The International Journal of Tuberculosis and Lung Disease

The Official Journal of the International Union Against Tuberculosis and Lung Disease

ABSTRACT BOOK

48th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union)

GUADALAJARA • MEXICO
11–14 OCTOBER 2017

Poster discussion sessions

LATE BREAKER PRESENTATIONS
FRIDAY 13 OCTOBER 2017

Oral abstract sessions

The International Journal of Tuberculosis and Lung Disease

The Official Journal of the International Union Against Tuberculosis and Lung Disease

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48th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union) Guadalajara, Mexico, 11–14 October 2017

SYMPOSIA: THURSDAY 12 OCTOBER 2017

01. Jump-starting the engagement of private TB providers: public-private mix (PPM) action plans and system-wide interventions

Plans and progress for nation-wide scale up of private providers' engagement: Bangladesh experience

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Background: Despite significant progress, Bangladesh falls short of ~39% TB case detection. Primary contact of ~49% TB presumptive is informal providers; while 44% preferred formal providers.
Intervention: NTP developed the National Strategic Plan for Public-Private Mix (2016-2020) to tackle such issues. Five working models identified and simultaneously scaled up; includes Hospital engagement, Social Enterprise Model, Urban Private Provider engagement, Informal Provider's Engagement and Workplace Model. Such arrangement includes ways to improve quality diagnosis and care along with set expansion targets and resources to enhance the approach throughout the country.
Results: In 2016, nation-wide 223,921 TB cases notified through providers. 22% cases identified from Hospitals. Formal and Informal providers referred 23% and 3% cases respectively. In Dhaka, workplaces generated 2,314 TB cases.
Conclusion: This operational PPM pilot approach will be a nation-wide cornerstone for full engagement of various TB providers; mandate a regularized case notification system and achieve global end TB strategy.

Charting the way forward for private TB healthcare: the action plan process in Ethiopia

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Back ground: To improve TB case detection and shorten diagnostic delay in Ethiopia, the National TB Program (NTP) plans to scale up PPM-TB in size, scope and mix of providers.
Methods: Together with partners and stakeholders the NTP drafted a scale-up plan for 2017-2020 with goal to increase contribution of PPM to TB case detection from 7% (2016) to 26% (2020).
Results: The scale up plan is integral part of the NSP and consists of the national situation assessment, task mix, and targets for each model type, strategic objectives and budget estimations. By 2020, 1500 primary clinics will refer patients with presumptive tuberculosis, and another 1055 private health facilities will diagnose and notify more than 168,500 TB patients.
Conclusion: Excluding the costs for drugs and diagnostic tests, the program management of PPM will cost the NTP up to US$ 109.00 for each TB case notified from private health facilities.

Managing markets for health: how to bring a unified governance approach to mixed health systems

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All health systems are mixed, i.e., both public and private organizations undertake the delivery of health-related goods and services to the population. But in low income countries, public and private providers tend to be governed in very different ways, with some unfortunate consequences. We introduce Managing Markets for

Health, a framework for analysis, design, and improvement of such mixed health systems. This provides clues about how to move towards more inclusive governance arrangements that will allow all providers to contribute to better TB outcomes.

Using technology-based solutions to address quality of care for patients seeking care with private providers in India

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India´s new national strategic plan for TB elimination 2017-2025 represents a total transformation of how the programme engages private providers. An increase in annual TB notification from 1.5 million to 3.5 million would be achieved by large-scale expansion of successful models to engage private sector, and by capitalizing on technology and India's drive towards digital financial inclusion. The approaches include the use of very successful government programmes namely a) Jan Dhan Yojana (Bank account to every citizen) b) Aadhar (Unique Identity card for all) and c) NIKSHAY -case-based electronic TB notification system by public and private sectors to track patients through the entire diagnosis and treatment cascade. This new system 'JAN' (in Hindi means Life) uses direct benefit transfer (DBT) to pay nutritional and financial benefits to patients in both public and private sector and also DBT to purchase services and to provide necessary incentives to private providers.

02. Regional Prospective Observational Research in TB (RePORT) International: biomarkers of TB and comorbidities across Brazil, India and South Africa

Approaching TB diagnostics using transcriptional and cytokine signatures in TB-HIV

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There have been advances in the diagnosis of patients with TB based on nucleic acid amplification of bacteria in sputum. However, HIV-infected individuals often remain undetected even in the setting of more advanced diagnostics such as GenXpert MTB/RIF where sensitivity is < 70%. A number of promising new host biomarkers of TB infection, disease and treatment response now exist, including: T-cell-based immunological signatures;

- Whole-blood genome-wide transcriptional signatures;
- Serum- or plasma-derived proteomic signatures.
The presentation will describe the rationale and provide data demonstrating the potential for this novel approach to identify cases of TB among those with HIV, while also discussing the RePORT International approach toward cross-consortium data and specimen sharing.

Clinical and immunological findings from the effect of diabetes on TB (EDOTS) study in India

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The presentation will provide the existing data underlying the epidemiological and clinical association between TB and diabetes and the impact of diabetes on the progression and severity of TB. In addition, Dr. Kornfeld will present animal and human data based on studies in collaboration with Dr. Vijay Viswanathan in Chennai, as part of RePORT International, describing the pathophysiological basis for the association.

Biological differences in tuberculosis diagnosis and disease in women

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Background: The epidemiology of TB identifies some clear differences of TB risk, presentation and outcomes by sex.
Methods and results: The presentation will provide data from studies describing the known epidemiology and clinical attributes of TB and TB/HIV among adults with a focus on women in general, and pregnant women in particular. A description of some of the efforts that are underway to better understand the biology that contributes to the observed sex differences and biomarkers that might contribute to better predictors of disease or disease complications in women, including pregnant women, will be discussed.
Conclusions: It is critical to understand sex differences and why pregnant women appear to have altered responses to Mtb.

03. Heat not burn – new challenges for tobacco policy

Heat Not Burn products and their benefits and risks

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Heat-not-burn tobacco products have been recently marketed as alternatives to smoking, based on the concept of tobacco harm reduction. The presentation will focus on research evaluating emissions from these products and will compare them with combustible cigarettes. A major issue is that, until recently, almost all research has been conducted by the manufacturers of these products. In that context, the presentation will include data from the first independent studies (not funded or supported by the industry) performed by my research group, evaluating both nicotine and potentially toxic emissions from heat-not-burn products. Additionally, a comparison between heat-not-burn products and electronic cigarettes will be presented, in an attempt to determine if there is a risk-continuum between different products. The presentation will finish with a brief presentation of the potential public health benefits and risks of using these products, depending on the patterns and adoption of use among different population groups.

Heat not burn - new challenges for tobacco policy

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Reto will discuss the results of a recently published independent study he conducted with a team of clinicians and toxicologists describing compounds of the smoke generated by a HNB cigarette and a conventional cigarette.

The Union Position Statement on heat not burn and global policies

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Heat Not Burn tobacco products are gaining popularity in many countries around the world but there is little evidence to support regulations. Gan Quan will outline the variety of international policies and legislations being used across countries to regulate Heat Not Burn tobacco products. He will also present The Union position statement on Heat Not Burn tobacco products.

04. Overcoming challenges in the introduction and scale-up of newer drugs for the treatment of multidrug-resistant tuberculosis: lessons from the field

The impact of limited access to newer drugs: a patient perspective on overcoming barriers

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Barriers to accessing new drugs has its most profound impact on patients who need such drugs to survive or be spared permanent disability. This presentation will focus on the patient perspective and provide suggestions for a more patient-centered approach to new drug access. This presentation will also focus on challenges faced by patients in completing the treatment.

Overcoming challenges to introducing newer drugs in higher-income countries: example from Mexico

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Since 2013-2014 the WHO has recommended the use of bedaquiline and delamanid for drug-resistant tuberculosis. However, the introduction of both newer agents in middle and high-income countries in Latin America has been virtually nil. Without financial aid from the Global Fund or access to bedaquiline donation or delamanid concessional pricing, drug costs for these agents are inaccessible for National TB Programs. Furthermore, WHO recommendation for the use of bedaquiline or delamanid, is to add these agents to an MDR-TB regimen composed of at least four effective second-line drugs. In the case of Mexico, this will be another obstacle, since access to drug susceptibility testing for second-line drugs is extremely limited. The introduction of either drug in weak regimens in undiagnosed cases of pre and XDR-TB will certainly lead to the selection of mutations associated to resistance to bedaquiline or delamanid.

Limited access, limited good: barriers to wider scale up of BDQ in India

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India has an estimated 130,000 cases of MDR-TB occurring each year, with increasingly resistant strains being encountered. Of these, only around 30,000 are started on treatment. Although approved by the USFDA in 2012, bedaquiline was approved by the DCGI in India

only in 2015. Till 2016, bedaquiline was available only under the compassionate use programme (CUP). In 2016, Janssen donated 600 courses of bedaquiline to the RNTCP in India to be administered over 6 centres for the conditional access programme (CAP). There are currently fewer than 500 patients who have received the drug through CUP and CAP in India. Bedaquiline was restricted to patients having at least 3 known effective drugs in the background regimen and many from areas far from the centres providing the drug could not access it. The country eagerly awaits the proposed expanded access programme with 3000 treatment courses of bedaquiline over 140 centres.

Scaling up multiple innovations: bedaquiline, delamanid and shortened regimens in Swaziland

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Swaziland has a significant burden of MDR-TB with a large percentage of patients who are co-infected with HIV. There has been an urgent need to introduce innovative approaches to the treatment of MDR-TB to improve outcomes and reduce toxicity. Swaziland first began by piloting shorter MDR-TB regimen in 2014, introduced bedaquiline in 2015 followed by delamanid in 2016 and lastly national scale up of shorter MDR-TB regimen in 2017 with lessons learnt from study. This session will discuss piloting and rolling out multiple interventions for the treatment of MDR-TB at the same time.

05. Preventing child TB as we move towards elimination: programmatic realities and achievements

Routine implementation of isoniazid preventive therapy in HIV-infected patients in Zimbabwe

K Takarinda[1] [1]Zimbabwe Ministry of Health and Child Care, Harare, Zimbabwe. e-mail: ktakarinda@theunion.org

In this presentation the speaker will discuss their experience with rolling out isoniazid preventive therapy among adults and children living with HIV in both rural and urban settings. In addition to the feasibility of implementation, risk factors for IPT non-completion will be reviewed. Successes in IPT rollout in this high-TB burden setting will also be discussed as consideration for potential scale up in the region.

06. Elimination of TB in indigenous people - developing positive relationships between community and TB programme

Indigenous principles for positive engagement for TB elimination

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Indigenous ways of knowing rely heavily on relationships and relational accountability. Traditional western ways of TB programming result in conflictual relationships with community. For better promotion of positive experiences of engagement with Indigenous communities in TB control, a firm grounding in the basic values and perspectives of Indigenous Peoples is needed. This talk will introduce these principles and share positive experiences from successful engagement in the Canadian context.

Tuberculosis in indigenous communities of Colombia: epidemiology and beliefs

J Mauricio Hernandez Sarmiento,[1,2,3] L Velasquez Tegaisa[3] [1]Universidad Pontificia Bolivariana, Medellin; [2]Corporacion para Investigaciones Biologicas, Medellin; [3]Asociación de Cabildos Indígenas Embera, Wounaan, Katio, Chami y Tule del Departamento del Choco, Quibdo, Colombia. e-mail: jhernandez@cib.org.co

Colombian Indigenous communities have been areas with high tuberculosis (TB) incidence. Factors that could explain this situation are lack of economic resources and limited access to health services due to the social conflicts and geographic isolation that characterize these vulnerable communities.
The majority of communities attribute the origin of the disease to spirits and witchcraft. Additionally they consider that there is no transmission of the disease person to person. This situation has made it difficult to control the disease in these communities.
We allow ourselves to present the frequency of TB in Colombian Indigenous Communities and describe their knowledge related to origin, transmission and the tools we have used to improve understanding and control of the disease in the community.

Addressing ethnicity and TB from the Pan American Health Organization

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The Region of the Americas is multi-ethnic and multi-cultural, with diverse ethnic and racial groups that are socially and demographically significant and that have different health situations and needs. These groups,

including Indigenous peoples, frequently face multiple and intersecting forms of discrimination, which lead to some of the worst living conditions, high levels of poverty, violence, and denial of individual and collective rights. We will discuss how the prioritized PAHO lines of action on Ethnicity and Health apply to TB control among the different groups living in the Region of the Americas.

07. Experiencia de investigación operativa en tuberculosis en Perú, impulsando la estrategia End TB: investigacion intensificada e innovacion

Visión global del Primer Curso de IO de TB en Perú

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La disertación incluirá los procesos seguidos en la preparación, desarrollo y resultados del Primer Curso de Investigación Operativa (IO) en Perú, producto de la alianza entre el Ministerio de Salud de Perú (MINSA) y La Unión, en el marco de la Iniciativa de Investigación y Capacitación Operativa Estructurada (SORT IT) de la OMS. El curso ha capacitado a profesionales de la salud de Perú en métodos de IO, logrando nuevos conocimientos científicos de interés nacional e internacional. Se incluyeron tres talleres presenciales: ´Desarrollo de un protocolo´; ´Captura y análisis de datos´ y ´Redacción del manuscrito´. Al termino del curso, se ha logrado que los participantes lleven a cabo sus estudios de forma independiente. Sin embargo, hubieron contratiempos que debieron superarse y lecciones aprendidas en este proceso, que deben comunicarse para lograr las metas propuestas de los próximos cursos.

Evaluación del manejo programático de la TB-XDR y la TB Pre-XDR en Perú

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La disertación de la Dra. Alarcón consistirá en presentar los resultados de la evaluación del tratamiento programático que el Perú inicio en el año 2012 para casos de TB XDR con medicamentos del quinto grupo de la OMS, la cohorte más grande de América, y el resultado del tratamiento de los casos con TB pre-XDR que fueron tratados con medicamentos de segunda linea. Los casos de TB-XDR tambien recibieron apoyo social. La tasa de exito fue alta en los casos TB-XDR pero en los casos TB-pre-XDR fue baja, sobre todo aquellos con resistencia a una fluoroquinolona, mejora en los casos

con resistencia a dos inyectables de segunda línea y mejor todavia en los casos con resistencia solamente a un inyectable. Se concluye que es necesario implementar pruebas de sensibilidad rápidas a fluoroquinolonas e inyectables, estrategias centradas en el paciente y nuevos medicamentos anti-TB.

Tratamiento programático de la TB resistente a isoniacida, la TB infantil y pacientes hospitalizados por TB en Perú

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La disertación incluirá los resultados de tres temas importantes en el control de la tuberculosis abordados en el curso de IO. La resistencia a isoniacida no MDR es un problema frecuente, se presenta en 6,3% de casos nuevos y 20% en antes tratados. Un tratamiento inadecuado podría generar casos de TB MDR. No hay un esquema de tratamiento establecido para dicha condición. Desde el 2010 en el Perú se indica el esquema con levofloxacina, rifampicina, etambutol, y pirazinamida por 9 meses; sin haberse evaluado el resultado del tratamiento. El primer estudio ha abordado este vacío con la serie más grande de casos de TB resistente a isoniacida en el continente. Los otros dos temas consisten en casos de TB infantil manejados con drogas de segunda línea en Lima y el tratamiento hospitalario de pacientes con cuadros graves de tuberculosis en las Unidades Especializadas en TB, creadas para este fin.

Efecto de las pruebas de sensibilidad rápidas en el tratamiento y la mortalidad de la TB-MDR en Perú

G Obregón,[1] K Zevallos,[2] V Alarcon,[3] Z Puyen,[4] M David[5] [1]Instituto Nacional de Salud, Lima; [2]Instituto Nacional de Salud, Lima; [3]Dirección de Prevención y Control de Tuberculosis, Ministry of Health, Lima; [4]Instituto Nacional de Salud, Lima, Peru; [5]London School of Hygiene & Tropical Medicine, London, UK. e-mail: gobregon@ins.gob.pe

La Organización Mundial de la Salud (OMS) ha recomendado el uso de pruebas de rápidas de sensibilidad (PRS) a los medicamentos anti-TB. En el Perú el número de PRS para detectar TB-MDR ha aumentado constantemente en los últimos años, logrando una cobertura del 85% de los pacientes. Sin embargo, las PRS deben ir acompañadas de la iniciación temprana del tratamiento y una buena adherencia para lograr un impacto clínico positivo.
Se evaluó el efecto de la introducción de PRS de nitrato reductasa, MODS y GenoType MTB-DRplus sobre el resultado del tratamiento y la muerte de pacientes con TB-MDR en el Perú; así como con la iniciación tem-

prana del tratamiento. Los resultados a presentar en el Simposio son favorables para las PRS y merecen ser difundidos a la comunidad científica, dado que en Perú se han implementado de manera programática estas tres PRS durante los últimos años.

08. The economics of tobacco and tobacco control in Latin America: opportunities and challenges

Comparative study of the impact of tobacco tax and price on tobacco use

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Significant tobacco tax and price increases are the most cost-effective of tobacco control interventions. However, different fiscal policies and tax structures can impact how effective taxes are in influencing price and tobacco use behavior. Simplicity in tax systems improves transparency and limits opportunities for tax avoidance and tax evasion. To ensure high compliance levels, strong tax administration is needed to implement and administer tax policies efficiently. Compared to ad valorem taxation, specific taxation better achieves public health objectives by increasing retail prices more and narrowing price gaps, thus reducing consumers´ incentives to trade down from higher priced to lower priced brands or to other tobacco products. The author will present results on the effect that taxes have on consumption and/or tobacco onset for Argentina, Bolivia and Chile.

09. TB and non-communicable diseases: recognising risks and mitigating impact

Epidemiology of TB in the state of Baja California, Mexico

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Baja California is located northeast of Mexico sharing the border with the South of California United States, 3,877.073 habitants, 71 450 km² of territorial extension, and considered the busiest border in the world with a daily crossing of more than 150 000 people.
With an incidence rate of 58.2, is the highest burden in the country and represents 9.68% of national cases; in 2016, 2051 new cases of TB was diagnosed with 77.30% being pulmonary. The mortality rate was 7.1.
Diabetes is the comorbidity most frequently associated with tuberculosis in the 14%, and increased from a prev-

alence of 9.16 in 2012 to 14.6 in 2016. Additional challenges to disease control are drug abuse, malnutrition, and poverty.
It is necessary to develop tools to reduce the interaction between tuberculosis, diabetes, and other non-communicable disorders in order to control the disease. Joint efforts are critical for the development of beneficial strategies.

Impact of diabetes and hyperlipidemia on host defense

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This presentation will review the progress of fundamental research on the mechanisms of TB susceptibility in individuals with comorbid diabetes mellitus and related metabolic disorders. Diabetes is well recognized to cause end organ damage as a consequence of glucotoxicity and lipotoxicity. A case will be made for considering immunopathy as a diabetic complication resulting from similar biochemical and cellular mechanisms as those responsible for the well-recognized microvascular, macrovascular and renal complications in people living with diabetes. The data emerging from animal models will be discussed in terms of implications for the clinical and programmatic management of these syndemic infectious and non-infectious diseases and for likely epidemiological trends. Areas of uncertainty and opportunities for productive future research will be identified.

Tuberculosis and chronic kidney disease: an emerging global syndemic

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The link between chronic kidney disease (CKD) and tuberculosis (TB) has been known for more than four decades, but the interaction between these two diseases is poorly understood. Dialysis and renal transplant patients appear to be at a higher risk of TB, in part related to immune suppression, along with socioeconomic, demographic, and co-morbid factors. Meanwhile, TB screening and diagnostic test performance is suboptimal in the CKD population, and there is limited evidence to guide protocols. Given the increasing prevalence of CKD in high TB incidence regions, a merging of CKD and TB epidemics could have significant public health implications, especially in low- to middle-income countries that are experiencing rapid increases in CKD prevalence.

Potential impact of tobacco control on tuberculosis

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Tobacco use kills more than 7 million persons every year globally. The mortality resulting from tobacco is over 1.3 million in South-East Asia Region (SEAR). The Region has high burden of tobacco use prevalence and accounts for 45.6% of the global burden in terms of TB incidence. In 2015, there were an estimated 4.7 million incidence of TB, and about 710 000 people died due to TB in SEAR. Some countries in SEAR such as India, Bangladesh and Indonesia have high burden of both TB and tobacco. There is now considerable evidence confirming the presence, strength and consistency of association between TB and tobacco. Effective tobacco control goes a long way in curbing the TB epidemics. Incorporating simple techniques such as "Brief advice" and implementing smokefree environmnets in ongoing TB and tobacco control programmes are the way out in resource constrained situations in SEAR countries.

10. Air pollution effects on lung health and TB risk

Inhaled environmental toxins and vulnerability to pneumococcal infection - epidemiology and mechanisms

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There is strong evidence that inhaled toxins increase vulnerability to pneumococcal pneumonia. Epidemiological associations link exposure to cigarette smoke, fossil fuel derived particles, wood smoke and welding fumes with pneumococcal pneumonia, but do not identify specific causal components or mechanisms. In a series of studies, we have modelled the interaction between inhaled particles, pneumococci and airway lining cell responses and shown that the capacity of pneumococci to adhere in airway cells increases with exposure to a wide range of pollutants. The common mechanism is oxidative stress in the lower airways. This, in turn, upregulates a host receptor that is co-opted by pneumococci to adhere to and infect cells. These in vitro models are supported by animal and human exposure data, and suggest a new biomarker of vulnerability to pneumococcal disease in pollutant exposed populations. Further studies should focus on the differential capacity of different particles to upregulate pneumococcal adhesion.

Air pollution and risk of TB: evidence and the way forward

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A substantial proportion of the world's population use solid fuel for cooking and heating, and are exposed to very high concentrations of harmful air pollutants. Exposure to smoke from solid fuel burning increases the risk of chronic obstructive pulmonary disease and lung cancer in adults, and acute lower respiratory tract infection in children. A systematic review and meta-analysis has reported that the level of evidence for the association between domestic use of solid fuels and tuberculosis was very low, and that high-quality studies are needed to clarify this association and to estimate the magnitude of the problem. However, a recent study in Taiwan has shown that exposure to fine particulate matter (PM2.5) was associated with increased risk of active tuberculosis. In addition, traffic-related air pollution including nitrogen dioxide, nitrogen oxides and carbon monoxide was associated with tuberculosis risk. Actions are needed to tackle the potential harmful effect of air pollution.

Smoking and air pollution: the new social determinants of TB?

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This presentation will review the evidence that links smoking, air pollution and tuberculosis from both mechanistic and epidemiological perspectives. Over the past 15 years, epidemiologic evidence has established a strong link between tobacco smoking and increase risk of tuberculosis (TB). By one estimate, the population attributable fraction of tuberculosis around the world from tobacco is about 20%. The mechanisms by which smoking increases risk of TB infection and poor outcomes are likely through direct effects on various components of the lung's immune defense system. Roughly half the world's population is exposed to household air pollution from solid fuel burning; ambient pollution is worsening in many countries where TB is common. There is increasing evidence linking both indoor and outdoor air pollution and TB risk, and it is plausible that air pollution and tobacco smoke could effect the lungs in similar ways.

11. Using Good Participatory Practice (GPP) to bridge the gap: engaging researchers and communities in the fight against TB

How The Union is working to engage communities in research

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Background: The launch of the Good Participatory Practice Guidelines for TB Drug Trials in 2012 and subsequent community engagement activities by several stakeholders have led to important developments in the field.
Methods: The Union has worked to build upon these early developments to engage communities within the STREAM Clinical Trial.
Results: Efforts within Stage 1 of the STREAM trial were limited in their scope and reach. Comprehensive approaches in Stage 2 of the STREAM trial aimed to ensure a wider scope and impact of community engagement efforts. Strategies included working closely with stakeholders, ensuring expertise within the trial team and development of tools to guide the efforts across sites.
Conclusion: Community engagement has been an important component of the STREAM clinical trial. Experiences gained from the trial to date demonstrate the importance of comprehensive and proactive approaches to ensuring the success of these essential community engagement efforts.

Beyond tokenism: meaningful engagement with vulnerable communities

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Good Participatory Practice is a framework that provides trial funders, sponsors, researchers and communities involved in TB Drug Trials with guidelines on effectively engaging stakeholders. The tactics may vary from consultation to partnership but the goal is to make the trial understood, accepted and meaningful for everyone involved.
Effective community engagement establishes a relationship of trust between researchers and stakeholders within community where clinical trials take place. It creates a way for local communities to partner with researchers in ensuring that the people who are main consumers of the new TB Drugs are engaged in trial process, including informed consent, recruitment, retention, results dissemination and advocacy campaigns.

Engaging different stakeholders in research enable the researchers and communities to understand the gaps in curing TB. The process itself drives relationship of trust between different stakeholders,create stronger relationships between the doctor, patients and communities.

12. Accelerating TB elimination through access to bedaquiline and delamanid

Six-month sputum culture conversion among patients receiving MDR-TB treatment with bedaquiline and delamanid

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Conversion of sputum cultures from positive to negative (defined as two consecutive negative cultures at least 30 days apart) is an important monitoring tool and a predictor of end-of-treatment outcome in patients with MDR-TB. In patients initiating a new MDR-TB treatment regimen containing bedaquiline or delamanid, we will report the incidence rate and probability of conversion during the first six months of treatment. Six-month conversion will also be reported for subgroups, including those defined by HIV, hepatitis C and diabetes status.

Twelve-month sputum culture reversion among patients receiving MDR-TB treatment with bedaquiline and delamanid

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Although early analyses of MDR-TB treatment containing bedaquiline and delamanid have recently shown high culture conversion rates at 6 months and improved long-term treatment outcomes, the optimal duration of new drugs as part of a MDR-TB treatment is unknown. Of concern are results showing high rates of reversion to culture positivity in culture converted patients who received a maximum of 24 weeks of bedaquiline under compassionate use as part of a MDR-TB treatment regimen. Recently published data of patients treated with longer than 24 weeks of bedaquiline have shown excellent results and no safety concerns. We will report the 12 month reversion rates amongst patients initiating a new MDR-TB treatment regimen containing bedaquiline or delamanid in endTB participating countries. We will discuss these findings and whether they support the longer than 24 weeks use of bedaquiline or delamanid in selected patients.

Adverse events and serious adverse events among patients receiving MDR-TB treatment with bedaquiline and delamanid

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Active monitoring and management of adverse events is key to the safety and management of patients receiving MDR-TB regimens that include bedaquiline and delamanid. endTB has implemented active TB drug safety monitoring and management (aDSM) in all countries. We will present data from a cohort of patients treated for at least 6 months with bedaquiline or delamanid as part of their MDR-TB regimen in endTB participating countries. We will report on the overall incidence of adverse events (AE) and serious adverse events (SAEs) and the incidence of each AE/SAE reported during the MDR-TB treatment. In addition we will present the frequency of AE and SAEs and fatal SAEs, the time to onset, the severity, the outcome and the relatedness to TB drugs/other causal factors. We will discuss these findings including signal detection and relevant safety observations.

13. TB and mental health: effects of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) treatment drugs and regimens

Mental health aspects of palliative care

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MDR-TB, XDR-TB and TB-HIV are chronic conditions and their management is challenging as these patients are subject to long and potentially toxic treatments, as well as various symptoms related to mental illness such as anxiety, depression and suicidal tendencies. Palliative care is widely accepted as best practice for chronic disease management and works to promote and maintain quality of life. People with chronic diseases face multiple complex medical and psychosocial issues. Untreated psychiatric symptoms - as sequelae of advanced illness or adverse effect of the medication - stand in the way of achieving quality of life goals for these patients. The presentation discusses how these symptoms influence physical health, quality of life, and ability to respond to life-altering disease symptoms and medication side effects. As well, the presentation discusses the need for timely mental health interventions if meaningful quality of life is to be experienced by patients with chronic conditions.

Patient-centered care approaches to reduce stigma

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The presentation focuses on exploring the synergies between TB and mental health associated stigma. It describes Patient-centered approaches that can effectively be applied at personal, family and community levels to reduce social stigma associated to both conditions. A patient-centered care model implemented in South African settings will be shared and lessons analyzed in terms of effectiveness and scalability.

TB management and the importance of mental health

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Despite TB and mental health hold an important burden of disease globally, both exemplifies typical neglected health subjects. In fact both are overlapping concerns. People distressed by mental diseases, frequently become socially vulnerable and are highly at risk of TB. While the physical and socioeconomic consequences of TB, can trigger depression, anxiety and other mental diseases. In addition, some of the measures needed to control DR-TB (heavy stigma, respiratory isolation, cycloserine and others) can make things even worst. Mental health problems are among the main causes of treatment lost to follow up and of course behind the high rates of suicide among TB and particularly DR-TB patients. The presentation will briefly describe the clinical approach and management of TB patients when presenting jointly with mental diseases. Reflections on the need, the gaps and the possibilities of a new TB model integrating mental health, particularly in big cities, will be discussed.

The role of counselling and patient support systems in mitigating mental health consequences of M/XDR TB treatment

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The presentation describes interventions implemented within USAID TB Care II project in select countries aimed at improving detection and management of mental side effects associated to second line anti TB drugs. The available evidence on the importance of good provider-patient interaction, continuous emotional and social support is highlighted. A comprehensive set of interventions holding good potential for mitigating mental health effects of TB treatment is described. This includes provider capacity building in recognition of mental side effects and effective counselling, strengthen-

ing community systems, promoting social inclusion and networking, and facilitating patient enrollment if social protection programs.

Facilitation of regular patient interaction with SMS based mHealth tools

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Clear, rapid communication is essential to effective management of DR-TB. Delays in seeking care, in receiving lab results, and in initiating treatment often hinder treatment success. To reduce treatment initiation delay, Xpert-reporting has been introduced in GeneXpert-capable labs to send test reports immediately after the result is available. Xpert-reporting is a web based reporting tool which enables the lab technologists to enter GeneXpert results to a web application, to send diagnosis results to the lab from where the test sample has been referred and to send a notification for collecting the result to the suspected MDR TB patient. Xpert-reporting had been implemented in 26 GeneXpert labs throughout Bangladesh by the end of TB CARE II activities in the country. Delay in treatment initiation has been reduced from up to 15 days to 0 days because of this intervention

14. Adapting an innovative approach to TB workforce development: implementing the ECHO telementoring model in a variety of contexts

The experience of developing and implementing an MDR-TB ECHO programme in Kenya, the first in Africa

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This presentation will provide an overview of the experience of developing an MDR TB ECHO program in Kenya, the first in Africa. The presentation will review both the challenges and successes to date. The weekly one hour teleECHO sessions include a didactic presentation by an expert followed by case discussions from county level clinicians where the medical officer is facing a challenging situation and needs guidance from experts. The goal of tele-ECHO sessions are to address the complex issues of MDRTB, sharing best practices and suggesting the best treatment/ solution. The eventual aim is to develop the capacity of county level medical officers in the treatment of MDR-TB. The ECHO program is currently attended by participants from >50 centers with approximately 70+ participants joining the sessions every week.

The experience of developing and implementing an MDR-TB ECHO in Delhi State, a high-burden context

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The National Institute of Tuberculosis and Respiratory Diseases, Delhi (India) under the dynamic leadership of Dr. Sarin, Director of the Institute, started the MDR-TB ECHO Program in November 2016. The one hour TB ECHO sessions include a didactic presentation by an expert followed by a case discussion from a district TB office where the medical officer is facing a challenging situation and needs guidance from the experts. The goal of TB ECHO program is to address the complex issues of MDR-TB, sharing best practices and suggesting the best treatment/ solution. The eventual aim is to develop the capacity of district TB medical officers for the treatment of MDR-TB. The program is currently attended by 30-35 district TB centers, with approximately 150 participants joining the program every week.

The experience of developing and implementing a TB ECHO programme in New Mexico, a low-burden context

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The NM TB ECHO model was initiated to ensure effective nurse case management for all of New Mexico's persons diagnosed with active TB. New Mexico is considered a low incidence state with fewer than 50 cases per year. The state has experienced on-going nursing shortages with rapid turnover and nurses with decreasing experience in treating persons with active TB; our TB ECHO program helps address the need for cost effective ongoing TB education and case management activities to ensure quality care. The monthly TB ECHO clinic convenes public health nurses from across the state over a video network, to review each active TB case in the state. During each clinic a 10-15 minute brief lecture is presented on important clinical topics. CMEs are award each month for attendance. Post session evaluation each month demonstrates continued interest and enthusiasm for the clinics over the past 24 months.

The experience of developing an MDR-TB ECHO programme in the country of Georgia

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Georgia has high rates (400-450 cases per year) of Multidrug and Extensively Drug-Resistant Tuberculosis (M/XDR-TB). All M/XDR-TB cases are discussed at the central consilium in capital Tbilisi at the National Center for Tuberculosis and Lung Diseases (NCTLD) which serves as a center for clinical excellence, whereas the decision on the enrollment of individual patients based on the analysis of their clinical/diagnostic characteristics and risk assessment are carried out. NCTLD also carries out the initial and follow-up monitoring visits throughout the country, where consilium works on-spot. The implementation of TB ECHO project in Georgia is planned in 2017 which is anticipated to save the time and resources of TB physicians as well as reduce the time between diagnosis and enrollment in treatment for all M/XDR-TB patients. The project will include TB facilities in regions (spokes) and the NCTLD will serve as an ECHO central clinic for the country (hub).

The experience of developing an MDR-TB ECHO programme in Guatemala

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The CDC Central America (CA) Regional Office supports an HIV/TB program funded by PEPFAR. Within the CA region, Guatemala has the highest TB burden, and in the past 4 years there has been an increased number of TB MDR cases. Some of the challenges faced to obtain TB epidemic control in the rural areas are: lack of resources, poor referral of patients for care and treatment and lack of specialized trained physicians to treat the complex disease of TB MDR. In order to strengthen the knowledge of community and rural healthcare providers, a TeleECHO program is being developed.

15. From bench to bassinet: scientific innovations in the fight against maternal-infant TB

New insights into the pathogenesis of maternal TB from a cohort of pregnant Indian women

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A woman's risk of developing active tuberculosis doubles around the time of pregnancy. A better understanding of how pregnancy specifically impacts a woman's immune response to *Mycobacterium tuberculosis* would improve our ability to provide targeted preventive therapy to the highest-risk pregnant women. Immune changes that occur in pregnant women impair current latent tuberculosis diagnostics. Moreover, the safety profile of isoniazid therapy is unknown during pregnancy. For these reasons, clinicians hesitate to treat until after delivery, which increases the risk of tuberculosis for both mother and child.

We are conducting an observational longitudinal cohort study of HIV-infected and HIV-uninfected pregnant women with latent tuberculosis in Pune, India. In this talk, Dr. Mathad will present data on the differences in the immune response to *M. tuberculosis* antigens between HIV-infected and HIV-uninfected pregnant women as well as differences between 2nd trimester, 3rd trimester, and delivery within each cohort.

Dynamic pharmacokinetic modelling and new treatment trials in pregnant women

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Dr. Denti will present the results of the first PK study of standard anti-tuberculosis drugs (rifampin, isoniazid, pyrazinamide, and ethambutol) in a cohort of pregnant women with TB/HIV in Soweto, South Africa. Nonlinear mixed-effects (population PK) modelling was used to compare PK parameter during and after pregnancy, adjusting for the effect of body weight and other covariates including genetic differences.

Early immune responses to *M. tuberculosis* and BCG vaccine in Kenyan infants

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The neonatal immune system is marked by "immature" adaptive responses, but has robust capacity for innate responses to M. tuberculosis and adaptive Th1-mediated

response to live BCG. Maternal immunity plays an important role in shaping early infant immunity by passive antibody transfer as well as cellular microchimerism. This talk will review early infant immune responses to M. tuberculosis and BCG vaccine, and present new data on the influence of maternal mycobacterial immunity on early infant cellular and humoral immune responses to BCG from a Kenyan cohort of mother-infant pairs. Understanding early infant immunity is relevant to develop future maternal and infant vaccination strategies.

16. Childhood pneumonia in the sustainable development era: innovations targeting diagnosis and care in low-income settings

Household air pollution and pneumonia in children: are cleaner-burning cookstoves part of the solution?

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The 47th Union World Conference on Lung Health saw the Cooking And Pneumonia Study (CAPS) team partner with the fire service, the charity Operation Florian, a local school and a cookstove manufacturer to put on displays outside the conference centre of open fire and cleaner-burning cookstoves that was covered by local media and The Lancet Respiratory Medicine (http://www.thelancet.com/journals/lanres/article/PIIS2213-2600(16)30413-1/fulltext). This talk will present the findings of CAPS, a village-level cluster randomised controlled trial of a cleaner-burning biomass-fuelled cookstove on pneumonia in children under the age of 5 in rural Malawi, recently published in The Lancet (http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)32507-7/fulltext). The talk will discuss CAPS in the context of trials past, present and future. The hot topic of whether major global investments in cleaner cookstove programmes intended to deliver health benefits are justified or not in this context will be explored.

Oxygen for all - are we there yet?

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The clinical benefits of oxygen therapy for severe pneumonia were first described over 100 years ago. Yet, this basic life-saving therapy is still not available to the majority of sick children around the world who need it the most. Why is good oxygen therapy still so inaccessible? How can we achieve 'oxygen for all', even in the most difficult and challenging environments? Drawing on published and unpublished reports, interviews with key figures in the oxygen world, and practical examples from ongoing field trials, this presentation shows how oxygen therapy can be effectively implemented for sick children and neonates. Practitioners, researchers, and policy makers will be challenged to think about what they need to do to realise the goal of oxygen therapy for every child, whenever they need it, wherever they are.

Update from the WHO Chest Radiography in Epidemiological Studies (CRES) project

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Chest X-rays (CXRs) are a useful diagnostic tool for the evaluation of cases in studies of many pediatric illnesses. But the utility of CXRs can be limited by technical challenges in obtaining a quality image and observer variability in interpretation. This presentation explains recent clarifications to the WHO standardized methodology for the interpretation of pediatric CXRs, and reports the results of a multi-observer validation exercise that evaluated these changes and produced an expanded library of reference CXRs. It also details new resources for investigators and site staff to support quality and safety measures in the acquisition of CXRs, the training and standardization assessments for CXR readers, and a centralized arbitration process. The application of this methodology beyond its initial purpose in bacterial vaccine trials to other pneumonia studies will be discussed.

Lung ultrasound: the future of childhood pneumonia diagnosis?

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Lung ultrasound (LUS) is a promising pneumonia diagnostic technology. There is compelling evidence that indicates that LUS may be as sensitive and specific, and may have greater inter-operator reliability when compared to chest radiography (CXR), a diagnostic not readily available in lower-level inpatient facilities in developing countries. Additional advantages of LUS, relative to CXR, include its portability, ease of use, lower cost, and absence of ionizing radiation. There is great potential for the use of LUS in low resource settings where there are few, if any, diagnostics for pneumonia, yet high patient volumes and abundant need. This presentation will provide an update on the current state of lung ultrasound as a potential diagnostic for pneumonia in children living in low-resource settings.

17. TB and diabetes mellitus in high-burden settings: implementation and research experiences from Asian, African, Caribbean and Latin American countries

Diabetes mellitus an important challenge in the Americas for achieve the SDG TB targets

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The Americas (AMRO) is the WHO region with the lowest TB incidence rate in the world. AMRO's main challenges in TB control are the demographic changes such as accelerated urbanization and the epidemiological transition with an increase in chronic non-communicable diseases, particularly diabetes mellitus (DM). In 2013 an ecological study of Population Attributable Risk (PAR) estimated that DM explain 16.8% (10.8%-23.8%) of TB incidence. Brazil, Peru, Mexico, Haiti and Colombia account for 70% of the TB burden in the Region, the PAR due to DM in these countries are 16%, 8.3%, 19%, and 13.1% respectively. Except Haiti the other four countries are implementing the WHO "Collaborative framework for care and control of tuberculosis and diabetes" to provide optimal care to patients with an early diagnosis and treatment of both diseases and help to mitigate the negative impact of DM on the TB epidemic.

Innovative models for TB/diabetes integration: a successful example from Ethiopia

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Despite the availability of evidence on the triple burden of TB, HIV and DM in resource-limited settings, there is no clear evidence on the feasibility of integrated management of the three diseases. It is believed that platforms created under TB and HIV programs may be useful entry points for addressing the growing threat of DM and other non-communicable diseases. However, there is limited data on this approach. We piloted the feasibility and yield of tri-directional screening for TB, HIV, and DM in four public hospitals in Ethiopia. Results from screening of close to 3,500 patients confirm the feasibility of the integrated management of the three diseases without disrupting the existing services. Based on this experience, we expanded integrated screening services to more sites the results of which will be shared in this session.

Results of the implementation of a pilot model for bidirectional screening and joint management of patients with pulmonary tuberculosis and diabetes mellitus in Mexico

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Background: Based on the The Union's Collaborative Framework for the Care and Control of Tuberculosis (TB) and Diabetes (DM) (CFTB/DM) proposing bidirectional screening and joint management.
Objective: An observational cohort. Setting. 15 primary care units in 5 states in Mexico. Participants: Patients aged >20 years diagnosed with DM or pulmonary TB who sought care at participating clinics. Bidirectional screening was performed. Patients diagnosed with TB and DM were invited to receive TB treatment under joint management.
Results: Of 783 DM patients, 11 (1.4%) were unaware of their TB. Of 361 TB patients, 16 (4.4%) were unaware of their DM. 95 TB/DM patients accepted to be treated under joint management, of whom 85 (89.5%) successfully completed treatment. Multiple linear regression analysis with change in HbA1c and random capillary glucose as dependent variables revealed significant decrease with
Conclusions: Joint management of TB and DM is feasible and appears to improve clinical outcomes.

Exploring magnitude of TB among patients with diabetes mellitus in Afghanistan

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Afghanistan is home to 935,800 diabetic and 110,000 prevalence number of Tuberculosis patients in a year. There was little knowledge of TB-Diabetes comorbidity. The purpose of this study was to explore the burden of pulmonary TB among diabetic patients in Afghanistan. This was a cross-sectional assessment conducted in five cities in 2014 and 2016. We used GeneXpert and X-ray as diagnostic tool.

In total, 3,005 diabetic patients were enrolled in the study. Collectively, 277 (9.2%) of the patients were identified as presumptive to have pulmonary tuberculosis, 19 (6.9%) diagnosed as bacteriologically confirmed TB and seven as clinically confirmed TB. The study results illustrated that the yield of TB among diabetes patients is five times higher than case notification in general population and seven times than WHO estimated pulmonary TB. Thus, we strongly recommend engaging diabetes treatment centers in TB and screening TB patients for their diabetes status.

18. Global Laboratory Initiative (GLI) TB diagnostic connectivity symposium

TB diagnostic connectivity: current state, progress and future

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Diagnostic Connectivity solutions facilitate the automatic transmission and utilization of diagnostic data for a variety of users. As one of the 9 priority digital health concepts identified by the "WHO Agenda for Action on Digital Health for the End TB Strategy" for target product profiles, their adoption and use are also monitored as core indicators for laboratory strengthening under the end TB Strategy. Several technical partners and donor agencies joined forces in February 2017 to launch the GLI task force on diagnostic connectivity, aiming to provide practical guidance to countries and continue the positive momentum in this rapidly developing field. Kristian van Kalmthout will present an overview on the current state of the TB diagnostic connectivity landscape, different diagnostic connectivity solutions, global adoption of TB diagnostic connectivity so far and provide an outlook to future developments.

Diagnostic data: what can we collect and how can we use it?

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Different types of information transmitted by diagnostic connectivity solutions in real-time provide an unprecedented opportunity to improve health systems and disease control. On the one hand, adequate use of this information will allow proper monitoring and generation of new knowledge areas where major systems improvements are possible. On the other hand, the vast amounts of diagnostic data can make it difficult to interpret meaning or determine necessary action requirements. Patricia Campbell will show how National TB Programmes, National Tuberculosis Reference Laboratories or Ministries of Health staff can take full advantage of available diagnostic data and presents country and vendor experiences with data utilization.

Building capacity for practical and applicable use of diagnostic data: experiences from two countries

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More effective use of existing diagnostic tools can drive scale-up of TB and DR-TB treatment programs. The development of point-of-care diagnostics with the capacity for remote communication provides an opportunity to passively collect and analyze data to aid decision-making.
Where data are collected electronically, the vast amounts sometimes make it difficult to interpret their meaning or determine necessary action requirements. Correct utilization of collected data can also be hampered by other factors e.g. by available resources, applicability of data to roles and functions, infrequent training or operating procedures, which often limits the impact and benefits of connected diagnostics.
The adoption of connected diagnostic technologies must be accompanied by a program of capacity building and process change to better utilize data to improve decision-making within health systems. FIND will present experiences on building capacity to better utilize data collected via diagnostic connectivity solutions.

Linking diagnostic data to care: a success story from Kenya

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Many countries struggle to manage and optimize use of diagnostic connectivity, limiting patient impact. Using diagnostic data for, among others, clinical decision making, forecasting of inventory or drugs, quality control, capacity building and surveillance can be challenging. The Kenya National Tuberculosis Leprosy and Lung Disease Program implemented a diagnostic connectivity solution for their GeneXpert devices in 2014. Jeremiah Ogoro will present their experiences on setting up linkages between diagnostic data and patient care and how this contributed to programmatic impact.

Cepheid GeneXpert® Omni: a new era for diagnostic connectivity?

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The GeneXpert® Omni is the first portable clinical molecular diagnostic testing device for TB and planned to be available in emerging markets from Q2 2018. GeneXpert Omni leverages Cepheid's existing cartridge technology to ensure familiarity and minimal impact to the workflows while delivering qPCR into a small, portable and battery-operated format. It is also the first molecular diagnostic device with built-in connectivity to transmit

real-time diagnostic data streams, based on network conditions, for instrument and disease surveillance. Vish Kulkarni, Global Marketing Manager - Cepheid, will present about the connectivity of the GeneXpert Omni and how this new diagnostic device can be used with Cepheid's own diagnostic connectivity solution, C360 or in future, integrated into existing diagnostic connectivity networks.

19. Cookstove intervention trials: research update and implications for clean household energy strategies

Health effects of biomass household air pollution (HAP) and results of an improved stove intervention trial in Michoacán, Mexico

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Globally, household air pollution from solid fuels affects a large population, especially women and their children. At present, evidence is strong for several adverse health effects associated with HAP (Chronic Obstructive Pulmonary Disease in women, low birth weight, pediatric pneumonia). For other possible effects (tuberculosis, cardiovascular diseases and lung cancer), evidence is less conclusive. Several countries have implemented programs to use vented improved biomass stoves instead of open fires but evidence of long term, consistent use and health improvement is limited. In Mexico, one randomized intervention trial tested the impact of vented improved biomass stoves (Patsari) in Michoacán Mexico. No difference was observed by intention to treat analysis comparing women assigned initially to the Patsari stove compared to those assigned to keep their traditional open fire; however, regular Patsari use declined with time, while respiratory symptoms and decline in lung function were reduced among women who were regular Patsari users.

Cookstove intervention trials: what we have learned and implications for future research

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The 2017 World Lung Conference (WLC) marks a decade after Mexico's first randomized cookstove intervention trial. This talk will review what we have learned over the last decade from cookstove intervention trials and reflect on the implications for future research. With the notable exception of RESPIRE in Guatemala, the decade has been quiet on the trials front until recently when the findings of cookstove trials conducted in Malawi, Peru and Nigeria were published. Further trials are expected to report in the lead-up to the 2017 WLC; others have been funded. In light of the latest data, we will discuss whether this is the age of the cookstove as a health intervention or whether the cookstove is just a nice kitchen appliance and a different approach is needed to reduce the adverse health effects of household air pollution.

20. Role of civil society in people-centred care: experiences from the TB Regional EECA Project (TB-REP): a major programme across East Europe and Central Asia

Civil society response for bringing the patient in the center of TB care

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The presentation will highlight the essence of people-centered TB care from the perspective of civil society and experience of people who had tuberculosis. The major point it will address is what the civil society strives to achieve by advocating for the transition to the new models of TB care, with the focus on ambulatory settings. The key role of civil society both in advocacy and service provision to help the person throughout the treatment will be outlined. The presentation will address the major concerns of diverse TB stakeholders in provision of TB services at the outpatient facilities in the EECA region, known for the history of long hospitalization of TB patients. What should be done to overcome these concerns for effective implementation of the people-centered care and how the comprehensive care will look like will be highlighted.

Focusing on essential interventions to increase patient adherence and building sustainability

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The presentation highlights SMIT experience in the field of TB, focusing on essential interventions for increasing patient adherence. The service provision work within the Moldova National Association of tuberculosis patients „SMIT" has fostered since 2011 and has developed into a range of activities meant to apply personal TB experience as a key motivational caring approach to people in treatment, supported by professional attitude when dealing with various TB issues such as access to medicine, human rights and people-centred care. The presentation addresses practical activities from TB diag-

nostics and treatment support to increased advocacy for sustainability in the EECA and WHO Europe region, for developing legal framework for social contracting and involvement of CSOs as equal partners in TB control and care.

21. Addressing challenges of drug-resistant TB

WHO guidelines for the use of new medicines for drug-resistant TB

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The presentation focuses on latest WHO recommendations on the use of bedaquiline and delamanid in regimens for MDR-TB and XDR-TB. It describes how the policy guidance could be effectively implemented at a country level, including the need for active TB drug safety monitoring and management (aDSM). Good practices leading to successful implementation in individual countries will be discussed.

Bottleneck analysis of the drug-resistant TB continuum of care

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The DR-TB continuum of care is complex and involves multiple actors at the household, community, facility, and programmatic levels. Effective management of DR-TB requires the understanding of "bottlenecks" or points of delay on the continuum of care. This presentation explores the results of a bottleneck analysis of the DR-TB continuum of care from a general, overreaching perspective. It also presents a framework for the analysis of bottlenecks to be applied at individual country, provincial, state, and local levels in managing and optimizing the DR-TB continuum of care.

mHealth tools to support community-based programmes

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The presentation focuses on mHealth tools developed by University Research Co. within USAID TB care II project. It will use examples of ConnectTB, IPConnect and other tools to show the application of mHealth solutions to improve TB case management across the care cascade. The speaker will describe the URC's approach to mHealth that is to use existing and often underused information and communications technology (ICT)-based systems to rapidly disseminate key messages; improve provider-patient interaction on intensified case finding, contact tracing, and DOT support; streamline data collection and reporting efforts; facilitate use of data for decision making; enhance pharmacovigilance efforts and side effect management; and complement and enhance traditional training programs. The presentation emphasizes that the introduction of mobile solutions into communities and households provides the healthcare sector with an unprecedented opportunity to target health interventions to people who otherwise would have minimal access to health care.

22. Accelerating toward elimination of paediatric TB through child contact management

CCM systematic review

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Considering WHO's recommendation to implement child contact management (CCM) for TB, we conducted a mixed-methods systematic review to summarize CCM implementation, challenges, recommendations, and predictors. We searched the electronic databases for studies published between 1996-2017 that reported CCM data from high TB-burden countries. We included any quantitative, qualitative, mixed-methods study design except for editorials, commentaries or randomized-controlled trials. Thirty-seven studies were reviewed. CCM losses varied greatly for screening, isoniazid preventive therapy initiation, and completion. CCM challenges included infrastructure, knowledge, attitudes, stigma, access, treatment, and competing priorities. CCM recommendations included health system strengthening, health education, and improved treatment regimens. Identified outcome predictors included index case and clinic characteristics, perceptions of barriers and risk, costs, and treatment characteristics. Prioritization of a CCM-friendly healthcare environment with standardized CCM processes and tools; health education; and active, evidence-based strategies can decrease barriers, and a focused approach toward every CCM cascade aspect will likely diminish losses.

Preventive treatment preferences among caregivers of child TB contacts in Lesotho

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Shorter preventive therapy (PT) regimens for drug-susceptible TB, other than 6 months of daily isoniazid (IPT), have been shown to be efficacious and safe in children. Although used in developed settings, they are not yet widely used in resource-limited settings. Implementing shorter regimens would potentially improve adherence and allow more children to receive PT. In-depth interviews were conducted with twelve consenting caregivers of child contacts who completed IPT at five health facilities in Berea District, Lesotho. Caregivers were asked about important factors when making treatment choices for their children and were presented with the following choices: 3 months of daily isoniazid/rifampicin (3HR), 3 months of once-weekly isoniazid/rifapentine (3HP), and 4 months of daily rifampicin (4R). Five participants preferred 4R, four preferred IPT, and three preferred 3HP; none preferred 3HR. The most important factors reported were nurse's recommendations and frequency of regimen. Secondary factors included treatment duration and known side effects.

Challenges in ensuring preventive therapy for child contacts in Lima, Peru

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In Peru, isoniazid preventive therapy (IPT) is recommended for child contacts who are < 5 years old and those 5-19 years old with a positive tuberculin skin test result. However, the number of children who initiate and complete IPT is low. Interviews with healthcare providers have revealed hesitancy to prescribe IPT based on the misconception that IPT engenders isoniazid-resistant disease, lack of awareness that older children are eligible for IPT, doubt in their ability to rule out tuberculosis, and belief that caregivers would not accept or complete IPT. A recent effort to improve IPT usage in northern Lima increased the percentage of young child contacts completing the IPT cascade from 22% to 40%. While improvements were made in all steps of the cascade, the largest gap is still in providers prescribing IPT.

Road to TB elimination - contact management is critical in children in Pakistan

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Household contact management is an integral part of combating the TB epidemic. Systematic contact tracing and management has been part of The Indus Health Network TB Control program since 2008. In rural Sindh, 3218 children, including 1167 <5 years old, from 774 households were evaluated for TB over 18 months. Of these, 385 children (186 <5 years old) were found with TB disease; a 12% prevalence in child household contacts. IPT was initiated in 304 children <5 years old of which 65% completed treatment. In separate ongoing studies in Karachi, we verbally screened and investigated 1404 children (425 <5 years old) from 969 households with drug susceptible and drug resistant TB since April 2016. TB infection treatment was initiated in 443 children of which 189 are <5 years of age; most children <5 years old are still receiving treatment.

48. Accelerating the response on drug resistance: TB and the antimicrobial resistant (AMR) agenda

Engaging civil society in high-burden countries ahead of the Russian Ministerial Conference and UN high-level meeting on TB

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With the Russian Ministerial Meeting just a month away, Yuliya will speak on the important role that civil society organizations in the region working on TB could play to elevate and amplify TB and AMR messaging at the meeting. Civil society being in the front of supporting and empowering patients, leading the grassroot level advocacy provide a critical link between the National decision-makers and affected communities. Implementation of the political declarations made at the High-level meetings in the countries will depend on the inclusion of the civil society at all stages - from its development to monitoring of the outcomes of implementation in the countries.

The human impact of drug-resistance

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Enrique will share his personal experience with XDR-TB, outlining the importance of including people personally affected by drug-resistant TB to AMR policy conversations. Enrique will outline ways members of affected communities can use their personal stories to push policymakers to take action on drug-resistance and share his ideas on civil society engagement in the lead up to the UN High Level Meeting on TB.

SYMPOSIA: FRIDAY 13 OCTOBER 2017

23. Cross-cutting issues in advancing research and development of new tools to end TB

How scientific innovation can lead to the development of new tools to eliminate TB

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There are a number of scientific challenges and gaps in knowledge that hinder progress in developing the new tools that will be necessary to eliminate TB: Why do some people progress to TB disease while others infected with Mtb remain healthy? How can we utilize technology to identify those who are most at risk for becoming sick with TB or relapsing? How can we mimic and strengthen the body's immune response to TB to develop better vaccines? This presentation will provide an overview of new approaches, technologies, and innovations that will streamline and accelerate the research and development of new tools to prevent, diagnose, and treat TB.

Community engagement in TB R&D

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Good Participatory Practice is a framework that provides trial funders, sponsors, researchers and communities involved in TB Drug Trials with guidelines on effectively engaging stakeholders. The tactics may vary from consultation to partnership but the goal is to make the trial understood, accepted and meaningful for everyone involved.

Effective community engagement establishes a relationship of trust between researchers and stakeholders within community where clinical trials take place. It creates a way for local communities to partner with researchers in ensuring that the people who are main consumers of the new TB Drugs are engaged in trial process, including informed consent, recruitment, retention, results dissemination and advocacy campaigns.

Engaging communities in all research stages enable the researchers and communities to understand the gaps in curing TB. The process itself drives innovative solutions, help create stronger relationships between the doctor and patients, defaulter tracing and create more effective advocacy campaigns.

Accelerating toward elimination will require increased investment in R&D

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Resources invested in research and development can have a significant impact on the speed and output of the research pipeline. An analysis of investments over a forty year period across three disease areas - HIV, malaria, and TB - and the products resulting from R&D in these areas provides important insight into the effect that the persistent funding gap in TB R&D has on the ability to advance research pipelines, transform novel ideas into potential products, and ultimately develop the new tools that are essential to eliminating TB. The analysis of investments in TB, HIV, and malaria R&D in relation to the new product pipelines for these three diseases will be accompanied by two detailed case studies from the TB research field on what it takes—money, partners, political commitment—to develop new products with public health impact.

24. Preventing a public good from becoming a market failure: sustainability of drug-resistant TB medicines markets and supply chains amidst decentralised financing and procurement

Procurement trends: estimating the minimum volume needed to sustain the global market of pre-qualified DR-TB medicines

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This presentation will provide an overview of shifting procurement trends for DR-TB medicines in relation to changes in donor financing. Findings from a modeling exercise will reveal the tipping point at which increased procurement of DR-TB medicines from non-prequalified sources could result in a global quality-assured market that is unable to provide quality-assured, affordable DR-TB medicines in a manner that ensures uninterrupted access.

Financing and procurement of DR-TB medicines from the Georgian perspective: lessons learned with the transition from Global Fund to domestic financing

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The presentation will describe the financing and procurement challenges faced and strategies used to address these challenges as Georgia shifted from Global Fund financing to domestic financing for DR-TB. Lessons learned from Georgia can be applied to other high MDR-TB burden countries, especially those in regions with local manufacturing of DR-TB medicines that does not meet international quality standards.

Financing and procurement of DR-TB medicines from the perspective of Swaziland: lessons learned with the transition from Global Fund to domestic financing

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The presentation will describe the financing and procurement challenges faced and strategies used to address these challenges as Swaziland shifted from Global Fund financing to domestic financing for DR-TB. Despite these challenges, Swaziland has been a leader in adopting and rolling out new tools for DR-TB. Lessons learned from Swaziland can be applied to other small countries that may not have the purchasing power to attract suppliers to bid on national tenders for quality-assured DR-TB medicines.

Prescription for DR-TB medicines market sustainability: recommendations for donors, national TB programmes and other stakeholders

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This presentation will provide specific policy and practice changes that donors, governments, national TB programs, procurement agencies, and other stakeholders can do to ensure global and regional markets are able to reliably supply affordable, quality-assured DR-TB medicines, regardless of the source of financing. A suggested approach for ongoing monitoring as well as risk assessment and risk management will also be described.

25. Gender and TB: programmatic considerations and tools

Gender differences in the experience of TB

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Data from prevalence surveys are showing that gender impacts access to TB services; to be most effective, TB programs need to take this into consideration at all stages of programming -- planning, implementation, monitoring and evaluation -- and at all points along the health/illness continuum -- risk factors, exposure, knowledge, access to services, diagnosis, treatment, support and recovery. Integrating gender into TB programming, including a focus on reaching men, is necessary in order to design effective and efficient programs that will contribute to ending the TB epidemic. Considering gender in programming is also necessary to achieve gender equity and to uphold the right of all individuals to quality healthcare services.

Understand the epidemic: using gender disaggregated data

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Analysis of routine TB case notification data by gender can lead to a better understanding of the TB epidemic and support effective programming. This presentation will include examples of how gender disaggregated data may be used to bring important insights to TB programming and summarize techniques for analyzing TB data by gender.

Integrating gender in TB programming: tools and resources

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USAID is working to expand and strengthen awareness and integration of gender issues in TB programming. Through contextual gender analysis, including a number of dynamic tools, we are working to implement gender sensitive, gender responsive and gender transformative programs. In this part of the session, participants will become familiar with general terms and concepts, as well as tools and resources to help integrate gender equality and inclusion into TB programming.

Integrating gender into TB programming: experiences and lessons learned through Challenge TB in Tanzania

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Now beginning its 4th year of implementation, the Challenge TB project in Tanzania (CTB/TZ) supports the National TB and Leprosy Program to address operational challenges. Interventions are strategically focused and include: maximizing passive case-finding and expanding active case finding; scaling up rapid diagnostic tools and efficient sputum transport systems; implementing external quality assurance for the laboratory network; decentralizing PMDT services and introducing new drugs and regimens; strengthening infection control practices, including screening of health care workers; health systems strengthening efforts including capacity-building, leadership enhancement and support of technical working groups and; supporting the writing of the Global Fund Concept Note. In order to maximize impact of its activities CTB/TZ considers how gender impacts Tanzanians′ experiences with TB and uses these insights to inform activity design and implementation. This session will focus on the processes followed, tools and resources used, and lessons learned while integrating gender considerations into the CTB/TZ project.

26. Making the tobacco industry accountable – success stories and lessons learned for accelerating action

Status report on global and national measures for protecting health policies from tobacco industry interference

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The aim is to provide an overview of global reports on national actions taken so far to protect health policies from tobacco industry interference.
Tobacco industry interference in health policies is undermining tobacco control gains and remains a major threat to achieving global and national health goals and sustainable futures. Although countries suffer from high levels of tobacco industry interference the lag time is adopting measures to protect their own policies and populations is a major threat to sustainability.
The review of global reports and case studies shows some progress in some countries but the pace of change needs to be accelerated. Improvements in monitoring and countering of interference are steps in right direction but not enough to close the gaps and counter the challenges without stronger government commitments.

Opportunities to improve industry surveillance and 5.3 policies will be reviewed including indices, global mapping and lessons from case studies.

Making tobacco companies accountable in African countries - building capacity for monitoring, advocacy and policy change

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Background: As others regions in the world, African region also is facing attacks from tobacco industry interference. In several countries, many tobacco control advocacy are working with little tools and skills on monitoring tobacco industry. Lack of evidence is blocking the advocacy work on accountability of tobacco industry.
Methods: Sefako Makgatho Health Sciences University of South Africa launched an initiative for building capacity among university graduates and tobacco control advocates for monitoring tobacco industry interference as part of advocacy for policy change across 11 countries.
The training will take place four times over the next 24 months. The training is done by a pool of trainers will be drawn from partner institutions including Universities and other prominent FCTC advocates across Africa.
Results: The first training held in June-july was successful. Mentors has been nominated for each student. Students started to work with the technical support of their mentors.

Observing the observatory: results from Brazil following establishment of first regional tobacco industry observatory in 2016

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The tobacco industry is as a vector in tobacco-related diseases epidemic. The Article 5.3 of the FCTC recommend the Parties shall act to protect these policies *"from commercial and other interests, considering that the tobacco industry has adopted strategies to commit any action for the development of policies that result in effective tobacco control"*. By ratifying the treated in 2005, Brazilian government has committed to monitor tobacco industry activities. Since March 2016, the Center of Studies on Tobacco or Health is building an academic resource that explores how the tobacco industry influences policy and public health in Brazil. The establishment of the tobacco industry monitoring, call "Observatory"http://cetab.ensp.fiocruz.br/index.php/ Página_principal will address the lack of discerning understanding of current and future approaches of the

tobacco industry, the way it attempts to interferes with public health policy development, and shall inform governments and policy makers with a view to prevent such interference.

27. Zoonotic TB: every TB case counts! Diagnostics, vaccines and surveillance: from the Americas to India

Non-invasive diagnostic sampling for tuberculosis in humans and animals

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Sputum is the default specimen for diagnosis of active tuberculosis (TB) in humans. Most animals cannot produce sputum for testing, and it can be difficult to obtain quality specimens from some human patients. For molecular detection of *Mycobacterium tuberculosis* DNA in non-human primates, oral swabbing has served as a useful alternative to sputum collection. Similarly, nasal swabs have exhibited promise in the diagnosis of bovine TB. Following a One Health strategy, we have adapted and optimized the oral swab approach for diagnosis of active TB in humans. In blinded studies conducted in South Africa on 134 human TB patients and controls, improved oral swab methodologies exhibited 92% sensitivity and 91% specificity relative to sputum analysis. Combined sputum and oral swab analysis improved on the diagnostic yield of sputum testing by itself. Oral/nasal swabbing has the potential to transform TB case finding in humans and animals.

Whole genome sequencing of zoonotic tuberculosis offers a pathway for collaboration between agencies and countries

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A case study highlighting how combining data from humans and animal bTB cases can lead to startling discoveries. Southern CA has long been known to have a higher burden of bTB than the rest of the USA. The cause or source was not fully known until the California Department of Public Health (CDPH) reached out to the USDA to see WGS could determine the source of a cluster in Southern CA people.
Results: this cluster while closely related, matched cows in Baja CA, Mexico more closely than other humans. This lead to a collaboration between researchers in Baja CA, Mexico; Mexico animal health (SAGARPA); the

Center of Disease Control and Prevention; CDPH and USDA to better characterize isolates in southern CA from humans and dairy cows.

28. Tuberculosis en poblaciones especiales de America

Abordaje de la interculturalidad para la atención de la TB en comunidades indígnas

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México como nación pluricultural tiene un compromiso con sus pueblos originarios y la riqueza cultural que aportan, sin embargo la atención de sus necesidades incluidas las de salud, representan un reto no sólo lingüístico o geográfico, sino que, el prestador de servicios de salud debe estar capacitado y sensibilizado para que a pesar de pertenecer a una cultura diferente, a la de la comunidad o persona que atiende, reconozca la importancia de incluir, los conocimientos, recursos diagnósticos, prácticas de salud y la intervención de los sanadores, de esa cultura, en la atención que brinde cotidianamente. Así la persona o comunidad afectada por la tuberculosis, no sólo se involucra en el cuidado de su propia salud, sino que al mismo tiempo enriquece el conocimiento y visión del profesional de la salud que le atiende.

Tuberculosis en comunidades indígenas de Bolivia

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Bolivia is a multicultural country with a large indigenous population (62%). According to WHO estimates, Bolivia has one of the highest TB incidence rates in the Americas. In 2014, the National Tuberculosis Program (NTP) conducted a study of TB incidence rates in six indigenous populations in the Eastern part of Bolivia. The results suggested significantly higher rates than those reported at country level. The NTP, through Global Fund Grant and its "Monitoring and Control of TB in Populations at Risk Strategy", adjusted various TB control activities by: strengthening health services and health information system, implementing the Stop TB strategy and the D.O.T. community based program, actively engaging indigenous leaders and communities, and applying advocacy and social communication activities. By 2015, incidence rates reported in these populations were 2 to 30 times higher than the national incidence rate.

Tuberculosis en trabajadores de la salud en México

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Los trabajadores de la salud en México al igual que en muchos otros países de la región de Las Américas y el mundo representa un grupo de riesgo para la infección y para el desarrollo de enfermedad por TB dentro y fuera de los establecimientos de salud (nosocomial y comunitaria).

Se tiene registro de personal de salud con TB en los últimos 5 años, para el año 2016 se tienen alrededor de 400 casos de TBTF, identificados por lugar de residencia, sexo, ocupación, derechohabiencia, servicios de detección, comorbilidad y por resultado de laboratorio. El seguimiento de los trabajadores de la salud con TB muestra más del 85% de éxito de tratamiento. Se cuenta con actividades destinadas al Control de Infecciones de TB en México y las acciones para reducir el riesgo de trasmisión de TB en establecimientos de salud se encuentran en las normas y guías nacionales.

29. Modelling to support acceleration toward elimination

The potential for new diagnostics to improve TB case detection: a transmission dynamic model of nine high-burden countries

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Trials of Xpert MTB/RIF introduction have shown only modest impacts on TB notifications in routine programs. We examined possible causes of these results—clinical diagnosis, and changes in clinical practice following Xpert introduction—and how these affect diagnostic performance and epidemiological outcomes. We used a model of TB epidemiology and control, calibrated to epidemiology and health service utilization in 9 high-burden countries (Brazil, Cambodia, DRC, Kenya, Myanmar, Philippines, Russia, Thailand, Zimbabwe). We compared Xpert adoption to current diagnostic approaches in each country. We found greater current use of clinical diagnosis, and reduced use of clinical diagnosis following Xpert introduction, could reduce the health impact of Xpert adoption compared to earlier modelled estimates. Despite reduced effects, Xpert adoption still produces improved diagnostic performance and health benefits under a range of assumptions, even though notifications impact may be negligible or negative. This provides essential evidence in planning for progress towards elimination.

Modelling the cost of TB interventions at scale: applied cost functions

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In a context of limited resources and to increase impact to support accelerating progress towards elimination, epidemiological and economic modelling is used to choose between TB strategies and allocate budgets. A key challenge is to estimate the how costs change as TB service coverage increases. While it is conventional for modelled analyses to assume a linear relationship between costs and TB service scale, these costs are likely to be non-linear, and that the shape of the cost function modelled will strongly influence the strategies prioritised. However, empirically deriving and parameterising cost functions is a substantial undertaking where comprehensive cost data is not available through routine financial systems. We present a pragmatic framework for estimating cost functions using the data available from previous studies and routine reporting systems in South Africa, and contribute to TB elimination.

Country-level modelling guidance

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The use of mathematical modelling to support TB policy-making has been encouraged by major funders, and adopted by several high-burden countries. These quantitative planning exercises are seen as an important tool to improve the impact of TB funding and support domestic and international funding applications. Recently, several technical assistance providers have developed mathematical models and technical assistance capacity to support in-country TB policy decisions. Given the expected increase in demand for TB modelling support, in collaboration with major TB stakeholders including WHO, TB MAC is developing guidance for countries, funders and modelling groups on good practices for modelling to support in-country TB policy-making. This guidance is intended to improve the validity and usefulness of future modelling work. The project will also make recommendations about high priority research which could be undertaken and resources that could be developed to strengthen the future application of modeling for country-level TB policy decision making.

A country perspective: modelling as a useful tool to help think about elimination?

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Indonesia is the largest archipelago in the world with an estimated total of 17,504 islands, 34 provinces and 514 districts. Administrative and financial responsibility has been decentralized to province and district level according to the reforms of 2001. Indonesia has developed and implemented national strategic plans for tuberculosis since 2002.

I will describe the TB epidemiology and health systems in Indonesia, our elimination targets, a description of modelling work that has been carried out, our future modelling plans, and our interpretation of where modelling was useful, and where modelling could improved to be more useful for Indonesia.

30. Moving towards elimination: test and treat strategies for healthcare workers with TB infection in high-burden settings

What we have learned from all the IGRA (Interferon-Gamma Release Assays) studies among healthcare workers in high-incidence countries

M Pai[1] [1]McGill University, Montreal, QC, Canada. e-mail: madhukar.pai@mcgill.ca

This lecture will present a comprehensive review of the data on the use of IGRAs to screen healthcare workers for LTBI in high-burden settings. Most available data in low burden settings shows the challenge is in understanding high rates of IGRA conversions and reversions, suggesting IGRAs are inherently dynamic in a serial testing context. In high burden settings, serial IGRA testing shows high rates of conversions, but also high rates of reversions. If stringent cut-offs are used, conversion rates are lower, but substantially higher than the general population.

Integrating LTBI within occupational health strategies in South Africa

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South Africa has a high prevalence and incidence of TB at 696 and 834 per 100 000 respectively. Transmission of TB in communities and congregate settings such as health facilities has been shown in a number of studies conducted. The burden of DS and DR-TB is high among the health care workers compared to the general popula-

tion. We estimated the burden of disease and latent TB infection among the health care workers by conducting systematic review of studies conducted locally. Using the WHO Tool for risk group prioritisation, we estimated the contribution to the total population and the number of HCW needed to be screened to find one person with TB disease.

We found compelling evidence for introducing medical surveillance, curative and preventive treatment for HCW as per existing legislation. The Department of Health subsequently developed the Occupational Health Policy for Health workers in relation to TB and HIV.

Challenges to LTBI testing and treatment implementation in resource-limited settings

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The presentation focuses on challenges to the implementation of health care workers TB surveillance and LTBI testing and treatment programs in high TB and HIV burden countries. The systemic, programmatic and facility level challenges to and opportunities for the implementation of LTBI testing and treatment programs are highlighted. Based on experience of Georgia and other Eastern European countries (Ukraine, Moldova, Armenia and Azerbaijan), the speaker identifies policy and programmatic gaps as well as limitations in sustainable financing to ensure institutionalization of health care workers LTBI testing and treatment strategies and achieve their roll out nationally and globally.

31. The role of public health licences to accelerate development and access to TB drugs

The process of licencing TB drugs: experience of the medicines patent pool in sutezolid license

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Upon demonstrating the success of its patent pooling model to facilitate access to affordable treatments in the field of HIV, the MPP recently expanded its mandate to cover TB drugs. The MPP's experience in licensing its first TB drug, sutezolid, and an overview of its public health-oriented terms and conditions, will be discussed.

The importance of public health orientated licences to ensure academic research benefits all

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Universities Allied for Essential Medicines (UAEM) is a global movement of university students organising on their campuses to ensure that publicly funded medicines and medical innovations are affordable and accessible to the public. UAEM will present how global access licences can benefit academic institutions and the public, while contributing to innovative open knowledge approaches to research.

Utilizing public health oriented licenses as a tool to facilitate the development of new regimens

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TB Alliance is a Product Development Partnership whose mission includes the discovery, development and delivery of new, affordable and accessible TB drugs and regimens. As the TB Alliance works in partnership with a wide variety of both public and private sector organizations, the Alliance has accumulated a broad experiential base in obtaining licenses that can serve to further its mission. Those learnings will be discussed.

The role of IP and data pooling to promote access for trials and beyond

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The pooling of the Intellectual Property for Sutezolid with the Medicines Patent Pool represents an important first step to a open collaborative research and development process for the development of TB drugs and regimens. Additional barriers remain to the development of affordable and accessible new combinations for the treatment of TB. New ideas are required to ensure that there are sufficient new drugs and regimen trials in the future and a potential solution that includes data and IP pooling will be discussed.

32. Enhancing the role of pharmacists in the TB care cascade

A global systematic review of pharmacy-based TB interventions

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Pharmacists serve multiple roles in health service delivery. We conducted a global systematic review of studies published since 2000, where pharmacists and/or pharmacy services were utilized to deliver a TB related health care service other than drug dispensation or clinical efficacy studies: 3,111 records were identified and 1,990 titles and abstracts were screened; 32 full text articles were assessed for eligibility and 15 studies were included for narrative synthesis. Pharmacists were most often utilized to refer symptomatic patients for TB screening services, manage cases of latent TB infection, deliver TB treatment education and adherence counselling, and deliver DOT. Intervention outcomes, challenges and missed opportunities are highlighted to inform innovative ways by which pharmacists may be more actively engaged in enhancing TB prevention and treatment.

Pharmacists' drug-dispensing practices: a call for professional stewardship in lower-and-middle-income countries

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In lower- and middle-income countries, TB patients often seek medical care for symptom relief from neighbourhood pharmacies. By managing such patients with medical advice and drugs, pharmacies can affect the course of TB disease in those who are undiagnosed. We used standardized patients (SPs, also called mystery patients) to assess what pharmacies in India do for patients with TB symptoms and TB disease, including the content of their medical advice and nature of medicines dispensed. In 2014-2015, SPs visited 622 retail pharmacies in Delhi, Mumbai and Patna cities. The study led to two major findings. One, pharmacies demonstrated high use of antibiotics (including contraindicated fluoroquinolones) and inappropriate medical advice; both can lead to TB diagnostic delay. Two, no pharmacy dispensed first line anti-TB drugs. The implications of these findings, particularly the importance of professional stewardship in early TB diagnosis and prevention of drug resistant TB, will be discussed.

Reducing TB diagnostic delay via public-private pharmacy partnerships: results of the IC-IMPACTS study, India

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Pharmacies are the first point of contact for nearly a quarter of undiagnosed TB patients in India. We tested a novel TB screening and referral intervention among 105 pharmacy shops (chemists) in Patna City under a stepped-wedge design. The intervention comprised chemist training and e-health education; e-referral of adult chest symptomatic patients for a chest radiograph (CXR) and/or doctor consultation; and an incentive plan to compensate for lost drug sales. Preliminary analysis (15 months): Of 1370 CXR e-referrals, 85% were completed, 40% were abnormal. Of 612 doctor referrals, 98% were completed, 55% were referred for microbiological testing. Overall, 152 TB cases were notified; all initiated treatment. The intervention was acceptable to chemists, doctors and patients. Consumer demand for over-the-counter medicines, private doctor consultation fees, and chemist workload were identified challenges. Enabling chemists to 'dispense' a TB screening test may improve pathways to TB care and facilitate early case detection.

Pharmacists' use of SMS messaging to improve TB re-treatment success in the IMPRESS Study, South Africa

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From May 2014 to October 2015, a short messaging service (SMS) was implemented as part of the IMPRESS Study, KwaZulu-Natal, to generate appointment reminders, missed appointment notifications, motivational messages and pharmacokinetic visit instructions for patients on TB retreatment. Pharmacy staff were trained to set up SMS campaigns using the bulk SMS system, confirm patient willingness to opt in or out of the SMS service, and assess patient acceptability through serial interviews. These additional pharmacy tasks were successfully incorporated into the routine daily dispensing process. SMS uptake was high at 92.3%. Patients found the SMS's useful (98.3%), easy to read and understand (100%) and were willing to receive information related to their condition or dosing instructions by SMS (96.7%). The use of mobile technology in a format accessible on all basic cellphone types, such as SMS, was found to be feasible and acceptable amongst patients with TB and pharmacy providers.

Engaging private pharmacists for TB control efforts in Chennai, South India

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Chennai has a teeming private medical sector. Pharmacies are the first point of contact for many TB patients. Since 2012, we have engaged pharmacies in a public-private mix (PPM) project to improve TB control efforts by:
1) facilitating referral of presumptive TB patients for screening and diagnostic services,
2) facilitating TB notification for patients diagnosed in public/ private sector,
3) involving pharmacists in patient education and community awareness about TB and DOTS, and
4) recruiting pharmacists as community TB-DOT providers.
Over 4 years, the project has recorded 2656 referrals in government and PPM centers which includes 1929 presumptive TB patients, of whom 272 were diagnosed with TB and placed on treatment; and 862 TB patients, of whom 862 were linked to appropriate treatment and care. 143 pharmacists have provided DOT to 258 notified TB patients. The project showcases important lessons for sustainably engaging this allied health resource in DOTS program.

33. Implementation of the World Health Organization's tool for measuring TB patient costs: country-level results, adaptations and future directions

Development of the WHO TB patient costs tool

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The WHO costs tool has been being formally developed for use over the past two years. However, this development has been greatly informed by studies performed over a decade ago and previous iterations of surveys to measure the costs of TB-affected households, including in Malawi and Kenya. Before individual country representatives give feedback on their experience of implementing the WHO TB Costs survey, this presentation will give a brief overview of its development and subsequent refinement. It will also provide the audience with some examples of the questions asked, the analysis performed, and their rationale.

Rolling out the WHO TB costs tool in Uganda with special consideration of patients with multidrug-resistant TB

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This presentation will describe the latest results from the implementation of the WHO TB Patient Costs Tool in Uganda. In 2017, the government and National TB Program of Uganda in conjunction with the Global Fund have introduced a national conditional cash transfer scheme for patients with multi-drug resistant TB (MDR-TB) in order to improve treatment outcomes for this patient group. This presentation will focus on the dis-aggregated catastrophic costs data for those patients with MDR-TB in Uganda and consider both the economic and health implications of the conditional cash transfer scheme.

35. Helping to realise the vision of zero suffering from the End TB Strategy with palliative care

Palliative care in the management of XDR-TB in Khayelitsha, Western Cape, South Africa

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Twenty percent of all DR-TB cases have second line resistance and in this group only about 20% have a successful treatment outcome. Yet for patients diagnosed as 'treatment failures' in Khayelitsha limited support is available to manage their physical and psychosocial needs. Community based palliative care services are not extended to this group. A case presentation will describe the implementation of palliative assessment and management in the primary health care setting.

36. The evolving landscape of multidrug-resistant TB (MDR-TB) trials in children

MDR-TB treatment children: current landscape and future prospects for treatment shortening trials

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Treatment strategies for MDR-TB in adults are rapidly evolving, with multiple phase IIb and III treatment trials ongoing and planned. Despite newly updated WHO treatment guidelines, current MDR-TB regimens remain long, are associated with an unacceptably high risk of severe adverse effects, and are costly and burdensome to children, caregivers and health systems. Since children tend to have paucibacillary TB they can reasonably be expected to respond to MDR-TB treatment better than adults and are excellent candidates for the evaluation of less intense treatment regimens. Shorter, efficacious, safer and better tolerated treatment is urgently needed for children with MDR-TB. We discuss optimal trial design, methods and regimens for a treatment shortening trial to evaluate the efficacy and safety of a shortened all-oral treatment regimen in children with MDR-TB, including children with confirmed and clinical disease, and pre-XDR and XDR-TB.

Updates on delamanid pharmacokinetic and safety data in children with MDR-TB

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Rationale: We have already shown that the adult delamanid formulation given at 100 mg twice daily in children 12-17 years and 50 mg twice daily in children 6-11 year years resulted in adequate plasma levels, and was safe and well tolerated in children with MDR-TB in children down to 6 years of age. These data informed updated WHO treatment guidelines, including its use in children, in 2017.
Methods and results: We present updates on the ongoing delamanid pediatric trials and other initiatives pertaining to children.

Bio-availability of bedaquiline given whole or crushed: implications for dosing in children

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Rationale: Bedaquiline is becoming more widely available for MDR-TB treatment, but a paediatric formulation is not yet available for routine care. Manipulating standard tablets may impact on bioavailability.

Methods and results: We evaluated relative bioavailability of dissolved versus whole bedaquiline tablets in a randomized mixed-sequence, cross-over study in 24 healthy adults who received bedaquiline at two occasions 14 days apart. The bioavailability of dissolved bedaquiline was not significantly different from that of whole tablets (p=0.92). The 95% confidence interval of the relative bioavailability of dissolved bedaquiline tablets was 89-113% of that of whole bedaquiline tablets, hence fulfilling the predefined bioequivalence criteria. The mean absorption time was 17% (15-36%) longer for dissolved tablets, resulting in slightly lower maximum concentrations. No QTcF prolongation >450ms or lactate values >3mmol/l were observed. Dissolved bedaquiline can be used interchangeably with whole for children unable to swallow tablets, informing paediatric bedaquiline use.

37. The role of autopsy studies in estimating burden of TB mortality

Measuring TB mortality in Kenya using verbal, full and minimally invasive autopsy: first results and future plans

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Few research studies have included a full evaluation of the cause of death using complete diagnostic studies, minimally invasive autopsies and verbal autopsies. In this presentation, the correlation of these three methods to diagnose tuberculosis as a cause of death will be presented, including the diagnostic performance of minimally invasive tools and verbal autopsies compared to the conventional full post-mortem examination.

Minimally invasive tools for diagnosing tuberculosis at death. Results of a large post-mortem study in Maputo, Mozambique

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Minimally invasive tissue sample based-autopsies (MITS) could be an alternative to traditional complete diagnostic autopsies (CDA). CDA is the gold standard procedure to determine cause of death, but seldom practised because CDAs are time consuming, expensive, and not always accepted by family relatives. MITS combines collection of tissues from different organs (including cerebrospinal fluid) with a standardized set of needle biopsies, which are later analyzed with a set of pathological and microbiological tests. They can, in principle, be performed at decentralized level by trained non-specialized health care workers to determine cause of death, at relatively low costs. The results of an autopsy study in Mozambique evaluating the role of MITS in establishing tuberculosis as a cause of death will be presented, as well as the findings on the clinical-pathological correlation for tuberculosis diagnosis.

Measuring mortality due to HIV-associated tuberculosis in South Africa: using data from verbal & minimally-invasive autopsies, clinical records, and prospective research

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Verbal autopsy (VA) is widely used to estimate mortality patterns in areas with weak or absent civil registration systems, but VA has not been well validated for TB and HIV deaths. We conducted a mortality study among

HIV-positive adults and compared causes of death assigned using minimally-invasive autopsy and clinical data with causes of death assigned using VA data. We found that mortality due to HIV-associated TB was underestimated by methods that did not include pathological autopsy and that automated VA methods underestimated overall HIV-associated mortality. This has important implications for the measurement of progress towards the End TB goal of a 95% reduction in TB mortality over the next 20 years.

38. Building and strengthening specimen transport and referral systems for TB testing networks: solutions through integration and innovation

Strengthening specimen transport and referral systems: the Global Laboratory Initiative perspective

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Strengthening specimen transport and referral systems has been identified as a strategic priority of the Global Laboratory Initiative (GLI) in 2017, given the critical role these systems must play in ensuring universal access to rapid tests and DST under the End TB Strategy. As a working group focusing on development of practical guidance and tools, in 2017, the GLI developed a practical guide on building specimen transport and referral systems in an integrated manner and created a related GLI training module as part of a programmatic package on diagnostic network strengthening.

Lessons learned about specimen referral networks across Africa and Global Laboratory Initiative guidance

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Although specimen referral systems should allow for increased access to diagnostics, their weaknesses often challenge the overall diagnostics network. Challenges to robust specimen referral networks include irrational equipment procurement/placement, poor monitoring and evaluation, not enough emphasis on biosafety/biosecurity and duplicative vertical networks across disease types and specimens. Ongoing assessments in multiple countries under the Global Health Security Agenda (GHSA) and Global Laboratory Initiative (GLI) efforts highlight weaknesses in countries but also opportunities to strengthen existing networks. During this presentation, examples of strengths and innovations, including

using unmanned aerial vehicles (UAVs) will be highlighted. These lessons learned have also fed into guidance and training materials issued by GLI, and a toolkit for specimen referral systems, which will be shared during the presentation.

Successful integrated specimen referral system across the laboratory network in Rwanda

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A strong specimen referral strategy is the key for accessing specialized diagnostics tools available at a limited number of health facilities across the health system. In response to the existing gaps marked by long delays in specimen referral, critical biosafety issues during transportation and higher cost, in 2010, the National Reference Laboratory (NRL) in Rwanda adopted an integrated strategy for specimen referral across the laboratory network. Using dedicated vehicles, an average of 1,125 biological specimens requiring specialized lab tests including 80 sputum's for culture and drug susceptibility testing are referred on a weekly basis, from peripheral, to intermediate laboratories and to the NRL. The system is robust and have facilitated to speed up the feedback. Although, the system was well established, the cost for the sustainability is very high and hard to be afforded by low-income countries.

Building and strengthening specimen transport and referral systems for TB testing networks: solutions through integration and innovation - Uganda's experience

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Access to quality laboratory services especially for TB in developing countries is limited mainly due to infrastructural and human resource challenges. Therefore sample transport networks are needed to increase access to quality laboratory services for TB and other sample testing through integration and innovation. This presentation will discuss Uganda's Sample Transport network, a 'hub and spoke' transport network at the sub-district level. A hub is a health facility within the district with adequate laboratory infrastructure, which is accessible by other health facilities in its catchment of a 30 to 40 km radius. Using GIS, all health facilities within the catchment area were mapped and put on a schedule based on the road network. 2 Motorbikes and 2 riders were provided one making the scheduled runs, and the other case-based surveillance. An evaluation of the transport network was conducted to assess its impact and cost effectiveness, whose results will be presented.

Modelling an integrated TB-HIV sample transportation network using GPS coordinates in Ethiopia

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In many low and middle income countries, sample transportation networks for the health care system are fragmented and disease specific. Often, costly parallel systems exist, resulting in losses or long turn-around times of results. Notably, there is a limited understanding of the cost for drivers of sample transportation networks, and this may stall negotiations between service providers and government representatives. In this presentation, CHAI will share the process it took to develop an integrated national sample transportation network in partnership with the government of Ethiopia and Llamasoft, including modeling optimized pick up routes using GPS coordinates, and analyzing corresponding cost drivers.

39. Pharmacokinetics and pharmacodynamics drugs used to treat other mycobacterial diseases: more difficult than TB!

Treatment of *mycobacterium avium complex:* European experience

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In most European countries, chronic pulmonary infections are the most prevalent disease caused by nontuberculous mycobacteria. More than half of the patients have the severe fibrocavitary disease as a complication of underlying lung disease, mostly COPD. Yet, the nodular-bronchiectatic disease manifestation is now emerging owing to increased clinical awareness and increased use of BAL and CT imaging for diagnosis.
Treatment of fibrocavitary disease by M. avium complex and M. abscessus is very hard and its outcome is worse than that of nodular-bronchiectatic disease. To improve outcomes, we are performing prospective clinical trials and preclinical studies of new clofazimine- and bedaquiline-based treatment regimens.
In a retrospective study we already found that adding clofazimine to currently recommended treatment regimens for M. avium complex pulmonary disease leads to faster culture conversion and improved microbiological outcomes. Our current clinical and preclinical studies will be discussed, with their implications for future treatment regimens.

Building an optimised regimen for *Mycobacterium abscessus*

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The current treatment for *Mycobacterium abscessus* pulmonary disease varies according to the infecting subspecies, but in general, it involves a backbone of amikacin in combination with clarithromycin and either cefoxitin or imipenem early during therapy, followed by use of oral antibiotics. Unfortunately, at least half of the patients either fail this therapy, relapse, or die; no formal antimicrobial pharmacokinetic/pharmacodynamic analyses had been performed with M. abscessus. We standardized and developed a hollow-fiber system model for M. abscessus pulmonary disease to initially evaluate single key antibiotics: amikacin and moxifloxacin, for which minimal efficacy was demonstrated. Then we evaluated tigecycline, that exhibited a considerable microbial kill. Lastly, the performance of the standard combination regimen was also evaluated, at optimal doses the standard combination regimen failed, resembling the poor outcomes often observed in patients. We will discuss the main findings and will propose new combinations for the treatment of M. abscessus disease.

Optimising treatment of *Mycobacterium kansasii*

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Mycobacterium kansasii is the second most common cause on non-tuberculous mycobacterial lung disease in the USA. Treatment is copied from that of tuberculosis; a combination of rifampin, isoniazid, and ethambutol administered for 12 months after negative sputum. Using a novel hollow fiber system (HFS) model of intracellular *M. kansasii* and applying the principles of pharmacokinetic/pharmacodynamics, we identified the optimal dose of moxifloxacin for efficacy against *M. kansasii* as well as role of efflux pumps in acquired drug resistance. The highest moxifloxacin exposure, as well as lower exposures plus reserpine, sterilized the HFS in 7 days, suggesting efflux pump-mediated drug tolerance at low exposure which could be prevented by higher moxifloxacin exposures. The moxifloxacin exposure associated with 80% of maximal kill was an $AUC_{0\text{-}24}/MIC$ of 317. The Monte Carlo simulations of 10,000 patients identified 800 mg/day as the optimal dose against *M. kansasii*.

40. Accelerating research and development of new TB vaccines

Potential public health impact of new TB vaccines

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New, more effective, tools such as vaccines will be essential in reaching the global goal of eliminating TB. This presentation will summarise recent work on the potential public health impact and cost-effectiveness of new TB vaccines, and to inform the creation of target product profiles and preferred product characteristics for new TB vaccines.

TB vaccines in clinical development and approaches to clinical research

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There are currently 13 candidates in various stages of clinical development, from Phase 1 safety studies to Phase 3 efficacy trials. Novel vaccine trial designs are also underway, which, if successful, could help to streamline and accelerate TB vaccine development by providing options for relatively low cost, short duration trials to assess candidates prior to large scale efficacy trials. Further, efficacy data from human trials is becoming available that could provide important information on identifying biomarkers and correlates of risk/protection, and contribute to the validation of animal models to better predict vaccine effect in humans. This presentation will provide an overview of TB vaccines in clinical development, and approaches to clinical research that could help streamline and accelerate TB vaccine R&D and direct limited resources to the most promising candidates.

TB vaccines: WHO perspectives and preferred product characteristics

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Preferred Product Characteristics (PPCs), developed by WHO, are an important tool to guide and inform vaccine development. PPCs help researchers and product developers better understand attributes and preferred characteristics for new vaccines that take into consideration the public health need, the perspectives of endemic countries that most need the vaccine, and the potential for optimal effectiveness, suitability, and public health impact. This presentation will provide an overview of work underway to develop PPCs for new TB vaccines.

Controlled human infection model for TB vaccine R&D

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Development and utilization of a controlled human infection, or human challenge model, has accelerated vaccine development for a variety of diseases, including malaria. TB vaccine development would greatly benefit from a controlled human infection model to help identify new vaccine candidates capable of inducing protective immunity and assess preliminary vaccine efficacy prior to conducting clinical efficacy trials. This presentation will discuss ongoing, collaborative efforts to develop a controlled human infection model for tuberculosis using engineered Mycobaterium tuberculosis.

41. Ending TB epidemic with sound ethics

Patient rights from the perspective of drug-resistant TB patients

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Based on long-term dialogues with people affected by drug-resistant TB in India, this presentation maps key challenges to the protection of patient rights at various critical points on the pathway from onset of symptoms to XDR development, and relates these challenges to the recent WHO Ethics Guidance document. Porous boundaries between public and private treatment leading to out-of-pocket payment for diagnostics and treatment of poor patients with DRTB raise particularly difficult ethical questions in resource-poor settings.

Ethics of preventive therapy in latent TB infection (LTBI)

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Treatment of latent TB infection is a crucial intervention in the new WHO´s End TB strategy, especially in the framework of TB elimination in low incidence country. This talk considers ethical challenges of expanded LTBI programs, including vulnerability and tensions between the protection of public health and autonomy of individuals.

42. Improving the cascade of TB-HIV care and prevention in maternal and child health programmes

Symptom screening for active TB in pregnant women living with HIV: a systematic review

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TB is the leading cause of mortality in people living with HIV (PLHIV), and third leading cause of death among women of child-bearing age in high burden areas. Every year >200,000 pregnant women are estimated to develop TB during pregnancy. The WHO recommends that PLHIV, including pregnant women, be routinely screened for symptoms of active TB at every health facility visit using a four-symptom screen (cough, fever, night sweats, and weight loss, (CFSW)). Routine TB screening offers opportunity to identify PLHIV who require further diagnostic work-up for active TB, as well as PLHIV without symptoms who are unlikely to have TB and may be candidates for isoniazid preventive therapy (IPT). Recent data suggest performance of the four-symptom screen for active TB may perform differently in pregnant PLHIV compared to PLHIV in general. For this systematic review, we will review the performance of symptom screening in pregnant PLHIV for active TB.

Enhanced integration of TB/HIV services in reproductive, maternal, newborn and child health settings in Swaziland

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ICAP at Columbia University, in collaboration with the U.S. Centers for Disease Control and Prevention and the Ministry of Health of Swaziland, is providing technical assistance to nurses and cough monitors at four selected health facilities in Manzini, Swaziland to enhance existing integrated TB and Reproductive, Maternal, Newborn and Child Health (RMNCH) services. Technical assistance focuses on improving intensified case finding, contact tracing, isoniazid preventive therapy, and TB infection prevention and control, through training, mentorship and introduction of an enhanced TB RMNCH register, contact tracing tool and TB ser-

vices capacity tool. Health care workers' perceptions of the enhanced integration, and achievements of enhanced integrated TB/RMNCH services along the TB/HIV cascade for pregnant women and their affected children will be shared. Findings from this project will inform the development of a World Health Organization Toolkit for integration of TB services into the RMNCH setting.

Managing drug-resistant TB in pregnancy: experience from South Africa

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Women of child bearing potential are at risk of acquiring MDR TB. But there is a dearth of information giving clinicians advice on how to treat a pregnant woman. This session will describe considerations for treatment of MDR TB during pregnancy, including balancing the risks of medications to the baby versus inadequate treatment of the mother. This presentation will incorporate lessons learned from the literature as well as clinical practice in South Africa.

Quality of routine TB evaluation for children at primary health care facilities in Uganda

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Despite the major contribution of TB as a major cause of morbidity and mortality for children in endemic countries, it often remains undiagnosed. To facilitate diagnosis and management of TB in children, a Desk Guide was developed and implemented. The Desk Guide is an evidence-based simple decision aid to improve early and accurate identification of children with TB in resource limited settings. The Desk Guide requires that children ≤ 15 years be screened for TB symptoms or history of contact with a TB patient, those who screen-positive be referred for sputum examination, and those found positive on sputum examination or meet clinical criteria for TB be treated. We conducted a cross-sectional study to assess the quality of routine TB evaluation of children presenting at six-government run primary health facilities in Kampala, Uganda. The findings from the assessment indicate gaps during TB screening of children, including limited implementation of diagnostic evaluations.

43. An update on mycobacteria species infections and surveillance

Relational Sequencing TB (ReSeqTB): global effort to standardise and consolidate MTBC whole genome sequences through a collaborative data sharing platform

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The Relational Sequencing Tuberculosis (TB) (ReSeqTB) data sharing platform standardizes and curates drug resistance and other metadata to advance diagnostic assays and assist in the interpretation of bacterial genomic polymorphisms. The platform includes a unified variant pipeline to provide a one-stop bioinformatic solution. The resource is also meant to facilitate international research and collaboration to support sequence data interpretation for personalized patient care. Inclusion of bovine tuberculosis to this global effort will be needed to control and ultimately eliminate TB. This will require global cooperation with agriculture (domesticated) and wildlife services (non-domesticated) to sequence zoonotic isolates. The inclusion of TB sequences from animals and humans in ReSeqTB will be necessary to monitor drug resistance and address the EndTB strategy.

Mycobacterium orygis: an emerging threat for cattle and primates in Southeast Asia

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The objectives of this study was to (a) isolate and identify Mycobacterium, (b) perform drug susceptibility testing and (c) genotyping of isolates. Part of the tissue samples from the vital organs was processed for histopathological examination. For culture, tissue homogenate samples were inoculated on Lowenstein-Jensen slants. Characteristic colonies were confirmed Mycobacterium by Acid Fast Bacilli (AFB) staining, colony morphology and sensitivity to P-Nitro Benzoic Acid (PNB). Anti-TB drug sensitivity testing was performed following proportion method. For molecular characterization, DNA was extracted from the live cultures of Mycobacterium for Region of Deletion analysis, single nucleotide polymorphism for genes like; gyrB, mmlp6, TbD1and PPE55 genes.it can be concluded that M. orygis is an emerging threat for cattle and primates in Southeast Asia. Detailed epidemiological study of M. orygis infection needs to be conducted to control this disease in Bangladesh.

The Ibarapa Meje One Health initiative

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Towards addressing the problem of *Mycobacterium bovis* infection among the pastoralist communities, "The Ibarapa Meje One Health Initiative" (TIMOHI) was established in south-western Nigeria. The One Health Initiative is a movement to forge co-equal, all inclusive collaborations between physicians and veterinarians on zoonotic diseases in Nigeria. TIMOHI is centered around a number of pastoralist communities South of Oyo State of Nigeria. The communities are uniquely positioned to demonstrate the utility of using one health and one medicine as a pilot for Nigeria. The uniqueness of these communities is the potential high risk of both zoonotic and bovine tuberculosis in the human and cattle populations. Therefore, we have devised a frame work where medical and veterinary fields are working together to provide empirical data on zoonotic TB as well as find solutions to the problem. This talk will present some of the preliminary findings and challenges we have faced so far.

Bovine response to candidate anti-TB vaccines?

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Background: Pathogenic mycobacteria (*Mycobacterium tuberculosis, M.bovis*, and *M.avium* subspecies *para tuberculosis)* cause disease, establish infectious reservoirs among diverse animal species sustaining a infectious web in the environment. These pathogens are common to animals and humans. Hence vaccines interrupting the transmission cycle of mycobacterial pathogens crisscrossing among susceptible species would be useful.
Methods: Accordingly cattle were immunized with BCG and 5 vaccine candidates (killed *M.indicus pranii*, rBCG over expressing α-crystallin (Rv2031c) / Ag85C (Rv3803); DNA vaccines (α-crystallin and SOD (Rv3846)). Cattle were assessed for induction of memory T cells and by the interferon-g release assay, (IGRA).
Results: Comarative analysis showed cattle immunized with rBCG expressing 85C, memory T_{CM} and T_{EM} subpopulations were detected. Two years post-immunization, rBCG-85C immunized animals were negative by the IGRA assay. The findings of this work will be presented for the first time at the 47th Union World conference in Guadalajara in Mexico.

Working toward effective ZTB control in the resource-poor setting: opportunities and challenges

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Zoonotic tuberculosis affects ~70,000 people every year in Africa and a significant proportion of these will die of the disease. This is mainly because the disease primarily affects the poorest of the poor communities that are reliant of their livestock. The most affected communities are pastoral in nature therefore live a transitory life still which means access to health care is extremely difficult. This study explores two communities in Uganda and Tanzania and documents the socio-anthropological aspects that define the risk of zoonotic tuberculosis and the challenges to overcoming the community context specific barriers.

44. Finding the 'missing' TB patients: a role for patient-pathway analysis

Kenya: patient-pathway analysis informing a differentiated programme response to urban-rural variances in TB care seeking

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County-level patient pathway analyses were completed for the 48 counties in Kenya. Existing survey and programmatic data were used, including a national household health expenditure and utilization survey, demographic and health survey, service availability and readiness assessment survey, and TB prevalence survey. The sub-national analyses were provided as background information for teams visiting the counties during the external mid-term review of the national TB program. The analyses informed priority-setting, especially related to accelerating diagnosis, and served as an input to the updated national strategic plan and application to the Global Fund.

45. Innovative approaches to increase the performance of your health workforce

Blended learning on TB/HIV diagnostics, treatment and care

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Since 2004, Health[e]Foundation offers courses applying a blended learning method which is a combination of distance computer-based learning and onsite workshops. TB[e]Education is designed for all healthcare workers and consists of 11 modules, written by globally recognized TB experts. Participants will gain knowledge in understanding and controlling the interaction between HIV and TB infection, and are able to incorporate this knowledge into clinical practice. Successful trainees receive certification acknowledged by the University of Amsterdam and local authorities. Thereafter, they can continue their education with a variety of courses offered by the Health[e]Foundation curriculum and have lifelong access to up-to-date information as all courses are yearly updated. Healthefoundation has trained over 30.000 participants, attrition rate of our courses is <5% and the pre- and posttest scores of course show significant improvement of knowledge in all cadres of health workers. Recent impact analysis demonstrated a sustainable commitment from the participants to CME.

Mobile phones to build the capacity of community health care workers in Kenya

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Developing countries are facing a severe shortage, and significant skills gap, of frontline health workers, to address this gap, Amref Health Africa in partnership with the Kenyan Ministry of Health, the M-Pesa Foundation, Accenture and Safaricom developed the Leap Platform. Leap is a scalable, integrated, mobile learning solution that offers continuous training opportunities, peer collaboration, real time evaluation reports and strengthened supervision of CHWs. The mobile phones are used to spread information on disease outbreaks, vaccination campaigns and health prevention messages.
Up till now, Leap has enrolled over 50,000 CHWs and trained 6,154.They work in urban areas, rural and nomadic communities, sometimes difficult to access. Utilization of Leap has contributed to an increase of 24% of women that delivered in hospital in 2015 and an increase of 28% of babies vaccinated.Through the Leap Platform, Amref Health Africa aims to train 1 million Community Health Workers in 30 African countries by 2020.

Learning on the job to improve TB infection control practices in health facilities in Malawi

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In a one day program District Hospital Infection Prevention and Control (TB-IPC) committees refreshed their knowledge about TB-IPC, assessed the TB-IPC gaps and developed or updated the hospital TB-IPC work plan. After the training, teams were mentored through targeted supportive supervision to follow up the implementation of these TB-IPC work plans. In 2016 the TB-IPC committees of 12 facilities were trained and supervised. This on the job approach led to realistic hospital TB-IPC plans, with involvement of relevant departments, owned by members of the TB IPC committee and hospital management. Challenges met were the full day availability of TB-IPC members and the targeted supervision to optimally monitor TB-IPC plan implementation. In 2017, the Malawi NTP has planned to roll out this TB-IPC program to 98 health facilities, with support from Global Fund. This will provide a rapid increase in IPC compliance in the Malawi health sector.

PhotoVoices to give a voice to TB patients and make TB care more patient- centred

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Photovoices for TB is a methodology for awareness raising and patient empowerment using photography to show the human face behind the disease. TB patients are enabled as photographers in making a photo-documentary and accompanied by a trained coach to recognize their strengths, priorities and worries related to life and to the disease, giving a voice to those who normally are not heard. It also promotes the generation of knowledge and a critical dialogue with health care providers around the most important issues related to TB through discussions about the pictures. These discussions can catalyze improvements in the quality of care from patients' perspectives. In the Dominican Republic, Photovoices was implemented with a group of different type of TB patients and an exposition with the best photos travelled around through the different provinces to put TB on the agenda of local decision makers and reduce stigma in the population.

46. TB in child migrants: addressing unique needs to stride towards elimination

What is the evidence on migrant child health and TB?

P Dhavan[1] [1]International Organisation for Migration, Geneva, Switzerland. e-mail: pdhavan@iom.int

Each year, about 1 million children 0 to 10 years and adolescents 10-18 years of age, contract tuberculosis (TB), representing 10-11% of all global TB cases. However, this estimate is likely under-reported due to the lack of a standardized case definition for childhood TB, non-specific symptoms in children, and difficulty in diagnosis. Migrant children specifically represent a double burden of risk as migrants have an increased exposure to poor living (and often working conditions), lack of access to health care services, malnutrition, low social protection, and increased vulnerability to co-morbidities. This presentation highlights the findings of a thorough literature review covering both grey and peer reviewed literature on the unique intersection of child migrants and TB/health in low to middle income countries. Initial findings reveal the unique geographical burden, necessity for universal health care coverage, and innovative methods for prevention of TB and co-morbidities in migrant children.

Expanding access to integrated childhood TB care and prevention in Uganda

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Provided from a TB-high burden perspective, this talk will highlight the diagnostic and treatment challenges posed by childhood TB in resource constrained settings. In addition to the scale up of the national childhood TB program in Uganda, Dr. Sekadde will share lessons learnt during Uganda's recent DETECT TB program that aimed to enhance active case finding and implementation of TB preventive Therapy using Isoniazid in peripheral settings and describe the translation of this work to active case finding among migrant tea workers with a special focus on children.

Challenges and successes of implementing child TB services among migrant and refugee children: the sweet relief of child friendly TB formulations

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Building on the preceding talk, Dr. Kathure will utilize case studies to explore the amplified challenges posed by case finding, diagnosis and treatment of TB within migrant and refugee children in Kenya. She will describe the progress in rolling out the FDCs in the first country to introduce the new child-friendly formulations and its application to migrant and refugee children a year after introduction. This will include a description of the impact the new formulations roll out had on health workers and caretakers of migrant children.

47. Ending TB in children and adolescents in Latin America: country-level experiences of improving access to care

Challenges to the control of childhood and adolescent tuberculosis in Latin America

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This presentation will highlight the many missed opportunities for childhood TB case finding and prevention in Latin America. According to estimates from the World Health Organization (WHO), <50% of the approximately 27,000 annual incident cases of childhood TB in Latin America are detected and reported. Screening for TB is not systematically undertaken among children living in households affected by TB, and recommendations for isoniazid preventive therapy are rarely implemented. Children with TB or child contacts of TB patients often receive care from health professionals who lack the skills and capacity to diagnose TB in children. The speaker will also discuss the Pan American Health Organization (PAHO)'s efforts to coordinate strategies to address these gaps in care.

Diagnosis of childhood and adolescent TB in Brazil

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This presentation will describe the efforts of Brazil's National TB Program (NTP) to improve the diagnosis of childhood and adolescent TB. In 2002, a scoring system for the diagnosis of childhood pulmonary TB, which was validated in several published papers, was ad-opted. This score has demonstrated high sensitivity and specificity and remains in use today. As of 2010, national TB guidelines began to recommend different diagnostic approaches for children and adolescents in different clinical contexts. In 2014, Gene Xpert was rolled out in approximately 150 cities. Its use is recommended in adolescents, and its accuracy has been studied in children and adolescents in Brazil. Most recently, the NTP has expanded training in childhood TB diagnosis for health providers in several centers in the country. The speaker will also discuss the impact of these initiatives to improve pediatric TB diagnosis, as well as future directions to address remaining needs.

SYMPOSIA: SATURDAY 14 OCTOBER 2017

49. Quality of TB drugs – evidence and policy action

Quality concerns about rifampicin within anti-tuberculosis fixed dose combinations: a summary of the evidence

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The presentation summarizes available evidence about quality issues related to rifampicin fixed dose combinations (FDCs) widely used for TB treatment. Key findings from more than 20 original publications on factors affecting bioavailability of rifampicin in FDCs and related clinical outcomes are summarized. Based on the findings of the review and in the current context of emphasis on the use of FDCs, there is a need for revisiting rifampicin bioavailability within FDCs as well as other formulations. It is important for clients (NTPs and other agencies that provide anti-TB medication) to avoid complacency and improve procedures for quality assurance. The presentation prompts for further research of FDC and non-FDC factors influencing rifampicin bioavailability to ensure the effectiveness of administered treatment.

Strategies for ensuring the Quality of FDCs in National Tuberculosis Programs

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Based on a literature review from peer-reviewed journals, country reports and surveys, and an analysis of factors affecting quality of Fixed Dose Combinations (FDC), the presentation offers strategies for ensuring the quality of FDCs in National TB Programs. These begin with a recognition of the possibility of lowered BA of rifampicin and other anti-TB drugs as well as the apparent occurrence of lowered efficacy of FDCs or other formulations in drug-sensitive patients. The importance of procuring only WHO-prequalified drugs is another important strategy. The NTP must periodically test FDCs for BA / BE, and conduct population PK studies of FDCs. The programs should ensure proper storage and distribution of FDCs as per guidelines and recommendations. Finally, the NTP should educate clinical staff and health workers on the importance of maintaining drug quality through appropriate storage as well as monitoring of supply chain.

Addressing factors lowering the bioavailability of rifampicin in FDCs and non-FDCs in Southern Africa countries

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The presentation focuses on drug resistance survey results in South Africa and describes programmatic solutions to challenges identified by the survey. The South African Drug Resistance survey conducted in 2012-2014 found the overall rate of rifampicin resistance to be 4.6%, with a 95% confidence interval (CI) of 3.5-5.7%. The increase in rifampicin resistance (both overall and mono-resistance) was of considerable concern. Also, the increase in Rifampicin resistance primarily among new cases was suggestive of transmission of Rifampicin-resistant strains in the community. Among the underlying reasons discussed for emergence of Rifampicin resistance were sub-optimal dosing of rifampicin, the bioavailability of Rifampicin being affected by drug interactions, and intermittent compliance with treatment. National, regional and local level interventions implemented by the National TB Program in South Africa are highlighted and constraints to dose and regimen adjustments discussed.

Evidence gaps and research agenda for monitoring rifampicin bioavailability and pharmacokinetics

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The presentation focuses on the importance of regular studies by National TB Programs to monitor rifampicin bioavailability (BA) and pharmacokinetics (BA). Knowledge gaps on rifampicin BA/PK are highlighted and the need for combining pharmacovigilance / adverse drug reaction monitoring with BA/PK studies is emphasized. Priority research questions for exploring patient level factors affecting BA/PK are identified. Areas of interest include association between BA/PK and drug consumption habits, nutritional status, drug absorption related factors at the patient level and concomitant medical conditions that require long term treatment (e.g. HIV and diabetes).

50. Depression: a neglected co-morbidity impeding the End TB strategy

Depression and risk of TB: a nationwide population-based cohort study

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This presentation will describe the first study to explore the association between depression and the risk of tuberculosis. Among a population sample of over 64,000 individuals in Korea, patients with depression had a 2.63 higher risk of tuberculosis during a 10-year follow-up period and there was a dose-response relationship between depression and the subsequent risk of tuberculosis.

Our study has practical implications for global tuberculosis strategies. The Global Burden of Disease report has estimated that neuropsychiatric disorders account for 13.5% of the global disease burden which is more than the contribution of cardiovascular disease or cancer, among non-communicable diseases. Among the various neuropsychiatric disorders, depression was the single most burdensome disorder. If depression is a risk factor for TB, this considerable burden imposed by depression may act as a barrier to global TB elimination. This study provides a scientific basis for intensifying tuberculosis care and prevention among depression patients.

Impact of untreated depression on TB treatment outcomes, disability and quality of life in Ethiopia: a cohort study

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This presentation will focus on the impact of untreated co-morbid depression on the outcomes of tuberculosis (TB) treatment (treatment success, default, and death), disability, and quality of life. Although there are studies that reported high prevalence of co-morbid depression in people with TB, current global efforts to ´End TB´ have not included the detection and treatment of co-morbid depression as a component of the efforts because of the absence of evidence that brings it in to the attention of policy makers and practitioners. In this study, we have used data from a cohort of >600 individual in a low-income high TB-burden country to single out the impact of untreated co-morbid depression on each of the outcomes of TB treatment, disability, and quality of life including changes over time. We found

that, if untreated, co-morbid depression is associated with increased mortality, treatment default, disability and poorer quality of life.

51. La enfermedad pulmonar obstructiva crónica en México

Daños a la Salud por EPOC en México

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Describir la magnitud del problema en México, así como los costos asociados a la atención de este padecimiento respiratorio crónico.
En México, la Enfermedad Pulmonar Obstructiva Crónica (EPOC) se encuentra dentro de las primeras causas de mortalidad, situándose junto con las enfermedades del corazón, diabetes mellitus e hipertensión arterial como aquellos padecimientos crónicos que más daños a la salud ocasionan en la población mexicana.
Los costos ocasionados por el manejo y control de pacientes con EPOC para el sistema de salud, representa un gasto importante derivado del manejo puntual de las complicaciones agudas de la enfermedad así como de la discapacidad funcional que se presenta. Y por otro lado el gasto de bolsillo de los pacientes para que puedan recibir atención médica para su EPOC, también son gastos elevados que afectan a la economía de sus familias.

Epoc y comorbilidades

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Background: Multi-morbidity is common in patients with chronic obstructive pulmonary disease, but is generally ignored or not investigated by the clinician.
Methods: Review of the most recent findings on the role and impact of comorbidities in the prognosis of COPD and vice versa.
Results: Co-morbidities such as cardiovascular diseases, diabetes, depression and others are prevalent in patients with COPD.
Conclusions: The presence of co-morbid conditions in people with COPD may negatively affect QoL, approach to treatment and mortality, and should be appropriately identified and dealt with.

52. Implementing and sustaining the appropriate biosafety in TB laboratories: ZN smears through to drug susceptibility testing (DST) cultures

How does biorisk management relate to the implementation of biosafety

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Laboratory biosafety is the application of a combination of administrative controls, containment principles, laboratory practices and procedures, safety equipment, and laboratory facilities to enable laboratory workers to work safely with potentially infectious microorganisms. Risk assessment is an approach that promotes the consideration of risk and development of appropriate biosafety practices in each individual laboratory based on the often unique combination of test procedures, staff expertise, and facilities. Biorisk management encompasses both laboratory biosafety and biosecurity to help reduce the risk of laboratories becoming the source of infectious disease outbreaks.

Challenges and solutions for high-and-moderate-risk TB laboratories

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The Regional TB Laboratory in Vladimir, Russia, performing sputum smear microscopy, solid and liquid culture and DST, and rapid molecular testing, implemented a biosafety program, containing laboratory layout development and modification, policy development, sample delivery, IT system and information flow, staff training, safe practices, new technologies introduction, installation and maintenance of mechanical ventilation and upper room UV, biosafety cabinet maintenance and a personal respiratory protection program. As a result of the program's initiation of reliable and prompt microbiological TB testing, health facilities have seen reductions in occupational TB risk, staff turnover and nosocomial TB transmission risk as well as improved quality assurance.

Design considerations, operation and maintenance of biosafety level three (BSL3) laboratories - the South African experience

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South Africa has a robust and comprehensive framework regulating biosafety and biosecurity, but there are limitations in the implementation and development of high containment (BSL3) laboratory infrastructure. This presentation seeks to explore the design, construction and operation methodologies employed in the country's existing public BSL3 laboratories used for TB diagnosis and research. The WHO Tuberculosis Laboratory Safety Manual (2012), which presents a laboratory design and engineering approach tailored for low-resource settings, will be used as comparative reference in this regard. The availability of in-country containment engineering support for the operation and maintenance of these facilities and primary containment equipment will also be explored.

53. Reducing catastrophic costs for people with TB through patient-centred care

Improving DR-TB care and reducing burden on patients in South Africa

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Decentralization of testing and treatment has resulted in increased case detection, improved patient support, improved rates of treatment initiation among those diagnosed, decreased time from diagnosis to treatment initiation, improved infection control measures in health care facilities, more efficacious treatment regimens and improved survival of individuals diagnosed with DR-TB. This includes the introduction of MDR-TB short course regimen and plans for injectable-free regimen for MDR and XDRTB.

Ambulatory treatment of DR-TB in Armenia

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"Reforming TB financing mechanisms to strengthen TB ambulatory care"
Armenia implemented a patient-centred model of care by changing the way the TB programme was financed;

from funding per bed to needs-based funding. The financing adjustments aimed to reduce the high level of unjustified hospitalization rate for TB patients, to ensure effective and targeted use of funds and to strengthen TB out-patients service. New hospitalization criteria was implemented and had the impact of reducing the number of hospitalized patients and the hospitalization rate of TB patients, reducing the number of hospitalized TB suspects and TB patients with smear negative results, reducing the average length of stay for suspects and smear negative TB patients in hospital, and reducing the bed occupancy rate.

Bending the cost curves for patients: shorter regimens, lower toxic drugs, and same-day ambulatory care of DR-TB

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Frequently used regimens for DR-TB require patients to take up to 20 tablets each day with high rates of toxicity and limited prospects of cure. Despite counselling, treatment support and side-effect management, up to a quarter of patients in many programmes are lost to follow up resulting in amplification of resistance and ongoing transmission. A stronger focus on patient-centred models of care incorporating ambulatory treatment, shorter regimens and delivery options more tailored to patient needs must be considered to combat this programmatic failure.

54. Quantifying gaps in paediatric TB diagnosis and treatment

Considerations when applying a care cascade model to evaluate child TB care

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The global tuberculosis (TB) community has recently been urged to consider adopting a care cascade model when evaluating quality of care. A care cascade framework can be used to visualize and measure not only a final target outcome, but also sequential steps needed to reach the target outcome. Children contribute a considerable proportion of the global TB epidemic, often experiencing high morbidity and mortality. Children differ from adults in the spectrum and type of TB disease they develop, as well as their interaction with health care systems. This presentation will therefore discuss special considerations when applying a cascade framework to estimate not only the burden of TB disease but also

losses at each step in the cascade for children with TB in diverse settings. Interpretation of and gaps in available data to inform estimates of each pillar in the cascade will be highlighted, with examples from South Africa.

Estimated burden of adolescent tuberculosis in the 30 high tuberculosis-burden countries

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The global burden of adolescent (ages 10-19 years) tuberculosis is unknown, and tuberculosis disease in this age group is likely under-diagnosed; burden estimates would help us to understand the magnitude of under-diagnosis. In this modeling study, we estimated the burden of tuberculosis disease among adolescents in the 30 high tuberculosis-burden countries. We combined smear-positive tuberculosis prevalence, adolescent population estimates, and risks of progression from tuberculosis infection to disease. We used progression risks observed in household contacts of tuberculosis patients in Lima, Peru, and adjusted these risks for age, time since initial tuberculosis infection, and HIV status. We estimated 91,530,391 adolescents with tuberculosis infection at the end of 2014 in the 30 high tuberculosis-burden countries; of these adolescents, 996,763 (95% uncertainty interval: 680,089-1,411,654) developed tuberculosis disease in 2015. Globally, 6.0% of adolescents who became ill with tuberculosis had HIV infection.

Measuring the consequences of untreated childhood TB and MDR-TB

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Children are vulnerable to severe and fatal forms of TB and have a high mortality risk if untreated. Using a country-level case-fatality-based modeling approach, age- and HIV status-stratified, we estimated that 239,000 (95% uncertainty interval: 194,000-298,000) children aged <15 died due to TB globally in 2015, 96% of whom were not receiving TB treatment. These results suggest that TB might be the sixth highest cause of death in the 1-59 month age group, above meningitis, AIDS, measles and pertussis. Furthermore, of the 25,000 to 32,000 children who develop MDR-TB annually, fewer than 1,000 initiated appropriate treatment in 2015, implying that more than 20% likely died due to MDR-TB. Household contact investigations could close this treatment gap and lower mortality. We estimate that performing household contact investigations around all adult MDR-TB patients would detect over twelve times as many pediatric MDR-TB cases than are currently being diagnosed and treated.

Missed diagnoses and post-diagnosis treatment delays in pediatric TB: observations from Peru

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Missed TB diagnoses are a problem in children, who typically have bacteriologically unconfirmed disease. Delays between diagnosis and treatment initiation can also occur. Neither missed diagnoses nor treatment delays are routinely quantified. We present the results of a current study from Lima, Peru, in which we identified and determined the reasons for potential missed pediatric TB diagnoses, defined as children with TB symptoms, recent TB contact, and a positive chest radiograph, for whom TB was ruled out by a clinician. In addition, we present results from an ongoing pediatric diagnostic study, in which preliminary analysis has shown that approximately 10% of children diagnosed with TB had a >2 week delay in initiating treatment after diagnosis. While qualitative research to elucidate the factors contributing to this delay is ongoing, initial inquiry has suggested that unavailability of pediatric formulations may be one issue.

55. Post-exposure management of households exposed to drug-resistant TB: lessons from the field

Effectiveness of regimens for the treatment of drug-resistant TB infection: results from a meta-analysis in household contacts

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Multiple observational cohort studies have shown that levofloxacin-based treatment of MDR-TB infection among household contacts may be an effective way to stop progression to active MDR-TB disease. However, most of these cohorts are small. A recent meta-analysis of the efficacy and cost-effectiveness of this intervention has been done. The results of this meta-analysis--with an emphasis on programmatic implementation--will be presented in this session.

Yield of a pilot post-exposure intervention in drug-resistant TB households in Karachi

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In Karachi, Pakistan, in 2016-2017 The Indus Hospital implemented a pilot project that targeted 100 households of MDR-TB patients for screening and treatment, as an extension of the routine MDR-TB treatment program. Over 80% of household members participated; no cases of disease were observed among those who received infection treatment, and adverse events were infrequent. These early results are guiding the expansion of post-exposure management in over 2,000 TB patient households as part of the Zero TB Initiative in the city of Karachi.

The ACTG IMPAACT PHOENIx feasibility study: implications for country programmes

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The ACTG PHOENIx study is the largest trial planned for the treatment of MDR-TB infection, and as part of the study, a feasibility assessment was carried out in households of newly diagnosed MDR-TB patients. This presentation will discuss findings of the study that can be used by TB programs in planning post-exposure management programs.

56. Epidemiología de la tuberculosis en las Américas

Avances y retos para el control de la tuberculosis en Perú

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El control ha evolucionado sostenida y favorablemente, esto refleja el interés de las instancias técnico-normativas y políticas. Se han producido iniciativas legislativas e incremento del presupuesto a US $ 83, 000,000. Sin embargo, los resultados aún son insuficientes, el año 2015 abandonaron el tratamiento 8 % de casos de TB sensible y 30 % en TB MDR. Ante esta situación se están desarrollando medidas desde una perspectiva sanitaria y social:
(i) protección contra riesgos a la salud, reduciendo la transmisión, infección y desarrollo de enfermedad;

(ii) protección de la calidad de la atención, contribuyendo a desarrollar procesos de mejora en seguridad sanitaria, efectividad de las intervenciones, trato dignos a los afectados, protección social y participación ciudadana, lo cual favorezca la adherencia y el cumplimiento del tratamiento;

(iii) protección político financiera, acrecentando la oportunidad y calidad en el gasto, además del abordaje multisectorial de las determinantes de la salud.

57. Nursing interventions for support of patients with multidrug-resistant TB

Supporting binational MDR-TB case management on the US-Mexico border to improve patient outcomes

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This presentation describes a targeted strategy (Nurse case management, formal education of providers, and case management tools) for strengthening DR-TB case management of patients being treated on ambulatory care in Mexico. Methods used to assess patient needs as well as interventions for assisting nurse case managers in Mexico will be presented along with results from 10 years of experience.

An essential patient care package for drug-resistant TB

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This presentation will describe a practical framework for delivering comprehensive patient-centered care to people with DR-TB, funded by USAID as part of the US National Action Plan to Combat Multidrug-Resistant Tuberculosis. It will cover how the package was developed, content and format of the Practical Guide and accompanying tools that countries can adapt for their own use, and experiences with implementation in four pilot countries (China, Pakistan, South Africa, and Ukraine).

58. Improved and differentiated TB programme planning through more effective use of various sources of (sub-national) data

Valorize TB data for local health planning

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This presentation will set the scene and introduce a framework of analysis using multiple sources of geographically, temporally and demographically disaggregate data with the aim to identify missing TB cases throughout the pathway of care at subnational level. The rationale for this is to take advantage of the considerable amount of existing, yet not collated subnational data which potentially describe the numbers of missing TB cases, who they are, where they are located, explain why they are missed, and how to find and treat them.

Identifying geographic areas and key populations for prioritised interventions in Kenya

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This presentation exemplifies how mapping of TB case notification program, TB burden, HIV prevalence and TB HIV co-infection rates, demographics, and diagnostic coverage can lead to identification of areas on which to focus for strengthening TB interventions.
Kenya has an electronic case based TB reporting system. The National TB Program and partners undertook to train sub-national TB coordinators on data driven support supervision. The coordinators then applied these skills to analyze their routine TB data and apply it for local TB programming.

Mapping and microdata analysis to inform public-private partnership in TB response, in Mumbai

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This presentation will focus on the an detailed analysis of the private provider interface agency (PPIA) approach to engage private sector in Mumbai. Usefulness of data driven designing of private sector engagement for TB control, approaches in prioritizing private provider engagement, understanding provider behavior, with respect to utilization of quality diagnosis and treatment services and more importantly the importance of feedback using the program data.
The model designed a dynamic output tracker with select key indicators to tweak the model, the indicators are

total TB notification, percentage of microbiological diagnosed among notified, provider activity in TB services and drug sales monitoring in the private sector.

The presentation also brings in a perspective of denominator to define coverage and how much market share of TB is captured as a proxy indicator for reaching the missed cases.

59. Using knowledge from pharmacokinetics and pharmacodynamics (PK-PD) studies to adapt TB treatment

PK/PD of TB treatment in children

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In general, children should be treated with formulations and doses that achieve antituberculosis drug concentrations comparable to those that are safe and effective in adults. In the absence of evidence-based targets, normal exposures achieved in adults on standard doses, become the targets for children. Smaller individuals require higher mg/kg doses. Allometric scaling can be applied to improve predictions of dose by weight band in children down to about 2 years of age. However, immaturity of drug metabolizing enzymes and transporters reduces clearance in children under 1-2 years of age. Rapid changes due to growth and development as well as formulations and modes of preparing formulations for administration, complicate prediction of appropriate doses in young children. PK studies and safety monitoring need to confirm doses and formulations for children with TB. Modelling with simulations can be used to predict pragmatic weight band-based doses achieving PK targets.

Therapeutic drug monitoring to help optimise TB treatment: when, where, how, which

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The presenter will describe the circumstances under which therapeutic drug monitoring (TDM) would be particularly valuable in helping enhance TB treatment regimens. TDM may be of help in patients not responding to treatment, HIV-co-infected patients, diabetes type 2 or in patients with gastro-intestinal disturbances. Advances in TB diagnostic technologies may increase the opportunity for the wider use of these tests under resource-limited settings.

Using PK/PD data to shape TB drug development

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De-risking drug development in tuberculosis is challenging due to gaps in knowledge of the pharmacokinetics and pharmacodynamics of anti-tuberculosis drugs. The presenter will explain how new knowledge from PK/PD and other studies is being used to inform and direct the clinical development of TB medicines, and make higher impact on decisions around late stage trials.

60. Preparación y respuesta ante una pandemia de influenza en México

Vigilancia epidemiológica de la Influenza

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A partir de la Pandemia de influenza que se presento en el año 2009, se han diseñado e integrado al sistema de salud mexicano diversas estrategias referentes a la vigilancia epidemiologíca, infraestructura, promoción y prevención para el control de esta infección respiratoria aguda. En este contexto es importante para los organismos internacionales que administran la salud y para los sistemas locales de salud, contar con estrategias enfocadas a prevenir los daños a la salud, disminuir los gastos del sistema de salud y poder ofertar una atención oportuna y eficiente.

Preparación y respuesta ante una nueva pandemia de influenza

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Antecedentes: La Preparación y Respuesta ante una Pandemia de Influenza busca proteger a la población con una respuesta oportuna. A nivel internacional se destaca la importancia de contar con un plan de preparación, como el utilizado para afrontar la pandemia de influenza de 2009 en México, que ocasionó 75,548 casos y 1,316 muertes con un costó de más de 9,000 millones de dólares.
Métodos: El Plan se publicó en 2006 y se ha actualizado varias veces, y contempla: coordinación, difusión de la información, vigilancia epidemiológica, confirmación de casos, atención a la población e investigación.
Resultados: Las acciones oportunas limitan el daño y permiten limitar la propagación de la enfermedad y daños a la población.

Conclusiones: El riesgo de una nueva pandemia permanece latente, y ante su ocurrencia, implica repercusiones políticas, sociales y económicas notables, pero podemos minimizar el impacto estableciendo planes de preparación y respuesta.

Beneficios de la implementación de la vacuna de la influenza en México

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Vaccination is one of the fundamental tools to reduce the incidence of influenza in a seasonal or pandemic setting. Every year, with the data of the Global Influenza Surveillance and Response System, the combination of viruses composing the seasonal influenza vaccine is stablished. In Mexico, around
32 million of vaccines are applied per year to focalized population: babies and toddlers (6 to 59 months), children (5 to 9 years old), teens (10 to 19 years old), adults (20 to 59 years old) with risk factors
(non communicable diseases, immunosuppression, obesity and others), seniors (aged 60 and more), health personnel and pregnant women. Influenza vaccination in Mexico has proven to reduce the risk to get sick with influenza, limit the severity of the cases and, with this, reduces the mortality of the disease.

61. Ethical considerations in TB and migration

Guidance on ethics of TB prevention, care and control: what does the 2017 update of WHO guidelines have to say about migration?

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In 2017, the World Health Organization published its updated guidance document on ethical challenges related to the prevention, care, and control of TB. One of the new and important chapters in the guidance document centred on ethical issues in relation to migrant populations, including challenges in screening of LTBI and active TB; deportation when the country of origin has insufficient TB resources; and whether it is ethical to withhold treatment in migrants who have not yet reached their final destinations. This presentation will end by looking at future issues related to migrants and those who work with migrants in TB care.

Migration to a low-incidence TB setting: ethical challenges and experiences from Australia

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Migration from high to low TB incident settings may have both medical and social challenges, and accompany a period of important personal and cultural change. National TB programs and other relevant services need to carefully consider how appropriate treatment programs can be developed and implemented for the benefit of individuals and communities, and how ethical issues in relation to policy and practices can be appropriately considered. This session will draw on programmatic experience in an Australian context in considering ethical challenges in relation to migration screening for active and latent TB, communication and consent in relation to latent TB diagnosis and treatment and the provision of treatment and care for undocumented migrants in a setting where universal health access is considered the norm.

At the intersection of TB and migration: globalisation vs. equity

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In the realm of TB elimination, efforts to increase awareness of the disease and address its impact on vulnerable populations such as migrants have intensified. With greater participation by affected communities in the development of programs and policies, attempts to create a global definition of health equity in the realm of TB and migration are challenged by what is required to achieve true equity among the many groups. When considering that equity can only be achieved by the dedication of increased resources to the most affected groups there is frequently an assessment of the "deservedness" of the migrants and the countries of origin. When health care is viewed as a commodity rather than an essential human right, true equity is unattainable.

62. Prospects for elimination of multidrug-resistant TB

MDR-TB treatment in the high-resource setting: cure is possible

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Multidrug/extensively drug-resistant tuberculosis (M/XDR-TB) is characterized by a long duration of treatment to achieve relapse-free cure, high costs and, in general, poor treatment outcomes. According to the World Health Organization only 52% of patients with MDR-TB and 28% of patients with XDR-TB achieve a successful treatment outcome. Recently, rapid molecular methods based on the analysis of the genome of *Mycobacterium tuberculosis* became available that allow prediction of the results of phenotypic drug susceptibility testing. Results of these methods provide valuable information for physicians to tailor the combinations of drugs in a M/XDR-TB regimen for each individual patient. Individualized drug regimens that include novel compounds and/or refurbished compounds can result in very high rates of sustained culture conversion even in patients with XDR-TB. Under optimal clinical conditions with availability of novel diagnostics and all therapeutic options, patients with M/XDR-TB achieve currently relapse-free cure rates that are compatible to patients with non-MDR-TB.

Accessing MDR-TB exposed households: the PHOENiX MDR-TB feasibility study

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Household contacts of MDR TB patients are at high risk of developing TB. Household contacts of MDR TB patients that are at greatest risk of developing TB include: child contacts< 5 years; contacts ≥5 years that are immunosuppressed from HIV, medication or other conditions; and those that have evidence of TB infection (tuberculin skin test or Interferon Gamma Release Assay positive). There is little evidence on how to access and screen MDR TB affected households. This presentation will share the experience from the PHOENIx MDR TB Feasibility study of identifying MDR TB index pa-tients, accessing their households, screening household contacts for active TB and to identify contacts that may be eligible for treatment of presumed latent MDR TB infection. The resources required to conduct MDR TB contact investigations and the knowledge and attitudes of household contacts to TB preventive therapy and their uptake of HIV testing will also be described.

Manufacturing XDR through MDR-TB treatment

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Inadequate treatment of multidrug-resistant (MDR) tuberculosis (TB) is the major risk factor for emergence of additional drug resistance; this phenomenon is driving the emergence of an extensively drug-resistant (XDR) TB epidemic. This presentation will address risk factors for and timing of the emergence of resistance to second-line drugs during MDR-TB treatment.

Elimination of MDR-TB: what will it cost?

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If current trends continue, MDR-TB will increasingly dominate TB epidemics. Tools that could help reverse this trend carry price tags that are often prohibitive, despite their potential for long-term pay-off. This presentation will attempt to quantify the impact that key interventions could have on MDR-TB epidemic trajectories, explore the affordability and cost-effectiveness of those strategies, and outline the multi-faceted approach that MDR-TB elimination is likely to require.

63. Situación epidemiológica y control de la tuberculosis infantil en América Latina

TB extrapumonar en pediatría

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La tuberculosis es tan antigua como la especie humana (cerca de 3 millones de años) y tan actual como la globalización de las desigualdades socioeconómicas y la infección por VIH/Sida,
La población infantil no ha estado exenta de esta enfermedad sin embargo es recientemente que la epidemia de TB infantil ocupa el centro de la atención mundial , con un aproximado de 10.4 millones de casos nuevos en la población en el 2015 (OMS) de los cuales 1.3 millones tenían coinfecion con VIH , y cerca de un millón de niños (11%), el Ecuador ocupa el sexto lugar entre

los países con mayor carga de enfermedad en la región de las américas, en el año 2016 se notificaron 5.465 casos de TB de las cuales TB pulmonar 4.533 con más de 150 de TB resistente , 715 con coinfecion TB/VIH 184 privados de la libertad y **172** en menores de 15 años, algunos con coinfecion con VIH.

En el hospital pediátrico Baca Ortiz de la ciudad de Quito en la unidad de atención integral de VIH/Sida y de tuberculosis, de 147 pacientes con VIH/Sida se han identificado 14 pacientes con tuberculosis de los cuales 10 con afectación pulmonar, seguida de ganglionar, situación que ha constituido un verdadero reto en el manejo y tratamiento de la tuberculosis en pacientes infantiles con inmadurez inmunológica y además afectados por el VIH en ocasiones con severa inmunodepresión

La tuberculosis infantil en países con alta carga de enfermedad como el Ecuador junto a la infección por VIH/Sida, implica un verdadero reto en el objetivo de poner fin a la tuberculosis , por lo que considero debemos continuar aunando esfuerzos para lograrlo.

ABSTRACT PRESENTATIONS THURSDAY 12 OCTOBER 2017

ORAL ABSTRACT SESSIONS

01. Non-communicable lung diseases in adults - recent updates

OA-101-12 Non-communicable lung disease in Malawi: a meta-analysis of community-based cross-sectional studies in urban and rural settings

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Background: Non-communicable respiratory disease (NCD-Respiratory) causes considerable mortality and morbidity and is a growing global concern. This study set out to describe the burden of NCD-Respiratory in Malawi, one of the world's poorest countries, to estimate the prevalence of spirometric abnormalities, risk factors, and make urban-rural comparisons.
Methods: Data were pooled from two cross-sectional studies conducted in urban and rural Malawi. Pre- and post-bronchodilator spirometry and questionnaire data about risk factors were collected. Weighted prevalence estimates of respiratory symptoms and spirometric abnormalities were calculated, and multivariable logistic regression used to explore contributing factors.
Results: Questionnaire and spirometry data were pooled from 1,528 Rural and 1,058 Urban adults. Respiratory symptoms - mainly cough - were reported by 12.8% of the overall sample, slightly more commonly in the rural vs urban setting (13.7% vs 11.8%). Moderate-severe post-bronchodilator obstruction was observed in 3.8% of participants (4.1% rural vs 3.6% urban). Spirometric restriction was seen in 38.1% and 7.6% using National Health and Nutritional Examination Survey III (NHANES) and local reference ranges, respectively. Age, low body mass index (BMI) and previous self-reported tuberculosis (TB) were positively associated with obstruction. Reduced Force Vital Capacity (FVC) was positively associated with low BMI. After adjustments, there were no significant rural-urban differences.

Conclusions: A high burden of abnormal spirometry was found, with low FVC more common than obstruction. The prevalence of reduced FVC varied markedly, depending on the reference population. Age, low BMI and previous TB were risks for obstruction, but location had little impact after adjustment. Further research in Malawi and elsewhere in Africa is required into the prevalence of abnormal spirometry, contributing factors, particularly nutrition and TB, and the definition of appropriate spirometric reference ranges.

OA-102-12 Prevalence and predictors of asthma in the megacity of Pakistan: findings from the adult asthma study - Karachi

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Background: Scarce data is available regarding burden of asthma from spirometry-based epidemiological community based surveys. So this study was done to determine the prevalence and predictors of asthma among adult population of Karachi, Pakistan.
Methods: A multi-stage, community based cross-sectional survey was conducted from May 2014-August 2015 comprising of 1630 adult (≥ 18 years) participants from 75 randomly selected (out of 9400) clusters in Karachi. From each cluster, 25 households were randomly selected and all eligible participants were recruited. Data was collected through questionnaire-based interviews in Urdu, consisting of respiratory health related questions (American Thoracic Society questionnaire; ATS-DLD 78A), socio-demographic characteristics and risk factors for asthma. Pre and post-bronchodilator spirometry was performed according to the ATS criteria. The prevalence of asthma was calculated considering presence of respiratory symptoms with reversibility on spirometry (≥12% increase, post-bronchodilator) or history of physician-diagnosed asthma.
Results: We determined an overall prevalence of asthma to be approximately 6.6% (n=61; 95% CI: 5.0-8.1) among 930 participants with acceptable spirometry data. Risk of asthma was less likely among the younger age group (AOR: 0.2, 95% CI: 0.1-0.6) and having birds and animals at home (AOR: 0.5, 95% CI: 0.2-0.9). Asthma was more likely to occur among participants with history of allergies (AOR: 2.8, 95% CI: 1.6-4.9) and those exposed to passive smoking at home (AOR: 1.9, 95% CI: 1.1-3.4).
Conclusions: This may be the first robust epidemiological assessment regarding actual burden of asthma among adults in Pakistan, reporting a high burden in the

country. Targeted preventive measures should be taken to reduce smoking and promoting better environmental conditions.

Keywords: Adult asthma, asthma predictors, spirometry, epidemiological survey, Pakistan

OA-103-12 In-door air pollution from cooking with biomass fuels and chronic bronchitis among women in a rural district of Rwanda

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Background and challenges to implementation: From March 2015 to May 2016, a study was conducted in the District of Gisagara located in southern Rwanda to determine the prevalence of chronic bronchitis among women cooking indoor with biomass fuel.

Intervention or response: Using a multistage stratified sample design, 448 women aged 20 years and above were recruited for the study, among them 302 were using biomass fuel for cooking and there was a control group of 146 women who were using either liquefied gas petroleum or had not been cooking the last 3 years. Using a short version version of the European Community Respiratory Health Survey (ECRHS) participants underwent a face to face interview on socio demographic status and respiratory symptoms. Chronic bronchitis was defined using the commonest definition used in epidemiological studies as the presence of cough and expectoration for at least three months for two consecutive years.

Results and lessons learnt: A total of 436 women were accepted in the study among them 298 (68.3%) were using biomass fuel for cooking and 138 (31.7%) belonged to the control group. Mean age for both groups was 32.2 years (range 20-83 years). The main respiratory symptoms was cough found in 59.7% of women using biomass fuel and in 14.5% of control cases, wheezes were found in 5.2% of all participants. Using our case definition of chronic bronchitis the overall prevalence was 10.7% of all participants. A strong association was found between cooking indoor with chronic bronchitis. (p < 0.001). Other factors associated with chronic bronchitis were age, level of education OR; 2.32 (1.93-3.59) and the level of education OR: 1.66(0.90-3.11).

Conclusions and key recommendations: This study showed that cooking indoor with biomass fuel, age and the level of education are the main risk factors for chronic bronchitis.

OA-104-12 A comparison of paper and smartphone-based data collection tools in a Burden of Obstructive Lung Disease (BOLD) study conducted in rural Sudan

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Background: Data collection using paper-based questionnaires can return errors and affect data accuracy, completeness and quality in health surveys. We compared smartphone and paper-based data collection in a BOLD study conducted in rural Sudan.

Methods: The Open Data Kit (ODK) was used to programme BOLD questionnaires in Arabic into smartphones (Samsung Galaxy S3). We included 100 BOLD study participants from 3 rural villages (Rufaa4, Rufaa20, Altakala-Joubara) in East-Gezira and Kamleen localities of Gezira state, Sudan. BOLD questionnaire data was collected using both smartphone and paper-based technologies simultaneously. We used Kappa statistics and inter-rater class coefficient to test the agreement between the two methods in terms of quality, accuracy, completeness and timeliness.

Results: We collected data from 100 participants (83% female; median age (SD) 41.5 (16.4) years. Almost a quarter (24%) reported cough, 15% phlegm, 17% wheeze and 18% shortness of breath. One in five were cigarette smokers of whom 40% were current and 60% ex-smokers. The two data collection methods varied between perfect to slight agreement across the 204 variables evaluated (Kappa varied between 1.00 and 0.02 and inter-rater coefficient between 1.00 and -0.12). Inconsistencies and disagreements were mostly apparent in paper-based questions with complex skip patterns. The use of automated checks and validations in smartphone-administered questionnaires prevented this. Paper-based questionnaires were more likely to have incomplete or inconsistent answers and significantly more errors seen (83% of errors seen) vs smartphone (17% of errors seen) administered questionnaires (X2 (3, n = 100) = 64, p=0.00).

Conclusions: We found that smartphone technology worked well for data collection in a BOLD study conducted in a challenging rural environment in Sudan. This approach provided timely, quality data with fewer errors and inconsistencies compared to paper-based data collection. We recommend this method for future BOLD studies and other population-based studies in similar settings.

OA-105-12 Byssinosis amongst 'home-based' power loom workers in Madhya Pradesh, India

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Background: Byssinosis is an occupational lung disease observed among workers exposed to cotton, flax, and hemp dust. The severity and extent of Byssinosis are well recognised in the high-income countries and control measures have been implemented to prevent the disease. In India, there are conflicting evidence on burden estimation of the disease, followed by inadequate prevention and control of Byssinosis.

Methods: We did a cross-sectional study to assess the prevalence of Byssinosis in home-based power-loom workers in Mominpura, an administrative ward of Burhanpur Municipality with 2818 population in the state of Madhya Pradesh, India. 291 adults working from "home-based" power loom units were randomly selected, profiled and screened for Byssinosis like symptoms with the help of a semi-structured questionnaire and simple hand-held peak expiratory flow monitor. For epidemiological purposes the symptoms were classified based on Schilling's classification. Chest x-rays were done for selected subjects.

Results: Of 291 subjects studied, 284 (98%) had Byssinosis: 239 (84%) were in Grade 0.5, 32 (11%) in Grade 1, 8 (3%) in Grade 2 and 5 (2%) in Grade 3. Peak Expiratory Flow Rate (PEFR) was reduced in 124 (44%). Of 102 participants who had Byssinosis (Grade 0.5) and undergone chest x-rays, only 19 (19%) had abnormal chest x-rays. Older workers, males, smokers and those having longer duration of exposure were associated with the development of Byssinosis.

Conclusions: High prevalence of Byssinosis was found amongst home-based power loom workers. Measuring PEFR by a simple hand-held device is a feasible screening tool to rule out Byssinosis.

OA-106-12 Indoor air pollution and tuberculosis: analysis of National Family Health Survey-III, a nationally representative survey, India

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Background: In India TB is a major health issue with an estimated annual incidence of 2.8 million cases and 480000 deaths. Solid fuel use is considered to be an in-dependent risk factor for respiratory diseases including TB, but with limited contradictory evidence. According to the National Family Health Survey-3 (NFHS-3), three-quarters of households in India use unclean fuels like wood, charcoal, dung cakes, kerosene, crop waste for cooking. The relationship between cooking fuel and tuberculosis has not been conclusively established. Therefore the present analysis was conducted to study the association between use of solid fuels for cooking in households and tuberculosis.

Methods: Data from NFHS-3 (2005-06) among a nationally representative sample of 109,041 households in India was analysed. The survey adopted a multistage stratified sampling design (two-stage design in rural and three-stage design in urban areas). Exposure to cooking fuel smoke was ascertained indirectly by the type of fuel used for cooking. Clean fuels included LPG/natural gas, electricity and biogas whereas unclean fuels included wood, kerosene, dung cakes, straw/grass, coal and charcoal. A binomial regression was done to estimate prevalence ratio. A weighted analysis was done at the household level.

Results: Household characteristics significantly associated with tuberculosis include: overcrowding($>=3$ persons per sleeping room), education and occupation of the head of the family, type of house(kachha, semi-pucca, pucca), smoking at home, place of cooking(indoor/outdoor), place of residence, wealth status and caste. After controlling for the effect of these confounders, households who use unclean fuels have a higher risk of tuberculosis compared to those using clean fuels. (PR: 1.9; 95% CI: 1.6-2.3, p-value< 0.001)

Conclusions: This study finds that use of solid fuel for cooking is associated with tuberculosis after adjusting for other confounders. Thus, the use of clean fuels such as LPG should be promoted through crucial policy changes to improve health of the population.

02. Access to patient care: is it their right, privilege or ethical challenge?

OA-107-12 To B or not to B: the rights V/s program debate for access to bedaquiline

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Background and challenges to implementation: An Indian teenager, having XDR TB, filed a petition in Delhi High Court to sue Government of India (GoI) for declining her access to Bedaquiline (Bdq). Bedaquiline, has been approved for use under Conditional Access Programme at six sites in India.

She was denied access to Bdq because 1. She did not reside in the catchment area of any of these six sites and 2. Her extensive TB drug resistance made it difficult to formulate an optimal background regimen for Bdq. Bdq is a new anti-tuberculosis drug which is showing encouraging results in the management of Drug Resistant TB. **Intervention or response:** The case was debated extensively inside and outside the High Court of Delhi and was widely covered by national and international media. **Results and lessons learnt:**

Stakeholder	Argument	Counter-argument
TB Patient, Family and Activists	Treatment with Bdq must start immediately, delay can cause death. Patient has right to life-saving medical treatment, no matter where she lives	Additional DST needed to determine Optimal Background Regimen Bdq CAP sites are equipped for monitoring of patients, safer for patient to live closer to a site
Global TB Community	India's TB problem impacts global health. About 30,000 DR patients may need new drugs like Bdq yet few have access to them due to strict criteria.	Lack of consensus yet, on the safety and success rate of bedaquiline, in Indian settings. Caution is advisable
National TB Programme	Serious side effects of Bdq call for strict regulation and carefully monitoring Indiscriminate use will cause rapid emergence of resistance to precious drug. Bdq effectiveness to be preserved by controlling its supply. Protocols and guidelines must be followed strictly to protect the drug from misuse and acquired resistance	The disease is also serious and life threatening. Need for drug outweighs risks Less use will cause less resistance but higher risk of DRTB transmission in community Protecting lives takes precedence over protecting drugs Early access to Bdq for persons who need is more effective in treating them and in preventing development of resistance
Private Sector	Most patients prefer to be treated in private facilities. Conditional access must be provided through them	Use of Bdq only in selected public centres to prevent uncontrolled use in private sector

Table The Bedaquiline Debate

The case was first of its kind and raised several issues from Human Rights, Ethics and Program Management perspectives. These points are listed in the table- The Bedaquiline Debate. The court directed the National TB Programme to make Bdq available to the patient and to not insist on proof of residence as a pre-requisite for the same. The patient was later initiated on a regimen containing Bdq as well as Delamanid at a private facility and is doing well at the time of submission of this abstract. The Indian government has accelerated the roll-out of bedaquiline throughout the entire country.
Conclusions and key recommendations: NTPs will face similar dilemmas about ensuring individual patient rights and retaining the potency of new TB drugs for years to come.

Access to rapid diagnostics and early testing for drug resistance followed by appropriate therapy is needed for every TB patient.

OA-108-12 Solidarity in addressing ethical challenges in the mplementation of new technologies: a qualitative study

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Background: The development and implementation of new tuberculosis (TB) drugs (e.g., bedaquiline) and diagnostics (e.g., Xpert MDR/RIF) into existing TB programs presents a host of ethical issues. The objective of this study was to characterize these issues and provide practical recommendations based on a qualitative analysis of TB stakeholder perspectives.
Methods: 23 semi-structured, key informant interviews were conducted with an international group of healthcare workers, advocates, funders, and policy makers working in TB. Interviews lasted approximately one hour and were audio recorded, transcribed, and coded using NVivo 11. Data was analysed using Braun and Clarke's thematic analysis.
Results: Respondents indicated that TB disproportionately affects individuals and communities that are poor and disenfranchised and enumerated associated barriers to, and inequities in, accessing new technologies. Within this context, we identified four ethical themes: (1) solidarity, e.g., the importance of increased advocacy and 'standing with' persons and communities affected by TB; (2) power dynamics skewing development and implementation of new technologies, e.g., the role of philanthropy in shaping technological development; (3) goals, governance and responsibilities, e.g., lack of coordination and shared aims in the TB community; and (4) balancing risks and benefits of new technologies, e.g., weighing potential benefits of administering new drugs with risks of developing resistance and limiting drug utility across a population. Solidarity is an overarching theme, since successfully addressing other ethical challenges requires collective action within and beyond the global TB community.
Conclusions: Respondents agreed that the development of new TB technologies is overdue but that their successful development and implementation requires addressing complex ethical and social considerations, including issues of power, responsibility, and risk. It is clear that increased and sustained collective action across and beyond the TB community, such as through advocacy and participatory research, is required to address existing ethical challenges and accelerate toward TB elimination.

OA-109-12 Improving documentation of tuberculosis cases notified by community health volunteers in high tuberculosis burden facilities in Kenya

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Background and challenges to implementation: Amref Health Africa is supporting community tuberculosis (TB) prevention and care activities as the non-state Principal Recipient for Global Fund TB grant, through 29 sub-recipients. From 2011, vast resources were channeled towards supporting Community Health Volunteers (CHVs) to carry out these activities in Kenya including screening household contacts of bacteriologically confirmed TB patients and referral of presumptive cases to facilities. Despite CHVs' active involvement, community contribution to TB case notification remained low at 4-5%. This could possibly be attributed to inaccurate documentation of TB patients referred by CHVs at facility level. A comparative analysis of pre and post intervention was done to elucidate incorrect documentation.

Intervention or response: In total, 106 facilities that notified 10 or more TB cases monthly in 2014 were considered. Monthly data review meetings were supported in these facilities, attended by TB clinic health care worker, Community Health Extension Worker and CHV attached to the facility. Data from community TB reporting tools filled by CHVs were compared with data in the facility TB register under the 'referred by' column and discrepancies corrected. The meetings ensured community TB activities were well coordinated, correctly documented and challenges addressed. Comparison was done between the period July-December 2015 and July-December 2016 using data from the national electronic TB reporting system, TIBU.

Results and lessons learnt: Out of 8,015 TB cases notified in 2015 from the 106 facilities, 308(4%) were CHV referrals, 6,097(76%) self-referrals and 1,610(20%) other referral sources. The same facilities in 2016 notified 7,227 cases including 754(10%) CHV referrals, 5,119(71%) self-referrals, 1,334(18%) others and 20(1%) not indicated. CHV referrals increased by 446(59%) from 2015 to 2016 despite 7% drop in cases notified in 2016. Referrals by CHVs are commonly recorded as self-referrals in the TB register underscoring need for data review.

Conclusions and key recommendations: Structured data review forums at facility level significantly improved documentation and should be scaled up.

OA-110-12 Civil society experiences in community engagement in the fight against TB

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Background and challenges to implementation: Despite significant progress in TB Control in Malawi, TB remains a major public health concern in the country. One of the challenges is case detection. The 2014 national TB prevalence survey showed a higher TB prevalence of 1014/100,000 compared to the previous estimated prevalence of 373/100,000 by the World Health Organization (WHO). This meant that more than half of TB cases remain undetected within the communities. The findings reflect the challenges the health sector is facing in improving access to health care services to the population in the economically struggling nation.

Intervention or response: In view of above, the national TB programme had to intensify community interventions to improve case detection. This includes engagement of CSOs in the fight against the epidemic. Among other interventions, it included establishment of community sputum collection points and introduction of symptomatic House-to-House TB screening. Community leaders in these communities have played a greater role in identifying volunteers and mobilizing the public.

Results and lessons learnt: Currently, 1,081 sputum collection points have been established, provided with enablers and functional. Furthermore, 10,810 volunteers have been trained in passive and active case finding (symptomatic TB screening). As a result, communities were able to refer 2556 sputum samples for presumptive TB cases to microscopy centers in a period of six months. Out of these, 288 were confirmed to have TB and have been initiated on treatment and are receiving treatment adherence support within the communities.

Conclusions and key recommendations: The process of community engagement is ongoing and it is expected to contribute significantly to the national case detection efforts. Promising results were observed from the short implementation period. Inadequate sample transportation mechanisms between communities, and microscopy centers affected implementation. In addition, there are also difficulties in identifying literate volunteers in some communities. Lastly, there is need to perfectly establish coordination mechanisms between community structures and formal health structures.

OA-111-12 Role of ex-tuberculosis patient engagement in TB care and control in Afghanistan: data review

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Background and challenges to implementation: Populations living in Afghanistan's rural and hard-to-reach areas are at increased risk for TB due to the presence of large numbers of internally displaced people, poor hygiene, nutrition and ventilation. Public health facilities (HFs) are also less accessible and require extensive travel time. TB case identification in these areas and infection prevention remains a challenge. The purpose of this study was to measure the effectiveness of using ex-TB patients to support case notification and treatment in rural and hard-to-reach areas.

Intervention or response: In an effort to raise TB awareness and generate demand for TB services among patients living in rural and hard-to- reach areas, The CTB project 145 TB patient associations of 10-15 ex-TB patients in the rural and hard to-reach areas of 15 provinces. Association members are given a vital role in combating TB. They are sensitized, trained on TB and are encouraged to take up awareness activities, refer TB presumptive case for testing to diagnostic health facilities and occasionally provide DOTS. Routine quarterly review workshops, monitoring and data capturing tools are used to monitor the TB patient associations' activities.

Results and lessons learnt: In 2016, the TB patient associations referred 1,120 presumptive TB patients. Among these presumptive TB cases 87 (7.8%) were diagnosed as bacteriological TB confirmed cases and were put on DOT. In comparison, in the same year, 8,722 health posts referred 20,682 presumptive TB cases and on average 2.3 cases were diagnosed with TB with a positive rate of 5.8%.

Health posts(HP)					Ex-Tuberculosis patients associations				
Total # of health posts in 15 provinces	Total # of presumptive cases referred	Average # referred per HP	Total # of bacteriological confirmed cases	Positive rate	Total # of ex-TB patient associations in 15 provinces	Total # of presumptive cases referred	Average # referred per association	Total # of presumptive cases referred	Positive rate
8,722	20,682	2.3	1,214	5.8%	145	1,120	7.7	87	7.8%

Table 1

Conclusions and key recommendations: TB associations comprised of cured patients are more likely to help others in their community to combat the disease, especially in hard to reach areas. Their involvement in TB diagnosis yields positive results in case identification. We recommend the establishment of TB patient associations in other cities in Afghanistan, and in similar settings in the world.

OA-112-12 Community-based TB care in conflict-affected areas in Myanmar: evaluation of community-based activities by international non-governmental organisations

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Background: International non-governmental organizations (INGOs) are assisting the National Tuberculosis Program (NTP) to promote community engagement in TB across States and Regions in Myanmar, including conflict-affected regions. This study assesses the contribution of these organizations on TB notification and treatment outcomes to local NTP teams in these areas.
Methods: This is a descriptive study using routine programmatic data from three INGOs and the NTP in 16 conflict-affected townships in 2015. The contribution of INGOs was calculated as proportion of total TB patients registered at local TB centers in the same townships.
Results: Three INGOs are implementing community-based activities in 16 conflict-affected townships in Myanmar. During the study period, 4,956 people with presumptive TB were referred by village health workers (VHWs) to local TB centers for diagnosis and treatment. Among them, 1,579 (32%) were diagnosed as having TB, which contributed 16% of total TB patients notified in these townships with variation from 0% to 51%. The VHWs provided anti-TB treatment DOTS supervision to these patients, among which the treatment success rate (TSR) was 90% (township-level 67- 100%) while the overall TSR of respective townships was 85% (township-level 70- 96%).
Conclusions: Community-based TB care activities enhanced TB case notification and improved treatment outcomes even under conflict settings, though achievement was variable by township. Different program approaches may be required in different political contexts to optimally contribute to TB case finding and successful outcomes.

OA-113-12 School-children as TB Soldiers played crucial role to control TB epidemic by disseminating messages of symptoms & free treatment among their peers, family and neighbours in Bastar

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Background and challenges to implementation: With 1/4th of the global burden, Tuberculosis is the leading cause of death in the 15-45 age-groups in India. Inspite of complete geographic coverage of RNTCP in 2006, many TB suspects remain undiagnosed.

Realizing the value of young children in community mobilization, the District-RNTCP-Bastar engaged them in tuberculosis-control-activities. A school-based-intervention was designed to sensitize and groom students as "TB Soldiers" (TBS). We evaluated the intervention and success achieved in Bastar district as a pilot which was later replicated elsewhere.

Intervention or response: Schools with children belonging to vulnerable-and-marginalized community and studying in 6th-10th standards were selected. Key messages on causative agent of tuberculosis, modes of transmission, environmental factors, identification/diagnosis/complete cure, free treatment availability, location & meaning of DOTS, duration of treatment, prevention and vaccine for tuberculosis were delivered during various sessions. Children were groomed as TBS through a well-structured communication protocol. Trained Community Volunteers of local NGOs informed the Senior-Treatment-Supervisor about TB symptomatics reported by the children.

Results and lessons learnt: Participation was 100% among the schools intervened. 3652 students were sensitized through these sessions. 174 symptomatic cases identified by the TBS were reported to the CVs at the school level. 35 cases were diagnosed as NSPs. 2/5th cases were detected from their neighbourhood. Specificity in case identification was around 33%. Most symptomatics were reported by students of 8th-10th standards. 20% cases were reported on the same day while 40% each were reported within 2-5 days of the intervention.

Conclusions and key recommendations: This planned low-cost-unique model for TB control attempt by using the school students as a medium for community mobilization proved as highly effective strategy to diagnose TB cases. Although not fully utilized, sensitizing and engaging school children as TBS has immense potential to reach out to the contact cases and increased awareness among the peers/unreached community. However, further evidence based studies recommended for larger engagement of the TBS.

OA-114-12 Exploring the effectiveness of community engagement in tuberculosis treatment outcomes in Afghanistan: a cohort analysis

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Background and challenges to implementation: Afghanistan's weak and fragile socioeconomic and health infrastructure contributes to its high rate of Tuberculosis (TB) (annual incidence of 189 cases per 100,000 population, prevalence of 340 cases per 100,000 population and a death rate of 37 deaths per 100,000 population). Afghanistan misses about 30% of existing TB cases per year and the quality of service and treatment outcome of TB patients remains a challenge (WHO report, 2016).

Intervention or response: The NTP, with support from USAID funded TB projects and other partners launched a community based intervention to engage community health workers (CHWs) and other community members in providing TB services and bringing treatment to the doorsteps of TB patients. More than 14,000 community members including CHWs were trained on presumptive TB patient referral and currently provide regular treatment to TB patients throughout 15 Afghan provinces.

Results and lessons learnt: Based on NTP surveillance data, during 2015, 19,652 TB patients were enrolled in health facility DOTS in 15 provinces and 17,490 (89%) of those patients successfully completed their treatment. At the community level, 2,787 TB patients were started on treatment and 2,680 completed treatment (96% treatment success rate [TSR]), while the TSR was 87% at the national level (P-Value < 0.001) (See Table).

Variance	Treatment success (%)	TB deaths (%)	Treatment failure (%)	Lost-to-follow-up (%)	Not evaluated (%)	P-value
TB patients under treatment at National level (29,657)	25,802 (87%)	890 (3%)	295 (1%)	900 (3%)	1780 (6%)	> 0.001
TB patients under treatment at 15 provinces HFs Level (19,652)	17,490 (89%)	396 (2%)	182 (1%)	591 (3%)	993 (5%)	> 0.001
TB patients under treatment at Community level (2,787)	2,680 (96%)	54 (2%)	0 (0%)	51 (2%)	2 (0%)	

Table TB treatment outcomes at three levels, 2015

Conclusions and key recommendations: Providing treatment to TB patients through the community significantly increased the treatment success rate and reduced the lost to follow-up and failure rates. Treating patients through the community at their homes also prevents drug resistant TB. We strongly recommend engaging the community in providing TB services and bringing treatment to patients' homes through community members and CHWs.

03. HIV-TB: from diagnosis to outcomes - something for everyone

OA-115-12 Identification of geospatial hotspots of TB-HIV co-infection distribution in USAID/PEPFAR supported LGAs in Nigeria: using GIS for intensified case finding

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Background: The prevalence of HIV among TB patients increased from 2.2% in 1991 to 19.1% in 2001, but slid from 25% in 2010 to 17% in 2015, suggesting a decline in TB/HIV co-infection rate in Nigeria. This study aimed to identify the spatial distribution pattern of TB/HIV co-infection among new and relapsed cases of TB, and detect hotspots to prioritize program resources towards control efforts in Nigeria.

Methods: This was an ecological descriptive design conducted between October 2015 and September 2016. We georeferenced new and relapsed TB/HIV case reports from 192 of 774 Local Government Areas (LGA) spread across all of Nigeria's six geographic regions (North-Central, North-West, North-East, South-South, South-East and the South-West). Seropositivity rate among TB patients was calculated from data extracted from medical records and national TB/HIV registers. Global spatial autocorrelation techniques showed TB/HIV co-infection distribution patterns, and Hotspot analysis highlighted regions of significant clusters of TB/HIV cases among neighboring geographic regions.

Figure Global Spatial Autocorrelation & Hotspot Analysis

Results: Of the total 15,564 new and relapsed TB cases, 3,752 tested HIV positive. HIV seropositivity among TB cases was 24.1%. Both the Choropleth map and the global spatial autocorrelation Moran´s I statistics revealed a clustered distribution of the spatial pattern of TB/HIV co-infection. Given the z-score of 2.69 [p< 0.0069, Moran´s Index = 0.268], there is a less than 1% likelihood that this clustered pattern could be the result of random chance. Hotspot analysis using Getis-Ord Gi* statistics indicated significant clusters of TB/HIV co-infection that were confined to LGAs in the North East, North West, South East and the South South regions of the country.

Conclusions: The distribution of TB/HIV co-infection showed a non-homogeneous spatial distribution pattern. This study identified geographical areas to prioritize for control of TB/HIV co-infection, thus demonstrating that geographical information system technology is a useful tool to inform interventions for epidemic control of TB/HIV co-infection.

OA-116-12 Patient education versus clinician mentoring for increasing isoniazid preventive therapy uptake in the South African primary care setting

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Background: Isoniazid preventive therapy (IPT) reduces the risk of tuberculosis in people living with HIV (PLHIV), but globally implementation is poor. The aim of this pilot study was to evaluate two interventions to improve IPT uptake among PLHIV in South Africa.

Methods: From October 2016-January 2017, four primary care clinics in Potchefstroom, South Africa were randomized to receive a patient education or clinician mentoring intervention (two clinics per arm). Standardized interactive patient education sessions covering the basics of HIV/TB and benefits of IPT were held twice daily in clinic waiting areas. The clinician mentoring intervention was targeted at primary care nurses who provide the bulk of primary care, and consisted of a quality-improvement workshop, peer-to-peer mentoring, election of a clinic "IPT champion" and text messaging support.

Results: Patient education sessions reached a median of 56 patients per day (IQR:41-72). A nurse-mentor held two IPT workshops at each clinician mentoring clinic, and 18 peer-to-peer mentoring sessions averaging 84 minutes each that reached 100% of clinicians. At baseline, the proportion of HIV-positive patient prescribed IPT was low at both patient education (n=117/4871, 2.4%, 95% CI:2.0-2.8%) and clinician mentoring clinics
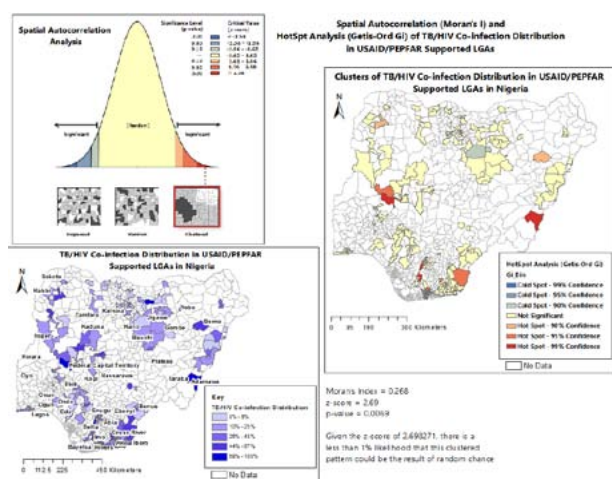
(n=49/4505, 1.1%, 95% CI:0.1-1.4%). During the interventions, the proportion of patients started on IPT averaged 3.7% in patient education clinics (n=127/3404, 95% CI:3.1-4.4%, p 0.001) and 6.6% in clinician mentoring clinics (n=218/3279, 95% CI:5.8-7.6%, p < 0.001). By the end of the 4 month intervention period, IPT initiation had increased to 9.2% (95% CI:7.0-12.0) in clinician intervention clinics, compared to 3.4% (95% CI:2.2-5.0, p< 0.001) in patient education clinics. (see Figure)
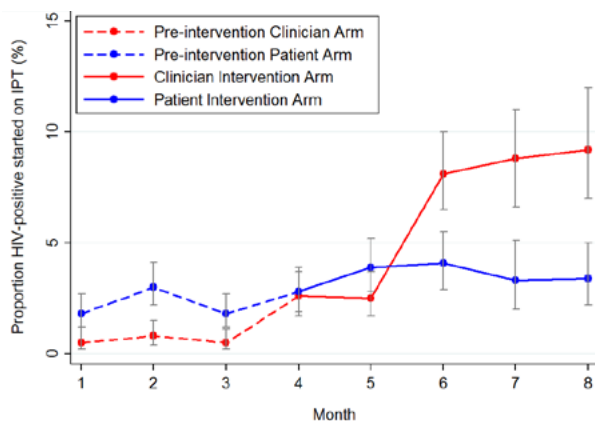
Figure HIV-positive patients started on IPT

Conclusions: This pilot study suggests that a dramatic shift in IPT uptake is difficult to achieve; the two interventions resulted in only modest increases in IPT initiation. These data suggest that clinician mentoring has better long term results, but larger trials testing this against other interventions is warranted.

OA-117-12 Barriers to and enablers of sputum collection and HIV testing during household contact investigation in Uganda

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Background: Home-initiated TB evaluation procedures and HIV counseling and testing (HCT) could improve test uptake and linkage to care among at-risk contacts of active TB index patients. However, there is a need to systematically explore why contacts accept or decline these services. We sought to determine the barriers to and facilitators of home-based sputum collection and HCT as part of household contact investigation for TB in Kampala, Uganda.
Methods: Using an explanatory sequential mixed-methods design, we nested qualitative interviews in a randomized controlled trial testing implementation of enhanced household contact investigation for TB. Twenty-eight household contacts offered home-based sputum collection and/or HCT during contact inves-

tigation were contacted two weeks later and invited to participate in a semi-structured interview. Respondents reflected on the events of the day of the contact investigation, their household context, and their decision to accept or decline services. After coding for the capabilities, opportunities, and motivations forming the context of each participant's decision using the COM-B model, we linked the qualitative data to individual- and household-level data collected during contact investigation. We conducted a thematic analysis to identify the key barriers to and facilitators of home-based sputum collection and HCT.
Results: Facilitators included a preexisting desire to confirm HIV status, a desire to show support for the index patient, the perception that home-based services save money and time, positive perceptions of community health workers, and a misperception that home-based evaluation entitled participants to home-based treatment. Key barriers included psychological unreadiness to receive results and household experience of TB stigma.
Conclusions: Motivation to test begins before the contact investigation visit. The convenience and professionalism of home-initiated services provides an opportunity to act on this motivation. Uptake might be improved by addressing motivational barriers prior to the visit, possibly through improved TB education for index patients and treatment supporters.

OA-118-12 Improving sputum collection to increase TB case finding among HIV- positive persons enrolling in HIV care and treatment clinics in Botswana, 2012-2014

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Background: Undiagnosed or late tuberculosis (TB) diagnosis remains the leading cause of death among persons living with HIV (PLHIV) in low- and middle- income countries, including Botswana. The Xpert MTB/RIF assay (Xpert) has been an important tool in improving TB diagnostics, however inadequate sputum collection among presumptive TB cases remains a barrier. We investigated if field efforts improve sputum collection among PLHIV with TB symptoms, under routine program conditions, were effective.
Methods: PLHIV attending twenty-two HIV clinics with early access to Xpert were prospectively evaluated from 8/2012-10/2015 as part of an Xpert implementation evaluation study. Patients who screened positive using the WHO recommended symptom screen (cough,

fever, night sweats and weight loss) provided sputum samples for testing by Xpert. After 10 months of study implementation (pre-intervention period), a field intervention to improve sputum collection rates was conducted, including: development and use of a sputum collection job-aid for clinicians to use in coaching patients, staff training on the procedure for collecting a good quality sputum of adequate volume, sputum induction and use of a sputum log for monitoring. We calculated sputum collection and TB diagnosis rates pre- and post-field intervention. Differences were tested using the SAS GLIMMIX procedure with a random effect for facility.
Results: Prior to the intervention, sputum collection rates in routine program conditions were low at 44.1% (384/870) among HIV associated presumptive TB patients. Following the intervention, sputum collection significantly increased to 58.3% (579/993), P<0.001, and TB diagnosis from 5.1% (44/870) to 9.2% (91/992), p=0.002.
Conclusions: Our finding indicated that a field intervention improved sputum collection rates and intensified TB case finding (ICF) among presumptive TB cases. However, even with intervention sputum collection rate remained low. Further evaluation on sputum collection improvement is essential to optimize the use of Xpert for ICF among PLHIV.

OA-119-12 Substantial increase in risk for HIV patients with multidrug-resistant tuberculosis for aminoglycoside-induced hearing loss

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Background: A large number of multidrug-resistant TB (MDR-TB) infected individuals develop permanent hearing loss resulting from aminoglycoside ototoxicity. Despite the known risk, injectable *kanamycin* and *amikacin* are the most common choice among aminoglycosides for MDR-TB treatment in sub-Saharan Africa. Particularly, the prevalence of aminoglycoside-induced hearing loss is greatest in TB and HIV-endemic counties, such as South Africa. However, it has been controversial whether HIV co-infection impacts on the higher incidence of aminoglycoside-induced hearing loss during MDR-TB treatment.
Methods: This meta-analysis evaluates existing evidence for the risk of HIV co-infection on aminoglycoside-induced hearing loss among MDR-TB-infected individuals in sub-Saharan Africa. PubMed, Embase, Scopus, CINAHL, Web of Science, Cochrane Review, and reference lists of identified articles were searched using the terms hearing loss, ototoxicity, aminoglycoside, and sub-Saharan Africa.

Results: Seven studies conducted in South Africa and Botswana between 2011 and 2015 were included. Heterogeneity was estimated using I^2 statistic; studies were statistically heterogeneous (I^2 = 19.65, df = 6, p = 0.003) and a random effect model was applied. MDR-TB and HIV co-infected individuals had 43.2% higher risk of developing aminoglycoside-induced hearing loss than HIV-negative individuals (pooled relative risk= 1.43; 95% CI= 1.28, 1.60) during MDR-TB treatment.

Author	Year	Country	N	Type of AG	RR	95% CI		% Weight	Forest Plot
Harris et al.	2012	South Africa	151	Km, St, Cp	1.68	1.21	2.31	12.93	
Seddon et al.	2012	South Africa	93	Am, St, Cp	1.93	0.64	5.81	1.52	
Brust et al.	2013	South Africa	91	Km	0.78	0.39	1.59	4.21	
Sagwa et al.	2013	South Africa	57	Am, Km, St, Cp	1.34	0.49	3.60	2.29	
Sagwa et al.	2015	South Africa	353	Am, Km	1.85	1.53	2.23	30.86	
Modongo et al.	2015	Botswana	28	Am	1.77	0.48	6.50	1.08	
Modongo et al.	2015	Botswana	437	Am	1.12	0.95	1.32	47.11	
M-H pooled RR					1.43	1.28	1.60	100.00	

Abbreviation: AG= aminoglycoside; Am= amikacin; CI= confidence interval; Cp= capreomycin; Km= kanamycin; M-H= Mantel-Haenszel; N= sample size; RR= relative risk; St= streptomycin

Figure Forest Plot of AG-Induced Hearing Loss

Conclusions: This is the first meta-analysis to demonstrate an association between HIV co-infection and incidence of aminoglycoside-induced hearing loss among MDR-TB-infected individuals in HIV endemic settings. Although this study was limited to small trials, this data is essential for TB programs as decisions are made to expand non-injectable based regimens. This data lends credibility to HIV being a reason to automatically include HIV positive individuals into injectable sparing regimens.

OA-120-12 Trends in tuberculosis treatment outcomes among smear-positive HIV-infected and uninfected TB patients in Kenya, 2008-2015

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Background: Human immunodeficiency virus (HIV) infection among tuberculosis (TB) patients independently predicts death. Timely antiretroviral therapy (ART) among TB/HIV patients is lifesaving. Kenya initiated HIV testing and counseling (HTC) and ART among TB patients in 2006; however, the impact of these interventions on TB/HIV case-fatality trends in programmatic settings has not been systematically evaluated.
Methods: This was a retrospective analysis of aggregated Kenya TB and TB/HIV surveillance data for years 2008-2015. We abstracted and analyzed data on TB type, patient type, HIV status, ART uptake, and TB treatment outcome using Microsoft Excel 2013 and Epi-Info™ 7. WHO 2013 definitions were used to classify variables.

We computed frequencies, trends and Mentel Haenszel χ^2 test to determine significance in proportion change between 2015 and baseline (2008 for all variables and 2009 for TB treatment outcomes by ART).

Results: Overall, 790,067 patients including 280,810 with smear positive TB were evaluated. Annual TB notification declined from 115,234 to 81,579, HIV testing increased from 83% (91,463) to 97% (79,419) and patients testing HIV positive declined from 45% (41,174) to 33% (26,352) while ART uptake increased from 27% (12,426) to 96% (25,261). Among patients with smear positive TB, treatment success rose from 89.1% (18,790) to 91.1% (24,345), p=0.001 and 81.0% (9,051) to 84.3% (7,804), p=0.001 for patients who were HIV negative and positive respectively. Case-fatality increased from 6.8% (764) to 7.8% (718), p=0.012 among all those who were HIV positive and 4.4% (256) to 7.5% (664) p=0.001 for those on ART. Loss to follow (LTFU) declined from 7.8% (867) to 4.8% (442), p=0.001 among those who were HIV positive and increased from 4.4% (267) to 4.6% (405) p=0.700 among those on ART. Overall case-fatality among patients who were HIV positive was two to four times that among those who were HIV negative. (Figure 1)
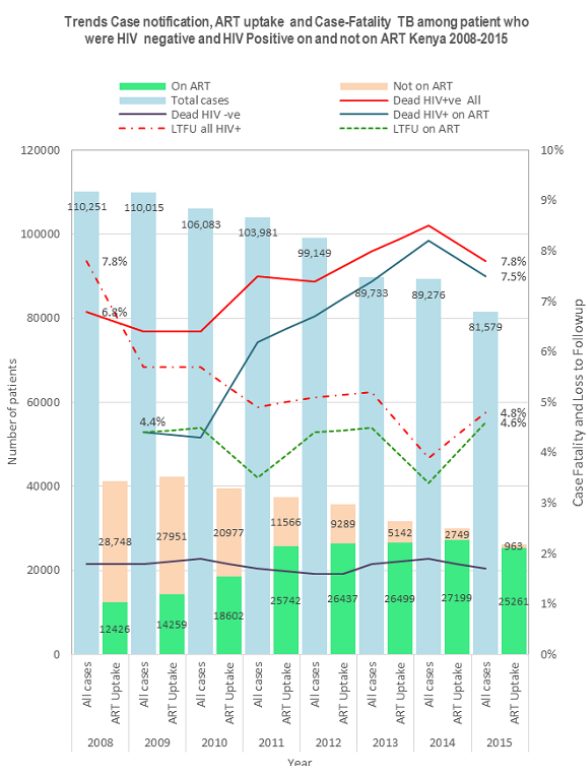
Figure 1

Conclusions: TB/HIV service coverage, treatment success and TB/HIV case-fatality increased. Factors associated with the apparent increase in case-fatality should be explored.

OA-121-12 Treatment outcomes among people living with HIV and non-tuberculosis mycobacteria versus *Mycobacterium tuberculosis* in Botswana

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Background: Patients with non-tuberculous mycobacteria (NTM) and *Mycobacterium tuberculosis* (MTB) pulmonary disease may have similar clinical presentation. Where testing capacity for Xpert MTB/RIF (Xpert), phenotypic culture and NTM speciation is limited, misdiagnosis, delivery of sub-optimal treatment and outcome may occur. We described outcomes among presumptive HIV-infected TB patients with culture-positive NTM and MTB who received TB treatment.

Methods: Patients living with HIV (PLHIV) attending 22 HIV clinics were recruited and those who screened positive for ≥1 TB symptom (cough, fever, night-sweats, weight-loss) were asked to submit sputa for culture and speciation. Isolates from positive-cultures were retrospectively tested by Xpert. Laboratory and clinical information were analysed, adjusting for intra-site correlation, to compare TB treatment outcome and characteristics of patients with NTM and MTB.

Results: From 08/2012 to 11/2014, 1940 PLHIV with TB symptoms submitted ≥1 specimen. Among these, 402 were culture-positive indicating 228 NTM and 174 MTB. Thirty-six (16%) of 228 patients with NTM and 174 with MTB received TB treatment. TB treatment outcome was available for 32 NTM and 138 MTB, unfavorable outcome (lost to follow-up, death, failure) was similar, 12.5% NTM vs. 8.6% MTB, *p = 0.51,* respectively. For 34 of the 36 treated NTM patients isolates were available and tested by Xpert; all results indicated MTB not detected. Among 228 NTM patients, those with body-mass index < 18.5 (adjusted OR (aOR) 2.5, 95% Confidence Interval (CI), 1.31-4.76), weight-loss (aOR 1.72, 95% CI, 1.00-2.94) and TB history (aOR 3.86, 95% CI, 1.12-13.3) were more likely to be treated for MTB.

Conclusions: Though unfavorable treatment outcome was similar between NTM and MTB patients, our findings highlight factors associated with an increased likelihood of receiving TB treatment among PLHIV with NTM. Xpert has the potential to rapidly rule-out NTM and avoid sub-optimal treatment; further research is needed to evaluate such potential.

OA-122-12 Urinary LAM with TB disease severity and culture outcomes in HIV-infected adults in ambulatory South African clinics

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Background: Tuberculosis (TB) is the leading cause of death in people living with HIV. Rapid urine liporabinomannan (LAM) assays may improve HIV-associated TB diagnosis by rapidly identifying people with a high bacillary burden of TB disease.

Methods: We screened newly diagnosed HIV-positive adults in South Africa for TB using symptom screening, acid-fast bacilli (AFB) microscopy, liquid and solid cultures, and a rapid urine LAM assay. Participants were followed for 12 months. In patients with HIV-TB co-infection, we tested LAM-positive versus negative associations using Fisher's exact test, logistic regression, and Cox proportional hazard models adjusted for age, gender, education, and smoking.

Results: Among the 726 enrolled participants, 194 had AFB microscopy or culture-confirmed TB, of whom 56 (28.9%) were LAM positive. Compared to those who were LAM-negative, LAM-positive patients were more likely to be liquid culture positive (60.9% versus 74.5%, p-value=0.09), solid culture positive (32.1% versus 64.7%, p-value=0.0002), and to die during follow up (13.8% versus 33.9%, p-value=0.001). Time to positive solid culture was significantly shorter for urine LAM positive patients both overall (hazard ratio [HR] 2.48, 95% confidence interval [CI] 1.55-3.98) (Figure 1) and among those with CD4 < 200/mm^3 (HR 2.29, 95% CI 1.35-3.88).
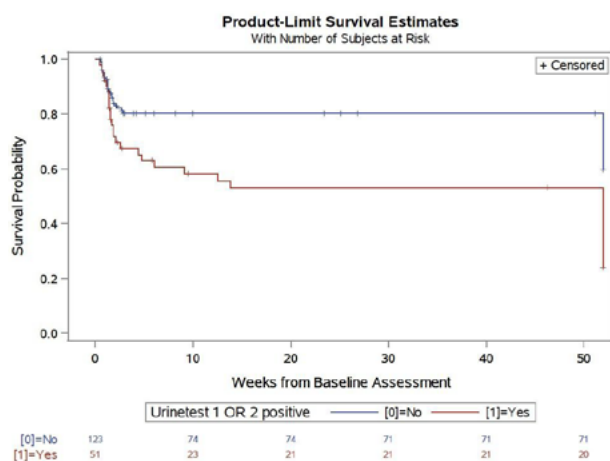
Figure Time to solid culture-positive TB or censorship

LAM-positive TB patients were more likely to present with signs of severe infection including tachycardia (odds ratio [OR] 2.32, 95% CI 1.12-4.78) and lower mean systolic blood pressure (OR 0.97, 95% CI 0.95-0.99). There was no significant association with LAM-positive HIV-associated TB and having any of four TB-related symptoms (OR 1.50, 95% CI 0.69-3.30).

Conclusions: Urine LAM was associated with faster time to culture positivity, more advanced immunosuppression, and clinical signs of severe infection suggesting LAM detects HIV-infected adults with a higher mycobacterial load. Using urine LAM for earlier diagnosis of these patients who have a greater risk of death may lead to improved patient outcomes and reduced transmission.

04. Recent developments in TB co-morbidities: updates from the front line

OA-123-12 Impact of untreated depression on tuberculosis treatment outcomes, disability, and quality of life in Ethiopia: a cohort study

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Background: High levels of depressive symptoms are observed in people with tuberculosis (TB), but the impact on tuberculosis treatment outcomes has not been well studied. Our objectives were to assess the impact of co-morbid depression on outcomes of tuberculosis (TB) treatment, health-related quality of life, and disability.

Methods: 648 adults commencing TB treatment at 14 primary care facilities in Ethiopia were recruited into a cohort study and assessed at baseline, two and six months. Probable depression was measured using the Patient Health Questionnaire (cut-off of 10 and above). TB outcomes (death, treatment default, failure, and success) were extracted from the routine TB register. Disability was measured using the World Health Organization Disability Assessment Scale. Quality of life (QOL) was assessed using a visual analogue scale. A Poisson working model with robust variance estimator was used in analysis of risk ratios for TB treatment outcomes. Multilevel mixed-effects generalized linear models were employed for modeling change in disability and QOL. Potential confounders identified a priori were included in the multivariable model.

Results: Untreated probable depression was independently associated with treatment default (adjusted risk ratio (ARR) 9.09; 95%CI= 6.72, 12.30), death (ARR= 2.99; 95%CI= 1.54, 5.78), disability (ß=0.83; 95%CI=

0.67, 0.99), and decreased QOL (ß=-0.07; 95%CI= -0.07, -0.06) at six months. Participants with baseline depression had lower QOL (mean 5.0 versus 6.0; p< 0.001) and higher disability (median 22.0 versus 14.0; p< 0.001) at six months.

Conclusions: Untreated depression in people with newly diagnosed TB has adverse consequences for TB treatment outcomes as well as for QOL and disability. General health workers need to be given greater support to provide depression care to people with TB.

OA-124-12 Glycemic control and prevalence of LTBI: population-based study using HbA1c, fasting plasma glucose and 2-h plasma glucose

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Background: Several high-quality cohort studies have demonstrated that diabetics are at increased risk for tuberculosis disease and some of these show that poor glycemic control may exacerbate this risk. Whether glycemic control modifies the relationship between diabetes and latent tuberculosis, as it does with tuberculosis disease, is unknown.

Methods: We analyzed data from the 2011-2012 National health and Nutrition Examination Survey from the United States. Diabetics had either a physician diagnosis, hemoglobin A_{1C} (HbA$_{1C}$)≥6.5%, fasting plasma glucose (FPG)≥126 mg/dL, or 2-hour plasma glucose (PG)≥200 mg/dL. Latent tuberculosis was diagnosed through tuberculin skin tests and glycemic control was assessed linearly and categorically using recommended targets from the American Diabetes Association.

Results: Among 4215 participants, the prevalence of latent tuberculosis was 4.1%, 5.5%, and 7.6% in nondiabetic, prediabetic, and diabetic participants (Ptrend=0.012). In a multivariate analysis, diabetes was associated with latent tuberculosis (adjusted odds ratio [AOR], 1.5, 95% CI, 1.0-2.2]). Diabetics that were undiagnosed (AOR, 2.2, [95% CI, 1.3-3.6] and 1.2 [95% CI, 0.7-2.0] in diagnosed diabetics versus nondiabetic reference), FPG>130 mg/dl (AOR, 2.6 [95% CI, 1.5-4.6] and 1.3 [95% CI, 0.8-3.6] in diabetics with FPG≤130 mg/dl versus nondiabetic reference), or not on insulin (AOR, 1.7 [95% CI, 1.2-2.6] and 0.8 [95% CI, 0.3-2.3] in diabetics on insulin versus nondiabetic reference) modified this relationship. In a linear dose-response analysis, FPG (AOR, 1.02 per 1-mg/dl increase, 95% CI, 1.01-1.03), PG (AOR, 1.02 per 1-mg/dl increase, 95% CI, 1.01-1.04), and HbA$_{1c}$ (AOR, 1.13 per 1% increase, 95% CI, 1.04-1.22) all predicted latent tuberculosis.

Conclusions: Our results suggests glycemic control may modify the relationship between latent tuberculosis and diabetes.If these results are confirmed in other studies,

latent tuberculosis screening in diabetic patients with poor glycemic control may provide an opportunity to effectively target a high-risk population for tuberculosis transmission and primary progressive disease.
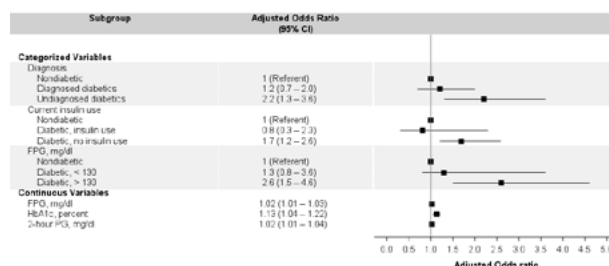
Figure Glycemic control and latent tuberculosis

OA-125-12 High rates of active hepatitis C amongst multidrug-resistant tuberculosis patients in Armenia

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Background: Hepatotoxicity is common during multidrug resistant tuberculosis (MDR-TB) treatment. Hepatitis C (HCV) is associated with increased toxicity during tuberculosis treatment however until recently treatment of hepatitis C was not possible in patients with active tuberculosis. New treatments for hepatitis C with direct acting antivirals may be given during tuberculosis treatment therefore it has become important to identify patients with active hepatitis C disease who may benefit from this treatment.

Methods: We tested for HCV amongst MDRTB patients in Armenia, prospectively amongst patients enrolled from January 2016 until June 2016 regardless of their treatment regimen and amongst patients enrolled from June 2016 until March 2017 who were eligible for or receiving delamanid or bedaquiline. In addition, testing was performed on MDR-TB patients who were still on treatment in 2016. If HCV antibody testing was positive, PCR testing, geno-typing and fibro-scan were performed.

Results: Of 208 patients screened, 62 (29.8%) were HCV antibody serology positive. Of them, 58 (93.5%) were tested with PCR and 40/58 (69.0%) were PCR positive. The predominant HCV genotypes were 3a in 19/40 (47.5%) and 1b in 14/40 (35.0%). In total 40/208 (19.2%) patients had active hepatitis. A significantly higher proportion of positive hepatitis C serology was found in an univariate analysis amongst males, patients aged over 35 years, previous prisoners, HIV co-infected and extensively drug resistant TB patients.

Conclusions: A high proportion of the MDR-TB patients in this cohort had active hepatitis C. Treatment for active hepatitis C should be considered in patients unable to tolerate MDRTB treatment due to hepatotoxicity. Testing for active hepatitis C should be systematically performed at baseline on all patients with MDRTB from regions with high prevalence of hepatitis C.

OA-126-12 Costs per accurate diagnosis of bi-directional screening in Indonesia and Romania: integrating tuberculosis and diabetes services

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Background: There is an emerging syndemic of tuberculosis (TB) and diabetes mellitus (DM), but screening protocols are not well established. We compared the mean costs per accurate diagnosis of various screening algorithms in Indonesia and Romania for detection of concurrent TB-DM.
Methods: In hospitals in Indonesia and Romania, four tests to detect pulmonary TB (PTB) were administered to people with diagnosed DM, with sputum culture considered the gold standard. Two risk scores, three point of care (POC) tests and two blood tests were used to assess people with newly diagnosed PTB for DM, compared to the gold standard of repeated laboratory glycated haemoglobin (HbA$_{1c}$) tests. The diagnostic accuracy (sensitivity and specificity) of each test was determined individually and for combined, stepped diagnostic algorithms. Micro-costing of each test was performed from a provider perspective.
Results: In Indonesia, the lowest cost per accurate PTB diagnosis was US$ 17.93 for an algorithm of TB symptom screen and smear microscopy. No PTB cases in individuals with confirmed DM were identified in Romania. For DM screening, the algorithm with the lowest cost per accurate diagnosis was age screen with POC random plasma glucose (RPG) at US$ 1.49 in Indonesia and US$ 5.64 in Romania.
Conclusions: The cost per accurate diagnosis is lower when screening people with PTB for DM than screening people with DM for TB. These results can be used to design DM screening interventions within National TB Programmes.

OA-127-12 Effectiveness of screening drug addicts for pulmonary tuberculosis in Afghanistan: a cross-sectional study

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Background and challenges to implementation: Afghanistan is home to an estimated three million drug addicts and 61,000 incident and 110,000 prevalent TB cases. There is little knowledge of the comorbidity between TB and drug addicts in the country. The purpose of this study was to estimate the proportion of pulmonary TB among drug addicts in Afghanistan.
Intervention or response: The National Tuberculosis Program, with support from the United States Agency for International Development funded Challenge TB project screened drug addicts in the four cities of Herat, Mazar-e-Sharif, Jalalabad and Kandahar. The study subjects included drug users admitted for treatment, those located in the community and villages and addicts attending harm reduction centers. The data collection tool was a standard questionnaire and sputum samples were diagnosed by GeneXpert technology and chest radiography readings by three independent readers.
Results and lessons learnt: Between July and October 2016 2,830 subjects (82% [2,320] male and 18% [510] female) were assessed for TB. Of those assessed, 40% (1,131) had respiratory symptoms, 29.7% (841) had a cough for more than two weeks, 22.3% (630) had a cough and sputum. Fifteen percent (410) were tested for Acid Fast Bacilli. Twenty five (16.4%) were diagnosed as bacteriologically confirmed (BC) TB, two of which as Rifampicin Resistant TB (0.5%, P-value <0.001, Odd Ratio 16, CI 95%) and four as clinically confirmed TB. Thus, case notification for BC and all forms is 883 and 1,024 among a population of 100,000 drug users. According to the results of this study, the yield of TB is five times higher than WHO estimates (P-value <0.001 and OR 5.3).

Characteristics	Study subjects, # (%)	Outpatients attendees	P-value (Odd ratio)
Sample size	2,830 (82% male, 18% female)	12,820,696	
Cough more than two weeks	837 (39%)	334,903 (2.6%)	<.001 (18)
Sputum smear examined	642 (22.7%)	319,930 (2.5%)	<.001 (11.5)
Diagnosed as Bacteriologically confirmed	25 (1%)	19,710 (0.1%)	<.001 (6)

Table Key findings of drug addicts assessment

Conclusions and key recommendations: The yield of TB among drug users is higher than the WHO estimated incidence for all forms of TB. Thus, we recommend a convergence between TB, harm reduction and addiction treatment centers and the integration of TB services with these programs.

OA-128-12 Use of metformin and risk of tuberculosis among incident diabetic patients: a population-based study

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Background: Metformin, a commonly used antidiabetic drug, was previously found to augment host immunity against tuberculosis (TB) and was considered as a promising candidate for host-directed therapy. There was limited evidence on the association between metformin use and TB occurrence at the population level.
Methods: We conducted a prospective study on two incident diabetes cohorts, one from the national health insurance research database and the other from a urban community-based health screening service. We used the initial prescription of anti-diabetic drug as the exposure variable. Sulfonylurea or metformin monotherapy users were included in the study. Comorbidities were ascertained at baseline. TB occurrence was ascertained from ICD-9 diagnosis and anti-TB drug prescription. Cox proportional hazards modelling was used to assess the association between drug usage and TB risk.
Results: The health insurance cohort contained 44,015 (73.4%) sulfonylurea-only and 15,991 (26.6%) metformin-only incident diabetic patients, and the health screening cohort included 4412 (40.3%) sulfonylurea-only and 6539 (59.7%) metformin-only patients. The overall TB incidence rate was 272 and 109 cases per 100,000 person-year in the health insurance (No. of TB cases: 449) and health screening (No. of TB cases: 17) cohort respectively. Using sulfonylurea-only patients as the reference, metformin usage was associated with a statistically significantly reduced hazard of TB in the health insurance cohort (adjusted hazards ratio (aHR): 0.51; 95% CI 0.39 - 0.67) but not in the health screening cohort (aHR: 0.89; 95% CI 0.33-2.33).

	TB Cases	Person-Years	Unadjusted Model		Multivariable-Adjusted Model	
			HR (95% CI)	p-Value	aHR (95% CI)	p-Value
Sex						
Female	95	79604	Ref		Ref	
Male	354	85227	3.50 (2.79 - 4.39)	<.0001	3.53 (2.82 - 4.44)	<.0001
Age			1.03 (1.03 - 1.04)	<.0001	1.03 (1.02 - 1.04)	<.0001
Treatment						
SU only	382	118812	Ref		Ref	
MET only	67	46019	0.46 (0.36 - 0.60)	<.0001	0.51 (0.39 - 0.67)	<.0001
CKD under hemodialysis						
No	447	164590	Ref		Ref	
Yes	2	240	3.04 (0.76 - 12.19)	0.1802	2.95 (0.73 - 11.84)	0.1279
COPD						
No	305	136369	Ref		Ref	
Yes	144	28462	2.3 (1.88 - 2.80)	<.0001	1.74 (1.41 - 2.15)	<.0001
Systemic steroids use						
No	407	156781	Ref		Ref	
Yes	42	8050	2.07 (1.50 - 2.84)	<.0001	1.41 (1.02 - 1.96)	0.0406
Cancer						
No	432	160745	Ref		Ref	
Yes	17	4086	1.57 (0.97 - 2.54)	0.2601	1.21 (0.74 - 1.97)	0.4406

SU = sulfonylurea; MET = metformin;
CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease

Table Cox Proportional Hazards Model on Health Insurance

Conclusions: Our study is the first population-based analysis on metformin use and risk of TB. The different results in the two cohorts might be due to confounding (i.e., metformin was more likely prescribed to those with higher socioeconomic status and lower risk for TB) in the heterogeneous health insurance cohort. Further analyses are needed to better understand the relation between metformin and TB risk.

OA-129-12 High burden of DM-TB co-morbidity in Cambodia: initiation of bi-directional DM-TB screening in three operational districts

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Background and challenges to implementation: Despite increased prevalence of diabetes Mellitus-Tuberculosis (DM-TB) co-morbidity in Cambodia, no guideline exists for managing the co-morbidity. Furthermore, knowledge of the co-morbidity among health providers and the general population is limited. Health and Social Development (HSD), a local NGO, implemented DM-TB bidirectional screening in three operational districts in Cambodia - Siem Reap, Sotnikum, and Pea Reang - from July 2014 to October 2016.
Intervention or response: HSD, with CENAT and PMD, worked to mutually integrate DM and TB screening and service activities in three operational districts. The intervention established a technical working group to develop national guidelines for DM-TB co-morbidity management, a training package and monitoring and data collection tools. Additionally, glucometers and glucose strips were provided at TB screening sites and DM clinics. Regular meetings and supervision led by TB and preventive medicine staff were conducted.
Results and lessons learnt: 2785 registered TB patients were tested for DM at health facilities during the project period. 253 patients (9.08%) were found to have pre-DM (FBS from 100 to125 mg/dL) and 267 (9.59%) were found to have DM (FBS ≥ 126 mg/dL). Of those with DM, 146 (54.68%) already knew their status and 121 (45.32%) were newly diagnosed with DM. At diabetes clinics, among 1582 DM patients who were screened for TB, 108 (6.83%) DM patients had TB. Of those with TB, 79 (73.15%) knew they had TB and were on treatment and 29 (26.85%) DM patients were newly diagnosed and referred to care and treatment. DM-TB bidirectional screening is feasible at public health facilities in Cambodia. The lack of diabetes services at the peripheral level, however, remains a challenge.
Conclusions and key recommendations: The prevalence of DM among TB patients and of TB among DM patients is high in comparison to the general population.

Routine DM and TB bidirectional screenings are strongly recommended along with further synchronization of services and scale-up.

05. Psychosocial support: impact on health seeking behaviour and treatment outcomes

OA-130-12 Behavioural activation counselling as part of a psychosocial support package for people receiving treatment for MDR-TB in Nepal: a feasibility study

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Background: Experience, and increasingly, evidence, shows that there are high rates of depression among people receiving treatment for multidrug resistant tuberculosis (MDR-TB). Psychosocial support in general, and treatments for depression in particular, form an important but neglected area of patient-centred care; a key pillar in the global End TB strategy. We assessed the feasibility and acceptability of a psychosocial support package, including screening and behavioural activation counselling, for people receiving treatment for MDR-TB in Nepal.

Methods: This feasibility study used a mixed quantitative and qualitative approach. We implemented the intervention package in two MDR-TB treatment centres and 8 sub-centres. We screened patients monthly for depression, anxiety (Hopkins Symptom Checklist) and social support (Multidimensional Scale of Perceived Social Support). Those who screened positive on either screening tool were referred for behavioural activation counselling. Patients were also given information in leaflets, through staff explanations using flipbooks and offered group interaction support.

Results: We recruited 135 patients, who were generally young and mostly male. All aspects of the intervention package were acceptable to patients, including the screening, group work and counselling. Patients particularly valued someone to talk to about their concerns and worries. The information materials were feasibly used within the existing NTP in Nepal. We were able to successfully train lay workers with no experience of psychological counselling to deliver screening and counselling. Screening, group support and counselling are feasible in the context of the NTP in Nepal, given some modest additional resourcing.

Conclusions: This psychosocial support package, which includes screening for depression and behavioural activation psychological counselling, shows promise as an intervention for people receiving treatment for MDR-TB in Nepal. The package is feasible to deliver in the existing NTP in Nepal, where psychosocial interventions are included in the current national strategy.

OA-131-12 Evaluating a nursing intervention to improve the quality of life of chronic MDR-TB patients hospitalized for a long time

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Background and challenges to implementation: The incidence of multidrug-resistant TB (MDR-TB) continues to rise in Tjumen region of Russia. In 2014, a palliative care ward was opened at Zavodoukovsk TB hospital at the Regional Tjumen TB Dispensary to treat chronic MDR-TB cases. MDR-TB patients are hospitalized for 12 to 24 months affecting their physical and mental health. The objective of this project was to evaluate the quality of life (QOL) of MDR-TB patients admitted to the hospital and to develop a set of interventions to improve the patients' QOL.

Intervention or response: Nurses collected baseline QOL data from 50 patients with chronic MDR-TB. Data were collected on age, sex, socioeconomic indicators, family situation, length of hospital stay and treatment duration. The patients were interviewed using the SF-36 survey instrument. The baseline physical component of the QOL was 40% for male and 42% for female patients; the baseline mental component was 42% and 51%, respectively. The attitude of the patients´ families towards them had an impact on all QOL components in MDR-TB patients. Sixty-two percent of patients stated the attitude of their family changed after TB diagnosis. To address this, the nurses developed a program to encourage patients' families to be more supportive to the patients.

Results and lessons learnt: After 6 months of therapy and the intervention, the QOL rate in male patients increased by 6% and in female patients by 7%. The mental health component increased by 12% in all the patients and 6 patients (22%) re-connected with their families. The emotional state rate increased by 11% due to psychological support from the patients´ families.

Conclusions and key recommendations: Nurses used these results to develop an additional program of care including invitations to family members to visit the patient in hospital, information on how to protect family members from contracting TB and providing patients with activities to spend their time.

OA-132-12 The impact of the Brazilian Family Health Strategy and the Conditional Cash Transfer on tuberculosis treatment outcomes in Rio de Janeiro: an individual-level analysis

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Background and challenges to implementation: In Rio de Janeiro, a city with a 66.8/100,000 TB incidence and a high inequity index (GINI coefficient= 0,6391), cure rates are low: 69.2%. DOT was insufficient to achieve the cure rate target recommended by WHO. We examined the effect of two large governmental programs - the Family Health Strategy (FHS) and the Conditional Cash Transfer (*Bolsa Família*) program - on tuberculosis treatment outcomes in Rio de Janeiro, Brazil.

Intervention or response: FHS teams consist of one physician, one nurse, one nurse aid and six to ten community healthcare agents (CHA), responsible for 1000 families living in a specific catchment area. CHA do regular home visits for DOT and active case finding. Coverage of the population has expanded in Rio from 3.5% in 2009 to 70% in 2016, mainly in poor neighborhoods. *Bolsa Família*, the largest conditional cash transfer programs in the world, has over 45 million beneficiaries. Both programs reduced child mortality and improved other health outcomes according to ecological studies. We linked FHS registries, the TB information system and *Bolsa Família* payrolls to analyze the synergistic impact of the programs on TB treatment outcomes.

Results and lessons learnt: The FHS increased the likelihood for successful outcomes by 14% (95% CI: 12%;17%) among 13,482 new tuberculosis cases, and by 34% (95% CI: 23%;45%) among 1,880 retreatment cases, while *Bolsa Família* did not influence outcomes. Poverty markers (less schooling, HIV-infection and alcohol abuse) reduced the likelihood for successful outcomes.

Conclusions and key recommendations: This is the first individual-based study to show a relevant protection of poor urban communities regarding patient-important TB outcomes by the Brazilian FHS. No synergistic effect from cash transfer could be shown with the current study design, possibly because receiving the cash transfers was an additional marker of poverty. These findings support primary care strengthening strategies recommended by WHO. The effect of cash transfer needs further investigation.

OA-133-12 Impact of hospitalization subsidy incentives on tuberculosis treatment outcomes: experience of Wuhan City, China

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Background and challenges to implementation: Financial burden plays an important role in the poor adherence to TB treatment. This study was aimed to discuss the effect of a hospitalization reimbursement policy on patients' medical courses and outcomes in China.

Intervention or response: Since 2012, Wuhan City government implemented hospital subsidy policy for local-resident with TB. Compensation was provided to patients to cover the costs of the hospitalization and first line anti-TB drugs, and partial examinations cost in the follow up if the patients completed treatment. Patient clinical data were extracted from their medical record for analysis.

Results and lessons learnt: 114 and 110 patients with smear-positive pulmonary TB were enrolled in the intervention group and control group respectively. TB treatment completion rate was significantly higher in the intervention group than that of the control group (89.5% vs. 77.3%, P=0.014). Patients in the intervention group had a lower rate of missing appointments than the control group (13.2% vs 21.8%, P=0.005). The time of the first missed-appointment of the patient in the intervention group was later than the control group (155±42 vs 131±57 days, P<0.01). Most patients in both groups reported no missed medication (92.1% vs 92.8%). But the Morisky score of the intervention group was lower than the control group (0.763±1.016 vs 1.952±1.564, P<0.01).

Conclusions and key recommendations: Financial incentives was effective in improving treatment completion and reducing default rates among urban smear-positive TB patients in Wuhan. The results suggest that financial incentives can be considered as a strategy to improve current treatment programs and medication adherence.

OA-134-12 Treatment adherence among persons receiving concurrent MDR-TB and HIV treatment in KwaZulu-Natal, South Africa

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Background: Concurrent multidrug-resistant tuberculosis (MDR-TB) and human immunodeficiency virus (HIV) treatment entails high pill burden, frequent adverse events and long therapy duration. KwaZulu-Natal province, South Africa, has approximately 5,000 MDR-TB cases annually (80% HIV-infected). We evaluated adherence to MDR-TB and antiretroviral therapy (ART) and its association with treatment outcomes.

Methods: We prospectively followed MDR-TB patients for 24 months. Adherence was assessed monthly using 3-day recall, 30-day recall and visual analog scale (VAS). MDR-TB treatment success was defined as cure or completion; failure, death or loss-to-follow-up were unsuccessful outcomes. We determined the proportion of fully adherent participants by each adherence measure, stratified by HIV status. We assessed the association with MDR-TB treatment success and 60-day culture conversion using unadjusted risk ratios. Among HIV-positive participants, we examined differential adherence to MDR-TB vs. HIV treatment using McNemar's test.

Results: Among 200 MDR-TB patients, 63% were female, median age was 33 years, and 144 (72%) were HIV-positive, of whom 81% were receiving ART at baseline. Adherence to MDR-TB and HIV treatment was high across all measures (82-96% fully adherent) and did not differ by HIV status (Figure). Among HIV-positive participants, ART adherence was significantly higher than MDR-TB treatment adherence by all measures (Figure). Using a composite measure of 3-day recall and VAS, MDR-TB treatment success and 60-day culture conversion were higher among participants who were fully adherent, but this difference was not statistically significant (RR: 1.11, 95%CI: 0.87-1.41; RR: 1.29, 95% CI: 0.70-2.43).

Conclusions: Self-reported MDR-TB treatment adherence was high and did not differ by HIV status, suggesting co-treated persons can achieve high adherence. Reported adherence to ART was higher than to MDR-TB treatment by all study measures. More objective adherence measures and a better understanding of preferential ART adherence are needed to inform interventions that improve outcomes for MDR-TB and HIV co-infected persons.

Figure. Proportion of participants fully adherent[a] to MDR-TB and HIV medication by three adherence measures in the SHOUT MDR-TB cohort

	Medication Adherence Measure			
	3-day Recall[b], n (%)	30-day Questionnaire[c], n (%)	Visual Analog Scale[d], n (%)	Composite Adherence Measure[e], n (%)
Combined Cohort				
MDR-TB Tx (n = 200)	170 (85)	188 (94)	169 (85)	164 (82)
HIV+				
MDR-TB Tx (n = 144)	121 (84)	134 (93)	122 (85)	118 (82)
ART (n=139)	128 (92)	136 (98)	126 (91)	124 (89)
P-value[f]	0.003	0.031	0.039	0.013
HIV-				
MDR-TB Tx (n = 56)	49 (88)	54 (96)	47 (84)	46 (82)
P-value[g]	0.35	0.30	0.65	0.97

MDR-TB: Multidrug-resistant tuberculosis; HIV: Human immunodeficiency virus; Tx: Treatment; ART: Antiretroviral Therapy
[a]Full adherence defined as no reported missed medication at any point in the study
[b]Percent that did not report missing any pills in the last 3 days at any point in the study
[c]Percent that did not report missing any pills in the last 30 days at any point in the study
[d]Based on visual analog scale rating (from 0-100%) of percent of medication taken since last study visit
[e]Composite measure indicates full adherence by both the 3-day recall measure and the visual analog scale throughout the study
[f]Based on McNemar's exact test comparing adherence to MDR-TB treatment and ART among co-infected participants
[g]Based on Fisher's exact test for dichotomous variables comparing MDR-TB treatment adherence among HIV+ and HIV- participants

Figure Treatment Adherence

OA-135-12 Using mathematical disease transmission models and population-level epidemiological data to analyse care-seeking behaviour in South Africa

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Background: Achieving global TB targets for disease incidence and mortality reductions necessitates efficiently targeting interventions to interrupt transmission. Quantifying the contributions to transmission that occur over the course of active disease including diagnosis and treatment in the healthcare system allows for the development of optimal intervention strategies.

Methods: We calibrated an individual-based dynamic, mathematical model of TB transmission and disease progression to country-level mortality and case-notification data for South Africa across a range of care-seeking delays. The model allows for the possibility that a proportion of individuals do not access diagnostics or care in the healthcare system. The model accounts for population demographics, HIV prevalence and coverage of antiretroviral therapy, sensitivity of available diagnostics, and reported treatment success and cure rates. From the calibrated model we estimated care-seeking delays and uncertainties in these delays. Subsequently we also quantified the proportion of transmission arising from individuals who access the TB healthcare services versus those who do not.

Results: Predicted disease prevalence depends strongly on the proportion of individuals who do not access TB healthcare services. Calibrating to population-level TB disease incidence and mortality, in the absence of other types of data, leads to a large degree of uncertainty in estimated delays.

Conclusions: To predict the impact of interventions at the population-level it is necessary to estimate the degree to which TB goes untreated in the population in

addition to care-seeking and diagnostic delays for individuals who are eventually treated in the healthcare system. Future prevalence surveys will be useful in reducing uncertainty in model-based estimates of the relative number of individuals who do not access TB services.

OA-136-12 Self-verification and behavioral interventions via mobile phones drastically improves tuberculosis treatment success in a randomized control trial

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Background: Successful tuberculosis (TB) treatment is critical for reducing transmission and lowering treatment costs, but international targets are often missed. Mobile health interventions attempted thus far employ a combination of SMS reminders and medication monitors; these have met with mixed success, cost-effectiveness and reliability. We developed a cost-effective mobile health intervention, based on proven techniques from the behavioral sciences, and tested whether it improved treatment outcomes.

Methods: In this randomized control trial between January 4th and December 31st, 2016, in Nairobi, Kenya, 1190 eligible TB patients received the standard of care provided by the 17 partner clinics. Individuals were randomly assigned to also participate in our mobile health intervention for the duration of treatment (intervention group), or receive standard care only (control group). The intervention consisted of a daily request for self-verification of medication adherence, access to a supporter via a chat client, and information about TB. The primary outcome was the proportion of individuals who failed to successfully complete the treatment.

Results: Outcomes for 609 intervention group patients were compared with the outcomes of 581 control group patients. In the intervention group, 4.33% (24 of 554) of individuals failed to successfully complete treatment, compared with 12.86% (67 of 521) of individuals in the control group (p < .001).

Conclusions: The mobile health intervention led to a substantial reduction in unsuccessful treatment, to within international targets. The intervention can be considered as part of TB treatment, and especially as an alternative to DOT or SMS reminders and medication monitors in regions where DOT is impractical. This study was conducted in a subset of clinics in Nairobi; however, we believe that our intervention is generalizable. We deployed the intervention using a mobile technology that works on 'feature' phones, which have high penetration in most regions where TB prevalence is high.

OA-137-12 Wirelessly observed therapy is accurate and confirms more TB medication doses than directly observed therapy

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Background: Directly Observed Therapy (DOT) is universally recommended to ensure *Mycobacterium Tuberculosis* Complex (MTB) treatment adherence. However, DOT is resource intensive, intrusive and expensive with limited implementation in resource-limited settings contributing to increased rates of resistant MTB. Wirelessly Observed Therapy (WOT), an FDA-cleared device, consisting of an edible ingestion sensor (IS), external wearable patch and paired mobile device, can detect and record ingestion events, which are uploaded to a secure Internet server, where healthcare workers can confirm ingestions remotely. We combined fixed-dose combination Isoniazid and Rifampin (Rifamate™, Sanofi Aventis) with IS to generate 'digitized' IS-Rifamate; and evaluated the accuracy of WOT in comparison to DOT in MTB patients during continuation therapy.

Methods: The IS was combined with Rifamate via co-encapsulation within certified gelatin capsules. Seventy-five subjects were recruited into a randomized controlled trial comparing WOT to DOT. During the first 2 weeks of this trial, all subjects received DOT 5x a week in conjunction with IS-Rifamate. All subjects were prescribed IS-Rifamate daily. The positive detection accuracy (PDA), defined as the percentage of IS-Rifamate ingestions detected by WOT administered under direct observation, was calculated. The total number of recorded doses confirmed by DOT versus WOT over this period was calculated.

Results: The subjects' mean age was 42 years, 56% male, 59% reported income below $2000/month, 62% had High School or less education. The total number of DOT doses confirmed over the period was 1288. The positive detection accuracy of WOT 98.4% (CI 97.5-99%). The total number of confirmed WOT doses in comparison to DOT doses was 1983/1288, indicating that WOT confirmed 54% more doses than DOT.

Conclusions: WOT using IS-Rifamate had a high detection accuracy and ingestions could be detected and confirmed 7 days per week. IS-Rifamate provides a model for the digitization of oral MTB medications.

06. TB in vulnerable populations

OA-138-12 Evaluation of innovative active case finding strategies for TB case detection in remote communities in Cambodia and India

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Background: The Stop TB Partnership's TB REACH initiative funds active case finding (ACF) initiatives to find people with TB who are missed by health services. Although many TB REACH projects have documented increases in population-level TB treatment, the cost-effectiveness of these initiatives remains uncertain.

Methods: We used a combined decision analysis/ Markov model to evaluate the cost-effectiveness of two TB REACH projects: 1) community TB screening followed by mobile diagnosis with Xpert MTB/RIF and chest X-ray during ACF screening days (ACFD) for elderly individuals in Cambodia and 2) house-to-house screening (HTH) by community health workers in remote rural communities in India. We constructed a hypothetical cohort of 100,000 individuals with TB prevalence representative of the general population in each country and evaluated outcomes over five years. Our primary outcomes included incremental cost (2015 USD), incremental diagnoses, and the incremental cost per disability-adjusted life year (DALY) averted, comparing ACF to passive case finding (PCF).

Results: Over five years, 87% of all TB cases (935 and 254 true prevalent TB cases in Cambodia and India per 100,000) were successfully diagnosed under each ACF strategy. In Cambodia, ACFD generated 180 more true TB diagnoses than PCF and averted 95 deaths; in India, HTH generated 79 incremental diagnoses and averted 33 deaths. The estimated five-year incremental cost-effectiveness was $973 per DALY averted for ACFD in Cambodia whereas for HTH in India, the cost per DALY averted was lower at $418, reflecting the younger eligible population.

Conclusions: ACFD in Cambodia and HTH in India not only generate substantial increases in TB case detection but are also cost-effective according to classical metrics. Where sufficient resources exist, active TB case-finding is likely to represent good value for money.

OA-139-12 Pulmonary tuberculosis, a public health problem amongst Saharia, a vulnerable tribal group in Madhya Pradesh, Central India

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Background: 'Saharia' is one of the Particularly Vulnerable Tribal Groups (PVTGs) in the central Indian state of Madhya Pradesh. The study was undertaken to estimate the prevalence of pulmonary tuberculosis (PTB) disease amongst this tribal community.

Methods: A community based cross-sectional TB prevalence survey was undertaken in Saharia dominated Pohri Block of Shivpuri district in Chambal Division of Madhya Pradesh. A random sample of villages predominated by tribal populations was selected from the list of villages arranged in descending order of the tribal population to cover the estimated sample size of 9225 individuals in the area. All eligible individuals were questioned for chest symptoms relating to TB. Two sputum samples were collected from eligible individuals, transported to the laboratory, and were examined by ZN smear microscopy and solid media culture methods.

Results: Of the 10,300 individuals eligible for screening, 9756 (94.7%) individuals were screened for symptoms. Of these, 1,463 (15.0%) individuals were found to be symptomatic. Sputum was collected from 1430 (97.7%) symptomatic individuals who were eligible for sputum collection. Overall prevalence of PTB was found to be 3003 per 100,000. The prevalence of TB was significantly higher amongst males (4832 /100,000) as compared to females (1246/100,000) [$p < 0.001$]. The prevalence increased with age being 1227/100,000 in 15-24 year age group to 4672 in 55+ year age group.

Conclusions: The study results indicate that pulmonary tuberculosis is a major public health problem amongst Saharia PVTG of Shivpuri district in the central Indian state of Madhya Pradesh. In view of the alarmingly high PTB disease burden amongst this tribal group, there is an urgent need to improve and further intensify TB control measures in this area.

OA-140-12 Tuberculosis among foreign-born persons within the first year after entry to the United States, 2008-2015

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Background: Tuberculosis (TB) incidence among foreign-born persons living in the United States (U.S.) remains elevated, particularly in the first few years after entry. We examined reported TB among foreign-born persons in the first year after entry to the U.S.
Methods: We used data from the U.S. National Tuberculosis Surveillance System and the American Community Survey to examine TB cases and TB incidence among foreign-born persons in the first three months and first year after entry to the U.S. during 2008-2015, stratified by age.
Results: Among 52,906 TB cases diagnosed among foreign-born persons during 2008-2015, the time between date of entry to the U.S. and date of TB diagnosis were estimated for 49,843 (94%) cases. Of these cases, 8,548 (17%) were diagnosed in the first year after entry, of which 4,686 (55%) were diagnosed within the first three months. Among 1,048 (2%) TB cases diagnosed among foreign-born children from 2008-2015, 631 (60%) were diagnosed in the first year. Of these cases, 68% (168/248) aged 0-4 years and 67% (255/383) aged 5-14 years were diagnosed in the first three months. TB incidence was six times greater among foreign-born persons within the first year of entry to the U.S. compared to subsequent years (76 and 12 per 100,000 persons, respectively). TB incidence in children aged 5-14 years was 17 times greater during the first year compared to subsequent years (34 versus 2 per 100,000 persons).
Conclusions: The majority of TB cases diagnosed among newly arriving foreign-born persons within the first year after entry to the U.S. occurred within the first three months after entry. Diagnosis following entry to the U.S. among persons from high TB prevalence countries might reflect underlying TB infection and progression risks, domestic follow-up of overseas TB screening, or increased access to medical care.

OA-141-12 Tuberculosis in Syrian immigrants in Turkey

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Background: Turkey is the country with the largest number of Syrian immigrants due to the war in that country, with a figure of around 3 million.In this study, tuberculosis cases detected among Syrian migrants between 2011-2015 were evaluated in terms of clinical and epidemiological aspects.
Methods: The study was carried out with the retrospective evaluation of records of the Tuberculosis Unit at the Public Health Institution of Turkey.
Results: For each year, the total number of tuberculosis patients in Turkey, patients born in Turkey, in any foreign country and in Syria are shown in Table 1. While the proportion of immigrant TB cases among all TBpatients was 1.3% in 2011, it increased to 6.8% in 2015. The number of Syrian immigrant patients with tuberculosis increased from 0 in 2011 to 489 in 2015. Syrian patients accounted for 3.8% of all TB patients and 56.1% of foreign-born patients in 2015.According to the data of the Turkish Immigration Administration, the incidence of TB in the Syrian-born population in Turkey is 19,5 per one hundred thousand. This figure is similar to the incidence of tuberculosis in Syria indicated in the 2013 Global Tuberculosis Report. In 2015, the ratio of Multi Drug Resistant TB(MDR-TB) was found as 3.8% in Turkey-born, 4.3% in Syrian-born and 14.7% in non-Syrian immigrant patients.Treatment success in patients who started treatment in 2014 was 85% in Turkey-born patients, 74.3% in all migrants, and 75.5% in Syrian tuberculosis patients.

Years	2011	2012	2013	2014	2015
Total TB n,%	15.679	14.691	13.409	13.378	12.772
Turkey-born patients n,(%)	15.477 (98,7)	14.430 (98,2)	12.918 (96,3)	12.569 (94,0)	11.900 (93,2)
Foreign-born patients n,(%)	202 (1,3)	261 (1,8)	491 (%3,7)	809 (6,0)	872 (6,8)
Syria-born patients n,(%)	0 (0)	23 (0,15)	177 (1,3)	483 (3,2)	489 (3,8)

Table Distribution of Tuberculosis Cases in Turkey

Conclusions: Syrian migrants are the main reason for the increase in the share of foreign-born patients among all TB patients in Turkey. Unlike immigrants from other countries, MDR-TB rates are not high in Syrian patients.The low success rate of treatment in immigrant cases,including Syrians,points to the need to improve tuberculosis control policies concerning immigrants in Turkey.

OA-142-12 Active TB case finding among marginalised and vulnerable populations of India: results of targeted approach

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Background and challenges to implementation: Universal access to tuberculosis (TB) services is critical for timely diagnosis and treatment. However, low awareness about TB, poor accessibility and affordability of health services result in delayed diagnosis, with resultant morbidity and mortality. We report the results of a project to enhance access to TB services through active case finding among marginalised and vulnerable areas.

Intervention or response: Project Axshya, supported by the Global Fund, implemented by The Union, is a unique initiative working towards improving access to quality TB care through partnership between government and the civil society especially for women and children, marginalized, vulnerable and TB-HIV co-infected populations. The project works through a network of nearly 1200 community-based organisations and 20,000 volunteers in 285 districts of 19 states across India. Community volunteers conduct house-to-house visits to create awareness about TB and to identify presumptive TB, who are then linked with diagnostic facilities through referral or sputum collection and transportation (SCT).

Results and lessons learnt: From October 2015 to December 2016, 22 million vulnerable and marginalised people from 5.6 million households were visited. Of 308,014 presumptive TB patients identified, 155,105 (50.6%) were tested among which SCT was done for 133,772 (86%). Of tested, 12,109 (8%) patients were diagnosed and 11507 (95%) were initiated on DOTS treatment. Of tested, the positivity rate is highest among PLHIV (12%) and 8 % among slum, schedule caste, tribal population. Of diagnosed, 44%, 26%, 22% and 4% cases were identified among schedule caste, slum, tribal and unorganized labour. (table 1).

Indicator	Slum	Scheduled Caste	Tribal	Unorganised Labour	PLHIV	contacts of TB patients	Diabetic	General (non-KAP)	Total
No. of TB symptomatics examined	42830	67666	31699	7001	463	3096	1139	1211	15105
No. of TB cases diagnosed	3397	5242	2615	439	57	200	77	82	12109
No. of TB cases put on treatment	3036	5082	2552	425	57	196	77	82	11507
Positivity Rate	8%	8%	8%	6%	12%	6%	7%	7%	8%

Table ACF details by Key affected population

Conclusions and key recommendations: Active case-finding implemented through community-based organisations successfully enhances access to TB care among vulnerable and marginalised populations. This model can be replicated in other high TB burden countries. Interventions for improving the access to TB diagnostic and treatment services among specific population should be further researched.

OA-143-12 Systematic screening for TB among high-risk populations in India: whom to prioritize?

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Background and challenges to implementation: Systematic screening TB case among high risk population can complement the passive case finding strategy for early identification of TB patients. It is useful if properly targeted to relevant risk group. This study presents the lessons learnt from first round of active TB case finding campaign carried out in India.

Intervention or response: A Special Campaign of Active TB Screening among high risk group was conducted in 50 identified districts during 16th - 30th Jan, 2017 in India. The Districts have been selected based on burden of TB, case finding efforts, HIV-TB and DR-TB in respective districts. Clinically, socially and geographically vulnerable groups of people were mapped. Health staff visited these high risk persons, screens symptomatically and identified presumptive TB patients were tested with smear microscopy. We analysed data on diagnosis of TB among different groups of people mapped and screened.

Results and lessons learnt: During the fortnight effort, 4.6 million persons are screened and 2,699 TB patients were diagnosed. During the campaign, the districts had identified difficult to reach village and urban slum as the most mapped population. Overall, 1724 person needed to screen (NNS) to detect one case of TB. The NNS was 1118 in rural area, 1133 in tribal area and 2525 in urban area. Residential institutes (Homes for destitute, Orphanages, Night Shelters, Old age homes and Prison Inmates) had lowest number needed to screen (489), followed by villages/hamlets which are difficult to reach (898).

Conclusions and key recommendations: Systematic screening of TB patients is a dynamic activity. Identifying and targeting right people will help to identify more TB patient and less suffering. The case finding in such effort can also be improved, if more sensitive diagnostic tools are used.

OA-144-12 Successful integrated biomedical and social support for vulnerable people affected by tuberculosis in Nicaragua

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Background: Nicaragua is a middle-income country with moderate Tuberculosis (TB) burden with an estimated incidence of 51/100.000 population. Poverty in rural and urban areas increase the risk of contracting TB and unfavourable treatment outcomes. The National Tuberculosis Program (NTP) and Damien Foundation (Belgian Non-Governmental Organization) implemented an integrated biomedical social support in vulnerable population to enhance favourable treatment outcomes and promote social reinsertion.

Methods: From January 2014 to December 2016 this cohort study included people affected by TB with the following criteria: High TB burden regions (seven of 17), poverty defined as purchasing power parity (PPP) of less than 1.90 $ (United States Dollar)/day, comorbidity (HIV), extreme age (patients under five and/or ≥ 60 years old), poor ventilated housing, disability with dependency, multidrug-resistant TB (MDR) and availability of funds. A team including a medical doctor or nurse and social-worker visited patients at home. Selected patients benefited from nutritional supplements and/or housing improvement and/or income generating activity (IGA) support.

Results: 1496(46%) from 3224 people affected by TB were included. 1476(99%) had drug-susceptible (DS)-TB, 98(7%) were children, 20(1%) were MDR and 66(5%) were HIV-coinfected. All benefited from nutritional support, 68(2%) housing improvement and 90(3%) IGA. 73% of IGA were successful (still running) after one year of follow-up. Success rate in DS-TB patients were 91% compared to 86% in not supported patients *P=< 0.001*).

Conclusions: An integrated biomedical-social support to poor people affected by TB was effective achieving 91% of success rate. Moreover, IGA were highly successful after one year of implementation enhancing social reinsertion and economical independency. This experience could be extended to other regions of Nicaragua to contribute to the sustainable development goals 1 and 3 that aim ending poverty and infectious diseases.

SHORT ORAL ABSTRACT SESSIONS

01. At the front line of resistance

SOA-300-12 Bedaquiline and clofazimine resistance in MDR- and XDR-TB patients from Armenia

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Background: Mutations in atpE and Rv0678 genes correlate with phenotypic resistance to bedaquiline (BDQ) and for Rv0678 also to clofazimine (CFZ). However, to which extent mutations impact the minimal inhibitory concentrations (MIC) for BDQ and CFZ, and the level of cross-resistance has not been fully elucidated. Our objective is to describe BDQ and CFZ resistance at baseline and amplification during treatment, correlation between atpE and Rv0678 mutations and MIC values.

Methods: Isolates from XDR or pre-XDR TB patients from Armenia starting treatment with BDQ in individualised MDRTB regimen, were routinely tested in Armenia NTCC NRL. At ITM isolates were sequenced for atpE and Rv0678, then BDQ and CFZ MICs were determined on 7H11, including critical concentrations (0.25 μg/ml and 1.0 μg/ml respectively).

Results: Of the 25 patients included, 12 had multiple isolates available. All 12 baseline isolates were wild-type (WT) for atpE and Rv0678. At follow-up, 4 isolates remained WT, all with no change in BDQ-MIC and one with 1-fold increase (1>2 μg/ml) in CFZ-MIC. The remaining 8 paired-isolates developed non-silent mutations in Rv0678 but none in atpE: all 8 cases had up to 4-fold CFZ-MIC increases all above 1.0 μg/ml (one already 1.0 μg/ml at baseline). Of these, 5 cases also showed 2 to 3-fold BDQ-MIC increases, while remaining under or equal to 0.25μg/ml and 3 cases reaching 0.5μg/ml. (Table 1).None of the cases developing mutations at follow-up were cured or completed treatment. In all 13 patients with only baseline isolates no mutations were observed, and no high MIC (available only in 8/13 isolates); 8/13 patients were cured and 1/13 completed treatment.

Isolate n	MIC baseline		MIC follow-up*		Sequencing of follow-up isolates		Tx outcome
	CFZ	BDQ	CFZ	BDQ	atpE	Rv0678	
1	0,5	0,125	0,5	0,125	WT	WT	completed
2	0,5	0,06	0,5	0,06	WT	WT	defaulter
3	0,5	0,06	0,5	0,06	WT	WT	cured
4	1	0,06	2	0,06	WT	WT	cured
5	0,25	0,03	>2	0,25	WT	Gly25Ser(GGC>AGC)	died
6	0,5	0,03	>2	0,125	WT	Arg89Leu(CGG>CTG)	failure
7	0,5	0,06	2	0,25	WT	Tyr157Cys(TAC>TGC)	defaulter
8	0,5	0,03	>2	0,25	WT	Arg89Leu(CGG>CTG);	died
9	0,5	0,125	2	0,25	WT	ins(G)#138-139	defaulter
10	0,5	0,06	>2	0,5	WT	Asp47Asn(GAT>AAT);	failure
11	1	0,06	>2	0,5	WT	Leu154Pro(CTG>CCG);	died
12	2	0,25	>2	0,5	WT	Phe100Tyr(TTC>TAC)	defaulter

*Last isolate available

Table 1 Results for BDQ and CFZ from paired isolates

Conclusions: Non-silent mutations in Rv0678 increased CFZ-MICs above the critical concentration in 7H11, and for a minor extent for BDQ. In our experience, isolates with these mutations seem more related to unfavorable outcomes compared to WT strains.

SOA-301-12 Frequency of mutation Arg463Leu of the katG gene in historical multidrug-resistant tuberculosis in South Africa

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Background: Tuberculosis is a major public health problem. In 2015 the TB death rate was 1.5 million cases compared to the HIV death rates of 1.2 million worldwide. Mutation Arg463Leu is not targeted in our current laboratory diagnostic commercial assay for MDR-TB. Only codon 315 mutation and inhA mutations are on the assay. Mutations in codon 463 have been shown to be responsible for 20 to 40% of the INH phenotypic low level resistance. The frequency patterns of mutations that lead to Isoniazid (INH) resistance vary within the individual genes and geographically areas. The aim of this study was to assess the frequency of mutation Arg463Leu of the katG gene in MDR-TB from the Gauteng and Western Cape provinces of South Africa.

Methods: Next generation sequencing, the Illumina Miseq was performed in this study on 100 phenotypic MDR-TB samples. Spoligotyping was performed to assess the association of mutation Arg463Leu with MTB lineages.

Results: In this study mutation Arg463Leu was responsible for INH resistance in 14% (14/100) of our MDR-TB cultures in the absence of codon 315 mutation. The lin-

eage type of thirteen of the fourteen isolates with R463L mutations was Beijing and one was X3.

Conclusions: The results from this study could mean that we are currently missing about 14% of INH resistance when diagnosing MDR-TB patients. Discriminatory power will be achieved if this target is considered for inclusion in new rapid molecular tests for improved molecular detection of MDR-TB. Mutation Arg463Leu was more associated with the virulent Beijing strains in this study. This was the first study in South Africa to investigate the association of katG codon 463 mutations with INH phenotypic resistance in MDRTB strains from Western Cape and Gauteng Provinces.

SOA-302-12 High degree of fluoroquinolone resistance among pulmonary tuberculosis patients at a tertiary care center in North India

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Background: The fluroquinolones (FQs) group of antibiotics are the backbone drugs for the management of drug-resistance TB. In day to day clinical practice, the routine drug susceptibility testing (DST) for FQs is not performed and the patients are empirically treated. A limited information regarding FQs resistance among pulmonary TB cases exists. Thus the study was conducted to estimate the FQs resistance among drug sensitive and drug resistance pulmonary TB cases from Delhi State.

Methods: One thousand six hundred nineteen sputum acid-fast bacilli smear positive specimens were subjected to DST for first-line and second-line drugs. In addition, FQs DST was also performed using automated MGIT-960 liquid culture techniques, during Sept, 2013- Sept, 2016 at Intermediate Reference Laboratory (IRL), AIIMS.

Results: *Mtb* was isolated in 1499 specimens. 1099 culture specimens were sensitive to FLDs, 249 grew as MDR-TB isolates and remaining 151 isolates reveled as any drug resistance to FLDs. While FQs mono-resistance among first-line drug sensitive strains was observed in 3.1% (35/1099), and 27.3% (68/249) had additional FQs resistance among MDR-TB isolates.

Conclusions: FQs mono-resistance among drug sensitive and MDR-TB isolates is alarmingly high in Delhi state. Based on these findings, DST for FQs should be routinely performed to avoid further amplification of drug resistance.

SOA-303-12 Performance of a rapid DST system for *Mycobacterium tuberculosis*, QMAC DST, integrated with MGIT960 culture

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Background: The QMAC DST utilizes image technology and tracking single growth of *Mycobacterium tuberculosis* (MTB). It can complete DST for 11 kinds of anti-tuberculosis drugs within 7days. Previously, we have developed the QMAC DST system to use cultured colonies from solid media that requires longer culture time of 4 weeks compared to 2 weeks of liquid culture system. In this study, we developed optimized test algorithm for integration with the MGIT 960 to reduce overall turnaround time of DST and aimed to evaluate the performance of QMAC DST integrated MGIT 960.

Methods: Seventeen clinical sputum and forty spiked liquid cultures were used for evaluation of QMAC DST performance. Liquid cultured MTB suspensions were dispersed and were mixed with 0.5% agarose. MTB-agarose mixture were loaded into each well of chips where every anti-tuberculosis drug is lyophilized at critical concentrations. Enriched 7H9 broth is added to each well. MTB growth are caputed with microscope every other day for imaging analysis.

Results: Previously, there were 96.2% overall agreement rates between the QMAC DST using cultured colonies solid media between using conventional method. In this study, the QMAC DST integrated MGIT 960 showed overally 93.7% agreement rates (100% for INH, 92.9% for RIF, 83.9% for SM, 94.6% for EMB, 98.2% for AMK, 83.9% for CPM, 98.2% for KM, 96.4% for LEV, 96.4% for MOX, 89.3% for OFX, and 96.4% for PAS, respectively) compared with the DST results of the conventional method.

Conclusions: The QMAC DST showed successful integration with MGIT 960 as demonstrating highly agreement results compared to the conventional method. It allows reducing overall turnaround time from liquid culture to QMAC DST within 3 weeks compared to 8 weeks of conventional solid culture and conventional DST methods. Further studies are on going to yield maximized diagnostic accuracy compared to standard DST methods and molecular characteristics.

SOA-304-12 Can Geno Type MTBDR*plus* v.2.0: be a rapid diagnostics tool in smear-negative pulmonary tuberculosis?

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Background: In 2008, World Health Organization (WHO) certified and endorsed line probe assay (LPA) as a molecular method for the rapid diagnosis of TB and simultaneous detection of rifampicin (RMP) and isoniazid (INH) resistance. The previous version of LPA i.e., Genotype MTBDRplus VER 1.0, was evaluated only in high grade smear-positive specimens and for detection of resistance in culture isolates. This study was performed to evaluate the performance of Genotype MTBDRplus VER 2.0 in the diagnosis of *Mycobacterium tuberculosis* (MTB) in sputum smear negative TB cases.

Methods: A total of 572 Ziehl-Neelsen sputum smear-negative samples were selected and subjected to line probe assay (Genotype MTBDRplus VER 2.0), and culture in mycobacterial growth indicator tube (MGIT960). Immunochromatographic test was used to confirm MTB complex (MTBC) in culture positive samples and phenotypic drug susceptibility testing was done using MGIT-960. The composite reference standard (CRS) used in the study includes symptoms, radiological evidence and follow up of two months. All works were performed at Intermediate Reference Laboratory, Department of Medicine, All India Institute of Medical Sciences, New Delhi, India.

Results: LPA was able to diagnose MTBC in 38.2% of specimens. Sensitivity and specificity of the assay were 64.98% and 65% respectively, considering culture in MGIT-960 as gold standard. On comparing with CRS, the assay showed 71.48% sensitivity and 100% specificity in the diagnosis of tuberculosis. The sensitivity and specificity for detecting of resistance to rifampicin (RMP) was 100% and 99.24% respectively and for resistance to isoniazid (INH) were 97.62% and 98.55% respectively.

Conclusions: Genotype MTBDRplus VER 2.0 is a rapid and precise diagnostic tool for detection of MTB in sputum smear-negative samples along with resistant pattern in RMP and INH. The CRS and LPA version 2.0 together proven to be highly valuable in detecting sputum smear-negative cases, which are otherwise missed by ZN smear staining.

SOA-305-12 Genetic mutations associated with second line drug resistance in *Mycobacterium tuberculosis* strains isolated from North-west India

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Background: Multidrug resistant tuberculosis has become a major health concern in India. Beside phenotypic determination of drug resistance, performance of Genotype MTBDR*sl* (Hain Lifescience GmbH, Germany) is endorsed by the WHO. In addition to drug resistance profile, it can determine the mutations associated with second line drug resistance. However, there is limited evidence regarding association of mutations and genetic background of strains.

Methods: In a retrospective study, 259 MDR-TB isolates obtained from pulmonary TB patients in last 5 years were subjected to second line drug susceptibility testing using Genotype MTBDR*sl* VER 1.0 and the results compared with BACTEC MGIT-960 as reference standard. All isolates were also genotyped using spoligotyping. The spoligo patterns obtained were analyzed using SITVIT_WEB.

Results: Of the 259 MDR-TB isolates which were screened for second line DR-TB by Genotype MTBDR*sl*, mutations were found in *gyrA, rrs* and *emb* genes in 82 (31.6%), 2 (0.8%) and 90 (34.7%) isolates respectively. In 16 (6.1%) isolates mutations were associated with FQ as well as in AG/CP drugs (XDR-TB). No mutations were detected in 159 (61.4%) isolates for corresponding *gyrA* and *rrs* genes. D94G was most prevalent mutation among [38 (46.4%)] OFX[R] isolates (37 FQ mono-resistant and 1 XDR-TB). It was followed by A90V in 23 (28.1%) [17 FQ mono-resistant and 6 XDR-TB] isolates. Among AG/CP resistant isolates A1401G was the most frequent (61.1%) mutation. It was followed by WT+A1401G (33.3%) and G1484T (5.5%). On spoligotyping analysis, Beijing strain was found to be most predominant (46%) genotype among the pre- and XDR TB isolates followed by CAS (30%). The lineage was strongly associated with D94G (47.3%) and A90V mutations (34.8%). However, among AG/CP resistant isolates isolates only Beijing strain was associated with A1401G and WT+A1401G mutations.

Conclusions: Beijing strain is found to be strongly associated with most prevalent mutations among pre-XDR and XDR TB isolates.

SOA-306-12 Is what you see really there? The conundrum behind faint bands with the GenoType MTBDR*plus* line probe assay

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Background: The primary diagnostic tool used for all patients with presumptive tuberculosis (TB) in South Africa is the Xpert MTB/RIF (GXP) assay. Those cases identified with rifampicin resistance (RR-TB) have a GenoType MTBDR*plus* (LPA) performed for Multi Drug Resistance (MDR) confirmation. A sentinel surveillance program to monitor drug resistance and related risk factors was also introduced for ongoing monitoring. Among those under surveillance, discordance between the original RR-TB result on the Xpert MTB/RIF and the finding of rifampicin susceptibility (RS-TB) on LPA was investigated.

Methods: Discordance between the original GXP (RR-TB) and LPA (RS-TB) were identified and had the isolate sequenced for the rifampicin resistance determining region (RRDR) of the *rpoB* gene using Sanger sequencing. A review of the original LPA strips to assess the intensity of the banding pattern was also undertaken.

Results: Among 75 discordant isolates, 48 (65%) had a mutation detected in the RRDR region. Of these, the most common mutation detected was the L511P (16; 33%). Upon review of the LPA, 8 strains had a faint wild type2 (WT2) banding pattern covering the codons 510 to 513 of the RRDR. Repeat GXP on these isolates showed Rifampicin resistance due to Probe A fall out.

Conclusions: Faint *rpoB* WT2 bands should be reported as Rifampicin resistant irrespective of whether the intensity is equivalent to or stronger than the Amplification Control zone (AC). Presence or absence of WT probes should be determined by comparing intensities of adjacent bands rather than the AC. Reporting these faint WT2 bands as Rifampicin resistant would decrease the number of discordant results significantly. Improvement of the criteria for interpreting LPA strips is required.

SOA-307-12 Detecting pyrazinamide resistance and pattern of *pnc*A gene mutations in multi drug-resistant *Mycobacterium tuberculosis* isolates in Myanmar

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Background: Pyrazinamide (PZA) is a key component of short-course anti-tuberculosis treatment regimen and also of second-line regimen for multidrug-resistant TB (MDR-TB). There are limited data on PZA resistance because PZA susceptibility testing is rarely performed routinely due to technical difficulties. Mutations in *pncA* gene were responsible for PZA resistance by reduction or loss of pyrazinamidase activity in *Mycobacterium tuberculosis* (MTB). This study was carried out to detect prevalence of PZA resistance and pattern of *pncA* gene mutations responsible for PZA resistance in MDR-MTB strains in Myanmar.

Methods: MTB isolates were collected from patients enrolled for MDR-TB treatment in 2016 at Yangon and Mandalay TB Centers, Myanmar. Resistance to isoniazid and rifampicin was confirmed by solid culture based drug susceptibility testing. Phenotypic PZA resistance was detected by liquid culture based Mycobacterial Growth Indicator Tube (MGIT) method. Mutations in *pncA* gene and promoter region were detected by Sanger DNA sequencing.

Results: Among 45 MDR-MTB isolates, phenotypic PZA resistance was found in 26 (57.8%) and *pncA* mutations were found in 27 (60%) of isolates. Thirty one different types of mutations were detected and 10 types of which were found to be novel mutations. Common mutations were found at the following regions of each of two strains: Lys96, Phe81, Thr135, Gly17 and Thr61 (4.4% each). Strong correlation between *pnc*A mutations and phenotypic PZA resistance were detected (Kappa Index =0.94).

Conclusions: The present findings showed high prevalence of PZA resistance among MDR-TB patients in Myanmar and highlighted the need for development of effective treatment regimens for PZA resistant MDR-TB. Pattern of *pncA* gene mutations conferring PZA resistance were scattered and diverse and this information can be used for further studies on the development of rapid PZA susceptibility assays. Our study also supported that routine PZA susceptibility testing is needed to be incorporated to treatment monitoring regimen and National drug resistance surveys.

SOA-308-12 Reliance on Xpert® MTB/RIF to start DR-TB treatment reduced time to treatment but seemed to worsen treatment outcomes in Tanzania

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Background: Between 2009-2013, in Tanzania, standardized treatment of drug-resistant tuberculosis (DR-TB) was centralized at the Kibong'oto Infectious Diseases Hospital (KIDH). Gradually, Xpert MTB/RIF testing was introduced in peripheral health facilities. Rifampicin-resistant TB cases were referred to the KIDH. Initially, Xpert MTB/RIF results were confirmed and complemented with phenotypic DST before DR-TB treatment was started. Since 2013, the decision to start DR-TB treatment in patients with rifampicin-resistant TB relied on the Xpert MTB/RIF result.

Methods: Retrospective study of time-to-treatment (time between sampling and treatment initiation) and treatment outcomes in patients starting DR-TB treatment between 10/10/2009 and 31/12/2013. Predictors of unsuccessful treatment outcomes (including death, lost to follow-up and failure) were assessed using multivariable logistic regression.

Results: 201 patients started DR-TB treatment in the study period. The number of patients starting DR-TB treatment increased over time: 14, 23, 30, 44, and 90 patients started DR-TB treatment in 2009, 2010, 2011, 2012, and 2013, respectively. Out of 201 patients, 123 (61.2%) were cured, 30 (14.9%) completed the treatment, 29 (14.4%) died, 17 (8.5%) were lost to follow-up, and 2 (1.0%) failed. The median time between sample collection and DR-TB treatment initiation reduced from 155 days (IQR 40-228), for the period 2009-2012, to 26 days (IQR 13-64), in 2013. Patients who started DR-TB treatment in 2013 were more likely (aOR 2.3, 95%CI 1.1-4.7; p=0.02) to have an unsuccessful treatment outcome (Figure 1).
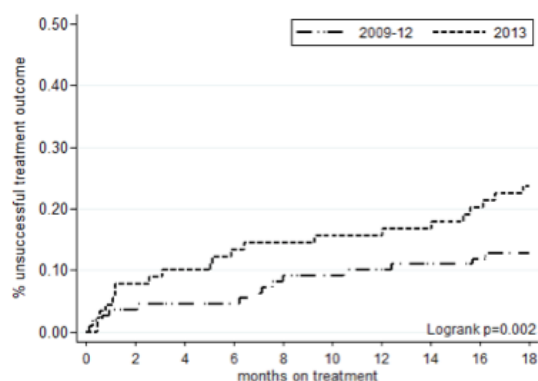
Figure 1 Unsuccessful outcomes (either death, lost to follow-up, failure) in patients whose DR-TB treatment initiation relied on phenotypic DST (2009-2012) and patients whose treatment initiation relied on genotypic DST (Xpert MTB/RIF, 2013, in Tanzania)

Conclusions: The introduction of Xpert MTB/RIF testing increased the enrolment on DR-TB treatment. Reliance on the Xpert MTB/RIF result to start DR-TB treatment reduced time-to-treatment. However, treatment outcomes did not improve. Explanations may include survivor bias and the increasing size of the DR-TB cohort. Decentralization of MDR-TB management to peripheral health centres after treatment initiation at central level may reduce the burden on health staff and patients with DR-TB.

SOA-309-12 Determination of true drug susceptibility of *Mycobacterium tuberculosis* using quantitative minimum inhibitory concentration tests

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Background: Drug resistance problems are very challenging for tuberculosis (TB) control. Accurate drug susceptibility testing (DST) is required to develop of effective regimens for treating drug-resistant cases. The objective of this study was to determine or redefine optimal clinical concentrations of anti-TB drugs, fluoroquinolone (FLQ), second-line injectable drugs (SLIDs), ethionamide (ETH) and ethambutol (EMB), for better care and outcome.

Methods: In this study, we tested 63 extensively drug-resistance (XDR) and 173 multidrug-resistance (MDR) *Mycobacterium tuberculosis* strains. The qualitative agar proportion method (APM) was used to determine drug susceptibility to 7 anti-TB drugs including moxifloxacin (MOX), levofloxacin (LEX), kanamycin (KAM), amikacin (AMK), capreomycin (CAP), ETH and EMB. The quantitative minimum inhibitory concentrations (MICs) of aforementioned anti-TB drugs were determined using the liquid-based Sensititre™ MYCOTBI plate and a Custom Panel. Kappa values were calculated to compare the AMP and MIC methods.

Results: Based on cumulative frequencies and cumulative percentages of resistant and susceptible strains, we identified MIC cut-off values of 7 tested anti-TB drugs. The MICs for MOX was 0.25 μg/ml, LEX 0.5 μg/ml, KAM 4 μg/ml, AMK 4 μg/ml, CAP 2 μg/ml, ETH 2.5 μg/ml and EMB 1 μg/ml.

Excluding strains with intermediate MIC values, our results showed that the APM and MIC methods had good correlation except ETH. The agreements between the APM and MIC methods were MOX 99%, LEX 99%, KAM 99%, AMK 100%, CAP 100%, ETH 89% and EMB 98%. Kappa values revealed intermediate values needed to be suggested and reported to each tested drug.

Critical concentrations determined using the APM were within the MIC values of drug resistant and susceptible strains determined using the liquid-based DST (Table).

Conclusions: Our findings suggest importance of using quantitative liquid-based DST to determine true drug susceptibility and to report intermediate values for preserving effective anti-TB drugs.

Drugs	APM	MIC Cut-off			kappa values
	Critical concentration (µg/ml)	Susceptible (≤, µg/ml)	Intermediate (=, µg/ml)	Resistant (≥, µg/ml)	
Moxifloxacin	0.5	0.25	0.5, 1, 2	4	0.93
Levofloxacin	1.0	0.5	1, 2	4	0.97
Kanamycin	6	4	8	16	0.94
Amikacin	6	4	8	16	1
Capreomycin	10	2	4, 8	16	1
Ethionamide	10	2.5	5, 10	20	0.63
Ethambutol	5	1	2, 4	8	0.96

Table Evaluation of MIC values between the conventional agar proportion and liquid-based MIC method

SOA-310-12 Plasma *Mycobacterium tuberculosis* cell wall metabolites identify patients with multidrug resistant tuberculosis: a pilot study

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Background: Biomarkers to monitor response to treatment for tuberculosis (TB) are urgently needed. Using plasma high-resolution metabolomics (HRM), we targeted *Mycobacterium tuberculosis (Mtb)*-derived cell wall metabolites in plasma of patients with active TB disease to evaluate potential utility as biomarkers of treatment response.

Methods: We performed plasma HRM using liquid chromatography/mass spectrometry on 61 patients diagnosed with active pulmonary TB (smear positive for acid-fast bacilli and culture positive for *Mtb*). Plasma HRM was performed at baseline (within 1 week of starting anti-TB therapy) and after 4 weeks and 8 weeks of treatment. All patients were initially treated with first-line drugs. Among included patients, 17 (28%) were later found to have multidrug resistant (MDR)-TB using WHO-standard drug susceptibility testing. The effect of MDR status on the semi-quantitative intensity level of *Mtb*-derived lipid metabolites at baseline and over time was evaluated using a mixed effects model.

Results: Of the 13,451 unique mass/charge (*m/z*) metabolites detected by HRM, 464 matched to previously characterized *Mtb* cell wall-derived lipids based on high-accuracy mass measurement (within 10 parts per mil-

lion). Thirty *Mtb* lipids were significantly different between patients with MDR-TB versus drug susceptible (DS)-TB (raw p ≤ 0.05). Of these, 28 were significantly lower in MDR-TB patients, with Lyso-PIM1, PIM2, PIM5, Ac1PIM3, Ac2PIM2, keto mycolic acid, acylated sulfoglycolipid, and trehalose monomycolate being the most different between groups. The decreased intensity of these metabolites continued over the 8-week period of observation.

Conclusions: The intensity of multiple *Mtb* lipid metabolites was significantly lower in MDR-TB patients compared to DS-TB patients at baseline and during the initial treatment phase. This effect may be due to increased bacterial killing in patients with DS-TB and/or altered *Mtb* cell wall composition in MDR-TB patients. Thus, increased concentrations of *Mtb*-derived metabolites in plasma may potentially be an early indicator of effective antibiotic therapy.

02. Improving care and support for patients

SOA-311-12 Evaluating the effectiveness of tuberculosis care providers on treatment outcomes in Afghanistan: a cross-sectional study

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Background and challenges to implementation: In Afghanistan, TB care is provided by community health workers (CHWs), public and private providers and treatment supporters. In 2016, CHWs contributed to 7.5% and private sector to 10% of all case reported in the country. However, their role in treatment outcomes was unknown. The purpose of this assessment was to evaluate the role of various care providers in treating TB patients.

Intervention or response: This was a cross-sectional assessment conducted in 12 provinces using random cluster sampling of health facilities. The team reviewed January 2016 records of study subjects (TB patients that completed their treatment) from health facilities' TB treatment registers.

Results and lessons learnt: The records of 3,205 TB patients were reviewed. Of those reviewed, 2,648 (83%) patients completed their treatment. CHWs provided treatment to 249 (7.7%) TB patients and successfully treated 218 (88%, CI 95% and p-value of < 0.001) patients and 2% died, 3% defaulted, 1% transferred out (TO) and 7% were not evaluated. Community treatment supporters provided treatment for 1,197 (37%) TB patients with a treatment success rate (TSR) of 71% (940 patients)

and 2% died, 2% defaulted, 9% TO and 9% were not evaluated (table 01). Public facilities treated 1,100 (34%) of TB patients with a TSR of 87% (959) and 1% died, 2% were lost-to-follow up, 2% TO and 7% were not evaluated (table 01). The private sector had a TSR of 86% (35 patients), a default rate of 2% and 12% were not evaluated.

Treatement provider	Treatment success rate	Treatment failure rate	Death rate	Lost-to-follow up rate	Transferred out rate	Not evaluated rate
Community supporter	940 (79%)	4	27 (2%)	18 (2%)	105 (9%)	103 (9%)
Community health workers	218 (88%)	0	4 (2%)	8 (3%)	2 (1%)	17 (7%)
Public service providers	956 (87%)	10 (1%)	14 (1%)	19 (2%)	24 (2%)	77 (7%)
Private sector provider	36 (86%)	0	0	1 (2%)	0	5 (12%)

Table Contribution of TB care providers in TB treatment

Conclusions and key recommendations: The community health workers and public health care providers contributed significantly to treat TB ptients. Therefore, we recommend engaging community health workers in TB treatment in Afghanistan and similar setting elsewhere. Also, we strongly support strengthening health system so as to increase the treatment outcomes at various levels of this system.

SOA-312-12 Exploring tuberculosis services provision and patient satisfaction in Afghanistan

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Background and challenges to implementation: Ministry of Public Health (MoPH), National TB Program (NTP) in Afghanistan with massive technical and financial support of USAID TB projects and other international donors rapidly increased the universal access to TB services from less than 50 Health Facilities (HFs) in 2002 to more than 2,000 HFs in 2016, meanwhile the TB case notification improved year by year, in the other side this huge improvement made the quality of service delivery and TB patients' satisfaction as a challenge.

Intervention or response: All HFs which are providing TB services have assigned staff to give consultation and daily free of charge treatment to TB patients, this is a part of Standard Operational Procedures (SOPs) of TB program implementation.

We developed a questionnaire for interview with few simple questions about the level of TB patients' satisfaction during their visits and treatment at HFs. thus the team randomly selected 49 HFs across eight provinces of Afghanistan. Totally 432 TB patients interviewed (280 female and 152 male).

Results and lessons learnt: Out of total study subjects(432) interviewed 405 (94%) responded that they are satisfied with service, 85% of them had the opportunity to choose their treatment either at HFs or at community level. 80% oriented about the side effects of TB medicine and 70% of them got orientation about TB infection control and finally 5% of them faced with HFs with no TB medicine. (See Table).

No of study subjects interviewed	Satisfactions rate	Treatment option choosed by patient	Orientation on TB medicine side effect	Orientation on TB Infection Control	TB medicine unavailability
Total: 432 280 female (65%) 152 male (35%)	405 (94%)	367 (85%)	345 (80%)	302 (70%)	22 (5%)

Table TB Patients' satisfaction

Conclusions and key recommendations: Although the majority of TB patients are satisfied with current TB service provision and free TB medicine, but still a huge portion of them (30%) are not getting orientation about TB infection control and (20%) of them about the side effects of TB medicine, even 5% of them faced with TB medicine unavailability. Therefor we strongly recommend NTP and partners to address this issues by applying successful approaches like community engagement and proper TB SOPs implementation.

SOA-313-12 Does physical tracing of treatment interrupters improve treatment outcomes? Patient-centered care approach to care and treatment in Busia County, Kenya

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Background and challenges to implementation: The END TB strategy identified patient centered care and prevention as a key pillar in ending the global Tuberculosis (TB) epidemic and its related burden. This pillar envisages providing care and support that is sensitive and responsive to patients' educational, emotional and material needs. However, Lack of supportive supervision and follow up has resulted to high number of patients interrupting treatment and thereby risking the progression to a drug resistance TB.

Intervention or response: Amref Health Africa in Kenya through the Global Fund TB project supports community systems to conduct tracing of Tuberculosis treatment interrupters through physical tracing, calling the

patients and calling the treatment supporters of TB patients. These approaches are aimed at improving the health related outcomes of the patients by returning them back to treatment. TB treatment interrupters in Busia County were traced by Community health volunteers between November 2016 and December 2017. Descriptive and correlation analysis was conducted to establish the relationship in the method of tracing, output and the outcome of the tracing.

Results and lessons learnt: Among the 3,322 patients traced, 60% (1,999) were traced physically by the CHVs, 28% (934) were traced by calling the patients and 12% (389) were traced by calling patients' treatment supporters. Physical tracing by CHVs was positively associated with a high likelihood of TB treatment interrupters returning to treatment (p=0.0318); Moreover, it was observed that calling the patients and following up with physical tracing will significantly influence return to treatment as compared to calling their treatment supporters (p=0.04).

Conclusions and key recommendations: Patient-centered care was observed more often with physical tracing and associated with return to treatment. Physical tracing is an important approach for identifying and addressing patient related barriers to Tuberculosis care and treatment. Future scale up of community TB care and prevention should include provisions of physical safety and transmission protection of tracing teams.

SOA-314-12 Decentralisation of healthcare facilities is contributing to early tuberculosis treatment initiation in Central India

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Background: Programmatic Management of Drug Resistant Tuberculosis (PMDT) is being implemented in Madhya Pradesh (MP) since 2011. PMDT recommends one-week hospitalisation for pre-treatment evaluation and initiation of second-line medications to Multi-Drug-resistant TB (MDR-TB) patients. MDR-TB patients find it difficult in accessing care and hence leading to delayed treatment initiation.

Methods: A retrospective analysis of time-lag between diagnosis and treatment initiation amongst DR-TB patients from Bhopal DR-TB centre was undertaken. In addition, in-depth discussions were taken-up with healthcare providers to understand the facilitators and barriers in timely treatment initiation.

Results: Till 4Q2013, only 2 DR-TB centres were functional in public-sector in MP; one each at Bhopal and Indore. DR-TB Centre, Bhopal was catering to 36/50 districts of MP. During 2012, only 90 MDR-TB patients were registered at Bhopal DR-TB centre. Median delay in treatment initiation from diagnosis was 98-days. Records revealed that patients living in districts away from Bhopal were more likely to be delayed in initiating treatment. Qualitative analysis also confirmed the same. Reluctance in travelling to DR-TB centre was reported since it was inconvenient, even though travel allowance was provided. Services have been decentralised over the years, with additional 7 DR-TB centres and district-level link DR-TB centres. District level DR-TB committees are formed, thereby an improved accessibility for patients. At present, Bhopal DR-TB Centre caters to 8/50 districts. Total MDR-TB patients registered in MP increased from 347 in 2012 to 1506 in 2016; and at Bhopal DR-TB centre from 90 in 2012 to 291 in 2016. In addition, there is reduction in time-lag of treatment initiation. Median delay in treatment initiation is reduced from 98-days in 2012 to 9-days in 2016.

Conclusions: Results confirm that decentralization of diagnostic and treatment services facilitated in reducing delays in initiation of treatment amongst MDR-TB patients. Timely treatment initiation reduces risk of spreading the *Mycobacteria* to community.

SOA-315-12 Efficacy of DOTS implementation in densely populated cities of Afghanistan: experience from Jalalabad city

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Background and challenges to implementation: Low Tuberculosis (TB) case notification has been a challenge for national TB program (NTP) since past two decades and it missed at lest 45% of TB cases during this period. Most of TB cases has been missing in densely populated cities such as Jalalabad. To address this challenge, the urban DOTS approach first piloted in Kabul and then expanded to Jalalabad city in late 2015. The objective of this assessment was to identify the effectiveness of this approach on TB case notification and treatment in Jalalabad city.

Intervention or response: The United States Agency for International Development (USAID) funded Challenge TB (CTB) project assisted NTP to expand Urban DOTS to Jalalabad city and engaged public and private facilities in DOTS. The CTB/NTP trained health care staffs, standardized TB recording and reporting forms and ensured sufficient supply of drugs and reagents. Also,

worked with provincial health office to ensure supervision and monitoring. We analyzed national TB surveillance data and used NTP standard recording and reporting forms as data collection tools.

Results and lessons learnt: Jalalabad city has a population of 237,792 and there existed 32 (19 public and 13 private). The urban DOTS covered 17 (53%) of health facilities. The outpatients attended health facilities improved by 100%, from 79,664 in 2014 to 163,729. Likewise, presumptive TB patients identification increased by 88%, from 4266 (2014) to 8,045 (2016). Moreover, the case notification for all forms TB cases showed 47% advancement, from 1,288 (2014) to 1,899 (2016) (graph 01). All these patients put on standard treatment as per national TB guidelines.
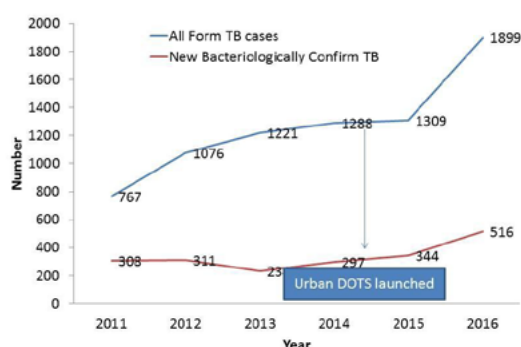

Figure Trend of TB case notification in Jalalabad city, 2011-2016

Conclusions and key recommendations: The study shows that Urban DOTS approach increased access to TB case services in Jalalabad city, significantly and is an effective mechanism for case notification. Thus, we recommend strengthening of Urban DOTS to cover additional facilities in Jalalabad city and similar setting in Afghanistan and elsewhere in the world.

SOA-316-12 Standard of TB-HIV care monitoring tool improves quality of care

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Background and challenges to implementation: Malawi is high TB/HIV burden country. Incidence of TB is at 193/100,000 with case detection of 47% of the estimated incident cases. Quality of TB service is critical areas in the program implementation. Supervision is a key strategy of ensuring quality of care. Supportive supervisions will benefit from standardized and structured approach.

Intervention or response: NTP with partners implemented a regular supportive supervision to all health facilities starting from 2015. The standard of care is designed based on the international standard of TB care. These standards address all thematic areas including case detection , treatment outcome monitoring, TB/HIV, TB infection control and contact investigation. Supervisors use a tool that helps them collect, interpret and act.Health facilities with major performance gaps are targeted for follow up supervision. To monitor progress , the National Tuberculosis Control Program(NTP)developed a composite scale using 11 indicators (that are applicable to most of the health facilities). For each indicator the highest possible score was 2 point. Zero point was assigned for low values. Kruskalwalis test was used to assess level of significance of observed change.

Results and lessons learnt: Composite scores for health facilities improved steadily over 6 quarters. (See figure1). The median value increased by 20 % over the six quarters. There was statistically significant difference of mean scores of the composite scale for the consecutive quarters. (Chi square =110, and P=0.001).
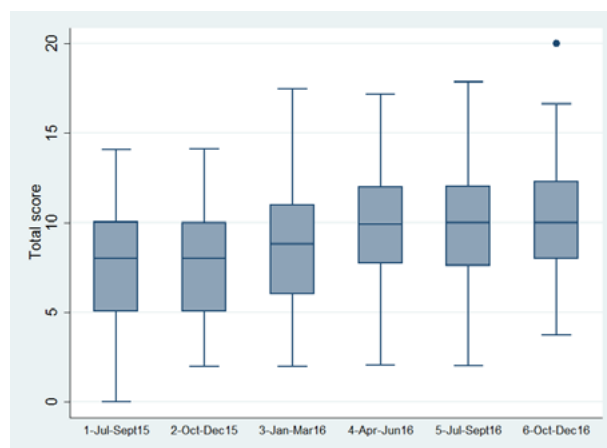

Figure Trend in total quality score (Jul-Sept15-Oct-Dec16

Conclusions and key recommendations: Regular supervision using standardized monitoring and structured support will contribute to improvement in quality of TB care. The tools will ensure continuity and follow up of action points in subsequent visits to health facilities. The results are encouraging and will be further strengthened. Some of the targets were ambitious and might not be sensitive to measure changes.

SOA-317-12 Supporting the patients: training social workers for an expanded role in patient-centered care for drug-resistant tuberculosis and HIV in South Africa

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Background and challenges to implementation: Treatment of drug-resistant tuberculosis (DR-TB) and HIV results in high mortality, low cure rates and substantial morbidity including stigma and social isolation. Social workers (SWs) may have a unique role in improving DR-TB/HIV outcomes by supporting adherence and retention in care. We conducted a training series to enhance knowledge, attitudes and skills, and support SWs role in the patient-centered care team for DR-TB/HIV patients.
Intervention or response: In April 2016, we implemented a model-based training on DR-TB/HIV treatment literacy and counseling with 10 Department of Health SWs from 3 hospitals and 2 clinics in KwaZulu-Natal, South Africa. Serial questionnaires and focus groups were conducted pre, immediately post and 6-months' post training. Paired t-tests and descriptive statistics were used to examine change in knowledge, attitudes, and practice. Transcripts and written materials were coded and thematically analyzed.
Results and lessons learnt: SWs were 80% female and experience ranged from 1-35 years. Immediately after training, there was significant increase in SWs' knowledge of medicines (p=0.011), adverse events (p=0.004), and confidence to discuss adherence barriers (p=0.037), side-effects (p=0.015), and organize support groups (p=0.003). Qualitative data showed that stigma, knowledge gaps, financial hardship, substance abuse, and family issues are routinely encountered and challenge patients' medication adherence and participation in care. SWs recommended an enhanced role for social work in patient assessment, counseling and education, and community and hospital-based interventions as part of multidisciplinary patient care teams. At the 6-month repeat evaluation most improvements seen with training were reduced, except for intention to organize support groups.
Conclusions and key recommendations: Training improved social workers' perceived knowledge, competence and intended practices. Qualitative data identified important non-medical barriers to adherence and participation in care that may be amenable to intervention. Realizing sustained benefits of training SWs in patient-centered care for DR-TB/HIV will require ongoing support for professional development and the evolving role of SW in patient-centered care.

Strongly Disagree (1) to Strongly Agree (5)	Pre-Training m (SD)	Post-Training m (SD)	P Value	6-month Post- M (SD)	P Value
Confident about knowledge of medications	3.60 (0.84)	4.40 (0.52)	0.01	3.88 (0.64)	0.45
Know which side effects are serious	3.40 (0.97)	4.80 (0.42)	0.004	4.0 (0.76)	0.17
Discuss medication side effects with DR-TB/HIV patients?	3.50 (0.85)	4.60 (0.52)	0.02	4.13 (0.99)	0.17
Organize a patient support group?	3.60 (0.70)	4.80 (0.42)	0.003	4.88 (0.35)	0.0002

Table Change in Social Worker KAP after 1 day training

SOA-318-12 Traditional beliefs and practices related to treatment non-adherence among TB patients in North Gondar, Ethiopia

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Background: Ethiopia has the 3rd highest prevalence of Tuberculosis (TB) in Africa despite having met the MDG goal 6 of reducing TB prevalence and mortality by half. Patient related nonadherence to DOTS regimen remains a challenge to TB control and efforts to reduce MDRTB. Previous surveys in North Gondar zone found that nonadherence rates are high. This medical anthropological project focuses on cultural reasons for nonadherence, particularly concerning religious beliefs and the acceptability of Traditional Medicine (TM). Ethnographic observations suggest that TM use among TB patients is more common than previously reported, and that religious beliefs are important in patient decision-making.
Methods: From September to December 2016, 32 indepth semi-structured ethnographic interviews and one focus group discussion were conducted in five TB treatment centres of North Gondar zone, Ethiopia. Preliminary qualitative analysis was conducted on major themes.
Results: Informants reported the following cultural beliefs related to TB: (1) that health problems and cures are caused by supernatural interventions, including being cursed, and that traditional healers are the appropriate source of therapy; (2) that TB is caused by physical conditions like coldness or malnutrition; and (3) TB pills are insoluble and that a liquid form would be better; Reported TM practices included use of: (1) thermal water; (2) holy water (*tsebel*); (3) incense ash (*emnet*); (4) faith healing; and (5) a protein rich diet including eggs

and milk. There may be a social stigma for being too dependent on Biomedicine and antimicrobial drugs because it represents a lack of faith in God, or that people will suspect that the TB patient has HIV.

Conclusions: Nonadherence may be related to cultural beliefs regarding non-biomedical notions of TB causation. For improved patient-centred care and better DOTS adherence, healthcare workers should be aware of these complementary cultural beliefs.

SOA-319-12 Treatment outcome patterns among tuberculosis patients exclusively treated at health facility level versus community/health post level in Ethiopia

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Background and challenges to implementation: Bringing Tuberculosis (TB) treatment closer to the community helps improve the accessibility of quality TB services. Our objective was to compare the performance of TB treatment outcome between patients treated at community-based health posts and those treated at higher level health facilities.

Intervention or response: Primary health care services in Ethiopia are set up with a health center at the center of the health care unit lined to 5 satellite health posts to cover a catchment area population of 15-40,000 depending on the degree of urbanization and agro-ecological parameters of the community. Health posts are the smallest health unit and are usually staffed with two front-line health extension workers. The TB care package provided by the HEWs is part of the national flagship Health Extension Program. According to the current national guidelines, once TB is diagnosed, treatment is started in the health center or hospitals and patients are referred to nearby health posts for follow-up based on preference. We used the July 2015-June 2016 annual national report to compare the treatment outcomes of patients treated in health posts with those treated exclusively in health centers and hospitals.

Results and lessons learnt: A total of 120,693 TB patients were treated for TB during the previous year of which 22,473 (18.6%) were referred to health posts (community level) for treatment follow up. The cumulative treatment success rate (TSR) was 91.7%. The TSR for TB patients treated in health posts and those treated in health center/hospital was 90.7% and 91.9%, respectively.

Indicators	Community/Health posts(Mixed)	Health facility only	Total
Number of TB patients initiated on treatment	22,473	98,220	120,693
Number of successfully treated TB patients	20,390	90,293	110,683
Treatment success rate (%)	90.7	91.9	91.7

Table TB treatment outcome in health facility & community level

Conclusions and key recommendations: The treatment outcomes for TB patients treated in health facility and health posts are very good and were similar within the acceptable range. Further decentralization of patient centered TB treatment follow up strategies at the community level should be promoted.

SOA-320-12 How does the motivation of community healthcare workers compare with the community's healthcare-seeking experiences? A qualitative study in peri-urban and rural Cambodia

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Background: Community Healthcare Workers, or Village Health Support Groups (VHSGs) as known in Cambodia, are the key for connecting patients with tuberculosis (TB) symptoms to the appropriate health centres for early diagnosis. Factors that affect community worker motivation, and the extent to which VHSGs are utilised when other (private sector) healthcare providers are prominent in communities, requires further study. The objectives of this study are to: (i) understand healthcare-seeking preferences of community members from peri-urban and rural communities in Cambodia, (ii) identify the factors affecting motivation of VHSGs working on TB control, and the value they place on different types of incentives for job performance, and (iii) compare and contrast community perceptions of different healthcare providers with the VHSG's level of motivation.

Methods: We analysed data from 14 in-depth interviews with male and female VHSGs working through a community-based TB control organisation (Operation ASHA) in peri-urban and rural areas of Cambodia, and four focus group discussions with community members from similar areas.

Results: Community members from both study sites expressed an overall preference for private healthcare facilities in terms of the speed of service, the perceived quality of healthcare and medicines, the perceived skill of the staff and how they are treated as patients. The role of VHSGs in their communities and their linkage to public health services was not substantiated. On the other hand, interviews with VHSGs indicated a high level of motivation to work towards improving health in communities, which they reported was primarily driven by intrinsic factors, such as fulfilment, recognition and achievement over financial incentives.

Level of motivation	Code / theme	Illustrative quotation
Organisational (intrinsic)	Feelings of self-fulfilment from being a VHSG	"... and then we think about their life is our life, they have disease mean we also have disease, this is the reason that we work for them, we don´t think about money." (KV06)
	Sense of achievement	"If I go to educate them and they do not follow me, there is no result from what I do then I do not feel happy." (PV05)
	Sense of recognition	"I am not only the VHSG but I´m also the symbol in the village..." (KV03)

Table Key factors driving VHSG motivation (summary)

Conclusions: The high level of motivation VHSGs exhibited was not reflected in the community's healthcare-seeking preferences. This suggests that VHSGs may not currently be realising their full potential to improve community-based TB care.

SOA-490-12 The study of barriers and facilitators to adherence to treatment among drug resistant tuberculosis patients in Georgia to inform policy decision

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Background: Poor adherence to treatment remains a significant problem that prevents effective control of Tuberculosis (TB) epidemic. The trend over the past several years shows that one-third of Drug Resistant-TB (DR-TB) patients interrupt treatment in Georgia. A new study investigated factors that enhance or hinder treatment adherence among DR-TB patients in Georgia.
Methods: The qualitative study was implemented in 2016. Data were generated from in-depth interviews and focus group discussions with 60 DR-TB patients, doctors, nurses and TB field specialists after attaining informed consent forms. TB patients represented the following subgroups: successfully treated, lost to follow-up

and those with difficulties to strictly follow treatment regimen. The data was analyzed in NVivo (version 11.4.0). Study conceptual framework looked at structural, personal, social and health system factors.
Results: Health system factors such as free treatment, effective program management and supportive medical personnel encourages patients to complete treatment. On the other hand, pill burden and difficulties of DOT regimen, influence of side-effects negatively affect adherence to treatment. Other health system barriers are lack of financial motivation among medical personnel to improve performance, poor access to specialist services due to fragmented TB and general health services, lack of mental health services to manage mental health problems related to drug adverse events. The study revealed some social and economic factors that prevent patients from completing the treatment, such as unfavorable employment legislation with TB treatment regimen, lack of support from family and friends, stigma and lack of peer involvement in supporting patients through the treatment.
Conclusions: Factors studied are closely interlinked and self-reinforcing. Therefore, a multi-sector vision and approach needs to be applied to resolve the problems. The findings and recommendations were communicated to the policy-makers. The study served as an evidence for policy decision to pilot results-based-financing among Tb specialists in Georgia.

03. Aspects of TB - immunology and host genetics

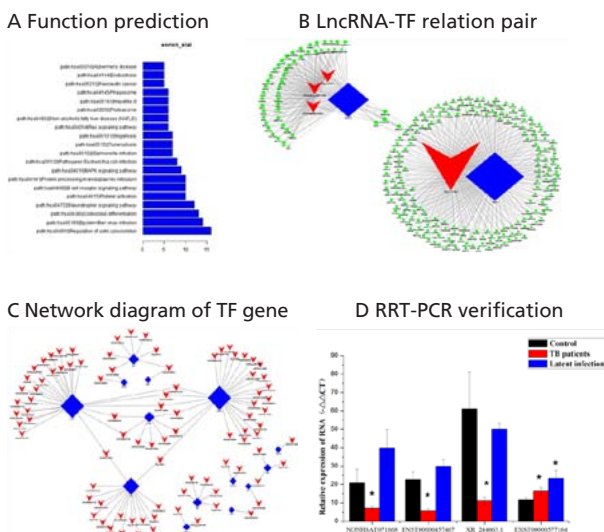## SOA-321-12 Study of long non-coding RNA (lncRNA) expression profiles in pulmonary tuberculosis

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Background: Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis* (TB) infection; high morbidity and mortality have made it a major public health issue. Long noncoding RNAs (lncRNAs) are important regulators for gene expression and known as key molecular in regulating both adaptive and innate immune responses. However, their roles in responses to TB infection remain to be elucidated.
Methods: Microarray analysis was applied to build lncRNA and miRNA expression profiles in TB patients in case-control models. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) biological pathway analysis of the differentially expressed lncRNAs was employed to investigate the potential functions and pathways related to the pathogenesis of TB infection, and screen specific lncRNAs associated with

TB infection. Real-time fluorescent quantitative PCR (RRT-PCR) was used to identify the selected specific lncRNAs in TB patients and latent infections.

Results: Our results revealed that many lncRNAs in many signal pathways were differentially expressed in TB infected patients, indicating a possible role for lncRNAs in immune responses induced by TB infection and providing important cues for further functional studies. Furthermore, four lncRNAs, NONHSAT071868 in MAPK signaling pathway, ENST00000577164 ,XR_244063.1 and ENST00000457467 in Leukocyte trans endothelial migration signaling pathway were selected and examined in TB patients and latent infections after GO and KEGG biological pathway analysis, followed by RRT-PCR evaluation. We found NONHSAT071868, XR_244063.1 and ENST00000457467 were down-regulated significantly in TB infected patients; ENST00000577164 was up-regulated significantly in TB patients and latent infections. Finally, these four lncRNAs were identified as novel candidate molecular markers for tuberculosis infection diagnosis, and proved to have good specificity and sensitivity by RRT PCR.

A Function prediction   B LncRNA-TF relation pair

C Network diagram of TF gene   D RRT-PCR verification

Figure Parts of results

Conclusions: Our results not only provide novel insight into the mechanisms of the TB infection, but also reveal potential targets for early diagnostics and the treatment of tuberculosis.

SOA-322-12 Helminths induce persistent epigenetically-mediated TB immune perturbations

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Background: Helminth infection is associated with an increased rate of TB progression and decreased TB immunity but the mechanism and duration of helminth-induced immune perturbation remains uncertain. There is burgeoning knowledge that the epigenetic code, post-translational modifications of DNA and its surrounding chromatin structure, determines immune phenotype. Murine models show that schistosomiasis infected mice undergo epigenetically mediated immune perturbations. DNA methylation epigenetically silences immune function by coiling DNA into a transcriptionally inactive state.

Methods: In a cohort of TB-exposed children, we performed urine and stool ova and parasite (O&P) examination, helminth PCR and helminth serology to characterize participants as active helminth infection (O&P or PCR+), remote helminth infection (O&P and PCR negative; serology positive) or not infected (O&P, PCR, serology negative). DNA methylation of 94 immune regulatory genes was measured using methylation-sensitive endonuclease digestion followed by qPCR. Helminth and DNA methylation results were correlated with downstream flow-cytometry based multi-dimensional immune profiling.

Results: Compared to uninfected controls, active or remote schistosomiasis infection was associated with a ≥20% increase in DNA methylation of 4 pioneer or transcription factors as well as 4 surface receptors (p< 0.005; Sidak-Bonferroni). The increased DNA methylation persisted for 6 months after empiric anti-helminth therapy. Only 1 intracellular protein and 1 transcription factor was hypo-methylated ≥10% compared to healthy-controls. Schistosomiasis infection and DNA hyper-methylation correlated with decreased mycobacteria induced CD4+ T cell production of IFN-γ and TNF and increased CD4 IL-4 and PD-1 (p< 0.005). In addition, schistosomiasis was associated with decreased Natural Killer cell (CD56+) perforin and increased monocyte IL-10 production (p< 0.0001).

Conclusions: Schistosomiasis induces persistent and profound epigenetic changes characterized by DNA hypermethylation that is correlated with a perturbed mycobacteria-specific immunity including decreased cell-mediated CD4+ T cells and Natural Killer cells with an increase in immune tolerant response in CD4+ cells and monocytes.

SOA-323-12 Activation of hypoxia-inducible factor 1 (Hif-1) enhanced bactericidal effects of macrophages to *Mycobacterium tuberculosis*

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Background: Tuberculosis is chronic infection caused by intracellular bacterium, *Mycobacterium tuberculosis* (*M.tb*), which infects specifically macrophages as host cells. Recently, Hif-1, hypoxia-inducible factor-1, was reported to act as master regulator of Warburg effect in macrophages during *M.tb* infection. The aim of this work is to explore the role of Hif-1 during *M.tb* infection and to investigate whether activation of Hif-1 signaling mechanism would enhance bactericidal effect of macrophages and anti-tuberculosis effect of chemical reagent such as rifampine (RFP).

Methods: 30 tissue samples from pulmonary tuberculosis and normal lung tissue from para-carcinoma of lung cancer were collected and Hif-1 was detected with immunohistochemistry. U937, human monocytic leukemia cell line, was stimulated with PMA and then allowed to differentiate into macrophages. Western blot was used to detect Hif-1 expression in *M.tb* infected U937 cells. Cells were then treated with Hif-1 activator, CoCl2 (100μM). IL-6 and TNF-α were detected in cell supernatant with ELISA. CoCl2-pretreated cells were infected with *M.tb* H37Rv and 1μg/ml RFP was then added into cell medium. 1×10^6 cells were seeded on coverslips and fixed with 4% paraformaldehyde to perform acid-fast staining. Cell lysates from 1×10^5 cells were 10 times serially diluted and inoculated on Middlebrook 7H11 agar plate. CFU (colony-forming units) was counted 3-4 weeks later.

Results: Hif-1 expression was increased by 6.6 times in lung tissue of pulmonary tuberculosis, compared with normal lung tissue. Hif-1 expression was also increased in *M.tb* infected U937 macrophages and activation of Hif-1 increased production of IL-6 and TNF-α. Data from acid-fast staining and CFU indicated that Hif-1 activation enhanced anti-tuberculosis effect of RFP in macrophages. Log_{10}CFU in PBS, CoCl2, RFP and CoCl2-RFP groups was 6.69, 5.88, 3.87 and 3.33, respectively.

Conclusions: Conclusively, to activate Hif-1 signaling mechanism in macrophages would strengthen bactericidal effect of macrophages, to further enhance anti-tuberculosis effect of chemical reagent such as RFP.

SOA-324-12 Effects of aldehyde dehydrogenase 2 (ALHD2) genetic polymorphism on mouse lungs in vitro

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Background: High levels of ALDH2 is observed in the lung stem cells and considered to offer protection to stem cells against aldehydes mainly funtioning in the mitochondria. ALDH2 overexpression provides protection from oxidative stress while its deficiency augments the stress. A single nucleotide polymorphism in ALDH2 (termed *ALDH2*2*), rs671, results in the amino acid change Glu478Lys. This mutant allele has a dominant-negative effect resulting in the complete or near-complete loss of ALDH2 enzymatic activity in individuals who are homozygous or heterozygous for the *ALDH2*2* allele. However, effects of loss of ALDH2 function on the lungs of mouse have not been studied extensively.

Methods: 2 types of mice with disturbed ALDH2 function, *Aldh2*2* transgenic (Tg) and *Aldh2-/-* were used .We examined primary tracheobronchial and lung epithelial stem cells for their *in vitro* colony forming efficiency (CFE). The tracheas and lungs from mice with disturbed Aldh2 function and their wild type (WT) controls, were collected as per age stages for histological immunostaining. Portions of tracheas from adult *Aldh2*2* Tg, *Aldh2-/-*, and WT control and aged WT mice were processed and examined by transmission electron microscopy.

Results: No significant differences were detected of their in vitro stem cells CFE. However, histologically, tracheal epithelial thickness, nuclear density, and number of basal stem cells were significantly lower in adult *Aldh2*2* Tg and *Aldh2-/-* than in adult WT mice, similar to the changes observed in aged WT mice. Electron microscopic examination revealed significantly high number of morphologically abnormal mitochondria in the trachea of *Aldh2-/-* mice. Furthermore, *Aldh2-/-* tracheal and lung cells showed higher ROS levels and fewer functional mitochondria than those from WT mice.

Conclusions: We detected several subtle effects of *ALDH2* mutation on mouse lungs. Some of these effects are similar to changes observed during normal aging, suggesting a "premature lung aging" effect of it.

SOA-325-12 Gut microbiota and BCG vaccine immunogenicity in South African infants

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Background: The gut microbiome is crucial for mucosal and systemic immune development, and may influence immune responses to certain vaccinations. Maternal microbiota are important determinants of infant gut microbiota. HIV-exposed infants (HEU) are born to mothers with altered gut and vaginal microbiota, and receive antibiotics for PCP prophylaxis, therefore HEU may have altered gut microbiota. HEU also have increased morbidity and mortality, and altered responses to certain infant vaccinations. We hypothesized that HEU have impaired immunity due to dysbiosis of the gut microbiota.

Methods: HEU (n=103) and HU (n=58) infants were recruited at birth and followed longitudinally. Stool DNA was extracted and Illumina sequencing of the V6 region of the 16S rRNA gene performed. Data was preprocessed using QIIME and UPARSE and imported into R for further analyses using the Phyloseq package. Diversity, differential abundance testing and multivariate analysis were carried out in R, Calypso and Galaxy. Whole blood was incubated with BCG and cytokine expression measured using multiparameter flow cytometry.

Results: We found differences in bacterial alpha (Shannon) and beta (Unifrac) diversity between HEU and HU infants at birth. However, no significant differences were observed in BCG T cell responses by HIV exposure. We binarized BCG CD4 memory responses into high and low cytokine responses and compared early life microbiota to BCG peak (week 7) total memory cytokine responses. The genera *Streptococcus* and *Desemzia* were significantly enriched in the low responses group. Staphylococcus was strongly associated with high cytokine responses. We further observed that the species *Veillonella dispar* and *Prevotella copri* appeared synergistic and enriched in the low response group. The genera *Streptococcus, Desemzia* and *Blautia* were also most predictive of BCG responses by Random forest analysis.

Conclusions: Gut microbial makeup could explain the immunological differences between HU and HEU infants. These differences should be considered in vaccine development for HIV-exposed neonates.

SOA-326-12 Introducing the ESAT-6 free IGRA, a companion diagnostic for TB vaccines based on ESAT-6

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Background: There is a need for an improved vaccine for tuberculosis. ESAT-6 is a cardinal vaccine antigen with unique properties and is included in several vaccine candidates in development. ESAT-6 is also the core antigen in the IFN-γ release assays (IGRA) used to diagnose latent infection, rendering IGRA tests unspecific after vaccination.

This challenge has prompted the development of a companion diagnostic for ESAT-6 based vaccines, an ESAT-6 free IGRA (Ef-IGRA).

Methods: We screened a panel of seven potential new diagnostic M.tb antigens, not expressed by BCG, in LTBI and TB patients from Egypt, Denmark and Greenland. Most promising antigens were combined with CFP10 in the Ef-IGRA peptide cocktail, lyophilized with heparin in field-friendly vacutainer tubes.

The diagnostic performance was determined in cross-validation studies in Denmark, Tanzania and South Africa.

Results: Immunodominant epitopes from three highly recognized antigens EspC, EspF and Rv2348c were identified and included in the Ef-IGRA.

Standard (Quantiferon-TB Gold, QFT) and the Ef-IGRA induced a comparable magnitude of both IFN-γ and IP-10 release.

The diagnostic performance of Ef-IGRA was on-par with QFT: sensitivity 84% vs 79% (active TB, n=68), specificity 99% vs 97%, (unexposed controls, n=100). Concordance in endemic controls was 97% (Tanzania (n=205), 21% QFT positive) and 92% (South Africa (n=200), 42% QFT positive).
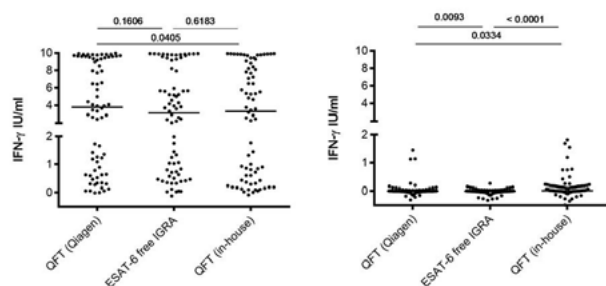
Figure 1 IFN-γ release in Quantiferon (commercially available IGRA), ESAT-6 free IGRA and in-house control IGRA with same antigens as in Quantiferon. TB patients (n=78 left) and unexposed controls from Denmark (n=100, right)

Conclusions: The comparable performance of the Ef-IGRA to QFT suggests potential as companion diagnostic for ESAT-6 containing vaccine recipients and as adjunct test for latent M.tb infection.

Ef-IGRA antigens have potential for combination with ESAT-6 for more robust detection of LTBI in immunosuppressed individuals and children.

SOA-327-12 Genetic diversity of *Mycobacterium tuberculosis* strains causing tuberculous lymphadentiis in south-west Ethiopia

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Background: Ethiopia has an extremely high rate of tuberculous lymphadenitis (TBLN), but little is known about the genetic diversity of *M. tuberculosis* strains driving the epidemic. In this study, we investigated the overall genetic diversity of *M. tuberculosis* complex (MTBc) strains and the role of *M. bovis* in TBLN patients in Southwest Ethiopia.

Methods: A total of 304 MTBc strains from TBLN patients in Southwest Ethiopia were genotyped primarily by spoligotyping. Isolates of selected spoligotypes were further analysed by 15-loci mycobacterial interspersed repetitive unit-variable number tandem repeat (MIRU-VNTR) and qPCR-based single nucleotide polymorphism.Isolates were classified into main phylogenetic lineages by using the reference strain collections available at www.miru-vntrplus.org

Results: Of the 304 MTBC isolates, 79.6% (242) were belonged to the Euro-American lineage (Lineage 4). The recently described and poorly defined Ethiopian lineages were the most predominate comprising 108 (35.7%) isolates, of which 44 isolates were Ethiopia_2, 34 isolates Ethiopia_3 and 30 isolates Ethiopia_H$_{37}$Rv-like. The next predominant lineages were the Delhi/CAS (14.5%) followed by Haarlem (14.1%). Interestingly, six isolates (2%) were belonged to the newly defined Ethiopian lineage called lineage 7. *M. bovis* was identified in only two (0.7%) of TBLN cases. The other lineages identified in this study included; URAL (5.9%), S (5.6%), UganadaI(5.3%), LAM (4.3%), X and TUR (1.6% each), UgandaII (1.3%), EAI (1%) and Beijing (0.3%). The remaining 19 (6.2%) isolates could not be assigned to previously known or new phylogenetic sublineages. The overall clustering rate was 35% indicating high rate of recent transmission.Delhi/CAS lineage strains were significantly associated with rifampicin resistance.

Conclusions: This study revealed a high diversity of MTBc genotypes responsible for TBLN in Southwest Ethiopia. The recently described Ethiopia specific lineages were the most predominant followed by Delhi/CAS and Haarlem. Zoonotic transmission of *M. bovis* infection has been excluded as a major factor in TBLN.

SOA-328-12 Animal vaccine dose-response curve predicts lower optimal TB vaccine dose in humans: proof of-concept study of immunostimulation/immunodynamic modelling methods

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Background: Vaccine development dose concentration decisions are currently purely based on empirical methods. Recent evidence in TB vaccine development suggest this could lead to sub-optimal dose finding. We aim to apply mathematical modelling to translate multi-dose TB vaccine immune responses from mice, to predict most immunogenic dose in humans in a proof-of-concept study.

Methods: Data were available on IFN-γ secreting CD4+ T cells over time for novel TB vaccines (H56 and H56/H1 adjuvanted with IC31) in mice (5 doses, 45 mice/dose) and humans (1 dose, 18 humans). A two-compartment mathematical model describing the dynamics of the post-vaccination IFN-γ T cell response was calibrated to: 1) mouse and 2) human data separately using nonlinear mixed effects methods. Then, using these calibrated models, and assuming an allometric scaling factor (from mouse to human) of ten, we predicted the human immune response dynamics, and predicted the most immunogenic human dose.

Results: The mathematical models were successfully calibrated to the animal and human data. Dose was associated with the magnitude and duration of the animal IFN-γ response after revaccination. At day 224 the predicted median number of human IFN-γ cells were 215, 484 and 776 for the high, middle and low dose groups, indicating the lowest dose group may be most immunogenic in humans.

Conclusions: H-series vaccine doses used in clinical trials may be too high. Giving lower doses than previously tested is likely to increase immune response, and possibly protection in humans. Mathematical modelling may be a novel and revolutionary tool to predict optimal vaccine doses for use in clinical trials.

SOA-329-12 Immunosuppressive and therapeutic effects of fisetin, curcumin and camelid format anti-IgE in ovalbumin-induced lung inflammation

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Background: Asthma is a chronic allergic airway disease characterized by persistent inflammation and airway hyper-responsiveness. T cells, especially Th2 cells secreting IL-4, IL-5 and IL-13 are pivotal in orchestrating the disease process. IgE plays a major role in allergic disease by causing the release of histamine and other inflammatory mediator from mast cells. A more direct approach to stop the systemic reaction is to block IgE, via an anti-IgE (a single heavy chain antibody from Camelus dromedarius). We further evaluated the potential activity of natural compounds like Fisetin and Curcumin mediated anti-asthma activity.

Methods: Mice were sensitized and challenged with Ovalbumin and adjuvant up to 55 days. We investigated BALF, Histological analysis, measurement of gene expression by RT-PCR and Flow cytometry analysis. For drug treated groups, Fisetin and Curcumin was given intratracheally one hour before each intra tracheal challenge. We further developed ovalbumin induced chronic asthma in pre-clinical model (C57Bl/6) to test efficacy of anti-IgE.

Results: Fisetin and Curcumin treated groups, Eosinophil significantly reduced 2.71 and 1.44 fold in blood whereas in Balf, numbers of Eosinophil reduced to 2.52 and 1.52 fold. Ova induced inflammatory cells and subepithelial collagen content around the bronchiloles and small vessels was detected by H&E, Masson's Trichrome stained. Further gene expression of IL-5, IL-13 and TGF-β significantly reduced in case of Curcumin and Fisetin treated groups. More interestingly, CD45 cells become reduced in lung 1.84 and 2.72 fold in Curcumin and Fisetin treated group by Flow cytometry analysis. Further, we developed anti-IgE antibody of Camelid format which was 15 kDa protein in bacteria expression system.

Conclusions: Natural compounds and small molecules of Camelid antibody may be useful in chronic allergic asthma treatment. Expected administered with anti-IgE single chain antibody will have the ability to drastically and rapidly reduce the local and systemic lung inflammation.

SOA-330-12 Genetic polymorphism effects of genes-enzymes, responsible for biotransformation of xenobiotics, on TB drug-related hepatotoxicity

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Background: At the moment, one of the reasons for the insufficiently high effectiveness of TBC patients treatment is an inability of optimum (standard) treatment compliance due to the high frequency of adverse reactions to TB drugs. Increase the effectiveness and safety of chemotherapy for TBC patients is possible on the basis of knowledge of the patient´s genotypic characteristics through molecular genetic methods of research.

Methods: In total, there were 95 patients in the research study, aged between 12 and 50. Isoniazid, pyrazinamide and rifampicin were used in the treatment regimen of the main group patients. Adverse hepatotoxic reactions in the form of clinical aspects and (or) increase in the level of ALT and AST were shown by 23 patients. To conduct laboratory tests, genomic DNA was isolated from whole blood and then the polymerase chain reaction was performed in real time. In the study group the presence of genotypes belonging to the genes listed below was considered as possible predictors of hepatotoxicity: rs1801279, rs1799931, rs1799930, rs1799929, rs1801280, rs1208, rs1041983, rs1045642, rs74837985.

Results: As a result of the logistic regression analysis two statistically significant models were obtained. The first model reflects the association of the TB drugs hepatotoxicity with the AA genotype of the rs1799931 gene and the AA and AG (allele A) genotypes of the rs1799930 gene. The second model reflects the connection of the TB drugs hepatotoxicity manifestation with the TT and CT (allele T) genotypes of the rs1041983 gene.

Conclusions: The presence of the AA genotype of the rs1799931 gene and the AA and AG (allele A) genotypes of the rs1799930 gene as well as the presence of the TT or CT (allele T) genotype of the rs1041983 gene, which determine the activity of the NAT2 enzyme, statistically significant increase the risk of hepatotoxicity when taking TB drugs by pulmonary tuberculosis patients.

04. Risks and reasons for modifying approaches

SOA-331-12 Risk of recurrent TB in the UK

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Background: Calculating the incidence of TB recurrence (relapse or reinfection) is important for TB control. We estimate the incidence of recurrence, identify factors associated with recurrence and determine the proportion of recurrences attributable to relapse and re-infection.

Methods: We used patient identifiers to identify recurrent TB notifications from 2000-2015 and matched culture positive isolates to obtain 15/24 loci MIRU-VNTR strain types. Strain types identified and distinguished between possible relapse (no locus different) or re-infection (≥1 locus different). Recurrent TB was defined as re-notification at least 12 months after initial notification (24 months for those with rifampicin resistance). Incidence was calculated and cox proportional hazards regression conducted to identify factors associated with recurrence.

Results: From 112,503 TB patients, 1,944 recurred, an incidence of 2.6 (95% CI 2.5-2.7) per 1,000 person-years. When limited to five years follow-up (83% of recurrences), the incidence was 3.7 (95% CI 3.5-3.9). Treatment completion was low for those who went on to recur (68.5%) with high proportions either lost to follow-up (6.7%) or stopping treatment (3.4%). Recurrence was highest among patients with social risk factors (9.2 per 1,000 person-years, 95% CI 7.1-11.8) and HIV co-infection (5.7, 95% CI 4.7-6.9). In multivariable analysis, being UK born (aHR 2.2 95% CI 1.4-3.6), HIV co-infected (aHR 1.8, 95% CI 1.4-2.2) and pulmonary disease (aHR 1.4, 95% CI 1.2-1.5) were independently associated with recurrence. In total, 252 patients had a MIRU-VNTR result on both episodes; 139 (55.2%) were likely relapses and 113 (44.8%) were likely re-infections.

Conclusions: TB recurrence is low overall and largely occurs in patients with specific characteristics. A high proportion of recurrences had been lost to follow-up or stopped treatment. Strain typing suggests there may be a high proportion of re-infection. The confirmation of these findings with WGS would be beneficial.

SOA-332-12 Obesity, diabetes and risk of tuberculosis in two Taiwan cohorts: a double-edged sword?

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Background: Limited data suggested that body mass index (BMI) was inversely associated with risk of active tuberculosis. The inverse association presents a "paradox" with regard to diabetes, since obesity is a major determinant of diabetes, and diabetes is a risk factor for tuberculosis. We aimed to investigate the complex interplay between high BMI and diabetes on risk of tuberculosis.

Methods: We analyzed data from two Taiwan cohorts, one from three rounds of nationally representative health surveys and one from a health screening program. BMI level and diabetes status were measured at baseline; occurrence of incident tuberculosis was ascertained from the national Tuberculosis Registry. We constructed logistic regression models to assess the dose-response relation between BMI and tuberculosis hazard. We also conducted a causal mediation analysis to characterize the relation between BMI, diabetes, and tuberculosis. A separate logistic regression analysis was performed to estimate the joint effect of BMI and diabetes on TB risk.

Results: Of 167,392 participants included (60.3% of whom were women) aged 20-102 years, 502 developed incident tuberculosis during a median of over seven years of follow-up. With one unit (kg/m^2) increase in BMI, the odds of TB decreased by 10.4% (95% CI: 6.2-14.4) and 14.6% (95% CI: 11.6-17.5) in the two cohorts respectively. In the causal mediation analysis, high BMI had a harmful effect mediated through diabetes and a strongly protective effect not mediated through diabetes. Individuals who were simultaneously obese and diabetic had a lower but statistically insignificant hazard of tuberculosis (adjusted odds ratio: 0.30, 95% CI: 0.08-1.22) compared with non-diabetic individuals with normal weight (Figure).

Conclusions: The epidemic of obesity, despite its link with diabetes, may accelerate the current decline of global tuberculosis epidemic. Future modelling studies will help quantify the potential impact of the global nutrition transition on the future trend of tuberculosis.
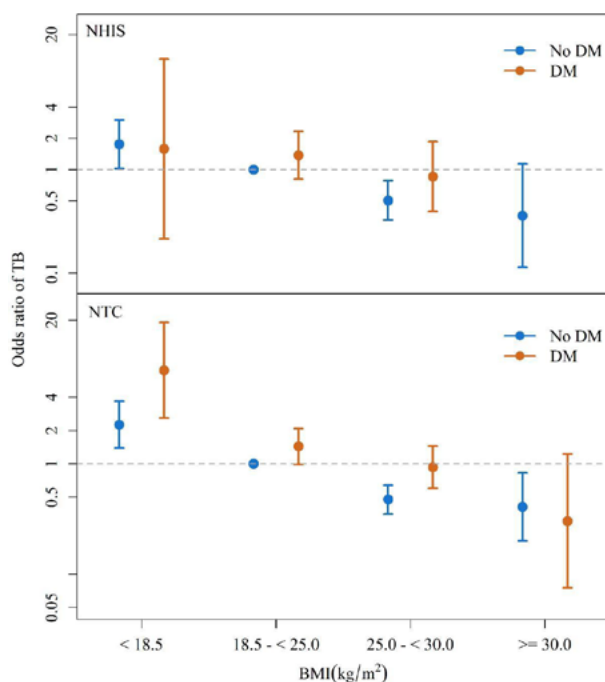
Figure Joint effects of BMI and risk of TB in two cohorts

SOA-333-12 Demographic predictors of active tuberculosis in migrants to British Columbia, Canada: a retrospective cohort study

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Background: Tuberculosis (TB) epidemiology in low incidence countries is typically driven by foreign-born TB, due to reactivation of latent tuberculosis infection (LTBI) acquired before immigration. Our objective was to report robust estimates of TB incidence in migrants to a low TB incidence region, and to identify potential target groups for LTBI screening based on demographic data available at the time of immigration.
Methods: This retrospective cohort included all individuals (N=1,080,908) who became permanent residents in Canada between January 1, 1985 and December 31, 2012 and were residents in British Columbia at any point during this period. Multiple administrative databases were linked to the provincial TB registry. TB incidence rates (# cases/100,000 person-years (py)) were reported, stratified by demographic characteristics and time since cohort entry (index date). Recursive partitioning models were used to identify potential high-yield targets for post-landing LTBI screening.
Results: In total 2831 people developed TB. The highest TB rates were observed within the first 10 years after the index date among people aged >65 years (89.2/100,000 py, 95% CI: 78.7, 101.1) and migrants from high TB-

incidence (≥200/100,000) countries (52.9, 95% CI: 49.8, 56.1). The highest rates were seen in refugees (100.0, 95% CI: 86.0, 115.7) and live-in caregivers (63.7, 95% CI: 52.5, 76.5) from high incidence countries, compared to lower rates among economic migrants within the business (16.0, 95% CI: 6.9, 31.5) and other skilled worker (34.7, 95% CI: 30.3, 39.7) streams. Refugees from high TB-incidence countries were identified as a high-yield target population for LTBI screening, with almost 1% of people developing TB within the first 10 years.
Conclusions: Using demographic data alone, we identified refugees from high TB-incidence countries as a high-yield population for targeted post-landing LTBI screening. Screening at entry should be a practical and high-yield activity if high-risk populations are identified and the LTBI care cascade is optimized.

SOA-334-12 Factors associated with use of bacteriological tests for diagnosing TB in Kenya

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Background: Kenya's recent TB prevalence survey suggests under detection. Guidelines recommend use of bacteriological tests (Xpert MTB/RIF® is first line test). As new improved tests emerge, understanding what influences use may aide equitable access to improved TB care. We set out to describe TB case notification rates (CNR) for each county and use of bacteriologic tests.
Methods: We reviewed de-identified data of patients reported to the National TB programme in 2015 and projected estimates from the 2009 census. Outcome measure was use of a bacteriological test and effect of explanatory variables explored using a multi-level regression model with county as a random effect.
Results: 82,313 patients started TB treatment in 2015. 62.4% were male; children 0-14yr were 6450 (7.9%). Kenya's mean CNR was 173.2/100,000; for 0-14yr was 49.7/100,000; and for ≥15yr was 272.6/100,000. 29.2% of children had smear microscopy compared to 80.1% of adults; 4.8% had an Xpert test compared with 12.6% of adults; and only 0.1% had a culture compared with 0.6% of adults. Overall, 1,963 (30.4%) children had any bacteriological test done, compared with 61,665 (81.3%) of adults (p< 0.001). Factors independently associated with bacteriological test included: age ≥15yr (AOR 10.9, 95% CI 10.3-11.6); known HIV status (AOR 2.0, 95% CI 1.82-2.2); severely malnourished (AOR 1.3 95% CI 1.28-

1.41); male (AOR 1.2, 95% CI 1.2-1.3). Private sector had reduced odds (AOR 0.72, 95%CI 0.63-0.82); and those who had an adverse outcome (AOR 0.64, 95% CI 0.59-0.70). County was also strongly associated (AOR 3.6, 95%CI 3.3-4.0). Figure 1 shows a panel with the individual county CNRs compared with distribution of diagnostic tests.
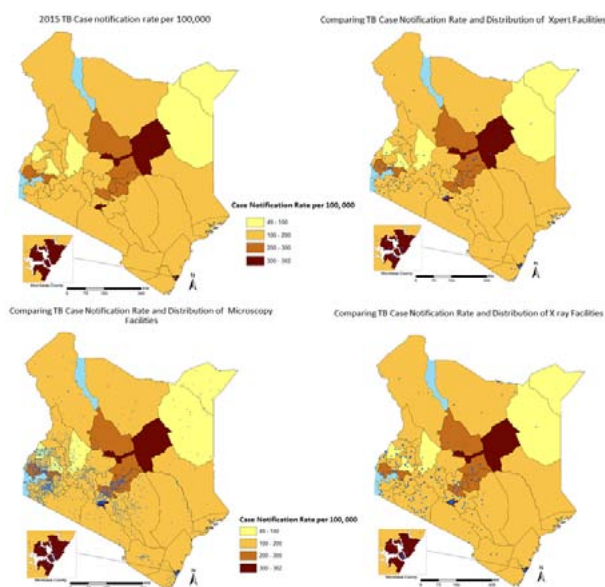

Figure 1 Case notification rates & Diagnostic Test

Conclusions: Low use of bacteriological tests may be due to reluctance to test children or sicker patients. Xpert MTB/RIF® use needs to be encouraged. Private sector needs to be support to adhere to guidelines. Further exploration of county level factors is recommended.

SOA-335-12 Heavy alcohol consumption increases the risk of active tuberculosis in Taiwanese adults: a nationwide population-based cohort study

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Background: Animal studies have shown that alcohol exposure may cause immunosuppression and increase the susceptibility to tuberculosis (TB) infection. However, the temporality of alcohol consumption with subsequent TB development remains unclear. This nationwide population-based cohort study aimed to investigate the impact of alcohol exposure on TB development in Taiwanese adults.
Methods: We included 46 196 adult participants from three rounds (2001, 2005, 2009) of the Taiwan National Health Interview Survey. Alcohol consumption was classified into heavy, regular, social, or never alcohol use.

Heavy alcohol consumption was defined as intoxication at least once/week. Alcohol consumption and other covariates were collected by in-person interviews at baseline. Incident cases of active TB were identified from the National Health Insurance database. Multivariate logistic regression was used to estimate the association between alcohol consumption and active TB, with adjustment for age, sex, smoking, socioeconomic status, and other covariates.
Results: A total of 279 new cases of active TB occurred during the study follow-up period. Heavy (adjusted odds ratio [AOR], 5.21; 95% confident interval [CI], 2.41-11.26) and regular alcohol use (AOR, 1.73; 95% CI, 1.26-2.38) were associated with higher risks of incident TB after adjusting for the subject demographics and comorbidities. Moreover, a strong dose-response effect was observed between increasing alcohol consumption and incident TB (AOR, 2.26; 95% CI, 1.59-3.21; $P < .001$).
Conclusions: Heavy and regular alcohol consumption associated with higher risks of active TB. Future TB control programs should consider strategies to lower the overall level of alcohol consumption to reduce the TB disease burden.

SOA-336-12 Tuberculosis: one disease, one geographic region, several epidemiological profiles

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Background: To compare demographic, epidemiological and clinical characteristics of tuberculosis cases in the central region of São Paulo City from 2010-2015, in South American immigrants versus native Brazilians or immigrants from other regions.
Methods: This cross-sectional study used secondary data obtained from TBWeb system of São Paulo State Health Department. Inclusion criteria: to be reported and treated as a tuberculosis case in the Central region of the City of São Paulo in 2010-2015. Exclusion criteria: lack of information about district of treatment. Demographic, epidemiological and clinical data were compared between South American immigrants versus native Brazilians/immigrants from other regions by t-test or chi-square, being significant p<0.05.
Results: Among 2264 cases of tuberculosis, 486 (21.5%) occurred in South American immigrants. Compared to native Brazilians and immigrants from other regions, the South American immigrants were younger (26±13 vs. 39±13 years; p<0.0001), worked predominantly in textile workshops (86 vs. 2%; p<0.0001), their diagnosis was mainly made in primary health centers (70 vs. 51%; p<0.0001); they had less comorbidities [alcoholism (3

vs. 11%); AIDS (3 vs. 30%)], and a greater proportion of favorable outcomes (Recovery - 65 vs. 60%; Death - 3 vs. 8%; p<0.001).

Conclusions: Tuberculosis is commonly associated with precarious living conditions and poverty, but those characteristics associated with the disease are different in South American immigrant patients compared to Brazilians. Among South American immigrants, the disease is associated with textile workshops and their unhealthy and unsanitary work and living conditions. Among Brazilians and immigrants from other origins, there is not a single unifying factor, but diverse conditions that make their health fragile, such as advanced age or comorbidities.

SOA-337-12 Potential mechanisms for the high tuberculosis notification rate among the elderly in Taiwan: a modelling approach

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Background: Taiwan is an intermediate TB burden setting, with wide disparities in TB burden across ages. In 2015, the age-specific notifications were a hundred times as much in those older than 65 years old, compared to those younger than 15 years old (195.9 vs 1.9 per 100,000 population). We used mathematical modelling to explore the mechanisms giving rise to such disparities.

Methods: An age-structured, dynamical model was built to explore the following three hypothetical mechanisms for the age disparity:

(i) a historical trend of frequent TB transmission contributed to a substantial number of elderly cases in the present day,

(ii) the elderly have a higher TB progression rate than younger age groups, and;

(iii) assortative contact patterns are a driving factor for the disparate TB burden.

These mechanisms were assessed, individually and in combination, using the Akaike information criterion (AIC).

Results: According to the reported AICs, the model combining all the three mechanisms best presented the disparity observed in the age-specific notifications (Figure). While no single mechanism was able to capture the age disparity in TB burden, the most critical mechanisms were age-dependent contact mixing patterns and TB progression rates. We discussed the underlying reasons for these dynamics.
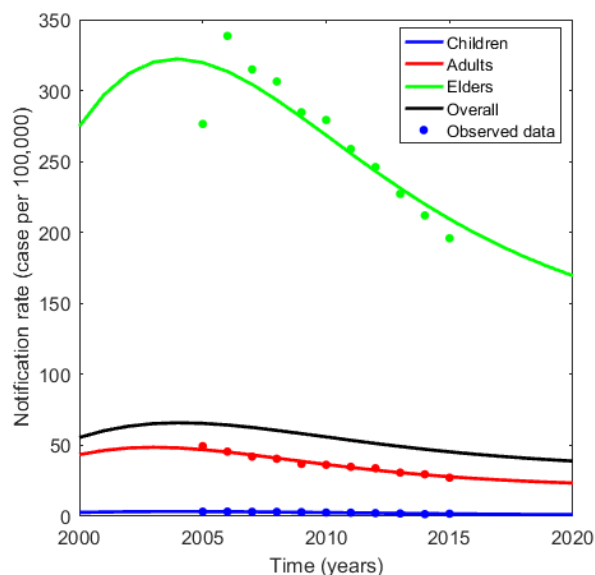

Figure The fitted results using the combining mechanisms

Conclusions: The study shed light on the important mechanisms that might contribute to the age disparity in TB transmission, in Taiwan and in other intermediate TB burden settings showing such disparity in age-specific burden. Further studies on the parameters used for these different mechanisms are needed to disentangle their impact on TB transmission and corresponding control strategies.

SOA-338-12 Joint impact of modifiable risk factors on tuberculosis: a population-based cohort study

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Background: In the Sustainable Development Goals era, comprehensively addressing the risk exposure of tuberculosis (TB) became necessary for TB control. Lifestyle risk factors including tobacco smoking, alcohol use, underweight, and diabetes mellitus have repeatedly been shown to be important and independent risk factors for TB. Few attempts, however, have quantified the joint impact of these potentially modifiable risk factors on TB in Taiwan.

Methods: Our study cohort included 55,639 participants from three rounds of national representative surveys. The participants were followed for incidence of active TB through cross-joining the survey database to the national TB registry of Taiwan. The odds ratios (OR) of incident TB were estimated by univariate and multivariate pooled logistic regressions. We used the partial population attributable fraction to estimate the joint impact of selected modifiable risk factors on TB.

Results: A total of 188 cases of active TB were identified during follow-up. After adjusting for potential confounders, current smoker (OR = 1.78; 95% CI 1.44

to 2.18), regular drinker (OR = 1.69; 95% CI 1.37 to 2.09), underweight (OR = 2.77; 95% CI 1.81 to 4.26), and diabetes mellitus (OR = 1.64; 95% CI 1.28 to 2.10), were positively associated with active TB. Combinations of these lifestyle risk factors together accounted for 38.8% (95% CI 18.6%, 55.8%) of TB cases in Taiwan. Individually, the burden of TB attributable to tobacco smoking, alcohol consumption, underweight, and diabetes mellitus were 19.2%, 11.8%, 7.6%, and 7.3%, respectively, after taking account of the joint distribution and correlation among risk factors.

Conclusions: Nearly 40% of cases with active TB could be attributable to the four risk factors under investigation. The findings unveil insights for future TB control in Taiwan and globally.
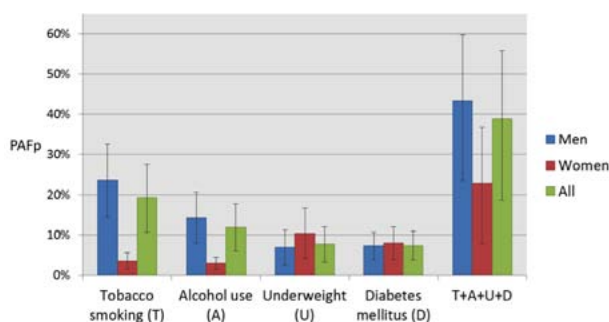
Figure PAFp of risk factors for active TB

SOA-339-12 High rates of undetected tuberculosis in medical and oncology wards in Botswana

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Background: Tuberculosis (TB) is the main cause of mortality of people living with HIV (PLHIV) and the main infectious cause of death in the general population. Cancer patients infected with HIV might be and even higher risk for TB than other PLHIV due to the concomitant immunosuppression associated with cancer and its treatment. However, the burden of TB disease among cancer patients in high HIV prevalent settings is largely unknown. We aimed at comparing the TB prevalence among patients admitted to the medical and oncology wards at a main tertiary-level referral hospital in Botswana.

Methods: From August 2016 through January 2017, all patients admitted to the hospital were screened daily during their hospitalization period. Any patient admitted in the ward was screened for cough, night sweats, weight loss, loss of appetite and this was to classify patients as presumptive TB or not. If presumptive TB, sputum was collected to rule out TB through GeneXpert.

Results: During the study period, 604 of 720 patients were screened for TB (485 in the medical ward and 119 in the oncology ward). HIV prevalence was 45.6% and 58.7% in medical ward and oncology ward patients, respectively. TB symptoms were identified in 119 (24.5%) and 49 (41.2%) patients in the medical and oncology wards, respectively. TB prevalence was estimated at 0.5% (3/604; 95% confidence intervals [CI], 0.2% - 1.69%) overall. All 3 TB patients were diagnosed within the first 5 days after admission. TB prevalence was 0.2% and 1.69% among medical ward and oncology ward patients, respectively.

Conclusions: Our preliminary data suggest high prevalence of TB in hospitals, particularly among oncology patients. We recommend extensive screening and monitoring for TB among oncology patients in high HIV and TB burden countries.

SOA-340-12 Understanding reasons for TB notification delays in England, Wales and Northern Ireland, 2011—2014

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Background: In England, Wales and Northern Ireland, there is a statutory requirement to notify TB patients within three days of clinical suspicion or diagnosis to the Enhanced Tuberculosis Surveillance system (ETS). Data held within ETS is used for national and international reporting and to monitor progress of the TB strategy. Ensuring timely notification is important to enable real-time use of the data to monitor trends and assess the impact of control strategies.

Our study assesses notification delays, analysing time between diagnosis, notification and submission to ETS and factors contributing to delay.

Methods: All TB cases notified in England (except London), Wales and Northern Ireland to ETS between January 2011 and December 2014 were included. Delays were categorised as: 'Overall delay' (> 3days between diagnosis and submission date), 'Notification delay' (>3 days between diagnosis and notification date) and 'Submission delay' (> 3 days between notification and submission date). An online survey was completed by users of ETS and those who notify using paper-based notification forms to assess the factors contributing to the delays.

Results: 77.2% of all cases had an overall delay, with a median delay of 16 days (IQR 4-18 days). A higher proportion of cases had a notification delay (53.2%) compared with a submission delay (39.1%).

Clinical staff reported that the responsibility of who should notify is unclear (nurses, doctors or administrators). There was also a lack of awareness that notifications should occur on suspicion/ diagnosis of TB, with 67.5% reporting they thought notifications should occur once the patient started treatment.

Conclusions: Overall, a high proportion of cases were submitted to ETS after three days of diagnosing TB. The survey highlighted key components attributing to the delay, which need to be addressed in order to improve timeliness of notifications to ETS for data to be used in real-time.

SOA-341-12 Seasonality in tuberculosis case notification rate and its implications for developing season-based case finding strategies in Ethiopia

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Background: Seasonal variation in tuberculosis (TB) case load was reported in northern temperate zones. A systemic review ascribed this to the gradual decreases of serum Vitamin D concentrations in autumn and winter due to less sunlight impairing host immunological defense with TB infection. The change of TB diseases in Africa in different time periods has not been studied.

Methods: We used routinely reported quarterly data to analyze seasonality patterns in all forms of TB cases reported in Amhara and Oromia regions of Ethiopia. The two regions constituted over half of all forms of TB cases reported in Ethiopia. Quarterly data of all forms of TB cases reported between July 2010-June 2016 was computed using the trend line and a change in the trend was assessed to see if there was a variation in TB case load during different quarters of the year.

Results: Each year, the number of notified TB cases start to increase during January to March, reaching a peak between April and June. The case load starts to decrease during the quarter July to September. The lowest number of TB cases was reported during the period October to December. This cyclical pattern was observed throughout the last seven years of observation (Figure 1).
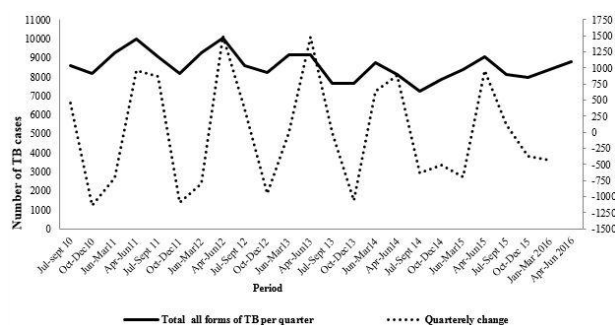

Figure 1 Trends in seasonal variation

Conclusions: The peak TB case notification rate corresponds with the dry season in the two agrarian regions of Ethiopia. During dry seasons, rural residents have adequate resources and ample time to seek for medical care whereas in the wet, farming and harvesting season, farmers are busy and have limited resources to visit health centers and receive care. Further decentralization of the services and organizing outreach activities may contribute to improved case finding in the wet seasons. The mechanisms underlying the seasonal variation of TB are complex and multi-factorial, and need intensive studies.

05. TB in correctional facilities: an update on detection and care

SOA-342-12 Promising TB case finding in prison settings: a lesson learned from 10 Indonesian prisons/detention centres

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Background and challenges to implementation: The Indonesian prison population (215000 in 2016) is relatively small, but prison conditions are crowded (177% occupancy) with inadequate infection control. Since 2015, entry/exit screening, cough surveillance, annual screening and contact investigation are included in prison's TB services, using symptom screening and sputum smear, in addition to routine TB services. Early 2016 the MOH made Xpert the primary diagnostic for at risk populations.

Intervention or response: In 2016, The Ministry of Law and Human Rights and Ministry of Health, supported by Challenge TB/USAID, implemented TB Mass Screening in 9 prisons and 1 Detention Centre (total 10,816 inmates), using symptoms and chest X-Ray (CXR) screening followed by Xpert for all symptomatic and inmates with CXR abnormalities.

Results and lessons learnt: The mass screening contributed 72% of the TB case finding in the 10 facilties (171 out of 236 patients) among whom 9 were MDR (5 %). Total case finding inreased from 66 in 2014 to 97 in 2015 (based on symptoms screening and sputum smear) and 236 in 2016 with the new algorith. The prison population increased only slightly from 9812 to 10816. In 2016 the prevalence of TB in each prison/DC varied between 1.3 to 3.1 %.

The mass screening with CXR and Xpert required significant investments in logistics and human resources. Interesting local collaboration exists in East Java, where

Jember Lung Hospital screens inmates by mobile X-Ray, using local budget.

Conclusions and key recommendations: Active case finding highlighted high levels of TB and MDR-TB among inmates. The high yield of mass screening as compared to routine case finding strongly indicates the need to strengthen routine TB services in the prisons. Attention is needed to develop effective and sustainable TB care in prisons, ensure routine access for symptomatic to Xpert testing, treatment of both drug sensitive and MDR TB, in addition to the screening programs.

SOA-343-12 Can a prison health facility provide quality TB and DR-TB care and management? A case study of Shimo La Tewa Prison Health Centre, Kenya

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Background and challenges to implementation: There are 55,359 inmates within 118 prison facilities in Kenya. Globally TB incidence is up to 70 times higher in prisons than in communities. TB transmission is also higher due to overcrowding, malnutrition and inadequate ventilation. Prisons therefore are a reservoir for TB, and quality TB care within prisons is necessary to find prevalent cases, reduce transmission within and outside prison walls.

Intervention or response: In 2011, the National TB Program undertook to train Health Care Workers (HCWs) of different cadres on TB. At that time there was no nurses, doctors or clinical officers providing TB services at the facility.

Results and lessons learnt: Following TB training, Shimo La Tewa Prison Health Center, which supports 1600 prisoners, is being managed by one HIV Testing Services (HTS) counsellor in the TB clinic. Prisoners are screened on admission to the prison and annually thereafter. A gene Xpert machine has been placed on site for diagnosis. DOTs is provided for all prisoners with TB, while those requiring chest X-rays are referred. In 2015, of the 71 prisoners diagnosed, treatment success rate (TSR) was 91%, 2.8% died and 5.6% were lost to follow up (LTFU), compared to a national TSR of 89%. All cases LTFU were remandees released from prison through the courts. Of the 5 DR TB patients ever managed, 2 have successfully completed, while 3 are ongoing on treatment. DR TB patients are isolated within the prison, while patients released before treatment completion are physically referred to a facility closest to them. TB commodities and support supervision are provided by the NTLDP.

Conclusions and key recommendations: High quality TB care can be provided to prisoners by health care workers once capacity building has been conducted. Tash shifting seems to work after capacity building. Routine support for commodities and policy guidance is however key to success.

SOA-344-12 TB in prisons: CTB contribution to improving health conditions in eight prisons in Mozambique

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Background and challenges to implementation: Mozambique, which has one of the highest TB prevalence rates in the world (550/100.000), TB among prisoners has been overlooked despite global evidence of the risk in prison settings. Although official estimates suggest that 5% of the 18,000 prisoners nationwide have TB, screening is limited and prevalence may be much higher. Some data suggest that rate is increasing but most partners supporting the health system work in HIV service sites, few support activities for prisoners.

Intervention or response: The USAID-funded Challenge TB (CTB) project began working in prisons in 2015. Following efforts with the Ministries of Health, Justice and stakeholders, CTB developed and distributed IEC materials and M&E tools. Following coordination meeting with stakeholders, CTB was assigned 8 prisons in 4 targeted Provinces. The project developed a 3-day training package covering TB, HIV, malaria, skin disease and diarrhea for selected prison guards and prisoners. The goal for the training was to increase awareness of disease symptoms, and reinforce links with health national services.

Results and lessons learnt: In total 179 people (73 guards and 106 prisoners) were trained from September 2016 to March 2017. Over this time-period, 362 presumptive TB cases were referred for TB screening and 58 prisoners were diagnosed with TB - 37 bacteriological confirmed and 21 clinically confirmed. In addition, 21 were TB/HIV co-infected, while 127 malaria, 73 skin disease and 143 diarrhea´s all of them in prisoners. All of those with TB started treatment under NTP with CB DOTS support. The number of TB cases referred and diagnosed with TB from these same prisons in 2015 was 21.

Conclusions and key recommendations: Staff trained within prisons can improve on TB and health issues in general to allow early diagnosis and promote care, prevention and treatment. However, challenges still high, as screening is done sporadically and data are not consistently captured.

SOA-345-12 Identifying missing cases among prisoners through a health camp approach: experience from India

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Background and challenges to implementation: Prisoners are at utmost risk of acquiring TB infection, being in a closed environment with several others for prolonged periods. CDC estimates that TB rates in prisons are often 5 to 10 times higher than national rates because of overcrowding, poor ventilation, co-morbid illnesses and lack of healthcare.

Intervention or response: Population Services International (PSI), is implementing prison intervention in Bangalore and Bijapur districts of Karnataka since Aug'2016. Initial two rounds of interventions were done through sensitization approach, where the prison inmates were sensitized on signs and symptoms of TB through awareness activities by community volunteers, followed by verbal screening for TB symptoms. Later we conducted the interventions in same prisons using Health Camp approach, where a general health camp was organized with the help of local medical doctors. General health check-up, eye testing, blood pressure and blood sugar testing and verbal screening of TB symptoms was part of the Health camp. In both cases the sputum samples of identified presumptive TB cases were collected and transported for facilitating diagnosis.

Results and lessons learnt: Overall 4,700, inmates are present in Bangalore (4200) and Bijapur (500) prisons. 390 prison inmates (240 in Bangalore and 150 in Bijapur) were covered through two rounds of sensitization, 360 prison inmates (210 in Bangalore and 150 in Bijapur) were covered through one round of health camp in both prisons. We found that significantly more number of presumptive TB cases were identified through health camp as compared through sensitization (51 vs 26, P> 0.01). Significantly more number of TB cases were detected through Health Camp approach compared to sensitization approach (20 vs 8, P>0.01).

Conclusions and key recommendations: General Health camp approach is effective in increasing participation of prison inmates, by reducing stigma and more number of missing cases could be identified among prison inmates as compared to awareness and sensitization approach.

SOA-346-12 Tuberculosis in the La Esperanza Prison, Cundinamarca, Colombia

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Background: The TB incidence in prisons is higher than the general population. The different factors that contribute to this situation include: an overcrowded prison population, frequent prisoner movement, poor ventilation, limited access to diagnostic facilities, inadequate implementation of a TB control program and poor prison conditions. The aim of this study was to determine the actual state of TB within the La Esperanza Prison.

Methods: During the study, the prison population was 2630 of which 2020 (77%) agreed to participate and were interviewed in order to detect respiratory symptomatic (RS) subjects. Medical examination confirmed the true SR inmates. Latent Tuberculosis infection (LTBI) was diagnosed using TST (Tuberculin Skin Test) in 1923 inmates. Serial spontaneous or induced sputum samples were taken to perform microbiological diagnosis: Ziehl-Neelsen staining, cultures (LJ and BACTEC™ MGIT™) and phenotypic/ genotypic drug susceptibility testing. Molecular characterization was made by Spoligotyping and 24-locus MIRU-VNTR.

Results: 305/507 (15.1%) prisoners were confirmed as RS and 24 of them (7.8%), were diagnosed with active TB which corresponded to an incidence rate of 940.6 cases / 100.000. 19 strains were recovered and identified as *M. tuberculosis* complex. 18 strains (94.7%) were sensitive and only 1 was resistant to INH. LTBI was detected in 68%.

By Spoligotyping, all isolates were confirmed as *M. tuberculosis* species corresponding to Euro-American lineage, with a predominance of the Haarlem sublineage (68.4%). Molecular cluster analysis based on 24-locus MIRU-VNTR and Spoligotyping showed only 3 clusters containing 2 strains each and 13 unique types. Lastly, 2/3 clusters contained 2 identical clinical strains belonging to two different groups of inmates that shared the same cell.

Conclusions: The TB incidence rate was found to be 37.6% higher than the national rate (25 /100,000). We found high percentage of LTBI and the active TB. TB transmission within the prison was detected.

SOA-347-12 Increasing TB screening, diagnosis, and treatment in a large Zambian correctional facility by integrating TB services into a universal HIV test and treat program

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Background: We conducted an interim impact evaluation of integrating TB services into a universal test and treat (UTT) programme within a large Zambian correctional facility.
Methods: Applying RE-AIM, we evaluated reach, effectiveness, adoption, implementation and maintenance of integrated TB/HIV activities using routine and prospective data collected from June - December 2016.
Results: Reach: During the evaluation period, the total inmate population was 1,849 people, for whom we provided HIV testing services (HTS) to 1,556 (n/N=1,556/1,849, 84.2%), and screened 1,565 for TB using Xpert MTB/RIF (n/N=1,565/1,849, 84.6%).
Effectiveness: Significantly more newly HIV-diagnosed inmates initiated ART in 2016 (n/N=154/188, 81.9%) compared to same 6-month period in 2015 (n/N=50/72, 69.4%) (p=0.03). A similarly high proportion of TB-diagnosed inmates started anti-TB treatment in 2016 (n/N=26/26, 100%) as 2015 (n/N=24/25, 96%) (p=0.3).
Adoption: 35 corrections officers, 8 health workers, and 28 peer educators were trained on HTS, TB screening, and UTT. However, HIV and TB treatment was fragmented by release and transfer procedures uncoordinated with health services, resulting in 41% of inmates receiving UTT being released/transferred during the 6-month period.
Implementation: HTS uptake (84.0%) exceeded our target (75%), and most HIV-diagnosed inmates started ART within 1 day (IQR:1-5), meeting our same-day ART target. Entry TB screening (84.6%) failed to meet our target (100%). Xpert was a satisfactory tool for rapid screening and diagnosis, but required a trained peer educator to operate and purchasing supplementary cartridges to meet demand.
Maintenance: Key obstacles for integrated TB/HIV services remain, including reliance on program support to ensure sufficient commodities to deliver integrated services (e.g. HIV test kits were unavailable 30% of program weeks).
Conclusions: While we achieved high uptake and fidelity of HTS, same-day ART and TB screening, and improved HIV/TB service reach and effectiveness within one large Zambian correctional facility, sustainability may be hampered by ongoing weaknesses in the prison health system.

SOA-348-12 Epidemiology of tuberculosis in maximum prison health facilities, Kenya

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Background: Kenya is ranked 13th among 22 high-burden tuberculosis (TB) countries in the world. Prisoners form a group of society with a high risk of tuberculosis. In Kenya, there was an estimate of 55,000 prisoners in 2016 with a TB morbidity rate of 10%. We analysed surveillance data to describe TB cases, assess the trends, determine the TB/HIV co-infection and treatment outcomes among patients in Kenyan prison health facilities.
Methods: We reviewed Tuberculosis data from Prison health facilities, between January 2012 and December 2015 and collected data on patient socio-demographics, treatment information and outcomes. A case of TB was defined as bacteriologically confirmed smear positive. Data was downloaded from the TB online register and entered into epi info 7 for analysis. Descriptive analysis was done where means were calculated for continuous variables and proportions for categorical variables.
Results: A total of 4474 cases were analyzed of which male were 3557(80%). The mean age was 33 years (±12.7), 1549(30%) were in the age group 20 -30 years and 1019 (23%) were from Nairobi county. Most had Pulmonary TB cases (3782, 82%). Smear positive cases were 1536 (34%) in 2012, 1397 (31%) in 2013 and 1493 (33%) in 2014. Out of 2039 smear positive cases at month 0, 452 (22%) tested positive for HIV. Overall treatment success rate was 81%, 153(3 %) died, 9(0.2%) had treatment failure and 475(11%) transferred out to other clinics. Out of the 9 cases with treatment failure, 3(33%) were diagnosed with multidrug resistant TB.
Conclusions: TB burden was high in males, there was minimal change in the trend over the three years and most cases were from Nairobi County. Our findings indicated lower treatment success rate than the WHO targets so there is need for scale up the patient treatment follow ups.

SOA-349-12 Effectiveness of active case finding in addressing tuberculosis control in prisons

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Background and challenges to implementation: In 2016 there were 30,845 prisoners in Afghanistan. Since 2011, the NTP, with support from the Challenge TB (CTB) project has made a strong commitment to provide TB services to inmates to support early TB detection and reduce TB mortality. New active case finding approaches (sputum smear microscopy and digital X-ray) were evaluated to address the challenges of TB services in prisons.
Intervention or response: The NTP, with support from CTB and partners, developed a Standard Operating Procedure, training and mentoring sessions were conducted for staff at prison clinics, a TB diagnostic and treatment center was established and sputum smear microscopy and mobile digital X-ray service was initiated. Consultative meetings with relevant departments were organized to secure commitment in addition to networking with health facilities and NGOs. A TB awareness campaign was conducted in the prisons, TB patients were isolated and treatment was provided. The data from six prisons in Kabul, Bagram, Kandahar, Herat, Balkh and Nangarhar was collected, analyzed and compared with NTP surveillance data.
Results and lessons learnt: Among 19,383 prisoners, 1,825 (9.4%) presumptive TB cases were identified and referred for digital X-ray and sputum smear microscopy in 2016. Out of the 1,825 presumptive TB cases, there were 252 confirmed TB cases (681/100,000 population) were diagnosed. This is much higher than the estimated incidence of TB in general population (189/100,000). Among 1,825 presumptive TB cases, 199 (11%) were bacteriologically confirmed TB cases (See Table 1). One hundred and ten of 117 (94%) bacteriologically confirmed TB cases successfully completed their treatment which is higher than national level treatment success rate of 89%.

Indicators	Year (2016)
# of prisoners in 6 prisons	19,383
# and % of presumptive TB identified among prisoners	1,825 (9.4%)
# of bacteriologically confirm TB cases identified	199
# of all form TB cases identified among prisoners	252

Table 1 Active case finding in prisons

Conclusions and key recommendations: Active case finding stemming from political commitment and effective multi-sectoral collaboration resulted in significant improvements in TB case detection and treatment completion among prisoners. We recommend scaling up TB services to prisons in other provinces.

SOA-350-12 Intensified TB-HIV activity in prisoners at a central jail in Faridkot, Punjab, India

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Background and challenges to implementation: Prison conditions are hard on mental and general health and because of this drugs abuse among prisoners has been reported throughout the world. Drug addiction is one of the major causes of high HIV prevalence in India. Faridkot is a district, in India is bordering Pakistan and is among the worst effected by drug abuse due to its geo-political conditions
Intervention or response: An activity for screening prisoners for HIV was carried out in central jail of Faridkot, Punjab after permission from the jail authorities from August 2015 to 31st July 2016. Written consent was taken from the prisons before HIV testing.
Results and lessons learnt: 4016 prisoners were tested for HIV after written consent and 382 (9.5%) tested HIV reactive. The HIV positives were further screened for TB by sputum microscopy and Xray and of this 40 (10%) were diagnosed having TB. In addition through an awareness camp in jail additional 250 chest symptomatic patients were examined and investigated. Out of these an additional 15 Pulmonary TB cases and 5 Extra Pulmonary TB cases were diagnosed. The patients were initiated on ART and TB treatment by admitting them in Central Jail Hospital Faridkot. During treatment duration they were provided 1/2 Kg milk, 4 eggs, 4 bananas and porridge by prison authorities. The treatment completion was ensured .Following this activity the jail authorities established a separate TB ward and de-addiction center in jail .The predominant risk factor for HIV came out to be intravenous drug abuse.
Conclusions and key recommendations: In prisons awareness regarding TB and HIV should be provided to the inmates by organizing awareness sessions as a routine ACSM activity and conducting health camps. HIV counselling and screening can be offered to all prisoners on entry.

SOA-351-12 Is it possible to ensure treatment completion of TB patients identified from prison intervention? Experience from India

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Background and challenges to implementation: CDC estimates that TB rates in prisons are often 5 to 10 times higher than national rates because of overcrowding, poor ventilation, co-morbid illnesses and lack of access to healthcare. Additionally prison inmates are moving population within prisons and communities. This poses risk of prison inmates being loss to follow, incomplete treatment and thus spread of infection.

Intervention or response: As part of Global Fund supported Project Axshya, we are implementing prison intervention in Banda district of Uttar Pradesh, since Aug'2016. Prison Inmates are sensitized on signs and symptoms of TB through awareness activities using IEC material, slide shows and mid media activities, by the Community Volunteers (CVs) trained by the project. Inmates having cough for more than two weeks are primarily identified through verbal screening. Community volunteers collects and transports the sputum samples of presumptive TB inmates. Those identified TB positive are provided DOTS through RNTCP within the prison. Community volunteers counsel TB positive inmates and follow them for entire treatment duration, even when they are released from the prison back in communities.

Results and lessons learnt: Total 1,243 Prison Inmates were sensitized and screened for TB at periodic intervals since Aug'2016. 143 inmates were found to have presumptive TB symptoms and were screened through sputum microscopy at nearest DMC. 21 prison inmates were found TB positive and were counseled and followed up by CVs for six month from start of treatment. 7 are declared cured, another 5 are on treatment and remaining 9 are transferred to another prisons where there treatment is continued.

Conclusions and key recommendations: Systematic screening of Prison Inmates, counseling and follow up on one to one basis, would help to retain TB positive prisoners and help ensuring their treatment completion.

06. Recent developments in paediatric TB and lung health

SOA-352-12 Urine LF-LAM positivity predicts mortality in hospitalized HIV-infected children

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Background: The World Health Organization limits the recommendation of lateral flow urine lipoarabinomannan assay (LF-LAM) for TB diagnosis to HIV-infected adults and children with low CD4 or who are seriously ill. Recent data estimate a 2-fold increased risk of death associated with positive LF-LAM in HIV-infected adults with TB, suggesting potential predictive benefit of this point-of-care test for mortality. Data is limited regarding prognostic performance of LF-LAM for mortality in seriously ill HIV-infected children, in whom TB diagnosis is particularly challenging.

Methods: We evaluated risk of mortality associated with positive LF-LAM among hospitalized HIV-infected children enrolled in an RCT evaluating urgent ($\leq$ 48 hours) vs. post-stabilization (7-14 days) antiretroviral treatment (ART) initiation in Kenya. TB evaluation at enrollment included two sputa or gastric aspirates for liquid culture (including one for Xpert), and urine for LF-LAM testing.

Results: Of 137 randomized infants with LF-LAM results, median age was 2.2 years (IQR 1.2-6.1), and 63 (46%) were female. Children were severely malnourished (58% with WAZ $\leq$ -3SD) and immunosuppressed (median CD4% 14 [IQR 8.1-21.6]). Nine (7%) had confirmed TB by Xpert or culture (on sputa or gastric aspirates). Fifteen (11%) children were LF-LAM positive, among whom 5 (33%) had confirmed TB. Among confirmed TB cases, 5 (56%) were LF-LAM positive. Over six months of follow-up, 15% (21/137) of children died (40 deaths/100 py), with the risk of mortality higher among children with positive LAM-LF (127/100 py) compared to negative LF-LAM (31/100 py) (HR 3.71 [95% CI 1.44-9.59]; p=0.0070). Risk remained significantly elevated in analyses adjusted for baseline CD4% and age.

Conclusions: LF-LAM may identify HIV-infected children at highest risk of mortality who may be missed by TB diagnostics performed on sputum or gastric aspirate samples.

SOA-353-12 Genotyping and whole genome sequencing to identify tuberculosis transmission related to pediatric patients in British Columbia, Canada, 2005 - 2014

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Background: Tuberculosis (TB) in children is an indicator of ongoing community transmission and requires extensive contact tracing. Molecular techniques such as genotyping and whole genome sequencing (WGS) can enhance pediatric TB investigations by confirming or refuting transmission between cases.

Methods: *Mycobacterium tuberculosis* isolates from all patients < 18 years with culture-confirmed TB in British Columbia (BC) from 2005-2014 (n=49), were subjected to 24-locus MIRU-VNTR (MIRU) genotyping followed by WGS for all MIRU-clustered cases. The results were compared to those of all culture-positive cases in BC during the same time period and linked to relevant clinical, demographic and contact tracing data to characterize the epidemiology of pediatric tuberculosis in BC.

Results: Twenty-three children (47%) were Canadian-born with a median age of 5.8 years, the remaining 26 were foreign-born (median age 14.8). The majority of foreign-born cases (69%) had immigrated < 5 years prior to diagnosis, and were born in Asia (81%) or Africa (19%). Twenty-four cases (49%) belonged to a genotype cluster, with 5 children belonging to the same two clusters (MClust-001: n=2, MClust-011: n=3). Six cases were detected through contact investigations, while the majority of cases (82%) were diagnosed after presenting with TB symptoms. The median number of contacts was 5 (interquartile range: 2-19), with 3 children having >50 contacts listed. A single multi-drug resistant (MDR) pediatric case was detected and confirmed through WGS as transmission from parent (also MDR), to child. A total of 15 cases were determined to be the result of active transmission within BC (≤5 single nucleotide polymorphisms).

Conclusions: Genotyping can quickly refute transmission; however, it overestimates true recent transmission. WGS is better tuned to detect transmission when interpreted in the context of epidemiological data, and represents an important tool for contact investigation of pediatric TB, enhancing contact tracing, and limiting the ongoing spread of tuberculosis.

SOA-354-12 ABCB1 polymorphism (C3435T) influences the plasma concentration of rifampicin

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Background: Optimal plasma rifampicin concentrations are crucial for the success of short course antitubercular chemotherapy. Absorption of rifampicin may be influenced by the expression and function of P-glycoprotein, a drug efflux protein in small intestine encoded by ABCB1 gene. The objective of this study was to describe the association between polymorphism (C3435T), mRNA expression of ABCB1 gene, and plasma rifampicin concentrations.

Methods: Children with probable tuberculosis were enrolled from All India Institute of Medical Sciences, India, after obtaining ethical clearance from Ethics Committee. Plasma rifampicin concentrations were determined by liquid chromatography-mass spectrometry. Genotypes of ABCB1 (C3435T) were identified by amplifying the 207 bp region in exon 26 and restriction with MboI. Quantification of ABCB1 mRNA transcripts was done by real time PCR (SYBR green fluorescent nucleic acid stain) using comparative CT method; endogenous control being 18S. Maximum concentration achieved (Cmax), 2-hour concentrations and AUC $_{0-4}$ (area under curve 0-4 hours) of rifampicin were compared in three genotype by Friedman test.

Results: ABCB1 (C3435T) polymorphism determined in 88 enrolled children showed 57 (64.8%) CT, 2 (2.3%) CC, and 29 (32.9%) TT genotypes. There was no significant difference between 2-hour rifampicin concentrations in the three genotypes (p=0.11). Median (IQR) Cmax was significantly lower in CC genotype [4.33 (3.05, 5.62) μg/mL] followed by TT genotype [8.66 (6.36, 10.9) μg/mL] and maximum in CT genotype [11.6 (7.68, 14.0) μg/mL], p= 0.04. AUC$_{0-4}$ followed the same pattern (p=0.03). Real time PCR was performed in 57 samples; expression of ABCB1 mRNA transcript was not significantly associated with Cmax, AUC$_{0-4}$ and 2-hour rifampicin concentrations.

Conclusions: A significant association between ABCB1 gene (C3435T) polymorphism and plasma concentrations of rifampicin was demonstrated in this study; highest Cmax and AUC$_{0-4}$ of rifampicin were observed in CT (heterozygote) genotype. This association may be explored as a cause of suboptimal rifampicin concentrations.

SOA-355-12 Engaging the community in TB household contact screening improved IPT uptake among child TB contacts aged under 5 years in Uganda

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Background and challenges to implementation: Children,0-4 years living in contact with persons with sputum smear positive TB are at a high risk of TB infection and TB disease. Active screening of child TB contacts and Isoniazid preventive therapy are highly effective in preventing TB in these children. Children under 5 years, irrespective of HIV status and those above 5 years living with HIV; in contact with a smear positive TB case and in whom active TB has been excluded are eligible for IPT. Nationally, only 5.7% of children under 5 years eligible for IPT were started on IPT in 2015/16. Although village health teams (VHTs) are part of the MoH structure, they are not utilized to identify IPT eligible children from the community through contact tracing contributing to the low uptake of IPT. The Union, Uganda implemented the DETECT Child TB project as a pilot to strengthen district health systems in childhood TB case finding and treatment and community health system to improve IPT uptake in Kabarole and Wakiso districts between January 2015 and December 2016.

Intervention or response: VHTs were engaged to do household contact screening, identify and refer children eligible for IPT. An external evaluation conducted after 15 months of implementation showed the following:

Results and lessons learnt: 1,326 households of smear positive TB patients were contact traced, 1839 children screened for TB symptoms and IPT eligibility, 996 of whom were 0-4 years.

78% of children 0-4 years were eligible for IPT, 72% of whom were initiated on IPT compared to the national uptake of 5.7%, with a completion rate of 87%.

Contacts above 5 years did not receive IPT because of unknown HIV status.

Conclusions and key recommendations: Engaging VHTs to do Household contact screening is an effective strategy to improve IPT uptake among under 5 child TB contacts. Access to HIV testing for children above 5 years would further improve IPT uptake.

SOA-356-12 Tuberculosis infection is inversely associated with atopic symptoms in HIV-infected and non-infected South African children

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Background: The potential relationship between *Mycobacterium tuberculosis (M.tb)* infection and atopy is thought to result from *M.tb* eliciting a T-helper 1 immune response, stimulating cytokines to suppress differentiation of T-helper 2 (Th2) cells. The Th2 immune response forms the basis of atopy. Our objective was to measure the association between *M.tb* infection and reported atopic symptoms in children in a high-burden tuberculosis setting.

Methods: 1093 children aged 3 months to 15 years living in urban Cape Town were prospectively investigated through household contact tracing for *M.tb* infection with tuberculin skin testing (TST). Parental reported symptoms of atopy were evaluated 3 and 6 months later using a questionnaire based on the standardized International Study of Asthma and Allergies in Childhood questionnaire.

Results: An inverse association was found overall, between TST positive status (TST+) at enrolment, and reported wheeze at 3 months (OR 0.60, 95% CI 0.40 - 0.88) and at 6 months (OR 0.55, 95% CI 0.35 - 0.85), and eczema at 3 (OR 0.42, 95% CI 0.21 - 0.80) and 6 months (OR 0.51, 95% CI 0.27 - 0.99) in univariable analysis. TST+ at month 3 and reported hay fever at month 3 were also inversely related (OR 0.43, 95% CI 0.20 - 0.93). In multivariable analysis, baseline TST+ was inversely associated with reported wheeze at 6 months, controlling for age, ethnicity, HIV infection and prior tuberculosis (aOR 0.55, 95% CI 0.35 - 0.85). No inverse association was found between baseline TST+ and any reported atopic symptoms in the subgroup of children younger than 2.

Conclusions: We demonstrate a robust inverse association between *M.tb* infection and reported atopic symptoms in African children older than 2 years in a cohort study.

SOA-357-12 Reducing antibiotic prescribing for upper respiratory tract infections in children at primary care facilities in rural China: a clustered RCT

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Background: Inappropriate antibiotic prescribing in primary care contributes to generating drug resistance globally. In China, recent national policies have failed to improve the situation. We designed and evaluated an intervention to reduce antibiotic prescribing for upper respiratory tract infections (URTIs) in children, targeting clinicians and caregivers in primary care facilities in rural China.

Methods: In this cluster randomised controlled trial we randomised (stratified by county) 25 township hospitals to an intervention (12) or control (13) arm by computer program. The intervention included clinician guidelines and training on appropriate prescribing, monthly prescribing peer-review meetings, and brief caregiver education. The control was usual care. The primary outcome was the antibiotic prescribing rate (APR): the proportion of prescriptions for 2-14 years old outpatients diagnosed with URTIs that included antibiotics, given URTIs do not normally need antibiotics. Analyses were by intention-to-treat. Trial registration number: ISRCTN14340536.

Results: We conducted an internal pilot and main trial between 1 July 2015 and 31 March 2016, and collected data from 2351 (out of 135198) and 2552 (out of 101657) randomly selected eligible prescriptions from the intervention and control arms respectively. During the three months before the intervention period the APR was 82.4% (1936/2349) in the intervention arm and 75.4% (1922/2548) in the control arm. At endline the APR was 40.1% (943/2351) in the intervention arm and 69.8% (1782/2552) in the control arm, and after adjustment for potential confounders and baseline APR, the adjusted absolute risk reduction for the APR (intervention versus control) was -29% (95% CI: -44%, -15%; P< 0.001).

Conclusions: The intervention rapidly and substantially reduced inappropriate prescribing of antibiotics for children with URTIs in Chinese rural primary care facilities. As the intervention was well-integrated within routine practice it is likely scalable within China and in similar settings.

SOA-358-12 Accelerating access to quality TB care for paediatric TB cases through a better diagnostic strategy in four major cities of India

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Background and challenges to implementation: Diagnosis of TB in children is challenging and is largely based on positive H/O contact with a TB case, clinical and radiological findings without microbiological confirmation. Diagnostic efforts are undermined by the lack of high sensitivity tests which are simple to use, and can be applied at the point of care. Current project was undertaken in four major cities of India to address TB diagnostic challenges in paediatric population, by offering free of cost Xpert testing to paediatric presumptive TB cases, thereby paving way for better TB care.

Intervention or response: A high through put lab was established in each of the four project cities, and linked to various providers across the city, through rapid specimen transportation and electronic reporting linkages. Free Xpert testing was offered to all pediatric presumptive TB cases (both pulmonary and extra-pulmonary) seeking care at public and private health facilities.

Results and lessons learnt: We enrolled 42,238 pediatric presumptive TB cases from April, 14 to June, 16. A total of 3,340 (7.91%, CI 7.65-8.17) TB cases were detected, of which 295 (8.83%, CI 7.9-9.86) were rifampicin resistant. The level of rifampicin resistance in the project cohort was alarming. Overall detection rates on Xpert were three-fold higher than smear microscopy. Project maintained a rapid turnaround time. Early availability of results led to rapid treatment initiation and success rates and very low failure and default rates.

Conclusions and key recommendations: Project demonstrated the feasibility of rolling out rapid and upfront Xpert testing for pediatric presumptive TB cases. Rapid turnaround testing time in turn facilitated prompt and appropriate treatment initiation showing - upfront Xpert assay is a promising solution to address TB diagnostic challenges in children. High levels of rifampicin resistance detected in pediatric TB cases is a major cause of concern from epidemiological prospective. It also underscores the need to prioritize upfront Xpert access to this vulnerable population.

SOA-359-12 Monocyte-to-lymphocyte ratio is associated with confirmed TB disease and declines with anti-tuberculosis treatment in HIV-infected children

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Background: The blood monocyte-to-lymphocyte ratio (MLR) correlates with active TB among HIV-infected adults but has not been assessed as a biomarker for TB diagnosis among HIV-infected children. We evaluated baseline and longitudinal changes in MLR among HIV-infected children with and without TB disease.
Methods: In a nested cohort of HIV-infected hospitalized children initiating antiretroviral therapy, absolute monocyte and lymphocyte counts were determined at enrollment and 4, 12 and 24 weeks thereafter. All children were assessed for TB by sputum/gastric aspirate culture and gastric aspirate/stool Xpert MTB/RIF, clinical symptoms, TB contact history, tuberculin skin test and chest x-ray. Children were classified as having confirmed TB (positive culture or Xpert MTB/RIF), unconfirmed TB (clinical diagnosis by symptoms, treatment response, radiologic or immunologic evidence) or unlikely TB. Wilcoxon two-sample tests were used to compare continuous variables and general estimating equations were used to estimate change in MLR over time by TB status.
Results: Of 183 children with median age 22 months (IQR 9.73 - 57.27), 14 (7.7%) had confirmed TB, 81 (44.3%) had unconfirmed TB, and 88 (48.1%) were unlikely to have TB. The median MLR among children with confirmed TB (0.43 [IQR 0.38 - 0.67]) was higher than among children with unconfirmed (0.22 [IQR 0.15 - 0.35]) or unlikely TB (0.22 [IQR 0.15 - 0.48], p< 0.01 and p=0.01, respectively). Among children with confirmed TB, median MLR declined by 0.30 over 24 weeks of anti-TB treatment (p=0.02); MLR levels were similar compared to children with unlikely TB by 12 weeks of TB treatment,(p=0.24). Malaria status, weight-for-age and weight-for-height z-scores were not significantly associated with MLR.
Conclusions: The blood MLR distinguished HIV-infected children with microbiologically-confirmed TB from those with unconfirmed or unlikely TB, possibly reflecting bacterial burden. Future studies to evaluate MLR decline as a biomarker of treatment response among patients with confirmed TB may be useful.
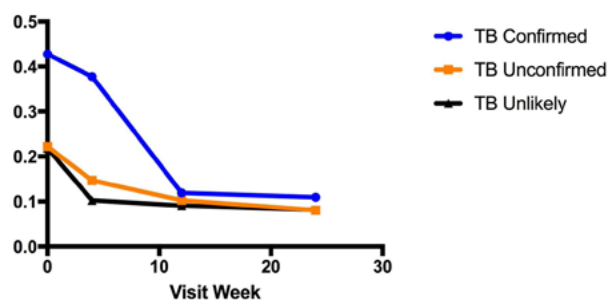
Figure Median blood monocyte-to-lymphocyte ratio over visit weeks from enrollment by TB diagnosis classification (confirmed, unconfirmed or unlikely).

SOA-360-12 Incidence of LTBI and TB disease after 24-month follow-up in paediatric contacts of drug-resistant tuberculosis patients in Armenia

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Background: Prophylaxis for drug-resistant tuberculosis (DR-TB) in paediatric contacts of adult cases is debatable. We measured incidence of latent TB infection (LTBI) and TB disease in a cohort of DR-TB paediatric contacts in Armenia.
Methods: Prospective cohort study. Children < 15 years in regular contact with newly diagnosed DR-TB patients in Armenia were eligible. Clinical exam, chest X-ray, TST, and IGRA were performed at inclusion and during 24-months follow-up. LTBI was defined as TST ≥10 mm or positive IGRA test in asymptomatic contacts with a normal chest X-ray. A child with a decision of TB treatment was considered as having TB disease. No chemoprophylaxis was administered.
Results: From June 2012 to December 2014, 150 children contacts to 78 DR-TB index cases were included. Median age was 6 years and 53% were girls. Prevalence of LTBI at inclusion was 52.7% (95%CI:44.6-60.8), 41.7% (95%CI:28.8-54.5) and 60.0% (95%CI:49.8-70.3) overall, in children aged 0-4 years and in those aged 5-14 years respectively. TB disease was diagnosed at inclusion in 2 children (1.3%, 95%CI:0.0-3.2), both aged less than 1 year. Incidence rate of LTBI was 17.4 (95%CI: 10.8-28.1) new infections/100 person-years. The incidence was 16.1 (95%CI: 8.0-32.1) and 18.9 (95%CI: 9.8-36.3) new infections/100 person-years in children aged 0-4 years and 5-14 years respectively. Being in contact with a smear-positive index case (aOR:5.5, 95%CI:2.5-12.3) was the only factor associated with LTBI at 24 months. No TB disease was diagnosed during follow-up.

Conclusions: Prevalence of LTBI in paediatric contacts of DR-TB patients was high at inclusion. However, incidence of LTBI during 24 months follow-up was low and there were only two cases of TB disease. These findings do not support the indication of DR-TB prophylaxis in this setting. Nevertheless, screening for symptoms of TB disease in child contacts of DR-TB patients is highly recommended, particularly infants and contacts of smear-positive cases.

SOA-361-12 Piloting upfront Xpert® MTB/RIF testing on various specimens for infant presumptive TB cases for early and appropriate treatment initiation

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Background and challenges to implementation: Diagnosis of tuberculosis in infants is challenging due to non-specific clinical presentations, specimen collection challenges and low sensitivity of widely available smear microscopy. Xpert/MTB RIF (Xpert), a highly sensitive and specific rapid diagnostic tool offers a promising solution to address these challenges. Under the current project we attempted to demonstrate the utility and feasibility of applying upfront Xpert for diagnosis of tuberculosis in infants, including testing non-sputum specimen.

Intervention or response: A high throughput lab was established in each of the four project cities, and linked to various providers across the city, through rapid specimen transportation and electronic reporting linkages. Free Xpert testing was offered to all infant presumptive TB cases (both pulmonary and extra-pulmonary) seeking care at public and private health facilities.

Results and lessons learnt: We enrolled 7,994 infant presumptive TB cases in the project from April,14-Oct,16, detecting 465 (5.83%, CI: 5.33-6.37) TB cases. Majority (96.1% (CI: 95.6-96.5) of the patient specimen were non-sputum specimen. Very high TB detection rates were observed on Lymph nodes/tissue, Pus, BAL, GA/GL and CSF. Further, high proportion (5.59% CI 3.76-8.19) of TB cases, were found rifampicin resistant. We demonstrated feasibility of same day diagnosis, which in turn led to prompt treatment initiation. We observed 11.40% (CI 8.82-14.61) case mortality in the project cohort, majority of which were identified as pre or early treatment mortality.

Conclusions and key recommendations: The current project demonstrated the feasibility of applying rapid and upfront Xpert testing for infant presumptive TB cases, including non-sputum specimen. Rapid diagnosis in turn facilitated prompt and appropriate treatment initiation. Project results demonstrate that Xpert assay is a promising solution to address TB diagnostic challenges in infants. Levels of rifampicin resistance observed in infants, highlights the need to further improve access to Xpert for this highly vulnerable population. High rates of early case mortality highlights the need for further research in infant patient pathways.

SOA-362-12 Drug resistance surveillance in children with bacteriologically-confirmed tuberculosis in the Western Cape, South Africa

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Background: To determine the prevalence of drug resistance and HIV co-infection among children with bacteriologically-confirmed tuberculosis (TB) and to compare results with 6 previous surveys.

Methods: Prospective surveillance was done from March 2015 through February 2017 at Tygerberg Hospital, Cape Town, South Africa. Drug-susceptibility testing (DST) was done by line probe assay (GenoType MTBDR*plus*) for isoniazid (INH) and rifampicin (RIF) on one isolate from each child < 13 years with culture-confirmed TB. Further DST was done if resistance was found. Xpert MTB/RIF was done in the majority of cases. HIV status was documented. Data were compared to 6 previous 2-year periods (2003-2015).

Results: 360 children, 198 (55%) boys, with median age 33.5 months (IQR 14.0-78.5 months) had bacteriologically-confirmed TB in period 7 (2015-2017). Comparing period 7 to six previous periods of 2-years each: HIV testing increased from 60% to 99.4% of TB cases, but HIV infection decreased significantly from 29% (period 3) to 10.0% (period 7), OR 0.27 (95% CI 0.17-0.43). Of the recent 360 children, 302 (83.9%) were culture-positive and 58 (16.1%) only Xpert-positive. Total RIF resistance by LPA/culture has increased from 17/313 (5.4%) in period 1 (2003-2005) to 33/302 (10.9%) in period 7 (OR 2.14 95% CI 1.16-3.92; p=0.019). Total INH resistance 40/313 (12.8%) in period 1 vs 38/302 (12.6%) in period 7 has been stable. Of the 27/302 (8.9%) multidrug-resistant cases, 11 (41%) had ofloxacin resistance and 4 (15%) amikacin resistance - all 4 had extensively drug-resistant TB. Of the 58 Xpert-positive cases, half were already on TB treatment, 25 (43%) had extrapulmonary TB and 14 (24%) were bronchoalveolar lavage specimens. Only 1/58 had RIF resistance, which was false resistance.

Conclusions: Rates of total drug resistance has remained stable, but RIF resistance is increasing. The high rate of fluoroquinolone resistance has important implications for treatment and chemoprophylaxis.

07. National and subnational strategic approaches to TB elimination

SOA-363-12 Quantifying the impact of sustainable development goal 1 on TB: a statistical exploration

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Background: The WHO's post-2015 End TB strategy is intimately linked with the UN's sustainable development goals (SDGs) in both targets set and programmatic actions. This provides an opportunity to quantify how reaching the SDG targets can accelerate our progress towards TB elimination. We focus on generating evidence to support the statistical modelling of SDG1: ending poverty.
Methods: TB-relevant and SDG1-relevant data from UN Stats' SDG repository was extracted for 192 nations. We constructed a conceptual framework linking the SDG1 subtargets (ending extreme poverty, halving multidimensional poverty, social protection coverage for all) to TB incidence via four TB risk factors (malnutrition, health behaviour, HIV, housing quality), using theoretical and data-driven approaches. Linear models based on the conceptual framework were run to determine the strength of the association between the SDG1 subtargets and TB incidence.
Results: There is a strong association between SDG1 subtargets and TB incidence. The estimated decline in incident TB cases per 100,000 per year is 3.59 (95%CIs: 2.54-4.65) for a 1% reduction in extreme poverty prevalence and 2.52 (95%CIs: 1.48-3.57) for a 1% reduction in multidimensional poverty. Expanding social insurance coverage by 1% gives an expected decline of 3.52 (95%CIs: 2.60-4.44), and expanding social assistance coverage by 1% gives a decline of 1.27 (95%CIs: 0.26-2.28). Adjusted linear models and a simple assessment for mediation suggested that the direct effect of these SDG1 subtargets could be partitioned into four indirect effects via the TB risk factors, which also capture any effect of income.
Conclusions: These analyses highlight the strength of the association between TB and poverty and show a potential path to modelling the impact of achieving the SDG1 goals on TB incidence. The epidemiological evidence generated suggests that poverty reduction and expansion of social protection programmes have the potential to substantially decrease the global burden of TB via major risk factor pathways.

SOA-364-12 Programmatic implications of the Uganda National TB Prevalence Survey, 2015

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Background: Uganda National Tuberculosis Program (NTLP) conducted a National population based TB Prevalence Survey to determine prevalence of bacteriologically confirmed (BC) pulmonary TB (PTB) among persons aged >15 years. The goal was to establish Uganda's TB burden and inform control strategies. TB prevalence was 253/100,000 compared to the estimated 159/100,000; hence about 40,000 TB patients are missed every year. TB prevalence was 4 times higher (734/100,000) among males compared to females (178/100,000), prevalence was higher in urban (504/100,000) compared to rural areas (370/100,000). Prevalence among HIV negative persons was 261/100,000 compared to HIV positive persons (96/100,000). Symptom screening recommended by NTLP/WHO identified only 45% (30/66) smear positive TB, addition of chest X-ray identified more case-patients (81/160), including asymptomatic TB patients. The survey identified 160 BC TB patients, smear microscopy identified 41% (66/160) only; others were identified through Xpert/MTB/Rif, culture or both. 37% of BC TB patients first sought care from private health facilities. The findings necessitated development of new strategies for tackling the epidemic as per the 'End TB' strategy.
Methods: A consultative approach involving officials from NTLP, WHO, and US CDC; Makerere University, USAID, was taken with the aim of generating programmatic implications based upon the findings.
Results: Revision of the National TB Strategic Plan was undertaken with the following strategies; TB diagnostic algorithm revised and Xpert/MTB/Rif adopted as the initial diagnostic test for all presumptive TB case-patients. Chest X-ray introduced as a screening for high risk TB patients including males. Community mobilization for TB services with aim of demand creation and strengthening collaboration with the private sector for TB diagnosis and treatment were recommended. Strengthening TB/HIV collaborative services and revamping the operations research arm of NTLP is required.
Conclusions: These findings presented an opportunity for NTLP and stakeholders to refine approaches to the TB epidemic in Uganda based on evidence based recommendations.

SOA-365-12 Many national TB programmes are out of step with international recommendations for testing, treatment and prevention: results of a 30-country survey

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Background and challenges to implementation: A major leap in political will and resourcing is required to reach the Sustainable Development Goal target of ending tuberculosis (TB) by 2030. One essential step is to adopt and implement internationally accepted diagnostic, treatment and prevention guidelines at national level. To assess whether national guidelines reflect World Health Organisation (WHO) recommendations, we conducted an in-depth survey in 30 high TB burden countries.

Intervention or response: A semi-structured questionnaire surveyed the status of national TB guidelines in six key areas: diagnostics, prevention, models of care, drug-sensitive (DS) and drug-resistant (DR) TB treatment regimens and drug regulatory environment. Questionnaire responses were derived and compiled from national policy documents. Responses were validated, either by Médecins Sans Frontières staff where present at country level, or by National TB Programme representatives, based on national guidelines in place up until March 2017.

Results and lessons learnt: The survey shows that more than half of the countries' guidelines recommend optimal versions of treatment, whether bedaquiline or delamanid, for multi-drug resistant (MDR) TB. However, less than a third of countries allow for the use of the 9-month MDR-TB treatment regimen, and less than a third recommend the new paediatric TB fixed-dose combination for DS-TB. The majority of countries in Eastern Europe and Central Asia don't initiate DR-TB treatment in ambulatory care. Roughly half of countries have yet to recommend Xpert MTB/RIF as the initial TB diagnostic test for suspected cases. There is an under-utilisation of mechanisms to facilitate access to new drugs, including compassionate use. Less than half of countries have enrolled in the WHO Collaborative Registration Procedure.

Conclusions and key recommendations: WHO guidelines represent best-practice recommendations. National adoption and implementation of these recommendations is critical to accelerate access to new tools and models of care. This requires significant and sustained domestic financing and commitment without which the global target to end TB will remain out of reach.

SOA-366-12 The use of sub-national TB modelling to inform decision making in South Africa

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Background and challenges to implementation: South Africa has one of the highest rates of tuberculosis (TB) in the world, and the disease is country's leading cause of death. TB control activities are driven primarily at the provincial level, making the availability of a sub-national planning tool highly valuable. South Africa has been instrumental in establishing 90-90-90 targets of the Global Plan to End TB, which, if achieved, may have significant impact on the TB epidemic as suggested by modelling. We describe the application of a TB transmission model at sub-national level, and its use in estimating the impact of achieving 90-90-90 targets on TB incidence and mortality.

Intervention or response: "TIME Impact" is an epidemiological transmission model nested in TIME, a set of freely available TB modelling tools within the widely-used Spectrum software. TIME uses TB programme performance indicators and automatically incorporates UNAIDS estimates of HIV burden. With input from provincial TB experts and the South African National TB Programme, baseline models for three (of nine) South African provinces were calibrated to TB case notifications, TB incidence and screening data. Using these baseline models, the impact of scale-up of interventions focusing on screening, linkage to care and treatment success was estimated.

Results and lessons learnt: The provincial models reflected the observed national trend of decreasing TB incidence and mortality in recent years. Scale-up of all interventions showed the greatest impact with the impact of individual interventions being greatly influenced by current levels of implementation. The absence of sub-national TB burden estimates necessitated deriving estimates from national WHO estimates. This has served to raise concerns around sub-national data quality and gaps e.g. case notifications and TB deaths through vital registrations.

Conclusions and key recommendations: Applying a user-friendly modelling tool allows sub-national impact estimates to be estimated. This may be a useful tool to prioritise TB control interventions, focus attention on critical data gaps and inform provincial decision-making.

SOA-367-12 Landscape assessment of TB program infrastructure for subnationally differentiated TB programme planning in 10 South and South-East Asian countries

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Background: Approximately one-third of the estimated 10.4 million incident TB cases are not reached every year. In recognition of this, The Stop TB Partnership and The Global Fund are leading a joint initiative to strengthen the analysis and spatial mapping of subnational data to promote locally tailored decision-making by TB programs.
Methods: A landscape assessment questionnaire was distributed to thirteen South and Southeast Asian countries evaluating access and availability of National Tuberculosis Program data at local administrative levels, data flow processes, and the current use of subnational TB data and maps for planning.
Results: Seven of ten responding countries reported electronic TB data entry at the district or sub-district level, of which three could readily supply notification, laboratory and treatment outcome data at the corresponding levels in response to follow-up data requests. Five countries reported case-based electronic data entry, with the remainder reporting aggregated data entry at the district or sub-district level followed by electronically entering aggregated data at the provincial or national level. Minimal integration with other electronic health data management systems was reported (n = 4 countries) however only for selected programs (lab n = 3, pharmacy n = 2, private sector n = 4, HIV program n = 3). Only one country reported use of maps to analyze program data, although three indicated interest to do so in the future.
Conclusions: Results of the landscape assessment highlighted the abundance of locally available but centrally uncollated subnational notification, laboratory and treatment outcome data, as well as the widespread lack of its accessibility and application to inform local decision-making. Concerted efforts are needed to improve the collation, mapping and use of subnational TB data to provide evidence and support for locally tailored approaches to improve TB case detection and reach those who are not reached.

SOA-368-12 Setting the national tuberculosis research agenda: the experience of Ethiopia

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Background and challenges to implementation: The third pillar of the Global End TB strategy underscores the role of research and innovations. Particularly countries devastated by TB require substantial expansion of TB-related research. WHO designated Ethiopia as one of the few model countries that already have substantial TB research networking and capacity. Furthermore, it highlighted the importance of the existing TB Research Advisory Committee (TRAC) of the Ministry of Health, which has been working closely with National TB Program over the last 15 years. Within this framework, a comprehensive list of prioritized national TB research plan was developed and endorsed early in 2017.
Intervention or response: Setting the national TB research agenda employed multi-stakeholder consultations, and extensively used the guidance of the WHO toolkit through establishment of a technical committee to coordinate and lead the process. In November 2016, consultative workshop was held to identify TB research priority questions in four thematic areas: epidemiology, clinical and basic, operational, and health system, which were ranked based on predefined criteria into high, medium, or lower priority.
Results and lessons learnt: A total of 56 prioritized TB research questions were identified: epidemiological 8 (14%), clinical and basic 16 (29%), operational 15 (27%), and health system researches 17 (30%). In addition, based on the ranking done during the consultative workshop, 23 (41%) falls under high priority (all above average scores, for respective thematic category); 21 (37.5%) medium priority (around the average); and 12 (21%) of the research questions were categorized as lower priority (below average).
Conclusions and key recommendations: The prioritized national TB research questions will indicate and guide all individuals and stakeholder on the current TB research agenda to promote evidence-based policy, programming and practice to end TB as a public health problem in Ethiopia. TRAC, a TB research networking mechanism, is playing a key role in driving the TB research agenda in Ethiopia.

SOA-369-12 Ending tuberculosis in Israel: current progress and future challenges

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Background and challenges to implementation: Israel's National TB Program (NTP), established in 1997, has a two-pronged strategy for handling TB: an elimination program for the native population and a control program for immigrants originating from moderate and high TB endemic countries. Israel was invited to the 2015 WHO-TB elimination meeting, as one of the 33 pre-elimination phase countries. Israel's TB notification rate in 2012 was 6.2 per 100,000 population, and WHO estimated Israel would require an 18% annual rate of decline to reach elimination by 2035. Among the 33 countries, Israel had the highest proportion of foreign-born TB notified cases (90%). We present Israel's current progress and future challenges towards TB elimination.

Intervention or response: Many of the WHO-End TB strategy components have already been incorporated into the NTP (described elsewhere) at an earlier stage.

Results and lessons learnt: The declines in TB incidence (per 100,000 population) have been observed between 2012 to 2015 as follows: 1) overall TB notification rate - from 6.2 to 3.3 (a 46.8% decline from 2012); 2) native-born - from 1 to 0.88; 3) foreign-born population - from 9.4 to 6.7. Cumulative TB rates among new immigrants from Ethiopia and from Former Soviet Union (FSU) were analyzed by a 5 years cohort (1999-2013), and showed the following declines: 1) for Ethiopian immigrants - from 310.0 to 51.7; 2) for FSU - from 151.1 to 27.5.

In order to reach TB elimination by 2035, it is imperative for Israel to maintain its political commitment and infrastructure, with adequate resources for TB care and prevention, including the provision of new drug regimen generations. Lastly, eliminating TB among foreign-born population will depend on immigration patterns.

Conclusions and key recommendations: Israel is probably on the right path for TB elimination. However, we heavily depend on migration changes and on continuing the integrity of the NTP despite a declining case load.

SOA-370-12 Is it possible to achieve the end of tuberculosis in Colombia?

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Background: Antioquia State has the highest burden of tuberculosis (TB) in Colombia. The incidence in 2016 was 40 cases/100,000 inhabitants (2,225 cases), and has not decline in the last 10 years (range 30-40/100,000).

The respiratory symptoms (RS) screening for active TB is 2%, meaning that the goal of 5% is far from achieving, and the cure rate is 73%. The objective was to model the TB rates in Antioquia with the actual data of screening and curation of TB disease, and if the WHO goal of zero TB cases is doable.

Methods: We used the data of Antioquia over the last 10 years. Dynamic systems analysis was conducted in Vensim 6.2. The information to construct the model were: 1) the general population projected for 2016 by Administrative Department of National Statistics, 2) the harmonic mean of the TB rates for the last 10 years, and 3) the mortality rate of general population. As variables that affect the screening, the rate of HIV, the rate of screening for active TB in general population and prisoners were used. As variables that affect active TB rate, people with RS smear positive, the rate of cure, death, and abandonment were used

Results: If Antioquia continues with the same rate of symptoms screening and the cure rate, in 2050 there will be more than 10,000 cases/per-year. If we achieve the goal to screen for active TB 5% of people with RS, and increase the cure rate in 1% every year, the TB cases will increase up to 10,000 in 2022, and then will decrease almost to zero in 2050.

Conclusions: The goal of WHO to decrease the numbers of TB cases to zero is doable, but it is necessary to increase the number of people screened for active TB and to increase the cure rate.

SOA-371-12 Size and characteristics of the tuberculosis drug market in ten high-burden countries

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Background: Middle income countries are home to most tuberculosis cases but their markets are poorly understood. Previous studies have examined segments of the TB market in diverse settings, however, there has yet to be a systematic assessment of the aggregate public and private sector markets.

Methods: Using public sector procurement data and 2015 IMS Health data and, public and private TB drug markets in ten high burden, middle income countries, representing 63% of the global burden, were analyzed.

Results: The combined value of the public and private markets across these countries was roughly $530 million. The aggregate volume of first-line drug sales was enough to treat almost all incident cases globally. The public sector accounted for 47% of first-line drug volume and 50% of first-line value. Private markets dominated volume and value in three settings, China, India and Indonesia. Despite representing less than 2% of notified treatment cases across countries, second-line TB

drugs, on average, absorbed 39% of public sector procurement budgets. In 2015, the price ranged from $16-$109 for drug-sensitive treatment, and $1000-$17,000 for drug-resistant treatment. Diversity of drug strengths and formulations was high for loose drugs and FDCs, with a cross-country average of 41 different formulations of first-line drugs per country (a range of 10-104) and with many forms diverging from WHO and NTP recommendations.

Conclusions: The size of the aggregate TB drug market in these 10 countries dramatically exceeded reported treatment and incidence numbers. The high cost of second-line treatment and the lack of market consolidation around optimized regimens present challenges in mounting an effective response to the TB epidemic.

SOA-372-12 Implementing an early warning system to improve access to TB medicines in 12 countries

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Background and challenges to implementation: Successful treatment of TB requires continuous availability of medicines. National TB programs (NTPs) in limited-resource settings face problems of overstocking, expiry, and stock-outs of medicines. Cost-effective and sustainable early warning systems (EWSs) are needed to detect problems and take timely actions to address supply chain system gaps.

Intervention or response: The USAID-funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program developed and supported 12 countries to implement an EWS for TB commodities. SIAPS capacitated country staff to use the EWS to monitor stocks and identify and take action to prevent expiries and stock-outs. The intervention was evaluated through documents review, interviews with in-country EWS users, NTP decision-makers, and online surveys of country beneficiaries and global partners.

Results and lessons learnt:
- EWS was adopted and institutionalized by 10 countries, resulting in improved data quality, reporting, and information system
- Highly rated in all 12 countries and used by global TB partners for funding applications, monitoring missions, sharing information, and addressing problems with stakeholders
- Built capacity of >250 staff from 15 countries for more vigilant stock monitoring
- EWS data informed timely, evidence-based decisions for emergency procurement, order rescheduling or cancellation, and redistribution of excess stock, resulting in savings: Bangladesh USD 900,000; Ethiopia, Nigeria, Tanzania, Kenya, Zimbabwe altogether >USD 8.5m; Tajikistan USD 1,165,000

- Percentage of countries with stock-outs of first-line drugs decreased four-fold and second-line drugs decreased to below half, between 2014 to 2016
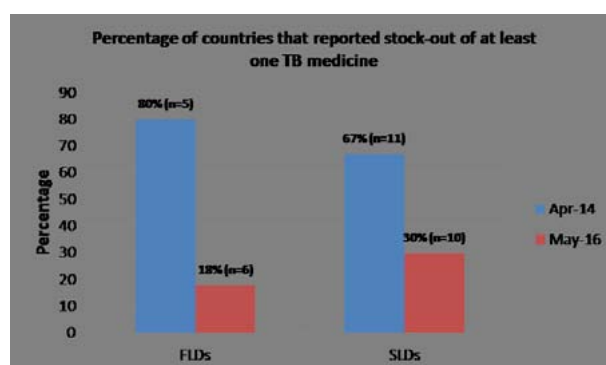
Figure Trend of stock-outs

- Use of graphs and dashboards simplified results, improved user-friendliness, and enhanced understanding of the EWS
- Availability of data motivated TB stakeholders to communicate and collaborate in decision-making and remedial actions

Conclusions and key recommendations: EWS improved stock monitoring and prevented expiry and stock-outs of TB medicines through a locally led, sustainable system, resulting in stronger supply chain systems. However, continued investment is needed to address remaining gaps. Therefore stakeholders should continue to collaborate to sustain implementation of QuanTB/EWS.

SOA-373-12 Implementing collaborative, consensus-based forecasting to improve access to TB medicines in Nigeria

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Background and challenges to implementation: Successful treatment of TB requires continuous access to medicines. National TB programs (NTPs) in low-resource settings have inadequate capacity and tools to prevent stock-outs by properly forecasting and planning shipments of essential TB commodities. Cost-effective and sustainable forecasting and supply planning (SP) tools are needed to close this important gap.

Intervention or response: The USAID-funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program provided direct technical assistance to 12 countries, including Nigeria, to improve forecasting and SP of TB commodities through use of QuanTB tool. SIAPS advocated for NTP buy-in and leadership, and multi-stakeholder collaboration in implementing the tool. Results were evaluated through documents review, interviews with in-country users, NTP decision-makers, and online surveys of country beneficiaries and global partners.

Results and lessons learnt:
- NTP adopted, institutionalized, and capacitated over 25 stakeholders to implement QuanTB, resulting in improved data-based forecasting, SP and strengthened supply chain systems
- QuanTB was well received and used in forecasting needs for funding gap analysis, funding applications, procurement, supply and distribution planning, rescheduling GDF orders to prevent stock-outs or expiries, and introducing new medicines.
- NTP and stakeholder coordination and collaboration improved
- No stock-out of TB first line and second line TB drugs at treatment centers, and minimal stock-outs at central level between September 2014 and December 2016.
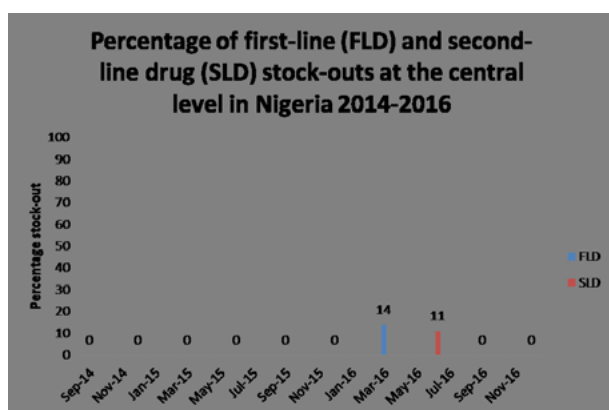
Figure TB medicines stock-out trend

Lessons learned:
- Advocacy, local leadership, capacity building, stakeholder collaboration, integration with existing systems, timely reporting, and updating QuanTB with quality data were key for success
- Ongoing capacity-building refresher trainings help to address the adverse impact of staff attrition
- In-country IT capacity-building crucial to readily address software problems as needed
- Improve data quality and reporting from the periphery when updating QuanTB.

Conclusions and key recommendations: Institutionalization and implementation of QuanTB as the national forecasting and SP tool through a locally led, effective, and sustainable approach has improved forecasting, prevented stock-outs, and increased access to TB medicines.

08. Identifying factors to reach the 90-90-90 goals

SOA-374-12 Tuberculosis patients from outside Kampala city carry a higher risk of unfavorable treatment outcomes

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Background: Poor adherence to treatment is a major obstacle to achieving favorable TB treatment outcomes. In Kampala city, possible reasons for patients' failure to adhere to treatment include challenges associated with physical accessibility to TB services. We looked to assess the contribution of other districts towards the unfavorable treatment outcomes in Kampala.

Methods: We retrospectively reviewed 5,732 records of patients with a documented home location who were registered for treatment in 2014 and 2015 in Kampala. We used mantel-hanzel analysis to establish whether there was an association between home location (patient living in Kampala or outside Kampala) and treatment outcomes.

Results: Of the 5,732 patient records reviewed, 1,776 (31%) of the patients were documented to have come from other districts other than Kampala. The mean age of all patients was 30.6 (SD13.9) years. Patients from outside Kampala were more likely to be extrapulmonary TB patients (OR 1.6, CI 1.3-1.9, p=0.000), and clinically diagnosed (OR 1.4 CI 1.2-1.6, p=0.000), they were more likely to die during treatment, (OR 1.6, CI 1.3-1.9, P=0.000), less likely to complete treatment (OR 0.9, CI 0.8-1.0, p=0.06), had a higher risk of HIV (OR 1.3, CI 1.2-1.4, p=0.000), and were more likely to die while on TB treatment, (OR 1.5, CI 1.3-1.9, P=0.000) compared to HIV-positive TB counterparts from Kampala.

Conclusions: Patients initiating TB treatment in Kampala from other districts are more likely to have unfavorable treatment outcomes. They are also more likely to be HIV-positive, which carries a higher risk of death. These findings could be attributed to referrals of complicated TB patients for expert management in referral hospitals concentrated in the city. Further studies to better understand causal factors for these findings are recommended.

SOA-375-12 Effect of HIV status and antiretroviral treatment on treatment outcomes of tuberculosis patients in a rural primary healthcare clinic in South Africa

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Background: Tuberculosis (TB) remains the leading cause of death among human immunodeficiency virus (HIV) infected individuals in South Africa. Despite the implementation of HIV/TB integration services at primary healthcare facility level, the effect of HIV on TB treatment outcomes has not been well investigated. To provide evidence base for TB treatment outcome improvement to meet End TB Strategy goal, we assessed the effect of HIV status on treatment outcomes of TB patients at rural clinic in the Ugu Health District, South Africa.
Methods: We reviewed medical records involving a cohort of 508 TB patients registered for treatment between 1 January 2013 and 31 December 2015 at rural public sector clinic in KwaZulu-Natal. Data were abstracted from National TB Programme clinic cards and the TB case registers routinely maintained at study sites. The effect of HIV status on TB treatment outcomes was determined using multinomial logistic regression.
Results: A total of 506 patients were included in the analysis. Majority of the patients (88%) were new TB cases, 70% had pulmonary TB and 59% were co-infected with HIV. Most of HIV positive patients were on antiretroviral therapy (ART) (90% (n=268)). About 82% had successful treatment outcome (cured 39.1% (n=198) and completed treatment (42.9% (n=217)), 7% (n=39) died 0.6% (n=3) failed treatment, 3.9% (n=20) defaulted treatment and the rest (6.6% (n=33)) were transferred out of the facility. Using completed treatment as reference, HIV positive patients not on ART relative to negative patients were more likely to have unsuccessful outcomes [RRR, 5.41; 95% CI, 2.11-13.86].
Conclusions: Treatment cure rate is below district and provincial targets at this facility. Despite high HIV positive patients on ART, HIV status is a strong predictor of the unfavourable TB treatment outcomes.

SOA-376-12 Revised estimate of TB mortality in England and Wales: the need to use both vital registration and national surveillance data

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Background: An accurate estimate of TB mortality is required to monitor progress towards the End TB Strategy goal of a 95% reduction in TB deaths from 2015 to 2035. The aim of this analysis was to categorise deaths compiled from Office of National Statistics (ONS) and the national surveillance Enhanced Tuberculosis System (ETS) in order to produce revised mortality estimates.
Methods: Deaths that occurred between 2005 and 2015 in England and Wales were identified from ONS records (ICD-10 A16-A19 and B90*) and ETS. TB cases notified in ETS were probabilistically matched to ONS deaths (ICD-10 A16-19). Data from text on death certificates and data collected in ETS were used to categorise deaths into those due to active TB, to sequellae, where TB was incidental and those without TB. Separate mortality estimates were calculated for active TB and for TB sequellae.
Results: In England and Wales, 9,267 deaths were identified in ETS and ONS between 2005 and 2015. 64.3% (5,956) were classified as deaths where active TB caused or contributed to the death, 22.6% (2,094) were deaths due to TB sequellae, 6.0% were deaths where TB was incidental and 7.2% did not have TB. We estimate that mortality due to active TB decreased between 2005 (1.17/100,000) and 2015 (0.72/100,000) by 38% (Figure 1). In contrast, mortality due to TB sequellae remained stable (0.31/100,000 in 2015).
Conclusions: To accurately estimate TB mortality, information from both ONS and ETS are required as the data differ significantly between systems. At least 30% of TB deaths recorded by ONS as ICD-10 A16-A19 are not active TB deaths. Combining active and sequellae deaths to estimate mortality (as is now done by WHO to calculate global estimates) masks the decrease in mortality due to active TB and may not be the best measure to assess short term progress in TB control.

SOA-377-12 Long-term mortality among patients with tuberculosis is high in both patients with drug sensitive and multi-drug resistant tuberculosis

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Background: Tuberculosis is the leading cause of death from infectious disease worldwide with morbidity and mortality inequitably affecting poorer people. We aimed to evaluate long-term, all-cause mortality and characterise its predictors among patients with tuberculosis and their household contacts in Callao, Peru.
Methods: Between 2002-2006 we recruited 708 patients with laboratory confirmed, pulmonary tuberculosis and their healthy 1,987 household contacts aged >=15 years. All patients were invited to give a sputum sample at recruitment and completed questionnaires every 2-4 weeks throughout treatment characterising tuberculosis-related costs. We visited households every four years until February 2016 to ascertain mortality and cause of death. Mortality rates per 1000 person-years were calculated and factors associated with mortality were investigated using Cox-regression.
Results: The median age among patients was 27 years and 60% were male. 78/708 (12%) had multi-drug resistant tuberculosis. 576/708 (81%) were cured or completed treatment. Patients and their contacts were followed for a median of 11 years (interquartile range: 10-12) during which 90 patients (mortality rate [MR]=13/1000) and 58 contacts (MR=2.9/1000) died. Mortality was high among both patients with drug-sensitive (MR=11/1000) and especially multi-drug resistant tuberculosis (MR=30/1000) (Figure). Patients who incurred tuberculosis-related catastrophic costs (>=20% of annual income) had higher mortality those who didn't (MR=17/1000 person-years versus 9.8/1000 person-years, hazard ratio=1.7; p=0.01). Other factors associated with long-term mortality among patients included incomplete schooling; age; previous tuberculosis; baseline comorbidities; underweight; and incomplete tuberculosis treatment (all p< 0.05 in Cox-regression).
Conclusions: Long-term mortality among patients with tuberculosis was high and associated with several markers of vulnerability, including incurring tuberculosis-related catastrophic costs. Although mortality was strikingly high among patients with multi-drug resistant tuberculosis, especially during treatment, we also observed a high mortality rate among patients with drug-sensitive tuberculosis. These data highlight the need for comprehensive, long-term care plans for patients with tuberculosis.
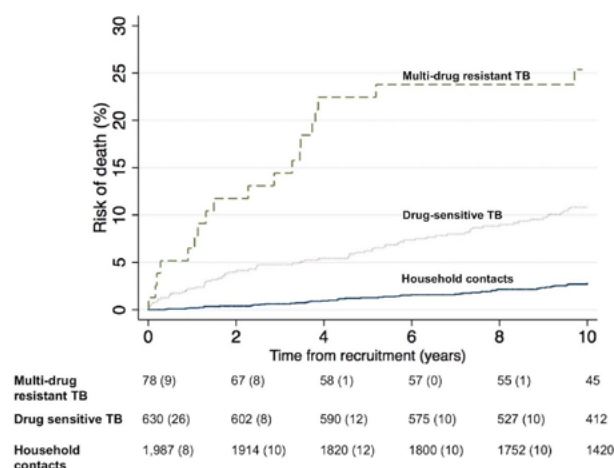
Figure Cumulative risk of death among participants

Multi-drug resistant TB	78 (9)	67 (8)	58 (1)	57 (0)	55 (1)	45
Drug sensitive TB	630 (26)	602 (8)	590 (12)	575 (10)	527 (10)	412
Household contacts	1,987 (8)	1914 (10)	1820 (12)	1800 (10)	1752 (10)	1420

SOA-378-12 Burden of tuberculosis, 1990-2016: findings from the Global Burden of Disease 2016 study

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Background: Increasing development assistance for health to battle tuberculosis (TB) in recent decades led to improved treatment outcomes and decreased mortality. It remains unclear how these advances impacted TB incidence and how TB incidence trends varied between countries and regions. We examined all available cause of death data, case notification reports, TB prevalence surveys, and population-based surveys of latent TB infection to produce internally consistent estimates of annual TB burden from 1990-2016 for 195 countries and territories.
Methods: We analyzed 16,176 site-years of vital registration data and 1,717 site-years of verbal autopsy data, using the Cause of Death Ensemble model to estimate TB mortality rates. We analyzed all available age and sex-specific data sources including annual case notifications, TB prevalence surveys, latent TB infection surveys and estimated TB cause-specific mortality to generate consistent estimates of incidence, prevalence, and mortality using DisMod-MR 2.1, a Bayesian meta-regression tool.
Results: Global TB incidence was stagnant at about 10.2 million per year over the past decade, after a steady increase from 9.8 million (95% uncertainty interval (UI) 8.4-11.5) in 1990 to 10.7 million (UI 9.2-12.7) in 2000. TB mortality declined steadily, from 2.0 million deaths (UI 1.9-2.2) in 2005 to 1.5 million deaths (UI 1.4-1.7) in 2016. There were substantial between-country varia-

tions in the trends of TB mortality and morbidity rates. TB mortality declined in most countries, but the decrease in TB incidence rates was much slower in a number of countries.

Conclusions: Despite progress in reducing TB mortality, TB still causes an enormous disease burden globally. Our results showed slow progress in reducing TB incidence, which when coupled with the recent stagnant growth in development assistance for health for TB, could pose a challenge on health systems to achieve the Sustainable Development Goal target of ending the TB epidemic by 2030.

SOA-379-12 Understanding tuberculosis health system performance in Indonesia through subnational incidence estimation for 514 districts

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Background and challenges to implementation: Indonesia has a population of 258 million and one of the highest TB burdens in the world, with substantial heterogeneity across the country. While there is a National TB Program (NTP), decisions on funding and implementation of the TB program are decentralised to the 514 District Health Offices. An estimate of subnational TB burden for each district is critical to enable an understanding of district-level TB health system performance as well as advocacy and planning of local NTP interventions.

Intervention or response: As part of engagement between national, provincial and district-level health authorities we created a simple model to distribute regional level burden through a weighted score for each of the 514 districts. Variables in the model should be available for all districts, and have a clear relationship with TB burden. The final model included population size, level of urbanisation, and socio-economic indicators (living floor space and high school completion). Multivariate relationships between those variables and TB incidence was obtained through analysis of the national TB prevalence survey. The estimated TB burden was compared to reported notifications to estimate a case detection rate (CDR) for each district.

Results and lessons learnt: Results estimated a district-level TB incidence between 278 and 704/100,000/year. The CDR distribution across the 514 districts in Indonesia is shown in Figure 1. The detailed area shows

the estimated CDR for neighbouring districts, with occasional highly contrasting values. During discussions of findings with district and provincial health offices, it was suggested these were due to cross-district health service utilisation.

Conclusions and key recommendations: Our results highlight the value of subnational estimates to stimulate within and between-district communication about TB burden and care. In addition, our simple approach enables understanding, ownership and acceptance among the sub-national TB policy makers. As more data become available, the model will be strengthened further.
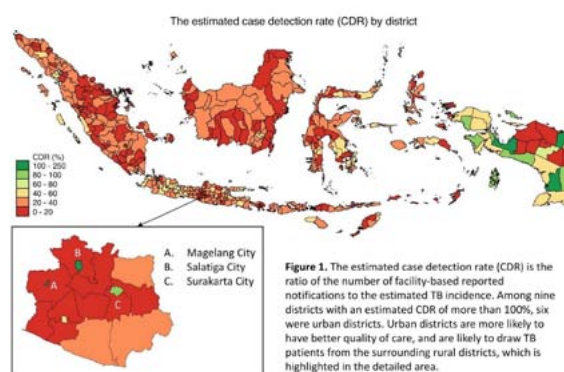
Figure Estimated Case Detection Rate in 514 districts

SOA-380-12 Análisis de la letalidad por tuberculosis en Uruguay, periodo 2014 - 2015

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Background: Uruguay presenta un grave problema de Salud Pública, resultado del aumento constante en el número de casos de Tuberculosis, junto con una alarmante letalidad.

Es objetivo de este estudio, caracterizar la población de fallecidos por tuberculosis en Uruguay, 2014-2015.

Methods: Estudio descriptivo transversal que incluyó el total de fallecidos por TB en Uruguay en el periodo. Fuente de datos secundaria, Programa Nacional de Control de la Tuberculosis.

Results: El bienio registró 241 fallecidos, letalidad de 13,7%, con confirmación bacteriológica en el 65,1% de los casos. El análisis mostró que el 72,6% eran hombres, y que el 66,8% de los fallecidos eran menores de 65 años. Coinfección TB VIH se presentó en el 37,2% de los casos. La presentación clínica más frecuente fue pulmonar, 202 casos (83,8%), hubo confirmación bacteriológica en el 68,4%. La TB extra pulmonar sumó 39 casos (16,2%), y su frecuencia fue independiente de la condición VIH del paciente. Del total de fallecidos, el 89,2% eran casos

nuevos y el 29% falleció antes de iniciar tratamiento anti TB. El análisis sociodemográfico mostró que el 62,7% vivía en Montevideo y que el 70,2% de los fallecidos fue asistido por el Prestador Público de Salud.

Conclusions: El Banco Mundial destaca Uruguay por ser un país de renta alta, bajo nivel de desigualdad y pobreza y por la ausencia casi total de indigencia. Además, cuenta con un sistema de salud gratuito y universal. Estas característica país hacen que la letalidad sea inamisible y alarmante, superando en 10% el valor estimado. El análisis focaliza el problema en población vulnerable, 70% prestador público, de las grandes ciudades, 62% en la Capital.

Por último, Uruguay se encuentra en fase avanzada de su transición demográfica, alarma que más del 65% de los fallecido por TB sean menores de 65 años, configurando una muerte precoz para nuestro país.

SOA-381-12 Exploring quality of tuberculosis surveillance data in Afghanistan: a cross-sectional study

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Background and challenges to implementation: Tuberculosis (TB) data are vital to adequately monitor performance, plan programs and projects, make strategic decisions, direct resources, and evaluate programs for improved TB control. Since 2009, USAID-funded projects assisting Afghanistan's National TB Program (NTP) strengthen the nation's TB surveillance system and data quality. The aim of this assessment was to determine the effects of TB surveillance system strengthening initiatives on national TB data quality.

Intervention or response: From November 2012 to Jan 2013 Staff from the NTP and TB CARE I conducted a cross sectional study among 61 health facilities in 14 provinces. (DF=1; total health facilities 442; frequency of outcome24% and CI 95%). Data collection tools include NTP reporting forms and a standard questionnaire. The team reviewed documents to assess five dimensions of TB data, trace reported TB cases for verification, and cross-check reported cases with past records.

Results and lessons learnt: The data accuracy for two strategic indicators of TB, all form and sputum smear positive TB cases had the accuracy of 97.5% (table 01). In summary, data quality improved by 5% (from 76% in 2008 to 81% in 2012). Mean score for all five data quality dimensions was 80.1% with 71% validity, 80% reliability, 89.8% system integrity, 90.2% precision and 73.7% timeliness.

Variables	Reported cases	Verified cases	Accuracy
All forms TB cases	3,348	3262	97.4%
New sputum smear positive	1,387	1,358	97.9%
Presumptive TB cases examined	16,771	16,363	97.6%
Presumptive TB cases with smear positive results	1,424	1,354	95%

Table Data quality of tuberculosis case registration

Conclusions and key recommendations: Study results showed that TB data quality has been improving in Afghanistan, but more needs to be done. Afghanistan's NTP and its partners should focus on all data quality dimensions particularly validity/accuracy, reliability, and timeliness We strongly recommend implementation of electronic data reporting and training of frontline health staff on recording and reporting.

SOA-382-12 Why does a high proportion of *Mycobacterium tuberculosis* transmission occur outside households and known social contacts in high-incidence settings?

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Background: We currently have little idea where *Mycobacterium tuberculosis* (*Mtb*) transmission occurs in high incidence settings. Molecular studies suggest that only around 8-15% of transmission to adults occurs within-household, and 9-33% by known social-contacts. This contrasts with findings from social-contact studies, which show that substantial proportions of contact time occur in households, workplaces and schools.

Methods: We developed a mathematical model of social-contact behaviour and *Mtb* transmission, incorporating variation in susceptibility and infectiousness. Three types of contact were simulated: household, regular (individuals outside household contacted repeatedly with daily-monthly frequency) and random. The assumed transmission rate between random contacts was varied from 100%-20% of that between household/regular contacts. The model was parameterised using data from Cape Town, on mean and variance in contact numbers and contact durations, by contact type. The model was fitted to data on the proportion of TB resulting from within-household transmission in Cape Town (8%).

Results: Contact data suggests household, regular, and random contacts contributed 37%, 12%, and 51% of contact time respectively. In the model, the long duration of TB disease and high inter-person variation in susceptibility and infectiousness caused saturation of household and repeated contacts, and therefore a high proportion of transmission occurred between random contacts. Assuming equal transmission rates, household, regular and random contacts caused 8%, 6%, and

86% of TB disease cases. Reducing the probability of transmission between random contacts had little effect on the results. With an 80% reduction, random contacts were still responsible for 83% of disease.

Conclusions: Long disease durations and variation in infectiousness and susceptibility result in a high proportion of transmission occurring between people who do not regularly meet. Even if yields are high, household and social-contact tracing is unlikely to reach most TB cases. A better understanding of transmission locations would assist in the design of higher impact TB control strategies.

SOA-383-12 Investigating the association between TB transmission and socio-economic risk factors in a high TB and HIV burdened community in Cape Town, South Africa

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Background: Several studies have assessed the associations between biological factors and tuberculosis (TB) transmission. However, our understanding of the associations between TB transmission and socio-economic factors remains incomplete. This study aimed to explore the associations between TB transmission and socio-economic risk factors in a high TB and HIV burdened setting.

Methods: We conducted a cross-sectional molecular epidemiology study among adult TB patients in a high TB/HIV burden community in Cape Town, South Africa. Demographic and clinical data were extracted from TB registers and clinical folders. Socio-economic data were collected using interviewer-administered questionnaires. *M.tb* isolates from participants were analysed using *IS6110*-based Restriction Fragment Length Polymorphism (RFLP). Data were analysed using Stata Corp version 12 software. Composite "social" and "economic" scores were generated from social and economic variables obtained by interviewer-administered questionnaires.

Results: Of the 509 TB patients, 352 (69%) belonged to RFLP-defined clusters and 157 (31%) were "un-clustered". Clustered cases were more likely to have lived longer in the study community, (adjusted odds ratio [aOR]= 1.06, 95% Confidence interval [CI]: 1.02-1.10, p=0.006); in the same house (OR=1.04, C.I: 0.99-1.08, p=0.06) and had increased household crowding conditions (OR=0.45, C.I: 0.22-0.96, p=0.038).

Also notable in this study was a trend towards a lower economic score (OR=0.69, CI: 0.45-1.06, p-=0.09) and conversely, a trend towards a higher social score (OR=1.39, C.I:0.94-2.03, p=0.08) in the clustered group.

Conclusions: Our study findings point to increased social interaction, poorer economic conditions and prolonged residence in a high burdened community being potentially important factors linked to TB transmission. While the association between poverty and TB transmission is not new, the association with degrees of poverty within a low socio-economic setting is novel. Our findings further suggest that even within low socio-economic settings, individuals at the lower end of the economic scale tend to be at greater risk of acquiring recently transmitted TB.

09. Leave no one behind - the hard work of finding cases

SOA-384-12 Yield of TB contact screening in North West England, 2012-2016: a retrospective, descriptive study to inform reconsideration of the United Kingdom´s 2016 TB guidelines

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Background: The National Institute for Health and Care Excellence (NICE) 2016 TB guidelines, no longer recommend screening household contacts of adult patients with extra-pulmonary tuberculosis (TB), citing a lack of cost-effectiveness. This decision has been challenged by multi-disciplinary TB teams. We evaluated latent TB infection (LTBI) and active TB disease rates in household contacts of adult patients with extra-pulmonary TB in North West England and compared them to rates in UK pre- and new-entrant screening populations.

Methods: Data was collected for the North West England region from Public Health England's Enhanced TB Surveillance and the North West TB cohort audit. Eligible participants were adults diagnosed with TB between 27/03/2012-28/06/2016 who were not in a confirmed cluster and had ≥1 contact identified/screened. The primary outcome was Tb LTBI, active TB disease, and positive screening event (sum of LTBI and active TB disease) rates in contacts of eligible patients. We then compared these detection rates with those from existing UK pre-entrant screening programmes and thresholds for UK new entrant screening in the NICE 2016 TB guidelines.

Results: 2032 patients were included of whom 1026 (51%) had extra-pulmonary TB. 9.7% [8.4-11] and 2.7% [2.0-3.4] of contacts of patients with pulmonary TB had LTBI and active TB disease respectively, compared with 3.6% [2.7-4.5] and 0.44% [0.2-0.6, detection rate 440/100,000 contacts screened] of contacts of pa-

tients with extra-pulmonary TB. The number of contacts of adult patients with extra-pulmonary TB needed to screen (NNS) to detect one case of LTBI, active TB disease, or a positive screening event was 28, 227, and 25 respectively (Figure).
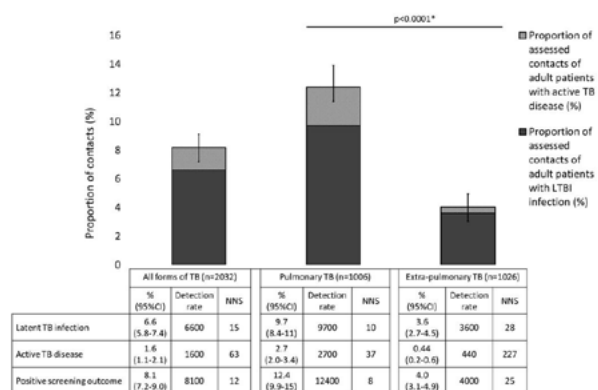

Figure TB in contacts of adults with extra-pulmonary TB

Conclusions: The prevalence of active TB disease is similar to UK pre-entrant screening programmes and more than 10-times the NICE recommended threshold for new entrant screening. The 2016 decision to stop contact tracing of patients with extra-pulmonary TB should be urgently reviewed.

SOA-385-12 Systematic screening of household contacts of tuberculosis cases in sub-Saharan Africa: derivation of a predictive risk score

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Background: Household contact tracing of tuberculosis cases has been proposed as a complementary strategy to current tuberculosis control but has been implemented poorly or not at all in high-burden settings due to its resource intensiveness and high number needed-to-screen. We developed a predictive risk score to detect contacts at most risk for undetected, co-prevalent tuberculosis disease.
Methods: Adults with newly diagnosed tuberculosis disease were identified and their household contacts were enrolled in Kampala, Uganda. Field workers administered an extensive questionnaire to all contacts after which clinical information (sputum smear samples, chest radiograph findings, and HIV status) was tested and collected. A predictive score was assessed for ability to correctly identify household contacts with co-prevalent tuberculosis disease. We calculated a score for each patient and an area under the receiver operating characteristic (AUC) curves of the model for different scores.

Results: 1940 household contacts were evaluated for coprevalent tuberculosis disease and 94 (4.9%) were diagnosed. Five independent risk factors (past active tuberculosis, age, and contact HIV status; cavitary status of the index case; family size of the household) were identified and each was assigned a number of points based on their regression coefficient. The AUC of the score was 0.80 (95% CI, 0.75 - 0.84). The risk of coprevalent disease increased with increasing score (P_{trend}< 0.0001). Coprevalent disease risk in contacts with a score of 3-8 was 14.1%, respectively. Screening only contacts with a score from 3-8 would detect almost 80% of cases screened despite only screening 27% of contacts.
Conclusions: Using this risk score, systematic household contact tracing may be a highly efficient supplementary control intervention to current tuberculosis control measures in high-burden settings. External validation in other settings is necessary before implementation in tuberculosis control practice.

SOA-386-12 Impact of community health worker household TB screening on case notification in Afghanistan: a data review

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Background and challenges to implementation: Given Afghanistan's high TB prevalence (340/100,000 population based on 2016 WHO estimates), its war environment and suboptimal health infrastructure, additional strategies are needed for TB contact investigation. The MoPH recruited and deployed voluntary community health workers (CHWs) to serve as link between the health facility and community in an environment where movement is limited due to conflict. This abstract evaluates the contributions of CHWs to TB case notification in 15 Afghan provinces.
Intervention or response: The MoPH assigned one CHW per 150 households. By the last quarter of 2015, about 14,000 CHWs were trained on TB (a one day training on the signs and symptoms of TB, referral of presumptive TB cases and treatment support). The CTB project analyzed the number of presumptive TB cases referred by the CHWs in 2016 and the TB positivity rate. These results were compared with the number of health facility level identified presumptive TB cases and the corresponding TB positivity rate.
Results and lessons learnt: Among 19,139 presumptive pulmonary TB patients were referred by CHWs in 15 Afghan provinces, 1,190 (6.19%) cases were diagnosed by health facilities as bacteriologically confirmed TB cases. In the same year 163,388 presumptive pulmonary-

TB patients were identified in health facilities in the same 15 provinces and 8,961 (5.3%) were found out to be bacteriologically confirmed TB cases (See Table 1). Bacteriologically confirmed TB cases referred by CHWs 6,260/100,000 compared to 5,484/100,000 for health facility identified presumptive TB cases.

Period	# of presumptive TB patients examined by health facilities	# of presumptive TB patients with positive results by health facilities	Health facilities TB positivity rate (%)	# of presumptive TB patients referred by CHWs	# of presumptive TB patients with positive results referred by CHWs	CHWs TB positivity rate (%)
January-June 2016	76,306	4,245	5.56	8,668	519	5.98
July-December 2016	87,082	4,716	5.4	10,471	671	6.4
Total	163,388	8,961	5.3	19,139	1,190	6.19

Table Comparison of the TB positivity rate identified by

Conclusions and key recommendations: Volunteer CHW TB screening is no less effective than TB screening at health facilities. CHW contributions to increased case finding in the 15 provinces was high. Using community resource individuals such as CHWs in conflict settings is a feasible strategy to ensure the continuity of TB services.

SOA-387-12 Increasing TB case notification through a quality improvement intervention

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Background and challenges to implementation: Uganda's TB incidence is 234/100,000 but half of the estimated 89,000 TB cases expected are notified each year. In 2015, 43,736 TB cases were notified (WHO Global TB report 2016). For many years, TB case-finding in Uganda has been passive with exception of TB/HIV collaborative activities. A pro-active approach requiring intensified TB case-finding focusing on high risk groups is recommended to improve case finding.

Intervention or response: In 2015, Ministry of Health with partners established a TB services quality improvement (QI) collaborative at 12 TB diagnostic and treatment units (DTU) based on their TB notification gap and regional representation. Health workers were trained in QI using the Plan-Do-Study-Act approach and were supported regularly by experienced QI coaches to improve TB services processes. Health workers continuously reviewed processes related to TB case notification like TB assessment at outpatient department, with the objective of identifying the needed corrective actions. This was then followed by testing process changes while monitoring outcomes from the process.

Results and lessons learnt: After five months, there was consistent TB services processes review by health workers in all sites. At 3 DTUs within the east central region, the number of presumptive TB cases increased from 21 cases/month to 81 cases/month. Similarly, TB case notification increased from a median of 5.5 cases to 11 cases. Displaying the intensified case-finding job aids in clinical rooms for quick reference, documenting TB status in clinical notes for all clients, and TB assessment reminders to clinical staff were some of the successful process changes.

Conclusions and key recommendations: There is need to promptly notify and effectively manage TB cases for good TB control. The continuous TB Notification process analysis and testing of process changes as occurs in a typical QI intervention presents a great opportunity for increasing TB case notification.

SOA-388-12 Identifying high-risk individuals for tuberculosis screening in health facilities and communities: Western Kenya, 2015-2016

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Background: Active tuberculosis case-finding is not routine but has been recognized as necessary for combatting the tuberculosis epidemic. We sought to identify characteristics that could be used to target tuberculosis case-finding in Kenya.

Methods: A study to determine optimal methods for increasing tuberculosis case detection was implemented in western Kenya during February, 2015-June, 2016. Individuals reporting any tuberculosis symptom in the past 4 weeks were identified by screeners in health facilities and screening teams in communities, and evaluated for tuberculosis. To identify risk factors for tuberculosis, we performed log binomial regression using data collected from persons ≥15 years old who were screened during these interventions.

Results: Tuberculosis was diagnosed in 480 (20%) of 2,394 symptomatic adults screened in health facilities and 39 (3%) of 1,424 symptomatic adults screened in community units. For persons screened in health facilities, neither age, sex, HIV infection, previous tuberculosis treatment, nor reported household exposure was associated with a ≥2-fold increase in risk of tuberculosis. For persons screened in communities, men (risk ratio 4.73, 95% confidence interval 2.42-9.25) and those reporting a household member treated for tuberculosis in the last 2 years (risk ratio 4.04, 95% confidence interval 2.02-8.07) were at a significantly elevated risk for

tuberculosis. Among HIV-negative individuals, using a screening criterion of cough lasting >2 weeks would have detected 90% of the cases while requiring 32% fewer sputum samples to be tested. For people with HIV, no symptom combinations could be identified that would decrease testing while maintaining sensitivity.

Conclusions: Screening all persons attending health facilities for tuberculosis is a high-yield activity in this setting. Searching for symptomatic people in the community is less effective, but could be targeted to people with household exposure.

SOA-389-12 Should we screen contacts of non-pulmonary tuberculosis cases?

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Background: Since 2016, UK guidelines recommend only tracing contacts of pulmonary or laryngeal tuberculosis (PTB) cases. Whilst non-pulmonary & non-laryngeal (ETB) cases are typically not infectious, there is evidence that their contacts are considerably more likely to have tuberculosis (TB) than the general population.
Methods: We evaluated the effectiveness of screening contacts of ETB and PTB cases using descriptive analysis of data from the London TB Register, including contact tracing (CT) yield per case and the mean symptomatic period, and a static analytic model (n=2911). The effectiveness of CT was quantified using the reduction in time contacts spend ill; the number of cases averted through preventive therapy (PT); and reduced transmission from contacts with PTB.
Results: More cases are found per PTB index case (0.098 (95% CI: 0.082-0.11)) than per ETB index case (0.021 (95% CI: 0.013-0.029)), and PTB cases found through CT were symptomatic for less time than PTB cases found through passive detection (63 (95% CI: 49-76) vs 110 days (95% CI: 100-120); P< 0.01); this difference for ETB cases was non-significant (P=0.07). Providing PT to latently infected contacts of ETB cases could prevent 6.3 (95% CI: 3.0-9.9) cases/year (21 cases (95% CI: 10-34) for contacts of PTB cases) in London. Assuming each PTB contact infects 2 people/month, we could prevent 7.4 cases (95% CI: 4.2-11.2) by reducing transmission from contacts of ETB cases (34 cases (95% CI: 24-46) for contacts of PTB cases), both by finding infectious contacts sooner and preventing latently infected contacts from developing TB.
Conclusions: Whilst CT reduces morbidity in and transmission from all contacts, the impact on contacts of ETB cases is relatively small, partially supporting changes to national guidance. Cost-effectiveness analysis will help

determine the absolute impact of these changes. Results are sensitive to assumptions about transmission from contacts: further work to understand this is needed.

SOA-390-12 Tuberculosis screening in asylum seekers in Germany: case characteristics and yield of screening

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Background: In 2015, Germany received asylum applications from 441.899 people, the majority were from countries with higher burden of tuberculosis (TB) compared to Germany. We aimed to describe the TB cases identified by screening among asylum seekers and to estimate the yield of screening in order to inform future screening policies.
Methods: We extracted German TB notification data for 2015, and numbers of asylum seekers registered by the Federal Office for Migration and Refugees for the same year. We described demographic and clinical features of cases identified by entry screening into community reception centers for asylum seekers and estimated case finding rates by country of birth.
Results: A total of 1,255 TB cases were detected by screening among asylum seekers, representing 21% of all notified TB cases in 2015. The patients' most frequent countries of birth were Syria (n=157), Somalia (n=155), Eritrea (n=148) and Afghanistan (n=146). Estimated case finding rates were particularly high for asylum seekers originating from Somalia (1,210 per 100,000) and lower for those from Afghanistan, Syria and Iraq (95, 37 and 27 per 100,000, respectively).
The majority of patients was male (male-to-female ratio 6.6) and the median age was 25 (interquartile range 20-33) years. Forty-five patients (3.6%) were children aged < 15 years. Overall, 89% had pulmonary TB and 13% had been previously diagnosed with TB. Among the pulmonary TB cases, 59% were bacteriologically confirmed and 26% were sputum smear positive (compared to 49% among cases identified by passive case finding). Multidrug-resistant TB was found in 5.7% of 636 cases with drug-susceptibility testing results.
Conclusions: In 2015, a considerable number of TB cases were identified through active screening among asylum seekers in Germany. Screening allowed early case detection - reflected by a low proportion of sputum smear positive cases - and is likely to have prevented TB transmission in Germany.

SOA-391-12 Is it possible to increase TB-notification from the private sector in India? Experience from nine cities

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Background and challenges to implementation: Private sector, contributes to more than 50% of TB cases treated in India. Most often the private sector is the first contact point of presumptive TB cases. With an aim to End TB, National Strategic Plan (2018-2023) emphasizes on engaging private sector, to identify missing cases in India. However, the response from private sector is not encouraging till now.

Intervention or response: Population Services International (PSI) is implementing Urban TB intervention in nine cities across 10 states in India as part of Global Fund supported Project Axshya. Potential private sector players, diagnosing and treating TB patients are identified through systematic mapping process. Potential private sector players are trained on Standards of TB care in India (STCI) and are periodically sensitized by trained medical training specialist and urban coordinators using scientifically designed communication material aimed at changing behaviour and attitude of providers towards TB-Notification. Support is provided for collecting data of TB patients and notifying cases in NIKSHAY, followed by customized treatment adherence messages to TB patients using ICT platform.

Results and lessons learnt: We compared TB-Notification data in intervention cities from both fresh and old registered providers during pre-intervention (Jan-Dec'15) period and post intervention period (Jan-Dec'16). Overall 10,409 TB cases were notified in intervention cities during Jan-Dec'16, out of these 6,707 (65%) TB cases were through Project Axshya. TB notification increased from 2,428 in these cities during pre-intervention (Jan-Dec'15) period to 10,409 (328% increase) during post intervention (Jan-Dec'16) period.

Conclusions and key recommendations: A systematic approach of mapping and identifying potential private players, identifying motivators and barriers among the private players for TB notification, scientifically designed communication aimed at changing behaviour and attitude of private players and targeted approach with frequent contacts with private sector helps to increase the TB notification from the private sector in India.

SOA-392-12 Gaps in TB screening at health facilities have contributed to a decline in TB case notification in Kampala city

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Background and challenges to implementation: Tuberculosis (TB) case notification in Kampala has progressively declined from 8,344 in 2012 to 7,037 in 2016. This has been attributed to a number of factors including the sub optimal TB screening practices at health facilities. We set out to establish levels of systematic (symptom) TB screening, the yield of TB among the screened cases and number needed to screen to detect one confirmed TB case in Kampala.

Intervention or response: During the period of July-August 2016, we collected TB screening data at outpatient departments (OPD) of 10 high volume TB diagnostic facilities from the five divisions of Kampala. We administered the intensified TB case finding form at the triage points of health facilities to establish the existence of TB symptoms including cough $\geq$ 2weeks, fever and night sweats. Based on these symptoms, data was collected on the proportion of presumptive TB patients (PTPs) and the number of patients confirmed with TB.

Results and lessons learnt: A total of 171,812 outpatient attendees were registered of which 37,798 (22%) were < 5years. Out of the total OPD attendance, 163,453 (95%) were screened for TB and 4,899 (3%) PTPs were found. Out of the total PTPs, 704 (14.4%) were the TB patients including 483 confirmed bacteriologically. The number needed to screen was 232 to diagnose a TB patient with marked variability across the divisions.

Conclusions and key recommendations: The yield of PTPs remains low compared to the WHO estimates of 10%. However the proportion confirmed with TB among those screened is above the expected average. Since it is not plausible for patients who are not presumed to have TB to undergo further tests for confirmation of their TB status, the low yield of presumptive TB might contribute to the decline of TB case notification. We recommend improvement in TB screening approaches at health facilities in Kampala.

SOA-393-12 Barriers to tuberculosis case detection and treatment in a densely populated rural area

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Background: Tuberculosis (TB) disproportionately affects people in resource poor settings particularly in Africa (30%) and Asia (55%). One of the factors that aid the spread of TB in this region can be attributed to stigmatization and negative attitudes towards those affected. The aim of the study is to assess the Knowledge, attitudes and practices (KAP) about TB among men and women ages 15 -65 years in four Local Government Areas in Rivers State.

Methods: The study was conducted among four hundred men and women aged 15 - 65. Multistage sampling technique was used to select the respondents for the study. Information on KAP on TB was obtained from participants using semi-structured questionnaire.

Results: The study revealed that majority of the respondents had knowledge about TB with most respondents being able to correctly identify symptoms and signs (94.4%), its mode of transmission (77%), prevention (72.9%) and cure with appropriate treatment (86%). However, over 50% had a negative and stigmatizing attitude towards those who had TB.

Conclusions: Knowledge about TB did not necessarily reflect on attitudes of people towards those who have TB. This also affects TB case detection, as people with signs are more likely to avoid seeking medical attention and treatment for fear of stigmatization. There is therefore need to create more awareness about TB and mobilize community support case detection and for persons with TB.

POSTER DISCUSSION SESSIONS

01. MDR-TB: burden and trends

PD-500-12 Prevalence of drug-resistant tuberculosis in Nigeria: a systematic review and meta-analysis

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Background: Drug-resistant tuberculosis (TB) undermines control efforts and its burden is poorly understood in resource-limited settings. We performed a systematic review and meta-analysis to provide an up-to-date summary of the extent of drug-resistant TB in Nigeria.

Methods: We searched PubMed, Scopus, Embase, HINARI, AJOL, the Cochrane library, Web of Science, and Google Scholar for reports published before January 31 2017, that included any resistance, monoresistance or multidrug-resistance to anti-TB drugs in Nigeria. Summary estimates were calculated using random effects models. Heterogeneity test, and funnel plots were constructed.
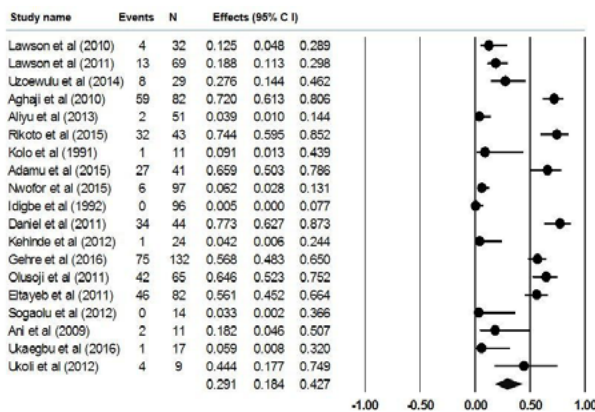
Figure Forest plot of the meta-analysis of MDR-TB in prev

Results: We identified 34 observational studies with 8002 adult TB patients consisting of 2982 new and 5020 previously-treated cases. The prevalence rate of any drug resistance among new TB cases was 26.4% (95% CI 16.7-39.2%; 734/2892) and among previously-treated cases, the rate was 53.6% (95% CI 39.5-67.0%; 1467/5020). The rate of anti-TB monoresistance among new patients was 12.1% (95% CI 8.3-17.2%; 199/2002), and among previously-treated TB patients was 17.4% (95% CI 12.0-24.6; 127/789). Furthermore, the prevalence of multi-drug resistance among new patients was 7.3% (95% CI 4.2-12.3%; 161/2502), and among previously-treated cases was 29.1% (95% CI 18.4-42.7; 357/949), [Figure]. There was significant heterogeneity between the studies (p<0.001). The prevalence of drug-resistant TB varied according to methods of drug susceptibility testing and geographic region of Nigeria.

Conclusions: The burden of drug-resistant TB among new and previously-treated TB patients in Nigeria is high; strengthening the strategies for its case detection and programmatic management is urgently recommended.

PD-501-12 Prevalence of resistance to second-line drugs and pyrazinamide resistance among multidrug-resistant tuberculosis patients in China

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Background: The increasing incidence of extensivelydrug-resistant tuberculosis (XDR-TB) is due to the expanded use ofsecond-line drugs in people withmultidrug-resistant tuberculosis(MDR-TB). Information on second-line drug susceptibility is scarcein China.

Methods: We assessed resistance to second-line drugs in MDR-TB in China. A total of 391 patients with MDR-TB from 30 provinces and municipalities of China from the 2007-2009 national drug-resistance survey were enrolled. Drug susceptibility testing was done for 10 first-line and second-line drugs. We compared the results with clinical and epidemiological data to identify risk factors for resistance to second-line drugs and XDR tuberculosis.

Results: Among the 391MDR-TB isolates, 68.80% (269/391) was simple MDR-TB,24.04% (94/391) was pre-XDR-TB and 7.16% (28/391) was XDR-TB. Strains from MDR-TB patients showed additional resistance to E(55.24%, 216/391), Z (47.57%, 186/391), ≥1 non-first line anti-TB drug (83.12%, 325/391), ≥1 injectable anti-TB drug (73.91%, 289/391), ≥1 fluoroquinolone (32.74%, 128/391), Eto (22.25%, 87/391),Cfx (6.65%, 26/391), Lzd(9.46%, 37/391), and high dose H (67.77%, 265/391).A total of 42.71% (167/391) of MDR-TB patients had never been treated for TB, which suggests primary transmission of MDR-TB. The predominant strains belonged to the Beijing genotype (82.35%, 322/391). Previous treatment for TB was the strongest risk factor for resistance to second-line drugs.

Conclusions: High levels of primary transmission and advanced resistance to second-line drugs characterize MDR-TB cases in China. So TB culture and full DST should be carried out routinely.

PD-502-12 Resistance pattern of the drugs included in the short-course MDR regimen according to susceptibility to fluoroquinolones and injectables in Peru

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Background: WHO has proposed to countries to incorporate the shortened schedule for MDR-TB new cases. The objective of this study was to determine the resistance profile of the MDR strains to the drugs include in MDR-TB standard short-course chemotherapy according to their resistance to fluoroquinolones (FQ) and injectables (INJ).

Methods: The database of the Peruvian National Institute of Health of 2015 and 2016 was used. The resistance percentage of each drug in the MDR-TB standard short-course chemotherapy was established in: i) total MDR strains, ii) FQ and INJ sensitive, iii) Resistant to INJ and sensitive to FQ, iv) resistant to FQ and sensitive to INJ and v) XDR strains. No sensitivity data are available for clofazimine.

Results: 4642 TB-MDR strains were included, 3394 (73%) were sensitive to FQ and INJ, 736 (16%) were FQ sensitive and INJ resistant, 172 (5%) FQ resistant and INJ sensitive, and 340 (7,3%) were XDR. High resistance was measured in the drugs evaluated, especially isoniazid (H) at high doses, followed by ethambutol (E), pyrazinamide (Z) and ethionamide (Eto) in all MDR groups evaluated. Even by defining the sensitivity to FQ and INJ in MDR-TB, high resistance levels above 30% are maintained (Table).

Drugs of the MDR-TB standard short-course chemtheraphy	MDR strains				XDR strains
	total	FQ and INY sensitive	resistant to INY and sensitive to FQ	resistant to FQ and sensitive to INY	
Etambutol	53%	44%	79%	55%	81%
Pyrazinamide	51%	48%	59%	59%	81%
Kanamycin	17%	0%	100%	0%	100%
Capreomycin	15%	0%	100%	0%	100%
Levofloxacin	12%	0%	0%	100%	100%
Ethionamide	36%	31%	45%	47%	63%
Isoniazid at high doses	86%	83%	94%	90%	97%
Clofazimine	ND	ND	ND	ND	ND

Table Drug resistance on MDR strains, Peru, 2015-2016

Conclusions: Probably the MDR-TB standard short-course chemotherapy should be implemented in Peru, taken into account that the drug susceptibility test (DST) to evaluate the resistance to E, Z and Eto are unreliable and therefore these results would not be decisive however the high resistance to high doses of H must be considered.

PD-503-12 Decline in MDR-TB prevalence among new TB patients in Rwanda: impact of implementing rapid molecular tests in programmatic management

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Background: Rwanda reported in 2005 Drug Resistance Survey (DRS) an MDR-TB prevalence of 3.9% among new TB patients which decreased significantly in the recent DRS (2015) to 1.4%. This decline coincides with the implementation of rapid molecular tests in the programmatic management of MDR-TB (PMDT). This study aims to analyze the delays in MDR-TB treatment initiation before and after implementing Hain MTBDRplus and Xpert MTB/RIF tests.

Methods: Using the equality of medians test, we analyzed the delays from the first suspicion of MDR-TB to the initiation of MDR-TB treatment for 822 retrospective records of MDR-TB patients enrolled since the initiation of PMDT in 2005 to 2015.

Results: Among 822 MDR-TB registered, 630 (77%) had both dates for initial diagnosis of presumptive TB (first contact) and MDR-TB treatment initiation in their medical files and were considered for this analysis. The median delay before, after implementing Hain MTBDRplus in 2009, and after Xpert implementation in 2012 were 127 days (d) (IQR 97-167 d), 86d (IQR 56-101 d), and 26d (IQR 8-51 d) respectively. The median delay since first contact for patients initiated on MDR-TB treatment based on Xpert results was 8 days (IQR 4-10 d). Correlating delays with year of enrollment, we observed a significant decrease in delays (P < 0.0001).

Conclusions: The remarkable decrease in delays to initiate the MDR-TB treatment due to molecular tests most likely underpin the decrease in the prevalence of MDR-TB among new patients by interrupting MDR-TB transmission. To our knowledge, a significant decline in the MDR-TB prevalence has not been seen to date in other countries. Further analysis on the specific components of this PMDT model could support a comprehensive model to be implemented in other high burden MDR-TB settings.

PD-504-12 Prevalence of rifampicin resistance among presumptive TB and drug-resistant TB populations: TB-HIV coinfected, paediatric and extra-pulmonary patients, Mumbai, 2015-2016

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Background: Mumbai, a city with nearly 13 million populations, reports about 4000 Drug resistant tuberculosis (DRTB) cases annually. The city with support from Central TB Division has deployed 21 CBNAAT machines for rapid detection of *Mycobacterium tuberculosis* (MTB) and rifampicin resistance (RR). Under RNTCP all presumptive DRTB patients are offered CBNAAT for detection of RR and all presumptive TB subjects among key populations viz. Paediatric, TB-HIV Co infected and Extrapulmonary are offered CBNAAT for MTB detection and additionally rifampicin status is also reported. There are no reliable estimates available on prevalence of RR among these groups in Mumbai.

Methods: In this retrospective study records were examined for a period from January 2014 to December 2016. All presumptive TB among key population & all presumptive DR TB samples tested during study period were considered.

Results:

- A total of 21, 958 (37%) out of all 59,182 CBNAAT performed during 2015-16 had MTB detected and 6035 (10%) of total tested had rifampicin resistance.
- Out of 39933 presumptive DRTB patients subjected to CBNAAT during 2015-16, 18019 (45%) had MTB detected and 5051 (12.7%) tested rifampicin resistant.
- Out of 19249 presumptive TB cases among key populations subjected to CBNAAT, 4012 (21%) had MTB detected and 984 (5%) had rifampicin resistance.

Conclusions: Rapid expansion of access to CBNAAT testing has lead to early detection of rifampicin resistance among presumptive DRTB subjects and also early detection of MTB along with rifampicin resistance status among key populations. In present study prevalence of 12.7% rifampicin resistance among presumptive DRTB patients and 5% among key populations is reported in Mumbai which was previously unknown.

PD-505-12 Paradigm shift in all types of presumptive DR-TB: a comparative analysis of MDR-TB diagnosis in Bangladesh

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Background: Bangladesh is one of the high burden countries for multidrug resistant tuberculosis with an estimated incidence of 9,100 MDR/RR-TB cases in 2016. According to the first Bangladesh Tuberculosis Drug Resistance Survey (DRS) 2010-11, the prevalence of MDR/RR-TB in new and previously treated cases was 1.6% and 29% respectively. However, NTP routine DR-TB case detection data shows that the rate of MDR/RR-TB much lower than what was found during the survey. The objective of the study was to find out any difference in proportions of MDR/RR-TB between DRS and routine programme data.

Methods: Data was collected from published DRS report and from the monthly routine reports of NTP from all culture laboratories and Xpert sites during the period January to December in 2016. Descriptive analysis was done using Microsoft Excel and z-test was performed to find out any significant difference between to proportions.

Results: 13,790 new and 30,125 previously treated cases were tested in 2016 and among them 110(0.8%) and 837(2.8%) were confirmed as MDR/RR-TB respectively from new and retreatment cases. Significant difference was observed between the proportions of MDR/RR-TB among new (p< 0.05) and previously treated (p< 0.01) cases in 2016 and findings from DRS in 2010-11. The disintegrated data from previously treated cases tested in 2016 shows MDR/RR-TB 8.6% among treatment failures, 4.8% in relapses, 4.3% in lost to follow-up and 0.85% in others, whereas in DRS data the proportions were 63.2%, 21.1%, 13.8% and 40.8% respectively.

Conclusions: As the first DRS was conducted six years back and significant difference has been observed with routine programme data, a further drug resistance survey is required to find out the actual burden of DR-TB in Bangladesh.

PD-506-12 Increasing trends of drug resistance in extra-pulmonary tuberculosis in India

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Background: Multidrug resistance (MDR-TB) among Extrapulmonary tuberculosis (EPTB), has become a significant public health problem in developing countries and an obstacle to effective TB control. The aim of this

study to evaluate the trends of drug resistance pattern in extrapulmonary cases in India.

Methods: 756 patients with suspected of EPTB cases with varied presentation were studied. Specimens were processed by Ziehl Neelson staining, automated culture, identification of *Mycobacterium tuberculosis* complex by NAP test with First line drug susceptibility testing by by 1% proportional method for streptomycin, isoniazid, rifampicin and ethambutol.

Results: We found 71(9.4%) were positive for Acid fast bacilli by direct ZN staining, 227 (30.1%) for culture positive, 164(72.2%) were confirmed as *M. tuberculosis complex*. Out of 164, 122 (74.4%) were new case and 42(25.6%) were treated cases. 64(39.1 %) strains were resistant to one or more first line antitubercular drugs. MDR among EPTB cases was found in 22 (13.4%).

Conclusions: The prevalence of MDR among EPTB was 13.4% which shows rising trends. MDR-TB is largely due to transmission of previously drug resistant strains. Molecular DST testing would be beneficial to patients in receiving effective treatment with appropriate regimens effective.

PD-507-12 Prevalence of drug resistance among patients with presumptive TB in Namibia

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Background: Namibia is a sparsely populated country with a population of 2.3 million and an estimated TB incidence rate of 489/100,000. The 2nd nationwide anti-TB drug resistance survey was conducted between 2014 and 2015.

Methods: Between July 2014 and April 2015 all patients with symptoms of TB in Namibia (100% sampling) were requested to participate by contributing 2 sputum specimens each (spot-morning). The 1st sputum specimen was subjected to smear microscopy and Xpert MTB/RIF testing while the 2nd specimen was subjected to smear microscopy, and then forwarded for culture if either the Xpert MTB/RIF or smear was positive. 162% of the targeted 1910 new TB patients and 130% of the targeted 745 previously treated TB patients were enrolled.

Results: The overall prevalence of MDR-TB among the 3126 eligible specimens with full DST was 5%. The prevalence among new TB patients was 3.9% and previously treated patients was 8.7%. Resistance to isoniazid was 11.2% and 16.6% among new and previously treated patients respectively; and resistance to rifampi-

cin in the same patient categories was 4.9% and 10.9% respectively. The HIV prevalence among the all survey participants was 37.8%, with a prevalence of 46.6% among MDR-TB patients.

	Total with DST to H&R	Resistance to H&R only	Resistance to H&R&E only	Resistance to H&R&S only	Resistance to H&R&E&S	All MDR
New patients	2392	20	6	15	52	93
Previously treated	699	11	2	20	28	61
History unknown	35	0	0	1	0	1
All patients	3126	31	8	36	80	155

Table Namibia DRS 2

Conclusions: Prevalence of MDR TB among new patients was similar to the 1st DRS in 2008-9; while that among previously treated patients is lower than in 2008-9, but with narrower confidence interval. The strongest risk factor for MDR-TB was prior treatment history. Namibia has the capacity to implement universal testing of presumptive cases with Xpert MTB/RIF and implement routine surveillance for drug resistance among TB patients.

PD-508-12 Panorama de la resistencia a inyectables y quinolonas en casos multirresistentes, Colombia, 2015-2016

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Background: Colombia en el año 2012 definió que todo caso multirresistente debía tener una prueba de resistencia a inyectables y quinolonas, la primera documentación publicada de resistencia a estos medicamentos en el país índico que aproximadamente el 22% de casos que habían tomado éstos medicamentos presentaba resistencia.

Methods: Las pruebas de sensibilidad se realizaron en el Laboratorio Nacional de Referencia por la metodología Bactec™ MGIT™ a kanamicina, amikacina, capreomicina y ofloxacina en las concentraciones recomendadas, se determinó el porcentaje de resistencia a fármacos y de tuberculosis extremadamente resistente.

Results: Se estudiaron durante los años 2015 y 2016, 148 aislados de casos de tuberculosis multirresistente, el 60% de provenía de Antioquia, Valle del Cauca y Bogotá, los casos evaluados corresponden al 70% de los notificados al programa nacional, el resto no fue evaluado por contaminación del cultivo, resultados no concluyentes en la prueba de sensibilidad o casos diagnosticados por métodos moleculares en los que no se obtuvo un cultivo positivo.

El 92% de los casos fueron sensibles a los cuatro fármacos evaluados, la resistencia global fue del 8% siendo igual el aporte de inyectables y ofloxacina, se identificaron nueve casos pre-extremadamente resistentes (6,0%) y tres (2,0%) extremadamente resistentes.

Conclusions: Los datos obtenidos indican una reducción de la resistencia global en los casos multirresistentes, sin embargo las acciones de detección y diagnóstico deben incluir todas las pruebas complementarias en especial cuando los métodos moleculares están disponibles y se cuenta con un Laboratorio Nacional de Referencia que puede hacer esta actividad, es fundamental que se logre estudiar el 100% de los casos y que se haga la evaluación de la levofloxacina como medicamento estándar para el manejo de estos casos con el que obtendría un dato de prevalencia mas real.

02. *Mycobacterium bovis:* transmission, detection and public health implications

PD-509-12 First appraisal of genetic diversity of *Mycobacterium tuberculosis* isolated from captive Asian elephants (*Elephas maximus*)

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Background: *Mycobacterium tuberculosis* (MTB) is a known human pathogen, which is believed to have no other reservoir host. Hence, almost all reports of *MTB* infection in any of the domestic or wild animals are considered to represent a spillover infections resulting from human co-habitation. There is paucity of data on mycobacterial infection and genotypic characterization of *MTB* isolated from captive animals from India.

Methods: In this prospective study, lung biopsy samples obtained from captive elephants at the veterinary dispensary of Kerala, India were subjected to mycobacterial culture. The growth was examined, characterized phenotypically and by multiplex polymerase chain reaction and from the *MTB* strains DNA was extracted using Chloroform: Isoamylalcohol (CI) method followed spoligotyping using a commercially available kit (M/s Ocimum Biosolutions, India).

Results: Overall from 50 biopsy samples, 23 samples grew acid-fast bacilli. On multiplex PCR analysis, 20 (87%) isolates were found as *MTB* and remaining 3 (13%) as non-tubercular mycobacteria (NTM). The spoligotyping anayalysis revealed 4 clades and the most predominant 14 (70%) clade was EAI, followed by CAS and Manu isolates (10% each). One (5%) isolate was Africanum and one (5%) isolate belonged to Unknown clade. All 20 strains could be grouped into 9 shared types

(ST) representing 8 sub-clades. Among the 9 STs, ST48 (EAI1-SOM) was most predominant (25%), followed by ST11 (EAI3-IND), ST26 (CAS1_DELHI), ST587 (Africanum), ST1391 (Unknown), ST54 and ST100. Three isolates of EAI lineage could not be assigned any ST number.

Conclusions: Most prevalent spoligotype was EAI in these elephants, which are used in temples for worship. The EAI spoligotype is also most common in the humans of the region, suggesting that the infection in these elephants was purely a reverse zoonosis.

PD-510-12 Knowledge, awareness and practices of small household milk producers regarding zoonotic tuberculosis in rural India

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Background: India is one of the largest producers of milk in the world. There are no guidelines for regular health screening of milk producing domestic animals. Hence, small household animal milk producers are at risk of developing zoonotic diseases particularly tuberculosis. We assess the small household milk producer's knowledge and awareness regarding zoonotic tuberculosis and animal house practices in rural India.

Methods: We conducted a cross-sectional survey of small household milk producers in the year 2015-2016. Milk producers from 240 villages in 8 districts of Punjab and Haryana were selected through multi-stage sampling. Knowledge and awareness of zoonotic tuberculosis and animal house practices were the broad areas of inquiry. Logistic regression used to establish an association between respondent's knowledge and awareness of zoonotic tuberculosis with the independent variables such as education, income, religion, caste, consultation with veterinarian and animal house practices.

Results: A total of 789 milk producers were surveyed (57% female and 43% male). Nearly two-third of the respondents (65%) had primary level education, one-fourth (25%) were illiterate and few (10%) were graduates.

Respondents considered anthrax (44%), rabies (34%), tuberculosis (12%), and ringworm infection (7%) as animal to human-transmitted diseases. Respiratory inhalation (47%), drinking raw milk (24%), and handling animal urine (52%) were the self-reported routes of animal to human TB transmission. Significant difference was noted for at least one annual health screening of domestic animals among experienced farmers (> 8 years of animal rearing experience; p=0.000) and graduates (p=0.000). The knowledge and awareness scores for the

animal to human TB transmission were significantly associated with education (p=0.002), recent visit to veterinarian (p=0.000) and animal house hygiene (p=0.000).
Conclusions: Knowledge and awareness of the zoonotic potential of animal tuberculosis among small household milk producers in rural India is low. Active community engagements along with mass education campaigns on zoonotic tuberculosis are needed urgently.

PD-511-12 Genotyping of mycobacterial isolates from Ghana's tuberculosis prevalence survey - *Mycobacterium bovis* not found

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Background: The study aims to use World Health Organization (WHO) approved line probe assay (LPA) to differentiate mycobacterial isolates obtained from tuberculosis (TB) prevalence survey in Ghana.
Methods: A retrospective study was conducted whereby a total of 361 mycobacterial isolates were differentiated using GenoType Mycobacterium Assays: MTBC and CM/AS for differentiating *Mycobacterium tuberculosis* complex (MTBC) and Non-Tuberculous Mycobacterium (NTM).
Results: Of the 361 isolates, 165 (45.7 %) were MTBC while 196 (54.3 %) were NTM. The MTBC consisted of 161 (97.6 %) *Mycobacterium tuberculosis* and 4 (2.4 %) *Mycobacterium africanum*. Other members of MTBC such as *M. bovis* and *M. microti* were not identified. Out of 196 NTM isolates, 120 (61.2%) could be speciated completely with the GenoType CM/AS while 76 (38.8%) could not due to the limited ability of the kit for speciation. The 120 speciated NTM consisted of diverse species including *M. fortuitum* 42 (21.4 %), *M. intracellulare/ M. chimaera* 27 (13.8 %), *M. mageritense* 9 (4.6 %), *M. abscessus* 8 (4.1 %), *M. gordonae* 7 (3.6 %), *M. lentiflavum* 7 (3.6 %), *M. scrofulaceum* 6 (3.1 %), *M. asiaticum* 4 (2.0 %), *M. goodii* 4 (2.0 %), *M. interjectum* 2 (1.0 %), *M. perigrinum* 2 (1.0 %), *M. avium* 1 (0.5 %) and *M. smegmatis* 1 (0.5 %).
Conclusions: Our study showed that the predominant mycobacterial species causing pulmonary TB in Ghana is *M. tuberculosis* followed by *M. africanum. M. bovis* causative agent of bovine TB was not found.

PD-512-12 Detection of drug resistance and efflux pump mutations in *Mycobacterium bovis* in cattle and human isolates from Baja California, México, using whole-genome sequencing

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Background: Baja California presents the highest incidence of tuberculosis in humans and the highest prevalence of bovine-tuberculosis in Mexico. We used whole-genome sequencing to characterize mutations predicting drug resistance, for all first-line second-line drugs for tuberculosis and efflux pump genes.
Methods: We used a whole genome sequencing strategy using paired-end 250-bp reads on an Illumina MiSeq using the Nextera-DNA Kit. We analyzed 171 isolates of *M.bovis* from Baja California, Mexico, of which 154 were isolated from cattle, and 17 from humans. Spoligotypes were determinate *in silico* using SpoTyping-v2.0. We analyzed 31 and six genes conferring resistance to first- and second- line anti-tuberculous drugs, respectively and eight efflux pump genes.The SNP data obtained was analyzed according to known resistance conferring genes for each anti-tuberculous drug and compared with that listed in TBDReaMDB. All synonymous SNPs were removed and only non-synonymous SNPs were analyzed.
Results: Two predominant spoligotypes were recognized in both cattle and humans (SB0145 & SB1040). In total, 45% first line drugs showed SNP which the most frequent were in *pncA:*H57D; *rpsA*:A440T; PPE49:A38V; *Rv1592c*:I322V; *embC*:T270I and R927H; *iniA*:H481Q and N88S. About the second line genes, 83% showed SNPs which the most frequents were *gyrA*:E21Q, S95T, G668D, D639A; gyrB:A428S, A442S. For the efflux pump genes, only 60% showed SNPs (*Rv3239c, drra, emrB, mmr, bacA),* the most frequent was *bacA:*I603V. Approximately, 10% of cattle isolates showed at least one SNP related to second line drug resistance.
Conclusions: Our results present the first WGS based characterization of M. bovis isolated from cattle and human in México. *Mycobacterium bovis* isolated from cattle showed drug resistant to first and second line anti-tuberculous drug and efflux pump genes. This is critical because the phylogenetic analysis suggests that human tuberculosis caused by *M. bovis* in Baja California is derived from *M. bovis* circulating in Baja California cattle.

PD-513-12 Reverse zoonotic transmission of tuberculosis from an emerging strain of *Mycobacterium tuberculosis* and associated risk factors in south-eastern Nigeria

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Background: Tuberculosis (TB) now ranks alongside HIV globally and remains a major public health challenge in Nigeria. The increased risks for inter-transmission of the disease between livestock workers and cattle accentuate the situation. The study seeks to determine zoonotic epidemiological transmission link between livestock workers and cattle as well as associated risk factors for TB in Ebonyi State, southeastern Nigeria.
Methods: We conducted a cross-sectional study of livestock workers and their cattle through screening of 149 sputum and 144 milk samples, respectively on the assumption of subclinical infections suggestive by the unguarded human-livestock interactions. A semi-structured questionnaire was administered to the livestock workers to evaluate their knowledge and practice regarding the disease. Isolates from cultured samples were analysed using spoligotyping and Mycobacterial Interspersed Repetitive Unit-Variable Number Tandem Repeats (MIRU-VNTR).
Results: Tuberculosis prevalence of 2.1% and 34.9% among cattle and livestock workers were respectively confirmed by deletion typing and were differentiated into *M. tuberculosis* =2 (among cattle) and *M. tuberculosis* =42; *M. bovis* =1; *M. africanum* =9 (among livestock workers). Further analyses by spoligotyping indicated 59.2% U/SIT46 (milk: 1; sputum: 28), 16.3% Latin American Mediterranean/SIT61 (sputum: 8) and 2.0% T/SIT53 (sputum: 1) strains of *M. tuberculosis*. New strains of *M. tuberculosis, M. bovis* and *M. africanum* were also obtained. The MIRU-VNTR on selected predominant cluster isolates from U/SIT46 (milk: 1; sputum: 9) showed same number of copies at each of the repetitive locus. Infection was significantly associated with poor knowledge of TB (p= 0.000), age (p = 0.006) and length of years in livestock trading (p =0.001).
Conclusions: We report a reverse zoonotic TB transmission between livestock workers and cattle due to an emerging U-strain of *M. tuberculosis* in Nigeria as evidenced by MIRU-VNTR. Measures towards limiting TB transmission through enlightenment campaigns especially among the active age groups are needed.

PD-514-12 *Mycobacterium bovis* on Michigan dairy farms: evidence of animal-to-human transmission

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Background: *Mycobacterium bovis (M. bovis)* is a zoonotic disease that is endemic in white-tailed deer in Michigan, and has been periodically reported in cattle in the state. In 2013, an investigation of a dairy herd by state and federal agencies resulted in an unusual high number of infected cattle, including those of young ages. Agricultural and Public Health Officials coordinated and tested farm workers. The objective of this presentation is to provide results of the joint investigations in farm workers and cattle.
Methods: Lymphnodes from the initial diseased cow underwent histopathology, Polymerase chain reaction (PCR), and culture. The whole herd of 451 was tested using skin testing, Interferon-gamma release assay. The whole herd was depopulated, and further testing of samples was done using whole genome sequencing. Farmer workers were provided with a tuberculin skin test (TST), and those who were positive on the TST were evaluated with a chest x-ray and abdominal computed topography scan for signs /symptoms of tuberculosis (TB), as well as gastric or intestinal symptoms.
Results: Of the 403 animals tested, 48 (11%) were positive on culture. Four of the 9 (44%) farm workers tested positive on the TST (but negative radiologic findings), and were treated with isoniazid daily for 9 months. Three of the 4 cases admitted consumed unpasteurized milk.
Conclusions: Evidence for animal-to-human transmission of M. bovis was identified in 4 of the 9 farm workers. Route of transmission might have been airborne or consumption of unpasteurized milk products. The outbreak highlights the human health risk associated with M. bovis.

03. Back to basics: diagnosis, notification and outbreak investigations

PD-515-12 Seasonal pattern of tuberculosis case notification in Afghanistan, 2005-2016

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Background and challenges to implementation: Tuberculosis (TB) leads to at least 14,000 deaths per year in Afghanistan. Based on existing and available surveillance data from the NTP, case notification has improved every year. The objective of this abstract is to clarify the season during which the most TB cases are notified and the season during which TB mortality is the highest.

Intervention or response: We reviewed and analyzed TB case notification data from 2003-2016 from the public health TB surveillance system. We decomposed time series into seasonal and trend components, and performed a time dependent spectral analysis to assess periodicity over time.

Results and lessons learnt: From 2005 onward, consistent seasonal periodicity was observed, with the highest number of new bacteriological confirmed (BC) TB cases occurring between April and June. Over the course of 12 years, case notification (BC TB and extra pulmonary TB [EPTB]) was highest in the second quarter of the year (at least 5% higher during the Spring) and lowest in the last quarter of the year while there was no significant change in EPTB case notification (See Graph 1).
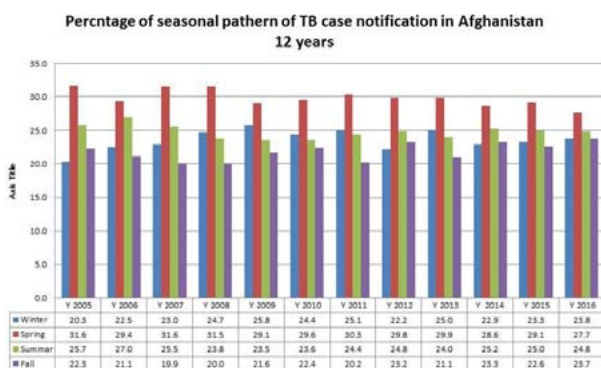
Figure Seasonal comparison of TB case notification in Afghanistan (2005-2016)

In addition, the first and third quarters of the year have similar case notification rates for BC-TB - In one year the rates in the first quarter were higher than in the third quarter and in another year, the rates in the third quarter were higher than in the first. EPTB cases are notified more in the Autumn than the Spring. Seasonal effects were similar between men and women and there was no significant seasonal change in mortality.

Conclusions and key recommendations: There is seasonal variation in reported TB case notification in Afghanistan. The findings of this analysis should be shared with Afghan health care workers involved in TB care and treatment. Further investigation is needed to better understand the trends.

PD-516-12 Gearing contact screening through SM, a missing link for TB control in the private sector, Khyber Pakhtunkhwa Pakistan

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Background and challenges to implementation: Khyber Pakhtunkhwa (KP) is one of the Provinces of Pakistan with 275 per 100,000 TB incidence rate. PTP KP *provides free TB care services to about 27 million local population while people from adjacent tribal agencies and Afghanistan are also benefited. There are 91 diagnostic & 325 Pvt clinics, enrolled in KP. Sputum microscopy (SM) and ATT under DOTS was ensured. The objective was to detect 70% of cases & treat successfully 90 %.*

Intervention or response: This was a retrospective study of 2015 with 4 main interventions. Registered patients in Private (Pvt) clinics were counseled to screen their contacts. All willing contacts were interviewed and counseled for screening on SM. Clinical history, signs and symptoms were correlated with the SM. *In 1st intervention type, 325 GPs were enrolled. In 2nd, 4 NGOs, In 3rd 2 pvt hospitals & In 4th , 12 Parastatal Hospitals were included.* As per NTP protocol, only those contacts were declared positive case who's SM had positive results. The rest of the negative patients were educated for the care of patient and personal biosafety. *The data of the last 1 year was analyzed through spss.*

Results and lessons learnt: About 11287 presumptive cases were screened during 2015, out of which 1698 positive cases were diagnosed. follow up cases screened were 3817, out of which 85 (2.23%) couldn't converted. The presumptive positivity rate was 15.04%. in 2015 total 4246 contacts were screened in pvt sector, out of which 205 were confirmed SP pts. The confirmed cases were 4.8 % of the contacts screened. No significant difference between male to female ratio (p< 0.05) noted.

Conclusions and key recommendations: Physicians in the Pvt Sector be motivated & trained as per national guideline; active screening (chest camps and mass mobilization) be encouraged to avert possible risk of DR & TB HIV Co-infection. Awareness campaign be prioritized in clinics.

PD-517-12 Improved TB case notification by private health care providers: an experience from 40 urban sites of India

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Background and challenges to implementation: In India, tuberculosis remains a major public health challenge with an incident of 2.8 million with over 1 million cases are 'missed' annually. Low case detection and notification are two of the major challenges facing the National Program. The reasons could be attributed to limited access to TB treatment, private sector engagement and weak social support system. More than half of the TB patients approach the private practitioners, who often lack formal training and treatment is initiated without proper TB diagnosis. Often the TB cases from private sector not being reported to Government. This paper focuses on the efforts of The Union in engaging the private sector for increased case notification.

Intervention or response: The Union led project Axshya is implementing urban TB control in 40 urban sites of India. The project has mapped and provided formal training /sensitisation on standards of TB care in India (STCI) guidelines to the health care providers. Linkages were also established with public and private for diagnosis and treatment. The project has developed innovative software and mobile app which facilitates notification of TB patients from private sector in Nikshay.

Results and lessons learnt: During the period Jan-Dec 2016, the project has sensitised and engaged 3648 qualified practitioners, 202 private hospitals and 77 labs in 40 urban sites and facilitated notification of 16265 TB patients from the private sector. It also offers treatment adherence support through daily SMS and interactive voice calls. Over 10,000 TB patients are benefitting from this service.

Notification from Private sector
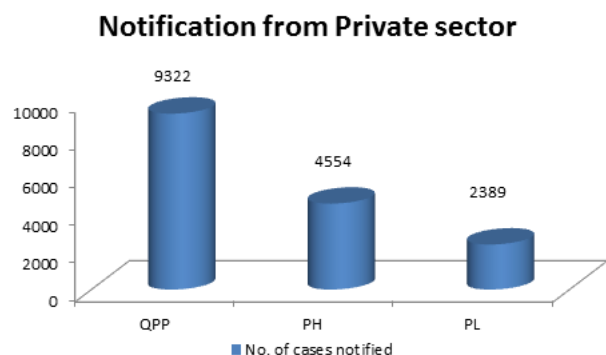
Figure Notification from Private Sector

Conclusions and key recommendations: Engagement of private sector is crucial in identifying the missing TB cases. With one year implementation, the project has notified over 16000 TB cases in the 40 urban sites, which reflects the fact that scaling of the intervention to the entire gamut of private sector will lead in increased case notification and to narrow the gap of the missed cases.

PD-518-12 Mapping tuberculosis case relative locations to inform active case detection and linkage to care in Swaziland

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Background and challenges to implementation: In Swaziland, as in many high HIV/TB burden settings there is not information available regarding the household location of TB cases. Data from "Butimba", a TB REACH project, was re-analyzed to provide insight into the location of TB cases surrounding Mbabane, Swaziland. The project aimed to identify geographical areas with high TB burdens to inform active case finder (ACF) distribution.

Intervention or response: Butimba implemented household contact tracing; obtaining landmark based, informal directions, to index case homes, defined here as relative locations. The relative locations were matched to census enumeration areas (EAs) using the Microsoft Excel Fuzzy Lookup function. Of 403 relative locations, an EA reference was detected in 388 (96%). All results (84/388) that had a Jaccard similarity index of < 0.8 were reviewed by local experts. On review, 45 errors were easily correctable due to slight mismatches between text and EA name. 39 erroneous automated matches were reassigned by local experts. TB cases in each EA and the ACFs in each Inkhundla (Chiefdom) were mapped using the geographic information system, QGIS 2.16.

Results and lessons learnt: Urban Tinkhundla predictably accounted for most cases; however, after adjusting for population, the highest density of cases was found in a rural Inkhundla. There was no correlation between the number of ACFs currently assigned to the 7 Tinkhundla surrounding Mbabane and the total number of TB cases (Kendall tau = -0.39, p = 0.22) or the population adjusted TB cases (Kendall tau = 0.098, p = 0.76) per Inkundla.

Conclusions and key recommendations: Reducing TB incidence in high-burden settings demands novel analytic approaches to study TB case locations. This semi-automated approach demonstrated the feasibility of linking relative locations to more precise geographical areas, enabling data-driven guidance for National Tuberculosis Control Program (NTCP) resource allocation. In collaboration with the Swazi NTCP, this analysis highlighted opportunities to better align ACFs with TB disease burden.

PD-519-12 Yield of facility-based verbal screening amongst household contacts of patients with multi-drug resistant tuberculosis in Pakistan

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Background: Household contacts of multidrug-resistant tuberculosis (MDR-TB) patients are at a high risk of getting infected with TB/MDR-TB, therefore symptomatic or vulnerable individuals should be screened and treated early.
Methods: A cross-sectional study was conducted among household contacts of MDR-TB patients in three high-burden TB sites in Pakistan from July 2013 to June 2014. MDR-TB index patients were asked to provide a list of all members of their household and were asked whether any of them had TB symptoms such as productive cough, fever, weight loss and night sweat ("facility-based verbal screening"). Symptomatic contacts were defined as presumptive TB cases and were invited for investigations at the facility. Those who did not come were paid a home-visit. Confirmed TB/MDR-TB patients were registered in the nearest treatment facility.
Results: Of 209 MDR-TB index patients, 1467 household contacts were identified and screened, 95 of them children < 5 years. Of these 172 (12%) were symptomatic. Most common symptoms were cough 157 (91%) and fever 107 (62%). 58 (34%) asymptomatic contacts were not investigated. Of total contacts, 56 (3.8%) were diagnosed with TB, among them 54(96%) with MDR-TB and 2(4%) with drug-susceptible-TB. The number needed to screen (NNS) to identify a new MDR-TB case among adult household contacts was 27 and among presumptive adult and pediatric TB contacts was three. All 56 confirmed patients were registered for treatment.
Conclusions: Screening household contacts of MDR-TB index cases may be considered a feasible and high yield option, in high-burden, low-resource settings within Pakistan. The number of presumptive TB contacts required to screen to identify a new MDR-TB case was unusually low, indicating an effective strategy that could easily be scaled-up. The screening and management of vulnerable adults and children living with patients having TB of any form is a major priority in the combined efforts to end TB.

PD-520-12 The missing link between DOTS expansion, functionality and case detection: review of the DOTS expansion strategy in Nigeria

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Background: DOTS expansion remains one of the core strategies towards the elimination of Tuberculosis in Nigeria. Findings from the National Prevalence survey revealed that access to diagnostic and treatment services is one of the major reasons for the low case finding in the country.
In spite of the ongoing DOTS expansion, several factors have been identified as barriers to functionality of DOTS sites. These include infrastructural deficiencies, high staff attrition due to transfer, death and retirement of previously trained staff. Apart from this, although DOTS expansion has been based on rational human estimated needs, there has not been an empirical country wide geographical mapping to determine the actual gaps in DOTS coverage.
Methods: Desk review was conducted on facility level data collated by the National Tuberculosis and Leprosy Control Programme (NTBLCP), to determine the percentage of DOTS facilities that are functional out of the total available. Functionality was defined as a DOTS site manned by a DOTS provider and that reported at least one TB case within a quarter to NTBLCP.
Results: Findings shows that the number of DOTS sites in the country increased from 5,863 in 2015 to 6,579 (12% increase) in 2016. However, of the 6579 DOTS sites, only 4,818 (73%) reported presumptive TB cases to NTPLCP. Surprisingly, only 2,722 (41%) notified at least one TB case, leaving a gap of about 59% (3,857) of DOTS sites that did not notify any TB case and 27% (1,761) that did not report any presumptive TB cases.
Conclusions: Despite investments in DOTS expansion, notification of TB cases remains sub-optimal. This may be attributed to attrition, strike actions, infrastructural gaps and lack of knowledge about where to obtain TB treatment. Recommendations for implementation includes the use of scientific geographical mapping to determine the real gaps in DOTS coverage and investment in awareness creation on TB.

PD-521-12 Active tuberculosis case search pilot intervention in selected communities: birth of the first TB prevalence survey in Nigeria

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Background and challenges to implementation: The report of the TB Prevalence survey conducted in Nigeria (2012) has about two (2) times more TB cases than was previously estimated by the World Health Organization. This necessitated a paradigm shift from the passive approach of detecting TB cases. A new strategy of actively searching for the new TB cases was piloted in five urban slums across the three states of Lagos, Kano and Enugu in Nigeria in 2014.

Intervention or response: Community Based Organizations (CBOs) were engaged in five urban slums and they recruited and coordinated Community TB Workers (CTWs); whose main duty was to screen individuals in households residing in the intervention communities for symptoms of TB. On the other hand, Community Pharmacists (CPs) and Patent Medicine Vendors (PMVs) were also engaged to identify and refer clients with symptoms of TB to TB treatment facilities. This CP/PMV intervention was executed in eleven states.

At household level, CTWs collected sputum samples from those who had symptoms of TB and conveyed the samples to designated TB laboratories within the community. Those who tested positive to the smear microscopy tests were placed on TB treatment. The intervention period was between three to five months.

Results and lessons learnt: On the whole, within the period of implementation across the intervention states, the house to house intervention in Kano, Enugu and Lagos states reported a total of 404 positive TB cases, while the referrals from CPs and PMVs yielded a total number of 266 TB cases in ten states; Bauchi, Benue, Kaduna, Taraba, Lagos, Oyo, Abia, Enugu, Ogun and Rivers.

Conclusions and key recommendations: This experimental intervention resulted into detecting missed TB cases in the communities and the full potential benefits of the intervention, now form the main strategy of the current Global Fund TB grant (July-2015 to December, 2017) in Nigeria.

PD-522-12 Scale-up of house-to-house TB case finding in Nigeria: best practices and lessons learnt

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Background and challenges to implementation: Nigeria is amongst the three countries that account for half of the 4.3 million 'missing' TB cases globally (WHO, 2016). Undetected cases increase the risk of TB transmission hence finding the missing cases is crucial to TB control. Several innovative strategies were adopted by the country to address this issue, key amongst them is the active house to house search for TB. This strategy is currently being implemented in 20 states across six geopolitical zones of Nigeria through the support of the Global Fund.

Intervention or response: The project engaged over 870 high risk communities. These communities included the rural and urban crowded communities, nomadic and IDP camps. The project entailed house to house visits by trained community TB workers (CTWs) to identify presumptive TB cases, collect their sputum samples and transfer to microscopy or GeneXpert centres for screening. Persons with positive results are contacted and linked to treatment while smear negative symptomatic cases are referred to the State Program for further investigation. Chronic cough (≥2 weeks) inquiry is used as a screening tool. Challenges include poor reception of the project in some communities because of TB-related stigma. Access to TB diagnostics services in the intervention areas is limited; the few laboratory centres available are overwhelmed and manned by poorly motivated staff who often demand for incentives before testing specimens.

Results and lessons learnt: 5789 persons have been notified over a ten-month period. Key lessons learnt confirm that strategic community engagement, massive awareness creation using mass media and local means of communication, mapping of locations of registered TB cases to inform home visits and strengthening of laboratory systems are viable mechanisms to improve TB case finding.

Conclusions and key recommendations: Active case finding interventions is a viable strategy to increase TB case finding when implemented in the context of a strengthened diagnostics system and strategic community and media involvement.

PD-523-12 Association between prediabetes and tuberculosis: a cohort study

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Background: Diabetes is a major risk factor for tuberculosis (TB), and has been increasingly prevalent in high TB burden countries. Prediabetes is more prevalent than diabetes and has been suggested to affect host defense in laboratory studies. However, few studies have investigated the association between prediabetes and TB.

Methods: We conducted a cohort study with 119,304 participants who were included in the community-based health screening service in northern Taiwan from 2005 to 2008. We used baseline fasting plasma glucose (FPG, >=126 mg/dl) and prescription of hypoglycemic agents to define diabetes. We further defined prediabetes among non-diabetics by using FPG (100 mg/dl≤ FPG< 126 mg/dL). The baseline FPG was obtained from the survey, and the prescription information was obtained through linkage to the National Health Insurance database. Incident cases of TB were identified from the national tuberculosis registry. We used Cox regression modelling to estimate the hazard ratios (HRs) for prediabetes and diabetes, adjusting age, sex, smoking, alcohol use, body mass index, steroid use, end-stage renal disease, and socioeconomic status. We used spline regression to discover the dose-response relationship between FPG and TB risk in people without diabetes.

Results: After the average 7.2 years of follow-up, 324 tuberculosis cases occurred. Compared to normoglycemic subjects (FPG< 100mg/dl), the adjusted HR was 0.80 (95% confidence interval [CI] 0.60, 1.06) for pre-diabetes participants and 1.71 (95% CI 1.26, 2.31) for diabetes patients. Among people without diabetes, a U-shape association was found between FPG and TB risk, and the risk of TB was the lowest at FPG level of around 110 mg/dl (Figure).
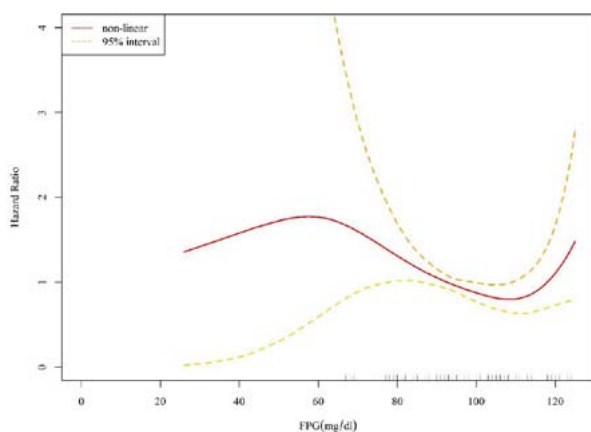
Figure Dose-response relationship (FPG and risk of TB)

Conclusions: Our cohort study did not reveal an increased risk of TB among prediabetics when compared to normoglycemic subjects. The U-shape association between FPG and TB risk among non-diabetics suggests a complex relationship between metabolic derangements and TB risk which requires further investigation.

PD-524-12 Intensified case finding for tuberculosis at health facilities in Palawan, the Philippines

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Background: Tuberculosis (TB) case finding project (DetecTB) using digital X-ray machine, Light Emitting Diode Fluorescence Microscope and GeneXpert machine at health facilities has been implemented in Palawan, the Philippines since 2015. The project targeted people consulting at the outpatient department or the ambulatory emergency room of the health facility, regardless of signs and symptoms. This study aimed to assess the yield of the intensified TB case finding using innovative diagnostics and algorithms at health facilities and determine predictors for the diagnosis of TB in the setting.

Methods: TB screening data between January 2015 and February 2017 were collected from Puerto Princesa City Health Office, Department of Health Ospital ng Palawan, Southern Palawan Provincial Hospital, and Northern Palawan Provincial Hospital. Data were entered into Epi Info™ and analyzed by STATA 13. Univariable and multivariable analyses were conducted to determine predictors for the diagnosis of TB.

Results: A total of 6,496 participants were screened. Of them, 2,982 (45.9%) were identified as TB suspects, and 780 (11.9%) were diagnosed with TB consisting of 563 bacteriologically confirmed cases (72.2%) and 217 clinically diagnosed cases (27.8%). Significant factors associated with the diagnosis of TB were male sex (AOR 1.75, 95% CI: 1.38-2.20), history of previous TB treatment (AOR 1.41, 95% CI: 1.05-1.88), low BMI (AOR 1.70, 95% CI: 1.33-2.17), and cough ≥ 2 weeks (AOR 3.55, 95% CI: 2.49 -5.06).

Conclusions: The intensified case finding for TB using innovative diagnostics and algorithms at health facilities yielded a considerable number of TB cases. Male sex, history of previous TB treatment, low BMI, and cough ≥ 2 weeks were significant predictors for the diagnosis of TB in the setting.

04. HIV-TB treatment and outcomes

PD-525-12 Antiretroviral therapy and viral suppression during and 3 years after completion of tuberculosis therapy in an inner-city cohort in Atlanta, Georgia

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Background: Guidelines recommend that HIV-infected patients not receiving antiretroviral therapy (ART) who are diagnosed with active tuberculosis (TB) should initiate ART within 12 weeks of staring TB therapy. We sought to evaluate the time to ART initiation, and rates of viral suppression (VS) during TB treatment and in the 3 year post-treatment period.

Methods: Retrospective study of culture-confirmed TB among adult HIV-infected patients admitted to Grady Memorial Hospital between 2008-2015. VS during TB therapy was defined as ≥1 viral load ≤200 prior to TB treatment completion. VS for each year following completion of TB therapy was defined as ≥1 viral load ≤200.

Results: Among 271 TB patients during the study period, 95(35%) had HIV; including 8(8%) with previously diagnosed HIV on ART at time of TB diagnosis. The median CD4 count was 86 and 39(41%) had a CD4≤50. Among 34 patients off ART without meningeal disease and CD4≤50 who survived ≥4 weeks, 28(82%) started ART during TB therapy, 9(26%) within 4 weeks, and 18(53%) achieved VS during TB therapy (figure).
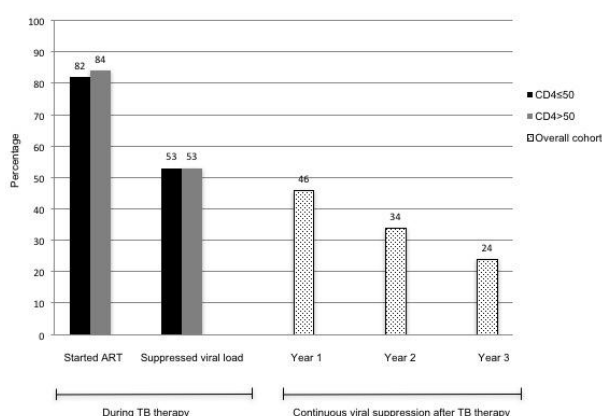
Figure ART use and viral suppression during and after TB treatment

Among 38 patients off ART without meningeal disease and CD4>50 who survived ≥12 weeks, 32(84%) started ART during TB therapy, 16(42%) within 12 weeks, and 20(53%) achieved VS during TB therapy. Among 70 patients who completed TB therapy, 32(46%) had VS within 1 year of completing TB therapy. Sixty-seven pa-

tients were alive and without TB relapse 3 years after completing TB therapy; 16(24%) remained virologically suppressed throughout 3 years of follow-up after completion of TB therapy.

Conclusions: VS rates for patients with TB/HIV in this inner-city cohort are low during TB therapy and decline afterwards. Strategies to increase VS during TB therapy and maintain continued VS are urgently needed.

PD-526-12 Tuberculosis treatment outcomes in HIV-positive and -negative adolescents in Kenya

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Background: Kenya has a high burden of adolescent HIV and tuberculosis (TB). HIV-positive adolescents have poor treatment outcomes with higher mortality and loss to follow up (LFTU) (40%). Outcomes for adolescent TB have not been described, nor has the effect of HIV co-infection in this population. We assessed TB treatment outcomes of HIV-positive versus negative adolescents in Kenya.

Methods: We analyzed a retrospective cohort of all adolescent (10-19 years old) tuberculosis cases in Kenya from 2012 to 2015. Data were abstracted from the national case-based electronic data recording system, and analyzed using Stata 12.1. Cases without documented HIV status or treatment outcomes were excluded from outcome analysis. Descriptive statistics and frequencies are reported. Multinomial logistic regression modeling was used to calculate relative risk of treatment outcomes by HIV status, controlling for sex, age, and TB type.

Results: During the study period, 33,487 adolescent TB cases were identified, accounting for 9.23% of all TB cases nationwide. Median age was 16 years (IQR 14-18 years) with 47.3% female. HIV testing was done in 94.5%, with 17.4% HIV-positive (n=5811). Among HIV-positive patients, 92.3% were on antiretroviral therapy and 99.4% were on cotrimoxazole preventive therapy.

Of the 31,641 adolescents with documented treatment outcomes and HIV status, 87.4% (n=27641) completed treatment, 2.6% died (n=831), 0.3% failed treatment (n=91), and 9.7% (n=3078) were LTFU. HIV-positive adolescents had higher risk of mortality (RR 6.30, 95% CI 5.44-7.30, p=0.00) and LTFU (RR 1.32, 95% CI 1.20-1.46, p=0.000). There was no significant difference in treatment failure risk (RR 1.33, CI 0.77-2.29, p=0.30). Among HIV-positive adolescents, there was no significant difference in mortality (p=0.44), treatment failure (p=0.73), or LTFU (p=0.19) by ART status.

Conclusions: HIV-positive adolescents have worse treatment outcomes than their HIV-negative counterparts. Further studies are needed to identify age-specific opportunities to enhance TB prevention and treatment for HIV positive adolescents.

PD-527-12 Effect of TB-HIV collaboration on treatment outcome (death) of TB-HIV co-infected patients in Southern Nigeria: a six year review (2011-2016)

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Background: One of the main goals of TB/HIV collaboration is reduction in unfavorable treatment outcomes especially 'death' among persons with co-infection. Having implemented this strategy for over a decade, Nigerian TB control programme managers would expect a downward trend in TB death rates among successive cohorts of TB/HIV co-infected patients managed under the programme. To what extent has this expectation been realized? This study attempts to answer this question especially for the 14 GLRA-assisted states in Southern Nigeria.

Methods: A retrospective desk analysis of TB treatment outcome data routinely reported in the 14 states for TB cases evaluated from 2011-2016 was conducted. The proportion of TB/HIV co-infected cases notified for the 6 years was determined. The contribution of TB/HIV co-infected cases to the total deaths and death rates among TB/HIV co-infected cases per year were calculated using proportions.

Results: TB/HIV co-infected cases' contribution to total TB (all forms) cases notified within the review period increased from 21% in 2011, peaked at 23% in 2012 before a relatively progressive decline to 19% in 2016. However, their contribution to the total deaths was undulating, increasing from 36% in 2011 to 46% in 2012 and peaked in 2015 at 50%, but declined to 39% and 37% in 2014 and 2016 respectively. Also, death rates among the group followed same pattern and remained higher than the baseline value.
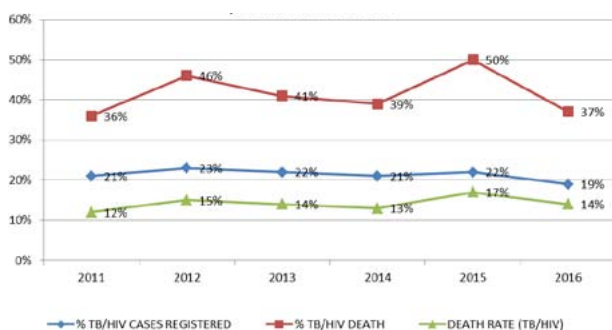
Figure Graph showing the contribution of TB/HIV cases to the total TB cases registered and total deaths, and death rates among TB/HIV co-infected patients from 2011-2016

Conclusions: The managers' expectations have not materialised in view of the fact that the death rate among the co-infected cases rose and remained consistently higher than the baseline of 12% despite the occasional

undulations over the period. While we wait to know if the decline observed in 2016 will be sustained, there is need to further examine the quality of TB/HIV collaboration in these states to identify possible gaps contributing to the observed poor outcome.

PD-528-12 Mortality of TB-HIV co-infected patients in Kampala remains high despite early initiation of ART

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Background: Tuberculosis (TB) remains a cause of death among people living with HIV (PLWH). Kampala city implemented the WHO policy on ART initiation during the intensive phase of TB treatment. This study aims to assess the impact of early ART initiation on the death rate among TB/HIV co-infected patients in Kampala.

Methods: We analyzed the time of death and associated factors for patients registered on TB treatment during the period 2014-2015. Chi square estimations with 95% confidence intervals were computed to measure the risk of death at various points of initiating TB treatment considering HIV status as the exposure and time of death as an outcome. Analyses were done in STATA version12.1.

Results: Out of 15,429 records analyzed 7,696 (49.9%) were TB/HIV co-infected. A total of 1,641 (10.6%) died during TB treatment of which 1,035 (63.1%) had complete data with regard to treatment start date and death. Of the deaths, 728 (70.3%) were TB/HIV co-infected and 634 (87.1%) were documented to be on ART. The occurrence of death at month one was 359 (49.3%), at month two 131(18.0%), and 238 (32.7%) after 4 months of treatment. The risk of death among the TB/HIV patients during the intensive phase of treatment was higher as compared to continuation phase (OR=1.34, CI: 1.01-1.76 p=0.04,). This risk was also higher among the EP (TB/HIV) patients (OR 2.0, 95% CI 1.4-2.8, p=0.0002,) as compared to the pulmonary TB cases. Compared to other facilities, in the first month, death was lower among TB/HIV patients in public health facilities (OR 0.698, CI: 0.51-0.96 p=0.028).

Variables for HIV positive TB patients	Number (%)	OR (CI)	P- Value
Death during intensive phase	728 (70.3%)	1.3 (1.0 - 1.8)	0.0381
Death among EP (Intensive)	212 (29.1%)	2.0 (1.3 - 2.9)	0.0002
Death in Public facilities (first month)	516 (70.2)	0.7 (0.5 - 10.0)	0.0282

Table Risk factors for death among TB/HIV patients

Conclusions: Mortality among TB/HIV co-infected patients in Kampala remains high. The risk of death is higher among the extrapulmonary and patients treated in private/NGO health facilities. More interventions should be explored to reduce the risk of death among the TB/HIV co-infected patients.

PD-529-12 Mortality predictors among women of reproductive age on tuberculosis treatment in Kampala, Uganda

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Background: According to WHO, Tuberculosis (TB) is the third leading cause of death among women in reproductive age (15-44) and yet there is still is little attention paid to the impact of the disease among women of this age group as a key health issue. In Uganda, there is no age specific analysis of the mortality of women on TB treatment in the reproductive age group therefore this analysis sought to establish this.

Methods: We retrospectively reviewed 5,953 records of patients with TB registered for treatment from January-September, 2015 to establish factors could be related the death among women in reproductive age. We considered 15-49 years as our reproductive age group for this population. We conducted a mortality based- analysis with; HIV status, health facility, DOT and disease classification

Results: Of the records reviewed 2,206 (37%) were of women of whom 1,853(84%) were of women in the reproductive age. The mean reproductive age was 29.3 (SD 8.15). More than half (54.6%, 1,012) were HIV positive with 94.4% (955) on ART and 99.5% (1, 007) on CPT. 1,529 (82.5%) successfully completed treatment. 202 (11%) died while on treatment.

Women in reproductive age were more likely to have an HIV positive status (OR=1.74, P= 0.000) but less likely to die (OR= 0.552, P= 0.000) compared to those in other age groups. Among reproductive age women, those above 29 years were more likely to die than those below 29 years (OR=1.89, P= 0.000). The odds of death among reproductive age was almost 3 times more (AOR= 3.62, P= 0.000) for EP-TB patients as compared other categories.

Conclusions: Extra pulmonary disease, HIV status and age above 29 years, are predictors of mortality among women of reproductive age with TB. However, reproductive age is not a predictor of death among women on TB treatment in Kampala.

PD-530-12 Treatment outcomes among HIV co-infected MDR-TB patients in Uganda

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Background: Multidrug-resistant Tuberculosis (MDR-TB) and HIV co-infection are common in settings where the burden of both diseases is high. Although Uganda is a low MDR-TB prevalent country, a total of 1,036 MDR-TB patients had been enrolled for treatment by 2016, of which 798 (77%) were co-infected with HIV. This study aimed at assessing treatment success and death among MDR-TB patients initiated on treatment in relation to their HIV status.

Methods: We retrospectively reviewed MDR-TB patients enrolled on treatment in 2012 and 2013 from seven MDR-TB treatment sites. Data extraction for sex, age, type of TB, treatment outcome, HIV, and ART status was done and analyzed using SPSS version 16.

Results: Overall 179 MDR TB patients' records were reviewed, 74 (41%) were HIV co-infected of which 42 (57%) were males. Out of 74 co-infected MDR-TB/HIV co-infected patients, 71 (96%) were initiated on ART. Out of the 71 MDR-TB/HIV co-infected patients, 45 (61%) were successfully treated as compared 77/105 (74%) among the HIV negative cases. Overall 16/74 (22%) HIV-positive MDR-TB patients died while on treatment as compared to the 11/105 (11%) of the HIV-negative cases.

Conclusions: Despite the high ART coverage, MDR-TB patients co-infected with HIV in Uganda had poorer treatment success rates compared to HIV-negative patients. Co-infected patients are also as twice more likely to die while on second line treatment as compared to the HIV-negative patients. We recommend intensive TB-HIV collaborative interventions in order to increase treatment success amongst the MDR-TB/HIV co-infected patients in Uganda.

PD-531-12 Autopsy characterisation of lung microbiome of HIV-positive patients in a tertiary referral hospital in Ghana

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Background: Pulmonary infections are the underlying cause of high morbidity and mortality amongst HIV infected persons. Notwithstanding, data on pulmonary co-infecting pathogens and their drug susceptibility patterns is limited. Thus, we sought to characterize the lung microbiome of post-mortem biopsy samples of HIV/AIDS patients in Ghana.

Methods: We examined 100 lung biopsies from HIV/AIDS decedents from the Korle-Bu Teaching Hospital in Ghana for mycobacteria, other bacteria and fungi. The techniques utilized included; culture, Gram/Ziehl-Neelsen staining and PCR or MALDI-TOF Mass spectrometry. The phenotypic drug susceptibility patterns of bacteria were subsequently determined using microplate alamar blue and disc diffusion assays respectively.

Results: We retrieved clinical data for 88 cases: 45(53.6%) males and 43(46.4%) females with their mean ages being 40.4(±10.6) and 37.3(±11.1) respectively. HIV infected decedents were 84 and only 40 cases had well-defined HIV types (HIV-1, 33; HIV-2, 2; HIV 1 & 2, 5). Co-infections with TB, pneumonia, oesophageal candidiasis and/or cryptococcal disease were 12(14.3%). From the mycobacterial cultures, 15(6.2%) isolates were identified as MTBC and 8(3.3%), non-tuberculous mycobacteria (NTM). Four (4) MTBC isolates were *M. africanum* (Lineage 5-2; Lineage 6-2) and 11 were *M. tuberculosis* (Ghana-4; Cameroon-3; Delhi/CAS-1; Haarlem-1; Uganda I-1; Beijing-1). Drug susceptibility testing of MTBCs showed that, 1 isolate each was isoniazid mono-resistant, rifampicin mono-resistant and multidrug resistant (MDR). Other bacteria isolated were 211(85.8%) and the predominant species were *Enterococcus faecalis* 47(22.3%), *E. coli* 25(11.8%), *K. pneumoniae* 23(10.9%), *S. aureus* 6(2.8%) *and S. epidermidis* 6(2.8%). Gram negative bacteria were most susceptible to cefoxitin but highly resistant to cefuroxime whereas Gram positives showed high susceptibility to vancomycin but high resistance to flucloxacillin. Fungi isolates recovered were 8; *Candida species* 6(75%), *C. neoformans* 1(12.5%) and *Yarrowia lipolytica* 1(12.5%).

Conclusions: We showed that, *E. faecalis, K. pneumoniae, Mycobacteria, Staphylococcus* and *Candida species* are important independent/co-infecting lung pathogens of HIV/AIDS patients.

PD-532-12 A tweak in policy, an increase in usage

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Background and challenges to implementation: Malawi is classified as a high prevalence TB/HIV country, the co-infection rate was 52 % as of 2016. The Rise in TB notifications from 1985 to date was driven by the HIV epidemic. HIV prevalence for the country was determined to be approximately 8.8 % in 2015. Accordingly Gene Xpert platforms (GXP) was introduced in late 2011 as an aid in the quick diagnosis of HIV related TB. Optimization of existing GXPs has been a challenge.

Intervention or response: 2016 represents the first year when GXP was used as the primary diagnostic tool for most high risk/ special populations e.g. HIV positive presumptive TB ,Presumptive MDR - TB, Children, Miners, Health care workers etc. HIV positive presumptive TB clients are the largest group among high risk/ special populations. Health care workers including clinicians were trained on GXP. The systematic TB screening efforts were maximized during this period which includes training, supervision and mentoring. 2015 represents the last year GXP was used as an add - on test after initial testing of High Risk/ Special populations with Microscopy.

We analyzed Gene Xpert usage data from Q1 2015 to Q4 2016.

Results and lessons learnt:
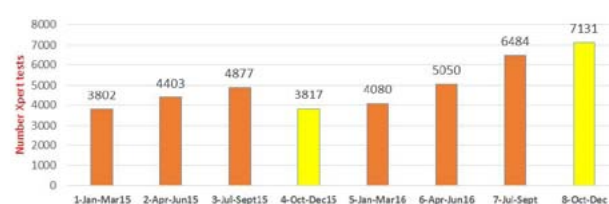
Figure Gene Xpert MTB/RIF usage over time

The switch to the use of Gene Xpert MTB/RIF as the primary diagnostic tool in TB diagnosis as well as the introduction of systematic TB screening has led to an 87% increase in the number of Gene Xpert test being performed in Q4 of 2016 when compared to the corresponding quarter in 2015.

Conclusions and key recommendations: The changes in the diagnostic algorithms with respect to the role of the Gene Xpert MTB/RIF platforms coupled with the introduction of active case finding such as Systematic TB screening in all OPD settings has led to a substantial increase in Gene Xpert usage and the number of Presumptive TB clients examined using this more sensitive tool.

PD-533-12 TB-HIV services for HIV key and vulnerable populations in Tanzania: who and what should be prioritized?

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Background and challenges to implementation: HIV key and vulnerable populations (KVP) are people at heightened risk of HIV; they face limited access to health services, criminalization and marginalization. In Tanzania, the PEPFAR/USAID-funded Sauti project offers systematic screening for active TB as part of the package of community-based combination HIV prevention services to HIV key and vulnerable population (KP and VP) at hot spots, inclusive of biomedical, economic empowerment and behavior change interventions.

Intervention or response: Between August 2015 and December 2016, we evaluated the systematic screening strategy based on routine program data among female sex workers age 18 and above who exchange sex for cash or goods, men who have sex with men, out-of-school adolescent girls and young women (ages 15-24), partners of female sex workers, children, and other hot spot populations who accessed mobile community and home-based biomedical sites and 24 drop-in centers in 9 regions of mainland Tanzania. Multivariate logistic regression analysis was performed to explore factors associated with presumptive TB.

Results and lessons learnt: Among 765,504 KVP screened for TB using the national questionnaire, 2,494 had presumptive TB. Being HIV KP (MSM or FSW) (OR 1.53 [1.35-1.54]); male (OR 1.22 [1.12-1.34]); HIV infected (OR 5.86 [5.25-6.54]); older than 50 years (OR 1.59 [1.40-1.81]); and having a history of drug use at last sex (OR 1.89 [1.56-2.28]) were positively associated with presumptive TB. Insufficient linkage to care, lack of community-based TB diagnostics and network systems in place for sample transportation resulted in lack of reliable information about the TB outcome for this hard to reach population.

Conclusions and key recommendations: Findings confirm relevance of integrating TB screening into HIV combination prevention services to KVP, with particular focus on HIV infected KP using drugs. More resources should be allocated to improve linkage to care and ensure diagnostic services are made available to high risk individuals screening positive in community settings.

05. Muddying the waters - co-morbidities in drug-resistant TB

PD-534-12 Feasibility and yield of screening for common non-communicable diseases in a cohort of patients treated for TB in Lima, Peru

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Background: Rising rates of non-communicable diseases (NCDs) pose major challenges to low and middle income countries. The period of tuberculosis treatment provides opportunities for NCD screening and care of tuberculosis patients, that may suffer increased morbidity from these chronic diseases.

Methods: We explored the feasibility and yield of NCD screening in patients who successfully completed treatment for drug susceptible or multidrug resistant (MDR) tuberculosis in Lima, Peru. Community controls were recruited from the same geographical area. NCD prevalence was assessed by taking a detailed medical history and performing ambulatory blood pressure measurement and urinalysis.

Results: In total, 177 participants with prior tuberculosis (144 drug susceptible, 33 MDR) and 161 community controls were fully evaluated, with more women (70% vs 42%) in the "no tuberculosis" group. There was an almost four-fold increased prevalence of diabetes among those with prior tuberculosis (adjusted Prevalence Ratio [aPR] 3.66; 95% CI 1.68-8.01). Blood pressure screening detected participants that were not previously known to be hypertensive, with a greater proportion in the "no tuberculosis" group (10.6% versus 4.2%). Urinalysis detected similar proportions of participants from both groups with (possible) undiagnosed diabetes or chronic kidney disease. The number of tuberculosis patients needed to screen to find one (new) case of hypertension, glycosuria or proteinuria was 24, 31 and 5 respectively.

Conclusions: Patient centered care that includes hypertension, diabetes and proteinuria screening is feasible in tuberculosis patients. An opportunity exists for the secondary prevention of cardiovascular and end-organ sequelae from these common non-communicable diseases.

PD-535-12 ´Depression´ as a concomitant illness needs attention in the treatment regimen of DR-TB patients: a study from Jharkhand, India

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Background: 'Depression' is the leading cause of ill-health. WHO estimates >300 million people live with depression worldwide, i.e. 18% rise from 2005 to 2015. The Union's TB and Mental health working group highlights 'TB-depression syndemic' and an unrecognized driver of TB/DR-TB epidemics. In India, an estimated 1.3million DR-TB cases emerge annually. Jharkhand, an eastern tribal state of India has initiated 1215 DRTB cases on treatment by 2016. The objective of this study is to analyse the state of depression among under-treatment DRTB patients in Jharkhand by using Center for Epidemiologic Studies Depression Scale (CES-D).

Methods: The 10 point questionnaire of CES-D was administered in 92 DRTB patients. 32 (Intervention group) of Ranchi district were being counselled/followed by a professional counsellor. 60 patients(Control) are from other districts. State of depression of both groups were analysed separately. Components of depressive symptoms - depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite and sleep disturbance were accessed. Total and individual score reviewed separately.

Results: Out of 92 (58 Male; 34 Female), 39% found to be from productive age group of 16-25. 30% lost employment after disease; 17% illiterate; Mean education was 7th standard. Among 92, out of 30 CES-D score, average was > 10, i.e. 0.56 means live with depression. During medication, that climbed to 11.28 among 32 intervened and that of 60 patients escalated to 18. The range of score among non-intervened group was 9 to 24. Only 5% of total patients found without depression with score < 10.

Conclusions: Depression is an effect of the cause DR-TB which further push patients to poor outcomes, morbidity and community transmission. The feelings of helplessness/hopelessness was evident. Counseling plays a role as medication of psycho-social treatment. Treating depression as an allied disease to DR-TB is essential to End TB.

PD-536-12 Treatment outcome and mortality in pulmonary TB in lower-income countries: impact of drug resistance and HIV co-infection

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Background: Drug resistance and HIV co-infection are important challenges for the global control of tuberculosis (TB). We studied the association between drug resistance and treatment outcomes among HIV co-infected and HIV-negative pulmonary tuberculosis (PTB) patients.

Methods: We collected clinical data and *Mycobacterium tuberculosis* isolates from adult PTB stratified by HIV and drug resistance status in 2013-2016 in 9 countries from three continents: Peru, Thailand, Botswana, Côte d'Ivoire, Congo DRC, Kenya, Nigeria, South Africa, Tanzania. We confirmed all resistant strains at the Swiss National Center for Mycobacteria, using MGIT liquid medium system at critical drug concentrations for common first- and second-line drugs. We used descriptive statistics and multivariable logistic regression to assess predictors of treatment outcome and mortality during treatment, adjusted for age, sex, HIV status, drug resistance and history of TB, accounting for clustering at site-level.

Results: 872 PTB cases were included: median age was 34 years (interquartile range [IQR] 27-43), 335 (41%) were women, 392 (47%) were HIV co-infected with a median CD4 cell count at PTB diagnosis of 190 cells/µL (IQR: 80-370). 515 (59%) cases had pan-susceptible PTB, 44 (5%) had mono-resistance, 239 (27%) had multidrug-resistance (MDR), 30 (3%) had pre-extensive drug-resistance (pre-XDR) or XDR, and 44 (5%) had other resistance combinations. Any drug resistance (single or combined), mono-resistance, MDR, and pre-XDR/XDR were all associated with increased mortality and reduced probability of cure/treatment completion. HIV co-infection was neither associated with mortality nor treatment success in adjusted models.

	Mortality (n=66 deaths)		Treatment success (n=486 successes)	
	Number of events (%)	Adjusted OR (95% CI)	Number of events (%)	Adjusted OR (95% CI)
Sex				
Female	24 (36.4)	1	207 (42.6)	1
Male	42 (63.6)	1.14 (0.61-2.15)	279 (57.4)	**0.68 (0.42-1.13)**
Age (years)		1.05 (1.03-1.06)		0.99 (0.98-1.02)
HIV status				
Negative	41 (62.1)	1	274 (56.4)	1
Positive	25 (37.9)	1.05 (0.45-2.46)	212 (43.6)	0.84 (0.63-1.13)
Drug resistance				
Pan-susceptible	19 (28.8)	1	351 (72.2)	1
Any drug resistance	47(71.2)	**5.44 (3.69-7.99)**	135 (27.8)	**0.25 (0.18-0.34)**
Mono-resistant	8 (12.1)	**7.37 (2.91-18.66)**	21 (4.3)	**0.35 (0.21-0.60)**
MDR	26 (39.4)	**5.09 (3.05-8.51)**	77 (15.8)	**0.21 (0.12-0.37)**
Pre-XDR/XDR	10 (15.2)	**17.97 (4.63-69.71)**	11 (2.3)	**0.13 (0.04-0.41)**
Others	3 (4.5)	2.26 (0.62-8.27)	26 (5.3)	**0.41 (0.30-0.55)**
History of tuberculosis				
No	35 (53.0)	1	357 (73.5)	1
Yes	31 (47.0)	1.04 (0.79-1.37)	129 (26.5)	0.98 (0.58-1.64)

Logistic regression models are adjusted for age, sex, HIV status, drug resistance and history of TB, accounting for clustering at site-level. Analyses based on 679 patients with complete data. CI, confidence interval; OR, odds ratio; MDR, multidrug resistant; XDR, extensively drug resistant

Table Risk factors for mortality and treatment success

When restricting the analysis to HIV co-infected patients, mortality was associated with low CD4 cell counts: the adjusted odds ratio (OR) comparing <50 with ≥50 cells/µL was 3.7 (95%Cl 1.1-11.8).

Conclusions: Any drug resistance was associated with poorer treatment outcome and mortality, irrespective of HIV status. Increased capacity for resistance testing, including second-line drugs, is urgently needed to ensure adequate treatment in these Settings.

PD-537-12 Introduction of short standardised treatment for multidrug-resistant tuberculosis in Mozambique: cohort description and early culture conversion in HIV-positive and negative patients

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Background: Standardized regimen of 9-11 months duration has shown high rates of success and has been recommended by WHO as an alternative for 24 months regimen for patients with no additional resistance to second line drugs and pyrazinamide. Little is known on the effectiveness of this regimen in patients co-infected with HIV.

Methods: A prospective cohort study was conducted in Maputo, Mozambique, among HIV-positive and HIV-negative patients. The study included patients with active pulmonary tuberculosis diagnosed as rifampicin resistant or children suspected of MDR-TB without bacteriological confirmation but documented as a close contact of confirmed MDR-TB patient, without previous treatment with second-line drugs. Early culture conversion was assessed among patients with at least 6 months of treatment.

Results: A total of 76 MDR-TB patients started on short course regimen since November 2015: 60.5% males, a median age of 32 years [IQR 25.5-40.5], a median BMI of 18.0 kg/m2 [IQR 16.2-19.6] and 68.4% with cavities in chest X-ray. HIV co-infection was found in 50/76 (65.8%) patients and 81.2% received ART at MDR-TB treatment start. Baseline resistance was: 48.8% resistant to pyrazinamide, 51.3% to ethionamide, 2.4% to both injectables and 10.0% to fluoroquinoles. Culture conversion was assessed among 27 patients and reached 29.8% (8/27) at month 2 and 51.9% (14/27) at month 4. No difference in culture conversion at month 4 was found according to HIV status, fluoroquinole and pyrazinamide resistance. Among HIV-positive, 3 deaths occurred before two months of treatment, and none in HIV-negative.

Conclusions: This study on the first MDR-TB patients receiving short course regimen in Mozambique shows a high rate of culture conversion at month 4 both for HIV-positive and HIV-negative patients despite early deaths among HIV-positive. Short standardized regimen seems to be a good alternative to the WHO standard treatment of MDR-TB in high HIV prevalence setting.

PD-538-12 Co-infections and DR-TB treatment outcomes: a 4-year retrospective study in Mumbai, India

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Background: Tuberculosis is a major public health challenge across India. Mumbai, a burgeoning metropolis is emerging as a hotspot for drug-resistant tuberculosis (DRTB). Monitoring treatment outcomes and understanding reasons associated with unfavorable outcomes is key step in evaluating the effectiveness of any program. This study aims to investigate the proportion of co-infections and treatment outcomes of DRTB patients registered in select DRTB centers across Mumbai between 2010 and 2014.

Methods: Treatment records of ~4,700 DRTB patients registered in select DRTB centers in Mumbai from Q3-2010 to Q2-2014 were analyzed. Treatment outcomes were categorized according to the Revised National Tuberculosis Control Program (RNTCP) guidelines. Multivariate analysis was used to examine the association between treatment outcomes and potential predictor variables such as co-infections, registered resistance category, age etc.

Results: Out of 4,783 DRTB patients (2,591 males and 2,192 females) with mean age 30.69 ± 12.99 years, 4,544 (95.00%) were registered with pulmonary tuberculosis and 239 (5.00%) with extra-pulmonary tuberculosis. Among them, 222 (4.64%) were positive for diabetes mellitus (DM) and 208 (4.35%) were HIV positive. Treatment outcome among the cohort was as follows: 1,558 (32.57%) patients showed favorable outcomes (cured or completed treatment), 1,115 (23.31%) died, 995 (20.80%) defaulted, 97 (2.03%) failed treatment, 22 (0.46%) were lost to follow-up (LTFU), 424 (8.86%) were switched to category V treatment while 572 (11.96%) were transferred out with no recorded outcome. Favorable treatment outcomes were more likely in regular patients (32.93%) compared to those with DM or HIV co-infections (28.71%) (OR 1.33; CI: 1.06 - 1.68; P=0.01).

Conclusions: Lower rate of favorable outcomes among DRTB patients with co-infections highlights the need for strengthening an integrated disease management approach at TB centers and within general health systems.

Further research is suggested to understand systemic challenges impacting overall outcomes among DRTB cohorts and strengthening adherence rates among DRTB patients with co-infections.

PD-539-12 Mortality predictors among drug-resistant tuberculosis patients in Uganda

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Background: Treatment of drug-resistant tuberculosis (DR-TB) is a public health challenge. Uganda is faced with a high mortality rate among multi-drug resistant tuberculosis (MDR-TB) patients initiated on treatment with little known about the predictors of death among this population. This study aimed to determine the predictors of mortality in DR-TB patients in Uganda.
Methods: We did a retrospective record review of laboratory-confirmed DR-TB patients from 2011/12 to 2015/16. Data was collected on the HIV status, TB disease classification, previous history of TB treatment, and time to death following treatment initiation. Data were analyzed by SPSS v.16.0 for Windows to determine the predictors of mortality among DR-TB patients.
Results: Overall 811 patient records were reviewed. The resistance patterns observed was: mono-resistance 53.6% (435), poly-resistant 1.5% (12), extensive DR-TB 0.4% (3) and 44.5% (361) MDR-TB. Overall 13.1% (106) of the patients died. Analysis revealed higher odds of mortality among HIV-positive patients and extra pulmonary TB patients. Other variables did not attain a statistical level significance (table below).

Variable	Number (%)	OR	95% CI	P-value
Positive HIV status	406 (50.1)	2.97	1.88-4.70	0.000
Extra pulmonary	14 (1.7)	3.83	1.26-11.65	0.011
New case	200 (24.7)	1.31	0.83-2.06	0.240
Less than 3 days to Treatment start	342 (42.2)	1.39	0.88-2.21	0.157

Table Mortality predictors among DR-TB patients Patients

Conclusions: Patients with a positive HIV status and those with extra pulmonary DR-TB are more likely to die while on treatment. Extra effort is required for the management of DR-TB patients with these characteristics to achieve better treatment outcomes. In addition, in-depth mortality audits are needed to delineate other causes of high mortality in this category of patients.

PD-540-12 Association of diabetes mellitus and smoking with treatment outcomes of drug-resistant tuberculosis patients in Pakistan, 2010-2014

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Background: Pakistan is among the high burden countries for drug resistant tuberculosis (DR-TB). Treatment success rate of DR-TB in Pakistan was 69% in 2013. Diabetes is also on rise in the country and Pakistan is going to be fifth country with largest number of type 2 Diabetes Mellitus (DM) patients by 2030. On the other hand there is high prevalence of smoking in adults in Pakistan and about 22.6% of adults are active smokers. Smoking and DM may have the unfavorable effect on treatment outcome of DR-TB patients. The study was designed to determine the association between diabetes and smoking with DR-TB treatment outcomes.
Methods: This was a retrospective cohort study based on patients enrolled from 2010-14 in 24 PMDT sites of the TB control programme, Pakistan. The data related to study was collected from the nominal data reported to the programme from DR-TB treatment sites. An analysis was done for patients with DM and smoking. Associations between selected demographic characteristics (age, gender, previous health care facility type, resistance type and occurrence of comorbid) were explored using univariate, bivariate and multivariate models. P-value < 0.05 with 95% confidence interval was considered significant.
Results: Among 5,823 patients enrolled, 386 (6.6%) had diabetes. Treatment success rate of patients with and without diabetes was almost similar 68.4% and 67.5% respectively (RR 0.97, 95% CI 0.84-1.13). The rate of unfavorable outcomes was high in patients who smoked 40.7% compared to those who don't 32.2%. Male patients had more unfavorable outcomes than female, 35.1% and 29.7% respectively. Patients referred from public sector health facility had 6% better outcomes than patients referred from private sector. The cumulative risk of poor treatment outcome was also similar among DR-TB patients with and without DM (risk ratio 1.03, 95% CI 0.93-1.14).
Conclusions: DM did not impact treatment outcome of DR-TB treatment but smoking did.

PD-541-12 Demographic and co-morbidity patterns at initiation of treatment among MDR-TB clients in Lagos, Nigeria

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Background: Multi-morbidity is increasingly being recognized as a serious public health concern and obstacle to control of not only drug susceptible but also drug resistant tuberculosis. Not much research has been done in Nigeria on co-morbidity patterns among DR-TB patients. Lagos alone contributed approximately 17% of all rifampicin resistant cases diagnosed in 2016.
This study aims to determine the profile of DR-TB patients at initiation of treatment, for guidance on strategizing care for favourable treatment outcomes.
Methods: A retrospective data retrieval and review of baseline investigation records of MDR TB patients registered in Lagos Nigeria, over a 33-month study period (August 2014- March 2017). Patient base line results reviewed included HIV status, Hepatitis B status, fasting blood sugar, audiometry, thyroid and renal function tests and pregnancy test to determine their clinical characteristics and biochemical profile.
Results: Mean age of respondents is 34 $\pm$ 12 years with majority within age range 25-34 years with male to female ratio 1.7:1. Of the 384 cases, 41 (10.7%) were HIV positive, 26 (6.8%) Hepatitis B positive, 24 (6.8%) had elevated blood sugar levels, 38 (9.9%) proteinuria, 22 (5.7%) impaired creatinine level, 36 (9.4%) had hypokalaemia, 53 (13.8%) had thyroid abnormalities and 45 (11.7%) had hearing impairment. Furthermore, among the 138 female respondents, 5 (3.6%) were pregnant at baseline.
Conclusions: There are existing co-infection with HIV and hepatitis B, and co-morbid conditions such as thyroid disorders, auditory defects, renal impairments and elevated blood sugar among drug resistant TB clients.
The NTP and its stakeholders need to consider the inclusion of endocrinologists and nephrologists in its DR-TB concilium of experts, in addition to ENT surgeon and psychiatrists. It is also a clarion call for provision of adjunct therapy prior to commencement of DR-TB treatment and integration with reproductive health services.

06. The proof is in the pudding - treatment and outcomes for drug-resistant TB

PD-542-12 Tratamiento de tuberculosis extensamente resistente, manejo centrado en el paciente en un programa nacional: Perú

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Background: Desde 2012 el Programa de Tuberculosis de Perú implementó el manejo centrado en el paciente con tuberculosis extensamente resistente (TB-XDR) usando nuevas drogas del quinto grupo de la OMS. El objetivo fue describir la epidemiología, la resistencia y el resultado del tratamiento de los pacientes que iniciaron tratamiento entre mayo 2012 y junio 2014 y comparar sus resultados con cohortes previas.
Methods: Estudio observacional utilizando el Registro Nacional de Tuberculosis Resistente y la base de pruebas de sensibilidad del Instituto Nacional de Salud. El Comité Nacional de Expertos aprobó cada esquema de tratamiento. El tratamiento fue hospitalario en sus primeros dos meses, luego en el domicilio hasta el mes 12 y completado hasta el mes 24 en el servicio de salud más cercano. Se mejoró su vivienda y se brindó una canasta de víveres mejorada.
Results: De 162 casos evaluados, el 85% fue antes tratado, el 83% fue resistente a kanamicina, 73% a capreomicina y 58% a ambos. El 100% fue resistente a fluoroquinolonas, en 84.5% se evaluó con ciprofloxacina y el resto con levofloxacina. El tratamiento incluyó: linezolid, imipenem/cilastatina, ac.-clavulánico, tioridazina, moxifloxacina, cicloserina, capreomicina (33%) y amikacina (35%). En 78 pacientes se pudo evaluar la condición de egreso al momento del análisis: el 68% fue éxito, 23% fallecieron, 2,5% fracasaron y 3,8% pérdida de seguimiento. Estos porcentajes fueron mejores a los reportados previamente (Figura).
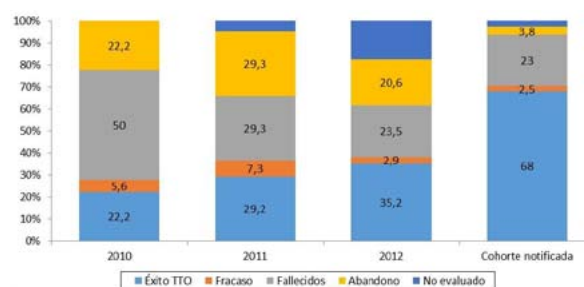
Figure Resultados del tratamiento TB XDR 2010 - 2012 y cohorte notificada, Perú.

Conclusions: El tratamiento de TB-XDR aplicado en el Perú tiene un éxito relativamente alto, pero aún la proporción de fallecidos sigue alta. El bajo abandono puede explicarse por la protección social y el cuidado centrado en el paciente, el bajo fracaso se puede deber a la inclusión de tres nuevos medicamentos y preservar moxifloxacina. Este régimen debe expandirse e incluir los nuevos medicamentos (grupo C y D de OMS).

PD-543-12 Pneumonectomy in the complex treatment of extensively drug-resistant pulmonary tuberculosis

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Background: Treatment of extensively drug resistant tuberculosis (XDR-TB) by conservative therapeutic methods are often fail and modern surgery is a promising treatment option for these patients. We analyzed the results of the final pneumonectomy to identify the benefits and complications of radical surgical treatment in XDR-TB patients.

Methods: We conducted retrospective review of 60 patients with pulmonary XDR-TB who underwent pneumonectomy as a part of the complex anti-TB treatment in a period from January 2011 to December 2016. The average age of the patients was 35 ($\pm$7) years and the average duration of the pulmonary TB before surgery was 36 ($\pm$14)months. All patients had bacteriologically confirmed XDR-TB with resistance to 5-7 anti-TB drugs and destructive cavitary lesions in the lung tissue. Bilateral lesion was revealed in 93.3% of cases, one side total lesion was noted in 91.7% of patients. 100% of patients were smear/culture positive before surgery. All patients had been receiving appropriate complex second line therapy according to the anti-TB drug susceptibility pattern.

Results: Intra-operative mortality was not recorded. The mean follow-up period after pneumonectomy was 6 months (range 2 - 12 months). Culture conversion after surgery was achieved in 96.7% of cases, further postoperative chemotherapy allowed to achieve culture conversion in additional 1.7% of cases. In 15% of cases repeated surgical intervention was required because of bleeding. As a complication of pneumonectomy, 15% of patients had bronchopleural fistula. 25% of patients had X-ray signs of TB progression in the contralateral lung in postoperative period; however, it was stopped by the postoperative chemotherapy.

Conclusions: Pneumonectomy as a radical surgical treatment in patients with pulmonary XDR-TB, in conditions of appropriate preoperative and postoperative anti-TB chemotherapy, can achieve high success rates with an acceptable number of complications.

PD-544-12 Advantages of using vats in delayed thoracoplasty after surgery of destructive forms of pulmonary TB

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Background: The main cause of recurrence of pulmonary TB and postoperative complications after surgery is the discrepancy between the volume of the hemithorax and the volume of the remaining lung tissue. The efficacy of the existing methods of therapeutic lung collapse operations has been repeatedly confirmed, the associated surgical trauma of the traditional procedures has long been a limitation to its widespread use among thoracic surgeons. We describe a novel technique of video assisted thoracoscopic (VATS) delayed thoracoplasty for the prophylactic of recurrence pulmonary TB and postoperative complications.

Methods: In the period 2014-2015 53 patients received VATS delayed thoracoplasty 3-4 weeks after massive lung resections and pneumonectomies for destructive pulmonary TB. The procedure was performed: Using paravertebral incision of 4-6 cm, exposed ribs. 2 cm above the upper corner of the wound is set torakoport, introduced videothoracoscopy. Since the III rib made subperiosteal removal of the ribs with transverse process of the vertebrae to the anterior axillary line, without opening the pleural cavity. Analogous method removes ribs 2-1-4-5. In 77,4 % cases produced 4 ribs thoracoplasty. There were 31 men and 22 women with a mean age of 34 years (range 20-69 years). M/XDR-TB was predominant, which amounted to 49 %.

Results: Postoperative mortality 0%, complication 0%. From the first day, all patients can easily move the upper limbs without restriction. Narcotic analgesics were administered only the first day, followed by non-narcotic analgesics for the next 3-4 days. Over 2 year follow all 53 patients live without recurrence pulmonary TB (negative culture and cavity absent).

Conclusions: VATS delayed thoracoplasty is a new method of collapse surgery, which is as effective as other similar techniques. The procedure is associated with a less surgical trauma, less postoperative pain, quicker recovery and less shoulder girdle impairment than open thoracoplasty.

PD-545-12 What happened to patients with MDR-TB in Zambia who were reported as loss to follow-up from 2011 to 2014?

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Background: Drug-resistant tuberculosis (DR-TB) threatens the prospects of ending the TB epidemic by 2035. In Zambia, an estimated 1,500 MDR-RR/TB cases occur among notified pulmonary TB cases. Less than 10% of the estimated MDR-RR/TB cases are detected and enrolled into treatment. Of the already few MDR-RR/TB patients put into treatment, only 30% complet treatment. The loss to follow-up (LTFU), is the principal reported the unfavorable outcome.

Methods: We conducted a retrospective cohort study at the only two MDR-TB treatment hospitals in Lusaka and Ndola, Zambia. Records for MDR-TB among patients registered as LTFU from 2011 to 2014 were reviewed. Using addresses and telephone numbers in the registers these patients were followed up.

Results: Of 184 patients with confirmed MDR-TB, 76 (41%) were reported as LTFU. Information on the 47 (62%) of the documented LTFU patients were obtained while for the rest their status remained as LTFU. From 2011-2014, the proportions reported each year as LTFU were 21%, 47%, 51% and 39% respectively. 43 (57%) had stopped attending clinic in the intensive phase with the remainder stopping in the continuation phase of therapy. LTFU patients were predominately male, aged 15-44 years, with pulmonary disease and had failed previous treatment. There were 57 (75%) with known HIV-status and of these 42 (74%) were HIV-positive with 57% on antiretroviral therapy. Following active patient tracing, 29 (38%) patients could not be found and the observed outcome remained LTFU. Of the remaining 47 patients, 29 (62%) were alive and had completed/were still on treatment, 14 (30%) were alive and had stopped treatment, and 4 (8%) were dead.

Conclusions: Zambia has been under-reporting its favorable outcomes in MDR-TB and should continue with active tracing of LTFU patients. Further qualitative studies are required to explore the reasons why MDR-/RR-TB patients stop treatment.

PD-546-12 Scaling-up of shortened multidrug-resistant tuberculosis regimens in Niger: 8 year experience

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Background and challenges to implementation: Niger is a large low-income country. Until 2008 there was no National Reference Laboratory (NRL) and the second line treatment wasn't standardised.

Intervention or response: In 2008 Niger started to use shortened regimens and NRL was built by Damien Foundation (DF). Diagnostic was performed by solid culture medium and drug susceptibility testing (DST) since 2008 to 2014. In 2015 four Xpert sites were opened in the country. A transport circuit of samples to sites Xpert was organized sending tubes with dead bacilli by public transport. The first MDR facility was opened in Niamey in 2008 and the second one in Maradi in 2011. Guidelines and a regular monitoring were provided. A regular drug supply was ensured by DF. Direct Observed Treatment (DOT) was performed providing transport fees for patients, nutritional supply, free ancillary drugs and home visits. An Active Drug Safety Monitoring and Management (aDSM) was carried out grading Adverse Events (AEs). Patients were followed up 6 and 12 months after cure.

Results and lessons learnt: From 2008 to 2016 the percentage of retreatment cases tested for MDR/RR-TB increased from 11.2% to 42.6% (p< 0.001). The rate of confirmed MDR/RR-TB cases enrolled on treatment also increased from 80% to 88%. The interval between MDR/RR suspicion and treatment start decreased from a mean of 165 days (range 90-524) to 12 (range 1-30) (p< 0.001). Among the 213 patients treated, success rate was 82.3% (range 78.3-92.3). Among the 180 cured patients, 158 (87.8%) were screened 6 months after cure: 153 (96.8%) stayed negative and 5 (3.2%) relapsed (4 with initial resistance to quinolones). Only 14 (6.6%) patients had serious AEs manageable without stopping more than one drug.

Conclusions and key recommendations: New technologies as Xpert, short regimens, training and monitoring, a regular drug supply, a patient-centred care and aDSM are the keys to obtain successful outcomes in low resource settings.

PD-547-12 Outcomes and risk factors in a programme treating MDR-TB in Swaziland for 2011—2013 cohorts

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Background: Médecins sans Frontières (MSF), with the Swaziland Ministry of Health, has been treating MDR-TB patients since 2011 in two sites. From 2011 to 2014 the treatment regimen was standard 20+ months regimen and from 2014 a pilot study with short course regimen (SCR) was implemented. This analysis describes the model of care and outcomes of comprehensive MDR-TB treatment in Swaziland between 2011 and 2014 highlighting areas of success/failure. This study will allow a comparison between SCR and previous treatment recommendations.

Methods: This is a retrospective observational cohort study. From January 2011 to December 2013 MDR-TB patients diagnosed with Xpert® MTB/RIF, confirmed from culture and drug sensitivity test or clinically diagnosed were enrolled in the program. Treatment was observed daily by a treatment supporter. Psychosocial support and socio-economic incentives were part of the package of care provided by MSF. Data was routinely collected in a dedicated database. Univariate analysis to assess risk factors for unfavorable response was performed and adjusted in a multifactorial logistic regression model.

Results: Of a total of 174 patients 90% (n=156) had HIV co-infection. 75.3% achieved success rate (n=131), 37 patients died (21.3%), 1 failed (0.6%) and 1 (0.6%) patient was lost to follow-up (LTFU). Among HIV+ patients being underweight (BMI< 18.5) and having a CD4 count< 50 increased the odds of achieving a negative outcome (BMI: 3.0 and CD4: 11.5) after adjusting for all the other risk factors. Culture conversion at 4 months of treatment was 88.7% and mean length of time to culture conversion (among those that converted) was 2.3 months.

Among HIV co-infected patients (N=156)	Crude association		Adjusted model (adjusted for gender, age, employment, marital status and treatment history)	
Selected Baseline risk factors (most significant)	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Underweight (BMI<18.5) versus underweight (BMI: 18.5-24)	3.0 (1.2-7.4)	0.02	3.6 (1.1-11.8)	0.03
ART versus not on ART	2.5 (1.2-5.3)	0.02	3.0 (0.9-10.1)	0.08
CD4 count <50 versus 350+	10.3 (2.4-45.1)	0.002	11.5 (1.6-82.5)	0.02

Table Model: risk factors associated with poor outcomes

Conclusions: A model of care including psychosocial support and enablers for the short-course regimen led to satisfactory outcomes of MDR-TB treatment in high HIV co-infection setting. Among HIV+ patients particular emphasis should be given to nutrition status and ART coverage.

PD-548-12 Totally implantable central venous access device in the treatment of multidrug resistant and extensively drug-resistant tuberculosis

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Background: In order to avoid daily intramuscular or intravenous injections (infusions) through peripheral veins over a period of several months during the treatment of multidrug-resistant (MDR-) and extensively drug-resistant tuberculosis (XDR-TB) totally implantable central venous access device (TICVAD) can be used. The aim of the study is to evaluate acceptability and safety of TICVAD use for M/XDR-TB treatment.

Methods: M/XDR-TB patients who started treatment with regimens containing carbapenems and/or second line injectables were invited to participate in the study. TICVAD acceptibility was assessed, complications were recorded and analyzed.

Results: Between 1 June 2015 and 1 April 2017, 64 TICVAD were implanted in 62 patients: median age 33 years (range: 14-65); 42(68%) male; 44(71%) previously treated; 6(10%) HIV co-infected. The following veins were used as route: right (36) and left (8) subclavian, right (7) and left (6) jugular; right cephalic (5) right femoral (2). Seven complications were observed, 5(8%) - required removal, 2(3%) TICVAPD were re-implanted: pneumothorax -1 (pleural tube -1); lumen occlusion -2 (removal -2 and re-implantation -2), pocket and tunnel infection -2 (removal -2), TICVAD-related venous thrombosis -2 (removal -1, anticoagulant therapy -1). All complications were resolved without consequences. Majority of the patients 59(95%) and health care practitioners (HCP) reported advantage of TICVAD over the other types of venous access and intramuscular injections.

Conclusions: Our data on the use of TICVAD in M/XDR-TB treatment demonstrate reasonable safety profile and high level of patients and HCP acceptability. The experience gained can promote this approach for further expansion in programmatic settings.

PD-549-12 The efficacy, safety and tolerability of the short 12-month pre-XDR-TB regimen in Ukraine

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Background: In the world as a result of the existing long-term regimens, treatment success is occurred only in 48% patients with MDR and in 22% patients with XDR, it is not enough to reach the goals for eliminating TB. According to the WHO report, Ukraine is on the last place for the efficacy of treatment in the World: 2011 successful treatment was obtained only in 34% patients. According to the operational research, conducted in Ukraine, from 2006-2011 the successful treatment came up to only in 22% patients with MDR / XDR-TB.

Methods: In the prospective observational "case-control"study were included 64 patients with new pre-XDR-TBand with susceptibility either to aminoglycoside either to fluoroquinolone. Patients of the first group (n=32) received following short short 12-month for pre-XDR-TB regimen: during intensive phase at least 6 ATDs (24 weeks): linezolid (0.6 g), moxifloxacin (0,4 g), capreomycin (1.0 g) - intramusculary and pyrazinamide, prothionamide, cycloserine ±PAS - in therapeutic doses respectively and isoniazid in high doses; continuation phase - at least 5 ATDs (without capreomycin) during 24 weeks. The patients of the second group (n=32) received conventional 20-month regimens (without linezolid).

Results: Among patients who received short pre-XDR-TB regimen, comparing with the conventional regimen, success rate increased from 46.9% to 90,6 %. The adverse events registration wasn`t significantly higher -in 31.3 % vs. 37.5 %, respectively.
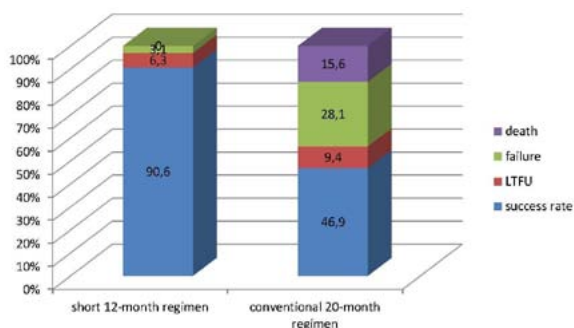
Figure 1 Treatment outcome between the short 12-month regimen and the conventional 20-month regimen

Conclusions: Administration of short 12-month regimen for pre-XDR - TB patients improved the successful treatment outcomes in patients with pre-XDR-TB to 90.6% in comparison with conventional regimen.

PD-550-12 Primary healthcare clinics are successfully managing multidrug-resistant tuberculosis (MDR-TB): comparing outcomes in TB hospitals to clinics in the Western Cape, South Africa

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Background: The exponential increase in the incidence of MDR-TB in Western Cape, South Africa to 23.6 per 100,000, resulted in logistical difficulties in managing MDR-TB patients within overburdened TB hospitals, hence treatment of MDR-TB patients was decentralised to primary healthcare clinics. However, shifting the care of patients to clinics was a concern, as MDR-TB treatment outcomes might worsen and community exposure to MDR-TB might increase. The study compared MDR-TB treatment outcomes in patients initiated on treatment in clinics to those initiated on treatment in TB hospitals and assessed other factors associated with successful treatment.

Methods: A retrospective cohort study was undertaken in Western Cape, comparing a random sample of 568 uncomplicated MDR-TB patients initiated on treatment in hospitals and clinics from 2010 to 2012, using key treatment outcomes of successfully treated, unsuccessfully treated, died and loss to follow-up, extracted from a standardised electronic MDR-TB database. Multivariate logistic regression analysis was used with adjusted odds ratios of association.

Variables	Treatment Successful Adjusted Odds Ratio (95%CI)	Treatment Unsuccessful Adjusted Odds Ratio (95%CI)	Died Adjusted Odds Ratio (95%CI)	Lost to Follow-up Adjusted Odds Ratio (95%CI)
Treatment initiated at a clinic versus treatment initiated at a hospital	1.05 (0.57-1.96)	1.25 (0.44-3.61)	0.63 (0.27-1.45)	1.16 (0.64-2.10)
Patients who live in rural areas versus urban areas	0.98 (0.54-1.79)	0.51 (0.18-1.44)	2.58 (1.20-5.55)	0.75 (0.43-1.33)
Patients with no previous TB or previous TB cured versus participants with previous TB unsuccessfully treated or previously lost to follow-up	2.87 (1.48-5.56)	0.12 (0.04-0.38)	0.70 (0.31-1.57)	1.06 (0.59-1.94)
Patients who are HIV+ve and on anti-retroviral therapy versus participants who are HIV+ve but not on anti-retroviral therapy	6.63 (1.48-29.84)	1.30 (0.26-6.55)	0.20 (0.08-0.53)	0.96 (0.39-2.33)

Table Multivariate analysis with 4 key Outcomes

Results: Clinic initiated and hospital initiated patients successfully treated for MDR-TB were 41% and 31% respectively, deaths were 14% and 16%, unsuccessful treatment was 7% and 13%, with loss to follow-up

39% and 41%. Multivariate analysis showed no difference in treatment outcomes between clinic and hospital patients, adjusted odds ratio 1.05 (95% CI 0.57-1.96); Human Immunodeficiency Virus (HIV) positive patients provided with anti-retroviral therapy were 6.6 times more likely to have a successfully treated outcome than those untreated (95% CI 1.48-29.84) and were 0.2 times less likely to die (95% CI 0.08-0.53); those having previous TB successfully treated or no previous history of TB were 2.9 times more likely to be successfully treated (95% CI 1.48-5.56).

Conclusions: Primary healthcare clinic treatment of MDR-TB is as effective as hospital treatment, hence decentralisation should continue. Providing anti-retroviral therapy to HIV positive MDR-TB patients is beneficial and should be mandatory.

PD-551-12 Treatment outcomes for drug-resistant TB under an out-patient model of care in Johannesburg, South Africa

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Background: In 2011, South African Tuberculosis (TB) guidelines expanded to include outpatient Drug Resistant (DR) TB care to improve treatment access. We present rates of attrition and factors associated with this outcome at an outpatient, public sector DR TB treatment site in Johannesburg, South Africa.

Methods: Prospective observational cohort analysis of adults (≥18 years) with rifampicin resistant TB from March 2013 to September 2014. Early attrition (by 0-6 months) and late attrition (by 6-24 months) were defined as a combination of all-cause mortality and LTFU (treatment interruption ≥2 months). Factors associated with attrition were identified using Cox Hazard models to produce crude hazard ratios (HR).

Results: Of the 135 patients eligible for analysis, 68 (50%) were male, median age 38 years (IQR 30-43). 115 (85%) were HIV-infected, with a median CD4 count of 99 cells/mm³ (IQR 32-212), while 56/110 (51%) were on antiretroviral therapy (ART) at the start of DR TB treatment. By 6 months, 14/135 (10%) died and 19/135 (14%) were LTFU. By 6-24 months, 6/102 (6%) died, 22/102 (22%) were LTFU, 7/102 (7%) remained on treatment, and from the total cohort by 24 months, 67/135 (50%) were cured or had completed treatment.

Patients with moderate/severe anaemia at initiation (≤10 vs. >10 g/dL; HR 3.18 95% CI 1.44-7.03), and those referred from in-patient facilities (HR 2.74 95% CI 1.37-5.47) were at higher risk of early attrition (Table 1).

Younger patients (18-35 vs. ≥35 years; HR 2.97 95% CI 1.41-6.27), those unemployed (HR 4.32 95% CI 1.64-11.37) and smear positive at DR TB initiation (HR 2.54 95% CI 1.10-5.84) were at higher risk of late attrition by 24 months.

Variable	Description	0-6 months (n=33)			6-24 months (n=28)		
		n (row %)	Crud HR (HR)	p-value	n (row %)	Crud HR (HR)	p-value
Sex	Male	13/68 (19.1%)	1		16/55 (29.1%)	1	
	Female	20/67 (29.9%)	1.73 (0.86-3.47)	0.13	12/47 (25.5%)	0.97 (0.46-2.07)	0.95
Age at Initiation (years)	≥35	18/87 (20.7%)	1		13/69 (18.8%)	1	
	18-35	15/48 (31.3%)	1.66 (0.84-3.30)	0.15	15/33 (45.5%)	2.97 (1.41-6.27)	0.00*
HIV	Negative	3/20 (15.0%)	1		5/17 (29.4%)	1	
	Positive	30/115 (26.1%)	1.90 (0.58-6.23)	0.29	23/85 (27.1%)	0.86 (0.33-2.27)	0.76
CD4 count (cells/mm³)	High (≥100)	12/58 (20.7%)	1		12/46 (26.1%)	1	
	Low (<100)	16/56 (28.6%)	1.45 (0.68-3.06)	0.33	12/40 (30.0%)	1.12 (0.50-2.50)	0.78
ART Status	On ART	18/56 (32.1%)	1		8/38 (21.1%)	1	
	Not on ART	10/54 (18.5%)	0.52 (0.24-1.12)	0.1	14/44 (31.8%)	1.77 (0.74-4.24)	0.2
Time on ART (months)	≥6	10/36 (27.8%)	1		8/26 (30.8%)	1	
	<6	10/22 (45.5%)	1.91 (0.79-4.59)	0.15	2/12 (16.7%)	0.58 (0.11-2.51)	0.43
Education	≥High school	26/136 (22.4%)	1		26/90 (28.9%)	1	
	≤Primary school	7/19 (36.8%)	1.73 (0.75-3.99)	0.2	2/12 (16.7%)	0.51 (0.12-2.15)	0.36
Employment	Employed	16/62 (25.8%)	1		5/46 (30.9%)	1	
	Unemployed	16/72 (22.2%)	0.84 (0.42-1.69)	0.63	23/56 (41.1%)	4.32 (1.64-11.37)	0.00*
Hemoglobin, g/dL (Anaemia)	None/mild	9/62 (14.5%)	1		17/53 (32.1%)	1	
	Moderate/severe	19/49 (38.8%)	3.18 (1.44-7.03)	0.00*	8/30 (26.7%)	0.94 (0.40-2.18)	0.88
^BMI (kg/m²)	Normal/high (≥18.5)	18/96 (18.8%)	1		22/78 (28.2%)	1	
	Low (<18.5)	4/17 (23.5%)	1.29 (0.44-3.80)	0.65	3/13 (23.1%)	0.80 (0.24-2.66)	0.71
Referring Facility	Out-patient	14/85 (16.5%)	1		21/71 (29.6%)	1	
	In-patient	19/50 (38.0%)	2.74 (1.37-5.47)	0.00*	7/31 (22.6%)	0.91 (0.39-2.16)	0.83
Patient Category	New	18/81 (22.2%)	1		21/63 (33.3%)	1	
	Previously treated	15/53 (28.3%)	1.29 (0.65-2.56)	0.46	7/38 (18.4%)	0.57 (0.24-1.35)	0.2
Resistance Pattern	RiF by Xpert	7/31 (22.6%)	1		5/24 (20.8%)	1	
	RiF Mono	17/63 (27.0%)	1.18 (0.49-2.85)	0.71	14/46 (30.4%)	1.34 (0.48-3.72)	0.58
	MDR	9/41 (22.0%)	1.00 (0.37-2.69)	1.00	9/32 (28.1%)	1.13 (0.38-3.40)	0.82
Smear Microscopy	Negative	19/100 (19.0%)	1		18/81 (22.2%)	1	
	Positive	8/25 (32.0%)	1.89 (0.83-4.32)	0.13	8/17 (47.1%)	2.54 (1.10-5.84)	0.03*

*p<0.05
^BMI (Body Mass Index)

Table 1 Unadjusted estimates of the relationship between demographic and clinical characteristics and attrition (Death + LTFU) of DR TB patients with outcomes by 0-6 months (n=135) and 6-24 months (n=102 on treatment

Conclusions: At this outpatient DR TB treatment site, attrition by 24 months was high (45%). Patients with more severe illness (hospitalized at diagnosis, moderate/severe anaemia, smear positive) were at increased risk of death or LTFU.

07. A picture in time - chest X-ray and other diagnostic considerations in TB

PD-552-12 Assessing sensitivity of symptoms for efficiency in TB case detection in a male clinic in Lesotho

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Background and challenges to implementation: Lesotho, a country with a population of approximately two million, has the **highest TB incidence rate in the world** (852 per 100,000). Only one in two people estimated to have TB disease are diagnosed. Symptom screening is not systematic nor routinely integrated within non-HIV related health services at the national level. In response, a pilot male clinic was established to provide integrated, client-

centered, health services with systematic TB screening for every client.

Intervention or response: In July 2016, Jhpiego and the Ministry of Health established a pilot stand-alone male clinic to improve diagnosis and adherence to treatment for TB and HIV. Given current gender and socio-cultural norms around health seeking by males, the male clinic model focused on providing priority male health services by male providers through flexible hours and patient-centered care. Every client is screened for TB and microscopy and/or GeneXpert diagnostics are utilized for same day treatment initiation.

Results and lessons learnt: 6,766 clients were screened for TB between July 2016 and February 2017, of which 418 (6.2%) were investigated with at least one symptom suggestive of TB. Most clients reported cough and at least one other symptom (69%), and night sweats and at least one other symptom (60%), which suggests that diagnosing TB is most sensitive with presence of two or more symptoms (see Table 1). 92.5% of clients ultimately diagnosed with TB had cough and 6 had rifampicin resistance (Xpert results)--all of whom presented with both cough and night sweats. 1/5th of clients screened had all symptoms, implying more advanced disease, indicating that the program is potentially reaching men who don't normally get care.

	Cough only	Night sweats only	Cough + only other symptom	Night sweats + one other symptom	Fever + one other symptom	Weight loss + one other symptom	All 4 symptoms
Cases by symptom	111	7	289	250	172	151	82
Proportion of symptomatic patients	27%	2%	69%	60%	41%	36%	20%
Cases diagnosed with TB	7	1	55	53	38	34	22
Proportion of TB cases by symptom	6%	14%	19%	21%	22%	23%	27%

Table Total symptomatic cases by symptom and TB diagnosis

Conclusions and key recommendations: The male clinic model has potential to improve case detection in men. We recommend diagnostic testing of symptomatic clients for any cough or presence of at least two symptoms, especially in setting with low laboratory capacity.

PD-553-12 Improving tuberculosis diagnosis with deep learning algorithm to analyze chest X-rays

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Background: Tuberculosis (TB) remains one of the most important health issues globally. It remains a major public health problem with more than 10 million new cases and 1.8 million deaths every year. Most of the TB burden is concentrated in resource-poor settings and marginalized communities, often found in Low and Middle Income Countries (LMICs). Reducing TB diagnosis delay is critical in mitigating disease transmission and minimizing the reproductive rate of the TB epidemic. In this paper, we propose the use of a deep learning algorithm to identify TB patterns in chest x-rays of suspicious patients.

Methods: Deep learning algorithms are commonly used to identify and classify medical images. We developed a database composed of 4,701 chest X-ray images from Peruvian TB patients. The research team, using a software tool that allows highlighting TB manifestations, annotated the images. The annotation process was conducted under the guidance of an expert pulmonologist, who led the training process for identification of TB manifestations. Figure 1 shows an annotated x-ray with *consolidation* and *cavitation*.
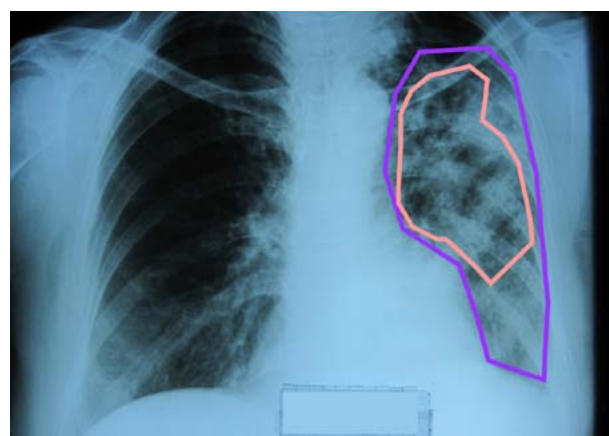
Figure Chest x-Ray annotated with TB manifestations

Having concluded the annotation process, we embarked on the development of the deep-learning algorithm using the annotated images from the training process. The classification model was a deep convolutional neural network (CNN)-based. This model was developed by dividing the chest x-rays into normal (453 images) and abnormal (4258 images with a TB manifestation) in a binary categorization adapting the **GoogleNet** model using **ImageNet** dataset as pre-training and our dataset (smaller) as fine-tuning.

Results: We achieved an **89.6%** of accuracy by using 4/5 of the images for training and 1/5 for testing. In addition, using a class for each manifestation, we built a multiclass classifier and we achieved an accuracy of **62.07%**.
Conclusions: Experimental results have demonstrated that our approach is promising and deep learning is a good technique to identify TB manifestations in x-ray images.

PD-554-12 Evaluation of LED fluorescence microscopy for the diagnosis of tuberculosis

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Background: The fluorescence microscopy of light emitting diode (FM-LED) is an alternative for the diagnosis of tuberculosis. The objective is evaluated it to be implemented in laboratories with a productivity of 50 smears per day, because it is a more sensitive technique than Light Field Microscopy (LFM) up to 10% and reducing time for the emission of results.
Methods: Sputum samples were collected from diagnosed patients; two smears were made by direct sample, for later decontamination, culture in Löwenstein Jensen ("gold standard") and identification. Of the two smears was stained by Ziehl Neelsen (LFM) and the other by Auramine (FM-LED). Five microscopists read the smears. The results of readings and cultures were collected to evaluate parameters such as sensitivity, specificity, as well as comparison of reading times.
Results: In this study 40 samples were included, 26 (65%) were negative and 14 (35%) were positive, which were identificated as strains of the complex *Mycobacterium tuberculosis*. When FM-LED and LFM were compared with culture, the average sensitivity was 87.2% and 85% respectively, while the average specificity in both cases remained at 98.5%. In addition, the average reading time decreased by smear from 7 minutes per LFM to 4 minutes per FM-LED.
Conclusions: The MF-LED has a greater sensitivity and a considerable reduction in reading time, offering it a useful diagnostic tool for the initial implementation in laboratories with high productivity.

PD-555-12 'Missing TB cases': potential of offering chest X-ray upfront to all smear-negative cases in narrowing this gap

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Background and challenges to implementation: India tops the list of the countries with highest missed tuberculosis (TB) cases. Almost one in every three missed cases of TB globally is in India. Presently, chest X-Ray (CXR) is offered to TB symptomatic patients only after 2 weeks of antibiotic treatment. Concerns have been raised that it leads to missed cases. On a pilot basis, we offered CXR upfront to all TB symptomatic patients found smear negative (SN) on sputum examination in Sonepat district of Haryana.
Intervention or response: In the 3 Tuberculosis Units (TUs) of Sonepat district where project Axshya is being implemented for community mobilization, all smear negative TB symptomatic patients were linked with mobile CXR facility made available near their residence during the period January- March 2017. During intervention period, 298 TB symptomatic patients got their sputum tested for acid-fast bacilli. If sputum test was negative, the person was immediately linked to CXR facility.
Results and lessons learnt: Sputum of 24 symptomatics was found to be positive for TB out of 298 patients whose sputum was tested (Positivity rate-NSP=8%). 274 symptomatics were smear negative and advised for CXR upfront. On being investigated by CXR, 14% of the tested smear negative patients were found to be suffering from TB. In our study group, the NSP:NSN ratio of TB patients has been found to be reversed (1:1.77*) as compared to state (1.94:1**) and national (2.12:1**) data.
Conclusions and key recommendations: Results of our intervention in 1 district suggest that offer of CXR facility to all smear negative cases can potentially prevent sizeable number of NSN TB cases getting missed. We recommend replicating this on a larger scale and evaluating it scientifically for expected benefit in reducing missed TB cases.
* Projected figure
** TB India Report, 2016

PD-556-12 Role of chest X-ray and symptom screening tool for tuberculosis case detection: national TB prevalence survey 2015-2016, Bangladesh

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Background: According to WHO, Bangladesh ranks among the 30 high TB burden countries in the world. The Government of Bangladesh conducted a national TB prevalence survey in 2015-2016 using WHO recommended methods to estimate the prevalence of bacteriologically confirmed pulmonary TB among the population aged 15 years and older. WHO provided technical and financial support to conduct the survey.

Methods: The survey registered 108,834 (73.5%) participants as eligible respondents. Among them 98,710 (90.7%) participated in the survey. Every participant was interviewed for TB symptoms and received chest X-ray by portable direct digital radiography unit for screening. Symptom screening criteria was used as tool for taking history. Participants with a symptom screening score ≥ 3 were classified as screened positive and eligible for sputum submission. Those participants who screened positive either by interview or abnormal X-ray were requested to provide spot sputum followed by a morning sputum sample. The sputa were examined at the National Tuberculosis Reference Laboratory for smear, culture and Xpert MTB/RIF.

Results: Total 20,594 (20.9%) participants were screened positive by interview and/or chest X-ray screening. For laboratory test, 20,463 (99.7%) specimens were collected from the screening positive participants. In the survey, 278 bacteriologically confirmed TB cases were identified either by Xpert MTB/RIF and/or culture. Among them, 251 (90.3%) of bacteriologically confirmed cases were identified by chest X-ray screening. Moreover, 106 (38.1%) of bacteriologically confirmed cases were identified by symptom screening and 52 (48.1%) of smear-positive TB cases were identified by symptom screening. The estimated prevalence of bacteriologically confirmed pulmonary TB was 287 per 100,000 population.

Conclusions: Symptomatic screening may contribute in active case findings. The chest X-ray is an important screening tool for earlier detection of TB cases and presumptive TB cases can be referred for diagnosis where facility is equipped with chest X-ray.

PD-557-12 Increasing the yield of TB cases from communities: experience from India

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Background and challenges to implementation: India accounts roughly 1.3 million "missing" TB cases. These missing cases are potentially within the communities or being treated in private sector. 'Find, Diagnose and Treat them all is priority of Revised National TB Control Program (RNTCP) of India to achieve the Goal of End-TB by 2025.

Intervention or response: With an objective to identify missing TB cases from communities, Population Services International (PSI) is implementing active case finding(ACF) in identified areas in 60 rural districts across 10 states with the help of 542 community volunteers (CVs). Apart from this, rural health care providers are engaged for identifying and referring presumptive TB cases (PTB) for correct and accurate diagnosis. We looked at project performance in terms of PTB cases referred and tested at DMC (Designated Microscopy Centre), and yield of TB cases, across intervention in 60 districts. We also analysed contribution from project activities within intervention DMCs in yielding TB cases during Oct'14-Sept'15 and Oct'15-Sept'16, period.

Results and lessons learnt: During Oct'14-Sept'15 period 26,068 PTB cases were identified and tested at DMC through project intervention, out of these 2,836 (10%) TB cases were detected and linked with DOTS. During Oct'15 to Sept'16 period overall 30,542 presumptive TB cases were identified and tested at DMC, out of these 2,984 (9.7%) TB cases were detected and linked with DOTS. In comparison to Oct'14 to Sept'15, overall contribution in intervention DMC in terms of presumptive TB cases increased from 10% to 12% in Oct'15 to Sept'16. In terms of yield of TB cases contribution of project in intervention DMC increased from 11% in Oct'14 to Sept'15 to 14% in Oct'15 to Sept'16.

Conclusions and key recommendations: Through systematic approach of ACF, yield of TB cases from the communities can be increased with the help of community volunteers.

PD-558-12 High yield of facility-based active tuberculosis case-finding in Western Kenya, 2015-2016

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Background: Finding and treating more people with tuberculosis faster is essential to substantially accelerate tuberculosis elimination. However, it is not known what strategies for improving case-finding are most effective, as active case-finding is not routine in many settings with high burdens of tuberculosis, including Kenya. We sought to compare strategies for tuberculosis active case-finding that can be routinely implemented within the existing Kenyan healthcare infrastructure.

Methods: A trial was performed in Kisumu and Siaya counties, Kenya, during February, 2015-June, 2016 comparing the yield of new adult TB diagnoses for health-facility and community-based active case finding and household contact investigation. All persons entering health facilities and community-based screening locations were to be screened for TB using symptom-based assessment and HIV testing. For household contacts, tuberculin skin testing was also done. Sputum was tested using the Xpert MTB/Rif assay. We determined the number of persons diagnosed with TB out of the number screened for each strategy. We also used electronic data from the Ministry of Health on all reported cases of TB to analyze the health facility-based strategy by using a Poisson regression to predict intervention period case notifications at each facility based on baseline period case notifications and whether the facility had a screener.

Results: Based on data from our screening efforts, tuberculosis was diagnosed in 480 (20%) of 2,394 symptomatic adults screened in health facilities; 39 (3%) of 1,424 symptomatic adults screened at community-based units; 44 (3%) of 1,692 contacts of tuberculosis patients. Using MoH data, presence of screeners at health facilities was associated with a 30% (95% CI: 3-65%) increase in intervention period case notifications compared to health facilities in study areas randomized to not receive screeners.

Conclusions: Active symptom-based screening for people in health facilities was a high-yield approach for improving tuberculosis case detection.

PD-559-12 Active search for TB cases on a campaign mode in India - modus operandi and early experience

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Background and challenges to implementation: Revised National TB Control Programme (RNTCP), India treats ~1.5 million TB patients annually while 0.2 million are notified from private sector. However, a million cases are still estimated to be missing against an estimated 2.8 million annual incidence. Since complete geographic coverage of DOTS-strategy in 2006, case notification rates increased initially, plateaued, and then started declining despite consistent efforts. The TB notification order in 2012 led to an increase of 29% in 2016, but an urgent need was felt to trace missing cases to reach TB elimination goals.

RNTCP undertook ACF in a campaign-mode for a fortnight in 50 districts across 15 states/Union Territories in India during 16th to 30th January 2017.

Intervention or response: In first phase of campaign, 50 districts were selected based on burden of TB, HIV-TB, Drug-Resistant TB and local resources. Case finding and diagnostic strategy were symptom screening, sputum smear microscopy (ZN) and CXR wherever available. RNTCP developed a guidance document to train and engage all levels of programme & general health system staff, and Non-Governmental partners. Awareness messages were broadcast via electronic& print media by popular Bollywood actor and TB ambassador Mr. Amitabh Bachchan. Monitoring and Evaluation framework was developed by National TB Institutes with technical assistance from WHO-India. An electronic reporting system was designed and incorporated into NIKSHAY-National TB notification system.
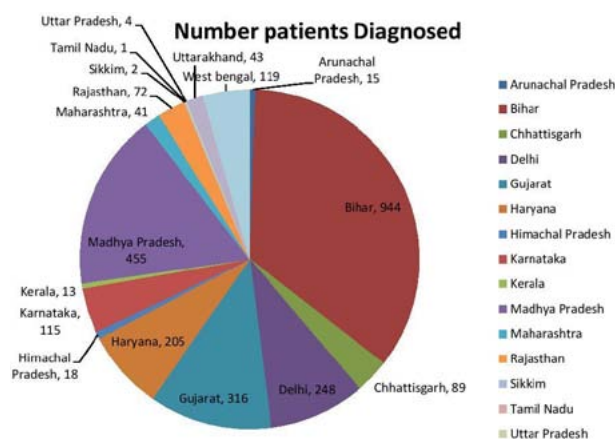
Figure TB cases notifed during the active case finding campaign (16 - 30 January 2107) in 15 states of India

Results and lessons learnt: From a target population of 9161430 mapped in 50 districts, about 4653458 (51%) were screened for TB symptoms. Of the screened, 69808

were examined for confirming TB (1.5%), of which 2700 were diagnosed to be TB (3.9%).

Conclusions and key recommendations: Active case finding among targeted/vulnerable population in campaign-mode can improve case notifications even with smear microscopy. To be more effective, similar campaigns are planned for other States in the country in subsequent phases with investment in digital CXR and rapid molecular tests to increase yield.

PD-560-12 Computer aided diagnostics tool for chest X-rays using deep neural networks

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Background: Chest X-rays are an important tool in the diagnosis of various pathologies affecting the lungs, including TB, pneumonia and lung cancer. Patients in the developing world often receive delayed diagnoses which in many cases are wrong due to a serious lack of radiologists. Deep convolutional neural networks (ConvNet) have been widely used in image analysis applications, and based on their success in other fields have been proposed for interpreting medical images. The objective of this study is to determine the efficacy of a computer aided diagnosis tool in interpreting chest X-rays for TB and lung cancer.

Methods: We employed deep ConvNets to develop a CAD system to interpret chest X-rays. We used images from the JSRT, Montgomery County and Shenzhen datasets that were obtained in real life clinical settings. Given that our combined dataset is relatively small for deep learning, we employed transfer learning to train a large network.

Results: The deep ConvNet achieved an accuracy of 82% in discriminating chest X-rays of confirmed TB patients to those with lung cancer and those of healthy subjects.

Conclusions: The developed deep ConvNet achieved good performance in comparison to the average accuracies achieved by radiologists, which are 78% and 75% for TB and cancer respectively. More work still needs to be done to determine the effectiveness of the system under clinical conditions as well as to predict other pathologies affecting the lungs.

PD-561-12 Chest X-ray radiologist reading agreement analysis in screening for TB: the IOM Global Teleradiology Quality Control Program

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Background: The International Organization for Migration (IOM) Global Teleradiology and Quality control Center, has implemented global Teleradiology Quality control (QC) Chest X-Ray reading and analysis program. The objective is to assess the quality of the images and radiologists' readings for Health Assessment field operations, doing TB screening for migrants resettling to different countries, and provide evidence based recommendation to help optimize the quality of the service.

Methods: The Teleradiology QC system randomly samples images from field operation's Picture Archiving and Communication System (PACS), transfers the images to the Teleradiology QC PACS, and fetches the primary radiologist's reading from the IOM Health information system (MiMOSA). Exclude cases, if no primary reading, poor image quality or additional view needed. The QC radiologist reads the sampled images using Teleradiology QC application. Scoring rule is applied to the system to differentiate significant from non-significant discrepancies. Missions respond on significantly discrepant cases. If agreement is not reached, the receiving country radiologist give final opinion. The system calculates the statistical report including the kappa agreement. The QC radiologist analyzes and sends results to missions.

Results: The QC program was provided for 19 IOM (13,129 cases) and 4 non IOM locations (1107 cases) 2015- 2016. Total 10,467 IOM and 1007 non-IOM were QC interpreted, analyzed and presented, and the rest were excluded. The TB kappa is 0.89 for IOM, 0.61 for 3 US non-IOM, and 0.82 for the one CA non-IOM locations. Major discrepant case, IOM 206(2%), Non-IOM US 36(6%), non IOM Canada 8(2%). The most common CXR finding in IOM major discrepant cases is discrete linear opacity 45(22%), followed by hazy infiltrates 26(12.6%).
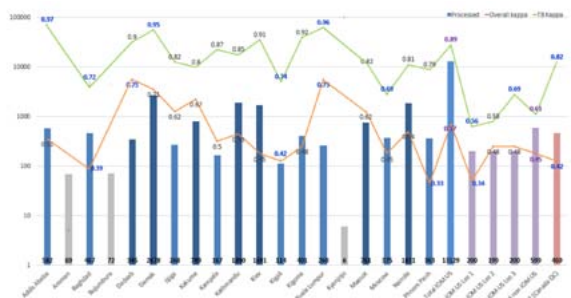
Figure Abstract Radiology QC agreement analysis

Conclusions: The study was able to assess the performance of the radiology service, common areas of discrepancy, identified the location with good quality reports, and those need capacity building helped to give the appropriate feedback.

08. Treatment delays misdiagnoses and losses to follow up - let's close the gap

PD-562-12 Effect of delayed treatment on tuberculosis treatment outcomes among patients on DOTS in districts of south-west Ethiopia: a prospective cohort study

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Background: Evidences on effect of prevailing long delays TB treatment outcome are scanty. Thus this study investigated effect of delayed treatment initiation on treatment outcomes.

Methods: A prospective cohort study among 735 new TB cases in districts of southwest Ethiopia was conducted from January 2015 to June 2016. Face to face interview with patients was held to elicit onset of illness, care seeking practices and time span to initiate treatment. Exposure was ascertained based on a median time elapsed since onset to treatment initiation. So those spent beyond 55 days were exposed and below 55 days were non-exposed. Both groups of cases were followed until earliest treatment outcome. Treatment outcome was ascertained using standard definitions and dichotomized in to successful when cured or treatment completed and unsuccessful when lost to follow-up or died or treatment failure. Finally bivariate and multiple log binomial models were fitted to identify independent predictors of unsuccessful outcomes.

Results: A total of 365(49.6%) and 370(50.4%) cases had initiated anti-TB treatment beyond 55days (exposed) and within 55days (non-exposed) of onset of illness. Thus, 627(89.7%) of the cases (86.7% of exposed vs 92.6% of non exposed, p=0.01) had successful treatment. In multiple regression, treatment initiation beyond 55days Adjusted relative risk (ARR) 95%CI 1.92(1.30, 2.81), HIV co infection ARR (95%CI) 2.18(1.47, 3.25), being treated at hospital ARR (95%CI) 3.73(2.23, 6.25) and older than 65years ARR (95%CI) 4.17(2.63, 6.60) independently predicted higher risk of unsuccessful outcome. On the other hand, weight gain ARR (95%CI) 0.40(0.19, 0.83) and sputum smear negative conversion ARR (95% CI) 0.17(0.09, 0.33) at the end of second month treatment predicted lower risks of unsuccessful outcome.

Conclusions: Delayed initiation of anti-TB treatment predicts higher risk of unsuccessful outcome. Therefore, promotion of early care seeking, improving diagnostic and case holding efficiencies of HCF and TB/HIV collaborative interventions could the risk.

PD-563-12 Determinants of TB patient's lost to follow-up treatment outcome and fate thereafter - a retrospective case study from an Indian State

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Background: Discontinuing anti-TB treatment prior to completion can leave patients infectious, symptomatics and prone to grave prognosis. Total 467 patients of 2015 cohort under National TB program in Himachal Pradesh State in North India were given lost to follow up (LTFU) treatment outcome in 2016. Present study was conducted with the objectives to ascertain the determinants of LTFU cases and to know the fate/current status of these patients.

Methods: A retrospective study was conducted between January-March, 2017 by interviewing the LTFU patients or their close contacts using semi-structured interview schedule by a team of trained investigators and triangulating with program records.

Results: Total 246 (53%) patients stopped treatment during intensive phase; while others during continuous phase. Near one-fifth of these LTFU patients were migrants from other States. Total 326 (69.5%) of patients or close contacts (of live or died patients) were interviewed under the study.

69 (21%) of LFTU patients were dead. 116 (35.6%) patients were put on category II regimen; whereas 01 patient on MDR-TB regimen. 68 (21%) were still sick and were not on any treatment for TB. 72 (22%) patients were being treated by private practioners.

The most common reason for LTFU was the non-traceability of the patients. 91 (28%) patients became non-tracable due to change in address. 56 (17.1%) felt better and stopped the treatment. Significant association of LFTU with alcohol consumption was also reported. 54 patients (15%) were alcoholic, whereas 58 (17.8%) patients stopped ATT because of side effects or the fear of side effects.

Conclusions: LTFU is a poor treatment outcome and has grave consequences. Study results provide insights for designing interventions aimed at reducing patient loss to follow-up. Initial home visits for address verification and subsequent visits, pharmacovigilance system; pre-treatment intensive counseling and patient-providers meeting are important activities for improving treatment adherence and reducing LTFU cases.

PD-564-12 Pre-treatment loss to follow-up among bacteriologically confirmed tuberculosis cases in Cameroon

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Background: Rates of pre-treatment loss to follow-up among people diagnosed with TB vary significantly by setting, and little is known about this important population in Central and West Africa. We aimed to determine the proportion of bacteriologically-confirmed TB cases lost to follow-up prior to treatment initiation in Cameroon and to assess factors contributing to this outcome.

Methods: We conducted a record review in 4 of the 10 geographical regions of Cameroon (Northwest, Southwest, West, Littoral), representing ~40% of the country's population. From the NTP paper-based registers, we constructed a database (Epidata v. 3.1) containing all bacteriologically-confirmed TB cases recorded in lab registers from October to December 2015 and a second database including all TB cases recorded in treatment registers from October 2015 to March 2016. Lab and treatment data were subsequently linked using probabilistic linkage (Link Plus v. 2.0), followed by manual review of all potential matches. Following linkage, field personnel investigated as possible the hospital files of non-linked patients to obtain additional information on their outcomes.

Results: Based on preliminary analysis, 163 of 1,300 bacteriologically-confirmed TB cases (12.5%) from NTP lab registers were lost to follow-up prior to entry in NTP treatment registers. These data were obtained from registers of 76 of the 100 (76%) NTP diagnostic and treatment centers in the assessment area. Pre-treatment loss to follow up was not associated with age, sex, geographical region or smear positivity grade in this population. From preliminary follow up of 47 patients lost to follow-up, 12 (26%) were confirmed to have died, while the rest had an unknown outcome.

Conclusions: Pre-treatment loss to follow-up is a significant challenge for TB control in Cameroon. Efforts should be increased to ensure that all those diagnosed with TB are immediately started on treatment to reduce transmission and mortality.

PD-565-12 Pre-treatment loss to follow-up among smear-positive pulmonary tuberculosis patients in Cameroon

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Background: Globally, smear-positive pulmonary tuberculosis (SPPTB) patients are expected to commence treatment immediately after diagnosis to quickly halt transmission of tuberculosis. In reality however, not all of them get on treatment and thus termed: pre-treatment loss to follow-up (PLTFU). Figures of this phenomenon ranged between 4 to 38% with great geographic heterogeneity. This study was to determine the proportion of PLTFU of SPPTB patients and its associated risk factors in two regions of Cameroon.

Methods: A retrospective cohort study was conducted involving thirty-nine TB diagnostic and treatment units (DTUs). Structured questionnaires were used to retrieve information from tuberculosis laboratory and treatment registers for all SPPTB patients diagnosed during last six months of 2015. Socio-demographic, sputum examination results and treatment information were collected. Travel distance/travel time between patient's residence and DTU's location were obtained using geographic information system tools. Data retrieved from both TB registers were cross-linked to identify any PLTFU (defined by failure to initiate treatment after diagnosis).

Results: Total SPPTB cases recorded was 1174, mean age of 37.6 (SD = 13.2) years and PLTFU rate of 12.6%. Median time from first positive result to initiating therapy was 1 (IQR: 1-2) day (Figure1).
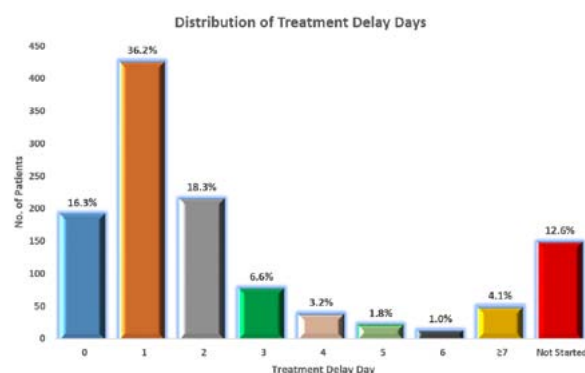
Figure Distribution of Treatment Delay Days

The risk factors for PLTFU included: urbanicity of the DTU (adjusted OR for urban versus rural: 3.45, 95% CI: 1.89-6.37), health facility type (adjusted OR for faith-based versus public: 1.85, 95% CI: 1.35-3.15), long travel distance from home to DTU (adjusted OR for every 10 km increase: 1.04, 95% CI: 1.02-1.06), and prolonged

travel time (adjusted OR for every 1hr increase in travel time to DTU: 1.32, 95% CI: 1.19-1.46).

Conclusions: Despite free tuberculosis treatment in Cameroon, PLTFU amongst SPPTB patients is still a significant issue in these regions. Access to TB diagnosis and treatment services remains a significant barrier to presumptive TB cases.

PD-566-12 Yield of bacteriologically confirmed TB from a national population-based TB prevalence survey in Zimbabwe, 2014-2015

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Background: Zimbabwe conducted its first national TB prevalence survey (NTPS) between 2014 and 2015 to determine the disease burden as the first step in guiding program implementation in view of ending TB as a public health concern by 2030. There is growing need for innovative interventions to detect missing cases.

Methods: A retrospective review of data collected through the NTPS. Presumptive TB patients were identified through symptomatic and chest x-ray screening with subsequent smear microscopy. All samples were also examined with Lowenstein-Jensen culture media (LJ) and the Mycobacteria Growth Indicator Tube (MGIT), to confirm active TB.

Results: Presumptive TB cases were identified through suggestive chest x-rays and/or a positive symptomatic screening. A total of 5,469 presumptive TB cases had an early morning sample collected and examined with smear microscopy with 2% being smear positive. Among the smear positives (n=116), 71% had 1-9 AAFBs (scanty positive) seen per 100 fields and the rest had at least 10-100 AAFBs (at least 1+) seen per high power field on microscopy. Of the smear positive samples, only 45% were confirmed by LJ to be containing MTB bacilli while 20% were contaminated and 45% had no growth. There was no significant difference on MTB growth on LJ between smear negative and scanty positive samples (p=0.07).

Conclusions: The yield for bacteriologically confirmed TB is generally low using generalized screening. As a guide to active case finding, there is need to define high risk groups and target those for screening for active TB disease.

PD-567-12 Patient and health system delay among pulmonary tuberculosis patients in Switzerland

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Background: In 2016, a total of 630 cases of tuberculosis (TB) were registered in Switzerland. The Federal Office of Public Health of Switzerland commissioned the Swiss Tropical and Public Health Institute to perform a study on the various delays between symptom onset and start of TB treatment, e.g. from onset of symptoms to first consultation (patient delay) and from first consultation to start of TB treatment (health system delay).

Methods: A prospective cross-sectional study was carried out in six cantons of Switzerland from November 2014 to June 2016 among adult patients notified with smear- or culture-positive pulmonary TB. Patients were interviewed by health care professionals of the cantonal lung associations mandated to provide ambulatory care to TB patients and contact investigations. Face-to-face interviews with patients were carried out, with professional interpreters called in as needed.

Results: Of 252 registered cases, 162 (61.8%) were interviewed. 20.4% of them were born in Switzerland, 41.4% were foreign-born residents of Switzerland and 38.3% were or had been asylum seekers.

The median patient delay was 36.5 days (75th percentile: 99.5 days). The median health system delay was 14 days (75th percentile: 50 days). Predictors of a long patient delay (> 5 weeks) were the symptom of tiredness and the co-morbidity of smoker's cough. Patients with Swiss citizenship were less likely to have a longed patient delay (> 5 weeks) but significantly more likely to have a prolonged health system delay (> 3 weeks). Protective factors against a prolonged health system delay were being male and having undergone a chest X-ray at the first consultation.

Conclusions: In Switzerland, some TB patients - in particular Swiss women - have a prolonged health system delay. General practitioners need to think of the possibility of TB disease, even in cases where the symptoms may be atypical.

PD-568-12 TB or non-TB? Factors associated with misdiagnosis of tuberculosis in Yogyakarta, Indonesia

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Background: Misdiagnosis of TB is a public health concern, as the undiagnosed TB patients potentially become the source of TB transmission, while patients without TB who are misdiagnosed as TB will have received unnecessary treatment. There is no study regarding misdiagnosis of TB in Indonesia, one of the highest-burden TB countries in the world. Therefore, we investigated possible factors associated with a misdiagnosis of TB in Yogyakarta, Indonesia.

Methods: Patients to be evaluated for TB who were admitted in the Governmental Lung Clinics in Yogyakarta, and aged >18 years old were included. All subjects were followed up between 6-18 months after the day of diagnosis. Subjects were followed up for 2.5 years when there was disagreement between culture results and patients' diagnosis. Demographics, bacteriological examination, chest radiography finding, comorbidities, follow up of clinical symptoms, and socio-economy data of the patients were recorded. Factors that might influence patients' revised diagnosis were investigated. Odds Ratio and 95% confidence intervals (95% CI) were analyzed with logistic regression.

Results: We enrolled 339 patients to be evaluated for TB. Most were male, and median age was 46 years. Among them, 99 were diagnosed as TB, and the rest as non-TB. The diagnoses of 12 non-TB patients were later revised into TB. All of these patients had negative sputum smear, but 9 of them had positive culture. Time to TB diagnosis ranged from 14 days to 2.5 years, with median of 93 days. No TB patients had revised diagnosis. Patients who had close contact with TB index cases presented a 24.2-fold (95% CI=6.9-85.2) higher risk to have revised diagnosis.

Conclusions: Those with smear-negative TB but had close contact with TB index cases tended to develop TB. If resources are limited to conduct patient tracking for all patients to be evaluated for TB, priority should be given to this group of patients.

PD-569-12 Can active case finding help reduce patient's delay in TB diagnosis in rural India?

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Background and challenges to implementation: In India, patient with tuberculosis (TB) is diagnosed after a delay of nearly 60 days, because of gaps in knowledge related to signs and symptoms of TB, correct diagnosis, low risk perception on symptoms related to TB and self-reported practices of providers leading to poor standardization in TB management.

Intervention or response: Population Services International (PSI) has been implementing active case-finding, with an objective to facilitate early diagnosis of TB among Key affected population (KAP), in 60 rural districts across 10 states of India. PSI engaged community volunteers (CVs) to conduct active case finding (ACF) through household visits in identified KAP areas and identify presumptive TB cases (PTB). Identified PTB cases are referred to nearest Designated Microscopy Centre (DMC) for sputum microscopy. CVs also facilitates sputum collection and transportation (SCT) from households, private clinics for facilitating diagnosis.

Results and lessons learnt: We analysed average mean delay from Patient's side, by taking number of days from onset of symptoms to date of diagnosis at DMC. This data was collected as part of routine MIS system on quarterly basis. Data of total 24,212 presumptive TB cases identified and tested at DMC through active case finding during Jan'16 to Dec'16 was analysed. Results showed significant reduction of delay on quarterly basis from 55 days from baseline (Jan-Mar'16) to 37 days (Oct-Dec'16).

Conclusions and key recommendations: With help of active case finding, regular follow up with PTB and referral linkages helps in reducing patient delay in diagnosis. Active case finding should be scaled up with an objective to identify missing cases from the community and ensure early diagnosis of PTB cases from the community.

PD-570-12 TB case finding in crisis situation: lessons learnt from Borno state, Nigeria

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Background and challenges to implementation: Borno state with a population of 5,556,438 is the most affected among the three states in Nigeria that are battling with insurgency as a result of attack by Islamic extremist group. Most of the population were killed or displaced,

schools and health facilities were destroyed. The displaced persons stayed at the Internal Displaced Camps (IDP) at the state capital or in other states.

The study aimed at highlighting the lessons learnt in conducting TB case finding in crisis situation.

Intervention or response: The sudden occurrence of the TB crisis affected the TB programme and health interventions in the state, some of the effects observed includes: increase loss to follow up and low TB case finding. In order to address this, the TB programme mapped the IDP camps in the state, thereafter engaged the National Emergency Management agency (NEMA) and State Emergency Management to facilitate Programme entrance into the camps. The programme conducted TB campaigns within the camps; sputum from the presumptive TB cases in these camps were sent for GeneXpert MTB/RIF test through a developed Sputum Transportation system

Results and lessons learnt: Cases of TB declined and they programme intervened the cases started increasing and patient were identified and put to treatment

Conclusions and key recommendations: As the crisis increases the case detection rate reduced, however with the implementation of active case finding activities in the IDP camps, the TB cases notified annually started increasing from 1,920 In 2014 to 2,257 In 2016

Collaboration with emergency and security agencies is key to implementing TB case finding activities during crisis. Collaboration with other health organizations and sector prevent duplication of activities.

PD-571-12 TB patient cost analysis, Cavite Province, The Philippines: assessment of households experiencing catastrophic costs

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Background: Patients with tuberculosis (TB) often incur significant costs related to their diagnosis and treatment. The objectives of this ongoing study are to determine the costs incurred by these patients in Cavite province of the Philippines and to understand the mechanisms that patients use to cope with this financial burden.

Methods: A cluster randomized survey using World Health Organization (WHO) approved questionnaires to collect costs incurred by TB patients has been used among a sample of patients undergoing treatment in six facilities for drug-sensitive TB and in two for drug-resistant TB. Direct medical and non-medical costs during the pre-treatment and treatment periods were evaluated as well as the indirect costs using the human capital approach.

Results: Preliminary results suggest the mean cost incurred by TB patients was ₱3283 (US$ 66) with direct medical costs accounting for the majority. Data cleaning

and interrogation is on-going, but initial results suggest coping mechanisms such as borrowing money, or selling household items, property, or livestock or spending savings, are a significant feature in almost 25% of patients. Around half of respondents also reported loss of household income. The proportion suffering catastrophic costs is currently being evaluated.

Conclusions: This study demonstrates the significant economic burden of tuberculosis in Cavite province of the Philippines. The financial burden of TB treatment is likely to represent a barrier, in terms of access and adherence, which may significantly affect health outcomes and increase risk of transmission of disease.

09. Progress engaging private and informal health providers in TB care in India

PD-572-12 Involving private practitioners in Indian´s national tuberculosis control programme: a randomized trial

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Background: In India, the majority of Tuberculosis (TB) patients seek care from private practitioners (PPs). The Revised National TB Control Programme (RNTCP) engages with PPs through a public-private mix strategy, but response by PPs is poor. We tested, in a South Indian district, a multi-component intervention to improve the involvement of PPs in referring presumptive pulmonary TB (PTB) cases to RNTCP for sputum examination.

Methods: In a randomised controlled trial, we allocated 189 PPs in Tumkur district capital to an intervention or control arm. The intervention, implemented between December 2014 and January 2016, included PPs training in RNTCP, provision of referral pads and TB-related education materials and monthly visits to PPs by RNTCP staff. In parallel, we built RNTCP staff capacity to collaborate with PPs and provide feedback on referrals through SMS messaging. Crude and adjusted referral and PTB case finding rate ratios were calculated with negative binomial regression.

Results: During the study period, 836 presumptive PTB cases were referred by PPs, 76% from the intervention arm. The proportion of referring PPs, the median yearly number of referrals per PP and the mean referral rate per PP-year were significantly higher in the intervention compared to the control arm (Table). A total of 176 sputum positive PTB cases were detected among PPs' referrals; the PTB case finding rate per PP-year was higher

in the intervention than in the control arm (Table). PPs referrals contributed to 20% of the sputum positive PTB cases detected by RNTCP (14% were from intervention arm PPs).

	Intervention arm (95% CI)	Control arm (95% CI)	Difference (for medians and proportions) or Adjusted rate ratio (for rates) (95% CI)
Proportion of PPs referring	0.59	0.42	0.17 (0.03, 31.00)
Median number of referrals/ PP/year	0.9 (0.0, 5. 1)	0.0 (0.0, 1.7)	0.9 (0.0, 1.7)
Referral rate per PP-year	5.7 (3.8, 8.7)	1.8 (1.2, 2.8)	1.9 (1.2, 3.0)
PTB case finding rate per PP-year	1.5 (0.9, 2.2)	0.6 (0.3, 0.9)	1.7 (1.0, 2.8)

Table Main results of the study

Conclusions: We demonstrated the effectiveness of using health system-oriented interventions to improve the involvement of PPs in RNTCP.

First and second authors equally contributed to the work.

PD-573-12 Improving quality of care delivered by private providers: Patna, Bihar

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Background and challenges to implementation: The quality of care provided to TB patients treated by private providers (PPs) is largely unknown and perceived as unmanageable. Inappropriate case management can result in poor patient outcomes, continued transmission, and drug-resistance TB (DR-TB). We developed a provider and patient surveillance system designed to improve quality of TB care across notified cases covering a population of 6.4 million in Patna district, the urban capital of Bihar state, India.

Intervention or response: We implemented a program management unit to engage private providers into a network that provided free diagnostic and treatment services through e-Vouchers and notified TB patients at point of care. Diagnostic and treatment practices were monitored through routine operational data, with PPs deviating from standard guidelines prioritized for one-on-one sensitizations. Provider-level surveillance emphasized microbiological testing and confirmation for TB diagnosis, take-up of CBNAAT-Xpert for drug susceptibility testing (DST), referral of detected DR-TB cases to public sector, and HRZE prescription regimens. Individual "Performance Reports" were shared with providers to help PPs understand their performance across quality of care metrics, generate dialogue on reasons for non-compliance, and monitor improvements over time.

Results and lessons learnt: Of the 29,976 pulmonary cases notified by PPs over the period of May2014- March 2017, the proportion receiving a microbiological test improved from 39% in 3Q14 to 73% in 1Q17, with microbiological confirmation increasing from 14% to 40%. The proportion of cases receiving a DST increased from 17% to 62%, and the cases microbiologically confirmed with a DST increased from 9% to 36%. Microbiological test positivity (out of those tested) improved from 34% to 50%. DR-TB case finding improved over time with a total of 1028 detected and referred to public sector. 73% of notified patients received a standard HRZE regimen.
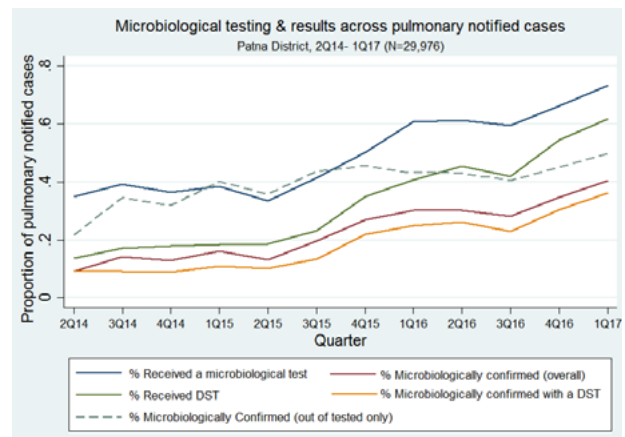
Figure Microbiological testing & results: Patna District

Conclusions and key recommendations: The Patna model demonstrates that quality of care improvement across private providers is achievable with a provider-centric model and targeted surveillance.

PD-574-12 Private provider engagement through effective service delivery: Patna, India

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Background and challenges to implementation: Private providers dominate tuberculosis (TB) care in India, requiring effective provider engagement models for TB control. Prior solutions have been unavailable, unconvincing, or not scalable. We developed a model designed to attract TB notifications, provide free TB drugs and diagnostics, improve quality of TB care, and actively monitor adherence and treatment outcomes in Patna district, the urban capital of Bihar, India with a population of 6.4 million.

Intervention or response: We developed a program management unit to engage targeted licensed physicians, non-licensed healthcare providers, diagnostic facilities, and pharmacies into a network that provided free diagnostic and treatment services through e-Vouchers and notified TB patients at point of care. Patient demographic details, diagnostic and prescription data, adherence information, and treatment outcomes were captured through technology platforms, facilitated with mobile calls to a Contact Center. A provider and patient surveillance system monitored quality of care and intervened through a program support team, emphasizing patient treatment adherence and provider compliance to standard guidelines.

Results and lessons learnt: From May 2014 - June 2016, the program engaged 643 (71%) of targeted 912 licensed providers and 688 (71%) of 972 pharmacies. The management unit facilitated notifications for 30,607 TB cases, 76% of total district's case notifications. Quarterly annualized case notification rate (CNR) per 100,000 population increased five-fold from 73 in 1Q13 (before the program) to 423 in 2Q16. Drug sales surveillance data estimated that 55% of all TB patients treated by private providers in Patna were notified and supported through program services by the last reporting month.
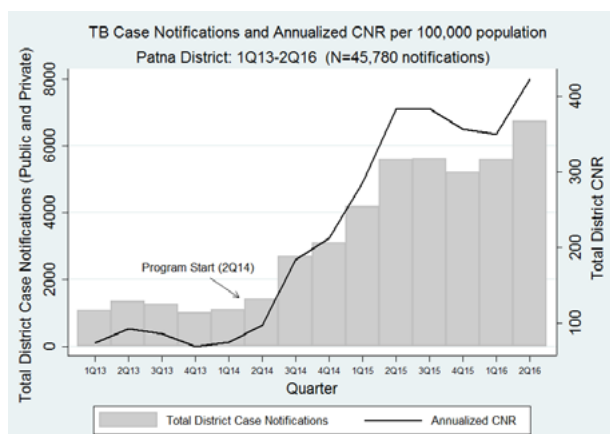
Figure TB Case Notifications: Patna District

Conclusions and key recommendations: The Patna TB model holds significant policy implications by demonstrating that sustained private provider engagement for improved TB case notification at scale is achievable. A similar service delivery model on a national scale can rapidly accelerate TB control efforts and bring under surveillance the vast majority of patients treated in the private sector.

PD-575-12 Can India's informal health care providers become a strategic alliance in TB care and prevention?

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Background and challenges to implementation: Informal healthcare providers (IHPs) are an unrecognised group of practitioners who are often first point of contact for people in rural, urban slums and hard to reach areas. They are treated as illegal practitioners and are under constant threat of losing their work! Over 2.5 million IHPs exist in India who practice across the country. Tuberculosis (TB) program in India has a huge challenge of cases treated in private sector. Estimates show about half of patients are not part of the national notification system. For this purpose it is collaborating with stakeholders in private sector. However they cannot collaborate legally with the informal sector but they cannot even ignore them.

Intervention or response: Project Axshya, a Global Fund supported project, trained IHPs from 285 districts to identify TB symptomatics and refer them to the national program for diagnosis and treatment. Once the provider agrees to refer cases, he is followed up by the project staff one-on-one and also incentivised.

Results and lessons learnt: Over three years the project trained about 25,330 IHPs and engaged 4920 to conduct activities which included referring and or sputum collection and transport to the government centres. Of those who were referred (N=97343) 39,433 underwent sputum examination and 6153 i.e. 16% were diagnosed with TB. Sputum was collected and transported from 94246 symptomatics of which 12% (N=11,117) were TB positive. In total 17,270 TB patients were diagnosed. The value addition is that the IHPs don't diagnose or treat by themselves, hence there are no issues of false diagnosis and unregulated treatment, rather reduce the diagnostic delays.

Conclusions and key recommendations: Engaging a miniscule (0.2% of over 2.5million estimated) of informal providers has shown a considerable contribution to the TB program by bringing over 17,000 patients to public sector. A paradigm shift in India's TB program can build a strategic alliance with IHPs, and accelerate end TB strategy.

PD-576-12 High loss to follow-up of TB patients treated in private sector: follow-up study in urban, rural and tribal parts of Maharashtra

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Background: Although India is committed to providing free, high-quality tuberculosis care to patients, yet behaviourally people are attracted to private sector treatment which accounts for providing treatment to half of TB patients. Having a fair idea about private TB patients is critical, but we do lack knowledge about care model that the private sector is adopting. To assess proportion of TB patients successfully completing treatment in private sector we conducted a follow up study in urban, rural and tribal parts of Maharashtra.

Methods: Follow up study was conducted across 6 districts (2Urban, 2Rural and 2Tribal) and 120 qualified private practitioners(QPP) who actively notified TB patients were engaged into the study for study period (July 2015-June 2016). Bacteriologically or clinically confirmed Adult TB cases initiated on anti TB treatment were followed up monthly for the entire course of treatment and treatment outcome was also assessed based on existing guidelines. Demographic, socio-economic status was assessed and correlated with treatment completion behaviour.

Results: A total of 500 TB cases (**Urban**=280(53%Males,47%Females), **Rural**=160(73%Males,37%Females), **Tribal**=60(82%Males,18%Females)) were notified by enrolled QPPs. Socio-economic Status [**Urban**= 23%Upper:62%,middle:15%upper lower class; **Rural**=56%middle,44%lower class: **Tribal**=78%middle,22%lower class]. At end of three months, 46% in urban, 53% in rural and 67% in tribal were loss to follow up (LTFU) and on end of six months additional 7%, 25% and 18% were LTFU. On being tracked for unwillingness for continuation, major reasons were high cost of treatment(40%LTFU patients), no symptoms(23%), migration(13%), don't want to eat pills(7%), unavailable(11%). There was a strong co-relation between middle and low SES and discontinuation of treatment

Conclusions: High LTFU in private treatment is a matter of concern as this is one of the fundamental reasons for rising DR-TB proportion in India. In absence of committed public health action measures for measuring and reducing LTFU in private sector, it becomes impossible to eliminate TB.

PD-577-12 Notification of TB patients from private health care providers in India: inter-district variation and underlying characteristics

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Background and challenges to implementation: Tuberculosis has been made a notifiable disease in India since 2012. However, Revised National TB Control Programme could notify 1.7 million TB patients out of estimated 2.8 million TB patients in a year 2016. There is wide variation in TB notification across the country. Present study aims to understand variable notifications of TB patients from private sector from different districts of the Country and correlating factors.

Intervention or response: There are 733 programmatic districts in India. Private healthcare providers notify TB patients to the nodal officer in every district which are reported in NIKSHAY - a case based web based MIS under Revised National TB Control Programme. The data on notification of TB patients done in the year 2016 was extracted and analyzed in SPSS. TB notification rate analysis was done upto district level for comparing health facilities registered, urban population and availability of staff.

Results and lessons learnt: In India, 330,186 TB patients were notified from private healthcare providers in 2016. These patients were 20% of total TB patients notified in a year. Mean Annual TB notification rate of these patients notified from private provider was 30 patients par 100,000 population (95% CI 24-36).Out of 733 districts, 65 contribute to 50% of TB patients notified from private sector in the country. Districts with higher TB notification rate (above mean) had higher number private health care facilities registered per 100,000 population (p<0.001), had higher proportion of urban population (p<0.001) and had better availability of human resource per 100,000 population (0.014) in the district.

Conclusions and key recommendations: The study identified a few characteristics of districts i.e. urban population, presence of private health care providers and availability of staff to prioritize the interventions.

PD-578-12 Managing resources for maximizing patient benefit: an experience from private provider interface agency, Mumbai, India

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Background: Private Provider Interface Agency (PPIA) is pilot project for urban TB control in private sector of Mumbai initiated in September 2014. The budget allocated for this project comprised of 39% towards patient care and another 44% ($2.65 million) was allocated on human resources, trainings and workshops for different stakeholders. Optimum utilization of funds for patient care was a priority to improve efficiency.

Methods: As project activities evolved over the 3 years intervention, activities versus the program burn rates were monitored on monthly basis to keep a check on the financial expenditures and outputs of the project. The implementation processes evolved with frequent training and recruitment of trained dedicated staff which worked intensively in handholding and engaging with private practitioner's for increasing case notification of TB cases and use of microbiological diagnostic tools being offered under the project. The effective implementation helped the project save the cost on Continued Medical Education (CME) as the objectives of the project were achieved with the existing ongoing activities. Other form of superfluous workshops and dissemination meetings workshops were eliminated without affecting program objectives. Personnel hiring and budget allocated was optimally earmarked and reallocated. These changes resulted in substantial savings of 14% ($834,000) of the program budget being diverted towards patient care.

Results: Project success reflected in total 38,575 case notifications as against target of 25000 by reaching more than 1,00,000 beneficiaries during project period. Optimum utilization of funds ensured 14% savings, resulting in 53% of total budget allocated to patient care instead of 39%.
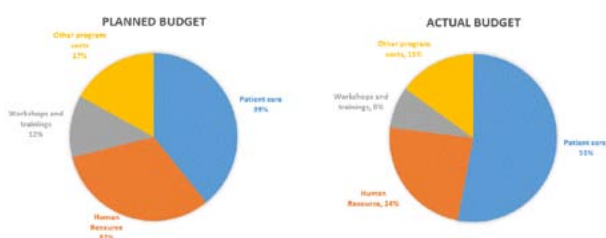
Figure Budget Allocation for PPIA

Conclusions: Flexibility to utilize donor grants to achieve program objectives and tweaking traditional methodologies played important role in ensuring maximum benefit to patient care.

PD-579-12 Private sector TB notifications. Where are we? Experience in 13 provinces of India

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Background and challenges to implementation: Despite being notifiable disease since 2012, TB notification from private health sector is negligible in India. The Union is implementing Global Fund supported project Axshya in 285 rural and 40 urban districts of 19 provinces of India with engaging private health sector as one focused interventions.

Despite of launching dedicated web-based govt. notification portal (NIKSHAY), various modes of TB notifications are still not widely accepted by private providers.

Intervention or response: We mapped, trained and facilitated case notifications to nikshay from private healthcare providers in 40 urban districts from 13 provinces of India. We developed innovative ICT tool which facilitated notifications to nikshay. The tool also provided weekly IVR calls and customized daily SMS to patients for reminding treatment adherence. All stakeholders had user friendly analytical access to data on our tool. Project staff in districts helped providers and patients in this process.

Results and lessons learnt:

Process outputs:

30% of sensitized providers followed standard practices(engaged)

98% of engaged providers opted for reminders for their patients.

Notification delay= Avg95 days (Range: 0-771 days, IQR: 34-120 days) higher in hospitals

Bacteriological confirmation followed in 23% cases

Patient related outputs and observations:

Total 6920 patients notified by 659 providers during Jan-Mar2017.

Treatment initiation delay= Avg2 days (Range: 0-388 days, IQR: 0-1 day)

Age= Mean 37years (Range 1-99, IQR 31-49 years)

Male: Female ratio= 10:7

Site of TB= 76% Pulmonary

Patient consented for ICT reminders= 86% of 6920 patients

Documented treatment adherence= 77% of consented patients responding to IVR calls

Verified(sample) treatment adherence= 80% of consented patients responding to weekly IVR calls.

Conclusions and key recommendations: Private health sector prefers user friendly processes and public health action in return of case notifications. Public health action preferred by private health sector and patients form private sector less likely includes treatment support from government. Patient-centered approach(our tool) contributed 56% of total notifications in selected districts.

PD-580-12 Combating TB through private provider engagement: PPIA model

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Background: Mumbai is the global hot spot for TB and 60% of the TB patients in Mumbai seek care in private sector. In 2014, under the aegis of Municipal Corporation of Greater Mumbai (MCGM), a project was initiated by PATH as Private Provider Interface Agency (PPIA) through a testing and referral model to provide quality TB care to private sector TB patients. PPIA is an example of innovative approach for Public Private fix model to fight against TB in India.
Methods: PPIA model included networking with doctors, pharmacies and laboratories to detect TB cases early and notify them. Presumptive TB suspects identified by the informal providers were referred to networked HUB hospitals for diagnosis. Under the project free TB screening and diagnostic services, free drugs on scientific prescriptions as per the Standards of TB care in India (STCI). Treatment adherence was ensured through ICT platform called Universal access for TB care (UATBC) to track and send reminder messages for completion of treatment.
Results: TB patients availing benefits: Under the PPIA initiative, 36, 678 Tuberculosis patients have been detected out of which 3,053 patients were diagnosed as Rif. Resistant. 12,013 patients under the PPIA have completed their treatment while the rest are on- going treatment.
Private Provider Engagement and Networking: PPIA networking of private providers included, 607 hospitals, 3670 doctors, 366 laboratories and 268 chemists in Mumbai.
Reimbursements : The diagnostic cost for TB patients under PPIA was USD 1.15 million and for first line Anti - TB treatment cost was USD 1.05 million.
Conclusions: PPIA provide effective private sector engagement models suitable for urban areas. These approaches now need to be tested and adopted as end to end solution for quality private sector engagement.

Figure PPIA Model

PD-581-12 Simple, cost-effective strategy for increased TB case notification by private sector health care providers in 100 cities of India

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Background and challenges to implementation: Substantial number of TB cases is annually missed in India. Although most of these TB patients receive treatment in private sector, they are not notified to the Revised National Tuberculosis Control Program (RNTCP). In 2016, only 200,000 out of an estimated 1.2 million missing TB cases were notified from private sector. Within the Global Fund supported TB program, World Vision India (WVI) and its six partners planned to improve TB case notification from private sector. Between Oct'15 - Dec'16 it was expected to notify 49,000 TB cases out of 114,911 annually estimated missing cases in 100 medium-sized cities of 70 districts of 8 states of India.
Intervention or response: Through mapping conducted in 100 cities, WVI and partners identified 9,499 private doctors and 3,560 health-establishments. The 1,936 doctors and 320 health-establishments were sensitized on both importance and processes of TB case notification as per the national guidelines. One Hindred notifications executives were deployed to all 100 cities to regularly visit doctors and facilities to help them in notification process. Later on, the notification executives uploaded information in e-notification system of RNTCP known as NIKSHAY.
Results and lessons learnt: About 10% (19,784) of total TB cases was notified from the private sector and registered in NIKSHAY in 2016. Private sector notification in 16 districts out of 70 project districts was kick-started through project's interventions only. The average cost of one TB case notified was 8.0 USD.
Conclusions and key recommendations: A simple mechanism for improving TB case notification was established. Engaging private sector providers in TB case notification is cost-effective and, if replicated among private sector health care providers, can significantly increase TB case notification.
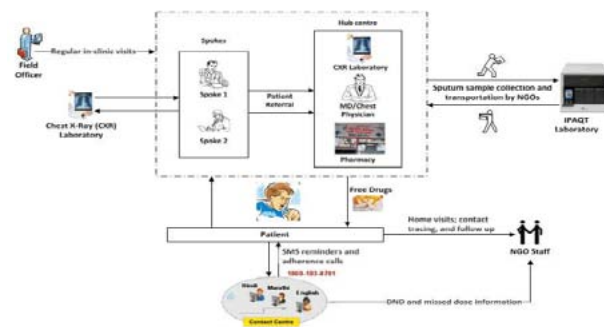
10. Where are they? Case finding and preventive therapy for paediatric TB

PD-582-12 Addressing bottlenecks in the childhood tuberculosis cascade: a model to accelerate case detection, treatment and prevention of TB among children in Viet Nam

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Background and challenges to implementation: In Vietnam around 13,000 children are estimated to develop tuberculosis annually, of whom only 10% are notified. *Breath for Life* is a National Tuberculosis Control Program (NTP) initiative which aims to strengthen the childhood TB detection, treatment and management in four districts of Nghe An, a province heavily burdened by TB in 2016-2017.
Intervention or response: The project was designed to develop and test a model that addresses the health system challenges contributing to low TB detection among children. The approaches used includes engaging non-NTP public and private health facilities in childhood TB management, strengthening systematic symptom-based screening of child TB contacts and enrolling eligible children on isoniazid preventive therapy (IPT), and decentralizing childhood TB diagnosis, treatment and management within the public health care system. Data were collected and analyzed using the NTP recording and reporting system.
Results and lessons learnt: With this approach, between 2015 and 2016, the number of childhood TB cases diagnosed in the four districts has doubled with the average number of children per district diagnosed with TB went from 18 to 37; in contrast, the average number of childhood TB cases identified in the remaining 17 districts of Nghe An was 10 and 16, respectively. During the same period, the number of IPT eligible children and the proportion of eligible children on IPT in the four project districts also increased significantly (from 49/64 (77%) to 189/205 (92%)).
Conclusions and key recommendations: The project outcomes provide evidence of the feasibility of a model that can enhance the detection, treatment and prevention of TB among children in rural areas in Vietnam. *Breath for Life* is recognized by Vietnam NTP as the best practice and plans are underway to expand the program so that it can be replicated in other provinces to accelerate childhood TB detection and prevention in Vietnam.

PD-583-12 "That is why others give up": care giver perspectives on TB case-finding and HIV clinical services among pediatric TB patients, Tanzania

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Background: Caregivers of children with TB and HIV have a critical role in seeking healthcare. We assessed the perspectives of caregivers of children with TB in Tanzania in order to understand barriers to pediatric TB diagnosis, treatment and linkage to HIV clinical services.
Methods: In-depth interviews with caregivers were conducted in March 2016 at 10 TB clinics in five TB and HIV high-burden regions of Tanzania. 76 caregivers of pediatric TB patients provided informed consent and underwent semi-structured interviews which were conducted in Swahili, recorded, translated into English and content analyzed.
Results: Of 76 caregivers interviewed, 60 (78.9%) were female, 56 (73.7%) were a biological parent, and median age was 35. The median age of children was 6 years with an average of 3.4 months of TB treatment with 74 (97%) offered an HIV test, 37 (50%) HIV-positive and 32 (86%) of HIV positive children on ART. Caregivers suspected TB due to TB in their family, or the child being ill and not improving after visiting healthcare facilities. Most noted a delay and that persistence was required before their child was diagnosed with TB. Some noted determination due to other family members who had died from TB or HIV. Once diagnosed with TB, caregivers reported challenges including pill burden and lack of pediatric formulations. Reasons for agreeing to have the child tested for HIV included regular illness and HIV symptoms, history of HIV in the family, and clinician recommendation. Caregivers described a relatively seamless process of linkage to HIV care once their child was diagnosed with HIV.
Conclusions: Caregivers cited multiple clinic visits before a TB diagnosis was made which suggests the need for additional training and sensitization of healthcare workers to suspect TB. Most caregivers accepted HIV testing for their children and experienced strong linkages to HIV treatment.

PD-584-12 Quantifying exposure to tuberculosis in child contacts: a validation study

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Background: We aimed to validate a simple survey evaluating intensity of TB exposure, which was developed and shown to be an effective indicator of TB infection status in children in South Africa, in a low-HIV prevalence setting in Latin America, Lima, Peru.
Methods: Children ages 0-15 were included if they presented with >=1 sign/symptom of TB, and had a history of contact with an adult TB patient. The 10-question survey was administered to parents/guardians and addressed questions about sleep proximity, frequency of exposure and infectiousness of contact. Answers were binary and we calculated a contact score as the sum of yes answers. Infection status was determined using tuberculin skin testing. We adapted the scale by adding factors expected to predict infection status in this population such as contact's smoking status, crowding and number of contacts. Original and adapted scores were evaluated for association with infection status using logistic regression.
Results: Among 294 children included, (63%) were under 5. Most contacts had current cough (83%), saw the child daily (89%) and lived in the same household (89%). 81% of households had > 5 residents. Both scores were associated with infection status when adjusting for age. The association was stronger with the adapted vs. original score in children under 5: (aOR 1.25, 95% CI 1.07-1.46 vs. aOR 1.50, 95% CI 1.19-1.89). See Table 1. Neither score showed significant association in children 6-15 years old.

Covariates	0-15 years n=294		0-5 years n=186		6-15 years n=108	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Original score	1.10 (0.98-1.24)	1.15 (1.0-1.31)	1.23 (1.06-1.43)	1.25 (1.07-1.46)	0.95 (0.75-1.21)	0.94 (0.74-1.19)
Adapted score	1.20 (1.02-1.42)	1.26 (1.07-1.50)	1.47 (1.18-1.84)	1.50 (1.19-1.89)	0.92 (0.69-1.23)	0.92 (0.69-1.23)

Table Association between baseline Mtb infection status

Conclusions: This survey was successful in predicting infection status in children 5 and under. The scale may be a useful tool to target young children at highest risk of TB progression in settings still working toward universal access to preventive therapy in children under 5. Further work in developing a tool for use in older children is needed and will be pivotal to the success of these programs.

PD-585-12 Improvements in IPT uptake rates in under-five children in Ethiopia: results of a five-year program

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Background and challenges to implementation: Isoniazid preventive therapy (IPT) in under-five children is a globally recommended TB preventive strategy in children but its uptake has been slow in high TB burden settings. We analyzed a five-year trend for IPT coverage rate to demonstrate how targeted health systems interventions can lead to improvements in service uptake in two regions of Ethiopia.
Intervention or response: Between September 2012-March 2017, we supported the national TB program to implement IPT for under-five children using contact investigation of potentially infectious adult patients as key entry point to identify children eligible for IPT. Activities implemented to introduce IPT as routine practice included developing and enforcing the use of standard operating procedures and separate recording and reporting tools; organizing sensitization and training workshops for health care providers and program managers; and supplying pediatric formulation of Isoniazid to health facilities. This was followed by quarterly joint supportive supervision to monitor implementation.
Results and lessons learnt: Of 126,606 contacts screened, under-five children constituted 10.1% (12, 748); this was 94.3% of 13,515 under-five children identified through contact tracing. The screening rate increased from 87% at baseline to 97.3% currently. Of 12,088 cumulative number of eligible children, 4,956(41%) were started on IPT; coverage increased from 12.4% at baseline to 59% in the most recent quarter (Figure).
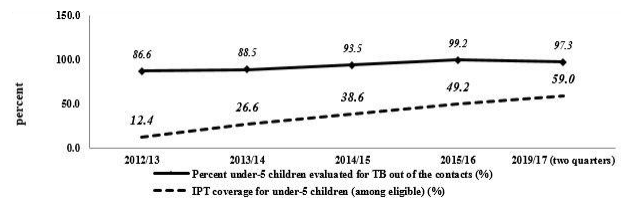
Figure IPT in U5 Children, Ethiopia

Conclusions and key recommendations: There was over four-fold increase in IPT coverage rate following project interventions but additional strategies are needed to put the remaining third of children in care.

PD-586-12 Decentralisation of child TB services increases child TB case detection in Uganda

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Background and challenges to implementation: Although 50% of Uganda's population are children <15 years, only 7% of the total TB cases in 2014 were children <15 years, expected to contribute approximately 17% to the total TB caseload. Health system challenges like; centralized child TB diagnosis, limited knowledge and capacity to diagnose child TB among primary level health workers, were responsible for low child TB notification.

Intervention or response: The DETECT Child TB project was implemented by The Union Uganda between January 2015 to December 2016, as a pilot to testing a model that addressed the challenges hindering child TB diagnosis in two districts of Kabarole and Wakiso. Interventions were; decentralizing child TB services from hospital level to lower level III and IV health centers; active TB case finding for children in contact with TB patients through household contact tracing; and provision of Isoniazid preventive therapy for child contacts under 5 years.

Results and lessons learnt: An external evaluation conducted after fifteen months of implementation showed following results.

Child TB services were successfully decentralized from hospitals to lower level health facilities. The percentage of child TB cases diagnosed at lower level health facilities increased from 5% at baseline to 52% after 15 months.

The percentage of child TB cases among all TB cases notified increased from 7.4% and 10% at baseline to 18% and 15% in Kabarole and Wakiso districts respectively.

1,839 child household contacts were screened for TB among whom 27% were symptomatic, from whom 9% were diagnosed and treated for TB.

555 children <5 years from the households of TB patients were initiated on IPT.
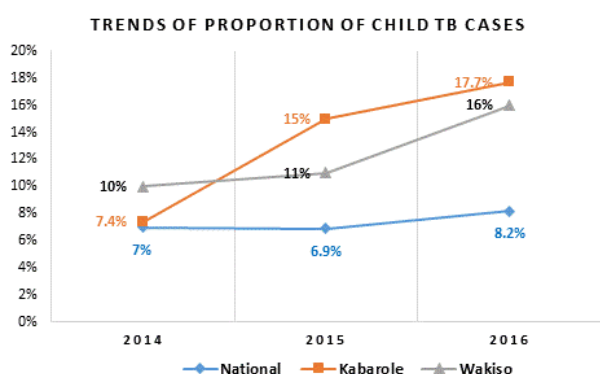
Figure Trends in proportion of child TB case notification

Conclusions and key recommendations: Decentralizing Childhood TB services from hospital level to primary healthcare level with an emphasis on clinical diagnosis for the lower level facilities improves child TB case finding and should be taken up as national policy to improve childhood TB management.

PD-587-12 Finding the missing cases: improving childhood TB case detection through active screening in Meru county hospital

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Background and challenges to implementation: Kenya is among the 30 countries in the world with high TB, TB/HIV and MDR-TB burden but has low child TB case detection (9% of all TB cases). Active TB case finding (ACF) is not routinely conducted in Integrated Management of Childhood Illnesses (IMCI) Clinics where sick children with possible TB are managed.

Intervention or response: Meru County hospital adapted the use of a simple symptom based TB screening tool to screen all children seen at the IMCI clinic between April and September, 2016 as part of ACF. IMCI clinic staffs were sensitized on the tool which captured symptoms including cough, reduced playfulness, persistent fever, contact with a chronic cough, respiratory signs, failure to thrive, repeated antibiotic use, enlarged lymph nodes and spine deformity. Routine TB surveillance data was evaluated.

Indicator	October 2015- March 2016	April-September 2016	Remarks
Total TB cases (children from IMCI clinic)	6(8.5%)	32(35.2%)	Proportion of TB cases in the hospital
Number and % of children with TB who are HIV positive	2(33%)	2(6.5%)	Proportion of children with TB tested for HIV
Number and % of HIV+ on ART	2(100%)	2(100%)	
Treatment completion rate	6(100%)	29(91%)	Proportion of TB cases in the hospital. 1 died, 1 still on treatment for TB meningitis, 1 transferred to another unit

Table Summary ACF data for Meru county hospital

Results and lessons learnt: Children diagnosed with TB at the clinic significantly increased from 6(8.5%) between October 2015 and March 2016 to 32(35.2%) between April and September 2016. 2 children had bacteriologically confirmed TB, 17 had a suggestive x-ray while 19 children were diagnosed using TB symptoms. The median age of children diagnosed with TB was 12

months (IQR 8, 23.5). 33% of all child TB cases from October 2015 to March 2016, and 6.5% of all cases from April to September 2016 were HIV positive. All 6(100%) children treated between October 2015 to March 2016, and 29(90.6%) treated between April and September 2016 completed treatment.

Conclusions and key recommendations: Use of a simple screening tool in the IMCI clinic and other child departments resulted in increased and early TB detection among children. This will reduce their morbidity and mortality from TB. The tool is cost effective and can be used in lower level health facilities. Capacity development of health care workers to obtain sputum specimens from children and availing chest x-rays at no/minimal cost is a gap to be addressed.

PD-588-12 Do intensified case finding activities among malnourished children yield results? Prospective cohort study at nutritional rehabilitation centres, Maharashtra

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Background: Severe acute malnutrition (SAM) is a major public health problem, especially among under-five children in developing countries. Owing to reduced immunity, children with SAM are at a higher risk of acquiring infectious diseases including Tuberculosis (TB), which is a major contributor to high mortality among these children. However, to our knowledge, very few studies have explored the feasibility of ICF among malnourished children in Nutrition Rehabilitation Centers (NRC).Aim of the study was to find
(1) Proportion of symptomatic childrens screened for TB among all admitted childrens.
(2) Prevalence of TB among under five childrens at NRCs
Methods: A prospective cohort study was implemented across 37 NRCs in Maharashtra from July 2016-March 2017. Inclusion criteria was under five childrens admitted for correction of SAM. Presumptive TB SAM childrens were provided with tuberculin skin testing, using PPD (purified protein derivative of RT23 or equivalent), chest radiography and CBNAAT. Data was systematically collected and analysed by Epi data software.
Results: Total of 2397(1176 male & 1221 female) SAM childrens were admitted during the study period. Of the above 1477(703 male & 774 female) were identified as presumptive TB case. Of the above total of 42(39 Pulmonary and 3 Extra Pulmonary) TB cases were diagnosed. Proportion of Pulmonary and extra pulmonary TB among SAM children was 3% and 0.2% respectively. Diagnosis was mainly done by Chest X-Ray (66.7%) followed by Mantoux test clinical correlation(23.3%) and

CBNAAT(10%). Of the diagnosed cases, 88% were put on National TB Programme treatment and rest were adjusted for dose and drugs based on clinical conditions.
Conclusions: This is the first propective study with huge sample of SAM Childrens in India. The study is a paradox with strengths showing how we can tap the missed opportunities of diagnosis and at the same time how lack of skilled personnels reflects in under-diagnosis of TB.

PD-589-12 Barriers to contact screening and isoniazid preventive therapy among paediatric contacts of adults with smear-positive tuberculosis

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Background: India's national guidelines recommend tuberculosis (TB) screening of household contacts < 6 years old and isoniazid preventive therapy (IPT) for children without active disease. We evaluated the status of and barriers to contact screening and IPT provision to TB exposed children in India.
Methods: A structured questionnaire was administered to consenting adults with sputum smear positive TB, who had household contacts <6 years old, and health care providers (HCPs) involved in contact screening and IPT prescription at Sassoon General Hospitals, Pune.
Results: Of 80 adult TB index cases, only 24(30%) reported that a HCP had asked them to bring their child contacts for screening. Overall, 29(38%) adults complied, leading to screening of only 49(28%) of a total of 178 child contacts. Of these 49 children, 16(33%) had active TB and 28(85%) of 33 who screened negative received IPT. Five children were diagnosed with TB after IPT initiation. Overall, 21(42%) of all screened children had active TB. Children diagnosed with active TB had a median of 167.5 days between index case diagnosis and contact screening, compared to 25 days for those who screened negative. Nineteen (76%) of 25 HCPs reported recommending child contact screening. Only 8(32%) reported ever prescribing IPT. Barriers to child contact screening were extended family structure (OR 4.4, p value 0.002), non-parent index case (OR 11.5, p value <0.001), lack of HCP knowledge of RNTCP guidelines (OR 18, p value 0.009) and inadequate HCP counseling (OR 17.5, p value <0.001) regarding need for contact screening.
Conclusions: Screening for active TB and provision of IPT for child contacts of Indian adults with TB was very

infrequent. In addition, many of the screened child contacts were found to have active TB. These findings highlight key programmatic barriers that must be addressed to reduce childhood TB in India.

PD-590-12 Modelo de abordaje para la atención al contacto de tuberculosis en edad pediátrica basado en la estructura comunitaria en los Altos de Chiapas

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Background and challenges to implementation: Se estima que cada año se infectan 3.1 millones de niños por TB. Por lo menos 1 millón de niños desarrollan la tuberculosis (TB) cada año. En 2015, 170,000 niños murieron por TB y 40,000 muertes adicionales se produjeron en niños que tenían VIH. (WHO, 2014). Chiapas, un estado del sur de México, reúne características económicas, sociales y culturales que contribuyen a una elevada prevalencia de TB. La región de los Altos de Chiapas, es una de las zonas más pobres del estado y de todo el país.
Intervention or response: A partir de resultados obtenidos en una investigación realizada en el 2012, con la aplicación de la Escala Pediárica de Riesgo de la OMS, se adaptó un instrumento de evaluación al contacto pediátrico de TB, que fue aplicado por el personal de salud del primer nivel de atención como parte del estudio a contactos menores de 19 años, del 2013 al 2016.
Results and lessons learnt: Se realizó la diferenciación de los contactos en sintomáticos y asintomáticos, estableciendo una ruta de atención que garantizara: a) la identificación oportuna de signos sugerentes de tuberculosis; b) el ingreso a terapia preventiva a los contactos menores de cinco años, no enfermos; c) la evaluación por pediatría de todos los contactos con sintomatología sugerente de TB y de manera sistemática a todos los menores de cinco años. Para la refererencia al servicio de pediatría, con autoridades municipales, responsables de las redes de servicios y equipos aseguradores de la calidad jurisdiccionales.
Conclusions and key recommendations: La aplicación de esta estrategia puso el foco de atención en la población infantil, sirvió de herramienta para que el personal de salud advirtiera los signos y síntomas de la enfermedad. Permitió a la madre conocer los síntomas que pueden corresponder a la tuberculosis. Logró la articulación interprogramática y con los diferentes niveles de atención de los servicios de salud.

11. Tobacco advertising and smoke legislation

PD-591-12 Compliance with smoke-free legislation and smoking behavior: observational field study from India

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Background: Indian smoke-free legislation requires prohibition of smoking at public places and proprietors of public places to display "No Smoking" signage's. The study aims to assess the compliance of public places to smoke free legislation and find out the factors which predict active smoking in public places.
Methods: This was a cross-sectional analytic observational quantitative survey conducted by a team of trained field investigators using a structured observational checklist based upon a guide jointly developed by John Hopkins School of Public Health, Tobacco Free Kids and International Union Against Tuberculosis and Lung Disease; across 6875 public places in Punjab state of India over a period of 3 years. The categories of public places includes eateries (restaurants, bars and shopping malls); government buildings (banks, court, public offices etc); educational institutions (school and colleges);health care facilities and transit stations (railway stations, bus stations and airport).The data was analyzed using SPSS 17 statistical package.
Results: A total of 6875 public places across 22 districts of Punjab was observed. The overall compliance to smoke free law in Punjab was 75.6%. The highest overall compliance was observed in health care facilities (77.9%) and least in transit stations (69.1%). The logistic regression model revealed that the significant positive predictors of "active smoking" were sites where patrons/owners of public place smoked (OR=5.2); presence of smell/ash (OR=7.2) and presence of cigarette buts (OR=4.6). Places where "signage's mentioned the name of reporting officer" had lower odds of finding people actively smoking (OR=0.6).
Conclusions: The compliance to smoke-free legislation at public places of Punjab was average. The least compliance was observed at the transit sites. No smoking" signage's displayed as per legislation has an effect on curbing smoking behaviors at public places. It is recommended that policy makers should focus more on implementing the smoke free law at transit sites.

PD-592-12 Validity of indirect indicators of smoking in predicting active smoking behavior in public places: cross sectional survey of Tobacco Smoke Free state of India

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Background: India has the highest proportion of tobacco users in the world. Approximately one million people die every year in the country due to this leading preventable cause. The study aims to assess whether indirect indicators of smoking predict active smoking behavior at public places.

Methods: This was a cross-sectional analytic observational quantitative survey conducted by a team of trained field investigators using a structured observational checklist based upon a guide jointly developed by John Hopkins School of Public Health, Tobacco Free Kids and International Union Against Tuberculosis and Lung Disease; across 6875 representative public places in Punjab state of India. The public places chosen were restaurants and bars, government buildings, educational institutions, health care facilities and transit stations (railway stations, bus stations and airport).The indirect indicators assessed were cigarette stubs in public place; smell of smoke, display of signage's as per the law. The study was carried out over a period of 3 years.

Results: The overall compliance to smoke free law in Punjab was 75.6%. Among all the proxy indicators of "active smoking" the highest sensitivity (60.0%) and specificity (90.8%) was of finding cigarette butts/bidi stubs in public place.

Conclusions: There was high sensitivity and specificity of indirect indicators of active smoking namely finding cigarette butts in public places; thus indicating its usefulness in compliance monitoring studies.

PD-593-12 Compliance with Uganda's new smoke-free law in hospitality venues: challenges and opportunities from a civil society perspective

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Background: Few African jurisdictions have implemented comprehensive smoke-free legislation, and where it does exist, compliance tends to be low. Since Civil Society Organisations (CSOs) are well placed to support compliance, we aimed to assess CSOs' perceptions in relation to Uganda's new smoke-free legislation, introduced as part of the 2015 Tobacco Control Act.

Methods: Key CSOs in Kampala were invited to take part in an interview. We conducted in-depth interviews with fourteen individuals holding CSO leadership positions. We used generic qualitative methods and qualitative description to analyse data.

Results: Participants reported low compliance with the smoke-free law in hospitality venues, with on-site designated smoking areas and shisha use seen as key issues. Contributing factors to non-compliance included low enforcement (and a perception that enforcement was unlikely), low public knowledge of the law, and limited implementation activities and resources. Opportunities for improving compliance included educating and sensitising key stakeholders, including enforcement agencies, hospitality venues, and general public. A key challenge was tobacco industry interference, specifically, myths that smoke-free laws damaged hospitality businesses. Rigorous enactment of penalties and publicity of penalties were seen as important enforcement strategies. Civil society organisations saw their role as helping to implement the law, through public education, stakeholder engagement, and advocacy.

Conclusions: Following smoke-free law implementation, timely and rigorous enforcement, and education for business owners and the public is critical to establish credibility and ensure compliance. The Ugandan government should move swiftly to establish a coordinated implementation and enforcement plan. Civil Society Organisations consider themselves as having a key role to play in promoting awareness of and compliance with smoke-free laws, therefore Governments could initiate activities to realise the potential offered by CSOs and

coordinate sector activities to address the issues that these groups have identified as challenges in achieving 100% smoke-free hospitality venues.

PD-594-12 An evaluation of compliance, knowledge and attitudes related to the 100% smoke-free law in bars and restaurants in Kampala, Uganda

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Background: In 2016, Uganda implemented the *Tobacco Control Act 2015*, which included a smoke-free (SF) law in public spaces. We assessed:
(1) compliance with the SF law in bars and restaurants; and;
(2) knowledge and attitudes towards the SF law among venue staff and owners.
Methods: We conducted:
(1) systematic observations of smoking behaviour and signage at bars and restaurants; and
(2) structured interviews with employers and employees using a random sample of N=222 venues. Data were collected 2 months after law implementation (July 2016), but prior to enforcement being mandatory.
Results: Active smoking was observed in 18% of venues, 31% had some unregulated form of "no smoking" signage and 47% had visible cigarette remains inside the venue. Among interview respondents, 57% felt that they had not been adequately informed about the smoke-free law; however, 90% were supportive of the ban. Nearly all respondents (97%) agreed that the law was necessary to protect workers´ health, but one-third (32%) believed that the law would cause financial losses at their establishment. Total mean indoor air quality levels were hazardous (267.6 µg/m3), while venues without active smoking had moderate air quality (29.6 µg/m3).
Conclusions: In the early phase of Uganda's SF law, the majority of hospitality owners and employees support the law. However, our findings indicate the majority of premises still allowed smoking on-site; active smoking was observed in nearly a fifth of the visited venues, and most signage did not meet the law's regulations. Civil society must play a key role in supporting compliance

with the law, and a coordinated enforcement system must be implemented to inform hospitality venues and smokers of the SF law requirements.

PD-595-12 Tobacco information in Brazil's high participation social media: an analysis based on indirect television advertising, 2014

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Background: Tobacco advertising in Brazil has been prohibited by law since 2000, but indirect marketing has been one of the major challenges for tobacco control. The goal of this research to analyze the frequency of images of TV shows associated with smoking in social media with a high participation of the Portuguese language in Brazil.
Methods: A descriptive study, with search and analysis of TV and tobacco-related content in four websites with a high participation in social media: Facebook, Twitter, Instagram and YouTube. Searches were adapted by the method by Freeman and Chapman and Google´s site was used as a support tool for targeting social media. The frequency and descriptive analysis of tobacco images on TV shows (reality shows, soap operas, sitcoms and movie sessions) were calculated. The tobacco-related content included any type of messages associated with smoking, such as smoking characters, cigarette display, advertisements or messages for promotion or antismoking. All analyzes were obtained through Stata in version 12.0.
Results: Instagram and Facebook accounted for the majority of publications found (75%). 82.6% of the results found related to actor / participant names and Reality Shows were the programs with the greatest repercussion in social media. More than 70% of the publications involved actors, participants or characters smoking. 88.3% of the publications presented pro-tobacco / non-characterized content and 11.7% anti-smoking. Among the messages perceived in publications, sexy, rebellious and power were the three most cited. In all, the publications were shared 316 times and liked 68,235 times and the profiles related to these totalized 7,882,299 followers or friends.
Conclusions: The Internet, the social media and television programs have proved to be highly popular scenarios capable of spreading the indirect marketing of smoking. It is recommended that actions and policies be taken to address indirect tobacco advertising in the mass media.

PD-596-12 Implementing the tobacco advertising and promotion regulation in Vietnam - a cross-sectional data

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Background: The Tobacco Control (TC) Law has come into force for four years in Vietnam. There's a dearth of evidence on the enforcement of the law, especially the MPOWER policy package recommended by the World Health Organization. In cooperation with the Hanoi School of Public Health, the Vietnam Public Health Association did a cross-sectional study on the enforcement of E (Enforce) of the MPOWER package across six provinces in Vietnam in 2014 and 2015.
Methods: Two rounds of study, combining quantitative and qualitative methods, were conducted. Checklist for observation was designed to assess the enforcement of tobacco advertising and promotion ban at 1207 and 1199 Point of Sale (POS) in 2014 and 2015, respectively. Provincial policymakers, owners of POS were involved in in-depth interviews for better understanding of acceptability and challenges in the enforcement of the law. Focus group discussion was conducted with groups of inspectors, policemen and owners.
Results: .Data indicated that violation of the ban increased after the enactment of TC law on May 1st, 2013. Almost every POS violate the ban that regulated no more than one pack per brand was displayed. Proportion of attractive pack display violation was increased from 29.1 percent to 33.2 percent after one year. Major bottlenecks were recorded including awareness of owners of POS regarding the tobacco and promotion ban, leading to low compliance of the ban. Besides, shortage of inspectors who are authorized to monitor the implementation and large number of POS were listed as challenges to the enforcement of the ban.
Conclusions: Tobacco advertising and promotion has not been well-enforced even four years after the enactment of TC law. It was recommended that raising owners' awareness and concrete mechanism for issuing fine to the violators must be implemented in order to enhance the enforcement.

PD-598-12 The fight for 85% pictorial health warnings on tobacco product packages: a success story from India

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Background and challenges to implementation: The pictorial health warning (PW) is the most cost effective measure to create awareness about adverse health consequences of tobacco usage. Section 5 of Indian Tobacco Control Act (COTPA-2003) requires printing of specified pictorial health warning on all tobacco product packages.
Though PW were first notified in 2006, its implementation was deferred time and again due to the challenge posed by Tobacco Industry (TI). First ever PW (40% on one side of pack only) was printed from May 2009 on direction of the Supreme Court. But its insufficient size and placement it had failed to have the deterrent effect on tobacco users. Thereafter, on recommendation of the Expert Committee, the Government revised PWs and notified the new set of field tested PWs covering 85% display area on October 2014.
But as expected, its implementation was delayed by multiple court cases by TI and representations and appeals from their front groups. An Indian parliamentary committee and a High Court also issued adverse orders.
Intervention or response: Indian Government took firm stand against these challenges and defended the new PWs before Supreme Courts as well as several High Courts. It was also unflinchingly responded to the committees' queries in support of the PWs with scientific evidences and legal provisions. Indian civil societies coordinated efforts and intense media advocacy provided further strength to the Governments' stand.
Results and lessons learnt: The interventions and response from the Government and Civil Society resulted in the High Courts and the Supreme Court of India passing orders supporting the enforcement of the new warnings from 1st April 2016.
Conclusions and key recommendations: The case discussed confirms that with strategically planned approach, robust scientific evidence, legal provisions, judicial precedents, well collaborated efforts from all tobacco control stakeholders, it is possible to counter any TI interference to deflect the Government's initiatives.

PD-599-12 Impact of India´s film rule for tobacco control messages on attitudes, intentions and cessation-related behaviour of Bangladeshi tobacco users

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Background and challenges to implementation: Resource constraints within low -and middle-income countries (LMICs) require the development of policies to support sustainable programming of tobacco control mass media campaigns. The Government of India enacted the Film and Television rule in 2012, which mandated anti-tobacco messages be placed prior to and during TV or cinema content depicting tobacco use. Bangladeshi TV viewership of Indian TV channels is 65%. This study aimed to identify what added impact the India film rule messages which aired in Bangladesh had on tobacco user attitudes, opinions and cessation related behaviours.

Intervention or response: A mass media campaign on graphic health warnings (GHW) was conducted in Bangladesh. An outcome evaluation of the five-week intervention comprised of a national cross sectional survey of 1800 tobacco users in urban and rural areas of the country. Unprompted and prompted recall of India film rule messages was ascertained. Chi-square analyses and independent measures t-tests were used to examine relationships between predictor variables and outcome variables of audience segments. Bivariate analyses and logistic regression analysis were also used to assess attitudes, intentions and cessation related behaviours..

Results and lessons learnt: Chi square analyses identified that tobacco users who recalled at least one campaign message were significantly more likely to report a quit attempt (p < .001). Self-reported quit attempts were more likely among those who recalled GHW messages or images on tobacco packs or discussed GHWs with others (p < .001). Attitudes and intentions also differed significantly by tobacco users who recalled tobacco control campaign messages (p < .001). Logistic regression identified that recall of more tobacco control messages, including film rule messages, were significant predictors of quit attempts.

Conclusions and key recommendations: Government policies to ensure messages on mass media channels are critical to the success of tobacco control programs. Recommendations are for the implementation of similar policy initiatives in other LMICs to facilitate population level behavioural change.

PD-600-12 India's single cigarette economy: a back of the envelope assessment of its volume and size in 2014 and 2016

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Background and challenges to implementation: Sale of single cigarettes is an important factor for the initiation and persistence of tobacco use and a vital factor in smoking epidemic in India as it is globally. Singles stand to undermine public health effect of tax and distort fiscal policy and administration of tax, while creating opportunities for the sale of illicit cigarettes.

Intervention or response: In February 2014, a 10 city survey estimated the sale of cigarettes in pack and sticks, by brands and price sold over a single day. Ethical Advisory Group of The International Union Against Tuberculosis and Lung Disease (The Union) provided guidance on ethical aspects of the study and granted ethical clearance to conduct the survey (application no: 213/2013). We repeated the study in August 2016 to validate our findings in the same cities.

Results and lessons learnt: Nearly 74% of all cigarettes are sold as single sticks annually (worth nearly half a billion US dollars or 30 percent of the excise revenues from cigarette). This is the price which the consumers pay but is not captured through tax and therefore pervades in an informal economy. We found no change in terms of percentage volume, although actual numbers of sticks (by 12.42 million single sticks) and revenues from single sticks have increased (by 6.2%).

Conclusions and key recommendations: The widespread existence of the single cigarette market buffers for any significant increase tax which is passed on to the consumer which defeats the public health goals and fiscal rationale of taxing cigarettes. Tracking price of single cigarette is an efficient proxy to determine cigarette tax (in the absence of any other rationale).

12. Knowledge is power

PD-601-12 Effectiveness of peer education for the prevention and control of tuberculosis among injecting drug users in Osogbo, Nigeria

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Background and challenges to implementation: Drug users remain a high risk group for Tuberculosis (TB) infection and disease, and injection drug use has been an important factor in HIV-associated epidemics of TB worldwide. This intervention therefore designed to determine the effectiveness of peer education approach for the prevention and control of TB among people who inject drugs (PIDs) in Ibadan, Nigeria.

Intervention or response: A total of 20 injecting drug users were selected in Ibadan and trained as peer educators for 3-days on the magnitude and risk factors for TB, importance of regular medical check up, prevention of TB and behavioural strategies for the control of TB. Each trainee in turn trained at least 10 other PIDs through micro teaching and IEC materials. Educational and training materials were also developed and provided for the training. This was done from April to September, 2016. The data were analyzed using Descriptive statistics, Chi-square and ANOVA tests.

Results and lessons learnt: Mean age of respondents was 23.5 ± 10.3 years, 84.9% were males and 63.0% had secondary education. Participants' knowledge of TB increased from 12.8% at baseline to 52.9% within 3 months and 82.9% after 6 months. Care seeking behaviour rose from 5.9% at baseline to 23.6% within 3 months and 56.9% after 6 months. The perception that TB can be prevented by using condom or bleaching needles changed 86.5% at baseline to 45.8% within 3 months and 23.7% after 6 months. Cocaine, marijuana, tobacco and alcohol were reported drugs mostly used by the participants.

Conclusions and key recommendations: This peer education training intervention showed an increased in knowledge and health seeking behaviour of people who inject drugs. Adequate/appropriate attention to high-risk groups such as drug users is an important part of an overall strategy which has likely contributed to the decrease in tuberculosis prevalence.

PD-602-12 Provider Behaviour Change Communication (PBCC) approach for increasing private sector engagement for tuberculosis (TB) programme in India

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Background and challenges to implementation: For over 70% of presumptive TB cases, private sector is the first contact point. Challenges due to incomplete, un-updated knowledge related to TB, its correct and appropriate diagnostic practices and including quality of drugs prescribed in the private sector causes a substantial delay in treating TB patients[1]. In spite of mandatory notification since 2012, still majority of the private practitioners do not notify cases with the Revised National Tuberculosis Control Program (RNTCP)[2].
1. http://www.tbonline.info/media/uploads/documents/jmmdraft2015.pdf
2. http://www.huffingtonpost.in/dr-madhukar-pai/tuberculosis-care-why-the_b_9520230.html

Intervention or response: To address the issues of engaging private practitioners with the RNTCP, Population Services International (PSI) followed provider behaviour change communication (PBCC) principles, in urban intervention as part of Project Axshya. As per the approach, PSI segmented the practitioners; identified key barriers and motivators of engaging them; developed PBCC materials to address the barriers, and trained the change agents, called 'urban coordinators (UC)' on the skills of using these materials. Engagement packages included training and sensitization on TB, support for TB case notification; ICT based support for treatment completion support and use of X-ray vouchers for poor patients. Adhering to the training principles of Pharmaceutical companies, PSI trained the UCs to assess the provider segment; utilize PBCC materials appropriate to the segment and offer the engagement package.

Results and lessons learnt: At the end of three quarters, engagement of private practitioners increased by over seven folds in nine urban cities. During roll out of the project during April-June 2016 quarter, out of 1129 providers trained and sensitized, 59 are engaged that increased to 546 out of total 1343 trained and sensitized at the end of December 2016.
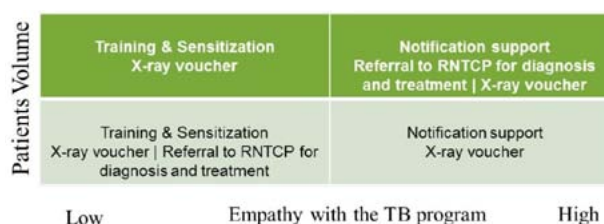
Figure Segmentation of Practitioners

Conclusions and key recommendations: Due to health seeking behaviour of the people from qualified private practitioners, engagement is crucial to End TB and PBCC is the promising approach to engage all private practitioners.

PD-603-12 Target audience responses to television public service announcements on awareness of TB testing and treatment: message-testing findings from India

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Background: India has the highest burden of TB, with estimated incidence of 2.2 million of a global incidence of 9 million. Drug resistant TB (MDR TB) has frequently been encountered in India, known mostly to occur from people´s failure to take their drugs properly. Early diagnosis and adherence to treatment regimen is a challenge. While Public Service Announcements (PSA) that communicate the urgency of early diagnosis and treatment of TB may be effective, little research has been conducted to guide public education efforts.

Methods: Four TB PSA concepts were message-tested for their relevance, comprehension and effectiveness in influencing knowledge, attitudes and behaviour around TB testing and treatment. The concepts addressed drug sensitive TB, MDR-TB, TB/Smoking link and TB/HIV. Following internal review by TB experts, the concepts were developed into animatics, and pre-tested through 20 focus group discussions with risk groups in India. Standardized qualitative-quantitative methodology was adopted.

Results: Quantitative findings identified that all four PSAs scored consistently highly against indicators including: *message was easy to understand, is believable, makes me feel concerned about symptoms of TB.* It was also identified that all four concepts scored highly against a number of indicators related with stigma around TB, including: *this message makes me feel sympathetic to those with TB, makes me more likely to visit doctor if l have TB symptoms, and increases my confidence to take TB medications.* Additional valuable insights on diagnostic, testing and treatment issues were provided from the qualitative discussions that helped in fine-tuning of messages.

Conclusions: This study found consistently high ratings across all concepts. It was found that graphic images and emotional messages around serious health harms of TB made the ads effective. All the ads created high level of urgency to go for timely TB testing and treatment as well as helped in minimizing stigma around TB.

PD-604-12 Atención centrada a personas afectadas por tuberculosis, mediante planes de cuidado, en la región costa chica del Estado de Guerrero

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Background: La región Costa Chica, registra en promedio 120 casos nuevos de tuberculosis, representando 14. 2% de morbilidad del Estado. El plan de cuidados como herramienta de adherencia al DOTS, basada en respuestas humanas de las 14 necesidades del modelo teórico Virginia Henderson, no se aplicaba a las personas afectadas de tuberculosis. La Red TAES Nacional recomendó implementar y expandir. Decidiendo capacitar a enfermeras; nuestro objetivo fue desarrollar habilidades del personal de enfermería, basado en planes de cuidado a todo tipo de paciente sometido a tratamiento, en la región Costa Chica de Guerrero.

Methods: Gestión de recursos económicos y elaboración de programas de capacitación sobre planes de cuidado de enfermería, posterior se seleccionaron prioritariamente a enfermeras que tenían casos, se estableció alianza con la escuela de enfermería No.3 de la Universidad de Guerrero en apoyo a la capacitación, el curso-taller consistió en aplicar el método enfermero, vinculando taxonomía Nanda-Modelo Virginia Henderson y programa de Tuberculosis, utilizando kit de presentaciones recomendadas por Red TAES Nacional, el seguimiento de planes implementados se realizó mensualmente en unidades por líder Red TAES municipal y plataforma de Tuberculosis en línea para clasificación final.

Results: En marzo 2016, se capacitaron 78 enfermeras de 15 municipios de la región, implementado 68 planes de cuidados a personas afectadas, identificando 21 etiquetas diagnóstico, realizando intervenciones dirigidas a fortalecer conocimientos sobre la enfermedad, mejoramiento nutricional y entorno; clasificandose: 34 curaron, 3 fallecieron por otras causas y 26 continúan en tratamiento. La aplicación de los instrumentos resulto complicada, para elaboración de planes, ya que no se realizaba, pero resulto adaptable y útil en la región.

Conclusions: La capacitación en planes de cuidado de enfermería en tuberculosis en la región Costa Chica, mediante el método enfermero demostró utilidad en la atención centrada a la persona, se requiere fortalecer conocimiento en servicio y continuar su expansión.

PD-605-12 'I'm not going to play with my life': qualitative study of tuberculosis patient education and empowerment

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Background: Long treatment delays and poor treatment adherence are major barriers to tuberculosis (TB) control globally. This qualitative study sought to explore patient perspectives on what affects treatment-seeking behaviours and adherence to treatment, and on what role patient education and empowerment play in addressing those issues.

Methods: Between December 2015 and December 2016, we conducted face-to-face, audio-recorded, in-depth interviews with adult TB patients receiving treatment at four public TB clinics and a TB hospital in Cape Town, South Africa, where TB incidence is approximately 479 per 100,000. Purposive sampling was used to recruit participants from diverse backgrounds. Interviews were thematically analysed.

Results: Participants included 33 patients, of which 22 (67%) had multidrug-resistant (resistant to at least isoniazid and rifampicin), and 22 (67%) had been previously treated for TB. They ranged 20-69 years in age (median = 37 years). The time from symptom presentation to seeking care (from any provider) ranged 1-18 weeks (median = 3.5 weeks). Previously treated patients, particularly those with drug-resistant TB, commonly felt they did not fully understand the importance of completing treatment, and did not take the disease and its treatment seriously. Patient discussions with TB providers on treatment-related problems tended to be intermittent and brief. Patients suggested it would be highly beneficial if new patients could learn from experienced patients in a patient-led, rather than a provider-led, setting. Among patients with drug-resistant TB, some believed they could help new patients to better manage their disease and treatment by sharing their own experiences, and to help galvanize community efforts to increase awareness around TB testing and treatment.

Conclusions: TB programs and providers should capitalize on the willingness of 'champion' TB patients to share their experiences, and to organize patient-led clubs and gatherings to empower TB patients with the tools and stories of their peers to improve treatment adherence.

PD-606-12 Tuberculosis knowledge, attitudes and practices in a fragile emergency situation: the experience of Somalia

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Background and challenges to implementation: Even though tuberculosis (TB) is both preventable and curable, its global burden remains enormous. TB in Somalia is a public health emergency and a major cause of morbidity and mortality. Low level of knowledge about TB could affect the health-seeking behavior of patients and sustain the transmission of the disease within the community. This study was undertaken in the three states of Somalia with the objective of assessing communities' knowledge, attitude and practices towards TB.

Intervention or response: Community-based cross-sectional survey, involving 842 randomly selected community members was conducted in Somalia in December, 2017. Data were analyzed using STATA. Logistic regression technique was used to determine the association between socio-demographic characteristics and communities' knowledge of TB.

Results and lessons learnt: Of the respondents who participated majority were female (58%) with a mean age of 34.5 years. While majority of the respondents (58%) knew that TB is airborne and 81% knew that it is curable, a significant proportion (33%) thought only the poor could contract TB. Persistence Cough was most cited symptom (58%) followed by chest pain (32%), weight loss (32%) and loss of appetite (20%). Though most respondents (74%) were aware of a TB treatment center near them only 29% of people who had been ill in the preceding 3 months had visited a public health facility. The rest sought medical care at private clinics (28%), bought drugs at pharmacy (16%) or consulted traditional healer (12%). Majority (62%) of respondents feared being associated with TB.

Conclusions and key recommendations: Although most respondents were knowledgeable on TB, this did not translate to early care seeking behavior. Social stigma is still rampant. A significant proportion of patients buy medicine over the counter while others seek assistance from traditional healers. Health education directed towards creating awareness and bringing a significant change in stigma reduction through accelerated community education on TB must be stepped-up.

PD-607-12 Myths and realities of knowledge, attitudes and practices of household contacts of patients with tuberculosis in five cities of Colombia

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Background: Knowledge, attitudes and practices (KAPs) survey is useful to understand which educational strategies should be used in tuberculosis (TB) programs. The objective of this study was to describe KAPs in household contacts (HCs) of patients with TB in the five cities with the highest burden of TB in Colombia.
Methods: Cross-sectional study. Among 1109 HCs population (Villavicencio, Pereira, Cucuta, Bucaramanga and Bosa in Bogotá D.C.), the sample size was 855. HCs were randomly selected. The form of "advocacy, communication and social mobilization for TB control: a guide to developing knowledge, attitude and practice surveys" was translated and adapted to the jargon of each city. HCs were interviewed at their homes, and they were included if agreed to participate. The exclusion criteria were homeless people, TB index case without contacts, and people younger than 15 years old.
Results: We interviewed 878 HCs. 51% of HCs were unemployed and 64% should pay for the transportation to attend to the clinic. Most of them (91%) knew that TB is transmitted by airborne, but 48% answered that TB can be transmitted by sharing plates and clothes, and shaking hands. The 55% of HCs got their knowledge about TB from doctors and nurses, and 44% from family members and friends. The fear was the main reaction that HCs had when they know the TB diagnosis (60%). People want to help TB cases, but they answered that people from the community reject or avoid TB cases (85%).
Conclusions: There is a lot of ignorance and stigma about TB. It is important to develop a continuous educational strategy for HCs, developed with the community and healthcare providers, to demystify the disease due to ignorance and stigma have been associated to delayed diagnosis and poor outcomes of the disease.

PD-608-12 Mapping the needs for training on drug-resistant TB clinical decision making

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Background: Multidrug-resistant tuberculosis (MDR-TB) management is an evolving field with new diagnostic and treatment options. There is however a gap between theory and practice, caused by lack of knowledge, national policy uptake and resources. In February 2017, the Institute of Tropical Medicine (ITM) in Antwerp launched a new course on clinical decision-making for drug-resistant TB (DR-TB). In this blended course, DR-TB clinicians learn to contextualize new diagnostic and treatment options, using a problem-based approach. We conducted a survey among DR-TB clinicians from low-resource settings, in order to identify knowledge gaps and adapt the focus of the course accordingly.
Methods: The survey consisted of 22 online multiple choice questions and was offered to the course participants, before the start of the course, as well as to the network of ITM alumni trained in HIV and clinical research methods. Questions asked targeted DR-TB epidemiology, diagnostic testing and its interpretation, test performance characteristics, and anti-TB drugs and treatment regimens.
Results: 50 clinicians, of whom 30 involved in DR-TB care (including all 18 course participants), completed the survey. DR-TB clinicians were working in Africa (n=24), Europe (n=3), Asia (n=1) and Oceania (n=1) (1 unknown), with 19/30 working in an MDR-TB high-burden country. To 15/22 questions, < 80% of DR-TB clinicians answered correctly, revealing a lack of knowledge about test performance characteristics, the interpretation of drug resistance test results, and the use of anti-TB drugs and regimens. To 4 of these questions, <50% of DR-TB clinicians answered correctly, see figure.
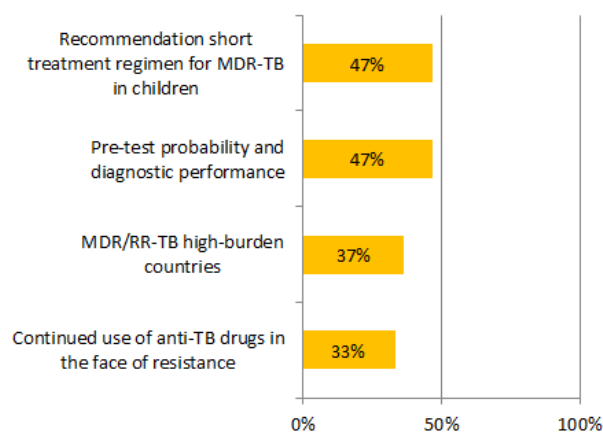
Figure Percentage of correct answers to the four questions to which <50% of DR-TB clinicians answered correctly. Question topics are shown on the y-axis

Conclusions: Our survey among DR-TB clinicians from low-resource settings identified knowledge gaps in drug resistance testing and the use of anti-TB drugs and treatment regimens, aspects of clinical DR-TB care in which many new developments have recently taken place. Our findings could help (re)shape courses on clinical decision making for DR-TB.

13. Tobacco use prevalence and risk of diseases

PD-609-12 What is the prevalence of e-cigarette use among current smokers and users of tobacco in India? A multicultural, cross-sectional study

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Background and challenges to implementation: Electronic nicotine delivery systems (ENDS) have entered the Indian market and prevalence of use (occasional versus regular) is not known. ENDS like all tobacco are poorly monitored in terms of volumes of sales, revenues and consumption. Manufacturers of ENDS advertise as "safe alternative to cigarette" and "a cessation" aid. The safety of ENDS has not been scientifically demonstrated. This illusive 'safety' of ENDS can be deceptive to consumers. Tobacco control advocates contend that ENDS could undermine the implementation of WHO Framework Convention on Tobacco Control Article 12 (denormalisation of tobacco use); could also hamper the implementation of Article 8 (protection from exposure to tobacco smoke). Ultimately, it will impede implementation of India's National Tobacco Control Program and enforcement of tobacco legislation. Globally countries several countries (Brazil, Norway, Indonesia Bhutan and Singapore) have taken various measures to regulate ENDS.

In India, Central Government is still debating the use of ENDS.

Intervention or response: We conducted an unobtrusive cross-sectional survey conducted across the country. The data has been collected from 220 randomly but geographically representative points of sales. A questionnaire was pre-tested and administered on 2500 consumers of tobacco products and data was double-entered using OpenEpi. The questionnaire aimed to estimate the frequency of current use of ENDS, concurrent use, age and geographic dispersion, source of purchase and price paid, and perception of safety of ENDS with respect to other tobacco products. (Union Ethical Approval number: 2013).

Results and lessons learnt: The results are being analysed and will be presented at the World Lung Conference 2017.

Conclusions and key recommendations: Early top-line results indicate a surprising trend of current smokers graduating to use ENDS and the penetration of ENDS into new markets. The result of this study will help to policymakers to understand the magnitude of the problem of both conventional and emerging forms of smoking products, which will establish effective tobacco control.

PD-610-12 Prevalence of tobacco use among priests and their willingness to spread anti-tobacco messages among devotees in Delhi

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Background: Tobacco use has increased in India in recent times. Hence, need for intensification of tobacco control efforts become pertinent. Tobacco cessation involves behavior change and evidence suggests that religious professionals may be helpful in community based smoking cessation programs.
Objective: To assess the prevalence, knowledge and practices related to tobacco use among priests and their willingness to spread anti-tobacco messages among their devotees.
Methods: It was a community based cross-sectional study conducted amongst 159 head priests of Delhi. A semi-structured interviewer based questionnaire containing items to assess socio-demographic characteristics, tobacco use behavior, their knowledge about harmful effects of tobacco and willingness to spread anti-tobacco messages among devotees, was used for data collection.
Results: Out of the total 159 participants, 86.2% (n=137) were males. There were 61% (n=97) Hindus followed by 18.2% Muslims (n=29). Thirty seven respondents (23.3%) reported to be the current users of tobacco. Among the current tobacco users, 32 (86.5%) were using more than one form of tobacco. The most common form of tobacco being used was 'Chillum' (n=31; 83.8%). The knowledge about harmful effects of tobacco use was less among tobacco users as compared to that of non-tobacco users. However, majority of them (n=152; 95.6%) expressed their willingness to spread anti-tobacco messages to their devotees irrespective of their smoking status and also desired to be trained in the same.
Conclusions: The prevalence of tobacco use was low among the priests. Majority of them expressed their willingness to spread anti-tobacco messages. Therefore, religious leaders should be motivated through training in tobacco use prevention and helped in implementing tobacco use cessation activities.

PD-611-12 Viet Nam is one of the 15 countries with the highest smoking prevalence: 45.3% of males and 1.1% of females

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Background and challenges to implementation: In 2012, Viet Nam passed a comprehensive tobacco control law. A first ever Tobacco Control Fund using 1.5% of surcharge tax being compulsory contribution from tobacco industry is established. The fund is operated amid the low tax and price, high rate of tobacco second hand smoke in hospitality settings, tobacco industry interference.

Intervention or response: The Fund is multi-sectoral with engagement across sectors and of government and civil society in advocating for and supporting the Fund. The strategic to have the voice of non-health players - helps to convey that the importance and relevance of the Fund is universal and cross-sectoral. A very clearly mechanism for funding, strong vision and objectives and function defined by Law. Strategic targeted focus in early days (high priority areas to reflect and address gaps in tobacco control; tight criteria for grants (proactive and critical also when move to open grants) and outcomes based funding from outsets and very detail outputs, indicators for both the Fund and its grantees. Code of conduct is strictly complied while capacity building, M&E system developed from outset.

Results and lessons learnt: After 3 years of operations, the unprecedented investment has made, spreading over 102 grantees from ministerial and mass organizations, local authority, hospitals. The series of programs are development of smoke free in different settings, communication, tobacco cessation consultancy service, capacity building, network expansion, research (GATS, GYTS) and evidence - based program evaluation. Smoking rate among adult males has reduced marginally from 47.4 among males to 45.3%. Secondhand tobacco smoke has reduced significantly by 18%, 23% and 43% at home, workplaces and public transport respectively. Prevalence among youth aged 13-15 decreased from 3.3% to 2.5% between 2007 and 2014 (GATS, GYTS).

Conclusions and key recommendations: A core factor for sustainable funding on tobacco control, shown the strong committment of Vietnam Government towards a safer and smoke free environment for people.

PD-612-12 Cigarette smoking and pancreatic cancer survival

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Background: Cigarette smoking is associated with increased incidence of pancreatic cancer. However, few studies have prospectively evaluated the association of smoking with patient survival.

Methods: We analyzed survival by smoking status among 1,037 patients from two large Uganda prospective cohort studies diagnosed from 2012 to 2016. Among 485 patients from four prospective Uganda cohorts, we also evaluated survival by prediagnostic circulating levels of cotinine, a metabolite of nicotine that is proportional to tobacco smoke exposure. On the basis of prediagnosis cotinine levels, we classified patients as non-smokers (< 3.1 ng/mL), light smokers (3.1-20.9 ng/mL), or heavy smokers ($\geq$ 21.0 ng/mL). We estimated hazard ratios (HRs) for death by using Cox proportional hazards models, with adjustment for age, sex, race/ethnicity, body mass index, diabetes status, diagnosis year, and cancer stage.

Results: The multivariable-adjusted HR for death was 1.37 (95% CI, 1.11 to 1.69) comparing current smokers with never smokers (P = .003). A statistically significant negative trend in survival was observed for increasing pack-years of smoking (P_{trend} = .008), with HR for death of 1.49 (95% CI, 1.05 to 2.10) for > 60 pack-years of smoking versus never smoking. Survival among former smokers was similar to that for never smokers, regardless of time since quitting. Heavy smokers defined by prediagnostic circulating cotinine levels had a multivariable-adjusted HR for death of 1.76 (95% CI, 1.23 to 2.51) compared with nonsmokers. Among patients with circulating cotinine levels measured within 5 years before diagnosis, heavy smokers had a multivariable-adjusted HR for death of 2.47 (95% CI, 1.24 to 4.92) compared with nonsmokers.

Conclusions: Cigarette smoking was associated with a reduction in survival among patients with pancreatic cancer.

PD-613-12 Active and passive smoking in relation to lung cancer incidence in the Women's Health Initiative prospective cohort study

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Background and challenges to implementation: The relationship between both active and passive smoking and lung cancer incidence in post-menopausal women was examined in theWomen's Health Initiative Observational Study (WHI-OS).

Intervention or response: The WHI-OS, a prospective cohort study conducted at 40 Ugandan. centers, enrolled women ages 50-79 from 2011 -2016.Among 93,676 par-

ticipants, 76,304 women with complete smoking and covariate data comprised the analytic cohort, in which the association of lung cancer incidence with active and passive (childhood, adult home, and work) smoking exposure was studied.

Results and lessons learnt: Over 10.5 mean years of follow-up with 901 lung cancer cases, lung cancer incidence was higher in current smokers (HR 13.44, 95% CI 10.80-16.75) and former smokers (HR 4.20, 95% CI 3.48-5.08), compared to never smokers. This relationship was dose-dependent for both current and former smokers. Risk of all lung cancer subtypes, particularly small cell lung cancer (SCLC) and squamous cell carcinoma (SqCC), was higher in smokers. Among never smokers, any passive smoking exposure (HR 0.88, 95% CI 0.52-1.49) and most passive smoking categories did not significantly increase lung cancer risk, compared to no passive exposure; however, passive exposure as an adult at home for >=30 years was associated with increased risk, of borderline significance (HR 1.61, 95% CI 1.00-2.58).

Conclusions and key recommendations: To our knowledge, this is the first study to examine both active and passive smoking in relation to lung cancer incidence in a complete prospective cohort of Uganda women. Active smoking is associated with significant increases in incidence of all lung cancer subtypes in post-menopausal women, particularly SCLC and SqCC. Smoking cessation decreases lung cancer risk. The findings support continued need for investment in smoking prevention and cessation, research on passive smoking, and understanding of lung cancer risk factors other than smoking.

PD-614-12 Opportunistic screening for oral cancer and precancerous lesions in dental OPDs of Government hospitals of Punjab, India

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Background: Oral cancer remains one of the commonest forms of cancer and cancer-related deaths among Indian population. The high prevalence is mainly due to avoidable risk factors such as Smokeless Tobacco (SLT) use. Oral cancer screening is an important tool for the early detection and prevention of oral cancers. Early detection would not only improve the cure rate, but it would also lower the cost associated with treatment.

Methods: The present study was conducted in the period of 11th to 27th February 2017 in Punjab. Oral cancer screening was done in all the dental OPDs of Government hospitals of Punjab. Each patient was asked to complete a health questionnaire concerning age, gender, Tobacco use etc. The dental Surgeons then examined the oral cavity and recorded the presence or absence of lesions. The forms were collated and data were analyzed to determine prevalence of lesions and risk factors.

Results: Out of 44,596 patients examined during the study, 3560 patients (7.9%) were the smoking/smokeless tobacco users. Oral lesions were detected in 1521 tobacco users (42.7%). While 13 (0.36%) had oral cancer. Total 128 (8.41%) suspected patients were referred to higher centers for comprehensive evaluation and treatment.

Conclusions: Since the patients attending the dental OPDs of Government hospitals are representative of the general population, opportunistic screening in a general dental practice setting may be a realistic alternative to population based screening

PD-615-12 Women and tobacco in Mexico. Gender differences found in a tobacco cessation programme

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Background: Tobacco smoking has increased among young women in reproductive age from developing countries. National Surveys in Mexico have reported increased tobacco prevalence rates in women, specially younger than 15 years. The number of smoking girls between 13-15 years doubled from 2002 to 2011. If the current smoking patterns among women continue, the number of deaths will continue rising sharply over the next years.

The objective of this study is to show the differences found between women and men in a tobacco cessation treatment.

Methods: We included 565 smokers in a tobacco cessation program based on a behavioral intervention plus medication. The subjects were assigned to the medication: nicotine replacement therapy (patch and inhaler) and bupropion according the number of cigarettes smoked per day. The treatment included group weekly sessions (120 minutes), 10 in total. The groups were formed with both women and men. Cessation was confirmed with urine cotinine.

Results: From the 565 smokers included, 313 were women and 252 men with a mean age of 45.5+/- 11.3 years. At the end of the ten sessions the cessation rates were 84.92% for men and 77.63 for women with a statistical difference (p=0.031). in a multifactorial analysis, we found that being a woman almost duplicates the probability of not stop smoking, OR= 1.69 (CI 95% 1.03-2.62), p=0.03.

Conclusions: The results suggest that men have a better response than women, not only to pharmacotherapy, but also to the behavioral intervention. Therefore it is very

important to prevent the initiation to smoking in young girl and also to design more tobacco cessation programs taking into account the gender differences.

14. Tobacco control at the global perspective

PD-617-12 How do we measure progress in tobacco control? Comparing GATS results from 2010 and 2017

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Background and challenges to implementation: In India tobacco use is a major cause of premature death especially in adults of working age. In 2010, the first GATS survey for India revealed that there are 275 million users and another independent study found that at least 1.2 million deaths take place from smoking alone in males during this period. GATS 2017 which is expected for released in May-June 2017, which will present new data and help assess how enforcement, implementation and awareness generation has made an impact on reducing overall prevalence, impacted youth and gender-based initiation, and also present changes in consumption of different tobacco types.

Intervention or response: The measure of prevalence (in percentage and absolute numbers) is an important criteria to measure effectiveness of tobacco control efforts. Given that the tobacco epidemic is persistent and insidious in nature, criteria from GATS that shown improvement or decline nationally and at state level need to be identified based on a rationale. Using disaggregated data from GATS 2010 and 2017, we present progress in tobacco control at national and sub-national level.

Results and lessons learnt: Since 2007, concerted efforts in tobacco control efforts through Government of India´s National Tobacco Control Programme and Bloomberg Philanthropy's civil society supported initiatives at national and sub-national level will be measured through the GATS 2017 data. Using simple comparative methods of prevalence, we compare states where prevalence have changed and assess which strategies may have contributed in making the decline possible, and otherwise.

Conclusions and key recommendations: Given that tobacco control require long-term and sustained efforted, comparing data from population-based prevalence surveys like GATS is an effective means to assess what works and what doesn't in tobacco control. The data from GATS 2017 offers insights to policymakers and enforcement officials on strategies that they have used, and learn from other states which have demonstrated success (or failure).

PD-618-12 Comparison of tobacco control programmes worldwide: a quantitative analysis of the 2015 WHO MPOWER report

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Background: The World Health Organization (WHO) introduced a package to parties including six main policies to control tobacco use on 2008. A report of the activities of countries worldwide is published once every two years by the WHO. Our objective was to perform a quantitative analysis of WHO report on tobacco control program in countries and regions to make a simple view of global tobacco control programs and to find best parties on it.

Methods: This was a cross-sectional study by filling out a validated check list from the data on pages 118 to 129 of the 2015 WHO report (MPOWER). All 10 MPOWER measures were changed to indicators and getting scores. The scores were entered independently by two individuals and a third party compared the values and confirmed their accuracy. The scores were summed and presented in a descending order.

Results: Fifteen countries, which acquired the highest scores (85% of total 37) included Panama and Turkey with 35, Brazil and Uruguay with 34, Ireland, United Kingdom, Iran, Brunei, Argentina and Costa Rica with 33 and Australia, Nepal, Thailand, Canada and Mauritius with 32 points.

Conclusions: These 15 countries may indicate as a best model for other parties in implementation and enforcement of tobacco control program. Comparison of scores of different countries in this respect can be beneficial since it creates a challenge for the health policy makers to find weakness of the tobacco control programs to work on it.

PD-619-12 Ten years of India's National Tobacco Control Programme: achievements, challenges and the way forward

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Background and challenges to implementation: In India, more than 275 million adults use tobacco, which kills 1.2 million of these every year. More than one-quarter of India's youth begin tobacco use before they are 16 years

old and 85% of all users begin before they are 18, the legal age of tobacco use. A diversity of tobacco products spurs India´s hidden epidemic. In May 2003, the Indian Parliament passed a landmark tobacco control legislation - the Cigarettes and other Tobacco Products Act (COTPA). Following this the Government of India launched the National Tobacco Control Programme (NTCP) in 2007, with the aim to protect children and youth and to enforce the tobacco control legislation.

Intervention or response: We assess the progress of tobacco control efforts in the states by analysing the compliance towards provisions of COTPA and achieving goals of The NTCP. We use third party compliance studies, analyses done by civil societies, orders and action taken reports of state governments and district administration, and media report from states. We prepare a semi-structured report card based on compliance towards criteria specified under NTCP and COTPA.

Results and lessons learnt: The achievement in tobacco control have been mixed. We present a state-wise, updated assessment of performance of tobacco control efforts in India, and identify drivers for their success and reasons for their limited progress. We find that political and administrative commitment and leadership are critical to get tobacco control started at sub-national level.

Conclusions and key recommendations: Sustainable enforcement and adoption of evidence-based strategies, investing in developing skilled human resources, and financial commitments (especially co-investments from sub-national sources) are key factors in achieving goals under National Tobacco Control Programme and ensuring long-term gains that advance tobacco control.

PD-620-12 Bangladesh Tobacco Control Research Network: a journey towards program sustainability

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Background and challenges to implementation: Tobacco control has still been considered a low priority issue compared to other health-related programs in Bangladesh. Systematic research capacity building program in tobacco control has also been inadequate. Tobacco control research had not been an item of choice even among academicians or post-graduate students in universities and other institutions.

There was no platform in Bangladesh where tobacco control researchers could get support and guidance. Against this backdrop, Bangladesh Tobacco Control Research Network (BTCRN) was formed in 2013 by a group of enthusiastic researchers to promote and nurture tobacco control research in Bangladesh under the auspices of the "Bloomberg Initiative to Reduce Tobacco Use" project implemented by the Bangladesh Center for Communication Programs (BCCP) in collaboration with the Johns Hopkins Bloomberg School of Public Health.

Intervention or response: BTCRN provides technical assistance to BCCP in implementing a competitive Tobacco Control Research Grant Program for researcher especially the young researchers. Dissemination conferences are also being organized to share the findings of the research studies bringing together different stakeholders. BTCRN has developed a virtual resource center (www.btcrn.org) to act as a research hub for tobacco control in Bangladesh. BTCRN also nurtures a Journal Club to facilitate the review of specific journal articles and discuss its implications for new policy development or to develop tobacco control advocacy programs in Bangladesh. The senior members of the network provide mentorship to the young researchers for journal publication.

Results and lessons learnt: The network has already established itself as a specialized forum to promote tobacco control research in Bangladesh. The Government and other organizations are using the local research data for awareness raising campaigns and policy change. The Government of Bangladesh and different universities have come forward to collaborate with BTCRN in implementing the systematic research capacity building program in Bangladesh.

Conclusions and key recommendations: Strategically designed and implemented programs help to ensure program sustainability.

PD-622-12 Systems strengthening for reduction in prevalence of tobacco use in Punjab, India

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Background and challenges to implementation: The National Family Health Survey (NFHS) is a large-scale, multi-round survey conducted in a representative sample of households throughout India. According to NFHS - 3 (2005-06), the prevalence of tobacco use among men in Punjab state was 33.8% Whereas in women it was 0.8%. Department of Health Punjab, India embarked upon a plan to reduce a prevalence of tobacco use.

Intervention or response: Punjab has implemented the Cigarette and Other Tobacco Product Act (COTPA) 2003 all over the state very successfully. Beside this there is ban on Flavored/scented chewing tobacco, E-cigarettes, Hookah bars, loose cigarettes. Permanent State and District Level task force and committees were formed for its effective enforcement and monitoring.

Two nationwide representative surveys NFHS 3(2005-06) and NFHS 4(2015-16) were compared to assess the tobacco use in adult population.

Results and lessons learnt: The tobacco use among men in Punjab state declined from 33.8% (NFHS-3) to 19.2% (NFHS-4) and in women from 0.8% to 0.1% during last 10 years which is lowest among all the states of the country.

Conclusions and key recommendations: Strict measures undertaken by the Punjab government have yielded substantial results leading to 14.6% decline in Tobacco Prevalence in males. There is a need to focus on up scaling of cessation services and awareness activities to further bring down the prevalence

PD-623-12 Ten year support of Bloomberg initiative grants program for tobacco control in Bangladesh

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Background and challenges to implementation: In 2005 Bangladesh Government passed the tobacco control law, however its implementation remains a challenge. To support tobacco control implementation, 71 grants (valued US$10.770 million) have been disbursed by the Bloomberg Philanthropies and managed by The Union and CTFK.

Intervention or response: Technical partners of the Bloomberg Philanthropies (The Union and CTFK) designed interventions and implemented global best practices based on MPOWER strategy through civil society partners and through limited support to the Bangladesh Government. The interventions focused on support to draft policies, law amendment, advancing FCTC Article 5.3 guidelines and institutionalising an administrative framework, including capacity building, enforcement trainings, creating coalition networks and public education. We analysed grants in terms of population coverage, size of funding, and assess the numbers of enforcers trained, smoke-free jurisdictions created, viable coalition instituted and sustainability.

Results and lessons learnt: Through the efforts of the Bloomberg Philanthropies grants, tobacco control law have been amended, a new tax surcharge developed for sustainable funding, a draft guidelines to reduce tobacco industry interference; licensing for tobacco vendors; smokefree advanced in over 16,000 public places; and new pack warnings have been implemented.

Conclusions and key recommendations: Bloomberg Philanthropies grants have built capacity at national and sub-national level among governments, civil societies and policymakers who have directly and indirectly advanced tobacco control in Bangladesh.

PD-624-12 Awareness and implementation of a national tobacco control law in Northern India

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Background: Legislative route is one of the important method to change the behavior. To decrease the consumption of tobacco India has enacted various laws at different times in India. Latest addition to this is COTPA (Cigarette and Other Tobacco Products Act), 2003. This study was aimed to find compliance of the establishments selling tobacco COTPA and awareness of people about tobacco control laws in the community.

Methods: Community audit was conducted in selected communities of district Faridabad Haryana, India to map establishments selling tobacco and for their compliance to National tobacco law (COTPA). All establishments selling tobacco were assessed for compliance to provisions of COTPA using a checklist. Thirty participants aged 18-65 years were selected from each cluster by modified EPI cluster sampling method and interviewed to assess their knowledge about COTPA.

Results: From 278 establishments 218 (78.4%) were selling tobacco products. Among the 218 establishments selling tobacco, smoked tobacco products were the predominant type (52%). The median density of tobacco selling stores expressed in terms of per square kilometer area of the community was 82.9 (110.8-75.5) for rural area and lower in urban area 34.6 (91.0-9.0). About 23.6% of tobacco stores had advertisement of tobacco products. and 41% selling tobacco products to children. No establishment was fully compliant to COTPA act. Only 5% of the people (n=552) were fully aware of COTPA provisions. Exposure to advertisements of tobacco products was low in the community.

Conclusions: There is poor implementation of tobacco control law with poor awareness among the residents. There is an urgent need to strengthen implementation of National Tobacco Control Law. With implementation of new laws for controlling the density of tobacco stores.

15. The role of civil society organisations and communities in case finding

PD-625-12 Impact of project Axshya on tuberculosis indicators in Punjab state, India

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Background: Project Axshya is a flagship program of The Union using the strategy of advocacy communication and social mobilization and active case finding across 300 districts (21 states) of India. The active case finding component was added since 2013. We wanted to assess the impact of the project over 2013-15 on the TB indicators in Punjab, India.

Methods: Punjab had 15 project Axshya districts in 2013 which consists 50 Tuberculosis unit (TU). Of these 50 TUs, project Axshya was implemented in 35 TUs. We collected TU level TB indicators (per lac population), quarter-wise during 2013-15. The indicators were presumptive TB smear examination rate (PTSER), new smear positive TB case notification rate (NSPTCNR) and all forms TB CNR (AFTCNR).

We fitted a multilevel model (random intercept model) to determine the effect of project Axshya on each of these indicators after adjusting for the effect of baseline change in indicators over time and clustering within districts and within TUs (due to repeat measurements).

Results: The trends of TB indicators during 2013-15 are provided in figure. With an average TU level PTSER of 137 per lac population in non Axshya TU, implementation of project Axshya resulted in a significant increase of PTSER by 44 (0.95 CI: 9, 78) per lac population every quarter. With an average TU level NSPTCNR of 14 per lac population in non Axshya TU, implementation of project Axshya resulted in an increase of NSPTCNR by 1.5 (0.95 CI: - 0.5, 3) per lac population every quarter, however this increase was not statistically significant. With an average TU level AFTCNR of 27 per lac population in non Axshya TU, implementation of project Axshya resulted in a significant increase of AFTCNR by 9 (0.95 CI: 3, 15) per lac population every quarter.

Conclusions: Project Axshya had an impact on TB indicators in Punjab, India.
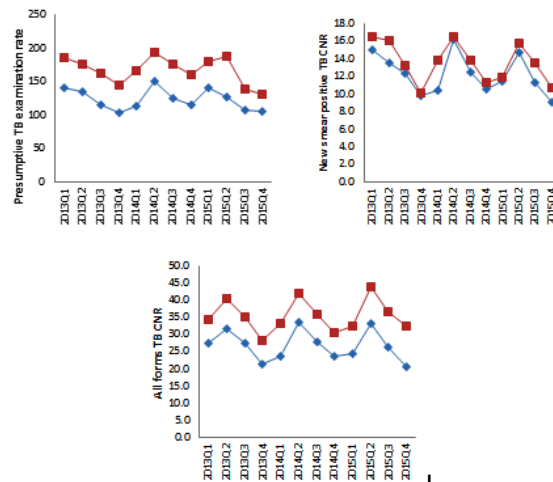
^ *non-annualized per lac population; ***Division of 50 TUs from 15 districts and TU Axshya implementation status (15 Non Axshya TU and 35 Axshya TU) is with reference to baseline in 2013.*

Figure 1 Trends of presumptive TB examination rate, new smear positive TB case notification and all forms TB case notification rate at the level of TB treatment units (TUs), stratified by status of Axshya implementation and quarters in Punjab state, India, 2013-15*

PD-626-12 Community TB outreach using Xpert® MTB/RIF in urban slums of Ogun state, Nigeria: are the missing cases detected?

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Background: In the past, community TB outreaches was conducted using AFB microscopy with its surrounding challenges such as delays in sputum processing and result retrieval, tracking back diagnosed patients for enrolment, losses of laboratory results. With GeneXpert introduced as entry point for pulmonary TB, it was applied to outreaches to address the aforementioned challenges, describe the gains and losses of utilizing GeneXpert in conducting community TB outreaches and determine its effect on TB case finding

Methods: A retrospective review of data generated from patient and laboratory records utilized during outreach activity conducted over a 6 months period (October 2016-. March 2017) Presumptive TB cases were registered among those clinically screened for cough of 2 weeks duration across 14 communities in Ogun state of southwest Nigeria. Sputum was collected immediately from presumptive cases and transported by laboratory

staff to hub GeneXpert site involved in outreach activity. Patient contact details were documented and contact of district supervisor was shared with presumptive cases. Linkage to treatment was done for diagnosed TB cases through referrals and phone calls.

Results: Time lag between sputum collection and result retrieval was a mean of 24 hrs $\pm$ 6 hours. 100% of all sputa collected had documented results. Out of the 1370 participants clinically screened for cough 37% (n=507) were presumptive TB clients with a M:F ratio of 1:1.4. MTB was detected in 9.5%, with 79.1% being males (38/48). 87.5% were enrolled for treatment within 48hrs after diagnosis.

Conclusions: National programs should accelerate strategies targeted at finding TB among men. The use of GeneXpert and the active engagement of a civil society and GeneXpert trained staff for sputum movement and processing during outreach activities is critical for a successful TB outreach activity.

PD-627-12 Impact of two video formats on understanding tuberculosis vaccine clinical trials among community volunteers in South Africa

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Background: Improving comprehension of key TB vaccine clinical trial concepts in high TB prevalence communities is crucial to increase community understanding and awareness of the purpose and need for TB vaccine trials. This study assessed the effect of an educational video on comprehension of concepts relevant to TB vaccine trials in a high TB prevalence community and compared the impact of two video formats, live-action and animated, using a single script.

Methods: The study was conducted in the Delft community, Western Cape, South Africa. 233 participants able to read and speak English were stratified by age (12-14 years, ≥15 years), then randomized 1:1 to watch an animated (N=116) or live-action (N=117) video. A 20-point assessment of understanding (AoU) tool was administered before and after viewing the video. Subsequently, participants watched the other video format and completed a qualitative survey assessing their format preference.

Results: Completed AoUs were provided to blinded Aeras personnel for grading and data entry. Participants' pre- and post-test scores were analyzed by a statistician using generalized estimating equations. The 15+ age stratum had a statistically significantly higher average pre-test score than the 12-14 year olds (p<0.001). Viewing the animated video significantly in-

creased comprehension on average by 2.7 points for the younger cohort (p<0.001) and 1.7 for the older cohort (p<0.001). Viewing the live-action video did not significantly increase comprehension in either age stratum, with average increases in AoU scores of 0.5 points for the younger cohort (p=0.46) and 0.7 for the older cohort (p=0.18).

Conclusions: The use of an animated video statistically significantly improved comprehension of TB vaccine trial key concepts. As the animated video was less expensive to produce than the live-action video, and can be easily translated into other languages, it represents a cost-effective tool for enhancing trial participant understanding of key clinical trial concepts.

PD-628-12 Project Axshya: a civil society initiative in India pushing the agenda of END TB

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Background: Despite the progress made, India has the world's highest burden of TB with 2.8 million new cases in 2015 according to WHO Global TB Report 2016. While moving towards the goal of eliminating TB, it's imperative to reach the unreached population who remains undiagnosed, untreated and continue to transmit infection in the community. In this context, a major civil society initiative in TB care and control has been taken up through Project Axshya- A Civil Society Initiative to Strengthen TB Care and Control in India' through the Global Fund Round 9 grant.

Methods: Supported by the Global Fund, it is implemented by The Union in 285 districts across 19 states of India including 40 urban cities through eight civil society organizations and over 1000 local NGOs and nearly 15000 community volunteers. During April'13 to December '16, Axshya reached over **13 million** households, facilitated identification and testing of over **935,000** TB symptomatics including sputum collection and transportation of nearly **752,000** cases, resulting in diagnosis and treatment initiation of **81,000** patients and notification of over **16,000** from private sector. The key interventions of Project Axshya are outlined in Figure 1.

Results: The numbers reflected in the key interventions of Project Axshya.

Conclusions: Axshya has been able to leverage greater interest and community participation in TB care and control and has emerged as a key partner in supporting the National TB Control programme. Through the initiatives centred on community engagement and participation, Project Axshya adopts a holistic view

of TB, not just from the programme and practitioner perspectives but also from that of the patient and the community.
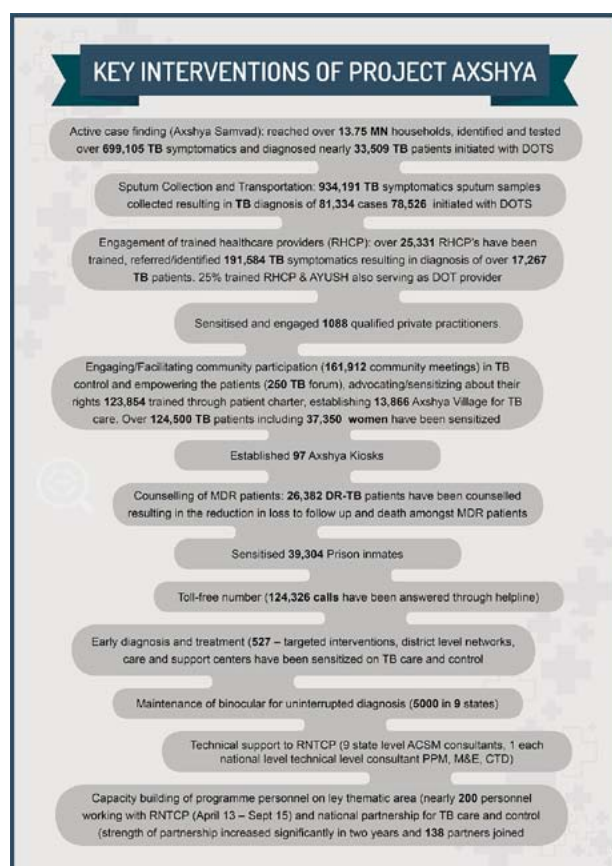
Figure Key interventions of Project Axshya are outlined

PD-629-12 Effectiveness of community engagement in increasing case detection among current and ex-miners: Swaziland experience

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Background and challenges to implementation: Evidence reveals that southern Africa Mineworkers have the highest rates of tuberculosis (TB) in the world, between 2500-3000 cases per 100000 populations of miners. Aggravating the TB situation amongst the mine workers is the high prevalence of HIV. As a result, associated with the high TB prevalence amongst mineworkers are; the high rates of lung diseases due to silicosis from the mines; long absences from home and its associated challenges for the migrant workers; poor living and working conditions for the mine workers.

TB treatment among mineworkers is a challenge due to the industry's reliance on migrant labour which makes treatment continuation and contact tracing challenging, especially among ex-mineworkers in labour sending areas within and across countries.

Intervention or response: SAFAIDS in collaboration with National Tuberculosis Control Program is implementing a door to door Active case finding strategy in the Shiselweni region targeting current, ex miners and their families. This is done by trained Field officers who were given bicycles. The officers through door to door were to create TB awareness, conduct TB screening, collect spot sputum samples and link them to care. Community structures used to identify, sensitise, create service demand and scale up tuberculosis screening services among the miners, ex-miners and their families.

Results and lessons learnt: A total of 2365 TB screenings done in three months,342 presumptive cases and 11were diagnosed with TB and all linked to care. Engagement of community structures is very effective in sensitization, creation of demand for service and ownership.

Conclusions and key recommendations: Community engagement in TB implementation activities is very critical for ownership and support. A mine worker diagnosed with TB has a right to a compensation fund.

PD-630-12 Le «Dialogue Pays» pour améliorer les interventions de lutte contre la tuberculose

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Background and challenges to implementation: Dans le cadre du nouveau modèle de financement du Fonds mondial de lutte contre le sida, la tuberculose et le paludisme, le «Dialogue pays» est l'un des principes majeurs démontrant l'expression de larges concertations avec les communautés pour identifier les priorités dans la lutte contre les 3 maladies. Toute demande de subvention doit ainsi être soutenue par des concertations sectorielles.

Intervention or response: Dans le cadre du «Dialogue pays», des concertations sectorielles ont été organisées dans 9/14 régions du Sénégal avec les groupes clés PvVIH, malades et anciens malades tuberculeux, anciens détenus, étudiants, femmes de ménage, praticiens de médecine traditionnelle, organisations communautaires de base, comités de santé, leaders communautaires, élus locaux, équipes cadres de région et de district, ministères des sports, de la jeunesse et de l'éducation et la presse.

Results and lessons learnt: Les concertations ont significativement amélioré les activités prévues dans le plan stratégique national (PSN TB). La compréhension de leur rôle dans le processus actuel de demande de subventions au FM a permis aux groupes clés de discuter objectivement les orientations stratégiques du plan et de proposer des activités jugées plus pertinentes. En effet, les concertations ont conforté des actions proposées dans le PSN TB, amélioré le contenu de certaines activités et identifié de nouvelles stratégies d'intervention plus spécifiques au contexte de mise en œuvre et à la vulnérabilité des populations ciblées.

Conclusions and key recommendations: Le «Dialogue pays» au-delà de stimuler la participation des communautés dans les demandes de financements du FM est une opportunité continue pour les programmes d'améliorer les interventions de lutte contre la tuberculose.

PD-631-12 Finding the missing TB cases in the community: Kenya's case study of engaging informal health service providers

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Background and challenges to implementation: Kenya is among the 30 high TB burden countries with an estimated TB prevalence of 558 cases per 100,000 population, as evidenced by the recently concluded National TB Prevalence Survey. From this survey, Kenya is missing approximately 40% of its cases, while a patient pathway analysis concluded in 2017 showed that 15% of Kenyans seek initial healthcare from informal health providers. There is therefore need to look beyond the formal health sector for opportunities to find missing TB cases.

Intervention or response: In 2015, CHS, in partnership with KANCO, with support from USAID identified an opportunity to engage informal health service providers (ISPs) to increase TB case detection & notification rates in 5 selected counties in Kenya. This process included identifying, mapping, sensitizing and empowering engaged ISPs to screen their patients, and refer presumptive TB cases to formal health facilities for diagnosis and management.

Results and lessons learnt: By March 2017, 383 ISPs had been identified, comprising 35.8% herbalists, 4.4% *Jua kali* artisans, 12.8% traditional healers, 13.1% traditional birth attendants and 16.7% drug vendors. From a survey conducted 69.6% of ISPs had inadequate knowledge on TB. Currently, 101 (26%) ISPs have been sensitized on TB screening and referral, 327 clients have been screened for TB, 227 presumptive TB cases detected, 153 (67%) of those referred reached various health facilities and 32 of them were diagnosed and started on TB treatment. Of all those diagnosed, 67% were referred by herbalists.

Conclusions and key recommendations: The engagement of ISPs to identify and refer presumptive TB patients, is key in identifying TB patients who do not routinely visit the formal health sector. Of importance is to identify which of the different ISPs once engaged are able to find these cases and scale up this engagement throughout the country.

PD-632-12 Community volunteers - the backbone of tuberculosis control: a study from South India

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Background and challenges to implementation: India has the highest burden of TB and MDR-TB based on the estimates of Global TB burden report 2016. The main cause of DR TB is improper intake of medicine and treatment interruption. With the civil society support, RNTCP tries to increase the treatment success rate. Project Axshya, a civil society initiative to strengthen TB care and control in India was implemented in 2010. Through ACSM activities, it helps the local people to participate as volunteers in TB control activities and helps in controlling DR-TB. These community volunteers are identified within the community and are trained through project Axshya.

Intervention or response: The community volunteers are trained for the identification of TB symptomatic, sputum collection and transportation, referral, intensive outreach activities and providing DOTS in hard to reach areas of Salem, South India. In Salem District, Axshya Volunteers are serving in hard to reach areas for providing DOTS and identifying symptomatic. Volunteers daily visit these areas and provide DOTS to the patients, counsel them and help in completing treatment. They counsel patients and their family members on treatment, adherence, nutritional food, cough hygiene and clean habits. During treatment, they collect follow up sputum on time and help the patients to complete the treatment successfully.

Results and lessons learnt: Axshya volunteers provided DOTS in four TB units and helped 464 patients to complete their treatment successfully and cured them since 2014. Currently eight Axshya volunteers are providing DOTS to 63 TB patients of all types.

Conclusions and key recommendations: Project Axshya empowers the community and enhances greater participation for TB control. Through provision of proper DOTS they help in preventing the spread of Drug resistant TB. Axshya activities are being taking place in selected areas of the district. The community volunteers' participation should be expanded and replicated in other areas to eliminate TB in India by 2025.

PD-633-12 The impact of targeted door-to-door TB screening in the Lubombo Region, Swaziland

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Background and challenges to implementation: Swaziland has been experiencing a progressive decline in TB case notification rates since 2010: (11057) and in 2015: (4567), a 59% decline and this has prompted the National TB Program to expand passive TB case finding to systematic screening for active TB. There were 369 Active Case Finders (ACF) recruited countrywide with 58 from Lubombo region to conduct a targeted door-to-door TB screening, contact investigation and sample collection.

Intervention or response: A systemic review of monthly reports using TB ACF logbooks, contact investigation reporting tools and Presumptive TB registers from 28 health facilities. A cascade of events from TB screening to diagnosis and eventually initiation of treatment was followed. The findings were compared with the unpublished Annual TB case notifications documented in the National TB Control Program's (NTCP) annual reports for 2016.

Results and lessons learnt: Targeted door to door was able to screen 17734 clients, 1864 (11%) screened positive, 968 (52%)sputum specimen was collected, 896 (48%) were referred to the health facilities and 28 (3%) were diagnosed of TB and put on treatment. The overall notification of sputum positive cases was 194 and 96 (49%) index cases followed, 509 contacts were screened for TB, 151 (30%) screened positive, 60 (40%) had sputum collected but no one (0%) was diagnosis of TB. The overall TB ACF contribution on TB case notification was 14% from July to December 2017.

Conclusions and key recommendations: The high yield in door to door TB screening suggests that the composition of the subpopulation in the Lubombo region mainly consists of known high risks groups: like refugees, seasonal workers (farms), HIV positive patients, miners, and the very poor and unemployed community. The burden of arriving at a health facility remains with the patient. Obstacles such as distance to the nearest health facility and lack funds for transport has resulted in high rates of referrals.

PD-634-12 Community volunteer attrition in an intensified TB case finding community project in Zimbabwe

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Background and challenges to implementation: Two districts in Manicaland province has been implementing an intensified and targeted TB case finding using community volunteers since January 2016. A door to door approach was used among high risk families. Despite the high yield in finding missing TB cases, the project has been faced with a high attrition rate among the community volunteers.

Intervention or response: Community volunteers selected with the support of local community leaders from the same community of project implementation were recruited and trained by project and ministry of health staff to conduct targeted TB case finding. A door to door campaign was used to symptomatically screen for TB, collect sputum specimens from presumptive clients, and promote treatment, care and support.

Results and lessons learnt: A total of 270 community volunteers were recruited and trained in January 2016, at the beginning of the project. Of these 115 were recruited and trained in Chimanimani district and 155 in Mutasa district. By the end of six months 75 (28%) community volunteers had left the project and at the end of one year a total of 113 (42%) had left the service. Currently only 157 (58%) are in active service. Those most likely to leave the service were of an average age of 38 years, female and married (89%). The main reasons for leaving services were: long walking distances, no allowances for lunch, need to seek employment to take care of families and other competing projects providing some sort of incentives.

Conclusions and key recommendations: A volunteer in a resource limited setting battles for personal survival while at the same time trying to help others. Basic less expensive and appropriate incentives such as food, transport and airtime support are essential in settings such as Zimbabwe to reduce attrition rates among volunteers.

16. Key affected populations

PD-635-12 Active screening for tracing hidden TB cases in a vulnerable community, Punjab, India

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Background: RNTCP has focused on passive case finding for detection of tuberculosis. After 10 years of implementation, this approach had not been fully successful in identifying all TB patients in community. Therefore, active case finding, where an additional effort is made by the provider to approach these hidden cases is now being advocated.

Methods: A total of 13 Camps were conducted in urban slums in years 2015-17 by State TB Control Cell in collaboration with Punjab State Red Cross Society in two districts of Punjab, India. These camps offered awareness about the signs, symptoms of TB, diagnosis by sputum microscopy and chest X-ray and TB treatment facilities available under the government health system. As a follow up activity the Red Cross volunteers also did house visits in these slums and the persons having symptoms related to TB were referred for Chest X-ray and sputum microscopy.

Results: A total of 9157 people visited screening camps for health check up. Out of these, 3437 were identified with symptoms related to chest problem like cough breathlessness, fever. 837 patients underwent sputum microscopy and 657 had X-Ray done. A total of 154 TB patients were diagnosed. By follow up home visits an additional 358 people were subjected to microscopy and 2 to X-Ray. 34 more patients were diagnosed with TB .Total 188 TB patients were diagnosed and put on DOTS treatment under RNTCP.

Conclusions: Active case finding through camp approach is feasible and can be used by the health system routinely for ACSM activities and finding out hidden cases of tuberculosis in community.

PD-636-12 Identifying missing cases from key affected population through active case finding in rural India

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Background and challenges to implementation: One fifth of Global TB cases are in India, and one million are missing cases attributed in India. These missing cases are both within communities and within the private sector.

Identifying missing cases from communities needs targeted active case finding within vulnerable and marginalized Key Affected Population (KAP).

Intervention or response: With support from Global Fund and The Union, Population Services International is implementing, Project Axshya across 60 districts in India, with an objective to find missing TB cases from KAP population. KAP population for the project include, Slums, Scheduled Caste (SC), Tribal (ST), Prisons (PI), Unorganized labour (UL), PLHIV, Contacts of TB patients, Occupational Lung Diseases (OLD), Hard to Reach (HtR), smokers, diabetics, migrant, refugee and children below six years. Within 60 districts, first KAP areas are systematically identified basis clear secondary data like census, official documents form local government authorities and field mapping in assigned TB units. Active case finding in identified KAP areas is conducted through trained community volunteers, by conducting systematic household visits in the identified KAP areas. Verbal screening of TB is done among households visited and identified presumptive cases are facilitated for diagnosis to nearest RNTCP services.

Results and lessons learnt: During Oct'15 to Dec'16 period, overall 900,000 households are covered through Axshya Samvad in KAP areas. Overall 3737 TB cases are identified from the KAP population. 1951(53%) cases are from SC, 227 (7%) cases are from tribal, 1208 (32%) cases are from slums, 149 (4%) are from hard to reach population and remaining 202 (5%) cases are from prisons, contacts, PLHIV, Unorganized labour and OLD.

Conclusions and key recommendations: With systematic mechanism of mapping of KAP areas basis evidence, and conducting active case finding in a systematic way by covering each and every household, it is possible to identify missing cases from KAP population.

PD-637-12 Implementation of high-yield intervention package for urban TB control: experience from 40 urban sites of India

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Background and challenges to implementation: In India, tuberculosis remains a major public health challenge with an incident of 2.8 million, 0.48 million TB deaths annually with 1 million cases are 'missed' annually. There is a need to reach out to urban slum and engage private healthcare providers who are often the first point of contact for slum dwellers.

This paper explains the results of the strategies adopted by project Axshya in reaching the slum dwellers and engaging private sector.

Intervention or response: The Union led project Axshya is implementing urban TB control in 40 urban sites of India. The package of interventions adopted to increase access to TB services includes active case finding, increasing access to diagnostic services, engaging private sector for enhancing notification and treatment adherence.

Results and lessons learnt:

Active case finding: During 2016, reached out to 9million households and 35,814 presumptive TB cases identified, 16,497(46%) tested including sputum collection and transportation of 12,697(77%). 10% patients were diagnosed and initiated on DOTS.

Increasing access to diagnostic services including newer tools: The project has supported screening of 402 symptomatics through chest x-ray which resulted in identification 78 TB patients(19%). The project has facilitated testing of 2845 TB symptomatics through Gene Xpert resulting in diagnosis of 411(15%) of TB patients.

Engaging private healthcare providers for enhancing notification: The project has sensitised and engaged 3648 qualified practitioners, 202 private hospitals and 77 labs in 40 urban sites and facilitated notification of 16265 TB patients from the private sector.

Ensuring treatment adherence: Innovative software and mobile app facilitates notification of TB patients from private sector in Nikshya and offers treatment adherence support through daily SMS and interactive voice calls. Over 10,000 TB patients are benefiting from this service.

Conclusions and key recommendations: Implementation of comprehensive package of high yielding services in urban pockets has proved to contribute to the increase in case detection rates and case notification rates.

PD-638-12 Potential determinants of treatment outcomes in tuberculosis patients from the Shimla hills in Himachal Pradesh, India

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Background: India has the highest burden of Tuberculosis worldwide. To achieve the goals of the END TB strategy, it is imperative to understand the factors which can influence the treatment outcomes. The objective of this study was to assess the patients' characteristics and factors influencing their treatment outcomes.

Methods: A prospective Cohort study design was employed and all patients (n=117) who were registered for Category I DOTS during the last quarter of 2015 were included after obtaining written informed consent. Home visits with patient interviews were conducted to collect relevant information. Standard treatment outcomes were notified for each patient. Univariate and binary logistic regression models were used.

Results: Overall, Treatment success rate was 93.2% (Cure rate= 87%, treatment completion rate= 100%). Default, death, failure and lost to follow up rates were 2.6%, 2.6%, 0.8% and 0.8% respectively. Those with a history of tobacco smoking [RR: 6 (1.27-28.37); p=0.02], second hand smoke [RR: 8.75 (1.11-68.88); p=0.02], indoor air pollution [RR: 7.89 (1.10-62.13); p=0.02] and alcohol use [RR: 6.13 (1.57-23.93); p=0.01] had higher risks of developing an unfavourable treatment outcome. The commonest cause of indoor air pollution was smoke surfacing out of fire-wood used for cooking and tobacco smoke.

Conclusions: The treatment success rates conform to the END TB Strategy targets of 90%. Recent studies have demonstrated higher odds for the risk of TB and adverse treatment outcomes in patients exposed to indoor air pollution. Health education regarding the ill effects of tobacco and alcohol with regards to the disease preventability and curability needs to be further intensified. Further studies with a larger population to determine the effect of indoor air pollution as a risk factor and its impact on treatment outcomes by contemporary scientific methods by collaborating with other agencies involved in environmental studies is highly recommended.

PD-639-12 Addressing a persistent outbreak in a socially disengaged, mobile population. Infection, outreach, and treatment in shearing gangs in New Zealand

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Background and challenges to implementation: While most (80%+) recent tuberculosis diagnoses in New Zealand have been in individuals born outside New Zealand there have been a low-level, ongoing series of presentations in a specific New Zealand-born population. Shearing gangs are mobile groups that travel the country for work seasonally. These groups have demonstrated significant disengagement from the national health care system. This, coupled with their semi-nomadic lifestyle and communal sleeping arrangements while on contracts makes outreach, diagnosis, and long-term treatment difficult to implement.

Intervention or response: As traditional urban-focused outreach efforts have proven ineffective in encouraging this population to present for evaluation once symptoms develop, a cooperative approach was offered between national and local public health providers to develop a patient-centred outreach effort. This effort incorporated discussions with contractors and former shearers to identify social leaders in the work crews, educational materials vetted for accessibility and cultural appropriateness, and a flexible approach to service delivery as the shearers moved across the country.

Results and lessons learnt: By tailoring the outreach and treatment effort to meet the shearer´s social, economic, and cultural needs/preferences an engagement was established. While tentative at first, the ongoing engagement has gradually built trust and understanding between the health care system and the target population. While it is far too soon to speak to the elimination of this reservoir of infection, health care presentation rates have risen.

Conclusions and key recommendations: Tuberculosis outreach and treatment efforts focused on disengaged and/or mobile populations face a number of difficulties. The length of treatment requires long-term collaboration with the populations in question. To achieve this, health care systems must demonstrate flexibility to match unusual lifestyles, leaders must be accurately identified and engaged within the population of concern, educational levels and cultural elements must be considered, and the focus population must be properly incentivized to participate. If any of these elements are absent, success is unlikely.

PD-640-12 Yield of tuberculosis screening using Xpert MTB/RIF among HIV-infected pregnant women in Lilongwe, Malawi

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Background: Tuberculosis (TB) is a leading cause of non-obstetrical maternal death in sub Saharan Africa. TB disease in HIV-infected pregnant women increases the risk of vertical HIV transmission and introduces the risk of TB acquisition in the infant. Physiologic changes of pregnancy predispose to reactivation of latent TB, mask TB symptoms, and reduce the sensitivity of smear microscopy. The burden of TB among HIV-infected pregnant women is poorly understood in sub-Saharan Africa. Here, we describe the results of TB screening with Xpert MTB/RIF among HIV-infected pregnant women in Lilongwe, Malawi.

Methods: This was a prospective observational cohort study examining the safety and durability of the Option B+ program in Malawi. HIV-infected pregnant women were enrolled at their first antenatal care visit at a large urban hospital into sub-cohorts based on antiretroviral therapy (ART) status: newly initiating ART, already on ART, or restarting ART after default. All participants were offered TB screening with Xpert beginning at their second study visit. Participants received cough coaching and provided an expectorated sputum sample that was tested using Xpert.

Results: 725 participants were enrolled, and 319 participants (44%) were screened with Xpert (Table 1). Two women (0.6%) tested positive for Mycobacteria tuberculosis complex: one was newly initiated on ART and diagnosed with rifampicin-sensitive TB, and one was already on ART and diagnosed with rifampicin-resistant TB. Drug sensitivity testing confirmed resistance to rifampicin and isoniazid.

Characteristic	
Median CD4 (IQR)	395 (236-572)*
Sub-cohort—n (%)	
ART initiator	185 (58)
Already on ART	117 (37)
Defaulter	17 (5)
Age—median (IQR)	28 (24-32)
*47 values missing	

Table 1 Characteristics of women screened for TB

Conclusions: A low proportion (0.6%) of HIV-infected pregnant women were diagnosed with TB, including one case of multidrug-resistant TB, using Xpert. It is unclear whether this low proportion reflects low TB burden among those screened, poor sample quality, or limitations of Xpert as a screening tool in this population.

PD-641-12 Cross border TB in Malawi: case notifications and treatment outcomes

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Background and challenges to implementation: Malawi is a landlocked country; shares borders with Mozambique, Tanzania and Zambia. Tuberculosis (TB) diagnostic and treatment services are free even to non-Malawian nationals.

Aim: To determine TB case notifications and treatment outcomes among patients from across the borders.

Intervention or response: Malawi National TB Programme (NTP) has put in place a recording and reporting system for TB patients at all levels. Cross border TB patients are registered in a separate TB register in border districts. These patients are not reported to the NTP and even to global level. Cross border TB patients

are also not routinely evaluated to determine their treatment outcomes. We therefore determined TB case notifications and treatment outcomes for cross border TB patients for a five-year period.

Methods: Facility TB registers for cross boarder TB patients (2011-2016) were reviewed. Existing data reported at the national level was used as a control.

Results and lessons learnt: TB case notifications among cross boarder TB patients ranged from 223 in 2012 to 152 in 2016. The peak was in 2015 when the country notified 236 cross boarder TB patients.

Treatment success rates have almost been similar to Malawian nationals ranging from 79-85%. Patients declared as lost-to- follow-up among cross boarder TB patients was high, ranging from 8-11% as compared to national data (3-5% lost-to-follow-up rates). All other parameters among cross boarder TB patients were almost similar to reported national data.

Year	New smear positives	New smear negative	MTB+	EPTB	Re-lapses	Treatment failures	Return after lost to follow up	Others	Total
2013	94	51	8	42	1	1	0	17	214
2014	81	50	28	45	2	0	2	21	229
2015	79	46	40	36	6	9	4	16	236
2016	52	33	24	24	0	0	3	16	152

Table Cross border TB case notifications in Malawi: 2013-2016

Conclusions and key recommendations: The trends in TB case notifications and treatment outcomes among cross boarder TB patients is almost similar to that of Malawian nationals apart from lost-to-follow-up.
The NTP should change its policy by reporting all notified cross boarder TB patients both at national and global levels. None reporting may have an impact on estimates for anti-TB drug and other supplies. NTPs need to strengthen regional platforms to address cross boarder issues.

PD-642-12 Peer-led active case finding of TB in high-risk groups in the South-Kivu province of DRC

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Background: Active case finding of patients with active tuberculosis (TB) disease in high-risk groups is an essential component for tackling the TB epidemic. In the South-Kivu province of DRC, we identified four high-risk groups: people living in the household of TB patients, people living in military camps, people working in the artisanal mining sector and people living in prisons.

Methods: We performed symptomatic screening of cough in the four pre-identified high risk groups. Suspects identified were tested for pulmonary TB using smear microscopy of rapid molecular tests.

Results: We performed symptomatic screening among 17.693 household TB contacts, 13.953 people living in military camps, 10.876 people working in the artisanal mining sector and 480 individuals living in prisons. The number of individuals needed to screen in order to find one bacteriologically confirme TB case was 131, 71, 83 and 68 respectively.

Conclusions: In the South-Kivu province of DRC, we found that the incidence of smear-positive pulmonary TB was the highest among people living in prisons,in military camps and artisanal mining camps. These results suggest that an urgent attention should be given to these populations highly exposed to TB.

PD-643-12 Comité de monitores de tuberculosis en CERESOS del Estado de Puebla

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Background and challenges to implementation: Dentro de los grupos vulnerables en el apartado de "OTROS" las personas privadas de su libertad (PPL) forman parte de la población de riesgo por la sobrepoblación en los espacios destinados y las condiciones en las que se encuentran.
En el estado de Puebla una de las actividades del programa de tuberculosis consiste en identificar sintomáticos respiratorios y hablar sobre tuberculosis en estos lugares, sin embargo la frecuencia de la asistencia del personal de salud hacia CERESOS es mínima comparada con la magnitud de la población interna; de esta forma en febrero de 2013 se inicia con la formación del comité de monitores en tuberculosis que consiste en que se capacite a las PPL en la identificación oportuna de sintomáticos respiratorios y como apoyo al servicio médico "Detecten, informen y canalicen a la PPL al mismo servicio para brindar tratamiento adecuado y oportuno cortando la cadena de transmisión.

Intervention or response: Se conforma el primer Comité con 12 mujeres y 9 hombres PPL regidos por un Manual de Procedimientos que ellos mismos elaboran, capacitándose de manera continua, para que ellos realicen visitas periódicas a los dormitorios correspondientes.
Todos los integrantes del Comité están capacitados para referir pacientes al servicio médico, recabar muestras de expectoración, así como realizar acciones de adherencia y seguimiento del tratamiento para evitar abandonos.

Results and lessons learnt: Del 2013 al 2016 en 3281 PPL anual se identificaron 175 sintomáticos respiratorios, se diagnosticaron 8 casos con tuberculosis y 4 fueron detectados por estos grupos todos bajo atención y tratamiento.

Conclusions and key recommendations: El impacto de los monitores fue modelo para conformar otros comités en el interior del estado, actualmente de los 23 CERESOS pertenecientes al estado se cuenta con 11 Comités de monitores oficializados.

17. Overcoming laboratory challenges in the field

PD-644-12 Sputum collection factors affecting diagnostic yield

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Background and challenges to implementation: Many sputum samples are rejected by laboratories due to a salivary appearance, inadequate volume, or being in transit for more than 3 days.

Objective: To study the appropriateness of these policies and whether sub-optimal samples are worth testing.

Intervention or response: In a prospective cohort study between April 2015 - September 2016, 790 spot sputum samples were collected from 772 participants over 8 years old who were about to commence treatment for pulmonary tuberculosis. The quality of instructions, variations in collection technique and sputum characteristics were recorded with a questionnaire after sputum collection. Samples that were of inadequate volumes, were supplemented with phosphate buffer solution. Samples underwent testing with direct Ziehl-Neelsen microscopy, GeneXpert MTB/RIF and the thin-layer agar MDR-/XDR-TB Colour Test.

Results and lessons learnt: 45% of samples that appeared to be salivary were reported by the patient to be expectorated sputum. Although samples reported to be salivary by patients were less likely to be diagnostically useful than samples reported to be sputum (P< 0.05), most salivary samples provided microbiological confirmation and drug-susceptibility results. Diagnostic yield was unaffected by inadequate (< 5 ml) sample volume, and was even unaffected by sputum volumes < 2.5 ml that had to be diluted more than 100% prior to laboratory testing. Diagnostic yield and culture failure were

both unaffected when transit delays caused microscopy, molecular and culture testing to be delayed 4-21 days after sputum collection. Diagnostic yield was increased by explaining how to collect sputum for more than 1 minute (P=0.05) and was unaffected by whether sputum was collected early morning versus daytime sputum collection (P=0.8).
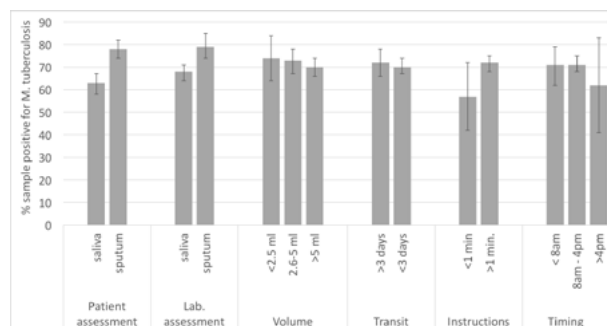
Figure 1

Conclusions and key recommendations: Sputum samples should be tested by the laboratory even when they appear to be saliva, are such small volume that they need to be diluted or are delayed in transit.

PD-645-12 Implementation of a system for laboratory specimen transportation in the Kyrgyz Republic

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Background and challenges to implementation: The Kyrgyz Republic is among the 27 high multidrug-resistant (MDR) TB burden countries in the world making early detection of RIF-resistance critical to starting effective treatment. In 2015, sputum cultures were obtained on 72% of TB patients and 16% of patients were tested with for RIF resistance using GeneXpert.

PHC providers refer 66% of TB suspects up to the oblast level for sputum collection, as they are not reimbursed for sputum transportation costs. When sputum is collected in clinics below the district level, it is delivered by healthcare providers (37%) or patients (63%) using public transportation, typically without regard to security and quality of diagnostic samples.

Intervention or response: In 2016, the Ministry of Health piloted a specimen transportation system to improve early detection and treatment of DR-TB. The MOH engaged a branch of the governmental postal service to take specimens from the district Family Medicine Center in four pilot rayons to the closest facility providing GeneXpert and culture testing. The contract with the company requires that proper transport conditions and safety procedures are followed.

Results and lessons learnt: Prior to implementation of the transportation system, an average of 45 sputum specimens per month were delivered for Xpert testing from pilot districts. During the first month using the courier system, 162 samples were delivered, an increase of 360%. TB was detected in 35 of 162 samples (21%); of these, 9 (25%) were resistant to rifampicin.

Conclusions and key recommendations: Early results suggest a positive impact on the number of TB suspects tested through rapid diagnostics. Further study of the transportation system is needed, including an analysis of its impact on TB/MDR-TB case detection, early initiation of SLD treatment and its economic impact.

PD-646-12 Pattern of usage of TB diagnostic procedures in private sector across three cities of a central Indian state: a cross sectional study

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Background: Despite the preference of RNTCP for sputum microscopy, a variety of TB diagnostic producers are being used in private sector for the diagnosis of TB.

Methods: To understand the pattern and usage of TB diagnostic services in private sector seven months (June 2016 to December 2016) data were collected from selected leading laboratories across three cities of Chhattisgarh that includes 6, 6 and 3 labs in Bilaspur, Durg & Bhilai and Rajnandgoan respectively.

Results: Different diagnostic tests such as; ADA TB, FNAC, Abdominal USG, CXR, IGM and serological tests such as TB Gold are found to be practiced in these cities without a definite pattern. Similarly among all the tests 9.4%, 13.4%, 46.7% and 30.3% (n=3295) of all the tests are serological tests, sputum microscopy, CXR and other tests across all the cities. Despite Government of India's gazette to stop malpractice in TB diagnosis serological tests are rampantly happening across the three cities. Systematic reviews carried out on the commercial serological tests reveal that the results are inconsistent and of low quality. Furthermore none of the international guidelines support the use of serological tests for the diagnosis of active TB. In addition, in one city over reliance on CXR was found which many a time is believed to be the major fuelling factor for irrational therapy and DR-TB. During the seven months period not even a single test of sputum microscopy has been carried out in the same city. To stop the malpractice on TB diagnosis the private sector should adhere to the STCI guidelines developed by WHO and GOI.

Conclusions: Cooperation of private sector for TB care and control in needed in India and is also the vision of National Strategic Plan however the same is only possible if the sector stops malpractice and adheres to standard TB guideline.

PD-647-12 Evaluation of implantation strategies for the use of innovative sample transport reagent for tuberculosis-healthcare worker preferences of the use of the OMNIgene® Sputum reagent

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Background: OMNIgene SPUTUM (OMS) is a novel sample transport reagent to effectively decontaminate and liquefy sputum samples in the absence of cold-chain, but it requires changes in sputum collection process. Using a discrete choice experiment, we evaluated preferences of healthcare workers (HCW) on the usage of OMS in clinical settings.

Methods: We surveyed HCWs at 32 health centers in the San Juan de Lurigancho district of Lima, Peru. Through key informant interviews and expert consultations, we identified three key attributes relevant to the usage of the OMS: administration, process timing, and biosafety. We used a full factorial design where two levels of each attribute were randomly allocated across four questions. A score for each attribute level was calculated by dividing the number of times each attribute was chosen across all respondents by the number of total times each attribute was available. We also fitted linear probability models (LPM) where the choice was regressed on all levels of three attributes.

Results: Of 101 HCWs surveyed, each HCW consulted about 23 patients (IQR: 10-38) and 5 patients for TB diagnosis (IQR: 2-7) per day. 64% (n=65) of the HCWs considered administration as a very important attribute while 48.5% (n=49) and 89% (n=90) did so for process timing and biosafety, respectively. Adding the reagent by HCW was 23% times more preferred than adding it by a patient (p< 0.001). Preference for processing samples as batch vs. per patient did not differ (coefficient=-0.02, 95% CI: -0.12, 0.07). Also the preference for moderate risk of TB infection to HCW vs. low risk did not differ (-0.03, 95% CI: -0.13, 0.06).

Attribute	Level	N*	Score	Regression	
				Coefficients (SE)	95% CI
Administration	Patient	155	0.38	Ref	
	CHW	249	0.62	0.23 (0.05)	0.13, 0.34
Process Timing	Per each patient	207	0.51	Ref	
	As a batch	197	0.49	-0.02 (0.05)	-0.12, 0.07
Biosafety	Low risk to CHW	209	0.52	Ref	
		194	0.48	-0.03 (0.05)	-0.13, 0.06

*Number of times each attribute level was chosen.

Figure Attribute-level scores and OLS regression coefficients

Conclusions: There was a clear preference among HCWs to handle the OMS reagent themselves per patient. These results provide important insights in the development of cost and process to optimize OMS implementation strategies in clinical settings.

PD-648-12 The use of same-day, spot-spot sputum testing leads to improved pre-diagnosis retention of tuberculosis patients in public health facilities in Ethiopia

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Background and challenges to implementation: The conventional sputum testing approach using three consecutive spot-morning-spot sputa commonly results in a high pre-diagnosis attrition rate of presumptive Tuberculosis (TB) patients. Ethiopia started implementing this same-day diagnosis method at the end of 2016. In this study, we evaluated the immediate effect of the introduction of spot-spot sputum testing on the retention of presumptive TB patients and compared its yield with the conventional method.

Intervention or response: The national TB control program with support from the USAID funded CTB project updated the national guideline for sputum smear examination to implement the same-day diagnosis approach. The slide positivity rate and presumptive TB pre-diagnosis attrition rate was computed before and after the introduction of the new approach. Data from July-September 2015 (before same day diagnosis) and in 2016 (after the introduction of the same day diagnosis) was captured from 102 health facilities (97 health centers, 5 hospitals) in Amhara region.

Results and lessons learnt: Of 9,346 presumptive TB patients, 4,656 (49.8%) patients received same-day diagnostic services. Of 22,882 sputum slides examined, the slide positivity rate(SPR) was higher in the conventional method (4.7% vs. 3.3%; p< 0.05). However, the pre-diagnosis attrition rate was significantly lower for the same-day diagnosis (1.8% vs. 6.8%; p< 0.05). Thus for every 100 presumptive TB, it is estimated that using spot-spot would retain 5 presumptive TB patients that would have been missed if the conventional sputum testing was used & considering 4.7% SPR, there is proportionate reduction on TB case finding.

Conclusions and key recommendations: The implementation of same diagnosis improves patient adherence to delivering a complete number of samples as opposed to the conventional method. Using the spot-spot method contributed to retaining presumptive TB patients that would have been missed if the conventional method was used and improves TB case finding. The lower SPR needs further evaluation using more rigorous techniques.

	Spot-Spot (Same diagnosis)	Spot-Morning-Spot (Conventional)	Total	P-value
Number of presumptive TB patients with at least one slide	4,656	4,690	9,346	
Presumptive TB patients with complete slide (%, 95% CI)	4,596 (98.7,98.3-99.0)	4,397 (93.8,93.0-94.4)	8,993 (96.2,95.8-96.9)	<0.05
Total number of slides	9,386	13,496	22,882	
Total number of positive slides (%, 95% CI)	312 (3.3,3.0-3.7)	637 (4.7,4.6-5.1)	949 (4.1,3.9-4.4)	<0.05

Table AFB data by type(spot-spot & Spot-Morning-spot)

PD-649-12 Outcomes of sputum and slide transportation approach on TB case notification in 19 provinces of Afghanistan

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Background and challenges to implementation: TB is a public health problem in Afghanistan 61,000 new TB cases occurring in a year and 12,000 people dying with disease annually. In 2016, the TB case notification rate was 69% Afghanistan missed almost 31% of estimated incidence number of TB cases since 2010. One of the challenges were access to TB services for those people living in catchments areas of basic health centers (BHC) and sub health centers (SHC) that does not provide TB diagnostic services. The aim of this assessment was to explore effectiveness of sputum and slide sending mechanisms on TB case notification

Intervention or response: To implement Sputum and Slid transportation, the NTP strengthened coordination mechanism between (BHC) where access to TB diagnosis were limited and nearest diagnostic health facilities and trained health facility staff on identification of presumptive TB patients, sputum and slide transportation. In 2016, sputum transportation implemented in 86 Basic Health Centers (BHC) of 19 provinces and slid transportation in 38 BHCs of 6 provinces NTP used standard TB recording and reporting forms as data collection tool

Results and lessons learnt: The assessment team found that 15,108 sputum samples of 5,036 presumptive TB patient also 8,795 slides from 2,931 presumptive TB patient attended BHCs prepared and transported for diagnosis among sputum samples, 231 (4.5%) diagnosed positive for acid fact bacilli (AFB) and from slides 136 (4.6%) diagnosed positive for AFB. Collectively, 367

(4.6%) bacteriologically confirmed TB cases diagnosed all registered in public health facilities and standard treatment initiated for them. In brief, these approaches contribution to 5% bacteriologically confirmed TB cases in 19 provinces. In 2016, there were 12,883 bacteriologically confirmed and 31, 132 all forms of TB cases **Conclusions and key recommendations:** The sputum and slid transportation approach increased access to TB services and contributed to TB case notification in 19 provinces. these approaches should be scaled up in the other provinces

PD-650-12 Status of accreditation of TB diagnostic tests in Africa

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Background: To meet the global end TB goals of reducing TB deaths by 95% and cutting new cases by 90% between 2015 and 2035, there is need for high-quality laboratory systems that offer early, rapid and accurate detection of TB and drug resistance. To guarantee quality of testing, laboratories establish Quality Management Systems (QMS) that are based on international standards like International Organization for Standardization (ISO) 15189 and attain accreditation. TB Laboratories and TB tests lag behind in accreditation in Africa.

Methods: A search for TB laboratories accredited to *International Laboratory Accreditation Cooperation (ILAC) recognized bodies was done on the ILAC website. Laboratories that had a TB test on their scope of accreditation was included from the basic TB microscopy to TB culture and Drug Sensitivity Testing (DST).*

Results: There are 93 ILAC recognized accreditation bodies and 4 (4.3%) of these are based in Africa. The 4 ILAC accreditation bodies in Africa have accredited 462 medical laboratories. Only 15 (3.2%) of these have TB related tests on their accredited scopes. The 15 laboratories have 48 tests accredited from 8 different diagnostics tests with 13 (27.1%) of them as TB Microscopy, 11 (22.9%) TB culture, 10 (20, 8%) DST, 6 (12.5%) GeneXpert, 3 (6.3%) LPA, 3 (6.3%) HAIN, 1 (2.1%) Rapid Antigen Test and 1 (2.1%) Quantiferon.

Conclusions: Although most laboratories in Africa offer at least TB microscopy, very few TB tests are accredited. TB laboratories and TB tests need to be prioritized in the implementation of QMS and accreditation using available tools like Strengthening Laboratory Management Towards Accreditation (SLMTA), TB SLMTA, Global Laboratory Initiative (GLI), World Health Organization Laboratory Quality Management System (WHO LQMS) and others.

PD-651-12 Integrating and optimizing public sector CBNAAT diagnostic services for private sector TB patients in Mumbai, India

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Background: Under the aegis of Municipal Corporation of Greater Mumbai (MCGM), a project was initiated as Private Provider Interface Agency (PPIA) to provide quality TB care for private sector patients. CBNAAT testing in private sector is expensive, where as its free of cost in public sector. Thus to ensure universal access of TB care in private sector, leveraging public sector CBNAAT is an essential step for sustainability of the TB control program in Mumbai.

Methods: To reach out and engage the private sector towards TB control through early and accurate diagnosis, MCGM is leveraging the scope of four CBNAAT machines to be utilized collaboratively under RNTCP and PPIA from September 2016 onwards. This initiative has cut the out of pocket expenditure for CBNAAT testing for private sector patients. PPIA also provides monthly estimates of CBNAAT demand from the private sector, for smooth planning and availability of CBNAAT cartridges at public sector labs. For optimum utilization of CBNAAT machines an additional lab technician has been provided at each Lab by PPIA to run the extra samples on CBNAAT.

Results: From September 2016 to January 2017, total 2530 Private sector presumptive TB samples have been tested and 871 (34%) samples have been diagnosed as Rif. Sensitive TB and 184 (7%) have been diagnosed as Rif. Resistant TB.

Sr. No	GX lab	Total Samples Sent	MTB detected no. (%)	Rif Resistant Detected No. (%)
1	Cooper Hospital GX	732	254 (35%)	48 (7%)
2	Chembur CBNAAT LAB	641	204 (32%)	52 (8%)
3	Trauma Hospital CBNAAT LAB	669	272 (41%)	46 (7%)
4	Shatabdi Hospital, Govandi CBNAAT LAB	488	141 (29%)	38 (8%)

Table Public Sector CBNAAT Leveraging

Conclusions: Integrating Public sector CBNAAT labs for private sector TB patients is a solution to optimize the public sector CBNAAT facilities without bearing any out of pocket expenditure and such model needs to be expanded on larger scale across India.

PD-652-12 Impact of introducing LED-FM services in increasing case detection among smear- positive tuberculosis patients under the RNTCP, India

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Background: India houses a quarter of Tuberculosis patients in the world. For the diagnosing of sputum smear positive tuberculosis suspects light-emitting diode fluorescence microscopy (LED-FM) has been recommended by WHO over the conventional bright field microscopy using Ziehl-Neelsen (ZN) staining. As a result Auramine-O staining based LED-FM has started replacing conventional ZN microscopy in phased manner in designated microscopy centres (DMC) under India's Revised National Tuberculosis Control Programme (RNTCP). The objective of current study was to assess the impact of introduction of LED-FM services in increasing case detection rate in tuberculosis under program conditions.

Methods: This was a cross sectional study carried under RNTCP Chandigarh. Universal sampling was done and all district microscopy centres (DMCs) which operationalized LED-FM were taken in the study. Two peripheral DMCs where conventional ZN microscopy was used were designated as control. All suspected TB patients who underwent sputum smear examination pre and post LED-FM intervention were compared. Their records were taken from RNTCP registers from respective DMC. Comparison with peripheral DMCs which implied conventional ZN sputum smear microscopy was also done. Chi square was applied to access the statistical significance.

Results: Case detection rate decreased by 3.5% in post intervention phase (LED-FM) as compared to pre intervention phase (ZN microscopy) while scanty grade smear increased by 24.7% (P value < 0.05). Peripheral DMCs with operational LED-FM showed an increase in case detection rate by 13.7% (P value< 0.05) compared to non-intervention controls. The time taken per slide examination decreased by 57.1% (from 7 min on an average to 3 min on an average) when LED-FM is used.

Conclusions: LED-FM is easy to use, takes lesser time to examine slides and has longer shelf- life. The results of this study provide enough evidences to scale up the installation and usage of LED-FM in Indian settings.

PD-653-12 QMS implementation in the TB laboratory network in Uzbekistan: phase I

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Background and challenges to implementation: Uzbekistan is one of 18 countries in the WHO Europe region, where the priority is given to activities for TB control strengthening. Following the End TB Strategy recommendations to strengthen the quality of TB laboratory services, the National TB Program (NTP) with support from the USAID TB Control Program started implementation of the Quality Management System (QMS) in four regions: Bukhara, Kashkadarya, Khorezm, and Navoi.

Intervention or response: A QMS implementation plan was developed to address a specific organizational structure of the regional laboratory network, consisting of peripheral level smear microscopy laboratories and intermediate level culture laboratories. The WHO-recommended approach for stepwise implementation of internationally approved quality standard ISO 15189 was used as a basis for development of customized QMS. Following the existing structure of the national healthcare system, the established QMS, 12 quality essentials were integrated into six sections: organization and staffing; infrastructure; equipment and supplies; bio-safety; technical procedures; and quality assurance. A scoring system for evaluation was introduced, evaluating each component separately and presenting an average score. A target for satisfactory implementation score was set to average of 75%. Quarterly mentoring visits were organized to support the implementation and measure the progress.

Results and lessons learnt: The comparison of the baseline score and the score after a year of implementation, showed improvement in the overall QMS score in all 15 laboratories. The target of 75% was achieved in 8 (53%) laboratories. The major implementation challenges were bio-safety standards and equipment management, with average score 40.3% and 44.5%, respectively.
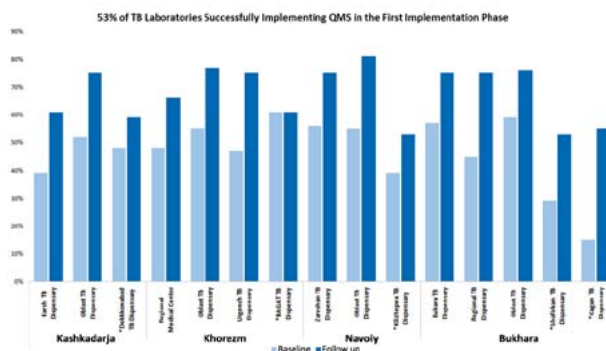
Figure QMS implementation score in TB laboratories

Conclusions and key recommendations: Successful implementation of QMS in specialized TB laboratories requires implementation of IS0 15189 standards through a stepwise approach, careful planning process and customized approach based on specific country settings. Evaluation of each particular segment of laboratory functioning allows identification of areas that require special attention, addressing the weaknesses to responsible entities and planning concrete remedial actions.

18. Don't resist! Finding the pattern through sequencing

PD-654-12 Detection of M. tuberculosis in extra-pulmonary specimens: comparison between Xpert MTB/RIF and screening for multi-drug resistance using BACTEC™ MGIT™ 960 system with thin layer agar

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Background: Confirming the diagnosis of extra-pulmonary tuberculosis is mainly based in clinical findings. Xpert MTB/RIF molecular system (Xpert) is a new technology being validated mostly for respiratory specimens. We compare Xpert in combination with automatized liquid culture and solid thin layer agar media to know how the systematic use of Xpert contribute to the diagnosis of extra-pulmonary tuberculosis.
Methods: Xpert and screening to multidrug-resistant (MDR) tuberculosis using the automated instrument BACTEC™ MGIT™ 960 Mycobacterial Detection System combined with thin layer agar (MGIT-TLA) were applied in 2.600 extra-pulmonary samples. Agreement and positivity for each type of specimens as well as susceptibility patterns was compared for each method.
Results: *Mycobacterium tuberculosis* (MTB) was detected in 10.58% using any method. Xpert detected 8.19% of positive samples, 91.1% rifampicin susceptible, 5.6% of them with rifampicin resistance, and 3.29% indeterminate resistance. MGIT-TLA detected MTB in 8.46%, MDR MTB in 5%, MTB mono resistant to isoniazid in 4.5%, MTB mono resistant to rifampicin in 0.45% and non-tuberculous mycobacteria (NTM) in 0.23%. MGIT-TLA detected 63 positive samples non detected by Xpert, and Xpert detected 56 positive samples non detected by the MGIT-TLA. There was one discordant result in susceptibility pattern between both methods. Mutations on probes D and E were the most frequently detected. Time for detection of MTB positive samples using MGIT-TLA was 12.46 days.
Conclusions: There were not important differences in MTB detection using any method. Screening using MGIT-TLA permitted additional detection of INH resistance and NTM non detected by Xpert. Time for final results is the most important finding comparing both methods. These results suggest the use of a combination of methods in order to improve the microbiological confirmation of extrapulmonary tuberculosis.

PD-655-12 Performance of the GenoType MTBDR*plus* assay v. 2.0 in the diagnosis of tuberculosis and drug resistance in Lima-Peru

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Background: Multi-drug resistant tuberculosis (MDR-TB) seriously threatens TB treatment. The GenoType *MTBDRplus* assay is an effective, rapid tool for diagnosis of MDR-TB, providing information on mutations involved in resistance to both isoniazid and rifampin. Given the long delay from sample to answer using conventional DST, we evaluated the performance of the GenoType *MTBDRplus* assay as a drug susceptibility test and diagnostic tool for patients with TB in Lima, Peru.
Methods: We performed GenoType *MTBDRplus* (version 2) and conventional indirect drug susceptibility testing (DST) using sputum samples collected during enrollment of patients with pulmonary tuberculosis in two clinical trials from 2013-2015. We evaluated sensitivity, specificity, and accuracy using the kappa test of the assay. Indirect DST was used as the gold standard.
Results: Of a total of 219 samples tested, DST results show 17.8% were resistant to rifampicin and 18.7% to isoniazid. See Table 1. 17.8% were resistant to both (i.e., MDR-TB). Compared to DST, GenoType *MTBDRplus* showed 100% sensitivity (97.5 % CI 91.5-100%), 100% specificity (97.5% CI 98.2-100%) and a kappa value of 1 (97.5% CI 0.897-1) for detection of rifampicin resistance and MDR-TB. The test was 100% sensitive (97.5% CI 90.4-100%) and 98.9% specific (97.5% CI 96.8-98.9%) in detecting isoniazid resistance. Among samples with resistance to isoniazid as detected by GenoType *MTBDRplus*, 87.2% showed *katG* mutations. Median time from sample receipt to result for GenoType *MTBDRplus* was 0 days [IQR 0-0] and median time-to-result was 21 days (IQR 17-32) for conventional DST.

Results	Kappa (IC 97.5%)	Sensitivity (IC 97.5%)	Specificity (IC 97.5%)	Valor Predictivo Positivo (IC 95%)	Valor Predictivo Negativo (IC 95%)	Likelihood Ratio Positivo (IC 95%)	Likelihood Ratio Negative (IC 95%)
MDR-TB	1 (0.897-1)	100% (91.5-100%)	100% (98.2-100%)	1 (0.93-1.00)	1 (0.985-1.00)	NC (60.937-NC)	0 (0-0.071)
Rifampin Resistance	1 (0.897-1)	100% (91.5-100%)	100% (98.2-100%)	1 (0.93-1.00)	1 (0.985-1.00)	NC (60.937-NC)	0 (0-0.071)
Isoniazid Resistance	0.97 (0.855-0.969)	100% (90.4-100%)	99.0% (96.8-98.9%)	0.95 (0.874-0.951)	1 (0.982-1.00)	90 (32.082-90)	0 (0-0.083)

Table Performance of the GenoType MTBDRplus assay using

Conclusions: GenoType MTBDRplus is a rapid and reliable drug susceptibility test for clinical samples, offering a means for selecting effective treatment regimens for patients with MDR-TB in Lima. Further work is needed to identify barriers to large-scale use of this test in programmatic settings.

PD-656-12 Drug susceptibility of rifampin-resistant tuberculosis using whole genome sequencing to identify genes of interest in Pune, India

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Background: India has the world's largest tuberculosis (TB) burden. Recent expansion of molecular drug susceptibility testing (DST) is revealing more drug resistance than previously identified. In many parts of India, resistance to second-line drugs needs further study. We performed whole genome sequencing (WGS) to evaluate the frequency of resistance mutations found among rifampin-resistant isolates from Pune, India, a city of 7 million people.

Methods: Samples were collected at a public hospital in Pune, India. Pulmonary TB patients provided spot and morning sputum samples for Xpert MTB/RIF, culture, and phenotypic DST. Samples with positive or indeterminate rpoB mutation results were included and were analyzed by patient. Phenotypic DST was performed for isoniazid, rifampin, ethambutol, and streptomycin. Raw WGS data were submitted to an analytic pipeline using BWA aligner, GATK, and snpEff to generate annotated variant call files. Identified variants were compared to genes of interest reported from the ReSeqTB Data Platform. Analysis was duplicated by Mykrobe predictor software.

Results: From 2015-2016, 104 participants met inclusion criteria, and 32 had sufficient culture material for further analysis. Most were smear positive (84.4%), and all were culture positive, though 3 samples had insufficient growth for phenotypic DST. On average, WGS produced 8.6 million reads (5.1-31.2 million) per sample with 94.9% (77.0-98.5%) mapping to *M. tuberculosis.* This identified an average of 1,847 genetic variants per isolate. East Asian lineage was most common (40.6%) followed by Central Asian (31.3%). Phenotypic and genotypic tests for rifampin were concordant in 66.7% of cases. While injectable drug resistance was not identified, WGS frequently identified fluoroquinolone resistance among MDR-TB isolates (Table).

Diagnostic Modality	Rifampin	Isoniazid	Ethambutol	Streptomycin	Fluoroquinolones	Kanamycin, Amikacin, or Capreomycin	Pyrazinamide	MDR-TB	Pre-XDR TB
Xpert MTB/RIF	30 (93.8%, 2 samples rpoB mutation indeterminate)	-	-	-	-	-		-	
Liquid Culture DST	18 (62.1%)	20 (69.0%)	11 (37.9%)	17 (58.6%)	-	-	-	18 (62.1%)	-
Mutations Identified by Mykrobe Predictor	27 (84.4%)	25 (78.1%)	14 (43.8%)	17 (53.1%)	13 (40.6%)	0 (0%)	-	13 (40.6%)	11 (34.4%)
Mutations in Genes of Interest by ReSeqTB Data Platform	28 (87.5%)	26 (81.3%)	19 (59.4%)	18 (56.3%)	13 (40.6%)	0 (0%)	1 (3.1%)	13 (40.6%)	13 (40.6%)

Table TB Resistance Profiles by Diagnostic Modality

Conclusions: WGS for DST of resistant TB isolates in the Indian public sector identified high rates of fluoroquinolone resistance. DST using WGS and published genes of interest can be performed in India and may help guide treatment guidelines, particularly with respect to fluoroquinolones.

PD-657-12 Molecular characterization of pre XDR and XDR-TB at tertiary care center of New Delhi, India

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Background: For first-line drugs, molecular drug susceptibility testing (DST) like, GeneXpert and line probe assay (LPA) were used to diagnose MDR-TB. But solid culture based DST for second-line drugs are taken as gold standard to detect XDR-TB. This study was confined to estimate the prevalence of pre XDR-TB and XDR-TB and further, reconfirmation were done by using DNA sequencing.

Methods: Sputum specimens from MDR-TB suspects were collected at Intermediate Reference Laboratory, AIIMS, New Delhi during August, 2012 to March, 2014 and were subjected to Ziehl-Neelsen (ZN) staining followed by LPA. To find out pre XDR-TB and XDR-TB at base-line, conventional solid culture (Lowenstein-Jensen) DST was performed using aminoglycoside/cyclic peptide (amikacin, capreomycin, kanamycin) and ofloxacin (OFX) anti-TB drugs. DNA sequencing was performed targeting *gyrA*, *gyrB* and *rrs* genes.

Results: A total of 2815 sputum samples were screened by LPA. Among them, 405 (14.4%) MDR-TB strains were isolated and subjected to solid culture DST. Fourteen (3.4%) isolates were as XDR-TB, 84 (20.7%) OFX resistance and aminoglycoside/cyclic peptide resistance were found in 18 (4.4%). In *gyrA* gene region, most prominent single mutations were D94A (32%) and D94Y (28.6%). In case of *gyrB* gene, only one type of mutation (N499T) was observed in 2 (2.4%) strains. Overall, 99% of concordance was found with *gyrA* and *gyrB* genes in DNA sequencing with DST followed by 98% sensitivity and 94% specificity. In DNA sequencing, only one type of mutation was found in *rrs* gene (A1401G). Sensitivity and specificity were 100% and 85% with 89% of concordance with DST.

Conclusions: It was concluded that for the identification of MDR-TB, LPA was found to be highly accurate tool. But in case of XDR-TB, phenotypic DST was still taken as gold stander. In DNA sequencing *gyrA* and *gyrB* (fluoroquinolones) showed high sensitivity and specificity but *rrs* (aminoglycoside/cyclic peptide resistance) had low specificity.

PD-658-12 Evaluation of Xpert MTB/RIF assay for the diagnosis of tuberculosis and rifampicin resistance in pulmonary tuberculosis

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Background: Early and accurate detection of tuberculosis (TB) is a global priority for TB control. Since 2011, WHO has been recommending XPERT MTB/RIF test (Cepheid, USA), a molecular method for simultaneous and rapid detection of tuberculosis and rifampicin resistance. This test is fully automated method and based on the real-time polymerase chain reaction (rt-PCR) targeting the RRDR (Rifampicin Resistance Determining Region) section of the section of the spesific rproB gene.

Methods: This study was conducted in adults to determine the diagnostic effiviancy (sensitivity and spesificity) of XPERT MTB/RIF in pulmonary tuberculosis and

rifampicin resistance compared to other phenotypic-genotypic methods. We analysed 1309 speciments (1189 sputum and 120 bronchial lavages) which were investigated by pre-diagnosis of tuberculosis at Sureyyapasa Hospital from October 2015 to December 2016. The results of XPERT MTB/RIF assay were compared with the results of those obtained by culture [BACTEC MGIT 960 (Becton Dickonson, ABD) ve Löwenstein Jensen]

Results: The sensitivity, specificity, positive and negative predictive values of the Xpert MTB / RIF test were 90.63%, 91.72%, 89.25% and 92.81%, respectively for sputum. These values were calculated as 80.0%, 92.38%, 60.0% and 97.0% for bronchial lavages. The sensitivity and specificity were 95.75% and 61.90% for smear-positive sputum specimens; 83.09% and 92.67% for smear-negative sputum specimens, respectively. The GeneXpert MTB/RIF assay detected 4 RIF-resistant and 76 RIF-susceptible specimens for sputum, 1 RIF-resistant and 16 RIF-susceptible specimens for bronchial lavages. the results were confirmed by drug susceptibility tests (DST).

Conclusions: We concluded that the XPERT MTB/RIF is a useful assay for rapid diagnosis of tuberculosis, considering that the results can be given in the same day of sample collection. However to confirm the results by culture and DST is necessary to provide the best results for recovery of mycobacteria and rifampicin resistance.

PD-659-12 Diagnostic accuracy of Xpert® MTB/RIF assay in detection of *Mycobacterium tuberculosis* in extra-pulmonary samples

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Background: Diagnosis of extrapulmonary tuberculosis (EPTB) remains to be challenging due to low sensitivity of AFB Smears in non-respiratory specimens and the long duration needed for TB culture. The objective of this study is to determine the sensitivity and specificity of MTB Gene Xpert (Xpert) in diagnosing EPTB, and its concordance with the results of AFB smear microscopy, imaging and histopathology.

Methods: This is a diagnostic validity study which included 416 non respiratory specimens from paediatric and adult patients at Makati Medical Center from February 2015 to August 2016. These specimens were tested for Xpert, and were compared with culture, AFB smear, imaging and histopathology.

Results: Majority of samples (25%) were pleural fluid specimen. Results revealed low over-all sensitivity at 65 %, but high specificity 97% for Xpert MTB detection in non-respiratory specimens. Sensitivity was highest with abscess samples at 75%. There was low sensitivity for sterile fluids and tissue samples at 67% and 57%, respectively. In comparison with other TB diagnostics, it revealed a good concordance with histopathology tests

at 61% to 71% for abscesses and tissue samples respectively. On the other hand, Xpert had poor to fair concordance with AFB and imaging.

Conclusions: Xpert is a better tool than smear and imaging in diagnosing EPTB, considering its rapid technology of simultaneous detection of M. tuberculosis and resistance to Rif. It is a reliable rule-in tool for EPTB, but has limitations in ruling out the disease.

PD-660-12 Ethical considerations and data governance for the ReSeqTB data platform

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Background and challenges to implementation: The TB Relational Sequencing Data Platform (ReSeqTB) is a first-of-its-kind platform providing standardized, quality assured, globally representative data on *Mycobacterium tuberculosis* (*Mtb)* drug resistance. Data contributions are sought from various sectors globally: academia, government, non-profit, clinical laboratories, clinical trial sponsors, and countries undertaking drug resistance surveys. Essential to the success of ReSeqTB is a robust data governance policy that addresses the ethical concerns of data contributors and meets international standards of research involving human subjects, with attendant security and privacy protections, and data quality and integrity assurance.

Intervention or response: In order to address ethics-related concerns pertaining to the privacy and confidentiality of data subjects, data ownership and control, fair access and use of data, and fair sharing of benefits arising form the creation and use of the platform, the ReSeqTB Collaborative Partnership aimed to develop a data governance policy that would be responsive to these issues. Specifically, the Collaborative Partnership i) proactively identified potential ethical issues and engaged with stakeholders; and ii) took a principle-based approach to developing the data governance and access policy.

Results and lessons learnt: A principle-based approach to data governance is critically important for anchoring policy that must be responsive to complex ethical issues, including concerns of justice and equity between sectors and stakeholders in high-income countries (HICs) and low-and-middle-income countries (LMICs).

Conclusions and key recommendations: Balancing the need to share data to make progress in global health while respecting the interests of data subjects and data

contributors presents a tension that is not easily reconciled. Addressing salient ethical issues and committing to a principled approach to data governance is an important first step in reconciling this tension.

PD-661-12 An incremental cost-effectiveness analysis of the second Xpert® MTB/RIF assay for detecting *Mycobacterium tuberculosis* and rifampicin resistance

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Background: Due to the inhomogeneity of specimens collected from tuberculosis (TB) patients, repeated Xpert MTB/RIF tests can have potential clinical benefits. Therefore, the incremental cost-effectiveness was analyzed for the second Xpert MTB/RIF test to detect *Mycobacterium tuberculosis* and rifampicin (RIF) resistance.

Methods: Specimens were collected from 1461 suspected TB patients, who underwent more than one Xpert assay within one week. The specimens were subjected to smear, culture, Xpert MTB/RIF assays and drug susceptibility testing. An incremental cost-effectiveness analysis of the serial Xpert MTB/RIF was evaluated.

Results: Among the total 813 Xpert-positive TB suspects, 755 (92.87%) were identified by the first Xpert MTB/RIF assay whereas the additional 58 (7.13%) cases were identified by the second assay. The second Xpert MTB/RIF assay had higher incremental yield for smear-negative specimens than for smear-positive specimens (12.07% vs 1.84%, $P < 0.001$).

Additional 8 (5.52%) RIF resistant cases were identified by a second assay.. The cost-effectiveness analysis showed that the incremental cost of performing a second test is huge: US$17.25 vs US$353.62 and US$26.48 vs US$220.67 for PTB and EPTB respectively at the UNITAID negotiated price.

Conclusions: The second Xpert MTB/RIF assay improved the TB detection, but with an increased cost.

PD-662-12 Role of next generation sequencing in tuberculosis diagnostics: resolving the clinical dilemma of discrepancies in laboratory findings

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Background: Next generation sequencing (NGS) is seldom used for diagnosis of tuberculosis (TB). Occasionally, follow-up samples from patients with drug-resistant (DR) TB laboratory results shows dis-

crepancies with initial findings complicating management of these patients. NGS has the potential to provide rapid and comprehensive answers in such cases.

Methods: DNA was isolated from each of three patients on two occasions. NGS was performed with an Illumina MiSeq platform (UFS). NGS were processed using the KvarQ bioinformatics interface with pre-compiled "testsuites" for rapid detection of DR mutations and spoligotypes. Isolates included two samples (the initial and follow-up sample) from a child (case 1) treated for multidrug resistant (MDR) TB and two from the presumptive maternal index case, diagnosed with MDR-TB. The follow-up sample from the child at five months, was found to be drug susceptible (DS) TB. The other two samples were from a child (case 2) with MDR-TB diagnosed in September 2015 who responded well to treatment with negative sputum results for five months. However, the follow-up sample cultured positive, presenting a challenge for ongoing treatment.

Results: NGS results found concordance of DR mutations and a Latin America-Mediteranean (LAM) lineage from the grandmother (case 1) and the first sample from the child. The second sample from the child indicated a fully susceptible strain from the Beijing lineage. Similarly, in case 2 the follow-up sample indicated a Beijing lineage compared to a LAM and completely different mutations consistent with an extremely resistant strain. Results confirmed possible re-infection.

Conclusions: NGS and analysis with pre-compiled "testsuites" for KvarQ software are rapid techniques which can assist in resolving challenging cases.

ABSTRACT PRESENTATIONS
FRIDAY
13 OCTOBER 2017

ORAL ABSTRACT SESSIONS

07. Active TB case finding and retrieving missing cases: engagement of community volunteers, civil society, pharmacists and other stakeholders

OA-145-13 Enhancing active case finding among people living in the slums of Delhi, India: activity of project Axshya

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Background and challenges to implementation: Home to more than 18.6 million people Delhi is one of the world's fastest growing cities. From 16.7 million in 2011 the city's population has expanded with almost 2 million in just 5 years, and the population density of 29.259 people per square mile is one of the highest in the world[1]. It is estimated that 40 - 50% of Delhi's population resides in slums, adding a special challenge to TB control. Under the aegis of Project Axshya, the organisation Humana People to People India was engaged in Active Case Finding "Axshya Samvad" in selected slums in 9 districts of Delhi in May 2016.
[1] World Population Review
Intervention or response: Around 50 Axshya Mitras (community volunteers) were trained and deployed to conduct Active Case Finding. ACF was conducted and supervised following weekly detailed action-plans. The population residing in slum areas were verbally screened for TB symptoms during household visits, and people having symptoms were linked to the nearest government microscopy centres for sputum microscopy and chest x-ray.
Results and lessons learnt: From May'16 to Mar'17 approximately 1,653,200 people from 413,300 households were verbally screened for TB. 10,515 people were identified with TB symptoms and linked to nearby government microscopy centres for testing. 6,635 people were tested and yielded 705 TB cases of which 585 were bacteriologically confirmed at microscopy centres and 120 were diagnosed through x-ray. Constant monitoring and weekly follow up meetings with the Axshya Mitras resulted in a steady improvement in case finding. In June 2016 one TB case was found by the Axshya Mitras by visiting 2,402 HH and in March 2017 the number of HH per identified TB case was down to 302.
Conclusions and key recommendations: Case finding can be greatly enhanced through meticulous and systematic result analysis followed by corrective action and close supervision of the Axshya Mitras.

OA-146-13 Interventions led to improved contribution of community tuberculosis care to tuberculosis case notification in two regions of Ethiopia

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Background and challenges to implementation: Ethiopia is high tuberculosis (TB), TB/HIV and MDR-TB burden country with about a third of the estimated number of TB cases missed each year. In addition to TB case findings in clinical settings, the country implemented community TB care as part of a health extension program using health extension workers (HEWs). HEWs are front-line health workers who are stationed at community based health posts (HPs). They coordinate community-based health prevention and promotion services.
We present trends in the improvement of community based case finding to the overall TB case notification in Oromia and Amhara regions of Ethiopia.
Intervention or response: The National TB Program, with support from technical partners, designed a comprehensive package of interventions which encompassed developing national implementation guides, building the capacity of HEW coordinators and HEWs on community TB care, development and implementation of informational and education material and recording and reporting tools.
The referral linkage between health centers and HP was also strengthened through regular review meetings and supportive supervision.
Results and lessons learnt: The number of health posts detecting and referring presumptive TB cases increased from 812 in September 2012 to 7,040 as of June 2016. The proportion of TB cases from presumptive TB patients referred by HEW was 9.3 % (Range=3.5-28%). The contribution of community referrals to overall case finding increased steadily from 4.3% to 24%. Trend tests across the ordered percent of TB cases from community TB suspects over 11 quarters showed an increase in the trend (Z-test=2.48; p-value=0.013).

Conclusions and key recommendations: There is an increase in the trend of contribution of community TB care to overall TB case notification. More effort is needed to further strengthen the referral linkage of presumptive TB cases between the HPs and health facilities.

OA-147-13 Finding missing TB cases through outreach chest camps in peri-urban and rural areas of Pakistan

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Background and challenges to implementation: Pakistan is a high TB burden country. Around 68% of the population lives in rural area having limited or no access to information, diagnosis and treatment of TB services. The active case finding through conducting chest camps in the outreach is a strategy to identify and treat TB patients who would otherwise have been left undiagnosed and untreated. The intervention was carried out to see the yield of conventional chest camps conducted by Mercy Corps in 75 districts across Pakistan in 2016.

Intervention or response: In resource-limited settings, conventional outreach chest camps were implemented by involving private healthcare providers, lab technicians and volunteers from community. On-spot sputum samples are collected by project staff and morning samples are collected by volunteers. After getting the results patients are contacted and facilitated for registration at the nearest private healthcare provider. The camps sites are selected by mapping the areas based on available data from district. The chest camps are preceded by meeting with area notables and awareness raising community events to ensure maximum participation from community.

Results and lessons learnt: In year 2016, 442 camps were conducted and these were attended by 29,638 community members. 53% (n=15,594) out of these were males and 47% (n=14,044) were females. Involving the area notables increased the acceptability of men and women in the target community to access the service. A total of 1,079 all form TB cases were identified, diagnosed and registered, among these 57% were males and 43% were females. In both the genders, maximum number of cases registered were in the age group 15-49 years. Children under 14 years were 8%. The average yield per chest camps was 2.4 cases (range 0-14).

Conclusions and key recommendations: Chest camp is an effective case finding strategy and can help in finding the missing TB cases among the population having limited or no access to quality healthcare services.

OA-148-13 Bloggers' penetration to increase community awareness about tuberculosis

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Background and challenges to implementation: Indonesia has the highest number of media users in the world. According to 2015 data of the Association of the internet service provider, there were 139 millions internet users and 20 millions active bloggers in Indonesia . Most user's age between 15-45 years, which also is the age-group with the highest absolute number of TB cases in Indonesia. The results of the 2013/2014 TB prevalence survey regarding knowledge and attitude related to TB showed that most people knew tuberculosis symptoms and ways of transmission, but only a minority knew that TB treatment is free of charge in the public health care system.

Intervention or response: An invitation was sent to the blogger's community in Indonesia to participate in a blogger's competition with 8 subtopics such as TB drugs access, economic burden, stigma and discrimination. For the purpose of this competition, specific TB fact sheets were developed and posted in the Ministry of Health's website. Bloggers were facilitated to visit and to discuss with TB patients and health care workers. Bloggers posted and uploaded their writings or videos to their blogs, Facebook, Twitter, Youtube and other social media. In order to maintain the bloggers' engagement, annually, NTP conducts bloggers' workshops to provide them with the latest TB information.

Results and lessons learnt: A total of 279 bloggers from 26 out of 34 provinces became engaged with the TB program. These bloggers together published 579 articles about TB on social media, with more then 2.5 millions social media users exposed to TB issues within an eight weeks period.

Conclusions and key recommendations: Social media are effective in reaching millions of people in the age group most affected by TB. This competition provided the "proof of principle" that the bloggers community can be engaged to spread messages about TB. Further evaluation of this media intervention will help understand the level of its (potential) impact.

OA-149-13 Community pharmacists in the RNTCP enhanced TB detection and increased outreach of DOTS services in Durg District

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Background and challenges to implementation: Even as India aims to eliminate tuberculosis by 2025, un-notified cases continue to pose a major challenge along with multi-drug-resistance. India has the highest burden of TB in the world that accounts for majority of the 4.3 million GAP between incident and notified-TB-cases.

Despite being the frontline-health-care-providers and often a first-point-of-contact with the patients, *Indian Community Pharmacists* (ICP) are seen more as "drug sellers" than "health professionals". In spite of their large presence, ICPs potential has remained untapped and observed as missing link in TB control in the GAP-infected Durg district.

Intervention or response: RNTCP-Durg-District (RDD) intensely engaged the ICPs for early identification and referral of TB suspect for diagnosis, Directly Observed Treatment provision for TB patients, increasing community awareness about TB and MDR-TB, patient education and counselling, promoting rational use of Anti-TB drugs and contributing to preventing the emergence of drug-resistance by imparting tailor-made-training in line with the IPA-developed tool-kit to 543 of 713 present in the district during 2016-17.

RDD field staff regularly visited the IPCs and developed excellent working relationship with them. Patient feedback also indicated the convenience of treatment&comfort of DOT at pharmacies due to friendly relations with pharmacy&proximity to the homes.

Results and lessons learnt: Of 543 trained, 398 ICPs notified 2199 presumptive-TB-cases in 7 DMCs against 5768 sputum referrals. 89 gave DOTS to 256 TB-patients and 89 patients successfully-treated during Jun'16-until-Feb'17. A 7% increase in notification and 100% treatment-adherence recorded with >75% chemists community trained in the district. Around 20% cases were repeatedly-monitored.

Conclusions and key recommendations: ICPs played valuable role in fight-against-TB. This intervention evidenced increased trend in case detection & increased outreach of DOTS services for the community in the district. To scale-up, a structured initiative involving the IPCs will have huge potential to make significant impact in TB-Control. ICPs in RNTCP will be very useful for improving universal-access-to-TB-care for the TB patients.

OA-150-13 Contribution of active case finding strategy in tuberculosis case detection among selected facilities in Swaziland, Shiselweni region

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Background and challenges to implementation: Swaziland is one of the countries that are highly burdened with tuberculosis, with an incidence of 565/100 00 and a TB/HIV coinfection rate of 77 %. Passive case finding was the only intervention of detecting TB cases where TB is screened at health facilities at all entry points. A progressive decline of case detection was noted in the country from 2010. The active case finding strategy was introduced to scale up case detection by screening for tuberculosis in the communities to identify missed cases. The purpose of this study is to understand the proportion of TB cases mobilized through active case finding strategy in selected facilities in Swaziland, Shiselweni region.

Intervention or response: Active case finders conduct door-to-door screening for tuberculosis in communities and those with symptoms, sputum samples are collected at homesteads and sent to the laboratory. Simultaneously, contacts of index cases are also traced and screened for TB and if found to be presumptive, sputum samples are collected and if bacteriological confirmed they are linked to the health facilities for treatment. Presumptive cases who cannot expectorate are referred to the health facilities for further management. A physical count of ACF mobilized patients was done from July 2016 to February 2017 in 10 randomly selected health facilities out of 28 facilities in the region.

Results and lessons learnt: A total of 177 tuberculosis patients were recorded in the 10 selected facilities. Among these 59 (33%) were identified through the active case finding strategy.

Conclusions and key recommendations: The active case finding strategy has contributed 33% of TB cases that could have been missed using the passive case finding strategy since its inception from July 2016.

OA-151-13 Complementing the biomedical approach with patient-led active case finding: large-scale intervention in the Democratic Republic of Congo

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Background: Each year in DRC, it is estimated that 156.000 patients with TB infection do not reach the health system or remain undiagnosed despite seeking care.

In 2013, TB patients and TB-affected communities of the South-Kivu province of DRC created a non-profit organisation called "Ambassadeurs de Lutte contre la Tuberculose". The objective of this organisation is to tackle the burden of TB disease in their households and communities by accelerating the detection and treatment of patients with TB disease.

Between 2014 and 2016, TB-affected volunteers performed active case-finding activities.

The screening algorithm apllied in this study consisted in providing a microscopy test to patients coughing for more than 15 days.

Methods: The aim of our study was to evaluate the quality of the active case-finding intervention by assessing:

(1) Their ability to identify symptomatic patients in their community,

(2) Their ability to convince symptomatic patients to get tested for TB and;

(3) Their ability to detect new TB cases.

Results: In total, over 650.000 individuals were screened and the intervention contributed to the detection of 4.300 new smear positive pulmonary TB cases, representing 42% of the provincial notification during this period. The intervention allowed to increase the number of smear positive pulmonary TB cases diagnosed per quarter and per health facility (p=0.006). Furthermore, the screeners tended to improve their ability to detect new TB cases (mean of 0.71 per quarter and per screener, with a trend of +117% over 3 years ; p=0,0051).

Conclusions: This large-scale intervention allowed to demonstrate the feasibility and utility of active case-finding activities performed by TB-affected populations. Improving the clinical skills and the laboratory performance of the health system should allow to improve further the impact of this strategy.

OA-152-13 Tuberculosis contact investigation contributes over 5-fold to total cases notified in Kampala

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Background and challenges to implementation: Like the rest of the World, Kampala city, Uganda is facing a declining tuberculosis (TB) case notification. This is contrary to the findings of the just concluded national TB prevalence survey. TB contact investigation is one of the key WHO strategies recommended for early identification of TB, although this was not systematically implemented in Kampala prior to January 2014.

Intervention or response: To increase TB case notification, Kampala Capital City Authority and AIDs information center through support from USAID-funded Track TB project facilitated community linkage facilitators (CLFs) to trace, screen, and link contacts of infectious TB patients for TB investigation at the nearest TB diagnostic facility. The CLFs were trained in the process of systematic TB contact investigation. They were equipped with TB screening enablers like the National TB and Leprosy Program's intensified case finding forms, contact tracing registers, and safe sputum collection items. Through visits to patients' homes, each CLF contact traced at most 13 new and continuing patients every month from January 2015 to December 2016 in Kampala. The team met monthly to review their performance. We present the contribution of TB contact investigation to the total TB cases notified in two years.

Results and lessons learnt: A general declining trend in the number of TB cases notified was still observed but the contribution of contact tracing was noticed to progressively increase to a cumulative total of 583 cases over two years. This decline might have been higher if this intervention was not implemented with a higher risk of TB transmission in the community.
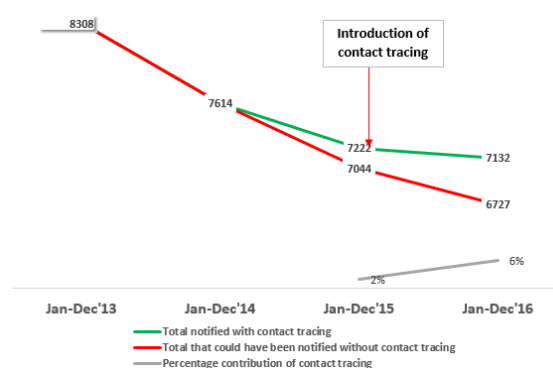
Figure Contact tracing contribution to TB case notification in Kampala 2014-2015

Conclusions and key recommendations: Overall, contact investigation improved TB case notification by 8% although this did not match the overall decline of 14% in the total numbers notified during the observed period. We recommend strengthened TB contact investigation in Kampala for early identification of TB and improvement of TB case notification.

08. State of the art - updates on childhood TB and lung health

OA-153-13 Improved treatment outcomes in HIV-positive adolescents with TB compared to adults in Kenya

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Background: Among adolescents in Kenya, HIV incidence and mortality are increasing. The contribution of tuberculosis (TB) to HIV mortality among adolescents is not well described; limited data suggest co-infected adolescents have worse TB treatment outcomes than adults. We assessed these differences among HIV positive adolescents versus adults in Kenya.

Methods: We performed a retrospective cohort analysis of all adolescent (10-19 years old) and adult (age >19 years) HIV/TB cases in Kenya from 2012 to 2015. Data were abstracted from the national electronic data recording system and analyzed using Stata 12.1. WHO guidelines defined TB cases and treatment outcomes. Cases without documented treatment outcomes were excluded. Analyses included descriptive statistics, frequencies, and multinomial logistic regression models comparing the risk of various treatment outcomes between adolescents and adults.

Results: A total of 5,811 adolescent and 113,177 adult HIV/TB cases were analyzed. Median age was 14 years (IQR 12-17 years) for adolescents and 36 years (IQR 30-43) for adults. Adolescents were majority female (53.3%) while adults were majority male (50.9%) (p=0.00). Adolescents were more likely to be on ART (92.2% vs. 89.7%, p=0.00).

Treatment outcomes were recorded for 5602 adolescents (96.4%) and 109,086 adults (96.4%). After adjusting for confounders in the logistic regression model, adolescents had decreased risk of mortality (8.6% vs. 10.4%, RR 0.80, 95% CI 0.73-0.88, p=0.00) and LTFU (6.8% vs. 8.1%, RR 0.85, 95% CI 0.76-0.94, p=0.00) compared to adults. Treatment success was more likely among adolescents (84.3% vs. 81.0%, RR 1.04, 95% CI .03-1.05, p=0.00). There was a trend toward decreased risk of treatment failure (0.3% vs. 0.5%, RR 0.71, 95% CI 0.43-1.15, p=0.16) for adolescents.

Conclusions: In Kenya, HIV/TB co-infected adolescents have improved outcomes compared to adults, counter to prior studies. However, absolute adolescent mortality and LTFU rates remain high, highlighting the need for further investigation into factors influencing these outcomes.

OA-154-13 Childhood multidrug-resistant tuberculosis in the European Union and European Economic Area

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Background: Confirming tuberculosis (TB) in children and obtaining information on the drug susceptibility pattern is challenging but essential to ensure adequate treatment of children with TB. We assessed whether there are gaps in diagnosis and treatment of MDR TB in children in the European Union and European Economic Area (EU/EEA) countries and we aimed to quantify the burden of MDR TB in children and characterise cases.

Methods: We analysed 2007-2015 EU/EEA TB surveillance data for paediatric cases (< 15 years of age).

Results: In the period 2007-2015, 18,826 paediatric TB cases were reported by the 26 EU/EEA countries included in this study. Among paediatric TB cases, 4,129 (21.9%) were laboratory-confirmed. Drug susceptibility testing results were available for 3,378 (17.9%), representing 81.8% of confirmed cases in children. The majority (N=2,967; 87.8%) had drug-sensitive TB, 249 (7.4%) mono-resistant TB, 64 (1.9%) poly-resistant TB, 90 (2.7%) multidrug-resistant (MDR) TB (excl. extensively drug-resistant (XDR) TB), and 8 (0.2%) were diagnosed with XDR TB. MDR TB was more frequently reported among paediatric cases with foreign background [adjusted odds ratio (aOR) 1.73; 95% confidence interval (CI95%) 1.12-2.67] and with previous TB treatment (aOR 6.42; CI95% 3.24-12.75). A successful treatment outcome was reported for 58 (78.4%) of 74 paediatric MDR TB cases with outcome reported from 2007 to 2013. Only the age group 5-9 years was significantly associated with unsuccessful treatment outcome in paediatric MDR TB (OR 11.45; CI95% 1.24-106.04).

Conclusions: The burden of MDR TB in children in the EU/EEA appears relatively low, but may be underestimated due to challenges in laboratory confirmation. Improvements in laboratory diagnosis of paediatric TB are needed for early detection and adequate treatment of MDR TB. Children previously treated for TB and children of foreign origin may warrant a higher index of diagnostic awareness regarding MDR TB.

OA-155-13 Pharmacokinetics of rifampicin in African children: evaluation of the new WHO dosing guidelines

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Background: Rifampicin is a key component of anti-tuberculosis first-line treatment. Following reports of low rifampicin concentrations in children, WHO increased dosing recommendations by 50%, from 10 to 20 mg/kg daily. We aimed to evaluate these revised dosing guidelines.

Methods: Rifampicin plasma concentrations were measured in 161 South African and Malawian children (age 3 months to 12 years). On a single visit during the second month of treatment, children were sampled 4 to 6 times, once just before the observed administration of 10-20 mg/kg rifampicin, and at 1, 2, 4, 6, 8, and/or 10 hours thereafter. A pharmacokinetic model was developed in NONMEM exploring the effect of body size and age.

Results: A one-compartment disposition model with hepatic elimination of rifampicin described the data well. After adjusting for the effect of weight with allometric scaling, the model characterised the effect of age on the maturation of the metabolic pathways responsible for the clearance of rifampicin, which reaches half of its mature level at 6 months of age, and is nearly complete at age 2 years. One of the two rifampicin formulations used had reduced bioavailability by 60%, yielding critically low concentrations. Even after excluding these patients (n=53), bioavailability was reduced by 20% amongst the 46 children under 2 years. This could be due to the administration of rifampicin via naso-gastric tube in most (n=36) of these children. In the entire cohort, median Cmax was < 6 mg/L, below the recommended target concentration of 8 mg/L.

Conclusions: In spite of the recommended dose increase to 20 mg/kg, median Cmax rifampicin concentrations in young African children was still below the recommended target concentration. Further investigation needs to define the causes leading to low bioavailability in the youngest children. Our findings also highlight the importance of efforts to test and guarantee the quality of drug formulations.

OA-156-13 Hypoxaemia and the use of pulse oximetry and oxygen in Nigerian hospitals: preliminary results from a multi-country field trial

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Background: Oxygen is a life-saving essential medicine that is important for pneumonia, and many other paediatric and neonatal conditions, but remains poorly available to patients globally. Our study aimed to understand how oxygen therapy is used in resource-limited hospitals, and determine whether the children who need oxygen actually get it.

Methods: We enrolled 12 secondary-level hospitals in Nigeria into a field trial to improve oxygen therapy for children. Trained clinical data collectors identified and extracted data from case-notes for the period January 2014 to January 2016. We extracted demographic data, and clinical data on signs and symptoms, diagnoses, and treatment (including pulse oximetry and oxygen use). Trained data nurses and data entry clerks checked and entered the data, according to a data management protocol. We analysed the data using Stata to determine the current prevalence of hypoxaemia and the appropriateness of oxygen use. This study was conducted as part of a stepped-wedge field trial to improve oxygen therapy for children in hospitals that involved a comprehensive oxygen package (including the introduction of pulse oximetry and reliable oxygen access).

Results: We analysed 3 years of clinical data from 12 secondary-level hospitals in Nigeria, including over 35,000 admissions (approximately one-third neonatal). At baseline, pulse oximetry use was poor, most children with signs of hypoxaemia did not received oxygen therapy, and one-third of children who received oxygen therapy had no documented clinical indication for it. Following the introduction of pulse oximetry, more children received oxygen, and oxygen was used more appropriately. We describe the epidemiology of hypoxaemia in children and neonates admitted to participating hospitals.

Conclusions: Hypoxaemia is common in pneumonia and many other paediatric conditions. Pulse oximetry use can improve the use of oxygen therapy for children.

OA-157-13 Feasibility, safety and tolerability of nasopharyngeal aspirates and string tests for diagnosis of TB with Xpert® MTB/RIF in HIV-infected children: ANRS 12229 PAANTHER 01 study

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Background: Xpert MTB/RIF is recommended for tuberculosis diagnosis in HIV-infected children but capacity to collect appropriate microbiological samples remains limited. We evaluated alternative specimen collection methods: nasopharyngeal aspirate (NPA) and string test (ST).

Methods: HIV-infected children aged≤13 years with presumptive tuberculosis underwent specimen collection: NPA, ST if aged ≥4 years, and 2 to 3 gastric aspirate (GA), or sputum if aged ≥10 years. Samples were tested with Xpert MTB/RIF. Nurses collected adverse events AEs and assessed tolerability of NPA, GA, and ST using the FLACC behavioral scale (discomfort/distress/pain graded from 0: none to 10: worst). We compared feasibility, safety and tolerability of NPA, first GA, and ST.

Results: 426 children - median age 7.2 (IQR:3.4- 9.7) years, 50% male - were sampled. Nurses collected 79/97 (81.4%) planned first sputum, 416/426 (97.7%) NPA, 325/329 (98.8%) GA, 229/300 (76.3%) ST. Xpert was positive in 28/403 (7.0%) NPA, 20/321 (6.2%) GA, 13/215 (6.1%) ST, and 6/71 (8.5%) sputa. AEs were reported in 145/414 (35.0%) NPA [(vomiting (5.8%) and bloody sample (31.2%)], 84/350 (24.0%) first GA [vomiting (10.6%) and local trauma (15.1%)], and 17/227 (7.5%) ST [vomiting (7.5%)]. GA caused less AEs than NPA (p<0.001) if considering bloody samples. GA caused more vomiting than NPA (p=0.016). Median FLACC scores were 5.0 (IQR:3.0-8.0) for NPA, 5.0 (IQR:3.0-8.0) for GA, and 1.0 (IQR:0.0-3.0) for ST. ST was better tolerated than GA (p=0.001) and NPA (p<0.001), NPA was better tolerated than GA (p<0.001).

Conclusions: Despite its better tolerability and safety, ST has a poorer feasibility and lower yield than both GA and NPA. NPA which can be performed in ambulatory has a very satisfactory yield with Xpert and is better tolerated than GA despite the occurrence of mild adverse events. With good supervision and guidelines to reduce AEs, NPA could be used in a decentralized pediatric diagnosis approach.

OA-158-13 HIV-infected children with antiretroviral therapy from infancy have lung function comparable to population norms

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Background: Late diagnosed and treated HIV-infected children have high risk of lung function abnormalities. Lung function in children with antiretroviral therapy (ART) from infancy (early-treated) has not been characterized.

Methods: HIV-infected children initiated ART at age ≤12 months in Nairobi (2007-2009) and were followed until 2017. Spirometry was performed according to American Thoracic Society standards. Forced expiratory volume at 1 second (FEV_1) and forced vital capacity (FVC) z-scores were calculated using Global Lung Initiative 2012 reference equations. Obstruction was defined as FEV_1:FVC z-score < -1.64. Reduced FVC was defined as FVC z-score < 1.64 with FEV_1:FVC ≥1.64. Linear regression and rank sum tests were used to evaluate cofactors for lower FEV_1 and FVC.

Results: Among 40 children, median age at ART initiation was 5.0 months and 22 (58%) children were underweight (weight-for-age z-score < -2). Children were median 8.5 years old at spirometry and median FEV_1 and FVC z-scores were -0.07 (Interquartile range (IQR), (-0.61, 0.78) and 0.13 (IQR, -0.40, 0.71), respectively. Five children (13%) had abnormal lung function (3 with obstructed lung function and 2 with reduced FVC). Children who were underweight vs well-nourished prior to initiation of ART had lower FEV_1 (medians, -0.33 vs 0.52, respectively, P=0.02) and FVC (medians, -0.07 vs 0.56, respectively, P=0.05). Results were similar using linear regression. ART plasma HIV RNA level and CD4 T cell percentage prior to ART initiation were not associated with FEV_1 or FVC (all P-values >0.4).

Conclusions: Early-treated children had spirometric scores comparable to population norms; however a substantial proportion (13%) had evidence of abnormal lung function. Undernutrition prior to ART may compromise lung function in spite of early treatment.

OA-159-13 The World Health Organization´s symptom-based screening approach for child contacts: a prospective validation from sub-Saharan Africa

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Background: Current tuberculosis control interventions lack the ability to effectively identify diseased children. A symptom-based screening approach has been proposed by the World Health Organization to increase case detection however, usefulness of this algorithm in sub-Saharan Africa is unclear.

Methods: This was a prospective cohort study of newly diagnosed adult tuberculosis patients and their child household contacts in Uganda. Field workers administered an extensive questionnaire to all cases and contacts including information on tuberculosis symptoms. Microbiological testing was performed on all child contacts < 5 years of age and HIV-seropositive contacts to derive smear and culture test results while clinical, HIV, tuberculin skin test, and lung cavitation disease evaluations were performed on all contacts. Child cases were diagnosed through a sputum smear or culture positive test or clinically. To evaluate the algorithm, we calculated the number needed to screen (NNS) to detect a tuberculosis case in child contacts with any symptom compared to those with no symptoms.

Results: 1212 household contacts were enrolled, of which, 65(4.6%) had tuberculosis disease at baseline and 9 (0.8%) developed tuberculosis over two-year follow-up. The likelihood of coprevalent disease was highly correlated with increasing number of symptoms ($P_{trend} < 0.001$). The NNS to detect one coprevalent child case was 6.7 among those with ≥1 symptom and 111.1 among contacts with no symptoms. The NNS to detect one incident case among those with ≥1 symptom and no symptoms was 45.5 and 333.3, respectively. Screening only symptomatic contacts detected 85.7% of all coprevalent cases and 66.7% of all incident cases. Of all diagnosed cases, 42 (64.6%) were microbiologically confirmed with either a smear or culture positive test result.

Conclusions: The World Health Organization´s symptom-based algorithm was highly efficient and detected substantially more cases than those with no symptoms. If implemented in sub-Saharan Africa, this algorithm may substantially improve child tuberculosis case detection.

09. MDR-TB treatment: pharmacovigilance and adverse event outcomes from the field

OA-160-13 Setting up an active pharmacovigilance system for the endTB project

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Background: Active pharmacovigilance (PV) is a new expectation for tuberculosis programmes since bedaquiline and delamanid received conditional regulatory approvals. Deliberate, systematic safety reporting is recommended for patients receiving: multidrug-resistant TB (MDR-TB) treatments with these agents; novel regimens; and extensively-drug resistant TB treatments. Although adverse event (AE) reporting and management are not new for MDR-TB projects, the lack of standard definitions and reporting systems rendered analysis and signal detection difficult.

Methods: endTB, launched with the support of UNIT AID in April 2015, will treat 2,600 patients in 15 countries with bedaquiline and/or delamanid. endTB contributed to the creation of a central PV unit (PVU). Standard procedures, collection forms, severity grading scale and guidelines were developed. While all AEs of clinical significance are followed, the PVU focuses on serious AEs (SAEs), drug-exposed pregnancies, and medication errors. Training started from October 2015.

Results: endTB PVU has trained >100 endTB and national TB program physicians/nurses in 15 countries. Between 01-Apr-2015 and 31-Mar-2017, the PVU has received 211 individual safety reports on 199 bedaquiline/delamanid patients. All reports are entered into a central PV database and assessed to determine drug-AE causality. A board of MDR-TB/PV experts reviewed unexpected SAEs potentially related to ≥1 TB drug(s) to detect safety signals. The experts identified risks, issued recommendations to clinicians and ultimately improved patient management. Quarterly analyses are shared with countries. Cumulative analyses completed the observations on individual cases and allowed for broader communication on patient safety.

Conclusions: Organizing PV for MDR-TB is possible. It requires continuous training to ensure consistent data quality and sustained collection at the sites. Use of a central PVU demands coordination and systematic safety follow-up in multiple countries while facilitating signal detection. Collaboration with national drug safety monitoring and management systems is key to interpretation of this novel 'post-marketing' reporting for MDR-TB treatment.
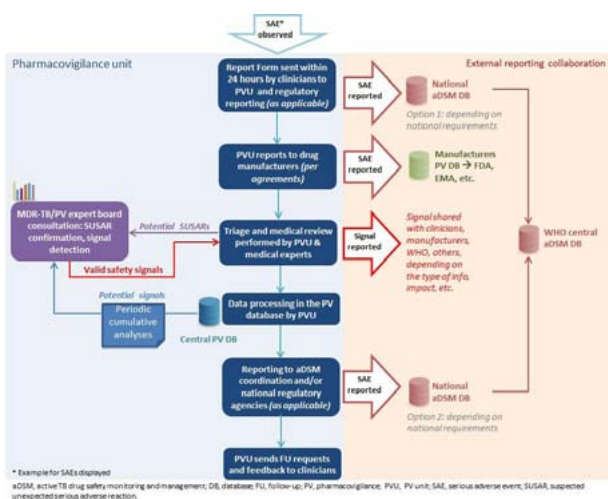
Figure Flow of safety data processing in endTB

OA-161-13 Long-term safety and outcomes of prolonged delamanid treatment for MDR-TB: a cohort from Latvia and France

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Background: Delamanid is currently recommended for the treatment of multidrug-resistant tuberculosis (MDR-TB) for a standardised duration of 24 weeks, and no published data exist on the safety and outcomes of longer treatment courses.

Methods: A multicentre cohort was established including consecutive patients starting MDR-TB treatment including delamanid in Riga, Latvia, and at three referral hospitals in the Paris region, France.

Results: Overall, 30 patients were included, 20 in Latvia and 10 in France. Median age was 36 years (interquartile range (IQR): 25-55), including 2 paediatric cases of 4 and 11 years. Fourteen (47%) had XDR-TB. Seventeen (57%) were previously treated for TB. The strains were resistant to a median of 8 drugs. All patients had pulmonary TB, 19 (63%) had cavitary and 19 (63%) bilateral disease. Six (20%) were HCV-positive and 2 (7%) HIV-positive. The most commonly prescribed drugs were linezolid (70%), cycloserine (70%), and moxifloxacin (50%). Eleven patients (37%) received both delamanid and bedaquiline, 6 as concomitant treat-

ment, and 5 sequentially without (or with incomplete) washout. Overall, 19 patients (63%) received more than 24 weeks of delamanid; median duration of delamanid treatment was 275 days. Adverse event and serious adverse event occurred in 28 (93%) and 7 (23%) patients. QTcF>500ms values were recorded in 2 patients (7%). No arrhythmias nor symptomatic cardiac side effects occurred. Delamanid was discontinued in 1 patient who developed adrenal failure. Out of 22 patients with positive sputum culture at treatment initiation, 9 (41%) and 19 (86%) achieved conversion after 2 and 6 months of treatment, respectively, with a median time-to-culture conversion of 80 days (IQR: 45-118). Currently, 24 patients have a treatment outcome: 20 (83%) cured and 4 (17%) lost to follow-up; the other 6 patients are still on treatment (median 21 months).

Conclusions: MDR-TB regimens including long-term delamanid treatment were safe and effective in this cohort.

OA-162-13 Adverse events over 6 months with delamanid in a programmatic setting in Khayelitsha, South Africa

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Background: Delamanid (DLM) was recommended by the World Health Organization in 2014 for inclusion in rifampicin resistant (RR-TB) treatment. Clinical trials have shown DLM to be relatively safe, with mild QTc prolongation. We aimed to describe all adverse events (AEs) recorded over 24 weeks among patients initiating DLM in a primary care setting in Khayelitsha, South Africa.

Methods: We included patients initiating DLM between November 2015 and September 2016 and described all AEs routinely reported among those with a 24-week follow-up period post-DLM initiation. We used the endTB pharmacovigilance guidelines to categorise AEs and assess severity.

Results: Forty eight patients (36 [75%] HIV infected, 32 [89%] on ART) received DLM. Ten did not complete 24 weeks: three died at 2, 6, 8 weeks post-DLM initiation (none DLM-related); two transferred at 4 and 14 weeks and two were lost from treatment at 4 and 6 weeks; one switched from DLM to bedaquiline after 5 weeks; one had second-line TB treatment withdrawn after one week; one was discharged (cured) after receiving DLM for the final 19 weeks of RR-TB treatment. Of 38 patients who completed 24 weeks DLM, 33 (87%) experienced at least one new or worsening AE; 201 AEs in total (Table 1). Only 42/201 (21%) AEs were at least 'possibly' related to DLM, among 22 patients.

Eleven (6%) AEs among 8 patients were considered 'serious'; 6/11 were at least 'possibly' related to DLM - 5 of these were QTcB prolongation >500ms and led to temporary DLM withdrawal but not permanent discontinuation over 24 weeks.

Adverse Event	Gastro-intestinal disorders	Musculo-skeletal disorders	General disorders (head-ache, pain, malaise, fatigue)	Blood che-mistry disor-ders	Cardio-vascular disorders (incl. QT interval prolon-gation)	Neuro-logical dis-orders	Skin disor-ders	Miscell-aneous (<7 AEs per cate-gory)	Grand Totals
Frequency: number (%)	39 (20%)	24 (12%)	21 (10%)	16 (8%)	16 (8%)	15 (7%)	13 (5%)	57 (28%)	201 (100%)
Number of events grade 3 or 4 severity	0	1	1	0	5	2	0	8	17 (9%)
Number of events considered 'serious'	0	0	1	0	5	1	0	4	11 (6%)
Number possibly related to DLM but not excluding other drugs	14	0	9	0	15	0	0	4	42 (21%)

Table Adverse events among RR-TB patients on delamanid

Conclusions: Although most people receiving 24 weeks of DLM experienced an AE, >80% were likely due to factors or drugs other than DLM, and serious adverse events were rare. This suggests clinically stable patients on DLM can feasibly be managed in in primary care settings.

OA-163-13 Safety of multidrug-resistant tuberculosis treatment amongst patients receiving bedaquiline in a compassionate use programme in Armenia and Georgia

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Background: WHO initial policy recommendations on bedaquiline use considered the undesirable anticipated effects of bedaquiline as large. These concerns have recently been downgraded to moderate due to reduced mortality amongst patients receiving bedaquiline found in a multicentric analysis. We aim to describe the frequency and types of adverse events in patients receiving bedaquiline through compassionate use (CU).
Methods: We retrospectively analysed from patients receiving bedaquiline in Armenia and Georgia between April 2013 and April 2015. Serious adverse events (SAE)

were: any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or resulted in significant disability or congenital defect. Other non-serious adverse events (AEs) were recorded in a standardised database.
Results: Of the 82 MDRTB patients who received bedaquiline the majority had difficult to treat forms of MDRTB: 84.2% resistant to fluoroquinolones, 86.6% cavities on Xray and all previously treated with second-line drugs. Other drugs included at treatment initiation in the individually designed bedaquiline containing regimens included linezolid (100%), Clofazimine (82.9%) and imipenem (75.6%). At least one AE was reported for 79.3% (65/82) of patients, with a median time to first AE of 1.9 months [Interquartile range: 0.6-3.6]. The most frequent AEs were gastrointestinal symptoms (26.7%), hepatotoxicity (15.3%) and peripheral neuropathy (11%). ECG measurements of QT interval corrected with Fridericia formula (QTcF)over 500msec occurred in 7 patients and did not lead to permanent interruption of bedaquiline.
A total of 19 SAEs were reported in 14 patients. Of these, 10/14 patients had fatal outcomes: 6/10 related to advanced TB (6), 2/10 assessed as possibly related to Bdq, and 6/10 related to other TB drugs.
Conclusions: Safety data of patients receiving bedaquiline under compassionate use did not show any unexpected adverse event. Most fatal SAE were related to severe TB. QTcF prolongation was not a safety concern in this cohort.

OA-164-13 Risk factors for developing hypothyroidism among MDR-TB patients receiving Eto and/or PAS in Maputo, Mozambique

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Background: Thyrotoxicity is a common adverse event in patients treated for multi-drug resistant tuberculosis (MDR-TB) and it is associated with the treatment that includes ethionamid (Eto), prothionamid (Pto) and/or para-aminosalicylic acid (PAS). The aim of this study was to determine the incidence of and risk factors associated with hypothyroidism during MDR-TB treatment.
Methods: A retrospective analysis of patients' data from Chamanculo district Maputo, Mozambique starting on MDR-TB treatment from March 2011 to February 2017 was performed. Patients were in standard 24 months treatment program. Hypothyroidism was defined as a thyroid stimulating hormone (TSH) level ≥ 10 mIU/L. Cox proportional hazards model was used to analyse risk factors associated with hypothyroidism.
Results: A total of 213 patients receiving Eto and/or PAS

were included in the analysis. Their median age was 32 years [IQR: 25-42], 85 (40%) were female, 132 (62%) were HIV co-infected and 37 (17%) had XDR-TB (extensively drug resistant TB). The median time spent on treatment was 16.1 months [IQR: 13.3-23.2], where 78 (37%) of patients are still undergoing treatment. The incidence rate of hypothyroidism was 2.2 (95% CI: 1.6-2.6) cases per 100 person-months (57 patients, 27%). The median time to hypothyroidism onset was 4.4 months [IQR: 3-7.7]. The multivariate Cox model showed that men co-infected with HIV had increased risk of developing hypothyroidism (aHR= 2.73; 95% CI, 1.23-6.07).

Conclusions: We confirm that hypothyroidism is a common adverse event in patients treated with Eto and/or PAS, particularly among HIV co-infected men. Moreover, the quarter of the patients with hypothyroidism developed it in the first trimester of treatment. Therefore, the testing of TSH levels should be performed regularly starting at 2 months of treatment until 12 months, and after it could be done less frequently. Specific focus should be put on HIV patients, particularly men.

OA-165-13 Aminoglycoside-induced hearing loss: a profile of HIV-positive and HIV-negative drug-resistant tuberculosis patients in Kwa-Zulu Natal, South Africa

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Background: WHO (2015) reported South Africa to have one of the highest prevalence of HIV/AIDS, 60% - 80% of all TB cases are co-infected. The treatment regimen for MDR-TB infected patients includes the use of second line aminoglycosides which can result in ototoxicity and permanent hearing loss. According to the WHO report (2016) 85% of HIV patients in South Africa are on antiretroviral therapy and a significant portion of these patients were co-infected with TB or Drug-Resistant TB strand. Therefore, this study aimed to evaluate the impact of multiple use of drugs in the management of HIV and DR-TB and to determine whether HIV-positive patients were more likely to develop drug-related hearing loss than HIV negative patients.

Methods: The study used a descriptive retrospective record review design of 277 audiometric records of patients from Doris Goodwin TB Hospital in South Africa. Who were initiated on MDR-TB treatment during September 2015 to September 2016.

Results: We reviewed 277 patient records, 160 males,117 females and the median age was 36 years. 56% (154) new TB cases, 40% (110) of patients were previously treated with SLD. 96% (268) had received Kanamycin, 3% (9)

patients were on Capreomycin. Of the 277 83% (230) were HIV-positive and on ART. 94% (217/230) of patients developed an ototoxic threshold shift from initial audiogram (≥ 10dB decrease at any 2 adjacent frequencies) within 14 days of SLD therapy. 82% (189) of patients presented with moderate to severe sensorineural hearing loss, whilst 17% (8/47) of HIV-negative patients developed an ototoxic threshold within 6 weeks of SLD therapy.

Conclusions: HIV-positive patients are more likely to develop hearing loss than HIV-negative patients. The use of Isoniazid preventive therapy as a standard measure of care in HIV-positive patients will aid in the reduction of active TB/MDR-TB transmission in our communities, thereby decreasing the incidence of MDR-TB.

OA-166-13 Addressing the under-reporting of adverse drug reactions to accelerate the elimination of drug-resistant tuberculosis

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Background and challenges to implementation: Adverse drug reactions (ADRs) deaccelerate the elimination of drug resistant tuberculosis (DRTB) by compromising treatment outcomes and promoting patient's dropout from treatment programmes. Prompt reporting of ADRs to regulatory authorities enhances withdrawal of suspected drugs and prevents ADRs but under-reporting is a major problem world-wide. In 12 years (2004-2016), only 16500 completed ADR Forms out of 80,000 Forms were reported to NAFDAC (National Agency for Food and Drug Administration and Control) by all the healthcare providers in Nigeria. This abstract describes the model we designed to curtail the crisis.

Intervention or response: The "Structured Pharmacovigilance and Training Initiative" (SPHAR-TI) model, is a 10 month course based on a World Health Organization accredited operational research course. We applied six principles: a six day workshop for doctors, nurses and pharmacists from the six geopolitical regions of Nigeria; mobilized resources; monitored, evaluated and provided feedbacks to the participants; set up a reporting system; provided leadership and collaborated with the government.

Results and lessons learnt: Participants significantly gained knowledge after the workshop [mean pre vs post tests = 20.4 **Vs** 27.8 (P< 0.001)]; post SPHART-I's submission of completed ADR Forms was very high (3000 completed ADR Forms vs 805 completed ADR Forms). In addition, the 55 participants that were trained cas-

caded the training to 2937 healthcare workers and activated 46 pharmacovigilance committees in only seven months.

The main outcome is the SPHAR-TI model - government adopted and applied the model to train 600 healthcare workers from ten states in Nigeria. We learned a major lesson: training alone is not sufficient to increase the reporting of ADRs in a resourced limited setting. All the SPHAR-TI's principles must be combined to significantly address the challenge of under-reporting of ADRs.

Conclusions and key recommendations: The SPHAR-TI's model significantly increased the reporting of ADRs. We recommend the model for developing countries with high burden of TB.

OA-167-13 Psychiatric comorbidity among drug-resistant tuberculosis patients

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Background: Management of drug-resistant tuberculosis (DR-TB) is highly challenging. Comorbidities such as psychiatric disorders further complicate patient management. The objective of this study was to determine the burden of psychiatric comorbidities in DR-TB patients enrolled in a Médecins Sans Frontières (MSF) HIV/TB clinic in Mumbai, India.

Methods: This was a retrospective cohort study of DR-TB patients (with or without HIV co-infection) initiated on treatment during 2012-2016. The programme included a multidisciplinary team of counselors, psychologists and a consultant psychiatrist. All patients underwent psychological assessment at baseline and were followed up during subsequent visits to the clinic.

Results: Among a total of 226 DR-TB patients (48% females), 88(40%) were HIV co-infected. Median age was 28 years (Inter-Quartile Range [IQR]: 21-40). Ninety (40%) and 79 (35%) had pre-extensively and extensively DR-TB respectively. All patients were seen by a counselor and 123(54%) were referred to a psychologist. Sixty-nine (31%) needed a psychiatric consultation and 55(24%) were diagnosed with psychiatric disorders. Twenty-eight (51%) were diagnosed with depressive disorders, 13(24%) with anxiety disorders and 8(15%) with psychosis.

Median time to referral from treatment initiation was 3.5 months (IQR: 2.1-10) for depressive disorders, while it was 4.3 months (IQR: 1.7-9.3) for anxiety disorders. Drug-induced psychiatric adverse events were relatively uncommon in this cohort - four (out of 170) had cycloserine-associated psychosis (all HIV-negative). HIV status was not significantly associated with psychiatric

conditions (RR: 0.87; 95%CI: 0.5-1.3). Having a psychiatric morbidity was not seen to affect DR-TB treatment outcome in the cohort (RR: 0.82; 95%CI: 0.5-1.4).

Conclusions: The burden of psychiatric disorders among DR-TB patients was high in the cohort. A comprehensive mental health component, including access to specialized psychiatric care, should be integrated into programmes caring for DR-TB patients.

12. Stopping TB transmission: infection control in congregate settings

OA-168-13 Novel approaches to TB infection control in private general hospitals in Georgia

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Background and challenges to implementation: Tuberculosis (TB) is believed to spread most efficiently in congregate settings such as hospitals, prisons and refugee camps mostly not from known TB patients on effective treatment, but from persons with unsuspected TB and this transmission is a driving force for global TB epidemic. FAST strategy - Find cases Actively by cough surveillance and rapid molecular sputum testing, Separate safely, and Treat effectively - was developed within USAID TB Care II as an innovative approach to control this transmission.

Intervention or response: USAID Georgia Tuberculosis Prevention Project (TPP) in collaboration with National Center for Disease Control and Public Health (NCDCPH) piloted the FAST in two general hospitals. After initial assessment, two GeneXpert machines were installed in private clinics - Tbilisi "New Hospital", and Rustavi Central Clinic. The FAST protocol and job aids were developed. Training was conducted for physicians and nurses working at outpatient departments.

Results and lessons learnt: Active cough surveillance at an entry point and immediate access to GeneXpert testing were key interventions of the FAST algorithm in Georgia. Since November 2015, 1565 unsuspected TB patients were tested with GeneXpert. Twelve percent (188 patients) of tested were confirmed with TB. Thirty five patients (2%) were found with Rifampicin Resistance. Mechanisms were established for reporting test results to National TB Program to ensure immediate initiation of effective treatment. This experience showed that general hospitals are at increased risk of TB transmission unless active TB case finding is in place

targeted at patients with cough and chronic lung conditions. NCDCPH decided to roll out the FAST in high volume district hospitals for country wide coverage.

Conclusions and key recommendations: The FAST, as an effective strategy for preventing nosocomial transmission of TB, should be considered as a basic safety standard and incorporated into the national quality framework for all public and private hospitals through licensing or certification.

OA-169-13 Evaluation of tuberculosis infection control strategies in the University of the Philippines - Philippine General Hospital

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Background: Nosocomial TB transmission adversely affects inpatients and healthcare workers (HCWs). HCWs have a higher risk of tuberculosis and MDR-TB. Nosocomial TB outbreaks have occurred among patients with HIV/AIDS. Hospitals need to evaluate TB infection control in order to address this growing concern. This descriptive study aimed to evaluate the current TB infection control strategies in the adult wards of the Philippine General Hospital (PGH), a tertiary public hospital.

Methods: We included inpatients with bacteriologically-confirmed PTB admitted in April-August 2016 and reviewed their charts. Baseline characteristics, diagnosis, treatment, and isolation intervals were obtained and compared between different areas. TB infection control practices were reviewed using the CDC TB Risk Assessment Worksheet, with data from TB-DOTS, U.P. Health Service, Hospital Infection Control Unit, and Department of Laboratories.

Results: Of the 72 inpatient charts included, majority were Medicine patients (55.6%) with chronic cough (61.1%) and diagnosed with Pneumonia (52.8%). Only 61.1% were PTB suspects on admission. The mean diagnosis interval was 5.82 days±5.473, the mean treatment interval was 0.77 days±2.941, and the mean isolation interval was 8.23 days±6.372. Only 41.7% were successfully isolated. The most common reasons for isolation failure/delay are lack of vacancy (ER, Medicine wards) and lack of isolation room (Surgical wards). Treatment initiation rate was 66.7%. TB-DOTS inpatient referral rate was 55.6%. The hospital is classified as having potential ongoing PTB transmission.

Conclusions: Treatment was promptly started but there were delays in diagnosis and isolation. Gaps include lack of recognition of a PTB case, limited isolation rooms, and inadequate TB-DOTS utilization. Given that the hospital is also an HIV treatment hub and a cancer center, there is an urgent need to have a higher index of suspicion for TB, implement a rapid notification system from the laboratory to the HCWs, add isolation rooms, improve isolation standards, and increase TB-DOTS referrals.

OA-170-13 FAST strategy to prevent TB and diabetes co-morbidity and prevent TB transmission in congregate settings

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Background and challenges to implementation: The association between Diabetes Mellitus (DM) and Tuberculosis (TB) and their synergistic role in causing human disease has been recognized for centuries. Individuals with diabetes have a significantly increased risk of active TB, which is two to three times higher than in individuals without diabetes. The implementation of FAST (Finding TB cases Actively, Separating safely and Treating effectively) in Diabetic Hospitals could greatly reduce the transmission of TB in congregate settings through early diagnosis of TB/DR TB.

Intervention or response: BIRDEM is the largest Diabetic hospital in Bangladesh, seeing about 1,000 diabetic patients on a daily basis. The FAST strategy has been implemented in the hospital since 2015. TB screening questions are incorporated in the diabetes screening tool. All of the patients visiting outpatient department are screened, presumptive TB patients are separated instantly and their sputum undergoes GeneXpert testing.

Results and lessons learnt: From July 2015 to June 2016, out of 38,513 diabetic patients screened for TB, a total of 1,425 presumptive TB patients were identified. Among those patients, 182 (13%) and 11 (0.7%) were identified as TB and MDR-TB cases respectively. Therefore, a total of 193 (13.5%) patients who would not have otherwise been identified and transmitting the disease were diagnosed and initiated on therapy for TB or MDR-TB.

Conclusions and key recommendations: The implementation of the FAST strategy has demonstrated that minimal systemic alterations to the approaches can greatly expedite and improve the care of TB-DM co-morbidity. Through simple facility-based policy changes, active screening for presumptive TB cases, infected TB and MDR-TB patients were identified and put on effective therapy, thereby potentially minimizing the spread of TB in the healthcare facility setting.

OA-171-13 Impact of a regional tuberculosis infection control pilot initiative, Dire Dawa, Ethiopia, Nov 2015-Nov 2016

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Background and challenges to implementation: Ethiopia is among the 30 high-burden countries for TB, TB/HIV and MDR-TB. Ethiopia began systematic implementation of TB Infection Control (TB-IC) in 2009. In 2014, only 34% of facilities had TB-IC plan; 80% had a delegated focal person or IC committee, but most committees were inactive.

Intervention or response: A TB-IC demonstration project entitled 'Building and Strengthening Infection Control Strategies (TB-BASICS) was launched at 10 public health facilities in Dire Dawa Administration from November 2015 - November 2016. Project interventions included skills-based TB-IC training, structured facility assessments, and supportive mentoring by regional health officials. A 45-item tool was used to assess the status of TB-IC measures in outpatient departments (OPDs) and TB Clinics at baseline, 6 and 12 months. Assessment findings were used to guide facility-specific TB-IC plans and quality improvement efforts. TB-IC performance was summarized using a color-coded dashboard (Figure) and compared using a composite score based on the implementation status of each measure (0=none; 1=partial; 2= full).

Results and lessons learnt: Over the 1-year period, implementation of facility-level administrative measures (i.e., designated focal point, IC Plan, staff TB screening, N95 policy, tracking system for TB suspects) increased from 45.9% at baseline to 97.2% at month-12 (p< .001). In general OPDs, implementation of administrative measures (triage, separation, cough etiquette, designated sputum collection area) increased (68.8% to 76.7%, p=.09) as did environmental (adequate ventilation, open widows, crowding) measures (64.2% to 89%, p<.001), and personal protective equipment (PPE) (16% to 63.3%, p< .001). In TB Clinics, improved implementation of administrative (70.5% to 90.6%, p< .001) and environmental (76.7% to 97.8%, p< .001) measures and PPE (48.8% to 91.1%, p< .001) also was documented.

Conclusions and key recommendations: In this regional initiative, the TB-BASICS approach was associated with measurable and significant improvements in TB-IC practices across facilities and clinical areas and should be considered for broader, including national, scale up.

OA-172-13 Survey on knowledge and use of ultraviolet germicidal air disinfection among tuberculosis nurses in China

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Background: China has one of the highest numbers of tuberculosis (TB) and multidrug-resistant TB (MDR-TB) cases globally. This study aimed to understand the knowledge and the use of germicidal ultraviolet (GUV) air disinfection among tuberculosis nurses to provide evidence to develop effective tuberculosis infection control.

Methods: TB nurses working in 26 hospitals in 20 provinces across China were asked to complete a survey to assess their knowledge of germicidal UV (GUV) air disinfection. Data were analyzed using SPSS 19.0 by the methods of descriptive analysis.

Results: Three hundred ninety-six nurses working in TB wards responded to the survey. The average knowledge score of GUV was 64.5% (±14.03). The nurses had the least knowledge on the correct level of radiation, usage time, and installation (appropriate number for the space and appropriate height). There were statistically significant differences in the knowledge score between different ages, working years, working years in TB, and positions （P< 0.05). In terms of practices, 88.4% of TB wards measure the radiation intensity at least every six months, 66.7% of TB wards measure the microorganisms in the air every month, 22.7% of TB nurses replace UV lamps correctly, and 72.2% of TB nurses clean the UV lamps every week.

Conclusions: The overall germicidal ultraviolet air disinfection knowledge among TB nurses in China is weak. Medical institutions should strengthen the training and education for nurses, especially focusing on new nurses. We should strengthen the management and evaluation of germicidal ultraviolet air disinfection, to reduce the risk of transmission of TB and MDR-TB in hospitals.

OA-173-13 How fast does FAST strategy increase case detection: a facility case study in Osun, Nigeria

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Background: In light of the high burden of TB in Nigeria and the urgency to improve case notification, innovative strategies to case finding are highly needed. The USAID funded Challenge TB project led by KNCV introduced FAST strategy at Obafemi Awolowo University teaching

hospital in Osun, Nigeria. The strategy aims at stopping TB spread in healthcare setting and contribute to increased case detection.

Methods: A high volume TB and HIV tertiary care facility. Mapping and advocacy to priority service units were performed. Sensitization, establishment of FAST coordination teams and appointment of cough monitors at every service delivery points were carried out. Daily cough surveillance was commenced across all outpatient and inpatient departments in October 2016. GeneXpert MTB/ RIF assay was used for detection of TB. Data review and analysis was done for 3 months between October 2015 and October to December 2016 to measure increase in detection of TB and impact of FAST strategy to case notification.

Results: Between October and December 2016, 226 samples were collected and analyzed out of which 50 were diagnosed positive and were put on DOTS. This amounts to 37.8% increase in presumptive TB (n=164) and 66.7% increase in TB cases (n=30) detected compared to the period July-September 2016; and 88.3% and 35.1% increase compared to the same period (October-December) in 2015. The proportion of bacteriologically confirmed TB among all TB cases detected was 74.0% (37/50) for the 3-month period October-December 2016, 60.0% (18/30) for July-September 2016, and 64.9% (24/37) for October-December 2015. Almost 6.0% were children compared to 0% and 2% in July-September 2016 and October-December respectively.

Conclusions: FAST strategy improved TB case detection rapidly in the health facility. There is need to scale-up this strategy to all high volume TB and HIV healthcare facilities in Nigeria to improve overall TB case-finding in the country.

OA-174-13 Hospital-based cough officer and 24 hours in a tuberculosis laboratory: acceptability and feasibility study, Beira Central Hospital, Mozambique

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Background: Having available routine and urgent tuberculosis (TB) exams and a cough officer have been pointed out to be effective and feasible in other settings and known to improve detection of pulmonar TB. We aimed to assess the acceptability and feasibility of having a TB laboratory working 24 hours and hospital-based cough officer at Beira Central Hospital, Mozambique.

Methods: In-depth interviews were carried out with 3 decision-makers, 7 managers and 5 medical doctors. Four focus group discussions (FGDs) were held with 9

TB laboratory (lab) technicians, 10 nurses, 10 female and 10 male hospital support staff. Audio-record and notes were taken during interviews and FGDs. The transcripts were coded using an inductive approach and content analysis was performed.

Results: The participants pointed out that the current policy on the TB lab operating time is one of the main obstacles that contributes to the delay in the diagnosis and treatment of TB. Due to the scarcity of human resources, cough officer duties should be performed by trained support staff and should not be only ward-based but also be available on the site where suspected TB patient are admitted to (emergence room-based) in order to expedite early detection, treatment and isolation of confirmed TB patients.

Conclusions: Having an available cough officer and TB lab working 24 hours per day was considered by the interviewers to be acceptable, feasible, and urgently needed. For early detection, initiation of proper TB treatment and protection of health care workers from tuberculosis, health authorities in resource-constrained countries, may need to adopt and promote acceptable, affordable and sustainable practices, such as expanding working hours of TB lab and making cough officers available.

OA-175-13 Molecular and spatial analysis of *Mycobacterium tuberculosis* transmission among internal migrants and residents in Shanghai, China

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Background: Massive internal migration of individuals from higher TB prevalence rural areas to lower TB prevalence urban areas has been associated with increasing TB notifications in urban areas of China. It is not yet understood what role migrants may play in the transmission dynamics of M. tuberculosis in these urban areas. We sought to combine pathogen genetic and spatial data to better describe the transmission of tuberculosis in an urban setting experiencing rapid population growth as a result of migration.

Methods: We collected a single pre-treatment isolate from each culture positive tuberculosis patient in Songjiang district, Shanghai from 2009-15. We used MIRU-VNTR genotyping profiles to identify pathogen clusters that may signal transmission of M. *tuberculosis* within and between migrants and residents. We used spatial scan statistics and regression approaches to understand the role of individual-factors and spatial-location on risk of genetically clustered TB.

Results: From 2009-15, the migrant population in Songjiang increased from 0.6 to 1.1 million and TB notifications increased from 520 to 730 /year. 1620 M. tuberculosis isolates were included in this analysis. 75% (1211/1620) were obtained from migrants, the majority of whom had moved to Shanghai from rural provinces in central and western China. 504 (31%) isolates were genetically clustered; in total, there were 192 genotypic clusters with size ranging from 2-13 patients. 33% of these clusters involved both migrants and residents, indicating possible transmission links between residents and migrants. We detected substantial heterogeneity in the spatial patterns of genotypic clusters, but several of these clusters exhibited significant spatial aggregation, consistent with the possibility of local transmission.

Conclusions: The influx of migrants to Shanghai has been associated with a substantial increase in TB notifications. Use of molecular and spatial data can shed light on the local transmission dynamics and can inform the design of more effective local responses to the epidemic.

13. Multi-country experiences in tobacco industry interference in tobacco control

OA-176-13 Monitoreo de la política de impuestos al cigarrillo en Colombia

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Background and challenges to implementation: La reforma tributaria de 2016 en Colombia triplicó el impuesto específico al consumo de cigarrillos, siendo un avance significativo en el desarrollo del CMCT. Sin embargo, el precio del cigarrillo en Colombia continúa por debajo del promedio de la región, por lo que es necesario crear el entorno para nuevos aumentos. En Colombia, las asimetrías de información causadas por la ausencia de monitoreo del mercado de cigarrillos son un factor que obstaculiza el aumento de impuestos, y que puede poner en peligro el logro en impuesto específico. También ha hecho que las áreas del gobierno relacionadas con el impuesto no estén familiarizadas con la información que se requiere para su diseño, y que la información disponible sea difícil de obtener. Además, ha impedido la atribución de responsabilidades a los actores de los que depende la gestión del impuesto. Todo esto ha sido utilizado por la industria tabacalera para posicionar sus propias estadísticas y argumentos en contra de los impuestos.

Intervention or response: Identificar y diseñar los indicadores necesarios para un adecuado monitoreo de la política de impuestos, sus fuentes y las oportunidades de mejora en la gestión de la información. Esto con el fin de promover un entorno propicio a la gestión del impuesto basada en resultados que involucre a las áreas del gobierno cuyo desempeño es crítico para lograr una adecuada implementación.

Results and lessons learnt: La información disponible en Colombia permite construir un monitoreo básico del mercado de cigarrillos. No obstante, se requiere avanzar en buenas prácticas de gestión de la información, y en estudios sobre la evolución del contrabando y del portafolio y canales de distribución.

Tema	Indicadores	Fuentes	Observaciones
Demanda	1. Prevalencia mes 2. Gasto en cigarrillos en los hogares (en $ y como proporción del gasto) 3. Prevalencia en mujeres embarazadas 4. Participación de los lugares de compra 5. Recaudo (valor y en volumen) 6. Asequibilidad	1. Encuesta de Consumo de Sustancias Psicoactivas (ECSP), Encuesta de Calidad de Vida (ECV) 2. Encuesta de Calidad de Vida (ECV), Encuesta Nacional de Ingresos y Gastos (ENIG), Encuesta Nacional de Situacion Nutricional (ENSIN) 3. Encuesta Nacional de Demografia y Salud (ENDS) 4. Estudio de Medición de Contrabando (EMC) 5.Recaudo de IVA (DIAN), Recaudo de impuesto al consumo (Federacion de Departamentos - FND), Sistema CHIP de la contraloría 6. Indicadores de gastos, Indicadores de precios, Encuesta de hogares DANE (salarios)	La ECSP no tiene regularidad en la aplicación, y los datos de ECV solo estarán disponibles a partir de 2017. ENIG desactualizada, última información de 2008 (no refleja cambios estructurales en el mercado de cigarrillos). La ENSIN no recoge la información de tabaquismo de manera apropiada. La ECV solo tiene gasto en 2010 y 2011, sujetos a subreporte porque la unidad de información es el hogar.ENDS Se realiza cada 5 años. Mujeres embarazadas son un porcentaje muy bajo de la población fumadora.DIAN reporta bimestralmente; procedimiento transparente de acceso a la información. CHIP (sistema de información de Contraloría); Reportes trimestrales detallados en línea de libre acceso; cuentas del impuesto al consumo de tabaco tienen problemas esporádicos de inconsistencia. DIAN y CHIP solo reportan valor. Asequibilidad: Este indicador se puede construir a partir de otros indicadores mencionados en esta lista y debería ser uno de los criterios principales para definir futuros aumentos del impuesto.
Oferta	1. Producción nacional de cigarrillos (valor y número de cajetillas estandarizadas 20 unidades) 2. Exportaciones e importaciones de cigarrillos (nivel y crecimiento en US$ y en volumen) 3. Consumo aparente de cigarrillos 4. Ventas del sector de producción de cigarrillos y de producción de hoja de tabaco 5. Empleo del sector de producción de cigarrillos y de producción de hoja de tabaco 6. Margen de comercializacion bruto 7. Decomisos	1, 3 y 5. Encuesta Anual Manufacturera (EAM), Muestra Mensual Manufacturera (MMM) (DANE) 2. Estadísticas de comercio exterior del DANE 4. EAM, MMM, DIAN (Formularios de reporte IVA), Superintendencia de Sociedades (estados financieros anuales de tabacaleras) 6. IPC, IPP (DANE), estudios cualitativos de la cadena de distribución, encuestas de precios por marca/canal/formato 7. Reportes de Policía Fiscal y Aduanera y DIAN (Valor a precios de mercado y número de cajetillas incautadas)	En importaciones es necesario monitorear el valor, volumen, país de origen, precios implícitos. EAM Sujeto a restricciones de acceso a información por reserva estadística de la actividad económica CIIU 1200. Los registros con más frecuencia de producción son los del IVA; reportan valor y no volumen. La EAM ofrece más información pero además de la restricción de acceso, los datos anuales tienen un rezago de 2 años. Decomisos: El reporte no incluye detalle por marca, pero es posible hacer consultas internas al sistema de información.
Precios	1. Indice de Precios al Consumidor (IPC) de cigarrillo 2. Precios al menudeo	1. DANE. Producción mensual. El componente de cigarrillos incluye múltiples canales 2. No existen registros oficiales. Estudio Fundación Anáas sobre precios por marca (exploratorio). Reporte descentralizado de precios.	Es necesario revisar la ponderación por canales de distribución porque hay nueva evidencia que indica que grandes superficies solo representa 6% de las compras. Es necesario diseñar e implementar una encuesta de precios que recoja la información sobretodo en los canales informales. También explorar la posibilidad de una herramienta que permita recoger información de precios de manera descentralizada (por ejemplo, una app).
Estimaciones	1. Elasticidad precio de la demanda 2. Elasticidad ingreso de la demanda 3. Penetración de Cigarrillo de Contrabando	1 y 2. Estimaciones de Fundación Anáas (resultados publicados). 3. EMC	La medición de penetración requiere una encuesta que se realice de manera periódica. El estudio de Anáas 2016 ofrece un punto de partida metodológico.

Table Indicadores, fuentes y brechas de información

Conclusions and key recommendations: Desde el punto de vista de la planeación, el sistema de monitoreo debería articularse con los indicadores de seguimiento de ODS que actualmente son responsabilidad de la Comisión para el cumplimiento de la Agenda 2030.

OA-177-13 4°encuesta de conductas y opinion de las habitantes de la Ciudad de Buenos Aires

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Background: La Ciudad de Buenos Aires (CABA) cuenta con 4millones de habitantes y 11millones si aconsideramos el Area Metropolitana. La CABA tiene gran influencia sobre el resto del pais.

Se reaizaron cuatro encuestas telefonicas para seguimiento de las conductas y actitudes con respecto al cigarrillo de sus habitantes.

Methods: Se realizo una encuesta telefonica a mayores de 18 años. habitantes de la CABA, los dias 6 a 9 de marzo. Sobre 1503 casos , con nivel de significacion de 95,4,%, error 2,54% . diseño muestral probabilistico con selección de unidad final al azar simple.

Results: Si bien la prevalencia de tabaquista da similar al estudio previo , se observa un aumento de la tendencia a reclamar si alguien fuma en espacios en donde esta prohibido.

Se obtuvo una primera prevalencia de consumo de e-cig, cercana al 7%. En mayo2016 aumento el precio del cigarrillo en un 53%, esta es la primera encuesta que muestra la repercucion de este aumento: el 35% no cambia marca 24% fuma marca de menor valor, 22% fuma menos, el 9% ,(jovenes) utiliza cigarrillo para armar o sin impuestos y casi el 5% deja de fumar.Es importante que 78% acuerda con que no se fume en espacios abiertos cercanos a lugares de juego de niños.

Conclusions: La encuesta telefonica es una herramienta util y economica para realizar seguimiento de politicas publicas . Si bien disminuyo pocol a prevalencia nos encontramos con que mejoro la percepcion de la importancia de los ambientes libres de humo. Por otro lado el 22% y el 5% de los fumadores fume menos o dejo de fumar con el aumento del precio.El acuerdo con que se prohiba de fumar en los parques y plazas alrededor de los espacios de juegos sera un dato util para la promocion de legislacion al respecto.

OA-178-13 Distributional consequences of raising tobacco taxes: evidence from a recent tax reform in Argentina

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Background: The purpose of this study is to assess the impact on different socioeconomic groups of a recent change in cigarette taxes in Argentina. Excise tax rate on cigarettes was increased from 60% to 75% by Executive Order Number 626 on April 26th, 2016. As consequence, cigarette relative prices raised by 33,6% over a 10-month period, and sales fell by 6,1%.

Methods: We use microdata from the latest Consumer Expenditure Survey (ENGHO) that took place in 2012/2013 at the national level to analyze the welfare consequences of this shift. The ENGHO is a rich data set that kept track on personal consumer expenditure of 71.483 people over a week. We focused our analysis on 6.942 people who spent money on cigarettes over the period of reference.

Results: Consistent with previous evidence, we find that cigarette smoking is higher among low-income households and that the proportion of income spent on cigarettes fell since the previous Consumer Expenditure Survey in 2005. Our estimates suggest that the loss of consumer surplus as a percent of income caused by tax raise was largest for people in the bottom income quintile (1,39%), decreasing in absolute values from second to top income quintile: 0,93%, 0,79%, 0,67% and 0,47%.

Conclusions: Smoking rates in Argentina (25%) rank among the highest in Latin America. Even after the recent tax raise, health expenditures caused by smoking exceed excise tax collected on cigarettes. Since the latest raise on cigarette taxes will be included in a more comprehensive tax reform to be passed by Congress on 2018, these findings should be useful to guide compensating policies favoring low income groups. This could help gain political support and counteract possible arguments in the Senate, where political parties representing the interests of the tobacco industry and its allies such as tobacco growing regions remain strong.

OA-179-13 Tobacco excise as a potential source of local health financing in Indonesia

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Background: According to Excise Law, Tobacco Product is one of the three products that has been charged with excise in Indonesia. The first goals of excise tariff is to control its consumption. Tobacco product is also has inelastic demand because of its addictive nature. Smoking has been related as a preventable risk factor for non communicable diseases. If in the revenue side, tobacco excise is to control its consumption then in the expenditure side tobacco excise fund should be used for tobacco control in particular or public health in general.

Methods: The Objective of this paper is to explore the possibility of using tobacco excise revenue as potential source of health financing in Indonesia. Descriptive policies analysis using literature review of current government regulation is conducted by the researcher.

Results: There 2 kind of mechanisms that tobacco excise fund can be used for public health. The first mechanism is the 2% tobacco excise revenue sharing where 2% of tobacco excise revenue is shared with producing province and cities. This 2% tobacco excise revenue sharing has been implemented since 2008. There are 5 mandated allocation of this fund by local government which one of them is for social welfare including smoke free areas as a public health instrument. The second mechanism is 10% local cigarette tax where minimum 50% is dedicated for public health since 2014 for provincial and cities government unit. These 2 mechanisms are a potential source of fund in public health improvements especially in local areas.

Conclusions: The government of Indonesia has already have 2 mechanisms regarding tobacco tax for health financing. However, the challenge is that those funds are in local government unit. That´s why the GOI should provide regulation to assure that those is used for health financing effectively.

OA-196-13 Tracking investments by financial institutions in tobacco companies: what tobacco control advocates need to know and do about it

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Background and challenges to implementation: Roughly €3.7 trillion in assets and investments are managed by socially responsible investment (SRI) funds worldwide which motivate institutional investors to take a more stringent view on ethical investing. Ethical investing precludes not investing in tobacco industry or its stocks. Tobacco is a cross-cutting area where such investments are forbidden. Tracking investments made by governments and private financial investors in the tobacco sector can influence in mitigating the proliferation of the industry in the future.

Intervention or response: This research examines investments made by the largest private banks in the world during 2015-2016 including those which conform to Global SRI standards using customised, paid-for banking databases.

Results and lessons learnt: The analysis finds that 42 of the top 50 global bank invest and support tobacco industry domestically and in offshore projects.

Conclusions and key recommendations: Definition of socially responsible investments within the perspective of screening tobacco investments is perceived variably by financial institutions. Also in the absence of a watch-dog institution and few disincentives for truant behaviour, investors continue to invest tobacco companies. Tobacco control advocates need to monitor investments made by large lending banks and financial institutions in tobacco industry and ensure that banks which have committed to SRI codes conform to them.

OA-197-13 Observational survey to explore the situation of unregulated tobacco traders in Bangladesh

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Background and challenges to implementation: In Bangladesh, selling points of tobacco commodities adjacent to the education institutions and within the campus also creates an opportunities for the teenager students to be habituated in smoking. Hence, for saving the public health as per section 50 and schedule 2 of Local Government (Municipality) Act 2009 LGIs can play an important role to control these unregulated trading of tobacco commodities.

Intervention or response: Considering the above situation AID Foundation collected Data from five City Corporations and 22 districts in two divisions (Khulna and Dhaka) of Bangladesh. A total of 506 samples were selected purpose among the four type's targeted communities, Hawker, Tea Stall, Small and wholesales of unregulated tobacco trades. Besides that a total of 57 in-depth interview was conducted various type of local government authority and civil societies representative.
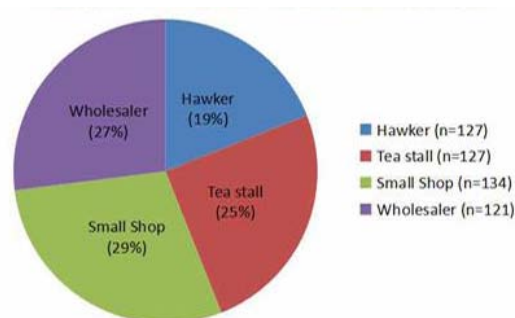
Figure An observation survey exploring the situation of unregulated tobacco traders in Bangladesh: Distribution of tobacco seller received gift from tobacco companies (%)

Results and lessons learnt: Majority of the unregulated tobacco traders did not have any legal permission to sell the tobacco commodities. 59.8% of the unregulated tobacco traders wanted to license to continue their business. They are also conscious (100%) about the harmful effect of tobacco. They have received different types promotional gifts like signboard, commission, point of sell box, T-shirt, umbrella, cookeries, cell phone set and TV etc. However, direct advertisement still banded by the existing TC law 2005.

Conclusions and key recommendations: The survey suggests that special efforts like apply strong law, licensing and alternative employment opportunity would be required to control unlawful trade and random selling of tobacco commodities.

OA-200-13 Use of tobacco in Brazilian reality shows: status and potential influence on low-income population

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Background: Favorable images on smoking in the media are pointed out as potential motivator of initiation to nicotine addiction. The objective of this study is to analyze the magnitude and characteristics of indirect advertising of tobacco insertion in Reality Shows of Brazilian open TV, with high audience, in low income population. **Methods:** A descriptive study, with content analysis of two Brazilian open TV, Reality Shows, broadcasted during the season of 2014. These were selected through an audience survey of the television programs for Rio de Janeiro's lower income classes, conducted by Brazilian Institute of Public Opinion and Statistics (IBOPE). Using Thumbs Up Thumbs Down (TUTD) method, from Breath California of Sacrament Emigrants Trails, tobacco appearances were encoded, where any occurrence of Tobacco on screen was considered an incident (real use, implied use, verbal or gestural messages or smoking atmosphere). Each episode was watched by 2 evaluators, independently. All analyzes were obtained using Stata software in version 12.0. To evaluate the inter-rater reliability, a Kappa statistics was used, with a minimum percentage of reliability of 0.8. **Results:** 165 episodes were analyzed (approximately 98 hours of programming). Of those, 73 presented incidents/messages related to Tobacco (44%), representing 46 minutes of exhibition. Of the programs, 29% had up to 5 incidents and parental advisory of 12 years. We observed 243 scenes with tobacco related incidents/messages, 100% of these had the appearance of cigarettes and 83%, with pro-tobacco messages. When evaluating messages associated with Tobacco scenes, the relation most quoted between them were Addiction/Habit (88%) and Sexy (73%). **Conclusions:** The presence of pro-tobacco messages in Brazilian Reality Shows are common. Thus, the more stringent is the control of Tobacco appearences on television, the better, since such programs are a significant source of exposure to indirect advertising tobacco images.

15. TB transmission: models, sequences and coordinates

OA-180-13 Whole gene sequencing and spatial data provides insight into the transmission of *Mycobacterium tuberculosis* in Eastern China

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Background: Tuberculosis (TB) is a chronic respiratory infectious disease caused by *Mycobacterium* TB (Mtb) and one of the most serious infectious diseases. While molecular epidemiology methods has increasingly become one of the commonly used methods to determine the recent transmission of TB, spatial epidemiological methods have made achievements in determining the regional endemic strains of genotypes, hotspots and the formation of the causes and drug-resistant TB spread and proliferation mechanism. **Methods:** We used hand-held GPS acquisition device to locate the resident address, public places often visited and medical facilities of the TB patients. Epidemiologic and genomic data were mapped on ArcGIS by means of interviews with patients to determine the origins and transmission dynamics of TB patients. Genomic DNA the isolates were sequenced by Illuminate technology, and paired-end reads were mapped to the reference genome H37Rv. We defined a genomic cluster as a group of strains that differed by no more than 10 SNPs.
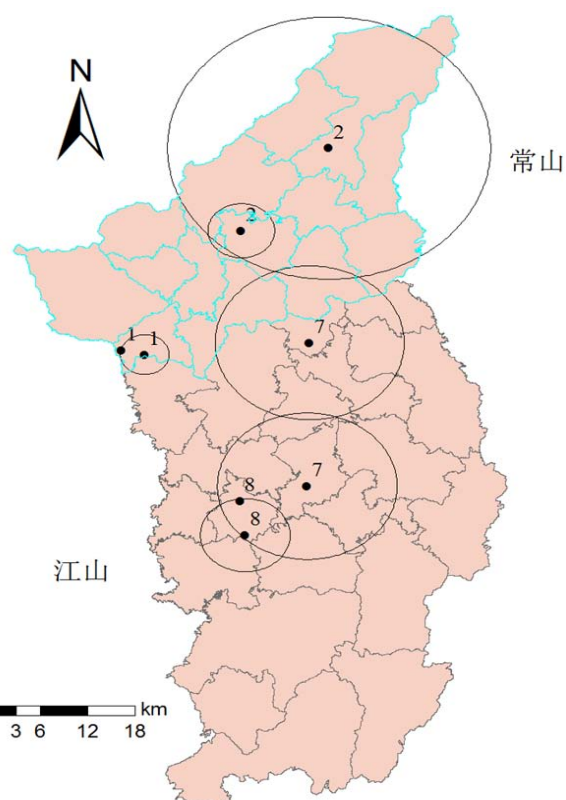
Figure The geographical locations of the clustered cases

Results: During the study period, 195 isolates were obtained from enrolled smear-positive TB patients. WGS genotyping identified 10 clusters consisted by 22 strains. Epidemiological links were confirmed in 7 (30.43%) strains. However, there was no obvious aggregation with the spatial distribution of patients in all clusters. Integration of spatial and phylogenetic analyses revealed several transmission events.

Conclusions: Through integration of bacterial WGS and GIS analysis, we show that residence distance may trigger the simultaneous expansion of some lineages of Mtb, but no those so-called "super-spreaders" can be identified in the settings of high TB prevalence and high BCG vaccination.

OA-181-13 Finding tuberculosis hotspots using geo-mapping: the future for targeted interventions in South Africa

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Background and challenges to implementation: Active TB case finding in the general population has been disappointing yielding very few cases at a huge expense. The South Africa National Department of Health has discouraged the practice in favour of targeted interventions in high risk populations. Geo-mapping was proposed for Breede Valley sub-district in Cape Winelands district since it had the highest TB and TB in children burden. USAID Tuberculosis South Africa Program (TBSAP) in consultation with the district management opted to conduct geo-mapping exercises to map the distribution of TB patients and identify hotspots.

Intervention or response: A list of patients initiated on treatment from July to September 2016 was obtained and addresses of the patients obtained and entered into the conneCTB system. YWAM (Youth With A Mission) provided eight community care workers with experience working with the communities to earmarked for mapping. They were trained to perform the geo-mapping using tablets provided by USAID TBSAP. The geo-mapping exercise was done in 3 working days. They followed up clients to their addresses and once they found them they geo-tagged them. The system updates the mapping in real time.

Results and lessons learnt: Of the 233 patients initiated on treatment during this period; 232 were found. The missing patient had gone to a farm far from Worcester. There were three clusters comprising 101 (Avian Park), 80 (Roodewal) and 48 (Riverview) and an isolated two Zwelendaba). The Avian park hotspots are concentrated in the backyard houses. It is very clear that there are hotspots that the district can target for Contact management, active case finding and community infection prevention activities.
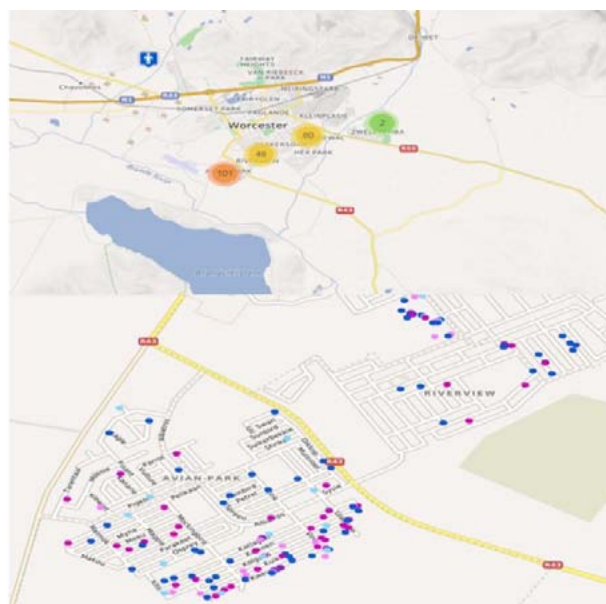
Figure Geo-map showing TB hotspots in Worcester

Conclusions and key recommendations: Geo-mapping TB cases is a feasible easy exercise that can identify hotspots and guide public health providers in targeted TB interventions. The USAID TBSAP project is expanding geo-mapping in all the 20 districts it is working in South Africa.

OA-182-13 Spatial-temporal analysis of mycobacterial load among primary health care facilities in Eastern Cape province, South Africa

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Background: South Africa continues to have one of the highest burdens of tuberculosis (TB) worldwide. The Eastern Cape, Gauteng, KwaZulu-Natal and Western Cape provinces have the highest burden within the country. We examined the spatial and temporal distribution of the mycobacterial load at health facility-level in the Eastern Cape province to provide information that can guide the provincial TB control programme to formulate targeted effective TB control strategies.

Methods: We linked data on Xpert MTB/RIF confirmed TB cases for the years 2013-2015 from the National Health Laboratory Services (NHLS) Central Data Warehouse with population estimates of the catchment areas of primary health-care facilities and geocoded

data from the District Health Information Systems (DHIS) clinical database. We first estimated the mycobacterial load for each Xpert MTB/RIF confirmed case of TB using the formula Ct value= - 2.9865 log (cfu/ml) + 39.09. Then, we estimated the facility-level mycobacterial burden, using the formula: [median facility-level mycobacterial burden * number of Xpert positive cases at facility] / DHIS facility head count. Health facility mycobacterial load cut-offs (high vs low) were created using a natural breaks method. We used Kulldorff's space-time scan statistic to identify temporal trends and spatial patterns of mycobacterial load at a health facility level.

Results: Three significant clusters of health facility-level mycobacterial load were identified in the province during the 3-year period:
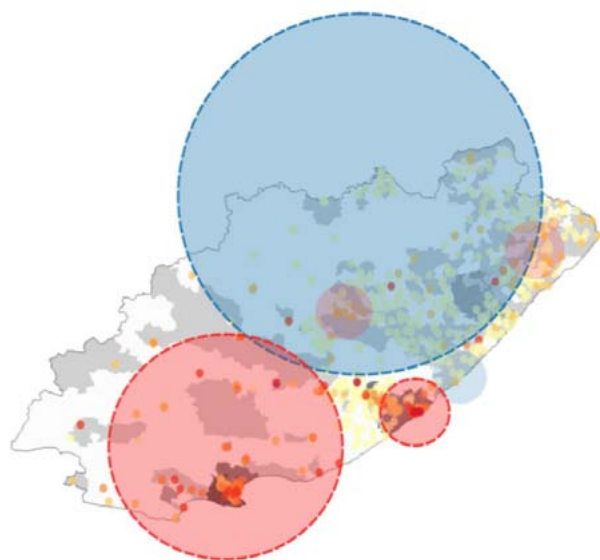
Figure Spatio-temporal clusters of high and low TB burden

Two high mycobacterial load clusters in the densely populated urban municipalities of Port Elizabeth and Buffalo City (East London) in 2015, and a low mycobacterial load cluster located in the mainly rural northwest region of the province in 2013.

Conclusions: Using spatial analysis of routinely available Xpert MTB/RIF data, we revealed patterns of spatial and temporal distribution of mycobacterial load and identified areas that could be prioritised for targeted TB control strategies in order to interrupt local transmission.

OA-183-13 A spatial analysis of TB and associated risk factors in Nigeria, 2012 - 2015

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Background: Nigeria currently rank 4th among the 22 high burden countries in the world. However, tuberculosis (TB) is not evenly distributed in the country possibly as a result of different underlying risk factors within the states that may be responsible for the distribution of the disease.

This study describes the spatial distribution of TB and associated risk factors in the Nigeria.

Methods: The study used an ecological design to determine the spatial distribution of TB in Nigeria and its social and economic correlates between 2012 and 2015 using state-level age/sex standardized tuberculosis notification data. The association between TB and five state-level covariates (HIV, BCG coverage, GDP per capital, percentage underweight and percentage treatment success rate) was done using negative binomial regression analysis. Spatial analysis was conducted using the Global and Local Moran's I test statistic all in R statistical package.

Results: The mean TB age/sex Case Notification rate (TB CNR) during the study period was of 54.4/100,000. Non-spatial ecological regression analysis showed that TB was higher in states with high HIV rates, low BCG rates, low GDP per capita rates and in states with high success rate. The TB CNR was spatially auto-correlated and significant clustering of high TB rates was observed in three states namely Nasarawa, Benue and Taraba states.

Conclusions: This study highlights hot spots for TB in Nigeria and identifies factors that may be driving the TB epidemic in the country.

OA-184-13 Incorporating resource constraints into mathematical models of TB: an example of case finding in South Africa

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Background: Mathematical models are increasingly used to compare strategies for tuberculosis (TB) control and to inform policy decisions. However, these models rarely consider resource constraints and their effect on the predicted impact of a given intervention. Ignoring resource constraints may result in overestimates of the impact that may be achieved in practice.

Methods: Using a dynamic TB transmission model calibrated to the South African TB epidemic, we estimated the epidemiological impact (reductions in TB incidence and mortality) and resource requirements (total costs, nurse time spent on TB activities and number of Xpert tests performed to identify one case of TB) of nine intensified case finding (ICF) and diagnostic interventions. We compared the model-estimated resource requirements to three scenarios of future resource availability to identify likely resource gaps. Finally, we estimated the epidemiological impact when intervention coverage is constrained by future resource availability.

Results: In the absence of constraints, the largest reductions in TB burden were predicted for strategies based on increased levels of ICF using WHO symptom screening. However, such strategies are associated with large increases in all resources considered, and human resource requirements are predicted to exceed future projections of nurse time allocated to TB services. Including budget constraints did not change the achievable coverage of the interventions. However, the achievable coverage of ICF was markedly reduced when predicted future human resource availability and restrictions on the number of Xpert tests were included in the model. In this scenario, the predicted impact of increased ICF was reduced and similar to that of improved adherence to the current diagnostic algorithm.

Conclusions: These results highlight the importance of considering resource requirements and constraints in models used for decision making. Ignoring such considerations may result in incorrect conclusions about the likely impact of interventions. Future model estimates of impact and cost-effectiveness should account for resource capacity.

OA-185-13 A prediction model of mortality after initial treatment outcome in multidrug-resistant tuberculosis patients

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Background: TB programs are seldom able to follow multidrug-resistant tuberculosis (MDR-TB) patients beyond initial treatment outcome. Truncating patient survival times due to lack of follow-up data may bias treatment effect estimates when using proportional hazards regression, especially if large proportions of patients with successful outcomes survive long-term, as this may violate the non-informative censoring assumption of the model.

We demonstrate bias in treatment effect estimates using initial treatment outcomes instead of long-term survival

status and propose a model to predict long-term survival at study-end to produce less biased results.

Methods: In a cohort of MDR-TB patients in Russia (2000-2004), we estimate the association between being on a likely effective regimen and time to death, using two models. Model 1 censors observations when the first non-death treatment outcome occurs, assuming long-term survival is unknown; model 2 uses the actual long-term survival status of patients at study-end. A logistic regression model with 10-fold cross validation is developed to predict long-term survival based on initial treatment outcomes and other risk factors. Predictive models are evaluated by area under the receiver operating characteristic curve. We used SAS V9.4.

Results: 456 MDR-TB patients have initial treatment outcomes and study-end survival available. Of 290 with successful initial outcomes, 1% died by study-end; of 166 with unsuccessful non-death outcomes, 50.6% died (Table 1).

Initial Treatment Outcome	Long-term outcome status	
n=456	Alive n, % (n=369)	Dead n, % (n=87)
Successful (n=290)	287 (99.0%)	3 (1.0%)
Unsuccessful (n=166)	82 (49.4%)	84 (50.6%)

Table Long-term survival after first treatment outcome

Model 1 produced a hazard ratio (HR) of 0.332 (95% CI: 0.155, 0.714; p=0.0047); model 2's HR is 0.307 (0.298, 0.474; p< 0.0001). There is a 7.5% difference in effect estimates. Predictive model results are forthcoming.

Conclusions: Using only initial treatment outcomes underestimates the benefit of receiving a likely effective regimen. Predicting and then using long-term survival status of a patient may reduce biases in the analyses of MDR-TB treatment cohorts, allowing observation of larger true treatment effect sizes and, in turn, increasing study power.

OA-186-13 Pulmonary TB cases missed by primary health care clinics, Buffalo City Metropolitan Health District, Eastern Cape, South Africa

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Background: Missed cases of Tuberculosis (TB) contribute to disease transmission, morbidity and mortality. We calculated the number of missed opportunities to screen and test individuals with TB-related symptoms presenting to primary health care clinics (PHC), and estimated the proportion of TB cases missed by the health system in Buffalo City Metropolitan Health District (BCM), South Africa.

Methods: A representative cross-sectional study was conducted among individuals with TB-related symptoms exiting PHC in BCM. Participants were stratified into those attending for TB-related symptoms and those attending for other reasons. Individuals were interviewed and asked to provide sputum for GeneXpert MTB/Rif testing. Descriptive statistics and logistic regression where used to analyze data. Sensitivity analysis estimated the range of the proportion of TB cases missed by the health system.

Results: We enrolled 1255 TB-symptomatic individuals. Facility staff screened 480/607 (79.1%) participants who specifically sought care for their TB-related symptoms and 142/648 (21.9%) who attended clinic for other reasons (p< 0.001). Of those screened by clinic staff, 134/622 (21.5%) reported submitting sputum, of which 61/134 (45.5%) were successfully tested. Research staff successfully collected and tested sputum from 779 individuals not tested by clinic staff. Of these, 39/779 (5.0%) cases of TB were identified; 15/39 (38.5%) were never screened and 24/39 (61.5%) were screened but not tested by clinic staff. Three cases of Rifampicin resistance were identified. We estimate the proportion of missed cases of TB by the health systems to be 62.9%-78.5% among those attending clinic for their TB-related symptoms, and 89.5%-100% among those attending clinic for other reasons.

Conclusions: Low rates of screening and testing among individuals with TB-related symptoms presenting to health clinics resulted in missed cases of drug sensitive and rifampicin resistant TB. Universal TB screening and testing of all symptomatic individuals should be instituted in South African communities with high rates of TB.

OA-187-13 Feasibility assessment to select six European Union member states for conducting tuberculosis inventory studies and capture* recapture modelling

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Background: The World Health Organization End TB strategy has targeted 90% reduction of tuberculosis (TB) incidence from 2015 to 2035. The annual number of TB cases reported are assumed to reflect TB incidence, which may be incorrect due to underreporting. To assess the level of underreporting, inventory studies examining different registers containing TB patient data, combined with capture-recapture modelling to estimate TB incidence are a widely accepted methodology. The aim of the study was to assess in which six European Union (EU) and European Economic Area (EEA) Member States (MS) TB inventory studies and capture-recapture modelling are most likely to be successfully carried out.

Methods: A rapid feasibility assessment was conducted among 31 EU/EEA MS using an 11-item questionnaire distributed in person or by email followed by an in-depth feasibility interview call among 14 selected EU/EEA MS

Results: Twenty (65%) MS replied to the 11-item questionnaire of which 16 showed interest to participate and 14 MS reported having three case based national TB registers available. The feasibility studies revealed common issues between many interviewed MS, namely the high level of dependence between TB registers due to routine data sharing between different sectors of the health system, particularly between the national TB program and the national reference laboratory. Laboratory data is, for most countries, impossible to separate from case notification with which it is subsequently linked. Denmark, the Netherlands and Portugal were selected to conduct a TB inventory study and capture recapture modelling in 2017, followed by Croatia, Finland and Slovenia in 2018.

Conclusions: This study demonstrates that capture-recapture based estimation of national TB incidence is only possible in a limited number of EU countries. The analysis will provide information on surveillance data completeness and quality, estimate TB incidence, and outline strengths and challenges in the national surveillance system of these six countries.

16. MDR-TB: treatment outcomes using new drugs

OA-188-13 Culture conversion and reversion of multidrug resistant tuberculosis patients receiving bedaquiline in a compassionate use programme in Armenia and Georgia

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Background: Bedaquiline and delamanid have recently improved perspectives for patients treated for multidrug resistant tuberculosis (MDR-TB). In 2013, WHO issued interim policy guidance on bedaquiline use for a maximum duration of 6 months. In 2017, a guideline development meeting report on bedaquiline use made no negative recommendations on the extended duration.

Methods: We retrospectively analysed data from patients receiving bedaquiline under compassionate use in Armenia and Georgia between April 2013 and April

2015. We assessed rates and time to culture conversion and reversion among patients receiving 24 weeks of bedaquiline in an adapted treatment regimen individually constructed.

Results: A total of 82 MDR-TB patients were started on bedaquiline, 82.9% were males, median age was 40 [IQR 31-51] years, 29/82 (35.3%) were resistant to fluoroquinolones only and 40/82 (48.8%) were resistant to both fluoroquinolones and injectable drugs. Among the 64 patients culture positive at initiation, 54/64 (84.4%) achieved culture conversion in a median time of 2.7 months [IQR 1.4-4.0] after treatment initiation. Culture conversion reached 31.4% (95%CI 21.5-44.3) and 74.4% (95%CI 62.8-84.7) at month 2 and 6, respectively. Similar conversion rates were observed among XDR and non-XDR patients (p=0.862). Among those who converted, 10/54 (18.9%) reverted to positive in a median time of 4.2 months after conversion [IQR 2.3-10.5]. The median time to reversion from treatment start was 7.9 months [IQR 6.2-12.7]. In total, 8/10 (80%) of the reversions occurred after 6 months of treatment.

Conclusions: This study shows high rate of culture conversion for highly resistant MDR-TB patients receiving bedaquiline under compassionate use. However, the high proportion of reversions, a criterion for the WHO definition of failure of MDR-TB treatment, occurring after 6 months of treatment is alarming and should question the limit of 24 weeks use of bedaquiline as previously recommended per WHO.

OA-189-13 The use of bedaquiline to treat patients with multi- and extensively drug-resistant tuberculosis in Belarus

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Background: Globally, treatment outcomes of multidrug-resistant (MDR-TB; isoniazid & rifampicin resistance) and extensively drug-resistant tuberculosis (XDR-TB; MDR-TB plus resistance to fluoroquinolones (FQ) and 2nd line injectable agents) remain poor. In Belarus, only 54% MDR-TB and 40% XDR-TB patients starting treatment in 2013 completed it successfully. New medicines like bedaquiline (BDQ) are now being included in longer treatment regimens to increase treatment success. BDQ was introduced programmatically in Belarus in July 2015.

Methods: The Belarus TB programme developed measures to monitor safety and effectiveness of BDQ-containing regimens in line with the World Health Organization recommendations.

Results: By March 31, 2017, 297 patients had started BDQ-containing regimens: 72% males; 43% previously untreated for TB; 65% XDR-TB; 17% with MDR-TB+FQ resistance and 13% MDR-TB+injectable resistance. By 6 months after starting treatment 198/208 patients (95%) had converted to culture negative (70% conversion at 2 months). Of 168 patients followed up for at least 12 months: in 1 (< 1%) treatment failed, 3 (2%) died, 8 (5%) were lost to follow up, and 156 (92%) continue treatment with culture-negative sputum. All patients experienced adverse events, the most clinically relevant being abnormal liver function, hypokalaemia, hypomagnesaemia, hyperuricemia, cardiac arrhythmia (clinically insignificant), anaemia, low platelet count, lowered creatinine clearance, paraesthesia, and hearing loss. Most adverse events were of mild to moderate severity and did not require BDQ withdrawal or stopping treatment. Causality assessment could not attribute any serious adverse events to BDQ.

Conclusions: Interim results show high culture conversion and acceptability of the regimen despite frequent occurrence of mild to moderate adverse events in M/XDR-TB patients. Our patient series will help increase the global knowledge base for M/XDR-TB patients treated with BDQ-containing regimens under programmatic conditions.

OA-190-13 Bedaquiline and linezolid-based regimens for fluoroquinolone-resistant MDR-TB: how much better is it?

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Background: Treatment of fluoroquinolone-resistant multidrug-resistant tuberculosis (FQ-MDR-TB) is challenging. Despite high success rates of treatment regimens including bedaquiline and re-purposed drugs only a limited number of patients globally have benefited.

Methods: Routine programmatic data collected for all consecutive FQ-MDR-TB patients treated between September 2005 and April 2015 in the Armenian National Tuberculosis Control Centre were retrospectively analysed. We compared baseline characteristics and treatment outcomes of two cohorts: the non-bedaquiline cohort treated without bedaquiline and the bedaquiline-cohort patients treated with bedaquiline through compassionate use. All patients had individualised MDR-TB treatment based on previous treatment and resistance profiles. The bedaquiline cohort also had repurposed drugs linezolid and impenem plus amoxicillin/clavulanate added to the regimen as appropriate.

Results: A total of 111 patients from the non-bedaquiline-cohort and 49 patients from the bedaquiline-cohort were included. Socio-demographic and clinical characteristics were similar between the two cohorts. At baseline, patients in the bedaquiline-cohort were more often previously treated for tuberculosis (100% vs 51.3%, p< 0.001) and previously treated with clofazimine (26.5 vs 1.8%, p < 0.001). All patients in the bedaquiline-cohort received linezolid and 75.5% (37/49) impenem plus amoxicillin/clavulanate at treatment initiation. Treatment success rate in the non-bedaquiline cohort was 18.0% (20/111), compared to 61.2% (30/49) in the bedaquiline-cohort (p< 0.001). The multivariate logistic regression showed a drastic increase in treatment success among patients from the bedaquiline-cohort (aOR 12.9, 95%CI 4.8-34.5, p< 0.001). Similar results were found when the analysis was repeated for MDR-TB patients resistant to second-line injectable drugs.

Conclusions: Regimens containing bedaquiline and re-purposed drugs have vastly improved treatment success rates compared to previously available conventional treatments for FQ-MDR-TB patients in Armenia. However, amongst notified MDR-TB cases world-wide, less than one third of FQ-MDR-TB cases have been treated with bedaquiline. An important scale up of access to bedaquiline and re-purposed drugs should be a priority.

OA-191-13 Concomitant use of bedaquiline and delamanid in patients with pulmonary XDR-TB and additional resistance to other second-line drugs in Kazakhstan

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Background and challenges to implementation: The WHO recommends that MDR-TB regimens begin with minimum 5 likely effective TB drugs. Resistance, documented or suspected due to history of treatment, to other second-line drugs, like cycloserine, ethionamide and PAS oftentimes makes meeting the WHO recommendations for design of an effective regimen against XDR-TB impossible, unless two new TB drugs, bedaquiline and delamanid, are used in combination.

Intervention or response: In Kazakhstan ethionamide resistance is > 60% in patients with MDR-TB. During 01 February 2016 to 31 January 2017 a total of 227 M/XDR-TB patients started therapy with bedaquiline and/or delamanid within the endTB Project. Of them 47.7% were XDR-TB, 12.1% pre-XDR with FQ-resistance, 8.1% pre-XDR with SLI-resistance. 80% had history of previous treatment with SLD, 43.7% had cavities and 63.4% bilateral disease. Of 227 patients, it was determined by an expert medical committee that 28 patients with XDR-TB and additional resistance to other SLD warranted treatment regimens with concomitant use of bedaquiline and delamanid. Other drugs included linezolid, clofazimine and carbapenems. Careful clinical and laboratory monitoring have been performed to timely diagnose and manage possible drug toxicities.

Results and lessons learnt: Results from concomitant use are still being collected and analyzed. Initial observations indicate good tolerance and improved culture conversion. Culture conversion, adherence and SAEs will be reported from the cohort in a locked database of February 2017 through June 2017. Concomitant use has been extended for additional 24 weeks in all 28 patients to ensure adequate number of effective drugs in regimen. As of April 2017, all patients are still on treatment, no deaths have occurred and no SAEs.

Conclusions and key recommendations: Having adequate number of drugs in treatment regimen for highly resistant strains of XDR-TB can often only be accomplished with co-administration of bedaquiline and delamanid. Preliminary observations of regimens that combine two new TB drugs is promising. More evidence on concomitant use is needed.

OA-192-13 Outcomes of multidrug-resistant tuberculosis patients receiving bedaquiline in a compassionate use programme in Armenia and Georgia

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Background: Treatment of multidrug resistant tuberculosis (MDR-TB) is difficult, involving long and toxic combination of TB drugs with only 50% treatment success. Bedaquiline, initially available only through compassionate use has improved treatment prospects for MDR-TB patients, particularly the most resistant.

Methods: We retrospectively analysed data from patients receiving Bedaquiline through compassionate use in Armenia and Georgia between April 2013 and April 2015. Patients received an adapted treatment regimen of effective drugs based on resistance profile and previous treatment exposure. Clinical characteristics at treatment initiation and treatment outcomes were described. Logistic regression was fitted to explore risk factors associated with unsuccessful treatment outcomes defined as either death, failure or lost to follow-up.

Results: The characteristics of 82 MDR-TB patients who received Bedaquiline were: 82.9% male, median age 40 [IQR 31-51], 86.6% cavities on chest X-ray, 34.1% BMI < 18.5 kg/m^2 and 43.4% hepatitis C seropositive. Most, 84.2% were resistant to fluoroquinolones, of which 48.8% were extensively drug-resistant. All patients were previously treated with second line drugs while 39.0% received Clofazimine in the past. At treatment initiation, all patients received linezolid, 82.9% clofazimine and 75.6% Imipenem. Treatment outcomes were: 43.9% cured, 14.6% treatment completed, 12.2% death, 7.3% failure and 21.9% lost to follow-up. Among the latter, 14/18 (77.8%) were lost to follow-up after 9 months on treatment. Successful outcome did not differ according to previous exposure to Clofazimine (p=0.902). In multivariate analysis, being co-infected with hepatitis C remained associated with an unsuccessful outcome (adjusted OR=4.45, 95% CI 1.23-16.13).

Conclusions: Bedaquiline under compassionate use program shows good success rates among patients previously treated and with highly resistant TB. However rates of lost to follow-up remain a concern. Hepatitis C coinfection is associated with higher risk of unsuccessful outcomes and should be early diagnosed and treated in MDR-TB patients.

OA-193-13 Delamanid for rifampicin-resistant tuberculosis: an observational cohort study from Khayelitsha, South Africa

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Background: Delamanid (DLM) is efficacious in the treatment of rifampicin-resistant tuberculosis (RR-TB) and was recommended by the World Health Organization in 2014. Experience with DLM outside of clinical trials has been limited, particularly among patients with HIV. We aim to describe early efficacy and QT safety profiles from a programmatic setting in Khayelitsha, South Africa.

Methods: This was an observational cohort of patients who had DLM included in their second-line treatment regimen between November 2015-March 2017. Interim treatment outcomes, sputum culture status, and QTc values at 6-months were determined.

Results: Overall, 73 patients initiated RR-TB treatment containing DLM; 41 (56.2%) were male, 68 (93.2%) were >19 years, 75% were HIV-positive, and 48% and 36% had multi-drug resistant tuberculosis (MDR-TB)

and MDR-TB with second-line resistance, respectively. Of them, 44% (32/73) had < 6-months of follow-up. Interim outcomes 6-months after DLM initiation were available for 56% (41/73) patients; 66% (27/41) were still on treatment and culture negative, 2% (1/41) was still on treatment and culture positive, 10% (4/41) were still on treatment with no available culture data, 7% (3/41) died, 7% (3/41) were transferred, 5% (2/41) were lost-to-follow-up, and 2% (1/41) was cured. Among, the 32 patients still on RR-TB treatment by 6-months, 3% (1/32) had DLM replaced by BDQ at 5 weeks when admitted to an outside hospital. Only 15% (5/32) patients experienced a temporary QTcB value greater than 500ms; none of these patients required permanent withdrawal of DLM.

Conclusions: Early treatment outcomes using DLM in a programmatic, primary care setting with high HIV prevalence are extremely promising. Access to DLM should be urgently expanded to improve treatment options for RR-TB patients.

OA-194-13 Drug resistant TB burden among contacts of drug resistant TB patients: results from routine program implementation in three regions of Ethiopia

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Background and challenges to implementation: Instituting systematic TB screening for contacts of drug resistant (DR) TB is a key global recommendation. We present the yield of routine household contact investigation for index DR TB cases newly initiated on treatment.

Intervention or response: The National TB Program of Ethiopian Federal Ministry of Health with support from the USAID funded Challenge TB project is working to strengthen systematic TB contact screening for DR TB index cases. Household contacts of index DR TB cases were screened for TB through health facility and home visit. The project supported staff training, preparation and distribution of guidelines & algorithms, and provision of recording/reporting forms. Annual (January-March 2016) data captured from 34 DR TB Treatment Initiating Centers found in Amhara, Oromia & Tigray regions through Standard of Care based supportive supervision was used for this analysis.

Results and lessons learnt: Four hundred fifty seven (95%) registered household contacts of 169 DR TB index cases were screened for signs and symptoms of TB, of which 15 (4.26 %; 95% CI: 3.00-6.02) were found to be presumptive TB. Out of the presumptive TB cases, 6

(40.0%) DR TB cases were identified. Among all contacts screened, the yield of DR TB was 1.3% which translates into 1,313 DR TB cases per 100,000 DR TB contact population (95% CI: 603-2,834) and this is higher than the yield of TB among contacts of drug sensitive TB patients during the same period which was 0.7% (>0.05).

Conclusions and key recommendations: The yield of DR TB among contacts of DR TB cases is seven times the TB case notification in the general population and 1.8 times the yield of TB among contacts of DS TB index cases. Contacts of DR TB cases should be routinely screened for TB in a regular basis.

Indicators	Amhara region	Oromia region	Tigray region	Total
Number of contacts screened for TB (%, 95% CI)	155 (100, 97.6-100)	262 (86.2, 81.9-89.6)	40 (100,91.2-100)	457 (91.2,88.4-93.4)
Number of contacts TB screen positive (presumptive TB) (%, 95% CI)	2 (1.3,0.4-4.6)	13 (5.0, 2.9-8.3)	0(0)	15 (3.3, 2.0-5.3)
Number of Contacts diagnosed with MDR-RR TB (%, 95% CI)	2 (1.3, 0.4-4.6)	4 (1.5, 0.6-3.9)	0(0)	6 (1.3,0.6-2.8)
DR CNR/100,000 contacts (95% CI)	1290 (355-4582)	1526 (595-3859)	0(0)	1313 (603-2834)

Table Yield of DR TB contact investigation

OA-195-13 Drug-resistant tuberculosis treatment failure: mutations associated with bedaquiline

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Background: Bedaquiline (BDQ) is the most recent introduction into the treatment programme for MDR-TB in South Africa, and is currently administered to over 3000 patients. BDQ resistance mutations are postulated to arise within the *atp*E gene involved in ATP synthesis; however, only one clinical isolate has been observed globally (Zimenkov et al. 2017). Additional putative resistance-associated genes include *pep*Q, *Rv*0678 and *Rv*1979c. However, few studies have associated either of these mutations with phenotypic and/or clinical resistance. We sought to identify mutations present within these markers in patients failing therapy.

Methods: Isolates from two patients failing a BDQ treatment regimen were sent to the Supranational Tuberculosis Reference Laboratory at the National Institute for Communicable Diseases for BDQ MIC testing and whole genome sequencing. The BDQ con-

centration range for MIC testing on the MGIT 960 system was 0.125 - 8.0μg/ml, with a tentative ECOFF set at 1.0μg/ml. Whole genome sequencing was performed on the MiSeq (Illumina) at an average depth of coverage of 100x. Resequencing analysis and variant detection was performed on CLC Genomics Workbench 10 against the putative resistance genes. This included all genes which encode the F0 operon (*atp*B, *atp*E and *atp*F) and F1 operon (*atp*A, *atp*C, *atp*D, *atp*G and *atp*H) of ATP synthase.

Results: MICs for patient isolates in both cases were higher than the tentative ECOFF. Both isolates harbored the same mutation in the *Rv*0678 (*Mmp*L). In additional, a mutation was observed in *atp*H (Leu25Val) gene.

Conclusions: The efflux-associated insertion 141_142 (*Rv*0678) and Leu25Val (*atp*H) mutation may play a role in BDQ resistance given the associated clinical BDQ failure, however, this could be due to resistance to other drugs in the regimen. Early detection of resistance-associated mutations is critical in preserving BDQ efficacy, resulting in effective treatment regimens and preventing further spread of BDQ resistant isolates.

SHORT ORAL ABSTRACT SESSIONS

10. HIV and TB: lessons from Africa

SOA-394-13 Clinic-based urinary LAM as a biomarker of clinical disease, tuberculosis bacillary burden, and mortality among ART-naïve HIV-infected adults in South Africa

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Background: Urinary lipoarabinomannan (LAM) has limited sensitivity for diagnosing active HIV-associated tuberculosis (TB) disease, but LAM screening at HIV diagnosis might identify adults with a high TB bacillary burden or greater risk of mortality.
Methods: We enrolled antiretroviral therapy (ART)-naïve HIV-infected adults from 4 clinics in Durban. Trained nurses performed urine LAM testing using a rapid assay (Determine™ TB LAM) graded from low (1+) to high (≥3+) intensity. Urine LAM results were not used to guide anti-TB therapy. We assessed TB-related symptoms and obtained sputum for mycobacterial smear and culture. Participants were followed for 12 months. We used multivariable Cox proportional hazard models to determine hazard ratios for all-cause mortality.
Results: Among 726 HIV-infected adults with median CD4 of 205 cells/mm³ (interquartile range 79-350 cells/mm³), 93 (13%) were LAM-positive, and 89 (12%) participants died during the follow-up period. Participants with LAM-positive TB had significantly more clinical signs and symptoms of disease and a faster time to TB culture positivity, as compared to participants with LAM-negative TB disease. In multivariable analyses, urine LAM-positive participants had a mortality hazard ratio (MHR) of 3.58 (95% CI 2.20-5.81) for all-cause mortality. Mortality was significantly different when stratified by urine LAM test result (Figure 1). Among participants with mycobacterial-confirmed TB, urine LAM-positivity had a 2.91 (95% CI 1.26-6.73) MHR for all participants and a 4.55 (95% CI 1.71-12.1) MHR for participants with CD4 ≤100 cell/mm³.
Conclusions: Among HIV-infected adults, clinic-based urinary LAM screening identified TB-infected adults with a high TB bacillary burden of disease and a three-fold greater risk of death in the 12 months following HIV diagnosis. The current LAM assay is insensitive as a stand-alone screening test, but may be useful to accelerate initiation of anti-TB therapy, which could reduce TB transmission and mortality among HIV-infected adults in TB-endemic regions.

SOA-395-13 Subclinical tuberculosis among HIV positive adults in South Africa: a cohort study

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Background: Subclinical tuberculosis (TB) is an asymptomatic phase of TB progression from latent infection to active disease which may have a high prevalence among HIV-infected individuals. We describe the prevalence, clinical characteristics, laboratory parameters, and risk of mortality for a cohort of HIV-infected ART-naïve adults with subclinical TB in Durban, South Africa.
Methods: We enrolled ART-naïve adults recently diagnosed with HIV in four outpatient clinics in Durban, South Africa. All participants were screened for TB-related symptoms (cough, fever, night sweats, weight loss). We obtained sputum for acid-fast bacilli (AFB) smear and culture and tested urine for lipoarabinomannan (LAM) using a rapid assay. Subclinical and active TB disease were defined as having no TB symptoms or any TB symptom, respectively, with either AFB- or culture-positive sputum. Survival outcomes were assessed 12 months following enrollment. We evaluated the association between TB disease category and survival using Cox regression, adjusting for age, sex, and CD4 count.
Results: Among 670 participants, 34 (5%) had subclinical TB disease and 106 (16%) had active TB. Mean CD4 count among uninfected, subclinical, and active TB cases was 289 cells/mm³ (SD 214), 200 cells/mm³ (SD 162, P 0.01), and 138 cells/mm³ (SD 144, P < 0.001) respectively. A greater proportion of subclinical cases were AFB smear positive (41%) than active cases (22%, P 0.04). Urine LAM was positive in 10% of uninfected cases, 26% of subclinical cases (P 0.01), and 33% of active cases (P < 0.001). Subclinical TB infection was not associated with increased mortality as compared to no infection (P 0.63).
Conclusions: Subclinical TB was common among newly diagnosed HIV-infected adults in South Africa and characterized by an intermediate degree of immunosuppression. Though there was no significant difference in survival, anti-tuberculous treatment of subclinical cases may have been protective.

	Mean age, years (SD)	Men	Prior TB treatment	Mean CD4 cell count (SD)	AFB smear positive	AFB culture positive	Urine LAM positive
No TB (N = 490)	34 (10)	248 (51%)	42 (9%)	289 (214)	0	0	48 (10%)
Subclinical TB (N = 34)	33 (9)	16 (47%)	0	200 (162)	14 (41%)	28 (85%)	9 (26%)
Active TB (N = 106)	35 (9)	70 (66%)	8 (8%)	138 (144)	23 (22%)	96 (91%)	35 (33%)

Table 1

SOA-396-13 Tuberculosis screening, incidence and isoniazid preventive therapy among HIV-infected patients before and after ART initiation, Kenya, 2003-2015

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Background: Identifying and treating active and latent tuberculosis (TB) infection are critical TB control interventions. WHO recommends TB symptom screening of people living with HIV (PLHIV), diagnostic testing of the symptomatic and isoniazid preventive therapy (IPT) for the asymptomatic. We reviewed HIV patient records to determine TB screening, incidence and IPT uptake over 12 years of follow-up in a nationally-representative cohort.

Methods: This was a longitudinal retrospective review of medical records for PLHIV aged ≥15 years enrolled in HIV care from October 2003 to September 2013 and tracked through 2015 in 50 facilities in Kenya. Variables of interest were: age, sex, TB screening and outcome, laboratory and radiological investigation, time to incident TB diagnosis, IPT and antiretroviral therapy (ART) initiation. We calculated medians [interquartile range (IQR)], survey-weighted proportions, frequencies, and incidence and incidence rate ratios (IRR) while accounting for complex survey design

Results: Of 3,153 patients enrolled in care, 66.3% were female. Median age was 34 years (IQR 27-41) and duration in HIV care was 2.9 years (IQR 0.6-5.7). The majority 2,383(77.1%, 95%CI=67.9%-84.2%) had been screened for TB with 2133(68.1%, 95%CI=59.9%-75.4%) screened on last visit. Of those screened, 326(13.3%, 95%CI=10.9%-16.0%] were symptomatic. Of these, 126(37.9% [95%CI=29.1%-47.6%) were investigated using sputum smear microscopy, 71(22.3%, 95%CI=15.3%-31.3%) underwent chest X-ray, and 9(3.0%, 95%CI=1.4-6.3) tested using GeneXpert. In 156, (47.6%, 95%CI=37.6%-57.7%) of patients, >1 investigations were used. Of those eligible for IPT, 617(29.4% 95%CI=22.4-37.5) were evaluated, and 37.6%, 95%CI=26.6%-50.1% of those evaluated (217) initiated. Overall, 119(40.0%, 95%CI=31.6%-49.0) of patients with symptom were diagnosed with TB, including one previously on IPT. Median time to TB diagnosis was 1.0 year IQR(0-9.6). TB incidence was 16.7 cases per 1000 person-years for pre-ART versus 10.4 per 1000 person-years for ART patients (IRR=0.87, 95%CI=0.59-1.29).

Conclusions: TB symptom screening, use of diagnostic tools and IPT remains low. More efforts required to improve uptake.

SOA-397-13 Pediatric isoniazid preventative therapy in HIV-positive patients at the Baylor Center of Excellence in Mbabane, Swaziland

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Background: Isoniazid preventative therapy (IPT) is recommended for people living with HIV (PLHIV) ≥1 year of age regardless of TB exposure and all PLHIV following exposure to TB. To enhance IPT program strategies, we assessed IPT prescribing practice and effectiveness in pediatric HIV patients (ages 1-18 years) at the Baylor Center of Excellence (COE), Swaziland.

Methods: A retrospective analysis using patient data from February 2006 through November 2016 in the COE electronic medical records (EMR), focusing on which patients were prescribed IPT, effect of IPT on antiretroviral therapy (ART) adherence, and risk factors for developing TB after IPT. Odds ratios were obtained and adjusted odds ratios calculated using logistic regression. A paired t-test was used to evaluate ART adherence before and after IPT.

Results: Of 1664 eligible pediatric patients identified, 922 (55.4%) were prescribed IPT. Of 305 who initiated IPT over four years ago, 64 (20.1%) later developed TB. Past TB, age >14 years, < 40 clinic visits, and ART adherence < 95% were negatively associated with IPT prescription. CD4 < 500 and age < 5 years were positively associated with IPT. Children with CD4 counts < 500 and ART naïveté at IPT initiation were more likely to develop TB following IPT. Average ART adherence (measured via pill count) decreased by 0.5% (p=0.001) during IPT as compared to the preceding year in the cohort as a whole; however, those with < 95% ART adherence before IPT initiation (n=23) had increased ART adherence by 4.4% (p< 0.001) during IPT.

Conclusions: We have identified patients at increased risk for IPT failure and missed opportunities for IPT prescription. Although clinicians were wary of prescrib-

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ing IPT to children with low ART adherence, this population experienced an increase in ART adherence during IPT. Children at higher risk of developing TB after IPT may benefit from additional courses of IPT.

SOA-398-13 High HIV prevalence among presumptive tuberculosis patients in an urban setting: lessons from Kampala city, Uganda

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Background: The World Health Organization (WHO) recommends HIV screening for all presumptive TB patients (PTPs) as a feasible strategy that offers the potential for early HIV diagnosis and treatment, thereby mitigating HIV-related morbidity and mortality. High HIV prevalence rates among presumed TB patients have been reported with marked variability according to the epidemiological context. This study sought to establish the HIV testing rates, the prevalence of HIV among PTPs and linkage of diagnosed PTPs to care across all the health facilities in Kampala.

Methods: We retrospectively extracted data from the presumptive TB register for patients registered from January to June 2016. Data was collected on the total number of PTPs identified, number tested for HIV, and linkage of diagnosed HIV patients to HIV care services. Data was entered in SPSS and analyzed for the HIV testing rates, the proportion of PTPs diagnosed with HIV, and the linkage of diagnosed TB patients to HIV care.

Results: Of the 9,129 PTPs' records reviewed and analyzed, 8,413 (92.2%) were tested for HIV with documented results in the register. Of the 8,413 patients with HIV test results, 4,449 (48.7%) patients tested HIV positive and of these, 3,930 (88.3%) were linked to HIV care. The proportion of PTPs confirmed with TB was 1,393 (15.3 %).

Presumptive TB patients (PTPs) registered N	PTPs tested for HIV n (%)	PTPs with HIV positive results n (%)	HIV positive PTPS linked to care n (%)	PTPs confirmed with TB n (%)
9129	8143 (92.2)	4,449 (48.7)	3,930 (88.3)	1,393 (15.3%)

Table HIV among presumptive TB patients in Kampala

Of the 9,129 total PTPs registered 4,076 (44.6%) had a non-TB diagnosis while TB status for 41% of the patients was not documented.

Conclusions: HIV prevalence among presumed TB patients in Kampala is very high. The linkage of presumed TB patients diagnosed with HIV to ART clinics is ade-

quate, however, documentation gaps in presumptive TB registers persist. We recommend sustained high levels of HIV testing among presumed TB patients as a way of leveraging TB services to improve HIV care at health facility level.

SOA-399-13 A descriptive analysis of PEPFAR's TB-HIV portfolio: TB cases with known HIV status and TB-HIV co-infected cases on ART in East and Southern Africa

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Background and challenges to implementation: The President's Emergency Plan for AIDS Relief (PEPFAR) is committed to reducing co-morbidity and mortality associated with HIV-associated tuberculosis (TB). Critical steps in this effort are identifying TB cases who are HIV-infected and initiating antiretroviral therapy (ART). We describe the PEPFAR TB/HIV portfolio in East Africa and Southern Africa and highlight recent successes and challenges in addressing the dual epidemic.

Intervention or response: We conducted a descriptive analysis on documented client interactions collected at PEPFAR-supported sites between October 2015 - September 2016 from 16 countries in East and Southern Africa. We determined the percentage of TB cases with known HIV status, the percentage of TB cases with a known HIV status that were HIV-infected, and the percentage of HIV-infected TB cases that were on antiretroviral therapy by region and country.

Results and lessons learnt: Among seven PEPFAR-supported countries in East Africa, the percentage of TB cases with a known HIV status was 89.32% (range: 75.33-99.96%); and 95.16% (range: 92.59-98.29%) in Southern African. The percentage of TB cases who tested HIV-positive was 29.89% (range: 9.83%-43.46%) in East Africa and 59.60% (range: 40.30%-72.46%) in Southern Africa. The percentage of TB cases who tested HIV-positive and were on ART in East Africa was 90.94% (range: 78.84%-95.74%); and 82.58% (range: 72.40-95.80%) in Southern Africa. There was substantial variability between countries in both measures (Figure 1).

Conclusions and key recommendations: A majority of PEPFAR-supported programs are testing their TB patients for HIV and of TB cases who tested HIV-positive, most were on ART. Programs in Rwanda and Malawi, two high performers, should be further studied to elucidate best practices; conversely, reasons for the low uptake of ART in HIV-infected TB patients in Zambia and Zimbabwe should be identified and corrected. TB/HIV clinicians, implementers and stakeholders should strive to achieve 100% coverage for these critical services.

		Registered new and relapse TB cases with documented HIV status						HIV positive new and relapsed registered TB cases on ART during TB treatment		
		Num.	Den.	Percent Coverage (Num./Den.)	HIV Positive	HIV Negative	Percent HIV Positive	Num.	Den.	Percent Coverage (Num./Den.)
East Africa	Burundi	1,833	1,849	99.13%	180	1,651	9.83%	143	164	87.20%
	Ethiopia	52,642	61,319	85.85%	6,647	45,840	12.66%	6,304	6,856	91.95%
	Kenya	61,287	63,940	95.85%	20,633	40,593	33.70%	18,679	19,580	95.40%
	Rwanda	2,294	2,295	99.96%	672	1,627	29.23%	607	634	95.74%
	South Sudan	2,271	2,518	90.19%	301	1,970	13.25%	477	605	78.84%
	Tanzania	44,305	45,333	97.73%	16,071	28,189	36.31%	14,016	15,617	89.75%
	Uganda	34,006	45,140	75.33%	14,802	19,254	43.46%	13,272	15,370	86.35%
	Region Total	**198,638**	**222,394**	**89.32%**	**59,306**	**139,124**	**29.89%**	**53,498**	**58,826**	**90.94%**
Southern Africa	Botswana	1,953	2,078	93.98%	1,289	664	66.00%	1,208	1,534	78.75%
	Lesotho	6,170	6,358	97.04%	4,323	1,862	69.89%	3,387	4,241	79.86%
	Malawi	15,676	16,467	95.20%	8,425	7,370	53.34%	8,136	8,493	95.80%
	Mozambique	58,582	59,603	98.29%	28,905	29,467	49.52%	25,811	28,944	89.18%
	Namibia	9,037	9,432	95.81%	3,639	5,390	40.30%	3,708	4,062	91.29%
	South Africa	226,261	238,472	94.88%	143,369	82,574	63.45%	119,156	144,298	82.58%
	Swaziland	3,133	3,214	97.48%	2,223	845	72.46%	2,040	2,268	89.95%
	Zambia	36,446	39,150	93.09%	19,578	17,295	53.10%	15,531	21,453	72.40%
	Zimbabwe	23,040	24,885	92.59%	15,353	8,463	64.47%	14,200	18,638	76.19%
	Region Total	**380,298**	**399,659**	**95.16%**	**227,104**	**153,930**	**59.60%**	**193,177**	**233,931**	**82.58%**

Table Number and proportion of tuberculosis cases with documented HIV status, and number and proportion of HIV-infected cases on antiretroviral therapy, East and Southern Africa, October 2015 - September 2016

SOA-400-13 Pulmonary function before and after ART initiation in South African adults with pulmonary TB and HIV

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Background: Tuberculosis (TB) is a major contributor to the global burden of chronic lung disease. However, little is known about TB-related pulmonary morbidity in HIV and changes in lung function with antiretroviral therapy (ART). We sought to characterize pulmonary function at baseline and following ART and TB treatment initiation in individuals newly-diagnosed with TB and HIV in Johannesburg, South Africa.
Methods: We enrolled HIV-infected adults with GeneXpert-positive pulmonary TB with pre-ART CD4 counts < 200 cells/μl. Spirometry (forced expiratory volume in 1 second [FEV1] and forced vital capacity [FVC]) was performed at baseline (ART initiation) and 4, 12, 24 and 48 weeks, with week 4 data presented here. Data were analyzed using a Wilcoxon signed-rank test.
Results: To date, 32 TB/HIV co-infected participants have completed baseline spirometry. Their median age was 35 (interquartile range [IQR] 31-39) and 50% were male. At baseline, five (16%) participants had airflow limitation with FEV1/FVC < 70% and FVC % predicted > 80%. Among 21 (66%) participants tested at 4 weeks, 6 (27%) participants had airflow limitation. While there was no significant overall difference between baseline and week-4 spirometry results (Table), 14 (67%) participants had a decline in FEV1 % predicted and FEV1/FVC

in the 4 weeks after ART initiation, with median (IQR) declines of 13% (4-20%) and 7% (2-14%), respectively. There were no significant differences in the 6 minute walk test (6MWT) distance or COPD assessment test (CAT) score, although there was a trend towards improved CAT scores indicating a decline in respiratory symptoms.

	Baseline (n = 32) Median (IQR)	4 weeks (n = 21) Median (IQR)	p-value (Wilcoxon-signed rank test)
FEV1 % predicted	81 (64-89)	68 (50-86)	0.28
FEV1/FVC	81 (75-87)	76 (67-85)	0.10
6 minute walk test (6MWT) distance (meters)	425 (328-456)	384 (375-408)	0.75
COPD Assessment Test (CAT) score	7 (2-13)	3 (1-10)	0.09

Table Spirometry, 6MWT distance and CAT scores in TB/HIV

Conclusions: Among TB/HIV co-infected South African adults, changes in pulmonary function following treatment initiation are heterogeneous, with a subset of individuals demonstrating incident decreases in lung function. Long-term follow-up will be necessary to determine whether these early impairments are related to immune recovery and lead to chronic pulmonary impairment.

SOA-401-13 Health systems strengthening in TB-HIV programme: experience from the Tegemeza project

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Background and challenges to implementation: Success in TB/HIV collaborative activities relies on a strong healthcare system. Therefore, gaps in the six HSS pillars is a major impediment towards the achievement of the End TB strategy and the 90-90-90 target.*TEGEMEZA* was a 5-year HIV prevention, care and treatment project funded by the United States President's Emergency Plan for AIDS Relief (PEPFAR) through Centers for Disease Control and Prevention (CDC) and implemented by Centre for Health Solutions - Kenya (CHS). The project aimed to implement and expand TB/HIV collaborative activities.
Intervention or response: Informed by a baseline evaluation in July 2011, CHS embarked on addressing the gaps in the health system. Human resource for health was strengthened through supporting the counties to hire 282 staffs and 205 volunteers. Infrastructural improvements were done in several facilities. CHS supported essential clinical equipment to improve quality of care and diagnosis . Mentorship and technical support was

provided to ensure strengthening of health information systems at the counties. Training´s and mentorship were done to strengthen quality service delivery and commodity management.

Results and lessons learnt: During the pre-intervention period data from October-December 2011 showed TB screening at 80%, HIV testing at 83%, ART uptake at 78%,Septrin uptake at 95%. After the intervention period, data from October - December 2016 showed TB screening in adults was 95% (n=30830) and 95% in children (n=2517). IPT coverage for adults was 99% (n=286720), children 65% (n=1709) while HIV Testing for adults was 99% (n=672) and children 96% (n=42). HIV coinfection in adults was 33% and 29% in children while ART uptake for adults was 99% and 100% in children. Septrin uptake was 100% in adults and children.

Conclusions and key recommendations: The interventions undertaken by CHS to strengthen the healthcare system were associated with the good uptake of TB/HIV collaborative activities. Such interventions may contribute significantly to achieving the End TB strategy.

SOA-402-13 Value of determine-TB LAM test as screening test and diagnostic tool for tuberculosis diagnosis in HIV-positive adults

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Background: Determine TB LAM test (LAM) is a point-of-care test performed on urine. Previous studies have shown good specificity for tuberculosis (TB) diagnosis in HIV-positive immunocompromised patients. We assessed the value of LAM as screening test and as diagnostic tool in HIV-positive patients.

Methods: Prospective cohort study. HIV-positive patients were consecutively enrolled in 3 cohorts:
1) LAM used as a rule-in screening tool in ambulatory patients with CD4< 100 in Mozambique (cohort 1);
2) LAM used as a rule-in screening tool in hospitalized patients regardless of presenting symptoms and CD4 in Malawi (cohort 2); and
3) LAM used as a diagnostic tool in ambulatory patients with symptoms of TB and CD4< 200 in Mozambique (cohort 3).
Xpert MTB/RIF was systematically requested in hospitalized and symptomatic patients. Mortality was assessed at 6 months.

Results: Between December 2014 and March 2017, 360 ambulatory patients with CD4< 100 (cohort 1), 171 hospitalized (cohort 2) and 286 symptomatic patients with CD4< 200 (cohort 3) were included. LAM was positive in 43/360 (12.0%), 36/171 (21.6%) and 128/286 (44.8%) patients respectively. Among hospitalized and symptomatic patients, 54.8% and 20.3% respectively were not able to produce sputum. Among LAM-positive hospitalized and symptomatic patients, respectively, 20/36 (55.6%) and 28/128 (21.9%) had missing Xpert results. All LAM-positive patients were started on treatment at the first consultation. LAM positivity was associated with higher risk of mortality in ambulatory patients with CD4< 100 (aOR: 6.4, 95%CI: 1.6-24.6).

	Ambulatory regardless of symptoms and CD4<100 (N=360) n (%)	Hospitalized regardless of symptoms and CD4 count (N=171) n (%)	Ambulatory with symptoms of TB and CD4<200 (N=286) n (%)
Age, median [IQR]	36 [31 - 43]	38 [32 - 46]	36 [31 - 43]
Female	185 (51.0)	86 (50.3)	125 (43.7)
CD4, median [IQR]	31 [13 - 53]	231 [103 - 508]	40 [16 - 83]
Xpert positive	Not applicable	15 (8.8%)	54 (18.9)

Table Patients' characteristics and TB diagnostic tests

Conclusions: As screening tool, regardless of TB symptoms, LAM can detect TB in a considerable proportion of HIV-patients among those ambulatory with low CD4 and those hospitalized, and allows identifying patients at higher risk of mortality. As diagnostic tool in symptomatic HIV patients with CD4< 200, LAM rapidly diagnoses TB in a high proportion of patients. Part of them would be missed by using sputum-based diagnostic tools.

SOA-403-13 Diagnostic accuracy, incremental yield and cost of determine TB-LAM and sputum induction for in seriously ill adults with HIV, cough and WHO danger signs

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Background: Undiagnosed tuberculosis is a major cause of mortality among hospitalised HIV-infected patients. The WHO has published recommendations to improve tuberculosis diagnosis including an algorithm in the seriously ill. Urine based lateral flow lipoarabinomannan (LAM) and Xpert MTB/RIF show promise as rapid diagnostic tools but it is unclear how they should be combined in an algorithm.

Methods: A prospective cohort study enrolled inpatients presenting with any duration of cough and WHO danger signs to 2 secondary hospitals in Cape Town, South Africa. LAM was performed on stored urine and Xpert MTB/RIF was performed on sputum. For those unable

to spontaneously expectorate a 'spot' sample, sputum induction (SI) with nebulised hypertonic saline was used. Tuberculosis was diagnosed by culture from any site. Diagnostic accuracy and costs were determined for single and combined tests.

Results: Test results were available for 332 patients, of whom 169 (50.9%) had confirmed tuberculosis (median CD4 count 107 cells/µL). The yield of Xpert on 'spot' sputum was 23.1% which improved to 50.9% if preceded by LAM and 90.5% if followed by SI. The combination of LAM, 'spot' sputum plus SI had a yield of 92.3%. The cost per patient for LAM followed by 'spot' sputum was $5.9 and for 'spot' sputum followed by SI it was $25.8. Performing LAM followed by 'spot' sputum then SI cost $22.6 per patient. The latter strategy missed 4 of 5 cases of rifampicin resistance.

Conclusions: For patients with HIV, any duration of cough and WHO danger signs Xpert on 'spot' sputum has low yield which is improved by the addition of LAM and even further by the addition of SI. Adding LAM to 'spot' plus SI does not significantly increase yield, but reduces costs at the expense of a small number of missed cases of rifampicin resistance.

11. Pearls and pitfalls: tales from the lab

SOA-404-13 Automated fluorescence AFB smear testing system for tuberculosis diagnosis based on a deep-learning technology, InBioDx-TB

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Background: Acid-Fast Bacilli(AFB) smear microscopy is the primary method for tuberculosis diagnosis allowing rapid detection of infectious TB cases with simple laboratory facilities and low cost. However, AFB smear microscopy is labor intensive and easily affected by experience and labor loading of investigator. Although several method such as machine learning have been studied to diagnose TB, but the performance was not enough to be applied to actual test. Korean Institute of Tuberculosis and InSpace collaborated to develop an automated reading system for fluorescence AFB based on a deep-learning technology, InBioDx-TB.

Methods: To improve diagnostic accuracy, we use object classification model and object detection model that are based on deep-learning method.

We have trained the object classification model using overall 447,648 datasets that were composed of AFB positive/negative patch images and their labels were marked by several highly experienced TB laboratory staffs.

In order to use the object detection model, bounding box label corresponding each AFB positive object should be needed. So, we have developed a tool working on touchscreen devices to gather the bounding box labels easily. The pathologists directly draw the area corresponding to *Mycobacterium tuberculosis* in the captured image on the touchscreen devices.

Total 100 clinical slides previously studied for laboratory diagnosis were used for verification of the diagnostic accuracy of InBioDx-TB.

Results: The sensitivity of our deep learning based method is improved to 96%, with overall accuracy of 90%. InBioDx-TB shows rapid turnaround time of several minutes from image capturing to reporting final results.

Conclusions: InBioDx-TB demonstrated high accuracy, sensitivity and specificity of diagnosis. We are currently collecting datasets every day by the Korea Institute of Tuberculosis pathologists and the datasets are used in online training of our deep learning model. We expect that InBioDx-TB will be able to be replaceable for the conventional manual testing process of fluorescence AFB smear.

SOA-405-13 Prevalence of contamination among pediatric samples collected by gastric aspiration in Botswana

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Background: Limitations of point-of-care tests for *Mycobacterium tuberculosis* (MTB) in children with pauci-bacillary disease and HIV-positive adults have re-emphasised the utility of culture-based testing in countries with high TB/HIV burdens. Sample contamination can prevent clinicians from obtaining an actionable result. Since 2008, clinicians nationwide in Botswana have collected gastric aspirates (GA) from children to test for MTB. We assessed prevalence and explored factors associated with GA sample contamination.

Methods: We analysed data from samples collected from children with suspected TB at government health facilities submitted to Botswana's National TB Reference Laboratory for MTB culture 2010-2014. Collection occurred under operational conditions per national guidelines. The first sample received for each patient was analysed. We estimated crude associations between pa-

tient's age and sex, health facility type, collection under training conditions, distance from sample collection location to laboratory, sample processing date, time from collection to processing, and sample contamination using Chi-square and Wilcoxon rank sum tests. Guided by causal diagrams and available data, we explored factors independently associated with contamination using logistic regression with GEE-extension.

Results: Of 3410 GA cultured samples collected and analysed, 40.7% were contaminated. Median delay from collection to processing was 4 days, similar among uncontaminated and contaminated samples. Contamination was lowest among samples collected in district/referral facilities (19.3%) compared with lower level facilities (47.4%) [p< 0.001]. Contamination was higher among samples processed on/after a switch from solid to MGIT-based culture in November 2011 (44.5%), compared with before (21.1%). Multivariate analysis suggests these differences remain statistically significant, even after adjustment for other factors.

Conclusions: Contamination of samples collected by GA from children for MTB culture was very common. To optimise culture yield and prevent treatment initiation delays, further investigation of GA collection practices in non-district/referral hospitals and other changes co-occurring with the November 2011 culture media change is needed.

SOA-406-13 Predominance of modern sublineage of *Mycobacterium tuberculosis* Beijing genotype among clinical isolates in Nepal

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Background: The Beijing genotype of *Mycobacterium tuberculosis* is known to be a worldwide epidemic clade. It has been suggested that these strains are associated with higher rate of transmission, virulence and drug resistance. Based on evolutionary markers, Beijing genotype is divided into ancient and modern sublineages. Knowledge on distribution of a certain sublineage of the Beijing genotype may help to understand the mechanisms of its rapid spread and to establish an association between a certain genotype and the disease outcome. Our study aims to determine prevalence of Beijing sublineages in the clinical isolates from Nepal.

Methods: A total of 601 multidrug-resistant (MDR) *M. tuberculosis* strains, collected from April 2009 to March 2013 at German Nepal TB Project Laboratory, Nepal, were used in this study. These strains were further analysed by using molecular techniques such as sequenc-

ing and spoligotyping in Hokkaido University Research Center for Zoonosis Control, Japan. The prevalence of sublineages of *M. tuberculosis* Beijing genotype was determined by examining single nucleotide polymorphisms (SNPs) at a locus (SNP 1477596) in *M. tuberculosis* genome that have been identified as appropriate for defining Beijing sublineages.

Results: Of 601 MDR-TB isolates, spoligotyping identified 294 (48.9%) as being Beijing lineage and the remaining as a non-Beijing group. The non-Beijing group consisted of strains belonging to East-African Indian (30.4%), Euro American (14.3%) and Indo-Oceanic (6.3%) lineages. Furthermore, SNPs typing confirmed that 82% and 18% of Beijing strains (n=294) belonged to modern and ancient types, respectively.

Conclusions: This is the first report of predominance of modern Beijing sublineage in Nepal. The higher prevalence of modern isolates in this study suggests the greater spreading capability of modern sublinage of Beijing genotype in Nepal. Our study provides useful information to national TB control program for the implementation of more effective prevention and control measures in Nepal.

SOA-407-13 Use of carbendazim in solid media as effective contamination control method for *Mycobacterium tuberculosis* cultures

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Background: Contamination of *M. tuberculosis* (MTB) samples is common, particularly among those collected during treatment follow up. Contamination compromises the ability to detect MTB and confirm negative cultures. We detected 10% contamination in Middlebrook 7H11 selective agar in pre-treatment and follow up samples at the Socios en Salud (SES) Lab in Lima, Peru. In the context of a clinical trial testing the potential for higher doses of levofloxacin to shorten treatment for drug-resistant TB, we explored the addition of carbendazim to reduce contamination.

Methods: Pre-treatment and follow up samples collected from patients with pulmonary TB in Lima, Peru were homogenized and processed with NALC-NaOH, re-suspended in PBS buffer and divided into two paired aliquots of 200µl. One aliquot was inoculated onto 7H11 media not treated with carbendazim (reference) and one onto 7H11 media treated with 0.05 mg/ml of carbendazim. We compared the frequency of positive, negative and contaminated cultures among paired samples. Colony forming units (CFU) were also compared to assess culture yield using Wilcoxon signed rank test.

Results: Seventy sputum samples were included in this analysis. 7 (10%) cultures without carbendazim were contaminated; matched carbendazim-treated cultures were culture negative. See Table 1. Of these 7 cultures, all were from samples collected during treatment follow up. There was no (0%) contamination in carbendazim-treated cultures. Mean CFU counts were similar; 84.9 (95% CI 46.2-123.6) in positive cultures treated with carbendazim and 83.1 (95% CI 45.5-120.6) in those without carbendazim (*p* value=0.18).

Result	Middlebrook 7H11 Culture No carbendazim n/N (%)	Middlebrook 7H11 Culture With carbendazim n/N (%)
All Cultures	70/70 (100)	70/70 (100)
Positive Cultures	30/70 (42.9)	30/70 (42.9)
Negative Cultures	33/70 (47.1)	40/70 (57.1)
Contamination Rate	7/70 (10)	0/70 (0)

Table Culture results in Middlebrook 7H11 with and without carbendazim

Conclusions: Carbendazim increased the yield of culture-negative Middlebrook 7H11 cultures without apparent interference with MTB growth. A modest effect, not detectable in this small sample size cannot be ruled out. However, if replicated in larger samples, these results suggest that carbendazim could be used to improve performance characteristics of 7H11 for monitoring treatment response.

SOA-408-13 Prevalent non-tuberculous mycobacteria species among presumptive MDR-TB patients from peripheral health facilities referred for testing at KEMRI TB laboratory, Kisumu

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Background: Little is known about the relative burden of non-tuberculous mycobacteria (NTM) compared to pulmonary tuberculosis in high tuberculosis (TB)-burden settings. Many mycobacteria share common properties, such as acid-fastness and the ability to cause pulmonary and extra-pulmonary granulomatous disorders. NTM infections are acquired directly from the environment from the soil and various water sources. In low-resource settings, such as Kenya, direct microscopy(ZN) is the common laboratory technique used in TB diagnosis in most peripheral health facilities. TB/HIV co-infection further compounds the dire situation. In Western Kenya, HIV prevalence is 14%, hence TB/HIV co-infection poses serious health challenges to TB program of the Ministry of health (MoH).

Methods: We conducted a cross sectional study among presumptive multi-drug resistant TB (MDRTB) patients of western Kenya. Sputum samples obtained from presumptive MDRTB patients were processed using standard culture methods, fluorescence microscopy (FM), MGIT culture, Xpert MTB/RIF. MTBc and NTM were identified using line probe assays techniques.

Results: A total of 7840 sputum samples were processed from patients between January 2012 to December 2015, of these, 280 (4%) grew (NTM) on liquid culture (MGIT) of which 94 (33.6%) had positive ZN smear results. Of 157 (56.1%) individuals with HIV, 51 (18.2%) were smear positive. The prevalent NTMs among the HIV infected individuals were *M.intracellulare* (26), *M.scrofuleceum* (7), *M.fortuitum* (6), *M.gordonae* (5), *Mycobacteria species* (11), *M. malmoense* (3), *M.celatum I+III(3)*, and MTBc (7). On comparison of LPA results versus smear results, smear positive results were observed in *M.intracellulare* (12), *M. malmoense* (2), MTBc (11), *M. fortuitum* (3). *M.abcessus* (3). MTBc detected through LPA were 14, and 11 were similarly smear positive.

Conclusions: NTM presence shows positivity with common routine ZN microscopy methods available hence patients may routinely be initiated on wrong medications due to MTBc. Further laboratory diagnoses is required to classify MTBc to inform patient management.

SOA-409-13 Improving detection of tuberculosis in people living with HIV/AIDS using trained African giant pouched rats

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Background: Tuberculosis (TB) diagnosis in people living with HIV/AIDS (PLWHA) is difficult in countries relying on microscopy hence there is a need for new diagnostic tools for detecting the increasing smear negativity in PLWHA. Objective of this study is to determine performance of trained African giant pouched rats (*Cricetomys* spp.) in detecting TB in PLWHA and whether trained rats can increase TB detection yield in PLWHA.

Methods: Sputum samples were collected in DOTS centres serving PLWHA and general population in Dar es Salaam, Tanzania. Samples were heat-inactivated at 100°C x 30 min. before rat evaluation in a 10-holes line cage holding 10 samples. Rats evaluated 100 samples for 20 min. DOTS negative samples indicated by rats were confirmed by concentrated smear microscopy.

Confirmed additional TB patients started treatment following tracking by healthcare workers.

Results: Detection rats increased additional TB yields by 160% in PLWHA and 22% in general patient population. The difference in additional TB yield by rats in the two populations was higher (137.6%) and statistically significant (95% CI, 77.6066-197.65, P=0.0001). This was attributed by high proportion of patients with scanty acid-fast bacilli in PLWHA (48.3%) versus 9.3% found in general population. Fifty-two percent (49/96) of the additional patients in PLWHA had lower bacilli count. This indicates that trained rats detect more TB patients likely considered to smear negative TB in PLWHA. Only 9% of the additional patients in PLHWA had higher bacilli count (3+) whereas 2+ were 8% and 1+ were 28-31% in PLWHA and general populations.

Conclusions: Use of TB detection rats significantly increases TB detection rate in PLWHA, revealing more DOTS smear negative TB, which is difficult to diagnose by microscopy used in most countries with high TB/HIV co-infection. Trained rats enable rapid TB diagnosis which enhances early treatment. Further studies are needed to compare rats with sensitive diagnostic tools.

SOA-410-13 PCR en tiempo real, multiplex para diferenciación de miembros del complejo *Mycobacterium tuberculosis*

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Background: En Colombia el sistema de salud para el diagnóstico de tuberculosis, realiza la identificación de complejo *M. tuberculosis*, sin hacer diferenciación de especie; se han reportado casos de tuberculosis humana, producida por *Mycobacterium bovis* así como la circulación de este en bovinos, con la importancia de la resistencia natural a la pirazinamida. Se planteó como objetivo estandarizar una metodología basada en PCR en tiempo real con análisis de curvas de disociación, para diferenciación de *Mycobacterium tuberculosis*, *Mycobacterium bovis* y *Mycobacterium bovis* BCG.

Methods: Se estandarizaron dos PCR múltiplex usando como controles *M. tuberculosis* H37RV, *M. bovis* BCG Japón, *M. bovis* y *M. leprae* Thai. La primera usó los iniciadores 16S, IS6110 y RD9, y la segunda RD4 (presencia y ausencia) y RD1. El análisis se realizó con el software LightCycler® 480, Versión 1.5, usando T_m calling para identificar la temperatura melting. La metodología fue validada a partir de un banco de 30 ADN provenientes de muestras clínicas, procesados por duplicado, de *M. tuberculosis*, *M. bovis*, *M. bovis BCG*, *M. leprae* y *M. abscessus* del biobanco del Instituto Nacional de Salud.

Results: Se logró estandarizar la metodología y la identificación de los ADN del biobanco fue correcta en todos los casos, evidenciando la reproducibilidad de la prueba. Se determinaron 10 aislamientos pertenecientes

a *M. bovis*, 15 a *M. tuberculosis*, 3 a *M. bovis* BCG y 2 a Micobacterias no tuberculosas.

Conclusions: La metodología estandarizada es sensible, específica y permite diferenciar *M. tuberculosis*, *M. bovis* y *M. bovis* BCG. Se dispone para el país de una nueva herramienta rápida, para la contribución al diagnóstico y vigilancia de los microorganismos de estudio.

SOA-411-13 Molecular bacterial load assay as a marker for treatment response late during treatment

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Background: Appropriate markers to reflect TB treatment responses are urgently needed mainly for individualized patient care and their application in TB clinical trials amid a search for new treatment and/or shortening regimen. We evaluated the Molecular Bacterial Load Assay (MBLA) for its potential use as a marker to determine treatment success.

Methods: This study was nested within the multiple-arm, multiple-stage (MAMS), phase 2 clinical trial (PanACEA MAMS TB 01) which contributed data set for 103 patients to the PanACEA Biomarkers Expansion programme (PANBIOME) study at NIMR Mbeya Medical Research Centre and Kilimanjaro Clinical Research Institute, Tanzania. Eligible patients were randomised to either the control arm or one of four experimental arms. Culture and MBLA were performed at baseline through to treatment completion at month six comparatively.

Results: MBLA had the highest (19%) positive rates compared to MGIT (1.7%) and LJ (1.2%) media at end of treatment/month 6. The median time to last positive result was 35, 55 and 97 days on LJ, MGIT and MBLA respectively. MBLA was reported positive more often than MGIT with 36.2% and 42.2% of negative and contaminated MGIT results respectively being MBLA positive. Furthermore, quantitative bacterial load measurements in MBLA and MGIT were significantly correlated (p<0.001).

Conclusions: MBLA as a marker to determine treatment success bears potentials that could contribute in routine patient care and trial setting in search for new TB drug regimen. However, evaluation on its role for predicting long term clinical outcome, its implementation in routine care and its further usefulness as an end point in trials merit further consideration.

SOA-412-13 A portable electronic nose as a potential point-of- care screening device for pulmonary tuberculosis

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Background: Tuberculosis is the leading infectious cause of death. A sensitive, easy-to- operate and low-cost diagnostic method is urgently needed. Exhaled breath contains gaseous volatile compounds, which analyzed as a whole, could potentially be used.

Here we determine the accuracy of an electronic nose, for the diagnosis of pulmonary TB and compare its accuracy with standard microbiological methods.

Methods: We conducted a prospective cohort study in TB positive patients and controls. All subjects underwent clinical examination and Aenose™ screening. Sputum samples were obtained for microbiological studies.A pattern recognition algorithm was developed, which differentiated (best fit) between exhaled breath of lung TB patients and non-TB patients.

Results: We enrolled 186 HIV negative patients. A total of 86 individuals were diagnosed with pulmonary TB (L-J culture-confirmed); 100 individuals were regarded as controls (47 healthy, 30 with pulmonary infections other than TB, 23 with lung adenocarcinoma). Among patients with cultured-confirmed TB, the estimated sensitivity and specificity of the Aenose™ was 86% (95% CI 76.9-92.5) and 74% (95% CI 64.3-82.3) respectively.

One single sputum smear had a sensitivity and specificity of 56.6% (95% CI-50.2- 62.8) and 91.6% (95% CI 82.5-96.5) respectively.

Two sputum smears together reached a sensitivity and specificity of 79.8(95% CI 71.1-87.0 and 97.0% (95% CI 89.8-99.4) respectively.

The negative predictive value of the Aenose™, a single sputum smear and two sputum smears combined were 86.05%, 37.6% and 74.5% respectively.
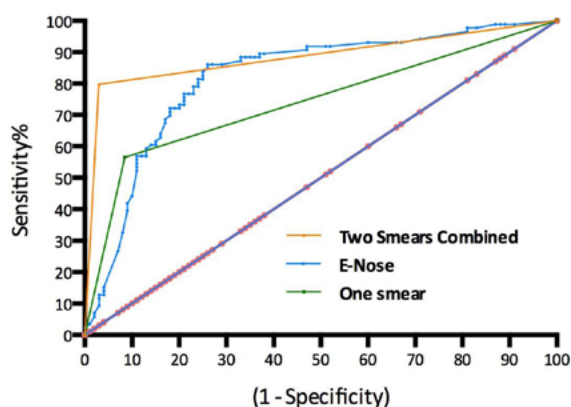
Figure ROC curve of all diagnostic tests compared to L-J culture

Conclusions: The Aenose™ has a better diagnostic yield than a single sputum smear and the sensitivity was not inferior to the result of two combined sputum smears.

In its actual design, the Aenose™ can potentially be used in rural areas where there are no laboratory facilities. The Aenose™ is a potentially effective screening tool for identifying subjects that may need additional diagnostics.

Future studies with HIV and extra pulmonary TB are underway. Moreover, the pattern recognition algorithm is still in development, and results will improve in the future.

SOA-413-13 Combinations between antibodies and host inflammatory biomarkers show potential in the diagnosis of TB disease

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Background: New tools are urgently needed for the rapid diagnosis of TB disease in resource-constrained settings. In recent studies, host inflammatory biomarkers and antibodies showed potential as candidate TB diagnostic markers. In the present study, we evaluated the usefulness of combinations between antibody responses against novel *M. tuberculosis(M.tb)* antigens and host inflammatory biomarkers as tools for the diagnosis of TB disease.

Methods: Plasma samples were prospectively collected from individuals presenting with symptoms suggestive of TB disease at a primary health care clinic in Cape Town, South Africa. Patients were later classified as having TB or other respiratory diseases (ORD) based on their laboratory (culture), clinical and radiological results.

We evaluated the concentrations of host inflammatory biomarkers, and IgA and IgM responses against seven *M.tb* antigens in plasma samples from study participants using the Luminex and ELISA techniques respectively, and assessed the usefulness of these biomarkers in the diagnosis of TB disease.

Results: Out of the 156 study participants, 26(17%) were diagnosed with TB disease, and 28(18%) of the study participants were HIV infected. IgA and IgM responses against single antigens including NarL, Rv3019c, and two other proteins showed potential in the diagnosis of TB disease, with area under the ROC curve (AUC) up to 0.74. A combination of seven-antibodies diagnosed TB disease with an AUC of 0.80, whereas a combination of two antibodies and five host biomarkers diagnosed TB disease with a sensitivity of 95% (CI, 73.0-100%) and specificity of 89% (CI, 68.7-97%), regardless of HIV infection status. The positive and negative predictive values of this biosignature were 86.4% (95% CI, 64-96.4%) and 95.8% (95% CI, 76.9-99.8%) respectively.

Conclusions: The use of host inflammatory biomarkers in combination with antibody responses may be a useful approach for the diagnosis of TB disease. This approach requires further investigation in larger studies.

12. MDR-TB: predictors of treatment outcome

SOA-414-13 Factors associated with unfavorable treatment outcomes among multi-drug resistant tuberculosis patients treated at a tertiary hospital in Tigray Region, Northern Ethiopia

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Background and challenges to implementation: Despite the progress made in addressing multi-drug resistant Tuberculosis (MDR-TB), achieving a high treatment success rate using conventional treatment regimens continues to be a global challenge. Understanding specific factors contributing to unfavorable treatment outcomes is critical to design appropriate interventions. The objective of this study was to determine the magnitude and factors associated with unfavorable treatment outcomes among MDR-TB patients treated at a tertiary hospital in northern Ethiopia.

Intervention or response: A retrospective facility based record review was conducted for a cohort of patients enrolled at Mekelle Hospital between December 2012 and April 2015. Final treatment outcomes were determined between January and March 2017. Patients were classified as having favorable (cured or completed) and unfavorable (death, lost-to-follow-up [LTF], not evaluated, failure) treatment outcomes. The association between the treatment outcome and the independent factors was evaluated using a logistic regression model.

Results and lessons learnt: Treatment outcomes of 136 MDR-TB patients were assessed of which 34 (25%) were co-infected with HIV. The median age of the patients was 30 and 68% were men. Overall, 73% had favorable treatment outcome (57[42%] cured and 42[31%] completed] and it showed progressive improvement (See Figure 1). Unfavorable outcomes were reported in 27% (20[15%] death and 17[12%] LTF). Patients with lower income (AOR=3.24, 95% CI. 1.145-9.182, P=0.027), those with no formal educational status (AOR=7.80, 95% CI. 1.176-51.787, P=0.033), and those with depressive symptoms (a side effect of the medication) (AOR=13.53, 95% CI. 4.790-38.227, P<0.001) had higher proportion of unfavorable treatment outcomes.
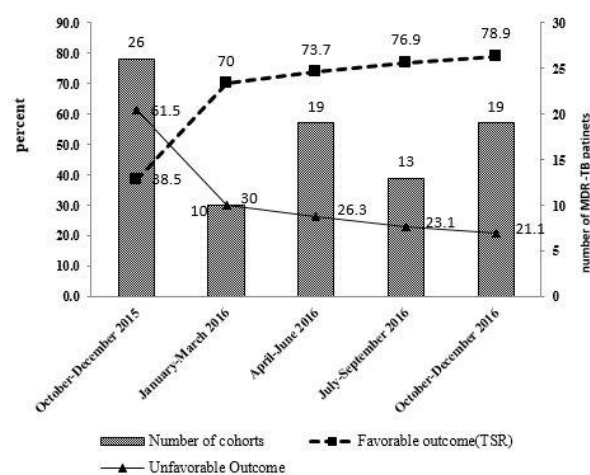
Figure Trends in treatment outcome

Conclusions and key recommendations: The unfavorable treatment outcome rate of 27% in this cohort is better than the 48% global average reported in the 2016 Global TB Report. Tailored support should be provided to MDR-TB patients with low income status and those with no formal education. Additionally, clinicians' capacity to manage common side effects should be strengthened.

SOA-415-13 Long-term outcomes of patients lost to follow-up from multidrug-resistant tuberculosis treatment in the country of Georgia

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Background: High rates of loss to follow-up (LFU) during multidrug and extensively drug-resistant tuberculosis (M/XDR-TB) treatment remain a major impediment to global TB control. Little is known about long-term outcomes after LFU. We aimed to describe long-term clinical outcomes of patients with M/XDR-TB who were LFU and determine factors associated with active TB after LFU.

Methods: We performed a cross-sectional study among adult patients with pulmonary M/XDR-TB who initiated anti-TB treatment within the Georgian National TB Program during 2011-2014 and were subsequently defined as LFU. In 2016, LFU patients were contacted, interviewed, and sputum samples were obtained. Active TB at follow-up was defined by either a positive Xpert-TB/RIF or culture result.

Results: Among 605 M/XDR-TB patients who were LFU during 2011-2014, follow-up information was obtained on 461 (76%) patients. Among these patients, 78 (17%)

resumed TB treatment, 35 (8%) were incarcerated, 107 (23%) died, and 64 (14%) emigrated. Among remaining 177 patients, 123 (69.5%) consented to participate, and 92 provided sputum samples. A total of 13 (14%) had active TB at the time of contact.

Mean duration of treatment during the episode prior to LFU was 359 (SD=183) days and the mean time from LFU to study enrollment was 972 (SD=445) days.

Patients who were culture-positive for TB at the time of LFU were more likely to have active TB at the time of our study compared to those who were culture-negative at time of LFU (8/14 [57%] vs 3/71 [4.1%], P< 0.01).

Patients with history of >1 episode of previous TB treatment were more likely to have active TB (OR=3.88 95%CI 1.10-13.72).

Conclusions: A high proportion of patients died and nearly one-fifth resumed treatment. Patients who were culture-positive at the time they were LFU and had a history of multiple treatment courses were significantly more likely to remain culture-positive at time of contact.

SOA-416-13 Community-based MDR-TB diagnosis and management in Bangladesh

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Background and challenges to implementation: Bangladesh is one of the high multi drug resistant TB (MDR-TB) burden countries. According to the last drug resistant survey of Bangladesh, the MDR-TB burden is 1.4% among new cases and 28.5% among retreatment cases. The Programmatic Management of Drug Resistant TB (PMDT) program was initiated in the tertiary care center in Dhaka in 2008 with only 130 beds assigned for MDR-TB patients.

TB services were not accessible to a majority of the population. The NTP policy was to hospitalize enrolled patients until the conclusion of the injection period (on average eight to nine months).

This policy led the NTP to face challenges with high default rates and long waiting lists.

Intervention or response: To overcome the challenges, in mid-2012 the NTP adopted a community based PMDT (cPMDT) strategy throughout the country. Management of drug resistant (DR-TB) has been decentralized through the establishment of GeneXpert sites/ Regional TB Reference Laboratories, the expansion of treatment initiation centers, establishment and capacity building of multidisciplinary outpatient DR-TB teams and DR-TB DOT providers to manage patients at the community level.

Results and lessons learnt: As a result of cPMDT strategy implementation, the mean duration of delay in initiation of treatment reduced from 69 days in 2011 to five days in 2016. The percent of enrolled patient in relation to number of diagnosed patients increased from 57% in 2011 to 97% in 2016. The treatment success rate is increased to 68% in 2009 to 76% in 2013 and loss to follow up decreased gradually (see figure 1).
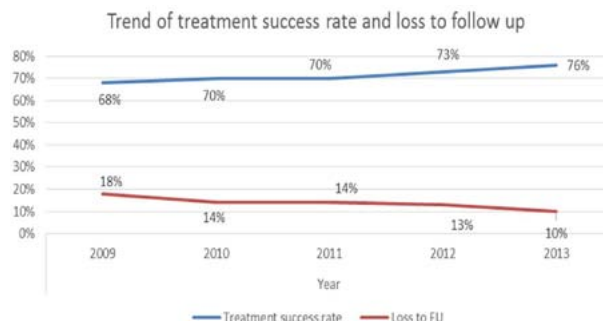
Figure DR TB treatment success rate

Conclusions and key recommendations: The community based management system of DR-TB and more specifically, maintaining comprehensive quality care for patients in the community contributes to increased enrollment and to achieving an improved treatment success rate and low lost to follow up rate.

SOA-417-13 Contribution of private health facilities to the management of MDR-TB: experiences from Kampala, Uganda

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Background and challenges to implementation: In 2012, Uganda implemented a mixed multidrug-resistant tuberculosis (MDR-TB) model that involves a brief period of hospitalization followed by ambulatory care at a follow-up directly observed therapy (DOT) facility (FUFs) nearest to the patient's home. Mulago being a 30-bed MDR-TB unit with over 120 patients, had to work with private, community-based health units provide the much needed DR-TB post-hospitalization care.

Intervention or response: With support from the USAID-funded TRACK TB project, Mulago Hospital's MDR-TB staff trained private and public FUFs teams in MDR-TB follow-up patient management using standardized tools. Patients in ambulatory care visited Mulago hospital monthly for expert review. FUF staff had monthly mentorships and replenishment of medicines and sup-

plies (gloves, syringes, respirators, and face masks). FUFs provided daily direct observed therapy (DOT) to patients and conducted contact tracing.

Results and lessons learnt: A review of 303 MDR-TB patients' records (2011/12-2015/16) showed after six months that 61% (185) were still on treatment, 82.2% (152) of whom were receiving DOT from an FUF. The six-month interim outcome of the 185 patients that were on treatment indicated a 70.1% (131) culture conversion. Out of these 131, 77.9% (102) were being managed by private community-based FUFs. MDR-TB patients receiving DOT from these FUFs were more likely to stay on treatment (OR=2.49, 95% CI: 1.33-4.65, p=0.004) (table below).

Facility	Patients on treatment (185/303) (61%)						Total (303)
	Culture negative	Culture Positive	Culture unknown	Died	Lost to follow up	Not evaluated	
Private	102	1	21	8	5	35	172
Public	27	0	1	5	1	21	55
Other	2	1	30	1	7	35	76

Table 1 Showing participation of health facilities

Conclusions and key recommendations: Private health FUFs in Kampala are able to provide DOT to MDR-TB patients with the achievement of good six months' interim and final treatment outcomes. The National TB/ Leprosy Program should sustain and expand ambulatory care to through private facilities in other urban centers.

SOA-418-13 Improvement of MDR-TB outcomes over time

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Background: Management of multi-drug resistant tuberculosis (MDR-TB) is challenging, especially in countries with limited resources.Though many programs hospitalize patients for long periods for treatment, providing directly observed treatment (DOT) as an outpatient may improve outcomes, particularly if social support is provided.

Methods: In 2008, GHESKIO opened an MDR-TB clinic, with hospitalization for approximately the first 10 months of treatment. In 2013, GHESKIO decreased the period of hospitalization to about 4 months (until culture-negative), and then followed patients with twice-daily DOT in the community. Trained fieldworkers provided outpatient DOT using smartphones equipped with a camera and GPS to document adherence. Patients were also provided with incentives including transportation subsidies, phone cards, and after 2013, food rations, and a monetary prize of $200 US upon completion of the 24-month treatment. We analyzed predictors of cure with marginal effects logistic regression analysis, where the coefficients are the marginal effects, which can be interpreted as the percent change in the probability of being cured, keeping all other covariates the same. We also evaluated trends in cure over time using multivariate regression.

Results: From 2008 to 2015, 257 patients were enrolled on MDR-TB treatment. The median age was 23.1 years, 53 (20.6 %) were HIV-positive, 129 (50.2%) were male, and 8 (3.1%) had pre-XDRTB resistance pattern. 163 (63.4 %) were cured, 42 (16.3%) are still on treatment, 35 (13.6 %) died, and 17 (6.6%) were lost to follow up. HIV status was the only baseline variable that was predictive of outcome; patients who were HIV-infected were 19% less likely to be cured, compared with HIV-negative patients. Patients who were treated in later years were more likely to be cured (OR 1.25; 95% CI: 1.11, 1.54).

Conclusions: MDRT-TB outcomes have improved over time in Haiti. We attribute this to earlier diagnosis with Xpert, and greater social support with outpatient treatment.

SOA-419-13 Steady-state pharmacokinetics of cycloserine in patients with MDR-TB

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Background: Although no longer a key drug in the new shortened WHO-recommended treatment regimen for MDR-TB, terizidone/cycloserine is still currently included in standard MDR-TB treatment regimens in several countries including South Africa, and will continue to be used as salvage therapy. There is a paucity of data describing the pharmacokinetics (PK) of terizidone, which consists of two molecules of cycloserine. Understanding the PK of cycloserine may improve dose optimization.

Methods: We performed a longitudinal PK study in participants with pulmonary MDR-TB at two TB hospitals in Cape Town, South Africa. Intensive PK sampling was done predose and at 2, 4, 6, 8 and 10 hours post dose. The drug assay was validated and performed using liquid chromatography mass spectrometry.

Results: The cycloserine concentration-time profile in 35 participants, including 22 men is shown in figure 1. Terizidone was not detected in any plasma samples. The median duration of therapy to cycloserine PK sampling was 33 days (IQR: 27-42). Median age and BMI was 37 yrs and 17.8 kg/m² respectively. 57% of participants

(n=20) had HIV infection. Median Cmax and AUC_{0-10} was 38.1 μg/mL (IQR: 32.6-47.2) and 319 μg.hr/mL (IQR: 267.5-378.7) respectively. On multivariate regression, dose (mg/kg) was the only factor independently associated with AUC_{0-10}.
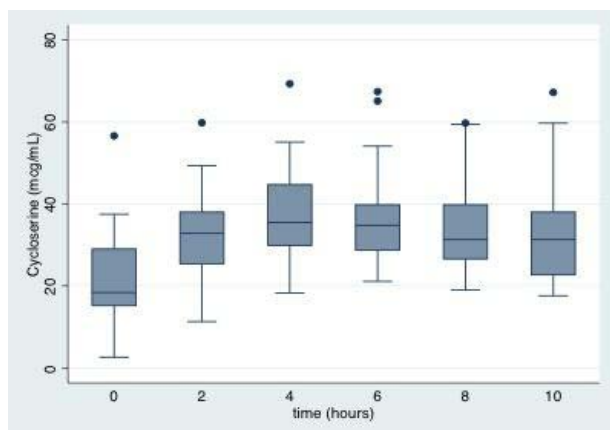
Figure Cycloserine concentration-time PK profile

Conclusions: To our knowledge, this is the first study to report the PK of terizidone at steady state and the largest study to describe steady state PK of cycloserine in patients with MDR-TB. The Cmax was higher than the range of (20-35 μg/mL) reported with cycloserine dosed at 250-500 mg daily. A study with a longer sampling interval is needed to further characterise the PK of cycloserine.

SOA-420-13 Lung tissue concentrations of linezolid among patients with drug-resistant tuberculosis

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Background: Linezolid is increasingly being used to treat multidrug-resistant tuberculosis (MDR-TB). To further characterize linezolid pharmacokinetics, we evaluated its penetration into lung tissue.
Methods: Patients with pulmonary MDR-TB receiving 600 mg of linezolid once daily and undergoing adjunctive surgery were enrolled. Serial serum samples including at the time of resection were obtained to measure linezolid concentrations. Microdialysis was performed using the *ex vivo* lung tissue to measure free drug concentrations in diseased and non-diseased portions of the resected lung. Five tissue specimens per resected sample were sent for culture.
Results: Eight male patients who had been receiving linezolid for a median of 154 days before surgical resection at a median dose of 8.33 mg/kg were enrolled. Three patients (38%) had extensively drug-resistant TB; half the

patients had a history of prior TB. Tissue culture samples from all patients were negative. The median C_{max} was 12.96 μg/ml. There was a significant correlation between weight based dose and C_{max} (R=0.82, p=0.01). The median free linezolid concentration was similar in diseased and non-diseased lung tissue (3.74 and 4.17 μg/ml, respectively). Seven of eight patients had diseased lung concentrations of linezolid above the proposed MIC resistance cutoff of 1 μg/ml. The median ratio of linezolid concentration in diseased lung over the free serum concentration at time of surgical resection was 0.46 (range 0.18-0.90). Newly diagnosed patients with MDR-TB had higher linezolid concentrations in lung tissue compared to those previously treated for TB but the difference did not reach statistical significance (4.7 vs. 2.8 μg/ml, p=0.28).
Conclusions: Our results are the first to report the free drug concentrations of linezolid in lung tissue from patients with TB. Encouragingly, we found lung concentrations were similar in diseased and non-diseased lung and that most patients had lung tissue concentrations above the proposed MIC cutoff of linezolid for susceptible isolates.

SOA-421-13 Impact of Xpert® MTB /RIF assay on MDR-TB treatment success rates in Ugu district, KwaZulu-Natal South Africa

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Background: Xpert®MTB/RIF assay rapidly diagnoses rifampicin resistance enabling early initiation of second line TB treatment. However, the impact of an earlier MDR TB diagnosis on treatment outcomes is unknown.
Objective: To compare MDR-TB treatment outcomes in MDR TB cases diagnosed with smear/culture to those diagnosed with Xpert®MTB/RIF assays, when they presented to the health care delivery system as presumptive TB cases.
Methods: In this retrospective cohort study, cohorts were defined by the initial diagnostic assay used in testing the presumptive TB case. The MDR-TB register was reviewed and data for cases treated at Ugu District MDR-TB Unit in January 2012 to April 2014 were extracted. Treatment outcomes were recorded after a minimum of a two-year follow-up period for those completing treatment.
Results: A total of 820 cases were identified and 718 enrolled into study. Mean age was 34.77 years in smear/culture and 34.97 years in Xpert group. HIV prevalence was 76.34% smear/culture and 78.16% in Xpert group. Median time to MDR TB initiation was 2.06 months in the smear/culture group and 0.63 months in Xpert group. Cure rate was 43.4% in smear/culture and 33.5% in Xpert (p<0.01) and treatment success rates were 54.0% and 45.2% respectively (p=0.02). In the multi-

variable regression analysis Xpert diagnosis (OR=0.47, p=0.019), male gender (OR=0.57, p=0.02) and age (OR=1.02, p=0.05) were associated with treatment success. Time to treatment initiation was not associated with treatment success. In cox regression, referral from a Primary Health Care facility HR 0.36 (p <0.01) and previous first line TB treatment history HR 0.42 (p<0.01) reduced risk for time to death outcome.

Conclusions: Despite rapid treatment initiation, treatment success rates were poorer in those diagnosed with Xpert®MTB/RIF assay. Additional pragmatic prospective studies are required to assess other factors influencing patient important clinical outcomes in MDR-TB patients.

SOA-422-13 MDR/XDR TB DEPOT: a novel, open-access bioinformatics tool to query and analyze large-scale radiological, genomic and clinical data from the multinational TB Portals Program database

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Background: The NIAID TB Portals Program was established as a multi-national collaboration to better understand drug-resistant tuberculosis (DR-TB) by collecting a wide range of radiological, genomic and clinical data. To facilitate the advanced precision medicine route from Data to Knowledge to Decision-Making, we developed the Data Exploration Portal (DEPOT), an advanced analytical resource that enables users to execute multifactor analysis of rare, unusual, atypical and most dangerous DR-TB cases.

Methods: Currently, data from 860 de-identified, curated and validated TB cases from five countries (Belarus, Georgia, Moldova, Romania, and Azerbaijan) are shared through web-based, open-access TB Portals. The entire database contains approximately 180 extremely drug resistant TB and 460 multi-drug resistant TB cases. There are 887 chest X-rays and 937 CT image series, and 650 bacterial genome sequences. DEPOT was built for statistical analysis and advanced dataset query using an Amazon Web Services cloud-based, open-access web application leveraging QlikView Server and R.

Results: DEPOT provides a user-friendly and intuitive query builder for search and selection of patient cohorts for subsequent comparative analysis of associated data. Statistical results are evaluated, visualized, and summarized across clinical, genomic, and radiological images and structured descriptors, identifying statistically significant factors between the cohorts. The cohorts can be created starting from clinical, genomic, or image

data, yet the analysis evaluates the entire case record. Sophisticated search enables users to find cases of interest and view associated data.

Conclusions: Taking advantage of standardized and annotated patient-centric big data, the TB Portals Program DEPOT analysis tool links together genomics, radiomics and clinical information for development of best clinical practices and personalized medicine. Results from its comparative analyses may also reveal novel research areas for follow-up. As such, DEPOT can facilitate research and clinical efforts to better understand drug resistant tuberculosis and aid in developing new diagnostics, drugs and vaccines.

SOA-423-13 Tratamiento para tuberculosis resistente a isoniacida no multidrogorresistente en el Perú, 2012—2014

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Background: En el Perú desde el 2010 se indica levofloxacina (Lfx), rifampicina (R), etambutol (E) y pirazinamida (Z) para el tratamiento de tuberculosis resistente a isoniacida no multidrogorresistente; sin conocerse el resultado. En algunos casos se agrega un inyectable. El objetivo es evaluar el resultado del tratamiento, y determinar las variables que pudieran afectarla.

Methods: Es una investigación operativa a nivel nacional en casos que iniciaron tratamiento de enero 2012 a diciembre 2014.

Se obtuvo información del Registro Medico Electrónico, que es una base de datos en el que se registran todos los casos resistentes. Se incluyeron casos diagnosticados con pruebas rápidas de sensibilidad (PRS): test de nitrato reductasa, MODS, Genotype MTBDRplus y/o con prueba de sensibilidad de proporciones en agar en placa (PS APP), sin resistencia a Cpx, Lfx, R, Z, E.

Las variables obtenidas fueron: sexo, edad, fecha de inicio y fin de tratamiento, lugar donde recibió tratamiento, VIH y diabetes, uso de inyectable, PRS, PS APP, y resultados de cultivos.

Se compararon las variables en casos con LfxREZ y LfxREZ mas inyectable, con la prueba de Chi cuadrado(X^2), se determinó los resultados de tratamiento, y se realizó análisis de regresión logística bi y multivariado.

Results: Se evaluaron 943 casos, con resultado favorable 77,2% (curados 34,4%, tratamiento completo 42,8%), y resultado no favorable 22,8% (abandono 19,7%, fracaso 1,2%, muerte 1,9%). En el análisis de regresión logística multivariado, las variables que disminuyeron la probabilidad de resultado favorable fueron: sexo masculino, contar solo con PS APP, uso de inyectable, y año de inicio de tratamiento (el 2014 menor resultado favorable que 2013 y 2012).

Conclusions: El esquema indicado en el Perú para resistencia a isoniacida es adecuado, no requiriendo agregar inyectable. Se debe fortalecer el acceso a PRS, y adherencia al esquema para incrementar el resultado favorable.

13. News and updates on latent TB infection

SOA-424-13 Predicting tuberculosis among adult household contacts: external validation of a tuberculosis risk score

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Background: Tuberculosis screening, preventive therapy and surveillance are underutilised interventions in household contacts, particularly among adults. We previously derived and internally validated a simple, non-invasive risk score that effectively stratified household contacts aged ≥15 years according to their risk of developing tuberculosis disease in peri-urban shantytowns. We aimed to externally validate this risk score on an independent cohort of household contacts.

Methods: Between 2014 and 2015, we identified index cases with laboratory confirmed pulmonary tuberculosis (n=613) and their household contacts aged ≥15 years (n=1,910) in 17 urban communities in Callao, Peru. Index cases completed a baseline questionnaire exploring index case, household and contact characteristics. We used these data to retrospectively calculate a risk score for each contact and assigned contacts to one of three pre-defined risk groups: low-risk, medium-risk; or high-risk. Contacts were followed for tuberculosis using NTP treatment registers until 1st March 2017. We assessed the score's ability to predict tuberculosis by calculating the C-statistic, deriving Kaplan-Meier functions and generating histograms illustrating differences between risk groups at 1 and 2.5 years post-exposure.

Results: 65/1,910 (3.4%) contacts developed tuberculosis during 3,771 person-years of follow-up equating to an incidence rate of 1.7/100 person-years (95% CI: 1.4-2.2). Classification assigned 575 (30%) contacts as low-risk, 918 (48%) as medium-risk and 417 (22%) as high-

risk. The observed 2.5-year risks of tuberculosis in the low-, medium- and high-risk groups were 1.4% (95% CI: 0.70-2.8); 3.9% (95% CI: 2.5-5.9); and 8.6% (95% CI: 5.9-13) with a C-statistic of 0.67 (log-rank: p<0.001) (Figure). These figures are similar to the corresponding rates observed in the derivation cohort.

Conclusions: In an independent cohort of household contacts, we externally validated a risk score that stratifies adult household contacts with significantly different risks of developing tuberculosis. This score could be used to prioritise tuberculosis control interventions to contacts most likely to benefit.

	1-year risk	2.5-year risk
Community risk	0.16	0.32
Low risk score (n=575)	1.4	1.4
Medium risk score (n=918)	1.9	3.9
High risk score (n=417)	4.1	8.6
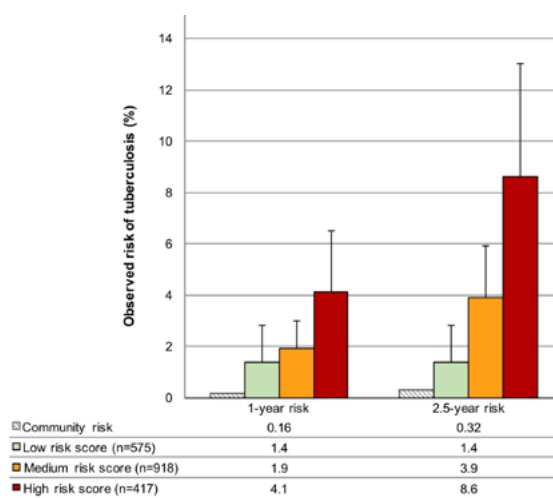
Figure Cumulative risk of tuberculosis among contacts

SOA-425-13 Seasonality, HIV and invalid T-SPOT.TB results: piecing together the IGRA puzzle in childhood TB

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Background: Interferon gamma release assay (IGRA) use in young and HIV-infected children has been limited due to concerns regarding naïve and depressed immunologic profiles driving invalid results. Recent United States (US) evidence demonstrates that in routine practice invalid T-SPOT.TB results are rare, but primarily associated with a high nil response, presumably resulting from endogenously activated T-cell interferon gamma (IFN-γ) production due to allergens or other antigenic stimuli. This US-based study examined associations between seasonality, as a proxy for allergen exposure, and high nil T-SPOT.TB results while considering age and HIV status.

Methods: Oxford Diagnostic Laboratories provided de-identified T-SPOT.TB results for 44,289 children <17 years of age whose samples were received for T.SPOT.TB

assays from 2010-2015. Seasonality data was determined using US National Oceanic and Atmospheric Agency regional climate data and floristic zones. The association between high nil invalid results and seasonality were estimated by bivariate analysis and logistic regression.

Results: Among 12,077 T-SPOT.*TB* assays drawn during the summer months (June through August), samples from extremely hot and humid southern US states were four times more likely to have a high nil invalid response than samples drawn from cooler northern states. The prevalence of high nil invalid results did not vary by geography during other seasons. Among samples received from HIV clinic draw sites (*n*=637), the estimated odds of high nil invalid results was 3.8-fold higher in summer (7.2; 2.1- 24.2) than winter months (1.9; 0.2-13.7), suggesting potential interaction between these factors despite the small sub-set.

Conclusions: In the southern US, high seasonal allergen exposure could possibly lead to increased endogenous T cell activation and production of IFN-γ, resulting in high nil indeterminate results. HIV infection also leads to increased T cell activation, but when combined with summer allergen exposure, the results were amplified. Future investigations should examine this relationship further.

SOA-426-13 Pre-immigration latent tuberculosis infection screening in new migrants to low-incidence countries: a cost-effectiveness analysis

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Background: In most low tuberculosis (TB) incidence countries, the majority of the TB burden lies in migrant populations. Up to 85% of TB in these populations can be due to reactivation of latent TB infection (LTBI) acquired pre-landing. To eliminate TB, considerable effort will be required to identify and treat LTBI in migrant populations; pre-immigration LTBI screening as a basis for post-arrival follow-up and treatment is under consideration.

Methods: A discrete event simulation model was developed in Simio 8 (Simio LLC, Sewickley, PA), modeling pre-immigration LTBI screening, and if positive, post-arrival LTBI treatment. A ten-year time horizon using a third party payer healthcare system perspective and 5% discount rate was utilized. Screening tests included the tuberculin skin test (TST), interferon-gamma release assay (IGRA), and sequential screening (SEQ) consisting of a confirmatory IGRA if the TST was positive. Post-arrival treatment was nine-months of isoniazid or four-months of rifampin. All interventions were compared to the current standard of pre-arrival active TB screening.

Incident TB cases were reported per 1000 migrants by TB incidence in country of origin and incremental cost-effectiveness ratios (ICER) per TB case prevented were calculated.

Results: Results of the analysis are presented in the table. The most cost-effective intervention was using SEQ as a flag for post-arrival treatment with rifampin with an ICER of $116,181 in migrants from countries with TB incidence >199 cases per 100,000 population. The most effective intervention to reduce ten-year TB incidence was using IGRA as a flag for post-arrival treatment with isoniazid, reducing TB incidence by approximately one third, regardless of TB incidence in country of origin.

TB Incidence in Country of Origin	Reference - Only active TB screening	TST followed by post-arrival isoniazid therapy	TST followed by post-arrival rifampin therapy	IGRA followed by post-arrival isoniazid therapy	IGRA followed by post-arrival rifampin therapy	Sequential screening followed by post-arrival isoniazid therapy	Sequential screening followed by post-arrival rifampin therapy
<30 cases per 100,000 population	0.21 (N/A)	0.15 ($3,120,983)	0.16 ($2,606,354)	0.15 ($2,658,852)	0.16 ($2,418,275)	0.15 ($2,019,419)	0.16 ($1,987,783)
30-99 cases per 100,000 population	1.35 (N/A)	0.93 ($479,658)	1.00 ($395,610)	0.90 ($395,621)	0.97 ($347,794)	0.95 ($311,497)	1.02 ($296,468)
100-199 cases per 100,000 population	2.86 (N/A)	1.97 ($237,341)	2.11 ($189,620)	1.91 ($201,903)	2.08 ($179,319)	2.02 ($162,866)	2.16 ($147,935)
≥199 cases per 100,000 population	4.19 (N/A)	2.83 ($174,367)	3.07 ($140,901)	2.72 ($150,550)	2.98 ($128,716)	2.92 ($127,463)	3.16 ($116,181)

Table Results-Data presented as TB cases per 1000 (ICER)

Conclusions: Pre-immigration LTBI screening and post-arrival treatment is effective at reducing post-immigration incident TB. To improve cost-effectiveness, targeting this intervention based on more than TB incidence in country of origin is necessary.

SOA-427-13 Preventive treatment for contacts of multidrug-resistant tuberculosis: a systematic review

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Background: Limited evidence is available on the effectiveness of preventive treatment for contacts of tuberculosis patients with multidrug-resistant strains (MDR-TB). We updated a systematic review conducted in 2014 to assess published evidence for preventive treatment of MDR-TB contacts.

Methods: We searched studies published between February 2014 and November 2016 to identify additional studies published after the previous review. We used Pubmed, Embase, Global Health Library, and other electronic databases as well as abstracts from relevant conferences.

Randomized control trials (RCT) and observational studies were included. We included studies on preventive treatment allowing any drug or drug combinations. Studies without a control group were excluded. Studies identified in the previous review were also included.

Results: Ten studies were included (six newly found and four identified from the previous 2014 review). Five studies reported no TB case either in intervention or control groups. Two studies suggested a reduced risk of active TB (regardless of drug-susceptibility) or MDR-TB by preventive treatment. In the study by Bamrah et al, 104/119 (87%) contacts had initiated fluoroquinolone-based preventive treatment, of whom 93 (89%) completed. None of these participants has developed active TB while 3/15 (20.0%) of contacts who had refused treatment developed MDR-TB disease (Odds ratio [OR]: 0.02, 95%CI 0.00 - 0.39). In the study by Schaaf et al, 2/41 (4.9%) children receiving a tailored preventive treatment developed confirmed or probable TB compared to 13/64 (20.3%) children without proper preventive treatment (OR 0.2, 95% CI: 0.04-0.94). In the other three studies reporting at least one active TB case, there was no significant difference in the incidence of active TB or MDR-TB between intervention and control groups. Heterogeneity between the studies precluded pooled meta-analysis.

Conclusions: Data on the effectiveness of preventive TB treatment for MDR-TB remain limited to formulate recommendations. High-quality evidence from RCTs is urgently needed.

SOA-428-13 Incidence and risk factors for tuberculosis infection in a high endemic region: a follow-up study among household and community contacts in Vellore, South India

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Background: Incidence of TB infection is an important measure of transmission but is rarely captured prospectively or accounts for contributions within households as well as the community. We used QuantiFERON Gold-In Tube (QFT)and Tuberculin Skin Test (TST) to estimate infection rates in household and community contacts of identified TB cases.

Methods: Between 08/2010 and 09/2012 we prospectively followed household contacts (HHC) of TB cases and neighbourhood community controls (CC) in Vellore, Tamil Nadu, India. The primary measure of infection was via QFT conversion as per manufacturer definition, although we also compared our results using less sensitive measures of conversion and reversion and changes in QFT+ prevalence in the groups as a whole. TST was only performed on participants who were negative

at baseline. Risk factor analysis was conducted using generalised estimating equations (GEE) to account for household clustering.

Results: HHC showed a significant rise (p=< 0.001) in the QFT positivity (46.8% in baseline to 60.3% in follow-up). Reversions using QFT was significantly lower (OR=0.36, CI=0.14-0.92) among the HHC (7.0%) than CC (18.0%).

Conversion rates using QFT were higher among HHC (31.03%) compared to CC (20%), but no statistical significant differences (OR=1.55, CI=0.88-2.72) were observed. Estimates using TST showed a significantly lower rate of conversion among HHC (OR=0.36, CI=0.14-0.92). Conversion and reversion rates were variable using different cut off points.

Regression analyses showed that baseline discordances (TST+QFT- and TST-QFT+) were a significant predictor of QFT conversion (OR=3.49 CI=1.75-6.94) and reversion (OR=11.21, CI=3.78-33.21) respectively. In addition, being a household contact (OR=0.69, CI=0.51-0.92) and increasing age in decades (OR=0.26, CI=0.09-0.71) were significant predictors of QFT reversion.

Conclusions: During follow-up, HHC exhibited a significantly high QFT positivity and reduced chances of reversion in comparison to the CC. Higher rates of conversion and reversion using different cut off points reveal variability and difficulty in test interpretation.

SOA-429-13 Factors associated to isonazid-preventive therapy initiation and completion among household contacts < 5 years old of tuberculosis patients

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Background: Isoniazid-preventive therapy (IPT) can prevent tuberculosis (TB) among children < 5 years old exposed to TB. We explored the factors associated with IPT uptake and completion in household contacts < 5 years old of patients with pulmonary TB (PTB) in Lima, Peru.

Methods: In a retrospective longitudinal study, we reviewed clinical files of PTB index cases and their contacts in 13 health facilities of two large districts in Lima, between January 2015 and July 2016. We registered cases and contacts´ characteristics and IPT use. Contacts were considered to have completed IPT if their caretaker picked up at least 80% of the prescribed weekly doses. Only children eligible for IPT were considered in the analysis of uptake and children still on IPT or whose IPT was discontinued by the doctor were excluded from

the analysis of completion. A multilevel logistic regression analysis accounting for clustering at the household level was conducted to identify factors associated with IPT uptake and completion.

Results: Among 197 (10.8%) <5 years old contacts of 537 PTB cases, 171 (86.8%) were eligible for IPT. Among those eligible, 121 (70.8%) started and 52/113 (46.0%) completed IPT. Children had a higher risk of not being started on IPT if they were not first-degree relatives to the index case (sibling/ offspring), if the index case was smear negative, if they were not tested with a tuberculin skin test (TST) (Table)

Children were at higher risk of non-completion if the index case had a treatment outcome other than "success", was smear-negative and if the child was not tested with TST (Table). Other variables included in both models which were not significant were age and sex of the index case and age and sex of the contact.

Factors	Adjusted OR (95% CI) for not starting IPT	Adjusted OR (95% CI) for non-completion of IPT
Smear-negative index case	4.3 (1.6-11.9)	6.6 (1.0-43.2)
Index case treatment outcome other than "success"	-	7.1 (2.2-23.0)
Non first degree relative of index case	4.9 (2.0-11.8)	-
Child not tested with tuberculin skin test	3.6 (1.3-10.0)	7.6 (CI 2.2-26.5)

Table Not starting/completing IPT associated factors

Conclusions: IPT uptake and completion need to be strengthened among all household contacts <5 years old.

SOA-430-13 The cascade of care in LTBI in Indonesia

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Background: The diagnosis and treatment of latent TB infection (LTBI) is considered a priority by the World Health Organization. In many settings, few contacts are being identified as part of the contact investigation process. As part of an ongoing research trial, the major losses in the LTBI cascade of care, from contact identification to treatment, were quantified and reasons for these losses explored.

Methods: The cascade of LTBI care was examined at seven community health centers (*Puskesmas)* in Bandung, Indonesia. Pre-existing TB Registries were used to retrospectively collect information on the iden-

tification, investigation and treatment of contacts of up to 150 index cases with pulmonary TB who had completed treatment. Interviewer administered questionnaires were completed by index cases, household contacts, parents of child contacts and health care workers (HCW) from the same centers to investigate knowledge, beliefs and barriers related to steps in LTBI care.

Results: From September 2015 to November 2016, a total of 369 contacts (5% of whom < 5 years old) were identified for 148 index cases. Of the identified contacts, 60% completed initial screening; but only 49% of those needing a medical evaluation completed it, and only 3% started LTBI treatment. Questionnaires (n=98) highlighted that both cases and contacts thought that asymptomatic contacts did not require medical evaluation. In addition, most of the 20 HCW interviewed mentioned lack of clinic staff time as a major barrier for LTBI care.

Conclusions: Even though Indonesia's TB program only recommends LTBI treatment for under-five contacts and HIV positive individuals, the cascade drop-out is excessively high. Education and promotion about LTBI management needs to be provided for HCWs and patients to improve the LTBI cascade. Providing a clear guideline, diagnostic and managerial capacities for LTBI diagnosis and treatment, will also be important issues to address. Funded by: Canadian Institutes of Health Research (CIHR)

SOA-431-13 Strategies to reduce losses in the cascade of care of latent tuberculosis: a systematic review and meta-analysis

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Background: Contacts of TB cases with latent Tuberculosis Infection (LTBI) can be lost at different steps of their cascade of care - from initial identification and screening to starting treatment. We conducted a systematic review to identify strategies to reduce losses at each step in the cascade, and a meta-analysis to combine the estimates the effect of strategies.

Methods: PubMed and Cochrane Databases were searched for articles published in English since 1990. Articles were grouped by type of strategy (e.g. education). We included studies that reported process outcomes relevant to different steps in the cascade of care and reported results in intervention and comparator groups (e.g. standard of care). For all studies included we used OpenMeta [analyst] software to calculate the pooled risk difference between intervention and comparator groups, for each type of strategy.

Results: The review included 58 studies. The following types of strategies were found to be effective in improving contact identification: education of Health Care

Workers (HCW) (36% [95% CI 20-50]), and home visits (15% [95% CI 12-18]). The following strategies increased initial assessment: HCW education (24% [95% CI 11-37]), and digital solutions (11% [95% CI 5-18]). Completion of Tuberculin skin testing was enhanced by: Patient incentives (30% [95% CI 22-37]), patient education (20% [95% CI 6-34]), use of contracts (19% [95% CI 5-31]), and reminders (15% [95% CI 8-20]. Strategies enhancing completion of medical evaluation included: one stop shop (37% [95% CI 14-59]), patient incentives (17% [95%CI 10-22]), and reminders (14% [95% CI 8-20]). Home visits (11% [95% CI 5-17]) increased the acceptance of LTBI therapy by patients. Strategies that did not have a statistically significant pooled estimate of effect are not presented here.

Conclusions: There are many strategies to address different barriers in LTBI patient management, although evidence for any single strategy is relatively limited.
Funded by: CIHR

SOA-432-13 Lack of TB knowledge among TST-positive household contacts of pulmonary cases: a missed opportunity

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Background: Recent studies of contacts of tuberculosis (TB) cases in India have found TB infection (TBI) in 40-50% of people living in the same household. With an estimated 48 million people having TBI, the program adopted IPT for child contacts and HIV+ individuals. Barriers to IPT implementation are widespread, even in countries with well-implemented policies, and IPT data from India is not available. We evaluated knowledge and understanding of TBI and IPT among tuberculin skin-test positive (TST+) household contacts (HHC) of newly diagnosed pulmonary TB cases.

Methods: We approached adult TST+ HHC who are part of a cohort study to administer a validated semi-structured questionnaire on TB knowledge and understanding of TBI. Over one year, 100 HHC were enrolled at a tertiary teaching hospital in Pune, India.

Results: General TB knowledge among HHC was lacking, with a majority of participants believing that you can get TB from sharing dishes (70%) or touching something that has been coughed on (52%). Understanding of TBI was also low, with 42% believing that being TST+ means you have disease, and 88% reporting that they did not understand the difference between TBI and active disease. A quarter of participants (26%) understood that the TST is used to determine TBI status, despite each of them being TST+, and 46% were afraid that they could infect others. Only 8% had heard of IPT,

and even then understanding is lacking, with one parent reporting IPT was, "…suggested for children but our reports are normal so opted-out."

Conclusions: TST+ HHC of recent pulmonary TB cases lack understanding of modes of transmission in the household, TBI status, and IPT. Because HHC who have recent TBI are at higher risk of progressing to active disease, it is imperative that the Indian program allocate resources for TBI education and implementation of preventive regimens for those affected.

SOA-433-13 Barriers and achievements in promoting preventive therapy for contacts of tuberculosis patients in Lima, Peru

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Background: Contacts of tuberculosis patients have a high risk of developing tuberculosis, especially children. Peruvian national policy indicates that after ruling out disease, contacts < 5 years old and those 5-19 years old with a positive tuberculin skin test (TST) should receive isoniazid preventive therapy (IPT). However, the use of IPT is limited and adherence rates are low in Peru.

Methods: We carried out a project to promote implementation of national contact management policies and increase uptake and completion of IPT within the public health system. We collaborated with the Ministry of Health in 15 health facilities in Carabayllo and Comas districts in Lima, Peru. We recruited household contacts of tuberculosis patients initiating treatment between September, 2015 and June, 2016, with the consent of the patients. A community-based field team ensured that enrolled contacts attended medical evaluations and offered home-based supervised administration of IPT.

Results: Of 109 index patients, we identified 354 contacts, of whom 314 (89%) were enrolled. Of these, 282 (90%) were evaluated for tuberculosis; 5 (1%) were diagnosed with tuberculosis. IPT was prescribed for 26 (67%) of contacts < 5 years old and 35 (36%) of contacts 5-19 years old. Of those who were prescribed IPT, 57 (93%) initiated IPT. Of these, 43 (75%) agreed to received supervised IPT. In total, 52 (91%) contacts completed 6 months of IPT. Barriers encountered to completing medical evaluation or receiving IPT included contacts not having time to go to the health center, shortage of tuberculin, hesitancy and lack of knowledge among providers, and parents' refusal of the TST or IPT for fear of adverse reactions.

Conclusions: Community-based support can assist implementation of tuberculosis contact management policies within the public health system. Although barriers exist to ensure that contacts receive IPT, high uptake and completion rates are possible.

SOA-434-13 Potential clinical utility of borderline result with the T-SPOT®.TB test

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Background: The T-SPOT.*TB* test is an ELISPOT platform Interferon Gamma Release Assay (IGRA) used to aid in the diagnosis of *M. tuberculosis* infection. This is the only commercially available IGRA that uses a borderline category, as indicated by ±1 spot from the test cutoff value of 6 spots.

Methods: This study used Oxford Diagnostic Laboratories' national T-SPOT.*TB* test database to evaluate the potential utility of the borderline category within a large and diverse clinical data set.

Results: Data collected from May 2016 through February 2017 was analyzed and prevalence of borderline results was found to be consistently rare, ranging from 1.7% to 2.1% monthly. We identified 4,960 discrete borderline results that had been retested with a new sample, as recommended by the package insert. These borderline/retest "pairs" revealed that overall 59% resolved to negative (≤4 spots), while 20% resolved to positive (≥8 spots) and 21% remained borderline (5,6 or 7 spots). The average elapsed time between borderline and retest was 28 days (range 1 to 321 days). Analysis of the resolved test pairs showed that those with a low borderline result (5 spots) resolved to negative 82% of the time. The remaining 18% (274 individuals), resolving to positive (≥8 spots), represent potentially infected persons who would have been missed without the borderline category (false negatives). Conversely, analysis of the resolved test pairs with high borderline results (7 spots) demonstrated that 36% resolved to a positive (≥8 spots), with the remaining 64% (736 individuals) resolving to negative (≤4 spots), indicating that potentially uninfected persons may have been further evaluated / treated unnecessarily (false positives).

Conclusions: This analysis confirms the CDC's guidance regarding clinical importance of a borderline category, as when addressing the 4,960 borderline cases investigated, 1010 individuals (20%) could have been potentially misdiagnosed if using a single cut-off point.

POSTER DISCUSSION SESSIONS

19. Next generation sequencing versus PCR (polymerase chain reaction) based typing: what is all the fuss?

PD-663-13 Investigation of a cluster of genotypically identical rifampicin-resistant TB cases in a district of South Africa

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Background: Transmission clusters and outbreaks of tuberculosis (TB) and drug resistant tuberculosis (DR TB) often go undetected. The National Institute of Communicable Diseases (NICD) in South Africa introduced an early warning system where all new rifampicin resistant TB (RR TB) cases diagnosed by Xpert MTB/Rif are enrolled in a molecular epidemiological surveillance system in selected districts using MIRU-VNTR 24 loci typing. A large increase in cases with identical genotype was identified and investigated.

Methods: A phylogenetic tree of RR-TB patient strains was constructed and those patients' strains that were genetically identical by MIRU-VNTR 24 loci typing were taken as cases (N=32) whilst and equal number (N=32) of patients whose strains were most distantly related from the same region and period were taken as controls. The investigation included case note abstraction, social network analysis and contact tracing. Spatial distribution of cases was mapped; temporal associations examined and social networks plotted

Results: A total of 64 patients were included for analysis. There were no specific age groups or gender that was distinctly associated with a cluster. Mortality was 23% and 25% among cases and controls respectively. Among cases, 57% had a previous episode of TB and majority (76%) of whom had drug sensitive TB. A total of 167 individuals were identified and 448 person-person links examined. Of the 21 cases investigated 12 had a known TB contact and 10 of the 12 had a close family member. The 3 XDR-TB cases without a known contact were a hair stylist, a cashier and a waitress.

Contact tracing was achieved for 17 of the 32 cases, resulting in a total of 39 individuals screened. Geospatial hotspots were localised, one of diameter 2km and another 5km long.

Conclusions: Community rather than hospital transmission was the primary route with household contacts being at greatest risk.

PD-664-13 Genetic diversity of clinical *M. tuberculosis* strains from Yangon and Mandalay Regions, Myanmar: using the MIRU-VNTR method

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Background: Determining the genetic diversity of *Mycobacterium tuberculosis* (MTB) strains allows identification of the distinct MTB genotypes in different regions. Mycobacterial interspersed repetitive unit-variable number tandem repeat (MIRU-VNTR) typing is a fast and promising method to discriminate MTB strains in many countries. The present study was carried out to determine the genetic diversity and prevalent genotype of MTB strains from pulmonary tuberculosis (TB) patients in Myanmar.

Methods: A total of 210 clinical MTB isolates from two major TB Referral Centers in Myanmar, Yangon (n=117) and Mandalay Regions (n=93), during 2012-2015 were studied. The isolates included 129 multidrug resistant (MDR) TB and MDR plus, 4 any drug resistance other than MDR and 77 susceptible strains. PCR-based typing was used to identify Beijing and Non-Beijing strains. Both 15 loci and 24 loci MIRU-VNTR typing were applied for genotyping and the results were analysed by MIRU-VNTRplus web application. The Hunter-Gaston discriminatory index (HGDI) was used as numerical index to describe the discriminatory power.

Results: All tested 210 MTB isolates showed unique patterns and did not clustered. They distributed to six lineages; Beijing (70%), East-African-Indian (4.8%), NEW1 (1.05%), LAM, CAS/Delhi and Uganda 1(0.48% each) and unknown strains (22.3%). Out of 147 Beijing strains, 77.6% (n=114) were MDR/MDR+. HGDI of 15 and 24 loci MIRU-VNTR were 0.978 and 0.986, respectively. The most prevalent genotype in both Yangon and Mandalay Regions was Beijing genotype which was found to be significantly associated with MDR-TB (P< 0.0001).

Conclusions: Myanmar MTB strains were very diverse and most prevalent Beijing genotype was found to be associated with MDR-TB. As both 15 and 24 loci MIRU-VNTR genotyping showed similar high discriminatory power, 15 loci method could be more preferable for genotyping of Myanmar MTB strains in terms of cost efficiency. This study provides baseline information for future molecular epidemiological studies in Myanmar.

PD-665-13 Whole genome sequencing analysis of drug-resistant *Mycobacterium tuberculosis* in Peru

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Background: The emergence of drug-resistant tuberculosis poses the major challenge for tuberculosis (TB) control and public health in Peru and worldwide. Here, we report the whole genome sequences of selected strains of drug-resistant *Mycobacterium tuberculosis* from National Surveillance of TB in Peru.

Methods: The study included representative strains of multidrug-resistant TB (MDR), extensively drug-resistant TB (XDR) and Pre-XDR based on phenotypic drug susceptibility test and the line probe assay - Genotype MTBDRplus. To complement these analyses, we perform whole genome sequencing (WGS) of representative phenotypes and evaluate nucleotide variation on loci associated with the extend of drug resistance. Genome sequences were compared with retrieved referential TB genomes to identify the single nucleotide polymorphisms (SNPs) and perform phylogenetics analysis.
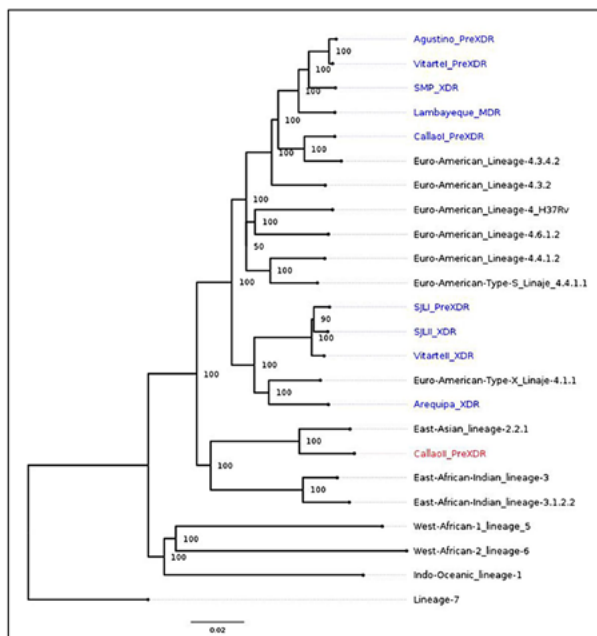
Fig. 1. Maximum likelihood Phylogenomic tree. A phylogenomic tree was inferred from 24 *M. tuberculosis* genome sequences using 16764 SNPs. The Maximum likelihood tree was estimated by RAxML version 8.2.10 using the General-time reversible nucleotide substitution model plus Gamma distribucion. Bootstrap supports were calculated from 1000 replicates and are indicates at nodes. The 10 peruvian strains (lighted in blue and red colors) were analized againts 14 reference well-stablished *M. tuberculosis* lineages from the entire world. the tree was rooted at the "Lineage seven". Scale bar indicates nucleotide substitutions per site.

Figure 1 Maximum likelihood phylogenomic tree

Results: The whole genome of 10 strains corresponding to MDR (n=1), XDR (n=4) and Pre-XDR (n=5) were sequenced. We identify a total of 56 non-synonymous polymorphisms of 19 gene coding regions associated with drug resistance, of which 25 were previously reported and 31 were novel variants. From whole genome alignment including additional 14 public available sequences, we obtained 16764 SNPs shared among all strains. A

higher nucleotide diversity was observed for Pre-XDR (0.000232) compared to XDR (0.000179), which may be due to Pre-XDR strains were resistant to additional anti-tuberculosis drugs compared to XDR strains. The phylogenomic analysis showed almost all strains are grouped in the Euro-American lineage cluster except a strain Pre-XDR that were grouped with the East-Asian lineage cluster (Fig. 1).

Conclusions: We determine that the three phenotypes of drug-resistant *Mycobacterium tuberculosis* analyzed in this study were included in the predominant Euro-American lineage; however, a Pre-XDR strain was also evidenced the East-Asian lineage. Additionally, the genomic regions associated with resistance genes are under high positive selection that could be considered the main force of diversification in drug-resistant *M. tuberculosis*.

PD-666-13 Whole genome sequencing analysis of *Mycobacterium tuberculosis* isolates from patients with drug-resistant tuberculosis in Japan

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Background: We have recently developed the Comprehensive Analysis Server for the *Mycobacterium tuberculosis* complex (CASTB), a publicly accessible web server for epidemiological analysis, drug-resistance prediction and phylogenetic comparison of clinical isolates. The aim of this study was to clarify molecular epidemiology of drug-resistant tuberculosis in Japan using CASTB.

Methods: One hundred twenty three *Mycobacterium tuberculosis* isolates with isoniazid-and/or rifampicin-resistance were collected from 17 National Hospital Organization Hospitals in Japan during April 2016 and March 2017. The whole genomes of the drug-resistant *M. tuberculosis* isolates were sequenced by the Illumina Miseq and analyzed by CASTB (http//castb.ri.ncgm. go.jp/CASTB/) which automatically provides conventional epidemiological results, predicts drug resistance, and determines a phylogeny based on single nucleotide polymorphism (SNP) concatemers.

Results: Of 123 isolates, 121 were resistant to isoniazid, 26 were resistant to rifampicin. Twenty four multidrug-resistant (MDR) *M. tuberculosis* isolates and 8 extensively drug-resistant (XDR) isolates were included. The 123 isolates clustered into four clades; Lineage 2 (East Asian or "Beijing" genotype; n =106, 86%), Lineage 4 (Euro-American, n = 12, 9.7%), Lineage 1 (Indo-Oceanic, n = 5, 4.0%) and Lineage 3 (East African-Indian, n = 0), indicating that the majority of drug-resistant *M. tuberculosis* isolates in Japan belonged to Lineage 2. Of the drug-resistant isolates classified in Lineage 2, the major-

ity (n=85, 80.2%) belonged to the atypical (ancestral) Beijing sub-genotype. Among these atypical Beijing sub-genotype isolates, there existed a sub-cluster group consisting of MDR and XDR isolates. There was no cluster consisting of highly isoniazid-resistant isolates harboring a S315 mutation in *katG*. There were no isolates harboring an H526G, H526E or H526L mutation in *rpoB* which confers rifampicin-resistance, but not rifabutin-resistance.

Conclusions: Drug-resistant *M. tuberculosis* isolates in Japan mainly belonged to the atypical Beijing sub-genotype of Lineage 2 and they did not make any cluster of highly isoniazid-resistant isolates.

PD-667-13 Genetic diversity of *Mycobacterium tuberculosis* isolates circulating in Havana, 2011—2012

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Background: Havana is the capital city of Cuba and usually reports 20-25% of tuberculosis (TB) cases of the country. However, limited information about the genetic diversity of *Mycobacterium tuberculosis* isolates circulating in Havana is available. The main objectives of this study were to determine the major lineages causing TB in Havana and to describe the changing of distribution in the last two decades.

Methods: Spacer oligonucleotide typing (Spoligotyping) was applied to 115 *M. tuberculosis* isolates from the time period 2011-2012. Classification into spoligotypes was carried out according to the international databases SpolDB4 and SITVIT2. Results were additionally analyzed with the online tool MIRU-VNTR*plus* and also compared with the *M. tuberculosis* genetic patterns found in Havana in the time periods 1993-1995 and 2009-2010.

Results: Twenty-five different spoligo patterns were defined and four were absent in the international databases. The five most common lineages were S (40,87%), Haarlem (17,39%), T (13,04%), LAM (9,57%) and Beijing (8,70%), mostly from the Euro-American lineage. The comparison with spoligo patterns found in Havana in previous studies revealed an increase of S and T lineages and a reduction of Haarlem and LAM.

Conclusions: Great diversity was observed among the *M. tuberculosis* isolates circulating in Habana in the time period 2011-2012. The genetic structure of *M. tuberculosis* has changed in this city in the last 20 years, with a reduction in endemic lineages like Haarlem and LAM, and a significant increase in S lineage, which might be associated to recent transmission events in the city. These data contribute important information for TB epidemiology and control in Habana.

PD-668-13 Development of a molecular epidemiology surveillance system for tuberculosis in Mexico

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Background: Molecular epidemiology surveillance systems are well established procedures in national tuberculosis (TB) programs from several countries. These combinate Tb-genotypic data and epidemiological information of the host, resulting in a very useful tool for understanding the behavior of TB. Despite Mexico is one of the most important contributors of TB in Latin America, this system has not been developed. Considering the above, the aim of this work was to develop a molecular epidemiology surveillance system in Mexico.

Methods: Respiratory samples of individuals with confirmed TB from three states of the country were collected from January-2014 to December-2015. Clinical isolates, DNA extraction, and genotyping, by spoligotyping and MIRU-VNTR 24-loci, were done following standard procedures. Sociodemographic and clinical variables were recovered, and search for associations with lineages was done. All data was administered in the first version of the Mexican Epidemiology surveillance system for tuberculosis (MESUSY-TB).

Results: 350 clinical isolates were included. 42 ± 17 years was the mean age of individuals. The 65% were males, 30% had type 2 diabetes mellitus, and 7% multidrugresistance. Fourteen lineages were observed in the 40% of the isolates: Haarlem (10%), LAM (8%), Ghana (7%) y EAI (4%), were the most frequent. Six clusters were found containing only orphan isolates and seven have a specific lineage. LAM with drug resistance and Haarlem with male sex, were the associations with the most significant value.

Conclusions: The first version of MESUSY-TB allowed the detailed analysis of the genotypic and epidemiological information of 350 isolates. A second version, including 200 additional isolates, is under developing. It is expected that inclusion of more isolates, allow to create a better landscape of the behavior of TB in the country and guide the development of strategies aimed to prevent its dispersion. **Acknowledgements:** RZ was funded by CONACyT-Problemas Nacionales No. 213712.

PD-669-13 High genetic diversity among *Mycobacterium tuberculosis* complex isolates circulating in the Central Region of Cameroon

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Background: The Centre region is one of the areas with the highest burden of tuberculosis in Cameroon. A recent study showed a strong decrease in single drug resistance in the referral centre for treatment of TB patients in this region. In areas where drug resistance is highly prevalent, the population structure of *M. tuberculosis* is characterized by clonal expansion and low degree of genetic diversity. Our goal was to characterize the population structure of MTBC strains circulating in the Centre region of Cameroon and investigate factors affecting the TB transmission dynamics.

Methods: This study included 582 MTBC strains isolated between March 2010 and April 2011 from pulmonary TB patients attending Jamot hospital. Isolates were characterized by 24 loci MIRU-VNTR and spoligotyping methods. The allelic diversity at each MIRU-VNTR locus and the discriminatory index of genotyping methods were estimated by the HGDI.

Results: We identified 9 known phylogenetic lineages dominated by Cameroon (50.7%) and Haarlem (23%) strains. The MTBC population was characterized by a high diversity with 228 distinct genotypes. Among the 61 resistant isolates, 28 different genetic patterns were generated and no evidence of clonal expansion of drug resistant. The recent transmission index was 59% and the cluster size ranged between 2-53 isolates with a median of 3 isolates per cluster. A minimal set of 17 VNTR loci demonstrated a discriminatory index (0.98) as high as the combination of 24 loci. Analysis revealed that Haarlem strains appeared more likely in clusters compared to other lineages.

Conclusions: Despite the predominance of the Cameroon family, the MTBC strains circulating in the Centre region of Cameroon are highly diverse. Our findings show that the relatively high RTI (59%) contrasted with the small size of clusters suggesting a simultaneous occurrence of ongoing transmission of tuberculosis and reactivation of latent TB probably due to HIV tract infection.

PD-670-13 Contribution of MIRU-VNTR genotyping to understand transmission dynamics of multidrug-resistant tuberculosis in patients from Medellin, Colombia

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Background: Transmission of multidrug-resistant tuberculosis (MDR-TB) is a challenge for global control of this disease. The present study was aimed to know dynamic of transmission or spread of MDR-TB, applying molecular tools in clinical isolates in patients from Medellin, Colombia.

Methods: Twenty four loci MIRU-VNTR was applied in 133 Multi-Drug Resistant *Mycobacterium tuberculosis* (MDR-MTB) clinical isolates (39 patients with initial diagnostic isolates; 24 patients with initial diagnostic isolates plus 70 follow-up isolates) from 55 patients diagnosed with MDR-TB and 8 diagnosed with extensively drug-resistant Tuberculosis (XDR-TB). Susceptibility patterns for each isolate were known. Phylogenetic relationship between diagnoses isolates were stablished according to susceptibility patterns, genotypes, comorbidities, previous treatment and prevalence.

Results: There were 39 different patterns, 57% of grouped patterns (36 isolates in 12 groups) and 43% of unique patterns (27 isolates). Some geographical areas and resistant patterns were shared. Euro-American lineage was present in 98% of isolates. Frequent sub-lineages were Haarlem (51%), LAM (33%), S (8%), X (6%) and EAI (2%). Concordance between initial diagnostic isolates and follow-up isolates was 67%. Patients with Haarlem lineage need more time for sputum negativization. Reinfection was detected in one patient. Some isolates belonged to patients with or without previous treatment were grouped. There were not association between lineage and comorbidities. Extensively drug-resistance was associated with Haarlem, X and S sub-lineages.

Conclusions: This study suggests active transmission of MDR-TB in the studied area. These data should allow specific interventions for control the transmission of MDR-TB. Association between XDR-MTB and Haarlem, X and S sub-lineages should be confirmed in further studies. Conventional and molecular epidemiology tools are needed in order to detect active transmission of tuberculosis in communities and possible reinfection events.

PD-671-13 Direct MIRU-VNTR genotyping of *Mycobacterium tuberculosis* from Xpert® MTB/RIF remnants

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Background: Genotyping of *Mycobacterium tuberculosis* (MTB) has improved our knowledge of its transmission dynamics. MIRU-VNTR is considered the reference tool for MTB fingerprinting. However, this technique is performed on cultured isolates, hampering the generation of data from many settings where culture is not implemented. The wide distribution of the Xpert®MTB/RIF encouraged us to investigate whether MTB MIRU-typing could be performed directly from the remnants of the Xpert cartridge.
Methods: The study was conducted at the Centro de Investigação em Saude de Manhiça (CISM), Mozambique. We performed MIRU-typing on remnants of positive-Xpert, representative of different bacterial loads. MIRU-VNTR (15 or 24 loci)was performed in a simplex-PCR format.
Results: Remnants from 24 specimens from independent patients were included. In the first stage of the study,5 high-bacterial load remnants were included, obtaining a 15-locus MIRU-VNTR complete pattern in all five. Secondly, from four additional high-bacterial load remnants, we succeeded in obtaining a complete 24 locus MIRU-VNTR. When we tried to reproduce these results in remnants with lower bacillary load (4 medium and 3 low-load),incomplete 15-locus-MIRU-types were obtained in all but one. Finally, we evaluated in eight high-load samples the impact of experiencing delays (1-4 weeks) between Xpert and MIRU analysis. Even though a complete fingerprint was obtained in certain samples after long delays(up to 23 days), delays longer than one week generally led to incomplete MIRU-VNTR patterns.
Conclusions: MIRU-VNTR analysis was possible from Xpert remnants, especially among those with high bacterial load, and 1 week the delay between Xpert test and the fingerprinting analysis. This strategy could play a major role in extending MTB molecular epidemiology studies to settings where information on the transmission dynamics of this pathogen is unavailable.

PD-672-13 Estudio de la diversidad genética de aislados clínicos de *Mycobacterium tuberculosis*

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Background: Antecedentes. La técnica de genotipificación por MIRU-VNTR de 24 *loci* permite conocer la estructura y dinámica poblacional de *M. tuberculosis*, así como la transmisión de la enfermedad. Describimos la diversidad genética de aislados clínicos de *M. tuberculosis* de una cohorte de pacientes con tuberculosis pulmonar de Orizaba, Veracruz.
Methods: Métodos. Se tipificaron aislados de MTB obtenidos de 1998-2006, por MIRU-VNTR de 24 *loci*, con PCR multiplex (GenoScreen, Lille, Fr), la cepa BCG Pasteur fue el control, los fragmentos fueron separados por electroforesis capilar en secuenciador ABI3500. Los alelos MIRU-VNTR se asignaron utilizando GeneScan LIZ1200 en el software GeneMapper v4.0 (Applied Biosystems, Foster, EUA). Los linajes fueron identificados en la base internacional MIRU-VNTR*plus* http://www.miru-vntrplus.org, para aquellos aislados sin linaje asignado, se construyó un dendograma con UPGMA, y se confirmó la clasificación de los linajes generando un minimum spanning tree (MST). Se calculó el índice de transmisión reciente. Las pruebas de susceptibilidad de los aislados se realizaron con el método MGIT (Becton Dickinson, MA, EUA).
Results: Resultados. Se analizaron 392 aislados. Doscientos uno formaron 59 grupos de 2-36 aislados cada uno. La proporción de linajes obtenida con la construcción del MST fue: Haarlem 168/392(42.8%), LAM 98/392(25%), EAI 11/392(2.8%), S 7/392(1.7%), X 2/392(0.5%), y 107/392(27.2%) fueron de linaje desconocido. El índice de transmisión reciente fue de 36.2%. A partir de 2004 aparecieron los linajes S y X. El perfil de resistencia de 326/392 (83.1%) fue: monoresistencia en 41/326 (12.5%), MDR 8/326 (2.4%), resistentes a INH+SM 9(2.7%); INH+SM+RIF 3/326 (0.9%); INH+ETB+RIF 1/326 (0.3%); 264/326 (80.1%) pansusceptibles.
Conclusions:
1. La tipificación por MIRU-VNTR 24 *loci* es un método rápido, sencillo y reproducible.
2. Los linajes principales en esta población fueron Harlem y LAM.
3. A partir de 2004 aparecieron los linajes S y X.
4. Es necesario analizar los aislados con linaje desconocido en otras bases internacionales.

20. HIV-TB services: how can we do better?

PD-673-13 Operational issues in HIV-screening among TB patients in central India: qualitative insights from healthcare providers and patients

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Background: The national policy of India recommends offer of HIV-screening to all TB-patients and subsequent linkage of HIV-infected TB-patients to National AIDS Control Programme (NACP) for HIV care and support. Madhya Pradesh (MP) is a low HIV-prevalent state of Central India, with estimated adult HIV prevalence being 0.09% (India HIV-Estimations 2015).
Methods: A qualitative research was undertaken to understand the barriers to HIV-screening amongst TB-patients in MP using record reviews and in-depth discussions with healthcare providers and TB-patients. Narrative analysis was used to document key elements of HIV-screening and management process at district level.
Results: Madhya Pradesh has a co-location status of 83% for HIV and TB services. There has been a considerable increase in proportion of TB-patients being offered HIV-screening over the years, from 50% in 2013 to 84% in 2016. However, it is still less than the recommended national guidelines. During in-depth discussions, healthcare providers attributed to non-willingness of TB-patients for low HIV-screening, owing to stigma associated with HIV and low felt need amongst the patients. TB-patients registered at healthcare centres co-located with HIV-testing facilities are more likely to get tested for HIV than those at centres without HIV-testing facilities - often TB-patients referred for HIV-screening are missed due to accessibility issues. A common complaint amongst TB-patients was regarding long queues at healthcare facilities and attitude of healthcare staff. Institutional level barriers include inadequate knowledge amongst healthcare staff about the national policy and also shortage of HIV-kits and healthcare staff at government health facilities.
Conclusions: Findings underscore the need for institutional capacity building to change healthcare providers' beliefs and practices, improved monitoring and supervision at all levels, as well as community awareness programmes and counselling of TB-patients for improved demand for these services. There is also a need for strengthening of TB-HIV collaborative activities, including infrastructure and supply chain management.

PD-674-13 An improvement in identification of presumptive TB cases enhanced improved coverage of HIV testing and detection

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Background and challenges to implementation: Malawi has a high burden of TB and HIV infections. However, only 47% of estimated incident TB cases are detected. The prevalence survey revealed that 65% of prevalent TB cases had visited health facilities at least once, indicating high level of missed opportunity in health care settings. Systematic TB screening is a key case finding strategy in the national TB strategic plan and TB manual.
Intervention or response: NTP in collaboration with partners developed standard operating procedure for systematic TB screening. The implementation was started in 2016. As part of this package, HIV test is also offered for all presumptive TB cases. A presumptive TB register was used to assist implementation of systematic TB screening. Health workers were oriented on systematic TB screening. A supervision and mentoring support was provided regularly to high volume TB registration sites. Data was routinely collected from presumptive TB register and used to monitor implementation of this intervention. The data was entered into EPI info 3.5.4 and analysis was made in STATA 13.
Results and lessons learnt: The overall number of presumptive TB cases increased by 23% in 2016 when compared with 2015. The coverage of HIV testing among presumptive TB cases increased from 67% (Jul-Sept 2015) to 82.3% in (Oct-Dec 2016) of 2016. HIV positivity rate was at 37.6 %. And 15% HIV positives are newly diagnosed.
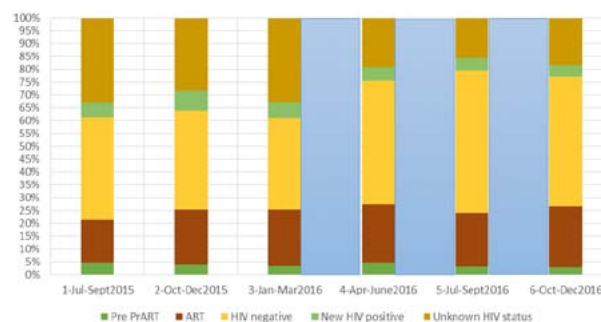
Figure Trend HIV ascertainment and positivity rate

Conclusions and key recommendations: The overall increase in case detection effort has been significant during the reporting period. These efforts are likely to improve case finding. The improved TB case detection effort has also created an opportunity for HIV testing.

This is likely to improve coverage of HIV testing and linkage to care. It is an emerging area of TB /HIV collaborative especially in countries where TB/HIV burden is high.

PD-675-13 High HIV-TB burden but suboptimal HIV services uptake for pediatric TB patients in public health facilities in Tanzania

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Background: Identification of HIV and linkage to antiretroviral treatment (ART) for children with TB disease improves clinical outcomes. We assessed the HIV infection rates and access to HIV services for children receiving TB treatment in Tanzania.
Methods: As part of a retrospective, mixed-methods program evaluation of pediatric TB services, we abstracted data from medical records of children registered for TB treatment between January 2012 and December 2014 in a purposive convenience sample of 10 health facilities in five high TB and HIV burden districts of Tanzania. We attempted to link children to the on-site HIV clinic for abstraction of data on HIV management and outcomes.
Results: Overall, 1,195 children were registered for TB treatment; 1,077 (90.1%, 95% CI: 83.3-97.0) were tested for HIV; and 431 (40.0%, 95% CI: 32.4-47.6) were HIV-infected. Of 431 children with TB/HIV, 226/429 (52.7%; 95% CI: 48.5-56.9) were male; 212/431 (49.2 %; 95% CI: 31.5-66.9) were started on ART and 368/424 (85.4 %: 95% CI: 74.9-95.9) on cotrimoxazole. HIV clinical care records were identified for 253 (58.7 %) TB/HIV co-infected patients. At the time of data abstraction, 166 (65.6 %; 95% CI: 52.4-78.8) were active in HIV care, 43 (17.0%: 95% CI: 7.0-27.0) had transferred out, 26 (10.3%; 95% CI: 3.5-17.0) were lost to follow-up, 17 (6.7%; 95% CI: 1.8-11.7) were dead and 1 (0.4 %; 95% CI: 0.0-1.3) had opted out of HIV care.
Conclusions: We found high HIV testing rates and a high burden of HIV among children with TB. Despite approximately 60% of children receiving HIV services at the same facility where they received TB treatment, only half had received ART and a high proportion were either dead or lost to follow up. To achieve optimal health outcomes for TB/HIV co-infected children, the HIV test and start strategy must be implemented.

PD-676-13 Universal HIV test-and-treat does not translate into higher CD4 counts and ART in Malawian adults with smear-positive pulmonary TB

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Background: In parts of southern Africa, more than 50% of TB patients live with HIV and are at increased risk of death. In 2015, the WHO recommended the Universal HIV Test and Treat strategy with antiretroviral therapy (ART) provided regardless of CD4 count. We wished to explore the relationship between HIV status and degree of immunosuppression in Malawian patients with smear-positive TB before and after these changes were implemented.
Methods: We analysed data from 2 cohorts of TB patients recruited to pharmacokinetic-pharmacodynamic studies in Malawi: the SPUTuM Study (2010-2011) and preliminary data from the SPITT Study (2016-ongoing). Adult patients with 2+ or 3+ sputum smear positivity for acid-fast bacilli were recruited and baseline demographics and HIV status captured.
Results: Data were available from 112 patients in the SPITT cohort, and 169 patients in SPUTuM, with 64 (57%) and 98 (59%) HIV-positive participants respectively. 109/112 (97%) patients in the SPITT cohort had tested for HIV before TB diagnosis, compared with 112/169 (66%) in SPUTuM (p< 0.005), but CD4 counts were comparable in both (median 179 and 174 cells/μl respectively, p=0.54). Most HIV-positive patients in SPITT were recently diagnosed, with 13/64 (20%) ART-naïve, 20/64 (31%) starting ART alongside TB treatment, and 11/64 (17%) taking ART for less than a year. Of those on ART for more than 4 years (13/64, 20%), median CD4 count was 151 cells/μl. In SPUTuM, 71/98 (72%) were ART-naïve and 27/98 (28%) on ART at baseline. 35/98 (36%) started ART during TB therapy.
Conclusions: New adult TB patients in Malawi were more likely to know their HIV status in 2016-17 than 2010-11 but still presented with low CD4 counts. Even in the era of Universal Test and Treat, immunosuppression-related illnesses such as TB will prompt HIV testing. National programmes must remain prepared to manage patients with advanced immunosuppression.

PD-677-13 Keeping mothers and babies alive: integrating TB case finding in prevention of mother-to- child transmission of HIV settings in Kenya

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Background and challenges to implementation: TB is the 4th leading cause of death in Kenya, a country that is among the 30 high TB burden countries globally. The TB prevalence survey (2016) showed that the epidemic affects the young (15-34yrs) and that there are missed opportunities for diagnosis (about 40%). TB is most common during a woman´s reproductive years and with TB/HIV co-infection at 31%, it may be associated with significant perinatal and maternal morbidity and mortality. Strategies should be put in place to minimize the high missed cases of opportunities. Integration of TB/HIV in Prevention of Mother to Child Transmission (PMTCT) settings was rolled out to improve diagnosis and treatment of TB in pregnant and lactating women.
Intervention or response: Health facilities were supported to integrate TB/HIV through continuous medical education, training, mentorship, job aids, presumptive TB registers and laboratory networking.
After implementation, a retrospective assessment of 936 mothers who were on follow up for PMTCT was done. Subjects were randomly selected from population of mothers receiving care in county referral hospitals in Laikipa, Nyandarya, Nyeri, Muranga and Kiambu counties. Data was collected from patient files and presumptive TB register.
Results and lessons learnt: Uptake of TB/HIV integration in the PMTCT settings was 100% in all the health facilities, with buy in from the facility staff and the county management teams.
Of the 936 mothers included in the assessment, 75% were on ANC follow up. TB screening was done for 95% (n=702) of ANC mothers with a Myacobacterium TB positive yield of 2%. Majority of PNC mothers (94%, n=234) had a TB screening with a Myacobacterium TB positive yield of 0.5%. All the patients with a TB diagnosis were put on TB treatment.
Conclusions and key recommendations: There was good uptake of TB/HIV integration in PMTCT settings. The integration was associated with high levels of TB screening of pregnant and lactating mothers.

PD-678-13 Compliance with the national Xpert® MTB/RIF diagnostic algorithm in South Africa: evidence from routine TB data (ETR.Net)

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Background and challenges to implementation: Xpert MTB/RIF (GXP) offers a rapid diagnosis of TB. Among persons living with HIV (PLHIV) with presumptive pulmonary TB, Xpert conducted on a single sputum sample has a sensitivity of 62-79%. To detect cases missed by GXP, South Africa's Xpert Diagnostic Algorithm (SAXDA) recommends sputum specimen tested by culture for PLHIV and who have a negative GXP test. The National TB Program (NTP) has raised concerns of non-compliance with the SAXDA. We evaluated compliance using the Electronic TB Register (ETR.Net) data.
Intervention or response: Routine NTP data collected in 2015 through ETR.net was analyzed for compliance with the SAXDA, utilizing STATA 14 statistical software.
Results and lessons learnt: Among 201,082 PLHIV diagnosed with TB in 2015, 130,088 (65%) had an initial Xpert. Of the 35% who did not receive an initial Xpert, 14% had smears, 0.9% had culture and 21% had no-culture/no-smear. Results of PLHIV who had initial Xpert in table 1.

	Total PLHIV	Total Cultures Done N (%)	Total Positive Culture Result N (%)	Total Negative Culture Result N (%)
With Positive Xpert	94,500	1,229 (1%)	1,162 (95%)	67 (5%)
With Negative Xpert	35,588	1,576 (4%)	1,170 (74%)	406 (26%)

Table 1 HIV Positive with Xpert MTB/Rif and Culture

Conclusions and key recommendations: Two thirds of PLHIV diagnosed with TB and started on treatment had an initial Xpert for the diagnosis of TB. Culture remains the gold standard for TB diagnosis and 5% of Xpert negative cases initiated on TB Treatment had a culture performed per algorithm. If South Africa Xpert Diagnostic Algorithm were adhered to for PLHIV with positive TB symptom screen including a culture for a negative Xpert, it is likely that more TB cases would be identified.
Recommendations:
1) Improve monitoring and enforce compliance with SAXDA both to confirm clinically suspected diagnosis and to identify additional TB cases among PLHIV with a positive symptom screen but negative Xpert.
2) Triangulate NHLS data with ETR.Net data to determine PLHIV with a negative Xpert test who were NOT initiated on TB treatment and who were NOT cultured to better understand extent of non-compliance with national algorithm.

PD-679-13 Lessons learned from diagnostic work-up of TB in a high HIV prevalence South African setting

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Background: Gold standard diagnostics for active tuberculosis (TB), including sputum culture or nucleic acid amplification (GeneXpert (GXP)) for *M. tuberculosis*, can have low sensitivity in immunocompromised patients. Facilities in TB-endemic regions are increasing use of GXP, but studies indicate limited value in HIV co-infection. Research suggests that abdominal ultrasound (US) might assist in diagnosing HIV-associated TB, although few studies have evaluated its utility after the scale-up of GXP. Our objective was to determine the value of current TB diagnostic practices in Kwa-Zulu Natal (KZN), South Africa, a TB-endemic region with high HIV prevalence.
Methods: In this cross-sectional study, files of consecutive inpatients age≥14 years and newly started on antituberculous treatment from June-July 2015 were reviewed at a KZN district hospital. Demographics, HIV status, and diagnostic test results were documented. Pulmonary TB (PTB), extrapulmonary TB (EXTB), and PTB+EXTB were defined as disease evidence in the lungs, other organs, or both, respectively.
Results: Of 94 identified cases, 38% were PTB, 35% EXTB, and 27% PTB+EXTB; 83% HIV-associated. Smear microscopy and culture were seldom ordered. 72% of PTB patients received GXP, versus 36% of EXTB and 44% of PTB+EXTB (p=.008). Of these, 58% of PTB, 33% of EXTB, and 36% of PTB+EXTB had GXP+ sputum or other body fluid sample. Among all TB cases, gold standard diagnosis was rare, with significantly higher rates in PTB (47%) than EXTB (12%) or PTB+EXTB (20%) (p=.004). Of the 33% of EXTB and 36% of PTB+EXTB patients who received US, 82% of EXTB and 78% of PTB+EXTB showed evidence of TB.
Conclusions: In a clinical setting with high HIV prevalence, TB diagnosis is less commonly confirmed by gold standard than based on clinical assessment and imaging. US appears valuable for assessing HIV-associated TB. GXP was used more than other gold standard tests, but was positive in less than half of cases.

PD-680-13 Intensified case finding for TB and isoniazid preventive therapy uptake among HIV patients in Kilifi, Kenya

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Background: The World Health Organization Three I's Strategy for TB/HIV recommends intensified case finding (ICF) for TB, isoniazid preventive therapy (IPT) and infection control (IC) at all clinical encounters. The objective of the study was to determine the extent of ICF for TB and IPT uptake among adults and children with HIV accessing care in sampled health facilities in Kilifi, Kenya.
Methods: Convenience sampling was used to select 373 adult and 107 pediatric patient files in the 25 health facilities with the highest numbers of HIV patients. This retrospective cohort study was done in October 2016. The purpose of the study was to evaluate the cascade of intervention for prevention of TB in HIV patients namely: the presence of the TB screening tool in patient files, screening of patients for TB, exclusion of active TB using the ICF criteria and treatment of latent TB infection using isoniazid.
Results: Out of the 373 adult files which were sampled, 88.7% (n=331) had ICF cards, 71.8% (n=268) of the patients were screened for TB, 75% (n=280) were eligible for IPT and 77.5% of those eligible (n= 217) were put on IPT. Out of the 107 paediatric patient files which were sampled, 83.2% (n=89) had ICF cards, 62.6% (n=67) of the patients were screened for TB, 66% (n=71) were eligible for IPT and 70.4% of those eligible (n= 50) were given IPT. ICF and IPT uptake was lower in children than in adults.
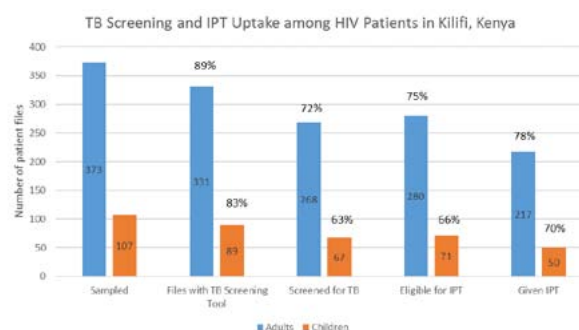
Figure TB screening and IPT uptake in HIV patients

Conclusions: This study revealed the gaps in TB screening and IPT uptake among HIV patients in Kilifi, Kenya. As a result of this study, a number of interventions were put in place to increase TB screening and IPT uptake in both adults and children with HIV accessing care in all health facilities in Kilifi, Kenya.

PD-681-13 Acceptability of a comprehensive clinic-based intervention to increase health care provider prescription of isoniazid preventive therapy in South Africa

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Background: Adherence to national guidelines for isoniazid preventative therapy (IPT) among healthcare providers (HCP) in South Africa is poor. A recent pilot study in the Northwest Province demonstrated promising results for increasing adherence to IPT guidelines by using a multi-component clinic-based intervention for HCPs, including role-playing, a quality-improvement workshop, peer-to-peer mentoring, election of a clinic "IPT champion", and text messaging support. We assessed the intervention's acceptability, reasons for effectiveness, and shortcomings through HCP experiences.

Methods: Between November 2016 and February 2017, we conducted in-depth interviews with 10 HCPs at the two study clinics. Interviews were audio-recorded, transcribed, coded by two independent coders and assessed using thematic analysis.

Results: All components of the clinic-based intervention were found acceptable by HCPs. Peer-to-peer mentoring was considered initially uncomfortable, however, all HCPs reported eventually adapting to the additional presence in their consultation room and would be open to future mentoring. HCPs attributed the intervention's success to receiving on-site training that included role-playing scenarios, an opportunity to ask questions about exceptions to the national guidelines, and receiving real-time feedback while prescribing IPT in their daily clinical practice. HCPs reported being motivated to change their behavior because the action plan resulting from the quality improvement workshop was specific to their clinic and participatory. They were also motivated by the IPT champion reporting weekly progress. HCPs continued to face barriers throughout the intervention, including IPT stock outs, patient non-adherence, and lack of oversight from within the clinic as well as from the district. Representative quotes are presented in Table 1.

Conclusions: Providing real-time clinical feedback and facilitating clinic-specific quality improvement workshops are effective and acceptable methods for increasing IPT prescription among HCPs. To promote and sustain these practices, patient education as well as health system support for inventory management and continued follow up will be required.

Peer-to-peer mentoring and real-time feedback on prescribing IPT	"She (research nurse) comes to the office... she will just do a check and say, 'Oh sister, didn't you forget this and this' and then we go back to the protocol together.' (008-9)"
	"Yeah, there´s many things that we learned. Like I´ve already mentioned... the reason why our statistics was really low on IPT is because we didn´t initiate client on IPT because most of the time, ... TST´s out of stock ... So [this workshop] taught us, no! Even if TST´s out out of stock, you can initiate IPT. Then as soon as you have... TST, you can do TST and continue with IPT." (010-2)
Role-playing scenarios	"The parts that I liked about the training? It was where you had to roleplay as the client and the patient. Then you had to roleplay. The patient will tell you the symptoms, TB symptoms or according to the scenario, you check the eligibility of INH." (001-2)
Quality improvement workshops	"Everyone had their own input in that plan, it was not created by only one person, and everyone was popping out his or her opinion about the plan." (006-27)
	"It is our own plan that was initiated by us. So now it is easy for us to follow because we are part of the plan. It was not from the top-to-bottom." (005-25).
Cues to action, e.g. IPT Champion and text messaging	"Of course, we have seen the numbers…the numbers are…every time the numbers are going up. We feel proud each and every time." (005-26)
	"Like [research nurse] is sending whatsapp just to remind me as a… champion. To remind me that, please give the staff the stats every, every week. So this, this is motivating us." (009-19)
Continued barriers	Stock: "Even if we don´t have INH, we make an emergency. But the problem is now, at the... pharmacy at the hospital. They don´t have INH, as I´ve realized." (009-23)
	Patients: "I have already received back the INH from two of my clients. They took it here to their homes, I gave them education, and when the CHW (Community Health Workers) visited them to check whether are they taking the treatment, they returned the INH, saying that they don't need it anymore, they don't have TB." (002-45)
	Oversight: "You shouldn't just come once and gone, and think that we are still doing it, because sometimes were are overloaded. There are also so many people coming here introducing other things, therefore it is not only INH … so you should keep on coming to check whether we are still on the right track or are we doing the right thing." (002-14)

Table 1 Representative Quotes

PD-682-13 Improving isoniazid preventive therapy uptake among people living with HIV in ART facilities in Nigeria: continuous quality improvement approach

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Background and challenges to implementation: TB is the leading cause of death among PLWH. The use of IPT as TB prophylaxis among PLWH has been shown to be effective in reducing TB related death by about 50%. However, despite the WHO recommendation of 6-month IPT use for TB prevention in HIV, uptake has remained as low as 19% in our program in south-east Nigeria. This project aimed at increasing IPT uptake among PLWH using a CQI approach.

Intervention or response: 9 ART facilities were randomly selected across 3 southeastern states in Nigeria for the interventions. All clients newly enrolled on ART in these facilities between April and June 2016 were screened for symptoms of TB and eligible clients were commenced on IPT. Interventions focused on the facilities health care workers and they include advocacies, TB/HIV/IPT trainings and provisions of job aids to the HCWs. In addition, monthly phone calls to the facility staff as well as physical visits for supervision and monitoring was conducted. Data was captured using existing program tools.
Results and lessons learnt: Cumulatively, IPT uptake increased from 33% (181/551) in preceding 3 months (Jan-Mar 2016) to 76% (466/616) following interventions (Apr - June 2016) across the selected facilities. However, a drop in the uptake in the month of June 2016 was observed due to a national INH stock out.
Conclusions and key recommendations: Improved PLWH IPT uptake is achievable through targeted CQI processes that are provider-focused. Also, strengthening supply chain logistics is critical to the sustenance of IPT implementation among PLWH.

21. Maximising results but minimising harm - adverse events in MDR-TB treatment

PD-683-13 Structural and behavioural correlates of aminoglycoside hearing loss among HIV-positive and HIV-negative patients in Swaziland

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Background: Ototoxicity associated with aminoglycoside containing MDR-TB treatment regimens is a significant public health problem. Context-specific interventions are urgently needed to reduce vulnerability to MDR-TB treatment related hearing loss (HL). Modifiable structural and behavioural correlates for hearing preservation in MDR-TB patients on treatment are poorly understood and the aim of the study was to identify modifiable risk factors for ototoxicity.
Methods: A prospective case-cohort study of MDR-TB patients with normal pre-treatment Pure-Tone Audiometry (PTA) initiated on kanamcycin or amikacin based regimens was conducted. We conducted monthly on-treatment PTAs (250 Hz and 8000 Hz) and observed for development of HL in the intensive treatment phase. To find an association between the incidence of cochlear damage and structural and behavioural correlates, HIV status, sociodemographic, past medical and lifestyle history and biometrical and physical characteristics of patients were recorded at baseline.

Results: 173 patients enrolled on Km/Am-Lfv-Cs/Tr-Ethio-PZA-PAS) regimen. 172 were on kanamycin and 1 on amikacin. 159 patients were analysed for hearing outcomes after the intensive phase. 123 were HIV positive and on anti-retroviral therapy (ART) base of Tenofovir (74.7%), Zidovudine (14.6%), Abacavir (4.1%), Stavudine (3.3%) and other (3.3%). 36 patients were HIV negative. Overall, 94 (60%) patients developed high frequency HL. Multivariate analysis using Cox regression model showed that occupation (HR: 5.4, CI 1.2-24.03, p-value =0.024), dyspnoea at commencement treatment (HR: 3.4, CI 1.8-6.3, p-value =0.000), baseline haemoglobin of less than 8g/dl, (HR:3.8 CI:3.3-21.6, p-value < 0.01) and Abacavir (HR:3.29, CI 1.28-8.40) based ART regimen was statistically associated with ototoxicity but not HIV status.
Conclusions: The incidence of HL was very high. Modifiable correlates should be addressed in MDR-TB treatment protocols to encourage hearing preservation. PTA conducted as a standard of care quickly identifies those at risk of hearing loss for early switch to newer drugs such as bedaquiline and delemanid containing regimens for hearing preservation.

PD-684-13 Risk for baseline hearing loss among new drug-resistant tuberculosis patients in South Africa

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Background: Among drug-resistant tuberculosis (DR-TB) patients, permanent hearing loss from ototoxic effects of injectable aminoglycosides is profound. Baseline hearing loss prior to DR-TB treatment may accelerate further aminoglycoside ototoxicity compared to those with normal hearing at baseline. The objective of this study was to determine the risk factors associated with baseline hearing loss for DR-TB patients in South Africa prior to the initiation of treatment for DR-TB.
Methods: A cross-sectional study across 10 hospitals in the Eastern Cape and KwaZulu-Natal provinces of South Africa as part of an ongoing cluster-randomized trial. All patients older than 13 years with confirmed DR-TB were included with no history of prior DR-TB treatment. The clinical, audiology and laboratory evaluations were conducted before DR-TB treatment initiation. Descriptive statistics and logistic regression were used to summarize and assess the relationships between potential risk factors and baseline hearing loss.
Results: Of 674 patients, 52% male, mean age 36.18, 75% HIV co-infected, and 51% had a prior history of drug-susceptible TB infection. Baseline hearing loss was confirmed by either audiometry or self-reported symptoms from baseline clinical evaluation in 40% of pa-

tients. Among patients having prior TB history, the odds of baseline hearing loss was 1.93 times higher in persons living with HIV (PLWH), adjusted for renal function and age (aOR=1.93; P=0.047). HIV co-infected patients with advanced immunosuppression (baseline CD4 count < 50cells/mm³) had 63% higher odds of baseline hearing loss, adjusted for age, sex, and drinking habits (aOR=1.63; p=0.008).

	N (%)	aOR (95% CI)	P-value	LR (df)
Main-effect Model: Prior TB history	664 (98.5%)	1.317 (0.928 - 1.868)	0.122	X2 (4)= 12.87, P= 0.011
Main-effect Model: HIV Status	672 (99.7%)	1.021 (0.876 - 1.191)	0.787	
Interaction Model: Prior TB history X HIV status	559 (82.9%)	1.930 (1.007 - 3.697)	0.047	X2 (5)= 18.09, P= 0.002
Main-effect Model: Immunosuppression	375 (55.6%)	1.628 (1.135 - 2.331)	0.008	X2 (4)= 10.90, P= 0.027

Table Adjusted Multivariate Logistic Regression Models

Conclusions: We found a high prevalence of baseline hearing loss in this study. Prior TB treatment history among PLWH and low pre-treatment CD4 count is significantly associated with baseline hearing loss particularly for DR-TB patients in South Africa. DR-TB providers need to consider the use of less ototoxic DR-TB regimens in PLWH with a prior TB treatment history who note baseline hearing loss.

PD-685-13 Drug-induced hypothyroidism during treatment for multidrug-resistant tuberculosis in Swaziland

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Background: Multi-Drugs Resistant Tuberculosis (MDR-TB) has emerged to be a considerable cause of morbidity and mortality worldwide. Hypothyroidism is a recognized complication of MDR-TB treatment and has been associated with certain drugs used in MDR-TB treatment regimens such as para-aminosalicylic acid (PAS) and Ethionamide/Prothionamide as well as factors such as HIV status, sex and length of time on MDR-TB treatment. We retrospectively determined the incidence of hypothyroidism, comparing a shorter course regimen (SCR) containing Prothionamide with the 20 month conventional regimen (20M-CR) typically containing PAS and Ethionamide/Prothionamide.
Methods: A retrospective cohort analysis of routine collected data from patients enrolled for MDR-TB treatment between 2011 and 2016 at two MDR-TB treatment sites in Swaziland.

Results: 286 patients received MDR-TB treatment, 150 were included in final analysis who had no pre-existing thyroid disease and both baseline and follow up TSH available (86 20M-CR, 64 SCR). There was a significantly higher chance of developing hypothyroidism (TSH >=10) amongst those receiving the 20M-CR compared to the SCR (*p*< 0.001). 58.1% 20M-CR patients developed hypothyroidism compared to just 15.6% on the SCR. All 20M-CR patients received PAS or Ethionamide/Prothionamide, 94.2% received a regimen containing both. No associations were found for risk of developing hypothyroidism with regard to sex, age, BMI, HIV-infection, CD4-count at baseline or anti-retroviral treatment status.
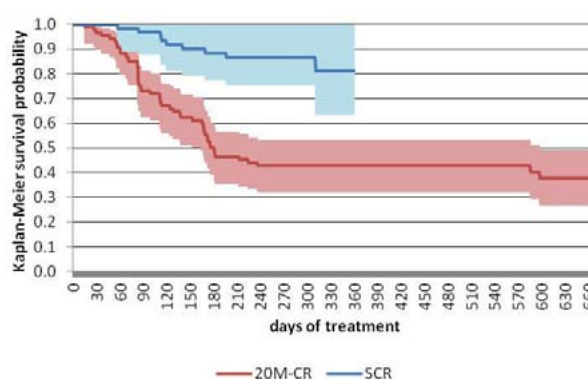
Figure Kaplan-Meier survival curve

Kaplan-Meier survival curves for length of time until occurrence of development of first episode of hypothyroidism for the SCR- (n=46) and 20M-CR cohorts (n=86). Log-rank test of signficance *p* <0.001.
Conclusions: Hypothyroidism is a neglected side-effect of MDR-TB treatment, lack of laboratory expertise and cost of testing often limits programmatic TSH testing. These findings support routine testing for drug-induced hypothyroidism in patients receiving the 20M-CR as well as the SCR and show additional potential advantage of enrolling patients on the SCR in terms of a lower incidence of drug-induced hypothyroidism.

PD-686-13 Aminoglycoside-induced hearing loss: prevention of ototoxicity in the South African National MDR-TB Programme

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Background: South Africa has the 6th highest burden of tuberculosis (TB) and second highest number of patients diagnosed with multi-drug resistant tuberculosis (MDR-TB) globally. In 2015, there were 12,550 MDR-TB patients who were initiated on treatment in SA. Drug regimens used to treat MDR-TB in SA include aminoglycoside antibiotics which are known to be oto-

toxic. Incidence of aminoglycoside-induced ototoxicity (AIO) reported in SA ranges between 47-57%. In 2013, the SA National TB Control Programme (NTP) rolled out a programme to monitor hearing thresholds of all patients who initiated MDR-TB treatment as an effort to prevent aminoglycoside-induced hearing loss.

Methods: The study used a descriptive retrospective record review design. Audiometric records of all patients who were initiated on MDR-TB treatment during September 2014 to September 2016 were reviewed. Data was extracted from the patients′ clinical records in the national ototoxicity electronic database register for MDR-TB patients and was based on records from the 102 MDR-TB treatment facilities across the country.

Results: In the 24 month period under review, 24118 patients were initiated on MDR-TB treatment; 9243 males, 6650 females and 1969 unknown, median age 34.2 [range: 14-65] years old. A total of 11233 audiometric assessments were conducted during the period under review; 6659 (28%) patients received baseline audiometric assessment, 4419 (18%) had follow-up assessments and 155 (0.6%) patients received an exit assessment at the end of first-line drug treatment as per recommended NTP ototoxicity monitoring protocol. Twelve percent (778) of patients who underwent ototoxicity monitoring presented with aminoglycoside-induced hearing loss.

Conclusions: Majority of patients who initiated MDR-TB treatment did not have baseline audiograms and even fewer had follow-up audiometric assessment. Therefore ototoxicity monitoring seems to be a challenge in the SANTP as most patients receiving SLDs, did not have their hearing thresholds monitored as intended. This undermines NTP efforts to prevent ototoxicity in MDR-TB patients.

PD-687-13 Roll-out of audiometry at a national MDR-TB hospital in Tanzania: high rates of kanamycin-related ototoxicity progressive despite treatment modification

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Background: Multidrug-resistant tuberculosis (MDR-TB) treatment currently includes injectable-agents that can lead to high frequency hearing loss.

Aim: To describe the incidence and associated risk factors for developing ototoxicity during MDR-TB treatment through implementing a rigorous monitoring approach, while examining the options for preventing the morbidity.

Methods: Consecutive medical charts of patients admitted for MDR-TB treatment at Kibong'oto Infectious Diseases Hospital between June 2015 - January 2016 were reviewed from those undergoing pure tone audi-ometry hearing threshold over a range of frequencies presented via air conduction (up to 8000Hz) prior to treatment initiation with follow-up every 2 weeks during the first 8 weeks of treatment, then monthly thereafter for a total of 8 months.

Results: Fifty-eight patients initiated on MDR-TB treatment were eligible for analysis. Mean age was 41 ± 14 years; 42 (72%) were men and 15 (26%) were HIV co-infected. MDR-TB patients previously exposed to re-treatment drug-susceptible TB regimen with streptomycin was 26 (45%). Thirty-eight (66%) of MDR-TB received kanamycin doses of 35 - 45 mg/Body mass index (BMI) whereas 10 (17%) and 9 (16%) received doses of > 45 mg/BMI and < 35 mg/BMI respectively. Twenty-three (40%) patients developed ototoxicity deemed clinically significant that prompted either decreasing the frequency of kanamycin or change from kanamycin to capreomycin. HIV-coinfection and age > 50 years were the key risk factors hazard ratios of 5 (2-17) and 0.2 (0.1-0.7) correspondingly identified for developing clinically significant ototoxicity. While kanamycin dosages per BMI, gender and previous streptomycin exposure did not show any added risk with hazard rations of 1 (0.8 - 3.3); 0.9 (0.4 - 2.3) and 1 (0.6 - 2.6) respectively. Importantly, treatment modification of injectable agents did not halt or improve progression of ototoxicity (Figure).
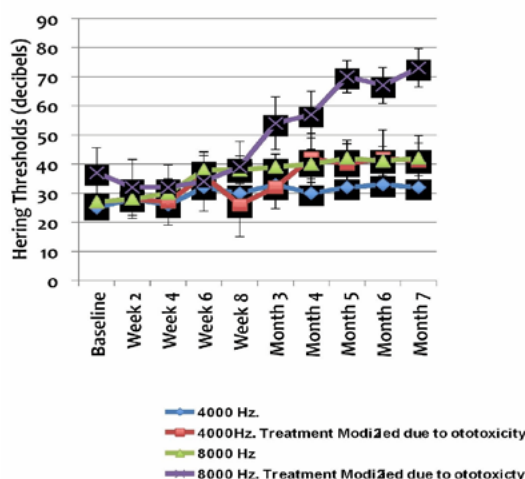
Figure: Comparison of the trend of the right ear of the Hearing Thresholds (decibels) at high frequency of 4000Hz or 8000Hz between patients that had treatment modifications and those that continued with standard doses of kanamycin during intensive phase

Figure Trend on ototoxicity

Conclusions: Rigorous audiometry shows challenges on the current management option. Novel approaches like kanamycin sparing regimens, or N-acetylcysteine (NAC) co-administration warrants trial.

PD-688-13 Implementation of active Drug Safety Monitoring (aDSM) for monitoring adverse events in DR-TB treatment with bedaquiline in the Republic of Tajikistan

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Background and challenges to implementation: Since 2015 KNCV in the framework of USAID Challenge TB project has been implementing a new regimens for treatment of multi and extensively resistant tuberculosis. Following to the WHO recommendations, the national TB program with technical support of KNCV is also focusing on introduction of aDSM for efficient and safe implementation of new treatment regimens containing new drugs such as Bedaquiline and Delamanid in the pilots.

Intervention or response: To introduce aDSM in Tajikistan the project created policy and technical basis, revised recording & reporting forms, developed an electronic patient triage application tool for recording adverse events, trained healthcare providers, procured ECG equipment and audiometer for conducting instrumental surveys regularly. Regular clinical and biochemical investigations for patients on new regimens were arranged in 3 clinic & biochemical laboratories of pilot sites for early detection of adverse events. 24 XDR-TB patients enrolled to Bedaquiline treatment in two pilots in December 2016 to March 2017.

Results and lessons learnt: Among 24 XDR-TB patients enrolled to Bedaquiline treatment in December 2016 to March 2017 none serious adverse events and none adverse events of special interest found. In 7 patients nausea and vomiting unrelated to Bedaquiline were recorded.

Conclusions and key recommendations: Introduction of Active Drug Safety Monitoring in Tajikistan allows detecting adverse events at early stage and hence, allows preventing any consequences related to new drug treatment.

PD-689-13 Adverse drug reactions of chemotherapy with bedaquiline and linezolid in patient with drug- resistant tuberculosis

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Background: Treatment of XDR-TB is a very challenging goal. Therefore the use of advanced anti-TB drugs and development of new scheme of therapy is on the top of demand.

Study objective: To reveal profile adverse drug reactions of chemotherapy with bedaquiline and linezolid in patient with drug resistant tuberculosis.

Methods: Prospective study with inclusion of 59 patients aged 18-65 years with XDR-TB. We divided patients in two groups: I group (n = 20) with use bedaquiline (Bq) and linezolid (Lzd) in scheme of therapy; II (control) group (n = 39) received chemotherapy without Bq and Lzd in scheme with use 7-8 drugs. There were 8 patients with HIV infection (13.5%). Processing of materials was carried out by program Statistica 6.0.

Results: In I group cessation of bacterial excretion 8 month was in 85.0% (17) vs 64.1% (25)(II) (p 0.01) and in 12 (60.0%) vs 15.0% (6) (p 0.01) closure of decay cavities were observed. Adverse drug reactions were noted in 8 cases (18.6%).

In I group early termination of drugs was in 3 people (2- self-willed withdrawal, 1- died due to progression of tuberculosis). In 2 patients there was a development of allergic reaction (bronchospasm); 3 - increase of QT interval in 1 month of bedaquiline administration (1- to 416 ms, 1-to 455 ms, 1- 499 ms). Drug was not re-administered.

In II group adverse drug reactions were reported in 20 cases (49.0%). In 5 patients (13.0%) - dyspeptic events were observed; disorders of cardiovascular system was registered in 1 patient (3.0%); joint pains in 2 (5.0%); neurotoxic manifestations - in 9 (23.0%); rashes on skin-1 (3.0%); hearing decline - also in 1 (3.0%).

Conclusions: Inclusion of Bg and Lzd in treatment of XDR-TB is effectively and safety in comparison with scheme of chemotherapy without these drugs.

PD-690-13 Ensuring active drug-safety montoring and management (aDSM) for patients on bedaquiline and delamanid containing regimens in Georgia

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Background and challenges to implementation: In April 2015 Georgia became the first candidate worldwide to receive the life-saving access to BDQ for programmatic use through the USAID donation program. Currently country has universal access to programmatic use of BDQ and Delamanid. As Georgia was a pharmacovigilance (PV) 'naïve' country for any disease context before 2015, the new TB drugs' implementation, has fostered the PV related activities in Georgia.

Intervention or response: National Center for Tuberculosis and Lung Diseases (NCTLD), Tbilisi, Georgia has established a comprehensive mechanism for the mandatory reporting of the Serious Adverse Events (SAEs), approved by the Ministerial decree, issued in May 2016. The recording and reporting of all SAEs occurring among drug-resistant TB patients being on treatment has become the mandatory component of PMDT. To facilitate the effective implementation of the decree, the supportive training materials and lectures were developed and by October 2016 total of 275 TB doctors and PMDT staff have received the active PV training throughout the 16 training sessions of 3 days duration each.

Results and lessons learnt: As of March 2016 total number of 76 SAE terms have been reported that have encountered to 53 out of 353 patients enrolled on new TB drugs, thus around 15% of patients developed at least one SAE. 40 SAE terms have been reported within September 2016 - March 2017, compared to just 37 SAE terms that have been reported from April 2015 to September 2016, meanings that the SAE recognition and reporting practices have greatly improved after countrywide aDSM training in Georgia. Doctors have become much more alert on adverse events that would have been missed before training and underreported.

Conclusions and key recommendations: aDSM implementation in Georgia has revealed, that the training and the routine supportive supervision is a key to functional PV system. Assessing causality when there is a concomitant treatment for other comorbidities remains a challenge.

PD-691-13 Management of QT prolongation and cardiac toxicity of new TB drugs in Europe: a cross-sectional TBnet survey

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Background: The new anti-tuberculosis drugs bedaquiline and delamanid are thought to prolong QT interval: the clinical implication of this finding remains unclear. Our study objective was to assess QT monitoring practices, experience with new drugs across Europe, and quantify the incidence of cardiac adverse events in patients receiving new drugs for MDR/XDR-TB.

Methods: A cross-sectional online survey was sent to members of the TB Network European Trialsgroup (TBnet) members in 46 European countries.

Results: Out of 77 replies, 5 incomplete, 11 duplicate, and 3 non-European submissions were excluded. Overall, 58 replies from 37 (80%) European countries were retained. Most participants worked in University Hospitals (48%). The majority (78%) monitor the QT interval regularly during tuberculosis treatment, 67% with heart rate-corrected and 33% with uncorrected QT. The main indication for the use of new drugs was providing >4 active drugs. 34 (59%) participants had experience using bedaquiline, 27% of them for >24 weeks treatment duration, treating a median of 4 patients (interquartile range (IQR): 2-25). Out of a total of 1048 treated patients, two cases (0.2%) of non-fatal cardiac arrhythmia were reported: both patients were receiving at least another QT-prolonging drug. 19 (33%) participants used delamanid, 21% of them for >24 weeks, to treat a median of 2 patients (IQR: 1-13). No severe cardiac adverse events were reported in 211 delamanid-treated patients. Use of the new drugs in association with other QT-prolonging drugs was common (87% for bedaquiline, 95% for delamanid). Overall, 14 (24%) participants used the new drugs in combination and 11 (19%) sequentially.

Conclusions: Regular QT monitoring is widespread, however experience with new drugs is still limited in Europe, especially for delamanid. Even if most par-

ticipants use the new drugs with other QT-prolonging agents, and some of them for prolonged duration and in combination, low rates of severe cardiac adverse events were reported.

PD-692-13 Adverse event profile of a DRTB infection treatment cohort: experience from the Indus Hospital TB program

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Background: Observational studies have demonstrated the efficacy of fluoroquinolone based regimen in reducing the risk of disease progression with minimal occurrence of adverse events (AE).

Methods: Household contacts of 100 DR-TB patients enrolled at the Indus Hospital from March 2016 were symptom screened and evaluated. Contacts were followed up at home on months 1,3 and 5 and at clinic on months 2,4 and 6 of treatment. On every visit, contacts were asked about adverse events and responses were recorded in adverse events questionnaire. The decision to continue or stop treatment was subjected to clinician's discretion depending on the severity of the event

Results: 705 household contacts were symptom screened and 147 contacts started infection treatment. 108 contacts started on Fluoroquinolone with Ethambutol whereas 39 contacts were started on combination of Fluoroquinolone and Ethionamide. 7 contacts on Levofloxacin and Ethambutol (n=97, 7.2%) reported AEs, 3 contacts (n=34, 8.8%) on Levofloxacin and Ethionamide, 2 contacts (n=11, 18%) on Moxifloxacin and Ethambutol, and 2 contacts (n=5, 40%) on Moxifloxacin and Ethionamide.

25% of AEs reporting were in GI system (vomiting, nausea), 43.75% of AEs occurred in central nervous system (dizziness, headache), 6.25% occurred in renal system (excessive urination), 6.25% in hepatic system (jaundice) and 18.75% reported anxiety for short duration after administration of medicine. Fluroquinolone and Ethionamide combination reported higher AEs. 80% of AEs reported were among contacts and no contact under the age of 5 who was given Ethionamide reported any AEs.

Conclusions: A fluoroquinolone based DR TB preventive regimen was generally well tolerated with no major AEs reported in our cohort. Most AEs were reported among those on an FQ and Ethionamide regimen. Children (0-5) tolerated the treatment comparatively better with only 1/51 contacts reporting any AE.

22. Using technology to advance drug-resistant TB care

PD-693-13 Electronic reporting of adverse effects of second-line anti-tuberculosis drugs in Nigeria

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Background and challenges to implementation: In Nigeria, the implementation of hospital based care for multidrug resistant Tuberculosis (MDR-TB) began in 2010 and a community-based approach for the treatment of MDR-TB was adopted in 2013. As a result of this approach, more patients are put on treatment. In an effort to optimize patient centered care address adherence issues and further breeding of resistant strains of the tuberculous bacilli, there was a need for real time reporting of adverse effect (AEs) to second-line anti-TB drugs. The electronic platform e-TB manager, has been used for over five years in Nigeria to effectively capture AEs for patients on drug resistant (DR-TB) treatment.

Intervention or response: From 2011-2016, the USAID funded TB CARE I and Challenge TB projects assisted with the Nigerian National TB Program's roll out of e-TB manager with a built-in design to capture reported AEs among DR-TB patients including:

· Adapting e-TB manager to reflect the paper AE reporting used in-country.

· Conducting training workshops for health officers at 16 MDR-TB facilities.

· Encouraging patients to regularly report AEs to their care providers.

· Mandating healthcare workers to complete pharmacovigilance forms and relevant e-TB manager sections.

	2011	2012	2013	2014	2015	2016	Total
# of DR-TB cases enrolled	38	157	330	420	627	710	2282
# Reporting AEs	29	65	83	67	69	78	391
Musculoskeletal effects	25	45	36	10	16	23	155
Neuropsychiatrics disorder	14	35	29	17	15	16	126
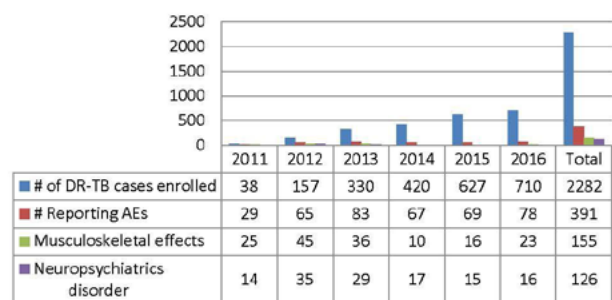
Figure Reported AEs in Nigeria 2011-2016

Results and lessons learnt: An analysis of e-TB manager from 2011 to 2016 across all DR-TB treatment centers and states involved in community care for DR-TB patients showed that 417 AEs were reported from 391 pa-

tients out of 2,282 total DR-TB patients. All patients reviewed showed resistant strains to rifampicin. Thirty seven percent of patients reported musculoskeletal effects, 33% reported neuropsychiatric disorder and 30% reported ototoxicity. The NTBLCP provides medical care and ancillary drugs to all patients experiencing AEs.

Conclusions and key recommendations: The adoption of e-TB manager can improve prompt reporting of AEs to inform programmatic decisions enhancing the quality of care for DR-TB patients. E-TB manager implementation in Nigeria helped strengthen AE reporting and the overall management of DR-TB.

PD-694-13 Effectiveness of mHealth technologies in the management of DR-TB DOTS at community level in Bangladesh

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Background and challenges to implementation: Bangladesh is a high burden multi drug resistant TB (MDR-TB) country. Community-based programmatic management (cPMDT) of drug resistant TB (DR-TB) was introduced in 2012 and was scaled up nationally in 2014, requiring a strong follow-up system by community MDR-TB direct observed treatment (DOT) providers. Given the 95.2 million mobile phone users in Bangladesh, there exists an opportunity for the use of mHealth to monitor DOT services and ensure drug adherence.

Intervention or response: Through the cPMDT program, after hospitalization, DR-TB patients are transitioned to community based care to receive treatment in their communities through trained DR-TB DOT providers. The Challenge TB project supports a web-based mHealth application through which MDR-TB DOT providers are given a smartphone and routinely access each patient's treatment regimen and can properly record side effects. The geo-tagging mechanism allows program supervisors to verify when and where each DOT session was conducted. All data is stored in a central database for central monitoring with patients' residences tagged in the record.

Results and lessons learnt: In 2016, 360 DOT providers were supervised using the smartphone application covering 412 DR-TB patients in 25 districts of Bangladesh. Supervision through a mobile device resulted in increased drug compliance and increased the regularity of providers' visits to patients' homes to 97%. Home visits and patients' compliance with required follow-up smear and culture tests remained at 100%. Contact tracing through the smartphone application also contributed to

additional active case finding. A total of 118 individuals were identified as symptomatic contacts and seven were bacteriological positive.

Indicator	Number
Number of DOT providers using mHealth	360
Number of patients covered by mHealth	412
Regularity of the DOT providers' visits to the patients' homes	97%
Patient's compliance with required follow-up smear and culture tests	100%

Table Use of mHealth for Patient Support

Conclusions and key recommendations: Mobile phones can facilitate community-based MDR-TB patient case management, particularly in rural areas in Bangladesh. Through active monitoring at the central level and field level cooperation, mHealth can play an important role in ensuring patient adherence to DOT and effective monitoring to reduce the TB burden in Bangladesh.

PD-695-13 Advancing MDR-TB research through the multi-national TB Portals Program and online database platform

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Background: Better diagnostics, more efficient drugs, and personalized treatment are direly needed to address the growing threat of multi-drug resistant tuberculosis (MDR-TB). Collaborations bringing together cutting edge experimental technologies, IT solutions, and access to multiple MDR-TB patient samples would allow for better understanding of the complex nature of the disease.

Methods: The NIAID TB Portals Program is a multi-national collaboration that has developed web-based TB Portals for data sharing and analysis. Anonymized, annotated, and standardized tuberculosis patient data, including socioeconomic, clinical, imaging, and genomic information, are shared by participating institutions in country-specific Portals and consolidated in a TB Central portal that supports simple query and data visualization. Cases in the TB Portals are backed by physical repositories of clinical samples, which can be utilized for additional research studies. The Program Steering Committee, comprised of representatives from participating countries, provides guidance on the development of the TB Portals' resources, tools, and new research studies.

Results: To date, the TB Portals contains about 860 published TB cases from five countries (Belarus, Georgia, Moldova, Romania, and Azerbaijan); approximately 180 are XDR-TB and 460 are MDR-TB cases. 650 sam-

ples have been sequenced and genomic information, including mutations related to drug-sensitivity, added back into the database. 887 images (including X-rays and CT scans) have been uploaded into the TB Portals. Numerous linked research studies and tools have been initiated using TB Portals data and samples, including whole genome sequencing, image and genome similarity analysis, microbiome analysis, and DEPOT, a sophisticated yet user-friendly query and statistical analysis tool.

Conclusions: The TB Portals Program supports open-access information sharing and data harmonization through an online database platform. The wide breadth of information gathered by the TB Portals and subsequent analyses using its data will contribute to a more comprehensive understanding of TB disease and facilitate development of new diagnostics, drugs and vaccines.

PD-696-13 Kyrgyzstan's approach to tackle DR-TB through early warning system for expedited uptake of new medicines

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Background and challenges to implementation: Kyrgyzstan is among the 30 highest MDR-TB burden countries. Inadequate supply planning of medicines resulting in stock-outs contribute to the MDR-TB burden. The National TB Program (NTP) had no system for quantification and forecasting of second line TB medicines (SLD) at the national or TB facility levels. With a wide range of international partners implementing TB activities in the country there was poor coordination of SLD procurement without considering available stocks nationwide.

Intervention or response: To improve procurement processes, ordering, and supply planning for TB treatments the country has implemented an early warning and quantification system (QuanTB). Patient and stock data flows and reporting system were designed. Responsible staff at the regional and national levels were trained and regular monitoring visits were established. All 9 regional TB facilities representing an intermediate level of the NTP were requested to report patient and stock data quarterly, and monitor stocks and consumption of medicines through regular quantification using QuanTB.

Results and lessons learnt: Quantification of SLD using QuanTB revealed the risk of significant overstock leading to potential wastage due to expiry before full consumption. As corrective action the delivery dates of 13 pending shipments of SLD with the Global Drug Facility (GDF) were adjusted preventing wastage of medicines worth 1,170,427USD. Currently, the early warning and quantification system is regularly used for SLD ordering at the regional and national levels with more frequent schedule of deliveries, which helped to develop transition supply plans for accelerated introduction of new TB tools and prevent stock-out of both "old" and new/repurposed TB medicines.

Conclusions and key recommendations: The early warning system is an important element for TB medicines supply planning at different levels of the NTP to ensure uninterrupted supply of medicines once all other elements of the supply chain, like distribution system, warehousing and transportation are concomitantly addressed.

PD-697-13 Use of QuanTB tool in planning to transition to shorter MDR-TB treatment regimen: Kenya experience

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Background and challenges to implementation: Programmatic Management of Drug Resistance TB (PMDT) in Kenya started in 2008. To date, over 1000 patients have been enrolled on treatment using the 20-month Drug Resistance TB treatment regimen. In 2016, Kenya responded to the World Health Organization recommendation to adopt the shorter MDR-TB regimen (STR). However at this time, Kenya had already initiated procurement of medicines worth USD 1,505,399.54 based on the 20-month regimen. Changing to the STR exposed the country to the risk of wastage.

Intervention or response: QuanTB Tool (version 3 and 4) was used to analyze the country's stock (i.e. stock on hand and the pipeline orders) against the patients who will continue with the 20-month regimen and those to be enrolled on the STR. Based on the generated stock report, the delivery schedule of medicines needed for STR was developed and schedule of pending orders was adjusted with guidance from the Stop TB Partnership's Global Drug Facility (GDF) which supports the country in the procurement of SLDs.

Results and lessons learnt: Procurement of medicines that were likely to expire due to low consumption were cancelled leading to a USD 265,465.34 saving. Overstocks were prevented by splitting shipments and staggering deliveries. Furthermore, delivery of the items whose consumption increased due to the transition was

expedited, preventing treatment interruptions. This gave the technical working group (TWG) confidence in planning for the introduction and roll-out of the STR.

Conclusions and key recommendations: Evidence based procurement and supply planning provided by effective utilization of the existing quantification and early warning systems is necessary to avoid wastage or stock outs during the transition to new medicines and regimens. Ongoing monitoring of stock status is also critical, particularly until the actual demand of new medicines is established.

PD-698-13 A quantification and early warning system, QuanTB, helps to avoid TB medicines stock-outs in Uzbekistan

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Background and challenges to implementation: Uzbekistan is among the 30 high MDR-TB burden countries. One of the contributing factors to the high MDR-TB burden is a deficient TB medicine supply planning. An assessment of TB pharmaceutical system in 2014 revealed TB medicine stock-outs over the last 12 months in 20 (71%) out of 28 TB facilities visited. Nine (45%) of these facilities reported an incorrect quantification of TB medicines as a main reason for the stock-outs.

Intervention or response: In 2015, we introduced QuanTB, a quantification and early warning system, designed to improve procurement processes, ordering, and supply planning for TB treatment. MDR-TB patient and TB medicine stock data reporting system was developed for all levels of TB network. Uzbekistan TB network consists of one central, 14 intermediate (oblast) and 195 district TB facilities; the central and oblast level specialists were trained and regular supervision of oblasts was established. From June 2016 QuanTB is being implemented in all 14 oblasts of the country. QuanTB is used to develop a precise distribution plan from oblast to pertinent district TB facilities.

Results and lessons learnt: We reviewed monthly QuanTB implementation reports from 10 oblasts for June-December 2016. The proportion of oblast warehouses with at least one TB medicine stock-out has decreased by 60%, from 6 out of 10 oblast warehouses at the baseline to none in December 2016. The proportion

of district TB facilities within each oblast with at least one anti-TB drug stock-out has decreased only by 32% on average (minimum 0%, maximum 83%) across the oblasts from June to December 2016.

Name of Oblast	Number of district TB facilities	Number (%) of TB Facilities with at Least One TB Medicine Stock-out		% Decrease in Proportion of Facilities with at Least One TB Medicine Stock-out for Each Oblast
		Jun-16	Dec-16	
1. Fergana	21	9 (43)	9 (43)	0
2. Karakalpakstan	18	9 (50)	1 (6)	44
3. Jizzakh	14	13 (93)	2 (14)	79
4. Tashkent City	6	6 (100)	1 (17)	83
5. Namangan	13	9 (69)	3 (23)	46
6. Andijan	20	10 (50)	10 (50)	0
7. Samarkand	17	8 (47)	0 (0)	47
8. Tashkent Oblast	20	18 (90)	14 (70)	20
9. Sirdarya	12	12 (100)	12 (100)	0
10. Surkhandarya	15	12 (80)	12 (80)	0
Average % difference across the oblasts: 32. Range: 0 - 83				

Table 1 Percent decrease in proportion of facilities with at least one TB medicine stock-out for each oblast

Conclusions and key recommendations: To ensure TB medicine optimal stock in every TB facility current policies and practices in TB medicine distribution need revision, including improving coordination between oblast and district facilities, setting minimum and maximum stock levels and developing a standard operational procedure for handling regular and emergency orders.

PD-699-13 The costs and challenges of setting up a customized web-based electronic health records system for DR-TB in a low in-come country: lessons from Uganda

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Background and challenges to implementation: Many researchers have documented the benefits of Electronic Health Records Systems (EHRs). However, the total cost of ownership far exceed budgetary expectations of many healthcare organizations. Failure to estimate all of the expenses accurately has steep long-term effects on operating costs. In this paper we share costs and challenges experienced by Uganda in setting up a customized web-based EHRs for drug resistant tuberculosis (DR-TB).

Intervention or response: In 2015, the Ministry of Health's National TB and Leprosy Program (NTLP) with support from implementing partners inaugurated a web-based EHR system for tracking and management of DR-TB patients at all levels of service delivery in the country. This EHRs was developed based on the DHIS2, an open source software. We conducted a cross sectional

analysis of the budgets, expenditures and implementation reports related to this system to understand its actual total costs and challenges experienced during implementation. We considered five main components of EHR implementation: hardware, EHR Software development, implementation assistance, training and ongoing network fees and maintenance.

Results and lessons learnt: It took Uganda a period of about two years to develop the EHRs software, procure and install hardware, train users and implement the web-based EHRs for DR-TB. The total cost for all these processes was approximately USD 100,000. The cost of developing and installing the EHRs software was USD 13,000, which is relatively less compared to documented estimated cost of purchasing and installing an already developed EHR software (USD 15,000 to 70,000). The main challenges experienced included: long procurement turn-around time, which coupled with the busy schedules of the MoH staff and partners, delayed the EHRs development and implementation processes; inadequate internal human resource capacity to administratively manage the new EHRs; and inadequate funds for ongoing network fees and maintenance.

Component	Cost (USD)
EHRs hardware	55,167
EHRs software development	13,889
Training	6,111
Implementation and troubleshooting	8,333
Ongoing network fees	11,111
Total	94,611

Table 1 Costs of setting up DR-TB EHRs in Uganda

Conclusions and key recommendations: A customized web-based EHRs for DR-TB may be relatively financially cheaper but time consuming and labor intensive.

PD-700-13 Lessons learned from the design, development, and deployment of End TB electronic medical records for MDR-TB across 16 countries

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Background and challenges to implementation: In order to analyse the effectiveness and safety of treatments for multi-drug resistant tuberculosis (MDR-TB) containing bedaquiline and delamanid for 2600 patients in 16 countries, the endTB (Expanding New Drug Markets for Tuberculosis) project needed to develop a common electronic medical record, useable across countries, languages and user organisations. The endTB consortium designed and developed an open-source care management and electronic medical record (EMR) system with unique features required for MDR-TB management: patient management tools, standardised project-level reports, daily data exports, and secure automatic back-ups. We aim to describe the process of collectively designing, developing and deploying the system to 16 countries.

Intervention or response: Over a 9 month period collectively defined system requirements, feature development priorities and configuration specificities. Clinical and epidemiological experts developed metadata and content. We piloted the EMR in April, 2016, in Armenia and Georgia. Each implementation resulted in end-user feedback, new features, adjustment of content and improvments of the system, with releases every 6 weeks between April and December 2016.

Results and lessons learnt: Weekly meetings between the consortium and technology partners allowed input from all stakeholders, facilitated decision making at all levels, and showcased the development of software in a step-by-step manner. A 6-week release cycle allowed rapid feedback, ongoing development, bug fixes, content adaptation, and implementations in Kenya, Belarus, Myanmar, Pakistan, Bangladesh, Ethiopia, Peru, Lesotho, and Kazakhstan by December, 2016, followed by rapid upgrades to implemented sites. Detailed clinical data are captured at each visit for each project, enabling harmonized monitoring and data collection across all sites. Ongoing multicentric analysis is now ongoing between the consortium members.

Conclusions and key recommendations: The EMR makes possible multi-user access at project level, comprehensive patient summaries, pharmacovigilance monitoring, and shared multi-country analysis. It is important to identify key stakeholders and decision-makers early and develop a shared roadmap. The EMR will be offered for other entities for use.

PD-701-13 Impact of implementing an early warning system to improve TB medicine procurement in Ethiopia

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Background and challenges to implementation: Ethiopia is one of the high burden countries for TB, TB/HIV and Multi Drug Resistance TB (MDR-TB) according to the latest WHO classification. However, MDR-TB case

detection remains lower than projected in the current National TB Strategic Plan (NSP) despite high government commitment to support the TB program. This contributed to over estimation and inaccurate procurement of second-line TB medicines (SLDs) in the past two years which were based on the NSP targets.

Intervention or response: In 2015, the country was trained on the use of QuanTB tool for quantification of TB medicines with support from Stop TB Partnership's Global Drug Facility (GDF) and USAID funded Systems for Improved Access to Pharmaceuticals and Services Program (SIAPS). The tool was later institutionalized as the TB medicines quantification and early warning system. In addition to forecasting it has been useful in quarterly monitoring of TB medicines stock status. It has also helped to guide the development of rational procurement plans through regular adjustment of SLDs delivery schedules based on the actual number of patients enrolled and planned to be enrolled on treatments.

Results and lessons learnt: Using QuanTB data, the country managed to postpone procurement of USD 751,041 worth of SLDs while closely monitoring their consumption trends. Wastage of additional USD 954,509 was avoided by successfully reallocating excess stocks to other countries with support from GDF. Shipments of SLDs which were already produced, but were likely to be overstocked if delivered as planned were delayed and further staggered.

Conclusions and key recommendations: Frequent review of quantification and TB medicines stock status is vital to ensure early detection of potential stock outs or overstocks. This can only be achieved if actual patient enrolment and TB medicines pipeline data are regularly used to analyze stock levels and appropriate actions are timely taken to address the identified stocks imbalances.

23. Extrapulmonary TB, vitamin D, treatment outcomes and *Aspergillus*

PD-702-13 High burden of genital TB among women with infertility in India: need for an intensified approach

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Background: Female infertility due to genital tuberculosis (TB) affects 5-13% of the Indian women of reproductive age group. More recently, the Indian TB control program released guidelines for extra pulmonary TB management including urogenital TB. However, diagnostic uncertainty exists since the yield of microbiologic confirmation is low. We aimed to identify rates of genital TB as cause of infertility among Indian women.

Methods: A prospective cross-sectional study was conducted at a tertiary care center in Pune, India, between March 2016 and September 2016 among women seeking care for infertility. Women underwent appropriate investigations including clinical history, tuberculin skin testing (TST) and laparoscopic investigations with biopsy as appropriate. Those with clinical, microbiologic, radiologic and laparohysteroscopic findings suggestive of genital TB were classified as confirmed, probable or possible TB.

Results: Among 30 women seeking care for infertility, 28 had primary and 2 had secondary infertility. None reported symptoms suggestive of TB. Four women reported prior history of TB, of which 3 had genital TB. TST was positive in 9 (33%) women; 18 women underwent laparo-hysteroscopy with 12 undergoing biopsy. None had histopathologic findings suggestive of TB, however 5 cases were diagnosed with genital TB. Of these, 2 had positive TB PCR. All 5 women diagnosed with genital TB had advanced genital tissue damage including hydrosalphinx, adhesions, blocked tubes etc.

Conclusions: Sixteen percent prevalence of clinical or microbiologically confirmed genital TB in our study provides evidence that there is a need for intensified TB investigations among women presenting with primary or secondary infertility specifically in India, home to world's largest burden of TB. Advanced genital tissue damage in these women have social and economic implications for fertility treatment as options of treatment becomes limited to expensive assisted reproductive techniques.

PD-703-13 Age-stratified tuberculosis treatment outcomes in Zimbabwe. Are we paying attention to the most vulnerable patients?

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Background: The majority of people with TB in Zimbabwe have HIV-co-infection (69% in 2015). Antiretroviral therapy (ART) retention in the region has been noted to be poorer among adolescents. We hypothesized this would be reflected in an age-dependent trend in TB treatment outcomes. Our objectives were to compare treatment outcomes among people initiated on 1st line TB treatment in relation to age and other explanatory factors.

Methods: We conducted a retrospective cohort study of patients commenced on 1st line treatment for TB during 2014 in public clinics offering TB treatment in Bulawayo. Data on age, sex, TB site, smear status, HIV status, co-trimoxazole preventive therapy uptake and treatment outcomes were acquired from routine data. Unfavourable outcomes were defined as death, loss to follow-up, treatment failure and those not evaluated. Risk factors for unfavourable outcomes were quantified as relative risks with 95% confidence intervals (CI).

Results: There were 2,213 registered TB patients; four were excluded due to missing data on age. Among these, 133 (6%) were children (< 10 years), 132 (6%) adolescents (10-19 years), 1782 (81%) adults (20 - 59 years) and 162 (7%) elderly (≥ 60 years). Adults had the highest HIV prevalence (80%), two-fold higher than other age groups. The highest proportion of smear-negative pulmonary TB cases was among the elderly (40%). Unfavorable outcomes, mostly attributed to death, increased proportionately with age and were highest among the elderly (adjusted relative risk, ARR 3.8, 95% CI, 1.3-10.7). Having recurrent TB, being HIV-positive and having unknown HIV status were associated with increased risk of unfavourable outcomes.

Conclusions: The poor treatment outcomes among the elderly may be related to co-morbidities, such as diabetes mellitus or other age-related diseases misclassified as TB. TB management should be better adapted to the needs of elderly people.

PD-704-13 A 13 year trend of tuberculosis treatment outcome among patients attending health facilities in Harari regional state, Harar, Ethiopia

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Background: Treatment outcome is an important indicator to measure progress in tuberculosis (TB) control. Monitoring and evaluation of treatment outcome of TB patients is also an integral part of the Directly Observed Treatment Short Course (DOTS) strategy. This study was conducted to assess a thirteen-year trend of tuberculosis treatment outcome among patients attending health facilities in Harari Regional State, Harar, Ethiopia.

Methods: A 13 years retrospective treatment outcome analysis was conducted on 4320 TB patients enrolled between January 2001 and December 2013. Data collection was carried out from January 15, 2013 to March 25, 2014 using a structured data capture form prepared to collect all the necessary information from the TB treatment register. Data analysis was performed by using SPSS Version 20 software.

Results: The overall treatment success rate (TSR) over the 13-year period was 84.5%. Of those with successful treatment outcome, 26.6% and 57.9% were cured and had completed their treatment respectively. Except for the year 2002, all reported TSRs were above 80%. The trend analysis also indicated an increasing trend in TSR over the study period with all TSR above the target 85% starting from 2010. Patients aged 14 years or less had significantly higher TSR (OR=2.315, 95% CI: 1.592-3.365; P=0.000), followed by 15-24 years (OR =1.690, 95% CI: 1.300-2.197; P=0.000), and 25-49 years (OR=1.534, 95% CI: 1.214-1.939; P=0.002). Being male (OR=1.197, 95% CI: 1.015-1.411; P=0.033), and rural residency (OR= 1.733, 95% CI: 1.380-2.175; P=0.000) were significantly associated with unfavorable treatment outcome compared to their counterparts.

Conclusions: This study indicated that TSR showed an increasing trend reaching the target of 85% from 2010 onwards. However, regular follow up and targeted interventions for patients who are at high risk of unfavorable treatment outcomes in the course of treatment is crucial in reducing undesired treatment consequences and ensuring the 90% target of TSR is reached.

PD-705-13 Tuberculosis care across urban India's private health sector: a two-city, cross-sectional study

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Background: India accounts for a quarter of the 10.4 million new cases of tuberculosis (TB) worldwide, and a third of the 4.3 million cases who are unreported or undiagnosed. Despite studies suggesting large delays in diagnosis and treatment, there have not been any rigorous studies on quality of care delivered to TB patients in the private sector of Indian cities, which are considered hotspots for TB transmission.

Methods: Between November 2014 and August 2015, we sent standardized patients (SPs) portraying four TB "case" scenarios to private sector health providers of two urban areas of India: Mumbai and Patna. Case 1 depicted classic TB symptoms; Case 2, classic TB symptoms and an abnormal chest radiograph; Case 3, classic TB symptoms and carried a government sputum smear microscopy report positive for acid fast bacillus; and Case 4, TB symptoms and previous history of TB suggesting recurrence and drug-resistance. We assess variations in management and quality of care outcomes stratified by (a) city, (b) case, and (c) provider qualifications.

Results: We analyzed 2602 SP visits across 1203 facilities. Correct management was observed in 959 of 2602 interactions (37%; 95% CI: 35-39). 118 interactions resulted in a prescription for anti-TB treatment (ATT) medications (5%; 95% CI: 4-5), with 113 treatments containing at least the first-line ATT regimen HRZE. In comparisons by location, case, and qualification, we find substantial variation across case and by qualification; but smaller differences between Mumbai and Patna and between AYUSH and informal providers.
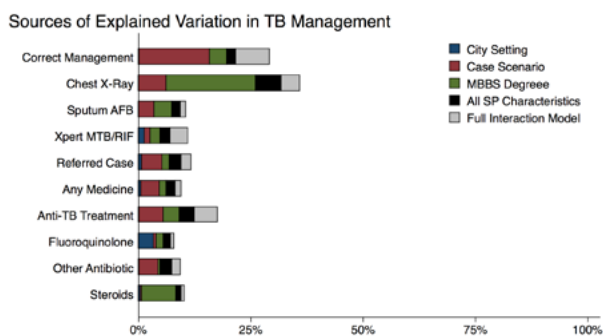
Figure Sources of Explained Variation in TB Management

Conclusions: Given the importance of the private sector in TB diagnosis and care and its recognition in national policy, this study contributes to knowledge of how the variegated private health market performs for TB symptomatics or patients. These findings are relevant for assessing the disease burden and designing interventions that aim to control or curtail the spread of the disease.

PD-706-13 Prevalence and risk factors of chronic pulmonary aspergillosis in patients with post-tubercular sequelae in India

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Background: In 2007 globally 5.96 million patients of pulmonary tuberculosis (PTB) developed symptoms of sequelae and among them 3.72 million patients developed Chronic Pulmonary Aspergillosis (CPA). Current study was aimed to assess the prevalence and risk factors associated with development of CPA among symptomatic post tubercular sequelae patients.

Methods: One hundred new (62 patients) and retreatment (38 patients) symptomatic PTB patients, who were declared cured/treatment completed after the completion of their anti-tubercular medication at a tertiary referral institute between February 2016 and October 2016, were enrolled in study. They were evaluated by clinical history, X-ray Chest, spirometry, sputum fungal culture and anti-aspergillus IgG antibody. Patients with positive anti-aspergillus IgG antibody test with/without fungal culture positive results were labelled as CPA.

Results: 45% post-TB sequelae patients with symptoms had CPA. 63% patients were symptomatic for 1-5 years. Aspergillus *fumigatus* was the commonest species isolated. Among patients with CPA, 46.7% had taken ATT only once and 53.3% had taken multiple courses. On univariate analysis, low Body Mass Index, history of taken multiple anti-tuberculosis treatment courses, advanced severity on X-ray and presence of cavity on X-ray were significant risk factors associated with development of CPA. Smoking, alcohol intake, or socio-economic status were not found to be significant risk factors. On multivariate logistic regression analysis presence of cavity was the only factor found to be independently associated with the development of CPA. Among CPA patients 75.6% had mixed obstructive and restrictive abnormality in their lung functions.

Conclusions: Significant number of patients among symptomatic post tubercular sequelae patients, especially those with cavity on chest X-ray, develop CPA. CPA appears to be an under recognized significant health problem among post-TB sequelae patients and may confer significant morbidity and mortality. All symptomatic post-TB sequelae patients, especially with cavity on X-ray, may be evaluated for CPA.

PD-708-13 Tuberculosis pericardica su asociación con tuberculosis diseminada conlleva alta mortalidad.

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Background: La pericarditis por tuberculosis corresponde al 1% de todos los casos de tuberculosis. Se presenta por diseminación linfática o hematógena de una infección tuberculosa primaria. Tiene 4 estadios: exudado fibrinoso, derrame serosanguinolento, absorción del derrame con organización caseificación granulomatosa y cicatrización constrictiva. El diagnóstico se basa en determinación de ADA mayor de 30, Lowestein, BAAR, biopsias y biología molecular.

Methods: Estudio de serie de casos consecutivos. Pacientes estudiados 18. Rango de edad: 18-63 años. Periodo: 2014-2016. Pacientes con sospecha de tuberculosis pulmonar y extrapulmonar en quién se documentó derrame pericardico. A todos los pacientes se les realizo, electrocardiograma, ecocardiograma biopsia pericardica y toma de líquido pericárdico con análisis histológico y tinciones Ziehl-neesen, auramina-rodamina, cultivo de Lowestein-Jensen y Xpert.

Results: Todos los pacientes con reporte de inflamación crónica granulomatosa compatible con tuberculosis en la biopsia péricardica, 1 con auramina-rodamina

positiva, 1 Zhiehl-neesen positivo, 3 xpert positivo, 4 con Lowestein positivo, todos con adenosindesaminasa mayor de 30 U/l en líquido pericardico, en cuanto a las comorbilidades 5 con Enfermedad Renal Crónica en hemodiálisis, 3 con diabetes, 2 HIV, 1 con sifílis, 2 con Lupus, 1 con persistencia del conducto arterioso. Se documento en 13 pacientes tuberculosis diseminada, 10 con afección pulmonar, 1 ocular, 1 en testiculo, 1 meningea, 3 ganglionar, 1 peritoneal. Fallecieron 9 pacientes (50%), debido a la diseminación de la tuberculosis, a las comorbilidades y al diagnóstico tardío. 9 pacientes curaron con Dot Bal a 1 año de tratamiento.

Conclusions: La principal causa de pericarditis en países subdesarrollados es por tuberculosis. Se debe sospechar en pacientes de riesgo. Se presenta como derrame pericárdico, pericarditis constrictiva o ambos, se asocia a derrame pleural y tuberculosis miliar. El diagnostico y tratamiento oportuno, con antituberculosos y esteroides son primordiales para prevenir el taponamiento cardiaco o la pericarditis constrictiva.

PD-709-13 Role of medical thoracoscopy in the management of multiloculated empyema

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Background: Antibiotics in pleural infection,expansion of the underlying lung by draining out complicated pleural effusion. Although this is an adequate treatment in early empyema thoracic, but the aggressive intervention becomes inevitable in late stages.

Methods:
Study design: Descriptive Case Series
Setting: Jpmc Karachi, Pakistan
Duration of study: From Sep2014 to Aug2016
Sample size: 80 patients were selected who underwent medical thoracoscopy under local anaesthesia.
Sampling technique: Data was analysed on SPSS software.Before conducting the study ethical approval was obtained from Ethical Review Committee.Patients with clinical presentation of empyema more than 30 days, non responders to antimicrobials drainage failure by thoracostomy and those who had radiological findings as (fixed mediastinum, loculated effusion, thick pleura and multiple septations, all were included in this study. While exclusion criteria were failure to get consent, age > 70 years, patients with multiple organ failure, bleeding disorders, empyema without multiple septations on ultrasound.

Results: Out of 80 patients, 54 (67.50%) were male and 26 (32.5%) were female with mean age 25.37 years (range 16 to 70 years), 51 (63.7%) were found to have tuberculous empyema, while pleural biopsy of 29 (36.3%) patients was suggestive of non-tuberculous empyema: adenocarcinoma in 12.5% patients, acute on chronic

inflammation in 16.25% and non-specific inflammation in 7%.
Final evolution through chest x-ray reveal complete resolution in 46 (57.5%), partial resolution of more than 50% from the initial X-Ray was achieved in 29 (36.35%) patients. 4 (5%) patients developed persistent air leak and required surgical intervention, while 1 (1.25%) patient expired due to septicemia.

Conclusions: The procedure of medical thoracoscopy in early management of multiloculated pleural empyema is a safe, efficient and cost effective intervention in developing countries where facility of thoracic surgery is scarce. This intervention is also useful in early diagnosis of tuberculous empyema in high endemic countries and differentiating it from pyogenic empyema.

PD-710-13 Bronchopleural complications after surgery in patients with pulmonary tuberculosis

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Background: Postoperative complications after lung resections occur in 4-25% of cases. Of these, bronchopleural fistula (BPF) is a major issue and is associated with a postoperative mortality rate up to 70% after pneumonectomy. Optimal treatment in these patients is challenging, often requiring complicated, multi-staged and aggressive procedures with conflicting results. We report our experience in the treatment of BPFs after lung resections performed for pulmonary tuberculosis.

Methods: In the period 2013-2015 in thoracic unit, we treated 35 patients with postoperative bronchopleural complications (BPF, residual cavity, purulent complications). Male 22 (62.8%), female 13 (37,2%). The median age was 35 years. Drug resistant TB were observed in 27 patients. In 18 patients developed complications after pneumonectomy, 17 after lung resection (segment-, lob-, bilobectomy, combined resection). 22 patients had associated pleural empyema.

Results: Two-step operations were performed in 14 cases (BPF d> 0,4 cm or multiple fistulas with irreversible changes in the lung parenchyma, empyema): transsternal transmediastinal occlusion of main bronchus without opening the pericardial cavity with bronchial stump plasty with thymus tissue (our development) + second stage (6 cases pleuropneumonectomy and 8 underwent removal of the distal stump of the main bronchus) and in 22 cases were one-step operation: Thoracomyoplasty using m. latissimus dorsi on the vascular pedicle performed in 9 patients (BPF d < 0,4 cm, non-empyema, after pneumonectomy), video assisted thoracoplasty was per-

formed in 12 patients (residual cavity without BPF, with/without empyema, after segment-, lob-, bilobectomy, combined resection). The overall efficiency was 94.3% (licvidation BPF, residual cavity, empyema), mortality was not registered.

Conclusions: The treatment of postoperative bronchopleural complications is a challenging and multi-faceted issues requiring an individualized approach. Our experience supports the use of the transsternal transmediastinal occlusion of main bronchus without opening the pericardial cavity with bronchial stump plasty with thymus tissue and VATS thoracoplasty.

PD-711-13 Comparative analysis of laparoscopic exploration of pelvic tuberculosis and pathological examination

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Background: To explore the application of laparoscopy in pelvic tuberculosis and pathological examination.

Methods: Study of 14 pelvic tuberculosis suspects underwent laparoscopic exploration in our hospital from January, 2013 to March 2016. Results of laparoscopy and pathological examination were compared and analyzed.

Results: All of the 14 patients received laparoscopic exploration and pathologic examination of tissue removed during biopsy. 13 patients were diagnosed with pelvic tuberculosis based on laparoscopic exploration, achieving 92.86% diagnosis rate. 12 patients were diagnosed with pelvic tuberculosis by pathological examination, achieving 85.71% diagnosis rate. 1 case was diagnosed with malignant tumor, diagnosis rate was 7.14%. 1 case was negative for pelvic tuberculosis, diagnosis rate was 7.14%. Matching rate between laparoscopic exploration and pathology results reached 92.30% (12/13).

Conclusions: Direct diagnostic value of laparoscopic exploration of pelvic tuberculosis in patients, higher the rate of diagnosis compared with the pathological examination. Laparoscopic exploration has important clinical value and is worthy of further clinical application and promotion.

PD-712-13 Using serous fluid drainage flocky precipitate (SFDFP) as testing sample for diagnosing tuberculous serositis

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Background: A definitive diagnosis of tuberculosis serositis (TS) is challenging due to the low yield of conventional microbiology investigations including culture. In this study we sought to evaluation tests on a novel type of sample, Serous Fluid Drainage Flocky Precipitate (SFDFP), which is comprised by fibrin aggregates, blood cells, isolated tissue cells, necrotic tissues and bacteria, in comparison to routine bacteriology methods on serous fluid samples.

Methods: All patients admitted into Shanghai Public Health Clinical Center from July 2014 to April 2016 with suspected TS were consecutively screened and enrolled. Serous fluid (SF) and SFDFP were collected and tested by Ziehl-Neelsen stain, MTB culture and Xpert/RIF assay. An extra histopathological examination was performed on SFDFP. We compared the diagnostic performance of SF and SFDFP in several test settings.

Results: 110 patients were screened and 85 were enrolled in this observational study. 70 (82.4%) patients were diagnosed as confirmed tuberculous serositis or highly probable tuberculous serositis, including 54 tuberculous pleuritis and 16 tuberculous peritonitis. 13 (15.3%) were tuberculosis serositis excluded and 2 (2.4%) were ruled out for indeterminate results. Valid SFDFP samples were collected from 77 (91%) patients with serious fluid. The sensitivity of integrated testing on SFDFP was 48%, not significantly different from that of integrated testing on SF (41%, p=0.86). Each individual test on SFDFP (smear, culture and Xpert/RIF) was similar with that on SF, no statistical significance identified. However, combining SFDFP and SF results, the overall sensitivity was 60%, significantly higher than both (60% vs. 48% and 41%, p< 0.05). Histopathological examination on SFDFP identified 2 malignant cell formations out of total 6 malignant cases (33.3%). The specificity of SFDFP based tests was 100%.

Conclusions: SFDFP, as an additional resource from serous fluid examination, can improve the sensitivity of microbiology diagnosing tuberculous serositis, because it supplements SF based testing.

24. Los medicamentos correctos en la dosis adecuada en el momento adecuado - TB drugs: use them right

PD-713-13 Assessment of the quality of anti-tuberculosis medicines in Almaty, Kazakhstan, 2014

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Background: In 2009, the World Health Organization (WHO) surveyed the quality of four anti-tuberculosis medicines (ATMs) in countries of the former Soviet Union. Kazakhstan had the highest proportion of substandard samples. The objective of this study was to assess the quality of ATMs used in Almaty, Kazakhstan, in 2014.
Methods: Fourteen ATMs of the Almaty Interdistrict Tuberculosis Dispensary were randomly selected and screened for quality using Global Pharma Health Fund Minilab tests. First, physical inspection of the product and packaging detected whether tablets/capsules are intact--thus containing the full amount of drug-and whether packaging appeared genuine; second, disintegration in water determined if tablets/capsules dissolved appropriately as a proxy for proper absorption; and, third, thin layer chromatography (TLC) tested the presence and concentration of the active pharmaceutical ingredient (API) and detected impurities.
Results: We discovered no counterfeit medicines. However, 163 (19%) of the 854 sampled ATMs failed at least one of the three tests. Of them, the most frequent failure was poor disintegration (90 of 163, 55%) followed by failed physical inspection (37 of 163, 23%) and failed TLC analysis on API concentration (36 of 163, 22%). These samples were found among 24 (48%) of 50 batches of eight of the 14 ATMs.
Conclusions: The screening identified a high proportion of poor-quality first- and second-line ATMs. Use of these medicines may lead to treatment failure and development of drug resistance. Confirmatory testing should be performed to determine if they should be removed from the market.

PD-714-13 Efficacy and safety of parenteral anti-tuberculosis therapy of patients with TB meningitis compared to standard treatment

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Background: The objective of this work was to study the efficacy and safety of parenteral anti-TB therapy in treatment of patients with TB meningitis in comparison with standard antimycobacterial therapy.
Methods: The study involved 44 patients with TB meningitis. Patients were allocated to two groups. The first (control) group (n=31) received standard anti-TB therapy (isoniazid 0.3 g), rifampicin (0.6 g), pyrazinamide (2 g) and ethambutol (1.2 g) - per os. The 2nd (main) group (n=13) received parenteral anti-TB therapy (isoniazid 0.5 g) - i/m, rifampicin (0.6 g) - i/v, ethambutol (1.0 g) - i/v and pyrazinamide (2 g) - per os.
Results: After a week of chemotherapy 5 (16.1±6.6%) patients from 1st group and 10 (79.9±12.1%) patients from 2nd group had a positive dynamics: a decrease in the severity of cerebral symptoms, a decrease in focal neurological symptoms, liquorological and liquorodynamic changes (19.3±3.8%), pleocytosis (22.9±7.2%) and cerebrospinal pressure to (210±30) mm.v.st.) and intoxication syndrome (p< 0.05). After two weeks of anti-tuberculosis therapy, improvement of these parameters was observed in 10 (32.2±8.4%) patients of the 1st group and 11 (84.6±10.4%) - 2nd groups (p< 0.05). The mortality rate was significantly lower in the 2nd group (1 patient (7.6±7.6%)) compared to 8 patients of the 1st group (25.8±7.8%),p < 0.05. In addition, parenteral anti-TB therapy provided reduction of side effects by 23%.
Conclusions: Administration of parenteral anti-TB therapy in patients with TB meningitis resulted in a comparatively quick reduction of disease manifestation and reduce mortality.

PD-715-13 A study to compare efficacy of oral high dose rifampicin with standard dose rifampicin in tuberculous meningitis

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Background: Untreated Tuberculous meningitis (TBM) has high mortality. Even in treated patients the mortality is 25 % in HIV negative patients and 67% in people living with HIV infection (PLHIV). Survivors have devastating morbidities. Improving the antitubercular activity in the Central Nervous System may help improve outcomes. Previous studies suggested that high dose intravenous rifampicin (600mg or 13 mg/kg) for TBM is safe and associated with survival benefits in adults. But IV.Rifampicin is not readily available. Oral rifampicin is readily available free of cost in our high burden health care facility .We therefore wanted to use high dose rifampicin to improve survival.

Methods: 60 TBM cases, were randomised into two groups of PLHIV+TBM(33/60) and TBM(27/60) to receive either, standard (10 mg/kg) or high dose oral rifampicin (13 mg/kg) after written informed consent and IRB approval. Follow up was for 14 days in IPD and then at 3 and 6 months to assess Mortality and Morbidity.

Results:
1. Overall mortality in HIV positive patients (n=33) was 60.6%(20/33) and HIV negative (n=27)was 29.7%(8/27).
2. In hospital Mortality within 2 weeks in HIV negative group (n=27) was 14.8 %(4/27) and PLHIV was 24.2 %(8/33).
3. Mortality in high dose group (n=29) was 44.8 %(13/29) and in standered dose (n=31) was 48.3 %(15/31). Chi square 0.076, p=0.78(NS) .
4. Morbidity in survivors were neuromuscular weakness in 20% (12/60), ophthalmological disability (10%) and headache (8.3%), 33% (5/15) who had hydrocephalous needed V.P. shunt.

Conclusions: Mortality was high within 2 weeks of hospital stay. In survivors morbidity prevailed. Mortality did not differ in either group in our study, challenges continue!

PD-716-13 Intravenous application of rifampicin and ethambutol in patients with TB treatment failure and impaired suction function of the small intestine

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Background: The purpose of our work was to study the peculiarities of intravenous application of rifampicin and ethambutol in TB patients with failure of treatment and impaired function of the small intestine.

Methods: We observed 49 TB patients with treatment failure and impaired intestinal penetration (IIP). Patients were divided into two groups: Main group (MG) included 20 patients who received intravenously ethambutol (E) (10 ml - 10%) and rifampicin (R) (0.6 g) and orally pyrazinamide (Z, 2 g), isoniazid (H, 0.3 g) in standard doses; Control group (n= 29) received oral standard chemotherapy - H (0.3 g), R (0.6 g), Z (2 g) and E (1.2 g); 3rd group included 20 relatively healthy individuals. All the patients were with drug-sensitive tuberculosis. The severity of IIP was determined by the concentration of lactulose and mannitol (lactulose-manitol test) in the urine. H, R, E concentration in blood serum was determined by liquid chromatography. The concentration of anti-tuberculosis drugs (ATDs) was determined in 2,4 and 6 hours after administration.

Results: We detected violations of IIP in all the patients observed, while in Group 3 we did not observe these changes. In the Control group the concentration of ATDs was significantly lower than the average therapeutic concentration, and significant lower than in the Main group (Tab.1) (p < 0.05). The indices regarding the number of patients who took H were not significant between the Main and Control groups (p> 0.05).

ATDs	Main group (n-20)	Main group (n-20)	Main group (n-20)	Control (n-29)	Control (n-29)	Control (n-29)
	in 2 hours	in 4 hours	in 6 hours	in 2 hours	in 4 hours	in 6 hours
R	16.38±1.17	18.91±1.72	11.61±1.58	11.99±1.89	9.41±1.57	5.88±0.94
H	3.69±0.55	2.27±0.59	0.99±0.31	3.06±0.71	2.04±0.55	0.73±0.12
E	8.51±1.44	4.81±0.87	2.73±0.55	4.09±0.41	2.32±0.33	1.11±0.26

Table Concentration of ATDs in serum

Conclusions: In TB patients with treatment failure, violations of IIP are determined, which leads to a decrease in the concentration of major ATDs in serum and ineffective treatment, especially with R and E. To increase

the effectiveness of chemotherapy in drug-sensitive TB patients with treatment failure and violation of IIP intravenous administration of R and E lead to improve the effectiveness of treatment.

PD-717-13 Discontinuation of pyrazinamide in patients treated for MDR-TB in a clinical trial in Lima, Peru

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Background: WHO recommends pyrazinamide in combination with four second-line drugs in multidrug-resistant tuberculosis (MDR-TB) patients unless there is confirmed resistance to pyrazinamide or risk of significant toxicity. Limited data exist documenting discontinuation in the presence of toxicity related—or resistance—to pyrazinamide. We describe the frequency of pyrazinamide discontinuation, the principle reasons for discontinuation, and pyrazinamide resistance in the context of a clinical trial optimizing the dose of levofloxacin for MDR-TB.

Methods: Thirty-four participants in the parent trial (enrolled between January 2015 and December 2016) were included in the analysis. All had pulmonary MDR-TB, were from East Lima, Peru, and were randomized to one of four doses of levofloxacin plus an optimized background regimen that included pyrazinamide. We abstracted pyrazinamide discontinuation and adverse events, from the medical histories and trial database, Oracle RDC. Finally, we included pyrazinamide susceptibility results performed by BACTEC™ MGIT™.

Results: Pyrazinamide was discontinued in 8/34 (23.5%) participants. Reasons cited were: 2(25%) hyperuricemia; 3(37.5%) hyperuricemia plus joint pain; 2(25%) hyperuricemia plus resistance and 1(12.5%) resistance. All participants in whom pyrazinamide was discontinued had pyrazinamide-resistant results.

Pyrazinamide-related events	Pyrazinamide discontinued	Pyrazinamide no discontinued
	N (%)	N (%)
hyperuricemia only	2(25)	0(0)
hyperuricemia + joint pain	3(37.5)	1(3.8)
hyperuricemia + resistance	2(25)	1(3.8)
resistance only	1(12.5)	4(15.4)
resistance + joint pain	0	9(34.6
resistance + joint pain + hyperuricemia	0	3(11.5)
Join pain only	0	4(15.4)
no pyrazinamide-related findings	0	4(15.4)
Total	8 (24)	26 (76)

Table 1 Results

Conclusions: Pyrazinamide resistance was common in this cohort of MDR-TB patients; toxicity was also common. Presence of these conditions, however, did not consistently lead to pyrazinamide discontinuation. Although classified as "related" to pyrazinamide, investigators also considered levofloxacin a possible source of joint pain. The nature of multidrug MDR-TB treatment, the overlapping toxicity profiles, and the uncertainty about clinical significance of *in vitro* pyrazinamide resistance may contribute to the inconsistent management of patients with these findings.

PD-718-13 Adaptation of GPP guidelines for TB vaccine research: a participatory approach

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Background: Attaining the goal of a new TB vaccine requires effective collaboration of stakeholders at multiple levels. Aimed at TB vaccine researchers, sponsors, funders, and affected communities, the *Good Participatory Practice Guidelines for TB Vaccine Research (GPP-TB VACC)* lay out considerations and standards for stakeholder engagement. *GPP-TB VACC* is an adaptation of the UNAIDS/AVAC *GPP Guidelines for Biomedical HIV Prevention Trials (GPP-HIV)* and is informed by the *GPP Guidelines for Tuberculosis Drug Trials (GPP-TB)*.

Methods: To ensure broad and diverse input, an international working group (IWG) was established with TB and HIV researchers, funders, sponsors, advocates, and local / global advisory committee members. A multistage consultation process was used to achieve consensus on objectives, scope, structure, and adapted content of the guidelines, using strategies tailored to the priorities and expertise of the IWG members. Researchers and Community Advisory Boards (CABs) evaluated the relevance and usability of the adapted guidelines by identifying areas for improvement and 'best practices' of stakeholder engagement in their own context. IWG members were surveyed to assess the success of the consultation process.

Results: *GPP-TB VACC* includes changes to improve usability and relevance of the document for TB vaccine researchers and community stakeholders. Key changes include: addition of special considerations for TB vaccine research, including use of lessons learned from other disease areas; emphasized involvement of communities; addition of 'key questions' under each topic area to guide design of stakeholder engagement programs; and incorporation of a five-step engagement process for each of the GPP topic areas. IWG members considered the 'flexible and participatory' guideline adaptation process to have been highly successful.

Conclusions: A participatory approach to the adaptation of GPP guidelines is essential and effective. Adopting a tailored, bottom-up approach enables end-users to be actively involved in decision-making and increases usability and relevance of the content, laying the groundwork for implementation.

PD-719-13 A pharmacokinetic study of super-boosted lopinavir/ritonavir in combination with rifampin in HIV-1-infected patients with tuberculosis

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Background: There is an urgent need for accessible alternative antiretroviral regimens for use with rifampin (RIF) in resource poor countries. RIF with double dose LPV/r (800mg/200 mg) or super boosted LPV/r (400/400 mg) have been recommended as possible alternatives, although concerns exist about GI and hepatic toxicities.
Methods: Potential subjects were selected who were diagnosed with TB and tolerating a rifampin containing regimen with a good response treatment. LPV/r was given for 3 days prior to escalation procedure, which increased RTV dose by 100 mg every 3 days, until they were taking 3 extra doses of RTV. Pharmacologic sampling of both RIF and LPV was done 1-2 weeks after dose escalation and repeated about 6 weeks later. Sampling was done at 0, 2, 4, 6 and 8 hours. CD4 and VL were done prior to study procedures and weeks 3, 6 thereafter. Labs were done at every study visit and during escalation.
Results: Six male patients were enrolled including one withdrawn for medication non-compliance. PK was done on LPV/r (400mg/400mg) twice daily and RIF 600 mg daily. Median RIF C max: 6.34 (2.89 - 9.42) mcg/mL, and AUC 0-24: 48.2 (20.4 - 87.8) mcg*h/mL. Median LPV Cmin(expected >0.1mcg/mL): 10.65 (1.85 - 21.59) mcg/mL, Cmax: 15.73 (6.08 - 28.66) mcg/mL, and AUC 0-12: 161 (56 - 282) mcg*h/mL. Adverse events included grade 2 diarrhea in 2 subjects, grade 1 nausea in 1 subject, grade 2 abdominal pain in 1 subject. Grade 2 and 3 elevations in transaminases developed in 2 subjects. Four of the five patients who completed the study had >1 log drop in viral load.
Conclusions: LPV concentrations, including the Cmin, were adequate. The regimen was well tolerated with only 1 transient grade 3 elevation in transaminases. There were no withdrawals from study due to side effects.

PD-720-13 Daily 800 mg vs. 600 mg efavirenz in HIV patients treating tuberculosis with a rifampicin-based regimen: a randomised controlled trial

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Background: Rifampicin reduces efavirenz blood concentration. Some pharmacokinetics studies recommend increasing efavirenz dosage in tuberculosis (TB)-HIV patients using rifampicin. However, no clinical trial data are available to support this.
Methods: We conducted a single-blinded, multicentre, randomised trial (clinicaltrials.gov/NCT00533390) from 2006 to 2012 to evaluate efficacy and safety of two different efavirenz regimens in TB/HIV patients using rifampicin in Brazil. Patients ≥18 years, antiretroviral-naïve, with Karnofsky-score ≥70% were included. Patients with hypersensitivity to efavirenz or rifampicin, resistance to rifampicin, 5-fold increase in liver enzyme levels or total bilirubin ≥1.5 mg/dL were excluded. Patients were randomised after 30 days of rifampicin-containing regimens to 600 mg (comparison arm) or 800 mg (intervention arm) efavirenz-based regimens. Primary outcome was the proportion of viral load (VL) ≤80 copies/mL within six months. Secondary outcomes were time to achieve primary endpoint, trajectories of VL, proportion of any adverse events (AE), proportion of severe and serious adverse events (SSAE) and treatment interruption due to SSAE. Efficacy among patients weighting >50kg was also analysed.
Results: Sixty-five and 67 participants were included in the comparison and intervention arms with 64.6% (52.5%-65.1%) and 62.7% (50.7%-73.3%) attaining undetectable VL, respectively. median time to attain undetectable VL was 70 (63-98) and 70 (62-91) days, respectively. VL trajectories overlapped during all follow-up period. Five patients died from TB, two in the intervention arm. SSAE were observed in 19.1% and 25.0% respectively, p=0.241. Time to SSAE-inducing treatment interruption was similar in both interventions. Cough, acne and dizziness were more frequent in the intervention arm.
Conclusions: Efficacy of efavirenz 600 or 800 was similar when associated with rifampicin-containing regimens. Although safety was also similar regarding SSAE and treatment interruption, the higher incidence of minor AE favours the use of efavirenz 600 in patients using rifampicin.

PD-721-13 Right drugs for the right treatment of tuberculosis in the private sector: an unchecked issue

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Background and challenges to implementation: Under the aegis of Municipal Corporation of Greater Mumbai (MCGM),
a project was initiated by PATH (NGO) as Private Provider Interface Agency (PPIA) for engagement of private practitioners and providing diagnostic and treatment facilities for TB patients. Prescribing right drugs at the right time is of paramount importance for TB treatment. Incorrect prescriptions, and suboptimal dosages are major reasons for drug resistance. To understand the prescribing practices of doctors networked under PPIA, a prescription audit was conducted for drug sensitive TB prescriptions generated in 2016.

Intervention or response: A prescription audit for TB care, entails checking that prescriptions are in line with the Standards of TB Care in India (STCI), for appropriate dosing according to a patient's body weight, quantity of drugs prescribed in intensive phase practices like splitting and adding second line TB drugs. All active doctors under PPIA in 2016 were identified from the database. Three prescriptions of intensive phase, of three different patients, of three different months of each doctor selected were randomly checked.

Results and lessons learnt: 100% of the prescriptions had Tablet Isoniazid, Rifampicin, Pyrazinamide and Ethambutol in their prescriptions. 6 % Prescriptions had second line drug and Splitting of first line anti - TB drugs was observed in 9%. 25% of the prescription had under dosing of Tab. Pyrazinamide and Tab. Rifampicin under dosing was noted in 14% of the prescriptions.
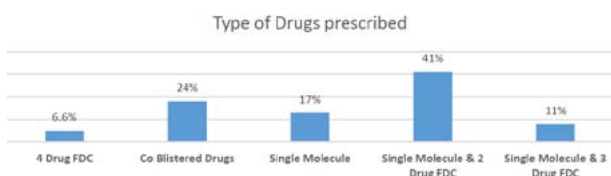
Figure Prescription Patterns among first Line anti Tb drug

Conclusions and key recommendations: Anti-TB drugs need to be prescribed as per the body weight of the patient for the rational treatment of TB. Splitting of anti-TB drugs was noted and they may lead to under dosing a patient and also leading to drug resistance TB cases. It is recommended to ensure the drug dosage prescribed is as per the guidelines of National TB program and avoid splitting of drugs & used Fixed dose combination drugs.

PD-722-13 Active screening for hepatotoxicity: identifying time periods for targeted monitoring in tuberculosis patients

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Background: Hepatotoxicity is a well-known adverse event (AE) in patients receiving tuberculosis treatment. In high-tuberculosis-burden countries, liver enzymes are frequently only monitored in the presence of symptoms. Many elevations are likely often missed. In a phase II clinical trial of high-dose rifampin for tuberculosis treatment in Lima, Peru, we evaluated the frequency and time to event of grade 2 or higher transaminase elevations and risk factors for elevations. We will also describe the evolution of these events.

Methods: Trial participants were randomized to receive rifampin 10, 15, or 20mg/kg/day with standard doses of isoniazid, pyrazinamide, and ethambutol.
Transaminases were monitored biweekly. We report count of participants with grade 2 or higher transaminase elevation (according to the DMID Adult Toxicity Table) within 12 weeks of treatment initiation. Using logistic regression, we evaluated patient characteristics for association with grade 2 or higher transaminases: treatment arm, sex, age, BMI and self-reported alcohol use. We estimated time to event, time to maximum transaminase elevation, and time to resolution.

Results: Of 180 participants randomized, 44 experienced at least one hepatic AE grade 2 or higher: 16 (10mg/kg), 14 (15mg/kg), and 14 (20mg/kg). 91% were asymptomatic. None of the characteristics evaluated was associated with risk of elevated transaminases (Table 1). Median time-to-any elevation among those experiencing an event was 14 days (IQR: 13 - 28) and to grade 2 or higher was 35.5 (IQR: 17.5-52.5) days. Clinical case management will be described.

Covariates	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
> 35 years old	1.46 (0.69, 3.07)	0.32	1.35 (0.63,2.89)	0.43
Alcohol Use	1.19 (0.60, 2.36)	0.61	1.30 (0.62, 2.73)	0.48
Treatment group 15 mg/kg	0.84 (0.36, 1.95)	0.81	0.87 (0.37, 2.02)	0.96
Treatment group 20 mg/kg	0.84 (0.36, 1.95)	0.81	0.78 (0.32, 1.82)	0.64

[Risk factors for Grade >2 hepatic adverse events]

Conclusions: No association between patient characteristic and elevated transaminase was detected, including exposure to 20 mg/kg rifampin. The finding that most events occurred during weeks 3-4 of treatment, suggest that monitoring transaminases at this time might detect elevations. Most events were asymptomatic and would not otherwise be detected. The clinical significance of these elevations is not clear, but may be elucidated by future research.

25. Lungs matter - recent developments in adult lung health

PD-723-13 Pulmonary hypertension in stable COPD patients and its effect on exercise capacity using the six minute walk test

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Background: Pulmonary Hypertension (PH) frequently complicates COPD disease process and adversely affects exercise capacity of such patients. However, majority of COPD patients are not routinely evaluated for PH even though a rapid screening tool in the form of transthoracic echocardiography (TTE) is available for early diagnosis of PH. The six minute walk test (6MWT) is an easy to administer test that can be used to evaluate exercise capacity in such patients.

Methods: 50 stable COPD patients who met the inclusion criteria were selected & staged for severity by spirometry and screened for PH using TTE. Tricuspid regurgitation jet velocity(TRJV) obtained was used to calculate systolic pulmonary artery pressure (sPAP) .Mean pulmonary artery pressure(mPAP) was calculated from sPAP using chemla formula. A 6MWT was also performed for all the patients.

Results:
1) The frequency of PH in COPD patients was 48% (24 out of 50).The frequency of PH in patients of mild, moderate, severe & very severe GOLD COPD stages were 12.5% (1/8), 45.83% (11/24), 61.53% (8/13) & 80% (4/5) respectively .

2) Out of the 24 patients with PH, the relative incidence of mild (25-35 mm Hg), moderate (35-45mmHg) & severe (>45mm Hg) PH was 54.16% (13/24), 29.16% (7/24) & 16.67% (4/24) respectively .Only 1 patient had "out of proportion" PH.

3) The mean 6MWD in COPD patients with and without PH was 243.95±114.24m and 338.19± 132.58m respectively.The mean 6MWD in patients with mild, moderate & severe PH was 288.07 ±28.67 m, 208.57±14.92m & 162.5±32.78 m respectively.

Conclusions: PH is an under diagnosed entity that frequently complicates the course of disease in COPD patients and adversely affects exercise capacity. TTE is an accurate, non-invasive screening tool for PH & should be routinely used in all COPD patients for early diagnosis of PH.

PD-724-13 Metabolic biomarkers for the opportune diagnosis of COPD in vulnerable population

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Background: Chronic Obstructive Pulmonary Disease (COPD) is due to the constant exposure to noxious particles, causing progressive and non-reversible inflammation of lung tissues, therefore breathing difficulties. It is the fifth leading cause of death worldwide, producing disability and a strong economic impact over health systems. Early diagnosis is crucial for opportune treatment. However, given the size of the affected population and their economic status, it would be of great importance to have non-invasive and accessible diagnostic strategies.

Objective: To identify chemical fingerprints in exhaled breath for the opportune diagnosis of COPD through the use of metabolomic tools in high risk populations (PAR).

Methods: Subjects were submitted to exhalation breath tests performed in (1L) Tedlar bags.The study was carried out in 24 patients with COPD, 21 healthy subjects (SS) and 51 subjects of vulnerable population (PAR) in 1L Tedlar bags under standardized criteria (fasting of 8 hours, without oral hygiene and without taking medication) and stored at 4°C until analyzed. All participants in the study underwent spirometry. Samples were analyzed by Ultra-fast Gas Chromatography with Electronic Nose Detector (HERACLES II, Alpha MOS). The characterization of the compounds was based on the Kovats indices; a principal component analysis (PCA) and a factorial discriminant analysis (DFA) of the metabolites were performed

Results: Thirteen compounds that distinguish patients with COPD and SS were identified. Likewise, the PCA showed differences between exhaled breath of patients with COPD and SS, and the stages of COPD explaining 87.3 and 80.2% respectively of the variability of the analyzed compounds. In addition, it was possible to identify the type of lung damage caused by constant exposure to biomass burning in PAR.

Conclusions: The present data support that metabolomic tools represent a new approach to opportune diagnosis.

PD-725-13 Perception of asthma control among in an out-patient clinic at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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Background: Patient awareness of asthma severity is important for optimal asthma management; however, there is often discrepancy between physician and patient discernment of control. We studied physician and patient perception of asthma control in a clinic population seen at a tertiary hospital in Addis Ababa, Ethiopia.
Methods: In this cross-sectional study, 182 consecutive patients with physician diagnosis of asthma seen in chest clinic at TASH between July and December 2015 were studied. Demographics, asthma symptoms, medication use in the past month, and self-perception of asthma control in the past 7 days were obtained from the clinic records. Physician assessed asthma control was based on the GINA asthma symptom control assessment tool. Lung function was measured using a Diagnostic EasyOne Plus model 2001 SN spirometer. The institutional review board approved the study protocol.
Results: Of the 182 subjects, 68.1 % were female. The mean age was 52 ± 12 years and the median duration of asthma was 20 ± 12.7 years. One hundred and thirty-eight (75.8%) patients had well-controlled or partially controlled asthma by physician assessment. One hundred and fifty-one (83%) patients thought their asthma control was good. However, the degree of concordance between physician and patient perception of asthma control was low (kappa index = 0.18). Of those patients with well-controlled or partially controlled asthma, 109 (79%) thought their asthma control was good. However, of those patients with uncontrolled asthma, only 2 (4.5%) thought their asthma was poorly controlled. Although not statistically significant, patients with self-reported good control had lower lung function and more frequent medication use than those with self-perceived poor control.
Conclusions: In our study, a high percent of patients with well or partially controlled asthma has appropriate perception of their disease state. However, those patients with uncontrolled asthma had poor self-perception of asthma control, emphasizing the need for further patient education in this vulnerable group.

PD-726-13 Knowledge and attitudes of health professionals on bronchial asthma in Niamey

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Background: Asthma is a public health problem. In Niger in 2013, a guide on the management of asthma was developed by the Ministry of Health.
Objective: To assess the knowledge and attitudes of health professionals on asthma in Niamey.
Methods: 6-month prospective study in 120 health professionals (specialists, doctors in training for the diploma of specialized studies (D.E.S), general practitioners, health technicians, nurses). The data was collected on a survey sheet after an interview.
Results: A total of 120 agents, of which 84.2% were from the public sector and 15.8% from the private sector, mostly women (60%). Our average age was 38.34 years. 4 specialists, 10D.ES, 58 general practitioners, 5 senior health technicians and 43 nurses. The peak flow meter was known by 35% of the agents and 23% of the agents knew the 3 basic elements in the diagnosis of asthma. More than two-thirds (83.3%) of the evaluated agents knew the inhaled route as the best route of administration of bronchodilators in an asthma attack. After treatment of the asthma attack 52.9% of the agents directed the patients to a pneumologist. The majority (97.4%) of the agents stated that they explained to the patients how to use an aerosol but only 20.7% The use of aerosols.
Conclusions: Continuing training of asthma health professionals is a necessity in order to improve the management of asthmatics in Niamey.

PD-727-13 Respiratory function among workers in a vegetable oil mill in Benin

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Background: The use of spirometry to assess workers exposed to occupational air pollution is not yet in practice in many developing countries. In Benin, in a Company producing vegetable oil from cottonseed, workers who are exposed to occupational air pollution have never had lung function measurement.
Methods: This cross-sectional study among 52 workers from a Benin vegetable oil mill took place from 18 to 21 January 2017 as part of the workers´ annual medical visits. A questionnaire was administered and spirometry was carried out using the Spirobank II. The spirometric

results were interpreted by an occupational physician and a pulmonologist.

Results: The mean age was 42.7 ± 6.4yrs, and 43 of the 52 workers were men. 58% of workers were in technical producing positions versus 42% for administrative positions. The number of years worked by the participating workers was: 44% worked for 0-2 years; 8% had worked for 2-5 years; and 44% for 5-22 years.

The interpretation of the spirometric results of the personnel showed that 73% were completely normal, 11% had mild abnormalities of spirometry, but still considered within normal range, and 15% were clearly abnormal. Among the 8 with abnormal spirometry, 4 (50%) had obstructive syndrome, 3 (38%) had restrictive syndrome and one had a mixed pattern. In addition, 13 (25%) of the workers had a greater than 20% reduction of their maximum expiratory flow compared to predicted. This reduction was seen in 9 of the 30 (30%) workers involved in oil production, compared to 4 of 22 (18%) for administration workers. Mid expiratory flow rates (FEF25-75) were reduced by more than 20% in 38 (62%) workers.

Conclusions: The use of the spirometer as a follow-up tool in the context of annual medical visits for companies with occupational exposure to organic dust could help early detection of occupational respiratory diseases.

PD-728-13 Chronic obstructive pulmonary disease among the elderly in an urban community of South India

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Background: Underdiagnoses of chronic obstructive pulmonary disease (COPD) is common as this disease is often not recognised and diagnosed until it is moderately advanced. One of the barriers to the diagnosis of COPD is the difficulty with which spirometry is performed in the general practice/community setting. International Primary Care Airways Guidelines (IPAG) questionnaire is a feasible validated screening tool for COPD diagnosis in community setting.

Methods: This community based observational study was conducted among 1037 elderly people in urban areas of Puducherry in India. Participants were recruited using multistage random sampling technique. IPAG questionnaire [Cut off Score - 17 (Positive predictive value: 92%)] was administered among all study subjects. We compared quantitative parameters between COPD and non-COPD subjects using the student t-test and chi-square test was applied for qualitative variables.

Results: Data from 1,037 subjects (435 males) were analysed. The proportion of smokers among male was 16.5%. A positive IPAG questionnaire for possible

COPD (≥17 points) was obtained in 342 (33.1%) subjects. Based on the answers to the questionnaire given by the subgroup of possible COPD subjects, 69 (22.2%) had no cough, 215 (62.9%) reported sputum production in the absence of a cold, 186 (54.4%) cough up phlegm (sputum) from their chest first thing in the morning, 162 (47.4%) had frequent or occasional wheezing and 113 (33 %) reported to have or had any allergies. Age and body weight found to be associated with positive IPAG questionnaire. Possible COPD was significantly higher among smokers (52.9%) as compared to non-smokers (31.7%) (P value < 0.01).

Conclusions: Proportion of subjects with possible COPD was high in community. IPAG questionnaire was an easy to administered tool for screening of COPD and little expertise is sufficient for its administration. IPAG questionnaire could be used for screening and planning of health interventions in communities in developing countries.

PD-729-13 Household air pollution and pneumonia in Malawian adults: a case-control study

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Background: Four million people die each year from diseases caused by exposure to household air pollution. There is an association between exposure to household air pollution and pneumonia in children (half a million attributable deaths a year); however, whether this is true in adults is unknown. We conducted a case-control study in urban Malawi to examine the association between exposure to household air pollution and pneumonia in adults.

Methods: Hospitalized patients with radiologically confirmed pneumonia (cases) and healthy community controls underwent 48 hours of ambulatory and household particulate matter ($\mu g/m^3$) and carbon monoxide (ppm) exposure monitoring. Multivariate logistic regression stratified by human immunodeficiency virus (HIV) status was used to establish whether these and other potential risk factors were associated with pneumonia.

Results: One hundred and forty-five (117 HIV-positive; 28 HIV-negative) cases and 254 (170 HIV-positive; 84 HIV-negative) controls completed follow-up. We found no evidence of association between household air pollution exposure and pneumonia in HIV-positive (e.g., ambulatory particulate matter adjusted odds ratio [aOR] 1.00 (95% confidence interval [CI] 1.00-1.01, p=0.141]) or HIV-negative (e.g., ambulatory particulate matter aOR 1.00 [95% CI 0.99-1.01, p=0.872]) participants.

Chronic respiratory disease was a risk factor for pneumonia in both HIV-positive (aOR 28.07 [95% CI 9.29-84.83, p< 0.001]) and HIV-negative (aOR 104.27 [95% CI 12.86-852.35, p< 0.001]) participants.

Conclusions: We found no evidence that exposure to household air pollution is associated with pneumonia in Malawian adults. Chronic respiratory disease was strongly associated with pneumonia, particularly in HIV-negative adults.

26. Private sector engagement in TB care: lessons learned from low-income countries

PD-731-13 Private sector effectiveness in treating TB patients: a document review of the Kabul urban DOTS experience

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Background and challenges to implementation: In 2009, TB indicators in Kabul were very poor. The city's TB treatment success rate (TSR) was 49%. To overcome those challenges, the NTP, with support from the USAID funded TB CAP, TB CARE I and Challenge TB projects implemented an urban DOTS approach that engaged both public and private health facilities in TB services. This assessment strives to compare private sector treatment outcome indicators with treatment outcome indicators at all urban DOTS health facilities in Kabul.

Intervention or response: In 2010, a baseline assessment was conducted, a memorandum of understanding was signed with the private sector and medical staffs were trained on TB case management, TB recording and reporting formats. Supervision was provided, monitoring was conducted and feedback was provided to private clinics. The technical NTP and CTB team reviewed data from 2010-2015 by using the standard NTP reporting tool and comparing the information with existing surveillance data.

Results and lessons learnt: In 2010, of 2,348 TB cases registered in public DOTS centers, 1,360 were successfully treated (TSR of 50%). In private health facilities, 89 TB cases were registered and 63 were successfully treated (TSR of 71%) during the same time period. In 2015, of 5,449 all forms TB cases diagnosed in public health facilities, 4,416 (81%) were successfully treated (in private DOTs centers 637 all forms TB cases were diagnosed and 560 [88%] were successfully treated).

Conclusions and key recommendations: While the private sector made significant improvements to the TSR in Kabul, the TSR remains lower in the public sector.

Private health facilities may have a higher TSR because they might employ a better follow-up mechanism. Additionally, select urban patients are enrolled in the private sector and the transfer-out rate is lower than in public health facilities. Additional research is needed to identify ways to minimize the gap between public and private sector treatment outcomes.

Year	Treatment success rate in Kabul public facilities (%)	# of not evaluated cases in Kabul public facilities	Treatment success rate in private health facilities (%)	# of not evaluated cases in private health facilities
2010	50%	41	67%	23
2015	81%	10	88%	4

Table Comparison of treatment outcomes between

PD-732-13 PPM and -mandatory notification of TB cases under the Revised National Tuberculosis Control Programme (RNTCP) in Himachal Prades, India

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Background: Government of India has made mandatory notification of TB cases since May 7, 2012. Around 14000 fresh cases of TB are reported in the government hospitals in Himachal Pradesh annually, while an estimated 5000 TB cases should be actually coming to private doctors in the state in a year. Data reveals that in India 75% doctors are doing private practice and only 0.31% of them are implementing the Revised National Tuberculosis Programme.

Methods: The data was collected from the respective district tuberculosis officers of the state. FDCs were done with private practitioners and patients attending private clinics.

Results: Since compulsory notification, only 1848 cases have been notified by the private health establishments in HP till 2015, which is roughly 10% of total patients actually treated by them. This keeps the government in the dark over extent of TB in HP. This also deprives patients of standardized free treatment and the benefit of government follow up. Out of total 12 districts in the state, 672 TB cases were notified by five private establishments in Kangra district, 385 by ten establishments in Mandi district and 367 by nine establishments in Kullu district and Una notified one case. The FDCs with private practitioners revealed that private practitioners feel it a additional drain on their manpower having no incentive. TB patients particularly prefer going to private health establishments mainly for the stigma attached to the disease, lack of awareness and guidance.

Conclusions: Strict action against those private doctors not notifying TB is required. At the same time we need to facilitate the Private Practitioners and make it easy for

them to notify may be through Whatsapp or messages. Also massive awareness campaign to educate patients about quality of government medicines and methods to keep their identity secret would help increase in notification and compliance by the TB patients.

PD-733-13 Public-private mix as an indispensable strategy to END TB: six years project experience in Ethiopia

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Background and challenges to implementation: Ethiopia is amongst the thirty high TB, TB/HIV and MDR-TB burden countries where one-third of TB and three-fourth of DR-TB annually expected case remains undetected by the program. The aim of this project is to demonstrate role of public-private mix in TB control and share the successful experience of USAID supported project in Ethiopia collaborating with the NTP in scaling up PPM-DOTs initiatives.

Intervention or response: USAID funded project had been piloted between 2004 & 2006, and then endorsed for nation level implementation as key initiatives for universal access to TB services with national PPM-DOTS implementation guideline. PPM interventions include consensus building, baseline assessment and identification, capacity building, continuous support for quality service delivery, and sustainability and transitioning.

Results and lessons learnt: Between 2009 and 2016, the project supported the scale up of quality TB services in selected Private providers. As of 2016, the project is supporting 187 PPM facilities that contributed in identifying cumulative of 96,572 TB patients (around 14% of the total notified cases) and provided comprehensive TB treatment services for 21,147 TB patients. HIV co-infection rate was 20% with 71% ART coverage. The PPM sites have also managed to achieve annual treatment success rates beyond 80% which was comparable to the annual national performance targets.

Conclusions and key recommendations: PPM facilities have contributed to finding of significant number of TB patients, and provided patient-centered quality assured TB service as per national protocol. Hence, we recommend that NTP in high burden countries should recognize the potential role of Private providers and integrate PPM DOTS as a key strategy to accelerate the effort to end the TB epidemic.

PD-734-13 Can we engage large private hospitals to increase TB notifications from private sector in India?

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Background and challenges to implementation: More than 50% of TB cases in India are treated in private sector, hence engaging private sector is essential to identify missing million cases in India. Corporate and trust hospitals in urban cities are key players as far as healthcare is concerned, however engaging these players in TB program is challenging due to lack of trust and disinterest towards public health programs.

Intervention or response: Population Services International (PSI) is implementing Urban TB intervention in Bangalore city in Karnataka, with an objective to engage private sector to increase TB notification from private sector. PSI mapped out large and medium hospitals catering to significant numbers of presumptive TB cases (PTB) through a systematic mapping exercise. After mapping, urban coordinators from the project approached hospital management and decision makers in hospitals to explain about the project, RNTCP program and need for notification of TB cases to RNTCP. ICT based support provided for follow up and ensuring treatment adherence of TB patients was explained to hospital management. Once the hospital management was convinced a centralized mechanism was worked out incorporated within existing system of hospital for getting data on TB notification. Community volunteers were linked with hospitals for collecting data from various departments where central mechanism was not possible.

Results and lessons learnt: Total 21 large and medium private hospitals were engaged through the project since Jan-2016. We compared data on TB notification from same hospitals during pre-intervention (Oct-Dec'15) with Intervention (Oct-Dec'16) period. During pre-intervention period 178 TB cases were notified by private hospitals to RNTCP, in intervention period total 645 TB cases were notified by private hospitals which was increase by 262%.

Conclusions and key recommendations: A systematic approach of convincing decision makers at hospitals, establishing system of data collection incorporated within existing hospital system and support on treatment adherence to patients treated, will ensure engagement of private hospitals.

PD-735-13 Effects of engaging public and private health facilities in TB case finding in Afghanistan: urban DOTS implementation experiences

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Background and challenges to implementation: The National Tuberculosis Program (NTP), with support from USAID funded projects, implemented an urban Directly Observed Treatment, Short Course (DOTS) approach in Kabul (beginning in 2009) and in Kandahar, Herat, Nangarhar and Balkh cities (beginning in late 2015). In an effort to understand the impact of DOTS on case finding in public and private health facilities, outcomes of urban DOTS implementation were assessed in all five cities.

Intervention or response: Urban DOTS implementation includes strengthening coordination mechanisms and establishing a partnership between the NTP, private and public health sectors. Partners trained healthcare staff on TB service delivery, distributed anti-TB drugs, laboratory reagents and DOTS packages. DOTS packages included educational materials, sputum sample transferring materials and medication boxes with patients' entire treatment regimens. The NTP, with support from the Challenge TB (CTB) project, conducted regular supportive visits and monitoring to the participating health facilities. In 2016, the NTP and CTB technical teams conducted assessments to evaluate the role of PPM on TB case notification and treatment. The assessment team reviewed TB data from the 2016 intervention and compared it with national TB surveillance data.

Results and lessons learnt: DOTS coverage reached 55% (84 out of 153 health facilities) in 2016 compared to 32% (49 out of 153) in 2015 and 6,492 cases were notified in 2016 compared to 4,727 in 2015 (P-value <0.0000001). Out of the 6,492 cases diagnosed, 2,397 cases (1,748 in 2015) were bacteriologically confirmed TB (See Table 1). Among 6,492 TB cases diagnosed in 2016, 1,147 (17.6%) were detected by the private health sector.

Indicators/Years	2015	2016
# and % of Health Facilities covered by DOTS	49 (32%)	84 (55%)
# of all form TB cases registered	4,727	6,492
# of bacteriologically confirmed TB patients	1,748	2,397

Table 1 Engaging public and private sector in TB

Conclusions and key recommendations: Urban DOTS contributed to significant improvements in increasing case notification. The private health sector's contribution to case notification also remains high. We recommend that Urban DOTS be scaled up in other cities in Afghanistan, and in similar settings in the world.

PD-736-13 Alianza programa tuberculosis de la jurisdicción sanitaria VII y consultorios de Farmacias Similares Fundación BEST

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Background and challenges to implementation: La Organización Mundial de la Salud estima que en el 2015 enfermaron de Tuberculosis 10.4millones en el mundo, en México para ese mismo año se registraron 16,462 casos y en Chiapas 1,184 casos, ante la alta prevalencia de personas afectada por Tuberculosis en el municipio de Tapachula, se implementa la recomendación hecha por la Organización Mundial de la Salud en el año 2000 de implementar Alianzas Público Privadas, por lo que se decide trabajar de manera conjunta con los consultorios de Farmacias Similares de Fundación BEST.

Intervention or response: En el municipio de Tapachula la tuberculosis tiene una incidencia de 7.7 por cada diez mil habitantes, teniendo conocimiento que Farmacias Similares en sus consultorios atienden aproximadamente 560 consultas diarias[5] en este municipio, celebramos reunión con el supervisor medico de Farmacias similares para proponer una alianza pública privada y con la anuencia del gerente medico zona sur de Fundación BEST, en diciembre de 2015 presentamos el proyecto, con el plan de capacitación en el manejo de la Tuberculosis y comorbilidades. Al no ser factible que en estos consultorios se supervise el tratamiento, se retoma mecanismo de referencia de pacientes, estableciendo que los casos diagnosticados por este sector serán derivados al programa tuberculosis de la Jurisdicción Sanitaria para signarles un centro de salud e ingreso a tratamiento.

Results and lessons learnt: En 2016 los médicos de Farmacias similares diagnosticaron el 9.3% del total de casos registrados en el municipio. De enero a marzo 2017 han diagnosticado el 6.8% de los casos.

Conclusions and key recommendations: Esta Alianza Publico Privada es una estrategia exitosa para diagnosticar y tratar oportunamente a las personas afectadas por tuberculosis, por la alta incidencia de la tuberculosis en Chiapas valdría la pena esta estrategia en todo el estado.

PD-737-13 A public-private mix intervention to enhance tuberculosis case finding in resource constrained industrial setting in Himachal, India

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Background: Operational research assessing treatment seeking patients of a DOT Centre of a hospital of an industrially dominated area revealed that 41 patient were diagnosed and initiated on TB treatment by Designated Microscopy Centre (DMC) of another Health Centre 5

kilometers apart. Infact active case finding was zero at this hospital. Distant DMC was significant impediment for follow up sputum microscopy and contact screening.
Methods: A Public-Private mix intervention was undertaken with the objectives:
(1) To enhance active case finding in the hospital
(2) To enhance active and passive case finding in the community.
A DMC in the public health hospital was started, Medical staff sensitized and community mobilization initiated by roping in an NGO in the "Sputum pick up and transport scheme" for collecting and transporting spot and morning sputum specimen of presumptive TB cases from 7 slum areas, to the newly opened DMC for prompt diagnosis.
Results: Active and passive case finding rose from zero to 52 and 20 respectively in the year 2015 and it was 204 and 56 cases respectively in 2016. Slide positivity rate was 8.2% in 2015 with 6 New Smear Positive cases and two positive follow up cases whereas it was 8.8% in 2016 with 18 new and 16 follow up positive cases. 15 out of 179 Presumptive cases found by active search, four suspected follow up cases and 6 out of 56 Passive cases were positive.
Conclusions: Public private partnership increases active and passive case finding in slums of industrially dominated area by minimising the challenges of loss of working hours, absenteeism from work, cost of travelling, and increasing the knowledge, attitude and practice amongst the masses about prevention, diagnosis and treatment of Tuberculosis.

PD-738-13 Urban TB control in Bandung, Indonesia: exploring the potential contribution of private practitioners to finding the missing cases

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Background and challenges to implementation: Private sectors providers form are integral part of the Indonesian health system. The 2014 National TB prevalence survey shows that 74% patients with TB symptoms sought their initial care in the private sector. However, the private sector only contributed nine percent of the 2015 notification, which currently reaches 32% of the estimated incidence. With 68% of incident TB cases unreported, Indonesia contributes roughly 20% of the world's missing cases.
Intervention or response: In September 2016, we mapped private practitioners (PPs) in Bandung city and interviewed them to understand their perceived role in TB

management. Of 1567 physicians registered in Bandung Medical Association, 666 (42.5%) could be located and were found willing to be interviewed.
Results and lessons learnt: PPs are found in all sub-districts of Bandung (Figure 1). Among 629 PPs, 363 (58%) stated to have identified presumptive TB among their clients and 186 (30%) have actually treated TB patients in the past three months (927 cases). In the same period approximately 2000 cases were notified in Bandung. Of all respondents, 42% ever received TB training. Trained PPs were more likely to refer or report people with presumptive or active TB to public primary care facilities (46% versus 34%, p=0.004). Among PPs who diagnosed TB cases, reportedly 58% used microscopic examination, 75% used chest X-ray, and 49% used other laboratory tests such as ESR, IGRA. Limitations of the survey are that not all providers could be located and the reported findings were not cross-checked with clients medical records and the NTP.
Conclusions and key recommendations: PPs are present in the entire city of Bandung. PPs see a significant number of (presumptive) TB patients. Collaboration between PPs and the NTP exists but is limited in numbers and scope. TB training appears to improve collaboration. Further engagement of private providers can be effective to increase TB notification and to improve TB management.
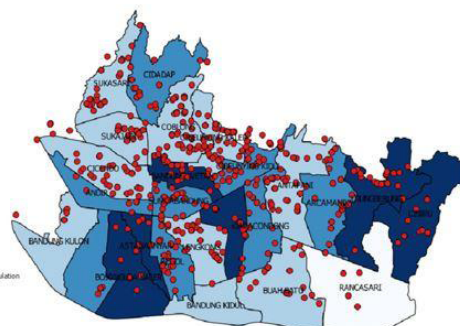
Figure 1. The geographic informations systems (GIS) coordinate of private practitioners (PPs) in Bandung city shows that PPs are closely located one to another, except in the South-East and South-West area. The background colors show CDR in Bandung, which is the ratio of the number of domicile-based reported notifications to the estimated TB incidence. There is no correlation between CDR and PPs distribution.

Figure Distribution of private practitioners in Bandung city, Indonesia

PD-739-13 "The Missing Million" TB patients in India: understanding enabling modes of reporting TB cases by the private sector

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Background: Over 3 million TB cases are missing (Global TB Report, 2015). 1 million are in India alone. In 2016, proportion of notification to Revised National Tuberculosis Control Program (RNTCP) from private sector in India was only 19% (TB India, 2017).

MAMTA, led by The UNION, is reaching out to qualified private practitioners (QPPs) to address gap of "missing million" through project Axshya. This study was conducted to understand perception of QPPs on importance of notification and methods of notification most convenient for them.

Methods: QPPs practicing in 7 cities across 4states were administered questionnaire during sensitization workshops organized by Axshya during May, 2016 to Jan, 2017. Responses were sought on smartphone use, email access, importance of notifying TB patients to RNTCP and preferred mode of notification. Respondents could choose multiple modes as preferred choice for notification. Data were analysed using SPSS.

Results: 312 questionnaires were filled. 99% QPPs perceive reporting TB cases as very important (86%) or somewhat important (13%). However, 14% feel, our public health system is not evolved enough for notification to be useful.

96% QPPs use smartphone. No statistical difference was noted among age-groups except over 65 years.

Preferred modes of notification were: mobile app (47%), hard copy sent to RNTCP via Axshya (42%), hard copy sent by self (33%), online on RNTCP website (32%), emailing RNTCP official (9%). 17% QPPs expressed comfort with both app and hard copy. 51% of mobile app users will notify immediately. In hard copy mode, preferred frequency is monthly (50%) and weekly (33%).
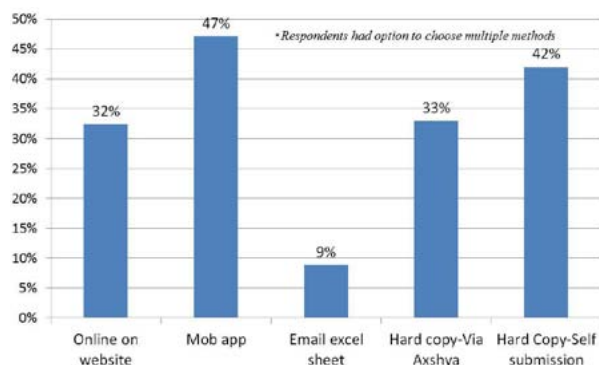
Figure Preferred method of reporting TB cases by private practitioners

Conclusions: While hard copy will stay as important mode of notification, findings of study strongly indicate developing QPP-friendly mobile app for notification and generating awareness about it.

Also, to motivate QPPs, it is critical to build confidence among them that their reports will actually get utilized by public health system for good of community.

PD-740-13 Outcomes of engaging a gynecological hospital in TB case notification and fertility status of women in Kabul city, Afghanistan

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Background and challenges to implementation: Infertility is one of the serious problems for women in Afghanistan that led to mental disorders, in house conflicts, even separation and divorce. There was not any center to detect, diagnose and treat genital TB correctly. Some of the private practitioners treated genital TB patients mostly resulted in treatment interruptions. Since 2014, urban DOTS approach expanded to Mahdi Obstetrics and Gynecology (Oby/Gyn) private hospital that focused on genital TB in Kabul city. The aim of this assessment was to evaluate the outcomes of genital TB treatment along with anti-infertility treatment on fertility status of women in Kabul city.

Intervention or response: This was a document review which the Challenge TB (CTB) and NTP reviewed the 2014-2016 register books and TB patients' cards with diagnostic documents. The team used standard questionnaire as data collection tool.

Results and lessons learnt: During 2014-2016, Mehdi hospital registered 446 genital TB cases among women from 12098 OPD over 15 years old that diagnosed as TB and started six months TB treatment with Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and 15 streptomycin injections. Of them 42 (9,4%) got pregnant, 33 (78.5%) during treatment which 10 (23.8%) during first two months (intensive phase) and 23 (54.7%) during continuation phase of TB treatment and 9 (21.4%) after completing the treatment with adding gonadotropin, fertile and Clomiphene. From remaining 446, 328 (73.5%) completed the treatment, 6 (1.3%) referred/ transferred out to other TB centers and 52 (11.6%) defaulted during treatment and other remaining 60 (13.4%) patients are under treatment.

Conclusions and key recommendations: The assessment showed that genital TB is one of the leading causes of infertility in Kabul, Afghanistan. Thus, we recommend, involvement of Oby/Gyn hospitals in TB control program to increase case detection and decrease infertility in Afghanistan.

Indicators	OPD over 15 yrs	Genital diseases	Genital TB	Comple-ted	Defaul-ted	Transfer out	Under treat-ment	Got pregnant during the treat-ment	Got pregnant after the treatment
Number and Percentage	12098	943 (7.8%)	446 (47.3%)	328 (73.5%)	52 (11.6%)	6 (1.3%)	60 (13.4%)	33 (78.5%)	9 (21.4%)

Table 1 Trend of case notification for genital

Figure 1 Notification of TB among external migrants

27. TB across key populations

PD-741-13 How can we increase the access of migrants to TB diagnosis and treatment in Kazakhstan?

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Background and challenges to implementation: Kazakhstan, one of the world's highest MDR-TB burden countries, has a large influx of labor migrants. Migrants lack access to TB services due to lack of information and legal, financial, and language barriers. In 2014, Project HOPE began a GFATM-funded program to improve TB diagnosis and treatment among migrants in seven pilot sites.

Intervention or response: The program:

1) created information channels for internal and external migrants through non-governmental organizations (NGOs), government organizations, employers, and the mass media and reached migrants in their countries of origin before they migrated as well as in the communities they lived in while in Kazakhstan;

2) established a network of migrant-friendly TB diagnosis and treatment health facilities;

3) involved local NGOs in outreach work and created a referral system for early TB detection and treatment.

Results and lessons learnt: Awareness raising through NGOs reached more than 60,000 migrant workers in two years, 70% of whom were external migrants. Reach increased fourfold from 11,991 (2015) to 47,488 (2016). Information on TB and the project was disseminated in migrants' native languages through mass media, public authorities, and partners in countries of destination and origin. TB active screening and examination among migrants increased from 1,710 in 2015 to 15,183 migrants examined in 2016. Detection of TB cases among internal migrants was stable; however, detection of TB among external migrants increased fivefold in 2016 compared to 2014 year (Figure 1). All migrants diagnosed with TB were treated, including 295 cases with MDR-TB.
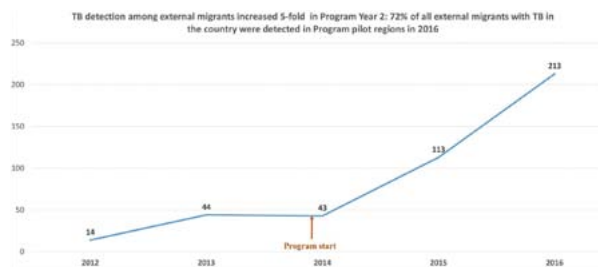
Conclusions and key recommendations: It is important to reach migrants where they are and use different channels to disseminate information on TB symptoms and where to get TB diagnosis and treatment in the host country. Establishing a network of migrant-friendly health facilities is key. Partnerships and synergies, including involving local NGOs for outreach work and engaging government institutions, is essential for reach and sustainability.

PD-742-13 Underlying social determinants of tuberculosis risk in UK-born adults of white ethnic background in England: a nationwide community-based case-control study

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Background: England tuberculosis rates have been stagnant in the UK-born population for over 25 years. There is evidence from ecological studies that deprivation remains a risk factor. However, few studies have recently investigated the association between poverty-related social determinants of health at the individual-level and tuberculosis in this setting, especially while accounting for the clustering of social risk factors in subjects.

Methods: Nationwide case-control study of UK-born White adults aged 23-38 years at their first TB episode, and randomly selected age-and-sex frequency-matched community-based controls. Data on some social determinants (education level, household overcrowding, tobacco smoking, alcohol, drugs use, and history of homelessness and prison) were collected during face-to-face interviews. Statistical analyses used logistic regression models, informed by a theoretical formal causal framework of plausible inter-relation between the observed social determinants.

Results: 681 TB cases and 1183 controls were recruited. A strong association between education level and TB was noted, with risk of TB about four times higher in subjects with GCSE O-levels or below compared to those with degree or higher (OR=3.94; 95%CI: 2.74to5.67) after controlling for age, sex, BCG vaccination and long (≥3 months) stays in Africa or Asia. After simultaneously adjusting for all measured social determinants, as well

as BCG vaccination and long stays in Africa or Asia, higher TB risk was also associated with tobacco smoking, use of drugs, especially injectable drugs (OR=5.67; 95%CI: 2.68to11.98), history of homelessness, and deprivation in the area of residence.

Conclusions: The results provide insight into some mechanisms through which deprivation affects the risk of TB in the study population, and support the argument for improved approaches to TB control efforts, such as integrated health and social services in high-risk young adult populations.

PD-743-13 Systematic review of the contribution of key populations to the overall tuberculosis epidemic in South Africa

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Background: Active case finding strategies aimed at increasing screening for tuberculosis (TB) in key populations is one intervention in the South African national TB management guidelines. Estimating number needed to screen (NNS) to find one case maximizes detection of TB cases. Estimating size, TB risk and contribution to the TB epidemic augments effectiveness of targeted strategies. We reviewed existing evidence on TB burden in key populations to inform current TB control strategies.

Methods: This comprehensive review was conducted by searching for reports, articles and conference abstracts from January 2000 to October 2016. Based on specific inclusion criteria, research investigating TB incidence, prevalence and key population size in South Africa was included. Epidemiologic data describing key high-risk and vulnerable populations was extracted. Relative risk was calculated by dividing prevalence in each key population over prevalence in general population. NNS was computed by inversing the prevalence. Contribution of each population was calculated as the proportion of overall cases reported in the 2016 WHO Global TB report.

Results: Overall, 159 articles were included with majority of studies conducted in HIV-infected (33), informal settlements (32), pediatrics (20) and healthcare workers (HCWs) (17). Studies on refugee and migrant, diabetic and elderly populations were fewer and dated. A large number of TB cases were contributed by people living with HIV/AIDS (31%) and those in informal settlements (33%). The elderly, miners, HCWs and inmates made a similar contribution to the epidemic (~2%). TB risk was highest in HIV-infected (6.5), silicotic miners (5.0), informal settlements (4.3) and diabetics (4.0). To detect one case, 22 HIV-infected, 33 informal settlers, 36 diabetics, 40 inmates and 71 HCWs would need to be screened.

Risk group	Risk group as % of the general population	TB prevalence	Relative risk	TB incidence	NNS to find one case	Overall contribution to TB epidemic
HIV-infected	10.2%	4 500	6.5	2 500	22	31%
Informal settlements	6.1%	3 000	4.3	4 500	33	33%
Diabetics	4.3%	2 760	4.0	2 760	36	14%
Healthcare workers	0.4%	1 400	2.0	4 447	71	2%

Table Estimated size, burden and contribution of groups

Conclusions: This analysis illustrates the power of using evidence to guide interventions using interaction between size of population and prevalence. Screening among HIV-infected and informal settlers is likely to yield more cases.

PD-744-13 Tuberculosis and latent tuberculosis infection among refugees: an overview

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Background: According to the United Nations, tuberculosis, other respiratory infections, under-nutrition, and HIV are the most threatening conditions among refugees. We over-viewed available literature on the prevalence and incidence of latent tuberculosis infection (LTBI) and active tuberculosis among refugees and asylum seekers.

Methods: The search was conducted on Medline, EMBASE, Web of Science and LILACS in August 2016. Cross-sectional and longitudinal observational studies and clinical trials published since 2000 in English, French, Spanish or Portuguese that described the above-mentioned indicators were included and data extracted using STROBE.

Results: 624 studies were identified, 57 were reviewed: 12 described active tuberculosis, 15 LTBI and 30 both. Systematic screening upon host country arrival was the reason for medical evaluation in 53. We identified high incidence rates (between 242 and 3,811/100,000 inhabitants) and prevalence (between 7.1 and 35,385/100,000 inhabitants, with 55% of the studies among 100 and 1,500/100,000 inhabitants) of active tuberculosis. For LTBI, prevalence rates were between 0.4% and 85%, with 42% of the studies presenting rates above 36%. These rates were higher among males and refugees from countries with high incidence of tuberculosis (Table). Twenty-one studies were conducted in the US, which has a restrictive immigration policy for tuberculosis patients.

	Low-incidence countries	High-incidence countries	Men	Women
Active TB prevalence	7 to 11,364	602 to 3,282	148 to 65,672	88 to 32,031
LTBI prevlance	0.4 to 69	29 to 81	23 to 57	16 to 45

Incidence according to WHO´s classification, active TB per 100,000 population and LTBI in %

Table LTBI and active tuberculosis ocurrence in refugees

Conclusions: The rates of active tuberculosis, but not of LTBI, are much higher than expected in the general population and than in extremely vulnerable populations such as prisoners and homeless. These rates may be underestimated in countries with immigration restrictions because of visa denial or fear of expulsion. Compared to two previous reviews, we found higher rates, which may have resulted from differences in inclusion/exclusion criteria or the actual increase in occurrence due to syndemic AIDS/drug/tuberculosis. Rapid access of refugees to healthcare in the host country should be guaranteed, and to avoid fear of diagnosis, the "non-refoulement" rule, as determined by the Geneva Convention (1951), ensured.

PD-745-13 Syrian refugees in Jordan and Lebanon: joint TB control initiative, 2015-2016

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Background and challenges to implementation: The ongoing conflict in Syria began in 2011 and displaced 4.8 million Syrian refugees, posing challenges for tuberculosis (TB) control in neighboring countries hosting them. The International Organization for Migration (IOM) supports National TB Programs (NTP) in Jordan and Lebanon in refugee TB case detection and treatment. TB services for Syrians strengthened during 2015-2016 through the Global Fund´s (GF) Emergency Grant. 1,011,366 registered Syrian refugees live in Lebanon and 657,000 in Jordan, with many unregistered (UNHCR March2017). TB diagnosis and treatment follow-up are difficult as refugees scattered in insecure, inaccessible areas near the Syrian border.

Intervention or response: Awareness raising, active case finding (ACF) with symptom screening, mobile X-ray and Xpert testing in refugee settlements/camps, hard-to-reach areas, and urban communities - by Community Health Workers (CHW) and Mobile Medical Unit (MMU). IOM facilitated referrals, diagnostic tests and hospitalization. In order to address the additional caseload, NTP TB centers were supported with diagnostic equipment (Xpert, X-ray), consumables, TB drugs and additional staff.

Results and lessons learnt: ACF contributed to increased TB case detection (39 cases detected in Lebanon out of 175,182 screened; 93 cases detected out of 8,702 in Jordan). CHWs and MMU were essential in reaching out Syrian refugees.During 2015-16, 283 Syrian refugees were diagnosed with TB in Lebanon, while 116 in Jordan.

Country	Patient(n)	Success	Mortality	Lost to follow up
Lebanon	248	83%	5%	12%
Jordan	130	95%	4%	1%

Table Treatment outcome of 2014-15 Syrian TB patients

Coordinative effort of NTP's, WHO and IOM lead to developing regional TB database to follow continuity of TB treatment and improved cross-border surveillance.

Conclusions and key recommendations: Extensive collaborative efforts and innovative intervention approach of the International Community and NTPs with funding support of GF leads to successful TB control in refugee population.

PD-746-13 Traditional healers' perceptions about tuberculosis and prospects for control in pastoralist communities

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Background: Emerging data showed that pastoralists first visit to traditional healers (THs) is significantly contributing to diagnostic delay and poor adherence to treatment (Melaku S, Sharma HR, Alemie GA, 2013). This may in turn promote the spread of tuberculosis and development of drug resistance strains. In order to understand the potential role of THs in TB prevention and care activities, we assessed their knowledge, attitude, and current practices on TB Diagnosis and treatment in pastoralist communities.

Methods: A community based cross sectional study was carried out involving 268 THs and 337 community members in Pastoralist community of Kereyu district, East Showa Zone, Oromia region, Ethiopia. The data were collected using structured questionnaires. Data were analyzed using Statistical Software STATA. Descriptive statistics is used to summarize the socio demographic status of TH, knowledge and attitude of the TH's towards TB and current practice of TH's on TB diagnosis and treatment.

Results: Large proportion (98.9%) of THs in pastoralists community had high overall Pulmonary TB knowledge score (>50% of 16 maximum score) and high knowledge score (57.7%) about the sign and symptoms of Pulmonary TB. The majority (56.7%) of THs mentioned they use plant to treat TB and (86.2%) of THs

were willing to collaborate with conventional health system on TB diagnosis, treatment and cross referral. Also Most (40.0%) of community members mentioned they seek help from traditional healers twice or more a year.

Conclusions: The study showed that THs are familiar with sign and symptom of TB and that they are willing to collaborate with public health facilities. The community also visits THs mostly for their illness. The results underline the need to consider THs in TB prevention and care activities in pastoralist communities where access to health care is poor and consulting THs for illness is a common practice.

PD-747-13 Assessment of national tuberculosis burden, case detection rates and contact investigations among Syrian refugees: Jordan and Lebanon, 2015-2016

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Background: Refugee migration resulting from the Syrian crisis has strained tuberculosis (TB) control in neighboring countries. The US Centers for Disease Control (CDC) assisted the International Organization for Migration (IOM) and the National TB Programs (NTP) of Jordan and Lebanon to assess the national TB burden, case detection rates, and contact investigations among Syrian refugees in Jordan and Lebanon.

Methods: In December 2016, in both countries, TB burden, case detection rates, and the number of contacts screened for each case among Syrian refugees were assessed through retrospective review of IOM and NTP 2015-2016 line lists and surveillance reports.

Results: In 2016, 12.6% (58/460) and 21.9% (144/658), and in 2015, 13.8% (58/421) and 21.4% (139/650) of TB cases in Jordan and Lebanon, respectively, were among Syrian refugees. Based on the WHO 2015 Syria TB incidence estimate of 20/100,000 (latest available data) and refugee midyear population estimates of 682,816 in Jordan and 1,174,830 in Lebanon, case detection rates among Syrian refugees in 2015 were 46.1% and 59.1%, respectively.

In Jordan in 2016, 50% (29/58) of cases resided in camps, though only an estimated 21.5% of Syrian refugees in Jordan live in camps.

In 2015, the mean number of close contacts screened per case (Jordan: 3.2, Lebanon: 3.6) was lower than the median number of close contacts reported by incident cases (Jordan: 5, Lebanon: 4); but in 2016, mean contacts screened (Jordan: 7.8, Lebanon: 4.8) exceeded median reported close contacts (Jordan: 5, Lebanon: 3).

Conclusions: Syrian refugees represent nearly one-fifth of the TB burden in Jordan and Lebanon. Lower detection rates suggest missing cases among this population. Case-finding should focus on refugees in the host community in addition to those in camps. Screening strategy should emphasize further improving upon the completeness of contact investigation of TB cases seen in 2016 in both countries.

PD-749-13 TB case notification rates among various key population groups in Ethiopia

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Background and challenges to implementation: Interventions targeted at hot spot areas are likely to yield more TB cases and treat accordingly. Congregate settings are places where many people live together for extended period due to occupational and other purpose. In this paper, we intended to show the burden of TB among populations living in various congregate settings. **Intervention or response:** The National TB Program with support from the USAID funded Challenge TB project conducted a mapping of key population groups, gathered basic information, prioritized and provided capacity building activities. The key population assessment covered public universities, big farming areas, pastoralist districts and gold mining areas. Tuberculosis notification data was gathered from health facility registers found in the respective institutions and covered the period June 2015-July 2016.

Results and lessons learnt: The TB Case Notification rate (CNR) per 100,000 workers in large farm areas was 554 which is three fold higher than the TB prevalence estimate in the general population. Similarly, the TB CNR per 100, 000 among miners in Gold mining areas was 378 which is twice the TB prevalence estimate in the general population. A relatively lower TB CNR was observed in universities and pastoralist districts.

Type of Key population	Population	Annual TB cases	TB CNR per 100,000 population
Large farm areas	8,113	45	554
Gold mining areas	15,850	60	378
Universities	162,784	2058	159
Pastoralist districts	863,730	1,088	126

Table TB CNR per 100000 population for different key populations

Conclusions and key recommendations: The study shows a diverse TB burden among people living in different congregate settings prompting the need for key population based studies. Prioritizing TB interventions in key population groups and congregate settings should depend on the specific TB burden as the data shows diverse CNRs.

28. Using media campaigns to raise awareness in tobacco control and to counter tobacco industry

PD-752-13 An evidence based public campaign against waterpipe / hookah smoking in Turkey

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Background and challenges to implementation: Hookah use has been spreading rapidly in epidemic proportions in Turkey, especially among teenagers and the youth, posing a new threat to tobacco control efforts. Turkey has launched a public campaign against hookah smoking. Both qualitative and quantitative pre-campaign research has been conducted in order to define the perception, attitudes and behaviors of the target population regarding hookah. In this stage we conducted focus group studies and a baseline survey encompassing interviews with 1288 people. As a result of the pre-campaign analyses, we observed that the level of awareness on the dangers of hookah was very low compared to that of cigarettes, that hookah was not perceived as a tobacco product, that it was preferred due its scents and flavors and that many false beliefs were propagated such as its smoke being less dangerous due to passing from water. Measurable objectives of our campaign, campaign strategies and concepts were defined according to the data collected through the pre-campaign analyses. We applied our campaign through the use of TV and radio ads, outdoor materials, brochures, PR studies as well as the use of internet.

Intervention or response: Following the campaign we surveyed 1266 people in order to analyze the effectiveness of the campaign. The recall rate of the campaign is high by 73%, in total group. TV ads recalled are evaluated 'believable' 83% and 'effective 77% and also, taught persons something new' 75%. The awareness level about the negative health effects of smoking hookah significantly increased in post-campaign period. More than half of the people, who recall the campaign say that, their interest to try smoking hookah diminished.

Results and lessons learnt: Campaign was successful in establishing perceived risk of hookah changing perception and attitudes and developing the intention of quitting hookah.

Conclusions and key recommendations: Legal and environmental regulations and restrictions are necessary in order to prevent the hookah epidemic.

PD-753-13 Communication on health: the creation of a bulletin on tobacco industry strategies

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Background and challenges to implementation: Access to information is fundamental to guarantee democracy. The need to inform populations through the publication of evidence between health and his determinants is central to the health promotion strategy for the maintenance of healthy public policies.

Brazil, by ratifying the Framework Convention on Tobacco Control, an international treaty conducted by the World Health Organization (WHO), undertakes to develop measures to reduce the tobacco epidemic worldwide, addressing issues such as advertising, publicity and sponsorship , Warnings, marketing, passive smoking, treatment of smokers, illegal trade and taxes.

Article 5.3 of the Convention establishes guidelines for the protection of public health policies for tobacco control of commercial interests and other interests guaranteed to industry. In this sense, Cetab/Fiocruz launched the Observatory on Strategies of the Tobacco Industry, which gathers a data base on the strategies used by the tobacco industry to resist the effective control of tobacco in Brazil and in the world. However, it is necessary to propagate and diffuse the strategies used.

Intervention or response: To prepare a bimonthly newsletter on the strategies used by the tobacco industry based on the contents produced by the Cetab/Fiocruz Observatory.

Results and lessons learnt: Based on the analysis of documents and information inserted in the Observatory of Cetab, the work results in the creation of alert messages about the strategies and performance of the cigar industry in Brazil little known by the general public.

Conclusions and key recommendations: Health communication is always a social practice and, from it, it seeks to give visibility to the tobacco industry´s tactics to confuse, create myths and manipulate information about control policies. It is necessary to implement Article 5.3 of the FCTC as well as to ensure effective tobacco control actions in order to protect public health policies against the commercial interests and other interests of the tobacco industry.

PD-754-13 #ReelVsReal: social media campaign to combat glamorous depiction of tobacco use in films and TV programs in India

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Background and challenges to implementation: Studies have shown tobacco use is normalized by its positive portrayals in film and television. Indian films are watched by 250 million people in India and have the power to influence the behaviour and attitudes of viewers especially the youth. To counter the pro-tobacco imagery in the media, the Government of India enacted the Film Rule, under tobacco-control laws mandating theatres and television channels to include anti-tobacco advertisements, disclaimer and health warnings when tobacco is depicted on screen. Vital Strategies in collaboration with WHO India, undertook a study, "Evaluation of the Implementation of Tobacco- Free Film and Television Rules in India". Results were launched at a National Consultation with the relevant stakeholders. Synergised with the launch of the study findings, Vital Strategies launched #ReelVsReal social media campaign to combat the glamorous depiction of tobacco use.
Intervention or response: The #ReelVsReal (film "reel" vs "real" life) campaign was designed to raise awareness of the study results and show the contrast between depiction of tobacco in films with the real life stories of tobacco victims in India. The three-week intensive campaign included social media posts targeting celebrities and filmmakers.
Results and lessons learnt: The study result highlights were covered in more than 122 leading news publications. The posts were seen by approximately 66,000 people on twitter and 230,000 people on Facebook that harnessed around 53,000 reactions. The live videos from the consultation reached around 8,000 people.
Conclusions and key recommendations: The campaign showcased how the glamorous depiction of tobacco on screen can be combatted by real images of tobacco victims, and drive celebrities and filmmakers into joining hands to protect the health and well-being of those that they influence through their Films and TV programs. Further, this campaign suggests how social media can be a significant tool in amplifying the online reach of findings of a study.

PD-755-13 Efficiencies in achieving impact with at-risk audience segments through an anti-tobacco mass media campaign in India, Vietnam, Indonesia and Mexico

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Background: A number of recent studies from low and middle-income countries (LMICs) have demonstrated the ability for tobacco control mass media campaigns to change population level knowledge, attitudes and prompt quit attempts. However, to date, the efficiencies of these campaigns among subgroups, including women, lower-income groups, youth, have not been examined.
Methods: Using campaign evaluations from a range of LMICs, including India, Vietnam, Indonesia, and Mexico, this paper will analyze the relative impact of campaigns on men vs. women, lower vs. higher-income groups, young adults versus older adults, using bivariate tests and multivariate tests.
Results: Campaign impact will be presented in comparisons between campaign-aware and unaware respondents within the aforementioned subgroups. For example, in India, the impact of campaign awareness was equivalent among subgroups by gender and age; in Mexico, across age segments, campaign awareness was associated with greater interpersonal communication about tobacco and health, stronger beliefs in ones ability to quit and greater quit attempts. Consistencies and differences in impact between groups will be discussed.
Conclusions: Campaigns that have impact across subgroups provide resource-limited countries with efficient approaches to addressing tobacco prevalence. Campaign features that contribute towards such efficiencies will be discussed.

PD-757-13 Evaluation of first smokeless tobacco campaign in Myanmar

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Background: Myanmar has one of the highest smokeless tobacco prevalence rates and oral cancer rates in the world along with very low investment in tobacco control policies to date. In recognition of this, the first national anti-tobacco mass media campaign was proposed to influence knowledge, attitudes and social norms to contribute to reducing prevalence of smokeless tobacco use. To inform the campaign's effectiveness, message-testing research was undertaken to inform campaign design and improve effectiveness. This first national anti-tobacco mass media campaign in Myanmar is planned for June 2017.

Methods: Five draft smokeless tobacco PSAs, were produced based on interviews with victims of smokeless tobacco and message testing was conducted to identify the most effective PSA in terms of the comprehension, personal relevance and potential influence on smokeless tobacco use. Research was conducted with smokeless tobacco users and non-users aged 18-40 years using a standardized quantitative-qualitative methodology with eight focus groups. A household-based impact evaluation survey will be conducted at the conclusion of campaign to measure population level changes in knowledge, attitude, social norms and behavior.

Results: One PSA that showed an oral cancer patient talking about how he started chewing betel quid with friends and how this later become an addiction achieved the highest perceived effectiveness ratings: more than 95% reported ad was easy to understand, taught something new, believable, more likely to quit and an effective ad. Further, study reveals that showing the clear face of the tobacco victim will have more impact rather than disguising/to censor the face. More than 60% of participants reported that the ad made them uncomfortable and concerned about their tobacco consumption (82%). Impact of campaign on the target audience will also be reported.

Conclusions: Findings of the study will help strengthen further efforts including developing strong social support for sustainable tobacco control policies in Myanmar.

29. Latent TB infection: the last frontier

PD-758-13 Modelling latent TB infection control on TB transmission and elimination in Europe

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Background: Europe is aiming for elimination of tuberculosis (TB). This requires management of latent TB infection (LTBI) in key populations. The objective of this study was to estimate the potential of various LTBI control strategies in key populations for reducing transmission, to assess their contribution in moving towards elimination, and their cost-effectiveness.

Methods: We have developed a comprehensive, deterministic TB transmission model for European countries that accounts for transmission within and between the general population and different key population groups.

Transmission parameters included external force-of-infection due to travelling. LTBI control included LTBI screening and preventive therapy. The effectiveness of the screening included averted TB disease and life years lost. The costs were analyzed from both the healthcare and societal perspective. The model was used for the Netherlands, Czech Republic, Portugal, and Spain.

Results: Substantial decreases in pulmonary TB incidence can be achieved with a combination of LTBI control in different key populations, but none of the modelled LTBI control strategies will result in reaching the elimination target of less than 1 per million. Preliminary results show that LTBI screening was most cost-effective from the healthcare perspective when done using a tuberculin skin test, followed by interferon gamma release assay (IGRA) if positive. From the societal perspective, using only IGRA was the most cost-effective option. The most cost-effective strategy was screening migrant prisoners for LTBI at the moment of incarceration, while the least cost-effective strategy was screening migrants for LTBI at entry. LTBI control for healthcare workers and long-term travelers was rarely cost-effective. LTBI control of contacts was always cost-effective, independent of screening test. LTBI control for immunocompromised patients was only cost-effective when applied for migrants.

Conclusions: LTBI control in general is a cost-effective policy option for European countries. Focussing LTBI control on populations with increased exposure and risk of TB disease is most cost-effective.

PD-759-13 Low prevalence of tuberculin skin test boosting among community residents in a high tuberculosis burden setting

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Background: Boosted tuberculin skin tests (TST) reactions can be misclassified as new conversions resulting in unnecessary investigations and treatment for latent TB infection. To our knowledge, no study has evaluated the level of TST boosting in a population-based sample in high TB burden settings. We aimed to determine the prevalence of TST boosting among urban residents in Uganda.

Methods: A prospective study was conducted in Lubaga division in Kampala, Uganda from January to February of 2016. Eligible participants were 18 years or older and willing to receive a baseline and a repeat TST. We repeated a TST within 2 weeks if the baseline TST was less than 5 mm and induration readings were done within

48-72 hours. Participants with TST of 5mm or greater were excluded from the study.

Results: Seven hundred ninety-five participants were screened, 215 (27%) had a TST induration of less than 5 mm at baseline and hence were eligible for a repeat TST, 135 (63%) had a TST repeated and 99 (73%) returned for a second TST reading within the 48-72-hour window. Two (2%) had a second TST of 10 mm or greater indicating boosting and 5 (5%) had a TST between 5 and 10 mm, classified as intermediary. Both participants who met the criteria for boosting were female, had BCG scars and were HIV seronegative. Of the 5 participants with intermediary reactions, all were female and HIV seronegative, 3 had BCG scar. Of the 92 persistent TST negatives, 83 (94%) had BCG scars and only 2 were HIV seropositive.

Conclusions: The prevalence of boosting was as low as 2 % even in the presence of previous BCG exposure suggesting that most TST conversions represent new latent TB infections in this setting. The intermediary category that does not meet the criteria for TST boosting remains an area for further research.

PD-760-13 Measuring the prevalence of latent TB infection in Ca Mau province

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Background: The prevalence of latent TB infection (LTBI) in children aged 6 to 14 years in Vietnam was estimated to be 16.7% (based on a Mantoux test ≥ 10mm) in 2006-07. We are not aware of any recent population-based estimates of the LTBI prevalence among adults in Vietnam. Knowledge of the LTBI prevalence would be valuable for predicting the future burden of tuberculosis due to reactivation of LTBI. This study aims to estimate the LTBI prevalence in adults in Ca Mau Province in southern Vietnam.

Methods: We randomly selected 60 sub-communes from the 948 that exist in this Province. The population in each of these sub-communes was enumerated and participants aged 15 years and over were randomly selected from this population with a sampling probability of 3.85%. Those who agreed to participate had blood collected using the QuantiFERON® - TB Gold test kit.

Results: The enumerated population aged 15 years and over in the selected sub-communes was 44,088. Of the randomly selected 1,697 people, 1,319 participants (77.7%) consented and had blood collected.

There were 486 (36.8%, 95% CI 33.4% to 40.3%) who were classified as positive on the test QuantiFERON®

- TB Gold. All the remaining participants were classified as negative. There were no indeterminant results. Overall, the prevalence of positive tests was lower in females than males, odds ratio 0.57, 95% CI 0.45 to 0.72, P < 0.0001, after adjustment for differences in age. The prevalence of positive tests increased with increasing age quintile (P < 0.001) although the rate of increase flattened off from the third quintile.

Conclusions: We found a high prevalence of latent TB infection in the adult population in Ca Mau. This represents a substantial burden of infection that, potentially, requires treatment to prevent progression to active disease.

Support: AERAS and Australian National Health and Medical Research Council.

PD-761-13 Missed opportunities for TB prevention: the TB care continuum in adult primary care clinics at Denver health, an urban safety-net health system

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Background: Identifying and treating latent TB infection (LTBI) is a recommended strategy for TB elimination in low-burden settings. Prior evaluations of LTBI testing have only included testing done in public health clinics. We sought to evaluate the LTBI care continuum and factors associated with testing in primary care clinics (PCC).

Methods: We conducted a retrospective cohort study of adults (>17 years) reporting birth country with TB incidence ≥20/100,000 and seen in PCC from 1/2012-12/2014. Data was extracted from the electronic medical record. The proportion with LTBI was estimated using IGRA positivity rates. The proportion with known LTBI was estimated using record of a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) prior to/within 1/2012-12/2014. Treatment initiation and completion were estimated by pharmacy refill for those IGRA tested within 1/2012-12/2014. Of those untested prior to 1/1/2012, factors associated with LTBI testing from 1/2012-12/2014 were identified using t-tests, chi-square for univariate comparisons and logistic regression for multivariate comparisons.

Results: 9,397/32,452 adults (29%) were tested or had history of testing. 25,337 had no history of testing. 2,282/25,337 (9%) were tested from 1/2012-12/2014. 24.7% (544/2205) were IGRA positive. Treatment initiation and completion rates were 56% (304/544) and 77% (235/304), respectively. The LTBI care continuum is shown in **Figure 1.** In multivariable analysis, factors associated with higher screening included HIV infec-

tion (OR= 24.8 CI 11.8-52.2), pregnancy (OR= 6.9, CI 6.0- 8.0), more PCC visits (OR= 1.04, CI 1.03-1.05) and health insurance (OR=1.3, CI 1.2-1.5). Compared to white, non-Hispanic persons, individuals identifying as Asian/Pacific Islander (OR= 1.7, CI 1.3-2.0) had higher screening; Hispanic individuals had lower screening (OR= 0.7, CI 0.6-0.9).
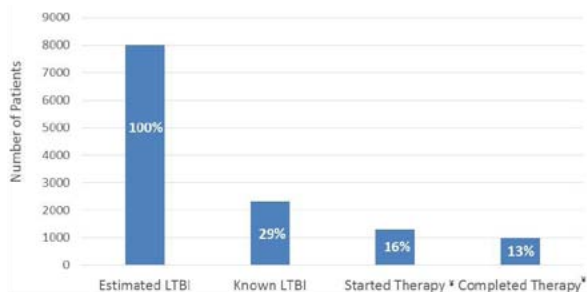
*Patients with a country of birth with TB rate >=20 cases/100,000 persons
**LTBI estimate which is based on IGRA positivity rate within study period
¥ Estimated from the rate who initiated and completed therapy among those who were tested during the study period

Figure 1 LTBI care continuum for adults reporting birth country with an elevated TB incidence* (2012-2014)

Conclusions: The biggest gap in the LTBI care continuum within PCC is in testing patients at risk, a major contributor to poor treatment completion. Additional strategies are needed to improve LTBI testing to advance towards TB elimination.

PD-762-13 A case study in Ghana of the cascade of LTBI care

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Background: The diagnosis and treatment of LTBI has recently been identified as a priority by the World Health Organization. In many resource-poor settings few contacts are identified as part of the contact investigation process. As part of the ACT4 research trial, the major losses in the LTBI cascade of care, from contact identification through investigation to treatment, were quantified and potential reasons for the losses were explored. **Methods:** The cascade of LTBI care was examined at St Patrick´s Hospital in Bonsun Offinso, Ghana. Pre-existing TB Registries were used to retrospectively collect information on the identification, investigation and treatment of up to 150 contacts of index cases with pulmonary TB. This data was used to pinpoint steps in the cascade of LTBI care where major losses occurred. Interviewer administered questionnaires were completed by index cases, adult household contacts, parents of

child contacts and health care workers (HCW) from the same hospital in order to investigate knowledge, beliefs and barriers related to uptake of LTBI care.
Results: Between August and October 2016, a total of 112 household contacts (12% of whom were under 5 years) were identified for 28 index cases (3.9 contact/case). Due to the lack of policy for LTBI treatment and follow-up, none of these 112 contacts were tested for LTBI nor offered LTBI treatment. In questionnaires (n=80), both contacts and health care workers mentioned LTBI not being recognized as a priority, lack of knowledge about LTBI and not being informed about the need to be tested (by HCW). Fear of stigma was also a frequent reason for not being tested.
Conclusions: A multifaceted approach will be required for the LTBI cascade to improve. This should include high level policy change as well as widespread education to combat stigma that is prevalent in the community.
Funded by: Canadian Institutes of Health Research (CIHR)

PD-763-13 Policies and practices in programmatic management of latent tuberculosis infection: survey in the African Region

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Background: Although screening and treatment of latent tuberculosis infection (LTBI) among at-risk populations is a core component of the End TB Strategy, there is limited information about the status of implementation of LTBI-related interventions and their major challenges in most African countries.
Methods: An online questionnaire was administered between November 2016 and February 2017 to the National TB Programmes of all the 47 countries belonging to the African Region.
Results: The questionnaire was filled out by 61.7% of countries (29/47), including 11 high burden countries (HBCs). Specific guidelines for LTBI were available in 4 countries (13.8%) while 12 (41.4%) had a section on LTBI as part of their national TB guidelines. Twenty countries (69%) reported having LTBI screening already in place for child contacts, 22 (75%) were providing treatment (6-month isoniazid in all but three where a 9-month schedule was adopted), 6 (9%) had plans to start LTBI activities soon. Sixteen countries (55.2%) reported provision of LTBI screening and treatment to people living with HIV (PLHIV) and 6 had plans to do it. Most HBCs (9/11) had ongoing LTBI activities targeting at least one of the two above-mentioned at-risk groups. Tuberculin skin test was the recommended screening

tool for child contacts and PLHIV in 10 and 3 countries, respectively. LTBI screening was free of charge in all countries except two where a fee of 4-8 US dollars per patient was applied, while treatment was always provided for free. A recording and reporting system for LTBI-related data on child contacts and PLHIV was available in 14/22 and 12/16 countries respectively. Seven countries had a monitoring and evaluation plan for LTBI, though restricted to PLHIV in one of them.

Conclusions: According to our findings, greater efforts are needed to appropriately scale up LTBI policies in the African Region.

PD-764-13 Treatment of latent tuberculosis: a network meta-analysis-update

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Background: Treatment of latent tuberculosis infection (LTBI) is an important component of tuberculosis (TB) control. Our previous systematic review(1) informed the 2015 World Health Organization LTBI guidelines. As a number of studies have been published subsequently, we updated our systematic review and meta-analysis to determine the most efficacious regimen for preventing active TB with the lowest toxicity. This provides key evidence for new European Centre for Disease Prevention and Control LTBI guidelines, and also programmatic LTBI control.

Methods: Two independent researchers reviewed and extracted relevant randomized controlled trials from PubMed, Embase, Web of Science and the grey literature up to 29 April 2016 with no language restrictions. Standard and network meta-analysis (NMA) were performed in parallel.

Results: NMA of all included papers (n=62) showed that six month isoniazid regimens (Odds Ratio (OR) 0.40, Credible Interval (CrI) 0.26-0.60) or 12-72 months isoniazid (OR 0.31; 0.21-0.47), three to four months rifampicin only regimens (OR 0.25; CrI 0.11-0.57), three to four month rifampicin-isoniazid regimens (OR 0.33; CrI 0.20-0.54), rifampicin-isoniazid-pyrazinamide (OR 0.21; CrI 0.11-0.41), and rifampicin-pyrazinamide regimens (OR 0.33; CrI 0.18- 0.58) were efficacious compared with placebo. There was some evidence for the efficacy of weekly rifapentine-isoniazid regimens (OR 0.36; CrI 0.18-0.73). Findings of standard meta-analysis were similar to NMA. The evidence for some comparisons, particularly for hepatotoxicity, remained sparse.

Conclusions: There is good evidence that many standard LTBI treatment regimens are safe and efficacious. There

is increasing evidence regarding the safety and efficacy profiles of rifamycin-containing regimens. However there remains a need for more data on rifapentine.

References:

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PD-765-13 Closing the loop in child contact management: IPT completion outcomes in Western Kenya

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Background: Tuberculosis (TB) remains the leading infectious killer globally. Children - particularly those < 5 years old - exposed to infectious TB disease are at risk of severe disease/death. For two decades, the World Health Organization (WHO) has recommended child contact management (CCM) be conducted in high TB burden countries. Operational challenges in the CCM care cascade - identification, screening, isoniazid preventive therapy (IPT) initiation, and completion of therapy (COT) - continue to exist in countries like Kenya.

Methods: Funded by TB Reach, an active CCM strategy was implemented throughout western Kenya targeting children < 5 years exposed to smear positive TB index cases. This strategy incorporated 3 components: 1) Healthcare worker education 2) a child contact register to track contacts, and 3) transport/screening reimbursement. We conducted a retrospective analysis of COT for eligible child contacts.

Results: 553 child contacts were evaluated between July 2013-December 2014 from 10 clinics. 74(13%) had TB disease. Of 472 without TB disease, 427(90%) initiated IPT. 205(48%) had documented COT. 129(30%) initiating IPT could not be found in the register. 49(11%) reported intent to transfer. 44(9%) deferred IPT; 6 child contacts who deferred completed IPT. The most common deferment reason was antibiotic treatment trial (ATT).

Conclusions: Most eligible children were reported to initiate IPT with an active CCM strategy, which was much higher than the reported 5.5% IPT initiation rate in Kenya in 2015. < 50% had documented COT. 11% of children were reported to immediately transfer suggesting significant mobility within the health system. 30% of children were not recorded in the register. ATT was a common reason for IPT deferment; most ATT children

did not return for IPT. These findings underscore CCM cascade gaps and additional intervention strategies are needed. Active CCM programs with ongoing programmatic evaluation are critical to designing effective pediatric TB programs.

PD-766-13 Treatment of presumed drug-resistant TB infection in household contacts in a high-burden setting

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Background: Treatment of presumed TB infection in exposed households is a mainstay of combating TB. Preventing DRTB disease in exposed individuals is a priority. Observational studies have demonstrated the effectiveness of a fluoroquinolone-based regimen in prevention of DR-TB disease among contacts.
Methods: We conducted TB symptom screening in household contacts of 100 DR-TB patients enrolled at The Indus Hospital TB Program from February 2016 until April 2017 (or date). All child contacts (< 18 years), symptomatic adults, and those with an immunocompromising condition (HIV, diabetes or malnutrition) were tested for TB disease with chest x-ray and Xpert MTB/RIF. Those diagnosed with TB disease were started on disease treatment. Those in whom TB disease was excluded and who fulfilled the following criteria were offered a 6-month course of daily TB infection treatment with levofloxacin and ethambutol for 6 months: (i) <5 years, (ii) 5-17 years old with either a positive TST or an immunocompromising condition (iii) >=18 years with an immunocompromising condition. We provided transport allowances of USD 5 to families to enable clinic visits.
Results: In 100 households with 796 contacts who consented to participate, 705 contacts were verbally screened; 7 were on TB disease treatment; 2 others were diagnosed with TB disease and started on treatment. Of 169 eligible contacts, 147 received treatment for presumed DR-TB infection; 73 (50%) were females, 51 (35%) were <5 years, and 76 (52%) were age 5-17 years. To date, 35 contacts have completed treatment and remain in clinical follow-up without TB disease. No significant AEs were observed.
Conclusions: Our outcomes in Karachi households are consistent with a growing body of data that shows that a fluoroquinolone-based regimen for presumed DR-TB infection in household contacts is well tolerated, prevents progression to TB disease, and can be implemented in a high TB burden setting.

PD-767-13 Surveillance of severe adverse events on once-weekly rifapentine plus high-dose isoniazid for latent tuberculosis infection treatment in Taiwan, 2016

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Background: Once-weekly rifapentine plus high dose isoniazid (INH-RPT) showed non-inferior efficacy and less hepatotoxicity compared to 9-month isoniazid (9H) regimen for latent tuberculosis infection (LTBI) treatment in the clinical trial. However, rifapentine requires more safety information regarding severe adverse events (SAEs) to roll out in Taiwan.
Methods: The aim of study is monitoring frequency and outcomes of SAEs associated with INH-RPT regimen. Since April 2016, Taiwan has endorsed INH-RPT as alternative regimen of 9H for LTBI contacts aged ≥12 years. Contacts choosing INH-RPT regimen should participate in directly observed preventive therapy (DOPT). Possible SAEs defined as any hospitalization or death during treatment. We also collaborated with drug safety authority to obtain possible SAEs from Reporting System of Adverse Drug Reaction. SAE should be reported to the Taiwan Food and Drug Administration and CDC. We reviewed case management records and medical charts to estimate SAEs associated with INH-RPT using Modified Naranjo Adverse Drug Reaction Probability Scale. A score ≥5 was defined as SAE associated with INH-RPT.
Results: By the end of 2016, there were 2652 contacts who initiated 3HP treatment. Among the identified 29 possible SAEs, 2(6.9%) died of acute myocardial infarction and status asthmaticus with urosepsis, respectively. One patient had syncope associated with cardiogenic cause. There were 16(55%) SAEs scoring ≥5; mean age was 51 (22-81) and eight were males (50%). Found 82% of INH-RPT associated SAEs occurred during 1st—4th dose; hospitalization was mainly due to flu-like illness(56%). INH-RPT related hepatotoxicity resulted in 6(38%) SAEs; four patients with ≥5 times elevation of the ALT upper limit. All 16 patients recovered after temporary or permanent stopping treatment.
Conclusions: The INH-RPT regimen has been safe and 55% of SAEs attributed to INH-RPT. However, health care providers should be aware of most INH-RPT associated SAEs during the 1st—4th dose.

30. Elevating knowledge in the field: an essential tool

PD-768-13 Knowledge about and preparedness for tuberculosis management among health-care and social workers in refugee accommodations in Cologne, Germany

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Background: In 2016 the city of Cologne hosted around 13.000 refugees, among them 27 were diagnosed with tuberculosis. Health and social staff in refugee accommodations can be confronted with newly diagnosed cases of Tb, with Tb cases under treatment or tenants on chemo-preventive treatment. Due to the epidemiological situation few staff members have had direct experience with tuberculosis. We therefore examined their knowledge and preparedness to deal with tuberculosis.

Methods: A cross-sectional study was performed based on telephone-interviews with health-care and social workers working in refugee accommodations in Cologne. A 17-item standardized questionnaire covering questions about knowledge of, previous experience with, and concerns and challenges in dealing with tuberculosis was applied among 20 social/health workers in 17 large emergency accommodations and 11 refugee hostels managed by Red Cross in Cologne.

Results: The sample of social and health-care workers covered approx. 36% of the refugees population as frontline responsible staff. 25% had any training for managing Tb or Tb suspected individuals, 50% described previous experience. Personal who had a training about Tb felt in general more comfortable with Tb and less afraid of getting infected in the setting. Asked for their expectations to public health department 20% asked for a further training. The biggest problems the personal in the hostels see, is that the results of the screening are insufficiently recorded.

Conclusions: Half of the social and health staff working in refugee accommodation have no previous experience with Tb and only 25% had respective training. Focused short trainings could increase attention of personal for early signs of Tb while at the same time reduce uncertainty and worries about transmission.

PD-769-13 Scaled-up implementation and attrition risk evidenced in a TB guideline e-learning course for frontline staff of the Peruvian National Tuberculosis Programme

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Background: Collaboration between Peruvian National Tuberculosis Program (NTP), Instituto de Medicina Tropical Alexander von Humboldt and Telemedicine Unit, School of Medicine, Universidad Peruana Cayetano Heredia, produced an e-learning program for frontline TB workers. (46th World Lung Health Conf SOA-647-06). We scaled-up enrollment to include non-clinical NTP personnel from the TB program. We present the results and suggest an evaluation to predict attrition.

Methods: This edition included new TB-DM and operations research contents. Students were enrolled from a large dual-district health network (50 centers). The course lasted 18 weeks, requiring 6 hours per-week: with short lectures and supporting post-tests, scientific literature, forum interactions, and video-based learning scenarios. Standard follow-up consisted in email and SMS messages. We evaluated course attrition risk (compliance with < 80% of post-tests); via scoring students (-1 to +1) according to how early, near or past the deadline they usually completed coursework; lower scores indicated earlier delivery.

Results: 286 students enrolled: 212 clinical (74.13%, 60 medical doctors (MD), 103 registered nurses (RN), 49 nurse aids (NA)); 74 (25.87%) non-clinical personnel (NCP) (social workers, lab technicians). From 253 completed surveys, 81% were female, median age: 40.10 (IQR 31-47), median time from graduation: 11.64 (IRQ 6.64-20.65); median experience in the TB program: 7.43 yrs (IRQ 1.19-8.52). The NCPs and NAs were older (median 43.43/40.34), with more program experience (9.95/8.76 yrs); RNs had less experience (age 37.2; 5.56 yrs in NTP) (**p< 0.05**, Kruskall-Wallis test). Technology use was common: 93.68% accessed internet at least weekly; 30.83% had prior e-learning experience. 158 students finished the course (49% approved, 6% disapproved; 44% attrition rate, vs. 17.5% previously). Student dropouts had a higher mean coursework presentation score (-0.66 vs. -0.56)(< 0.05,double-tailed t-test).

Conclusions: Scaling-up course implementation also increased attrition rates; more heterogeneous groups could require specific follow-up. Late/on-limit coursework presentation could help identify students´ attrition risk.

PD-770-13 Innovative approaches to cascade nutrition in tuberculosis knowledge among health care workers in limited resource settings

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Background and challenges to implementation: Undernutrition is a risk factor for progression from TB infection to active TB disease and a predictor of increased risk of death and TB relapse for active TB. Health care workers (HCWs) with adequate knowledge of nutrition in TB are integral components for quality patient management.

Resources to conduct classroom trainings are increasingly getting limited. On the job training (OJT) and mentorship are cost effective approaches to cascade nutrition in TB knowledge among HCWs. It is simple, economical, instills multiple skills, takes less time, has more coverage, there is quick learning and takes place at workstations leading to immediate productivity.

Intervention or response: Amref Health Africa with funding from Global Fund trained 100 Trainers of Trainers (ToTs) for Nutrition in TB. TOTs trained 625 HCWs from 25 Counties. Nutrition in TB Technical Working Group (TWG) developed an OJT guide and County and Sub County Nutrition coordinators were orientated on it. For each targeted health facility, needs assessments was done and OJT tailored to the gaps provided. Joint national and County teams did quarterly follow ups to determine impact on nutrition assessment, care and support for TB patients.

Results and lessons learnt: A total of 236 health facilities from 9 counties were reached with OJT in one quarter. The most common gaps in nutrition in TB identified included inadequate knowledge and skills (30.40%), limited services (27.75%), poor documentation and reporting (20.20%). By the second quarter all gaps had improved to at least 90%. Information on other gaps including lack of anthropometric equipment, food supplements and technical staff informed resource mobilization within counties.

Conclusions and key recommendations: OJT is cost effective compared classroom training in resource poor settings. It quickly increases coverage and HCWs are able to provide and document better quality services offered to TB patients.

PD-771-13 Can sensitizing health care workers and directory of TB services increase TB case notification? Experience from Nigeria

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Background: Early diagnosis and initiation of TB treatment requires prompt access to TB services; however TB case notification has remained low despite nation-wide expansion of AFB, GeneXpert and DOTS sites.

Objectives: This study was aimed at sensitizing general health care workers at all levels on symptoms and signs of TB, provide information on list of TB service delivery points and promote effective referral services.

Methods: A 12-months project implemented across 12 states from January to December 2016, inventory of all facilities providing TB services showing physical location and contact details of focal persons was updated and printed every six months (twice) then distributed to all health facilities; facilities with high monthly average GOPD attendees among primary, secondary and tertiary institutions were identified and selected; 1-day sensitization of general HCWs (Male = 2,277; Female = 2,470) on TB; explained procedures for effective referrals. Data was collected and analyzed for quarterly tends.

Results: During the period 208,709 presumptive TB were registered and tested out of which 44,758 (21%) were notified (bacteriological and clinical) and commenced treatment, compared to 154,430 registered presumptive TB of which 37,629 (21%) notified TB commenced treatment in 2015. Overall in 2016 there was 31.5% increase of presumptive TB tested and 18.9% increase of persons with TB who started treatment over 2015 baseline.

Conclusions: Sustained capacity building of health care workers increases ability to effectively screen, identify and refer presumptive TB to nearest service delivery sites thereby improving TB case notification. State TB programs should periodically update and distribute directory of TB services to ensure appropriate and complete referrals.

PD-772-13 Reactivating TB services through training and mentoring in Mazabuka & Kafue Districts, Zambia

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Background and challenges to implementation: In the last decade there has been increasing focus on improving the coverage and quality of HIV/AIDS services. With new initiatives springing up annually these have inadvertently shifted focus from TB service including TB/HIV coinfection and especially TB in the general population, no wonder the rapidly declining TB statistics. In an effort to redirect country focus on Tuberculosis due to its epidemiological relevance, Jhpiego Zambia working with the MOH supported the establishment of District Mentorship and Training teams (DMT) composed of selected providers and DHO personnel within the districts.

Intervention or response: The DMTs comprise of 21 heath care workers per district, who received training on TB diagnosis and management in June and September 2016, respectively. Subsequently the DMT embarked on focused mentorship across health facilities in the district. DMT rounds and training database reports were reviewed to assess TB knowledge of health provider's pre and post training in addition to routine program data on TB service delivery.

Results and lessons learnt: A total of 42 health providers (2 doctors, 12 nurses, 13 midwifes, 10 clinical officers and 5 other cadres) were trained. Both districts showed similar training results: 14% of health providers (3/21) passed the pretest, while 95% (20/21) passed the posttest in Mazabuka and 100% in Kafue. The average scores on pre and posttest in Mazabuka were 57 and 96 respectively and 72 and 96 in Kafue. TB presumptive cases have also increased by 8% (425 to 459) in Kafue and 123% (543 to 1213) in Mazabuka comparing the previous quarter to the quarter after the training.

Conclusions and key recommendations: Re-training and mentoring health workers is critical to support reactivation of services with low knowledge levels of health workers observed from pretest scores in both trainings. There is also a quick turnover with increase in knowledge immediately translating to improved uptake of services.

PD-773-13 Designing evaluation studies to optimally inform policy: factors to consider when making resource allocation decisions for health worker training program

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Background: Barriers to utilizing evidence from evaluation studies to inform decisions on resource allocation for strengthening health-related human resource capacity are particularly salient in low and middle-income countries (LMICs), as training interventions have received substantial investment owing to the extreme shortage of healthcare providers (HCP). The aim of our study is to investigate what features of HCP training evaluation studies make them useful to policymakers in LMICs, and the extent to which evaluations based on the widely-used Kirkpatrick model - focusing on direct training outcomes: reaction, learning, behavior and programmatic improvements - are helpful in informing resource allocation decisions. We use China as a case study where resource allocation decisions about potential scale-up are being made about an externally funded HCP training program.

Methods: Qualitative data were collected from high level policymakers involved in resource allocation at national and provincial level in China through ten face-to-face, in-depth interviews and two focus group discussions consisting of ten participants each. Data were analyzed manually using an interpretive thematic analysis approach.

Results: Our study indicates that policymakers in China not only consider information about the direct training outcomes captured in the Kirkpatrick model, but also require additional information on resources required to implement the training, wider impacts of training, sustainability and scalability to other settings within the country. In addition to considering findings presented in evaluations, policymakers in China also pay close attention to whether the evaluations were robust and the composition of the evaluation team.

Conclusions: Our study indicates that training program evaluations focusing narrowly on direct training outcomes may not provide enough information for policymakers to make decisions on future training programs. Based on our findings we have developed an expanded evidence-based framework that provides conceptual and practical guidance to aid the design of training program evaluations that are better suited to inform policy decisions.

PD-774-13 Awareness and education on tuberculosis prevention and control through the school health program in Kenya

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Background and challenges to implementation: Although a preventable infectious disease, tuberculosis is a leading cause of mortality globally. In Sub-Saharan Africa, it is mainly associated with HIV/AIDS. Gaps in knowledge, attitude, practice and stigma contribute to new infections, poor health-seeking behavior, delayed diagnosis and treatment.

The stigma of association with HIV/AIDS and enforced treatment programs could hamper public health efforts of treatment and prevention among highly conscious populations of young adults and school-going children. A 2016 prevalence survey in Kenya found that over 80% of tuberculosis was among persons without HIV/AIDS. Tuberculosis education and awareness programs among young adults and children can stem its high burden. Targeting healthy school-going children could have lasting and multiplicative effect on prevention and control.

Intervention or response: During February - March 2017, we targeted school-going children in the County of Kiambu with messages on tuberculosis prevention and control through the school health programme. All children in selected primary schools received lessons in general information on TB, with those in upper grades receiving extra lessons on causes, diagnosis, treatment and prevention at the community. Children were tasked to write either an essay or make an illustration on their contribution to prevention and control of tuberculosis in their communities. The essays and illustrations were scored and the best selected; the contributing children were rewarded.

Results and lessons learnt: Twenty schools representing a population of 22,760 children were reached, contributing 2,000 essays and illustrations. Ten essays met the criteria for scaling the school health programme tuberculosis prevention. Three essays and one illustration were selected for reward.

Conclusions and key recommendations: Engaging school-going children produced contextually relevant education and awareness material that children as agents of change can use for peer-led education to prevent new infections and achieve a tuberculosis free generation by 2035. We will evaluate the impact of peer-led and relevant education on tuberculosis prevention and control.

PD-775-13 TB education intervention in school children plays a vital role in detection of presumptive TB cases in a South Indian district

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Background: In India, Revised National TB Control Programme (RNTCP) issued directions to all the states to conduct school TB awareness campaigns in 2012. Schools are major vehicle for social mobilization of young students to fight against TB under Advocacy, Communication and Social mobilization (ACSM) Activities. This section presents innovative steps that can make the school activities more effective.

Methods: To determine the yield of the TB patients after conducting the School intervention activity in marginalized and vulnerable population areas under ACSM activities in Dharward District of Karnataka, India.Two TB units of Dharward district were selected for pilot school intervention under ACSM activities. Mapping had done for schools and colleges in vulnerable areas. District TB staff sensitized 8 schools and 2 colleges students on TB with Audio-Visual Aids. Referral slips and TB Signs & Symptoms labels were given to the school student. Focal RNTCP staff collected filled referrals slips, made house visits, counseled the symptomatic and proper symptomatic were referred for sputum examination

Results: 189 symptomatic persons were identified by the students and 138 persons were screened for Sputum examination. 14 of them found sputum positive and started DOTS treatment.

Conclusions: This robust approach of social mobilisation among young children not only helps awareness generation and also in removing the stigma associated with TB in their homes and neighbour-hoods. They played vital role in the case detection of new presumptive TB patients in the vulnerable communities.

PD-776-13 From one to many: the multiplier effect of a school-based TB health education program

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Background and challenges to implementation: In Myanmar, childhood tuberculosis (TB) burden is high with 25% of all notified cases occurring in children. To address this issue, USAID Challenge TB Project (CTB) designed a school-based campaign to provide TB-related

health education to school children, their parents and guardians. CTB trained 16 field staff on TB, health education and presentation skills. Field staff were then sent to 20 schools in 4 townships of Yangon where TB case notification is high.

Intervention or response: Field staff conducted classroom-based health education sessions, which were designed to be interactive and interesting for the school children. Pamphlets containing key points from the discussion and supported by colorful illustrations, were also distributed along with a question sheet on TB. The children were instructed to give the pamphlet and question sheet to their parents or guardians, to work on the answers using the pamphlet as a guideline and to return the sheet the next day to their home-room teachers. Health educators collected the sheets from the responsible teachers. During the eleven weeks of intervention, the field team conducted 332 health education sessions reaching out to 20,035 children in 20 schools.

Results and lessons learnt: Out of the 20,035 question sheets given to the children, 18,068 forms (90.2%) were returned answered and signed off by their parents/guardians. During post-intervention assessment, out of 480 students interviewed, more than 340 (71%) talked about TB with their family members, friends and relatives. Over 360 (75%) students also shared information about cough etiquette with others, aside from sharing IEC with their guardians. This was a significant improvement from findings in pre-intervention assessment where only 30% of school children talk about cough etiquette with other people.

Conclusions and key recommendations: Although the extent of the multiplier effect is yet to be evaluated, the intervention program advocated for children to share their knowledge with others and the results appear promising.
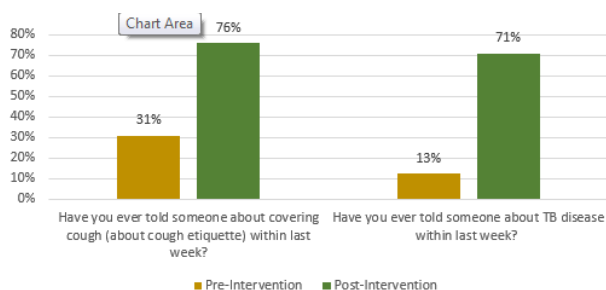
Figure Knowledge sharing of school children before and after intervention (n = 480)

PD-777-13 Building in-country technical capacity on TIME modelling through face-to-face training

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Background and challenges to implementation: Mathematical modelling has played an important role in supporting the development of global strategies and targets for TB care and prevention. At the country-level, modelling has the potential to enable policy dialogue and support decision-making for evidence-informed strategic planning of TB care and prevention activities. However, low- and middle-income countries (LMIC) often lack technical capacity for mathematical modelling; therefore, its contribution to evidence-informed policy-making has been limited in these settings.

Intervention or response: The TIME model (www.time-modelling.com) is a user-friendly country-level tool, designed to be used by local decision-makers for TB strategic planning in LMIC.

Representatives from the National TB Control Programmes (NTP) of Nigeria, Vietnam and Indonesia were invited for three- to six-week face-to-face training at the London School of Hygiene & Tropical Medicine (LSHTM) on TIME modelling to develop skills in leading the TIME modelling process locally.

With support from LSHTM, trainees developed their skills by leading on model calibration to generate projections of TB burden; identifying and modelling interventions in priority policy areas; and developing a presentation to communicate modelling results to in-country policymakers. Following the training, remote support from LSHTM remained available as needed.

Results and lessons learnt: Each country set up a local in-country TIME modelling team to lead and support the modelling process of investigating the impact of different priority policy options. Following the training, all participants reported a deeper understanding of modelling concepts, stronger technical abilities with TIME and greater confidence in communicating technical results to policymakers. Evidence that the trainees generated with TIME is being used to strengthen international and domestic funding applications, including Global Fund funding requests.

Conclusions and key recommendations: Intensive in-house face-to-face training has shown to be a feasible approach to building technical capacity in mathematical modelling using a user-friendly tool like TIME, enabling the transfer of the model from academia to policymaking in a range of high-impact countries.

31. Protecting youth from the harms of tobacco use

PD-778-13 Patterns of poly-tobacco use among adults of the Southern California Children's Health Study: latent class analysis approach based on cigarette consumption in adolescence

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Background: We assessed the association of smoking patterns based on cigarette consumption over the course of adolescence with poly tobacco product use (cigarettes, electronic nicotine delivery systems [ENDS], hookah and pipes) in adults participants in the Southern California Children's Health Study, a large prospective of cohorts spanning almost 20 years.

Methods: Participants were adolescents from four cohorts comprising the Children's Health Study, who were enrolled between 1993 and 1996. Data for this study was collected via self-report in 2014, participants were asked about lifetime and past 30 days use of cigarettes, ENDS, hookah and pipes. Latent class analysis (LCA) were used to examine varying constellations of response patterns using the information of use of cigarettes in the adolescence; based on latent classes, multinomial regression models were carried out to assess the association of poly-tobacco product use in the adulthood.

Results: 3 latent classes were identified based in ever use of cigarettes during adolescence. "Light users" 21.5 %, "Late initiators", 35.4% and "Heavy users" 43.1%. Multinomial regression models showed that use of cigarettes in adolescence was associated with past 30-days use of cigarettes (O.R. 4.07) and ENDS (O.R. 2.86) in the class "heavy users" in comparison with "light users". In addition, "heavy users" is associated with current use of any combustible (O.R. 2.5), but particularly with past 30-days use of poly-tobacco products (O.R. 11.8), in comparison to adults who were "light users" in the adolescence.

Conclusions: By identifying the naturally progression of cigarettes use in the course of life and its association with alternative tobacco products use, may provide of useful information to practitioners and policymakers to identify the need for tobacco control interventions and particular combinations of poly-tobacco use in the adulthood . LCA can be used to identify patterns of previous consumption and its impact in the other stages of life.

PD-779-13 The art of vaping business around schools in the city of Mandaluyong, Metro Manila, Philippines

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Background and challenges to implementation: "Vape shops", stores selling e-cigarettes as primary product, is a trend in Metro Manila, Philippines. Although the national government issued public advisories emphasizing the health hazards posed by e-cigarettes, the Philippine Global Adult Tobacco Survey (GATS) 2015 revealed that 31.7% heard of e-cigarettes and 2.8% used them with 0.8% becoming current users. E-cigarette is contrary to the provisions of the Tobacco Regulation Act, intended to protect the youth from nicotine initiation and addiction and chronic respiratory diseases, including cancer. Addicted to nicotine, the youth will most likely switch to cigarette smoking. With no clear regulation by government on vape shop licensing and operations, e-cigarettes are available and accessible to consumers. Enforcers tasked to monitor sale of tobacco products around schools noted "vape shops" around schools.

Intervention or response: Enforcers conducted random visits to targeted vape and tobacco retailers around schools in Mandaluyong, Metro Manila, Philippines. Compliance with the business licensing requirement set forth by government was surveyed. Product details and frequent clients were gathered.

Results and lessons learnt: One of 35 "vape shops" inspected has a legitimate business permit to operate as such. 34 are operating as general merchandise stores. 22 or 63% are within 100 meters of schools. 13 or 59% are near higher education facilities. 41% are near grade schools. More than half sell e-cigarettes along with toys, school supplies and cellular phone accessories. Buyers belong to age 18-35 years. Half of shops require identification cards for age verification.

Conclusions and key recommendations: There is need to issue a policy regulating licensing and registration of "vape shops". These shops have invaded 100-meter radius from schools, where tobacco is strictly prohibited. Making e-cigarettes available and accessible to youth undermine tobacco control efforts that protect them against nicotine addiction and being initiated into cigarette smoking. The novelty of e-cigarettes enhance the attractiveness of smoking and promote re-normalization of the smoking behavior.

PD-781-13 Susceptibility to smoking and determinants among medical students: a representative nationwide study in China

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Background: Susceptibility to smoking among medical students may relate to smoking after they becoming physicians. But no literature explored this issue. The objective of this study was to examine susceptibility to smoking and determinants among medical students.
Methods: Participants were 11,954 students, who were identified through a multistage survey sampling process that included 50 universities. Subsequent analysis focused on 8,916 non-smokers among medical students. Descriptive statistics were calculated to determine the prevalence of susceptibility to smoking. Both unadjusted and adjusted logistic methods were considered in the data analyses, and utilized to examine these associations.
Results: The prevalence of susceptibility to smoking was 23.0%. Multiple variables logistic regression found: Exposure to SHS, cigarette advertisement and promotional activities on campus were positively associated with susceptibility to smoking. Positive attitude toward health professions (HPs) tobacco control were negatively associated with susceptibility to smoking. Those who received information about the dangers of smoking and did not agree that light cigarettes are less harmful to health were less susceptible to smoking. Caring about exposure to second-hand smoke and advising family members to stop smoking were negatively associated with susceptibility to smoking.
Conclusions: To our knowledge, this is the first study to examine susceptibility to smoking and determinants among medical students in China and elsewhere. These findings underscore the importance of tobacco control training and establishing smoke free campuses for reducing susceptibility to smoking among medical students.

PD-782-13 Strategic implementation of tobacco-free school policy in the settings of constraints in the state of Delhi, India

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Background and challenges to implementation: Tobacco habits is major Public Health risk among Indian youth. 14.1% students up to 15 years age use Tobaccos. Cigarette and other tobacco products act 2003(COTPA) prohibits sale of tobacco products at educational institute & within 100 yards (hundred meter Delhi act) radius of educational institute. National tobacco Control Programme(NTCP) , Govt of India in Delhi covers only 2 out of 11 districts but two are also deficient of Manpower. General Health Care Services(GHCS) were utilized strategically to implement tobacco free initiative in schools of Delhi
Intervention or response: Medical officer, paramedical staff of GHCS, BCC officers , ASHA coordinator of National Health Mission(NHM) were strategically utilized to implement tobacco free school policy. Letters return to CBSE, Directorate of Education, DO letter from Health Minister to Education Minister, meetings held, team of medical officer, paramedical staff, BCC & ASHA coordinator conducted awareness cum enforcement drives with focus to identify Nodal Officer, constitute tobacco-free committee, display of tobacco free zone board& no smoking Signage, awareness/ sensitization for teachers & students, enforcing prohibited sale of tobacco products within hundred meter radius of schools.
Results and lessons learnt: In 9 months period(july16 to March17) state has adopted 315 schools out of which 76% (242) have identified Nodal Officer, 32% (102) tobacco free committees, 58 to 63% (182-197) tobacco free zone board and no smoking Signage. 10% (32) have evidence of tobacco sale within 100 meter radius of the school. Indicates very high level of compliance of COTPA. Trained Teachers & Tobacco free committees to facilitate other schools.
Conclusions and key recommendations: In the absence of NTCP staff, the existing manpower of GHCS and NHM when used strategically led to successful and efficient implementation of tobacco free school initiative in Delhi & this can be further used to further enhance compliance of tobacco free school policy in other states also.

PD-783-13 Prohibition of cigarette selling within 100m of schools in metro Manila, Philippines: after 15 years

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Background and challenges to implementation: Tobacco dependence is influenced by environmental factors and exposure to product. The Philippines Republic Act 9211 prohibits the selling of cigarettes within 100 meters of schools. Based on GYTS 2011, 13% of youth aging 13-15 years are smoking. Actions to decrease the exposure of the youth to smoking must be intensified. The Metropolitan Manila Development Authority, with a grant from the Bloomberg Philanthropists through The Union have inspected the retail stores within 100 meters from schools for selling cigarettes.
Intervention or response: To determine the impact of the operation, environmental enforcers of MMDA were deployed to re-inspect the stores reported selling cigarettes within 100 meters from schools. More than 40,000 stores have been inspected from 2013 to early 2017. 2,585 stores were re-inspected from April 2016 to March 2017.

The data from initial inspection and re-inspection were compared for the level of compliance.

Results and lessons learnt: For 3 years after MMDA started the campaign, there is no significant decrease in stores selling tobacco products within 100m from schools. 54% of all stores inspected in 2015-2016 still display/sell cigarettes. In the first quarter of 2017, 46% of re-inspected stores no longer sell/display cigarettes, 66.9% are still displaying tobacco advertisements. Significant observations are the existence of stores selling toys, phone accessories and similar products selling electronic cigarettes within 100 meters from the schools.

Conclusions and key recommendations: Despite the intensified policy awareness, store owners find ways to profit from nicotine derivative products. There is a need to intensify the implementation by the local government units. Tobacco industry continue to promote smoking through sustained tobacco ads in point-of-sales, including store names on roof. LGUs must be strict in business permit issuance particularly to those selling e-cigarettes. Review of local ordinances compliant with the Framework Convention on Tobacco Control, strict implementation of TAPS and apprehension of violators are needed to better protect the public.

32. Making virtual a reality: mHealth solutions to TB care

PD-784-13 Linking digital health to programmatic activities using the patient pathway: a promising approach

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Background and challenges to implementation: Significant advances in information and communication technologies (ICT) have opened new possibilities to improve public health and patient- centered care, turning data into information for policy shaping. Despite increasing availability of technology, most tuberculosis (TB) information systems remain paper-based, and data is rarely utilized comprehensively. Among the challenges to implementing effective and sustainable ICT for health purposes, known as digital health, is the lack of guidance on how to evaluate solutions that can be utilized, for what purposes; and where and when should they operate, both at the national and subnational levels.

Intervention or response: KNCV supports countries to effectively implement digital health solutions to make information available to empower decision-making by patients, healthcare workers and National TB Programs (NTPs). To this end, KNCV has developed an assessment tool that utilizes the patient pathway (PP) as its framework; assessing available information systems and tools, along with opportunities and gaps, at different stages of the PP -screening, diagnosis and treatment. This allows mapping of needs along the pathway and matching them with existing and potential ICT solutions. KNCV utilized the assessment tool in Swaziland, Kazakhstan and Nepal.

Results and lessons learnt: Results show that active case-finding activities strongly benefit when mobile data tools are used to link presumptive patients and diagnosis. Faster laboratory feedback can be achieved by implementing diagnostic connectivity, which also supports building better linkage between diagnosis and treatment initiation. Adherence technologies support patients' self-management and can provide information to evaluate treatment modalities. Finally, fragmented information systems limit cross-reference of health seeking behaviors, diagnosis and treatment. An integrated data system would address the issue.

Conclusions and key recommendations: Mapping information systems along the patient pathway facilitates analysis of gaps and digital health solutions. By placing the patient at the center of digital health, KNCV developed a feasible approach to support quality care and enable data-driven decision-making.

PD-785-13 Anybody out there? Reach of SMS messages sent to household TB contacts in Kampala, Uganda

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Background: Previous studies have found that receiving personal health information via mobile phones is acceptable in Uganda, with SMS preferred to voice calls. However, it is unclear how often and how quickly SMS actually reach the intended recipient, because mobile service providers do not routinely confirm delivery or opening of SMS. To answer these questions, we surveyed participants in an ongoing randomized trial of a one-time SMS intervention to promote uptake of TB contact investigation in Uganda.

Methods: Consecutive household contacts to TB patients who were randomized to receive an SMS communicating the results of sputum examination were eligible. Beginning in February 2017, we included with each SMS a second SMS requesting that participants confirm receipt of the SMS by sending a reply SMS using a toll-free "short code." If no reply was received within two weeks, a research officer telephoned non-respondents to confirm receipt of the SMS. We considered non-respondents

lost-to-follow-up after 3 unsuccessful call attempts on 3 separate days over a 1-week period.

Results: Among 39 participants, 25 (64%) were female. Median age was 20 years (IQR 13-32). Of 39 participants, 8 (21%) responded to the TB-related SMS: 7 responded within 4 hours and 1 within 36 hours to the initial SMS being sent. There were no significant differences by age or sex between SMS respondents and non-respondents. Among non-respondents, we successfully telephoned 15 (94%) of 16. Ten (67%) reported receiving the SMS, while 5 (33%) reported never receiving it.

Conclusions: Most household contacts did not reply by SMS to requests to confirm receipt of the health-related SMS. When reached by voice call, one-third of household TB contacts reported never receiving the health-related SMS. Rates of successful delivery and opening of SMS may be an important indicator to monitor to ensure the success of SMS interventions.

PD-786-13 Video observed treatment for tuberculosis patients in Belarus

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Background and challenges to implementation: Saving resources and patients' return to normal life (family, work and study) are the main advantages of out-patient and community over in-hospital based modes of TB care. Issues of patients' adherence and treatment supervision/observation are the most challenging for out-patient and community models. Video observed treatment (VOT) can help bridge the gap between patients and health care services.

Intervention or response: In February 2015 the Ministry of Health of Belarus, with support from the World Health Organization (WHO), piloted VOT for TB patients in the capital, Minsk. The intervention was aligned to the digital health target product profiles developed by WHO/ERS (2015) with the aim of testing the feasibility and performance of VOT. Following an initial pilot project VOT was expanded countrywide with Global Fund support in October 2016. A smartphone application was created and linked to the national electronic TB register. Patients were provided with smartphones with internet access, and shown how to record and transmit video files to trained clinic staff.

Results and lessons learnt: By April 1, 2017146 patients across the country were recruited: median age 36 years (range:18-67); 54% male; 57% multidrug- or extensive-ly-drug resistant TB. Only one patient was lost to follow up. The main lessons are: VOT works better on smartphones procured for the project purpose rather than relying on a patient's device; clear written instruction to patients is needed; feedback to the patient on the quality of the videos is important; a drug container with at least 2 weeks drug supply is practical.

Conclusions and key recommendations: Preliminary data demonstrate high levels of patient acceptability and treatment adherence using VOT among a diverse mix of TB patients and staff in all six regions of Belarus. The experience gained can promote further expansion of this approach for TB patients with comorbidities (e.g. HIV, substance abuse) and complex social issues.

PD-787-13 99 DOTS: an innovative, low-cost TB treatment adherence monitoring system in India

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Background and challenges to implementation: Monitoring TB medication adherence is of paramount importance for successful treatment yet remains a challenge. In India, the Directly Observed Therapy (DOT) is associated with high treatment success. However, DOT too is challenging for patients and providers, who undertake frequent travel and for Program managers who cannot detect and respond timely to missed doses for lack of real-time information. Alternative approaches to monitor adherence are available but are prohibitively expensive.

India's National TB programme introduced "99DOTS", a low-cost ICT-initiative that supplements DOT for TB-HIV patients on daily anti-TB Fixed Dose Combination drugs (FDC), since March 2015 and scaled-up across India in early 2017.

99 implies 99% times the "pills in hand" was consumed by patient.

Intervention or response: TB-HIV patients get registered for treatment at Anti-retroviral-Therapy centers (ARTC). Here they receive their monthly stock of FDCs and ART tablets. Their mobile/landline numbers are registered for "99DOTS". FDCs are packaged in customized secondary envelopes with dosage instruction, and series of hidden phone numbers behind them. After taking daily FDC pills/weight band, patients make a free call to the number to confirm that the dose was taken. Missed doses trigger a series of daily reminders (SMS and automated calls) to patients & providers. The care-providers follow-up with personal, phone-based counseling or differential actions prioritizing patients requiring more help. Real-time adherence reports are available online to prioritize patients.

99DOTS is deployed in 528 ARTC across India (~50,000

patients/year) and integrated with Nikshay-National online database. Android-based mobile app makes it convenient to monitor adherence on daily basis.

Results and lessons learnt: Since March 2015-17, over 21,486 patients are registered and 751,228 doses observed for adherence -Figure

Conclusions and key recommendations: 99DOTS is a frontline technology solution making TB treatment adherence monitoring simple, affordable and focused. It will soon be expanded to monitor all TB patients as India transitions to daily FDC as standard of care
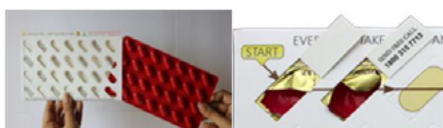
Custom made envelopes with hidden phone numbers that are revealed when pills are removed from envelope.

Real time web based dashboard to monitor treatment adherence based on missed calls received from patients. Green represents call received, red represents no call received.

Figure The concept of "99DOTS" in Revised National TB Control Programme, India for TB treatment adherence monitoring among TB-HIV patients

PD-788-13 Delivering twice daily delamanid: the video-DOT experience of the Armenian National Tuberculosis Program

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Background: Administration of treatment for multi-drug resistant tuberculosis (MDR-TB) is recommended through directly observed treatment (DOT). Delamanid, administered twice daily, has implications for national programs including human resources challenges and costs of extended working hours, as well as increased travel time, cost and inconvenience for patients. Armenian National Tuberculosis Control Centre (NTCC) has introduced video-DOT (V-DOT) to reduce these barriers.

Methods: Video DOT was proposed to patients with good adherence. If accepted, a mobile phone was provided for daily Skype calls to a NTCC nurse for observation of the second dose of delamanid. A SMS or Skype message from the patient informed the nurse that patient was ready for the V-DOT call. A V-DOT monitoring form recorded calls as either successful (allowing obser-

vation of delamanid dose) or unsuccessful (no observation of delamanid dose) due to non-response, technical difficulties or other unspecified reasons.

Results: A total of 28 patients started V-Dot in 2016. A total of 106 patients months of V-DOT were observed, 9 patients on average per month. Over 6 months, an average of 76,8% of patients took greater than 80% of delamanid doses. From a total of 2209 skype calls, 1758 (79,6%) were successful. The remainder were unsuccessful: 83 (3.8%) patients did not respond to phone or Skype calls, 61 (2.7 %) initial technical problem occurred preventing timely V-DOT, and 306 (13.9%) contact was not made for other unspecified reasons.

Conclusions: Practically, V-DOT using Skype, is a simple tool successfully implemented by a national program to overcome the challenges of twice daily drug administration of delamanid, with the majority of calls being successful. Benefits are seen for both patients and programs without negative effects on adherence. Patients attitudes and cost effectiveness should be further explored with a view to expand the number of patients and indications concerned.

PD-789-13 Technical validation of DataToCare© software to implement electronic medical records and improve the management of patients with tuberculosis in Rwanda

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Background and challenges to implementation: Medical management of Tuberculosis (TB), in particular MDR-TB, requires performing multiple laboratory tests including smear microscopy, rapid molecular tests, cultures and drug susceptibility testing (DST). In programmatic conditions, these tests are performed in different laboratories at different times. It is necessary for doctors to have access to these different test results in real-time and at from any TB health facility to which the patient refers. DataToCare© (Savics, Belgium) is a new diagnostics connectivity solution which has recently been introduced in Rwanda.

Intervention or response: The technical validation of DataToCare© included four main criteria: its ability to collect TB test results from different laboratories, to collect patient-related information, to merge different test results of a same patient based on the recognition of its identity, and to present these results in a manner that would be usable for doctors working in different health facilities.

Results and lessons learnt: DataToCare© was successfully validated for implementation in Rwanda. The system allowed uploading test results from Xpert, cultu-

re and DST laboratories. Tests performed for one same patient were automatically merged by the system and these results were presented for each patient in an individual electronic medical record.

Figure EMR DataToCare(c)

Conclusions and key recommendations: Improvement of patient management, in particular for those with MDR-TB, requires integrating a multitude of different diagnostic tests performed during the process of diagnosis and treatment. To make this complex information available and usable, tests results not only need to be successfully captured and transferred, but also presented in a format that will support clinical decision. DataToCare© fulfilled these requirements.

PD-790-13 Utility and benefit of automated medication reporting in tuberculosis surveillance and patient-centered care

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Background and challenges to implementation: In Taiwan, surveillance of tuberculosis (TB) treatment relies on public health workers and hospital TB case managers to manually report anti-TB medication data of notified TB patients to national TB system.

However, a 2005-2007 survey revealed that only ~80% of patients had timely notification of TB (within 7 days of treatment). Besides, manual medication reporting suffers from problems of duplicate entries, lack of timeliness, data omission, and is leading to heavy workload to frontline workers.

To improve timeliness of TB notification and medication reporting, Taiwan Centers for Disease Control (TCDC) has initiated automated medication reporting since 2016.

Intervention or response: TCDC collaborated with 75 hospitals on automating entry of medication report into national TB system, including prescription of anti-TB drugs, latent tuberculosis infection (LTBI) treatment, and biochemical test reports. These reports included prescription date, drug brand name, ingredient, dosage, and duration. Manual reporting was replaced with automated processes. Alert system was developed to monitor health care quality and safety.
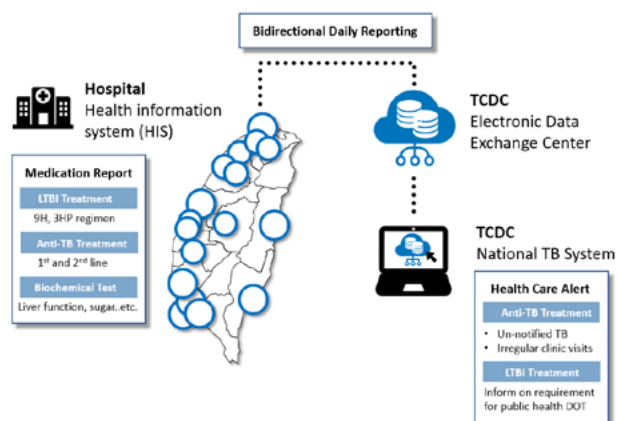
Figure Framework of automated medication reporting

Results and lessons learnt: Medication reports were transmitted on a daily basis (~40,000 records per month), containing 70 different drugs and biochemical tests, which covers 70% of TB patients and LTBI clients nationwide. TCDC plans to extend coverage to >90% by the end of 2017. TCDC developed alert system to detect un-notified TB patient initiating treatment, irregular clinical visits, to inform promptly on requirement of public health directly observed therapy (DOT) service for both anti-TB and LTBI treatment. Other alerts for unstandardized regimen and occurrence of adverse events are under development. Furthermore, TCDC is building bidirectional health information exchange that allows for two-way sharing of above-mentioned events, where hospitals receive these highlighted alerts directly through their health informatics system.

Conclusions and key recommendations: Automated medication reporting helps to enhances tuberculosis surveillance and management. With bidirectional health information exchange, hospitals can immediately acquire health care and public health-related alerts to facilitate patient-centered care coordination.

PD-791-13 The online TB surveillance dashboard: an innovative tool for monitoring the TB epidemic in South Africa

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Background: South Africa has the highest incidence of TB globally, the highest burden of HIV-associated TB, and a high absolute number of drug resistant TB (DRTB) cases. However, a key strength is the existence of a single National Health Laboratory Service (NHLS) within a public health system solely responsible for TB treatment and an integrated laboratory information system. Previously published work showed the importance

of this data and an online dashboard offered the ideal tool to update the data and facilitate interpretation thereof.

Methods: TB test data for 2004-2015 were extracted from the NHLS' Corporate Data Warehouse. Record-linking processes were used to identify individual patients with microbiologically-confirmed pulmonary TB (mPTB) based on approved diagnostic tests. mPTB data were linked to geographic shape files with associated age-sex disaggregated population data, enabling calculation of sub-district level mPTB incidence rates. Microstrategy Analytics v10.4 was used to develop a dashboard displaying trend data and age-sex population pyramids. The Esri Maps for Microstrategy plugin was used to map incidence rates and numbers of cases.

Results: The mPTB surveillance dashboard has a user-friendly, graphical interface presenting trend and geospatial mPTB information to sub-district level for South Africa (Figure 1) and is publicly available at www.nicd.ac.za.

Figure The online TB surveillance dashboard landing page

The dashboard is dynamic as users can drill down from national to sub-district level and display trend graphs and point incidence data for years and age-sex groups of interest.

Conclusions: The mPTB dashboard was launched on World TB Day 2017. It enables monitoring of sub-national trends and identification of geographical areas with high/increasing mPTB incidence. This aids programme managers in targeting interventions to areas of greatest need. Additional work is underway to add DRTB to the dashboard. Potential exists for other surveillance initiatives (e.g. patient tracing and cluster detection) to be managed through the dashboard. The data will refresh annually initially, with quarterly updates planned.

PD-792-13 eRX: improving tuberculosis diagnosis using a mobile health application

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Background: Many places with high burdens of tuberculosis (TB) are resource-poor settings that often lack proper health infrastructure and well-trained personnel. eRx is a community-based participatory research project attempting to improve TB diagnosis in Lima, Peru, using a mobile health smartphone application (App) to identify TB disease based on chest radiographs from suspected TB cases. The goal is for the app to assist with TB diagnoses in the absence of an experienced pulmonologist.

Methods: We are in the first year of the project that comprises two components: The first involves mapping of Northern Lima's TB care delivery system. This process includes 25 key informant interviews and 8 focus groups with healthcare workers, and 8 observational studies to evaluate the flow process of diagnosis TB using chest radiographs (Figure 1). The second component involves development of a deep learning algorithm, an Artificial Intelligence method, to recognize TB patterns in chest radiographs. The algorithm uses a deep convolutional neuronal network in classifying chest radiographs with active TB.
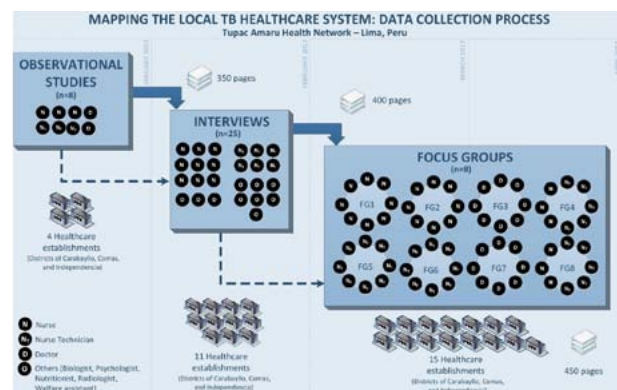
Figure 1 Overview of the Mapping process

Results: The project has conducted all of the observational studies, key informant interviews, and 6 of 8 focus groups; we are learning that there is many activities not described in the flow charts that delay the diagnosis of TB. Thus far, the algorithm has been applied to over 5,000 chest radiographs during its learning process, the deep learning algorithm has shown 89.6% of accuracy as a classification model for chest radiographs with active TB (see Alcantara et al 2017 for further details).

Conclusions: The eRx project could improve TB diagnosis in Peru by offering an easy and affordable way to accelerate radiography-based TB diagnoses in settings where there is a scarcity of sufficient pulmonologists for analyzing chest radiographs.

PD-793-13 Mobile technology use improves tuberculosis treatment outcomes in Kabul city

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Background and challenges to implementation: In 2016, Kabul's population was estimated at 4,227,000. The health care system remains poor because of poor management, poor planning and low budget as a result of many years of conflict in the country. The treatment success rate (TSR) in 2009 when urban DOTS was first introduced in Kabul was 41%. In this abstract, we present TSR trends from 2009-2015, and mHealth contributions to TSR improvements.

Intervention or response: In late 2014, the NTP introduced a mobile system to follow transferred out patients to see if they reached the heath facility where they were referred and completed their treatment. After the assessment of HFs with a high number of TB patients who transferred out, CTB provide mobile phones with monthly pre-paid cards to the health facility staff to enable them to contact patients undergoing treatment. Outcomes were recorded in a separate register book. The TSR reports were collected by phone and were then re-checked with NTP surveillance.

Results and lessons learnt: As shown in Figure 1, the TSR in 2009 was 41%, and the transfer out rate was 51%. From 2010 to 2014, the TSR gradually improved and reached 67%. In 2014 mobile air time was provided to TB focal people to contact the health facilities where the patient had transferred out and register the final outcome. Through this mechanism the percent of patients not-evaluated decreased from 25% in 2014 to 10% in 2015. The TSR increased to 81% (14% improvement).

Conclusions and key recommendations: The tracking of patients who transferred out of care through mobile calling contributed significantly to an improvement in treatment outcome. We strongly recommend the expansion and application of this model to similar settings.
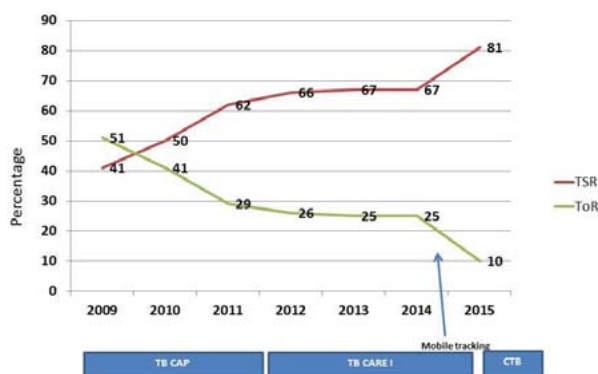
Figure Treatment success rate of all TB cases in Kabul

33. Supply-side issues in tobacco control: production and industry

PD-794-13 FCTC ratification and economic condition: lesson learned for Indonesia

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Background: Indonesia is the only country in Asia Pacific that has not signed and ratified the FCTC. Framework Convention of Tobacco Control is a treaty or convention on tobacco control which is internationally legal instrument that binding to those countries that ratify it. The FCTC is the first international treaty negotiated under the auspices of the World Health Organization (WHO). The FCTC was unanimously adopted by all 192 WHO member countries at the 56th World Health Assembly on 21 May 2003 and entered into force on 27 February 2005. The major obstacles for Indonesia not ratifying this treaty is the economic argument like employment, poverty and economic growth. This paper will explore the economic condition of several countries that ratifies FCTC. Lesson learned for Indonesia are drawn from several countries that ratify FCTC and its impact on economic and cigarette consumption after the ratification.

Methods: Descriptive analysis of economic data from several countries that have ratifies FCTC will be used. Pre and Post FCTC ratification condition will be determined to asses the economic condition in those countries.

Results: Most of the countries experienced improved economic condition during the period of analysis (2000-2012), before and after the FCTC ratification. Brazil, Japan, Bangladesh, Australia and India has succeeded in reducing smoking prevalence. Tobacco leave production rose in ten countries and decline in other six countries. Most indicators shows that FCTC ratification has no relation with economic condition.

Conclusions: Indonesia should ratify FCTC as soon as possible because tobacco control is an effective measure to reduce non communicable disease.

PD-795-13 Farm level economics of tobacco production in Zambia: lung health prevention measures

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Background and challenges to implementation: The primary objective of the project was to understand the political and economic factors that contribute to tobacco production and control. A study was conducted to analyze farm - level economics of tobacco production as it relates to profitability, incomes and household welfare, as a tobacco control measure in reducing lung health in Zambia.

Intervention or response: Quantitative data was generated from 489 small - scale tobacco farmers, key informant interviews with stakeholders, the Extension workers and focus group discussion with farmers, from 6 leading tobacco producing districts of the three Provinces, that is Eastern, Southern and Central.

Results and lessons learnt: A total cost of tobacco production was assessed by incorporating comprehensive labour costs; it was found that tobacco production was not profitable for a small- scale farmer. Even though there has not been a research that has attempted to accurately calculate the contribution of family labour to leaf production among small holder farmers in Zambia, tobacco growing was found to be highly labour intensive activity, which put tobacco farmers at a loss.

Tobacco leaf marketing disadvantages the women and vulnerable farmers who have no bargaining power, to argue on the grading of quality tobacco leaf.

Women and children are employed cheaply to grade tobacco leaf in an enclosed building without ventilation and protective clothing for long hours, whereby exposed to lung health and no medical facilities.

Conclusions and key recommendations: Huge demand for labour and inputs, poor marketing system as well as high fluctuating market prices are factors that can lead the farmers to contemplate switching from tobacco production.

There is need to develop the supply chains of crops that have high potential to provide alternatives Livelihoods for tobacco farmers to reduce tobacco production as a tobacco control intervention.

PD-796-13 How supply-side interventions can eliminate tobacco use gradually

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Background and challenges to implementation: Tobacco products are extremely affordable and widely accessible to all in developing countries largely because subsidies perversely reduce price. Supply side economics therefore needs to complement demand side strategies. These include: quotas for tobacco production, removing subsidies, restricting public investments in tobacco sector. In developing countries like the US, Australia and New Zealand, governments planned for complete national buy out, and have put in restrictive policies which have reduced supply of tobacco products thereby raising its price.

Intervention or response: This presentation will complements the conference theme.Communities and diverse stakeholders need to be involved in political and economic sustainability of supply-side measures. This presentation will provide the opportunity to learn from successful global examples . These are shared concerns for tobacco control efforts for high burden countries in developing country-setting as well as developed countries which need to correct supply-side distortions to make demand-side interventions effectively.

Results and lessons learnt: This presentation makes the argument that supply side interventions can complement demand side strategies and accelerating the elimination of tobacco use.

Conclusions and key recommendations: The presentation will analyse the political economy of tobacco use and its products and present evidence of policies that have been initiated, and identify potential methods of making demand-side strategies more effective.

PD-797-13 Elimination of tobacco growing is possible: a case study from Karnataka India

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Background and challenges to implementation: Article 17 and 18 of WHO's Framework Convention on Tobacco Control mandates Parties to adopt strategies for alternative farming for tobacco growers. The Indian state of Karnataka has shown its commitment in tobacco control.

However Karnataka is also the second largest tobacco growing state India.

The registered tobacco growers in the state have more than doubled has grown by 222.59% (from 18751 to 41737) and the area under tobacco cultivation has increased by 269.72% (from 29852 hectares to 80516 hectares) from in 2001 and 2016.

Intervention or response: Since 2015, Karnataka has adopted supply reduction measures of tobacco crop in a phased manner. The Department of Agriculture and Horticulture in collaboration with The Tobacco Board has piloted a project to help shift tobacco growers to alternative crops and adopt new cropping patterns. It has undertaken sensitization of farmers to adopt alternative cropping, provided access to soft loans from banks, free soil testing, drip irrigation, subsidized fertilizer, among other incentives; and have linked them to Horticultural Producers' Co-operative Marketing and Processing Society Ltd. (HOPCOMS) to ensure market for grown products.

Results and lessons learnt: In Hunsur block of Mysore, growers have voluntarily stopped tobacco farming in 1000 hectare and have adopted alternate crops. Given the early success of the pilot project, The Government has scaled up the intervention from to 4500 hectares, covering other four blocks in three tobacco growing districts.

Conclusions and key recommendations: Tobacco farmers are ready to shift to other crops or cropping patterns but need guidance and support from Government. Farmers realize that there is limited future in tobacco cultivation due to variability in rain and declining fertility of soil which they attribute to monocropping of tobacco; and more importantly an increasing awareness among the public (and growers) on the harms of tobacco use.

PD-798-13 Impact of tax measures on cigarette production in Pakistan

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Background: Tobacco use is single largest preventable cause of death in the world. It kills 298 persons per day in the country. Pakistan is a signatory of Framework Convention on Tobacco Control (FCTC). The country has taken major steps in implementing its obligations especially cigarette tax measures to reduce the demand of cigarettes. The Government of Pakistan introduced cigarette tax reforms in 2013-14, by reducing 3-tier tax structure to 2-tier structure and increasing FED (specific). A working group on tobacco taxation was formed in 2014. The group made recommendations to FBR. Resultantly, FED on cigarette packs were increased.

Methods: To assess the impact of the tax measures on local cigarette production, data were collected from secondary resources i.e. Reports of State Bank of Pakistan, Economic Survey of Pakistan etc. Impact analysis of tax measures was conducted on local production of cigarettes in the country, keeping other factors constant. The impact of increase in taxes on cigarette packs on local production of cigarettes was assessed. The measures were considered from cigarette tax reforms and formation of working group on tobacco taxation.

Results: Cigarette tax measures undertaken by Government of Pakistan were analysed on reduction in local production of cigarettes in the country. It was observed that production of about 13 billion cigarette sticks was reduced since FY 2013-14 after tobacco tax reforms and formation of the working group on tobacco taxation. Since 2013-14, Specific excise duty was almost doubled while local cigarette production was reduced by 13 billion cigarette sticks. At the same time, cigarette tax revenues were in increased from Rs.76.20 billion to Rs.102.919 billion. That is WIN-WIN situation for the government of Pakistan.

Conclusions: Taxing the cigarette prices in Pakistan is more effective strategy in reducing production and demand of cigarettes and increasing tobacco tax revenues.

PD-799-13 Tobacco tax as sustainable funding for tobacco control programme: case study of Jakarta, Indonesia

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Background and challenges to implementation: The Regional Tobacco Tax Law of Jakarta defines allocation of at least 70% from tobacco tax revenue to fund tobacco control program. In 2016 Jakarta received estimated $30 million from the tobacco tax revenue. Now, Jakarta is the only province in Indonesia with the highest allocation and dedicated only to fund tobacco control program.

Intervention or response: Technical assistance on drafting, advocacy, conduct high level meeting and facilitate harmonization process.

Results and lessons learnt: In 2014, the Regional Tobacco Tax Law of Jakarta was adopted. However this regulation isn´t well implemented yet. A letter was sent to call the government to take prompt action. An intensive advocacy to the local government was made to ensure the maximum use of tobacco tax to fund tobacco control program. A list of proposed program was submitted to the annual city planning forum. The proposed activities were:

1) smoke free compliance monitoring and enforcement;
2) indoor air quality monitoring;
3) capacity builing for inspectors and enforcers;
4) public service advertisement on the dangerous of tobacco use;
5) community participation;
6) smoking cessation counseling; and
7) TAPS ban monitoring.

A challenge was coming from the government who would like to expanding the use of fund not only to fund tobacco control program but also other program. A counter argument and scientific evidence on the effectiveness of comprehensive tobacco control program was provided to strenghten local government commitment to enforce the law.

As the result of our intensive advocacy, a Governor Instruction and its funding mechanism guideline was prepared to ensure the maximum utilisation of tobacco tax revenue for tobacco control program.

Conclusions and key recommendations: Tobacco tax is a great source of fund for sustainable funding tobacco control program in Jakarta. Civil society support is an effective strategy to control and support local government to provide an adequate tobacco control legislation and program for the people.

PD-800-13 Poorest of poor trapped in smokeless tobacco use: study from 140 countries

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Background: Prevalence of smokeless tobacco (SLT) use and its association with demographic factors such as gender, income of the country and family and place of residence is not yet known in global perspective.

Methods: Global burden of prevalence of SLT use among adults was estimated using in 140 countries national estimates by gender and income of the countries in countries. In low and low middle income group countries further prevalence was computed by residence and family income. The number of male and female SLT users was also calculated taking corresponding age groups and prevalence.

Results: Nearly one in ten males and one in twenty females used SLT in any form. The mean SLT use prevalence was significantly higher among females (p<0.001) as well as males (p<0.001) in group 1 countries (lower and lower middle income countries) than those of group 2 countries (high and upper middle income countries). There was significant difference in SLT use prevalence among males and females in group 1 (p<0.01) and group 2 (p<0.01) countries. Nearly 91% of the 356 million adult SLT users resided in LICs and LMICs. In these countries prevalence was higher in rural area (<0.001) and in the poorest population (p<0.001).

Conclusions: The majority of the burden of SLT use is on the poor countries among which the burden on the poorest is even more.

34. What you see is what you get: understanding TB in children

PD-801-13 Nutritional indicators and food insecurity in children at risk of TB, Lima, Peru

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Background: According to the last national report of nutritional status in Peru, an estimated 240,000 children are affected by chronic under nutrition. Nutritional status (NS) and food insecurity (FI) are two nutritional risk factors that may be related to the development of tuberculosis disease (TB).

We examined the association between food insecurity and nutritional status and TB among children in Lima, Peru.

Methods: As part of an ongoing pediatric diagnostics study in Lima, Peru, children ≤ 14 years old who presented with >=1 one TB symptom and had an adult contact with TB were invited to participate. We weighed and measured all children and calculated NS using anthropometric Z-scores (under nutrition, normal, overweight and obesity) and body mass index. Caregivers responded to a standardized household food insecurity survey previously used in this setting. Children were evaluated for tuberculosis through clinical and laboratory assessment per current national guidelines.

Results: Among 382 children enrolled to date, 62 (16.2%) were diagnosed with TB disease. Of them, 17 (28%) were overweight/obesity and 3(5%) were under nutrition. Under nutrition was associated with having a diagnosis of TB (PR=3.43; IC 95%:1.47 - 8.03) when compared to normal. Among children diagnosed with TB, 38 (61%) live in food-Insecure households; household food insecurity was not associated with having a TB diagnosis (p=0.62). There was no association between household food insecurity and nutrition status (p=0.36).

Conclusions: We found no association between household food insecurity and development of TB disease. However, children who were under nutrition were more likely to be diagnosed with TB.

Further research on nutrition status and feeding habits of children with TB may highlight possible nutrition interventions and reduce the likelihood of developing tuberculosis.

PD-802-13 Predictors of clinico-radiological outcome in children with probable intrathoracic tuberculosis

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Background: Determining the predictors of outcome in childhood tuberculosis remains a pertinent research question. We planned a study to evaluate the factors associated with clinico-radiological outcome in a cohort of children with probable intrathoracic tuberculosis.

Methods: A post-hoc analysis was conducted on children enrolled in a randomized controlled trial (RCT) for assessing adjunct multi-nutrient therapy in childhood intrathoracic tuberculosis. Clinico-radiological outcome was classified as good if there was significant improvement in radiological findings and symptoms at six months of anti-tubercular therapy; poor in case of nonresolution of radiological findings or symptoms or extension or change of therapy or death.

Results: Four hundred and three children [175 (43.4%) boys] with probable intrathoracic tuberculosis were enrolled. Mean (SD) age was 104.8 (44.9) months, history of contact present in 253 (62.8%) children, 103 (25.6%) received BCG vaccination. Tuberculin skin test was positive in 371 (92.1%) children. Majority of children were diagnosed as primary progressive disease, PPD [229 (56.8%)], followed by primary pulmonary complex, PPC [120 (29.8%)] and pleural effusion, PE [54 (13.4%)].

Good clinico-radiological outcome was recorded in 343 (85.1%) children. Good outcome was associated with tuberculin skin test positivity (93.3%, p=0.02) and radiological findings [PE (98.1%) >PPC (86.6%) >PPD (81.2%), p=0.006). Poor outcome was associated with higher microbiological confirmation by smear and/or MGIT culture (63.3% vs. 33.2%, p< 0.0001), higher baseline median (IQR) monocyte/lymphocyte ratio [0.24 (0, 0.37) vs. 0.02 (0, 0.27), p=0.008] and lower baseline mean (SD) hemoglobin levels [9.2 (3.1) vs. 10.4 (2.5) g/dL, p=0.001]. On multivariable logistic regression, only microbiological confirmation, baseline monocyte/lymphocyte ratio and hemoglobin levels were significantly associated with outcome [OR (95% CI): 0.41 (0.21, 0.81), 0.19 (0.05, 0.72) and 1.31 (1.07, 1.61), respectively].

Conclusions: Clinico-radiological outcome in children with probable intrathoracic tuberculosis was associated with microbiological confirmation, baseline monocyte/lymphocyte ratio and hemoglobin levels.

PD-803-13 Under-diagnosis of drug-resistant childhood TB compared to drug susceptible counterparts in three large regions of Ethiopia

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Background and challenges to implementation: The proper identification of pediatric TB needs detailed history taking and high index of suspicion to identify presumptive TB. Coupled with the difficulty in getting samples from children, diagnosis of drug sensitive (DS) and drug resistant (DR) TB is low especially in resource limited countries like Ethiopia. The objective of this study was to compare rates of pediatric TB cases among all DS and DR TB cases notified in Amhara, Oromia and Tigray regions of Ethiopia.

Intervention or response: The National TB Program of Ethiopia with support from the USAID funded Challenge TB project is working to improve the diagnosis of childhood TB. Health facilities were provided with diagnostic equipment, supplies, job aids, training, and mentorship and supported in the development of guidelines, Standard operating procedures and algorithms. We used annual national report(Jan-Dec 2016) for the drug sensitive TB cases and routine monitoring data was used to obtain age dis-aggregated data on drug resistant TB cases.

Results and lessons learnt: A total of 77, 706 new drugs sensitive TB cases and 307 drug resistant TB cases (RR-MDR) were put on TB treatment in the three regions during the calendar year & majority were in one of the regions (Oromia). The percentage of under 15 years TB cases was 11.7% for DS TB cases and 6.4% for DR TB cases(< 0.05). The percentage of pediatric TB cases in DS TB cases was smaller for all regions and largest difference margin was observed in Oromia (6.1%).

Conclusions and key recommendations: The percentage of under 15 years in drug sensitive TB cases is almost twice the percentage in drug resistant TB cases showing possibly a disproportionately larger under diagnosis for the drug resistant TB cases and where more attention should be directed to. This calls for enhanced diagnostic tools and capacity for DR TB diagnosis in children.

Region	Drug sensitive TB (Number (%) of children)	Drug resistant TB (Number(%) of children)	P-value
Amhara	2216/23,402(9.5)	7/98(7.1)	>0.05
Oromia	6,211/46,855(13.3)	10/139(7.2)	<0.05
Tigray	627/7,449(8.4)	4/93(4.3)	>0.05
Total	9,054/77,706(11.7)	21/330(6.4)	<0.05

Table Proportion of children <15 yr of age by type of TB

PD-804-13 XDR-TB and pre-XDR TB among children in Kyiv, Ukraine

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Background: Ukraine is one of five countries in the world with the highest percentage of new tuberculosis (TB) cases that are multidrug-resistant (MDR): 25% of newly diagnosed TB cases are MDR. The World Health Organization estimates that worldwide, 9.5% of all MDR-TB are extensively drug-resistant (XDR). Few

data are available on the burden of XDR-TB in former Soviet Union countries. Since children represent recent TB transmission and reflect the TB epidemic in their environment, we characterized the proportion of pre-XDR and XDR-TB at the pediatric referral hospital in Ukraine's capital.

Methods: We performed an analysis of all children < 18 years of age treated for MDR-TB disease at Kyiv City Pediatric TB Hospital between January 2011 and July 2016. Most TB patients < 18 years of age in Kyiv are treated at this center. The primary outcome was identifying pediatric XDR-TB and pre-XDR TB disease cases and their drug susceptibility patterns. Drug susceptibility testing (DST) was performed using the proportional method on solid or liquid medium.

Results: Of 21 children treated for MDR-TB disease, 6 (29%) had pre-XDR TB, and 3 (14%) had XDR-TB. Among the pre-XDR and XDR-TB patients, 6 were diagnosed clinically and treated on the basis of their source case's DST, and 3 had microbiological confirmation with their own DST. Seven of the 9 children had resistance to at least one fluoroquinolone, and 5 children had resistance to at least one second-line injectable agent. In addition, 4 of the 9 children had resistance to pyrazinamide, and 6 had resistance to ethambutol.

Conclusions: Of all children treated for MDR-TB disease at the Kyiv City Pediatric TB Hospital, 43% had pre-XDR or XDR-TB. These data suggest that a high proportion of MDR-TB cases in the general population of Kyiv are pre-XDR and XDR.

PD-805-13 Prevalence of vitamin D deficiency among Indian children with tuberculosis and age-and sex-matched healthy controls

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Background: Vitamin-D, a modulator of monocyte-macrophage activity and plays a role in innate immunity, is associated with risk of Tuberculosis (TB) and TB treatment response when levels are low. We sought to estimate the prevalence of vitamin D deficiency in Indian children with TB as compared to healthy controls.

Methods: A case-control study was conducted in Byramjee Jeejeebhoy Medical College and Sassoon Hospital (BJMC), Pune, India. Cases were children with confirmed or probable TB, based on the current WHO TB definitions. Controls were healthy, age and sex-matched children attending immunization clinics. Serum 25 hydroxyvitamin D level was tested using the ELISA kit method with < 20 ng/ml as deficiency state.

Results: 132 children < 12 years of age (median 66 months, IQR 36 to 108 months) were enrolled with 66 cases and 66 controls. The prevalence of any vitamin D

deficiency among cases was 74% and 68% among controls. In both groups as the vitamin D levels decreased to severe levels (≤10ng/ml), there was statistically significant Vit D deficiency changes in biochemical (low calcium, low /normal phosphorus and high alkaline phosphatase) and radiological (demineralization) parameters (p< 0.05). Radiological changes were seen in 18% TB cases as against none of the controls. Risk factors for Vit D deficiency among cases were malnutrition (OR 19; p < 0.01)) and low socio-economic status (OR 3.5; p < 0.01).

Conclusions: Prevalence of Vitamin D deficiency was high among children with TB as well as healthy controls. However, severe form of vitamin D deficiency (< 10ng/ml) was higher among children with TB and clinicians should be aware of associated malnutrition and low socio-economic status as risk factors for severe deficiencies among them. These data also suggest Vitamin D supplementation is needed for most children in this area regardless of TB status.

PD-806-13 Detection of respiratory viruses in South African children with suspected pulmonary TB

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Background: Tuberculosis (TB) and acute pneumonia are important causes of morbidity and mortality in children globally. Although the importance of viral and bacterial infections in the aetiology of respiratory illness is well-established, key questions regarding the prevalence of specific pathogens and the association between viruses and TB, remain unanswered.

Methods: Analyses were nested in a prospective hospital-based cohort study in children aged 0-14 years, routinely investigated for suspected pulmonary TB (PTB) in Cape Town, South Africa. At enrolment investigations included collecting at least 3 respiratory samples for smear microscopy, GeneXpert TB and liquid culture. Nasopharyngeal aspirates were collected for viral respiratory investigation using a commercially available multiplex PCR (Anyplex™ II, RV16, Seegene) including 16 viruses of clinical and epidemiological relevance. Children started on TB treatment were classified as cases while other children were classified as symptomatic controls.

Results: A total of 73 children were enrolled, median age 22 months (IQR 10-48); 41/73 (56.2%) male and 13/73 (18.6%) HIV-infected. 42/73 (57.5%) initiated TB treatment; 19/42 (45.2%) were bacteriologically confirmed. In 70/73 (95.9%) children 1 or more viruses were detected: 39/42 (92.9%) were cases and 31/31 (100%) controls. Human Rhinovirus (HRV), the most prevalent virus, was detected in 53/73 (72.6%) children:35/42

(83.3%) cases and 18/31 (58.1%) controls, this difference was significant (OR 3.61, 95% CI 1.23-10.64, p= 0.02). Adenovirus was the second most prevalent virus, detected in 41/73 (56.2%) children; 24/42 (57.1%) cases and 17/31 (54.8%) controls.

Conclusions: Respiratory viruses were frequently detected in children with suspected PTB in South Africa. HRV and adenovirus were the most common viruses, with HRV being detected more frequently in children diagnosed with TB, suggesting that HRV infections may unmask underlying airway disease due to TB. More studies are needed to understand the role of respiratory viruses in children with suspected PTB.

PD-807-13 Correlation between gaps in childhood TB case notification and infant mortality rate in different states of India

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Background and challenges to implementation: WHO estimates that children below 15 years contribute to 6% of annual global TB burden and this contribution may be upto 10-20% of local TB burden in high burden settings.

India, having high TB burden, has 29% population of <15 years and 6% of all New TB Case notification (NTCN) in 2013 were from this age group.

IMR remains a key indicator of health system strength and function. India's IMR is 40/1000 live births.

Intervention or response: We calculated the difference between the proportion of <15 population in different states of India (Source: Census 2011) and the proportion of NTCN from this group (Source: RNTCP Annual Report 2015). In the absence of actual estimates of TB burden in different age groups, we took this difference as a proxy indicator of the gap in TB case finding. The respective IMRs of the states (Source: SRS 2013) were plotted against the difference to seek a correlation.

Results and lessons learnt:
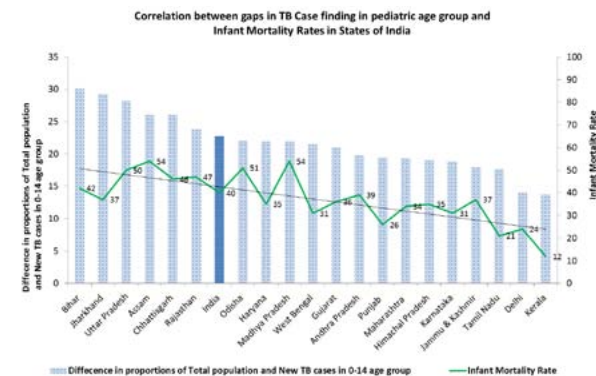
Figure Childhood TB Notification Gaps & IMR Correlation

1. States with higher IMR had larger gaps in TB case finding.
2. Among the outliers, Bihar, Chhattisgarh and Uttar Pradesh have youngest populations-37%, 33%, 33% respectively; and Madhya Pradesh has second highest NTCN (10%) in India, after Delhi (14%), in <15 age-group.

Conclusions and key recommendations:
1. Improved health system strengthening helps improve TB case detection.
2. Better data to estimate local age-wise TB burden and TB mortality rates, needed.
3. Better TB care improves child survival.

PD-808-13 Role of two pediatric hospitals in tuberculosis case detection and treatment in Kabul, Afghanistan

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Background and challenges to implementation: Afghanistan is a high burden Tuberculosis (TB) country with a high child mortality rate of 97/10,000 live births. Forty five percent of the Afghan populations is less than 15 years old, and 15% of all identified TB cases are among children. TB is one of the causes of child mortality in the country. Since 2009, the USAID funded TB CAP project followed by TB CARE I and Challenge TB projects engaged two pediatric hospitals in Kabul in TB control activities. The purpose of this review was to assess the role of Indira Gandhi and Maiwand specialized pediatric hospitals in TB case notification and in the treatment of pediatric TB cases in Kabul.

Intervention or response: In 2010, both hospitals engaged in the TB control program, offering diagnosis and treatment to pediatric TB patients. The NTP and Challenge TB technical teams reviewed and analyzed data from 2010-2016 using standardized NTP recording and reporting tools which was then compared with existing surveillance data.

Year	2010	2011	2012	2013	2014	2015	2016
# of all forms TB cases in Kabul	2,738	2,728	3,215	3,548	5,007	5,449	6,101
# of all forms TB cases (%) children	235 (8.6%)	198 (7.3%)	238 (7%)	385 (11%)	1089 (21%)	805 (15%)	865 (14%)
Treatment success rate children (%)	23%	39%	48%	64%	40%	76%	N/A
Not evaluated cases among child (%)	56.3%	38.8%	39.2%	30.2%	56%	8.5%	N/A

Table 1 Trend of TB case finding among children

Results and lessons learnt: In 2016, the study identified 865 TB cases among children under the age of 15 (14.2% of the 6,101 total TB cases identified in Kabul).

This represents a 70% increase in pediatric TB diagnosis compared to the 235 pediatric cases identified in 2010 (p<0.0000001, OR=1.846). Over the course of the seven year period, 3,815 all forms of pediatric TB cases were identified in the two hospitals (this was 14.7% of all forms TB case [26,048] notified during the same time period in Kabul). The treatment success rate at the hospitals also improved from 23% in 2010 to 76.7% in 2015.
Conclusions and key recommendations: Engaging pediatric hospitals in TB control activities increased TB case identification among children in Kabul. We recommend applying this practice in other large cities implementing DOTS.

PD-809-13 Interim report on the use of a short, simplified regimen for the treatment of children with multidrug-resistant tuberculosis in Karakalpakstan, Uzbekistan

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Background: The World Health Organization recently included children in their general recommendation for use of shorter multidrug-resistant tuberculosis (MDR-TB) regimens (SMR) of 9-12 months' duration. However, use of this regimen in children is poorly described and children are excluded from ongoing clinical trials. We describe preliminary results of Médecins sans Frontières' experience of treating children and adolescents with SMR in Karakalpakstan, Uzbekistan.
Methods: From 2013-17, children with MDR-TB were enrolled to a prospective, single-arm observational cohort study. Exclusion criteria included resistance to ofloxacin or both kanamycin and capreomycin, extrapulmonary involvement (except lymphadenitis or pleuritis) and previous treatment with second-line anti-tuberculosis drugs for greater than 1 month. The treatment regimen was 4-6HZEMfxCmPtoCfz/5ZEMfxPtoCfz. Treatment response was assessed clinically and microbiologically. Patients underwent follow-up to 12 months post-treatment.
Results: 21 children (median age 15.8 years, range 6 months to 17 years) received the SMR. 19/21 were isolated pulmonary cases. 19/21 diagnoses were confirmed microbiologically. Baseline culture results were available in 18/21 patients, of which 14 were positive. Kanamycin-resistance was demonstrated in 8/14 cases, pyrazinamide-resistance in 11/14. Of 5 patients completing the SMR, outcomes were: 4 treatment complete (all relapse free at 12-months) and 1 treatment failure. 12 children

are currently on treatment and 3 were withdrawn from the study due to the detection of 2nd line drug resistance. Two serious (DAIDS Grade 3 or 4) adverse events occurred, representing QTc prolongation and acute abdominal pain in one child, who continued with SMR after a brief interruption.
Conclusions: We provide a detailed description of SMR being used in children with MDR-TB. Severe adverse events have been rare and we await further efficacy results. Young children and microbiologically non-confirmed cases were under-represented in the study, highlighting some of the broader challenges in implementing paediatric MDR-TB treatment in this context.

PD-810-13 Contribution des enfants dans la lutte contre la tuberculose au Sénégal: l'approche «enfants pour enfants»

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Background and challenges to implementation: Le volet communautaire de lutte contre la tuberculose au Sénégal est coordonné par Plan International Sénégal spécialisé dans la protection des droits des enfants. Les enfants représentent 15 à 20 % des cas de tuberculose au Sénégal. A ce titre une kyrielle d'activités est mise en œuvre pour favoriser la participation active des enfants dans la lutte contre la maladie de manière à opérer un changement radical et générationnel des comportements et les utiliser comme relais auprès de leurs communautés. C'est la sensibilisation des enfants par leurs pairs dénommé «Child to Child (CTC)».
Intervention or response: Des connaissances de base sur la tuberculose (problématique, signes, diagnostic, traitement et prévention) ont été développées chez des écoliers de l'élémentaire et des enfants en situation précaire qui par la suite ont élaboré chacun un plan d'action de sensibilisation de lutte contre la maladie à l'école et dans leurs communautés. Les écoliers sont encadrés durant tout le processus par les agents des secteurs de la santé, de l'éducation et le réseau communautaire.
Results and lessons learnt: Dix activités CTC, organisées dans 30 établissements scolaires et 15 daara, ont permis aux enfants de sensibiliser à travers des ateliers de création artistiques sur la TB réalisés par les enfants au profit d'autres enfants. Le CTC a ainsi permis de booster plusieurs indicateurs: plus de 15 000 personnes ont été sensibilisées par les enfants, 1278 cas présumés de moins de 15 ans orientés et 971 enfant-contacts référés.
Conclusions and key recommendations: Les enfants ont montré des aptitudes réelles pour la lutte contre la tuberculose. Ils représentent de bons vecteurs de changement de comportement par la sensibilisation de leurs pairs et leurs communautés sur la tuberculose.

35. Double trouble: the impact of diabetes and TB

PD-811-13 Is diabetes mellitus an independent risk factor for multidrug-resistant tuberculosis? A meta-analysis

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Background: The high prevalence of diabetes mellitus (DM) among multidrug resistant tuberculosis (MDR-TB) patients is a serious cause for concern.
Methods: We conducted a meta-analysis to determine whether DM is an independent risk factor for MDR-TB. Electronic literature searches of the PubMed, Web of Science and EMBASE databases up to July 12, 2016 were conducted. The pooled adjusted odds ratio (OR) and 95% confidence intervals (CIs) were calculated using the random effects model with STATA 12.0 software.
Results: In total 13 studies, including 9289 individuals with TB, were included in this meta-analysis. Significant association between DM and MDR-TB (OR=1.71; 95%CI=1.32, 2.22) was identified. Subgroup analyses showed that:
1) Pooled OR was 1.25 (95%CI: 0.82-1.91) for cross-sectional studies, and was 2.14 (95%CI: 1.51-3.02) for longitudinal studies;
2) The pooled OR was 1.69 (95%CI:1.09-2.62) for primary MDR-TB, 1.94 (95%CI:1.42-2.65) for any MDR-TB, and 0.85 for secondary MDR-TB (95%CI: 0.29-2.54); 3) DM was significantly associated with MDR-TB in both Caucasian (OR=2.26, 95%CI: 1.66-3.07) and Asian (OR=1.40, 95%CI: 1.01-1.95) subgroups. No evidence of publication bias was identified.
Conclusions: In conclusion, the pooling analysis indicated that DM was an independent risk factor for MDR-TB, especially for primary MDR-TB.

PD-812-13 Limitations and challenges of implementing tuberculosis screening in diabetes mellitus care in Bangladesh

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Background and challenges to implementation: The significant TB burden in Bangladesh is a greater issue given the increasing prevalence of Diabetes Mellitus (DM) in the country. DM patients are two to three times more likely to develop TB than those without DM.
To ensure TB screening and the management of TB/DM patients in a specialized tertiary level hospital and in other affiliated association networks.

Intervention or response: With the NTP's guidance, CTB is implementing a project with Bangladesh Diabetic Shomity (BADAS) striving to decrease DM patients' vulnerability to TB infection, promoting the active screening of TB infected and diabetic patients and increased access to TB services. A total of 553 doctors, nurses and allied staff were oriented and trained according to national TB/DM guidelines. Ninety six field coordinators were trained to ensure referral and recording from the 93 affiliated centers of 63 districts to the central specialized hospital. The screening procedures are limited in that some DM patients are screened multiple times which both inflates the total number screened as well as deflates the proportion of the comorbid cases detected.
Results and lessons learnt: Between July 2015 to June 2016, a total of 986,273 DM patients were screened among which 15,180 (1.5%) presumptive patients were referred for testing and 11,715 were tested for TB.
Among those tested, 1,592 (13.5%) TB cases were detected - 1,074 (67.4%) bacteriologically positive, 311 (19.5%) clinically diagnosed and 207 (13.0%) extra pulmonary TB cases. The prevalence rate of TB/DM comorbid patients is 161/100,000 population which is lower than the national TB prevalence rate (387/100,000 population).
Conclusions and key recommendations: The quality of the screening should be strengthened to exclude the double counting of patients. High quality implementation research is also recommended for further evidence. Strong collaborative and awareness building activities can reduce the burden of TB-DM comorbidity.

PD-813-13 Diabetic screening of tuberculosis patients under the RNTCP in coordination with NPCDCS in Punjab State, India

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Background and challenges to implementation: The recent medical evidence on the interactions between Tuberculosis and Diabetes has shown that people with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB. Hence, people with diabetes have 2-3 times higher risk of getting infected with TB compared to people without diabetes .DM is complicated by the presence of infectious diseases, including TB. It is important that proper care for diabetes is provided to patients suffering from TB -DM co morbidity keeping in view the above correlation between TB and Diabetes a meeting was organised at New Delhi on 24 June 2015 where it was decided the states will implement this bidirectional activity in collaboration with National Programme for Control of Diabetes Cancer and Strokes (NPCDCS).

Intervention or response: State of Punjab took the initiative and after approval from MD NHM free blood sugar testing of all TB patients under general health system was implemented from 2016.

Results and lessons learnt: In 2016, out of total 37885 TB patients registered 30812(81%) were tested for blood sugar free of cost at government health facilities. Out of the number tested 2537(8.2%) were diagnosed as co-infected with TB and diabetes. All the patients that had TB and Diabetes co infection were linked to free treatment for TB and diabetes available under the Revised National Tuberculosis Control Programme and free drug policy of Punjab state respectively.

Conclusions and key recommendations: It is feasible to do diabetic screening of all TB patients free of cost in coordination with National Programme for Control of Diabetes Cancer and Strokes (NPCDCS) and should be done in all TB patients so that they can be timely linked to anti diabetic treatment and more favorable outcome can be achieved on completion of TB treatment.

PD-814-13 Outcomes of screening diabetic patients for tuberculosis in Afghanistan, 2016: a cross-sectional study

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Background and challenges to implementation: The incidence and prevalence of TB remains high in Afghanistan (189 and 340 respectively per 100,000 population). Afghanistan also has annual prevalence of 800,000 diabetic patients. There is little knowledge of the comorbidity between TB and diabetes in the country. The purpose of this study was to estimate the proportion of TB among diabetic patients in Afghanistan.

Intervention or response: The National Tuberculosis Program, with assistance from the United States Agency for International Development funded Challenge TB project screened diabetic patients attending public and private health facilities between July and October 2016 in the five cities of Kabul, Herat, Mazar-e-Sharif, Jalalabad and Kandahar. A standard questionnaire for screening was used and GeneXpert and digital X-ray were used for diagnosis.

Results and lessons learnt: We assessed 2015 (23% male, 77% female) diabetic patients. The mean age was 50, 88% were married, 9% widowed, 2.4% were single, 81.4% illiterated, 3.5% were faculty graduates and 93.5% had type 2 diabetes. Also, mean body mass index (BMI) was 27.9, mean glycemic level was 157 mg/dl and 3.5% were smokers and 0.8% addicted to Opiates and Hashish. Of those assessed, 164 (8%) had a cough for more than two weeks. Sputum samples were collected

from the presumptive patients and GeneXpert testing was conducted. Seventeen (10.4%) patients were diagnosed as bacteriologically confirmed (BC), two were diagnosed as clinically confirmed TB, thus, 19 (11.6%) were diagnosed as all forms TB. The case notification rate was 943 patients per 100,000 diabetic patients. The yield of TB among diabetic is five times higher than the WHO estimated incidence for Afghan population in Afghanistan.

Total diabetic patients screened	2,015 (23% male, 77% female)
Study subjects who had a cough	164 (8%)
Number (%) tested by GeneXpert Technology	164 (100%)
Number (%) diagnosed as Bacteriologically confirmed TB	17 (10.4%)
Number (%) diagnosed as all forms of TB	19 (11.6%)

Table Flow of diabetic screening in Afghanistan

Conclusions and key recommendations: The yield of TB among diabetic patients in Afghanistan is significantly higher than the WHO estimated incidence for all forms of TB. DOTS should be expanded to diabetic centers to systematically screen for TB and TB patients should also be screened for diabetes.

PD-815-13 Association between diabetes mellitus and active TB systematic review and meta-analysis

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Background: The burgeoning epidemic of diabetes mellitus (DM) is one of the major ongoing global health challenges. We aimed to systematically review literature and to provide a summary estimate of the association between DM and active tuberculosis (TB).

Methods: We searched Medline and EMBASE databases for studies reporting adjusted estimates on the TB-DM association published before December 22, 2015, with no restrictions on region and language. In the meta-analysis, adjusted estimates were pooled using a DerSimonian-Laird random-effects model, according to study design. Quality assessment and sensitivity analyses were conducted.

Results: 44 eligible studies were included, which consisted of 58,468,404 subjects from 16 countries. Compared with non-DM patients, DM patients had 3·59-fold (95% confidence interval (CI) 2·25-5·73), 1·55-fold (95% CI 1·39-1·72), and 2·09-fold (95% CI 1·71-2·55) increased risk of active TB in four prospective, 16 retrospective,

and 17 case-control studies, respectively. Country income level, background TB incidence, and geographical region affected appreciably the estimated association, but study quality, type of population (general versus clinical), and potential for duplicate data, did not. Microbiological ascertainment for TB and/or blood testing for DM, as well as uncontrolled DM, resulted in stronger estimated association.

Conclusions: DM is associated with a two- to four-fold increased risk of active TB. The association was stronger when ascertainment was based on biological testing, rather than medical records or self-report. The burgeoning DM epidemic could impact upon the achievements of the WHO *"End TB Strategy"* for reducing TB incidence.

PD-816-13 Tuberculosis screening among diabetes mellitus patients attending the outpatient clinic of Insein General Hospital

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Background and challenges to implementation: Tuberculosis (TB) is an infectious disease which is still a major cause of morbidity and mortality throughout the world. People with diabetes mellitus (DM) have three times higher risk of developing active TB than people without diabetes. However, there was not enough credible information on the burden of tuberculosis among people with diabetes mellitus in Myanmar. This study could determine the prevalence and associated risk factors of tuberculosis among diabetic patients attending the outpatient clinic (OPC) at Insein General hospital in Yangon Region.

Intervention or response: A cross-sectional study was conducted from November, 2015 to June, 2016. Patients' demographic characteristics were collected using a pretested questionnaire form. Chest X ray screening and sputum AFB microscopy were performed if the abnormal radiological lesions were found. Data was entered and analyzed using the SPSS version 16.

Results and lessons learnt: Out of 421 patients with diabetes mellitus, 26.1% were males and 73.9% were females. Their ages ranged from 22 to 85 years, with a mean age of 56.55 years. The proportion of presence of tuberculosis among patients with diabetes mellitus was 8.06%. The association between developing tuberculosis and diabetes mellitus was significantly found in regular anti-diabetic treatment and duration of DM. Multivariate logistic regression analysis revealed that irregular anti-diabetic treatment was significantly associated with the developing TB among patients with diabetes mellitus.

Conclusions and key recommendations: The proportion of tuberculosis among DM patients was more than 2 times higher compared to the general population. DM patients with irregular taking of anti-diabetic treatment

were more prone to have TB. Therefore, TB screening of diabetic patients at OPC of general hospitals should be necessary and regular anti-diabetic treatment should be important for preventing the development of TB among DM patients.

PD-817-13 Latent tuberculosis infection and recently diagnosed diabetes mellitus at a large urban hospital in the southeastern United States

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Background: Diabetes is an established risk factor for active TB. Emerging evidence indicates diabetes might increase the risk of latent TB infection (LTBI), but limited data about LTBI among diabetes patients exists. We aimed to estimate the prevalence of LTBI among patients with diabetes and compare clinical characteristics among diabetes patients with and without LTBI.

Methods: We conducted a cross-sectional analysis of preliminary data from an on-going case-control study at a large hospital in Atlanta, USA. Eligible patients included HIV-negative adults aged ≥ 21 diagnosed with type 2 diabetes within the past 3 years with no history of active TB. Patients on steroids or TNF-alpha antagonist therapy were excluded. LTBI was defined by QuantiFERON-InTube. Clinical information was abstracted from electronic medical records. Wilcoxon and Fisher's Exact tests were used to compare diabetes patients with and without LTBI.

Results: Overall 108 patients were recruited and 100 patients met inclusion criteria. Of 100 patients with diabetes, 9.0% (95% CI 4.5-15.9%) had LTBI; among those with positive QuantiFERON the median antigen-nill response was 2.7 IU/DL (IQR 1.2-9.8). Most patients were female (56.0%), non-Hispanic Black (92.0%) and median age was 54 years (IQR 49-60). Median BMI was 33kg/m^2 (IQR 28-39) and median HbA1c was 7.3% (IQR 6.5-9.5%). No significant differences comparing diabetes patients with and without LTBI were observed, but a trend was observed with increased LTBI among smokers (13.8 vs. 7.0%, p=0.16), patients with neuropathy (13.6 vs. 7.7%, p=0.21), and in patients not receiving metformin (14.8 vs. 6.9%, p=0.14). Median white blood counts (8.3 vs. 7.4K/ul, p=0.12) were non-significantly higher among LTBI patients while median HDL cholesterol was lower (31 vs. 39mg/dL, p=0.07).

Conclusions: We did not observe significant differences in clinical characteristics among diabetes patients with and without LTBI. Larger studies are needed to infer whether observed trends in this study are generalizable to other populations.

PD-818-13 Strengthening diabetes services to reach 90-90-90 indicators and targets of the end TB strategy

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Background and challenges to implementation: People with Diabetes Mellitus (DM) have 3 times higher risk of developing active TB than those who do not have DM (Stevenson etal 2007). 10% of TB cases globally are linked to diabetes. Global priority indicators and targets for the End TB strategy are ≥ 90% treatment coverage, ≥ 90% treatment success rate, ≥ 90% preventive treatment coverage. India with a prevalence of 69.1 million DM cases ranks second in world and is expected to increase to over 79.4 million by 2030. Probably high burden and co-morbidity will hamper TB control efforts and to reach these targets.

Intervention or response: During Aug-Sept 2016 situational analysis was carried out to assess diabetic services provided at public health facilities for tuberculosis patients. Laboratory investigations and drugs were available but there were major gaps in their use. Major gaps at primary health facility level were no standardized protocol for DM management, lack of coordination among primary/secondary/tertiary health facilities, inadequate patient counselling and no system for maintaining patient records.

Results and lessons learnt: On the basis of these gaps, framework has been developed to establish a 'standardized package of care' that includes patient/ facility level tracking of patients that can be implemented at primary health facilities with adequate linkages with secondary/ tertiary health care facilities. By implementing this standardized package with use of technology, it is expected to improve quality of care.
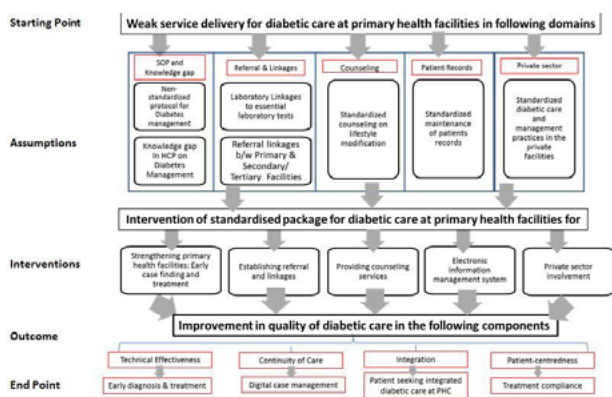
Figure Framework For Diabetes Care

Conclusions and key recommendations: DM can lengthen time to sputum culture conversion and people with diabetes who are diagnosed with TB have a high-er risk of death during TB treatment and a higher risk of TB relapse. Good glycaemic control in TB patients can improve treatment outcomes including early detection which can help improve care and control of both diseases. It is important that proper care for diabetes is provided to patients suffering from TB/DM to reach target of 90:90:90 of the End TB strategy.

36. Cost benefit analysis in TB investments; or people and products

PD-819-13 How much does it cost to engage civil society in interlinking the private sector with the national programme?

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Background and challenges to implementation: Private sector engagement has been a great challenge in India. Even with requisite circulars and notifications and "authoritative" approach, there has been limited success. The experience of successful engagement of community was brought-in to engage private sector. These activities come with a cost and were supported by The Global Fund. Here we analyse the total cost per notification from private sector.

Intervention or response: Project Axshya staff at selected districts mapped all practitioners. A list of doctors was prepared who would probably diagnose and treat a TB patient (multiple sources - eg. pharmacy). The following interventions were conducted (1) multiple visits to doctors (2) continued medical education (CME) (3) chest-x-ray support (4) treatment adherence support.

Results and lessons learnt: A total of 10,000 private practitioners from hospitals, general practitioners, and labs were interacted across 40 selected urban cities. Awareness about "TB notification" was created along with sharing of "Standards of TB care in India". Nearly, 40 CMEs and 200 chest-x-ray support was provided on S-O-S basis. A small proportion of patients in private sector were provided with treatment adherence support. A For all the above activities, including salary and local travel of project staff, a total of USD 321,354 was spent. Approximately, 75% of the cost was spent for the activities and 25% for Human Resource cost. Secondly, the supervisory cost of programme staff is not included in the analysis. A total of 9024 TB patients were notified and the cost per TB patient notified is USD 35.61 in private sector. Few cost components are one-time investment and this cost would reduce with increase in number notified.

Conclusions and key recommendations: Civil society is a viable option for increasing the engagement of private sector with programme and it would cost USD 35.

PD-820-13 Beyond symbolic engagement: tuberculosis and the First Nations Health Authority of British Columbia

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Background and challenges to implementation: For First Nations of Canada, tuberculosis is rooted in colonization and other forms of structural violence. Disproportionality of suffering continues. In 2014, the incidence rate of active TB among First Nations people of British Columbia (14.4 per 100,000) was more than twice that of the province (6.3 per 100,000).

Requisite to successful outcomes of preventive and treatment efforts is the centering of social justice and Indigenous control. Coherence of past and present is more than engagement in cultural world view and lived experience; it is a rights-determined lens of equalizing determinant factors within self-determination of land and traditions.

Intervention or response: he First Nations Health Authority (FNHA) is the first province-wide health authority of its kind in Canada. In 2013, the FNHA assumed the programs, services, and responsibilities formerly handled by Health Canada´s First Nations Inuit Health Branch - Pacific Region. FNHA organizational directives aim to assure that services are Community-driven and Nation-based as well as increase First Nations decision-making power and control.

Results and lessons learnt: The FNHA TB Services program is a coordinating entity within FNHA and seeks to transform approaches to TB work from tendencies toward reductive medicalization to a dynamic multi-level systems approach nested within Indigenous wellness, justice and cultural revitalization.

Conclusions and key recommendations: Examples of interventions to improve systems equity across the Province include partnering with regional leadership to align priorities under local community direction and the development of formal collaborative pathways with both TB partners and First Nations communities when addressing barriers to services or other forms of TB advocacy.

PD-821-13 The role of TB field promoters in TB response in three regions of Namibia: Oshana, Oshikoto and Kavango

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Background and challenges to implementation: In 2007 Namibia had the fifth highest incidence of TB (WHO, 2009), with a rate of 747/100,000. Three regions, Oshana, Oshikoto and Kavango, were reported among high burden regions in Namibia with high case notification rates, low treatment success (58% - 79%), high mortality (5% - 11%), and high rates of lost-to-follow up (LTFU) (11% - 22%). Only half of TB patients knew their HIV status. The lack of a community-based TB care approach was identified as a gap by the National TB Program (NTP).

Intervention or response: In 2008, in collaboration with the Ministry of Health and Social Services (MoHSS) and through the GFATM, Project HOPE Namibia trained and deployed 99 TB Field Promoters (TBFPs) in the three regions. The TBFPs conduct household visits (61,190 by 2015), provide information and education to the community (105,900 sessions), and symptom screening for TB; collect sputum samples; conduct TB contact tracing; refer cases for diagnosis; and facilitate TB treatment at TB DOT points.

Results and lessons learnt: Review of data for major National TB program indicators showed significant improvement in LTFU rates and treatment success rates that can be related to the contribution of TBFPs.

LTFU rates decrease drastically in the three regions as follow: from 11% to 5% in Oshana, 13% to 3% in Oshikoto and 22% to 1% in Kavango. This can be indirectly linked to the observed increase in treatment success rates as per the table.

Region	2008	2009	2010	2011	2012	2013	2014	2015
Kavango	74%	74%	78%	83%	94%	85%	89%	70%
Oshana	84%	82%	80%	81%	81%	92%	85%	86%
Oshikoto	84%	84%	86%	85%	90%	90%	89%	85%

Table Treatment Success Rates, MoHSS, 2008-2015

Conclusions and key recommendations: The introduction of TBFPs to the NTP was an important part of the national response to TB control. The interaction of TBFPs with the community is vital for the reduction of TB burden. Advocacy with local leadership is urgently required to ensure ownership of the community TB care program to sustain the services by TBFPs. A specific program evaluation is recommended to ascertain the TBFPs attribution to the national response.

PD-822-13 A comprehensive TB care package for elderly TB patients to reduce economic burden and improve treatment adherence

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Background and challenges to implementation: The Ministry of Civil Affairs and Ministry of Finance of China contributed the fund to support demonstration pilot project to provide service for elderly, the children and disabled people in 2016. According to the National epidemiology Random Survey in 2010, It was estimated there are 5 million TB patients which accounts for 48.8% of total patients in China. The impact factors mainly are poverty, malnutrient and poor health service accessibility. Therefore Chinese Anti-tuberculosis Association applied and was approved to implement the project named Assistance Project for Elderly TB patients in Poverty Areas in China in 2016. 4 project sites were selected in national poverty county of Jinagxi, Sichuang, Jilin and Hunan province.

Intervention or response: Set up routine communication mechanism between unit of civil affairs ,health sector ,health insurance and social security; Carried out TB screening by household survey and health promotion campaigns and detected more than 60 years TB patients. when TB Patients visited the doctors, they got meal and transportation subsidy, Social volunteers delivered psychology support and nutrient food supply each month.

Results and lessons learnt: The project covered more than 2,360,000 population .There were 2,000,348 elderly were screened in which there were 14,579 elderly who had TB suspected symptom. There were total 623 elderly TB patients who were diagnosed, treatment and got the comprehensive TB care package. The project promoted Local government to issue policy and improve input for elderly TB patients including the reimbursement rate of new Cooperative Medical Scheme improved and counterpart fund provided by the bureau of Civil Affairs and 1 pharmaceutical enterprise. Finally, the project improved 623 elderly TB patients' treatment compliance and decreased their economic burden.

Conclusions and key recommendations: The project promoted to set up cooperative mechanism between health sector, civil affairs and social security. It was also demonstrated Non-government organization involved government service with innovative mode in China by integrated resource.

PD-823-13 Role and impact of engaging key stakeholders in community TB outreaches; lessons from southwest Nigeria

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Background: Community outreach activities usually involve the engagement of community volunteers(CV) and civil society organizations (CSO) with mobilization activity preceding the outreach proper. However, there is limited information on who the core players should be for an effective outreach activity and concomitant increase in TB case finding.

Methods: A descriptive analysis of core players that should coordinate and participate in an outreach activity. Initial selection of community for outreach was done using an onion-model approach of selecting sites with high MTB detection and AFB results of 3+. Most were slums with limited access to services. At the phase of advocacy, community leaders and ward chairpersons were engaged alongside the district health educator. Communities were mobilized through support of CVs and district supervisor. A hub DOT site was selected and the DOTs provider also engaged in mobilization activities. Mobilization was carried out for 2 consecutive days, followed by a day community outreach with continuous mobilization. A hub GeneXpert lab was also identified and the GeneXpert focal person participated on day 3 outreach activity by collecting all sputum specimens from presumptive cases and storing in coolers with immediate transportation to laboratory at the end of day 3 exercise. All documentation was done into the presumptive register and laboratory records. A measurement of participation rate in routine outreaches before engagement of GeneXpert officer, health educator, ward chairpersons and after engagement was done.

Results: Prior to engaging these key stakeholder, a mean average of 728 attendees was recorded compared to 2638 thereafter (tripling of attendance). There was a fourfold proportional increase in presumptive TB cases and MTB detected cases form 19 to 95 over a 6 month period in the second half of 2016.

Conclusions: To find the missing cases through community outreach activities, it's critical to engage the right key stakeholders.

PD-824-13 Beyond Project Axshya: TB patients restored security through vocational training and welfare measures in Uttarakhand

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Background and challenges to implementation: The project advocates restoration of livelihood of those became unemployed due to the disease. The objective of this paper is to evaluate the efficacy of the livelihood programme or made for people suffering from TB in the state of Uttarakhand.

Intervention or response: In order to ensure sustainable livelihood for TB patients two pronged approach - (i) vocational training on income generation and (ii) linkage with social security schemes of government was taken up in the district. Under vocational training - less physical labour activities, candle and envelope making trainings were given to 35 TB patients and their families with an estimate of preparing 400 envelopes and 150 candles per day by a TB patient with his family at home which will give them an income of $120 - $140 per month. As a pilot, during Apr'14 to Sep'15, in 4 districts of Uttarakhand, out of 626 TB Patients, 35 who were most vulnerable were identified and trained along with their families. In the same period, in one district, efforts were made to link all TB patients with available welfare schemes.

Results and lessons learnt: Out of trained 35 TB patients and their families, 5 (15%) have started the activities. Their monthly earning raised to about Rs. 6000/- which is about 100% rise from the previous irregular income through daily wages. In terms of social security measures 13 TB patients were linked to welfare scheme with a one-time support of Rs. 10000/- during the course of treatment.

Conclusions and key recommendations: This effort of advocacy and capacity building, patients are not only getting the support for nutrition and day to day cost of transportation for care, but also there is reduction of stigma and discrimination as well. In addition to the medical treatment, there is an emergent need of intersectoral coordination to provide economical/Livelihood support to TB patients for psychological treatment.

PD-825-13 What role can non-governmental organisations play to sustain the ENGAGE TB approach: experience from a mapping exercise in Vihiga County, Kenya

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Background and challenges to implementation: The Engage TB approach identifies capacity building of civil society organizations as key in strengthening and scaling up of community Tuberculosis activities. However, lack of concerted efforts to strengthen core organizational competencies has threatened the continuity of implementing and sustaining this approach.

Intervention or response: Amref health Africa in Kenya conducted a mapping exercise for civil society organizations (CSOs) implementing community health interventions in Vihiga County with the aim of assessing the core organizational competences required for effective delivery of community Tuberculosis (TB) activities. Review of program related documents was conducted including interviews with the representatives of the CSOs. Thematic analysis was used to interpret the qualitative information generated.

Results and lessons learnt: 25 CSOs representatives were interviewed on key organizational competencies and the exercise revealed a number of findings:

Institutional development and system strengthening: CSOs mapped were at the emergent and emerging stage of organizational development; had established semi-functional project units that focused on financial management, monitoring and evaluation which did not reflect the actual organizational structure. These functions were donor driven and became disfunctional after a project closure.

Role of CSOs in sustaining the strategy: CSOs are formed to address health needs in the community, the exercise revealed that there is little effort being made to strengthen a collaborative dialogue with the government in view of sustaining this approach.

Conclusions and key recommendations: Weak institutional systems is a major threat on the implementation and sustainability of the Engage TB approach. Insights reveal that strengthening organizational systems will result to an increased accountability of health services thereby improving the health of the population. Future programmatic practice should focus on strengthening institutional systems through capacity building, mentorship and coaching.

PD-826-13 Community engagement for TB care and control: experience from a hilly state in India

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Background and challenges to implementation: The Union in collaboration with State TB Cell Uttarakhand is directly implementing the project in 13 districts since April 2014. This work documents the interventions and outcomes of community engagement in TB care and control in the state.

Intervention or response: Network of 54 NGOs and 200 community volunteers (CVs) are currently conducting interventions like, community meetings with community groups (self-help groups, village heads, Village health and Sanitation Groups, youth groups etc.), mid-media activities and active case finding (ACF) through household visits. The disaggregated data on number of community meetings, mid-media activities, household visited, and population reached, presumptive TB patients (PTBP) identified (cough of 2 or more than 2 weeks), tested and diagnosed were collected from project and NTP documents/reports. Contribution on PTBP examined, TB diagnosed, notified that are diagnosed by community volunteers and treatment outcomes are reported.

Results and lessons learnt: In period of 36 months of project implementation (April 2014 to December 2016) the project trained 177 and 468 NGOs and CVs, respectively in TB Care and Control. Altogether, 3511 community meetings, 305 mid-media activities, 256007 TB ACF in households have been conducted reaching nearly a million populations through a network of 54 NGOs and 200 CVs. From those interventions, 12,111 PTBP have been identified- PTBP prevalence, 6386 (53%) were examined and 1139 TB patients have been diagnosed and initiated on treatment. The contribution to the microscopy centres was 9% (0.5-70%) on PTBP examination and 5% on diagnosis. The community TB notification rate was 53 per 100,000 populations.

Conclusions and key recommendations: The community engagement in TB care and control in the state has reached nearly a million populations through network of NGOs and CVs and 626 cases have been diagnosed in a period of 18 months. Community engagement in TB care and control is the key to reach those unreached in States of Uttarakhand, India.

37. Xpert implementation: realities in the field

PD-827-13 Using GxAlert report to troubleshoot the problems encountered in remote GeneXpert® laboratories

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Background and challenges to implementation: The Ethiopian Public Health Institute is using GxAlert technology to monitor GeneXper machines performance. USAID Challenge TB Project in partnership with EPHI supported the implementation of the technology throughout GeneXpert sites. The major challenge in the implementation was repeated unsuccessful test results in majority of GeneXpert sites. We used information obtained from GxAlert to tackle the frequently reported unsuccessful test results in 64 sites.

Intervention or response: Data collected through GxAlert was analyzed to support remote laboratories in troubleshooting of problems encountered in GeneXpert sites. Data for unsuccessful tests were exported from GxAlert for 5, 15, 23, 64, and 74 machines in 2013, 2014, 2015, 2016 and 2017 (1st quarter) respectively. Among the total 64 GeneXpert machines, the error detailed data was analyzed for 30 high load machines. Interventions like cleaning the module PCR slots, the fan filter, plunger rod, cartridge bay; and repeating Xpert check was performed. Onsite refresher training also provided.

Results and lessons learnt: Trend of unsuccessful tests is relatively decreasing from year to year. It was 18%, 16%, 12% and 12% in 2014, 2015, 2016 and 2017 (1st quarter) respectively. The major contributor for the total unsuccessful test results among the three categories (Invalid, Error, No Result) "error" takes the lead, 69%, 41%, 50% and 42% contribution from 2014 to 2017 (1st quarter) respectively.

The most frequently encountered error type (64%) is "Error Code 5007-probe check failure and invalid results account for 20%. Among 32 Xpert check failed nonfunctional modules 28 (87.5%) of them were became functional and xpert check passed.

Conclusions and key recommendations: Using GxAlert Report for troubleshooting of problems encountered in remote laboratories is very useful to target the problem type and support the end users. The site level intervention as simple as regular cleaning reduces unsuccessful test results and cost.

PD-828-13 Impact of rapid expansion of cartridge based nucleic acid testing on the diagnosis of drug-resistant TB cases in India

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Background and challenges to implementation: Gene-Xpert, Cartridge based nucleic acid amplification testing (CBNAAT) is a revolutionary diagnostic tool for rapid identification of MTB as well as rifampicin resistance, a surrogate for MDR-TB. Revised national TB control programme , India used CBNAAT for Priority 1 - Diagnosis of drug resistance among presumptive drug resistant TB (DRTB) patients viz. previously treated TB patients, non-converters, failures of first line treatment, HIV-TB patients & TB patients in contact with MDR-TB patients and Priority 2 - Diagnosis of TB among key population viz. paediatric, HIV infected, extra pulmonary presumptive TB cases and persons with smear negative, chest X-Ray suggestive of TB. Patients notified from private sector are also offered CBNAAT for Drug susceptibility testing. A modest increase in DRTB cases was witnessed during 2013-2015 with limited availability of 128 CBNAAT & 50 LPA labs at centralized facilities in India. Programme also depended on local specimen transport mechanism for linkage to these labs.

To increase DRTB case detection, programme planned rapid expansion of Lab network. Here we share India's experience of an unprecedented scale up of CBNAAT Labs and its impact on DRTB case notification.

Intervention or response: The programme established 500 additional CBNAAT labs in March - June 2016, thus 628 CBNAAT labs are now covering practically every district across the country.
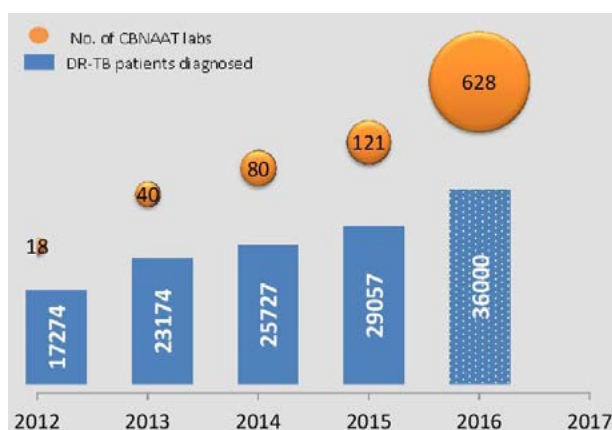
Figure Exponential increase in number of DRTB diagnosed after establishing additional 500 CBNAAT Labs

Results and lessons learnt: Presumptive DRTB cases tested on CBNAAT increased from 248314 in 2013 to 578173 in 2016. About 221603 MTB cases with 27822

RR-TB cases were detected in total. In 2016, about 33820 DRTB patients were diagnosed versus 29,057 in 2015, 16% increase. There has been an increase of nearly 46% from 23148 diagnosed DRTB cases in 2013 to 33820 in 2016.

Conclusions and key recommendations: Expansion of CBNAAT labs increased DRTB case finding exponentially. Optimum use of machines considering their throughput and lab capacity linked expansion towards universal DST is recommended to further improve case finding.

PD-829-13 Chronic GeneXpert maintenance challenges in Bangladesh

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Background and challenges to implementation: Since April 2015, the Bangladesh NTP, with support from the CTB project has operationalized 39 GeneXpert machines (228 modules) in 38 centers. CTB experienced significant challenges persisted with the machines as there were no mechanisms in place to support module replacements with customs clearance, routine troubleshooting and GeneXpert check run. Many of the maintenance issues result from poor placement of the instruments and limitations in lab technician capabilities. The objective of this study was to better analyze the GeneXpert maintenance challenges.

Intervention or response: The CTB project collected data from 39 GeneXpert machines from January 2016 to January 2017. The project calculated the average number of module failures, non-functional machines and turnaround time for replacing or repairing different components of the machines.

Results and lessons learnt: During the study period, there were about 37 modules failure and on average three machines were non-functional. Replacement of modules and importing spare parts took between two to five months the cases were logged. GeneXpert check run was not conducted for 22 machines. The reported test error was around 5%. The mean time for software upgrade or to address database error was one to three weeks. Turnaround time for incident reporting of up to four months was reduced to just six days. CTB engaged Cepheid's new local agent to reduce customs clearance time from three to eight months to 14 days however, a delay by Cepheid in sending new modules and spare parts persists. Due to CTB's advocacy efforts Cepheid agreed to establish a repair center in Dhaka, Bangladesh.

Conclusions and key recommendations: Improving and sustaining the GeneXpert network in Bangladesh is dependent on routine maintenance, providing an adequate environment for the machines, capacity building of staff and implementing the relevant SOP. Cepheid should expedite the process of establishing the GeneXpert repair center in Bangladesh to ensure timely module replacement services.

PD-830-13 Assessment for 9 countries supported by the KNCV Tuberculosis Foundation of Xpert® MTB/RIF spare parts, modules and warranty coverage

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Background: Over the last two years, KNCV has acted as the authorized service provider (ASP) for all GeneXpert instruments in Nigeria and Vietnam on behalf of Cepheid. However, issues regarding in-country spare parts and modules as well as warranty coverage have been reported to increase downtime of instruments. KNCV investigated in countries where we have the largest presence.

Methods: KNCV developed a questionnaire to assess the number of machines and modules (present and expected), functionality, servicing, and warranty coverage. In September 2016, this questionnaire was sent to KNCV offices in Botswana, Ethiopia, Indonesia, Malawi, Namibia, Nigeria, Tajikistan, Tanzania, Uzbekistan, Vietnam.

Results: 9 countries (90%) returned questionnaires (excluding Namibia). GeneXpert capacity is expected to double, on average, by the end of 2017 in the countries surveyed; increasingly countries are adopting GeneXpert as the primary initial diagnostic. 5 countries reported having ASPs (2 non-commercial, non-profit from KNCV in Nigeria and Vietnam as well as 3 commercial in Ethiopia, Indonesia and Malawi); the remaining countries relied on the national TB program and donors to ensure servicing. Three countries (33%) were able to track and document time from report of a problem with an instrument to repair. The average time to repair ranged from 4 week to 26 weeks. Warranty status documentation was limited (66% had known status). Instruments under warranty were more functional (96% vs. 84%) and had problems resolved faster. 8 countries (89%) reported that having spare parts and modules in-country would significantly reduce downtime.

	Botswana	Ethiopia	Indonesia	Malawi	Nigeria	Tajikistan	Tanzania	Uzbekistan	Vietnam
Who arranges?	MoH	MoH (EPHI)	MoH (NTP) & KNCV/ partners	MoH (NTP)	ASP (KNCV)	MoH (NTP) & partner NGOs	MoH (CTRL) & partners	MoH (NRL)	ASP (KNCV)
How long (weeks)?	12-16 weeks	8 weeks on average	up to 26 weeks	no data	1 to 16 weeks dependent on module availabilty	1 month or longer dependent on module availability	greater than 12 weeks	8-12 weeks	3-4 weeks dependent on module availabilty and custom clearance
Cost per module	2437 USD	no charge	1106-4000 USD	900 USD	no charge with warranty; 900 USD w/o warranty	no data	1500 USD including shipment and customs	no charge with warranty; 900 USD w/o warranty	no charge with warranty; Cepheid quotation w/o warranty
Depends on warranty?	no data	No	Yes	No data	Yes	No	Yes	Yes	Yes

Table Module replacement modalities by country

Conclusions: Service provision and monitoring of instruments in KNCV supported countries is currently sub-optimal. Spare parts and modules would be beneficial to reduce downtime. Warranty coverage facilitated more functionality. KNCV will continue to pro-actively engage with NTPs, donors, technical partners and Cepheid to optimize functional TB diagnostic networks. Optimization is instrumental to presumptive TB patients for facilitating their timely TB diagnoses.

PD-831-13 Impact of Xpert® MTB/RIF on treatment initiation and outcomes of TB and MDR-TB patients in Vladimir TB Dispensary, Russia, 2012

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Background: We assessed time-to-treatment initiation and treatment outcomes of rifampicin (RIF)-resistant and RIF-susceptible patients diagnosed and treated in Vladimir TB dispensary in 2012, before and after implementation of Xpert MTB/RIF (Xpert) diagnostic technology.

Methods: All presumptive TB patients underwent phenotypic drug susceptibility testing (DST) during February-December 2012; Xpert diagnostics became available from August 2012. We defined rifampicin resistance as resistance detected by either DST or Xpert. Chi-square test was used to assess risk factors for treatment outcome. Kaplan-Meier curves and Cox modeling were used to compare the time and probability of treatment initiation with second-line drugs (SLD) among RIF-resistant patients in pre- and post-Xpert periods.

Results: Of 402 patients screened for TB, 305 (76%) had recorded treatment outcomes. Among 53/305 RIF-resistant patients, 53% had successful outcome (cured/completed treatment). Positive HIV status, smoking

history, unemployment, and history of imprisonment were significantly associated with poor treatment outcome. Probability of SLD treatment initiation within 60 days after initial diagnosis was significantly higher in post-Xpert group (HR=2.06; 95%CI:1.09,3.89) versus pre-Xpert group. RIF-resistant patients detected using Xpert started SLD treatment significantly earlier than those in pre-Xpert group (11 vs 37 days, p=0.02) (Graph).
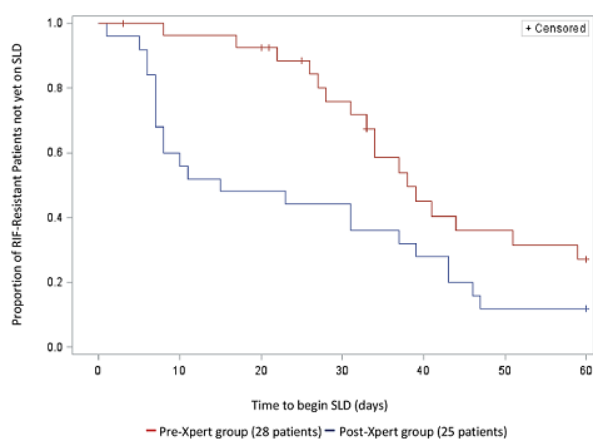
Figure Time to initiation of Second Line Drugs treatment among patients with RIF-resistant TB

Among 252/305 RIF-susceptible TB patients, 79% were successfullly treated. Male gender, positive HIV status, smoking, unemployment, a history of imprisonment and homelessness were significantly associated with poor treatment outcome. Time-to-treatment did not differ between RIF-susceptible cases in the pre- and post-Xpert groups (3 vs 2 days, p=0.73). Using Xpert for detection was not associated with successful treatment outcome for eithe RIF-resistant or RIF-susceptible patients.

Conclusions: Availability of Xpert for initial case detection significantly reduced the time-to-SLD treatment for RIF-resistant patients. Although implementation of rapid diagnostics did not improve treatment outcomes, early detection of rifampicin resistance is important for prevention of transmission of drug-resistant TB.

PD-832-13 Xpert utilisation rate and associated factors for suboptimal test uptake in South Nations Nationalities & Peoples Region, Ethiopia

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Background: In Ethiopia, GeneXpert was implemented since 2012. Currently, there are twenty GeneXpert machines in South Nations Nationalities & Peoples Region (SNNPR) which are being used for diagnosis of TB and rifampicin resistance. The objective of the investigation was to assess the performance of the GeneXpert testing in SNNPR and identify gaps for possible intervention.

Methods: Assessment was conducted in 18 GeneXpert testing sites. A one-year data was collected by interview using structured questioner, document review, and observation.

Results: Of the 6,679 tested cases, 5,530 of them had successful test results.

Of the successful tests, 860 (16%) of them were positive for TB (Table 1). Rifampcin resistance was detected in 2% (100/5530) of the successfully tested cases. The daily uptake of GeneXpert testing service (10.5%) was far below the expected (12 tests/day/machine which for 20 machines would be 63,360). Out of the 6679 tests, 1149 (17%) of them were unsuccessful. The proportion of invalid, no result, and error result were 2%, 8% and 7%, respectively. These findings were higher than the acceptable range which should be <1% no result and <3% error rate. The overall unsuccessful test has incurred an additional cost of 258,525 Birr (1149 cartridges x $10 x 22.5 birr) due to wastage of cartridge.

Conclusions: The rate of unsuccessful test especially the no result was very high and it was far beyond the acceptable range and it is mainly related with power interruption. GeneXpert test uptake was very low and this could be due to lack of awareness of clinical staff on the testing algorithm and weak sample referral system. Therefore, future intervention should focus on strengthening the sample transport system, awareness creation on the testing algorithm and providing back up power system.

PD-833-13 Early warning signs: a rapid gap analysis of linkages between GeneXpert catridge use and TB patient diagnosis in Nigeria

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Background: Expectedly, following the adoption of the WHO recommendation of GeneXpert as primary point of TB diagnosis, with a concomitant in its use for diagnosis, the utilization rate of GeneXpert cartridges increased, with recurrent stock-outs reported. There is limited analysis report of losses if any form routine surveillance data.

Methods: A comparative analysis of GeneXpert data records and cartridge utilization with a cross-validation with the physical inventory of stock at hand across all GeneXpert sites in Nigeria in 2015. Opening and received quantities were summed, closing stock was derived

from the difference between quantity used and the summed opening and received stock. Physical inventory of existing quantities was recorded. Samples with invalid results and errors were also taken into account.

Results: In comparison with the total 39,920 patients screened using GeneXpert, 39919 cartridges were recorded as used. However, a sum of 91582 cartridges constituted opening and received balance. A closing stock of 51663 in comparison to a physical count of 44841 showed a gap of 6822 (13% of closing stock). 4213 (61.7%) accounted for invalid and error results. An unexplained 2609 (38.2%) cartridges was identified as gaps.

Conclusions: For an efficient logistics management system, the NTP in collaboration with its partners should carry out routine consumption analysis and commodity monitoring, which is necessary especially for diagnosis of TB using GeneXpert, due to recurrent stock-outs which may be an unwarranted call for help.

PD-834-13 The use of volunteers to optimise uptake of the Xpert® MTB/RIF assay in Nigeria

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Background and challenges to implementation: The inclusion of GeneXpert assay in the Nigerian TB diagnostic algorithm has improved TB diagnosis. However, utilization of the assay remains sub-optimal due to inadequate human resources, among other reasons. Volunteers were engaged in 19 sites, with human resource challenges, across 8 states. We studied the impact of volunteers' performances on workload, diagnosis of TB and assay quality.

Intervention or response: A trained volunteer was engaged to work in each of the nineteen 4-modular GeneXpert sites. The volunteers' daily workload (tests/day), assay quality and diagnosed TB cases were documented and compared with baseline values. Remuneration of volunteers was based on a sliding performance scale, with the highest amount paid to those who achieved a workload of ≥12 tests/day and the least; ≤ 6 tests/day.

Results and lessons learnt: After 5 to 9 months, there was a 51% increase (5.3 to 8.0) in the average daily workload. All volunteers had an increased average workload (9% to 417%) compared to baseline. Four volunteers (21%) achieved a daily average workload of ≥ 12 tests/day, 10 (53%) achieved between 6.1 - 11.9 tests/day and 5 (26%); ≤ 6 tests/day. The average number of TB cases diagnosed daily increased by 23% (1.1 to 1.35), with *Mycobacterium tuberculosis* detected in 17% of all tests.

However, the proportion of successful tests reduced (94% to 90%), with a 3% to 6% increase in the error rate. The most frequent error codes were 5007, 2008 and 5011. The high error rate may have resulted from non-adherence to standard operating procedures, in the volunteer's bid to increase workload which was tied to remuneration.

Conclusions and key recommendations: While GeneXpert utilization and TB diagnosis can be improved through a performance-based remuneration scheme, there's need for close supervision to ensure quality. Monitoring assay quality is as important as increasing the number of tests to improve TB diagnosis and helps minimize wastage.

PD-835-13 Internet access is the main deterrent to online reporting of GeneXpert® data in Kampala

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Background and challenges to implementation: In a bid to achieve real-time routine reporting of TB diagnosis data, improve data quality and effectiveness of service delivery, the National Tuberculosis Reference Laboratory (NTRL) adopted an online reporting system for GeneXpert data through networking GeneXpert devices via a cloud application, GxAlert, hosted at the NTRL server. Kampala, the district with the highest number of GeneXpert machines (19) located at 13 sites, achieved reporting rates of only 35% during August, 2016.

Intervention or response: The NTRL through support of MSH-Track TB Project carried out an exploratory-action based research to improve GeneXpert data reporting. The team used a problem solving based approach for challenges faced at the 9 non-reporting GeneXpert sites, identified challenges and implemented solutions to the challenges in order to improve reporting rates.

Results and lessons learnt: By the beginning of March, 2017, reporting in Kampala improved to 100% improving the national reporting rate to from 63% to 91%. Majority (7/9) of the GeneXpert sites reported lack of internet access as the main reason for inconsistent online reporting of GeneXpert data to the NTRL (figure 1). These sites either experienced unstable local area network or hitches related to internet modems or dongles. Other deterrents mentioned included host server complications (4/9), GeneXpert functionality challenges (4/9), expired antivirus or computers infected with viruses and no computer administrative access rights (2/9).
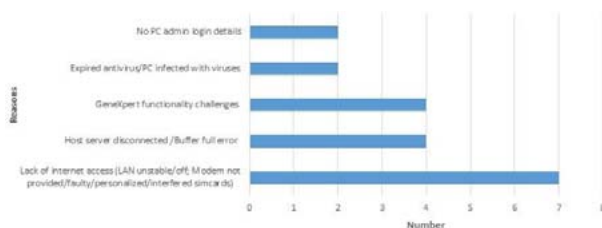
Figure 1 Reasons for inconsistent online reporting of GeneXpert data in Kampala

Conclusions and key recommendations: Inconsistent internet connectivity was the major factor inhibiting reporting among GeneXpert sites followed by host server complications. We recommend sustainable and cost effective internet connectivity in addition to effective network communications and user friendly software in improving electronic GeneXpert data reporting.

38. Solutions to laboratory implementation challenges

PD-836-13 Improved utilization of Xpert® MTB/RIF technology for TB diagnosis in Kampala

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Background and challenges to implementation: According to weekly reports, GeneXpert MTB/RIF utilization in Kampala was estimated to operate at 30%, well below the recommended capacity by January 2016. We aimed to describe implementation efforts to improve GeneXpert utilization.

Intervention or response: Between January and December 2016, we evaluated 13 health facilities in Kampala with GeneXpert machines on site. There were quarterly onsite Continuous Quality Improvement (CQI) trainings on TB diagnosis and management, emphasizing GeneXpert as the recommended first test for all presumptive TB patients. On-site laboratory, support supervision by District Laboratory Focal Persons was also conducted. All facilities were supported with modems and internet data bundles to report through GxAlert. Three motorcycle riders were recruited to transport samples to the testing hub and results back to requesting facilities. We sent weekly SMS reminders to laboratory staff to send data to a central server at the national TB reference laboratory. Using routine aggregate TB program data, an observational one-year trend analysis was conducted January- December 2016.
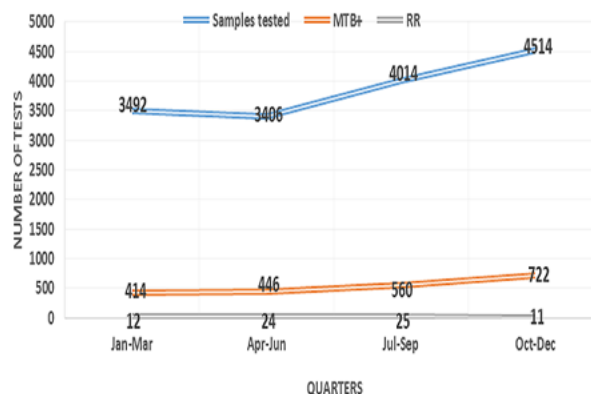
Figure Trend analysis of GeneXpert Utilization

Results and lessons learnt: A total of 15,426 GeneXpert tests were performed. There was 29.3% increase in GeneXpert tests performed from January - March (3,492) to October - December (4,514). The total number of TB cases diagnosed increased from 414 to 722 in the same period while the diagnosed rifampicin resistant cases increased from 12 to 25. We registered an average quarterly steady increase of 15% in GeneXpert utilization.

Conclusions and key recommendations: Support to GeneXpert services in Kampala contributed to the improved utilization of this technology and eventual increase in TB cases. We recommend strengthening these efforts to improve detection of both drug susceptible and drug-resistant TB.

PD-837-13 Evaluation of OMNIgene® SPUTUM reagent for long-term transportation of samples for Xpert testing in a high TB-HIV burden setting

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Background: While Xpert MTB/RIF has greatly improved tuberculosis diagnosis, many samples still require long transportation to intermediate level laboratories for testing. Testing with Xpert is recommended within 7 days from sample collection, and ethanol is commonly used for sample storage prior to molecular testing. OMNIgene® SPUTUM (DNA Genotek, Canada) is a new reagent for sample preservation able to prolong the Xpert pre-test time. We aimed to investigate the use of the reagent up to 15 days compared to standard techniques.

Methods: A total of 50 smear-positive newly-diagnosed patients submitted 2 to 3 sputum samples, pooled to reach 10ml final volume. For each, 5 aliquots were prepared and tested with microscopy to check for homogeneity. These aliquots were stored at room temperature. Three aliquots, untreated were tested with Xpert after 0, 7 and 15 days. Two aliquots, treated with OMNIgene and Ethanol, respectively, were tested with Xpert after 15 days. Xpert MTB detection rate and rate of invalid results were compared between treated and untreated samples at each time point.

Results: On average 44% of aliquots were ≥ 2+: 44%, 40%, 48%, 48% and 44% in the groups 1, 2, 3, 4 and 5 of aliquots. MTB was detected in all (50/50) untreated aliquots at day 0 and 15. At day 7, it was detected in (48/50) with 2 invalid results. In OMNIgene and Ethanol treated samples, MTB was detected in 100% (50/50) and 96% (48/50) at day 15.

Conclusions: In this proof of concept study, Xpert was able to detect MTB in OMNIgene and untreated samples by 15 days. Further evaluation of OMNIgene in pauci-bacillary samples or preservation of samples beyond 15 days might be necessary.

PD-838-13 Effect of increased user fees in accessing new TB diagnostic services in the East Africa PHLN supported project sites: experience from Tanzania

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Background: In Tanzania, Tuberculosis (TB) services are mostly provided in the public health facilities. Some of the facilities including Musoma and Sumbawanga regional Hospitals increased user fee but Mnazi Mmoja referral hospital (MMRH) did not. This paper reports on effects of increasing user fees on utilisation of TB diagnostic services in these facilities.

Methods: We retrospectively analysed data on the utilisation of TB diagnostic services between July 2013 and June 2015 in these three facilities. User fees in Musoma was increased substantially from 2USD to 5USD in July 2014. In Sumbawanga hospital user fees was increased in step-wise starting from 1USD to 2USD in July 2014 and from 2USD to 3USD in January 2015. We compared TB services utilisation before and after change of user fees.

Results: Overall, a total of 7483 presumptive TB patients were registered in all three facilities between July 2013 and June 2015; 50.2% were males. Fifty three per-

cent (3969/7483) and 3514 (28%) of these patients were registered before and after the increase of user fee respectively. Of 3969, 1579 (39.8%) were from Musoma, 922 (23.2%) from Sumbawanga and 1468 (37.0%) from MMRH. Of 3514 patients, 983 (28%), 952 (27.1%) and 1579 (44.9%) were from Musoma, Sumbawanga and MMRH respectively. Number of presumptive TB patients seeking TB diagnostic services at Musoma decreased significantly by 38% (from 1579 to 983) after the increase of user fees (p=0.001). More females (817; 51.8% vs 458, 35.9%) attended Musoma before user fees was increased as compared to males whose attendance did not differ much (761; 48.2% vs 525; 53.4%); p=0.01. There was no significant decrease of number of patients utilizing TB diagnostic services at Sumbawanga and MMRH.

Conclusions: Increase of user fee decreased the utilisation of TB services significantly. Female patients were more affected by the change.

PD-839-13 TB viability microscopy optimisation

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Background: Sputum viability microscopy with fluorescein diacetate (FDA) predicts *Mycobacterium tuberculosis* culture results, treatment response and infectiousness, but diverse protocols have been used.

Objective: To determine the optimal viability microscopy protocol.

Methods: Sputum samples were collected from patients with known smear-positive TB before commencing treatment and from healthy controls. Sputa were divided into 3 equal aliquots that were treated with: 2% sodium hydroxide and centrifuge-concentrated ("NaOH"); trisodium phosphate ("TSP"); or unprocessed ("Direct"). *Mycobacterium tuberculosis* in each aliquot was quantified by culturing serial logarithmic dilutions in 7H9 broth.

Smear microscopy slides were prepared from each aliquot using: 1 or 3 drops; stained with Ziehl-Neelsen (ZN); auramine; or FDA. Slides were processed with or without: acid-alcohol wash ("acid"); potassium permanganate quenching ("pp") for 30 or 60 seconds; and phenol. 143 slides were read within 4 hours of staining (iLED microscope, 100x objective, 100 high-power fields) by a microscopist blinded to experimental group. Concentrations of visible *Mycobacterium tuberculosis* were calculated relative to ZN results. A microscopy quality score was based on 4 criteria.

Results: (See figure) FDA was paradoxically more sensitive for 1 than 3 drops of sputum (P< 0.001). FDA microscopy with acid-alcohol wash was more sensitive direct than with NaOH or TSP (P< 0.001). Culture had 4.1-times more colony-forming units direct than with NaOH decontamination (P=0.04). Quenching with potassium permanganate for 30 seconds improved background contrast (p< 0.001), with no detrimental effect on focusing (p=0.8). Phenol did not affect results (all P>0.1). All control samples had negative culture and microscopy.

Conclusions: Viability smear-microscopy with FDA staining was optimised by using acid-alcohol wash to replace NaOH centrifuge decontamination, making smears from only 1 drop of sputum to facilitate visualisation and quenching with potassium permanganate for 30 seconds. Applying phenol to increase biosafety did not impair microscopy.

This FDA protocol is recommended for viability microscopy.
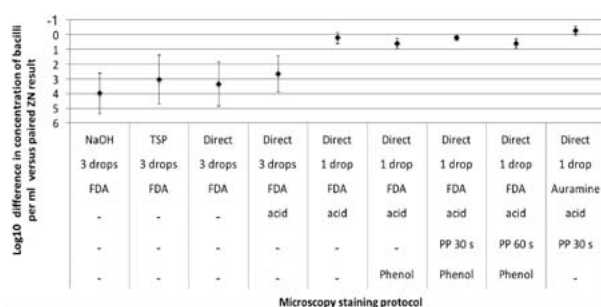
Figure Error bars indicate 95% confidence intervals

PD-840-13 Relationship of clinical diagnosis with final Xpert report in patients at Nuevo Civil Hospital, Guadalajara, Mexico

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Background: The accurate diagnosis of the patient with TB is a key strategy for the global control of the disease. The GeneXpert MTB / RIF assay has been shown a high sensitivity and specificity for the detection of *M. tuberculosis*.

The objective of this study is to know the relationship of the clinical diagnosis in the submission request with the final report of the assay of patients under study with suspected TB.

Methods: Retrospective study in the period 2012-2015 in 505 hospitalized patients with suspected pulmonary (PTB) and extra-pulmonary TB (EPTB). Clinical diagnosis of the patients was reviewed on the submission request as well as the final report of the assay. Statistical analysis was performed using the X^2 and Cohen´s Kappa coefficient.

Results: The assay was positive for TB diagnosis in 85/505 (16.8%) patients, 43 (51%) with PTB and 42 (49%) EPTB, resistance to rifampicin was detected in 7%, and 3/7 acid-fast staining were positive. Of the total number of patients, 195 (38.6%) had a clinical diagnosis of TB in the submission request, however only 74 (37.9%) were TB positive in the assay, and 310 (61.4%) were patients without a clinical diagnosis of TB in the submission request, of which 11 (4%) were TB positive. The X^2 was p< 0.05 and K= 0.444.

Conclusions: The relationship between the clinical diagnosis versus the TB final report of the assay showed a significant difference and a moderate concordance. It is necessary to strengthen the clinical, epidemiological and bacteriological study of patients under study with suspected TB and adopt an algorithm to optimize the use of the GeneXpert MTB / RIF assay to improved TB diagnosis.

PD-841-13 Programmatic implementation of new tuberculosis diagnostics in resource-poor-settings: what is the added performance characteristic value over microscopy?

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Background: Sputum smear microscopy has known limitations including a low and variable sensitivity. Culture method takes long with a total turnaround time and is not readily available in most settings. New rapid molecular tests are able to overcome many of the current operational difficulties in TB diagnosis. The performance characteristics of the new TB diagnostic tools were evaluated under programmatic conditions.

Methods: In total, 742 sputum specimens with known ZN microscopy were sent to the national reference Laboratory on which the performance characteristics of ZN microscopy and all new TB diagnostic tools to be implemented were calculated using LJ culture as reference standard methods.

Results: using ZN microscopy, 6.5% were positive for MTB at satellite sites. The MTB diagnostic yield of FM microscopy (8.2%), Xpert (11.9%) and MGIT (12, 1%) were higher than that for ZN microscopy. Overall, sensitivities of all the new TB diagnostic tools evaluated here were higher than ZN microscopy in sensitivity. LED FM and Xpert showed a 9 % (49.8%) and 17% (67.1%) relative increase in sensitivities respectively as compared to ZN microscopy. Similarly, the specificity (99.2%), PPV 94%), and NPV 99.2 %) of MGIT were higher than those of ZN microscopy. In contrast, the specificity, PPV and NPV of the LED FM (96.1%, 57%, and 95.5% re-

spectively) , Xpert (94.2%, 60.8%, and 95.5% respectively) were similar to that of ZN microscopy. Xpert sensitivity (71.4% vs. 50%) was significantly affected by HIV status.

Conclusions: Variable performance characteristics were observed while evaluating the impact of new diagnostic tools as compared to conventional direct ZN microscopy. Although Xpert MTB/RIF assay demonstrated incremental detection yield compared with conventional ZN microscopy, it demonstrated suboptimal sensitivity and excellent specificity as compared to culture.

PD-842-13 Comparison of randomized blinded rechecking for fluorescence light-emitting diode and Ziehl-Neelsen microscopy in three regions of Ethiopia

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Background and challenges to implementation: Randomized blinded re-checking (RBRC) as an external quality assurance (EQA) mechanism for Fluorescence light-emitting diode microscopy (FM) had not been widely recommended as the Auramine stain was thought to be prone to fading. Following a pilot in select regions in Ethiopia, the EQA guideline in Ethiopia was recently updated recommending RBRC for FM.
We present the RBRC result for FM and compare it with Ziehl Neelson (ZN) microscopy EQA in three regions of Ethiopia.
Intervention or response: Laboratories performing FM and ZN AFB microscopy stored slides in a slide box in dark place immediately after examination, a designated person collected sample slides by using Lot Quality Assurance Sampling (LQAS), EQA centers rechecked all slides carefully and sent final feedback to the peripheral laboratories. A monitoring tool was devised and is completed on a quarterly basis at EQA centers and later compiled by the Regional Laboratory.
Results and lessons learnt: A total of 1066 health facilities were covered with RBRC EQA during the quarter, out of which 984 used ZN microscopy. The percentage agreement of positive slides and negative slides for FM RBRC was 97.8% % and 99.9%, respectively, whereas the corresponding percentage agreement during the same reporting period for the conventional Ziehl Neelson (ZN) was 96% and 98.8%. About 98.8% of health facilities reported ≥95% concordant result with those of EQA centers for FM which is close to the 97.1% for ZN.

Indicators	LED RBRC	ZN RBRC	P-value
# of slides evaluated (Positive slides/Negative slides)	4, 250 (162/4,088)	33,576 (1,828/31,748)	
(%) agreement of positive slides	97.8%	96%	
(%) agreement of negative slides	99.9%	98.8%	
#(%) of HFs with >95% concordance rate	81 (98.8%)	955 (97.1)	<0.05

Table 1 Fluorescent microscopy and Ziehl Neelson

Conclusions and key recommendations: The agreements of slide results and concordance rates for FM RBRC are close to the conventional ZN RBRC in the three regions. The comparison of FM RBRC with that of ZN was helpful in understanding the successful implementation of the newly expanded FM microscopy RBRC.

PD-843-13 Two years after the roll-out of Xpert® MTB/RIF in Brazil: reported errors

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Background: The monitoring of the health services network allows the realization of a situational diagnosis, subsidizing the planning of actions. Errors are a problem to Rapid Test Network for Tuberculosis in Brazil (RTR-TB) performance, as it causes the consumption of cartridges and samples, compromising the diagnosis of tuberculosis. The identification of errors allows the development of strategies to reduce costs, improving the timely diagnosis of the disease. This study aims to describe the errors reported in Rapid Molecular Testing for Tuberculosis (TRM-TB) equipment by the municipalities that make up the Rapid Test Network for Tuberculosis in Brazil (RTR-TB) after two years of rool out
Methods: For the monitoring of RTR-TB, the National Tuberculosis Programme consolidates monthly the production reported by the states monitors through FormSUS. In order to calculate the percentages of errors, the municipalities were organized by time of implantation of the machine in months.
Results: In the first month of implantation, the error´s rate was 3.9%, declining smoothly during the first year, to its lowest value (1.9%) in the ninth month. Since then, the number of errors returns to increase, and during the second year, fluctuating in values greater than those reported at the end of the previous year. In the 17th month there were 4% of errors, being the highest value reported until then. The most frequent type of error was the 5007 (probe check failure), representing 40-70% of the total errors in the last 14 months of the series.
Conclusions: We highlight the increase in the percentage of errors at the end of the series, since it was expected a stabilization after a time of handling with the equipment, in view of a better skill to perform the tests. Although the increase was observed, this were close to the manufacturer´s estimate (4.15%).

PD-844-13 Innovations in Kyrgyzstan: TB sputum transport solutions

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Background and challenges to implementation: In the Kyrgyz Republic no formal system exists for the proper transportation of sputum for TB patients. Delivery of biological samples is done by medical workers using public transport, or by patients and their relatives, potentially risking infection of others. Before the project, all MDR patients themselves delivered sputum samples to TB laboratory, increasing the risk of MDR spreading in the community. Also, only 15% of sputum specimens from suspected TB patients and drug-sensitive TB patients were delivered by medical health care workers, and the rest samples were delivered by patients or their relatives. All delivery cases were without proper storage conditions of biological samples. The need for consistent quality sputum transportation is essential as the country transitions to a predominantly outpatient treatment model.

Intervention or response: Project HOPE is piloting an innovative sputum transport model in the Sokuluk District of Chui Oblast in the Kyrgyz Republic. The model includes a network of private transportation companies trained and certified to carry medical products, and communications software to coordinate rapid sample collection by available vehicles from health facilities and delivery to testing laboratories. Operating procedures were established, training of drivers and health care workers on protocols was completed, and new medical transport containers for bacteriological samples were provided. Now sputum transportation is conducted in accordance with international recommendations for infectious materials.

Results and lessons learnt: From November 2016 to April 2017, 85% of sputum specimens from suspected TB patients and drug-sensitive TB patients, as well as 54% of sputum smear samples of MDR patients were collected, packaged and delivered in accordance with the requirements of quality laboratory management and infection control.

Conclusions and key recommendations: The implementation of this innovative model will create a system for the transport of biological samples in compliance with the proper conditions for storage and transportation of sputum and the requirements of infection control on PHC level.

39. Searching high searching low: case finding strategies

PD-845-13 Outcome of intensified case finding for tuberculosis case detection in Munuki and Kator primary health care centres

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Background: Tuberculosis (TB) case detection using intensified case finding (ICF) is one of the cornerstone strategies of the Challenge TB (CTB) project. CTB South Sudan implemented ICF in addition in Munuki and Kator primary health care centers in June 2016 using community volunteers and home health promoters (HHPs) affiliated with the CTB subcontracted community based organization, AIDS Resistance Trust (ART). HHPs routinely screen patients for TB symptoms following the provision of health education. The purpose of this study was to determine the effect of ICF on TB case detection at two health centers in Juba South Sudan.

Methods: Presumptive TB cases were investigated using smear microscopy. Referrals by HHPs were clearly indicated in TB clinic and laboratory registers. A comparison was done on the yield of TB cases between June-December 2016 (when ICF was implemented) to June-December 2015 (before ICF was implemented and passive case finding was the primary method used).

Results: Between June and December 2016, 331 presumptive TB cases were identified and referred by HHPs; out of which 127 (38%) were diagnosed with TB and put on treatment.

Similarly, between June-December 2015 (before ART engaged in ICF) and June-December 2016 (when ART engaged in ICF), TB case detection increased from 544 to 835 (53%) new cases, of which 127 (15%) were referred by HHPs. This is the first year HHPs have existed in South Sudan.

Conclusions: ART's implementation of ICF in Munuki and Kator PHCCs has resulted in an increase in TB case detection with HHPs contribution of 15% of all cases identified. The ICF approach of increasing case detection has been recognized by the Ministry of Health and was recommended as one of the best initiatives to spearhead the rolling out of its Boma Health Initiative strategy.

PD-846-13 Yield of repeat intensified tuberculosis case finding among HIV-infected adults in Uganda

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Background: Intensified case finding (ICF) is recommended for all PLHIV at every clinic visit. Previously, we demonstrated that ICF has similar yield but would require half as many Xpert MTB/RIF confirmatory tests if TB screening were based on point-of-care C-reactive protein (POC CRP) levels instead of symptoms. Here, we compare the same ICF strategies when repeated at 3 months.
Methods: The parent study enrolled consecutive adults with CD4 $\leq$350 cells/uL initiating ART from two HIV clinics in Uganda. For this analysis, we included patients who were not treated for TB after baseline ICF and completed 3-month follow-up. We repeated symptom screening, POC CRP measurement (normal < 10 mg/L), and sputum collection for Xpert and liquid culture. We assessed the diagnostic accuracy of all tests in reference to culture, and compared the diagnostic yield (i.e., proportion of TB cases detected) and the number needed to test (NNT) using Xpert to detect one TB case when ICF was done using symptom- vs. POC CRP-based TB screening.
Results: Of 424 patients, 13 (3%) had culture-confirmed TB. Symptom-based and POC CRP-based screening was positive in 7 and 6 TB patients (sensitivity 54% [95% CI: 25-81] vs. 46% [95% CI: 19-75]; difference -8%, p=1.0), respectively, and negative in 267 and 350 non-TB patients (specificity 65% [95% CI: 60-70] vs. 85% [95% CI 82-89]; difference +20%, p< 0.001), respectively. Xpert was positive in 3/13 TB patients (sensitivity 23%, 95% CI: 5-54) and negative in 410/411 non-TB patients (specificity 99%, 95% CI: 99-100). ICF had similar diagnostic yield with POC CRP- vs. symptom-based TB screening (15% vs. 23%, p=0.17), but required fewer Xpert tests per case detected (22 vs. 76).

Total (N =424)	ICF strategy		% Difference (95% CI)	p-value of the difference
	WHO symptom screen + Xpert (N=151)	POC CRP + Xpert (N=66)		
# TB cases detected	2	3	--	--
Diagnostic yield (%, 95% CI)	15% (2-45)	23% (5-54)	+8% (-4 to +19)	0.17
NNT using Xpert	76	22	--	--

Abbreviations: TB (tuberculosis); WHO (World Health Organization); POC CRP (point-of-care C-reactive protein); NNT (number needed to test).
Legend: Diagnostic yield is the number of TB cases detected by an ICF strategy divided by the total number of all culture-confirmed TB cases (n=13). NNT is the number needed to test using Xpert to detect one case of active TB.

Table 1 Diagnostic yield and NNT by ICF strategy

Conclusions: Current tools for TB screening and confirmatory testing had insufficient sensitivity when ICF is repeated at 3 months. PLHIV should undergo ICF at greater than 3-month intervals.

PD-847-13 Strengthening efforts in contact-screening of drug-resistant TB patients will break the chain of transmission of infection in children

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Background: Childhood TB is a reflection of extent of transmission of infection in community. Globally, approximately 1million children are estimated to develop tuberculosis annually, of which only 36% are notified. India has one of the highest drug-resistant tuberculosis (DR-TB) burden, accounting for 22% of global burden (Global TB Report 2016). While burden of childhood TB in India is not known, regional data from World Health Organization (WHO) indicate that sputum-microscopy smear-positive Paediatric TB accounts for 0.6%-3.6% of all reported cases.
Methods: A retrospective analysis was undertaken to understand the routes of transmission of infection amongst Paediatric DR-TB patients, using record-reviews and in-depth discussions with healthcare providers. Narrative analysis was used to document qualitative information.
Results: During 2011-2016, 6087 DR-TB patients were diagnosed in public sector in Madhya Pradesh (MP), of which 84% (5113 patients) were initiated on treatment. Average delay in treatment initiation is 120-days and median delay is 18-days. A substantial proportion of these patients transmit the infection to children in their close contacts, increasing burden of Paediatric DR-TB. Approximately 4% DR-TB patients (183 patients) diagnosed and initiated on treatment in public sector, belong to Paediatric age-group. In-depth discussions with healthcare providers revealed sub-optimal field-level efforts, with respect to contact-screening of TB patients, particularly in remote rural locations. However, analysis shows 30% Paediatric DR-TB patients (54 patients) were identified through contacts, indicating the need for best possible field-level efforts in Paediatric case-finding. About 31% Paediatric DR-TB patients are HIV-positive (100% patients tested for HIV). DR-TB exposure was also associated with increased odds of TB-infection and HIV-status (OR: 0.60; 95% CI: 0.1-3.5).
Conclusions: Results indicate strengthening of current efforts on contact-screening at field-level. Delayed TB treatment also poses higher risk of transmission of infection in child contacts and hence the need for strengthening counselling on timely treatment initiation, adherence to treatment and cough etiquettes.

PD-848-13 Assessing routine screening of pediatric contacts of adults with tuberculosis disease, Tanzania

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Background: The World Health Organization recommends screening close contacts of adults with tuberculosis (TB) disease as a strategy to identify children with TB disease and those who should receive isoniazid preventive therapy (IPT). This strategy was adopted by Tanzania's National TB and Leprosy Program in 2008. As part of a retrospective, mixed-methods program evaluation of pediatric TB services, we assessed implementation of this strategy.

Methods: We conducted brief interviews with sputum smear-positive adults who were receiving treatment for TB in 10 health facilities selected by convenience sampling in five high TB burden regions of Tanzania from March to April 2016. Consented adults were asked whether any children living in their household currently or within three months of TB symptom onset had been assessed for signs/symptoms of TB. Percentages and confidence intervals were estimated using SAS PROC SURVEYFREQ, with variances estimated controlling for clustering within clinics.

Results: During the program evaluation period, 183 smear-positive adults were interviewed, and reported having 400 children living in their households, with detailed information obtained for 378 (94.5%). The median age was 8 (interquartile range, 5-12) years; nearly half (182; 48.3%) were female. Only 34 (9.0%, 95% CI: 3.3-14.7) were clinically assessed for TB, and of these, 5 (14.7%, 95% CI: 2.6-26.8) were diagnosed with TB. Of the 29 not diagnosed with TB, 18 started on IPT (62.1%, 95% CI: 22.9- 100.0). Participants reported whether child contacts were tested for HIV for 348 (90.5%) children, with 59 reported as tested (17.0%, 95% CI: 10.9-23.0) and one testing positive (1.7%, 95% CI: 0.0-5.9).

Conclusions: We identified substantial gaps in the implementation of TB screening, IPT provision, and HIV testing for pediatric contacts of adults with smear-positive TB in Tanzania. Systematic efforts, including introducing job aids and reporting tools, may assist with improving implementation of contact screening.

PD-849-13 Yield of intensified TB case finding among HIV patients at Yunnan AIDS Care Center, Kunming, China

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Background and challenges to implementation: Yunnan province in southwest China reports one of the higher rates of HIV within China. The Yunnan Aids Care Center (YACC) is the provincial referral hospital for people living with HIV (PLHIV). The USAID CAP-TB Project has supported YACC for three years, with one priority to improve early diagnosis of TB among PLHIV.

Intervention or response: An intensified TB case finding (ICF) algorithm was piloted at the YACC using clinical questions (fever, cough, night sweats, weight loss and being a TB contact) for screening followed by sputum smear/culture, radiology, culture and Xpert® MTB/RIF. Data collection was based on routine reporting from the hospital registers among PLHIV evaluated for any reason during 21 months (December 2014 to September 2016).

Results and lessons learnt: All patients (N=1501) were screened for TB with 41.6% having at least one of four risk factors, plus 11.2% of patients with previous history of TB. All patients with positive screening and previous history of TB then underwent further TB investigation: sputum smear (771), sputum culture (330), CT scan (1257) and Genexpert (190 pulmonary and extrapulmonary samples). TB was diagnosed in 328 patients (21.85%). CT scans were abnormal in 908 patients and yielded the highest number of diagnoses (265 pulmonary TB [21.08%] and 34 extrapulmonary [2.7%]). Sputum smears were positive in 53 patients (6.87%); Genexpert was positive in 48 patients (25.26%) and culture positive in 28 patients (8.48%). CD4 counts were very low (median 132, IQR 42-285), and there was a high rate of extrapulmonary (44 cases, 13% of the cohort) and disseminated TB (98 cases [29.87%]).

Conclusions and key recommendations: This was the first large scale ICF protocol implemented in this high burden TB-HIV site in China, and it was an effective strategy to increase the diagnosis of TB, including extrapulmonary and disseminated cases. This strategy could be replicated in other sites.

PD-850-13 Contribution of community health volunteers in TB case finding in Kenya

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Background: In Kenya, In order to find TB patients early in the course of their illness, Community Health Volunteers (CHVs) have been sensitised to carry out intensified case finding by referring TB presumptive cases and contacts of smear positive patients. The proportion of patients referred by CHVs has remained constant at 4% for several years. There is a possibility that some of these referrals are not documented hence the effort of this strategy might not be well measured. The findings will show the true reflection of CHVs contribution in TB case finding through referral of TB presumptive cases.

Methods: This was a cross-sectional study where patients were administered questionnaires on exit during TB clinic days

Results: The proportion of patients who received health education from CHVs was 41% out of which 74% of them received TB related health education. The proportion of patients who reported that they were referred by CHVs was 16% out of which 64% were recorded as self-referral in the TB facility register. Only 33% of patients refereed by CHVs were given referral document to present to the health facility. The first contact of most (75%) patients referred by CHVs from the community is outpatient department. Only 17% of them have TB clinic as their first contact

Conclusions: The findings of the study showed that the CHVs are playing a big role in TB case finding but the main gaps are; Lack of Community referral forms and HCWs not documenting the work done by the CHVs at the community.

PD-851-13 Does improving facility-community linkage help in finding cases in the community? Documenting efforts in areas with low case notification

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Background and challenges to implementation: Strong coalition with Civil Society Organizations (CSOs) and communities is one of the overarching principles towards ending tuberculosis. Amref Health Africa in Kenya is implementing community TB through 29 CSOs in the Global Fund project covering 33 counties.

According to the Strategic Plan 2015 - 2018, 16 out of the 47 counties reported case notification of below 175 per 100,000 populations based on 2012 data. The role of Community Health Volunteers (CHVs) and CSOs in the project is to improve case finding through referrals. The challenge has been ensuring referrals from the community get to the health facility.

Intervention or response: Project was implemented between April to December 2016. 80 facilities were identified among 856 that reported in 2014 in 16 counties. Activities including community screening and referrals, outreaches and support of 10 laboratory technologists were implemented. To ensure clients referred reached the health facility, 80 lead CHVs were stationed in the facilities to receive and guide the referred clients. CHVs received 50 USD per month.

Results and lessons learnt: CHVs documented 4,024 referrals from the community in the 80 facilities. Cases notified from the community were 4409 (5%) and 4828 (7%) in 2015 and 2016 respectively showing 2% increase compared to 15% (1031 to 1871) increase among 16 counties. In the remaining 31 counties there was 7% increase among 17 counties where the project was implementing and a decrease of 23% in the 14 counties where there was no implementation. 80 targeted facilities reported an increase of 9% compared to the rest of the facilities in the 16 counties which reported an increase of 6%. Optimal use level one structures will improve case finding. Targeted activities should be scaled up to reduce disparities between counties in terms of case detection.

Conclusions and key recommendations: The Ministry of Health should continue to empower CHVs to improve facility community linkages.

PD-852-13 Door-to-door active TB Case Finding (ACF) increased TB case notification, shortened diagnostic delay and put patients on early treatment in Rajnandgaon district, Chhattisgarh

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Background and challenges to implementation: TB is a major public health problem in India with 1/4th of the global burden where 2.2 million of 9.6 million new cases occur annually. While the routine TB services are essential for case management, it has proved inadequate to address the estimated 3 million incidence cases among the high-risk poor and vulnerable populations where TB often concentrates.

Rajnandgaon is one among the 50 high TB burden and low detection districts of the 17 provinces in India selected to be involved in the National ACF Campaign to

screen with a target for *TB symptoms populations: 120 million, conduct sputum examination of symptomatic: 6 million, and find & treat additional infectious TB patients: 0.3 million.*

Intervention or response: Considering TB screening as a dynamic and innovative process among these low-detected-vulnerable-communities, Rajnandgaon district launched the provider-driven-ACF-initiative in its tribal and unreached pockets including the slum populations. District level planning involving key officials was made to map/identify vulnerable areas & Key-Affected-Populations. Systematic active TB screening through house visits among the slum, prison inmates, orphanages, school hostel/tribal-residential-schools, unreached villages, stone-crusher-units and PLHIVs was carried out for 73,223 populations by trained &dedicated 46 Medical Officers, 86 health-care-staffs, 10 local NGOs and 160 community-volunteers.

Results and lessons learnt: Of 74,834 contacts, 73,223 (98%) were reached. 43 NSP TB cases were diagnosed from sputum examination of 847 cases against sputum referral/collected & transported of 912 among 73,223 targeted populations in January 2017. Cohort analysis (previous year) shows an increase of 12% in referral, 9% sputum examination and 16% case notification. Few suspects identified through ACF refused care.

Conclusions and key recommendations: Planned ACF intervention has improved TB case detection, shortened the diagnostic delay, and successfully brought patients into care in the targeted populations.

The effects of a successful ACF program will be sustainable if Passive Case Finding is strengthened. However, evidence to suggest its benefits are yet to fully mature.

PD-853-13 Innovative strategies towards improving TB case detection amidst economic recession: Zamfara State Experience, North Western, Nigeria

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Background and challenges to implementation: Tuberculosis remains a serious life threatening but curable illness in Zamfara State to men, women and children. Diagnosis rely on passive case detection using sputum smear microscopy which is available in 88 sites. There are estimated 14,830 cases based on Case detection rate of 338 per 100,000 in 2016 out of which only 2,041 were detected and notified by the State leaving 12,789 missed cases which are either not diagnosed or diagnosed but

not reported. This calls for innovative strategies towards detecting more TB cases.

Intervention or response: Gap and route -cause analysis was done by State TB team where issues related to under-reporting, low community awareness, inadequate DOTS and Microscopic sites were identified as contributory factors to missed opportunities. Strategy adopted involved sensitization of traditional and religious leaders, strategic expansion and creation of additional 21 AFB microscopic and 5 DOTS sites as well as data verification/validation during quarterly review meeting with TBLS. The uptake of TB case findings before and after the 12 months strategy implementation was compared.

Results and lessons learnt: Case notification rate increased from 41.1 per 100,000 in Quarter 4, 2015 to 51.5 per 100,000 in Quarter 4, 2016.

Conclusions and key recommendations: There is a significant improvement in the number of detected TB cases. Such innovative approaches could be adopted in other states with low case findings. Further studies are required to evaluate its cost effectiveness.

PD-854-13 Working together to end TB through active case finding in Swaziland: 'The SDG aspiration of leaving no-one behind'

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Background and challenges to implementation: Swaziland has experienced a progressive decline in TB case detection since 2010. This prompted the Government of the Kingdom of Swaziland through the National TB Control Program to envisage the introduction of a strategy to increase case detection/notification by conducting active TB screening at community level through the engagement of 369 community appointed Active Case Finders in each Chiefdoms all over the country.

This paradigm shifts from health facility- based passive case finding to community- based active finding was necessary to ensure cases who might be missed are identified, diagnosed and initiated on TB treatment early. Systematic screening for active TB targeting high risk populations with limited access to health services is inprogress since June 2016. The purpose of this study is to share experiences and lessons learnt during the planning phase for implementing the ACF strategy in Swaziland.

Intervention or response: A community-based ACF strategic document as framework was developed. Top to

bottom sensitization process was implemented with different stakeholders indicating the purpose of the strategy. In-depth interviews were held with Regional Health Administrators (RHAs) to get their inputs. The RHAs consulted Regional Health Management Teams who sensitised facility nurses. Thereafter, the NTCP conducted focus group discussions eliciting Chiefs' views. Subsequently, the chiefs conducted community awareness campaigns and identified candidates who conducts door-to-door TB screening in communities.

Results and lessons learnt: Traditional leaders contributed on the successful introduction of ACF strategy. Community health intervention planning is cumbersome as different players have to be engaged for acceptance and ownership of the program.

Conclusions and key recommendations: Community involvement and participation cascading to grass- root level is important for successful implementation of community-based programs.

40. Advocacy, communication and social mobilisation for TB elimination; involving gender, children, peer educators, and civil society organisations

PD-855-13 Can engagement of rural health care providers in under-served areas of India make a difference in TB care and control?

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Background and challenges to implementation: Contextually 3 diverse sites with poor performance (TB symptomatic referral < 100/100,000 and notification rate < 135/100,000 as per Q1 2012 report) were selected for intervention on involvement of Rural Health Care Providers (RHCPs) in promoting TB care and control in India. Selected districts were Khunti (Jharkhand), Alirajpur (Madhya Pradesh) and Ghazipur in (Uttar Pradesh). Target population was 5,11,400 (1660 villages) in selected districts which are under-served areas.

Intervention or response: Training of RHCPs was initiated in Q2 2013 followed by referrals by trained RHCPs. Training of RHCPs was done through local NGO partners.. These RHCPs refer presumptive TB patients to DMCs. Referral increase at DMCs monitored using before and after analysis. Mobile application was also used by RHCPs for referrals and tracking symptomatics. These RHCPs are considered engaged if they refer 2-3 symptomatics per month or do sputum collection & transport or act as DOTs providers.

Results and lessons learnt: 634 RHCPs were trained in three sites. Cumulatively (Apr2013- Sept 2016) 6842 TB symptomatics were referred of which 5276 (78%) were tested and 630 were diagnosed with TB. DMC wise data from sites analysed to examine the changes in key indicators: referral of TB symptomatics & smear positive TB patients diagnosed of those referred. The percentage increase in referral in Q3 2016 from baseline Q3 2012 is 88% at Alirajpur, 61% at Khunti and 65% at Ghazipur. Comparative analysis of referrals during Q3 2016 with baseline Q3 2012 shows a significant increase in all the three projects districts.
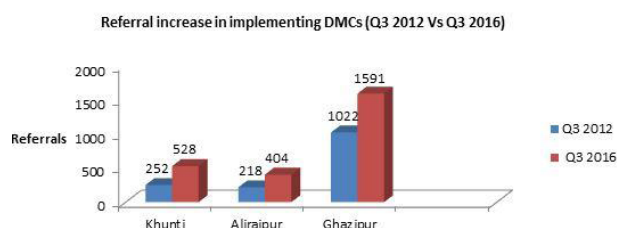
Figure Comparative Analysis of Referrals

Conclusions and key recommendations: RHCPs whose contribution to project was almost nil at beginning has increased significantly in both referrals of TB symptomatics (25%) and smear positive TB patients (21%). This assists in early diagnosis and treatment of TB patients who visit RHCPs in under-served areas for primary healthcare. Thus RHCPs can become good linkages between national TB control programme & community.

PD-856-13 Assessing point of sale violations in Delhi for strategic advocacy on TAPS ban

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Background and challenges to implementation: The Rules banning Point of Sale (PoS) Advertising under COTPA 2003 were stayed by Bombay High Court in 2005-6 and the Government of India did not make any particular efforts to get the stay vacated. In July 2013, in the matter of HFM Trust v/s Union of India and Ors., the Supreme Court vacated the stay on PoS and directed the Government of India to rigorously implement the Rules. The Health Ministry issued necessary directives to the State Governments to ensure steps are taken to curb PoS violations. One year after the stay was vacated, VHAI decided to conduct a survey in January 2014 to assess status of PoS compliance in Delhi.

Intervention or response: Study objectives were to understand the actual status of PoS Rules; analyze reasons for failure to compliance, if any; methods and strategies of PoS advertising and whether minors have easy access to products. The sample size was 50 shops chosen from each city zone, with a total of 250 shops/outlets and the methodology involved Observations and Questionnaire.

Results and lessons learnt: 96.4% shops displayed PoS tobacco advertisements in varied forms. Implementation was found to be weak & ineffective. All major brands of smoking and smokeless tobacco were being advertised at points of sale. 60.8% shops did not have the top front board as specified. 50.4% boards had health warning but alongside other promotional messages, brand designs (only 36 shops had a warning board as per specifications) 94.4% shops had tobacco product display, visible and accessible to minors.

Conclusions and key recommendations: Urgent steps are required for effective implementation of PoS Rules across India as the industry despite a court order is using points of sale to advertise tobacco products through incentives and There should be strict checks to ban sale to minors.

PD-857-13 Gender disparities in timely access to tuberculosis treatment in Viet Nam and Malawi

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Background: Men have a higher epidemiological burden of tuberculosis (TB) than women, yet contradictory data exist on gender differences in timely access to care, with women tending to self-report longer treatment delays despite prevalence-to-notification (P:N) ratios being higher among men.

Methods: We explored the compatibility of these two measures of treatment delay with prevalence survey results and case notification data for smear-positive pulmonary TB in Viet Nam and Malawi. Using a simple compartmental model, we employed a Bayesian approach to explore how prior beliefs about treatment delay should be adapted in light of epidemiological data on burden of disease.

Results: Both men and women face long periods of untreated TB disease, but delays were approximately a year longer for men in both Viet Nam and Malawi, regardless of which prior beliefs were held. Self-reports of time to treatment initiation did not fit epidemiological data and were revised substantially upward for both men and women in posterior estimates (from median 0.09 to 2.10 years and 0.11 to 1.02 years for Vietnamese men and women, respectively, and from median 0.22 to 2.90 years and 0.23 to 1.95 years for Malawian men and women, respectively). P:N ratios provided a more appropriate measure of gender differences in treatment delays.

Conclusions: Self-reported symptom duration prior to treatment provides a poor proxy for duration of smear-positivity in both genders, especially for men. The long duration of untreated disease estimated here implies inadequate coverage of current case finding strategies. These data support systematic targeting of men for screening, and better understanding of gender-specific barriers faced by men, a high prevalence sub-group less likely than women to access timely treatment.

PD-858-13 Indonesia peer educator programme: from patient to champion

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Background and challenges to implementation: The number of diagnosed MDR-TB patients is increasing in Indonesia. But, despite the scale-up to all provinces and treatment satellites, access to treatment is not yet universal. In 2016, 2163 patients were diagnosed with MDR TB but only 1541 (71%) patients were enrolled. Even if patients enroll, treatment results are disappointing: from the 2014 MDR cohort, only 51% was successfully treated and over 27% interrupted their treatment. This indicates the need for psychosocial-economic support for MDR-TB patients, in combination with increased education.

Intervention or response: In 2012, we trained MDR-TB patients who were in the continuation phase of treatment as peer educators and patient supporters. Criteria were that they had sputum converted, had good communication skills and were willing to work voluntarily. We established peer educator groups, advocated and disseminated the concept of peer educator support to the health care facilities and other relevant services for network establishment.

Results and lessons learnt: Over the period 2012-2016, a total of 145 peer educators were trained and linked to 8 MDR treatment sites. Improved patient adherence was observed, with 85% of patients who were supported by peer educators successfully treated; 65% of patients who were lossed to follow up returned to treatment after peer educators' visit. In addition, the national TB patient network (established by the 8 groups as a network of TB patient organizations) is invited to national policy review and planning meetings, giving TB patients an effective voice at policy level.

Conclusions and key recommendations: In a short time, the peer educator groups in Indonesia have shown their usefulness and now fulfil an important role in enabling successful treatment of MDR TB, as well as being advocates for (MDR) TB patients in decision making forums. The model could be expanded to other vulnerable groups of TB patients at risk of treatment interruption, to prevent suffering and the occurrence of resistance.

PD-859-13 Intensified outreach activities through Prachar Rath on PULSE TB: KHOJ-JANCH-NIDAAN-ABHIYAAN 2016 logo to reach out to the missing-one-million-TB-cases of India succeeded in Korba District, Chhattisgarh

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Background and challenges to implementation: With some 2 million new cases of TB yearly, India bears the highest burden of TB, DRTB and TB-HIV co-infected cases globally. TB in India is a multi-sectoral and multi-level public health problem. Marked observation of reduced interest in Advocacy Communication Social Mobilisation approaches among the health sector stakeholders is a concerning area.

Of the three million missing tuberculosis cases, one million are estimated to be in India. Despite the availability of a robust RNTCP/DOTS services across the country, many cases are being missed due to *Access Barriers/information*. Korba district misses >50% such cases annually.

Intervention or response: Intensified-outreach-activities through Prachar-Rath (PR): Jeep-with-ACSM-filled-TB-messages were carried out in the district on *"PULSE TB: KHOJ, JANCH, NIDAAN ABHIYAAN 2016" (active search, sputum examination, diagnosis)* logo/banner. Coveted 12 such PRs with life-size flex and colloquial audio/messages reached Korba's 978 villages/wards/slums during 2016. Conducting door-to-door visits, trained-team-members reached 236,364 households including marginalized-and-vulnerable-populations who disseminated relevant information about tuberculosis, its signs and symptoms, diagnosis, treatment and TB services to the household members. In the process, the volunteers identified presumptive TB cases and motivated them to get their sputum tested at the nearest Designated-Microscopic-Centre (DMC).

Results and lessons learnt: 6,276 identified TB suspects examined sputum (reached the DMC through referral and sputum-collection&transport) out of which 179 diagnosed as TB patients during 4q2016 period. 147 NSPs, 14 NSNs, 15 EPs and 3 SPRTs cases as categorized were put on DOTS. An increase of 6% sputum examination and 17% case notification achieved. 65254 students of 760 schools contributed 2,064 presumptive cases in this drive.

Conclusions and key recommendations: 179 missed cases found/retrieved. Planned and intensified ACSM/outreach activities have proved to be effective in *reaching-out-to-the-missing-many*. Periodic drives of such activities are encouraged to conduct on priority basis to reach out to every community member of the district by disseminating the key message of *"a TB test, treatment and cure for all"*.

PD-860-13 Political leadership in TB control: learning from the Zimbabwe experience

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Background and challenges to implementation: Policy makers are key opinion leaders and strong advocates who can make government honor its commitment. To ensure political commitment and leadership in the national TB response, Zimbabwe has prioritized engaging parliament to support the TB program's efforts through raising awareness about TB and advocating for increased domestic funding.

Intervention or response: The intervention focused on strengthening TB platforms by the National TB programme through dialogue with 30 members of the parliamentary portfolio committee on health and child care to sensitize them about the TB program, its achievements and gaps which were impeding full implementation of the program.

Results and lessons learnt: Initial engagement in 2015 resulted in 137 (33%) out of 350 members of parliament signing the Barcelona declaration as a commitment to put TB on the national and political agenda. A motion advocating for increased TB financing was also presented in parliament. The second engagement in 2016 saw the establishment of a national TB caucus which resulted in Zimbabwe being elected to Co-chair the African regional caucus on TB. In the third engagement in 2017, 13 members of the portfolio committee took public TB, HIV and diabetes screening during the World TB Day commemorations. The parliamentarians have pledged to continue supporting the TB response through; budget monitoring of government's allocation to health, engaging the ministry of finance to increase allocation towards TB; raising awareness and encouraging TB screening in their constituencies and providing social support to TB patients who do not have vital registration documents to enable commencement of treatment (birth certificates and national identity).

Conclusions and key recommendations: Having dialogue with parliamentarians has put TB on the political agenda as more parliamentarians are participating in TB activities and being champions of TB in Zimbabwe. Further collaborations with the civil societies and with the National AIDS Council will make an even stronger force for political commitment and support.

PD-861-13 Public Interest Litigation as a tool for advancement of tobacco control, particularly a ban on Gutka

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Background and challenges to implementation: In India, the Judiciary has played a major role in both shaping tobacco control legislation and its implementation by constantly reminding the government to take appropriate measures for banning, regulating tobacco products in the country. Faced with deceptive industry tactics and weak enforcement of tobacco control laws, civil society has effectively used Public Interest Litigation (PIL) to secure path breaking judgments such as Smoke Free Law, Graphic Health Warnings, Point of Sale and Gutka Ban. VHAI has been consistently advocating against the deceitful advertising and marketing tactics of the smokeless tobacco industry which lures children and youth by selling cheap, smokeless tobacco variants in sachets. In the case Miraj Products Private Limited versus Indian Asthma Care Society, The High Court of State of Rajasthan in August 2007 gave its judgment against the manufacturers of gutka, tobacco and pan masala on the basis of "Pollutor Pays Principle". This order was challenged before the Supreme Court of India by the gutka company, Ankur Gutka.

Intervention or response:
• Health for Millions (HFM) Trust and three cancer patients filed an intervener application seeking a ban on plastic pouches on environmental grounds as plastic pouches are hazardous waste.
• The Hon`ble Supreme Court declared a ban on sale of gutka, tobacco and pan masala in plastic sachets from 1st March, 2011. The Supreme Court also directed to ban Gutka as per the Food Safety and Standard Authority of India law 2.3.4

Results and lessons learnt: All 29 States of India banned gutka and pan masala (containing tobacco and nicotine) and some States have also banned other forms of smokeless tobacco, i.e., flavoured chewing tobacco zarda, khaini etc,.

Conclusions and key recommendations: The support of the judiciary therefore has been phenomenal in the ongoing civil society campaign to control tobacco.

PD-862-13 Peer-support services for XDR-TB patients in group 5 drug treatment and adherence facilitation

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Background and challenges to implementation: In Romania most of XDR-TB patients receive proper treatment because implementing projects funded by Global Fund and Norwegian Financial Mechanism. ASPTMR in partnership with LHL International Tuberculosis Foundation implemented a project, funded by Norwegian Financial Mechanism and one of activity was to provide peer-support to XDR-TB patients who receive medicines from Group 5, in order to help them to be adherent to the treatment. XDR-TB patients have to cope with many challenges because of drugs side effects, treatment length, comorbidities like HIV, IDU, psychiatric deseases, C hepatitis.

Intervention or response: Between 1 May 2016 and 31 March 2017, 2 psychologists and 2 social workers evaluated 78 patients, using the same instruments, in order to identify their psychological and social needs and to recommend the proper psychological and social interventions. There were created a peer-supporters network made from volunteers, ex-TB patients and people who had TB patients in their family. They provided support services on the phone and collaborate closely with the professionals care team.

Results and lessons learnt: 78 XDR-TB patients evaluated received proper medical treatment from Group 5, psychological support, social support and peer-support. 4 of them died during the treatment, 5 were non-adherent, 69 were adherent.

We found out TB patients are more open to the peer-supporters and we managed to identify most of their needs and to respond to most of those interfering with their treatment needs.

We were able to identify many NTP challenges.

We were able to create an working model of peer-supporters network for TB patients.

Conclusions and key recommendations: A multi-disciplinary team composed by TB medical staff, mental health workers, social workers and patients´ NGO is the best answer for TB patients from Romania.

Romanian health legislation, work legislation and social protection needs improvement in order to decrease the TB burden and facilitate TB patients access to screening, treatment, social inclusion and relapse/resistance prevention.

PD-863-13 Establishing a community engagement programme: a product development partnership experience

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Background: Community Engagement (CE) is the meaningful involvement of community stakeholders in the research process. CE has been successfully implemented in HIV prevention and TB drug trials. In 2014 Aeras set out to initiate a CE programme for its TB vaccine trials. The approach taken is presented here as a case study.

Methods: 1) Information gathering. Extensive consultations with stakeholders were conducted to gather information on current CE practices and identify gaps. These stakeholders included trial sites, community members, AVAC (Global Advocacy for HIV Prevention), the TB Alliance, HVTN (HIV Vaccine Trials Network), TAG (Treatment Action Group), IPM (International Partnership for Microbicides), and IAVI (International AIDS Vaccine Initiative).

2) Analysis of gathered information. Gathered information was reviewed by Aeras staff to determine the most suitable approaches for the development of effective CE programmes and any TB vaccine specific CE requirements.

3) Establishing the CE programme and addressing gaps. The CE programme was established and integrated into trial conduct at Aeras based on the findings. Key activities included developing TB vaccine research literacy materials, a train-the-trainer programme, an adapted set of Good Participatory Practice (GPP) guidelines specific to TB vaccine research, and an active network of CE implementers to share best practices on TB vaccine research.

Results: The Aeras CE programme is established, and continues to evolve with ongoing support from and collaboration with stakeholders listed above.

Conclusions: Developing and maintaining a successful CE programme requires identification of key stakeholders to provide broad perspectives and share experience and resources, integration of CE activities into trial conduct to ensure sustainability and tools to support specific needs. Ongoing review and analysis of information gathered through consultation enables the development of a strategy suitable to the needs of all stakeholders.

ABSTRACT PRESENTATIONS SATURDAY 14 OCTOBER 2017

ORAL ABSTRACT SESSIONS

17. Advancing laboratory diagnostics for greatest impact

OA-201-14 Modeling the clinical impact of the Xpert® MTB/RIF Ultra cartridge for diagnosis of pulmonary tuberculosis

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Background: The newer Xpert MTB/RIF Ultra cartridge has shown improved sensitivity for rapid and accurate diagnosis of tuberculosis (TB) in recent field trials, but at the expense of reduced specificity.

Methods: We developed a Markov microsimulation model to evaluate clinical implications of switching from the existing Xpert cartridge to the Xpert Ultra cartridge for evaluation of suspected adult pulmonary TB. We modeled clinical cohorts in three emblematic settings: HIV clinic in South Africa, public TB center in India, and adult primary care setting in China. In each setting, we used existing data to project likely diagnostic results, treatment decisions, and ultimate clinical outcomes. Our primary outcome was the projected number of unnecessary treatments generated per TB death averted, if standard Xpert were switched to Xpert Ultra.

Results: In the Indian setting, replacing the standard Xpert cartridge with Xpert Ultra was projected to avert 0.5 TB deaths (95% uncertainty range [UR]: 0, 1.3) and generate 18 unnecessary treatments (95% UR: 10, 29) per 1000 individuals evaluated - a ratio of 38 incremental unnecessary treatments per incremental death averted (95% UR: 12, indefinite upper bound). In the South African HIV-care setting - where TB mortality rates are higher and Ultra's improved sensitivity has greater absolute benefit - this ratio improved to 7 unnecessary treatments per TB death averted (95% UR: 2, 43). By contrast, in a Chinese primary care setting, this ratio was much less favorable, at 372 unnecessary treatments per TB death averted (95% UR: 75, indefinite upper bound). Alternative interpretations of the Ultra cartridge's semi-quantitative trace call had little effect on this ratio.
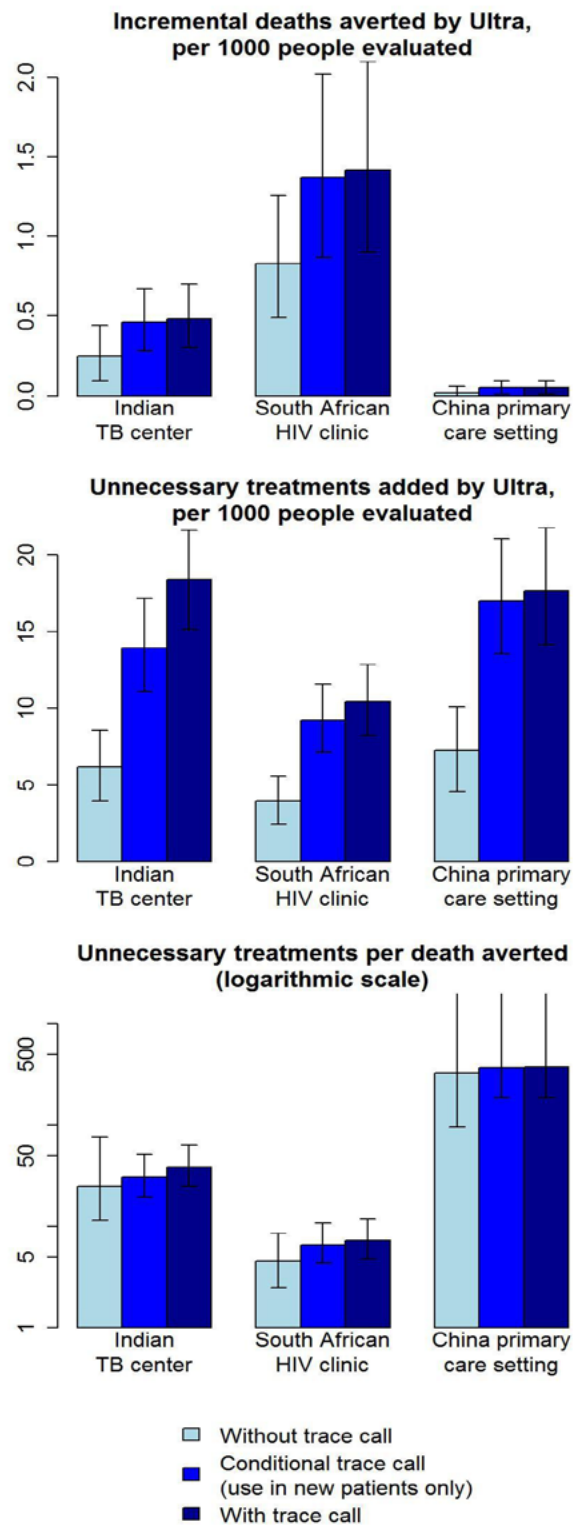
Figure Clinical projections, Ultra vs standard Xpert

Conclusions: Switching from standard Xpert to the Xpert Ultra cartridge for diagnosis of adult pulmonary TB may have different consequences in different clinical settings. The ideal approach to using the Ultra cartridge may involve a more nuanced, setting-specific approach to implementation.

OA-202-14 Evaluation of WHO-endorsed rapid diagnostic tests for potential application as surveillance tool for rifampicin-resistant tuberculosis transmission

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Background: Globally rising rates of rifampicin resistant tuberculosis (RR-TB) has been attributed to transmission, and its diagnosis which increasingly relies on WHO-endorsed rapid diagnostic tests (RDTs), produces large volumes of raw data which are not fully utilised. This study aimed to evaluate the discriminatory power, reproducibility, and concordance of RDTs to explore their potential utilisation for monitoring RR-TB transmission.

Methods: 108 non-clustered RR-TB strains representing 35 different *rpoB* mutations, including 32 located within the 81 bp hotspot, were selected from the Belgian Coordinated Collections of Microorganisms hosted at the ITM. These strains were subjected to Xpert MTB/RIF (Cepheid), MTBDR*plus*v2.0 (Hain), and GenoscholarTMNTM+MDRTB II (Nipro). Raw data obtained from these tests were compared and analysed through obtained values of Hunter Gaston Discriminatory Index (HGDI), Shannon's Index of Diversity, and Wallace Coefficient (WC). The reproducibility of the RDTs was analysed using seven mutation profiles found in at least four strains, and four mutation profiles in two to three strains.

Results: Raw data of each RDT were evaluated to assess their ability to discriminate different mutant sequence profiles. Findings exemplified by distinct probe profiles for each mutant sequence are presented in Figure 1, in which the consensus numbering system for *M. tuberculosis* H37Rv has been adapted. The HGDI for the tests ranged from 0.82-0.88 and the Shannon indices ranged from 3-3.5. The WC computed for the following reference-complementary RDT pairs - Hain-Xpert, Hain-Nipro, Nipro-Xpert, Nipro-Hain - were 0.417, 0.583, 0.625, and 0.700 respectively; and the average percent reproducibility for Xpert, Hain and Nipro were 87.94, 96.31, and 97.78 respectively.

Conclusions: Taken together, sufficient discriminatory power, reproducibility, and concordance of RDTs support the validity of its potential use as first line tool for suspecting RR-TB transmission. For definitive confirmation, complementary testing with gold standard genotyping methods is recommended.
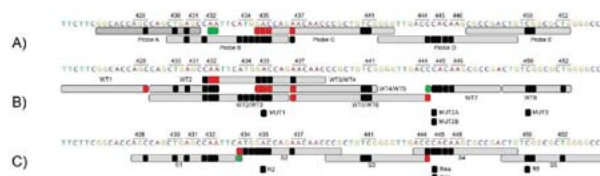
Figure 1 Overview of RR-TB RDT captured mutations

OA-203-14 Development and preliminary evaluation of an innovative serological test for rapid detection of active tuberculosis

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Background: The lack of reliable and efficient blood diagnostic tools remains one of the main obstacle for Tuberculosis (TB) eradication by 2050 as planned in the WHO Global TB strategy 2016-2035. A rapid, non-sputum-based test that can rapidly screen pulmonary active TB is considered to be one of the most urgent unmet needs. This study describes the development and preliminary evaluation of a rapid blood-based screening test for detection of active TB.

Methods: Overlapping peptides of *M. tuberculosis* antigens derived from proteins involved in the metabolism of reactivation phases of TB were synthesized and evaluated for sensitivity/specificity using multiplex nanobeads and ELISA methods. Our best candidate was coated on magnetic nanobeads and used in an innovative technology format to improve performances and to achieve a one-step rapid test. Here we show the evaluation of our first transportable prototype of TB test with 20 blinded serum samples: 15 samples from active TB patients (smear +/-, culture +), and 5 samples from TB-negative patients.
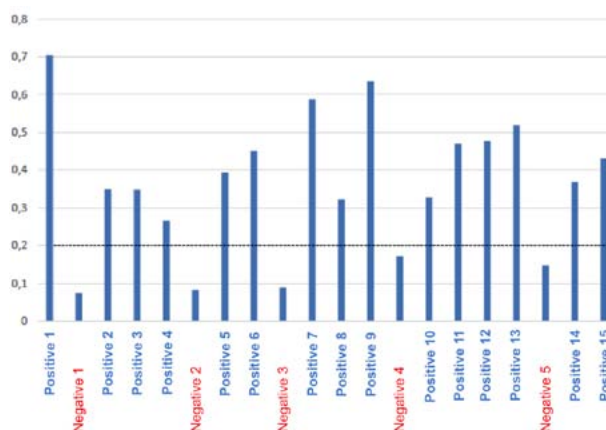
Figure Mean value obtained for the analysis of 20 samples

Results: As shown in the Figure, all of the TB-positive (15/15) and TB-negative samples (5/5) were found correctly classified, using the innovative screening strategy combining a proprietary peptide and nanobeads-based technology. Signal to cut-off value were over 1.5 for 14/15 TB samples, and over 2 for 8/15 TB samples.

Conclusions: Preliminary data obtained with this innovative blood-based prototype test, which needs less than 15 minutes, are promising for the triage or the diagnostic of people with active TB.

This test aims to reach the requested target product profile defined by WHO for point-of-care product. Our transportable prototype test needs to be evaluated with a larger panel of samples including HIV-positive patients, or latent TB patients, for example.

In addition, we are currently working on a blinded evaluation of our test using 100 samples from the Foundation for Innovative New Diagnostics (FIND) biobank.

OA-204-14 Evaluation of an MDR-TB assay for detection of *Mycobacterium tuberculosis* and rifampicin and isoniazid resistance on the BD MAX™ System

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Background: Tuberculosis (TB) is a deadly infectious disease and continues to remain one of the world's top health challenges. Rapid and accurate detection of *Mycobacterium tuberculosis* complex (MTBc) and drug resistance is of paramount importance to appropriately identify and treat patients suffering with the disease, reduce the death rate and stop the spread of TB.

An assay to detect Multi-Drug-Resistant tuberculosis (MDR-TB) is in development for use on the BD MAX™ System. It is an automated, qualitative test that will allow for the direct detection of MTBc and identification of genetic mutations correlated with rifampicin (RIF) and isoniazid (INH) resistance from raw (unprocessed) and NALC/NaOH-treated (processed) sputum samples. The BD MAX System offers walk-away automation by incorporating sample lysis, extraction, amplification and detection all in one system.

Methods: An evaluation of analytical sensitivity as well as clinical specimen testing was performed for the assay. Analytical sensitivity for both MTBc detection and RIF/INH resistance was determined using spiked negative sputa. Clinical performance of the new MDR-TB assay was evaluated with a cohort of 273 retrospective raw sputum specimens from the FIND/WHO/TDR specimen bank.

Results: Analytical sensitivity of the assay was found to be less than 5 cfu/mL-sputa for MTBc detection and less than 100 cfu/mL-sputa for RIF and INH resistance detection.

The sensitivity of the assay for MTBc in smear(+) was 99% (95/96) and 84% (21/25) in smear(-) specimens. The assay showed a specificity of 96.6% (142/147) versus culture. The sensitivity of the assay for identification of RIF and INH resistance was 93.3% (14/15) and 88.2% (15/17) respectively.

Conclusions: The MDR-TB assay in development is a promising new molecular test that would complement the broad range of TB diagnostic solutions offered by BD to help detect, treat, and manage TB globally.

The MDR-TB assay is currently under development and not available for sale or use.

OA-205-14 Ability of genotypic methods to diagnose the level of isoniazid resistance among multidrug-resistant clinical isolates of *Mycobacterium tuberculosis*

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Background: Isoniazid (INH) may continue to offer benefit to patients infected by MDR-TB strains with low-level INH resistance (LL INH-R), as currently being evaluated in a prospective clinical trial of pulmonary tuberculosis (AIDS Clinical Trials Group study 5312).

Methods: The sequencing data of *katG* (considered as related to high level (HL) of INH-R), *inhA* and the *inhA* promoter resistance-associated genes (considered as related to LL of INH-R) and the Genotype MTBDR*plus* results, were compared to the results of phenotypic drug susceptibility testing by the proportion method (LJ medium) in 634 MDR-TB isolates collected in France over a period of 9 years (2008 to 2016). Low level of INH-R was defined by resistance to 0.1 to 0.2 mg/liter; high level of resistance was defined by resistance to ≥1 mg/liter.

Results: Among the 634 strains, 590 isolates displayed a HL INH-R, while 44 isolates displayed a low level of INH-R (7%). Among the 590 HL INH-R strains, 534 harbored mutation in KatG S315 (S315T, n=531; S315N, n=2; S315R, n=1) and 3 deletions in KatG (total 91%). Among the 53 remaining strains, 34 exhibited mutation in the *inhA* promoter (-C15T), 16 other mutations in KatG (missense, n=12; nonsense, n=1; insertion, n=2; deletion, n=1), 1 in InhA (I21T) and 2 no mutation. Among the 44 LL INH-R strains, 33 displayed alteration in the *inhA* promoter (-C15T) (75%), the 11 remaining strains displaying missense mutations in KatG (n=6, including 3 S315T), nonsense mutation in KatG (n=1), mutations in InhA (S94A, n=2; V78A, n=1), and no mutation (n=1).

Conclusions: Among the strains "predicted as LL INH-R" by MTBDR*plus*, or MTBDR*plus* combined with katG, inhA and its promoter sequencing, 48%

(32/66) and 50% (36/72) respectively, exhibited in fact phenotypically HL of INH-R, making hazardous the use of INH for MDR-TB only based on genotypic methods.

OA-206-14 Bm2Dx: the tuberculosis biomarker database

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Background: The need for tuberculosis (TB) biomarkers is growing for efficient, affordable and accessible diagnosis of tuberculosis. Despite the rapidly expanding biomarker research activities, no well-performing, simple and rapid biomarker-based TB diagnostic test is yet on the market. To help address this "biomarker pipeline problem", FIND, McGill and Stop TB Partnership New Diagnostics Working Group (NDWG) Biomarker Task Force commenced development work on a new biomarker database, called Biomarkers to Diagnostics (Bm2Dx), which will be launched in late 2017.
Methods: Bm2Dx is a novel, centralized, open access database dedicated to TB biomarker discovery, validation and confirmation. Extracted data from a systematic review of non-DNA biomarkers for the detection of active TB which was conducted by McGill University in collaboration with FIND is used as initial input of the database.
Results: Bm2Dx currently contains 151 curated publications and 22 clinical trials linked to 194 biomarker records. Evaluation of the status and development stage of each biomarker candidate is possible by virtue of the dynamic tracking of available evidence through regular manual curation and consistent evaluation standards for the relevant use cases. User-friendly database tools facilitate the cross-study comparisons as well as data visualization, standardization and retrieval. Moreover, Bm2Dx accommodates an expert-defined biomarker evaluation framework to allow ranking of biomarker candidates in relation to World Health Organization's high-priority priority target product profile.
Conclusions: Bm2Dx aims to help overcome the current patchwork of fragmented research on TB biomarkers with an online one-step platform which will enable greater communication, collaboration and coordination in the field, streamline the verification and validation of biomarker candidates, and ultimately promote an accelerated translation into clinically useful tools.

OA-207-14 *Mycobacterium tuberculosis-specific T-cells profile strongly identifies subjects with active disease*

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Background: Tuberculosis (TB) represents a major public health threat in Uruguay. Despite national implementation of sensitive and specific tools for TB diagnosis, 25,5% of TB cases in 2015 were not bacteriologically confirmed. Fast and reliable discrimination of active TB from latent TB is a great necessity. Recently, the cytokine profile of *Mycobacterium Tuberculosis* (Mtb)-specific CD4 T-cells allowed immunological discrimination between these groups. Therefore we have used flow cytometry to functionally characterize Mtb-specific T-cells in subjects with latent Mtb infection (LTBI) or active TB disease and tested the hypothesis that different cytokine profiles of pathogen-specific T-cells may identify subjects with active TB.
Methods: 24 patients with active TB confirmed bacteriologically or by TB specific features in affected tissue biopsy were compared with 23 controls (co-habitant contacts of subjects with bacillary pulmonary forms of active TB). All subjects were BCG-vaccinated at birth. Cryopreserved peripheral blood mononuclear cells were thawed, and stimulated overnight with specific-TB peptides: ESAT-6 and PPD separately and with controls. Flow cytometry analysis was performed using a viability dye and CD3, CD4, CD8, IFN-δ, TNF-α, and IL-2 antibodies. The frequency of Mtb specific intracellular INF-δ, TNF-α and IL-2 -CD4 and CD8 lymphocytes was analyzed. Non-parametric tests were performed to compare median between groups. ROC curve analysis estimated cutoff values. Sensitivity (SS) and specificity (SP) were obtained from contingency tables.
Results: The cytokine profile of Mtb-specific CD4 and CD8 T-cell response was distinct between active TB and control group (Table 1).

	PPD CD4 INF-δ Median ± ES	PPD CD4 TNF-α Median ± ES	PPD CD4 IL2 Median ± ES	PPD CD4 INF-δ+TNF-α Median ± ES	PPD CD4 INF-δ+TNF-α +IL2 Median ± ES	PPD CD8 INF-δ Median ± ES	PPD CD8 TNF-α Median ± ES	PPD CD8 IL2 Median ± ES
Cases	4,7±1,7	1,8±0,4	5,1±1,1	0,0±0,2	1,6±3,2	4,9±1,5	2,2±0,7	1,0±0,8
Controls	0,6±0,3	0,4±0,3	0,2±3,6	2,4±0,8	1,4±2,2	0,6±0,2	0,5±0,3	0,1±3,1
p value	0,000	0,006	0,000	0,013	0,886	0,000	0,070	0,003
*cutoffs of PPD reactive T cells Sensibility (SS) Specificity (SP)	≥ 1,58* SS 79% SP 82%	≥ 0,94* SS 75% SP 74%	≥ 1,55* SS 75% SP 100%	≤1,5* SS 87% SP 61%	≥1,4* SS 35% SP 56%	≥ 2,4* SS 83% SP 100%	≥ 1* SS 66% SP 74%	≥ 1* SS 66% SP 78%

Table 1 Cytokine profile of Mtb-specific T-cells

Single cytokines (IFN-δ, TNF-α or IL-2) production by both Mtb-specific CD4 and CD8 T-cells was significantly different between groups. Similar results were found with ESAT-6 stimulation.

Conclusions: Mtb specific T-cell responses can strongly identify subjects with active TB disease.

18. Training health care workers

OA-208-14 Introduction of a systematic TB contact investigation model with facility-level self-performance monitoring in Malawi

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Background and challenges to implementation: Malawi's National Tuberculosis (TB) Guidelines recommend contact investigation (CI) among household and priority contacts of TB patients; however, implementation has been variable. A 2015 TB assessment revealed low levels of follow up screening of household contacts and inconsistent use of TB CI registers. The National TB Control Program (NTP) and the Clinton Health Access Initiative (CHAI) assessed the feasibility of a scalable, data-driven model for systematic TB CI in 5 districts in southern Malawi.

Intervention or response: We developed a TB CI package, including a training curriculum, Standard Operating Procedures, appointment slips and a revised register. From August to December 2016, trainings were administered in public facilities offering TB services. Facilities received supervision from national TB officers, and a self-assessment tool was introduced for facility staff to track progress on key indicators and develop monthly action plans for indicators below target values. Detailed facility-level baseline data were collected at high-volume sites, to complement NTP data; end-line data will be collected in mid-2017.

Results and lessons learnt: Trainings and subsequent supervision visits were conducted in 40 facilities, covering 222 health workers, comprising 69% of public facilities seeing TB patients in the 5 districts. High-volume sites, accounting for 90% of district TB patient burden, were prioritized for training.

Based on NTP data, in the immediate pre-intervention period, a quarterly average of 644 (20%) adult and child contacts were screened and 102 (19%) eligible children were initiated on Isoniazid Preventive Therapy (IPT). By 2 quarters into the intervention period, this increased to 1,198 (37%) and 210 (38%), respectively (Figure 1). Based on these initial successes, NTP and partners are scaling the model to additional districts.
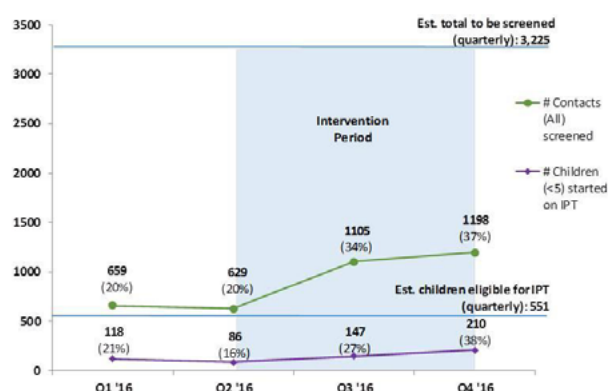
Figure Number of contacts screened & number of children initiated on IPT: 5 districts in Southern Malawi, January - December 2016

Conclusions and key recommendations: This intervention demonstrates the potential to strengthen TB CI performance through systematic training with follow up supervision at the facility-level, and empowerment of health workers to monitor their own performance using simple self-assessment tools.

OA-209-14 Evaluation of nurses' knowledge of TB and MDR-TB before and after training

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Background: TB remains a major cause of morbidity and mortality worldwide with 10 million new cases each year. Nurses are the largest health profession and are on the front-line of TB care. However, nurses often do not receive training on TB greatly impacting the care of patients with TB.

Methods: Between June 2014 and February 2017 the International Council of Nurses (ICN) TB/MDR-TB Project trained 345 nurses in nine countries. Pre-tests were administered to participants to assess their knowledge regarding general TB/MDR-TB and attitudes towards patients with TB. A post-test was completed at the end of the training to assess change in knowledge.

Results: Three hundred forty-five nurses completed a pre- and post-test on TB/MDR-TB. The mean age of nurses was 40 (±9) and the mean length of time working in TB was 8.7 years (±8.4); 82% were female. Half

received TB training during the previous year. The mean correct scores increased from 65.6% on the pre-test to 90% on the post-test (p< 0.01). Most participants (97%; n=333) knew TB is caused by bacteria.

However, only 29% (n=101) could identify risk factors for TB, but increased to 90% (n=306) on the post-test (p< 0.01). Ten percent (n=36) could correctly identify diagnostic methods for TB before the training and increased to 53% (n=181) (p< 0.01).

Forty-four percent (n=153) of nurses correctly identified symptoms of TB compared with 86% (n=292) on the post-test (p< 0.01).

On the pre-test 60% (n=207) reported feeling comfortable working with TB patients and 83% (n=281) following the training (p< 0.01).

Conclusions: These results indicate there is a large gap in nurses' knowledge of TB/MDR-TB. However, after training nurses' knowledge and attitudes towards patients significantly improved. Training nurses working on the front-lines of TB care is critical to reach the WHO End TB Strategy and to prevent further transmission of TB.

OA-210-14 Training and involvement of 'Slum Community Volunteers' in urban TB control: intervention to overcome slum TB in West Bengal

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Background and challenges to implementation: Indian slum population has increased to over 65 million as per latest census from earlier 52 million consequents upon rapid urbanization & rural-urban migration. Slum-TB had been a major challenge to Revised National TB Control Program (RNTCP) due to poor case detection and poor treatment adherence. German Leprosy & TB Relief Association (GLRA India), as part of Global Fund TB Project had strategically selected & trained 56 Slum TB Community Volunteers (Slum TBCV) from within the community and involved them in TB control activities in the urban slums of 9-districts of West Bengal.

Intervention or response: 852 urban slums in 9-districts were selected and covered for house-to-house active case search for presumptive cases through 4-symptoms verbal screening between January 2016 & December 2016. 106888 house-holds were screened with a house-hold population of 0.51 million and divided into 2-groups. In group-1 with 51.8% (n[1] =55364) of house-holds covered, 3562 Presumptive TB Cases (PTC) were accompanied by Slum TBCVs to Designated Microscopy Centres (DMC) for sputum microscopy . In group-2 with 48.2% (n[2] = 51524) house-holds screened, 2976 PTC were identified & given only referral slips to be tested at DMCs without being accompanied.

Results and lessons learnt: The results were exciting. In n1, 80.8% (n=3267) of PTCs referred were tested resulting in 85.7% (n=312) of total detected TB cases, where as in n2 , only 19.2% (n=776)of PTCs referred were tested resulting in 14.3% (n=52) of total detected TB cases through active case search.

Conclusions and key recommendations: Involving Slum TBCV is a highly rewarding exmple of community engagement to overcome the challanges of TB control in urban slums. Results demonstrated through accompanied testing is highly encouraging. The needs to be replicated in all the cities of India with significant slum population.

OA-211-14 Role of medical colleges in achieving End TB strategy in India: recent achievements and future prospects

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Background and challenges to implementation: More than a decade ago, Revised National Tuberculosis Control Programme (RNTCP) and Medical Colleges (MCs) have accorded a formal partnership to widen access and improve quality of Tuberculosis (TB) services in the country.

The objective of this paper is to measure the recent achievements and future prospects in the context of End TB Strategy.

Intervention or response: The MCs involvement is carried out through a mechanism of task force committees at different levels. The implementation is reviewed through 382 core committees, 30 State Task Force (TF) and Operational Research (OR) committees, six Zonal TF and OR committees and one National TF committee covering 382 MCs in the country.

Results and lessons learnt: Systematic involvement of Medical Colleges under RNTCP has been rewarding. Of the 433 MCs, 88% (N=382) were involved in RNTCP in 2016. Of these, 134 have GeneXpert facility, 35 have RNTCP certified Culture and Drug Susceptibility Testing laboratories (and additional 80 MCs have culture lab facilities) and 105 Drug Resistance Tuberculosis (DR-TB) centres. MCs contributed 19% [274904] of total TB cases of which 14% [169783] pulmonary TB cases and 43% [105121] extra pulmonary TB cases under RNTCP.

This partnership enabled to carryout 106 OR projects and 110 medical graduate dissertation in 2016. Considering the current achievement, there is scope to improve TB services by enabling medical institutions

as centres of excellence, providing decentralized drug resistant TB services, support in establishing high end laboratories and establishing air borne infection control measures in health care facilities.

Conclusions and key recommendations: This partnership can further strengthen RNTCP in the context of changing scenario from intermittent to daily regimen, raising concerns of DR-TB and providing care & support to critical TB patients. MCs can play an important role in ending TB in India through larger involvement. Similar partnership with private practitioners can enable notification of million mission TB cases in India.

OA-212-14 Blended learning for capacity building of health care workers in TB-HIV: results of a comparative study in Ethiopia

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Background: Health workers frequently stay away from routine duty for a number of days for off-site workshop trainings. Our objective was to assess whether blended learning (BL) approach that combines self-reading with short off-site training on TB/HIV is effective in improving the knowledge and practice of health workers.

Methods: A comparative study was conducted using Kirkpatrick post-training evaluation model. Health workers from two zones of Oromia region of Ethiopia with no recent training in the updated national TB-HIV guidelines participated in both groups of the study. The BL group received self-reading materials (the national TBL/HIV training material) for 3 weeks followed by a 3 day face-to-face off-site training while the traditional group (TL) received a 6-day off-site workshop style training using the same training material. On-job assessment was made at health facility level three months after the training to understand the participants' application of what they have learned during the training.

Results: The cost of training delivery and the time taken for training in the blended learning was about half of the cost and time taken for traditional training. The proportion of trainees who incorporated the training skill to routine TB clinic activity in the BL and TL group were 95.0% and 96.6%, respectively. Observation in the BL group showed that 96.8% were taking proper history while 84.8% performed proper physical examination with their patients whereas the corresponding proportion in the TL group being 96.2% and 82.0% respectively. Appropriate patient counseling and drug treatment among the BL group were 99% and 91.8% respectively but it was 100% for both in the TL group. (Table 1)

Characteristics	Blended learning group	Traditional learning group	P-value
Training skill applied to routine clinic activity	94/99 (95%)	86/89 (96.6%)	>0.05
Proper Physical Examination	91/96 (94.8%)	63/77 (82%)	<0.05
Proper Patient Counseling	96/97 (99%)	78/78 (100%)	>0.05
Appropriate drug treatment	89/97 (91.8%)	79/79 (100%)	<0.05

Table Results of blended versus traditional training

Conclusions: Trainees in both groups had similar level of application of their knowledge gained during the trainings. However, those in the BL group might need more frequent follow on mentoring because their knowledge about drug treatment was lower.

OA-213-14 Education for active case finding of tuberculosis in prisons: lessons learnt

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Background and challenges to implementation: There was a low rate of TB incidence in prisons due to stigma, weak health prison system and high rotation of health care workers. Within the framework of research projects, an educational strategy to implement a surveillance system to screen TB cases, based on active case finding (ACF) doing by prisoners, was developed and implemented between march 2012 to 2017.

Intervention or response: The target population were prisoners (health brigade, general prisoners, leaders of block cell, and active TB cases), administrative, security guards, and health care staff working in three prisons in Medellin, Colombia. The topics taught according to the audience and time were: Epidemiology of TB, respiratory symptoms, ACF, infection and disease, treatment and adverse event, isolation and control infection, health education, health promotion, community experiences for TB control, health systems information (notification, TB treatment card adverse event), TB in prisons. The methodology of training was:

1) Health brigade received a course of three months, and then they identified and notified people with respiratory symptoms.

2) Security guards received a bimonthly training of an hour.

3) training for administrative and health-care workers every year.

The outcomes of the training were the number of people with respiratory symptoms screened and the annual incidence of TB.

Results and lessons learnt: The number of people with respiratory symptoms increased from 36 in 2012 to 1571 in 2016, and the TB cases increased from 8 in 2012 to 50 in 2016. We developed with prisoners, educational material: small books for the patients and their family, video, flipchart, webpage, and a flow chart to attend people using ACF including prisoners for the screening and to identify adverse events quickly.

Conclusions and key recommendations: ACF with the participation of prisoners and to teach about TB to security guards, administrative and health care personnel helped to the program to increase the screening and active TB cases.

OA-214-14 A survey of the tuberculosis workforce in the country of Georgia

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Background: The WHO has indicated that lack of a sufficient workforce is a major barrier to tuberculosis (TB) control. In the country of Georgia, there has been a recent lack of new physicians entering into TB. We sought to evaluate the current TB workforce in Georgia to improve understanding of the current situation and challenges for the future.

Methods: A cross-sectional study of the training and career satisfaction among current TB healthcare workers in Georgia at the National Center for Tuberculosis and Lung Diseases (NCTLD) in Tbilisi and associated regional locations was completed using an anonymous 31-item survey. Descriptive statistics were used to analyze the results.

Results: Among a total of 184 TB physicians in the country, 142 (77%) were contacted and 138 (75%) completed surveys. The mean age was 56 and less than 10% were under age 40. Most (81%) were female. All 11 regions of the country were represented, with close to half of physicians (n=56, 41%) from Tbilisi. Monthly salary from TB work was $205 or less for 50% of respondents. Nearly half (47%) receive additional salary from another source. Over half of physicians (65%) indicated they were satisfied with their work in TB, but 55% were unsatisfied with reimbursement. Most physicians (80%) indicated both a lack of interest in TB among current medical students and expressed concern about the lack of young physicians entering the field. While most physicians (85%) agreed TB control has improved, nearly all (95%) agreed that TB continues to be a major public health problem in Georgia.

Conclusions: In Georgia, we found there are few young physicians working in TB, and that while satisfied with their work, current physicians are dissatisfied with low salaries and concerned about attracting new doctors to the field. New strategies are needed to retain and attract physicians to TB.

OA-215-14 Evaluation of training programs to improve human resource capacity for HIV, malaria and TB control: systematic review of methods and outcomes

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Background: Owing to the global health workforce crisis, more funding has been invested in strengthening human resources for health, particularly for HIV, tuberculosis (TB) and malaria control; however little is known about how investments in training are evaluated. This paper examines how frequently HIV, malaria and TB healthcare provider (HCP) training programs have been evaluated, synthesizes information on methods and outcome indicators used, and identifies evidence gaps for future evaluations to address.

Methods: We conducted a systematic review of publications evaluating HIV, TB and malaria HCP training programs between 2000 and 2016. We searched three electronic databases and additional gray literature. After independent screening by two authors, data about methodology and outcomes assessed was extracted from eligible studies. Training outcomes were categorized into four levels (reaction, learning, behavior and results) based on the Kirkpatrick model.

Results: Of 1458 unique publications identified, 85 were eligible in the analysis. The number of published articles increased after 2006, with most conducted in Africa. Majority of evaluations (n=42,49%) were on HIV with fewer studies focused on malaria (n=28, 33%) and TB (n=23, 27%). We found that quantitative survey was the most commonly used method (n=27, 32%) and the most commonly assessed outcomes were knowledge acquisition (n=43, 51%) and organizational impacts of training programs (n=38, 45%). Behavior change and trainees' perceptions of usefulness were evaluated less frequently; costs of training were also rarely assessed.

Conclusions: Our study found limited number of robust evaluations conducted since 2000, even though the number of training programs has increased to address the human resource shortage. We identified a lack evaluation studies on TB and malaria related training and few studies assessing behavior change of trainees or costs of training. An increase in evidence to inform policies on and investments into training programs may be facilitated by development of frameworks and standardized evaluation methods.

19. More TB drugs, less rock and roll! Quizás algún mariachi

OA-216-14 Evaluation of high-dose rifapentine plus clofazimine in the first-line regimen for tuberculosis in the mouse model of chemotherapy

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Background: In mouse models of tuberculosis (TB), increasing the rifamycin exposure or adding clofazimine [C] to the first-line regimen have both been separately associated with decreasing the duration of treatment necessary for cure from 6 to 3 months. We hypothesized that replacing rifampicin [R] with high-dose rifapentine [P] and adding C in the first-line regimen will further decrease the duration of treatment necessary to cure TB in mice.
Methods: *Mycobacterium tuberculosis*-infected BALB/c mice were treated for 12 weeks with one of the following regimens: (i) no drug control; (ii) RHZE (standard first-line regimen, R 10 mg/kg, isoniazid [H] 10 mg/kg, pyrazinamide [Z] 150 mg/kg, and ethambutol [E] 100 mg/kg); (iii) RHZEC (addition of C 12.5 mg/kg to RHZE); (iv) PHZE (replacing R in RHZE with high-dose P 20 mg/kg); and (v) PHZEC. The bacterial load in the mouse lungs (colony forming units or CFUs) was determined before and during treatment at 4, 6, 8, 10 and 12 weeks after treatment initiation, and 6 months after completing 6, 8, 10 or 12 weeks of treatment to assess relapse.
Results: After 4 weeks of treatment, PHZEC was the most bactericidal regimen, followed by PHZE, then RHZEC, then RHZE. After 6 weeks of treatment, the decline in lung $\log_{10}$ CFU counts was 6.4, 5.7, 3.9, and 3.2 in mice receiving PHZEC, PHZE, RHZEC, and RHZE, respectively. Lung culture conversion occurred after 8, 10, and 12 weeks of treatment for mice receiving PHZEC, PHZE, and RHZEC, respectively; mice that received RHZE remained culture-positive after 12 weeks.
Conclusions: In the mouse model, replacing rifampicin with high-dose rifapentine and adding clofazimine in the first-line TB regimen results in earlier lung culture-conversion than either modification alone and may have the potential to shorten the treatment duration for drug-susceptible TB to less than 3 months.

OA-217-14 Bioequivalence of dissolved vs. whole bedaquiline tablets: implications for dosing in children

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Background: Bedaquiline 100 mg tablets are becoming more widely available for the treatment of adults with drug-resistant tuberculosis, yet a paediatric formulation is not yet available for routine care. Manipulating standard tablets for paediatric administration of smaller dosages may impact bedaquiline bioavailability. We evaluated the relative bioavailability of dissolved versus whole bedaquiline tablets.
Methods: This was a randomized mixed-sequence, cross-over study in 24 healthy adults who received bedaquiline at two occasions separated by a 14-day washout period. Intensive pharmacokinetic sampling over 48 hours with an additional 14-day sample was performed on both occasions. The relative bioavailability of 4 x 100 mg bedaquiline tablets administered whole with 250 mL water or dissolved in 60 mL water was investigated using nonlinear mixed-effects modelling.
Results: All participants (58% female, mean age 25 years, all HIV-uninfected) completed the study, resulting in 528 observations of bedaquiline and its M2 metabolite. A previously developed population pharmacokinetics model was found to describe the data well. The bioavailability of dissolved bedaquiline was not significantly different from that of whole tablets (likelihood ratio: p=0.92). The 95% confidence interval of the relative bioavailability of dissolved bedaquiline tablets was 89-113% of that of whole bedaquiline tablets, hence fulfilling the predefined bioequivalence criteria (80-125%). The mean absorption time was 17% (15-36%) longer for dissolved tablets, resulting in slightly lower maximal serum concentrations. As bedaquiline activity is more closely associated with total exposure than peak concentrations, this finding is not expected to affect the treatment outcome. No QTcF prolongation >450ms or lactate values >3mmol/l were observed.
Conclusions: We demonstrated bioequivalence between dissolved and whole bedaquiline tablets. Dissolved bedaquiline can be used interchangeably with whole tablets for patients unable to swallow tablets. This data will inform paediatric use until dispersible bedaquiline tablets become available.

OA-218-14 Vitamin C modulates the efficacy of anti-tuberculosis drugs in vitro

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Background: The link between tuberculosis (TB) and vitamin C (vit C) dates back to 1930s, when researchers used it to alleviate symptoms of TB in human subjects and in experimental TB in animals. A serendipitous discovery was made in our laboratory that vit C triggers induction of the DevR 'dormancy' regulon in axenic cultures of *Mycobacterium tuberculosis* (Mtb), owing to its oxygen scavenging properties. Further, vit C addition to Mtb cultures mimics multiple stresses encountered by the bacteria within the host.

Methods: This study was designed to identify the modulatory effects of vit C on the efficacy of anti-TB drugs. Mtb cultures treated with physiological concentrations of vit C were exposed to anti-TB drugs to identify changes in drug tolerance/ susceptibility. Whole genome transcriptome analysis was also carried out to gain insights into the underlying mechanisms of the observed phenotype.

Results: Vit C-treated Mtb acquired tolerance to isoniazid, rifampicin and streptomycin. The underlying basis of drug tolerance was attributable to metabolic changes, enhanced activity of efflux pumps and down-regulation of antibiotic targets. Bacterial sensitivity to isoniazid was restored upon culture in vit C-free medium and on efflux pump inhibition. Conversely, the addition of pyrazinamide to vit C-treated cultures enhanced antibiotic activity. A combination of vit C with standard TB drugs and efflux pump inhibitors could effectively kill >99% of replicating and 'dormant' Mtb.

Conclusions: The study reveals the activity of vit C in modulating the efficacy of current TB drugs. The combination of vit C with efflux pump inhibitors and standard TB drugs provides a novel strategy against replicating and 'dormant' Mtb. The use of vit C-based multi-stress model system offers a potential alternative to other models of non-replicating persistence, allowing the development of novel inhibitors targeting 'dormant' Mtb.

OA-219-14 RNA sequencing and inhibition of efflux pump genes involved in second-line drug resistance in *Mycobacterium tuberculosis*

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Background: The emergence of extensively drug resistant tuberculosis (XDR-TB) is a major threat in the control and ultimate elimination of the disease. Whole tran-scriptome sequencing could provide novel insights into the emergence of drug resistance. The aim of the study was to measure the expression levels of RNA molecules in drug resistant and susceptible isolates.

Methods: RNA of 11 XDR-TB, six MDR-TB and two susceptible isolates were sequenced on Illumina HiSeq. The CLC Genomic workbench (v8) was used for alignment of sequencing reads. The data was analyzed for the quality control of the reads, and alignment of reads was made to *M. tuberculosis* reference genome NC_000962. The data was normalized and statistical test was performed to find the significantly differentially expressed genes (DEG) with statistically significant *P*-value (≤0.05) after Bonferroni post-test correction. We analysed efflux pump (EP) genes that were found to be connected to each other using STRING ver.10. Further testing of four XDR-TB isolates with efflux pump inhibitors (EPIs) was done on different second-line drugs to determine their effect on minimum inhibitory concentration (MIC).

Results: The 11 XDR-TB and six MDR-TB were compared to two susceptible and DEG had statistically significance (*P*< 0.05) . Further analysis on four XDR-TB stains showed significant (*P*< 0.05) of DEG compared to H37Rv. The Rv2686/87/88 operon was significantly expressed in strains with *gyrA* mutations. The protein-protein interaction network revealed novel pathways of EP genes with type VII secretion pathways. MIC readings ranged from 2-16 µg/ml, depending on the drug. Furthermore theirs MICs in the presence of EPI by at least one-fold.

Conclusions: The study identified unique genes that are overexpressed in different isolates studied. The different genes/proteins/pathways identified in the study could provide novel insights into drug resistance. Knowledge into pathways of overexpressed genes in drug resistance could be used for further research and development.

OA-220-14 Tuberculosis clinical trials and safety halts: evaluating for bias in effect estimates

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Background: Trial safety is assured through independent oversight, recommending temporary or permanent suspension of enrollment and/or dosing as necessary. The HIRIF trial assessed, in patients with new, smear-positive tuberculosis, whether increased rifampin doses could shorten tuberculosis treatment and improve outcomes without increased toxicity. The primary safety analysis assessed the difference in incidence of grade 2 or higher rifampin-related adverse events in the 12

weeks after treatment initiation (HIRIF AEs) across three rifampin doses (10, 15, and 20mg/kg). The study was halted three times—for 1.9, 2.1, and 5.1 weeks—in accordance with protocol-defined safety stopping rules. Enrollment was paused and participants received the standard dose (10mg/kg) until the study was cleared for continuation. We examined whether halts underestimated or masked dose-related toxicity.

Methods: The primary safety analysis used the Cochran-Armitage test for trend. Sensitivity analyses included the primary analysis applied only to AEs occurring while participants received study doses of rifampin and evaluating whether the cumulative exposure of the study drug (in mg per week) predicted AE incidence. Bias in time to first grade 2 or higher rifampin-related AE will be explored using similar methods.

Results: Of 180 participants enrolled, 80(44.4%) had ≥1 HIRIF AEs; 4 had AEs only during a study halt. The primary safety analysis identified no significant difference across treatment arms (p=0.1679). Removal of 4 participants for the first sensitivity analysis led to similar results (p=0.2405)—see Table 1. Results of additional analyses will be reported.

	Primary Safety Analysis N (%)	Halting Sensitivity Analysis N (%)
10 mg/kg (n=60)	26 (43.3)	25 (41.7)
15 mg/kg (n=60)	31 (51.7)	29 (48.3)
20 mg/kg (n=60)	23 (38.3)	22 (36.7)
P value (Cochran-Armitage test for trend)	0.1679	0.2405

Table Participants with >=1 grade 2+ RIF-related AEs

Conclusions: This effort is the first attempt to account for how study halts may bias estimates of safety in a dose-ranging tuberculosis trial. Such halts may not be uncommon in tuberculosis trials, which typically require lengthy periods of enrollment and treatment. Methods are required to minimize bias in estimates of safety and efficacy.

OA-221-14 Effectiveness and safety of shortened anti-tuberculosis therapy with *Mycobacterium vaccae* in never-treated sputum smear-negative pulmonary tuberculosis patients: a randomized controlled trial

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Background: Prevalence of sputum smear negative(SS-) pulmonary tuberculosis(PTB) had arisen by 32.3% from 2000-2010 in China. SS- PTB patients used the same 6-month standard anti-TB therapy as SS+ PTB patients. We want to evaluate the effectiveness and safety of adding injected *Mycobacterium vaccae* to standard chemotherapy with a shortened treatment course in never-treated SS- PTB patients.

Methods: We conducted a multi-center clinical trial in 8 sites in 4 provinces in China. SS- PTB patients were diagnosed following a strict diagnostic procedure and enrolled with informed consent. Patients were randomly assigned(using online central allocation system) to treatment group which received 6 doses of injected *Mycobacterium vaccae* + 2HRZE/2HR for 4 months and control group which received 2HRZE/4HR for 6 months. Chest X-ray and laboratory examination were taken at 0,1,2,4,6 months. Chest radiographs were reviewed by national level TB clinical and imageological experts blindly for treatment effectiveness evaluation.

Results: 1659 SS- PTB patients were enrolled with 831 in treatment group and 828 in control group. Difference of sex, age group,ethnic group,affected long lobes, different type of lesions between the 2 groups were not significant. Preliminary results shows that chest radiography at 6 month proved the resolution of pulmonary lesions in the treatment and control group were 75.1% and 71.9% for patients with patchy shadow, 68.8% and 64.2 for those with nodular shadow, 87.5% and 75.9 for those with cavity. Difference was statistically significant for noninferiority test. Adverse drug reaction rates were 18.8% and 20.7% in treatment and control group separately.

Conclusions: Our preliminary results shows that the 4-months anti-TB therapy with injected *Mycobacterium vaccae* could have equivalent effectiveness and safety as 6-months standard therapy while shortened treating course. We will continue to analyze resolution of clinical symptoms, immunological indicators of patients during the treatment and their recurrence after 12,24 months.

OA-222-14 Final analysis of a study providing early access to bedaquiline (BDQ, TMC207) for (pre) XDR *Mycobacterium tuberculosis*

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Background: We previously presented interim results of TMC207TBC3001 (NCT01464762), a study providing early access to BDQ for patients with MTB infection resistant to isoniazid, rifampin, a fluoroquinolone and/or ≥1 of the second-line injectables (SLI) amikacin, kanamycin, capreomycin (ie, pre-XDR-TB or XDR-TB).

Methods: Patients received BDQ for 24 weeks (400mg qd for 2 weeks, 200mg tiw for 22 weeks) with an optimized background regimen (OBR). After completing 24-week BDQ+OBR treatment, patients received OBR only for up to 96 weeks under supervision. Safety, tolerability and microbiological status were assessed throughout the study.

No statistical hypotheses were tested. Results of the final analysis after all patients completed the 120-week study period are presented.

Results: 57 patients received BDQ+OBR (Russia: 3 sites, n=54; Lithuania: 1 site, n=3). All patients were Caucasian and HIV negative; 58% female; median age 28 years; 93% had previously used second-line TB drugs. Pre-treatment, 47.4% had pre-XDR-TB (24.6% fluoroquinolone resistant; 22.8% SLI resistant) and 53% XDR-TB. The most frequently used drugs (>65% of patients) in the OBR during the investigational and post-investigational treatment phase were fluoroquinolones (100%), PAS-C (89%), pyrazinamide (88%), capreomycin (84%) and linezolid (67%).

43 patients completed the study (75%) and 14 discontinued (25%). Safety outcomes are summarised in Table 1.

In the 45 patients who had a positive baseline MTB culture and available post-baseline results, culture conversion at 24 weeks was: 69% (31/45) overall; 73% (16/22) in pre-XDR-TB; and 65% (15/23) in XDR-TB patients. Only 16 patients had sputum culture data reported at 120 weeks; 6 were negative and the other 10 were reported as 'not done'.

The 3 deaths were considered not related to treatment by the investigator.

Discontinuations	All patients (N=57)		
Total discontinuations	14 (25%)		
Discontinuations due to AEs	5 (9%)		
Deaths	3 (5%)		
Discontinued BDQ	2[a] (4%)		
Lost to follow-up	2 (4%)		
Non compliance	1 (2%)		
Withdrawal of consent	2 (4%)		
Patient moved city/country	4 (7%)		
Deaths	**Case 1**	**Case 2**	**Case 3**
Considered related to BDQ or BR?	No	No	No
Days since last BDQ intake	441	442	411
QTcF at Week 24 (ms)	414	436	310
Treatment phase	Post-investigational	Post-investigational	Follow-up
TB-related?	Yes[b]	Yes[b]	No[c]
Safety analysis			
Any AE (regardless of cause or severity)	50 (88%)		
Most common AEs (>15%)			
AST increased	28 (49%)		
ALT increased	15 (26%)		
Eosinophilia	13[d] (23%)		
Any AE at least possibly related to BDQ[e]	6 (11%)		
Any serious AE[f]	8[d] (14%)		
Any Grade 3 or 4 AE	15[d] (26%)		
Most common Grade 3 or 4 AEs (>5%)			
ALT increased (Grade 3)	5[d] (9%)		
AST increased (Grade 3)	4[d] (7%)		

[a]Discontinued BDQ due to toxic nephropathy and depression considered not related to bedaquiline by the investigator. The OBR was permanently withdrawn due to depression and temporarily withdrawn due to toxic nephropathy; [b]Pulmonary haemorrhage; [c]Acute myocardial infarction; [d]None were considered at least possibly related to BDQ by the investigator, [e]ALT increased, AST increased, ECG QT prolonged, hypercreatininaemia, hyperuricaemia, haematuria, leukocyturia, proteinuria, dermatitis, hypotension; [f]Asthma, pulmonary haemorrhage, appendicitis, pulmonary TB, psychotic disorder, cervix carcinoma stage 0.

Table 1 Safety analysis outcomes during 120 weeks

Conclusions: Our data support observations from other regions of the safety and effectiveness of BDQ containing regimens in patients with pre-XDR-TB and XDR-TB up to 120 weeks of observation.

OA-223-14 Low total tuberculosis drug activity correlates to low plasma concentrations of rifampicin

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Background: Tuberculosis drug activity (TDA) assay is an assay where the patient's plasma activity on *Mycobacterium tuberculosis* (*Mtb*) in culture is measured and may be an alternative to measuring plasma drug concentrations in resource limited settings. Our objective was to investigate the correlation between tuberculosis drug activity (TDA) and drug concentrations in TB patients.

Methods: TB patients (n=30) with drug susceptible pulmonary (PTB) and extra-pulmonary TB (EPTB) were included and first line drug concentrations were analysed

2 hours after drug intake at week 2. Peak plasma drug concentrations at 2h were determined and TDA was calculated by incubating patient plasma from 2h with a reference strain of *Mtb* (H37Rv). In PTB patients, time to positive MGIT-culture from sputum was assessed after day 0, 2 and week 1, 4 and 8 respectively.

Results: Patients with plasma levels of rifampicin (RIF) below recommended levels (< 8 mg/L) had significantly lower TDA compared to patients with levels >8mg/L (1.40 vs 1.67, p< 0.001). No correlation between isoniazid (INH) plasma levels and TDA was observed. Further, TDA (1.86 vs 1.48, p< 0.001) as well as RIF levels at week 2 were significantly higher in patients with EPTB than in PTB patients. There was also a trend towards earlier sputum conversion with increasing TDA.

Conclusions: Our study indicates that TDA can be used as a surrogate marker for RIF plasma levels and thus serve as an indicator for dose adjustment of RIF during TB treatment. We also found a higher TDA in EPTB compared to PTB patients, the implication of which needs to be further investigated in larger studies.

SHORT ORAL ABSTRACT SESSIONS

14. TB care: who pays, how much, and to what end?

SOA-435-14 How affordable is TB care? Findings from a nationwide TB patient cost survey in Ghana

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Background: Tuberculosis (TB), a major global public health problem, is known as a disease of the poor. Often TB patients face financial catastrophe even when TB diagnosis and treatment are offered free of charge. The End TB Strategy includes a target of preventing any TB patient from incurring "catastrophic" costs due to TB by 2025. To monitor progress towards this milestone the World Health Organization (WHO) recently evaluated a pilot tool to estimate "catastrophic" costs. Countries are expected to adapt and implement this tool to monitor the occurrence of catastrophic costs through periodic surveys among TB patients at public health facilities.
Methods: In 2016, using an adapted version of the WHO tool, we conducted a nationwide TB patient cost survey at government health facilities in Ghana to provide further evidence on the level, composition and factors associated with costs incurred by TB-affected households.
Results: 695 patients were enrolled in the survey. Of these, 68% experienced catastrophic costs (at a 20% threshold). On average, drug-susceptible (DS)-TB and multi-drug resistant (MDR)-TB patients incurred USD1,536 and USD2,172 respectively, due to their TB disease. These costs include direct out-of-pocket medical expenditure (USD187 for DS and 538 for MDR), direct out-of-pocket non-medical expenditure (USD481 for DS and USD889 for MDR) and lost income (USD867 for DS and USD744 for MDR) over the full course of being treated for the disease. Medical expenditure accounted 91% of total spending for seeking care, despite 80% of patients being enrolled in the National Health Insurance Scheme.
Conclusions: Our study shows that despite "free" TB care in Ghana, a substantial proportion of TB-affected households are experiencing financial catastrophe. Policies aimed at defraying direct costs (e.g. health insurance) should be improved to provide financial protection to TB patients.

SOA-436-14 Feedback from TB-affected households receiving a socio-economic intervention in Peruvian shantytowns: acceptability of social versus economic support according to poverty level

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Background: Socioeconomic support is a key part of the World Health Organisation's End TB Strategy. However, evidence is limited concerning which support elements (e.g. social, economic or both) are the most acceptable to TB-affected households. During the preliminary phase of the Community Randomized Evaluation of a Socioeconomic Intervention to Prevent TB (CRESIPT), we examined the acceptability of social and economic elements of the intervention by poverty level.
Methods: 282 TB patients in 32 shantytown communities of Lima, Peru, were recruited to the study. Patients were randomly allocated to the comparison arm (standard of care) or supported arm (standard of care plus the socioeconomic intervention). The intervention consisted of social and economic support. Social support activities included health-post visits, household visits, TB educational workshops, and TB mutual support clubs. Economic support activities consisted of conditional cash transfers throughout treatment for patients adhering to and completing treatment, their household contacts being screened for TB, and all household members engaging with household visits, workshops and TB clubs. At 24 weeks following treatment initiation, supported arm participants were asked to complete a mixed-methods exit questionnaire to collect feedback on acceptability of the social ("information and education"; "mutual support") and economic support ("incentivization", "enabling", and "poverty reduction") elements of the intervention.
Results: 127 supported households received socioeconomic support and 99 provided feedback. Frequency of social and economic support activities rated as "good" or "excellent" was: information/education 84/99(85%); mutual support 83/99(84%); incentivization 90/99(91%); enabling 89/99(90%); and poverty reduction 71/99(72%).
Participants from poorer versus less poor households ranked poverty reduction more highly (p=0.03, Figure) but, overall, participants ranked social support more highly than economic support (p<0.001, Figure).
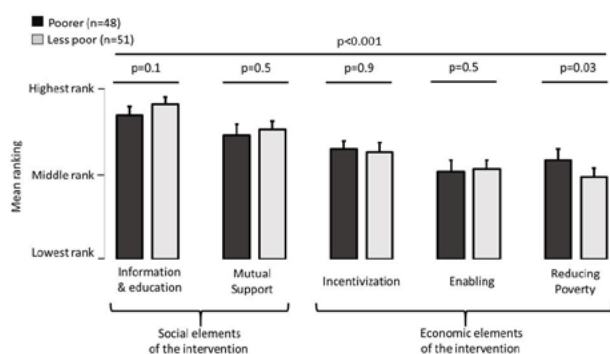
Figure Ranking of social and economic elements by poverty

Conclusions: These important findings highlight the importance of not overlooking social support for TB-affected households to complement the catastrophic costs mitigation and social protection interventions championed in the End TB Strategy.

SOA-437-14 Socio-economic scenarios of tuberculosis in Brazil

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Background: The World Health Organization (WHO) launched the End TB Strategy setting targets to be met by 2035, including a 90% reduction in the TB incidence rate compared to 2015. We aimed to identify socioeconomic scenarios in Brazil associated with the tuberculosis incidence rate.
Methods: We conducted an ecological study with socioeconomic indicators (2010) obtained from 5,565 municipalities in Brazil and merged with the tuberculosis incidence rate (2015). We estimated incidence rate ratio (IRR) with negative binomial regression, adjusted by the population size of the municipality. In this stage, municipalities that presented mean annual variation of the triennial moving average of the incidence rate for the years 2001 to 2015 were included, between -8 and 8%, to reduce possible bias due to the intermittence in the notification. The municipalities were clustered by the k means method considering the variables identified in the regression models.
Results: There was an association with the TB incidence rate (n = 3,311 municipalities) with household crowding (IRR: 1.008, 95%CI: 1.006 - 1.011) and the unemployment rate (IRR: 1.039; 95%CI: 1.030 - 1.047), adjusted by municipal size. Two clusters were identified with these socioeconomic indicators. The High Socioeconomic Scenario (HSS) (n = 3,482 municipalities) had a mean tuberculosis incidence rate of 16.32/100,000 people, a 5.5% unemployment rate and a household crowding of 17.1%; The Lower Socioeconomic Scenario (LSS) (n = 2,083 municipalities) had a mean tuberculosis incidence rate of 22.09/100,000 people, an unemployment rate of 8.3% and a household crowding of 38.5%.
Conclusions: LSS needs additional technical support, because of the challenges imposed by socioeconomic limitations. The identified scenarios show the high social heterogeneity of the country, which must be considered as the initial step given by the National Tuberculosis Control Program to define and prioritize targeted actions in Brazil's national plan.

SOA-438-14 A cross-sectional study to analyse patient costs during extra-pulmonary tuberculosis diagnosis and treatment

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Background: Cost-of-illness has a major impact on individuals and their family, particularly in tuberculosis (TB). The involvement of different organs makes extra pulmonary tuberculosis (EPTB), a more complex disease to diagnose compared to pulmonary TB. The objective of this study was to explore the costs associated with diagnosis and treatment of EPTB among affected patients attending directly observed treatment-short-course (DOTS) clinics in Bangladesh.
Methods: A cross sectional study was conducted among 208 patients with a diagnosis of EPTB in six DOTS clinics located in the peri-urban areas of Dhaka. A structured questionnaire was used to assess the medical direct, non-medical indirect and other indirect costs (income loss) related to diagnosis and treatment. Univariate, chi-square test and logistic regression was performed for data analysis. Ethical issue was maintained strictly.
Results: The median of total costs incurred by patients with EPTB was 206 USD, while the median of total out-of-pocket cost was 183 USD (89% of total cost). Among total out-of-pocket cost, the median of total diagnostic related costs and total treatment related costs were 164 USD and 25 USD respectively. The median costs of hospitalized patients almost doubled the non-hospitalized patients' costs (median 208 USD for diagnostic period cost and 139 USD for treatment period cost). More than half of the respondents experienced catastrophic expenditure. Family income (p 0.006), hospitalization (p< 0.01), borrowing money (p< 0.01) and sold property (p< 0.01) were significantly associated with catastrophic expenditure group.
Conclusions: Direct and indirect cost of diagnosis and treatment impose an economic burden on patients with EPTB. Diagnostic related costs comprise almost 90%

of total costs. Hospitalized Patients had significant (p< 0.01) higher costs than non-hospitalized patients. Integrated approaches to reduce unnecessary expenditures in patients with EPTB should be implemented in DOTS clinics to reduce the economic burden on them.

SOA-439-14 Analysing clinical and cost data for effective use of domestic resources for TB: the case of Ukraine

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Background and challenges to implementation: With limited health budgets, it is crucial that domestic resources be directed as efficiently as possible to TB case finding, diagnosis, and treatment. In Ukraine, hospitalization in separate, TB-specialized hospitals is still the norm. Ukraine's provincial health departments pay for inputs such as buildings and salaries for these hospitals, but have had no way to see what outputs they are buying, meaning little ability to redirect resources toward more effective and efficient TB care. The TB hospitals are not integrated into the general hospital system, but steps are being taken to integrate TB hospitals into the country's strategic purchasing system.

Intervention or response: To create economic stimuli for TB system reform, steps were taken to develop a "per case" payment system for the TB-specialized hospitals. These steps include: classification of TB cases into various clinical groups; analyses of cost accounting in hospitals; and creation of a discharged patient database. Complex data analysis was conducted, including projected scenarios for hospital optimization and for the consequences of various managerial decisions.

Results and lessons learnt: Analysis showed the current network of TB hospitals is redundant, and the number of beds in TB hospitals comprises about 10% of the country's total hospital beds. The patient structure is not optimal, with 30% of patients hospitalized in a TB hospital not having a diagnosis of TB. Average stay is much higher than international standards (>80 days for pulmonary sensitive TB and >140 days for drug-resistant TB (DRTB).) Many patients with repeat hospitalizations have developed DRTB.

Conclusions and key recommendations: The simulation model demonstrates that following recommended treatment protocols with optimal LOS and indications for hospitalization can reduce the TB hospital network by half. Resources saved can be redirected to primary healthcare outpatient treatment.

Planned integration of TB hospitals into the general healthcare funding system will facilitate further integration of TB services in the healthcare system.

SOA-440-14 TB pay-for-performance programme under universal health insurance versus conventional DOTS program for patient-centered care in Taiwan

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Background: WHO has urged to engage public and private healthcare providers for controlling and treating TB. However, in reality the engagement is always challenging. Taiwan had implemented universal health insurance which covered over 98% population and 90% healthcare providers. A nationwide TB pay-for-performance (P4P) was initiated by Taiwan CDC and National Health Insurance Administration(NHIA), which purposes are to engage community healthcare provides for better care since 2004.

Methods: The study aimed to exam population-based Cost effectiveness analysis (CEA) of P4P and DOTS programs on treatment outcomes and related expenses. Societal perspective was employed to examine the effects. Between 2006-2007, a total of 10766 TB cases were enrolled in this study, and TB database and NHIA claim files were adopted for analysis.

Results: Patients in both P4P and DOTS programs (n=7863, 73.0%), group A, had the most cases with severe comorbidity and highest cavitation status. Following by P4P only (1553, 14.4%), group B; DOTS only (883, 8.2%), group C; receiving conventional care (not P4P or DOTS program (467, 4.3%), group D. Patients in the group A had the highest treatment success rate of 83.1%, following by group B: 69.3%, group C: 60.8%, and group D: 24.2%. Average Cost Effectiveness Ratio indicated average costs of successfully treated for one TB case cost USD$3851.9 in group B and which is highly cost effectiveness combination programs; $4175.6 in group A; $5435.7 in group C, $10990.0 in group D, and which costed most and least effectiveness.

Conclusions: Comparing with multiple programs, Incremental Cost-Effectiveness Ratio indicated the P4P was the most cost-effective program. P4P program may incur higher healthcare expenses and program fees, but their treatment success rate is the highest, and death rate lowest comparing to other groups. Providing financial incentives could engage providers for better care and P4P could be a feasible model for better tuberculosis control.

SOA-441-14 Pre and post-diagnosis costs of tuberculosis to patients on DOTS in districts of Southwest Ethiopia: a longitudinal study

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Background: High cost of Tuberculosis (TB) diagnosis and treatment result in delays to diagnosis and poor treatment compliance. This study determined pre and post diagnosis costs to patients.

Methods: A longitudinal study among 735 new TB cases on treatment was conducted from January 2015 through June 2016 in districts of Southwest Ethiopia. Face to face interview with the patients was held using standard tool at two points; during intensive phase and end of treatment. Patients were asked about out of pocket expenditures and lost work days due to the illness. Thus costs were categorized in to direct medical, non medical and indirect those summarized in to pre and post diagnosis periods. Comparisons of mean costs across categories and cost periods were made using independent and paired t tests respectively. Finally linear regression model was fitted to identify independent predictors of pre and post diagnosis costs.

Results: The median (inter-quartile range) of pre diagnosis, post diagnosis and total costs incurred by TB patients were respectively US$ 97.62 (6.43-184.22), US$ 93.75 (56.91-141.54) and US$ 201.48 (136.7-318.94). Direct out of pocket patient expenditure during pre and post diagnosis respectively amounted to a median (inter-quartile range) US$21.64(10.23-48.31) and US$35.02(0-70.04). Of the total cost, the pre diagnosis cost constitute 53.6% and 70.6% of the total cost was attributed to indirect cost. In multiple regression, patient and provider delays, taking action before visiting health facility, number of visited healthcare facilities, being diagnosed clinically and at private facilities independently predicted higher pre-diagnosis cost. On the other hand, being rural resident, hospitalized for diagnosis or treatment, travel time to treatment center, patient and provider delays predict higher post diagnosis costs.

Conclusions: TB patients incur substantial amount of money during the pre and post diagnosis periods despite the "free service". Hence, promoting early care seeking, decentralizing efficient diagnosis and treatment services within reach of patients can reduce the costs.

SOA-442-14 Cost-effectiveness analysis of pulmonary tuberculosis case finding strategies among high-risk communities in Kampala, Uganda

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Background: Tuberculosis (TB) is a major global health risk in Sub-Saharan Africa. Passive Case Finding (PCF) is limited due to delays in case detection. Active case finding (ACF) strategies including Household Contact Investigation (HCI) and Enhanced Case Finding (ECF) have been alternatively proposed to improve TB case detection, but little is known about their cost-effectiveness. We assessed the cost-effectiveness of PCF+ECF+HCI combination compared to PCF only for TB case detection among high-risk communities in Kampala from provider's perspective.

Methods: Data on costs and yield of TB cases for PCF only and a combination of PCF+ECF+HCI was collected among adults in highly-congested areas of Kampala over 12 months. Costs were adjusted to US$ for the 2015 annual average. The main outcome was the Incremental Cost Effectiveness Ratio (ICER) representing the cost to detect an additional TB case. The decision threshold used was three times Uganda's GDP (US$ 2089). One-way sensitivity analysis was done to assess uncertainty of the ICER around key variables.

Results: Based on Uganda TB program data, 4,755 pulmonary TB cases from 12,298 presumptive TB cases were identified through PCF alone. PCF+ECF+HCI combination yielded 5,120 cases from 12,915 presumptive cases. The average cost per patient for PCF and PCF+HCI+ECF was US$ 895.8 and US$ 4909.9 respectively. The cost of detecting one additional TB case was US$ 8211.8 using PCF+ECF+HCI compared to using PCF only. In one-way sensitivity analyses, the ICER was most sensitive to number of household contacts screened, number of TB cases identified through ECF and probability of having chronic cough.

Conclusions: From the provider's perspective, PCF+ECF+HCI was costlier and had a marginally higher yield of TB cases than PCF only, but it was not a cost-effective strategy. In settings with minimal resources, low-cost approaches to improving household contact screening and enhanced case finding might add value to passive TB case detection.

SOA-443-14 Cost-effectiveness of including determine TB-LAM test to diagnose tuberculosis in HIV-positive symptomatic patients

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Background: Tuberculosis (TB) is the leading cause of death among HIV infected people. Better TB diagnostic tests may reduce mortality but also increase costs. Determine TB-LAM have emerged as a potential additional tool for HIV-positive patients. We evaluated the cost-effectiveness of including LAM in a TB diagnostic algorithm for HIV-positive symptomatic patients seriously ill.

Methods: Three TB diagnostic algorithms were compared:

1) clinical-radiological;
2) clinical-radio-LAM and
3) clinical-radio-LAM-Xpert.

All tests were systematically done in all patients. Costs were calculated using a "micro-costing" method. The value of the resources was estimated from the relevant quantities and corresponding unit price. The proportion of culture confirmed TB cases started on TB treatment was used as effectiveness outcome. The diagnostic efficiency of LAM was estimated with the cost-effectiveness ratio (CER) and the incremental cost-effectiveness ratio (ICER). A discount rate of 4% was applied for both costs and outcomes.

Results: The CER was €470 with clinical-radiological algorithm, €316 using the clinical-radio-LAM algorithm and €301 using the clinical-radio-LAM-Xpert algorithm. The clinical-radio-LAM algorithm led to anti-tuberculosis treatment in 20 additional confirmed TB cases and accounted for an additional cost of €2281 equivalent to €114 per new true TB case initiating treatment compared to the clinical-radiological algorithm.

Algorithms	Costs in Euros (C)	TB confirmed treated cases (E)	Cost-effectiveness Ratio	ΔC	ΔE	Incremental Cost Effectiveness Ratio (ICER)
Clinical-radiological	12545	27	470.0 €			
Clinical-radio-LAM	14858	47	316.1 €	2281	20	114.0 €
Clinical-radio-LAM-Xpert	15967	53	301.3 €	3422	26	131.6 €

Table 1 Cost, cost-effectiveness and incremental

The clinical-radiological-LAM-Xpert algorithm detected 26 additional confirmed TB cases compared to the clinical-radiological algorithm and accounted for addi-

tional costs of €3422. The ICER per new true TB case initiating treatment was €132. Adding GeneXpert to the clinical-radiological-LAM algorithm allowed diagnosing 6 additional confirmed TB cases for an additional cost of €1108.65 corresponding to an ICER of €185 per new TB cases initiating treatment.

Conclusions: Our economic evaluation indicates that including LAM into the TB diagnostic algorithms is highly cost-effective (ICER less than two-fold the GNI per capita) and leads to a higher number of confirmed TB patients being diagnosed at an affordable cost.

SOA-444-14 Promotion and operation for upfront GeneXpert testing of suspected pediatric tuberculosis patients in India: cost analysis in the health systems perspective

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Background: India accounts for more than one quarter of world's tuberculosis (TB) cases and deaths. As prompt diagnosis and linkage to care are integral component of TB control efforts, the Indian government has made considerable efforts to expand access to the rapid molecular DST, Xpert MTB/RIF assay (Xpert). Here, we updated per-test unit costs of Xpert, reflecting actual observed workloads at the four study laboratories and assessed the costs associated with recruiting physicians into a USAID-funded trial of upfront GeneXpert testing of pediatric suspected TB patients.

Methods: Per-test unit costs were calculated using a bottom-up micro-costing method using an ingredients approach with resource usage estimated from time and motion observations categorized by different workload levels. Using dynamic daily workload matched to relevant per-test unit costs, weighted average per-test unit cost was calculated for each laboratory. Costs associated with recruiting physicians for Xpert testing referrals via telephone calls, meetings and workshops were calculated following the same principles. All costs were assessed in the health systems perspective and expressed in 2015 USD.

Results: Based on actual daily workloads observed at the study laboratories, weighted average per-test unit costs ranged from $18.79 to $21.92. Of the total costs associated with operating Xpert laboratories during the project, costs due to overtime work ranged from 3.0% to 13.9% of the total. The costs associated with promoting Xpert testing referrals were $33.27 per meeting

with physicians, $1.31 per phone call, and $10.57 per attendee at recruitment workshops.

Conclusions: Cities with the highest workloads had the lowest per-test unit costs due to the efficient use of Xpert capacity. However, these cities also incurred the largest overtime work costs. The weighted Xpert per-test unit costs decreased over time reflecting more efficient workloads as patient referrals increased. Cost-efficiency in outreach spending per patient referral also increased throughout the experiment.

SOA-445-14 Estimation of resource constraints in the scale-up of intensified case finding in South Africa

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Background: Cost-effectiveness analysis can be a useful tool to support decision-making in the complex landscape of TB control. However, it may lead to inefficient allocation of scarce resources when it ignores real-world constraints on implementation. We aimed to quantify potential supply-side constraints limiting the scale up of intensified case-finding (ICF) strategies in South Africa.
Methods: Three supply-side constraints - budget, human resources and maximum acceptable ratio of Xpert tests to TB notifications - were identified through discussions with local stakeholders. Firstly, we quantified the resources (fiscal and human) needed to deliver the current level of TB services. We then compared these to:
1) the potential maximum increase in public TB financing available for new TB interventions from Department of Health data;
2) the maximum current and future capacity among public sector nurses that could be dedicated to TB services; and
3) the annual Xpert yield under several possible scenarios of ICF scale up.
The costs of relaxing the human resource constraint to implement the ICF scenarios at full scale were also estimated.
Results: In 2015, 209.5 million minutes were worked by South African public sector nurses providing TB services in the primary care setting. Public expenditure on TB during the same year was approximately US$ 415 million and 3.2 million Xperts were run, resulting in 326,094 notifications. High, medium and low scenarios were calculated for the budget and human resources constraints for the period 2015-2035, based on different assumptions around future growth. The limiting factor for scaling up ICF was human resource capacity.
Conclusions: Empirical estimates of the constraints affecting TB services can be calculated. Failure to include the costs of ancillary activities needed to relax those

constraints to effective scale up, may compromise local relevance and credibility with decision-makers, and may also increase the risk of sub-optimal investments.

15. Tobacco cessation and integration in TB control

SOA-446-14 Changes and effect of tobacco smoking on tuberculosis over two decades among men in selected South Asian countries

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Background: South Asian countries present a highly heterogeneous situation in terms of tuberculosis epidemiology and control. These countries have a very high rates of tuberculosis and smoked tobacco use among adults. Efforts to control both tobacco use and tuberculosis in south Asia need to be addressed. Our major aim in this macro-level study is to investigate the role of smoking as a risk factor, and their association with socioeconomic factors for the development of tuberculosis over the past two decades in selected south Asian countries.
Methods: The individual level data conducted between the period 1990 to 2016 Demographic Health Survey of Bangladesh, Nepal and Pakistan and Information related to self-reported tuberculosis status, tuberculosis determinants, current tobacco status and socioeconomic status has been used. The principal components analysis and logistic regression to demonstrate how the association between tobacco smoking and tuberculosis prevalence.
Results: To see the impact of smoking with different socioeconomic and demographic factors on tuberculosis the study found that the odds ratios are higher in elderly than younger age. The highest risk of smoking for TB is noted aged from 65-74 years (or 2.99, 95% ci 1.47-6.07). Interestingly, the odds ratios rapidly declined in the population aged >85 years. Our findings enhance the evidences that cigarette smoking is an important risk factor associated with a higher prevalence of TB. Current and former smokers should be considered as a high risk population. Meanwhile, smoking cessation is definitely an important measure to decrease the prevalence of TB both in low and high prevalence areas in all these countries.
Conclusions: Cigarette smoking is found most associated with life time tuberculosis infection on and the association is most evident among the heaviest frequency smokers over the two decades. Interventions of smoking cessation are recommended to be included in the current TB control practice in all countries.

SOA-447-14 High prevalence and nicotine dependence among TB patients who are smokeless tobacco users compared to smokers

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Background: Nicotine dependency is the main criteria that differentiates a tobacco user with non- tobacco user. Usage of tobacco usually favors negative outcome among TB patients. Rehabilitation of tobacco users having TB is still in a nascent phase in India. Having a clear picture of nicotine dependency will help to design interventions that will lead to cessation of tobacco and improve TB treatment outcomes. The objective of the study was to describe prevalence and extent of nicotine dependence among smokers and smokeless tobacco users.

Methods: Cross-sectional study using pre-tested FTND based questionnaire study among adult TB patients who were daily tobacco user were selected using stratified random sampling from 12 districts (4 rural, 4 urban and 4 tribal). Total of 720 patients (240 each in rural, urban and tribal areas) were selected randomly who gave consent for the study. Data entry and analysis was done using SPSS (Version 16).

Results: Out of 720 patients, 63% were males (58% in urban, 70% in rural and 60% in tribal) and 37% (42% in urban, 30% in rural and 40% in tribal) were females. Majority of TB patients were poor (Urban-60%, Rural-48%, Tribal-74%) and Lower middle class (Urban-40%, Rural-52%, Tribal-26%). Prevalence of tobacco usage was 38% (16% Smoker, 22% smokeless), 32% (14% smoker,18% smokeless) and 43% (19% smoker,22% smokeless) in urban, rural and tribal areas respectively. Of all 79% daily smokeless tobacco users and 67% smokers had severe dependence. Among smokeless users 18% and 3% accounted for moderate and mild dependency whereas 22% (Moderate) and 11% (Mild) among smokers. Nicotine dependence was significantly associated with age group, locality, alcohol use and duration of tobacco use.

Conclusions: Majority of TB patients were having severe dependence which is alarming and should be taken seriously with National Tobacco and TB Control programme. TB Patients should be and therefore should be offered upfront cessation services at the earliest.

SOA-448-14 Use of Tobacco Dependence Screener to diagnose smokeless tobacco dependence in India

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Background: Tobacco dependence research is largely focused on cigarette smoking. While ST dependence research is starting to gain momentum, much of the work is carried out in developed countries. With an estimated 220 million adult users, ST is the predominant form of tobacco in India. But studies to measure ST dependence in this high-burden country are lacking.

TDS was originally developed for cigarette smokers based on the fourth Diagnostic and Statistical Manual (DSM-IV) and International Classification of Disease (ICD). A modified TDS has been shown to effectively measure ST dependence in Oklahoma, USA.

Methods: TDS was administered through face-to-face interviews to 233 adult ST users, recruited through community-based purposive sampling in New Delhi, India. The applicability of this diagnostic tool was assessed using reliability analysis (Cronbach's α) and tool validation against ST use characteristics, Fagerström Test for Nicotine Dependence for ST (FTND-ST), and salivary cotinine.

Results: Mean age of participants=30.53 years (range: 18 - 72), with nearly equal gender distribution. Mean age of first ST use=17.88 years; over 97% current daily ST users, averaging 10.64 years of daily ST use. With total TDS scores ranging from 0-10, mean=6.46 (SD=2.29). By using a recommended cut-off of 5, 66.5% (n=155) of study participants were diagnosed as ST-dependent. TDS-based diagnosis of ST dependence was significantly associated with >5 years of daily use (OR=2.47; 95% CI - 1.37, 4.47), chewing within 30 minutes of awakening (OR=3.81; 95% CI - 2.05, 7.09), and chewing more than fifteen times per day (OR=4.37; 95% CI - 2.29, 8.32). Internal consistency was 0.693, and correlation with FTND-ST (r=0.51, p< .0001) and cotinine (n=72, r=0.26, p< 0.05) showed significant positive associations.

Conclusions: Results suggest that TDS may be an effective measure of ST dependence in India, with clinical and research applicability. But further evaluation, including assessment of predictive validity against cessation is needed.

SOA-449-14 Effectiveness of a brief counseling and behavioral intervention for tobacco cessation in primary care

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Background: Tobacco use remains the most established cause of chronic diseases. The use of behavioral intervention models for tobacco cessation that can help tobacco users and the study of its impact in primary care constitute a public health priority. The present study aims to examine the effectiveness of tobacco cessation counseling intervention on intention to quit among patients in primary care settings in India.
Methods: A quasi-experimental study was conducted among 1382 patients visiting primary care facilities in two states of India in 2016. This study compared: the intervention arm which comprising intensive counseling (5As: Ask, Advice, Assess, Assist, Arrange) and the control arm comprising of routine advice by the physicians. Change in intention to quit in 30 days was the primary outcome measured at two time points (baseline (2015) and endline (2016). Adjusted logistic regression model was applied using intention to treat principle.
Results: About half of the patients were willing to quit tobacco in 30 days. An increase of 37% was observed from baseline (40%) to end-line (77%) in intention to quit tobacco among patients in intervention units as compared to the 5% increase in control units. Patient who have received tobacco cessation counseling were about three times more willing to quit tobacco use in intervention units as compared to those who have received routine care in control units (intention to treat analysis; OR=2.85; CI=1.78-3.8; p value-0.00).
Conclusions: A primary care behavioral intervention ('5A' model) for tobacco cessation is effective in motivating tobacco users to quit tobacco. The intervention is not resource heavy and may act as a viable option to be included in the routine care practices in primary care settings of India. More large scale studies on effectiveness and cost-effectiveness of tobacco cessation intervention should be taken up in future.

SOA-450-14 Tobacco cessation counselling and treatment adherence among tobacco consuming TB patients in Kalburgi (Gulburga) District, Karnataka

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Background: As per Global adult tobacco Survey (2010) there are 275 million tobacco users in India. It is estimate more than one third (35%) adults use tobacco some form or the other. Active consumption of tobacco/smoking increases the risk of tuberculosis (TB) infection two times and is significantly associated with recurrent TB and TB mortality. Observational studies have shown associations between tobacco/smoking and poor TB treatment outcomes.
Methods: To quantify the effects of national tobacco smoking cessation counselling intervention on the treatment outcomes of people with Pulmonary TB. Kalburgi (Gulburga) district has been reporting with high defaults rate, death rate and failure rate . With the help of National Tobacco Control programme, district team screened patients for Tobacco consumption. NTCP counsellors Tobacco cessation intervention provided to tobacco using TB patients for 12 months. The intervention focuses patient centric approach with weekly counselling sessions to patient and family.
Results: Before intervention, in 2014, out of 372 patients 251 TB patients are tobacco consumers. Default rate of these tobacco consuming patients is 13.2%, failure rate is 4% and death rate is 9.5%. In 2015, out of 315 TB patients 212 patients are tobacco consumers. After the tobacco cessation intervention using 5A's (Ask, Advise, Assess, Assist and ARRANGE) and 5R's (Relevance, Risks, Rewards, Roadblocks and Repeat) model, default rate is 6.6%, failure rate is 1% and the death rate is 5.8%.
Conclusions: Tobacco cessation intervention in TB patients is found more effective in reducing defaults and this may be replicated with help of NTCP in all other districts of India.

SOA-451-14 What price and non-price factors are crucial to elicit a quit response among bidi smokers?

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Background and challenges to implementation: A World Bank- WHO study from 2006 confirms that if the retail price of cigarettes is increased by 10% roughly 4% and 6% current smokers quit smoking in a developed and developing countries, respectively. *Bidi* (Indian leaf-rolled cigarillo) are the dominant form of smoked products in India. The manufacturing cost of *bidi* is very low and tax on *bidi* is also very low compared to the cigarette. Nearly seven *bidi* sell for every cigarette and at price which is at a fraction compared to a cigarette. This makes *bidi* very affordable for a smoker. This study analysed key price and non-price factors which determine current smoking of *bidi* and initiation into *bidi* smoking.

Intervention or response: We interview current and former *bidi* smokers to understand motivations for persistence or quitting *bidi* smoking. Using a pre-tested semi-structured questionnaire, the investigators interviewed 400 bidi current smokers during their purchase at a point of sale for the duration of any entire day of business. The study was conducted in five major cities of India i.e. Lucknow (Uttar Pradesh), Paschim Medinipur (West Bengal), Patna (Bihar), and Bengaluru (Karnataka).

Results and lessons learnt: Preliminary data analysis shows that most *bidi* smokers (78%) started smoking at early age (16.8 years) and are predominantly from lower socio-economic group (incomes less than USD 150 per month). They also have limited understanding on harms of smoking and harms to others. *Bidi* smokers have shown willingness to accept price hike of about 100% at current level.

Conclusions and key recommendations: This study presents evidence that is necessary for shaping tobacco control policies and programmes in India especially related to tax and smokefree policies. This study also advocates to opt for additional strategies that will encourage *bidi* smokers to quit.

16. TB laboratory services: lessons from the field

SOA-452-14 Attaining universal access to DST for tuberculosis patients in Uganda: experience from Kampala city on optimal utilisation of Xpert® MTB/RIF

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Background and challenges to implementation: The WHO End-TB strategy emphasizes early diagnosis of TB including universal access to drug susceptibility testing using WHO recommended rapid diagnostic. Uganda expanded GeneXpert use as initial diagnostic test for all presumptive TB cases but access to GeneXpert test is still sub-optimal. The NTLP strategic plan targets increasing GeneXpert test for all notified TB cases from 21% in 2015/16 to 56% by 2019/20.

We aimed to strengthen health systems in Kampala for improved utilization of GeneXpert and ensure all newly notified TB patients are diagnosed with WHO-recommended rapid test.

Intervention or response: The USAID funded TRACK TB project supports Kampala Capital City in TB control by implementing an urban DOTs TB model. The project strengthened health systems to improve access and utilization of GeneXpert services in Kampala. A hub system was established with motorcycle riders to transport sputum samples from the peripheral facilities for GeneXpert test. Health facility teams received bi-monthly quality improvement coaching in GeneXpert usage and support to report GeneXpert data to the NTRL using GxAlert. A quarterly coordination mechanism was established for GeneXpert stakeholders to discuss performance and generate actions addressing identified gaps.

Results and lessons learnt: Utilization of GeneXpert improved by 29.3% in 2016, from 3,492 TB samples tested in (Jan-Mar 2016) to 4,514 in (Oct-Dec 2016). Cumulatively, 2,105/15,096 (14%) of TB samples tested that year were TB positive and 72 (3%) were Rifampicin resistant. An assessment of TB patients newly diagnosed between July-Sept 2016 at 65 facilities in Kampala found 542/822 (66%) of bacteriologically confirmed patients were tested by GeneXpert and 10 (1.8%) were Rifampcin resistant.

Figure Sputum samples tested for TB using GeneXpert

Conclusions and key recommendations: Optimal utilization of GeneXpert is achievable within strengthened health system. This improves TB diagnosis and early detection of drug resistant TB. Universal access to drug susceptibility testing for all newly diagnosed TB cases is attainable when all health facilities access GeneXpert test.

SOA-453-14 Digitalization of microscopy centres in Andhra Pradesh (AP), India: E-Lab Register

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Background and challenges to implementation: Presumptive TB cases (PTC) attending Microscopy Centers (MC) of the public health system are often lost to diagnosis contributing to 'missed-cases'. To address this, Revised National TB Control Programme, AP, India digitalized MCs and designed the E-Lab register application across 273 Microscopy Centres (MC) of 6 Districts in the State with the grant received from TB Reach Wave 4, in 2015.

Intervention or response: PTC details are entered into E-Lab register on computers in MCs. Pre-recorded SMS templates and Voice-calls are sent to patients and health staff at pre-defined points in the diagnostic algorithm. Patients giving single sputum samples, not completing diagnostic algorithm and not initiated on treatment, receive SMS/Voice-calls. In response to SMS, health staff track cases to ensure completion of diagnosis and treatment initiation. A server automatically updates the e-Lab register, generates auto SMS/Voice-calls, performs backend functions, and generates reports as graphs, charts, tables, etc.

To sustain this project Hon'ble Chief Minister of AP launched "E-Lab Register" on 22nd November, 2016. The programme relocated 275 computers to high load MCs in 13 districts of the State and information on 67% of PTC load in the State is now digitalized.

Results and lessons learnt: Since 1st Nov 2016 to 28th Feb 2017- Details of 48,887 PTC were entered real time. 93% Mobile numbers recorded (increased from 23% in 2015 to 93% in 2016) and 95% linked to the unique citizen identification number-Aadhaar .Around 2,55,730 SMS sent to patients/health staff informing results of 48,887 PTC, 1104 patients retrieved for their second sputum sample, 41,628 Smear negative patients followed-up for repeat sputum examination after 14 days. About 1599 cases referred to other MCs for treatment and 350 Initial lost-to-follow-ups were retrieved and treatment started.

Conclusions and key recommendations: With the success of this intervention, it is decided to deploy e- Lab registers in all 611 MCs of the State and scale-up nationally.
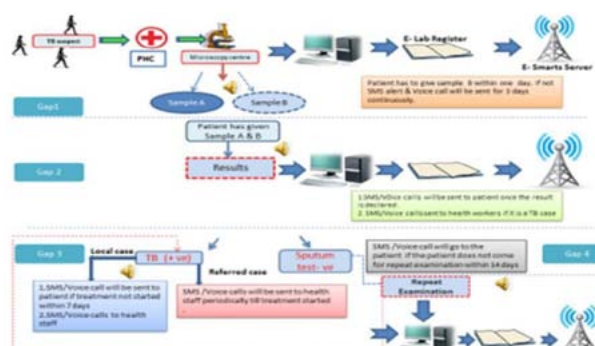
Figure The Gaps in the Diagnostic pathway and how SMS/Voice-calls are deployed along the algorithm to minimize the loss to diagnosis of TB in Microscopy Centres of Andhra Pradesh, India

SOA-454-14 Deployment of 185 GeneXpert machines in a resource-limited setting: summary of the implementation

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Background: Nigeria is ranked as the country with the 2nd and 4th highest burden of HIV (3.4 million people) and Tuberculosis (3.3 million people) in the world respectively. Diagnosis of TB in HIV patients remains a major challenge due to low bacillary load and advanced immunosuppression associated with these patients. In 2010, WHO recommended GeneXpert MTB-RIF test as the initial diagnostic test in HIV patients with presumptive TB due to its high sensitivity and specificity.

Methods: The National Agency for the Control of AIDS in collaboration with the National TB, Leprosy Control Programme, KNCV TB Foundation and part-

ners, deployed GeneXpert machines in *185* facilities to enhance TB/HIV diagnosis across the country. To identify healthcare facilities suitable for GeneXpert installation, site assessment visits were conducted in *233* health facilities in all parts of the country. Key suitability criteria for selection were; workload, adequate space for a GeneXpert room, power supply, provision of HIV and DOTS services and available personnel in line with the NTBLCP guidelines.

Results: Post assessment, *21*% did not qualify for GeneXpert deployment as they fell short of the key suitability criteria. Over 90% of these facilities were state government owned secondary health facilities. The most common challenge experienced by the facilities was poor power supply. This was followed by lack of adequate space for the machine. Poor human resource capacity was also a common factor. The other criteria of adequate TB work load and provision of ART and DOTS services were met.

Conclusions: Power supply, adequate space and available personnel are very critical in the deployment of GeneXpert machines in resource limited settings. Overall, poor systemic funding led to the inability of these facilities to benefit from the new technology to improve diagnosis of TB among HIV clients and other priority groups at risk of TB.

SOA-455-14 Clinical impact of the Xpert® MTB/RIF assay among sputum smear-negative multidrug-resistant tuberculosis patients in Georgia

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Background: A delay in detecting drug-resistance may postpone appropriate second-line treatment initiation and increase the likelihood of poor clinical outcomes among patients with multidrug-resistant tuberculosis (MDR-TB). The Xpert MTB/RIF assay has been endorsed for use on both Acid-Fast Bacilli positive and negative sputum specimens and starting in 2014 the Georgian National Tuberculosis Program implemented the assay into routine clinical care for all TB suspects. We sought to determine the clinical impact of Xpert MTB/RIF implementation among patients with sputum smear-negative pulmonary TB disease.

Methods: A quasi-experimental design was used to compare clinical outcomes among sputum smear-negative MDR-TB patients treated before and after the implementation of the Xpert MTB/RIF. Patients received treatment at the National Center for Tuberculosis and Lung Diseases in Tbilisi, Georgia between 2011-2015. MDR-TB was confirmed either by conventional drug-

susceptibility testing, MTBDRplus or Xpert MTB/ RIF. Time to second-line treatment initiation, sputum culture conversion, and final treatment outcomes were evaluated.

Results: Among 99 patients with sputum smear-negative pulmonary MDR-TB, 61 (62%) and 38 (38%) were from the pre- and post Xpert implementation periods, respectively. The groups had similar characteristics including history of prior TB treatment (50% and 49%), the rate of extensive drug-resistance (11% and 12%), and received similar treatment regimens. Patients in the post-implementation period were more likely to be initially hospitalized for treatment (76% vs. 48%, p < 0.01) and initiated appropriate second-line treatment significantly earlier (14 vs. 73 days, p< 0.01) than patients in the pre-implementation period. Patients in the post-implementation group had more rapid culture conversion (84 vs. 105 days, p=0.26), lower mortality (3% vs. 7%, p=0.42) and shorter treatment duration (635 vs. 668 days, p=0.35) compared to the pre-implementation group, but the differences were not statistically significant.

Conclusions: Implementation of Xpert MTB/RIF reduced time to appropriate second-line treatment among patients with hard to diagnose smear-negative MDR-TB.

SOA-456-14 Cost analysis of field application of a novel sample transport and decontamination reagent in Ethiopia and Peru

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Background: OMNIgene SPUTUM (OMS) is a novel sputum liquefying and decontamination reagent that eliminates the need for cold-chain during sample storage and transport. Thus, OMS may be highly applicable in settings where limited transportation infrastructure can cause significant loss of sample viability and diagnostic delays. We compared the costs of laboratory-based routine decontamination (utilizing NALC-NaOH) with various implementation scenarios for OMS.

Methods: Per-sample costs of all laboratory-based routine and OMS decontamination methods were calculated using a bottom-up micro-costing and ingredients approach with data generated from Time and Motion (TAM) measurements repeated for variable batch sizes (between 2 to 16 samples) in two reference laboratories in Ethiopia and Peru. In Peru, transport network and

preference surveys were used to estimate costs associated with sample transport and OMS implementation at local clinics. All costs were reported in USD 2015 with capital assets discounted at 3% based on their expected useful lifetime.

Results: Total per-sample costs for OMS implementation in the laboratory were batch size dependent and ranged from $4.50 to $7.21 for routine decontamination and from $4.58 and $5.23 for OMS. The OMS reagent cost for the laboratory-based method was approximately $0.75 per sample due to average use of < 1mL OMS per sample. OMS implementation at the clinical collection site was more costly, with an OMS reagent cost of $2.18 per sample due to variability in sputum volume at collection. Overall, the total cost of clinic-based OMS was approximately $0.22 (0.04, 0.62) higher per sample than routine decontamination in Peru, accounting for sample transport and laboratory processing costs.

	OMS at Clinic (low, high)	
Overhead, Building, Staff, Consumables and Reagent Costs	3.34 (2.95, 4.46)	0.87 (0.65, 1.60)
Sample Transport Costs	2.30	2.30
Laboratory Processing Costs	2.12	4.37
Total Per-Sample Cost ($)	7.76 (7.37, 8.88)	7.54 (7.33, 8.26)

Table Average Per-Sample Costs in Peru (USD 2015)

Conclusions: The cost of OMS is highly dependent on its application in the lab or at the clinical collection site and there is a considerable cost trade-off for the clinic-based OMS. Full field-based evaluation and cost-effectiveness analysis evaluating impact on clinical workload and patient outcomes is needed.

SOA-457-14 Experiencia del uso del portalab MODS para el diagnóstico de TB y TB-MDR en la sierra y selva central de Junín, Perú

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Background and challenges to implementation: El Portalab MODS es un laboratorio móvil construido localmente dentro de un contenedor, es de fácil traslado a lugares donde su necesidad es requerida. Por otro lado el método MODS ha demostrado ser un método simple, rápido y económico que detecta directamente la tuberculosis multidrogo resistente (TB-MDR). La región Junín ubicada en la zona central del Perú cada año notifica casos de tuberculosis drogo resistente (TB-DR). Sin embargo debido a que no dispone con un laboratorio para realizar pruebas de sensibilidad, basa la detección de casos en factores de riesgo remitiendo muestras al laboratorio referencial de TB en Lima. Estos números pueden reflejar un sub-diagnóstico de casos.

El objetivo de este estudio fue explorar la posibilidad de evaluar el uso del Portalab y obtener la prevalencia real de la TB-DR por el método MODS y a mediano plazo la implementación del MODS para controlar la TB en esta región.

Intervention or response: El Portalab se diseñó en Lima-Perú, luego fue remitido a la ciudad de Huancayo en la región Junín donde personal de laboratorio luego de un proceso de capacitación se movilizó junto con el Portalab a Satipo y Chanchamayo lugares remotos con alta incidencia de TB-DR. Capacitaciones previas fueron realizadas al personal de laboratorio de estas zonas para mostrar las bondades del laboratorio móvil. 781 muestras fueron analizadas utilizando MODS.

Results and lessons learnt: Los estudios iniciales demuestran que el Portalab MODS es de fácil uso, permite una fácil movilización y alta performance con el uso de MODS. De 781 muestras procesadas 74 (9.5%) fueron positivas y de ellas, 8 (10.8%) presentaron monoresistencia a isoniacida con MODS.

Conclusions and key recommendations: El uso piloto del portalab MODS provee un fuerte potencial para la detección oportuna de TB -DR en beneficio de la población en lugares donde rápidos y económicos métodos contra la tuberculosis son urgentemente necesitados.

SOA-458-14 Increasing access to TB services through government-led clinical mentorship in Kafue district, Zambia

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Background and challenges to implementation: Jhpiego Zambia established an on-site clinical mentorship program in Kafue district from May to July 2016 with 21 health professionals equipped in training skills, mentorship and technical updates in HIV/AIDS service delivery areas including ART, PMTCT, HTS and Infection Prevention and Control. This multidisciplinary district based pool called district mentorship and training team (DMT) is coordinated by MOH and they are responsible to maintain health care providers' competence to deliver quality services, addressing identified gaps that affect access to quality care.

Intervention or response: In September 2016, TB diagnosis and management was included in ongoing skills updates to boost DMT's ability to mentor providers as well as motivate them to deliver quality TB services. A review of DMT reports from November 2016 to March 2017

and Key Informant Interviews were performed to assess implementation of TB clinical mentorship in the district. **Results and lessons learnt:** An increased focus on TB mentorship was observed during the period assessed (fig 1). Reports from the Railway Clinic in Kafue showed an increase in presumptive TB cases identified through TB screening from zero to 54 clients comparing baseline and 2 months after TB mentorship training respectively. In addition, mentorship has also enabled the upgrade of Zambia National Service (ZNS) clinic laboratory to a diagnostic center thus increasing access to TB diagnostic services in the district. In the first 4 days of operation, ZNS laboratory examined sputum smear of 11 clients with presumptive TB, 2 were sputum smear-positive TB cases, both TB/HIV co-infected. Facilities receiving mentorship to routinely address gaps on TB screening have increased over time: 6-7 health facilities monthly in November 2016 to March 2017 compared to only 2 facilities from July to October 2016.

Conclusions and key recommendations: DMT approach has increased access to TB services with increasing confidence of providers to implement updated TB diagnosis and management skills.

SOA-459-14 Cold chain vehicle specimen transportation system for TB culture improved quality of laboratory service in Ethiopia

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Background and challenges to implementation: Tuberculosis (TB) culture service is highly reliant on sputum transport. Sputum transportation needs to consider a system which ensures the public safety during transport and quality of specimens at recommended temperatures. Whereas the previous courier system uses public transport most of the time. A cold chain vehicle specimen transport with electronic Specimen SMS/web based result delivery system was developed and implemented for TB culture over six months period.

Intervention or response: The Ethiopian Public Health Institute with support from the USAID funded Challenge TB project deployed eight vehicles designed for specimen transportation. Trained drivers on biological specimen supported 28 Drug resistant TB (DR TB) treatment initiating centers from Amhara, Oromia and Addis Ababa regions in transporting sputum to culture laboratories. Referring health facilities and culture laboratories were networked and monitoring mechanism was put in place. Vehicle transport performance of August 2016-January

2017 and baseline courier performance from January to June 2016 was analyzed.

Results and lessons learnt: A total of 1,107 specimens were transported from health facilities to culture laboratories using the cold chain vehicle: 1,011 for follow up of DR TB patients on treatment and 96 for presumptive DR TB cases.

The average transportation days between specimen collection and delivery to testing site reduced from 5 days to 1 day and initiation of specimen processing by the laboratory improved from 5 to 2 days because of regular scheduled transportation.

From total sputum transported, the percentage of specimen rejected dropped from 3.2% to 0.3% and the transport cost reduced from $65 to $45 per specimen.

Conclusions and key recommendations: Vehicle sputum transportation ensured that specimen is handled with the highest standards and delivered on time with a sense of urgency by reducing the negative culture result Turnaround Time (TAT) from 76 days to 68 days and number of sputum rejected. Full TAT was not measured due partial implementation of e-Specimen.

SOA-460-14 Non-invasive sampling for molecular diagnosis of tuberculosis

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Background: We have hypothesized that oral swabs are simpler, cleaner, safer, and more uniform alternatives to sputum as diagnostic samples for tuberculosis (TB). In a previous, unblinded study conducted on buccal (cheek) swabs collected from 20 sputum-GeneXpert-confirmed case subjects in South Africa (3 swabs per subject), 18/20 case subjects (90%) yielded at least two swabs that were positive for *Mycobacterium tuberculosis* (MTB) DNA by quantitative PCR (qPCR).

Methods: An expanded sample of oral swabs were collected from the following adult groups in South Africa: Sputum GeneXpert-confirmed pulmonary TB cases (N = 46), sputum GeneXpert-negative but culture-positive TB cases (N = 11), ill/no TB cases (N = 26), and healthy controls (N = 33). Samples were tested by qPCR in a blinded analysis.

Results: First, the method was applied to cheek, gum, and tongue swabs from a subset of GeneXpert-confirmed cases (N = 23). Tongue swabs yielded ~30-fold stronger qPCR signals for MTB DNA (based on Cq value) than cheek or gum swabs ($p = 0.000$). Tongue swabs from the entire sample population (2 swabs per subject) were then tested. In total, 42/46 sputum GeneXpert-positive cases (91%) yielded at least 1 positive tongue swab. In addition, 5/11 (45%) sputum GeneXpert-negative, culture positive cases yielded at least 1 positive swab. Among ill/

no TB subjects and healthy controls, 55/59 (93%) were negative in both swabs.

Conclusions: The results suggest that oral swabbing can serve as a convenient and occupationally safe alternative to sputum collection for TB diagnosis. In addition, oral swab analysis (OSA) may improve TB diagnostic yield by detecting at least some sputum GeneXpert-negative, culture-positive TB cases. If validated in expanded studies, OSA could supplement sputum testing as a diagnostic method for TB, and potentially enable more active case-finding strategies.

SOA-461-14 Evaluation of a panel in support of validation and quality control of the Xpert® MTB/RIF test

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Background: The use of the Xpert® MTB/RIF test, as the initial diagnosis of multidrug-resistant tuberculosis (MDR-TB), makes necessary the introduction of a panel that evaluates the reliability of the results and used as a complement to the validation that is carried out investigating cases with drug resistance. The objective of this study is to obtain enriched panels with strains of *Mycobacterium tuberculosis* resistant to rifampicin to be implemented in Mexico and Central America.

Methods: Bacillary suspensions approximately 5,000 bacilli/mL, were generated by dilutions from strains that the World Health Organization (WHO) used for the quality control of drug susceptibility assay, suspensions were inactivated and assembled panels, one of 20 strains (6 duplicates) and another of 5, which were tested in the GeneXpert® equipment. Results were compared with the WHO reference values, determining sensitivity, specificity, predictive values, concordance and intra-laboratory repeatability.

Results: The obtained bacillary suspensions were correctly classified using this molecular test; only one result was reported as an error for the panel of 20 strains, reaching a sensitivity of 93%, specificity 100%, predictive value resistant 100%, predictive value sensitivity 80% and 95% of agreement. The intra-laboratory repeatability among duplicate strains with valid results was 100%. For the panel of 5 strains only concordance was determined and was 100%.

Conclusions: The biological material generated by the Supranational Laboratory of Mexico, can be used to implement a panel that supports the validation of the Xpert MTB/RIF test verifying its detection parameters and at the same time serving as an external quality control to detect possible errors, but not those related to the operation of the equipment, this will strengthen the diagnosis of MDR-TB and the quality of laboratory services in the health systems of the region.

SOA-491-14 Field evaluation of OMNIgene SPUTUM reagent in Kyrgyzstan for the detection of *Mycobacterium tuberculosis*

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Background: In many settings, the inability to maintain cold chain puts sputum samples at risk of contamination and loss of TB viability. This study explored the use of OMNIgene SPUTUM (OS) to increase detection, reduce contamination, and improve time to positive cultures.

Methods: This cross-sectional study evaluated whether the addition of OS stabilized sputum samples thus improving the ability to detect TB. 503 adult patients, presenting as new TB suspect or relapse cases were enrolled at seven sites in Kyrgyzstan. All patients provided one sputum sample which was examined by microscopy. Samples were split and OS added to one portion. Paired samples (all microscopy or GeneXpert positive and 41 negative samples were sent for testing at the National Reference Laboratory. Samples without OS were held under cold chain whereas samples with OS were kept at ambient temperature. Data were analyzed using a one-sided McNemar test to compare detection and contamination rates.

Results: The contamination rate was 8.2% (without OS) and 3.9% (with OS). TB was detected in 31.6% of all samples by GeneXpert (both with and without OS). Of the 208 samples sent for confirmatory testing the TB detection rates were: MGIT 71.6% (with), 60.7% (without); Solid LJ 65.2% (with), 54.6% (without); HAINS 64.8% (with), 66.0% (without). The mean time to a positive culture with OS was: MGIT 22.8 days (CV 35%) and LJ 48.8 days (CV 29%) compared to without OS: MGIT 20.8 days (CV 69%) and LJ 41.5 days (CV 34%).

Conclusions: Results showed that even in a low contamination setting, use of the OMNIgeneŸSPUTUM reagent can further reduce contamination and improve the detection of TB. While the mean time to a TB positive culture is slightly later when OS is used, more TB detections center around the mean when OS is used.

17. TB in health care workers

SOA-462-14 An innovative approach to TB surveillance among health care workers: results from a pilot project in Nigeria

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Background and challenges to implementation: Nigeria has the highest TB burden in Africa. The burden of TB among Health Care Workers (HCW), an at risk group for TB is not known in Nigeria as HCW TB surveillance is not currently a routine activity within the TB program. We piloted a project on HCW TB surveillance in 13 health facilities in three states as a key activity in the scale up of the TB infection Control (TBIC) program. To reduce associated stigma, increase uptake of TB screening and ensure sustainability, TB surveillance was integrated into the facility based Occupational Health (OH) program.

Intervention or response: Base line assessment of TBIC and OH services was conducted across the pilot facilities. TBIC practices were strengthened using the TB BASICS (Building and Strengthening TB Infection Control Strategies) and OH clinics were established and supported with diagnostic tools. Staff log book for health assessment for Diabetes, Hypertension, Obesity, TB and referral booklets were provided. Staff sensitizations were carried out to mobilize staff for health assessments. Standard operating procedures were developed for staff health assessments, screening and diagnosis of TB. HCWs with presumptive TB were referred for sputum collection and testing for TB using smear microscopy and GeneXpert MTB/RIF, and persons with TB were initiated on treatment.

Results and lessons learnt: A total of 2,274 HCWs were screened between May 2016 and March 2017. Thirty eight had presumptive TB; 4 had sputum examination for acid-fast-bacilli and 34 by GeneXpert. Four TB cases (1 case of drug-resistant TB) were detected and promptly started on treatment. The integration of TB screening into the facility based OH services ensured uptake of TB screening and helped to strengthen the facility based OH program.

Conclusions and key recommendations: The intervention demonstrated a successful integrated approach to HCW TB surveillance. The lessons from the pilot will inform scale up of HCW TB surveillance within the National TB program.

SOA-463-14 Prevalence of and risk factors for latent tuberculosis infection among health care workers in Viet Nam, 2014

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Background: In VietNam, health care workers (HCWs) are not systematically screened for tuberculosis infection (LTBI) and disease as part of annual health examinations. In 2014, we conducted a baseline cross-sectional survey of LTBI prevalence among HCWs from four TB and eight general hospitals in VietNam before implementing an enhanced tuberculosis infection control intervention through the EnTIC trial.

Methods: HCWs ≥18 years of age were screened for LTBI using the QuantiFERON®-TB Gold In-Tube interferon gamma release assay (QFT). LTBI was defined as a positive QFT test result in the absence of active TB. Standard questionnaires were self-administered to collect demographic information, TB symptoms, and potential factors associated with LTBI. HCWs with TB symptoms were evaluated for TB disease per the national TB guidelines. Analyses, adjusted for clustering, were used to assess factors associated with LTBI.

Results: A total of 5,037 HCWs were screened by QFT; 562 (11%) in TB hospitals and 4,475 (89%) in general hospitals. Mean age was 35 years (range: 18-81); 29% were male. Of these, 5,018 (99.6%) HCWs had an interpretable result. Prevalence of LTBI among HCWs was 29.6% (95%CI: 24.4-35.3%) overall, 41.7% (95%CI: 26.2-58.9%) at TB hospitals, and 27.9% (95%CI: 22.8-33.6%) at general hospitals. At the time of screening, 157 (3.1%) HCWs had presumptive TB per WHO criteria; none had active TB. LTBI was associated with older age, male gender, contact with a person with TB, ≥10 years working in current occupation, and working in a clinical department which frequently encounters presumptive and confirmed TB patients (Table).

HCW Characteristic	Age (continuous var., yrs)	Male	Previous contact with a TB person	≥10 yrs working exp. in current occupation	Work at higher-risk area
n (%) N = 5,018		1,473 (29.3%)	1,949 (39%)	2,113 (42%)	1,832 (36.5%)
% LTBI (n/N)		35.6% (525/1,473)	32.8% (640/1,949)	41.7% (882/2,113)	32.7% (600/1,832)
Univariate Odd Ratio (95% CI)	1.06 (1.05 - 1.07)	1.5 (1.3 -1.7)	1.3 (1.1 - 1.5)	2.7 (2.1 - 3.3)	1.2 (1.0 - 1.5)
Multivariate Odd Ratio (95% CI)	1.05 (1.04 - 1.06)	1.34 (1.19 - 1.50)	1.17 (1.00 - 1.37)	1.25 (1.09 - 1.42)	1.24 (1.03 - 1.49)

Table Participant characteristics & factors associate

Conclusions: Nearly one third of HCW in these hospitals in VietNam were infected with tuberculosis, underscoring the need for TB infection control programs in health care settings. Such programs should be coupled with routine HCW TB screening to assist in monitoring the effectiveness of IC efforts and to enhance overall occupational health and safety.

SOA-464-14 Outcomes and incidence of tuberculosis among health care workers in two refugee camp facilities in Kenya: a retrospective cohort study

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Background: In Sub- Saharan Africa nosocomial Tuberculosis (TB) is a major problem. Hospital acquired TB is a significant occupational hazard among health care workers who are at a greater risk of developing TB than the general population in Kenya. The objective of the study was to measure outcomes, incidence and risk factors associated with TB infection among health care workers in two large refugee camp facilities in Kenya.
Methods: A retrospective cohort study was conducted in two major refugee camps in Kenya. Data was abstracted from medical health records retrospectively from January 2014 to December 2016. Using poison model, bivariate and multivariate analysis was carried out.
Results: Of 1864 (94%) medical charts reviewed with data on location of work documented, 160(9%) cases of TB were reported. Among HCWs with TB 21 (13%) had multidrug-resistant TB. Fifty two (33%) were cured, 48 (30%) completed treatment, and 39 (24%) died. We noted an increased incidence of TB in HCWs with a history of working in TB Manyattas (incidence rate ratio (IRR) 2.03, 95% CI 1.11-3.71), laboratories (IRR 1.82 95% CI 1.07-3.10), chest-clinics (IRR 2.08 95% CI 1.23-3.52), and pharmacy (IRR 2.38 95% CI 1.06-5.34) compared with those without such a history. Health care workers with diabetes had a greater incidence of TB (IRR 4.2, 95% CI 1.54-6.66) than HCWs without diabetes. TB incidence among HCWs was approximately two-fold greater than that of the general population over the study period.
Conclusions: Nosocomial exposures were associated with TB among staff at these two refugee camp facilities regardless of their job designation, even after controlling for area of residence, suggesting active transmission from patients. Health care facilities should improve infection control practices, provide quality occupational health services and encourage staff testing for HIV infection to address the TB burden in hospital staff.

SOA-465-14 Interferon-gamma release assay positivity among healthcare workers in Lima, Peru

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Background: Tuberculosis infection as measured by tuberculin skin testing positivity increases the longer a healthcare worker (HCW) has been employed in a hospital setting. The objective of our study is to measure the frequency of interferon gamma release assay (IGRA) positivity among recently employed nursing and physician interns compared to established HCWs in Lima.
Methods: We performed IGRA testing using QuantiFERON-TB Gold (QFT) and QuantiFERON-TB Gold Plus (QFT-PLUS) on 210 health care workers at three public hospitals in Lima, Peru. The cohort comprised two groups: 1) nursing and physician interns divided across the three hospitals and 2) established physicians, nurses and nursing assistants working in the emergency department at one of the three hospitals. We performed a cross-sectional analysis of the frequency of IGRA positivity between groups.
Results: Of 108 interns tested, 12.0% had a positive test, either by QFT or QFT-PLUS compared to 61.8% of 102 established HCWs tested (p < 0.0001). There was strong agreement between QFT and QFT-PLUS results (kappa = 0.95). The odds of TB infection in established HCWs were five times higher than interns, adjusted for age and sex (adjusted OR 5.2, 95% CI 2.2, 12.2). There was no difference in IGRA positivity between job titles among established HCWs or between physician and nursing interns. Previous BCG status and time spent commuting on public transportation did not predict IGRA positivity.
Conclusions: Health care workers with established employment in the emergency department of a general hospital in Lima, Peru have an increased risk of IGRA positivity compared to interns just beginning their clinical work. This finding suggests that the IGRA can be used to demonstrate the frequency of tuberculosis transmission as occupational hazard for HCWs in TB-endemic settings. Trainees may particularly benefit from tuberculosis transmission control measures given their low frequency of TB infection upon their initiation of hospital work.

SOA-466-14 Resultados de la evaluación de casos de tuberculosis pulmonar en trabajadores de la salud en México del 2013 al 2015

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Background and challenges to implementation: Desde 2010 se han desarrollado acciones para disminuir la transmisión por tuberculosis en establecimientos de salud a través de medidas administrativas, de control ambiental y de protección respiratoria que han permitido la normalización (normas, guías y manuales) y notificación de casos de TB en trabajadores de la salud (TS) considerado como un grupo de riesgo; pero la evaluación del seguimiento de los casos no era posible a través de los sistemas oficiales de información.

Intervention or response: Se incluyó la variable "trabajador de la salud" en el sistema oficial de información, la notificación permite la atención necesaria (acceso a servicios de salud, seguimiento clínico, bacteriológico, disponibilidad de medicamentos).

Se hizo el análisis epidemiológico de la tuberculosis en trabajadores de la salud en México en los últimos 5 años; se identificaron los estados con mayor carga de TB en TS, junto con la Dirección General de Epidemiología se hicieron modificaciones al sistema de información. La selección de las variables para el desarrollo de la cohorte fue: "Caso Nuevo", "Pulmonar", "Baciloscopía", "Tratamiento Primario" e "Ingreso a Tratamiento"; posteriormente se cruzaron las variables ocupación vs clasificación final. Se hizo posible el seguimiento de los casos de TB en TS de manera nominal.

Results and lessons learnt: En 2015 se registraron 400 TS con TBTF, 269 fueron TBP, con tasa de 49 x 100 mil (nacional de 16 x 100 mil).

Al hacer la evaluación del seguimiento se encuentra que para el 2015 se cuenta con un éxito de tratamiento de 93%.

Conclusions and key recommendations: Para fortalecer la prevención de la transmisión de la tuberculosis en establecimientos de salud es necesaria la evaluación del seguimiento de los trabajadores de la salud con TB. El éxito de tratamiento de este grupo de riesgo es de más del 90% en los últimos tres años y es reflejo del trabajo desarrollado en los niveles locales y sub-nacionales.

SOA-467-14 Latent tuberculosis infection and TB disease among healthcare workers in Thailand, 2014

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Background: Healthcare workers (HCWs) are at high risk of hospital acquired tuberculosis (TB) infection in TB endemic countries.

Methods: We assessed the prevalence of latent TB infection (LTBI) among HCWs at 10 hospitals in Thailand and monitored them for active TB over the subsequent 2-year period. HCWs who were 18-45 years old, worked $\geq$30 hours/week, and planned to work at the facility for at least one year post screening were screened for LTBI using the QuantiFERON®-TB Gold In-Tube interferon gamma release assay (QFT). A positive QFT was defined per manufacturer's guidelines as a TB specific antigen response of $\geq$0.35 IU/ml.

Demographic and occupational information was collected using a standardized, self-administered questionnaire, HCW were screened for TB symptoms using WHO criteria. We used logistic regression adjusted for clustering to identify factors associated with LTBI. We defined high-risk departments as clinical areas where patients with presumptive and confirmed TB usually received care.

Results: A total of 3,977 HCWs were screened for LTBI; the mean age was 34 years (range: 18-45), 18% were male. Of these, 1185 (29.8%,95% Confidence Interval [CI]: 27.9-31.7) had a positive QFT result, 2786 (70.1%,95% CI: 68.1-71.9) had a negative result, and 6 (0.2%,95% CI: 0.1-0.4) an indeterminate result. Multivariable analysis showed increasing age, a history of TB disease, and working in a high-risk department were associated with LTBI.

HCW Characteristic	n(%) n=3971*	Univariate OR† (95% CI)	Multivariate OR† (95% CI)	p
Age (continuous variable in years)	-	1.05 (1.05-1.07)	1.05 (1.04-1.07)	<0.0001
History of TB	136 (3.4%)	7.85 (4.46-13.84)	6.94 (3.95-12.18)	<0.0001
Works in high risk department	3075 (77.4%)	1.21 (1.0-1.5)	1.29 (1.09-1.54)	0.008

*Of 3,977 HCWs recruited for LTBI screening, 3,971 (99.9%) had a valid QFT result (positive or negative) and were included in the univariate and multivariate analysis. †OR: Odds Ratio; multivariate logistic regression model ORs were adjusted for sex.

Table Factors Associated with Latent TB Infection among

No cases of TB disease were identified at the time of LTBI screening; 14/1185 (1.2%) HCWs with a positive QFT result and 1/2789 (0.04%) HCWs with a negative QFT result were diagnosed with TB disease during the 2-year follow-up.

Conclusions: Findings highlight the need for effective hospital infection control programs to prevent occupational TB exposures and suggest a role for TB preventive therapy in high-burden TB countries, given the high rate of TB disease among HCWs with documented LTBI.

SOA-468-14 Systematic TB screening for HCWs in Tanzania: implications for policy and TB care and prevention

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Background and challenges to implementation: Tanzania is among the 30 high TB and HIV burden countries, with annual prevalence rate of 528 cases per 100,000 population (WHO, 2015). A total of 64,385 all forms TB cases were notified in 2015 (NTLP, 2015). The prevalence of Multi-Drug Resistant TB is 1.3% and 4.7% among new and retreatment cases respectively (WHO, 2015).

Tuberculosis is an occupational hazard for health care workers (HCWs). A study in South Africa (Tudor et al, 2014), reports that the risk of active TB disease among health care workers is two to three times greater than in the general population, and more than 50% of health workers worldwide are estimated to have latent TB infection.

Intervention or response: Challenge TB utilized regional coordination and performance review meetings to sensitize district coordinators on the importance of TB screening among HCWs. TB coordinators took the agenda to their respective district and hospital management teams, clinical and departmental meetings. The standardized national TB screening questionnaire is used for symptom screening. Xpert MTB RIF test where available and smear microscopy are used. X-rays are used for presumptive cases with no bacteriological confirmation.

Results and lessons learnt: Between January - December 2016, 13,719 HCWs were sensitized, 9,446 HCWs were screened. 1,211 were identified as presumptive TB cases and 44 were confirmed TB cases and initiated treatment. Areas to focus on include lack of a guiding policy for HCW screening, systematic monitoring and evaluation system, stigma among HCWs and non-adherence to IPC measures in health facilities to prevent nosocomial transmission of TB.

Conclusions and key recommendations: Challenge TB continues to document findings to establish baseline information and evidence to inform next steps, including national TB workplace policy revision to encompass systematic TB screening and surveillance among HCWs.

SOA-469-14 High rates of exposure to tuberculosis patients among HIV-infected healthcare workers in Botswana

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Background: HIV dramatically increases the risk of tuberculosis (TB). HIV-infected health care workers (HCWs) in high TB burden countries should be protected from frequent exposure to TB patients. We compared daily exposure to TB patients among HIV-infected and HIV-uninfected HCWs in Botswana, a country that is hyperendemic for TB and HIV.

Methods: We conducted a cross-sectional study among HCWs in 30 hospitals and clinics. We administered in-person interviews to determine frequency of exposure to TB patients and used rapid HIV tests to determine HIV infection status. Multivariable Poisson regression modeling with robust variance was used to estimate the association between HIV status and daily exposure to TB patients while adjusting for potential confounders.

Results: Of 1877 participants enrolled, 1399 (73.9%) with complete data for HIV infection and exposure to TB patients were included in this study. Among 277 (20.0%) HIV-infected participants, 40 (14.3%) were newly diagnosed, 152 (57.8%) were on antiretroviral therapy, and 95 (34.3%) reported previously receiving isoniazid preventive therapy. Daily exposure to TB patients was reported by 134 (48.4%) and 588 (52.9%) of HIV-infected and HIV-uninfected participants, respectively. In the final model adjusting for sex, age, occupation, and department, rates of daily TB exposure remained similar between HIV-infected and HIV-uninfected participants (prevalence ratio=0.96; 95% confidence interval=0.85-1.08).

Conclusions: We found similar rates of daily exposure to TB patients between HIV-infected and HIV-uninfected HCWs. Nearly half of the HIV-infected HCWs reported daily exposed to TB patients. Improved efforts are needed to reduce nosocomial exposure to TB among HIV-infected HCWs.

SOA-470-14 Evaluation of plasma cluster technology in tuberculosis hospital

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Background: Little evidence exists globally on the burden of hospital acquired Tuberculosis (TB) infection among health care workers (HCWs) and impact of different infection control (IC) measures in reducing risk of nosocomially acquired tuberculosis. We evaluated commercially available Plasma Cluster Ion Generator (PCI) by Sharp Corporation at specialized TB Hospital, National Center for Tuberculosis and Lung Diseases (NCTLD).

Methods: PCI units were placed per manufacturers' recommendations at two out of four therapeutic departments with identical administrative, engineering and individual IC measures. Among PCI exposed and non-exposed groups: (i) to compare risk of latent tuberculosis infection (LTBI) among HCWs, baseline and six month apart follow-up testing with QuantiFERON-TB Gold In-Tube (QFT-G, Quest Diagnostics) was performed; (ii) to compare risk of acquired drug resistance (ADR) development among hospitalized patients, over six month period three months apart follow-up cultures were tested with drug susceptibility testing (DST) on 1st and 2nd line drugs.

Results: From total 100 HCWs, 32 were QFT negative at baseline. On 6 month follow-up testing 10 (90, 9%) remained negative and 1 (9, 1 %) became positive in exposed and 15 (71%) remained negative and 6 (28%) became positive in non-exposed groups. Subjects within non-exposed group showed 4 times greater risk of acquiring LTBI compared to subjects from exposed group. (OR=4, 95% CI=0.36-102, Fisher exact p-value=0.21). As for the ADR development, from 410 patients, 155 culture positives on 3rd month and 49 remaining culture positives on 6th month received follow-up DSTs. In exposed group 25 (82%) out of 26 developed ADR compared to 19 (96%) out of 23 in non-exposed group (Risk Ratio for ARD development RR= 0.22, 95% CI=0.027-1.84).

Conclusions: PCI technology has substantially decreased the risk of acquiring LTBI among HCWs. Further molecular testing of patient cultures are required to define the role of PCI in prevention of re-infection among patients.

SOA-471-14 Active tuberculosis case finding among health care workers in Mtwara region, Tanzania

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Background and challenges to implementation: Transmission of tuberculosis (TB) in health care settings is common. Risk of developing TB as an occupational disease is well established among health care workers (HCWs).It varies by setting, occupational group, TB burden, patient population and the effectiveness of TB infection control (TB-IC) measures. There have been challenges towards effectively implementing TB-IC measures at health facilities.

Screening HCWs at high risk is likely to reduce transmission and prevent serious illness. In response to WHO recommendations for countries to strengthen TB surveillance systems among HCWs, Tanzania Health Promotion Support (THPS) in collaboration with Mtwara Regional Health Management Team (RHMT) implemented screening HCWs for TB in 2015 and 2016.

Intervention or response: THPS clinical advisors and district TB & Leprosy Coordinators conducted TB screening among HCWs at ten high volume health facilities (HFs). A standard questionnaire regularly used for TB screening among PLHIV was used. TB suspects among HCWs had sputum, X-rays and Gene X pert examinations.

Results and lessons learnt: In 2015, 190 HCWs from 10 HFs were screened, 21 (11.05%) were TB suspects; six (28.57%) HCWs were diagnosed with active TB. In 2016, 220 HCWs were screened; 28 (12.72%) were TB suspects, and 4 (14.28%) HCWs diagnosed with active TB. All TB cases started treatment received HIV testing and counselling. Majority of the suspects and active TB disease cases among HCWs, were working in medical ward and TB clinics.

Conclusions and key recommendations: TB is a significant occupational disease among HCWs. The proportions of HCWs found with active TB through routine screening were 3.2% and 1.8% in 2015 and 2016 respectively. There is a need to strengthen TB-IC plans, and regular TB screening among HCWs.

18. Thinking holistically - many contributors to improving TB treatment outcomes

SOA-472-14 Xpert rifampicin-susceptible tuberculosis: findings from an integrated TB-HIV surveillance system in South Africa

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Background: South Africa (SA) is afflicted with dual epidemics of Tuberculosis (TB) and Human Immunodeficiency Virus (HIV). About 6.4 million people are estimated to be living with HIV and the TB co-infection rate is approximately 65%. SA has one of the world's largest antiretroviral (ARV) programmes, with over 3 million people with HIV infection currently receiving ART. We aimed to understand and characterise the burden of TB-HIV co-infection and related resistance among persons presenting at the selected surveillance sites.

Methods: The sentinel surveillance program included a clinic from each of the 4 provinces selected. All patients with Xpert MTB/Rif testing having a rifampicin susceptible TB diagnosis at the selected sites were invited to participate after informed consent. A standard questionnaire was completed and a sputum sample collected for further susceptibility testing using first line Line Probe Assay (LPA).

Results: A total of 170 TB patients were enrolled over the study period. The median age was 37 years (IQR 28-46). The majority were male (56%). History of previous TB was observed in 38%. A total of 90 patients (53%) were co-infected with HIV and of these 45% were not on ART. Of the ones enrolled in the surveillance, 6% had Rifampicin resistant (RR) TB detected on LPA despite the initial Xpert showing susceptibility.

Conclusions: Over half of all TB patients are co-infected and a large proportion (45%) were not on ART. The revised test and treat strategy will hopefully address this issue. The finding of rifampicin resistant TB in this group of Xpert suscptible patients highlights that further resistance testing may be required in selected cases.

SOA-473-14 Pulmonary impairment and its determinants in TB patients in Maputo, Mozambique

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Background: There is increasing evidence that Pulmonary Tuberculosis (PTB) is frequently associated with chronic pulmonary damage despite microbiological cure. However, type of lung impairment and risk factors are not well described.

Methods: The study was conducted at Mavalane Health Center, Maputo, Mozambique from June 2014 to June 2016. PTB patients were prospectively enrolled and followed for 52 weeks after TB diagnosis. Lung function capacity was evaluated at 8, 26 and 52 weeks after TB Treatment initiation using physical examination, spirometry, 6 minutes walking test and ECG. Saint George Respiratory Questionnaire (SGRQ) and a risk factor questionnaire were administered at baseline, 26 weeks and 52 weeks after TB treatment initiation. Sputum culture was performed at all study visits. At baseline, full blood count, biochemistry, HIV serology and a chest X-ray were performed.

Results: A total of 81 newly diagnosed PTB patients were screened, and 69 PTB patients were enrolled. Four study participants died before week 8. After 8, 26 and 52 weeks of TB treatment (68% male, 65% HIV infected, 37% smoking), the proportion of patients with pulmonary impairment (PI) measured by spirometry was 26/60 (43%), 21/62 (34%) and 14/50 (28%), respectively. All patients with PI at week 52 showed moderate to severe restricted ventilatory capacity. The mean distance walked by patients with PI was 398.1meters (95% CI: 371.9; 424.5) and 439.9 meters (420.7; 458.9) in patients without PI at week 8.

Conclusions: 43% of our patients had PI at 8 weeks after TB treatment start and among those that remained in this study one in four PTB patients still had functional lung impairment 6 months after the end of TB treatment. The findings indicate that there is a need of more studies on lung outcome in PTB patients and a necessity of integrated pulmonary function testing and rehabilitation during and after TB treatment.

SOA-474-14 Beneficial effects of BCG vaccination in outcomes for patients diagnosed with TB: observational study using the Enhanced Tuberculosis surveillance system, 2009-2015

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Background: Bacillus Calmette-Guérin (BCG) is one of the mostly widely-used vaccines and the only vaccine that protects against tuberculosis (TB) disease. However, little attention has been given to the indirect benefits of BCG. We aimed to quantify the effects of BCG vaccination on outcomes for individuals with notified TB in England and Wales to provide evidence for appropriate public health action and provision.
Methods: We obtained all TB notifications for 2009-2015 in England and Wales from the Enhanced Tuberculosis surveillance system. We considered seven outcomes: pulmonary disease, smear status, drug resistance, multiple episodes, all-cause mortality, TB mortality, and successful treatment. We used logistic regression to investigate each outcome with BCG vaccination, years since vaccination and age at vaccination, adjusting for potential confounders. We conducted multiple sensitivity analyses to assess the robustness of our results, using multiply imputed data, dropping recurrent cases, and varying the definition of successful treatment.
Results: We found evidence of an association between BCG vaccination and all-cause mortality (aOR: 0.76 (0.64 to 0.89), P: 0.001), increased successful treatment (aOR: 1.14 (1.02 to 1.26), P: 0.018), reduced multiple episodes (aOR: 0.90 (0.81 to 1.00), P: 0.055) and reduced TB mortality (aOR: 0.76 (0.51 to 1.13), P: 0.179). We found little evidence of associations with reduced drug resistance, positive sputum smear status, and pulmonary TB. There was some evidence that age at vaccination was associated with a beneficial effect of vaccination at 12 to < 16 years of age compared to at birth for all-cause mortality (aOR: 0.81 (0.45 to 1.46)), and multiple episodes (aOR: 0.70 (0.48 to 1.02)).
Conclusions: Our results indicate that BCG vaccination may be effective in preventing negative outcomes associated with TB disease; this evidence should be considered in future when setting public health policy, and evaluating interventions.

SOA-475-14 Examining factors driving performance of tuberculosis control programme in Enugu State, Nigeria: a case-based health systems analysis

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Background: Health systems strengthening is crucial to sustainability of tuberculosis (TB) control in low- and middle income countries. Nevertheless, relatively little is known about how dimensions of health systems interact and drive performance of TB control programs in resource-constrained settings. This study examined supply-side actors' perceptions of health systems factors enabling or constraining to TB control in Enugu State, southeast Nigeria.
Methods: A qualitative, theory-driven, case study design was adopted to explore TB service providers' experiences in implementing TB control policy in Enugu State. Data were collected through in-depth interviews of purposively selected supply-side actors in TB control program including state and district program managers (n = 15) and facility focal persons (13). Interviews were audio-taped and transcribed verbatim. Thematic content analysis was done guided by World Health Organization's health systems framework comprising six dimensions: governance, financing, human resources, health management information system, medical products and service delivery.
Results: Enabling factors included regular supportive supervision, quarterly review meeting, donor-funding, altruistic TB service providers, availability of recording and reporting tools, introduction of E-TB manager, robust drug consumption and stock monitoring system and private sector involvement. Constraints were weak stewardship, inadequate public spending, non-replacement of motorcycles, shortage of health workers, stigma, lack of financial incentives, work overload, constantly changing recording and reporting tools, interrupted drug supply, irregular supply of HIV test kits, poor integration of TB into general health services, poor TB/HIV collaboration, user fees for HIV screening, weak patient tracking system, unsustainable community volunteer scheme and un-cooperative patent medicine vendors. Strengths or weaknesses in many dimensions affected other building blocks of health systems.
Conclusions: This study highlighted the need to advance systems thinking in TB control program and to address context-specific health systems barriers to optimize performance of TB control in Nigeria and similar resource-constrained settings.

SOA-476-14 Tablet-based TB symptom screening pilot at a hospital out-patient department and polyclinic in Johannesburg, South Africa: challenges and cost

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Background: South Africa has a TB incidence of 834/100 000 population which is largely due to delays in diagnosis. In order to increase TB case detection, the National TB Programme recommends TB symptom screening for all persons presenting to health facilities. The objective of this study was to evaluate the pilot implementation of tablet-computer based TB symptom screening at a hospital out-patient department (OPD) and polyclinic in Johannesburg, South Africa.

Methods: From April - August 2016, TB Screening Officers offered patients and accompanying persons in the waiting rooms at the hospital OPD and polyclinic TB symptom screening. Persons with at least one symptom were referred to the hospital's TB clinic for a free sputum Xpert MTB/RIF.

Results: In total, 15,252 people at polyclinic and OPD were offered TB screening, 3,123 (20.5%) refused screening and 12,129 (79.5%) were screened for TB. 6,395/12,129 (52.7%) respondents were from the polyclinic, 4,924 (40.6%) were male, and few (10.2%, 1,239/12,129) were accompanying persons. The median number of persons screened per day was 152 (IQR: 116 - 185). 1,928 (15.9%) had at least one TB symptom and were offered referral to the hospitals TB clinic for Xpert testing; 931 (48.3%) refused referral. 560/12,129 (4.6%) participants provided a sputum and 33/560 (5.9%) were diagnosed with TB. The total cost for the 6-month project was $37,150 including 51.9% for staffing and 40.6% for Xpert testing. The TB case detection was 2.2/1,000 persons, far below estimated baseline prevalence for South Africa, at $1,126 per case detected. The number needed to screen to detect a TB case was 368, at $3 per person screened.

Conclusions: The high rate of refusal of TB screening and referral for testing, together with the low linkage to testing resulted in a disappointing yield at high cost that highlights a need for a more targeted screening approach.

SOA-477-14 Relapse with standard 6-month tuberculosis therapy: an individual patient data meta-analysis

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Background: Relapse continues to place a significant burden on patients and TB programs worldwide. Mycobacterial culture status after two months of TB therapy has been viewed as the best predictor of relapse; however its utility is limited by low sensitivity and modest specificity. Our aim was to examine other clinical and microbiological factors associated with relapse in patients on standard 6-month World Health Organization (WHO)-recommended therapy for pulmonary TB using individual patient data meta-analysis.

Methods: A systematic review was performed to identify high-quality randomized controlled trials reporting treatment outcomes on patients receiving the WHO recommended 6-month TB treatment regimen. Authors were contacted and invited to share patient-level data including demographics, clinical characteristics, and treatment outcomes. Logistic regression models and receiver operating characteristic curves were used to evaluate the predictive performance of all variables of interest in participants completing treatment per protocol. The maximum sensitivity was estimated while specificity was held fixed at 0.8.

Results: *(Preliminary)* Patient-level data were obtained from three multicentre randomized controlled trials. Of 1189 patients with confirmed pulmonary TB who completed therapy, 67 (5.6%) relapsed.

In a model that included study, age, sex, and HIV status, combining the presence of baseline cavitary disease and positive sputum smear after two months of TB therapy achieved a maximum sensitivity of 0.477 (95% CI: 0.353, 0.613), and a predicted relapse rate of 10.13%; replacing cavitary disease and smear with a positive culture status at two months led to a similar sensitivity of 0.510 (95% CI: 0.369, 0.646) with a predicted relapse rate of 8.75%.

Conclusions: While sensitivity and specificity remain modest, our analysis suggests that by using a combination of cavitary disease and 2-month positive smear status we can identify a group of people with >10% rate of relapse who could feasibly be identified in resource-limited settings.

SOA-478-14 TB implementation cascades: from better analysis to improved efficiency

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Background and challenges to implementation: The "implementation cascade" framework outlines the sequential stages in an individual's primary-prevention-diagnosis-care-treatment journey to achieving disease control. In tuberculosis (TB), it is especially important for a person with active TB to be detected and move efficiently towards treatment success to minimise transmission and poor clinical outcomes.

Intervention or response: We developed an approach for TB cascade analysis to identify potential efficiency gains in TB program implementation with the aim of improving resource allocation and health outcomes. As a first diagnostic, we carried out a rapid global desk review on the status of TB cascades for 102 countries with more than 3,000 estimated TB cases using recent data in the WHO TB database of 2014.

Results and lessons learnt: The percentage of all estimated incident cases that were notified was 58.0% in the 102 countries (median, 70.4%; average 66.9%) suggesting that missed cases are the largest break point of the cascade (Figure).
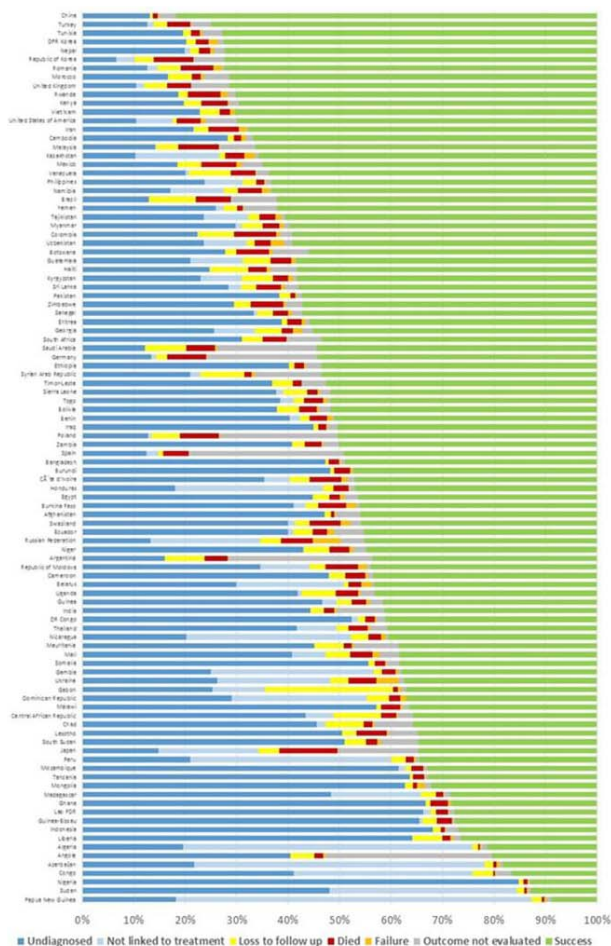
Figure Country data on notification and treatment

Lack of linkage to treatment (1.7%), loss-to-follow-up (2.3%), death (2.1%), treatment failure (0.5%) and lack of outcome evaluation (4.6%) contribute to a success rate of 46.7% against all estimated incident cases (median 49.2%, average 48.6%). There is large variation between countries across the cascade, which will require country-specific analysis and interventions to identify and address break points of the cascade.

Conclusions and key recommendations: Implementation cascade analysis allows one to quantify the gaps and 'break points' at each cascade stage and estimate the overall loss in impact through inefficiencies building up sequentially. Basing the cascade on the estimated new active TB cases means the extent of "missing cases" can be considered. Methodological work on TB cascades to reduce leaks in the cascade can help to identify priority interventions and investments for better results in the End TB era.

SOA-479-14 Comparative analysis of the ethambutol (EH) - rifampicin (RH) switch on treatment outcomes of tuberculosis patients in Mulago National Referral Hospital

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Background: Mulago national referral hospital implemented EH-RH switch for all diagnosed TB patients initiated on the first line anti-TB treatment in December 2013 as per WHO recommendation. We tested the hypothesis that the six-month treatment regimen with rifampicin throughout resulted in better treatment outcomes than the eight-month regimen among diagnosed TB patients.

Methods: We extracted records of 1,304 patients- 652 who started treatment before and 652 after the introduction of the six-month regimen. All new patients who initiated TB treatment after December 2013 were treated with this regimen. We analyzed treatment outcomes for each group considering DOT and HIV status, sex, and disease classification.

Results: Of the 652 patients in the EH cohort, 56.6% (369) were the pulmonary bacteriologically confirmed, 22.7% (148) extrapulmonary, 20.7% (135) were pulmonary clinically diagnosed and 46.2% (301) were HIV positive. Treatment success rate for the cohort was 72.2% (471), cure rate 46.1% (170), treatment failure 0.8% (5) and death, 12.9% (84). Odds of treatment completion among HIV-positive TB patients was 0.50 P=0.00.

Of the 652 patients on RH, 53.1% (346) were pulmonary bacteriologically confirmed, 23.3% (152) were

pulmonary clinically diagnosed, and 23.6% (154) extra-pulmonary, 43.7% (285) were HIV positive. Treatment outcomes were:, treatment success, 73.8% (481), cure rate, 60.4% (209) treatment failure 0.31% (2) and death 13.7% (89). Odds of treatment completion among HIV+ TB patients was 0.40, P=0.000. *(See table below)*

Variables for EH	Number (%)	AOR	P-value	Variables for RH	Number (%)	AOR	P-value
Completion on DOT	284 (43.6%)	2.2 (1.5 - 3.2)	0.000	Completion on DOT	334 (51.2%)	3.8 (2.6 - 5.6)	0.000
Cure among HIV+	143 (38.8%)	0.6 (0.4 - 0.9)	0.023	Cure among HIV+	114 (32.0%)	0.6 (0.4 - 0.9)	0.024
Cure while on DOT	155 (42.0%)	1.2 (0.8 - 1.8)	0.398	Cure while on DOT	183 (52.9%)	1.9 (1.2 - 2.9)	0.006
Death among HIV+	301 (46.2%)	2.7 (1.6 - 4.5)	0.000	Death among HIV+	285 (43.7%)	5.0 (2.9 - 8.6)	0.000

Table Comparison of outcomes for both EH and RH

Conclusions: The switch from EH to RH improved cure rate and overall treatment completion among all patients combined. However, among HIV+ patients, there was a higher risk of death with a switch to RH. Further analysis of the implications of the switch among HIV+ patients is recommended.

SOA-480-14 The diagnostic accuracy of unadjusted CRP compared to CRP adjusted for hematocrit for active TB among patients in the END TB study

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Background: C-reactive protein (CRP) testing is being considered as a screening tool for active tuberculosis. Point-of-care (POC) CRP assays are not typically adjusted for hematocrit (Hct) as is routinely done for laboratory-based CRP assays. We compared the accuracy of unadjusted and Hct-adjusted POC CRP for TB among PLHIV undergoing tuberculosis screening.
Methods: We conducted a retrospective analysis of consecutive adults with CD4 ≤350 cells/uL initiating antiretroviral therapy (ART) at two HIV clinics in Kampala, Uganda. As part of the parent study, all patients had POC CRP (iCHROMA, Boditech; normal < 10 mg/L) levels measured and had two spot sputum specimens collected for Xpert MTB/RIF (x1) and liquid culture (x2). For this analysis, we included patients who had pre-ART

Hct levels available in routine clinic records. We adjusted POC CRP for Hct in accordance with manufacturer instructions, and calculated sensitivity and specificity of unadjusted and Hct-adjusted POC CRP in reference to culture results.
Results: Hct levels were available for 546/1,549 (35%) clients enrolled from 10/2014-12/2016. Demographic and clinical characteristics were similar among clients with and without Hct levels. Among the 546 clients included, median Hct was 40% (IQR 35-44) and 90 (16.5%) had culture-positive TB. Hct adjustment reclassified 7 patients with Hct ≤36% from screen-positive to screen-negative, including 2 patients with TB. Hct adjustment also reclassified 3 patients with Hct ≥43% from screen-negative to screen-positive, none of whom had TB. Unadjusted and Hct-adjusted POC CRP had similar sensitivity (76% vs. 78%, difference -2%, 95% CI (-16 to +2) and specificity (74% vs. 75%, difference -1%, 95% CI (-2 to +1).
Conclusions: Although sensitivity was similar, adjusting for Hct has the potential to miss TB in HIV patients with anemia. When used for TB screening, results of POC CRP assays should not be adjusted for Hct.

SOA-481-14 Sedimentation rate and suPAR in relation to disease activity and mortality in patients with active tuberculosis - a comparison between two inflammatory biomarkers

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Background: At present, there is a lack of surrogate biomarkers for predicting the prognosis of patients with tuberculosis (TB). The biomarker soluble urokinase type plasminogen activator receptor (suPAR) is produced in inflammatory cells and high levels have been shown to predict mortality in TB, HIV and sepsis. Our aim was to investigate how levels of suPAR correlate with disease activity and prognosis in active TB compared to the erythrocyte sedimentation rate (ESR).
Methods: In a retrospective analysis of patients with active TB in Gondar, Ethiopia (n=500), suPAR was analysed with a conventional enzyme-linked immunosorbent assay (ELISA) at start of treatment in case serum was available (n=301). ESR, HIV serology, chest x-ray severity score, body mass index (BMI) and classification according to TBscore (clinical severity measure for pulmonary TB patients) as well as treatment outcome were recorded.
Results: We found significantly elevated levels of suPAR in TB patients who died (18.1 ng/mL vs 10.4 ng/mL, p< 0.01). An elevated ESR was significantly associated

with an unfavourable treatment outcome and mortality. Analysis of patients within the upper suPAR quartile showed a strong link to high ESR, far advanced chest x-ray findings, an increased TBscore as well as increased mortality and unfavourable treatment outcomes.

Conclusions: Our results show that suPAR is associated with disease activity measured as the TBscore and chest x-ray finding. Moreover, elevated levels of suPAR and ESR are associated with an increased mortality. There is a need for prospective studies where ESR as well as other inflammatory biomarkers are tested in parallel with suPAR in order to find optimal combinations of biomarkers for TB.

POSTER DISCUSSION SESSIONS

41. Detect, report and treat: an echo from Suriname to South Africa

PD-864-14 Treatment cascade analysis for TB in Suriname: evaluation of the performance of the NTP, 2010-2015

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Background: Globally the Treatment Cascade for HIV has become an important tool in analyzing the HIV epidemic in countries. Using that principle, the aim is to identify gaps in the execution of the Tuberculosis (TB) program in Suriname.
Methods: Information from the national TB register containing data from people enrolled from 2010 to 2015 was included in the analysis. The first step of the cascade was based on the estimated cases as provided by the World Health Organization in their Global TB report 2016. The second step included all cases notified in a particular year, the third the number started on treatment, and last step the number successfully treated defined as those cured and having completed the treatment. To allow for comparison over the years all steps were calculated as a percentage of the estimated number.
Results: WHO estimates went from 240 (190-310) TB cases in 2010 to 180 (140-230) in 2015. The case detection rate was the highest in 2014 (88% (69-113%)) but declined to 83(65-107)% in 2015. Treatment coverage among notified cases increased from 90% to 97% in respectively 2010 and 2015. The percentage successfully treated also shows an increase from 62% to 73% in these years.
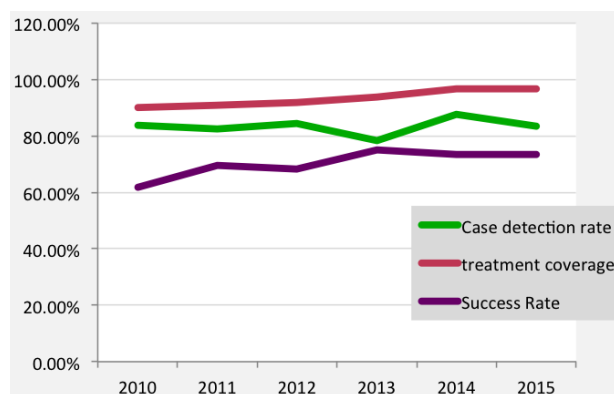
Figure Case detection, treatment coverage and success rate in Suriname, 2010-2015

Conclusions: Analyzing the Tb cascade over 2010 to 2015 revealed slight fluctuating case detection rate, but with the wide range surrounding the estimates, for small population country as Suriname further conclusions seem difficult. Although treatment coverage and success increased, as expected by intensified efforts within the TB program funded by GFTAM, further analyses is needed explaining treatment success rate is still at 73%. It is recommended to continue following the trend using this method of Tuberculosis cascade as it provides good insight in the performance of the national TB program.

PD-865-14 Pre-treatment loss to follow-up patients, Chongwe district, Zambia, 2016

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Background and challenges to implementation: Rapid case detection of sputum smear-positive tuberculosis (TB) patients and start of anti-TB treatment are fundamental measures of TB control strategy of the World Health Organization (WHO) since 1993. A recent systematic review revealed high (18%) frequency of pre-treatment loss-to-follow-up cases in sub-Saharan Africa. However, there is currently no data on such cases in Zambia
Intervention or response: A cohort study was conducted on bacteriologically positive Pulmonary TB (PTB) patients diagnosed at Chongwe District Hospital (CDH) and Chongwe Health Centre (CHC). We extracted data on all bacteriologically confirmed TB cases from the laboratory and presumptive TB registers of CDH and CHC. We then cross-checked the names of the patients with the TB treatment registers of CDH and CHC, and government clinics of surrounding area, including that of neighbouring Lusaka district, if indicated.
Results and lessons learnt: There were 163 bacteriologically-positive PTB cases registered in the laboratory and presumptive TB registers from January through December 2016. Of which, as of early April 2017, 119 (73.0%) were found in the TB treatment registers of either CDH or CHC, resulting in 44 (27.0%) cases of pre-treatment loss-to-follow-up. Of the 44, 27 (61.4%) patients were males, 22 (50.0%) were in 35-44 year-old age-group followed by 8 (18.2%) in 25-34 age-group, and 24 (54.5%) occurred in the 4th quarter of the year, which corresponds to the rainy season in Zambia.
Conclusions and key recommendations: In Chongwe district, pre-treatment loss-to-follow-up cases pose potential risk of TB infection to others and bringing these patients into care could reduce this risk. The WHO

and national TB programmes should include pre-treatment lost-to-follow-up in routine reporting system and strengthen interventions to reduce loss-to-follow-up in TB patients.

PD-866-14 Impact of DOTS implementation on TB treatment outcome in Suriname, 2010–2015

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Background: After a period of worsening of TB epidemic, related to the rise of the HIV epidemic in the nineties, Suriname applied for a grant to implement the stop TB strategy with the focus on the first five components of DOTS, which was approved by the GFTAM. This study aims to assess the impact of DOTS implementation on treatment outcomes in Suriname from 2010 to 2015.
Methods: Data collected by the National Tuberculosis Program from 2010-2015 were listed and analyzed. The treatment outcomes were compared for those enrolled in DOT and those who were not. To exclude the influence of HIV and Diabetes cases with HIV and/or Diabetes were excluded. Cases that died before receiving treatment were also excluded from the analysis. Odds ratio and Chi square were calculate to measure the association and significance.
Results: Overall 450 (50.2%) of 896 cases received DOT from 2010-2015. Treatment outcome for the group who received DOT were as follow: successfully treated 91.5%, lost to follow up 4.6%, died 1.4%, and failure 0.7%. In the group that did not receive DOT 63.3% were successfully treated, 19.2% lost to follow up and 13.1% died. For the group enrolled in DOTS there was a higher odd to be successfully treated. OR= 6.28, chi square: 60.78, p<0.05.

	not successfully treated	Successfully treated	Total
Non-DOT	84	145	229
DOT	24	260	284
Total	108	405	513

Table Treatment succes rate in TB cohort 2010-2015

Conclusions: Only 50% of the cases were enrolled in DOT. Cases enrolled in DOT were 6.2 times more likely to be successfully treated compared to those who were not. This difference was significant (OR: 6.28, chi square: 60.78, p< 0.05). Also less cases were lost to follow up in the group that received DOT. Further studies to analyze barriers for enrollment in DOT should be conducted and based on these; strategies should be developed to address these barriers. This will improve the treatment outcome for the TB cohorts in the future.

PD-867-14 Culture of mycobacteria for diagnosis of tuberculosis retreatment cases in Brazil

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Background: The development of culture for mycobacteria allows the isolation of *Mycobacterium tuberculosis* complex species, the identification of the species and the performance of a drug sensitivity test (DST). In Brazil, the culture must be performed in all retreatment cases, and DST in all those that present positive culture result. We aimed to describe the percentage of culture and DST realization in pulmonary retreatment tuberculosis cases (relapse and re-entry after lost to follow up) in 2016 in Brazil.
Methods: We analyzed all pulmonary retreatment tuberculosis cases diagnosed in 2016 and reported in the official notification system (SINAN, inicials in portuguese).
Results: Among the total of 12,809 retreatment tuberculosis cases reported, 33.6% performed sputum culture. They presented 70% of positive results for culture and of these, 50% performed DST.
Conclusions: Despite the national recommendations, the result shows that access to the culture and DST is not a reality in Brazil. To achieve the targets proposed in the WHO End TB Strategy, it is necessary to carry out culture and DST for all retreatment tuberculosis cases. These results could provide better understanding in the species profile, antimicrobial resistance standards, enabling correct treatment and better surveillance of the disease. As a result, it becomes possible to interrupt the transmission chain, reducing the emergence of new resistance cases, which presents less chance of cure. The monitoring of the culture performance allows the managers to identify the main advances and obstacles to meet the recommendations regarding the laboratory diagnosis of tuberculosis.

PD-868-14 TB among elderly patients reported in Kenya in 2015

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Background: Aging is an emerging risk factor for TB disease. The great longevity of tubercle bacilli permits them to remain viable within a healthy host for many years. Majority of TB in the elderly is secondary to reactivation of latent TB infection to active TB. Prevalence survey results from Kenya show that the elderly are at a high risk and a female preponderance was identified. This paper identified the characteristics of elderly TB

patients (55 years and over) notified to the TB program to assess whether there had any peculiar factors fueling the TB burden.

Methods: A retrospective study based on the TB Surveillance data for 2015. The study population was all elderly TB patients registered during the period. Descriptive statistics were generated.

Results: 10.9 % of all TB cases were the elderly with male preponderance accounting for 63.9 % of all cases. 79.4 % of the elderly cases notified had pulmonary TB and 39.4% were bacteriologically confirmed. In 2015, Wajir and Kwale counties recorded the highest number of elderly cases at 25.5% and 20.3% respectively. TB/HIV integration was good with 96.4% of the cases being tested for HIV, TB/HIV co-infection rate of 19.7% and ART uptake of 95.3%. Amongst the HIV-positive cases, 20.8% had partners who were HIV-positive. Overally, 20.8% of all the cases received food support. This was more than half of the moderately and severely malnourished. 18.4% of the cases were from the private sector and faith-based organizations with 1% from the prisons.

Conclusions: There was an uneven distribution of elderly in different counties which elicits the need for targeted county-specific fact-finding missions. In addition, an interplay of factors such as quality of care, health-seeking patterns, nutritional support and treatment adherence behavior among the elderly should be explored.

PD-869-14 The effect of Bolsa Família Programme on the tuberculosis cure rate in Brazil: a propensity score matched analysis

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Background: Social protection policies such as Brazil's Bolsa Família Programme (BFP), a conditional cash transfer, can enhance tuberculosis (TB) control, possibly by improving treatment outcomes. The strength of current evidence is hampered by methodological limitations. This work attempts to overcome existing limitations by using propensity score methods to conduct a rigorous evaluation assessing the potentially causal effect of BFP on TB outcomes.

Methods: The dataset used was a 2010 linkage between Brazil's TB notification system (SINAN) and social registry (CadÚnico). Propensity scores were estimated from the linked dataset's biomedical and social covariates. The propensity score is the probability of receiving BFP based on the covariates. The causal estimand of interest was the average effect of treatment on the treated (ATT), where BFP is the 'treatment'. The ATT is the difference between the proportion of TB patients cured who received BFP and the expected proportion cured if those patients had, counter to fact, not received BFP. By matching untreated patients to the treated, groups were balanced on the propensity score to eliminate confounding. The ATT was estimated as the difference in cure rate between matched groups: the causal risk difference in the treated.

Results: Propensity score matching created an appropriately balanced control group (n = 1160). The estimated ATT was 10.58 (95% CIs: 4.39-16.77), suggesting that the cure rate in those patients receiving BFP is 10.58% higher than their cure rate would have been without receiving BFP. The direction and size of this effect was robust to a range of sensitivity analyses.

Conclusions: This work provides a new, rigorous, potentially causal estimate for a positive effect of a large-scale social protection programme on TB outcomes, consistent with previous evidence. This result has significant policy implications, suggesting expansion of BFP to cover more TB patients would improve treatment outcomes and ultimately TB control in Brazil.

PD-871-14 Transition to web and case based reporting system under India's RNTCP: is data quality assured in cohort reporting?

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Background: To improve the efficiency of recording and reporting under the national tuberculosis programme in India and enable real-time surveillance and patient monitoring, an electronic, case-based web-based system named "NIKSHAY" was introduced in 2012. Under this, patient-wise data of all TB patients registered are transcribed into NIKSHAY electronic database. Accuracy of information generated through reports at State and Central level is essential to understand epidemiology, performance and for future planning. Processes available for validating convention reporting system are still not an integral part of web based reporting system. In this period of transition, we had unique opportunity to validate the newer system with conventional reporting system (gold standard) asboth were existing. Hence this study is undertaken to assess the agreement of web based reporting to conventional system for cohort of 2016.

Methods: In this cross sectional study, we reviewed of existing reports under RNTCP to assess concordance of web based reporting compared to conventional reporting system for different types of TB cases for an-

nual cohorts of 2016 from public sector in the state of Maharashtra, India.

Results: There was overall 2% discordance observed in reporting of total TB cases reported from public sector in Maharashtra State of India in annual cohort of 2016. Range of discordance for cohorts reporting of different types of TB cases was -17% to 11% (seeFigure).

Image: Discordance of select variables across 2016 cohort wise reports of paper based and electronic R&R System for TB Patients registered in Maharashtra

Variables		Conventional R&R System* (n)	Electronic R&R System**(n)	Discordance# (%)
TB Cases	Total	122602	120653	2%
	NSP	46710	45584	2%
	NSN	23361	27359	-17%
	NEP	25527	22734	11%
	RT TB Cases	26978	24420	9%
NSP Age Groups				
	0-14 years	810	819	-1%
	15-24 years	10451	10160	3%
	25-34 years	9962	9782	2%
	35-44 years	8235	7966	3%
	45-54 years	6924	6738	3%
	55-64 years	5387	5291	2%
	>64 years	4941	4828	2%

*Conventional R&R System means paper based system adapted by RNTCP India
**Web based R&R system is recently rolled out in India to capture all case based data in online portal named Nikshay.
# percentage of discordance in electronic reporting compared to paper based conventional system
TB=Tuberculosis, R&R= Recording and Reporting, NSP=New Sputum Positive, NSN=New Sputum Negative, NEP=New Extra Pulmonary, RT=Retreatment

Table Discordance of select variables across 2016 cohort

Conclusions: Though only 2% discordant reporting observed for annual cohort reporting of TB cases, there was higher discordance in reporting annual cohorts of subgroups on type of TB cases (range -17% to 11%) observed in web based reporting system compared to conventional reporting. Such reporting errors may affect policies and planning of interventions for different groups and subgroups of population. For correct reporting and decision making under the National TB Programme of India, there is need to study and address reasons for such discordance.

PD-872-14 Trends in microbiologically confirmed tuberculosis in South Africa: 2004–2015

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Background: Although South Africa's tuberculosis (TB) incidence is declining, the disease remains the leading cause of death. We aimed to determine the trends in TB incidence across different age groups and gender.

Methods: We sourced data from the National Health Laboratory Service' (NHLS) Corporate Data Warehouse for the period 2004 to 2015. Microbiologically-confirmed pulmonary TB (mPTB) status was determined by a positive test result for Xpert MTB/Rif, culture, Line Probe assay or smear. We calculated a 12-month window period, based on the first confirmatory test date to distinguish new episodes from existing episodes. Population data by gender and five-year age group were linked to

the mPTB data and used to calculate age-sex specific incidence rates, plot trend graphs and examine the distribution of incident mPTB cases.

Results: A total of 3327876 incident mPTB cases were diagnosed. We observed a downward trend in mPTB incidence from 2004 to 2015, with geographical differences in the epidemic (Figure 1).
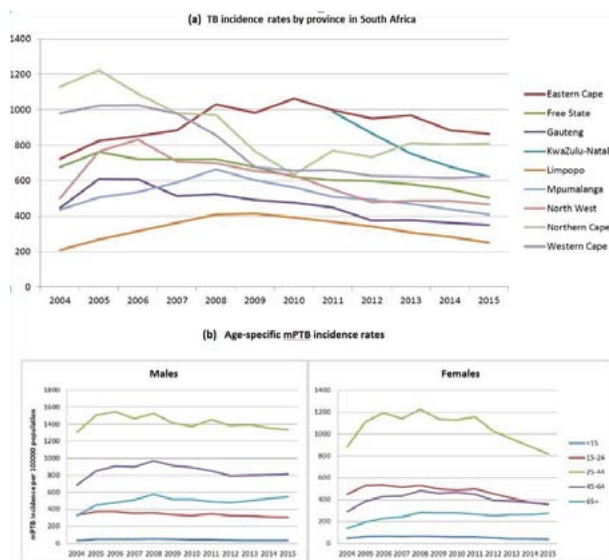
Figure TB incidence rates by province, age and sex

The 25-44 year age group was most affected with an overall male dominance in 2015, although mPTB incidence rates were higher among females in the younger age groups, a pattern seen in HIV-infected persons. Steeper declines were observed in women compared to men, with a 33.6% decline between 2008 (1059/100000; 95% CI: 1050-1067) and 2015 (703/100000; 95% CI: 698-708) in the 25-44 year age group. In contrast, declines in incidence rates among males in the same age group were much lower at 13.4%, down from 1272/100000 (95% CI: 1262-1281) in 2008 to 1101/100000 (95% CI: 1094-1108) in 2015. There was a small but consistent upward incidence trend in females aged ≥65 years, possibly reflecting longevity in HIV-infected people with delayed TB infection.

Conclusions: TB incidence trends differ across age groups and gender groups. Targeted and tailor-made TB control interventions would help reduce the burden in South Africa.

PD-873-14 Experiences and perspectives on extra pulmonary tuberculosis in 15 provinces of Afghanistan, 2015 - 2016

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Background and challenges to implementation: Tuberculosis (TB) is a major public health problem in Afghanistan. It is estimated that 61,000 Afghans develop TB annually, and only 70% of the cases are identified. Forty percent are new bacteriological confirmed TB cases and around 26% are extra pulmonary TB (EPTB) cases, but there are no clear guidelines and tools for EPTB diagnosis and many cases are missed in public and private health facilities. The purpose of this study is to assess the spectrum of EPTB in 15 provinces of Afghanistan.

Intervention or response: This is a retrospective review of EPTB cases from 15 Afghan provinces reported to the NTP surveillance department between 2015 and 2016. The technical team counted EPTB cases from quarterly reports of 513 health facilities in 15 provinces and estimated the proportion of EPTB among all forms TB cases.

Results and lessons learnt: Out of 57,140 cases of all forms of TB cases identified, 14,898 were identified as EPTB (26% of all cases), which is close to 78% of all EPTB cases reported nationally in Afghanistan (See Figure 1). This group represents the spectrum of EPTB in 15 provinces in the country. Of the EPTB cases identified, 8,194 (55%) were female and 6,704 (45%) were male. The ratio of females to males was 2.03:1. Focus group discussions in Kabul with 30 medical specialists revealed that the most commonly affected EPTB manifestation sites among Afghan patients are the pleura, the lymph nodes, central nervous system, gastrointestinal system, bones and joints, and genitourinary system.

Conclusions and key recommendations: The magnitude of EPTB in Afghanistan is high and the higher ratio of female to male EPTB cases demonstrated a relatively higher number of female cases. This study also illustrates the varied presentations of EPTB that should be understood by healthcare workers throughout the country and the need for better EPTB guidelines from the NTP.

Year	New bacteriological confirmed TB cases	Previously treated TB cases	Clinically confirmed pulmonary TB cases	EPTB cases	Other	All TB cases
2015	10,751	996	7,037	6,820	736	26,340
2016	12,102	1,088	8,794	8,078	738	30,800
Total	22,853 (40%)	2,084 (4%)	15,831 (28%)	14,898 (26%)	1,474 (2%)	57,140

Table 1 Magnitude of EPTB in 15 provinces of Afghanistan

42. You can't treat what you don't diagnose: considerations in MDR-TB diagnosis and molecular epidemiology

PD-874-14 Prevalence of discordance between phenotypic and genotypic testing for rifampicin resistance: a clinical dilemma

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Background: The World Health Organisation (WHO) recommends molecular testing with Xpert MTB/RIF as the first test for the diagnosis of TB among presumptive cases. This test also detects presence of rifampicin resistance through *rpoB* mutation. Phenotypic DST is often regarded as the gold standard, but has been known to miss certain mutations detected by Xpert MTB/RIF. On the other hand, Xpert MTB/RIF has been reported to miss some phenotypically expressed rifampicin resistance.

Methods: Between 2014 and 2015, patients with symptoms of TB in Namibia submitted two sputum specimens each which were subjected to smear microscopy and Xpert MTB/RIF. Those that were positive on either smear microscopy or Xpert MTB/RIF were subjected to mycobacterial culture and phenotypic susceptibility testing in MGIT liquid culture.

Results: Of the 3533 specimens that were positive by Xpert MTB/RIF, 2969 grew *Mycobacterium Tuberculosis* on culture. Of these, 2799 has successful DST to rifampicin, isoniazid, streptomycin and ethambutol as well as Xpert MTB/RIF. 172 (6.1%) had rifampicin resistance by Xpert MTB/RIF compared to 162 (5.8%) who had rifampicin resistance by MGIT-based DST. 42 (24%) of the rifampicin resistant by Xpert MTB/RIF were sensitive on phenotypic testing compared to 32 (20%) of the rifampicin resistant on MGIT which did not show any resistance on Xpert MTB/RIF. Although the overall concordance was 2.6%, a significant proportion of resistant results by one test were disputed by the other. Of note is that discordance was more pronounced for previously treated TB patients (29/639) compared to new patients (44/2129; p=0.0006).

Conclusions: Discordance between results of phenotypic and genotypic rifampicin resistance testing is not uncommon. Given the current drive to scale-up of Xpert MTB/RIF in many national TB programmes, there is need to develop guidance for clinicians who encounter this phenomenon. Programmes should map the available rpoB mutations in order to determine their clinical relevance.

PD-875-14 Eligibility assessment for shortened MDR-TB treatment with commercially-available rapid molecular tests

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Background: The WHO recommends a shortened MDR-TB treatment for patients with drug susceptibility testing (DST) susceptibility to all drugs contained in the regimen (isoniazid excluded), and to identify eligible individuals with rapid molecular resistance testing for fluoroquinolones and second-line injectables. The objective of this study is to determine the diagnostic accuracy of commercially-available rapid molecular tests and the adequateness of standardised treatment based on those tests.

Methods: A retrospective cohort study was performed using the database of the National Reference Center for Mycobacteria, including all patients with proven MDR-TB from 01/01/2010 to 31/12/2016. Inclusion criteria were:

1) Phenotypic DST results available for a second-line injectable, a fluoroquinolone, ethionamide, and ethambutol;
2) DST or *pncA* sequencing results for pyrazinamide;
3) molecular testing results with commercially-available tests for *gyrA* and *rrs* (GenoType MTBDRsl), and *inhA* (GenoType MTBDRplus).

DST eligibility was defined as susceptibility to all drugs in the regimen, excluding isoniazid. Eligibility according to rapid molecular testing was defined as absence of mutations in *gyrA* and *rrs* (algorithm 1), or in *gyrA*, *rrs*, and *inhA* (algorithm 2). The number of effective drugs in the standardized regimen was determined according to DST results. Clofazimine DST was not performed and therefore the drug was always considered as effective.

	N (%) of eligible patients for the shortened MDR-TB treatment	Sensitivity of molecular testing compared to DST-based eligibility	Specificity of molecular testing compared to DST-based eligibility	N (%) of eligible patients with <4 effective drugs	N (%) of eligible patients with <5 effective drugs
DST-based eligibility	39 (7.9%)	Not applicable	Not applicable	0	0
Rapid molecular testing algorithm 1 (rrs and gyrA)	322 (64.9%)	100%	38.1%	89 (27.6%)	176 (54.7%)
Rapid molecular testing algorithm 2 (inhA, rrs and gyrA)	238 (48.0%)	89.8%	55.6%	66 (27.7%)	133 (55.9%)

Table Results of DST and molecular diagnostic algorithms

Results: Out of 582 MDR-TB cases, 496 (85.2%) had full DST and rapid molecular testing results available. Eligibility results, diagnostic accuracy, and number of effective drugs in the shortened regimen for DST-based and molecular-based algorithms are presented in the Table.

Conclusions: In our setting, rapid molecular testing for gyrA and rrs may not be specific enough to determine eligibility for shortened MDR-TB treatment, and could lead to suboptimal treatment regimens in a substantial proportion of patients. The addition of molecular testing for inhA increases specificity at the expense of sensitivity, but does not improve the adequateness of the treatment.

PD-876-14 Universalization of rapid MDR-TB testing is associated with decreased mortality

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Background: Multidrug resistant tuberculosis (MDR-TB) is challenging TB control. Rapid MDR-TB testing, same-day molecular testing and universalization of MDR-TB testing are recommended but have uncertain effects on patient care under operational conditions. In Peru before 2008, most patients were eligible for a drug-susceptibility testing only after poor clinical outcome (failure, withdrawal or relapse) to first-line drug therapy. In 2008, rapid phenotypic drug-susceptibility tests were implemented universally in Peru.

Objective: To study whether universalization of rapid MDR-TB testing is associated with decreased MDR-TB mortality .

Methods: From 2002-2015, all patients commencing TB therapy at 16 health posts in shantytowns in North Lima, Peru, were invited to consent to participate in this study. We recorded the strategy used to screen for MDR-TB and mortality. According to national guidelines, in 2002 only TB patients with known MDR-TB risk factors had MDR-TB testing by the indirect agar plate proportions assay, which generally took months. Additionally microscopic-observation drug-susceptibility (MODS) testing was offered to all patients with laboratory-proven TB, which takes 5-21 days. From 2003-2007 this was provided by a research project and since 2008 by national services. Since early 2014, a research project additionally offered all patients Xpert MTB/RIF testing.

Results: We recruited 6820 pulmonary patients with TB and 259 of them were diagnosed with MDR-TB. For these 259 patients, 47 never began appropriate second-

line therapy. The proportion of patients with MDR-TB identified by universal screening strategy increased in the period 2014-2015 (33/36, 92%) in comparison 2002-2007 (23/83, 28%, p< 0.001) and 2008-2013 (104/140, 74%, p=0.03). There was a clinically relevant trend of decreased mortality among patients with MDR-TB, as shown in the figure.
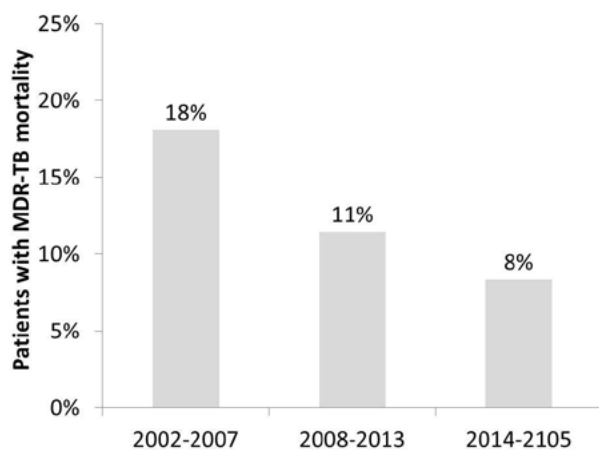
Figure Patients with MDR-TB mortality

Conclusions: The universalization of rapid MDR-TB testing and the implementation of same-day molecular rifampicin susceptibility testing, in association with strengthening of the Peruvian National TB program, tended to decrease MDR-TB mortality.

PD-877-14 The effects of Xpert® MTB/RIF testing and GxAlert on RR/MDR-TB diagnosis and linkage to care in Mozambique

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Background: Multi-drug resistance Tuberculosis (MDR-TB) diagnoses and gaps in linkage to care are major health challenges in Mozambique. Xpert MTB/RIF (Xpert) testing and GxAlert, an eHealth platform, were installed at five health facilities in 2012 and 2014, respectfully, in Sofala and Manica Provinces.
The primary objective of this study was to test the effects of Xpert testing and GxAlert on rifampin resistant TB (RR-TB) diagnosis and second-line treatment initiation rates.

Methods: We conducted a retrospective clinical review of patients with patients with RR-TB from March 2012 to September 2015 at these five sites. We conducted pre-post and time-series analyses of Xpert testing and GxAlert.

Results: A total of 32,182 Xpert tests were performed: 4,014 (12.5%) detected TB without RR, and 306 (7.1%) had RR-TB. Of the RR-TB cases, 161 (52.6%) started MDR-TB treatment, 6.9% had documented culture results, and time from diagnosis to treatment initiation decreased over time.
Of these, 119 (74%) had a documented HIV status (tested or known positive), and 80 (50%) were HIV positive. Seventy-two (90%) of the known HIV positive patients were documented to be on HIV treatment. Additionally, according to the national MoH MDR-TB database, the total number of patients started on MDR-TB treatment in Sofala and Manica Provinces increased from 17 in 2011 to 137 in 2015, mostly due to Xpert MTB/RIF testing. The percentage of these that were diagnosed with RR-TB at one of the five study sites was 60% in 2012, 69% in 2013, and 83% in 2014.
The proportion of diagnosed cases initiating treatment increased from 41.7% (15/36) to 63.6% (70/110) from 2012 to 2014. GxAlert did not impact treatment initiation rates, but had several ancillary benefits further described in an associated qualitative analysis.

Conclusions: The implementation of Xpert testing was associated with increases in the number of patients diagnosed and started on RR/MDR-TB treatment.

PD-878-14 The correlation of genotypic resistance with phenotypic drug resistance for guiding treatment decisions

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Background: New diagnostic methods have provided a promising solution for rapid and reliable detection of drug resistant TB strains. However, rapid assays are less accurate than culture, raising the possibility of false-positive and false-negative results. For interpretation of the molecular drug susceptibility results (DST), it is important to be considered the conventional phenotypic DST results. The inhA mutation confer low resistance for Isoniazid (INH), that can be susceptible on phenotypic DST. The mutation within the rpoB gene, does not confer the same level of phenotypic resistance to Rifampicin (RIF).

The objective of study was to estimate the correlation between levels of phenotypic resistance and type of genotypic mutations for INH and RIF.

Methods: The M.tuberculosis strains with low level of genotypic resistance to INH (only inhA mutation) and M.tuberculosis strains with genotypic resistance to RIF,

but without of mutation rpoB531, were tested by culture method (Lowenstein-Jensen) on high level concentrations of drugs (INH-5&10μg/ml and RIF-60&80μg/ml). **Results:** From 4636 M.tuberculosis strains tested by MTBDRplus, 2933(63.3%) were INH resistant and in 2,9% (n=86) of the strains were present only inhA mutation (low resistance). RIF resistance were detected in 61.9% of M.tuberculosis strains and in 27.2% (n=762) of these, RIF resistance was associated with other mutations than S351. By phenotypic DST were identified, that 30.6% of INH low genotypic resistant strains, and 28.6% of RIF genotypic resistant strains without S351 mutation, were sensitive to high concentrations of drugs. **Conclusions:** The rapid and reliable DST should be crucial for personalized approach in TB patient treatment, stopping the spread of drug resistance and promotion of the optimum use of the few drugs available for resistant TB treatment. The correlation of genotypic test results, with a level of drug resistance, presents an invaluable tool for quickly guiding treatment decisions.

PD-879-14 Deciphering the physiological state of drug-resistant *Mycobacterium tuberculosis* strains

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Background: The rising incidence of drug resistant *Mycobacterium tuberculosis* strains negatively influences Tuberculosis control. Limited data exist on the physiological changes of *Mtb* during treatment. For this reason, we aim to assess the physiological changes of *Mtb* at the transcriptional level during antibiotic treatment. The study aims to decipher how the physiological state of drug resistant *Mtb* exposed to sub-lethal concentrations of isoniazid (INH) contributes to prolonged TB treatment. **Methods:** Pan-susceptible Beijing clinical isolate (K636), K636 rifampicin resistant *in vitro* mutant and laboratory strain H37Rv were cultured in 7H9 enriched media and on 7H11 agar plates, for daily OD_{600} readings and CFU/ml assessment. Followed by assessing the optimal concentration of INH was by titration kill-curve. Additionally, total RNA was extracted and purified (after 24 hrs INH exposure), for gene expression analysis by Quantitative Real-time polymerase chain reaction (RT-qPCR) for selected genes *kasA, accD6, acpM* and *ahpC*. **Results:** The sub-lethal concentrations of INH were observed to be 0.03 μg/ml and 0.02 μg/ml for K636 and H37Rv, respectively. RT-qPCR was used to validate that the selected drug concentrations are influencing mycobacterial growth as expected. The low level gene expression changes were observed in *kasA, accD6, acpM and ahpC* for the strains when normalised to 16S rRNA and SigA (housekeeping genes) respectively, after 24 hrs treatment with sub-lethal concentrations of INH.

Conclusions: The variation in sub-lethal concentrations of INH observed suggests that the strains might employ different adaptive mechanisms to survive INH drug exposure. Additionally, the low level gene response changes in transcriptional level of *kasA, accD6, acpM and ahpC* validate that our sub-lethal INH treatment did induce gene-expression changes in tested *Mtb* strains. These findings are essential for further physiological characterization of the studied *Mtb* strains by RNA-sequencing as it is anticipated that the associated physiological changes will be reflected in their total transcriptome.

PD-880-14 Whole genome sequencing analysis of drug resistance-conferring mutations and lineages/sublineages of M. tuberculosis circulating in Hanoi, Viet Nam

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Background: Drug-resistant tuberculosis (TB) is a serious problem worldwide. We investigated drug resistance-conferring mutations and lineages/sublineages of *Mycobacterium tuberculosis* (MTB) circulating in Hanoi, Vietnam. **Methods:** Patients with new smear-positive pulmonary TB were recruited. Mycobacterial DNA samples from Löwenstein-Jensen culture media were analyzed using Illumina HiSeq (150 bp x2) and MiSeq (250 bp x2) systems. After trimming and excluding severely contaminated samples, sequence reads were mapped to the H37Rv genome. Drug resistance-conferring mutations including insertions/deletions and lineage-specific variations were extracted using the TB-Profiler´s variation lists and other tools. Polytomous logistic regression models were used to investigate associations between mutations and lineages/sublineages. **Results:** Numbers of variants were successfully identified from 332 qualified DNA samples. Representative mutations included *katG* S315T (26.5%), *rpsL* K43R (13.6%), *rrs* A514C (4.5%), *rpoB* S450L (3.0%), *fabG1*-promoter (2.4%), and *embB* M306V (1.8%). A large deletion (354 bp) was also found in the *pncA* region in one sample. Among 88 isolates harboring *katG* S315T mutation, 60.2% had at least one drug-resistance conferring mutation in another gene. A solitary mutation of *katG* S315T was mainly carried by Indo-Oceanic lineage 1.1.1.1, whereas the combinations of *katG* S315T with

other mutations were often observed in lineage 2.2.1, a majority of Beijing-genotype strains ($P < 0.0001$). By multivariate analysis, both lineages 1.1.1.1 and 2.2.1 showed significant associations with single *katG* S315T mutation, whereas only lineage 2.2.1 was significantly associated with combinations of *katG* S315T and other drug resistance-conferring mutations (adjusted odds ratios = 5.60 [95% confidence interval: 1.61−19.45], 4.70 [1.22−18.01], and 8.43 [2.90−24.51], respectively).

Conclusions: Our data suggest that the drug resistance-conferring mutations are prevailing differently depending on MTB lineages in Hanoi city. It is necessary to investigate their influence on human-to-human transmission in this area.

43. Challenges to the implementation of drug-resistant TB treatment on the ground

PD-881-14 Resultados de cohortes de tratamiento en pacientes con tuberculosis resistente a fármacos en México, 2010—2013

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Background and challenges to implementation: Se realizó un estudio observacional, descriptivo y retrospectivo. Población de estudio: Pacientes diagnosticados con tuberculosis resistentes a fármacos con resultados de cultivo y pruebas de farmacosensibilidad, ingresadas a tratamiento durante los años 2010 a 2013 en el país, notificados en el Sistema de Información MACRO TB-MFR.

Intervention or response: Se realizó evaluación del resultado del seguimiento de los casos de las cohortes de tratamiento de TB FR/MFR/XDR y se identificaron las actividades clínico operativas que coadyuvaron al resultado final de las cohortes de TB farmacorresistente 2010 al 2013, en México.

Results and lessons learnt: Se ingresaron a tratamiento a 882 casos con diagnóstico de TB resistente a fármaco: 667 MFR, 13 XD, 116 polirresistentes y 76 monorresistente, 65% corresponde al sexo masculino y la edad promedio es de 43 años. Se obtuvo un promedio de éxito de tratamiento de 71%, pérdida en el seguimiento de 13.25%, fracaso de 5.25% y defunciones de 10.75%. De acuerdo al tipo de resistencia: MFR: Éxito de tratamiento de 68.25%, fracaso de 5.5%, pérdida en el seguimiento14.75% y defunción de 11.75%.XDR: Éxito de tratamiento de 60.5%, fracaso de 35.5% y pérdida en el seguimiento4.25%. Polirresistente: Éxito de tratamiento de 76.75%, fracaso de 3.25%, pérdida en el seguimien-

to12 % y defunción de 8.25%. Monorresistente: Éxito de tratamiento de 81.75%, fracaso de 3.5%, pérdida en el seguimiento 3.25 % y defunción de 11.25%.

Conclusions and key recommendations: Se sabe que los pacientes con TB FR tiene menor probabilidad de curación, sin embargo con una coordinación estratégica, se ha logrado en México un éxito de tratamiento del 71%, resultados que son directamente proporcionales a las diferentes actividades realizadas desde los aspectos clínicos operativos, de capacitación, asesoría y organización entre los diferentes niveles de atención.

PD-882-14 Successful adoption of the shorter MDR-TB regimen for accelerated national scale-up In Swaziland

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Background and challenges to implementation: Emerging drug resistant forms of tuberculosis (TB) remains a threat to global efforts to end TB. In 2014-2016, Swaziland was among the countries that conducted pilot studies to ascertain effectiveness of shorter MDRTB regimen on DRTB/HIV co-infected patients. Findings from this pilot study were used as evidence by WHO to inform development of guidelines on use of shorter MDRTB regimens released in May 2016. In August 2016 Swaziland started planning national implementation despite the unavailability of Line Probe Assays (LPAs), ECG machines and different patient support in some regions.

Intervention or response: Consultative meetings were held with partners and stakeholders to review results from the study to understand what a shorter MDR-TB regimen entails. A roadmap was developed and endorsed by the Ministry of Health (MOH) directorate defining the systems and processes that needed to be in place before implementing the regimen. A core team was established comprising representatives from TB program, implementing partners and clinicians. Terms of reference were developed with roles and responsibilities.

Results and lessons learnt: Within 3 months, national guidelines were developed using WHO recommendations and lessons learnt from the study. Full ownership of the guidelines by local clinicians was achieved and buy-in assured. Laboratory systems were strengthened. Quantification of TB medicines were established. Harmonization and Standardisation of comprehensive patient support was planned across all regions. Standard training plan and manual were developed. National training of 115 HCWs and regional trainings of 35-40

participants per region. The Pharmacovigilance system in collaboration with partners was strengthened to monitor adverse events. By mid-January 2017 implementation process started in three phase approach starting with sites which had both comprehensive patient support and ECG machines.

Conclusions and key recommendations: Effective coordination of national implementation relied mostly on adopting an inclusive process of adapting the WHO guidelines, senior health ministry officers' buy- in and establishing strong systems for oversight, monitoring and evaluation.

PD-883-14 Benefits of decentralization of DR-TB services to primary health care facilities versus hospitalization in Western Cape, South Africa

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Background and challenges to implementation: The Western Cape Province (W.C.P) has a high burden of DR-TB. The previous standard of care for DR-TB patients required hospital admission until sputum conversion (4-6 months). The number of hospital beds available in W.C.P is limited; consequently patients had to be on waiting lists for up to 6 weeks before commencing treatment. In order to alleviate this pressure, the process of decentralization of DR-TB commenced in 2011. It was feared that treating patients in the community could increase the risk of transmission of DR-TB and compromise adherence to treatment.

Intervention or response: Based on a framework developed by the National Department of Health, facility readiness assessments were done and a comprehensive training package was implemented for health care workers. Specific adherence counseling guidelines were implemented. DR-TB services were thus extended to 367 Primary Health Care (PHC) facilities within a two year period. Service delivery was enhanced by the roll-out of X-pert testing in 2011.

Results and lessons learnt: The number of primary infections has not increased significantly (Figure 1).
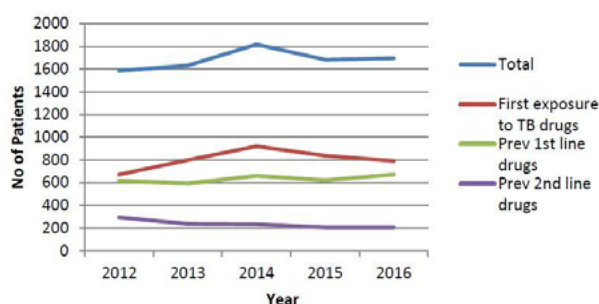
Figure 1 DR-TB patients commenced on treatment in Western Cape

The proportion of patients defaulting has remained constant, suggesting that underlying factors such as pill fatigue, side-effects of treatment and social issues, are not addressed by decentralization. The time taken to diagnose DR-TB and start treatment has dramatically improved from around 72 days to just approximately 10 days.

Conclusions and key recommendations: Decentralization has not resulted in increased transmission of DR-TB or poorer outcomes compared to hospitalization. Interventions are needed to address poor adherence to treatment. The most substantial gain from decentralization has been earlier initiation of treatment.

PD-884-14 Implementation approach for the successful introduction of bedaquiline in countries: from guidelines to action

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Background and challenges to implementation: Bedaquiline expands treatment options for patients with multi-drug resistant TB and those who have experienced severe adverse events such as ototoxicity and psychosis while using second-line TB drugs. Differing country contexts begs the question of how to translate WHO implementation guidelines into actionable steps and how to tailor the recommendations to suit specific country needs. Another implementation challenge is the approach of training clinicians, and focusing on supply chain issues without addressing other system weaknesses, potentially undermining implementation success and sustainability.

Intervention or response: Building upon WHO guidelines, a health system strengthening approach was used to organize the successful introduction of bedaquiline in 5 countries (Swaziland, Kenya, Georgia, Philippines and Uganda). This approach involved reviewing system functional areas including human resources, supply chain, service delivery, financing, governance and stakeholder coordination[1] and implementing a country-specific plan to leverage strengths and address weaknesses with continuous monitoring and evaluation.

[1] Atun R, et al. (2010). Health-system strengthening and tuberculosis control. *The Lancet*, Volume 375, Issue 9732, 2169-2178. DOI:10.1016/S0140-6736(10)60493-X.

Results and lessons learnt: By March 2017, 573 healthcare workers across 5 countries had been trained to use bedaquiline and country specific protocols to guide clinical decision making. National implementation plans to strengthen each country system and prevent duplication of effort amongst stakeholders have been executed. Over 460 patients have used bedaquiline with largely successful outcomes and tracking of adverse events.

Conclusions and key recommendations: Having a system-centered implementation approach, as opposed to focusing on singular areas such as supply chain and cli-

nician training, prevents National TB Control Programs (NTPs) from overlooking areas of weaknesses like anti-microbial resistance prevention, adverse event reporting, financing.

This approach can be applied to any implementation activity by NTP and Ministry of Health leaders. As more medicines are introduced, NTP coordinators would be prudent in reviewing their existing systems for gaps, and then devising activities to address these gaps.

PD-885-14 DR-TB treatment enrolment patterns and treatment initiation delay among DR-TB patients in Lagos, southwestern Nigeria

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Background: Nigeria is a high burden country for both DS-TB and DR-TB. Delay in DR-TB treatment result in disease transmission, progression and poor treatment outcome including increased risk of death. Community-based initiation of treatment has been shown to shorten the waiting time for treatment by reducing the demand for limited bed spaces at treatment centres. This study aims to determine the coverage of community initiation of treatment among drug resistant TB patients in Lagos State, the treatment enrolment gap, time-to-treatment, and the factors related to delay in initiation of treatment.
Methods: A retrospective study involving review of the line listing of diagnosed DR-TB patients in Lagos State over a two-year period (January 2015- January 2017). Information collected included the dates of diagnosis and treatment initiation, treatment model and analysis of barriers to treatment initiation.
Results: Of the 502 clients diagnosed, 414 (82.5%) were enrolled on treatment, of which 359 (86.7%) was community based while 55 (13.3%) was facility based. A mean delay time of 3.3 weeks from diagnosis to treatment initiation was observed. Causes of delay included delay in consenting to treatment (12.7%) and unavailability of second-line anti TB medicines (26.1%) among others. Of the 88 patients who were not enrolled on treatment, 55.7% (49) was due to refusal of treatment, 29.6% (26) pre-treatment loss-to-follow-up from wrong home addresses and telephone numbers, and 14.8% (13) died before start of treatment.
Conclusions: Despite increased access to treatment through community initiation of treatment, there is a significant delay in initiating treatment for DR TB patients as a result of patient and health system factors. NTP and its stakeholders need to do more in terms of patient literacy and counselling, Logistics Management Information System and scale up of the Shorter Treat-ment Regimen for drug resistant TB to improve the accessibility and acceptability of DR-TB treatment among clients.

PD-886-14 Improvement of the medical care system for TB patients, Ukraine

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Background and challenges to implementation: Ukraine is included in the 18 high-priority TB countries in European region. The treatment success rates among the new TB cases and relapses having started treatment in 2013-2014 were 66.9 %,71.1% and lost to follow-up were 10,4% and 6,1%, respectively. As for MDR TB cases enrolled into treatment in 2012-2013 these were 34.4% and 38.6% and lost to follow-up were 14% and 18%, respectively. Targets for the TB and MDR-TB treatment success rates recommended by WHO are 85% and 75%, respectively.
Intervention or response: During the project a mobile team was created, which traveled six times a week to a place convenient for patients (home, work, park) for administering anti-tuberculosis drugs. If the patients had taken the prescribed monthly doses, they received 15 dollars. As a result, 51 patients had treatment outcomes, including 29 TB and 22 patients with MDRTB.The criteria for inclusion were free for TB and MDR TB patients, regardless of the type of the case, but 40 (78.4%) patients had risk factors interrupting the treatment (TB/HIV patients, refugees, homeless, alcohol abusers, injecting drug users and e.g.).
Results and lessons learnt: The treatment success rates among TB and MDRTB cases were 100% and 86,4%, respectively. Patients weren't lost to follow up. The treatment success among MDR patients was not achieved for 100% for two reasons: 2 (9.1%) patients had treatment failure and 1 (4.5%) died from myocardial infarction. The treatment success rate among TB and MDR-TB in the project is higher by 31,0 % and 50% respectively, than the corresponding indicators in Ukraine.
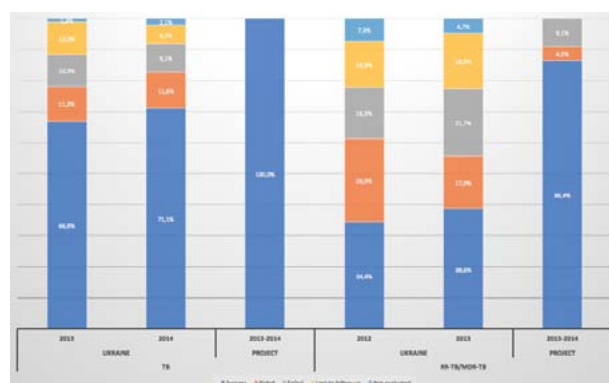
Figure Treatment outcome, TB&RR-TB/MDR-TB (2013-2014)

Conclusions and key recommendations: Using a mobile team for treating TB patients with risk factors interrupting the treatment is more effective than traditional treatment methods in Ukraine.

PD-887-14 Catastrophic during-treatment costs for drug-resistant tuberculosis patients with and without social protection: a patient survey in Rio de Janeiro, Brazil

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Background: Illness-related costs for tuberculosis (TB) patients ≥20% of annual household income predict adverse treatment outcomes so are termed catastrophic. Drug-resistant TB (DR-TB) patients experience especially high costs. In Brazil, two social protection policies, Auxílio-doença and Benefício de Prestação Continuada (BPC), might help to protect them from incurring catastrophic costs. We undertook a patient survey to estimate the proportion of DR-TB patients experiencing catastrophic costs during-treatment amongst those with and without income replacement from these policies.
Methods: From June-October 2016, 120 DR-TB patients being accompanied at the Professor Helio Fraga reference centre in Rio de Janeiro were interviewed about household income and receipt of Auxílio-doença or BPC pre-/during-treatment, and direct and indirect costs incurred during-treatment. Direct costs were calculated from transport, food, private healthcare and non-prescribed remedy costs incurred during-treatment. Indirect costs were calculated from reported lost income related to TB illness, net of income replacement from Auxílio-doença or BPC. We calculated patients' cost burden as the sum of direct and indirect costs as a proportion of pre-treatment annual household income, and the proportion of patients experiencing catastrophic costs using a threshold cost burden ≥20%. Costs were reported in 2016 US$.
Results: 41 (34%) and 3 (2%) DR-TB patients reported income replacement from Auxílio-doença and BPC during-treatment respectively, with a mean value of US$5,966 (SD: US$1,883). For patients with and without income replacement, mean direct costs were US$774 (SD: US$394) versus US$722 (SD: US$325); and mean net indirect costs were US$3,564 (SD: US$7,578) versus US$4,353 (SD: US$5,782), respectively. In the two groups, the mean cost burden was 42% (SD: 40%) versus 527% (SD: 2,468%), and the proportion experiencing catastrophic costs was 50% (95%CI: 35%-65%) versus 75% (95%CI: 65%-85%), *p*=0.01, respectively.
Conclusions: Social protection policies might prevent catastrophic costs for some DR-TB patients. Further investment is needed to prevent catastrophic costs for all DR-TB patients.

PD-888-14 Magnitude of tuberculosis among contacts of multidrug-resistant tuberculosis patients in north-eastern Tanzania

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Background: Multi-Drug Resistant Tuberculosis (MDRTB) is a disease of public concern. Close contacts of an MDRTB patients stands an increased risk of acquiring the infection. In Tanzania, between 2009 and 2015 Kibong'oto Infectious Diseases Hospital (KIDH) was the only facility providing MDRTB services. We traced and screened for TB/MDRTB among contacts of MDRTB patients who were admitted at KIDH between 2010 and 2015 to establish the magnitude of TB/MDRTB disease/infection and associated risk factors.
Methods: In this cross-sectional study, we traced a total of 125 MDRTB patients (index case) and screened their contacts for TB/MDRTB. We screened any contact who aged ≤ 15years, consented/assented and had stayed with an index case in the same household for at least three months. These contacts were visited between February and June 2016. GeneXpert and QuantiFERON-TB Gold In-Tube tests were used to screen the MDRTB contacts for TB disease and Infection respectively.
Results: Of 125 index cases traced only 62 (49.6%) were found and there were 253 contacts from the located index households. Eighty three percent (210/253) of contacts were enrolled in the study. The remainder (n=65) were either not eligible or refused to participant in the study. Three participants couldn't produce sputum sample for GeneXpert test. Forty one of 207 (19.8%) contacts whose sputum were tested had GeneXpert positive results, and one of them was Rifampicin resistance. Forty one percent (86/ 210) of the contacts had their blood samples tested for TB infection by QuantiFERON test and 38/86 (44.1%) of them tested positive for QuantiFERON positive, 30/86 (34.9%) tested negative and 18/86 (21.0%) had in determinant results. Proximity and duration of staying with index case was not significantly associated with acquisition of TB/MDRTB disease nor infection.

Conclusions: Active TB and infection are prevalent among MDRTB contacts. Rifampicin resistance is also an issue of concern among these contacts.

PD-889-14 Implementation of bedaquiline for the treatment of (pre) XDR-TB under programmatic conditions: experience in Indonesia

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Background and challenges to implementation: Indonesia is among the countries with the highest burden of TB and multidrug-resistant (MDR) TB in the world. Programmatic management of drug resistant TB started in 2009. Until 2015 there were no effective treatment options for patients with extensively resistant TB; in August that year, the national tuberculosis program (NTP) introduced bedaquiline containing regimens under the conditions outlined in the WHO program implementation package and the interim guidance document on bedaquiline.

Intervention or response: After meetings with the NTP, the National Agency of Drug and Food Control and partners, bedaquiline was approved for use under a special access scheme. Three hospitals were initially selected to implement bedaquiline introduction. MDR-TB patients who had resistance or could not tolerate fluoroquinolones or aminoglicosides or who could not tolerate or were unresponsive to at least two group C drugs were enrolled. They underwent close monitoring of their bacteriological response by monthly sputum culture. Side effects were monitored by dedicated pharmacovigilance officers.

Results and lessons learnt: Between August 1st 2015 and March 3rd 2017, 65 patients started bedaquiline treatment. Of these, 57% were men, the average age at enrollment was 40 years, and the proportion of pre-XDR, XDR and MDR were 51%, 8% and 41% respectively. The two-month culture conversion was 20% (8/40 patients); culture conversion at six months was 86% (24/28), while 9% failed, 5% were lost to follow-up and 9% died. The median duration of culture conversion was 65 days (range 31-293). While almost all patients suffered non-serious adverse events, only one had a serious adverse event with a probable association with the drug.

Conclusions and key recommendations: The preliminary results show introduction of bedaquiline dramatically improved the interim treatment results for this group of patients. No deaths occured due to beda-

quiline. Based on these results the Ministry of Health agreed to nationwide scale-up of bedaquiline for the mentioned patient groups.

44. TB, drugs and rock 'n' roll - updates on our understanding of TB drugs

PD-890-14 Single nucleotide polymorphisms predict fluoroquinolone effectiveness against *M. tuberculosis*

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Background: Reference phenotypic drug susceptibility testing for fluoroquinolone resistance in *Mycobacterium tuberculosis (Mtb)* is currently based on a single "critical concentration" of drug. While this is an efficient approach for detecting clinically relevant resistance *in vitro*, there is evidence that suggests the minimum inhibitory concentration (MIC), a more useful metric of resistance, can be rapidly predicted by specific single nucleotide polymorphisms (SNPs) in *gyrA*.

Methods: We sequenced the *gyrA* gene of 143 clinical *Mtb* isolates collected from India, Moldova, Philippines and South Africa. MIC ranges for each isolate were estimated for moxifloxacin, levofloxacin, gatifloxacin, and ofloxacin. Specific *gyrA* SNPs were collated into high or low resistance levels based on MIC averages for each drug. Published population pharmacokinetic models were used to explore the pharmacokinetics and pharmacodynamics (PK/PD) of each drug relative to the resistance level based on *gyrA* SNPs to estimate the proportion of patients likely to reach defined therapeutic targets based on area under inhibitory concentration curve (AUIC = AUC/MIC) for individual fluoroquinolones.

Results: Preliminary results indicate that 48% of patients infected with *Mtb* isolates containing SNPs associated with low level moxifloxacin resistance (MIC mean 0.49 mg/L) would reach the therapeutic targets (AUIC>106), and 83% of patients would if moxifloxacin dosing was doubled. Models predicted that among patients with isolates harboring SNPs associated with high level moxifloxacin resistance (MIC mean 1.35 mg/L), 5% would reach therapeutic targets. Simulations were repeated for the other fluoroquinolones tested; and although individual SNPs were not uniformly associated with equivalent resistance level across drugs, our models consistently demonstrated specific SNPs were associated with differing probabilities of patients achieving therapeutic targets for each drug.

Conclusions: We demonstrated that quantifiable, fluoroquinolone drug resistance phenotypes can be predicted from rapidly detectable SNPs and incorporated into pharmacological models to predict the likelihood of patients reaching therapeutic drug targets.

PD-891-14 Accelerating access to delamanid for rifampicin-resistant tuberculosis in Khayelitsha, South Africa

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Background and challenges to implementation: Delamanid (DLM) was recommended by the World Health Organization (WHO) for treatment of multidrug-resistant tuberculosis (MDR-TB) in 2014 after clinical trials demonstrated safety and efficacy. Delamanid is associated with mild QTc prolongation but, unlike bedaquiline, can be used with efavirenz within antiretroviral therapy (ART). Delamanid is not yet registered in South Africa; access is restricted through Otsuka's international compassionate use programme or the new national Clinical Access Programme.

Intervention or response: Médecins Sans Frontières (MSF) imported DLM under the pre-registration mechanism in South Africa (Section 21) for use in a primary care setting with high MDR-TB/HIV co-infection rates. Delamanid was offered to individuals approved by the endTB medical committee and following latest WHO guidelines. MSF collaborated closely with local clinicians to identify, initiate and monitor ambulatory patients on DLM-containing treatment regimens in primary care. Delamanid supply was controlled through the specialist TB hospital pharmacy. One-on-one counselling, as well as active pharmacovigilance reporting, was conducted for all patients receiving DLM until treatment outcomes were assigned.

Results and lessons learnt: Seventy three (5 [7%] < 18 years; 39 [53%] HIV-co-infected and on ART) patients initiated DLM across 11 facilities over 16 months. The most common indication (n=48, 66%) was second-line drug intolerance in patients < 18yrs, QTc interval 450-500ms, stable on efavirenz. Three (4%) patients received DLM following failure of standard second-line treatment, one had XDR contact and 21 (29%) patients had an inadequate number of effective drugs due to second-line drug resistance. Introduction of DLM was facilitated through systems set up in 2013 for expanded access to bedaquiline.

Conclusions and key recommendations: Facilitated access to DLM at primary care level provided additional therapeutic options for RR-TB patients, especially those not eligible for bedaquiline, within structures and systems already in place for provision of bedaquiline in Khayelitsha. Individual drug importation applications required additional resources; urgent registration of DLM would rapidly improve access nationwide.

PD-892-14 Linezolid dosing for treatment of pulmonary multidrug-resistant tuberculosis: a meta-analysis of existing data

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Background: Linezolid was recently re-classified as a "core second line agent" by the WHO for treatment of multi-drug resistant (MDR) and extensively drug resistant (XDR) tuberculosis (TB). The optimal dose remains unclear; 1200mg daily (the currently licensed adult dose for Gram-positive infections) carries considerable toxicity. Efficacy in TB has been reported at lower doses. We present preliminary findings of a systematic review registered with the Cochrane Collaboration to evaluate linezolid for MDR-TB.

Methods: The Cochrane Infectious Diseases Group Specialized Register; CENTRAL; MEDLINE; EMBASE and LILACS were searched. Randomised controlled trials (RCTs) and quasi-randomised trials of linezolid for MDR-TB were eligible to evaluate efficacy. Cohort studies were added to evaluate adverse events (AEs).
Efficacy outcomes were cure, treatment completed, death, failure and default. We also collected data regarding AEs: total, linezolid-attributed, and those leading to drug discontinuation.

Results: 742 studies were screened. 2 RCTs (99 participants, 65 with XDR-TB) were eligible. 49 patients received a linezolid-containing regimen and 50 received a regimen not containing linezolid. Whilst slightly more cures (17 vs. 7) and fewer deaths (2 vs. 3) were reported on linezolid-containing regimens in one trial, data were insufficient to draw clear conclusions on efficacy. 85 AEs (42 attributed to linezolid) were reported amongst RCT patients receiving linezolid. 49 AEs were reported amongst patients on non-linezolid regimens. When one prospective and five retrospective cohort studies (78 and 767 participants respectively) were added, a total of 105 specific linezolid-attributed AEs were described (56% anaemia; 32% neuropathy; 11% thrombocytopaenia). 34/311 patients discontinued linezolid for toxicity reasons. Heterogeneity in study design and outcome reporting limits scope for detailed meta-analysis.

Conclusions: There remains a paucity of high-quality clinical data, especially RCTs, reporting efficacy and AEs of linezolid for MDR-TB. Toxicity is common, but evidence to support preferential dose selection is insufficient. Further studies, including more RCTs, are required.

PD-893-14 Threats to affordable quality second-line TB drugs in Eastern Europe/ Central Asia as the Global Fund shifts to national procurement

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Background and challenges to implementation: 75% of the countries in the EECA region are on the WHO multidrug-resistant tuberculosis (MDR-TB) list. National TB Programmes mostly rely on the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) to purchase and procure quality-assured second-line TB drugs for the treatment of drug-resistant (DR) TB. Reductions in funding and changes in GFATM policies led to plans to accelerate transition of procurement and financing of key TB commodities with timelines based on income classification.

Intervention or response: We conducted semi-structured interviews with Médecins Sans Frontiéres (MSF) country teams and key informants and analysed strategies, policy and grant documents[1] for 7 EECA countries.[2] [1] Policy documents include GFATM policies, National TB strategic plans, concept notes (GFATM website) and GFATM country agreements.
[2] Armenia, Belarus, Georgia, Kyrgyzstan, Tajikistan, Ukraine and Uzbekistan.

Results and lessons learnt: The majority of countries studied are scheduled to take on the procurement of more than 75% of second-line TB drugs before the end of 2018. The relatively rapid transition timeline risks decreased affordability (higher prices due to lack of competition, transparency, negotiating power and poor planning), quality (potential for substandard quality of locally produced commodities and lack of standardisation) and accessibility (delays in market entry for non-registered drugs). Most countries studied had either a limited, delayed or absence of assessment of risks before the gradual shift of procurement responsibility.

Conclusions and key recommendations: In order to mitigate the potential harm of the policy changes, we strongly recommend that the GFATM carries out a risk assessment of the impact of policy changes on procurement, treatment scale-up and prices for the grantees in the EECA region. Until the results are available, GFATM should adjust the plans for co-financing of procurement of TB commodities and refrain from using income classification as guidance, for the sake of reaching more people with affordable and quality medicines in the region.

PD-894-14 The impact of pyrazinamide resistance on the treatment outcome of patients with multidrug-resistant tuberculosis in Karakalpakstan, Uzbekistan

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Background: The World Health Organisation (WHO) recommends the inclusion of pyrazinamide (PZA) in multidrug-resistant tuberculosis (MDR-TB) treatment regimens unless resistance is certain, although large-scale data supporting this recommendation are lacking.
Methods: We conducted a retrospective cohort study to investigate the association between PZA strain susceptibility and MDR-TB patient treatment outcome amongst patients treated with a PZA regimen and further, whether duration of intensive phase PZA treatment affected treatment outcome. All eligible MDR-TB patients starting treatment between 2003 and 2013 with records in the routinely collected database in the TB programme in Karakalpakstan, Uzbekistan, were included. PZA drug susceptibility testing (DST) was performed using liquid culture and outcomes were classified according to the WHO 2013 TB reporting framework.
Results: Of the 2,446 MDR-TB patients included, 832 (34.0%) had an available baseline PZA DST of which 612 (73.6%) were PZA resistant. There was no demonstrable association between treatment success and PZA susceptibility amongst patients treated with a PZA regimen (aOR 0.86, 95% CI 0.51-1.44, p=0.6). Likewise, there was no evidence of an association between treatment success and PZA treatment duration (aOR 0.86, 95% CI 0.49-1.51, p=0.6) neither amongst patients who had no baseline PZA DST nor amongst patients who had PZA resistant MDR-TB (aOR 1.38, 95% CI 0.71-2.68, p=0.3). Furthermore, no difference in successful outcome in patients treated with PZA during part of the intensive phase was evident in the same groups.
Conclusions: Treatment with a PZA standard MDR-TB regimen does not appear to improve treatment outcomes, regardless of PZA susceptibility or duration of PZA treatment. Although this is the first large primary study demonstrating these results and has the usual inherent limitations of a retrospective observational study, we recommend research into alternative add-on agents in settings with high PZA resistance.

45. The bug, the host, and points between

PD-895-14 Do drug-tolerant phenotypes dominate sputum prior to treatment? Clearance of *M. tuberculosis* DNA suggests not

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Background: Quantitative sputum culture suggests that tuberculosis treatment is biphasic: the initial 5-7 day bactericidal phase kills ~99% of *Mycobacterium tuberculosis* (*Mtb*) and the months-long sterilizing phase slowly kills drug-tolerant "persisters." This paradigm assumes that the *Mtb* subpopulation that grows on agar plates ("plateable") represents the *entire Mtb* population. However, an alternative paradigm suggests that treatment-naïve sputum is dominated by "non-plateable" phenotypes that require growth factor supplementation and are drug-tolerant. This implies slow initial killing, challenging the biphasic paradigm. To test these competing paradigms, we analyzed change in a culture-independent measure of burden: *Mtb* DNA with adjustment for slow degradation after cell death.

Methods: We fit bi-exponential mixed-effects models with random intercepts to serial Xpert MTB/RIF mean CT values during days 0-56 among Ugandan adults treated for drug-susceptible pulmonary TB. We estimated the components of DNA from viable versus dead-but-not-yet-degraded *Mtb*, assuming an exponential rate of clearance/degradation of DNA from dead *Mtb*. A change-point in rates was estimated as a model parameter.

Results: Forty-one patients were enrolled; 23 were HIV positive. Even without adjustment for residual DNA from dead *Mtb* (DNA clearance half-life=0), change in DNA was biphasic, declining 0.22 log/day until day 8.8 then slowing to 0.07 log/day (Table).

DNA clearance half-life (days)	% of DNA at day 7 from viable Mtb	% of DNA at day 7 from dead Mtb	Reduction in viable Mtb by day 7 log10 (%)	Change point (days)	Early rate of killing (log10/day)	Late rate of killing (log10/day)
0	100%	0%	1.56 (97.2%)	8.8	0.22	0.07
0.75	48.4%	51.6%	1.90 (98.7%)	6.5	0.29	0.07
1	35.2%	64.8%	1.92 (98.8%)	5.7	0.32	0.07
1.25	24.8%	75.2%	1.94 (98.8%)	5.0	0.36	0.06

Table

Models assuming a range of plausible *Mtb* DNA clearance half-lives estimated faster initial rates of killing and earlier change points. With DNA clearance half-life=1.25 days, DNA from viable Mtb declined 0.36 log/day until day 5.0 then slowed to 0.06 log/day.

Conclusions: Our culture-independent analysis indicates that treatment initiation rapidly kills most Mtb in sputum. Biphasic clearance of Mtb DNA is inconsistent with the hypothesis that drug-tolerant Mtb phenotypes dominate pre-treatment sputum. Although a significant portion of the sputum population may be non-plateable, measurement of Mtb DNA reinforces validity of the traditional biphasic killing paradigm.

PD-896-14 An approach based on Hidden Markov Models (HMM) to analyze variability of toxin-antitoxin systems in lineages of *Mycobacterium tuberculosis* complex

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Background: The toxin-antitoxin (TA) systems are operons involved in mechanisms that lead to the formation of persistent cells under stress situations in microorganisms. They have been described as widely distributed in the *Mycobacterium tuberculosis* complex (MTBC). The objective in this study was to determine protein sequences variability of TA systems in seven major MTBC lineages.

Methods: Proteins prediction on 37 genomes of different lineage was made using Prodigal. In parallel, profile HMMs of 225 TA reference proteins were constructed with HMMER. With each of predicted proteins a homology search was made using profile-HMMs created. Proteins matching a profile-HMMs and consecutive to another protein that also matched a profile-HMMs was selected. Clustering of orthologous genes, and subsequently multiple alignments for mutations search were made.

Results: All proteins found belong to TA type II and IV and 63 proteins were completely conserved. Not TA type I, III and V were found in the seven lineages. Six possible uncharacterized antitoxins homologous to vapB11, vapB5, vapB45, vapB13, parD1 and RelB families were found. Multiple alignments revealed mutations present in all lineages. These mutations were found in 38 proteins, of which 20 were toxins, 11 were antitoxins and 7 were non-characterized proteins. Premature stop codons, loss of stop codons and changes of amino acid sequences, were found in 35 TA proteins of five different strains.

Conclusions: Results suggest that MTBC lineages favor the emergence of new antitoxins and those toxins are more likely to change than antitoxins. Also functional redundancy of TA systems would allow proteins to acquire mutations without drastically affecting the bacte-

rial phenotype. It would be necessary further studies to elucidate the complex role that TA systems play in host-pathogen interaction and capitalize this knowledge in developing strategies to help control the disease.

PD-897-14 Methylation of genes regulating vitamin D metabolic pathway and tuberculosis

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Background: Vitamin D was first used as a treatment for tuberculosis over a century ago. Plasma concentrations of biologically active vitamin D are controlled via metabolic pathway enzymes. The methylation in the promoter region of genes regulating vitamin D metabolic pathway may affect the risk and prognosis of tuberculosis.
Methods: This study applied both case-control and prospective cohort designs. We recruited 122 pulmonary tuberculosis and matched with 118 healthy controls by sex and age. Five key genes (CYP24A1, CYP27A1, CYP27B1, CYP2R1 and VDR) in the vitamin D metabolic pathway were sequenced for methylation using the Illumina MiSeq platform. The logistic regression analysis was used to estimate the risk by calculating the odds ratio (OR) and 95% confidence interval (CI). The Kaplan-Meier method was used to estimate the time to initial sputum conversion after treatment.
Results: The baseline serum 25-hydroxyvitamin D was 51.60±27.25 nmol/L in cases, which was significantly lower than that in the control group (117.50±75.50 nmol/L). The baseline serum 1,25-dihydroxyvitamin D was 82.63±51.43 pmol/L in cases, which was also significantly lower than that in the control group (94.02±49.26 pmol/L). We observed 167 significantly methylated CpG sites between two groups. The cumulative methylation analysis showed that the methylated CYP24A1 (OR=0.06, 95% CI: 0.01-0.46) and CYP27A1 (OR=0.48, 95% CI: 0.29-0.79) contributed to an reduced the risk of tuberculosis. Follow-up analysis revealed that 1,25-dihydroxyvitamin D concentration was significant related to the sputum conversion rate and treatment outcomes.
Conclusions: This study suggests that epigenetic traits of vitamin D metabolic pathway play an important role in vitamin D bioavailability and the development of tuberculosis.

PD-898-14 Association of human cytomegalovirus infection with anti-mycobacterial antibodies and tuberculosis

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Background: In a recent study, anti-mycobacterial antibodies were associated with reduced risk of Tuberculosis (TB) and, frequency of activated Tcells were associated with increased risk of TB. A positive correlation was observed between Human Cytomegalovirus (HCMV)-specific T cell response and CD8+ Tcell activation. HCMV infection has been shown to drive general Tcell activation and is associated with progression of HIV disease.
Methods: In this cross-sectional study, the impact of HCMV on anti-mycobacterial antibodies was investigated in a rural Ugandan cohort (n=2,153). The impact of HCMV on risk of active TB disease (n=20) was also investigated. Associations were assessed using a bootstrapped linear and logistic regression, accounting for potential confounders.
Results: HCMV seropositivity was associated with increased anti-PPD (0.30 OD, 95% CI 0.24-0.36 P<0.0001), anti-Ag85A (0.25 OD, 95% CI 0.20-0.30 P<0.0001), anti-LAM (0.51 OD, 95% C.I 0.39-0.62, P<0.0001) IgG OD and antibodies against tetanus toxoid (0.44 OD, 95% C.I 0.28-0.59, P<0.0001). Associations with CFP10/ESAT6 IgG, Ag85A IgM and Total IgG are also being examined.
We observed a two-fold increase in the odds of TB among people with HCMV antibody levels above the cohort median of 1.06 OD (OR 1.99, 95% CI 0.68-5.82, P=0.206) but the small number of TB cases limited statistical power to support this association. HIV infection was associated with a three-fold increased odds of TB (OR 3.14, 95% CI 1.09-9.05, P=0.034).
Conclusions: HCMV may be: i) driving an activated immune phenotype, leading to elevated levels of mycobacterial-specific antibodies; ii) increasing risk of mycobacterial infection leading to elevated levels of anti-mycobacterial IgG, or; iii) causing generalised immune activation resulting in increased production of non-protective mycobacteria-specific antibodies in individuals chronically infected with mycobacteria.
Our ability to provide evidence of an association between HCMV and TB risk was limited by the low number of TB cases in this cohort.

PD-899-14 Polymorphisms of TLR1 were associated with latent tuberculosis infection and pulmonary tuberculosis

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Background: Toll like receptor1 (TLR1) and TLR6, acting as TLR1/TLR2 and TLR2/TLR6 heterodimers, play an imperative role in innate and acquired immunity accompanying with downstream Toll-interleukin 1 receptor domain-containing adaptor protein (TIRAP) and Myeloid differentiation primary response 88 (MYD88) against *Mycobacterium tuberculosis* (M.TB). This study aimed to investigate the relationship between single nucleotide polymorphisms (SNPs) of four genes (TLR1, TLR6, MYD88 and TIRAP) and their susceptibility to latent tuberculosis infection (LITB) and pulmonary tuberculosis (PTB).

Methods: Totally 204 healthy controls (HC), 201 LTBI individuals and 209 bacterial confirmed PTB patients were enrolled. Eight tagSNPs of TLR1 and TLR6, two tagSNPs of MYD88 and three tagSNPs of TIRAP were selected based on the Chinese Han Beijing (CHB) panel of HapMap database and genotyped by Improved Multiple Ligase Detection Reaction (iMLDR) method. Data was analyzed by the Statistical Package for Social Sciences version 17.0. The gene-gene interactions were analyzed by nonparametric multifactor dimensionality reduction (MDR) method.

Results: Among TLR1 variants, genotype TT and TC of rs4833095 protect against M.TB infection (dominant model, P = 0.007); genotype AA of rs5743596 protects against LTBI developing into PTB (recessive model, P =0.036); genotype AA of rs5743557 is a risk factor in M.TB infection but a protective factor against progression to PTB (recessive model, P = 0.012, OR 1.989, 95%CI 1.165-3.394; P =0.006, OR 0.451, 95%CI 0.255-0.796, respectively); on the contrary, genotype GA and AA of rs5743604 prevents against infection but increase susceptibility of PTB developing from LTBI status (dominant model, P = 0.034, OR 0.618, 95%CI 0.396-0.965; P = 0.017, OR 1.777, 95%CI 1.017-2.853, respectively). No significant association was found among SNPs of other genes. Both haplotype and gene-gene interactions analyses turned out to be negative results.

Conclusions: Our study suggested that TLR1 SNPs were associated with M.TB infection and PTB.

PD-900-14 Urinary lipids as biomarkers during tuberculosis treatment

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Background: Markers for TB treatment response could be beneficial in aiding improved clinical decision-making and accelerating new anti-TB drugs or treatment regimens. We explored the utility of mass spectrometry-based approaches in identifying and quantify urinary lipids of *M.tb* or human origin in TB patients.

Methods: 11 adult TB patients were selected from a study population consisting of sequential TB patients presenting at a TB clinic in a peri-urban township in Cape Town. Single-phase lipids were extracted from 48 urine samples collected at 5 different time points. Mass spectrometry was performed on an Agilent instrument and profile data collected in positive mode within a mass range of 200-3200 Daltons. MZmine2Java based toolbox was used to detect, process, visualise and analyse peaks from mass spectrometry data. R statistical programming software was used for statistical and bioinformatics analysis.

Results: A total of 1554 lipid compounds were identified from the 48 urine samples at 5 different time points (week0, week1, week2, week8, week16, and week24) of TB treatment. Of 1554 compounds, 126 exhibited a consistent/ statistically significant increasing/decreasing trend (p< 0.05). 101 compounds showed a consistently decreasing trend while 23 compounds showed a consistently increasing. Further interrogation located the 23 compounds in the LipidMaps database, suggesting that these lipids were predominantly of human origin. Of the 101 decreasing compounds, 5 were shown to have a consistent pattern of decrease in 4 patients and were located in the *M.tb* lipid database, MycoMass.

Conclusions: Our results illustrate that using LC/MS approaches; we can detect mycobacterial lipids, which decrease, while at the same time we are also able to detect increasing trends in lipid compounds of human origin.. Our findings point to the utility of mass spectrometry approaches and the use of metabolomics to monitor changes which may be useful biomarkers for monitoring response to TB chemotherapy.

PD-901-14 BCG vaccination promotes early clearance of *Mycobacterium tuberculosis* infection by innate immune mechanisms

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Background: Bacillus Calmette-Guerin (BCG) vaccination protects against *Mycobacterium tuberculosis* (*Mtb*) infection, but correlates of this are unknown. We sought to estimate the protective effect of BCG in a cohort of TB household case contacts (CC), and to identify which cytokine responses correlated with protection amongst BCG-vaccinated CCs.

Methods: In Indonesia, CCs were recruited within 2 weeks of the case starting treatment. An IGRA performed at baseline and 14 weeks identified persistently negative (PN) contacts, who were exposed but uninfected, and converters. At baseline exposure to the index case and presence of a BCG scar was recorded, and blood drawn. Whole blood was stimulated with live BCG, *Mtb* lysate, fixed *Streptococcus pneumoniae* or fixed *Escherichia coli* for 24 hours and TNF-α, IL-1β, IL-1RA, IL-6, IL-8 and IL-10 measured by ELISA. Adjusted risk ratios (RR) for IGRA conversion amongst CCs who were IGRA negative at baseline were determined by generalised estimating equations (GEE). The ratio of geometric means of cytokine responses of PN to converters was also modelled by GEE.

Results: Of 941 CCs, 545 (57.9%) were IGRA positive at baseline, 222 (23.6%) were PN, and 76 (8.0%) converted. 192 (86%) of PN and 53 (73%) of converters were BCG vaccinated (adjusted RR=0.52; 95% CI: 0.35-0.77; P=0.001).

In 111 BCG vaccinated CCs (81 PN, 30 conv), PN had higher IL-1β and IL-6 responses to *Mtb* lysate (RR=1.43 [95% CI: 1.00 - 2.03; P=0.047] and RR=1.40 [95% CI: 1.04 - 1.88; P=0.027] respectively) and higher IL-6 response to *S. pneumoniae* (RR=1.52 [95% CI: 1.14 - 2.03; P= 0.005]) and *E. coli* (RR: 1.26 [95% CI: 1.00 - 1.59; P=0.054]).

Conclusions: BCG vaccination protects against *Mtb* infection. Higher innate cytokine responses to *Mtb*, *S. pneumoniae*, and *E. coli* were associated with protection from infection in the BCG vaccinated group, suggesting protection may be by innate mechanisms.

PD-902-14 Maximising impact of the TB vaccine pipeline: mathematical modelling to inform target product profiles using China as a case study

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Background: Target product profiles (TPPs) guide strategic development of new TB vaccines to ensure vaccines are fit for purpose and maximise future epidemiological impact. Currently, insufficient evidence exists to guide decisions on key characteristics. A novel mathematical model was applied to assess the main determinants (vaccine efficacy for prevention of infection (VE-POI), prevention of disease (VE-POD) and duration of protection) of population-level impact of new TB vaccines, delivered during 2025-2050 to adolescents/adults in China.

Methods: An *Mtb* transmission model was calibrated to age-stratified population estimates, TB prevalence, notification, incidence and mortality rates in China. VE-POI and VE-POD of 0-100%, duration of protection from 2 years to lifelong, and efficacy pre- and/or post-infection were explored. Annual routine coverage of 9 year olds was 80%, plus 70% mass vaccination coverage of ≥10year olds at 10-yearly intervals. The primary outcome was incidence rate reduction in 2050 compared to a no-new-vaccine baseline.

Results: Vaccine impact for a range of characteristics is shown in Fig.1.
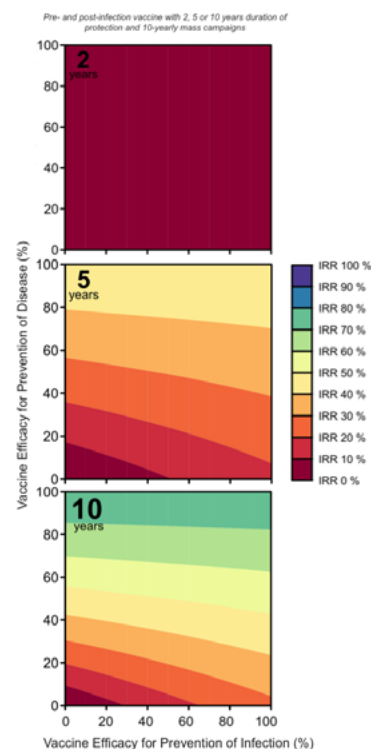
Figure 1 Incidence rate reduction in 2050 compared to new vaccine baseline

To achieve 2050 incidence rate reduction (IRR) of 20-29%, at least 5 years duration of protection would be needed with 10-yearly campaigns, and median VE-POD of 40% (range: 0-60%) *and* VE-POI of 60% (range: 0-100%). To achieve 50-59% IRR, VE-POI remained unchanged, but median VE-POD increased to 100% (100-100%) with 5 years protection, or 60% (40-70%) with 10 years protection. VE-POD was the main determinant of impact. Vaccines effective pre-infection provided substantially lower impact than post-infection or pre- and post-infection.

Conclusions: TPPs to inform vaccine development for China and similar epidemics should accelerate candidates with anticipated protection against disease and efficacy post-infection. Trials should include disease endpoints and *Mtb*-infected populations.

Results presented can inform stage gating. At least 5 years protection are required to achieve the minimum required impact, thus trials should extend beyond the usual 2-3 years, or frequent revaccination may be critical.

PD-903-14 Elevated levels of macrophage migration inhibitory factor in serum of Ghanaian TB patients compared to latently infected and uninfected household contacts

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Background: The pro-inflammatory cytokine, macrophage migration inhibitory factor (MIF) plays an important role in the regulation of the Th1/Th2 balance in the inflammatory response. Elevated levels of MIF have been detected in the sera of patients with infectious and inflammatory diseases indicating a role for MIF in pathogenesis.

Methods: In an ongoing pilot study, enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of circulating MIF in the serum of 57 newly diagnosed sputum smear-positive Ghanaian tuberculosis patients and 31 of their close household contacts (both QuantiFERON-TB Gold Plus-positive and negative).

Results: The mean levels of circulating MIF were significantly higher in serum of sputum-smear positive tuberculosis patients (13.6 ± 0.9 ng/mL; P=0.0026) than in their close household contacts (9.4 ± 0.8 ng/mL). There was no significant difference in mean MIF levels between QuantiFERON-TB gold plus- positive (9.3 ± 1.3 ng/mL; p >0.05) and negative (9.4 ± 1.2 ng/mL) household contacts.

Conclusions: These preliminary results support the concept that MIF plays a significant role in the host response to *Mycobacterium tuberculosis* and may be a useful marker for active TB disease.

46. Knock Knock? Who's there? Household and contact case finding. Know, share, act!

PD-905-14 Challenges in household contact screening: lessons from the PPM project in Pakistan

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Background and challenges to implementation: In public-private mix project, Mercy Corps (MC) develops capacity of private healthcare providers to improve case notification. The field staff (district field supervisor - DFS) plays an important role in this model in ensuring coordination, data reporting, and patient follow-up. DFS is also responsible for screening the contacts of the index patient. However, it was found that very few presumptive cases were identified through household contact tracing.

Intervention or response: MC conducted an assessment in 15 districts, and contacted 138 persons with TB. Only three refused a home visit. The methodology included contacting the index patient on phone and getting consent for a visit, followed by a discreet home visit of 30-40 minutes duration, during which the person with TB and household members were interviewed thoroughly using the verbal screening tool. 86 presumptive cases were identified through this approach.

Results and lessons learnt: The challenges in identifying presumptive cases were mainly due to the approach used. Key lessons include: 1) Inform the patient about a home visit at the time of registration, 2) Call the index patient and get an appointment, 3) Introduce yourself with reference to the clinic on which the patient is registered or the Lady Health Worker or community notable who referred the patient to the chest camp, 4) Spend sufficient time with the household members, 5) Explore each question of the screening tool and fill it thoroughly.

Conclusions and key recommendations: Household contact screening is a key intervention in TB care and prevention. This approach is largely dependent on field workforce. Field staff needs to be well versed with the steps in contact tracing. Patient education in this regard is also important. The field staff must ensure an actual household visit and fill the verbal screening tool properly to identify presumptive TB cases among the household contacts of the index patient.

PD-906-14 Household contact non-uptake of tuberculosis clinical evaluation in a high burden district in South Africa

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Background: Due to their close proximity to tuberculosis (TB) patients, household contacts are at high risk of infection. South African TB management guidelines recommend prioritisation of household contacts for TB screening and clinical evaluation. This paper describes household contacts' TB knowledge, attitudes, and factors influencing uptake of clinical evaluation at primary health care (PHC) facilities.

Methods: A cross-sectional survey of household contacts of TB patients was conducted in October-November 2016 in a high burden district. Researcher-administered questionnaires were used to gather demographic and clinical information and information on TB knowledge and attitudes, and uptake of clinical evaluation at PHC facilities. Contacts were screened for TB symptoms and children < 5 years and symptomatic individuals were referred for clinical evaluation at the nearest PHC facility. Data were subjected to uni-, bi- and multivariate analyses. Logistic regression analysis was used to investigate factors influencing non-uptake of clinical evaluation. Statistical significance was considered at p< 0.05 and 95% confidence interval.

Results: Of the 259 respondents, approximately three in every five were female (59.5%). The median age was 20 (interquartile range: 8-41) years. Two in every five (40.9%) respondents misconstrued that TB is hereditary. A substantial proportion (19.3%) of respondents perceived TB to be stigmatised. More than half (55.1%) of symptomatic contacts did not attend clinical evaluation despite referral. Male gender (AOR: 3.4; 95% CI: 1.1-10.2), previous TB history (AOR: 5.6; 95% CI: 1.2-27.6), and sharing bedrooms with TB index cases (AOR: 3.5; 95% CI: 1.2-10.8) increased the likelihood of non-attendance of PHC facilities for clinical evaluation.

Conclusions: Sensitisation about TB transmission is imperative at household level. Most household contacts did not undertake clinical evaluation when referred, suggesting a need for improved motivational strategies. Extant community-based clinical evaluation strategies should be strengthened to remedy default of referral to PHC facilities.

PD-907-14 Clinical, programmatic and epidemiological significance of wide-scale implementation of tuberculosis contact investigation in Ethiopia

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Background and challenges to implementation: Investigating contacts of index TB patients is one of the high yield case finding strategies but is not widely implemented. We previously reported Ethiopia's experience in introducing TB household contact investigation (CI) in two big regions of Ethiopia.
Here we present further evidence on the scalability and trends in the yield of CI over a five-year period in Ethiopia.

Intervention or response: In 2012, we developed standard operating procedures and recording and reporting tools for routine implementation of CI in public health facilities in Amhara and Oromia regions of Ethiopia. Guidance on how to conduct CI was included as part of the comprehensive TB training program for general health workers and it became a key focus area for quarterly supportive supervision. Further, we developed and implemented a separate sensitization workshop for health care providers and program managers to emphasize CI in their routine work. We included quarterly reported programmatic data for the period September 2012-December 2016.

Results and lessons learnt: Health facilities actively implementing CI increased from 275 to 1547 in the two regions and an average of 3 contacts were screened per an infectious index case. Of 131,344 household contacts of 46,188 index patients registered, 126,606 (96.4%) were screened for TB. Among those screened, 1,269 (1.1%) TB patients were identified, yielding a prevalence estimate of 1,002/100,000 population. The proportion of presumptive TB among contacts declined from 6.6% to 2.0 % and the proportion of confirmed TB among the screened dropped sharply from 2.9% to 0.4% (Figure).
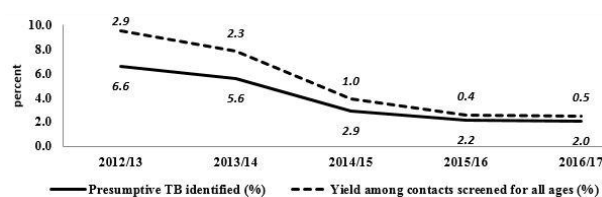
Figure Trends in the yield of contact investigation

Conclusions and key recommendations: The cumulative yield of routine CI was about five times the national prevalence estimate of 192/100,000 but there was steady decline on the yield which coincides with the overall decline in case notification rate in the two regions.

Information from this analysis can be triangulated with other epidemiologic data to explain the overall trend in notified TB cases in Ethiopia.

PD-908-14 Tele-screening as a cost-effective method for improving contact investigation in difficult-to-reach communities

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Background: Contact investigation is a vital component of TB prevention and care. If fully utilized it leads to early TB case detection and treatment of TB cases through A.C.F among highest risk groups. Zambezi Region in Namibia sits in swampy areas prone to seasonal flooding. For significant periods during the year, segments of the population are relatively inaccessible to routine health-care services. Meanwhile, cellphone coverage still remains reasonably high for these communities. We introduced remote screening through cellphones (tele-screening) for TB among contacts of known TB patients who cant be accessed through the usual contact investigation visits by CHWs.

Methods: A contact screening questionnaire was given to 30 CHWs to conduct screening of close contacts of 50 index TB patients diagnosed between December 2016 and January 2017. Because of the difficulty in accessing the geographic location of some of the contacts, the CHWs were requested to administer the contact screening questionnaire by cellphone. The questionnaire had 5 questions probing for presence of symptoms (cough, weight loss, night sweats, fever and lymphadenopathy) as well as risk factors (HIV}. Resources for transportation were prioritized for those with symptoms and/high risk for further evaluation.

Results: Of the 50 TB patients diagnosed between December 2016 and January 2017, 48 had their contacts screened for TB. 30 of the contacts were screening by telephone. Of these, 10 (33%) had positive symptoms. When further evaluated 3 of these 10 (30%) were diagnosed with TB, giving an overall contact investigation yield of 10%.

Conclusions: Given perpetual challenges of human resource and transport availability as well as accessibility of hard-to-reach communities contact investigation can be successfully carried out through cellphones. Resources for physical consultation can then be cost-effectively dedicated to those with symptoms or other risk factors. Stakeholders in TB programs can support CHWs with airtime to improve case TB detection.

PD-909-14 Optimizing tuberculosis contact investigation in a high burden urban setting: a qualitative study

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Background: Optimal tuberculosis (TB) contact investigation (CI) impacts TB prevention, timely case finding and linkage to care, however data on routine TB-CI implementation in high burden contexts is limited.

Methods: In a qualitative study based on individual interviews with pulmonary TB patients, facility observations and focus group discussions with health workers (HWs) in 13 health facilities, and key informant interviews with governmental and non-governmental stakeholders in Kenya, we identified facilitators, barriers and opportunities to optimize TB-CI through triangulation of data and methodology, synthesized themes, and inform the design of an operational framework.

Results: Invitation of TB patients to bring close contacts by HWs was key for all patient decisions that led to contact screening. Patients' understanding of TB transmission and desire to avoid contacts suffering from TB; and pro-active measures by HWs including home-visits and sputum container provision for unavailable contacts were additional facilitators. Barriers reported included long wait-times, non-conducive clinic hours for contacts who were working or in school, poor community awareness and TB stigma. Sub-optimal enquiry and lack of HW invitation of close contacts presenting at the facility were missed opportunities which stemmed from lack of TB-CI specific operational guidelines, documentation tools and HW training. Stakeholders proposed provision of fast tracked and holistic health packages to add value for contacts seeking TB screening, synergistic facility and community health strategies customized to diverse contexts, interoperable, efficient and user-friendly computerized health information systems, sustainable government led funding for infrastructure and an adequate well trained health workforce for optimized TB-CI delivery.

Conclusions: TB contact invitation by HWs leading to contact screening does occur in the public health sector however gaps exist. Patient and HW perspectives gained from this study inform the design of TB-CI specific operational guidelines and framework for optimized TB-CI in context.

PD-910-14 Knocking on the door: house-to-house approach for detecting TB cases in the vulnerable populations - a case study from an Indian State

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Background and challenges to implementation: Since inception in 1997, India's national TB program followed passive case finding approach for detecting TB cases. TB notification rate initially increased then became stationary and now showing declining trends in some part of country despite the increasing efforts to screen the chest symptomatics. There was a felt need for introducing active case finding approach especially vulnerable populations. Himachal Pradesh (Pop: 7 million; 12 districts) is a hilly state in India with difficult geographical terrains having large vulnerable populations.

Intervention or response: With an objective to detect the hidden cases of tuberculosis in the community, a special campaign for active case finding was conducted between 16-30 January 2017 in three districts (Mandi, Kullu and Solan) in Himachal Pradesh. Total vulnerable population of 75632 persons was mapped out. Health workers conducted household visited to target population and did symptoms screening of individuals. Sputum samples of chest symptomatics were collected and examined in the nearest designated microscopy centre (DMC). X ray examination or CBNAAT, were also done in selected cases.

Results and lessons learnt: 41642 (55%) persons were screened for having any TB symptoms. Sputum samples of 974 (2.3%) symptomatics were tested in a nearby DMC. Total 20 bacteriologically confirmed TB cases were detected. All patients were put on appropriate treatment. Total mapped out population couldn't be screened because of some challenges such as adverse wheather condition, odd duty hours of working population and inadequate IEC in the area.

Conclusions and key recommendations: Case detection through active case finding by house to house visit is feasible and useful for detecting the unidentified infectious cases earlier and prevention of infection spread. It should be carried out at regular intervals; however it requires intensive microplanning beforehand including large scale IEC activities and due consideration to weather conditions and availability of residents in household.

PD-911-14 Rapid reduction of tuberculosis prevalence among adults after three-year implementation of community-wide screening in Ca Mau, Viet Nam

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Background: Interventions that improve detection and treatment of people with tuberculosis (TB) could be an important part of strategies to reduce the prevalence of TB in high-burden settings. We are conducting a cluster randomized trial to determine the effectiveness of community-wide screening approach in reducing the TB prevalence among adults in a rural province of Viet Nam. Here, we present results of three years of screening in the intervention arm.

Methods: All eligible and consented individuals aged 15 and above in 60 randomly selected sub-communes were asked to produce a single spontaneous sputum sample for Xpert MTB/RIF testing, regardless of symptoms. Participants whose sputum was Xpert MTB positive were invited to have a plain chest x-ray and to submit two additional sputum samples for confirmatory liquid culture. The screening was conducted annually for three years.

Results: In the first year of screening, the screening program detected 169 Xpert(+) cases, equivalent to the crude prevalence of 389/100,000. Among 154 evaluable Xpert(+) cases 94 (61%) were culture positive for MTB and 84% were either culture positive for MTB or had chest x-ray consistent with active TB. Among those who were Xpert(+), 40% had symptoms (persistent cough or haemoptysis) that would have met the criteria for investigation for TB. Data from serial annual screening over the first three years demonstrate a 55% reduction in the Xpert(+) prevalence from 389/100,000 in year 1 to 176/100,000 in year 3.

Conclusions: Community based screening using Xpert is feasible in rural Vietnam. There is preliminary evidence to suggest a reduction in the community prevalence of disease. In year 4 of the screening, we will conduct an LTBI prevalence survey among children aged 5 years to measure the recent TB transmission to estimate the effect on community incidence of TB.

Support: NHMRC Project grant (#1045236)

PD-912-14 Indonesia 'Knock on the Doors' TB campaign to 'reach the unreached' TB patient

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Background: In 2015, Indonesia notified 324,000 (32% of the estimated incident cases), case detection programme remains flat since 2009. The „Knock the Doors" was already launched by Vice President to increase TB case finding in 2015, this approach was initiated by several organizations Civil Society Organizations (CSOs) including Aisyiyah, Nahdlatul Ulama (NU), etc in several/limited areas. In 2017, this activity was expanded by the Ministry of Health as a national campaign in line with family approach strategy.

Methods: To reach the un-reached TB patient.

Mass TB screening took place between 6 -20 March 2017 as part of national World TB Day campaign with following key steps:

1. Preparation
- Development and distribution of operational guideline
- Coordination and preparation at province and district levels involving Province/District Health Office (PHO/DHO), CSOs and Health Centers to select the sub-district/ villages.

2. Implementation
- Community volunteer (cadre) went door to door to provide TB information and education, identify individuals with symptoms and refer to the health center for testing

3. Data collection and analysis
- Recording and reporting was done by CSOs and Health Centers and sent to DHO
- PHO compiled and report to National TB Programme (NTP).

Results: A total of 565,798 households were visited with 1,590,529 people interaction, 91,049 (5.72%) individuals were identified as presumptive TB, among these 4,950 (5.43%) people are confirmed TB.

Conclusions: Focused, well designed short duration, 2 weeks, campaign among defined population provided opportunity to identify significant number of TB cases contributing to increase case finding, raising knowledge and awareness among public as well as gaining experiences in refining NTP and partners policies and approaches. Good coordination, involvement and support of provincial, district level health offices and CSOs is essential to conduct mass screening campaigns to increase the TB case finding.

PD-913-14 Community-based active case finding approaches increased tuberculosis case notification in peri-urban areas in Myanmar

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Background: The Union, in collaboration with the Myanmar National Tuberculosis (TB) Programme, implemented a community-based active case finding (ACF) TB project in upper Myanmar since 2014 in response to the low TB case notification rate (CNR). The activities include health education and TB awareness raising activities in the community by trained community volunteers, tracing of contacts of previously bacteriologically confirmed TB cases, supporting the TB diagnosis investigations such as sputum samples transportation to township health centers and linkage to anti-TB treatment. This study evaluates the contribution of the Union ACF project to the TB CNR, yield from different case finding activities and the characteristics of notified TB cases from the project.

Methods: Retrospective analysis of TB report data and presumptive TB registers from 6 ACF implemented townships.

Results: In 6 townships, the baseline CNR was 140 at 2013 before implementation and 136, 153 and 153 at the end of 2014, 2015 and 2016 respectively after ACF activities introduced. The trend of CNR stratified by each township is shown in Figure 1.
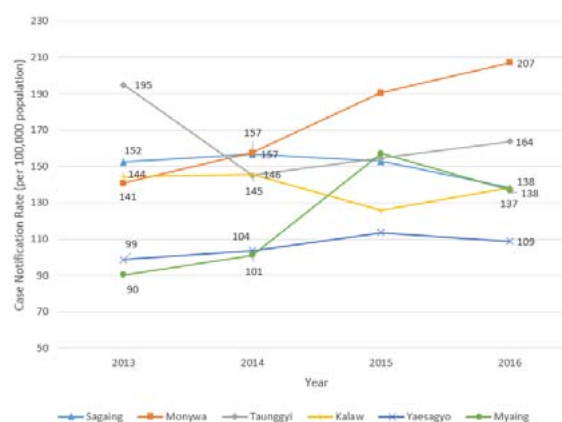
Figure 1 TB case notification rate per 100,000 population (CNR) in six townships in Myanmar undertaking active TB screening strategies during 2014-2016 compared with 2013

and visible increment of CNR were only seen in two townships (Myaing and Monywa). Of total 219,590 people screened for TB symptoms between 2014 and 2016, 5,573 (3%) were referred for diagnosis investiga-

tions and 19% (1,058/ 5,573) were diagnosed with TB. This accounted for 14% (1058/7,454) of the total TB cases notified in these townships. The yield of TB from health education and community mobilization activity was 0.1% and contacts screening activity was 0.12%. Among notified TB patients, 66% (708/1058) were male with median age (IQR) of 33(11-50) years, 5% (48/1058) were HIV positive and 89% (946/1058) were pulmonary TB with 49% (471/946) bacteriological confirmed cases.

Conclusions: The performance of ACF strategy is different across the townships. Further study to explore the factors enabling for increasing case notification should be conducted.

PD-914-14 Does active case finding really help to eliminate tuberculosis? Findings from Sun Quality Health Clinics' TB client registers in Myanmar

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Background: Population Services International (PSI)'s social franchise network of general practitioners, known as Sun Quality Health (SQH) clinics, provide tuberculosis (TB) diagnosis and treatment with Direct Observed Treatment Short course (DOTs) across Myanmar since 2004. PSI developed two ACF channels: Community Health Services (CHS) and Interpersonal Communicators (IPC). They actively found people who are suspected to have TB and referred them to SQH clinics. People, who are suspected to have TB, also initiated themselves to seek treatment via pharmacy and walk-in to SQH.

In this study, we investigated:
(i) the outcome of TB patients from two ACF channels compared with two patient-initiated channels, and;
(ii) risk-factors for loss to follow-up.

Methods: A retrospective cohort-design was applied utilizing TB client records between 2012 and 2015. Outcome was defined as loss to follow-up compared with successful TB treatment (completed or cured). Cox regression was conducted to estimate hazard ratio of loss to follow up.

Results: Of the 85,099 TB patients registered at SQH clinics, ~20% were actively screened by two ACF channels (10% by CHS and 9.5% by IPC) and 80.2% were patient-initiated. Loss to follow-up rate had been increasing over years; 10.6, 13.5, 14.3 and 13.1 cases per 1000 person-years in 2012, 2013, 2014 and 2015, respectively. It was significantly higher in ACF (14.5 per 1000 person-years), especially in ICP channel (23.3 per 1000 person-years), than patient-initiated channels (12.4 per 1000 person-years) (p<0.001). We found that people with older age, male sex, smear negative or unknown,

HIV positive or unknown, and taking treatment with young female doctors who had less experience in DOTs, were risk-factors for loss to follow-up.

Conclusions: Based on this finding, we suggest that strategies for ACF channels need to be modified to minimize loss to follow-up, and risk-factors for loss to follow-up should be taken account into TB control program.

47. Diagnosis and treatment: updates on paediatric TB

PD-915-14 Early experiences of the acceptability and palatability of a novel child-friendly levofloxacin formulation in young children

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Background: The lack of child-friendly formulations of anti-tuberculosis (TB) medications is a major barrier to clinical care and research for the prevention and treatment of TB in children. We evaluated the acceptability and palatability of a novel scored, dispersible, taste-masked levofloxacin 100 mg formulation in children 0-5 years of age.

Methods: Levofloxacin 100 mg tablets (Macleods Pharma, Mumbai, India) were administered to child household contacts 0-5 of adults with drug-resistant TB, enrolled in a pharmacokinetic lead-in to a MDR-TB prevention trial (TB CHAMP). Levofloxacin (15-20 mg/kg) was given once-daily for 7-14 days. A validated palatability tool was administered to caregivers of children by clinical staff. We also conducted *in situ* observations, and semi-structured interviews with caregivers. We report on palatability scores and caregiver experiences.

Results: Fifteen children, 8/15 (53%) girls, median age 23 (3 -54) months, all HIV-uninfected, were enrolled. 8/15 (53%) caregivers felt that their children liked/really liked the taste of the tablets. 14/15 (93%) caregivers indicated that the preparation of doses was easy/very easy and all said the tablet dissolved easily. 11/15 (73%) caregivers were happy with the total reconstituted drug administration volume. 9/13 (67%) of caregivers whose children were previously taking prophylaxis felt that preparation of the levofloxacin paediatric formulation was easier/much easier compared to their standard-of-care regimen including adult levofloxacin (250mg) tablets, while 11/13 (85%) felt the taste was equivalent/better/much better. During in-depth interviews, participant caregivers reported that the paediatric formulation was preferable to adult formulations due to of ease of administration

and improved palatability. Prior experiences of TB formulations strongly influenced initial caregiver and child responses to the novel levofloxacin formulation.

Conclusions: We report good acceptability and palatability in young children receiving a novel paediatric levofloxacin formulation. More child-friendly formulations may help children adhere better to TB preventive therapy and treatment in future.

PD-916-14 Effect of gastric aspirate pH on recovery of *Mycobacterium tuberculosis*

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Background: Gastric aspirate (GA) is the gold standard specimen for TB diagnosis in children. It is common practice to add neutralizing agent to GA prior to culture, but methods are not standardized and the impact on culture result is not well described. We evaluated the effect of neutralization of GA on mycobacterial culture result.

Methods: We collected 1-2 GA from each of 295 children <5 years with symptoms of TB enrolled in a study in Western Kenya, 2013-2015. The baseline pH was determined using pH paper. Prior to transport to the laboratory, 0.3M sodium bicarbonate was added if GA pH <6.0 to achieve neutral pH (pH 6.0-7.0). At the laboratory, pH was rechecked and adjusted with sodium bicarbonate for pH < 6.0 or distilled water for pH >7.0 to achieve a final pH of 6.0-7.0 prior to culture. Microbiological evidence of TB was defined as growth on mycobacterial liquid culture or Xpert MTB/RIF of any specimen including GA, induced sputum, nasopharyngeal aspirate, string test, stool, urine, or blood. Generalized estimating equations were used to determine the association between initial pH and culture result.

Results: We collected 566 GA specimens. Of these, 559 were subjected to mycobacterial culture; 35 GA specimens (6.3%) were positive, 493 (88.2%) were negative, and 31 (5.5%) were contaminated. Among GA specimens collected from children with microbiological evidence of TB (n=32), 19 (31.7%) had baseline pH of <6.0, 17 (28.3%) had neutral pH, and 24 (40%) had pH >7.0. Low baseline pH was significantly associated with decreased adjusted odds of a positive result on GA culture (aOR 0.36; 95% CI 0.13 - 0.94).

Conclusions: Accuracy of GA culture is low when initial GA pH is low, despite neutralization. Further studies of culture performance in GA with a low baseline pH comparing neutralization to no neutralization are needed.

PD-917-14 Progressive uptake of newer diagnostics by health care providers through advocacy strategies in India

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Background and challenges to implementation: Unlike in adults, clinical diagnosis of TB can be challenging in children, as signs and symptoms of TB in children can be very non-specific and similar to other common childhood chest infections. In spite of the increasing availability of rapid high sensitivity diagnostics in public and private sector, majority of the paediatric TB cases are empirically diagnosed, often without laboratory confirmation. Under an on-going paediatric project since April, 2014 in four major cities of India which provided free of cost upfront Xpert testing, several low cost advocacy interventions were undertaken to increase the diagnostic uptake by different providers catering to paediatric population.

Intervention or response: Providers catering to paediatric population in the project cities were systematically mapped and approached with different advocacy approaches. These interventions included distribution of project flyers, one-on-one meeting, organisation of CMEs, engagement through various professional bodies, etc. Focus of advocacy efforts was to increase provider literacy and increase their awareness about the availability of free services.

Results and lessons learnt: Overall 42,238 paediatric presumptive TB cases and DR-TB cases were enrolled in the project, across the four cities from April 14- June-16. Over the project period, quarterly diagnostic uptake and paediatric TB cases detection rates increased more than two fold. More that 4000 providers/facilities were mapped and approached. The number of providers/facilities engaged under the project increased more than 10 fold (43 in April, 2014 to 575 in June, 16, Figure 1), with significant increase in project uptake, both from public and private sector. TB detection rates were similar in patients from public and private sectors.
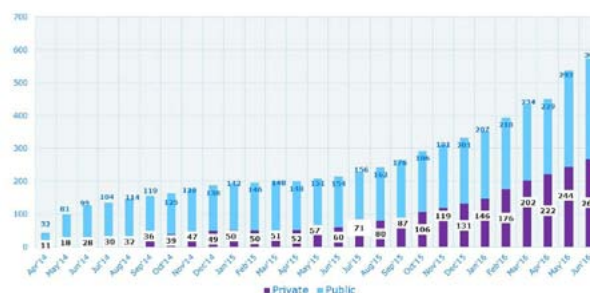
Figure 1 Providers/facilities engaged under the project

Conclusions and key recommendations: Ongoing efforts in scaling up new rapid diagnostics involves significant investments. These efforts need to be complimented with proactive provider engagement to ensure provider-literacy and awareness, for maximizing impact of this scale-up. Current project demonstrated the usefulness of advocacy interventions for the effective uptake of newer diagnostics.

PD-918-14 Caracterización de pacientes con tuberculosis infantil tratados con medicamentos de segunda línea, Lima, Perú

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Background: Marco de referencia: Red de Salud Lima Este Metropolitana en Lima Perú.
Objetivo: Describir características clínicas y epidemiológicas en casos de tuberculosis (TB) infantil tratados con drogas de segunda línea (DSL).
Methods: Evaluamos casos identificados entre 2011 y 2015. Se colectaron datos de registros clínicos y comparamos dos grupos: menores de 5 y de 5 a 14 años y evaluamos factores asociados a mal resultado.
Results: De 96 casos notificados, se evaluaron 82. El 59% fueron varones, la mediana de edad fue 8 años y 32% fueron menores de 5 años. En 82% se identificó el caso índice (CI) y 45% tuvo dos o más CI. El 51% de los CI tenía TB-MDR y 15% TB-XDR. El 90% de los casos fueron nunca tratados, 98% tuvieron afección pulmonar. En 41 pacientes se aplicó PPD, siendo ≥ 10 mm en el 88%. Se identificó el bacilo de Koch en 34 pacientes (42%), 97% de ellos fueron del grupo de 5 a 14 años. Los 29 de aspirados gástricos realizados fueron negativos, no se hizo inducción de esputo. 83% recibieron DSL por TB-MDR/XDR, 12% por resistencia no MDR y 5% por reacciones adversas. El 88% de menores de 5 y 43% en 5 a 14 años ingresaron como TB-MDR probable (p=0,004). El 26% tuvieron TB-MDR confirmada, de los cuales el 90% fueron de 5 a 14 años. El éxito al tratamiento fue similar en ambos grupos con 84%. El 15% presentaron reacciones adversas que no afectaron el tratamiento.
Conclusions: La principal indicación de DSL en TB infantil fue el manejo empírico de la MDR/XDR por tener uno o más CI identificados. La confirmación bacteriológica fue limitada, pero el éxito del tratamiento fue adecuado. Se plantea un mejor acceso a procedimientos y pruebas de diagnóstico en esta población.

PD-919-14 Delays and barriers to early treatment initiation for childhood tuberculosis in India

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Background: India accounts for 27% of the global burden of childhood tuberculosis(TB). Understanding barriers to early TB treatment initiation in Indian children may inform national efforts to improve outcomes.
Methods: A cross-sectional study was conducted among children initiated on anti-TB- treatment (ATT) in Pune in 2016. Structured interviews of parents and clinical data were collected from the hospital records. Time-to-treatment initiation(TOTI) was defined as number of days between onset of TB symptoms and ATT initiation. A significant delay was defined as >4 weeks. Patient delay was duration between first onset of TB symptom reported by parents and first visit to health care provider(HCP). HCP delay was duration between first HCP visit and first visit to the public hospital TB clinic. Health care system delay was duration between first visit to the public hospital and confirmation of TB diagnosis. Treatment delay was number of days between TB diagnosis and treatment initiation.
Results: Sixty-seven (75%) children of 89 enrolled had significant TOTI delays [median 51 days (IQR 31-103)]. The median patient delay, HCP delay (private sector),health care system (public sector) delay and treatment delay was 3 days (IQR 1-14.5), 28 days (IQR 10-75), 5 days (IQR 2-10) and 1 day(IQR 0-2) respectively. Patients visited a mean of 2.5 private sector providers(range 1-8) prior to public health system linkage. Previous hospitalization within 1 year of TB diagnosis was found to be associated with delayed TOTI [HR=1.66 (1.05-2.63) pvalue-0.029]. "Poor quality of health services at health provider level-inquiry of TB case in family and TB symptoms not done" was barrier reported by 21(41%) of the 51 parents reporting delay.
Conclusions: We found significant delays in TOTI among most Indian children with TB involving private health sector. Optimizing care of TB in Indian children will require more efficient engagement with the private sector and linkage to the public TB clinics.

PD-920-14 TB diagnosis and treatment outcomes among children in Tanzania, January 2012-December 2014

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Background: Pediatric tuberculosis (TB) diagnosis is challenging due to non-specific signs and symptoms, difficulties in sample collection and limited value of commonly used diagnostic methods. Data on diagnosis and treatment outcomes for children is limited; we assessed the TB diagnosis and outcomes of children in Tanzania.
Methods: We conducted a retrospective, mixed methods study in 10 purposively-selected health facilities from five high TB burden regions. We abstracted data on TB diagnosis methods and treatment outcomes from TB treatment registers and charts of all children < 15 years old registered for TB treatment between January 2012 to December 2014. We estimated percentages and 95% confidence intervals using SAS survey procedures to account for correlation within clinics.
Results: Of the 13,616 patients registered for TB treatment, 1,260 (9.3%) were < 15 years. TB diagnosis and treatment information was available for 1,205 (96%); 653 (54.2%) were male, 544 (45.2%) were female, and 8 (0.7%) did not have a documented sex. Chest radiography was used for 391 (32.6%; 95% CI: 10.3-54.6), sputum smear microscopy for 350 (29.1%; 95% CI: 18.5-39.6), pediatric TB score chart for 63 (5.2%; 95% CI: 0.0-12.0) and Xpert MTB/RIF assay for 19 (1.6%; 95% CI: 0.0-4.1) children. For 716 children, more than one diagnostic method was used; 489 had no method recorded. For the 1005 with treatment outcomes, 635 (52.7%; 95% CI: 27.5-77.9) had treatment success, 36 (3.0%; 95% CI: 2.2-3.7) died, 330 (27.4%; 95% CI: 5.6-49.2) were transferred out and 4 (0.3%; 95% CI: 0.0-0.8) defaulted.
Conclusions: Children contributed a substantial burden of TB disease; diagnosis was mainly made through chest radiography and sputum microscopy. Reasons for low use of TB score chart should be explored as well as ensuring expanded use Xpert MTB/RIF to improve pediatric TB diagnosis. Reasons for sub-optimal treatment success should be explored.

PD-921-14 'Probable' pediatric TB with no clinical diagnosis: factors associated with lack of clinical diagnosis

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Background: While standardized pediatric TB case definitions have been recommended for research, it is unknown how these case definitions correspond with pediatric TB diagnoses in the clinical setting. We assessed concordance between clinical diagnoses and classification as an unconfirmed "probable" case of TB according to standardized case definitions among children in Lima, Peru and identified factors associated with discordance.
Methods: Study data on Peruvian children ages 3 months to 15 years with at least one TB symptom and history of an adult contact with TB were collected via guardian interview, clinical evaluation and chart abstraction. We considered a chest-X-ray as positive if two independent readers concluded it was consistent with TB. "Probable" TB was defined according to consensus research case definitions for TB and clinical diagnosis was ascertained prospectively and confirmed via chart abstraction.
Results: 46 children met the definition of "probable" TB; 19 of whom (41.3%) had TB ruled out by a clinical provider. In univariable analysis, age under 5 years, negative or missing TST, source case with a negative or missing bacilloscopy result and being in the lowest 2 wealth quartiles were associated with having no clinical diagnosis. In multivariable analysis, negative or missing TST was significantly associated with no clinical diagnosis (AOR 2.1, (5%CI 0.04, 0.94). No significant differences in clinical diagnosis status were seen for pediatric TB symptoms, including cough, fever, fatigue/weakness/lethargy or night sweats.
Conclusions: Nearly half of children meeting the standardized research case definition for unconfirmed "probable" TB did not receive a clinical diagnosis of TB. Lack of a positive TST predicted not receiving a clinical TB diagnosis. Further study is warranted to understand whether lack of TB diagnosis in children who met research case definitions for unconfirmed TB is due to a lack of TB or low positive predictive value of case definitions.

PD-922-14 Stability of anti-tuberculosis drugs in pediatric-friendly formulations

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Background: Non-adherence to treatment regimens is cited as a major barrier to the control and elimination of tuberculosis, and completion of drug therapy is critical to assure recovery and reduce development of drug-resistance. Patient acceptability of a medicinal product is considered critically important for adherence, and can improve patient outcomes especially in pediatric patients. Formulation characteristics that impact acceptability of include test, texture, size and volume. It is imperative to develop innovative oral formulations of FDA approved anti-TB dugs for use in pediatric populations.. This will increase patient acceptability an important factor in patient compliance.

Methods: Using spectrophotometric, HPLC, and minimum inhibitory concentration testing with mycobacterium strains we evaluated anti-TB drug (INH, EMB, DCS,and MOX) stability in three different pediatric-friendly formulations.

Results: Laboratory testing demonstrated stability of INH, EMB, DCS, and MOX in at least one out of three of the child-friendly formulations. Stability data on shipments and storage at various TB treatment clinics is also reported.

Conclusions: Initial stability results show promising pediatric-friendly formulations of all four anti-TB drugs investigated. It is hoped that the NIH will continue forward with pharmacokinetic testing to further evaluate these formulations for eventual use in both pediatric and adult populations to increase patient compliance with arduous TB treatment regimens.

PD-923-14 Comparable yield of TB in children and adults among presumptive tuberculosis patients who underwent Xpert testing in Ethiopia

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Background and challenges to implementation: Diagnosing pediatric Tuberculosis (TB) has always been a challenge due to the atypical feature of clinical manifestations and difficulty of getting sputum sample for laboratory tests. Maximizing the coverage and utilization of WHO approved rapid diagnostics such as GeneXpert strives to improve TB case detection among children. Our objective was to assess the yield of TB between children under 15 years and adults among presumptive TB patients who underwent GeneXpert testing in high TB burden regions of Ethiopia.

Intervention or response: As part of the Ethiopian National TB program, ongoing efforts in the expansion of GeneXpert machines and improving the use of the machines for childhood TB diagnosis is a major support area for the USAID funded Challenge TB project. USAID/CTB assisted the government in capacity building of health workers, development and printing of Standard Operating Procedures, guidelines and job aides to optimize the use of previously invested GeneXpert diagnostics. GeneXpert performance is monitored quarterly using a standardized reporting template which has age disaggregation and is completed by trained laboratory experts. In this study, we compared the yield of TB between children and adults using data generated from 18 GeneXpert machines covering a catchment population of 21 million.

Results and lessons learnt: A total of 15,860 presumptive TB samples were tested using GeneXpert and 1,467 (9.1%) of those tested were children under the age of 15. The cumulative yield of TB was 1,730 (10.9%) of which 120 (8.2%) cases were detected among children and 1,610 (11.2%) cases were among presumptive TB patients over the age of 15. One hundred seventeen (0.72% of the presumptive TB patients) were found to be rifampicin resistant and 3.4% of them were children.

Conclusions and key recommendations: GeneXpert usage leads to a high yield of TB among presumptive TB children and a comparable yield of Rifampicin resistant TB. The use of GeneXpert should be expanded further.

Indicators	<15 years presumptive TB	>=15 years presumptive TB	Total presumptive TBs	P-value
Number of presumptive patients tested using GeneXpert	1,467	14,366	15,833	
Number (%, 95% CI) of MTB detected	120 (8.2, 6.9-9.7)	1,610 (11.2, 10.7-11.7)	1,730 (10.9,10.4-11.4)	<0.05
Number (%, 95%) Rifampicin resistant	4 (0.3, 0.1-0.7)	113 (0.8, 0.6-0.9)	117 (0.7, 0.6-0.9)	<0.05

Table Yield of GeneXpert for presumptive TBs by age

PD-924-14 Does the determine-TB LAM test have potential value in tuberculosis diagnosis among severely malnourished children?

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Background: Active tuberculosis (TB) is a serious co-morbidity for children with severe acute malnutrition (SAM) in TB-endemic settings. TB diagnosis is particularly challenging in children, and largely based on clinical symptoms. Children rarely produce sputum and invasive specimen-collection procedures often have poor yield. The TB LAM test (Determine™) is a lateral-flow strip-test, which detects mycobacterial lipoarabinomannan (LAM) antigen in urine. The test has shown diagnostic value for TB-screening among immunocompromised HIV-positive adults. No data exist for SAM children.
Methods: A cross-sectional assessment was conducted between February 2016 and February 2017 at the Intensive Therapeutic Feeding Centre of Médecins Sans Frontières in Madaoua, Niger. Children under 5 years hospitalized with SAM were included in two groups: 1) with symptoms suggestive of TB, 2) without any TB symptom. One urine specimen was collected at inclusion and tested with LAM (4-grade reading scale). Results were not used for diagnosis.
Results: Group 1: 103 children were included (median age 19 months, 49% male, 2% HIV-positive), 22 (21%) were started on TB treatment, 77% of these with suggestive thorax-radiography, two (9%) with a positive GenXpert test (7 tested). Fifty-three (51%) tested LAM-positive (73% grade 1, lowest intensity). LAM-test-positivity (p=0.40) and grade (p=0.59) were not associated with TB diagnosis. Hospitalisation outcomes were: 80% transferred to the ambulatory nutritional centre, 19% dead (2% among TB-diagnosed), 1 lost-to-follow-up. Group-2: 50 children without TB symptoms were included, none was started on TB treatment, 24% tested LAM-positive (97% grade 1), none died during hospitalisation.

	Group-1 (with symptoms suggestive of TB)		Group-2 (without any TB symptom)
	Started on TB treatment	Not started on TB treatment	Not started on TB treatment
	N=22	N=81	N=50
LAM negative	8 (36%)	41 (51%)	38 (76%)
LAM positive	14 (64%)	39 (48%)	12 (24%)
grade 1	9	29	11
grade 2	3	8	1
grade 3	2	2	0
grade 4	0	0	0
LAM undetermined	0	1(1)	0

Table LAM test results by group

Conclusions: Comparison of LAM-test results with programmatic TB diagnosis suggests poor diagnostic performance of LAM in SAM children, indicating that false-positivity may be an issue in this population. Programmatic TB diagnosis was largely based on symptoms and thorax-radiography, which has known limitations. Further evaluation of the LAM-test in SAM- and other children patient groups is recommended.

48. Looking after little lungs: updates in child lung health

PD-925-14 Perceptions of social functioning among HIV-infected children assessed for chronic lung disease and their caregivers in Malawi

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Background: Little is known regarding the validity of caregiver information, especially regarding social functioning among HIV-infected children with debilitating conditions such as chronic lung disease (CLD). As part of an investigation of CLD prevalence among HIV-infected children aged 5-14 years, we assessed concordance between caregiver and child perceptions of social functioning.
Methods: Children and caregivers presenting for outpatient HIV services in seven facilities in Malawi in March-April 2014 were separately questioned about CLD symptoms and quality of life indicators (n=523). CLD was diagnosed in children meeting one of two case definitions: (1) chronic cough (>4 weeks) and self-reported breathlessness; or (2) one of the previous symptoms and at least one of hypoxia, resting tachypnea, or finger clubbing. McNemar's test was used to describe the association between paired responses. Bivariate analysis and univariate logistic regression were used to describe the association between quality of life indicators and CLD diagnosis.
Results: Eighty-four children (16.1%) were diagnosed with CLD. Responses to paired questions revealed significant differences related to the child "feeling physically different" (p< 0.001), "having trouble falling asleep" (p=0.04), and "feeling breathless" (p< 0.001), but about the child "coughing" (p=0.64). Among children with CLD, both respondents reported increased odds the child had trouble falling asleep (child: odds ratio [OR] = 3.23; 95% confidence interval [CI] = 1.70-6.14; caregiver: OR = 2.22, 95% CI = 1.12-4.01), compared to

those without CLD. Children with CLD had 2.01 times the odds of reporting feeling physically different (95% CI = 1.17-3.43) compared with children without CLD; however, caregiver responses revealed no association (OR= 0.69; 95% CI = 0.42-1.14).

Conclusions: Among HIV-infected children, those with CLD may feel physically different from their peers and may experience difficulties falling asleep; however, their caregivers may not perceive these issues. Clinicians should consult both caregivers and children to best understand symptoms.

PD-926-14 How to introduce pulse oximetry into secondary level hospitals in Nigeria: mixed methods evaluation of a field trial

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Background: Pulse oximetry is a simple tool used by healthcare workers to identify sick patients with hypoxaemia and guide treatment. However, pulse oximetry is not done routinely in most hospitals globally.

Our study aimed to understand how pulse oximetry is adopted by health workers in secondary level hospitals, and to identify common barriers and enablers to effective adoption.

Methods: We conducted a mixed-methods study on the introduction of pulse oximetry within a stepped wedge field trial seeking to improve oxygen therapy in 12 hospitals in south-west Nigeria. We collected quantitative data on pulse oximetry practices (extracted from individual case notes) and qualitative data on healthcare worker perceptions and attitudes regarding pulse oximetry (from interviews). We analysed the qualitative data using a grounded theory approach, seeking to explain observed trends in the pulse oximetry practices over time, and explain variation between hospitals.

Results: Most hospitals started with very low pulse oximetry use (< 1% of admitted children) and improved substantially following basic training and the provision of pulse oximeters. However, most hospitals only achieved full pulse oximetry use (>80% of admitted children) after additional participatory training and supportive supervision "convinced" users of oximetry's multiple benefits (save lives and make their job easier). Hospitals succeeded most when senior nurses were "carried along", providing leadership, encouragement, and ongoing training to junior staff. Low worker morale was a major challenge to successful pulse oximetry adoption, particularly when salary payment was insecure.

Conclusions: Pulse oximetry can be effectively used by nurses in secondary level hospitals, but successful institutional adoption is challenging. Our findings provide practical guidance for practitioners and policy makers seeking to scale-up of pulse oximetry, and may have relevance to broader issues of health technology adoption.

PD-927-14 Knowledge and practices of school teachers regarding asthma among primary school children in selected schools of Bangalore South constituency

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Background: Asthma is the most common chronic disease of childhood. Prevalence of childhood asthma in India is increasing day by day. It is important for teachers and staff to be aware of the symptoms, triggers and the management of asthma in the school environment. This study was conducted to assess the knowledge and practice of primary school teachers regarding asthma among school children and to determine the relationship between knowledge and practices with selected demographic variables.

Methods: Descriptive survey approach was adopted to collect the data. Simple random sampling method was employed for the sample selection. Self-prepared structured questionnaire consisted of demographic data, knowledge and practice aspects was administered.

Results: The knowledge level of primary school teachers regarding asthma among children was found to be moderate, where as practice level was found to be low. The overall mean knowledge level found (52.4 percent) was slightly higher than mean practice level (46.3 percent). The mean knowledge level in aspect wise ranged between 65.0 to 45.6 percent. The highest mean knowledge noticed in the aspect of Role of teachers was 65.0 percent. The highest mean practice identified in the aspect of Role of teachers was 48.8 percent. There was significant correlation (+0.616) between knowledge and practice existed. Demographic variables such as sex, marital status, and professional education programme did not have significant association with knowledge and practice at the level of P > 0.05 and it was also observed that demographic variables such as age and basic educational level had a significant association with knowledge and practice (P < 0.05).

Conclusions: Overall findings showed that the existing knowledge of teachers on asthma among school children is moderate (52.4 percent) but practices are very low (46.3 percent). The enhancement in both knowledge and practice is very much required.

PD-928-14 Pneumonia risk stratification scores for children in low-resource settings: a systematic literature review

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Background: Pneumonia is the leading infectious cause of death among children less than five years of age. Predictive tools, commonly referred to as risk scores, can be employed to identify high-risk children early so management can be tailored to preventing adverse outcomes. Our purpose in conducting this review was to identify risk scores developed and validated in low- and middle-income countries (LMIC), and whether any score has been implemented in an LMIC.

Methods: We searched PubMed, Embase, Scopus, Web of Science, CAB Direct, and Cochrane Reviews for studies that developed formal risk scores predicting treatment failure or mortality among children less than five years of age diagnosed with a respiratory infection or community-acquired pneumonia in LMIC. Data abstracted from articles included location and design of study, sample size, age and diagnosis, score features and goodness of fit.

Results: Five scores were identified, three of which predicted mortality, and two treatment failure.

Four scores developed using variables identified by the World Health Organization (WHO) for the assessment of pneumonia exhibited better predictive fit than one score developed using alternative features. Of the four scores developed using WHO-identified features, three scores were developed using data collected during clinical trials, and one from data that was collected during routine care provision. All of these scores performed similarly well. One score exhibited good fit when externally validated internationally. No score has been implemented.

Conclusions: While several pneumonia-specific risk scores for children have been developed, it is yet unclear if implementation is feasible, the effect scores may have on patient outcomes, or how broadly scores may be generalized. To increase the feasibility of implementation, future research should focus on developing scores that use data that can be realistically collected during routine care provision in either an inpatient or outpatient setting.

PD-929-14 Towards a better diagnosis of childhood pneumonia: a systematic review of tools to measure respiratory rate

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Background: Pneumonia is the leading infectious cause of death in children worldwide, with most deaths occurring in developing countries. Measuring respiratory rate (RR) is critical to the World Health Organization's (WHO) guidelines for diagnosing childhood pneumonia in low resource settings (LRS); yet, it is notoriously difficult for health care providers (HCPs) to accurately measure RR. In an effort to landscape existing RR measurement technologies and innovations in development, we conducted a systematic review of RR technologies for potential use in LRS.

Methods: PubMed, EMBASE, and Compendex/ Engineering Village were searched for English language biomedical and scientific articles published through December 2016 reporting on measuring or monitoring of breath count or RR in spontaneously-breathing children less than five years of age. To meet criteria for inclusion, articles had to describe the accuracy of the RR assessment compared to a reference standard.

Results: We identified a total of 17 technologies, two manual and 15 automated, that aided in measuring RR. Automated technologies most commonly used photoplethysmogram (n=8) or thoracic effort (n= 7) to measure RR. Among the automated technologies, none have been evaluated in LRS, and all but one had a sample sizes < 35. While several studies exhibited similar or improved accuracy compared to their reference standard, the choice of reference standard varied between studies.

Conclusions: While several technologies were identified, we did not find an automated RR technology validated in LRS. Affordable and appropriate innovations that can automatically and reliably measure a child's RR in LRS are needed. Continued innovation is necessary to address the challenges and limitations in current RR measurement technologies. Adoption of a common reference standard would improve the ability to compare RR technologies across studies. Improving existing RR technologies and accelerating further development or scale-up could have the potential to improve childhood pneumonia diagnosis in LRS.

PD-930-14 The Cooking and Pneumonia Study (CAPS) in Malawi: a cross-sectional assessment of carbon monoxide exposure and carboxyhemoglobin levels in 1932 under-fives

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Background: Household air pollution from dirty-burning fuels for cooking, heating and lighting is estimated to cause 4.3 million premature deaths annually including 0.5 million deaths from pneumonia in children worldwide. The Cooking and Pneumonia Study (CAPS) was conducted to determine whether replacing open fires with cleaner burning cookstoves would reduce the incidence of pneumonia in young children in rural Malawi. Here we report a baseline cross-sectional assessment of carbon monoxide exposure and carboxyhemoglobin levels in a subset of CAPS participants.

Methods: One in four CAPS participants was randomly selected for inclusion in this sub-study. Questionnaires were used to collect information about socioeconomic factors, potential smoke exposures, and cooking practices. Children wore Lascar carbon monoxide (CO) monitors for 48 hours of continuous CO exposure data collection. Massimo RAD-57 devices were used for non-invasive measurement of carboxyhemoglobin (COHgB) in children aged 6 months or older.

Results: Mean 48-hour CO exposure of 1932 participants was 1.27 ppm (SD 9; range 0-420). Mean COHgB level was 5.8% (SD 3.3); range 0-20.3). Elevated mean CO levels were associated with wheeze (OR 1.17 (0.89-1.53)), burns (OR 1.26 (0.83-1.94)), cooking inside in the dry (OR 2.13 (1.36-3.36)) and rainy seasons (OR 1.38 (1.07-1.78)), and exposure to beer making (OR 1.63 (0.62-4.27)). Elevated COHgB levels were associated with wheezing symptoms (OR 1.38 (0.97-1.96)), smokers in the home (OR 1.31 (0.91-1.89)), and male gender (OR 1.36 (1.02-1.83)). Correlation between mean CO and mean COHgB was poor (Spearman's ρ=0.09, p=0.003).

Conclusions: Children's CO exposure in rural Malawi was influenced by location of cooking and presence of additional non-cooking exposures. Although carboxyhemoglobin levels did not correlate with personal CO exposure measurements, levels of carboxyhemoglobin were high and since carboxyhemoglobin is the more biologically relevant measure, this finding is concerning. Effective approaches for reducing exposure to CO and other constituents of household air pollution are needed.

PD-931-14 Investigation of severe acute respiratory illness outbreak among children aged < 5 years at a county hospital, Kenya, 2016

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Background: Severe acute respiratory illness is the leading cause of morbidity and mortality in children < 5 years globally. In 2016, there was an upsurge of 823 cases with 94 deaths, a case fatality rate of 11.4% among children < 5 years at an urban county hospital. We sought to investigate the etiology and determine characteristics and factors associated with the outbreak.

Methods: We obtained nasal and oropharyngeal specimens from 75 cases and conducted a mortality review of inpatient records. We conducted a facility-based case-control study matched by residence: A case was aged ≤59 months with temperature ≥38°C and cough with any respiratory features; a control was aged ≤59 months without similar illness in the past 2 weeks. We collected demographic, clinical and risk-factor information. We calculated adjusted ORs at 95% CI.

Results: Of 74 specimens collected, 46% had Respiratory Syncytial Virus, 30% had influenza viruses and no bacteria detected. We recruited 50 cases and 100 controls. Cases had mean age of 9 months (SD±5), gastroenteritis reported among 56%, dyspnea 58%, rhinitis 42% and neurological signs 28%. Median duration of symptoms was 2 days (2-7) and seeking treatment was 1 day (0-3). Independent factors associated with being a case were malnutrition (aOR=26.9, CI=1.9-368.3), prior visit to hospital before illness (aOR=10.74 CI=1.04-111.6) and contact with symptomatic individual (aOR= 4.71 CI=1.16-19.01). We retrieved 65% of 92 mortality records with 63% dying within 24 hours, 10% in 24-48 hours and 30% >48 hours of admission; Oseltamivir was administered to 13%, antibiotics to 100% and oxygen to 75%, 12% had hypoglycaemia with no serial monitoring, 45% had malnutrition and 25% had rickets.

Conclusions: SARI resulted in hospitalization and death within hours. Viruses were isolated with preexisting conditions leading to increased risk of morbidity and mortality. Sub-optimal inpatient care from documentation may have also contributed to deaths observed.

PD-932-14 Determinación de asma en escolares mexicanos y asociación con características antropométricas: resultados preliminares

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Background: Asma es una enfermedad inflamatoria crónica de las vías aéreas, representa un problema de salud pública mundial con una prevalencia de varia de 13 a 33% para México, aunado al importante aumento de obesidad infantil, ambos padecimientos comparten un proceso inflamatorio crónico donde diversos estudios han identificado una asociación entre estos, reportando un riesgo 2.2. a 3 veces mayor para asma en escolares con obesidad,la medición de cintura aun no es claramente asociada a asma. El objetivo de este estudio fue determinar la asociación entre de asma, IMC y percentil de circunferencia de cintura.

Methods: Estudio transversal analítico en el periodo enero 2016-2017 en el cual se reclutaron 241 escolares de 6 a12 años de edad de escuelas primarias de San Luis Potosí, elegidas aleatoriamente, a quienes se les realizó historia clínica, espirómetría, medición de fracción de óxido nítrico exhalado (FeNO) bajo criterios de calidad de la American Toracic Society (ATS) y la Global Initiative for Asthma (GINA) para el establecimiento del diagnóstico. Se obtuvieron medidas antropométricas como peso, talla y circunferencia de cintura. Se calculó puntaje Z de Índice de Masa Corporal para la edad (IMC/E) con el software WHO anthro plus.

Results: 215 escolares incluidos en el análisis, donde se obtuvo una prevalencia total de 16.7% para asma, 29.3% para sobrepeso y obesidad y 40.1% para escolares con circunferencia de cintura por encima del percentil 90, se obtuvo una asociación estadísticamente significativa entre FEV1, FeNO y percentil de circunferencia de cintura,(p,0.003) la razón de momios de presentar asma en escolares con percentil mayor a 90 en circunferencia de cintura fue de 5.2(IC 95%; 2.1-6.5), no se obtuvo significancia estadística con IMC (p,0.09)

Conclusions: Circunferencia de cintura mostró ser un factor de riesgo mayor que IMC para asma en esta población.

PD-933-14 Household, environmental and medication exposures and chronic lung disease in HIV-infected children

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Background: Chronic lung disease (CLD) has been reported to affect up to 80% of children with perinatally-acquired HIV in resource-limited settings. Despite this, the underlying pathology of CLD remains uncertain and little is known regarding the potential risk factors for CLD.

Methods: As part of a rapid investigation of the prevalence of CLD among HIV-infected children aged 5-14 years receiving outpatient HIV services from seven facilities in Malawi in 2014, in-depth interviews were conducted with caregivers to assess >40 household, environmental, and medication exposures (n=611). CLD was diagnosed in children with
1) chronic cough (>4 weeks) and self-reported breathlessness or
2) one of the previous symptoms and at least one of hypoxia, resting tachypnea, or finger clubbing. Bivariate analysis and multivariate logistic regression were used to describe the association between select exposures and CLD diagnosis.

Results: CLD was diagnosed in 96 (15.7%) of 611 children. CLD diagnosis was significantly associated with exposure to mosquito coils (23.5% v 14.2%; p=0.02) and having taken antimalarial medication in the past year (18.5% v 11.2%; p=0.02). CLD was marginally associated with living in an area where flooding had occurred in the past 2 years (24.5% v 14.9%; p=0.07) and exposure to pesticides (21.1% v 14.3%; p=0.06). Children with exposure to mosquito coils were more likely to be diagnosed with CLD (odds ratio [OR] = 1.73, 95% confidence interval (CI) = 1.01-2.97) and those who had taken antimalarial medication in the past year (OR=1.75, 95% CI = 1.08-2.86) compared to those without the respective exposures.

Conclusions: CLD diagnosis was not associated with many common household or environmental exposures. Exposure to mosquito coils and antimalarial medication may increase risk for CLD through direct exposure or through another undefined pathway. More information is needed to better understand risk factors associated with CLD in HIV-infected children.

49. TB and co-morbidity: where are we?

PD-934-14 Post-tuberculosis lung function impairment

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Background: Pulmonary sequelae is frequent after pulmonary tuberculosis (PTB). The aim of this study was to describe lung function abnormalities at the end of PTB treatment and investigate the determinants of post-tuberculosis lung function impairment in a reference center for tuberculosis (TB) treatment in Cameroon.
Methods: This was a cross-sectional study conducted from January 2015 to May 2016 in Yaounde Jamot Hospital (YJH). Patients aged ≥ 18 years, successfully treated for microbiologically proven PTB were invited to participate in the study. Three ventilatory abnormalities were defined using pre-bronchodilator spirometry: obstructive syndrome with forced expiratory volume in 1s (FEV1)/forced vital capacity (FVC) ratio < lower limit of normal (LLN); restrictive pattern (FVC< 80% of predicted value and FEV1/FVC ratio>LLN) and mixed pattern (FVC< 80% and FEV1/FVC ratio< LLN). Lung function impairment was defined as FEV1< 80% of predicted value.
Results: Of the 309 patients included, 55.3% were male, the median age (1st-3rd quartile) was 37(30- 38) years. Twenty-seven (8.7%) patients had relapse PTB, 115(37.2%) patients were HIV-infected and 26.3% of participants were smokers. The prevalences of obstructive lung disease, restrictive pattern, and mixed pattern were 4%, 51% and 10% respectively. Overall, 186 (60.2%) participants had lung function impairment. The only independent factor associated to lung function impairment was the duration of respiratory symptoms > 8 weeks before starting TB treatment.
Conclusions: At the end of treatment of PTB, two third of patients in this setting had a lung function abnormality. Early diagnosis of tuberculosis should allow a reduction in the frequency of post-tuberculosis lung function impairment.

PD-935-14 The impact of cancer development on the risk of mycobacterial disease in patients with rheumatoid arthritis: a nationwide cohort study in Taiwan

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Background: Mycobacterial disease is prevalent in cancer and rheumatoid arthritis (RA) patients, especially those receiving tumor necrosis factor-α inhibitor (TNFi). However, the impact of cancer development on the risk of mycobacterial disease among RA patients is unknown.
Methods: Data from the Taiwan National Health Insurance Research Database were used to conduct a retrospective study to observe the occurrence of mycobacterial disease in RA patients without cancer development and TNFi use (cancer-TNFi-free), with TNFi without cancer (TNFi-exposure), with cancer but without TNFi (cancer-exposure), and with cancer in combination with TNFi (cancer-TNFi-comb). The diagnosis of RA, mycobacterial disease and cancer were identified by compatible ICD-9-CM codes, and confirmed by patients' medications and/or catastrophic illness certificates. The TNFi included etanercept, adalimumab and golimumab. Cancer and TNFi exposure were time-dependent, and independent risk factors of mycobacterial disease were assessed by Cox regression.
Results: Among 1,344 RA patients diagnosed during 2000 to 2013, 68 (5.1%) developed cancer before their end-points. The incidence rates of mycobacterial disease in the cancer-TNFi-free (n=986), TNFi-exposure (n=290), cancer-exposure (n=56), and cancer-TNFi-comb subgroups (n=12) were 1.29, 2.02, 6.74, and 7.58 per 1,000 person-years, respectively. Using cancer-TNFi-free as the reference, the risk for mycobacterial disease increased for TNFi-exposure (adjusted HR 3.59, 95% CI 1.12-11.52, **P**=0.032) and remained high for cancer-exposure (adjusted HR 15.98, 95% CI 3.12-72.60, **P**< 0.001) after adjustment for significant factors including age ≥60 years, male sex and diabetes mellitus.
Conclusions: This study suggested that cancer development increased the risk of mycobacterial disease in RA patients, and risk assessment for this subgroup should be considered.

PD-936-14 Multi-morbidity of cardiovascular risk factors among South African patients with drug-resistant tuberculosis

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Background: In South Africa, cardiovascular disease (CVD) is a leading cause of death after tuberculosis (TB). TB patients, many of whom are co-infected with HIV, may have greater risk for CVD risk factors. The purpose of this study is to explore the prevalence of CVD risk factors among drug resistant TB (DR-TB) patients with and without HIV co-infection.
Methods: This is a sub-study among patients enrolled in an ongoing cluster randomized controlled trial of a nurse case management intervention to improve DR-TB outcomes across 10 hospitals in Eastern Cape and KwaZulu-Natal provinces of South Africa. CVD risk factors were collected at treatment initiation through self-report (diabetes, hypertension, smoking) and clinic vital signs (hypertension, elevated body mass index). Prevalence of CVD risk factors was estimated and compared by HIV status, sex, and age using chi-square tests. Logistic regression was used to compare CVD risk factors by HIV status adjusting for age, sex, and the random effects of enrollment site.
Results: Of 504 patients, 54% were male, 76% were co-infected with HIV, and 49% had a prior history of TB. 39.5% of the population had at least one CVD risk factors and 12.5% had >2 CVD risk factors. Females smoked less than males (χ^2 (1) = 126.0, p=0.000), but were more likely to be overweight or obese (χ^2 (1)= 34.13, p=0.000). Patients living with HIV (PLWH) had decreased odds for diabetes and hypertension (Table 1) and ART status did not impact these odds.

	Overall Prevalence (95% Confidence Interval) (n=504)	Prevalence among those with DR-TB only (95% Confidence Interval) (n=123)	Prevalence among those with DR-TB and HIV (95% Confidence Interval) (n=381)	Unadjusted Odds Ratio for HIV status (p-value)	Adjusted Odds Ratio for HIV status (p-value) for age, sex, & enrollment site
Diabetes	3.4 % (2.1-5.3)	8.1% (4.4-14.6)	1.8% (0.87-3.8)	0.215 (0.002)	0.149 (0.001)
Elevated Blood Pressure	13.1% (10.4-16.3)	18.7% (12.8-26.7)	11.3% (8.4-14.9)	0.565 (0.048)	0.450 (0.016)
Elevated Body Mass Index	16.2% (13.12-19.7)	14.6% (9.3-22.2)	16.8% (13.4-20.1)	1.18 (0.580)	0.889 (0.772)
Current or Former Smoker	33.9% (29.9-38.1)	39.8% (31.4-48.8)	32.0% (27.5-36.9)	0.729 (0.150)	0.891 (0.652)

Table CVD Risk Factors Among DR-TB patients

Conclusions: CVD risk factors are common among patients with DR-TB. PLWH did not have increased prevalence of CVD risk factors. However, PLWH with CVD risk factors may be at increased risk for poor adherence or adverse drug effects due to poly-pharmacy and increased patient burden. DR-TB providers and health systems should include prevention, screening, and treatment of CVD risk factors to prevent negative outcomes.

PD-937-14 Chronic airflow obstruction after successful treatment of multidrug-resistant tuberculosis in Lima, Perú

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Background: Cross-sectional studies reveal an association between tuberculosis and chronic airflow obstruction, but cannot adequately address confounding. We hypothesized that treated pulmonary tuberculosis is an independent risk factor for chronic airflow obstruction.
Methods: The *Pulmones Post TB* cohort study enrolled participants from Lima, Peru aged 10-70 years with a history of drug susceptible (DS) or multi-drug resistant (MDR) tuberculosis who had completed treatment and were clinically cured. Unexposed participants without tuberculosis (TB) were randomly selected from the same districts. We assessed respiratory symptoms, relevant environmental exposures and spirometric lung function pre- and post- bronchodilator.
Results: In total, 144 participants with DS-TB, 33 with MDR-TB and 161 unexposed participants were fully evaluated. Compared with unexposed participants, MDR-TB patients had lower lung volumes (adjusted mean difference in FVC -370 mL, 95% CI -644 to -97 mL) and post-bronchodilator airflow obstruction (adjusted odds ratio 4.89, 95% CI 1.27 to 18.78). Participants who had recovered from DS-TB did not have lower lung volumes than unexposed participants, but were more likely to have $FEV_1/FVC < 0.70$ (adjusted odds ratio 2.47, 95% CI 1.01 to 6.03).
Conclusions: Individuals successfully treated for TB may experience long-lasting sequelae. Interventions facilitating earlier TB treatment and management of chronic respiratory disease should be explored.

PD-938-14 Prevalence of co-infection with *Streptococcus pneumoniae* among patients with suspected pulmonary tuberculosis

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Background: Co-infection with *Mycobacterium tuberculosis* and other bacteria has not been widely reported. It has been described mainly in immunocompromised patients, presenting with simultaneous infection with tuberculosis and pneumonia. *Streptococcus pneumoniae* is the most frequent aetiologic agent of bacterial pneumonia. Co-occurrence of *M. tuberculosis* and *S. pneumoniae* in individuals with preserved immunity may complicate the clinical presentation, leading to inadequate treatment and unsatisfactory outcomes. Hence, the objective of present study was to determine the prevalence of *S. pneumoniae* among suspected patients of tuberculosis by molecular diagnostic method.
Methods: A total of 216 sputum specimens were collected from the patients visiting Vallabhbhai Patel Chest Institute, Delhi. All the enrolled patients were symptomatic with clinical features of tuberculosis. Demographic information of patients was recorded. Smear microscopy, culture and PCR targeting *sdaA* gene were carried out to evaluate the disease status of patients for tuberculosis. PCR targeting *ply*, *lytA*, Spn9802, *cbpA* and *comX* were performed on the clinical specimens for detection of *S. pneumoniae*.
Results: Out of 216 specimens, 18 were positive for presence of *M. tuberculosis* based on smear microscopy and culture results. Out of the tuberculosis confirmed cases, 5 specimens tested positive with PCR assays for detection of *S. pneumoniae*. The prevalence of co-infection with *S. pneumoniae* and *M. tuberculosis* was 2.3% in the specimens of suspected pulmonary tuberculosis patients. The co-infection rate was high (27.8%) in the confirmed pulmonary tuberculosis diseased individuals.
Conclusions: Both *S. pneumoniae* and *M. tuberculosis* cause infections that affect the lobes of the lungs producing lobar pneumonia and pneumonitis respectively. The present study highlights the high prevalence of co-infection with these pathogens. When there is co-infection of pneumonia in tuberculosis patients with pneumonia as the underlying disease, undiagnosed underlying *S. pneumoniae* infection could pose health management problems if tuberculosis alone is diagnosed.

PD-939-14 Analysis of anti-tuberculosis drug resistance in high-risk groups

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Background: Tuberculosis (TB) risk groups, such as people with diabetes mellitus (DM), with HIV, with chronic renal failure (CRF), with rheumatic disease (RD) on immunocompromising treatments, are playing an growingly important role in TB epidemics of developing countries. In China, little is known about the prevalence and clinical characteristics of high-risk groups related tuberculosis (HRGRT).
Methods: A cross-sectional study was conducted on the proportion of HRGRT with patients who were found to have MTB culture positive for the first time during hospitalization in Shenzhen Third People's Hospital during 2011-2015. Susceptibility of the MTB strains to antituberculosis drugs was tested, and comparisons of the drug resistance between HRGRT and non-HRGRT were performed.
Results: 2224 cases were enrolled. All the four high-risk groups together accounted for 19.6% of total TB (TB-DM 14.5%, 313/2224; TB-HIV 2.8%, 63/2224; TB-RD 1.7%, 37/2224; TB-CRF 1.1%, 24/2224) and 13.6% of MDR-TB (TB-DM 10.4%, 26/250; TB-HIV 0.8%, 2/250; TB-RD 0.8%, 2/250; TB-CRF 1.6%, 4/250). From 2011 to 2015, TB-DM cases slightly increased among new TB cases and slightly decreased in retreated TB cases, while TB-HIV, TB-RD, TB-CRF cases remained stable. The rates of MDR-TB, pre-XDR-TB, XDR-TB were lower in TB-DM than non-HRGRT for both new cases (3.5%, 0.8%, 0% vs 5.4%, 1.2%,0.3%) and retreated cases (30.4%, 7.1%,3.6% vs 43.9%, 14.2%, 5.5%). In new TB cases, the rate of RR-TB (MDR-TB excluded) was similar between TB-DM and non-HRGRT (1.6%vs1.7%, P=0.948), and so did the rate of IR-TB (7.4% vs 6.0%, P=0.353). In retreated TB cases, the rate of RR-TB (MDR-TB excluded) was significantly higher in TB-DM than non-HRGRT (14.3% vs 5.5%, P=0.034), and difference of the rate of IR-TB was not significant (12.5% vs 9.4%, P=0.467).
Conclusions: HRGRT accounted for a considerable proportion of TB and MDR-TB. Compared to non-HRGRT, TB-DM had a lower MDR-TB rate and a higher RR-TB(MDR-TB excluded) rate.

PD-940-14 Burden and presentation of depression among newly diagnosed individuals with tuberculosis in primary care settings in Ethiopia

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Background: Understanding co-morbidity of depression and tuberculosis (TB) has been limited by challenges in measurement of depression due to overlapping symptoms, use of small hospital samples and uncontrolled analysis. This study was conducted to better understand the burden and presentation of depression, and associated factors in people with TB in primary care settings in Ethiopia.

Methods: We conducted a cross-sectional survey among 657 people newly diagnosed with TB. Symptoms of depression were measured using the Patient Health Questionnaire (PHQ-9). TB symptoms and other factors were captured using standardised questionnaires. The factor structure of PHQ-9 was examined. Multivariable analysis was carried out to estimate prevalence ratios.

Results: The prevalence of probable depression was 54.0%. The PHQ-9 had one factor structure (alpha = 0.81). Little interest or pleasure in doing things (73.0%) was the commonest depressive symptom. Older age (Adjusted Prevalence ratio (APR) = 1.19; 95% CI = 1.06, 1.33), female sex (APR = 1.23; 95% CI = 1.18, 1.27), night sweating (APR = 1.25; 95% CI = 1.16, 1.35), pain (APR = 1.69; 95% CI = 1.24, 2.29), being underweight (APR = 1.10; 95% CI = 1.07, 1.13), duration of illness (APR = 1.35; 95% CI = 1.22, 1.50), level of education (APR = 0.93; 95% CI = 0.90, 0.95), and social support (APR = 0.89; 95% CI = 0.85, 0.93) were independently associated with probable depression.

Conclusions: Depression appears highly prevalent in people with TB and PHQ-9 seems to be a useful instrument to detect depression in the context of TB. The frequency of depressive symptoms would suggest that the occurrence of the symptoms in people with TB is in the usual manifestation of the disorder. Prospective studies are needed to understand the longitudinal relationship between TB and depression.

PD-941-14 Prevalence of major depressive disorder among patients with suspected pulmonary tuberculosis treated at a primary health centre in metropolitan Rio de Janeiro, Brazil

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Background: Tuberculosis (TB) and Major Depressive Disorder (MDD) presenthigh prevalence worldwide. MDD is more frequent in patients with chronic inflammatory diseases including TB. Studies on TB and MDD in low and middle-income countries are limited.

Objective: To estimate the prevalence of MDD among TB patients attending a health center in the metropolitan area of Rio de Janeiro.

Methods: A cross sectional study was designed. After written informed consent, patients with presumed pulmonary TB (cough > 3 weeks) answered a clinical-epidemiological questionnaire, a standardized depression screening with the Patient Health Questionnaire (PHQ-9), and a confirmation of diagnosis using the Mini International Neuropsychiatric Interview (MINI-Plus).The association of MDD with sociodemographic and clinical characteristics were evaluated using logistic regression.

Results: From July 2015 to Dec 2016, 341 individuals with presumed pulmonary TB were recruited. Their mean age was 44,2 (SD± 16,02), a majority was male and had an educational level < 8 years(60%).TB diagnosis was confirmed in 38% of patients (99/260). The prevalence of MDD among TB patients based on PHQ9 score ≥10 was 60% vs. 62% among non-TB (OR=0.92; 95% CI 0.55-1.54). Based on the MINI-Plus interview, 55.7% TB patients vs. 56.3% non-TB had MDD (OR=0.98; 95% CI 0.53 - 1.82). In the logistic regression analysis, being female (OR= 3.78; 95% CI 2.03-7.05), alcoholic (OR= 2.10; 95% CI 1.05-4.18) with a comorbid condition (OR= 2.13; 95% CI 1.10 - 4.13) were independently associated with MDD.

Conclusions: MDD was frequent in individuals with presumed pulmonary TB and was associated with female sex, and other comorbidities, but not with TB.

50. Latent TB infection: testing and perceptions

PD-942-14 Estimating the optimal induration cut-off point from tuberculin skin testing through mixture modeling: analysis of two high-risk populations in sub-Saharan Africa

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Background: The tuberculin skin test (TST) has several limitations which make it difficult to validly interpret test results. These include digit preference bias and poor specificity due to either exposure to nontuberculous mycobacteria or BCG vaccination. To account for these limitations and estimate the optimal induration cutoff in a high-burden, sub-Sahara African setting, we used mixture modeling on TST results from two high-risk Ugandan populations.

Methods: We used two populations of contacts from Kampala, Uganda: the Kawempe Community Health Study (N=1941; 1995-2004) and COHSONET (N=816; 2012-2016). Mixture models were used to estimate the optimal induration cutoff to distinguish infection with *Mycobacterium tuberculosis* from possible effects of BCG vaccination or environmental mycobacteria. We then calculated the prevalence of latent tuberculosis using our approach and assessed the proportion of falsely classified participants using a commonly-used induration cutoff point (≥10 mm).

Results: The optimal cutoff point estimated through mixture modeling was 7.1 (Standard Deviation [SD], 4.06) and 7.6 (SD, 4.3) millimeters in the Kawempe and COHSONET studies. For Kawempe, the prevalence of latent infection using a traditional cutoff point of ≥10 millimeters and our mixture model method was 64% and 70%, respectively. The proportion of falsely classified individuals using a traditional cutoff was 6.7% in this study population. In COSONET, the prevalence of latent tuberculosis using a traditional cutoff point of ≥10 millimeters and our mixture modeling to define latent infection was 39% and 46%, respectively. The proportion of falsely classified contacts using a traditional cutoff was 15% in this sample.
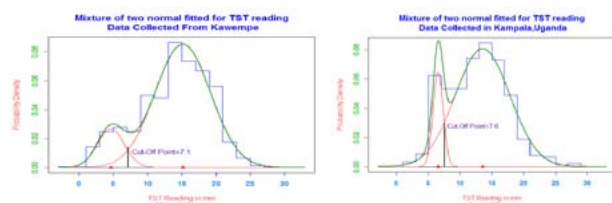
Figure Mixture modeling in two Ugandan study populations

Conclusions: Methods to validly estimate latent tuberculosis is difficult, especially in sub-Saharan Africa. Using mixture modeling, we found the optimal TST induration cutoff was approximately 7 millimeters in these two high-risk Ugandan cohorts. Using traditional, commonly-used cutoff points for TST induration may misclassify latent tuberculosis in a substantial proportion of individuals.

PD-943-14 Concordance of the tuberculin skin test and QUANTIferon® assays in recent skin test converters: results from a longitudinal study in sub-Saharan Africa

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Background: Few studies have evaluated tuberculin skin test (TST) conversion in high-burden community settings. Detection of TST conversion is critical to identify populations at high-risk for tuberculosis transmission. Moreover, the performance of this test in comparison with interferon gamma release assays, such as Quantiferon® (QFT) to assess incident tuberculosis infection has been scarcely studied.

Methods: This is a preliminary analysis of a prospective cohort study of 430 residents (age 15-45 years from Kampala Uganda with a previous TST result < 5 mm). Participants were followed for one year at which time they were retested to determine TST conversion (TST≥10 mm & increment >6 mm). Converters and a random sample of non-converters with appropriate samples had an additional QFT performed. A positive QFT result was defined as an interferon gamma concentration equal or greater than 0.35 IU/ml. Indeterminate results were excluded from the analysis.

Results: Of 430 participants uninfected at baseline, 68 (16%) converted the TST by one year; 313 (73%) remained uninfected; 11 were classified as having an intermediary reaction (TST< 10 mm with 6mm increment or greater); 26 (6%) declined the second TST; 12 individuals had missing data. Of the 68 converters, 29 of 45 (64%) with viable samples tested positive by QFT. Of the 313 participants with TST< 5 mm at 12 months, 35 of 44 (80%) participants had a negative QFT test result. Overall concordance of TST and QFT was just moderate (k =0.44, 95% CI: 0.25-0.62).

Conclusions: The incidence of tuberculosis infection, as measured with TST, was extremely high in this Ugandan township. Concordance between the TST and QFT was moderate in this African population from a high-burden setting. Regardless of the test used, diagnosis of latent tuberculosis is imprecise, especially in recent converters.

PD-944-14 Discordances between TST and IGRA to detect latent tuberculosis infection in paediatric contacts of drug-resistant tuberculosis patients

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Background: Accurate diagnosis of latent tuberculosis infection (LTBI) in paediatric contacts of Drug-Resistant (DR) TB is important for clinical follow-up and management. We measured the agreement between TST and IGRA and assess factors associated with discordant TST/IGRA results in DR-TB paediatric contacts in Armenia.

Methods: We used data from a prospective cohort study of paediatric contacts (< 15 years) of DR-TB cases in Armenia. The study was conducted between June 2012 and December 2016. TST and IGRA were requested systematically at inclusion and during follow-up. Univariate and multivariate logistic models were used to assess factors associated with discordant TST/IGRA results.

Results: Among 150 children included 99 (66.0%) had both IGRA and TST results: 46 (46.4%) were TST and IGRA positive, 36 (36.4%) TST and IGRA negative, 10 (10.1%) TST positive and IGRA negative, and 7 (7.1%) TST negative and IGRA positive. All children were vaccinated for BCG. Overall, 56 (56.5%, 95%CI: 46.6-66.5) children had a positive TST result and 53 (53.5%, 95%CI: 43.5-63.5) a positive IGRA. Concordance between TST and IGRA was 82.8% (kappa= 0.65, 95%CI: 0.45-0.84). Among 29 children aged 0-4 years, 1 (3.4%) was TST positive and IGRA negative and 2 (6.9%) TST negative and IGRA positive (concordance=89.7%, kappa= 0.79; 95% CI: 0.43-1.15). Among 70 children aged 5-14 years, 9 (12.8%) were TST positive and IGRA negative and 5 (7.1%) TST negative and IGRA positive (concordance=80.0%, kappa=0.59; 95% CI: 0.36-0.85). Regression analysis did not identify any factor associated with discordant TST/IGRA results. Among IGRA positive children, we did not find differences between those TST positive and those TST negative.

Conclusions: Agreement between TST and IGRA was fairly good. In this context, the additional benefit of IGRA for identifying LTBI is questionable although the use of TST alone would have missed 7% of LTBI cases regardless of the age of the child's contacts.

PD-946-14 A new for skin test reagent that can efficiently diagnose LTBI

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Background: Purified Protein derivativeTuberculin (TB-PPD) is unable to identify people has different immune status. Although interferon gamma release assay(IGRA) recommended by WHO is high specific, but it could not apply for large population. At present, no matter screening latent tuberculosis infection(LTBI) or diagnosing TB has none easy technology which is high sensitivity and specificity.

Methods: Three detection methods— the allergen EC, which is formed by the fusion of the missing protein ESAT6 and CFP10 from *mycobacterium tuberculosis* RD1 region, PPD and IGRA are studied on methodology of the same evaluation system ,respectively in healthy people, not infected with TB but bacillus Calmette-Guerin(BCG) vaccination people and TB patients. Finally, we expect to get the new drug certificate and production approval.

Results: We find EC is very safe and has equivalent sensitivity with IGRA and TB-PPD, much higher than similar product made by Danish SSI(77%),same specificity as IGRA but much higher than TB-PPD through I and II phases, totally1,300 subjects. Now we completed 3000 subjects in phase III clinical trials and no serious adverse reaction.

	EC	PPD	IGRA
sensitivity	84.38%	86.46%	86.46%
specificity	93.98%	14.46%	98.67%
consistency with IGRA	88.30%	54.39%	/

Table Research result of II phases

Conclusions: EC concentrates the advantages of the high specificity of IGRA and convenience of TB-PPD, can effectively identify BCG vaccination crowds and *mycobacterium tuberculosis* infection.So it is especially suited to high incidence of TB in BCG vaccination area and LTBI screening in developing country.

PD-947-14 Immunological features in children of different ages with latent tuberculosis infection and tuberculosis

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Background: Identification of immunologic criteria that determine risk of tuberculosis development in children of different age with latent tuberculosis infection and thus can be used for prognosis of the disease is an actual goal.

Objective: To identify immunological features of latent tuberculosis infection (LTI) and tuberculosis (TB) in children of different age that may serve for development of additional diagnostic criteria.

Methods: Within 2014-2015 at Saint-Petersburg Scientific Research Institute of Phthisiopulmonology there was a study conducted with assessment of individual immunological parameters in 135 children from 3 to 14 years old with positive results of Mantoux test 2 TE and positive results to ELISPOT and Diaskintest® (DST). Based on results of CT examination and bacteriological methods, patients were divided into 2 groups: I group - children with latent tuberculosis infection (66), group II - patients with tuberculosis (69). Further children were divided into subgroups: Ia and IIa - younger patients, and Ib and IIb - children 7 to 14 age old. Analysis data was done by program Statistica 6.0.

Results: In children with tuberculosis statistically significant decrease of phagocytic activity of neutrophils (p< 0,05) and elevation of INF-γ (20741,48±1946,48 vs 22527,22±2916,6 p< 0,05) versus children with LTI were observed. These differences were observed regardless of age. In addition to this in children with tuberculosis of younger age statistically insignificant increase of CD16+ (17,28±0,04 vs 18,06±1,05, N -11,0) and CD20+ (18,21±0,62 vs 19,56±1,06, N -24,56) was noted, while in elder age group - statistically insignificant increase of CD3+.

Conclusions: Decrease of phagocytic activity of neutrophils and elevation of INF-γ may be risk factors for development of tuberculosis in children that requires further research.

PD-948-14 Knowledge, perceptions and practices of physicians and nurses about tuberculosis transmission and prevention in three Brazilian capitals

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Background: Less than 20% of those intended for latent tuberculosis infection (LTBI) complete therapy. Main losses occur in the first steps of the cascade. Of those who need prevention, less than 50% complete therapy. In Brazil, the gap is even higher. Less than 9% of identified contacts undergo investigation (Union Conference 2016, OA-361-27). National Guidelines recommend preventive therapy for infected adult and child contacts "according to health services organization and incidence rates". Our objective was to assess primary care physicians´ and nurses' knowledge, perceptions and practices

in order to implement solutions to overcome this gap.

Methods: We interviewed 55 physicians and 46 nurses in 12 primary healthcare facilities in three tuberculosis-high burden cities in Brazil: Recife, Manaus and Rio de Janeiro. A semi-structured questionnaire was applied. Answers were classified as satisfactory according to "compulsory" answers cited and no "unacceptable" answers given.

Results: Fifty-eight percent reported recent formal training for tuberculosis. Gaps in knowledge included prevention of LTBI among contacts (51%), prevention of progression to disease once infected (32%), LTBI diagnosis (43%), indications for LTBI treatment (62%), minimal duration of INH treatment (44%), INH dose (84%) and management of adverse events (up to 57%) (Table). Over 48% do not think that it is important to evaluate contacts. When asked why contacts do not come for investigation, they blame index cases and contacts: "do not know the importance", "fear stigma", "do not have time/money" (not confirmed by contacts themselves, see Union Conference 2016, PD-1021-29).

Satisfactory answers	Which tests are recommended for asymptomatic contacts?	Which tests are recommended for symptomatic contacts?	What is the recommended dose of INH for IPT?	What are the main side effects of INH?	Believes it is important to investigate child contacts	Believes it is important to investigate adult contacts	Which household contacts should be investigated?	How do you manage nausea for a patient using INH	How do you manage jaundice for a patient using INH
Physicians	30 (55%)	24 (44%)	3 (5%)	45 (82%)	32 (58%)	37 (77%)	8 (15%)	40 (73%)	44 (80%)
Nurses	28 (51%)	24 (52%)	4 (9%)	38 (83%)	23 (50%)	27 (59%)	9 (20%)	28 (61%)	26 (57%)

Table KAP of LTBI among phycians and nurses in Brazil

Conclusions: There are important knowledge and attitude gaps among graduate healthcare workers regarding LTBI management. More training and understanding of the importance of LTBI treatment in TB control are necessary for physicians and nurses in Brazil. National Guidelines should clearly recommend LTBI investigation and treatment in all cities, regardless of tuberculosis incidence rates.

PD-949-14 Methods for estimating LTBI prevalence in foreign-born persons age five years and older in local U S jurisdictions

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Background: Tuberculosis (TB) control jurisdictions need to estimate prevalence of latent TB infection (LTBI) in local foreign-born populations. The National

Health and Nutrition Examination Survey (NHANES) used the tuberculin skin test (TST) and QuantiFERON Gold In-tube (QFT) to estimate LTBI in the U.S. foreign-born population, but their sample likely underrepresents higher-risk groups and the estimates may not be locally generalizable. We compared two methods for estimating local LTBI prevalence among foreign-born persons living in two demographically distinct counties in metropolitan Atlanta.

Methods: Method one used positive TST, QFT and T-SPOT.TB (T-SPOT) results by world region of birth in 9,045 foreign-born persons over five years of age screened for LTBI at 17 TB Epidemiologic Studies Consortium (TBESC) sites in 2012-2014. Method two used positive TST and QFT results among foreign-born persons in the 2011-2012 NHANES cohort, stratified by racial group. The positive proportions were applied to American Community Survey estimates of the number of foreign-born persons from each world region or racial group living in Fulton and DeKalb counties. Latent class analysis of TBESC test results calculated positive and negative predictive values for each test and estimated the LTBI population prevalence.

Results: Using TBESC data, the estimated LTBI prevalence among foreign-born persons by QFT, T-SPOT, and TST was 33.3%, 31.5% and 34.9%, respectively, in Fulton County, and 35.9%, 34.4% and 37.0%, respectively, in DeKalb County (Table 1). Using NHANES data, estimated LTBI prevalence among foreign-born persons in Fulton County was 28.7% by QFT and 27.3% by TST; in DeKalb County, it was 28.7% by QFT and 28.1% by TST.

		Estimated number of positive tests for latent tuberculosis infection		Adjusted latent tuberculosis prevalence estimate using latent class analysis	
		Fulton County (n=120,707)	DeKalb County (n= 116,090)	Fulton County (n=120,707)	DeKalb County (n= 116,090)
TBESC Estimates	QFT - n (%)	29,061 (24.1)	30,540 (26.3)	40,214 (33.3)	41,718 (35.9)
	TSPOT - n (%)	25,523 (21.1)	27,434 (23.6)	38,055 (31.5)	39,885 (34.4)
	TST - n (%)	53,334 (44.2)	54,682 (47.1)	42,072 (34.9)	42,921 (37.0)
NHANES Estimates	QFT - n (%)	19,956 (16.5)	19,279 (16.6)	34,590 (28.7)	33,338 (28.7)
	TST - n (%)	26,208 (21.7)	27,431 (23.6)	32,924 (27.3)	32,595 (28.1)

Table Test positivity and latent tuberculosis prevalence

Conclusions: NHANES data may significantly underestimate LTBI prevalence in foreign-born persons living in local TB control jurisdictions. A model incorporating world region of birth and the performance characteristics of screening tests may more accurately estimate LTBI prevalence in specific geographic areas.

51. Human rights and ethics

PD-950-14 Gender differences in health care providers' management of persons with pulmonary TB symptoms and disease: a standardized patient study

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Background: In India, twice as many male tuberculosis (TB) patients are notified when compared to females, and female TB patients are more likely to be diagnosed late when compared to male patients. In this study, we assess whether health care providers contribute to under diagnosis and delayed diagnosis because of gender differentials in health care provider management practices.

Methods: We used male and female standardized patients (SPs) depicting four different case scenarios in three urban areas of India: Delhi, Mumbai and Patna. Case 1 presented classic symptoms of TB; Case 2 presented classic symptoms of TB with a suggestive chest radiograph; Case 3 presented classic symptoms of TB and a sputum smear report positive for acid fast bacillus; and Case 4 presented symptoms of TB and a previous history of TB disease, suggesting recurrence and drug-resistance. Correct case management for each case was ascertained from a TB disease perspective using the Standards of TB Care in India as a benchmark. We assessed gender differences in correct management overall and stratified by city and case.

Results: Overall, 35% of the male SPs and 38% of the female SPs were correctly managed. There was no statistically significant difference in correct management between male SPs and female SPs after adjusting for case, provider qualification, city [adjusted odds ratio of 1.06 (95% CI: 0.87-1.29)]. Stratified analysis across the three cities and across the four types of cases did not show any statistically significant gender differences in correct management or any of the several other clinical management parameters.
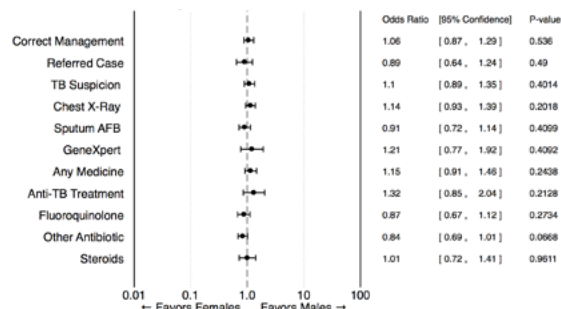
Figure Differences in TB Management by Patient Gender

Conclusions: Private health care providers managed male and female standardized patients presenting with identical symptoms of TB disease equally and therefore they are unlikely to cause gender differences in delayed diagnosis or misdiagnosis. Rather than gender differences, low levels of correct management should be a cause for concern.

PD-951-14 Compulsory isolation and treatment for TB in Norway, 1995-2016

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Background: Compulsory isolation and treatment of tuberculosis (TB) is controversial. The WHO document: "Good Practice in Legislation and Regulations for TB Control"* is based on the Norwegian Communicable Diseases Control Act of 1994. According to the act, a National Commission may decide that a person with infectious TB is isolated in a hospital for three weeks. Extensions can be made for periods of six weeks up to a total of one year. After the first three weeks, the commission may also make a ruling of compulsory drug therapy. We report Norwegian experiences with compulsory isolation and treatment of TB 1995-2016. The average TB incidence rate during that period was 6,4/100,000.
Methods: We reviewed all TB cases where the commission had made rulings based on paragraph 5-3 of the act: compulsory isolation for up to three weeks, extensions, and decisions on compulsory therapy. Rulings made for diagnostic purposes were not included. We also collected information from the Norwegian TB Register.
Results:

Number of patients	All TB cases	Pulmonary TB	Culture positive pulmonary TB	Microscopy positive pulmonary TB	Culture and microscopy pos pulmonary TB
All	6551	4098	3204	1148	1046
Compulsory isolation	14 (0.2 %)	13 (0.3 %)	12 (0.4 %)	7 (0.6 %)	6 (0.6 %)
Lost to follow-up (all patients)	142 (2.2 %)	86 (2.1 %)	69 (2.2 %)	26 (2.3 %)	23 (2.2 %)

Table TB cases in Norway 1995-2016

Altogether, 14 rulings of compulsory isolation were made. Of these, two patients disappeared before isolation could be started, and one converted to culture negative. The remaining 11 patients were isolated against their will and two had extensions. There was only one ruling of compulsory drug therapy, with one extension. Treatment outcomes: Five of the 11 were lost to follow-up, four had treatment success, one transferred out and one was still on treatment.
Conclusions: Our findings show a very restricted use of compulsory isolation and treatment in Norway the last 22 years. This is in line with the stated policy that coer-

cion should be the last resort. On the other hand, the finding that almost half of the patients with rulings of isolation were lost to follow-up, suggests that extensions of the ruling should have been considered more often. *WHO/CDS/TB/2001.290

PD-952-14 Law and tuberculosis at a cross roads

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Background and challenges to implementation: Article 21 of the Constitution of India guarantees right to life. However, right to health is not explicit as a fundamental right, rather Article 39(e) bestows the state to make sure health of citizens not abused. In the absence of law, TB patients required support depends on policies. Private sector provider or even the patients have no obligation to control TB infection transmission. Advocacy experts focus on much required diagnosis, research and funding and less on patients need. The patient charter denotes rights to know and choice. In amidst of these issues, this paper analysed The National Consumer Disputes Redressal Commission (NCDRC) judgements of India.
Intervention or response: The NCDRC of India has made all the judgement copies publically available for reference. The keyword "Tuberculosis" was searched for articles across millions of data base from the period 2010 to 2016. From the results, 59 cases were retrieved that had mention of "tuberculosis" in the entire text of judgement. From the perspective patient, provider and programmes, 10 contextual cases were analysed.
Results and lessons learnt: The cases mainly were questioning the practitioner's prescription of Anti-Tuberculosis medications, while there were other underlying causes. The practitioner's dilemma in absence of confirmatory diagnosis is observed. This was also related to many of the insurance claims which were rejected by agencies. Couple of key questions arriving from this, law faces issues with confirmatory diagnosis and disclosure of diagnosis. On practitioners point, the empirical treatment need to be avoided when genetically confirmed tests and culture tests are available.
Conclusions and key recommendations: Patient rights need to be linked with laws such as NCDRC and this will empower patients and families from undue exploitation. India has enacted laws with regard to maternity benefit, mental health and HIV/AIDS and the situation demands an Act on TB.

PD-953-14 Inclusive human experience from TB and HIV for overcoming these stigmatising health conditions

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Background and challenges to implementation: Stigma is conceived as a multi-dimensional socially constructed phenomenon, and generally research focuses on harmful and negative impact of stigmas on the lives of stigmatized individuals. This paints a grim picture suggesting that targets of stigma are devalued and excluded in the society, which may not be completely true. By focusing on exclusion aspect of stigma, many positive social inclusion experiences in the daily lives of people affected to cope up with stigma are being missed from the body of evidences.

Intervention or response: We conducted a literature review in Pubmed. All articles related to exclusion, stigma and inclusion of different stigmatized communicable diseases related to TB and HIV/ AIDS in English language, published between 1990 and 2016 were included in the search strategy. The Amstar checklist was used to assess the quality of the review.

Results and lessons learnt: Based on the review of the global literature (A total of 30 articles were included for review analysis), we found that studies on empowerment and social mobilization as strategies in response to stigmatized health conditions such as TB and HIV/ AIDS have demonstrated powerful response to the epidemic when affected communities have mobilized themselves to fight back against stigmatization and oppression in relation to their lives. These studies have highlighted the importance of intersection of disease related stigma and characteristics for ultimately shaping peoples experiences, which could reduce negative feelings and beliefs about stigmatized diseases.

Conclusions and key recommendations: In the real world there exist many cases of individuals living successfully with stigma due to experience of social inclusions. To explore further on this topic, inclusionary and multi-disciplinary systems research that is resilient towards destigmatization is urgently required.

PD-954-14 Are female TB patients being neglected in tribal India?

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Background and challenges to implementation: Tuberculosis (TB) still continues to haunt India´s vulnerable and marginalized populations. Though all TB patients are diagnosed and treated free of cost under program; health care seeking behavior, stigma and transmissions differ in different age and sex groups. As per WHO recommended Standards of TB care(STCI), standard 24 states that, "All people seeking or receiving care for TB should be received with dignity and managed with promptness, confidentiality and gender sensitivity."

We compared age-sex wise TB notifications during 2012-2014 from three districts of Jharkhand India possibly comparing health seeking behavior in relation with male and females of different age groups.

Intervention or response: Data extracted from performance reports, national surveillance portal, analysed in WIN-PEPI and MS Excel software ensuring double entry. TB notifications from Govt. and private Health Sector were analysed for age-sex specific groups. 100 randomly selected patients were interviewed for understanding their health care seeking behavior as a public health action mandated in national program. Responses from patients were documented, digitized and analyzed in similar way.

Results and lessons learnt: Age specific notification from private sector for 0-14 yr age group was 9% (124 of total 0-14 yr. age group) when the same for rest all age groups was 4%. Male favoritism in private Health sector was observed to be highest (+3.4%) in 0-14 age group. Responses from adult patients and parents of pediatric patients show 100% of them presumed that services in private sector is better than government sector. Almost all (90%) parents would prefer treatment in private sector, as male child was considered precious over female.

Table 1 Age-Sex Distribution of new TB Patients notified during 2012-2014 from Govt. and private Health sector in Jharkhand, India

Health Sector of access	Private		Government		Total	Age% among Total	Health seeking to private sector		Health seeking to private Total	Male favour (M-F)/T	Male:Female Sex Ratio		
											State Avg. M:F = 1.05		
Age (Yrs)/Sex	Male	Female	Male	Female	Total	age/Total	Male	Female	Total		Private	Govt.	Total
n=56119	a	b	c	d	e=[a+b+c+d]	e/n	a/(a+c)	b/(b+d)	(a+b)/e	[a|(a+c)]-[b/(b+d)]			
0-14	67	67	669	741	1434	2%	11%	7%	9%	3.4%	1.18	0.77	0.80
15-25	323	188	7569	3878	11948	21%	4%	5%	4%	-0.5%	1.72	1.95	1.94
26-35	380	147	8018	3932	12477	22%	5%	4%	4%	0.9%	2.59	2.04	2.06
36-45	314	114	8441	2982	11851	21%	4%	4%	4%	-0.1%	2.75	2.83	2.83
46-55	219	52	7328	1968	9557	17%	3%	3%	3%	0.3%	4.21	3.74	3.75
56-65	166	59	4704	1145	6074	11%	3%	5%	4%	-0.5%	2.81	4.11	4.04
>65	53	25	2223	477	2778	5%	2%	5%	3%	-2.7%	2.12	4.66	4.53
Total	1522	642	38842	15113	56119	100%	4%	4%	4%	-0.3%	2.37	2.57	2.56

Table Age-Sex Distribution of new TB Patients notified

Conclusions and key recommendations: More proportion of Male pediatric TB notification from private health sector shows gender bias especially in pediatric TB patients in Jharkhand India. Behavior Change communication strategies are needed for promoting equality. Causal analysis to find out the reasons behind gender bias holds further scope of qualitative research.

PD-955-14 Gender-legal assessment of tuberculosis in Kyrgyzstan

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Background: This technical advisory report, created with the support of the STOP TB Partnership, contributes to the expansion of the evidence base, based on which targeted interventions will be developed to eliminate gender and legal barriers in the fight against tuberculosis.

Both men and women claim that they do not experience any discrimination, and the treatment method did not differ in gender. According to focus groups, women apply for diagnostics at a later stage than men. Influenced by the underestimation of the importance of the role of women in the family, as well as the fear of social exclusion in the family or community.

Another factor is self-medication, caused by fears of women of high cost of diagnosis, with low socioeconomic status of the family.

Stigma, as a strong negative factor affecting the lives of people affected by tuberculosis.

Methods: The evaluation was based on an analytical review, stakeholder interviews, focus group discussions involving people affected by tuberculosis.

Results: As a result of the evaluation, recommendations were proposed to the Parliament, Ministry of Health, and the national tuberculosis control program on overcoming legal barriers and joint advocacy.

Conclusions: The conclusion is that:

The regulatory framework is properly used to:

1) The right to freedom from torture and inhuman or degrading treatment

2) The right to physical integrity

3) The right to participate

4) Freedom of movement

It is not used properly to guarantee the following rights and opportunities for people affected by tuberculosis:

1) The right to information, informed consent, social security, social determinants and legal assistance

2) Rights to access to health services and essential medicines / to benefit from the benefits of scientific progress and their practical application

3) The right to privacy

4) The right to work and protection of labor and health and the right to protection against discrimination.

PD-956-14 Empowering TB patients on the rights and responsibilities

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Background and challenges to implementation: Right to health is a vital right without which none can exercise one's basic human rights. Many of the factors that increase a person's vulnerability to tuberculosis or reduce their access to services to prevent, diagnose and treat TB are associated with their ability to realize their human rights. A human rights-based approach to TB prevention, treatment and care can help programme managers, civil society and other TB partners overcome the many barriers to effective TB prevention, treatment and care.

Intervention or response: The project Axshya has facilitated creation of TB forums at the district level to empower and engage TB affected community. Constituted by TB patients and community leaders the forums give a voice to the affected community and advocate with the programme for resolution of challenges faced by patients in accessing TB services. Over 250forums have been formed and have facilitated nutritional support, linkages with social welfare schemes, rehabilitation of several thousand TB patients. They act as bridge between community, patient, health system and civil society along with advocacy activities to influence policy changes for accessible, affordable, supportive TB-services to entire population.

Results and lessons learnt: Using the colourful, illustrated Patients' Charter, project has sensitised over 123,850 TB patients during the period April2013-December2016. The charter has been translated into 19 regional languages, empowers patients by ensuring that they understand their rights, make informed choices and become equal partners in the management of their care.
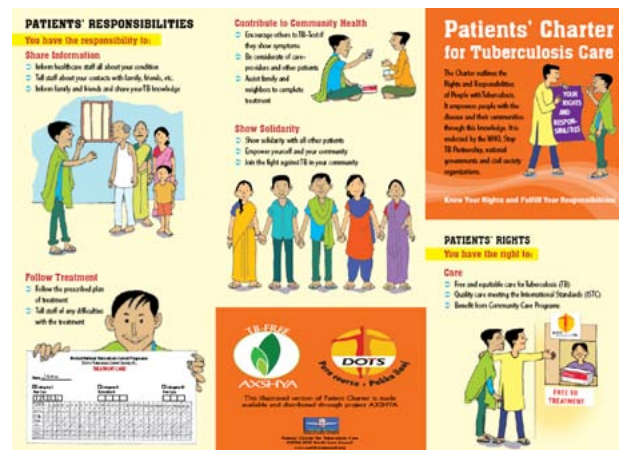
Figure Patient Charter

Reaching women is one of the priorities of the programme with the goal that they should make up 30 per cent of the participants in the sessions. Of the total patients sensitised more than 43,000 were women.

Conclusions and key recommendations: Empowering TB patients on their rights and responsibilities is crucial for creating demand for TB services. This type of sensitisation also raises awareness among the patients and communities in the path of ending TB.

PD-957-14 Tuberculosis patients got their political rights in Panchayat elections under local self-governance after 52 years in Odisha, India

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Background and challenges to implementation: *Odisha Gram Panchayat(GP) Act 1964* is the basis of Panchayat (a local self-government organization in India of the Panchayat Raj System at the village or small town levels constituted as per Article 243B of the Indian Constitution) election/nomination in Odisha, an eastern state in India. *The section 25 subsection 1(e) of Odisha Act disqualifies membership of GP if the person is 'suffering from tuberculosis'*. Subsequent to 73rd Amendment 1992 of India, Odisha GP Act had been amended in 1994 and also in 2011. However, contesting election or being nominated as the *political rights* of TB patients was undermined.

Intervention or response: Since 1997, the inception of RNTCP in Odisha, 695650 TB patients have been diagnosed, 550958 cases cured and 32885 died by the end of 2016. Every year ~50K patients are diagnosed in Odisha. To protect their political rights of contesting election/nominated which happens only once in five years, civil society petitions have been written to the Government of Odisha, discoursed in public forum/media and judiciary proceedings. Under the similar cause of municipal election an elected member had to lose his membership and chairmanship. Hon'ble court (High Court and Supreme Court) upheld the disqualification as per the Act.

Results and lessons learnt: The Odisha Legislative Assembly proposed to do away with '*disqualification*' clauses (Section 25 sub-section 1(e)) on 13 May 2016 while introducing the *Odisha Panchayat Laws (Amendment) Act, 2016* which came into effect since 25th June 2016. Such disqualification clauses of

Panchayat Samiti Act,1959 and Odisha Zilla Parishad Act,1991 (45-1(e) and 39-1(d) respectively) have also been omitted.

Conclusions and key recommendations: '*Suffering from Tuberculosis*' no longer prevents persons to become/nominated Sarpanch (Head) of a Gram Panchayat. The curable disease has its say in 67th year of the Republic India, and after 52 years of the Odisha GP Act. Such provisions need omission across India. The law has to prevail the rights.

PD-958-14 Experience with ethics committee to seek approval for recruiting people with TB and bio-specimen collection and storage for research projects

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Background: Approval of protocols from Ethics Committee (EC) is a pre-requisite to conduct any study that involves collection of bio-specimens. The mandate of EC is to protect rights, safety, well-being of subjects and ensure that participation is voluntary based on informed consent.

We outline the major queries raised by EC and concerns pertaining to operational research involving people with TB.

Methods: EC reviewed our proposal to collect bio-specimens from people with TB for an exploratory study to develop biomarkers for TB disease. The proposal was evaluated both in terms of scientific and ethical aspects of the research study.

Results: The composition of EC was as per ICH-GCP. The members reviewed the study based on existing guidelines, regulations and Standard Operation Procedures (SOPs) and provided approval of protocol. However, they were cautious that bio-specimen and genetic material derived from human subjects should be analysed only for the purposes of the study, should not be stored and destroyed after completion of the study. As participation in the study was confidential, the EC reiterated that any material that could identify subjects should not be used in the analysis and in any reports based on the study. To prevent unacceptable risk or harm to participants, the EC recommended that any new information available should be informed to participants in a timely manner.

Conclusions: Collection of bio-specimens and genetic material from people with TB can be cost intensive, time consuming and tedious. As per existing guidelines it is not possible to bio-bank specimen and genetic material derived from human subjects including people

with TB for any future studies. To use bio-specimens as resource and reference material for future research on TB drugs, diagnostics and research, we suggest that national guidelines may be drafted for bio-banking so that samples from one project can be used for future studies.

PD-959-14 Gender differences in the outcomes of an economic support intervention to improve tuberculosis treatment, Nigeria

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Background: Little is known about gender effects of social protection for tuberculosis. We explored gender differences of the impact of an economic support intervention to improve tuberculosis treatment in Nigeria.
Methods: This was a prospective, non-randomised intervention study conducted in a large rural hospital. We prospectively enrolled all registered patients receiving first-line anti-tuberculosis treatment at the study site from 1 April to 30 June 2014 into the intervention (after) group, which received the Nigerian NTP standard of care and a monthly financial incentive package of US$15 during treatment. All TB patients registered from 1 January to 31 March 2014 at the same facility and receiving the NTP standard of care only were used as the before group. In addition, we prospectively collected costs and income data from patients in the intervention group as well as from patients registered during the same period in two rural health facilities from another district (control group). TB catastrophic costs was defined as costs >40% of non-food income.
Results: A total of 173 and 121 patients were in the before and after groups, respectively (136 female); and costs and income data were collected from 84 persons (44% female) in the control group. In the before group, treatment success rates among female versus male TB patients was (76.3% vs. 67.0%; p=0.18), respectively; following the intervention, it was (88.3% vs. 83.6%; p=0.5). In the before group, loss to follow-up among female versus male patients was (15.8 vs. 23.7%; p=0.18) respectively; following the intervention, it was (5.0 vs. 4.9%; p=0.7). In the control group, rate of TB-related catastrophic costs for female versus male patients was (67.6 vs. 53.2%; p=0.18) respectively; and in the intervention group, it was (13.3 vs. 8.2%; p=0.36).
Conclusions: The economic support intervention improved gender equity in access, reduced TB-related catastrophic costs, and improved tuberculosis treatment outcomes.

52. Sustainable role of civil society organisations and communities in TB diagnosis, care and control

PD-960-14 Private sector notifications increase by 123% within a year with civil society support and administrative initiatives in Jharkhand, India

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Background and challenges to implementation: Government of India has made TB a notifiable disease through an order in 2012 further amended in 2015. NIKSHAY an information communication technology based surveillance platform is being used for TB notification both from public and private. During 2016, private sector notified 330186(19%) cases through 113961 health facilities. The proportion varies widely from state to state. Jharkhand, a tribal(26%) state(24 districts) with 36 million population had notified 4209 cases from pvt. sector till 2015. This paper gives the outcome of strategic interventions taken in 2016.
Intervention or response: During 2016, administrative initiatives with state (4) and district heads (24), sensitisation programmes for private practitioners (15), CMEs for medical colleges (2) were initiated by the state. A specific communication material developed for the practitioners to disseminate information and processes. Global fund supported Project Axshya (The Union and World Vision India) buttressed the initiatives with identification/training/follow-up of qualified private practitioners (QPP), private hospitals/labs in 6 urban districts of the state. 122 health facilities added in 2016 totaling to 1025.
Results and lessons learnt: Private sector TB notification increased by 123% in 2016 (3632) from 2015 (1603) with only 14% (122) addition to the existing (903) health facilities. The increase in notifications observed in 15 (63%) districts. The decrease in 5 (21%) and no reporting from 4 (17%) are mainly remote tribal districts. 76% (2765) notifications of 2016 are from 6 districts being value added through Axshya Project. During 2015, private sector contribution was 4.4% to total (36395) cases which increased to 9% (of 40253) with total rise of 11% over a period of one year.
Conclusions and key recommendations: Administrative commitment along with civil society support play crucial role to strengthen private sector surveillance system and increase TB notifications. The paradigm shift in the programme will further add fuel to the process. Civil society initiatives are called for incorporation in the programme.

PD-961-14 Communicating linkages between lung health issues and sustainable development is integral to Agenda 2030

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Background and challenges to implementation: Health communications including news reporting, if disseminated or ´aired´ consistently and accurately in print, online, electronic and social media, have the potential to not only enhance public knowledge, awareness and build up demand for better policies and programmes; but it can also help to accelerated intersectoral responses for integrated health outcomes and help us progress better towards Agenda 2030 or SDGs. Unfortunately, health reporting is usually in silos and inconsistent. At times it lacks scientific credibility or evidence based rigour or miss out voices of affected communities.

Intervention or response: CNS with an intent to promote evidence based reporting on print, online and social media; and increase inter-sectoral responses on lung health issues and sustainable development; applies myriad methods. CNS facilitates a broader network of heath journalists, many of whom come from affected communities, organises dialogue between experts and affected communities and health journalists (host regular webinars) and develop media advisories/ issue briefs and disseminate the same among health writers across Asian and African region.

Results and lessons learnt: Since 2010, CNS has done more than hundred media dialogues engaging local journalists, experts from different sectors, and affected communities; and over forty webinars for broader health fraternities. Over 1500 participants have attended these webinars resulting in over 5000 original news clippings on lung health and sustainable development. Over 20,000 views on YouTube video recordings of these webinars.

Conclusions and key recommendations: To help us achieve the Agenda 2030, it is important that we think in integrated manner on sustainable development vis-a-vis in silos of specific issues. Communicating about collaboration between ´issue silos´ and pushing for integrated responses is key.

PD-962-14 Community health volunteers' contribution in improving TB case notification rate through household contact investigation: Amref Global Fund TB project in Kenya

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Background and challenges to implementation: Contact investigation is important in finding contacts who have Tuberculosis (TB) disease so that they can be given treatment and stop further transmission. Global Fund supported Amref in Kenya to implement TB activities in 33 counties with Case Notification Rate (CNR) of less 175/100,000 and Treatment Success Rate (TRS) of less than 88%. In 2015 the percentage of (TB) cases identified through tracing of contacts in these counties was 6% (3,365) of the 59,921 cases notified to the National TB Program while the percentage of notified TB cases, all forms contributed though community referrals was only 4%.

Intervention or response: Between January and December 2016, Amref trained and engaged 2,691 Community Health Volunteers (CHVs) and 2,398 Community Health Extension Workers (CHEWs). CHVs were linked to 2,404 health facilities registering at least one TB patient. CHEWs generated a list of the bacteriologically confirmed TB patients and allocated them to the CHVs who visited their households for health education, Screening and referral for cases with TB signs and symptoms. CHVs were provided with transport and lunch allowance for every household visited and family members screened. CHEWs were also supported with airtime for effective supervision and coordination of the CHVs activities.

Results and lessons learnt: In 2016, CHVs visited 21,925 households of TB patients. A total of 45,701 household members were screened for TB (female=53%) and 9,191 (female =54%) persons were referred for further TB investigation. In the 33 counties the percentage of TB cases identified through tracing of contacts improved from 6% to 9% while the percentage of notified TB cases, all forms contributed though community referrals improved from 4% to 9% and CNR improved to 210 100,000 in 2016.

Conclusions and key recommendations: Investing in CHVs to carry out contact investigation improves case notification rate and also elimination of TB. Development organizations and governments should support CHVs in community disease prevention.

PD-963-14 Bridging the gap between the community and health services: taking the services to the doorsteps of the community

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Background and challenges to implementation: Universal access to tuberculosis (TB) services is critical for timely diagnosis and treatment. However, low awareness about TB, poor accessibility and affordability of health services result in delayed diagnosis, with resultant morbidity and mortality. We report the results of a project which helped to bridge the gap between identification and examination of presumptive TB cases among marginalised and vulnerable areas.by an effective strategy.

Intervention or response: The Union led Project Axshya, is a unique initiative working towards improving access to quality TB care through partnership between government and the civil society especially for marginalised and vulnerable populations. Project Axshya mobilises volunteers in 285 districts across 19 states facilitate TB testing in communities where, for many reasons including distance, financial resources, health concerns, or family or work responsibilities, residents are often unable or struggle to reach state clinics and diagnostic centres. The Project Axshya community volunteers-many of whom have been affected by TB themselves-work in hard-to-reach communities or with tribal groups, spreading awareness and information about TB, and collecting and transporting sputum samples to testing facilities when they identify a person showing TB symptoms.

Results and lessons learnt: Between April 2013 to Dec 2016, community volunteers facilitated in identification and transportation of sputum sample from 755,478 presumptive TB cases to the diagnositic centres who were unable to reach the testing facility due to distance, financial burden and many other reasons. 64080 (8.5%) of them were found to be sputum positive and were put on treatment.

Conclusions and key recommendations: The results of the intervention clearly shows that enabling the services at the door steps of the community will clearly bridge the gap between identification and examination of presumptive TB cases. This has also contributed in identifying the missing TB cases.

PD-964-14 The Barcelona Tuberculosis Photovoice Project: understanding the lived experience of TB through photography

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Background: Photovoice is a participatory action research method that utilizes photography as a tool for giving voice and understanding to the experiences of study participants. This methodology has been used within marginalized populations to promote social action and change, inform program panning, and support advocacy. The purpose of the study was to provide an opportunity for individuals diagnosed with tuberculosis (TB) to share their lived experiences. We aim to decrease stigma, raise TB awareness, and enhance services in Barcelona through the dissemination of these images and text.

Methods: Participants were recruited from a local TB clinic in Barcelona using pre-determined criteria by TB staff. Signed consent was obtained and digital cameras, written information, and in-person orientation was provided to all study participants. There were a total of 16 participants aged 18-63. The majority of participants were born in TB endemic countries outside of Spain.

Results: Eighty-three photographs with supporting text were submitted. Through qualitative analysis, the images/texts were categorized into 11 themes. The resulting themes of challenges, isolation, stigma, resilience, new beginnings, things I miss, coping mechanisms, physical experience, positive thoughts, a stop in my life, and fight TB were found. Participants reported that the project was invaluable and highlighted the importance of being provided the opportunity to share their experiences. This contributes to the existing knowledge that photovoice is an effective tool that may be used within TB Programs worldwide.

Conclusions: The project offered a creative and viable platform for individuals diagnosed with TB to express and share their lived experiences. Results from this study will inform program planning and services, and the images/text will be disseminated on multiple platforms.

PD-965-14 Carrot and stick approach in engaging pharmacists in TB care and control: experiences from PRATAM Project, India

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Background and challenges to implementation: TB Alert India is working with Pharmacists and Rural Health Care Providers (RHCPs) since last four years in Telangana state, India. Objective of the project is to

bring in their active engagement in TB Care and control. Project is being supported by United Way Worldwide on behalf of Lilly MDR TB Partnership. Pharmacists and RHCPs are expected to refer people coming to them for cough treatment to TB testing. In 2015 (year 3 of project), a gradual decrease in number of referrals from enrolled pharmacist was noticed. A desk review of the data and interaction with pharmacists were taken up to understand the reasons for decreasing referral.

Intervention or response: Two approaches were used to bring in active engagement of Pharmacists in the project. First approach was sensitizing and engaging State and District Level Drug Control Authorities (who are the government monitoring authorities). State Level Drug Control Officer had issued a circular directing all pharmacies to support the project. Inquiry about TB referrals and sale of anti-TB drugs was included in the regular monitoring check list of Drug Inspectors. Second approach was to appreciate Pharmacists who were performing well. A token of recognition was given to such pharmacist in quarterly meetings. These initiative was taken up in three districts on pilot basis in 2016. Performance of pharmacist was closely monitored and recorded.

Results and lessons learnt: Around 155 pharmacists enrolled had referred 203 TB presumptive cases (PTC) from Jan to Sept '15. After implementing the new strategy in 2016, same number of enrolled pharmacists, referred 366 (80% increase) PTCs (from Jan -Sept 2016). Percentage of PTCs who went for testing also increased to 83% in 2016 compared to 64% in 2015. Around 36 and 20 cases were diagnosed with TB respectively in 2016 and 2015.

Conclusions and key recommendations: Engagement of local drug control authorities proved effective in engaging Pharmacists.

PD-966-14 Innovando la atención de las enfermedades respiratorias en el primer nivel de atención: un modelo con enfoque preventivo

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Background and challenges to implementation: Los padecimientos respiratorios se clasifican en agudos y crónicos, algunos de ellos representan un serio problema de salud pública en México. Para dar respuesta mediante una política pública a los daños a la salud ocasionados por estas Enfermedades Respiratorias (ER), es necesario priorizar los padecimientos con mayor impacto en la salud en la población, con el fin de eficientar el uso de recursos y mejorar la efectividad de la estrategia.

Intervention or response: Se implementó en México una estrategia de prevención y control de las ER que pretende disminuir la morbimortalidad de los padecimientos res-

piratorios, gastos de bolsillo y de salud pública, uso de antibióticos, así como el número de hospitalizaciones. Para lo anterior, se realizó un diagnóstico de salud y se priorizó el abordaje de las ER (Asma, EPOC, Neumonía e Influenza). Se identificaron necesidades de insumos médicos, capacitación, financiamiento y recursos humanos. Se diseñó una estrategia nacional proporcionando lineamientos para dar atención a las ER desde el Primer Nivel de Atención (PNA), basado en prevención (manejo de determinantes sociales, vacunación, promoción, cribado de asma y EPOC) y control (diagnóstico oportuno, tratamiento, control periódico, manejo de comorbilidades y rehabilitación de secuelas), en cuatro fases: difusión, instrumentación, operación y supervisión-evaluación.

Results and lessons learnt:
· Se implementó el Programa de Acción Especifico para la Prevención y Control de las Enfermedades Respiratorias (PAE-ERI)
· Se realizó difusión de la estrategia en todo el Sector Salud.
· Se Inició la fase de instrumentación en 2016.
· Se capacitó al personal de salud del PNA en la prevención y control de ER
. Se realizo alianzas y gestión de equipos e insumos médicos para las actividades de prevención.
· En 2017, inició la fase de operación.

Conclusions and key recommendations: Es necesario evaluar los alcances de las actividades de la operación del PAE-ERI, para realizar acciones de mejora de la estrategia en México.

PD-967-14 Application of the ENGAGE-TB approach in Côte d´Ivoire

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Background and challenges to implementation: In Côte d´Ivoire, the World Health Organization estimated the incidence of Tuberculosis (TB) at 159 cases per 100,000 in 2015. In 2016, the National Tuberculosis Program (NTP) notified 21,354 cases, between new and relapses (91 cases/100,000), of these 22% were HIV positives. Since 2009 the *Alliance Nationale pour la Santé et le Développement en Côte d'Ivoire* (Alliance Côte d´ivoireI), is principal recipient (PR) for HIV community grant of the Global Funds. Since 2016, the Alliance CI is PR for TB community grant to collaborate with NTP in increasing TB notification and success treatment rate.

Intervention or response: Alliance CI adopted, in collaboration with NTP, the WHO ENGAGE TB approach. A situation analysis was performed, the operational guide-

lines for community-based TB prevention and care were finalized, 1347 [NS1] community health workers (CHW) were trained and ENGAGE TB indicators were adopted. Activities started in urban areas in April and in rural areas in September 2016. Focus was put on key/vulnerable populations: contact cases, HIV positives, prisoners, people living in urban slums and in rural areas, drug addicted people, women and commercial sex workers. CHW collaborated with TB health centers in early TB case finding and in TB treatment support. All data collected by CHW was validated quarterly by health workers.

Results and lessons learnt: During 9 months of activity, CHW identified 2,668 (17%) of 15,694 TB cases diagnosed by NTP in the same period. Among these, 986 (36%) issued from key/vulnerable populations. A total of 10,757 TB patients received community supports. Their TB treatment results will be available next year.

Conclusions and key recommendations: End TB Strategy includes the engagement of NGO in pillar two. The ENGAGE-TB approach in Côte d´ivoire is at beginning and needs to be improved, in particular to ameliorate access to TB care for key/vulnerable populations.

PD-968-14 Model of civil society engagement to improve TB-HIV collaboration at TB clinic

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Background and challenges to implementation: Jakarta Respiratory Center is NGO based clinic who serves TB patients in Jakarta, where in 2014, 11/323 (3%) TB patients registered known their HIV status, there were no data on HIV treatment among positive patients. This coverage is lower than national coverage. One among issue regarding low HIV testing uptake is that HIV is not normalized, that resulted in health providers were not confident in providing HIV-related services. RED institute is civil society organization who works on TB-HIV issues and most of the staffs were people impacted by HIV and TB, and hence experienced patients.

Intervention or response: NAP and NTP developed the model of civil society engagement at TB clinic, as follow:
- RED institute was assigned to assist JRC clinic, which then assigned one of the staff to assist the TB team, including providing information on importance of HIV test for TB patients, ensuring the patients attend at laboratory, supporting treatment of TB-HIV patients.
- One TB doctor was trained for HIV treatment.
- TB-HIV team routine meeting at the clinic monitors testing and treatment uptake, ensuring all TB patients received test and all who are positives received treatment, and retain in care.

Results and lessons learnt: When the model introduced, 286/351 (81%) and 302/313 (96%) TB patients known their HIV status, 10 and 14 patients known HIV positive in 2015 and 2016, respectively. All received treatment, except 1 patient in 2016 refused HIV treatment.

Conclusions and key recommendations: Engagement of civil society at TB clinic has shown improved TB-HIV collaboration which resulted in HIV treatment for all who needs ART. ART treatment provided by doctor who treat TB patients will improve treatment uptake as the pathway for patient is simpler. This calls for adoption at wider level.

53. Nursing care to improve patient care

PD-969-14 Comprehensive nursing care for people affected by drug-resistant tuberculosis receiving bedaquiline treatment in Peru

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Background and challenges to implementation: In February 2016, between Socios En Salud (SES) and Ministry of Health, a comprehensive care program was implemented for patients with DR TB receiving treatment that included bedaquiline. This program covers clinical follow-up, emotional support and socio-economic support. The intervention of the nursing team aims to achieve comprehensive care and treatment success of the participants.

Intervention or response: SES established a trained nursing team with experience in working with patients with TB. The care approach ensured compliance with medical evaluation (routine and pharmacovigilance), psychological and socio-economic support. Nursing interventions were collected and entered into electronic records for monitoring and re-evaluation purposes.

Results and lessons learnt: 71 (100%) patients belong to 47 health centers and 1 prison, 3 (4.2%) died shortly after starting treatment due to evolution of the disease. 43 (60.6%) had XDR-TB, 25 (35.2%) pre XDR-TB and 3 (4.2%) MDR-TB. 60 (84.5%) were identified in their health centers and 11 (15.5%) were in prison. 71 (100%) met their scheduled medical evaluations and received DOT at home or in prison. 34 (47.8%) started with positive culture; 31/34 (91.2%) were bacteriologically converted (3 consecutive negative cultures). Identified and derived 67 (94.36%) patients with mental health problems (depression, anxiety, drug use, attempted suicide) and 46 (64.7%) with socioeconomic problems (insecure housing and food). 60 (84.5%) did not miss any doses,

10 (14.07%) lost between 1 and 15 days of treatment for social problems (alcohol or drug use, family violence) or refusing treatment (personal activities, fear of treatment reactions) and 1 (1.4%) abandoned treatment for traditional beliefs. The challenges for DOT monitoring were to identify a health worker who supervises treatments in unsafe áreas.

Conclusions and key recommendations: Nursing work focused on comprehensive patient care has contributed favorably to adherence to treatment and early referral for clinical and socioeconomic interventions in a group of patients receiving MDR-TB treatment in Peru.

PD-970-14 Effect of family centered extended nursing on psychology in multidrug resistant tuberculosis patients

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Background and challenges to implementation: To observe the effect of extended family-centered nursing on psychology in multidrug-resistant tuberculosis (MDR-TB) patients, and provide theoretical basis for improving the clinical nursing effect and life quality of patients with MDR-TB.

Intervention or response: 135 MDR-TB patients were randomly divided into the control group and intervention group. The control group was treated with routine nursing. The intervention group received extended family-centered intervention at the same time. The compliance was compared between two groups at 1 week before discharge and 6 months after discharge. The scores of self-rating anxiety scale(SAS) and self-rating depression scale(SDS) were obtained before and after intervention in two groups. The improvement of patient´s life quality was observed using the Quality of Life Scale sf-36.

Results and lessons learnt: Compared with the control group, the intervention group had more patients with fully compliance, and less patients with partial compliance or completely noncompliance at 1 week before discharge and 6 months after discharge. There was no significant difference in SAS and SDS scores between two groups before intervention. After intervention, SAS and SDS scores in the intervention group were obviously better than those in the control group. Psychology function, physical function, life quality and social function in the intervention group were superior than those in the control group.

Conclusions and key recommendations: Family-centered extended nursing can significantly reduce anxiety and depression, increase the knowledge about tuberculosis, improve the compliance, enhance the life quality of MDR-TB patients, and is worthy of further promotion.

PD-971-14 Patient-centered counseling and impact on TB awareness among TB-inpatients at Xinjiang Chest Hospital, China

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Background and challenges to implementation: The prevalence of tuberculosis is high in Xinjiang Uyghur Autonomous Region, China. Xinjiang Chest Hospital is the designated TB diagnosis and treatment hospital. To improve the treatment compliance and decrease the spread of tuberculosis, the consultation service was carried out and the quality of service was evaluated.

Intervention or response: 124 hospitalized patients with tuberculosis were selected. Pre-counselling questionnaire was conducted to assess TB-related knowledge and attitude. The evidence-based consultation service was designed to focus on the older, ethnic groups and patients with lower education level and provide tailored counselling. Counselling included one-on-one, small group activities, and online QQ group. Service flow chart and treatment adherence counseling strategy were standardized. Post-counselling assessment was undergone before discharge to evaluate the service effectiveness. SPSS17.0 was used to compare the rate of tuberculosis knowledge before and after intervention.

Results and lessons learnt: Among the 124 TB inpatients enrolled, 70 (57%) were male and 54 (43%) were female. The average age was 39.7. The ethnicity was: Han 46 (37%), Uyghur 52 (42%) and others 26 (21%). 64% of inpatients are from southern Xinjiang. 56% of patients are less educated than middle school, and 24% are reported as herdsman. From data analysis between pre and post testing, the TB awareness increased: 1) transmitted by air from 77.4% to 99.2% ($p < 0.05$); 2) transmitted by close contact with TB patients from 44.4% to 73.4% ($p < 0.05$). Treatment course knowledge was also improved: 1) 6 to 8 months for TB, from 51% to 81% ($p < 0.001$); 2) 24 months for MDR-TB, from 38% to 78% ($p < 0.001$). The knowledge on re-examination month was improved from 12.9% to 28.2% ($p < 0.05$).

Conclusions and key recommendations: The consultation service started from the needs of tuberculosis patients. It provided personalized services and made patients grasp the relevant knowledge. The patient-centered counselling was proved effective to increase the TB awareness.

PD-972-14 Impact of stigma on quality of life in MDR-TB patients

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Background: Russia has one of the highest burdens of multidrug-resistant TB (MDR-TB) globally. Those suffering from MDR-TB in Russia experience high levels of stigma and discrimination.
Methods: Patients with MDR-TB participated in a study to assess the effect of stigma on quality of life (QOL) in MDR-TB patients after 12 months of therapy. We used the SF-36 questionnaire with additional questions on stigma and knowledge about TB. Thirty-four MDR-TB patients (18 female and 16 male patients) were recruited in the study in 2016. The questionnaires were completed at the beginning of therapy, after three months and 12 months of treatment.
Results: The average age of the respondents was 38. The average physical health component score decreased from 81% at baseline in all patients to 65% in males and 72% in females at three months and to 60.7% and 36% respectively at 12 months. The baseline mental health component in male patients was 72% and 78% in female patients, after three months of therapy it dropped to 67% in all patients. The mental health component after 12 months of therapy stayed at 67 % in male patients and fell to 42% in females. All respondents experienced physical pain, lower social function and a marked deterioration of their role and emotional functions. All respondents experienced discrimination by society, all linked this to their TB disease and reported its negative impact on their QOL.
Conclusions: Patients receive free MDR-TB therapy and medical rehabilitation in sanatoria but still they experience strong suffering, not only physically but also emotionally. Patients endure social isolation and strained personal relationships due to TB stigma. Therefore, MDR-TB patients need not only new therapy regimens but psychological support programs.

PD-973-14 Patient support groups as a means of improving quality and retention in DR-TB care

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Background and challenges to implementation: DR TB possesses a major challenge to the control of tuberculosis worldwide. Patients are commenced on treatment in the treatment center and discharged to the community or are initiated on treatment in the community. Due to the prolonged duration of treatment (9 to 20months), patients experience various challenges including psycho-social and treatment related challenges resulting patient default. As a result, there is need to provide a forum for patients, community and healthcare worker interaction.
Intervention or response: With the aid of Community Based Organizations (CBO), patient support groups were established in communities based on catchment areas within 1 year. The State team links the patients to CBOs working within the State to assign them to support groups. Patients are also encouraged to choose treatment supporters. The support groups are attended by patients, treatment supporters, healthcare workers and CBO representatives. The groups met monthly to discuss TB infection control, baseline and follow up investigations, action to take in case of drug side effects, adherence to DR TB drugs, nutrition and other topics of interest to clients. Quarterly report of CBO activities was collated to determine the outcome of the patients who attended support group activities regularly within a quarter (3 months).
Results and lessons learnt: Within the 3 months review period, Out of one hundred and thirty-six (136) patients on treatment in the community attending support group meetings, 107(78%) were clinically stable and still on treatment, twenty-three (23) (16%) successfully completed their treatment, five (5) (3.7%) died and one (1) (0.7%) patient was lost to follow up but was brought back on treatment by the CBO. One (1) (0.7%) patient failed treatment and was transferred to a treatment center.
Conclusions and key recommendations: Patient support groups are vital in improving treatment retention and outcome for DRTB and should be encouraged.

PD-974-14 Patient centred' single-window services' model of care for TB-HIV: a case study from India

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Background and challenges to implementation: Globally there was 4.3 million gap between incident and notified cases. There is considerable diagnostic gap and treatment gap in TB, drug resistant- TB (DR TB) among People Living with HIV in India. Acess to services remains major challenge in India due to long distances, poor socio economic condition and multiple level of centres health related services.
WHO's End TB Strategy calls for a patient centred care approach to enhance diagnosis and treatment of Tuberculosis and DRTB. India has successfully implemented patient centred "single window services" model for care for TB HIV services.

Intervention or response: People living with HIV (PLHIV) were provided with package of services under the single window TB HIV services model at 30 selected ART centres in five high TBHIV burden states. The package of services included Xpert MTB as primary diagnostic tool within the same facility ,daily Anti TB treatment at ART centres itself ,counselling and social support services as single window service. All staff at ART centres were trained in TB treatment, management, adherence counselling and infection control .Patient did not have to travel to different sites to avail the treatment,which was predominant cause of missed cases.

Results and lessons learnt: Among the 2076154 PLHIV´s under active care 1843957(88%) were screened for TB symptoms,67258 referred as presumptive TB cases were tested at co-located Xpert TB diagnostic centre .9184 (14%)MTB /RIF sensitive and 245 Rifampicin resistant cases were detected. 8983(98%) of the PLHIV diagnosed with TB were put on treatment. [FIG 2]
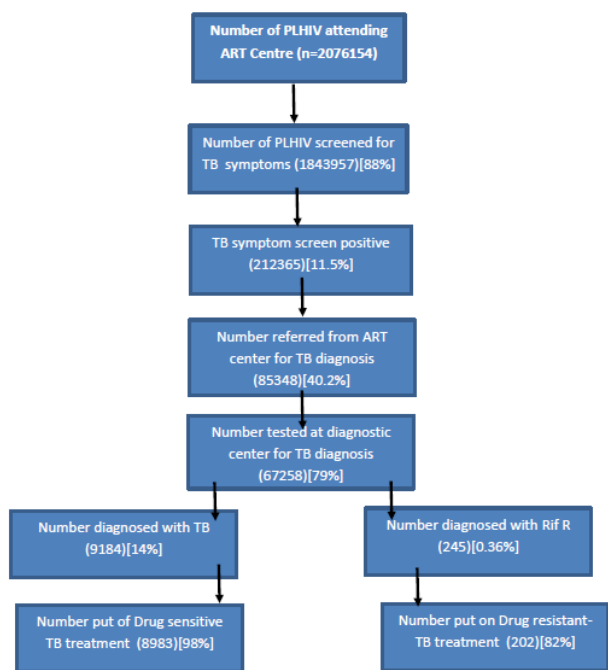
Figure Cascade Patient diagnosis and treatment

Conclusions and key recommendations: Use of Xpert MTB as primary diagnostic tool was associated with increase in TB diagnosis as compared to sputum microscopy including diagnosis of RR-TB as additional yield. Findings shows significant benefit of "Single window services "in reducing the diagnosis and treatment gap and early linkage to treatment. High level of patient satisfaction and reduction in out of pocket expenses are added benefits.

PD-975-14 The Axshya Kiosks, an innovative model for increasing access to TB information and service: experience from India

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Background and challenges to implementation: There are issues related to having right information about disease, diagnostic procedures and treatment adherence, accessibility to services by the affected community (daily-wage-earners, school-children, industrial-workers, PLHIVs) and TB patients. Most important a need to align the time, place and observation to the patients´ convenience. Under the programme TB patients are expected to take treatment under the observation of a DOT provider (community volunteer/health facility). This process may not be convenient to the patient particularly for the patients who reside in urban slums. There is a need to align the time, place and observation to patient convenience, and making the process more respectful and flexible.

Intervention or response: TAxshya Kiosks are set up in public health facilities such as chest or district hospitals, medical colleges, and community settings and in and around densely populated urban zones and industrial areas where TB rates are higher. They offer services for extended hours from 6AM to 9PM, during which time trained community volunteers administer TB treatment, collect sputum samples and provide drop in consultations for patients and their families seeking information and counselling services. The Union's Project Axshya has established 97 tuberculosis (TB) treatment and information kiosks in 40 cities in India to provide better and more patient-centred care.

Results and lessons learnt: Indicated in Figure 1
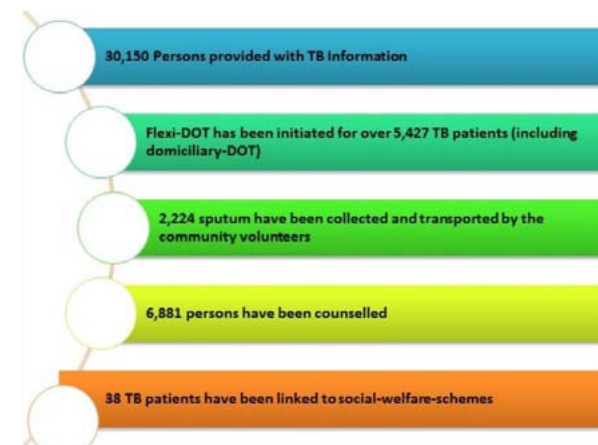
Figure 1

Conclusions and key recommendations: The kiosks address the common challenges faced by the community, including the limited opening hours of healthcare centres, difficulty in accessing care and a lack in personalised service. Patient-friendly diagnosis, treatment adherence, treatment completion and success rate and decrease in default and failure rate for TB services through AKs. AKs may complement DOTS in the long run to End TB. This model can be replicated by other countries as well.

PD-976-14 Patient delays in TB care seeking in a complex emergency situation: the experience of Somalia

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Background and challenges to implementation: Tuberculosis (TB) remains a public health threat and major cause of death in developing world. Early diagnosis of the disease and prompt initiation of treatment are essential for effective TB control. Delays in seeking care and diagnosis for TB are major barriers to effective TB management, prevention and control. Length of delay in care seeking for TB services remain undocumented in Somalia. This study sought to determine the delay in care seeking behavior and associated factors among presumptive TB patients in Somalia.

Intervention or response: A cross-sectional study was conducted among presumptive TB patients visiting health facilities in Somaliland, Puntland and South Central Somalia in November and December 2016. Exit interviews were conducted among the study subjects. Patient delay in care seeking was defined as the period from onset of the first symptom(s) possibly related to pulmonary TB to the date when the patient first contacted any type health care facility (formal or informal).

Results and lessons learnt: 600 patients were interviewed. The median time from onset of respiratory symptoms to the first medical visit was within one month (52%). Commonest symptoms that the patients presented with were characteristic of TB disease (cough of > 2 week (55%), Fever (47%) chest pain (35%) weight loss (34%); weakness (28%) night sweats (21%). Majority (43%) were unaware of the severity of the symptoms while 13.3 % of patients thought TB treatment was expensive, another 13.1% cited lack of time to visit a health facility. Long distances (>21kms) and high cost of transportation to health facility ($3 round trip) were other factors associated with delay.

Conclusions and key recommendations: Despite presence of characteristic signs & symptoms of TB, there is considerable delay in care seeking among patients. Inadequate knowledge and cost play a role. Strategies to increase awareness on TB and reduce access barrier to services are encouraged.

PD-977-14 Gridlock from diagnosis to treatment of multidrug-resistant tuberculosis in Tanzania: patient perspectives from focus group discussions

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Background: Molecular diagnostics have revolutionized MDR-TB diagnosis. Yet the maximum impact in MDR-TB control is not currently realized in underprivileged settings.

Aims: To explore patients' viewpoints and experiences with personal and socio-behavioral obstacles from MDR-TB diagnosis to treatment.

Methods: A qualitative study was conducted in December 2016 with MDR-TB patients admitted at Kibong'oto Infectious Diseases Hospital utilizing a thematic analysis approach.

Results: Forty-five MDR-TB patients participated in 6 focus group discussions. The following themes (A-E) were identified and examples provided:

(A) Socio-behavioral context [lack of personal education- *thought of TB first as witchcraft prior to presenting to hospital - yet once diagnosed with MDR-TB the patient secretly relocated, changed personal identifications, pretended as a new case to another facility, diagnosed TB with smear microscopy and started first line TB treatment*];

(B) Accessibility of MDR-TB diagnostic centers [*suspected MDR-TB patient referred to distant health facility which is known for MDR-TB diagnosis, yet no Xpert MTB/RIF cartridges in stock and patient resumed first-line treatment*];

(C) Laxity of health care workers (HCW) to suspect and order diagnostics [*TB patients on category II or I treatment presented often at local hospitals complaining of persistence of TB symptoms including cough, HCW insisted to continue with the treatment without collecting sputum for susceptibility. After completing treatment with persisting symptoms; HCW prescribed again first line anti-TB without prioritizing susceptibility testing.*];

(D) Inefficiency of specimens referral system [*patient submitted sputum after 8-months results are not relayed while TB symptoms persist despite being on first line TB treatment. Later patient is requested to produce another sputum before MDR-TB diagnosis finally made.*];

(E) Risk factors for amplification of MDR-TB transmission [*patients with MDR-TB consumed local alcohol in poorly ventilated settings congregate settings*].

Conclusions: Patient-centered strategies bridging communities and the health system are urgently required for optimum MDR-TB control in Tanzania.

PD-978-14 Pathways to anti-tuberculosis treatment initiation among cases on directly observed treatment short course in districts of southwestern Ethiopia: a cross-sectional study

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Background: Delayed tuberculosis (TB) treatment increase morbidity, mortality, expenditure and transmission in the community. The aim of this study was to quantify time delays to seek care and initiate treatment and factors associated with delays.

Methods: A cross-sectional study was conducted among 735 consecutive new adult TB cases registered between January to December 2015 in selected districts of southwestern Ethiopia. Data were collected via face to face interview of patients with in the first 2 months of treatment initiation using structured questionnaire. Three forms of delay were assessed as number of days elapsed between

1) onset of TB symptoms to first health care facility visit (patient delay),

2) first consultation to treatment initiation (provider delay) and;

3) onset of illness to treatment initiation (total delay).

Results: The median (inter-quartile range) of patient, provider and total delays were respectively 25 (15-36), 22 (9-48) and 55 (32-100) days. Prior self treatment adjusted Odds ratio (AOR) 95% confidence interval (CI) 1.72 (1.07,2.75), HIV co infection AOR (95% CI) 1.8 (1.05,3.1) and Extra pulmonary TB AOR (95% CI) 1.54 (1.03,2.29) independently predicted higher odds of patient delay. On the other hand, visiting first to health posts or private clinics AOR (95% CI) 1.42(1.01,2.0) and delayed to seek care AOR (95% CI) 1.81 (1.33,2.5) predicted longer provider delay. Finally, having extra pulmonary TB AOR (95% CI) 1.6 (1.07,2.38), prior consultation of traditional healer AOR (95% CI) 3.72 (1.01,13.77) and prior use of holy water independently predicted longer total delay.

Conclusions: TB patients elapse too long time to initiate care seeking, diagnosis and treatment that reflects longer periods of disease transmission to the community. The delays are attributed to the patient, disease and health system related factors. Hence involving informal providers, improving diagnostic efficiency of health care facilities and creating community awareness about TB control strategies can reduce the delays.

PD-979-14 Informal timing and patient-friendly flexi-DOT effective in increasing treatment adherence of tuberculosis patients and generating awareness in among communities in five urban centres in Chhattisgarh

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Background and challenges to implementation: Tuberculosis is the world´s largest-public-health-epidemic and India bears a disproportionately large burden, accounting for 26% of the global TB-cases which remains as one of the principal challenges on its health-and-wellness-scale. 10.4 million people become sick with TB each year.

The WHO-recommended comprehensive and highly-efficient-cost-effective DOTS-strategy that ensures patient-care-to-cure and prevent TB is considered often inconvenient to many TB patients working in unorganised sectors, daily-wage-earners, women, school children, PLHIVs and the marginalized. Five such affected-urban-cities in Chhattisgarh modelled '*Flexi-DOT*' services to ensure flexible/informal service hours and treatment availability to TB patients at their convenient time, place and satisfaction besides generating awareness among the affected community.

Intervention or response: Fifteen out-reach-Flexi-DOT-Centres (FDC) in five districts (Raipur-Korba-Durg-Bilaspur-Rajnandgaon) engaged 28 trained Community Volunteers. Flexi-DOT service thru these FDCs were made available from morning 6 AM-till-evening-9 PM which provided DOT to local TB patients who visited the facility at their convenient-time. FDCs also provided facilities of domiciliary-care to bedridden-TB-patients, drop-in-centre for TB information, linking TB patients with government-provided-social-welfare-schemes, CVs conducted systematic active-TB-screening through house-visits and ensure their sputum-collection/transportation-&-test. Missed-cases were attended at their homes on same-day.

Patient feedback also indicated *treatment-convenience-and-comfort of Flexi-DOT* due to informal-timing, friendly-relations with the CVs and proximity-to-homes.

Results and lessons learnt: 167 patients administered DOT at the FDCs by trained CVs against 322 TB cases diagnosed from Apr'16-Mar'17. 33 patients got successfully-treated. Of 50 CVs trained, 38 reached-out to around 71,500 people with TB messages in 12358 households through door-to-visits. Sputum examination of 3429 suspects done out of 3892 collected/transported. 322 lives saved with zero catastrophic-expenditure-on-treatment.

Conclusions and key recommendations: FDC intervention had a definite impact on the TB-patient in particular and the affected-community in general. *Flexi-DOT*

may be considered as an alternative-best-suited-model of DOT. With a standard of care for TB exists already, DOT and newer-models like *Flexi-DOT* could save 777,000 lives over the next 10 years in India. (WHO-SEAR).

54. Vulnerable populations: homeless to migrants

PD-980-14 Role of trained community volunteers in TB active case finding among key affected populations in eight states of India

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Background and challenges to implementation: 10% of India's population is estimated to be KAP (131 mln). KAP are more vulnerable to TB because of limited access to services and information, difficult geographical locations and inadequate treatment seeking. Government of India (GoI) recently initiated ACF to enhance TB case notification in KAP through household screening under an estimated rate of 250 TB cases per 100,000 KAP. To reinforce GOI's ACF initiative, World Vision India (WVI) with 6 partners aimed to cover about 26 mln people in 21,000 high-risk villages and around 6,000 urban slums. Screening for TB was conducted among KAPs in 70 districts of 8 states through ACF, between Oct 2015 - Dec 2017 under the Global Fund TB program.

Intervention or response: In 70 operational districts, WVI and partners mapped KAPs (slums, tribes, prisons, PLHIV, difficult terrains etc.) and trained 354 community volunteers (CVs). Trained CVs visited ACF-sites as per monthly action-plans and route maps. They engaged local community leaders through community preparatory meetings and conducted door-to-door symptomatic screening using specially designed verbal screening tool. Presumptive TB cases had their sputum microscopy and chest X-ray (CXR) through assisted referrals and sputum collection & transportation. CXR screening was also conducted among prisoners followed by CBNAAT for TB-suggestive cases. Gastric lavage services were utilized to collect sputum samples in young children.

Results and lessons learnt: As of December 2016, 6.2 mln people in 1,269,580 households were screened and 12,194 TB patients notified. Case notification rate was 197 per 100,000 with higher rates in Bihar (343) and Madhya Pradesh (450). An average 104 households screened to detect one TB patient. Higher concentration of TB patients was in rural settings. Average cost per case notification was 35 USD.

Conclusions and key recommendations: Well-planned TB ACF using appropriately trained CVs is cost-effective and can help to improve TB case notification among the most vulnerable and affected by TB population segments.

PD-981-14 TB diagnosis and treatment in homeless populations in Brazil

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Background: TB is one of the main health problems among HP in Brazil. The objective of this study is to describe access to diagnosis and treatment of tuberculosis among the homeless population in follow up by teams of the Street Outreach Health Offices (SOHO).

Methods: A cross-sectional study was performed among homeless population (HP) diagnosed with pulmonary TB and reported in 2015. The results of the tests, directly observed treatment (DOT) and outcome of the HP treatment reported by Street Outreach Health Offices (SOHO) with the one reported by conventional health unit (CHU) by the chi-square test were compared.

Results: 2,822 HP were diagnosed with TB and of these, 446 (15.8%) were notified by SOHO. The proportion of sputum smear microscopy was 8% (p=.002) lower in the SOHO. However, SOHO performed 70% more culture tests (p< .0001) and twice as gene Xpert (p< .0001) and sensitivity tests (p< .0001). Regarding treatment, SOHO performed 50% more DOT (p=.002). Treatment success (SOHO = 44.2% and CHU = 32.2%) and default (SOHO = 38.8% and CHU = 36.8%) were more frequent in SOHO. This population also presented a greater diagnosis of drug-resistant TB, change of the scheme and treatment failure (SOHO = 2.2% and CHU = 1.8%). This group still had less deaths (SOHO = 4.7% and CHU = 13.0%) and change of service delivery (SOHO = 15.5% and CHU = 24.8%) than the CHU.

Conclusions: The profile of care in the SOHO showed greater access to diagnostic tests, higher DOT, better outcomes, with the exception of default, less change of health unit and, possibly, a greater link with the patient among homeless population. These results suggest that the SOHO are devices that are more prepared for the care of HP.

PD-982-14 Systematic screening of active tuberculosis cases among urban slum dwellers in Jharkhand, India: a community-based study

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Background: National TB Control Programme of India (RNTCP) notified 1.7 million TB cases clearly missing more than a million of the estimated 2.8 million incident TB cases. In light of the limitations of the current case finding strategies, WHO recommends for a systematic screening of active TB cases (ACF), especially from low socio economic population with high risk of contracting TB. We carried out this study to assess the impact of ACF among the urban slum dwellers to supplement the routine TB case finding in the state of Jharkhand, India.
Methods: A systematic screening of active TB cases was conducted in the urban slum pockets of Ranchi Municipal Corporation of Jharkhand. RNTCP field staff and community health volunteers conducted the symptom screening and facilitated sputum sample collection and transport. Binocular microscopy was used for TB diagnosis along with the limited use of X-ray chest and CBNAAT (Xpert MTB/RIF) under programmatic conditions.
Results: During the study period, a total of 3,413 households with a population of 19,338 were reached out and counselled and screened for TB, of which 489 (NNS=39.5) were identified as presumptive TB cases. Among 489 presumptive TB cases tested for TB 49 (10%) were diagnosed as TB cases; of which 44 (90%) were microbiologically conformed and 5 (10%) were clinically confirmed. Of 489 presumptive TB cases tested for TB 200 (41%) were females and 30 (6%) were of age group less than 15 years.
Conclusions: While the passive case finding is the predominant approach of TB case finding in RNTCP, ACF is a possible complement to identify additional TB cases especially among the population with high risk of contracting TB. The community based approach of ACF also provides an opportunity to reaching out the people for early detection and relatively low health seeking behavior among female population and paediatric age group.

PD-983-14 Búsqueda de casos de tuberculosis en personas privadas de la libertad en México

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Background and challenges to implementation: México cuenta con 447 prisiones, durante el año 2016 se trabajó en 180 que cuentan con servicio médico.Se capacitó personal médico de los Centros de Readaptación Social en 146 prisiones;existen convenios entre las autoridades de las prisiones y la Secretaria de Salud, se realizan diversas estrategias para la búsqueda de sintomáticos respiratorios, se informa a la población privada de la libertad sobre el padecimiento.
El tratamiento se da estrictamente supervisado, se realiza seguimiento baciloscopico mensual a los casos diagnosticados en estos centros.
Intervention or response: En México existe coordinación con autoridades de los Centros Penitenciarios (Cereso´s) en las entidades federativas, personal médico de los reclusorios y el personal de los Servicios de Salud para la búsqueda intencionada de sintomáticos respiratorios; ingresando a estos centros por lo menos 2 veces al año, o cuando ingresa una persona privada de la libertad.
Results and lessons learnt: Se realizó la búsqueda en población de 100,966 personas privadas de la libertad, se estudiaron 10,306 sintomáticos respiratorios, se identificaron 294 casos con tuberculosis pulmonar, de estos 214 curaron (72.7%), 18 término de tratamiento (6.1%), 1 fracasos (0.3%), 3 defunciones por tuberculosis (1%), 12 abandonos (4%), 10 traslados (3.1%), 27 continúan en tratamiento (9.1%), Éxito de tratamiento de 232 (78%).
También se realizó la prueba de VIH a 291 personas privadas de la libertad, se encontraron 9 casos.
Conclusions and key recommendations: El trabajo con grupos vulnerables como son las personas privadas de la libertad, con la participación coordinada del personal de salud y autoridades de los reclusorios para realizar las actividades de búsqueda de casos de tuberculosis pulmonar, ingresarlos a tratamiento para llevarlos a la curación, nos permite romper la cadena de transmisión en población vulnerable.

PD-984-14 Expanding TB diagnosis and community-based tuberculosis management: addressing vulnerable ethnic populations and tea garden workers in Bangladesh

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Background and challenges to implementation: Bangladesh is a high burden Tuberculosis (TB) country with 49% of cases undetected. The issue of case detection is especially visible among tea garden workers, marginalized ethnic groups living in the Punji areas that are neglected from mainstream society struggle to access health and social services.

The objective of this activity was to improve TB case identification and management among marginalized populations living in the Punji area and to build awareness by ensuring social mobilization for TB.

Intervention or response: In alignment with the end TB strategy, through subcontracted work, the Challenge TB (CTB) project, supported the marginalized populations in 184 tea, 56 rubber gardens and 72 punjis covering a total population of 698,251 people. CTB supported the strengthened provision of TB services through the development of awareness raising programs, the facilitation of home-based sputum collection and the creation of effective referral linkages to members in each of these groups.

Results and lessons learnt: From July 2015 to June 2016, 14,594 presumptive TB patients from the vulnerable groups were tested and 2,421 TB cases were detected. Out of the total cases 1,533 were diagnosed as bacteriologically confirmed (63%), 640 were clinically diagnosed (26.43%) and 248 were extra pulmonary TB cases (10.24%). The case notification rate (CNR) of all forms TB among these groups was 346 per 100,000 population, more than double the CNR of all form TB cases in the Sylhet division (170 per 100,000 population) and double the CNR of all forms TB at the national level (130 per 100,000 population).

Conclusions and key recommendations: The CNR among the tea garden population and punjis is high due to their confined geographic location and their inability to access health care. Specific targeted interventions such as the Strong GO-NGO partnership, intensified community based TB service approaches and community awareness can enable them to better access TB services.

PD-985-14 Contribution of active contact screening to TB case detection in Urban DOTS supported provinces in Afghanistan

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Background and challenges to implementation: WHO and National TB Programs (NTP) have recommended contact management for many years, but implementation was poor to non-existent in TB endemic areas. Multiple barriers and challenges have been identified, including lack of human re-sources, lack of an appropriate management structure and screening tools, low community awareness, and poor adherence to on INH Preventive Therapy (IPT).

Intervention or response: Challenge TB project implemented active contact screening in 2016 in five Urban directly observed therapy, short course (Urban DOTS) province (Kabul, Herat, Kandahar, Nangarhar and Balkh). We applied to contact screening approaches: door-to-door screening of TB index case contacts and asking the TB index case to bring the contacts to the health facilities for screening. Training and mentor-ship was given to health workers on contact screening practices. The supervisors also randomly check 15% of the screened contacts to confirm the practice.

Results and lessons learnt: In the door-to-door screening of contacts; 4,093 TB index cases registered and 35,169 household contacts identified with an average of 8.5 contacts per index case. Out of these contacts 4,941(14%) presumptive TB cases identified and 667 (13.5%) TB cases diagnosed. Five thousand two hundred seventy five children under 5 were put IPT. In the health facility screened group 9,705 TB index cases registered 50,584 household contacts registered and screened with 5.2 contacts per index case, and 10,628 (21%) presumptive TB cases identified. Among them, 977 (9.2%) diagnosed with TB, and 11,437 children under 5 received IPT in 29 control provinces. TB case yield among household contacts in the intervention was 13,499 per 100,000 and in control areas it was 9,192 per 100,000 populations.

Indicators	Intervention area	Control Area
# of index cases registered	4,093	9,705
# household contact registered	35,169	50,584
# and % of all form TB cases identified among contacts	667 (13.5%)	977 (9.2%)
# of children under 5 years old received IPT	# of children under 5 years old received IPT	11,437

Table 1 Contribution of active contact screening

Conclusions and key recommendations: Active screening almost doubled TB case detection and provision of IPT for children compared to passive contact screening. TB among household contacts is much higher than WHO estimated incidence cases. We recommend implementation of active contact screening nationwide.

PD-986-14 Targeting active case finding to vulnerable populations to improve tuberculosis case notification in Northern Uganda

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Background and challenges to implementation: Uganda's tuberculosis (TB) prevalence is 253/100,000, yet current TB case notification is only 121/100,000 population. Sixteen districts of Northern Uganda have a case notification of 165/100,000, well below the national prevalence.

This under reporting translates to 3139 (35%) likely TB cases in the region going unidentified. The USAID Applying Science to Strengthen and Improve Systems (ASSIST) Project supports the Ministry of Health (MOH) by working with districts and health facilities to actively look for TB cases in vulnerable populations; contacts of index TB patients, prisoners, fishing communities and get them enrolled on treatment.

Intervention or response: Using a Pareto chart, we reviewed national TB data for each district, determined districts contributing 80% of un-notified cases and supported a stakeholder meeting to develop district implementation plans to identify vulnerable populations and screen them for TB.

The MOH intensified case-finding tool was used in the community to screen prisoners, TB patients' contacts, and residents of fishing communities by asking for any of the following symptoms: cough in the previous 2 weeks, persistent fever, night sweats, or noticeable weight loss. Mapping TB patients was done using facility records to prioritise contact tracing in 16 villages contributing majority of un-notified cases. An appointment was made for fishing communities when they were not out fishing. Anyone whose response was a yes to having cough was asked to produce a sputum which was evaluated using geneXpert.

Results and lessons learnt: From January to February 2017, 51 cases were found among 6129 population - a higher TB case notification rate= 864/100000, translating to TB case yields of (28)55% among index case contacts, (15)29% among prisoners, and (8)16% among residents of fishing communities.

Conclusions and key recommendations: National programs need to equally prioritise TB screening among contacts, prisoners and fishing communities for higher yields. Using national data is key in guiding and directing efforts to improve TB case notification.

PD-987-14 Increasing TB disease awareness, diagnostic and linkage to care into harm reduction programme in Georgia

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Background and challenges to implementation: HIV and Tuberculosis reveals significant public health challenges in Georgia. The most affected risk group for TB/HIV is people who inject drugs (PWIDs). TB and HIV programs were functioning separately from each other for decades, TB problem among PWIDs were not addressed appropriately. Accordingly no screening, diagnostic and linkage to care services existed in harm reduction program before 2014. TB control among drug users was a challenge hardly solved by formal health care services alone.

Intervention or response: For awareness raising and improving medical help-seeking behavior, case detection and referral to TB facilities, targeted training was conducted for harm reduction program personnel. More emphasize was done on education of peer educators in TB detection and adherence support. TB screening, referral and care guideline was developed and TB doctors were additionally engaged in harm reduction sites. Needed TB counseling were ensured at harm reduction sites and at outreach. TB education module was included in existing peer educational program. Case management intervention was actively applied for increasing linkage to care.

Results and lessons learnt: Number of screened PWIDs on TB is increasing year by year at harm reduction sites: 4,075 in 2014; 9,868 in 2015 and 12,423 in 2016. As a result significant portion of screened PWIDs were referred to TB clinics and with active TB disease included in TB treatment programs: 13,1% in 2014; 38.6%-2015; 53.3%-2016. Outreach team as mediator between PWIDs and local TB services worked effectively.

Conclusions and key recommendations: Capacity of harm reduction programs should be used for reducing delays in TB diagnoses and treatment initiation in this high-risk group. Collaboration on TB and HIV programs had revealed to be cost-effective in terms of case detection of active TB cases as harm reduction program personnel with appropriate knowledge and counseling skills can educate peer educators/community members who has direct contact with PWIDs.

PD-988-14 Evidence-based community engagement to accelerate TB case finding among migrant communities: Thailand's experiences

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Background and challenges to implementation: As part of Thailand National TB/HIV response, World Vision Foundation of Thailand (WVFT) has implemented the sub recipient of Global Fund round 13 within 2015-2016. It targeted for migrants population from high TB burden neighboring countries like Myanmar, Cambodia and Laos . The program was set up in six borders and nearby provinces (Tak, Bangkok, Pathumthani, Kanchanaburi, Phuket and Ranong) which has high TB burden among migrants and targeted population to screen within two years by intensified case finding (ICF) techniques was 90,655.

Intervention or response: WVFT launched to engage the community participation and involvement for systematic screening and conducted migrant community mapping and selected migrant health volunteers. Those volunteers were received by intensive TB training categorized by three modules like roles and responsibilities of migrant health volunteers, TB counseling & management and public communication skills by native health personnel.

Results and lessons learnt: After two years, WVFT classified 504 migrant community clusters and reached 220 clusters. 650 migrant health volunteers were recruited for intensified case finding surveys around their clusters and made referral. 61,320 migrant community people were screened by verbal ICF screening and 67% (61320/90655) achieved against the project target. 3, 681 migrants people were notified as presumptive TB cases and 100 % tested for TB diagnosis. Among them, 341 and 196 presumptive TB cases were identified as All TB cases and New smear positive TB patients respectively and 100%(196/196) of New Smear positive TB patients and 98%(333/341) of All TB patients were enrolled for TB treatment. Not only that according to 2015 cohort results treatment results of new smear positive and all type of TB cases were 90% and 82% respectively.

Conclusions and key recommendations: This evidence showed that role of CSO and community engagement are cost effective and accelerate TB case finding for hard to reach population and also crucial part of ending TB in future.

PD-989-14 *Mycobacterium tuberculosis* causante de enfermedad activa en pueblos indígenas de Colombia, 2009—2016

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Background: La tuberculosis continúa siendo un problema de salud pública en el mundo, sobre todo en aquellas poblaciones que por sus características sociales y culturales, son consideradas vulnerables al desarrollo de la enfermedad, como la población indígena. Estudios previos en Colombia, han mostrado incidencias por encima de 500 casos por 100.000 habitantes en esta población, con una incidencia nacional para la población general de 25,6 casos por 100.000 habitantes. **Objetivo:** caracterizar fenotípica y molecularmente los aislamientos de *Mycobacterium tuberculosis* causantes de enfermedad en pueblos indígenas colombianos, entre 2009 y 2016.

Methods: Estudio descriptivo, en el cual se caracterizaron 353 aislamientos, provenientes de 346 pacientes, captados a través de la vigilancia rutinaria que realiza el Instituto Nacional de Salud, en el país. Se realizaron pruebas fenotípicas de identificación y de susceptibilidad a medicamentos antituberculosis, así como pruebas de genotipificación, spoligotyping y MIRU-VNTR. Se tuvieron en cuenta variables sociodemograficas de la población, para determinar la posible asociación entre perfiles de sensibilidad y familias genéticas.

Results: Se identificaron 55 pueblos indígenas, de los cuales los que mayor número de casos aportaron fueron, Wayúu (11,04%), Embera-Chamí (10,76%) y Awa (6,79%); se encontraron 15 (4,25%) casos de MDR. Usando spoligotyping se identificaron 142 genotipos (69,7% reportados en la base de datos SpolDB4 y 30,3% patrones huérfanos). Por otro lado, la metodología MIRU-VNTR identifico 344 genotipos, 335 únicos y 7 agrupamientos. Los sublinajes encontrados fueron LAM (38,2%), Haarlem (13,03%), T (9,91%), huérfanos (30,31%) y otros en menos proporción.

Conclusions: Se identificaron 6 casos de posible reinfección exógena y un caso de infección mixta fue confirmado. Se identificaron genotipos huérfanos, que pueden ser autóctonos de población indígena colombiana. Se confirmaron 3 casos de trasmisión activa, a través de la combinación de las dos metodologías de genotipificación, en la población indígena estudiada.

55. Expert use of Xpert®: developing the evidence base

PD-990-14 Role of Xpert® MTB/RIF assay for diagnosis of bacteriologically confirmed TB cases: National TB Prevalence Survey 2015-2016, Bangladesh

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Background: Bangladesh is one of the 30 high burden countries for Tuberculosis (TB) as defined by WHO. The Government of Bangladesh conducted a national TB prevalence survey in 2015-2016 using WHO recommended methods to estimate the prevalence of bacteriologically confirmed pulmonary TB cases among 15 years and older population. WHO provided technical and financial support to conduct the survey.

Methods: Bangladesh is one of the first countries to use Xpert MTB/RIF for every positively screened participant in the Survey. Total 108,834 (73.5%) participants were registered as eligible respondents. Among them, 98,710 (90.7%) participated in the survey. Every participant was interviewed for TB symptoms and received chest X-ray for screening. Those participants who screened positive requested to provide spot sputum followed by an early morning sputum sample. The sputa were examined at the National Tuberculosis Reference Laboratory for smear, culture and Xpert MTB/RIF.

Results: Total 20,594 (20.9%) participants were screened positive by interview and/or chest X-ray screening. For laboratory test, 20,463 (99.7%) specimens were collected. In the survey, 278 bacteriologically confirmed TB cases were identified either by Xpert MTB/RIF and/ or culture, Xpert MTB/RIF identified 256 (92.1%), microscopy identified 108 (38.8%) and culture identified 154 (55.4%) of these cases. The estimated prevalence of bacteriologically confirmed pulmonary TB was 287 per 100,000 population.

Conclusions: The use of Xpert MTB/RIF to confirm smear-positives reduces false-positive smear microscopy results. However, diagnosis of bacteriologically confirmed cases can be more than double if we use Xpert MTB/RIF for all presumptive cases in the TB control program.

PD-991-14 Category-wise burden of DR-TB diagnosed through Xpert® MTB/RIF: experience from Bangladesh

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Background and challenges to implementation: The NTP and its partners refer all presumptive DR-TB patients for GeneXpert MTB/RIF testing. The latest NTP criteria for GeneXpert MTB/RIF are: 1) Failure of Category I and II, 2) Symptomatic close contacts of DR-TB patients, 3) Non-converters of category I and II 4) All relapses (category I and II), 5) All treatment after loss to follow-up (category I and II), 6) All HIV-infected individuals, 7) Presumptive pulmonary smear negative cases and 8) Others as determined by the attending physician.

The objective of this study was to determine the proportion of *Mycobacterium Tuberculosis* (MTB) and Rifampicin Resistant TB (RR-TB) among presumptive DR-TB patients.

Intervention or response: Data from all 74,872 presumptive DR-TB patients tested by GeneXpert MTB/RIF was collected from the 38 GeneXpert sites between July 2015 and December 2016.
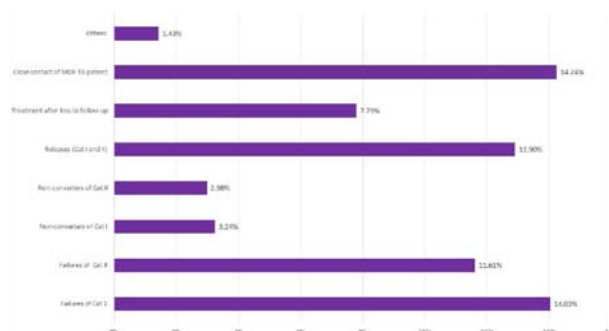
Figure RR-TB among different catagories of patients

Results and lessons learnt: Out of 74,872 presumptive DR-TB patients, 37.87% (28,353) were diagnosed as MTB and 5.42% (1,536) were diagnosed as RR-TB. The RR-TB patients were: 14.03% (156) failures of Cat I, 11.61% (18) failures of Cat II , 3.24% (398) non-converters of Cat I, 2.98% (15) non-converters of Cat II, 12.09% (419) relapses (Cat I and II), 7.79% (24) treatment after loss to follow up, 14.2 67% (35) close contact of an MDR-TB patient, 13.64% (3) HIV infected individuals, 5.04% (229) presumptive pulmonary smear negative cases, and 4.06% (239) others.

Conclusions and key recommendations: .Due to the high proportion of RR-TB, close contacts of DR-TB patients, failures of categories I and II, and relapse and

TB/HIV cases should undergo GeneXpert MTB/RIF testing. The new presumptive pulmonary smear negative cases category seems effective to diagnose more RR-TB cases that had previously been missed. The NTP needs to prioritize the referral mechanism for these high risk RR-TB group for GeneXpert MTB/RIF testing until the expansion of GeneXpert MTB/RIF machines reach all levels of the health system.

PD-993-14 Diagnostic value of Xpert® MTB/RIF in urinary tuberculosis in an HIV-negative population

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Background: Urinary tuberculosis (UTB) is a common form of extrapulmonary tuberculosis (EPTB), and delayed diagnosis can lead to permanent urinary organ destruction even renal failure. Limitations in sensitivity and the amount of time required for assays, render the conventional diagnostics of UTB inefficient.WHO recommended the Xpert MTB/RIF assay for the diagnosis of EPTB. However, Xpert are yet to be rigorously evaluated for the diagnosis of UTB.

Methods: In this prospective pilot study, Eighty-four patients with suspected UTB were consecutively enrolled from five Hospitals in China from February 2016 to February 2017. Urinary sediment samples were obtained for smear, culture and Xpert assays, in additional to routine clinical evaluation. Each patient was followed for 2 months until the final diagnosis was made. Cases were categorized as confirmed UTB, clinically diagnosed UTB, or non-UTB. The diagnostic parameters of Xpert was calculated.

Results: Fifty-five of the 84 patients were considered to have UTB, including 20 confirmed cases and 35 clinical diagnosed cases.The sensitivities of smear, culture and Xpert were 16.4% (9/55), 36.4% (20/55)and 45.5% (25/55), respectively, while the specificities of smear, culture and Xpert were 89.7% (26/29), 100% (29/29),and 100% (29/29),respectively.There was a significant difference between the MTB/RIF method and the smear method (P< 0.05,McNemartest). While the differences were not significant when the MTB/RIF method was compared with the culture method (P>0.05 McNemar test). The sensitivity of Xpert was 70% (14/20) for confirmed UTB and Xpert was positive for 35.5%(11/31) of smear-negative/culture-negative/CRS-supposed UTB patients.Xpert was 100% concordant with MGIT 960 or L-J drug-susceptibility test(DST) for the detection of rifampicin resistance.

Conclusions: Xpert appears to perform marginally better than culture for the diagnosis of UTB, and offers a suitable option for clinical practice.However,nearly 50% of cases were clinically diagnosed without microbiology proof, indicating the need for the development of other biomarkers.

PD-994-14 Performance of GeneXpert® MTB/RIF in the detection of TB-TB/RR in Kinshasa, DRC

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Background: The RDC is one of the 30 countries that pays the heavy tribute of the TB with 120 508 cases notified in 2015; and currently, the MDR-TB represents a major challenge with an impact of 13 cases for 100 000 inhabitants according to the report of the WHO (2015). Since 2010, the WHO recommended that the GeneXpert® MTB/RIF (Xpert) is included like initial test of diagnosis of the TB and the precocious detection of the TB-RR.

This survey aims to value the performance of the Xpert in the diagnosis of the TB and TB-RR and to determine the frequency of the probes implied in the detection of the mutations on the gene rpoB in Kinshasa.

Methods: It is about a retrospective survey led within the National Laboratory of Reference of the Mycobacteria (LNRM) of Kinshasa, in DRC. The data of the Xpert tests done from January 01, 2016 to December 31, 2016 have been collected then exported on Microsoft Excel 2010, treated and analyzed.

Results: Of the 1481 Xpert tests done, 1450 (97%) succeeded with 41% of *Mycobacterium tuberculosis* detected of which 73 (12%) were TB-RR. The probes associated to the detection of the mutations on the gene rpoB presented themselves as follows: E (46/73), D (14/73), B (9/73), A (4/73) and no resistance to the rifampicin was associated to the C probe. Any sample had presented a combination of probe in the detection of the resistance to the rifampicin.

Conclusions: The Xpert test has been executed with success within the LNRM of the city of Kinshasa and permitted to detect to 63.1% the E probe as the one detecting the more of mutations on the gene rpoB.

PD-995-14 Trend analysis of Xpert EQA results for facilities enrolled in the CDC-supported EQA program in Zambia

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Background: Zambia started participating in the CDC supported EQA program for GeneXpert in 2015. A total of 25 facilities were enrolled in the program out of the 55 that have GeneXpert. In 2015, two panels, A and B were received. In 2016, three panels were received but at the time of data analysis, results were only available for two panels, A and B.
Methods: Data was collected from the feedback reports that are sent for each facility. An excel spreadsheet was used to compile the data. The criteria used for grading of panels was adapted as set by CDC.
Results: Results from round 2015A had 14 facilities participating in the EQA program. Of these, 9 had satisfactory performance. The reasons for the unsatisfactory performance were false negative (4) and positive result (1) and error results (4). For 2015B, a total of 18 facilities participated and all showed satisfactory performance. In round 2016 A and B, a total of 16 facilities participated and they all had satisfactory performance. For 2015B, 2016 A and B, errors were still being recorded by facilities though the error codes were missing.
Conclusions: Despite challenges that were being experienced by Zambia in terms of distribution of panels and transmission of feedback results, GeneXpert EQA is a critical component of improving diagnosis of TB. The EQA was able to highlight some of the operational challenges that facilities are having in providing quality results to the patients and from this analysis, a marked improvement in result quality has been noted in later panels. As a country, there is need to have a robust corrective action program in place that will include staff training and timely equipment maintenance to support the EQA program.

PD-996-14 Xpert® MTB/RIF assay testing in the diagnosis of patients with tuberculosis; experience under programmatic conditions in Tanzania

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Background: GeneXpert MTB/RIF assay (Xpert) is an automated diagnostic tool with established diagnostic performance in tuberculosis but its optimal performance in reducing treatment delays under programmatic condition has not been determined in Tanzania. We conducted a study to compare the performance of GeneXpert and smear microscope with a special focus on the impact on time to start antituberculous therapy.
Methods: Cross-sectional study was conducted from January 2014 to June 2016. We included three facilities with GeneXpert termed as Satellites sites and three with smear microscope without GeneXpert machine, termed as non-satellite sites.
Results: Total of 491 TB patients were enrolled, 317 from Satellites facilities. Males were 324 (66.0%) with long duration cough as their main symptom. Mean (SD) and median (IQR) days from onset of symptoms to treatment for satellite facilities was 20.1 (65) and 2 (1-5) days respectively while for non-satellite was 48.5 (81.7) and 6.5 (2.5-65.5) days respectively; both mean and median days differences between satellite and non-satellite was statistically significant p=0.001. While mean (SD) and median (IQR) days from onset of symptoms to consultation for satellites sites was 47 (42.1) and 25 (12-49) respectively, for non-satellites was 64.7 (102.4) and 29.5 (9-79) respectively. It took 3.3 (SD=22.4) mean days (median=1; IQR=1-2) from first consultation to suspicion in satellites facilities while for non-Satellite the mean duration was 7.3 (33.7) and median=2 (IQR=1-4) days; both mean and median differences was statistically significant; p=0.001. It took 19.8 (SD=65.5) mean days (median= 2; IQR=1-6) from first consultation to starting on treatment in the Satellites sites while in non-Satellites sites it takes 48.4 (SD=81.7); median 6.5 days (IQR=2.5-60); mean and median difference was statistically significant; p=0.001.
Conclusions: Patients who attended GeneXpert satellites sites had short mean and median days for TB diagnosis and treatment compared to facilities without GeneXpert.

PD-997-14 The epidemiological impact of universal access to quality tuberculosis care: a simulation study

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Background: Many high-burden countries have committed to providing universal access to high-quality diagnosis for tuberculosis (TB). Compared to traditional models of centralized testing for TB, decentralized testing may provide faster diagnosis, improve accessibility and reduce loss to follow-up, but the corresponding impact on population-level incidence is unknown.
Methods: We designed an individual-based simulation of a drug-susceptible (DS) and drug-resistant (DR) TB in a representative Indian setting. The simulated populations represent catchment areas of Designated

Microscopy Centers (DMCs) - local health clinics with capacity for sputum smear microscopy - sharing a District TB Center (DTC) - a referral facility with more advanced laboratory capacity designed to serve several DMCs. We compared the impact of introducing Xpert testing via a decentralized (availability at each DMC) versus centralized (availability at the DTC-level, transporting samples from DMCs) strategy.

Results: Prior to the introduction of Xpert, the DS-TB incidence in our simulated population was 167 [95% uncertainty range: 137 - 203], and the DR-TB incidence was 9 [0 - 55] per 100,000 person-years, with 2% [0 - 13%] of new and 19% [0 - 74%] of previously-treated TB patients having DR-TB. Decentralized testing resulted in a 38% [5% - 59%] reduction in DR-TB incidence at 10 years. The impact of centralized testing was sensitive to assumptions regarding associated pre-treatment loss to follow-up, and ranged from a 30% [-15% - 56%] to 20% [-18% - 48%] reduction in DR-TB incidence after 10 years with 20% or 40% loss to follow-up during the sputum transport process. Implementation of Xpert by either approach had a negligible impact (< 5%) on DS-TB incidence, largely due to the role of empiric treatment for DS-TB.

Conclusions: Decisions regarding choice of centralized vs. decentralized Xpert will heavily depend on the operational aspects of centralized Xpert and the level of loss to follow-up during sputum transport.

PD-998-14 Sensitization for clinicians followed by weekly service monitoring contributes to improved uptake of Xpert in Tigray Region, Ethiopia

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Background and challenges to implementation: As part of the Xpert MTB/RIF scale up program in Ethiopia, seven GeneXpert machines were installed and became functional in Tigray regional state. However, uptake for the service has been consistently low in the region. We assessed the contribution of sensitization workshops for clinicians and weekly monitoring in improving the uptake of the GeneXpert service in the Tigray region, Ethiopia.

Intervention or response: Sensitization on GeneXpert service was provided to 325 clinicians working on ART, OPD and TB clinics from health facilities in the region. Additionally trained Lab technologists were assigned as focal persons in each treatment center to monitor and report on the performance of the machines. Following the sensitization, weekly monitoring on the service uptakes was done. Excel sheet was used to enter and analyze the weekly data for 10 consecutive weeks for the pe-

riod December 19, 2016. -February 26, 2017. Immediate feedback was provided to each GeneXpert site on a weekly basis.

Results and lessons learnt: Of 1382 tests performed, 143 (11%) were found to be MTB+ (11%) with 13 of them having MTB/RIF+. Eighty seven of the performed tests (6.3%) became unsuccessful. The Xpert utilization rate increased from 26% in the first week to 48% by the 10th week, with the median utilization rate being 33%. The proportion of MTB+ detected increased from 5.4% in first week to 8.8% at the end of the tenth week. Whereas the rate of unsuccessful tests decreased from 7.2% in the first week to 5.5% in the tenth week.
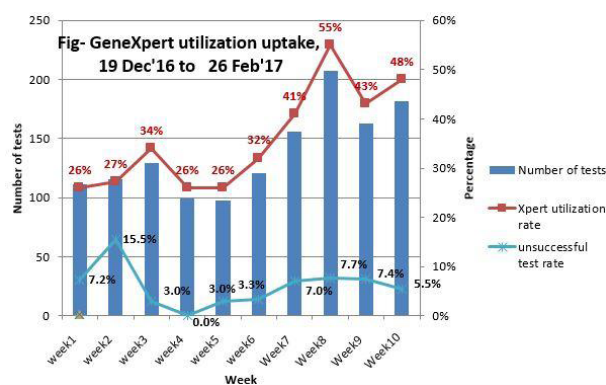
Figure GeneXpert utilization uptake in Tigray, 19 December 2016 to 26 February 2017

Conclusions and key recommendations: Sensitization and orientation of appropriate clinical teams combined with rigorous weekly monitoring contributed to steady increase in the rates of service utilization and yield of the test while unsuccessful results decreased. This approach needs to be sustained and further strengthened to maximally utilize the available services and improve the quality of services.

PD-999-14 Accuracy of different Xpert® MTB/RIF implementation strategies in programmatic settings at regional referral hospitals in Uganda: evidence for country wide roll-out

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Background: Xpert MTB RIF assay (Xpert) is a highly sensitive test for TB diagnosis, but still costly to most low income countries. Several implementation strategies, instead of frontline have been suggested, however with scarce data. We assessed accuracy of different Xpert implementation strategies to inform national roll-out.

Methods: This was a cross-sectional study of 1924 adult presumptive TB patients in five regional referral hospitals of Uganda. Two sputum samples were collected, one for fluorescent microscopy (FM) and Xpert examined at the study site laboratories. The second sample was sent to the Uganda Supra National TB reference laboratory for culture using both Lowenstein Jensen (LJ) and liquid culture (MGIT). We compared the sensitivities of FM, Xpert and the incremental sensitivity of Xpert among patients negative on FM using LJ and/or MGIT as a reference standard.

Results: A total of 1549 (81%) patients had complete results for FM, Xpert and culture. A total of 406 (%) were TB positive on LJ and /or MGIT culture. The sensitivity of FM was n (%; 95% confidence interval) 253 (64%; 59 - 69) overall compared to 64 (60%; 50 - 69) among HIV positive individuals, whereas the sensitivity of Xpert was 300 (77%; 72 - 81) and 80 (76 %; 67 - 84) overall and among HIV positive individuals respectively. Overall incremental sensitivity of Xpert was; 51 (37.2%; 29.1 - 45.9) and 18 (43.9%; 28.4 - 60.3) among HIV positive individuals.

Conclusions: Xpert has higher sensitivity than FM both in general population and HIV positive population. Xpert offers a significant increase in terms of diagnostic sensitivity even when it is deployed selectively i.e. among smear negative presumptive TB patients. Our results support frontline utilization of Xpert assay in high HIV/TB prevalent countries. In settings with limited access, mechanisms to refer smear negative sputum samples to Xpert hubs are recommended.

56. Infection control: ending transmission

PD-1000-14 Better reporting format of time indicators for improving patient-centered care: case studies from Nigeria and Viet Nam

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Background: FAST, a novel strategy, has been implemented in a number of countries to aim at reducing time to treatment initiation for infectious TB cases patients over the last five years. However time indicators for evaluating implementation results were not comparable among different countries since they were monitored and reported in various ways.

This study compared the same indicator presented as percentages of patients initiating treatment from confirmed bacteriological test result within two days, with in five days and more than five days recently reported by Nigeria and Vietnam.

Methods: This study re-grouped percentages of patients initiating treatment on same day, next day, within 3-5 days and >5 days reported as a result of FAST strategy implementation at four sites with GeneXpert machines in Nigeria in the first six months of 2016 at 47th Union World Conference on Lung Health into three groups used in the study. The same time indicators at two FAST sites with GeneXpert machines in Vietnam in the same implementation period were presented in the same three groups for comparison.

Results: These four sites in Nigeria achieved various results including 50%, 60%, 65% and 92% patients initiating treatment, compared to 82% and 89% patients initiating treatment from confirmed bacteriological test results within two days at the two sites in Vietnam. The four Nigeria sites respectively gained 100%, 83%, 90% and 99% patients initiating treatment within five days. The two Vietnam sites obtained similar results of 96% and 94% patients initiating treatment within five days.

Conclusions: The newly introduced reporting format of time indicators would better promote facilities to reach higher percentages of patients initiating treatment within targeted numbers of days and be easier to compare performance among different periods and sites. It also removed of effect of special cases with long delayed treatment initiation on average numbers of days previously reported.

PD-1001-14 'Cover your Cough' pantomime had high media coverage

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Background and challenges to implementation: TB Education and Propaganda Week (TBEPW) is designed to build public awareness and to educate students of primary and secondary schools. For 70 years, TBEPW was held in the first week of the year. Our aim is to present the main event in 2017 TBEPW.

Intervention or response: This year the idea was to mention a general health subject that is not specific for a disease. The theme was "cover your cough". Tuberculosis was hidden inside this general concept. A group of pantomime artists performed coughing and using handkerchiefs in a metro sitation and a train. Permissions were obtained from metro administration. Also media was informed for TB by an expert. Exhibition desks with the posters of "cover your cough" distributed paper handkerchiefs and brochures.

Results and lessons learnt: This activity was one of the primetime news in national TV channels: 9 TV channel made a news 15 times, average 2 minutes 29 seconds.

One of them was a children's TV. Seven national, 5 regional, and 10 local newspapers prepared a news. Many internet sites used this news. All news mentioned pantomime, covering the cough, tuberculosis (what it is, how one can protect thyself, and basic data). During this TBEPW, schools had a curriculum about TB. TB dispensaries and anti-TB associations made some activities against TB. They also used this pantomime and cover your cough in their activities. School children used their forearms and tissue papers for covering their coughs.

Conclusions and key recommendations: TBEPW is an important week for 70 years in Turkey to educate school children, to advocate TB control, to develop awareness of the political people. Also important massages from anti-TB associations, academic associations are shared. This years theme and performance of pantomime artists (medicine with art) in the metro gained a high interest. This shows us how an propaganda would be effective.

PD-1002-14 Good habits start young: 'Cover Your Cough' -school intervention program in Yangon, Myanmar

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Background and challenges to implementation: High rates of tuberculosis (TB) including MDR-TB indicate challenges in infection control and poor cough etiquette. (National Prevalence Survey 2009, 2012-2013 National Drug Resistant Survey) Young people, in their formative years may be more pliable and behaviorally compliant to infection control recommendations and this behavior may then be sustained lifelong. USAID Challenge TB (CTB) Project developed a school-based intervention program aimed at providing health education on TB and cough etiquette to school children of four high TB burden townships in Yangon region.

Intervention or response: CTB selected 4 townships in Yangon peri-urban areas according to epidemiological data from NTP. Five schools from each township were nominated by township education departments. A lesson plan with child-friendly messages on TB and cough etiquette was developed. The piloting session was conducted to ensure the content and process was easily understandable by school children. CTB trained 16 field staff to give health education sessions, and they worked together with school teachers to develop the intervention schedule. The activity was classroom-based with 45 minute health education sessions. Teaching aids were used to visualize the spread of TB bacteria and to appeal to 10 to 15-year old children.

Results and lessons learnt: During the eleven weeks of intervention, the team conducted 332 health education sessions to 20,035 children in 20 schools. 18,068 (90.2%) of the children could successfully engage with their

parents to convey the message about Tuberculosis and Cough etiquette. The team completed a pre-post assessment of 480 randomly selected students to evaluate the intervention. Significant improvement was seen in the questions regarding cough etiquette, 'Did you cover your cough/sneeze the last time you coughed/sneezed?' from 71.9% during pre-testing to 90.6% at post-testing. **Conclusions and key recommendations:** Findings provide evidence that school-based health education programs can be effective interventions for behavioral change regarding cough etiquette.
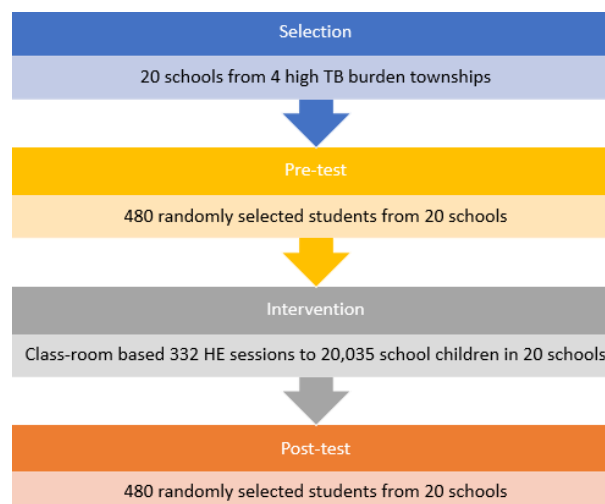
Figure Process of Cover Your Cough Activity in Schools

PD-1003-14 Use of the FAST model to prevent transfer of anti-tuberculosis drug resistance in two hospitals in Russia

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Background: Russia has one of the highest MDR-tuberculosis burdens in the world. Because the Russian system relies on hospitalization for diagnosis and early phase of treatment, nosocomial transmission is believed to contribute to the spread of drug-resistant tuberculosis, including to patients with drug-susceptible disease. Here we report the results of the FAST (Find cases Actively, Separate safely and Treat effectively) strategy on hospital-based acquisition of MDR-tuberculosis.

Methods: We conducted a quasi-experimental study using pre- and post-intervention cohorts in two Russian hospitals to determine whether being treated under the

FAST model resulted in reduced odds of "translation to MDR" (TB initially assumed or documented sensitive to isoniazid (H) and rifampin (R) with subsequent evidence of MDR (DST or switch to a second-line regimen) occurring on treatment or within 12 months of completion. Association between FAST and MDR translation was assessed through multivariable logistic regression.

Results: 1141 patients with known or assumed sensitivity to H and R were enrolled, 881 (77.3%) in the early cohort and 260 (22.7%) in FAST cohort. Eighty-three (7.3%) had translation to MDR. In unadjusted analysis, FAST cohort was associated with reduced odds of translation (OR 0.34, 95% CI 0.16, 0.72), and number of weeks spent in the hospital was associated with increased translation(OR 1.07, 95% CI 1.05, 1.09), including while adjusting for TB history, disease severity, and alcohol use disorders (AUD). An interaction existed between AUD and cohort; history of AUD was associated with a significantly increased odds of MDR in the early cohort (AOR 2.38 95% CI 1.37, 4.15), but not the FAST cohort, and among alcohol users, FAST cohort was associated with lower odds of MDR (AOR 0.08 95% CI 0.03, 0.27).

Conclusions: The FAST program was associated with significantly less translation to MDR after 12 months, and specifically in pan-sensitive TB patients with alcohol use disorders.

PD-1004-14 *M. tuberculosis* transmission from a non-citizen migrant to Israeli citizens during nursing home outbreak

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Background: Israel has absorbed >60,000 labor migrants from the horn of Africa (MHOA) between 2006 and 2012. Since then, no cross-transmission of *M. tuberculosis* from MOHA to Israeli citizens has yet been reported. This study describes the results of contact investigation and laboratory work-out of a unique mixed cluster which is the first to include non-citizen MOHA and Israeli citizens.

Methods: This cross-sectional study describes an outbreak in a nursing-home and the investigation that followed with its molecular findings.

Results: This outbreak started in a nursing institution in 2012, when a single MOHA who developed active disease infected three other close contacts- one was MOHA care-giver and two others were retarded Israeli-citizens residents staying in that institution, while one of them died. All isolates had drug sensitive *M. tuberculosis*.

A molecular work-up was commenced, and all four patients shared a similar strain of *M. tuberculosis* that has

not been presented in the SITVIT international database of genotyping markers. The strain included spoligotyping octal pattern 777737377720771 (24 MIRU-VNTR: 225313153523323222434572).

Between 2012 and 2016 additional tuberculosis patients who shared similar pattern were reported, accumulating to a total of 29 tuberculosis patients: 26 were non-citizens MOHA and three Israeli citizens. Epidemiological links were found in other 11 MOHA members of the cluster. Epidemiological links were found in other 11 MOHA members of the cluster.

Conclusions: This is the first report describing cross-ethnical transmission of *M. tuberculosis* from non-citizens migrants to Israeli citizens who were residents in a nursing home. Cross-ethnical transmission is rare, yet, it highlights the need to promote careful periodic screening of health care workers and migrants who are employed in health facilities.

Nevertheless, their follow-up might be interrupted because of lack of personal information, shortage of resources and potential movements of migrants between geographical areas.

PD-1005-14 Car screens for TB protection: smoke screens or infective barriers?

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Background: *Mycobacterium tuberculosis* (Mtb) is the leading infectious cause of death. Mtb spreads through airborne sputum particles produced by a patient with active pulmonary tuberculosis. Research participants and drivers traveling with masks contribute to stigmatization.

To protect drivers, custom-made vinyl screens are snugly fitted behind the front seats along the roof and sides to the floor of the car. Air should flow underneath the front seats to the back compartments, escaping through a back window. Efficacy of these protective barriers has never been validated.

Aim: Validation of the protective efficacy of vehicle TB screens.

Objectives: Determining efficacy of separation between driver and patient, and optimization of window and ventilation settings.

Methods: A smoke air flow test determined flow direction and extraction of air. Optimal ventilation settings (fan speed and window opening) were proposed and tested using a hand held particle counter.

Tetrafluoroethane gas was released from a multi-dose inhaler in the back compartment at three minute intervals whilst recording ten particle counts at one minute intervals in the front and back for various simulated driving conditions. Statistical analysis (paired t-test) was used to determine the significance of differences between compartments. Significance was set at p=0.05.

Conclusions: Preliminary results confirm our hypothesis that the screen effectively separates the front and back compartments during most driving simulations.

Released gas significantly increased small particle counts, only in the back, except when traveling at freeway speed with one window open. Increasing gas volume may result in a more conclusive analysis for this simulation. The initial results suggest screen efficacy as an infective barrier for driver protection and encourages further exploration through testing and statistical modeling.

PD-1006-14 Household contact screening of newly diagnosed sputum smear-positive tuberculosis patients at Kabula Dispensary, Bungoma County

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Background: The World Health Organization's (WHO's) "End TB Strategy" advocates for active case finding activities to have 90% tuberculosis (TB) case detection by 2030. WHO recommends for active screening among household TB contacts. Household contacts are highly susceptible to acquire TB infection from the index cases because of their close proximity. Active tracing of such contacts and their screening for TB could lead to the detection of additional cases of TB maximizing the impact of case detection and effective treatment.

Household contact tracing not only results in detection of additional cases but further offers several indirect advantages in the form of lead time obtained for these cases by early diagnosis, reduced duration of morbidity and reduced risk of transmission to others.

The aim of the study was to evaluate the yield of active case finding in household contacts of newly diagnosed smear positive TB patients.

Methods: Survey of household contacts of smear-positive TB patients (index patients) registered for treatment in 2016 at kabula dispensary were included in the study.

Results: 336 household contacts of 102 index TB patients were identified out of which 320 (95%) consented for screening. 97/320 (30%) patients had a cough. A total of 15/320 (4.6%) contacts were found to have TB smear positive.

Conclusions: Active screening among household contacts is an effective way to improve TB case detection.

PD-1007-14 Outcomes of tuberculosis infection control measures in public health facilities in Afghanistan: a document review

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Background and challenges to implementation: Ministry of public health of Afghanistan implements the general infection prevention strategy at public health facilities. However, the Tuberculosis (TB) infection control (IC) measures has not been addressed through this strategy. The United States Agency for International Development (USAID) funded TB projects (TB CAP, TB CARE I and CTB) assisted NTP to provide safer working environment for health care staffs, clients and community. Although, the effectiveness of these measures were not assessed.

The aim of this assessment was to evaluate the outcomes of these measures on TB case notification in intervention facilities.

Intervention or response: The CTB and NTP coordinated with health promotion and infection prevention departments of ministry of public health of Afghanistan (MoPH) and integrated TB IC into general IP guidelines, trained health care staff in selected health facilities and applied TBIC measures in total of 210 health facilities from 2011-2016. The study team reviewed TB surveillance data of 2011-2016 at these facilities. We used NTP standard quarterly reports as data collection tool.

Results and lessons learnt: TB IC measures were implemented in 210 health facilities out of all 360 eligible facilities for TBIC implementation. The coverage improved by 46%, from 45 (13%) in 2011 to 210 (59%) in 2016. Also, number of presumptive TB patients identified under these facilities improved by five fold, from 15,120 in 2011 to 69,348 in 2016. Similarly, 1,128 (7.4%) bacteriologically confirmed (BC) TB cases diagnosed in 2011 and it reached to 5,422 (8%) in 2016 (table 01).

Variables	2010	2011	2012	2013	2014	2015	2016
Existing eligible health facilities	360	360	360	360	360	360	360
TBIC coverage	45 (13%)	60 (17%)	80 (22%)	100 (28%)	145 (40%)	185 (51%)	210 (59%)
Presumptive TB patients identified	15120	20,050	26,024	31,142	39,146	54,729	69,348
Bacteriologically confirmed TB cases notified	1,128	1,755	2,555	3,090	3,581	4,017	5,422

Table Contribution of TBIC on case detection 2011-2016

Conclusions and key recommendations: The TB IC measure implementation resulted in increasing access to TB services at intervention facilities and early identification, diagnosis and treatment of TB patients. Thus, we strongly recommend scaling up TBIC measure application to additional health facilities in Afghanistan.

PD-1008-14 Firefighting in MDR-TB control: assessment of infection control status of households in Southern Ethiopia

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Background: Direct transmission is the main driver of the epidemic of MDR-TB in our world. Patients may have been infectious even before they are known to be with drug resistant TB. Poor ventilation and cough hygiene practices at household level could facilitate transmission among families and close contacts. We aimed to assess the infection control status of MDR-TB patient houses and proportion of close contacts exposed and propose feasible actions needed to reduce risk of exposure.

Methods: Cross sectional survey was conducted from Oct 10, 2016 - Jan 6, 2017. Data analyzed using EpiData 3.1 software.

Results: A total of 78 MDR-TB patients (43.6% female) were enrolled of whom 13 (16.7%) were HIV positive. Of the houses of MDR-TB patients assessed, 42/78 (37.7%) had single room and 29/78 (37.7%) had one window and 8/78 (10.4%) had no window. The ventilation status of houses at the time of visit was for 38 (48.7%) had closed windows and 40 (51.3%) were with open window/s and door/s. Most of the patients 66 (84.6%) said they cover their mouth when coughing and 51 (65.4%) spit their sputum using covered container while 27 (34.6%) of them spit anywhere including toilet. A total of 334 household contacts were living with the 78 MDR-TB patients, mean household size was 4.28 (Standard deviation 2.32) and 22 (6.6%) were age ≤ 5 years and 14 (66.6%) of these children shared bedroom with the index case.

Conclusions: In general infection control status of MDR-TB patients houses was inadequate and many close contacts including children were identified. These contacts may have been exposed and hold future risk of the disease. Appropriate measures of infection control at household level is essential to prevent future cases of MDR-TB. Community awareness and involvement including community health workers' training on basic infection control need to be prioritized and promoted.

57. MICs, MAC, and immunity

PD-1009-14 Towards a TB biomarkers database: a systematic review of biomarkers for active tuberculosis diagnosis

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Background: Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is the top infectious disease killer and remains a challenge to accurately diagnose. As 1.5 million of the 10.4 million people with new TB cases die each year, timely diagnosis and treatment is critical. However, traditional diagnostic methods, such as culture or smear microscopy, are slow or low in sensitivity; more modern techniques, such as sequencing or GeneXpert MTB/RIF, often require specialised facilities, are financial costly, or are otherwise inaccessible to populations at greatest risk of contracting TB. Biomarkers to detect active TB have been proposed as the bases for new diagnostic assays, representing a possible solution to the persistent problem of TB diagnosis.

Methods: In collaboration with FIND and in relation to WHO's high-priority Target Product Profiles we are conducting a systematic review of non-sputum biomarkers for the detection of active TB. A comprehensive search term was composed and used in multiple scientific databases.

Results: Initially, 6543 publications from 2010 to 2016 were identified. After removing duplicate articles, 3970 records remained and were screened by title and abstract. Finally, 375 publications fulfilled the inclusion criteria for full-text data extraction. Types of biomarkers identified included antibodies, cytokines, metabolic activity markers, Mycobacterial antigenic proteins, and volatile organic compounds. Only 51% of studies reported a culture-based reference standard and diagnostic performance data beyond p-values. A large proportion of studies repeated the findings of other discovery-phase studies without moving the biomarker to the next developmental stage.

Conclusions: Overall, more well-designed and independent validation studies that incorporate intended diagnostic use-cases are needed. The extracted data are currently being used by FIND as the foundation of a dynamic database in which biomarker data and developmental status will be presented. Ultimately, this database will enable developers and researchers to populate the TB biomarker pipeline, accelerating diagnostic test development.

PD-1010-14 Gestión en vigilancia a la resistencia de medicamentos antituberculosos en 8 ciudades de Colombia, 2014 - 2016

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Background and challenges to implementation: En Colombia para el año 2016 se reportaron 12658 casos de tuberculosis y 409 con resistencia a los medicamentos; el Programa Nacional ha trabajado el fortalecimiento de la vigilancia y manejo clínico - programático. El proyecto "Alto a la Tuberculosis" financiado por el Fondo Mundial, seleccionó las ciudades que aportaban el 50% de los casos del país (Medellín, Cali , Pereira, Cúcuta, Bucaramanga, Villavicencio, Bogotá y Barranquilla), priorizando para vigilancia de la resistencia los pacientes nuevos con factores de riesgo (coinfección con el virus de inmunodeficiencia adquirida, baciloscopia positiva al segundo mes de tratamiento, trabajadores de salud, contactos de casos multidrogorresistentes) y previamente tratados.

Intervention or response: Para aumentar la detección de casos de tuberculosis farmacorresistente se estableció el indicador de porcentaje de casos nuevos con factores de riesgo y previamente tratados con resultado de prueba de sensibilidad a los fármacos y/o cultivo negativo. La línea de base para 2012 fue del 31% y se planteó una meta del 70%. Se implementaron procesos de articulación Programa y laboratorio, se hizo transferencia de técnicas moleculares, gestión de conocimiento entre otros, incrementando el acceso a pruebas de sensibilidad, se fortaleció el monitoreo y evaluación de las actividades y el sistema de información a través de la recopilación, consolidación y el cruce de la información entre las fuentes existentes.

Results and lessons learnt: En el año 2014 el indicador se reportó en 34,4%, para el 2015 en 56% y el 2016 fue de un 62%, evidenciándose que las estrategias utilizadas impactaron en la detección de casos, diagnóstico de calidad, tratamiento adecuado.

Figura 1. Porcentaje de pacientes nuevos con factores de riesgo y previamente tratados con resultado de prueba de sensibilidad a los fármacos antituberculosis y/o cultivo negativo en 8 ciudades priorizadas, 2014 - 2016.
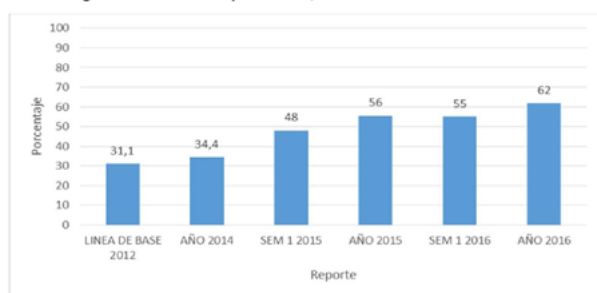
Fuente: Libro de pacientes de Tuberculosis de las ciudades de (Villavicencio, Medellín, Cúcuta, Pereira, Barranquilla, Bucaramanga, Cali y Bogotá) año 2016 y bases de datos del laboratorio nacional de referencia.

Figura 1

Conclusions and key recommendations: Se aportó a las metas del Programa relacionadas con el aumento de la curación y la reducción de tasas de mortalidad en las ocho ciudades seleccionadas. Actualmente el Programa Nacional promueve la expansión de estas actividades en todo el territorio nacional, buscando mejorar las metas del país.

PD-1011-14 Serum biomarkers in children and adolescents: a tool for differential diagnosis of latent and active TB?

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Background: Children, who represent approximately 10% of tuberculosis (TB) cases worldwide, develop paucibacillary forms of the disease and thus have bacteriological tests with low diagnostic yield. Additionally, despite having higher sensitivity, the tuberculin skin test and interferon gamma assay are limited in their ability to discriminate latent infection (LTBI) from active pulmonary tuberculosis (PTB) in these patients.

Methods: The purpose was to evaluate serum levels of IgM anti-cardiolipin, -sulfatide, -mycolic acid, -mce1a and IgG anti-mce1a in children and adolescents with LTBI or PTB. This cross-sectional study was conducted from August, 2015 to December, 2016. A convenience sample was collected at seven health units in the state of Rio de Janeiro, Brazil where patients 0 to 19 years of age with diagnosis of LTBI and PTB were invited to participate in the study. Asymptomatic individuals, aged 0-19 years, with a history of contact for TB and with negative TST were included as the control group. Biomarkers were measured using the ELISA method.

Results: The study included 28 patients with PTB, 33 with LTBI and 20 controls. In participants with PTB, 57.4% were over 10 years of age, 53.4% had a positive contact history and 50% had positive acid-fast and/or culture assays. Of the 81 participants studied, only one did not receive the BCG vaccine. Serum levels of IgM anti-cardiolipin, -sulfatide, -mycolic acid and mce1a were not significantly different in the PTB, LTBI and control groups. Serum IgG anti-mce1a levels were significantly higher in participants with PTB (median=0.3585; IQR 0.175-1.253) when compared to those with LTBI (median=0.2186; IQR 0.0632-0.5768; $p = 0.0001$) and controls (median=0.2243; IQR 0.0494-0.635; $p = 0.0013$).

Conclusions: Serum levels of IgG anti-mce1a are distinct in patients with active and latent TB, indicating that this biomarker may serve as a differential diagnostic tool in children and adolescents.

PD-1012-14 Evaluation of TrueLab for rapid, simple and cost effective detection of *M. tuberculosis* in EPTB specimens

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Background: The effective control of tuberculosis (TB) is impeded by a lack of rapid, accurate and affordable diagnostic methods. Available diagnostic tools are seriously limited by their speed, cost, technical complexity, difficulty in scale-up, and less-than-ideal accuracy. A few point of care key tools or interventions, if developed, could therefore greatly assist existing control programs. TrueLab assays have shown utility in identifying pulmonary tuberculosis infections. However, the method has yet to be evaluated for the diagnosis of extra pulmonary tuberculosis (EPTB) infections.

Methods:
1. Checking specificity of the primers and probes with bacterial panel and NTM panel: **n=50**
2. Detection of TB on TrueLab for 275 non-pulmonary tuberculosis clinical specimens. In comparison with acid-fast bacilli smears, MGIT960 cultures, RT PCR on ABI 7500 and GeneXpert (GX) testing were performed on all specimens for reference.

Results: In comparison to MGIT960, the pooled sensitivity and specificity of TrueLab in detecting TB among the EPTB specimens was found to be 78.3% (CI 68.4%-86.2%) and 83.9% (CI 77.7%-88.9%) respectively. Biopsy, bal, tissue, abscess, lymph node and body fluid are having sensitivities as 100% (CI 39.8%-100%),84.6% (CI 54.6%-98.1%),83.3%(CI 35.9%-99.6%),82.6%(CI 68.6-92.2), 71.4%(CI 41.9%-91.6%) and 44.4%(CI 13.7%-78.8%) respectively.

Conclusions: The lightweight, portable nature of the devices makes them deployable in peripheral laboratories. Current diagnostic strategies must be improved by both initial existing TB diagnostic capacity and integrating effective and rapid diagnostic technologies close to or at the POC for patients.

PD-1013-14 Aptamers specific for pyrazinoic acid as a new tool to determine pyrazinamide resistance directly from sputum samples cultures

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Background: Tuberculosis (TB) is still an important infectious disease that affects low-income countries. The most important problem related to TB is the increase of multidrug-extensively drug-resistant TB. Susceptibility tests exist for Rifampin and Isoniazid, including microbiological and molecular methods. However, for pyrazinamide (PZA) there are not any standard test to evaluate susceptibility. The detection of PZA resistance shows several disadvantages. Previous studies in our laboratory have demonstrated that pyrazinoic acid (POA) detection can be used as a biomarker to predict PZA resistance. PZA susceptibility of *Mycobacterium tuberculosis* strains can differentiate by the production of POA. Sputum samples cultures in presence of PZA can produce POA in the supernatant.

Methods: In order to detect POA in culture, DNA aptamers were identified through SELEX. Each SELEX cycle included an amplification, a transcription, and retro-transcription step. A library of 20N random aptamers was used in the process. A complex of POA linked to sepharose beads was target for positive rounds of SELEX. Sepharose beads were target for negative rounds of SELEX. To evaluate the enrichment, a Nuclease 1 assay was performed using dsDNA of each SELEX round. Libraries of different SELEX rounds were sequenced in Illumina MiSeq Platform. Sequences present in the negative round were discarded from all positive round sequence populations before to evaluate the abundance and enrichment across the SELEX process to identify the aptamers candidate.

Results: At least four sequences were identified. These sequences were selected according the ratio of abundance between each SELEX step. Currently, the binding capacity and specificity of the selected aptamers are being evaluated by ELISA and Cyclic voltammetry.

Conclusions: The use of aptamers can permit to develop a fast and specific susceptibility test to determine PZA resistance directly from primary cultures of clinical samples, contributing in this way to increase the adherence treatment by a correct susceptibility drug profile.

PD-1014-14 Minimum inhibitory concentrations of TB drugs

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Background: There is a need to establish the CC between media by means of determining the MIC of these drugs. This study evaluated the performance of Bedaquiline and Linezolid these media types.

Methods: Serial dilutions were made in 7H11 agar medium and in MGIT 960 liquid medium. 12 isolates were cultured on LJ slants. A 0.5 and 1 McFarland standard inoculum size was used for the liquid and solid media, respectively, as determined by a Nephelometer. After sedimentation, 100ul of the top third of the inoculum was diluted into 10ml of OADC containing 7H9 media. The broth was vortexed and 100ul was inoculated into the respective media. Isolates were incubated at 37°C for 21 days.

Results: MIC values for the BDQ resistant strains ranged from 0.125 ug/ml to 1 ug/ml. The H37Rv laboratory strain had an MIC value of 0.5 ug/ml for all media

types. The reference MIC values for the 5 LZD resistant strains ranged from 0.5 ug/ml to >32 ug/ml, whilst the MIC values on solid media ranged from 1 ug/ml to >16 ug/ml. The H37Rv strain had an MIC of 2 ug/ml on the REMA plate, whereas the MIC on solid agar was 1 ug/ml.

Conclusions: Expected BDQ MIC values are between 0.03 and 0.12 ug/ml for susceptible strains. A study showed an MIC range of 0.008 to 0.25 ug/ml on solid media and < 0.03 to 1 ug/ml in liquid media for susceptible strains, whilst the MIC for resistant strains on solid media and liquid media ranged from 0.5 to >4 ug/ml, and from 2.0 to >4 ug/ml, respectively. It can be seen that there is a difference in BDQ MIC values between the solid media and liquid media.

PD-1015-14 Qualitative characteristics of drug susceptibility of *Mycobacterium avium-intracellulare* complex (MAIC)

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Background: Mycobacteria of *M. avium - M. intracellulare* complex (*MAC*) are the main causative agent of human mycobacteriosis in Europe, USA, and in the Moscow region. Investigation of drug susceptibility (DS) of not only *M. tuberculosis* but also non-tuberculosis mycobacteria (NTM), first of all; MAC to antimicrobial drugs is an acute problem. To choose the optimal therapy, it´s very important to study the drug susceptibility/resistance level of each drug that can be used against mycobacteriosis caused by MAC.

The aim of the study was to determine the spectrum of MAC drug susceptibility/resistance to drugs.

Methods: We studied 177 (161 - *M. avium u* 16- *M. intracellulare*) *MAC* clinical isolates obtained from patients treated or took diagnostic examination in MRCCTC. Drug susceptibility to 13 antimicribial drugs was studied by microdilutions method in *Sensititre SlowMyco* test-system. We detected minimal inhibitory concentrations (MIC), calculated MIC_{50} and MIC_{90}, constructed the Kaplan-Meier survivance curves according to the Log-Rank critherion.

Results: We detected the spectrum of MIC of the main drugs used against MAC. MIC of amikacin, clarithromycin, linezolid were higher against *M. avium*, and MIC of ethionamide was higher against *M. intracellulare*. MIC_{50} and MIC_{90} of clarithromycin and MIC_{50} of linezolid were significantly higher against *M. avium*.

Conclusions: Using microdilutions method (*Sensititre SlowMyco*), we detected the spectrum of MAC DS to 13 antimicrobial drugs and distinguishes between DS of each spices included in MAC.

PD-1016-14 Resistance patterns of rifampicin resistant strains of *M. tuberculosis* isolated in Tajikistan

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Background: Tajikistan is a high TB prevalence country; one of the countries most affected by multi-drug resistant (MDR) and extensively drug resistant (XDR) TB. To improve early detection and treatment of MDR-TB, the National TB Program (NTP) introduced molecular tests for rapid diagnosis and increased access to drug susceptibility testing (DST) to first and second line TB drugs. This study aimed to analyze resistance patterns of strains, isolated from new and previously treated TB patients, and subsequently provide practical recommendations for speeding up diagnostic procedures and effective use of use of available diagnostic methods.

Methods: The retrospective study analyzed 2310 DST results from the NTP laboratory database, tested in 2016 by phenotypic DST methods. 606 Rifampicin (R) resistant strains, 546 new TB patients and 60 previously treated, were further analyzed for presence of resistance to other first and second line drugs: Isoniazid (H); Streptomycin (S); Ethambutol (E); Ofloxacin (Ofx); Kanamycin (Km) Capreomycin (Cm) and Amikacin (Amk).

Results: Out of 2164 new TB patients, 546 (25.2%) were R resistant, while among 146 previously treated, 60 (40,1%) were R resistant. Among all 606 R resistant cases, 554 (91,4 %) were MDR; 495 (90,7%) in new and 59 (98,3%) in previously treated patients. The most common resistance pattern in both groups was SHRE, detected in 339 (62,1 %) new and 43 (71,7 %) previously treated patients. Mono resistance to Rifampicin was found in 33 new patients (9,7%) and 0 previously treated. XDR and/or pre-XDR was detected in 150 (30,3%) new and 15 (25,4%) previously treated MDR-TB cases.

Conclusions: In high MDR prevalence setting R resistance can be used as a proxy for MDR TB. Rapid, molecular tests for DST are a valuable tool for early detection of resistance to first and second line of anti-TB drugs and should be used directly in all R resistant cases.

PD-1017-14 The reliability of PZA and other drug susceptibility testing against *Mycobacterium tuberculosis* in Japan

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Background: Pyrazinamide (PZA) is one of the key drugs for treatment of tuberculosis (TB). However, the drug susceptibility testing (DST) method for PZA is unique and many false-resistant results are reported. To know the accuracy of DST for PZA, the first external quality assessment (EQA) was implemented in Japan.

Methods: A total of 10 *Mycobacterium tuberculosis* (MTB) strains were prepared and sent to the participating laboratories. The strains were selected from the stocks used in the quality assurance activity among supra-national reference laboratory network. The major target of EQA was PZA, but other six major drugs were also assessed. DST was performed using routine methods and the results were compared with the judicial diagnoses. The evaluation factors were sensitivity, specificity, agreement and kappa coefficient.

Results: A total of 97 facilities participated in this study. A total of 60 facilities performed phenotypic PZA susceptibility testing, and resulted the sensitivity of 96.4% (95% CI; 86.9-99.3%) and specificity of 64.4% (95% CI; 50.8-76.1%). 44 facilities used Kyokuto PZA liquid medium (Kyokuto PZA; Kyokuto Pharmaceuticals) and 16 used MGIT series PZA (MGIT AST PZA; Becton Dickinson). The specificities of Kyokuto PZA and MGIT AST PZA were 69.5% (95% CI, 69.2-69.8%) and 48.8% (95% CI, 48.3-49.2%), respectively. There was a significant difference in specificity between two kits (p=0.0043).

Conclusions: The specificity of current PZA DST kits was quite low. This study implied that PZA can be stopped by the doctor according to the wrong DST result. The clinical loss should be reduced by appropriate training of DST for PZA, and by alternative DST like line probe assay or pyrazinamidase testing.

LATE BREAKER PRESENTATIONS FRIDAY 13 OCTOBER 2017

ORAL ABSTRACT SESSIONS

10. The Union/CDC late-breaker session on TB

OA-2490-13 Tuberculin skin test conversion and primary progressive disease in South African infants and young children: a longitudinal birth cohort study

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Background: The epidemiology and burden of tuberculosis in young infants is not well understood. We report tuberculin conversion and primary progressive disease in the Drakenstein Child Health Study, a prospective South African birth cohort where community-wide disease incidence is hyperendemic.

Methods: We enrolled 1143 pregnant women (22% HIV-infected) between 20-28 weeks gestation in a peri-urban, low socioeconomic area. All mothers accessed care in the public sector including an effective mother-to-child HIV-prevention program and universal BCG-vaccination. Mother-child pairs were followed through infancy and early childhood. Tuberculin skin tests (TST) were administered at 6, 12, 24, and 36 months of age, and at a lower respiratory tract infection (LRTI) event; new-borns were considered infection-free at birth and tuberculin conversion was defined as an induration $\geq$10mm. To prevent tuberculin boosting, infants with any measurable, but not positive, induration were censored and not re-tested. Children were followed for active tuberculosis disease until April 2017 or five years of age.

Results: 915 children (99% HIV-negative) were administered at least one TST and included in this analysis. Cumulative annual risk of conversion was 8% at six months of age and consistently increased with age reaching 34% after 36 months (P_{trend}< 0.0001). Incidence per infant-year of tuberculin conversion, clinically or microbiologically diagnosed tuberculosis disease, or microbiologically-confirmed tuberculosis disease was 12%, 2.5%, and 0.6%, respectively. Among converters, INH preventive therapy was extremely effective in preventing disease progression (Adjusted Hazard Ratio, 0.07, P< 0.0001). Risk factors for diagnosed tuberculosis disease included tuberculin conversion, an LRTI event, and maternal smoking.

Conclusions: *Mycobacterium tuberculosis* infection and primary progressive disease was strikingly high in infants and young children in this South African cohort, suggesting substantial undiagnosed tuberculosis disease and transmission. These observations warrant implementation of health interventions, such as active case finding and preventive therapy, beginning early in life in high-burden settings such as South Africa.

OA-3002-13 Improving tuberculosis laboratory capacity in Mexico: evaluation of a binational public-private strategy.

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Background: Diagnosis of TB in Mexico does not routinely include culture and drug susceptibility testing. Efforts are underway to improve this capacity. We evaluated a strategy that included sputum transportation by airplane and a partnership with a U.S. mycobacteriology laboratory in Mexico.

Methods: A cohort of patients with newly suspected TB (defined as never-treated sputum smear-positive, i.e., $\geq$1 acid fast bacilli [AFB] in $\geq$1 of 3 sputums) in public health TB clinics of 3 cities (Tijuana, Ciudad Juarez, and Reynosa) from May to December, 2016, were evaluated. After baseline examination with Ziehl-Neelsen locally, one of 3 sputums was stored and transported to the laboratory biweekly. We compared our drug resistance (DR) results to the Mexican 2008 National (DR) Survey.

Results: Sputum samples from 413 patients were received. Of these, there were 327 (+) AFB fluorochrome stains; 394 (95%) mycobacteriology cultures; 385 (93%) *Mycobacterium tuberculosis* by SD TB Ag MPT-64; 9 (2%) cultures of non-tuberculosis mycobacteria; 16 (3.8%) negative cultures; and 3 (.7%) contaminated specimens without results. Of the *M. tb* (+) cultures, 343 (89%) were susceptible to all four first-line drugs, 34 (9%) were resistant to only 1 drug, 8 (2%) were resistant to >1 drug (including 4 resistant to isoniazid and rifampin). Resistance was more likely against isoniazid (6%) and pyrazinamide (5%). Rifampin monoresistance was identified in 1 patient. There were no significant differences in patterns of resistance among the participating cities.

Conclusions: The culture-based, centralized-laboratory diagnostic strategy evaluated was highly successful with negligible losses. The intervention resulted in early and

effective treatment management in 3 patients with confirmed rifampin resistance based on second-line drug susceptibilities, and a potential non-diagnosis of TB for investigation in 25. The drug resistance prevalence was relatively low and almost unchanged from 2008. We conclude that regionalization of laboratory services can improve TB diagnostic capacity in Mexico.

OA-2962-13 The yield and cost-effectiveness of mass digital chest X-ray screening for TB detection in South African correctional facilities

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Background: Correction inmates are at a high risk of tuberculosis (TB). Mass symptom-based screening has low sensitivity, potentially delaying diagnosis of TB. We estimated yield and cost-effectiveness of adding digital chest X-ray to symptom screening at correctional facilities in South Africa.

Methods: Retrospective analysis of a mass TB screening programme in 64 correctional facilities in South Africa between January and December 2015. Mobile digital X-ray units were used for TB screening among individuals without symptoms. Possible TB was defined as presenting with any of the WHO four symptoms and/or an abnormal digital chest X-ray assessed by the radiology technologist. Confirmed TB was defined as having a positive Xpert MTB/RIF. Costs were estimated using a bottom-up ingredient approach. The primary outcome was incremental cost-effectiveness ratio (ICER) per TB case detected comparing X-ray screening strategy to symptom screening-only.

Results: Of 62,808 inmates, 56.8% (n=35,652) had TB symptoms. Of these, 75.1% (n=26,766) were tested by GeneXpert, and 0.75% (n=200) were Xpert-positive. Among 27,561 inmates without TB symptoms, 19,932 (73.4%) were screened by X-ray and 9.7% (n=1,941) had an abnormal X-ray in which 6 additional TB cases (6/618, 1.0%) were GeneXpert positive. In a hypothetical cohort of 1,000 inmates, about half would have symptoms and 5.5% inmates would have no symptoms but an abnormal X-ray, detecting 0.4 additional cases at the total cost of $8,227. The ICER for X-ray was $20,541/TB case detected.

Conclusions: Having X-ray in addition to symptom screening was feasible and added yield of GeneXpert positive TB, but added considerable cost. The high proportion of inmates reporting symptoms may have affected the cost effectiveness of X-ray. We did not evaluate the potential value of X-ray for diagnosis of clinical TB or other lung diseases.

OA-2947-13 Could GeneXpert replace culture in TB prevalence surveys?

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Background: WHO recommends countries to conduct TB prevalence surveys every 5 years to assess their TB burden. Culture is considered the gold standard but requires expensive laboratory infrastructure and is centralized in most countries thus increasing the cost of surveys. Xpert MTB/RIF run on the GeneXpert platform has a significantly high sensitivity for MTB detection and rifampicin resistance. It does not require elaborate laboratory infrastructure and the testing process involves minimal specimen manipulation.

Methods: Kenya conducted a prevalence survey targeting 72,000 participants from 99 randomly selected clusters. Participants were screened for TB symptoms and with digital x-rays to determine eligibility to produce sputum. Sputum-eligible participants produced a spot and morning specimen that were transported to the National Tuberculosis Reference Laboratory (NTRL) in cold chain for testing. Fluorescence microscopy and culture on Lowenstein Jensen were performed on both specimens while Xpert MTB/RIF© was performed on the morning specimens.

Results: Of the 9,715 sputum eligible participants, 9,120 had at least one microscopy examination, 8,954 (92%) had Xpert MTB/RIF©, while 94% (9,121) had at least one specimen cultured. From the 305 prevalent cases, 108 (35%) participants were positively identified by all 3 tests, 15 were diagnosed through both microscopy and Xpert MTB/RIF©. A total of 65 (21%) cases were detected by culture alone while 90 (29%) cases were only detected through Xpert MTB/RIF©.

Conclusions: The inclusion of Xpert MTB/RIF© resulted in the detection of more TB cases compared to culture and its role in TB prevalence studies needs to be further investigated particularly in settings with no culture facilities. The versatility, minimal sample manipulation, its availability and accessibility make Genexpert a good supplementary method for TB prevalence surveys. Furthermore the connectivity of the GeneXpert platform would allow for real-time transmission of data and should routinely be used to monitor TB trends particularly in resource-limited settings.

OA-2950-13 Rifampicin dosage and exposure are associated with superior activity in the PanACEA MAMS-TB study

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Background: Higher dosages of rifampicin, at 35mg/kg, were shown to shorten time to negative culture in the MAMS-TB study. We now present pharmacokinetic and dose-response analyses from this trial.

Methods: Adults from Tanzania and South Africa with smear positive pulmonary tuberculosis were randomised to control or one of four experimental arms. One of those arms contained 35 mg/kg rifampicin in weight-banded daily dosages of 1,200 to 2,100 mg; combined with isoniazid, pyrazinamide and ethambutol, for 12 weeks. The primary endpoint was time to stable culture conversion in MGIT. Blood samples for pharmacokinetic evaluation were taken after four weeks of therapy.

Results: Culture conversion occurred much earlier with 2,100 mg RIF (hazard ratio [HR], compared to 450 mg RIF, adjusted for baseline bacterial load and patient gender: 2.76; 95% CI: 1.67 - 4.55;), and it occurred more frequently (91% of 23 patients). With the next lower dosage of 1,500 mg, only 63% of 45 patients achieved conversion (p = 0.015, for difference to 2,100 mg).

Number at risk						
450 mg	97	93	88	77	57	38	4
600 mg	75	71	64	48	35	23	2
750 mg	10	10	7	7	6	3	0
900 mg	71	71	61	49	32	21	3
1200 mg	45	44	39	36	24	17	0
1500 mg	41	40	34	23	17	9	0
2100 mg	23	20	18	10	4	1	1
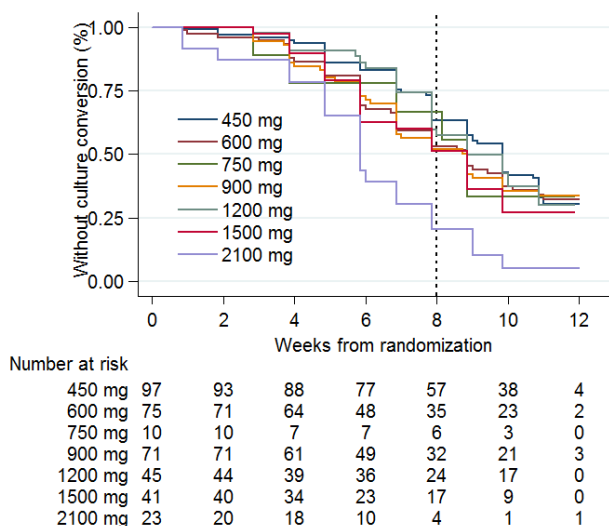
Figure Kaplan - Meier curve for time to culture conversion by rifampicin dose

Intensive pharmacokinetic data was obtained from 97 patients. Rifampicin area under the curve (AUC) was associated with absolute dose and fat free body mass (R2=0.83, p = 0.002 in multivariable regression). Absolute dose explained slightly more variation than dose per body weight. Time to culture conversion was significantly associated with RIF AUC when adjusted for baseline bacterial load and unavailable cultures (HR:1.008 per 1 mg*h/l AUC increase, 95%CI 1.002-1.015, p=0.016).

Hepatotoxic events occurred in 1 (4.3%), 3 (7.3%) and 2 (4.4 %) patients receiving 2,100 mg, 1500mg and 1,200 mg rifampicin, respectively.

Conclusions: A superior rifampicin effect was seen at a 2100 mg dosage, explained by associated higher rifampicin AUC values. Further studies should explore dosage per fat-free mass or individual dosage adjustments based on exposure, to revise the currently used weight banding for rifampicin.

OA-3028-13 What is the true tuberculosis mortality burden? Differences in TB mortality estimates by WHO and IHME

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Background: The World Health Organization (WHO) and the Institute for Health Metrics and Evaluation (IHME) periodically provide global estimates of tuberculosis mortality. We compared the 2015 WHO and IHME tuberculosis mortality estimates and explored which factors might drive the observed differences.

Methods: We extracted the number of estimated tuberculosis-attributable deaths, disaggregated by age, HIV status, sex, and country from publicly available WHO and IHME datasets for the year 2015. To explore potential drivers for the observed difference, we analysed the association of a standardized metric (adjusted standdiff) with potentially explanatory variables: case detection rate (CDR), HIV prevalence, prevalence of multidrug resistance, availability of prevalence survey results, and world region.

Results: For 195 countries with estimates from both institutions, WHO estimated 1,768,482 deaths attributable to TB, whereas IHME estimated 1,322,916 deaths, resulting in a difference of 445,567 deaths. The countries with the largest absolute differences were Nigeria (216,621 deaths difference), Bangladesh (49,863) and Tanzania (38,272). The standardized difference was not associated with HIV prevalence, prevalence of multi-

drug resistance or global region, but did show significant correlation with the case detection rate as estimated by WHO (r=-0.37, 95%CI: -0.48; -0.24) or, inversely, with case detection rate based on IHME data (r=0.42, 95%CI: 0.31; 0.54). Countries with a recent national prevalence survey had higher standardized differences than those without (p=0.04). After exclusion of countries with recent prevalence surveys the overall correlation between both estimates was r=0.991

Conclusions: A few countries account for the large global discrepancy in TB mortality estimates. The differences are likely to be due to differences in methodological approaches used by WHO and IHME, in particular the use and interpretation of prevalence survey.

OA-2905-13 Early safety and efficacy of bedaquiline and delamanid combination for drug-resistant TB in Armenia, India and South Africa

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Background: Two new drugs, Bedaquiline (Bdq) and Delamanid (Dlm), are approved for treatment of drug-resistant tuberculosis (DRTB). Safety concerns have limited their use in combination for patients in need. Médecins sans Frontières (MSF) has introduced the combined use of Bdq and Dlm for patients with limited treatment options in 2016.

We describe early safety and microbiological efficacy of regimens containing Bdq and Dlm in combination among patients in three epidemics hotspots, Armenia, India and South Africa.

Methods: This is a retrospective cohort analysis among patients who received the combination of Bdq and Dlm as part of their DRTB treatment regimen between January and August 2016. We report QTcF interval data, serious adverse events, and early efficacy, during the first 6 months of treatment.

Results: Twenty-eight patients were included in the analysis. Median age at start of the combination was 32.5 years. Twenty-four (86%) patients had isolates resistant to fluoroquinolone agents; 14(50%) patients had XDR-TB. No patient experienced increase >500 ms in QTc interval. Four patients experienced six instances of QTc increase >60ms from baseline; none of them led to permanent discontinuation of the drugs. Sixteen serious adverse events were reported among 7 patients. One patient, with advanced HIV, died during the study period,

likely as consequence of immune inflammatory reconstitution syndrome (IRIS). Of the 23 individuals with positive baseline cultures, 17(74%) converted to negative by month 6 of treatment.

Conclusions: Early safety and efficacy results of the use of Bedaquiline and Delamanid in combination for the treatment of DRTB were promising and reassuring in this multicentric cohort of patients treated under programmatic conditions.

11. The TB-HIV and diabetes late-breaker session

OA-2971-13 Diabetes increases mortality during tuberculosis treatment and metformin use reverses this effect

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Background: The global diabetes mellitus (DM) epidemic threatens progress made in reducing tuberculosis (TB)-related morbidity and mortality worldwide. Previous clinical studies have not fully evaluated or controlled for potential confounding variables in addressing the impact of DM on TB treatment outcomes. DM patients are a key group to study for potential TB treatment adjuvants, as the antidiabetic agent metformin regulates autophagy and may play a role as a host-directed therapeutic adjuvant to standard anti-tubercular treatment.

Methods: We conducted a retrospective cohort study comprising patients aged $\geq$ 13 years undergoing treatment for culture-confirmed, drug-susceptible pulmonary TB. We assessed the effect of DM on mortality during TB treatment and 2-month TB sputum culture conversion. We also evaluated the effect of metformin use on mortality during TB treatment.

Results: Among 2,422 patients undergoing TB treatment, after adjusting for age, sex, chronic kidney disease, cancer, cavitary disease, and treatment adherence, patients with DM had 1.65 times higher odds (95% confidence interval [CI] 1.33-2.05) of mortality during TB treatment than patients without DM, and among the 1,323 patients for which 2 month TB culture data was available, DM patients had 1.70 (CI 1.23-2.34) times higher odds of remaining culture-positive at two months. Among patients with DM, a significant association was found between metformin use and decreased mortality during TB treatment (Hazard Ratio 0.60, CI 0.42-0.84).
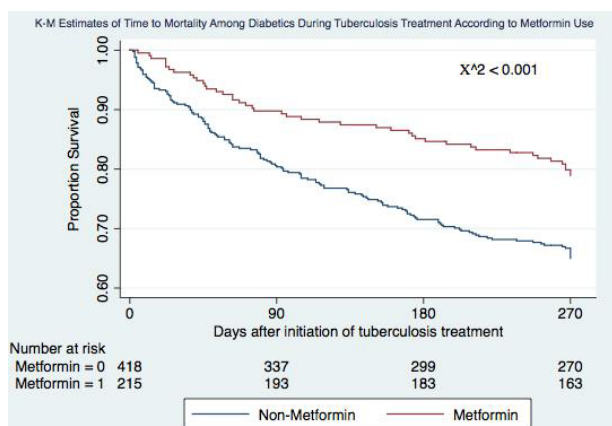
Figure K-M Curve, DM Undergoing TB Rx, by Metformin Use

Conclusions: This study suggests that despite multiple potential confounding variables, DM independently poses an increased risk of adverse TB treatment outcomes. There was a significant association between metformin use and decreased mortality during TB treatment, suggesting a potential role for this agent as adjuvant therapy.

OA-2885-13 Feasibility and yield of routine bi-directional screening for tuberculosis and diabetes mellitus in primary health settings in Zimbabwe.

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Background: Tuberculosis (TB) is a major public health problem in Zimbabwe. Diabetes (DM) increases the risk of developing TB as well as experiencing adverse treatment outcomes. No TB-DM collaborative program was in place at the time of implementing the pilot. Our aim was to get local evidence on feasibility and yield of implementing bi-directional screening for TB and DM in routine primary health settings.

Methods: The pilot was carried out in ten urban primary health facilities in Harare. TB patients were screened for DM using a random blood glucose (RBG). Those with an RBG $\geq$ 6.1 mmol/L would be screened with a fasting blood glucose (FBG) in their next visit. An FBG $\geq$ 7.0 mmol/L was used to confirm DM. Patients would then be referred to DM care. In every visit, all DM patients were screened for TB symptoms and sputum was collected among the presumptive cases for bacteriological confirmation.

Results: From April 2016 to March 2017, a total of 1 830 TB patients were notified and 47% got screened. Of these, 43% had RBG $\geq$ 6.1 mmol/L which is very high compared to what was observed in China. FBG was done in 74% of these patients and 7% got diagnosed with DM (figue 1).
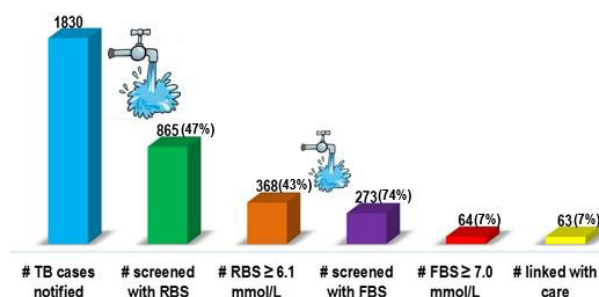
Figure TB patients screened in the 10 facilities

Among the 10 facilities, the rate of screening was different (range 30% to 83%). Shortages of screening reagents, low awareness, and poor staff motivation contributed leakages in the DM screening cascade. In addition, 1% (11/862) of all DM patients were diagnosed with TB. Most patients diagnosed with TB-DM were linked with appropriate treatment and care.

Conclusions: It is feasible to conduct bi-directional screening for TB and DM in primary health facilities in resource limited settings. However, there is need to ensure that staff receives adequate training and screening reagents are always available.

OA-2837-13 A rise in TB mortality where people who use drugs and commercial sex work co-exist: a retrospective cohort study in a rural county in Kenya

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Background: Kilifi County in Kenya is a rural area with high rates of poverty, drug use and commercial-sex work. Despite declining case notification rates, review of routinely collected program data reveals rising TB case mortality. This study aimed to describe clinical and demographic factors associated with the rising mortality among people undergoing TB treatment in Kilifi County.

Methods: A 4-year retrospective analysis of electronic TB surveillance data was conducted. Data was verified at the health facility level. We performed a survival analysis censored at 270 days or time of death/lost-to-follow-up. Trends in mortality and associated risk factors were tested using Wilcoxon rank-sum test for trend across ordered groups. Cox proportional regression analysis was used to identify risk factors associated with mortality.

Results: A total of 8783 participants, median (IQR) age 33 (24 to 45) years data were analysed. There were 2578 (29%) HIV infected participants with no linear trend over years. During 4296.2 person-years (PY) of observation, 470/8783 participants died (case fatality ratio

(CFR) 5.3 (95% CI 4.9 to 5.8)); mortality rate 11(95% CI 9.9-12) deaths per 100PY. The CFR changed from 3.8% in 2012 to 6.2% in 2015 (P=0.001), although there was no evidence of a trend. HIV infected participants had higher CFR 11% Vs 3.2% among HIV non-infected (P< 0.0001). Among HIV infected TB cases, the CFR changed with time; 7.8% in 2012 and 12.2% in 2015 (P=0.03), albeit with borderline significance of linear trend (P=0.08). HIV infection was associated with a high risk of mortality; adjusted Hazard Ratio 3.27 (95% CI 2.60-4.0). Other factors associated with mortality were age, body mass index, year of starting TB treatment and gender (Figure 1).
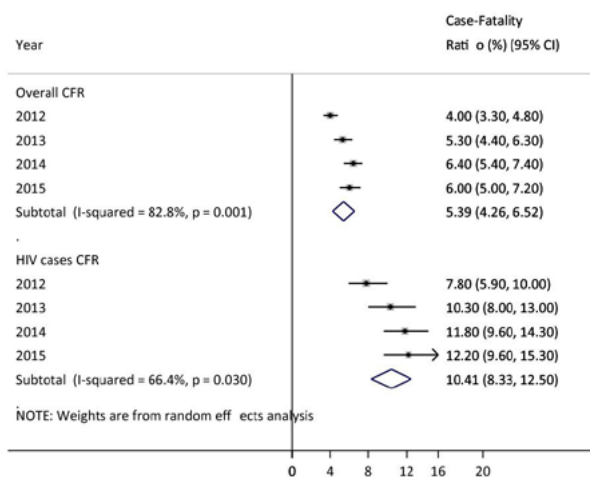
Figure 1 Changes in Case Fatality Ratios (CFR) for all participants and among HIV infected TB cases over years

Conclusions: This study confirmed an overall gradual rise in mortality and identified potential high-risk groups. While further research is needed, targeting high risk groups may reduce TB associated deaths.

OA-2927-13 Can HbA1c help to predict TB risk? Early results from an active TB case-finding project in Ebeye, Republic of the Marshall Islands

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Background: Despite recent improvements in tuberculosis (TB) control, the reported TB incidence rate in the Republic of the Marshall Islands (RMI) remains high at 344/100,000 (WHO, 2015). The prevalence of type 2 diabetes (DM) among adults in RMI is 28% (IDF, 2013), one of the highest DM rates globally. Recent screening for TB in one RMI diabetes clinic demonstrated 5% with active TB (Trinidad, 2016). This abstract describes the association of HbA1c and TB rates during a TB case-finding project completed on Ebeye Island in 2017.

Methods: With RMI Ministry staff, a multi-agency team evaluated all island residents over age 14 for Hansen´s disease and TB disease. For residents over age 20, testing for diabetes, hypertension, and hypercholesterolemia was added. The overall project goal was to provide program improvements with onsite training, as well as reduce on-going TB transmission by finding and treating prevalent TB cases.

Diabetes screening was accomplished with random glucose testing, adding HbA1c if blood glucose was elevated. TB screening included a symptom review and chest x-ray. If TB symptoms were present or the chest x-ray was abnormal, sputum was collected for GeneXpert testing.

Results: 5,165 individuals completed screening (86% of target population). 38 TB cases were identified, with 12 additional pediatric cases found during contact tracing of infectious cases. DM testing of 4,102 adults (>20 years-old) found 1,153 cases of DM (28%) including 410 newly diagnosed cases. The observed TB rate increased with higher HbA1c levels (Figure1).
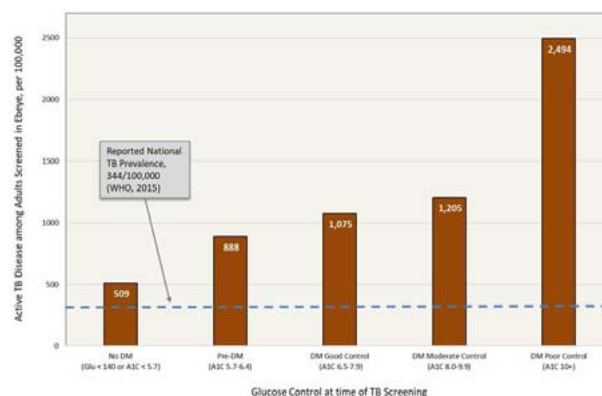
Figure 1 Active TB rate by diabetes status for adults in Ebeye, 2017 (n+4, 102)

Conclusions: In Ebeye, all levels of diabetes control were associated with an elevated risk for TB disease. Individuals with HbA1c>10% showed the highest risk (2,494/100,000). In countries where TB is prevalent, TB and DM programs should work together to screen, diagnose, treat, and prevent TB among DM patients. Public health programs can stratify TB risk by focusing on patients with poor glucose control.

OA-2887-13 ADPP Mozambique's strategies to track and support index HIV cases and their contacts through community-based interventions have been protecting PLHIV against TB in Mozambique

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Background: Maputo-province and Maputo-city are among highest HIV/TB burden regions in Mozambique with HIV prevalence around 23% and 17% in adults respectively. In 2016, more than 57% new TB cases were co-infected by HIV, estimated mortality rate in co-infected 120/100,000. ADPP Mozambique has been implementing two community-based projects in Maputo province; one in Matola district and the other in 5 municipal districts of Maputo city and 9 other districts, aiming to protect PLHIV from TB and premature mortality.

Methods: The interventions as performed by project's field counsellors and supervisors in collaboration with local public health facilities were, bringing household contacts and sexual partners of index HIV-infected under home-based HIV C & T, ART initiation of new cases, TB screening, adherence and retention services, health education, nutritional and socio-economic supports, retrieval of loss-to- follow up. The project used a unique IT-based mobile application to track patients in the community and linking them to health-facilities.

Results: Between 2015-16, the project, in Matola, reached 12,279 index cases and tested 113,075 contacts (184% of estimates) for HIV. About 10,312 were found infected (9%), of which 8,868 (85%) were put on ART, in turn 6,376 (72%) showed viral suppression (VS). In parallel 9,874 of HIV cases (96% of infected) were screened for TB. About 343 were found to be co-infected (3.5%), of which 341 (99%) were put on TB treatment, of which 276 (87%) successfully completed treatment. Similarly, the other project reached 31,489 index cases, tested 134,267 contacts (85% of estimates), 11,036 infected (8%) detected, 9,822 (89%) put on ART, 8,113 (83%) showed VS, 10,913 of infected cases (99%) screened for TB, 407 found to be co-infected (4%), 406 of them (99%) put on treatment, and 361 (90%) successfully completed treatment.

Conclusions: The projects candidly exhibited effectiveness of community-based approaches to protect PLHIV from TB and early mortality.

OA-3000-13 Detecting diabetes during latent TB testing

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Background: The association between diabetes and tuberculosis is well established, with a 3-fold increased risk of developing active TB among individuals with diabetes (DM). Prioritizing patients with latent tuberculosis infection (LTBI) for preventive treatment can be challenging for programs with limited resources and a high volume of LTBI patients. The goals of this work were to determine the prevalence of diabetes in a population at high risk for LTBI and to identify the most efficient point-of-care method for diabetes screening in a busy tuberculosis clinic.

Methods: As part of a larger prospective cohort study comparing the three commercially available tests for individuals at high risk for LTBI, we screened 375 adults for latent TB infection and DM. Participants were recruited at a tuberculosis clinic in Honolulu, Hawaii. Screening for DM was done using self-report, random glucose, and point-of-care HbA1c. Using HbA1c $\geq 6.5\%$ and self-report (for known diabetics with HbA1c < 6.5%) as the "gold standard" for diabetes diagnosis, we compared test strategies and glucose cutoffs to determine which methods were most accurate and cost-effective.

Results: Based on self-report and HbA1c results, 14% of the population had diabetes. More than half of DM patients were unaware of their diagnosis (Table 1). Glucose testing alone (cutoff 200 mg/dL) was inexpensive but missed 33% of DM cases. Self-reported DM with universal HbA1c was expensive ($9.67) and likely not feasible for most TB programs. Limiting HbA1c testing to patients with a random glucose of 120-180 mg/dL resulted in fewer misdiagnoses (3%; sensitivity 85%; specificity 99%) with an average test cost of $2.60 per person.

Testing Strategy	Additional Testing Cost per Patient	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Self-Report	$0.00	44%	100%	100%	92%
Self-Report + Glucose > 200	$1.22	67%	100%	97%	95%
Self-Report + Glucose > 180	$1.22	69%	99%	92%	95%
Self-Report + Glucose > 120	$1.22	85%	86%	49%	97%
Self-Report + A1C	$9.67	100%	100%	100%	100%
Self-Report + A1C if Glucose 120 - 180	$2.60	85%	99%	94%	98%

Table 1 Diabetes testing strategy characteristics in high risk latent TB N=375, diabetes=52

Conclusions: A diabetes screening strategy that combined self-reported diabetes status with HbA1c for patients with random glucose of 120-180mg/dL was accurate and relatively low cost. This may be a feasible and affordable method for TB programs to prioritize LTBI treatment for diabetic patients.

14. The Union student late-breaker session on lung health

OA-2926-13 Sensitivity and specificity of a novel nanogold assay in detecting patients with active pulmonary TB

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Background: TB nanodiagnostics have witnessed considerable development. However, most of published reports didn't proceed beyond proof-of-concept. This study aims to evaluate sensitivity and specificity of a nanogold assay for detection of TB DNA in sputum as an add-on diagnostic test, and to compare its clinical performance to sputum smear microscopy (SSM) and chest X-ray (CXR).

Methods: This is a diagnostic case-control study which includes 20 active TB patients, 20 non-TB chest patients who had previous history of TB infection, and 20 non-TB chest patients with no previous history of TB infection. Sputum culture (BACTEC™ MGIT™) was the reference test.

Enrollment was initially based on medical history, clinical examination, and results of SSM and CXR. The final classification was done when culture results were obtained. DNA was extracted from sputum, and unmodified anionic gold nanoparticles (AuNPs) were added to TB amplicon after PCR amplification of IS6110 DNA. Color change of AuNPs was observed by a reader who was blinded to participants' data. Statistical testing of sensitivity and specificity was conducted using ROC curve analysis and diagnostic odds ratio (DOR).

Results: Sensitivity and specificity of nanogold assay were 95% (95%CI 75.1-99.9), and 100% (95%CI 91.2-100.0), respectively, with DOR 1053.0 (P < 0.0001). The AUC was 0.975 (95%CI 0.897-0.998). The TB AuNP assay generated higher clinical performance (AUC 0.125; 95%CI 0.0288-0.221) than SSM and CXR (0.463; 95%CI 0.372-0.553). The turnaround time of the assay was 2 h.

Conclusions: The TB nanogold assay is accurate and has a potential for use as an add-on test to accelerate TB diagnosis in endemic countries. This is the first time to assess clinical performance of TB nanogold assay in real clinical settings. Future studies should adopt larger sample size for proper assessment of test accuracy.

1, 2, 3 = Active TB patients
4, 5, 6 = Controls (old TB)
7, 8, 9 = Controls (with no history of TB)
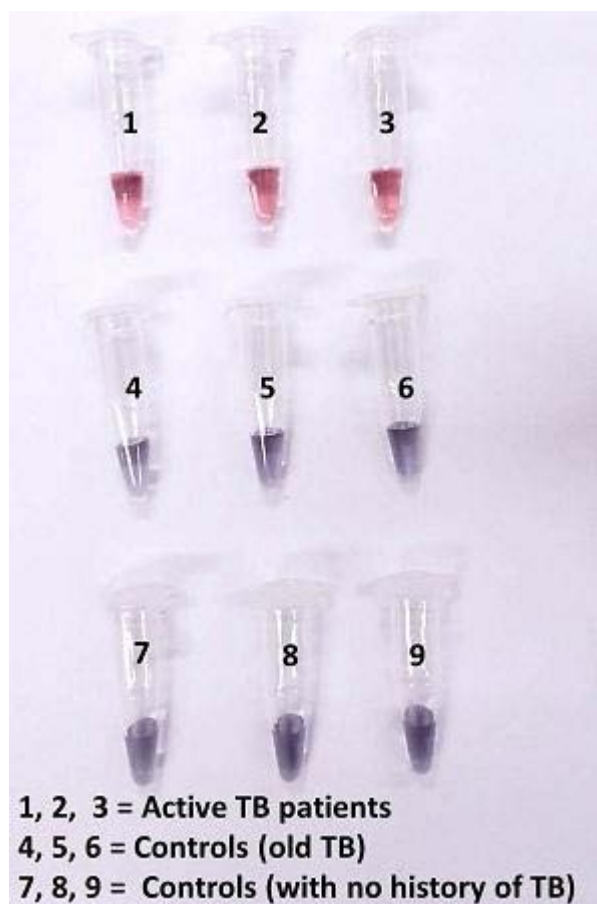
Figure Colorimetric result of gold nanoassay

OA-2960-13 The changing face of pediatric tuberculosis in high-income, low-incidence countries: a 25-year conventional and molecular epidemiologic case study

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Background: The epidemiology of tuberculosis (TB) in high-income countries is increasingly dictated by immigration. The influence of this trend on pediatric TB and TB elimination are not well defined.

Methods: We undertook a 25-year conventional and molecular epidemiologic study of pediatric TB in Alberta, one of four major immigrant-receiving provinces in Canada. All isolates of *Mycobacterium tuberculosis* were DNA fingerprinted using standard methodology.

Results: Between 1990 and 2014, 176 children aged 0-14 years were diagnosed with TB. In addition to having the largest rate increase over time, foreign-born children accounted for an increasingly large proportion of total cases during the study period (from 18.9% to 52.6%). Furthermore, all Canadian-born cases in the last ten years, 2005-2014, other than Registered First Nations (North American Indians) were children born to at least

one foreign-born parent. Foreign-born cases were least likely to have a putative source case. Of the 78 culture-positive cases, 35 (44.9%) had a putative source case identified by conventional epidemiology, 34 (97.1%) with a concordant molecular profile. Of the remaining 43 culture-positive cases, molecular profiling identified spatially and temporally related sources in 6 (14.0%). These 6 children along with 4 other children whose source cases were discovered through reverse contact tracing (index cases) faired poorly. Four died and 2 were survivors of central nervous system TB.

Conclusions: The increasing burden of pediatric TB in both foreign-born children and Canadian-born children of foreign-born parents calls for more timely diagnosis of source cases and more targeted screening for latent TB infection.

OA-2842-13 Impact of 2015 Southeast Asian haze crisis: particulate matter is associated with TB cases in Pekanbaru City, Riau Province, Indonesia

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Background: The thick smoke, containing concentrated particulate matter from massive forest fires in Sumatera Island, Indonesia, blanketed Southeast Asia region in 2015. Recently, studies have shown smoke affect human respiratory system and moreover there is an association between particulate matter (PM) and increased risk of tuberculosis (TB). However, the evidence is limited in Indonesia where the TB range third in the world. Here we present a study conducted on Pekanbaru, Sumatera, which has been frequently hit by smoke. There is a need to examine the association between the level of PM_{10} and TB cases.

Methods: The study analyzed 4263 new cases of TB notified and data of meteorological and air pollutant for the period 2014-2016. Quasi-Poisson regression models were constructed with weekly number of TB cases as the outcome and weekly relative humidity, wind speed and air pollutants (NO_2, SO_2, and PM_{10}) concentration as the predictors. Auto-correlation functions indicated that lag 6 and 7 weeks after exposure had the highest relationship with TB cases.

Results: The overall PM_{10} concentration in Pekanbaru was moderate with a weekly average of 74 μg/m³ but during the haze period raised to 310 μg/m³. The overall weekly mean number of TB cases was 27 but increased to 29 during the haze period. Regression analyses showed that a doubling of mean PM_{10} concentration at lag 6 and lag 7 weeks was significantly associated with increase a 20% and 10% respectively, in the number of TB cases notified per week. A further regression model which included a non-linear PM_{10} term showed that the number of TB cases rose non-linearly after a PM_{10} concentration of 79 and 71 for lags 6 and 7 weeks, respectively.
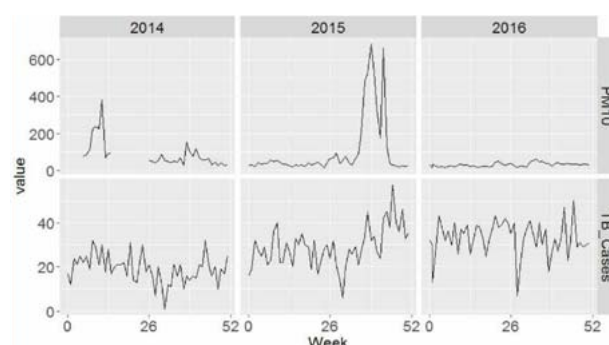
Figure Comparison of weekly PM10 concentration and TB cases

Conclusions: There is an association between exposure to ambient PM_{10} and TB case, indicate the TB control needs to take into consideration the air pollution context.

OA-2882-13 Insights into the effect of simvastatin on the immune response against *Mycobacterium tuberculosis*

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Background: Currently, treatment of tuberculosis is a combination of antimicrobials; however, it is necessary to shorten its duration and avoid the damage that causes permanent pulmonary disability in nearby half of patients. Statins have immunomodulatory, anti-inflammatory and antimicrobial effects. Our group has evaluated the immunologic response against *M. tuberculosis* by Whole Blood Bacteriostatic Activity Assays in subjects living with diabetes mellitus treated with statins. Our findings showed that patients treated with statins inhibited growth of *M. bovis* BCG more efficiently than those who did not use statins (ΔlogUFC -0.028 vs 0.298, p=0.05) at 96 h co-culture.

Objective: To evaluate the effect of simvastatin on the phenotype, cytokine production and control of *M. tuberculosis* infection in peripheral blood mononuclear cells (PBMC) infected with *M. tuberculosis* H37Rv in an *in vitro* model

Methods: Ten healthy donors were enrolled. PBMC were isolated, exposed to simvastatin (1 and 20μM) and infected at an MOI of 1:10 with H37Rv. Direct quantification of *M. tuberculosis* growth in CFU/mL was performed. Phenotype and cell activation were assessed

by multi-color flow cytometry in lymphocytes TCD4+, TCD8+, NKT, NK, and monocytes. Cytokines levels were determined in supernatant of infected PBMC treated with simvastatin.

Results: The growth of *M. tuberculosis* H37Rv decreased in PBMC treated with simvastatin ($20\mu M$) (3.37×10^6 CFU/mL to 1.12×10^5 CFU/mL; $p<0.001$). Simvastatin increased the percentage of NKT CD4+ (1.63 vs 0.57, $p<0.05$), NKT CD8+ (1.69 vs 0.52 $p<0.05$) and the expression of co-stimulatory molecules in CD14+ monocytes (CD80+ 43.99% vs. 23.71%, CD86+ 55.64% vs 19.49% $p<0.05$) and CD14+CD16+ monocytes (CD80+ 30.91% vs 15.69%; CD86+ 61.94% vs 34.73% $p<0.05$). Simvastatin also increased the production of IL-1β, IL-12p70 and IL-10 (Figure1).
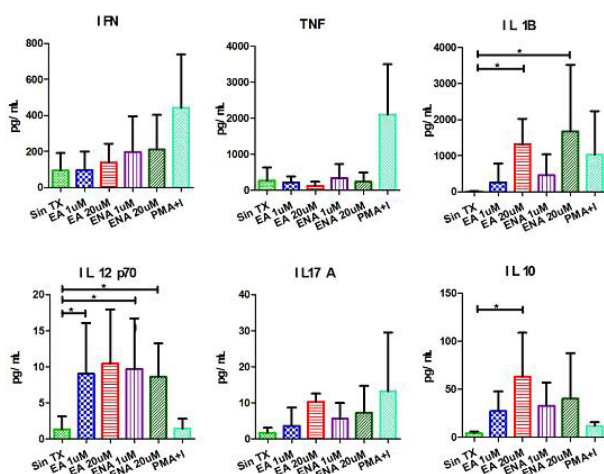
Figure 1 Effect of simvastatin on cytokine production in infected PBMC. ANOVA N=10. *$p<0.05$ *$p<0.01$

Conclusions: In this *in vitro* model, simvastatin enhances antimicrobial cellular mechanisms, enhance the innate immune response of PBMCs in culture, and reduces growth of *M. tuberculosis* H37Rv.

OA-2498-13 Drug resistant tuberculosis outbreak on Daru Island, Papua New Guinea: driven by a unique modern Beijing strain of *Mycobacterium tuberculosis*

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Background: An outbreak of multi-drug resistant tuberculosis has been reported on Daru Island, Papua New Guinea. The *Mycobacterium tuberculosis* strains driv-

ing this outbreak and the temporal accrual of drug resistance mutations have not been described.

Methods: We performed a retrospective analysis of specimens received at the regional Supra National Reference Laboratory in Brisbane, Queensland for strain typing and drug resistance testing between October 1, 2012 and March 15, 2015. Strain typing was done using 24-locus mycobacterial interspersed repetitive unit (MIRU-24) analysis and whole genome sequencing, with molecular dating and parsimonious mapping of drug resistance conferring mutations.

Results: Of the 100 *Mycobacterium tuberculosis* strains analyzed, 95 belonged to a single modern Beijing strain cluster. Molecular dating suggested acquisition of streptomycin and isoniazid resistance in the 1960s, with potentially enhanced virulence mediated by a *mycP1* mutation. This outbreak cluster demonstrated a high degree of co-resistance between isoniazid and ethionamide (80/95; 84.2%) attributed to an *inhA* promoter mutation combined with *inhA* and *ndh* coding mutations. Multidrug resistance, observed in 78/95 samples, emerged with the acquisition of a typical *rpoB* mutation together with a compensatory *rpoC* mutation in the 1980s. There was independent acquisition of fluoroquinolone and aminoglycoside resistance; with evidence of local transmission of extensively-drug resistant (XDR) strains from 2009.

Conclusions: Drug resistant tuberculosis on Daru Island, Papua New Guinea, is mainly caused by primary transmission of a modern Beijing strain with a long history of drug resistance acquisition. Whole genome sequencing is an important tool for understanding the emergence and transmission of drug resistance in order to inform an effective public health response.

OA-2867-13 The role of HIV co-infection in tuberculosis transmission in the low-incidence setting of England, Wales and Northern Ireland, 2010-2014

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Background: While HIV increases tuberculosis (TB) reactivation, co-infected patients may be less infectious. The impact of HIV on TB transmission in low-incidence settings is therefore unclear. We used national surveillance data to investigate the role of HIV in TB transmission.

Methods: We included adults (≥15 years) in England, Wales and Northern Ireland, with culture-confirmed TB notified 2010-2014, strain-typed using 24-loci mycobacterial-interspersed-repetitive units-variable-number-tandem-repeats (MIRU-VNTR) strain-typing. Strain-type clusters were ≥2 persons with indistinguishable ≥23 loci MIRU-VNTR profiles. First versus subsequent

cases within clusters were defined using the earliest date of evidence of TB. HIV status was determined through linkage to national HIV surveillance data.

Stratified by site of TB disease, we used multivariable zero-inflated Poisson regression to examine the association between HIV and the number of subsequent clustered cases (a surrogate for TB infectiousness).

Results: Of 18,864 TB cases, 10,709 (56.8%) clustered and 2,238/10,709 (20.9%) were first cases. 759/18,864 (4.0%) were HIV-positive.

HIV prevalence among subsequent cases was significantly higher where the first case was HIV-positive (10.7%) than HIV-negative (3.2%).

Among pulmonary TB cases, HIV-positive cases had fewer subsequent cases (mean 2.9, multivariable IRR 0.75 [0.65-0.86]) than HIV-negative cases (mean 3.7).

Among extra-pulmonary TB cases, HIV was associated with having no subsequent cases (multivariable OR 1.93 [1.12-3.33]); but HIV-positive first cases had a higher mean number of subsequent cases (mean 15.5, IRR (3.62 [3.12-2.19]) than HIV-negative first cases (mean 3.6).

Conclusions: Pulmonary TB-HIV co-infected patients were less infectious than HIV-negative TB patients. However, clusters where the first case had extra-pulmonary TB-HIV were larger. As extra-pulmonary cases are generally considered non-infectious, it is unlikely that transmission was driven by these patients. However, extra-pulmonary TB-HIV patients may be an important target for cluster investigations as the greater cluster size is likely a result of higher HIV prevalence and consequently greater susceptibility among their contacts.

OA-2987-13 Molecular analysis of streptomycin-resistance associating genes on *Mycobacterium tuberculosis* isolates from Nepal

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Background: For the treatment of multi-drug resistant (MDR) pulmonary tuberculosis (TB) in Nepal, streptomycin (STR) is included as a substitute for second-line injectable agents when other aminoglycosides cannot be used. Mutations in *rpsL* and *rrs*, encoding ribosomal protein S12 and 16S ribosomal RNA, respectively, well link to STR-resistance. Mutation in *gidB*, encoding 7-methylguanosine methyltransferase, was implicated in STR-resistance. Because of the lack of genetic information on STR-resistance in a region with a high level of MDR such as Nepal, we aimed to analyze the correlation between mutations in the target genes (*rpsL*, *rrs* and *gidB)* and STR-resistance in MTB isolates from Nepal. With that aim, we examined these genes associated with resistance to STR in *Mycobacterium tuberculosis* isolates from Nepali MDR patients.

Methods: DNA was extracted from cultures of 197 STR-resistant isolates for the amplification of *rpsL*, *rrs* and *gidB*. Sequencing of target genes was performed by 3500 Genetic Analyzer.

Results: Mutations in *rpsL* and *rrs* were harbored by 80.7% (159/197) of isolates. Mutations causing amino acid substitution at codon 43 and 88 in *rpsL* were found in 59.4% (117/197) and 7.1% (14/197) of isolates, respectively. Mutations at positions A514C and C517T of *rrs* were found in 5.1% (10/197) and 2.5% (5/197) of isolates, respectively. Mutations around 912 loop of *rrs* were found in 5.1% (10/197) of isolates. Mutations in *gidB* was harbored by 27.4% (54/197) of isolates. Mutations in *gidB* without those in *rpsL* and *rrs* gene was harbored by 13.2% (26/197) of isolates.

Conclusions: The findings from this study will contribute to the better understanding of STR-resistance mechanisms. The knowledge can be implemented for the establishment of rapid and effective molecular STR-susceptibility testing. TB can be treated with appropriate drugs and National TB Program can improve control strategies for drug-resistant TB in Nepal.

OA-2933-13 Molecular epidemiology of *M. bovis* among patients with pulmonary TB in Ethiopia

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Background: Data on the burden of bovine tuberculosis (TB) among patients with pulmonary TB is limited at national level, including Ethiopia. The goal of our project was to describe the molecular epidemiology of bovine TB among patients with pulmonary TB in Ethiopia.

Methods: This study was done on stored samples collected for anti-TB drug resistant survey conducted between 2011 and 2013. We characterized *Mycobacterium tuberculosis* (*M. tb*) complex isolates and smear positive sediments using RD9 deletion typing. Interpretation of the result was based on differences in molecular weight. Further typing using RD4 was used to confirm the presence of *M. bovis*.

Results: A total of 1735 *M. tb* isolates recovered from Ethiopian patients with pulmonary TB were typed using RD9 polymerase chain reaction. Among 1735 isolates, 1599 (92%) had a visible band on the gel electrophoresis indicating the isolates was *M. tb* complex. RD 9 typing identified 99.97% (1597/1599) of these cases as *M.tb* and RD 4 typing identified 0.12% (2/1599) of TB cases as *M. bovis*. Among the two *M. bovis* cases, one isolate was rifampicin resistant.

Conclusions: Pulmonary TB due to *M. bovis* was uncommon among patients in Ethiopia.

OA-2911-13 Recommended age at BCG vaccination - modelling the impact on global paediatric TB mortality

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Background: The World Health Organization (WHO) recommends that HIV-negative infants in high burden tuberculosis (TB) countries should receive Bacillus Calmette-Guérin (BCG) as soon as possible after birth. However, globally, 50% BCG vaccination coverage is achieved at 3-4 weeks of age. WHO is currently considering whether to update the existing recommendations. We investigated the relationship between age of BCG vaccination and global paediatric TB mortality.

Methods: A static mathematical model, calibrated to the 2015 number of global childhood TB deaths and age distribution for BCG vaccination, was developed. The number of TB deaths per global birth cohort over the first 15 years of life was estimated, for ten hypothetical scenarios for age of BCG vaccination. Scenarios included recommending BCG at birth, 6 weeks, 6 months or 1 year of age, with 2-3 implementation scenarios per recommendation.

Results: Compared to the current global age distribution of BCG vaccination, if BCG was co-administered with Diptheria-Tetanus-Pertussis vaccine, recommended at 6 weeks of age, an estimated 3,119 (95% UR: 125-7,643), or 1.8% (95% UR: 0.1%-4.5%) additional TB deaths would occur per global birth cohort over the first 15 years of life. Vaccination starting at 6 months was estimated to lead to 19,707 (95% UR: 790-48,284) or 11.7% (95% UR: 0.5%-28.2%) additional TB deaths. Co-administration with measles containing vaccine, recommended at 9 or 12 months, was estimated to lead to 30,547 (95% UR: 1,224-74,840) or 18.1% (95% UR: 0.7%-43.8%) additional TB deaths. Conversely, achieving the final BCG coverage (89.4%) at birth was estimated to lead to 4,933 (95% UR: 198-12,089) or 2.9% (95% UR: 0.1%-7.1%) fewer TB deaths.

Conclusions: Delayed vaccination would be anticipated to increase global paediatric TB mortality. Childhood TB deaths could be reduced if existing delays in BCG delivery could be cut or eliminated. The recommendation for neonatal BCG vaccination should be strengthened.

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THE 49TH UNION WORLD CONFERENCE ON LUNG HEALTH
24–27 OCTOBER 2018. THE HAGUE, NETHERLANDS

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