

JOINT PARTNERS FORUM FOR STRENGTHENING AND ALIGNING TB DIAGNOSIS AND TREATMENT

WHO Executive Board Room
Geneva, 27-30 April 2015



JOINT PARTNERS FORUM FOR

STRENGTHENING AND ALIGNING TB

DIAGNOSIS AND TREATMENT

REPORT

27-30 April 2015

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Photos courtesy of Ernesto Jaramillo and Medea Gegia

All presentations from the meeting are posted on the WHO website <http://www.who.int/tb/laboratory/gli/en/>

List of abbreviations

ARV	antiretroviral
Bdq	Bedaquiline
BRICS	Brazil, Russia, India, China and South Africa
CEM	cohort event monitoring
CHAI	Clinton Health Access Initiative
CoE	Centers of Excellence
CU	Compassionate Use
CXR	chest x-ray
DCS	Dried culture spot
Dlm	Delamanid
DR-TB	drug-resistant tuberculosis
DST	drug -susceptibility testing
EQA	External Quality Assessment
ERS	European Respiratory Society
FDC	fixed-dose combination
FIND	Foundation for Innovative New Diagnostics
GDF	Global Drug Facility
GDI	Global Drug resistant TB Initiative
GLI	Global Laboratory Initiative
GSM	Global System for Mobile Communications
GTB	Global TB Programme
HSP	Human Spirit Project
IRD	Interactive Research and Development
LAM	lipoarabinomannan
LAMP	Loop mediated isothermal amplification
LMICs	Lower middle income countries
LPA	Line probe assay
LTBI	latent tuberculosis infection
MDR-TB	multidrug-resistant tuberculosis
NAAT	nucleic acid amplification test
NFM	New Funding Model
NTP	National TB Programme
PEPFAR	United States President's Emergency Plan for AIDS Relief
PLHIV	People living with HIV/AIDS
PMDT	programmatic management of drug-resistant tuberculosis
POC	Point-of-care
PV	Pharmacovigilance
QMS	quality management system
RESIST TB	Research Excellence to Stop TB Resistance
rGLC	regional Green Light Committee
RR-TB	Rifampicin resistant tuberculosis
SCM	Supply Chain Management
SLD	second-line drugs
SLIPTA	Strengthening Laboratory Management Towards Accreditation
SLMTA	Stepwise Laboratory Quality Improvement Process Towards Accreditation
SRL	Supranational Reference Laboratory
STAT	Scale-up Treatment Action Team
SWIFT	Society Working on Implementation to Fight TB
TB	tuberculosis
TB/HIV	tuberculosis/human immunodeficiency virus
TPP	target product profile
TRP	Technical Review Panel
UNITAID	Innovative Financing to Shape Markets for HIV/AIDS, Malaria and Tuberculosis
USAID	United States Agency for international Development
VL	Viral load
WHO	World Health Organization
XDR -TB	Extensively drug-resistant tuberculosis

Background

The overall goal of the Joint Partners Forum was to bring together representatives from country TB control programmes, international institutions and initiatives, non-governmental organizations, academic and research institutes from developed and developing countries, patient communities, the TB Supranational Reference Laboratory network, industry representatives and funding agencies, working in partnership to address the challenges of increasing access to early diagnosis and treatment of all persons with TB, including drug-resistant TB and TB/HIV.

Meeting objectives included the following:

- Provide an overview of the WHO End TB strategy to control the global TB epidemic post-2015;
- Present priorities and achievements of the Global Laboratory Initiative and Global Drug-resistant TB Initiative;
- Disseminate developments in WHO policy guidance on TB diagnostics and new drugs, and provide updates on the TB diagnostics pipeline and clinical trials for new drugs and regimens;
- Share lessons learned and challenges for wide-scale implementation of Xpert MTB/RIF and other rapid diagnostic tests to ensure effective use of resources and identify synergies with TB/HIV integrated activities;
- Evaluate the status of the SRL network and its activities;
- Share best practices for the alignment of diagnosis and treatment for the programmatic management of drug-resistant TB (PMDT); and
- Present progress of regional initiatives for scale-up of laboratory strengthening and PMDT.

Joint Partners Forum was organized by the World Health Organization (WHO) Global TB Programme with the financial support from USAID, PEPFAR, Global Fund and Fondation Mérieux.

Session 1: Introduction

Chairs: Tom Shinnick and Charles Daley

Monday April 27th

Session 1: Introduction		Chairs: Tom Shinnick & Charles Daley
09:00	Welcome	Mario Raviglione
09:05	Opening remarks	Karin Weyer Lucica Ditiu
09:15	Ending the global TB and MDR-TB epidemic post-2015: the WHO End TB strategy	Mario Raviglione
09:40	Discussion	
09:55	Achievements and priorities of the Global Laboratory Initiative (GLI)	Tom Shinnick
10:15	Achievements and priorities of the Global Drug-resistant TB Initiative (GDI)	Charles Daley
10:35	<i>Coffee break</i>	
11:05	Looking ahead: the new TB diagnostic pipeline	Catharina Boehme
11:25	Alignment of diagnosis and treatment of drug-resistant TB: current global situation and challenges	Fuad Mirzayev
11:45	Discussion	
12:30	<i>Lunch</i>	

The Joint Partners Forum for aligning and strengthening TB diagnosis and treatment was opened by Mario Raviglione, Director of the WHO Global TB Programme (WHO/GTB). Welcome remarks were also made by Karin Weyer, Coordinator of the Laboratories, Diagnostics and Drug Resistance Unit of the WHO/GTB, and Lucica Ditiu, Executive Secretary of the Stop TB Partnership.

Ending TB and MDR-TB: The WHO End TB Strategy

Mario Raviglione (WHO/GTB director)

Mario Raviglione described the WHO End TB Strategy (2016-2035), including its objectives, components and targets, and highlighted its relevance to the theme of the current Joint Partners Forum. The presentation also described the global situation of TB and MDR-TB, and provided an overview of the priority activities needed to control the MDR-TB epidemic, including preventing the development of drug resistance through high quality treatment of drug-susceptible TB, expanding rapid testing and detection of drug-resistant TB cases, providing immediate access to effective treatment and proper care, preventing

transmission through infection control, and increasing political commitment with financing.

Global Laboratory Initiative (GLI) & Global Drug-resistant TB Initiative (GDI)

Tom Shinnick (CDC) and Charles Daley (National Jewish Health)

The structures, objectives, activities and priorities of the Global Laboratory Initiative (GLI) and Global Drug-resistant TB Initiative (GDI) working groups were presented by Tom Shinnick and Charles Daley respectively.

The GLI's mission is to serve as a platform of coordination and communication for TB laboratory strengthening, including global policy guidance, laboratory capacity development, interface with other laboratory networks, standardized lab quality assurance, coordination of technical assistance, effective knowledge sharing, advocacy and resource mobilization; GLI projects are conducted by GLI partners in a collaborative spirit with GLI core group review and coordination. GLI achievements for 2014-2015 have included the 6th Annual GLI Partners Meeting in 2014, co-sponsoring of a meeting to

develop target product profiles for new TB diagnostic tests, finalization of the Xpert MTB/RIF training package, development of a draft of TB Laboratory Consultants Manual, continued rolling out of the GLI Stepwise Process towards TB Laboratory Accreditation, and formation of a GLI for Africa core group and finalization of its work plan. Proposed priorities for the GLI for 2015-2016 include assisting countries develop the laboratory component of their National TB Strategic Plan, promoting the use of the GLI accreditation tool with other tools for improving QMS, finalizing development of new GLI tools, disseminating and promoting use of GLI tools, developing strategy to improve human resources for laboratory management, and working with GDI to promote scale-up of diagnostics and PMDT in parallel.

The GDI's mission is to serve as a multi-institutional, multi-disciplinary platform organizing and coordinating the efforts of stakeholders to assist countries to build capacity for PMDT in the public and private sectors, with the ultimate aim

of universal access to care and appropriate treatment for all patients with drug-resistant TB (DR-TB). The strategic priorities of GDI are to facilitate integration and coordination of efforts to align diagnostic services for patients with access to high-quality care, to develop targeted advocacy strategies and resource mobilization for DR-TB management scale-up, to build global consensus on the management of DR-TB for patient-centred care delivery, to promote strategies to facilitate patient access to high-quality DR-TB care through a long-term, in-country capacity building approach, to facilitate effective knowledge sharing among partners and harmonize coordination with existing technical assistance mechanisms, and to support prioritization of research to generate evidence for PMDT. There are three task forces within GDI, which support prioritization of research to generate evidence for PMDT, to build global consensus on the management of DR-TB for patient-centred care, and to develop targeted advocacy strategies and resource mobilization for DR-TB management and scale-up.



Looking ahead: the new TB diagnostic pipeline

Catharina Boehme (FIND)

Catharina Boehme gave an overview of the TB diagnostics pipeline, describing the technologies that are in various stages of development and evaluation. Target Product Profiles were developed by the GLI and New Diagnostics Working Groups in 2014, which have provided the optimal and minimally required characteristics of diagnostic and screening tools for guiding developers. New NAAT (nucleic acid amplification test) platforms address needs including decentralization, improving time to diagnosis, improving MTB detection, higher throughput and multiplexing, and extended and timely drug susceptibility testing (DST). The functionality and expected timelines of anticipated NAAT tools were described, including Xpert MTB/RIF Ultra and XDR, Alere q TB and DST, Molbio-Truenat, and Ustar Easynat. Advancements in sequencing technology and biomarker research and development were also described. Challenges that prevent TB diagnostics from having their intended impact in countries were discussed, and the examples of Xpert and PIMA were used. The prerequisites for achieving universal rapid diagnosis and DST were described, including the implementation of novel tools as comprehensive solutions, novel testing strategies, strong and integrated lab systems, and a transformed diagnostic ecosystem. TB LAMP and Urinary LAM assays will be reviewed by an independent expert group convened by WHO in June 2015 for potential recommendation. First and second-line line probe assays will be reviewed in Q4 2015, along with the role of sequencing as a gold standard for molecular test evaluation. DST methods for bedaquiline and delamanid will be evaluated fully and recommended in Q1 2016. Considerable discussion ensued, including on the strengths and shortcomings of current and future genotypic tests, and the priorities envisioned for retooling by programmes when new diagnostics are introduced.

Alignment of diagnosis and treatment of drug-resistant TB: current global situation and challenges

Fuad Mirzayev (WHO/GTB)

Fuad Mirzayev presented on the alignment of diagnosis and treatment of drug-resistant TB. The presentation highlighted the global problem of the MDR-TB and discussed the gaps between MDR-TB cases detected and enrolled on treatment based on country reports to WHO as part of the annual Global TB reports. The presentation also described the challenges national TB programmes face aligning diagnosis and treatment of patients with MDR-TB, achieving favourable treatment outcomes, summarised observations and mapped out several potential solutions, including preventing isolation between diagnostic and treatment streams of work, linking information systems as feasible, implementing innovations across systems, using well-designed and cost-effective algorithms that are widely discussed and agreed with all relevant healthcare providers and implemented within patient-centred and contextualized models of care.

Session 2: Advancements and opportunities in diagnosis and treatment

Chairs: Rumina Hasan and Agnes Gebhard

Session 2: Advancements and opportunities in diagnosis and treatment		Chairs: Rumina Hasan & Agnes Gebhard
14:00	Introducing new anti-TB drugs and regimens	Christian Lienhardt
14:15	WHO approach to pharmacovigilance of anti-TB drugs	Ernesto Jaramillo
14:30	The current state of knowledge: genotypic vs phenotypic drug-susceptibility testing (DST)	Daniela Cirillo
14:45	Discussion	
15:00	Achievements and challenges of the Supranational Reference Laboratory (SRL) network	Harald Hoffmann
15:20	Designation of 3 SRL Centers of Excellence (CoE) in the Russian Federation	Karin Weyer
15:30	<i>Coffee break</i>	

WHO role in the introduction of new TB drugs and regimens: issuing normative guidance

Christian Lienhardt (WHO/GTB)

The presentation provided background information on the pipeline of new drugs for TB, and then focused on the WHO policy framework to develop guidance on new TB drugs. Several essential challenges related to the definition of the optimal background regimen were also described. WHO now has a mechanism so that each time a new drug or regimen emerges it triggers the process to develop policy recommendations. The process follows the principles established by WHO's Guidelines Review Committee. GRADE methodology is used to assess the quality of evidence and formulate the recommendations (strong or conditional).

WHO Approach to pharmacovigilance of anti-TB drugs

Ernesto Jaramillo (WHO/GTB)

The presentation focused on the rationale and the main concepts behind pharmacovigilance, which has now become important because more drugs are being used ahead of results of phase III

clinical trial. Treatment should not worsen a patient's suffering. In this context active PV is being recommended by WHO: active in the sense that questions and an array of laboratory and clinical tests are applied at defined periods of time, before, during and after treatment without waiting for the patient to report complaints.

PV is a relatively new activity for national TB programmes and therefore the national government centres responsible for PV. Several basic steps are recommended for setting up a system in settings using new anti-TB medicines. It is important that certain early steps are however in place before new drugs are started: having an agreement on the collection of data, and the parameters in place for collection of data with all the personnel involved appropriately trained.

The current state of knowledge: genotypic versus phenotypic drug-susceptibility testing (DST)

Daniela Cirillo (SRL Milan, Italy)

The presenter described in detail the two approaches to testing and hence, the use of different methods to test for antibiotic susceptibility is leading to discordant results between different phenotypic tests. This discordance is drug dependent and strains with a

minimum inhibitory concentration close to the breakpoint are the ones which are most affected. Discrepancies between different molecular test results may be due to the targets included in the tests: their gold standard remains sequencing. The speaker gave examples to illustrate challenges posed to the interpretation of discrepant results, e.g. 10% of RR-TB mutations are not detected by in vitro testing, especially in liquid culture and these mutations are associated with poor treatment outcomes.

It was highlighted that Xpert MTB/RIF and LPA can generate false positive resistance results in the case of silent mutations and false susceptible results may occur if the molecular assay does not target relevant mutation. In fluoroquinolones, resistance is most frequently associated with mutations related to DNA gyrase (*gyrA>gyrB*). In pyrazinamide, mutations in the *pncA* gene disrupt the conversion of pyrazinamide to the active metabolite. There is excellent correlation between pyrazinamide resistance and *pncA* mutations but DST on liquid media showed inconsistent results with poor reproducibility. In conclusion, the identification of mutations is needed for the accurate diagnosis of resistance.

High-confidence genetic markers of resistance may replace conventional DST while certain markers for low-level resistance can be used to improve clinical management. The Relational Sequencing TB Data Platform represents a joint effort to create a common platform to investigate the relationship between mutations, phenotypic, surveillance and clinical data.

Achievements and challenges of the Supranational TB Reference Laboratory (SRL) network

Harald Hoffmann (SRL Munich, Germany)

The Supranational TB Reference Laboratory network (SRLN) acts as a technical resource for WHO, works to strengthen TB lab capacity worldwide, and supports the largest and longest-standing surveillance network (>20 years) for antimicrobial resistance in the world. The SRLs establish partnership agreements with national TB reference laboratories (NRL) to provide technical assistance and support. SRL staff undertake regular missions to the NRLs that they supervise and a standardised report of findings is then made. In the last few years the SRLN is active in a new molecular surveillance project on

fluoroquinolones and pyrazinamide, involving five countries and possibly more in future. This surveillance is not only providing information on the levels of drug resistance to drugs which are crucial for new TB regimens but also promoting the use of whole genome sequencing as a reliable technology for surveillance.

Designation of the national TB reference laboratories as Centres of Excellence (CoE) in the Russian Federation

Karin Weyer (WHO/GTB, Laboratories, Diagnostics and Drug Resistance unit)

In the past the BRICS countries in particular have expressed the desire for their NRLs to get better recognition of the efforts they make to improve the diagnostic competence of the labs in their respective countries. Last year, the Ministry of Health of the Russian Federation applied for three of its TB reference laboratories (Central TB Research Institute of Moscow, Ural Research Institute for Phthisiopulmonology in Yekaterinburg and TB Research Institute in Novosibirsk) to be considered as Centres of Excellence of the Supranational TB Reference Laboratory Network. A mission was held by staff from WHO/HQ to assess these facilities in December 2014; it found that the three establishments had a very good infrastructure and were staffed by competent and well-trained staff. It was thus recommended to designate them officially as Centres of Excellence. Dr Weyer, coordinator of the WHO/GTB Unit for Laboratories, diagnostics and drug resistance, welcomed representatives from the three institutions and provided them with certificates of appointment. Teresa Kasaeva, from MoH of the Russian Federation, expressed her gratitude for the positive assessment of the laboratories. She stated that while the Russian Federation had made much progress in TB control in recent years such an award was very prestigious and a significant acknowledgement of the efforts made by these laboratories.

Discussion, Q&A:

A number of issues on PV have been clarified following discussions with partners and are elaborated in documents such as the Companion Handbook and the FAQs that GTB has published. However, due stress has to be made on the fact of uncertainty associated with new drugs and therefore close scrutiny of patients treated with

these drugs is important. With respect to funding of PV there are possibilities to get support from the Global Fund and there is no need to cut down on resources devoted to other programme activities. The representative from Belarus provided a country example and noted that the Belarus experience with pharmacovigilance for linezolid (bedaquiline is expected to be delivered shortly) showed that while it requires significant funding and is labour intensive it is absolutely feasible. There are training needs and reorganisation of work and the national TB register. If the data were better organised electronically it could save a lot of double data collection.

The discussion also went on the usefulness and reliability of molecular tests. The answer highlighted that molecular tests provide more rapid results; much of the misunderstanding and confusion may be related to inappropriate use of the phenotypic test and country-based simple sequencing may provide a solution.

The participants were also interested in knowing the relevance of certain mutations for the practitioners in different parts of the world. It was explained that the country should be aware of the local geographical variations and prevalent forms of drug resistance by improving surveillance. The technologies are relatively new and are reliable but the doctors should not lose sight of the clinical picture in the individual patient.



Designation of the national TB reference laboratories as Centres of Excellence (CoE) in the Russian Federation.

Session 3: Introduction and access to new anti-TB drugs

Chairs: Mario Raviglione and Gavin Churchyard

Session 3: Introduction and access to new anti-TB drugs		Chairs: Mario Raviglione & Gavin Churchyard
16:00	WHO's role in the introduction of new drugs: normative, technical assistance and monitoring	Christian Lienhardt
16:15	Update on bedaquiline "donation programme", and USAID's perspectives on introduction and access to new drugs	Ya Diul Mukadi
16:25	Introduction of delamanid: progress and plans	Charles Wells
16:35	Field experience of introducing new drugs, Access Initiative, and call to action on the introduction of bedaquiline and delamanid	Grania Brigden
16:45	UNITAID's perspectives on introduction and access to new TB drugs	Philippe Duneton
16:55	Introduction and access to new drugs under the Global Fund's new funding model	Mohammed Yassin
17:05	Stop TB Partnership/GDF's role in making new drugs accessible	Joel Keravec
17:15	Discussion	All
18:15	Summary of session and way forwards	Mario Raviglione & Gavin Churchyard
18:30	<i>End of Day 1</i>	

An introduction to the session was provided by Dr Mario Raviglione, Director, GTB Programme, WHO Geneva. He stressed that it is an exciting time to be in TB control since, after a gap of many decades, there are new anti-TB drugs, namely bedaquiline and delamanid, available. Although these drugs are licensed in a few countries and WHO has issued interim guidelines on how these drugs should be used, access and uptake at the country level has been slow. This slow uptake prompted MSF and 88 other civil society organizations to publish a public "Call to action" open letter on 10 March 2015 with a number of requests to industry and other stakeholders. The session is intended to update all on the current situation and future plans of a wide range of stakeholders.

WHO's role in the introduction of new drugs: Supporting introduction in countries

Christian Lienhardt (WHO/GTB)

The presentation provided an overview of the public health challenges of introduction of new TB drugs in countries, the key principles of the WHO's

Strategic Plan for the rational introduction of new TB drugs and regimens, Policy Implementation Package and a generic implementation plan for the introduction of bedaquiline in countries. Finally an update on the work that WHO has done with the five 'early implementing countries' and the lessons learnt, was presented. The key aspects for WHO/GTB in this work are: to engage with and support national authorities and stakeholders early in the preparation of policies for introduction of new TB medicines at programmatic level; to ensure that new TB medicines/regimens are introduced in an optimal way to protect patients from misuse and prevent emergence of resistance; and to ensure that introduction of new drugs follows WHO policy recommendations and appropriate plans are made to ensure feasibility and inform policy-making. In summary, a model of introduction of bedaquiline (Bdq) according to WHO recommendations, seems to work and can be used for other new drugs and regimens as they become available, however the process needs to be streamlined for more countries and other new drugs. Consultants need to be trained, and updated information needs be delivered to donors, regulators and the regional GLCs.

Bedaquiline Donation Program and USAID's Perspectives On Introduction and Access to New Drugs

Ya Diul Mukadi (USAID)

The introduction of new drugs sits within the US Government's 2015–2019 TB Strategy and offers an opportunity for strengthening the quality of the management of MDR-TB. Within the current USG TB strategy, the introduction of the new drugs will be supported through the following 3 objectives: a) improve access to high-quality, patient-centred TB, DR-TB, TB/HIV services, b) strengthen TB service delivery platforms, and c) accelerate research and innovation. Details of the news about the bedaquiline donation program between USAID and Janssen, launched on 1 April 2015, were provided to the meeting. This program responds to a call for action from TB community for more access to new TB drug including bedaquiline. The purpose of the program is to assist countries in

combatting MDR-TB through improve access to appropriate MDR-TB medicines. It is a four-year program for up to 30,000 treatment courses of bedaquiline to be delivered to eligible patients in up to 100 low and middle income countries. Countries that are eligible to request TB funding through the Global Fund are eligible to participate in and receive the bedaquiline donation program. Others can be added based on mutual agreement between USAID and Janssen. The donation will be provided to eligible countries under conditions that "reasonably meet the requirements set out in the WHO Interim Guidance" and delivered to countries through the Global Drug Facility (GDF). Countries can also request technical assistance to strengthen or develop any of the five areas listed in the WHO Interim Guidance. It is anticipated that the program will remove price as a potential barrier to MDR-TB scale-up, and also provide the mechanism by which evidence will be gathered on the use and impact of bedaquiline in a real-world setting.



Delamanid for MDR-TB: Current Development Progress and Ongoing Access Plans

Charles Wells (Otsuka)

Otsuka believes the way forward for successful introduction of delamanid requires: long-term strategic planning; careful introduction in quality TB management programs accompanied by robust risk management plans; country level

support for implementation; prevention of additional drug resistance; and strengthened pharmacovigilance systems. Sometimes these core principles may be perceived as conflicting with the urgency to make delamanid available as soon as possible, to as many people as possible, worldwide. Following this discussion on Otsuka's philosophy for introduction of new drugs, an update on the delamanid Phase III trial and paediatric development programme was provided.

Dr Charles Wells on behalf of Otsuka announced its "FightTB Back Initiative" to enable access to delamanid for the management of MDR-TB patients. The plan is centred around a "20 by 2020" goal, which is to ensure delamanid reaches 20% of all diagnosed and treated MDR-TB patients in quality programmes by 2020. On top of its ongoing compassionate use (CU) and expanded access programmes, Otsuka intends to incorporate a targeted access donation program as a preliminary step to meet the community's "Call to Action." Discussions are ongoing with several stakeholders to supply delamanid in approximately 20 low and middle-income countries (half in the 27 highest-burden countries) starting in 2015. Other components of the plan include innovative research and development of new products for MDR-TB, optimized patient management, and collaborative capacity building, including working with communities using new approaches to ensure delamanid is administered safely and responsibly to minimize the threat of DR-TB.

Through the initiative, Otsuka anticipates that over 30 countries will have delamanid in routine use by the end of 2016. Discussions are ongoing to see whether delamanid can be made available through several other access channels including via GDF. Otsuka concluded by calling on the TB community to increase the development and availability of paediatric formulations for other MDR-TB medicines, help increase access for new TB drugs through advocacy for regulatory harmonization, and work together to strengthen pharmacovigilance systems for improved data collection and safety monitoring.

Call to action on the introduction of bedaquiline and delamanid

Grania Brigden (MSF – on behalf of 88 co-signatories)

SDRA approval of bedaquiline (Bdq) was granted in December 2012 and for delamanid (Dlm) in April 2014. WHO issued guidance on programmatic use of Bdq in June 2013 and for Dlm in November 2014. The WHO has been working with five early implementer countries for the introduction of new drugs for a year and the USAID donation programme for Bdq started in April 2015. Positive clinical experience with Bdq has been building from France, Georgia, Armenia, RSA, Latvia (CU programmes). All of this is offering hope to both patients and clinicians, but

only 600 patients are on Bdq and less than 50 patients on delamanid outside of clinical trials. Delamanid as yet is only registered in the European Union, Japan, and South Korea. And there has been minimal use of repurposed companion Group 5 drugs needed to support introduction of new drugs. This slow uptake of the new drugs prompted MSF and 88 other civil society organizations to publish a public "Call to action" open letter on 10 March 2015 with a number of requests to industry and other stakeholders. A proposed solution is the establishment of an 'action team' comprised of actors committed to meet time-bound goals for increasing access to new and repurposed DR-TB drugs in 50 top high-burden countries through greater collaboration, coordination and accelerated activities i.e. DR-TB STAT!! (Scale-up Treatment Action Team). The time-bound goals are grouped under a number of broad headings including: "Quick start" with linked patient targets; optimal DR-TB treatment; regulatory status; procurement; and pharmacovigilance. Examples of previous similar collaborative mechanisms for expanding drug access were provided e.g. the collaboration between UNITAID and CHAI in relation to access to Paediatric ARVs. The speaker ended with posing a number of queries to the meeting, namely: can we achieve these targets; how can the key actors work together to ensure all patients requiring new drugs have access to them; what other barriers need to be addressed; and what actions need to be taken to achieve these goals within the next 6 months and 12 months? Success is to be measured by number of patients on treatment.

UNITAID's perspectives on introduction of and access to new TB drugs

Philippe Duneton (UNITAID)

The meeting was reminded that the TB market is small and fragmented compared to that for HIV and Malaria, and that an integrated approach to diagnosis and treatment is needed. Scoping of the TB market and landscape shows that there is poor access to diagnosis (DST) and treatment of MDR-TB is complex, costly, and long. There is an urgent need for evidence to improve and simplify treatment, and to consolidate demand. Many countries have limited capacity for treatment and monitoring, whilst for the manufacturers, pharmacovigilance and reporting systems are often poorly established in low- and middle-

income settings. Interventions are urgently needed to facilitate access. Projects by which UNITAID aims to support access to new TB medicines are: the endTB project with PIH, MSF and IRD (details of which were presented in session 7); the Strategic Rotating Stockpile via GDF, Stop TB Partnership (details of which were presented in session 3); and the Speeding Treatments to End Paediatric TB project (STEP TB) with the TB Alliance. Looking ahead, UNITAID has a strong interest in additional complementary approaches to increase the access to new TB drugs.

Introduction and access to new drugs under the Global Fund's new funding model

Mohammed Yassin (The Global Fund)

Dr. Yassin presented the challenges and opportunities relating to scale up of DR-TB services. The Global Fund has supported the expansion of PMDT services with increasing allocations of funds. The number of MDR-TB cases treated by Global Fund-supported programmes increased from 64,000 in 2012 to 150,000 in 2014. Global Fund grants have also supported the procurement of over 2'000 GeneXpert machines and 2 million cartridges in 2013-14. GF looks to countries having a balance between basic TB and DR-TB services, with close alignment in the scale up of diagnostic services with those for the management of the detected cases. Global Fund support is contributing to the change in the mode of MDR-TB treatment – including catalysing “reform” and scale-up of ambulatory treatment, and the leveraging of additional resources. The Global Fund supports the introduction of new drugs and shorter regimens for MDR-TB, along with support to build capacity for active pharmacovigilance and other required areas in accordance with WHO recommendations. For example 15 countries have included funding requests for the treatment of pre-XDR and XDR-TB cases, including the use of bedaquiline. The funding requested is for 2,000 cases, establishing/strengthening active pharmacovigilance, and the provision of the required technical assistance (TA) and capacity building. With the creation of the bedaquiline donation programme between USAID and Janssen, countries can re-programme any funding allocated for bedaquiline to support PMDT activities and scale-up treatment depending on

need and priorities. GF support allows countries to receive technical assistance through the regional GLCs. The previous GLC memorandum of understanding between Global Fund and WHO, is to be revised and extended. The aim of the new agreement will be: to contribute to overall TB and DR-TB control; disbursement of funds will be performance-based and services quality assured; strengthen coordination and collaboration between WHO, USAID, STP/GDF; and support the introduction of new diagnostics and new drugs. Consultations are ongoing with a wide range of TB partners on the best options for future TA for PMDT and align with End TB Strategy, Global Stop TB Plan and the new Global Fund Strategy Stop TB / GDF Access Strategies and Support for New Drugs Uptake

Joel Keravec (GDF, Stop TB Partnership)

Dr Keravec stressed that the key issues and access challenges for new drug introduction should be addressed by a Supply Chain Management (SCM) systemic approach. Key interventions are required to support a rational uptake strategy and a framework for early adoption, with dedicated strategies for introduction, implementation and monitoring are important. New drugs (e.g. Bdq & Dlm) will be distributed along with existing SLDs. There is therefore the opportunity to build on existing systems & tools and further improve access and SCM initiatives, such as GDF Strategic Rotating Stockpile, MDR-TB costs decreases, as well as Technical assistance tools like QuanTB to support proper introduction and build on on-going Harmonized regional registration initiatives to address the regulatory issues, However countries' procurement systems and SCM models are different. Hence a “one fits all strategy” is not appropriate, rather more appropriate are market-based and country-clusters specific approaches, in line with key elements of WHO recommended implementation package for new drugs introduction and Stop TB partnership advocacy framework.

Discussion, Q&A:

The meeting was informed that over 100 patients are being treated with Bdq via NTP in South Africa. However whether South Africa can access Bdq via the donation program is still being discussed. Also during the discussions, questions from the audience highlighted the urgent need for having a DST to the new drugs available. An update of the current work was provided by Daniella Cirillo, from

which it appears that a standardised method for Bdq and Dlm susceptibility testing may be available by the end of 2015.

The major focus of the discussions was on the "call for action" from MSF and the other 88 co-signatories, albeit with the exciting announcement from Otsuka on their plans for making Dlm available. A major concern raised in relation to the call was of the need to avoid overlap of platforms, particularly as there may be competition for the same space. It was stressed that duplication of actions and confusion needs to be avoided at all costs. It was clarified by those who signed the "call for action" that its objective was not to establish any new platform, and that they also want to avoid duplication of structures and efforts. Rather if appropriate, the activities called for should be done within existing structures, but there is a need for faster action. The desire is to bring all the relevant players together in order that they collaborate and communicate better, and wider access to the new

drugs is achieved quickly. A suggestion was that the GDI, with its Task Force structure, could provide the most appropriate "house" for this activity, and that the "call for action" would bring a real sense of focus and purpose of intent with it. It was agreed that this discussion would be taken forwards during an open session of the meeting of the GDI Core Group on the morning of Friday 1 May 2015. A number of country representatives stressed that the slow uptake of the new drugs by countries was not just related to financing, but often related to the numerous approval hurdles that had to be overcome. Hence in addition to the extra resources and TA (in which the rGLCs have an important role to play) needed for the introduction of new drugs and scale up of PMDT services generally within countries, what is needed is stronger advocacy rather than the establishment of yet another global process or mechanism.

Session 4: Implementing innovations

Chairs: Alaine Nyaruahirira

Tuesday April 28th

Session 4: Implementing innovations		Chair: Alaine Nyaruahirira
09:00	Progress on adaptation and use of the SLMTA (Strengthening Laboratory Management Towards Accreditation) tool for TB laboratories	Heidi Albert
09:30	Discussion	
09:45	A model for specimen transportation: experience of Pakistan	Sabira Tahseen
10:00	Re-organization of the laboratory network in Belarus	Aksana Zalutskaya
10:15	Discussion	
10:30	<i>Coffee break</i>	
11:00	Advancements in e/m- Laboratory Information Management systems: outcomes of the 2015 WHO/ERS meeting	Chris Isaacs
11:15	Panel discussion on advancements in remote connectivity tools for GeneXpert - GXAlert - GenXchange - South Africa	Moderator: Dennis Falzon Moses Joloba, Jeff Tackle Emmanuel Andre Alaine Nyaruahirira

Progress on adaptation and use of the SLMTA (Strengthening Laboratory Management Towards Accreditation) tool for TB laboratories

Heidi Albert (FIND)

Heidi Albert gave an overview of various tools that can be used by TB laboratories to support quality improvement and work towards accreditation, such as SLIPTA (Stepwise Laboratory Quality Improvement Process Towards Accreditation), SLMTA (Strengthening Laboratory Management Toward Accreditation) and GLI stepwise process towards TB Laboratory Accreditation. SLIPTA is an auditing framework to evaluate the progress of laboratory quality management systems and fulfil ISO 15189 standards, whereas SLMTA is a task-based training and mentoring program. GLI stepwise process is an online tool. She went on to describe the TB-SLMTA programme and TB Laboratory Quality Management Systems Towards Accreditation Harmonized Checklist (incorporating SLIPTA and GLI clauses), developed by FIND, based on the SLMTA and SLIPTA approaches. TB-SLMTA is specific for TB laboratories and is being rolled out in 31 TB labs in 6 countries: Dominican Republic, Lesotho, Tanzania, Cameroon, Ethiopia and Vietnam. TB-SLMTA programme includes

training of trainers' workshop, 3 country workshops and structured mentoring, and baseline and exit assessments to measure impact. 51 participants have graduated as trainers from 19 countries to date. Lessons learned show that sufficient and well-targeted investment; motivated staff and management support, well-coordinated mentoring and country level support contribute in a relatively short time frame to achievement of the sustainable accreditation.

A model for specimen transportation: experience of Pakistan

Sabira Tahseen (NRL/NTP-Pakistan)

Specimen transport in Pakistan has evolved from specimen transport within the same city using local arrangement, such as motorcycles, to intercity transport of specimen using courier services from clusters of surveys to NRL. Based on lessons learned, effective specimen transport system has now been established between various PMDT sites and TB culture and DST laboratories in each province. Pakistan now is planning to enhance screening for drug resistant TB by scaling up the specimen transport system to obtain improved access to, wider coverage of new molecular diagnostics such as Xpert MTB/RIF.

The aim is to establish transport linkages in initial stage between 20% of high volume BMUs notifying 50% of country TB cases and Xpert sites. This National scale up pilot has experienced some challenges due to low interest of in-country service providers to offer courier services for infective specimen, maintaining cold chain during the transportation, low computer literacy of laboratory staff at district level and expanding GeneXpert and culture DST network which often requires change in initially established transport linkages

Re-organization of the laboratory network in Belarus

Aksana Zalutskaya (NRL Belarus)

NTP/NRL suggested re-organizing the laboratory network in Belarus to gain efficiency and shorten the time of diagnosis and introducing new diagnostics technologies while assuring the necessary bio-safety measures. The first situation analysis including the assessment of the laboratory capacity was performed in Brest Oblast leading to a nationwide analysis. TB laboratory network was re-organised by reducing drastically the number of culturing points and district TB laboratories and re-organizing the Level II and Level III laboratories within the oblasts. NTP/NRL adopted the Health regulations for TB institutions and issued guidelines for the laboratory diagnostics of TB for use across the laboratory network. NTP/NRL organised nationwide trainings for TB laboratory specialists to assure the quality of diagnostics. Besides, laboratory component of the TB register has been mainstreamed and revised; algorithm of TB diagnostics with the use of molecular techniques has been updated; and infection control has been strengthened. A national strategic plan for the prevention and control of TB and MDR TB in the Republic of Belarus in 2015-2020 has been developed.

Advancements in e/m-Laboratory Information Management systems: outcomes of the 2015 WHO/ERS meeting

Chris Isaacs (FIND)

Chris Isaacs presented the plans to develop target product profiles (TPPs) for improved information management in TB laboratories. A joint WHO/ERS consultation was attended by more than 90 participants on 25-26 February

2015 in Geneva. Four working groups were set up to work on TPPS: Patient care, “DOT” & mCessation; Surveillance and Monitoring; Laboratory Information Management Systems and e-Learning. The laboratory work stream consisted of national end users, technical partners, laboratory experts and funding agency representatives. Based on a pre-workshop survey, the following factors were considered as the most important: storing data from diagnostic devices and data entry applications, making data available to applications and sending SMS to clinicians and patients. The second most important product is a diagnostic device that can send results to a laboratory information system and /or a patient electronic health record. Third most important was a paperless laboratory information system tailored to the needs of clinical laboratories in low and middle income countries. The whole architecture of the proposed solution would be in three parts: diagnostics data connectivity, data repository and presentation. The Laboratory Information Management Systems working group came up with the concrete plans, users profiles and next steps, such as setting up a core work group to further develop the connected diagnostics TPP and to address key strategic issues, drafting TPP for data repository / gateway, engaging with and providing support for manufacturers to implement connectivity and evaluating connectivity benefits for priority use cases.

Panel Discussion on advancements in remote connectivity tools for GeneXpert

(Moderator: Dennis Falzon, Speakers: Moses Joloba, Emmanuel André, Alaine Nyaruhirira, Jeff Tackle)

Introduction of GxAlert in Uganda:

Moses Joloba

GxAlert is an online diagnostic device collecting GeneXpert results in real time from Xpert sites connected to the system. Uganda reported that the introduction of GxAlert has improved monitoring of the Xpert machines, inventory management of cartridges preventing stock outs, data management from Xpert instruments and a better follow up of the patients put on treatment. GeneXpert machines with high error rates are detected through a monitoring dashboard in real time. Currently there are 22 GenXperts connected

to GxAlert in Uganda and the results show that 87% of the 22 sites report in real time quality data. However some challenges have been faced with due to the lack of computer proficiency to extract, aggregate and send data to the programme and treatment sites. Sometimes monthly Xpert data collection and recording is not systematic and the Xpert results are not documented to the outdated paper lab registers.

GenXchange

Emmanuel André

GenXchange collects both test- and patient-related information using SMS technology. It is currently being used in the DR Congo as a means to manage data generated by GeneXpert machines. However, its vision is wider and it is envisaged that it will provide more comprehensive laboratory data management as per international standards (management of consumables and equipment, alerts for stock-outs). The presenter described how the system is intended to help support laboratories, countries and international institutions undertake quality management and epidemiological surveillance using data on patients and test results, logistics

Country Experience on update on quality management using EQA and RemoteXpert

Alaine Umubyeyi Nyaruhiira (MSH and Lesly Scott, NHLs , SA)

Although internationally-approved external quality assurance (EQA) programs have been well-defined for TB laboratory tests, large scale EQA for Xpert MTB/RIF testing has not yet been assessed or endorsed. Consequently, most countries have not initiated EQA for Xpert MTB/RIF. In response to this gap, the Ghana National TB Program (NTP) in collaboration with TBCARE I developed an EQA process for Xpert MTB/RIF using dried culture spots (DCSs) and it was piloted at four hospitals. Xpert MTB/RIF online reporting system called TB GX Monitor was installed. Xpert MTB/RIF results were uploaded onto the TB GX Monitor and DCS panels were tested. Four hospitals scored with three panels each 100% staff level proficiency in Xpert MTB /RIF testing process. Ghana pilot project provide a field-tested model for national scale-up and the NTP endorses the program and expand the process to all new sites through the National TB

strategic plan (2014-2019) supported by Global Fund. However, verification and 3x/year EQA is not sufficient for overall quality management.

The presenter also reported briefly about a beta trial in South Africa of Cepheid's Remote Xpert platform, a web portal which is intended to provide a comprehensive view of the diagnostic data generated by GeneXpert machines including their performance, in order to monitor their usage and coordinate their maintenance. The NHLs has been working with Cepheid to evaluate and improve the system. Results of the trial are expected to be communicated shortly.

Discussion and Q&A:

Participants were interested in the cost of the date repositories well as the cost of the data transmission to the users especially in developing countries. They were explained that the cost to store is free of charge and the data transmission is preferred through GSM rather than through SMS and messenger and the average cost of GSM connectivity is \$10/month. It was highlighted that financial resources are needed and there is now an opportunity for industry to be involved in the process of developing the pilots.

Besides, presenters were asked about the ways of providing the common programmatic interface or a framework between countries. It was stated that, common set of APIs, extraction of data from a centralised repository both in host country and a cloud based platform. Then the data transmission settings are by country based settings e.g. GSM in a country.

As different systems are being introduced to manage data generated by GeneXpert machines, programmes are requesting help in choosing which software to adopt. A tentative matrix summarizing the main futures of the system was presented to give an idea of landscape of different products.

Participants were also interested in the cost of implementation of the EQA panel using DSC's , they were explained that one panel costs now 115 US \$ delivered by NHLs in South Africa and this doesn't take into account any freight cost which will vary country to country. However, this cost is 1/10 lower compared to other materials used for EQA.

Session 5: Update on Xpert MTB/RIF implementation

Chair: Bill Coggins (CDC)

Session 5: Update on Xpert MTB/RIF implementation		Chair: Bill Coggins
13:30	2010-2015: uptake and impact of Xpert MTB/RIF	Wayne van Gemert
13:45	Use of Xpert MTB/RIF for diagnosing paediatric TB	C.N. Paramasivan
14:05	Moving beyond risk groups for Xpert MTB/RIF testing: the role of chest X-ray as a screening tool	Anja Van't Hoog
14:25	Private sector Xpert MTB/RIF scale-up: successes and challenges of the TBXpert social business projects	Aamir Khan / Imran Zafar
14:45	Discussion	
15:00	<i>Coffee break</i>	

2010-2015: uptake and impact of Xpert MTB/RIF

Wayne van Gemert (WHO/GTB)

The global roll-out of Xpert MTB/RIF has been rapid, with 3,763 GeneXpert instruments (17,883 modules) in the public sector of 116 countries eligible for concessional prices by the end of 2014. The number of Xpert MTB/RIF cartridges procured under concessional prices stabilized in Q2-4 2014 at around 1.2 million per quarter; South Africa continues to procure about 56% of the global number of cartridges. Comparing numbers of instrument modules to cartridges by country reflects that most countries are not yet using their instruments as efficiently as South Africa, which is able to perform an average of 3 tests per module per day. As an example of a multi-country initiative to widely roll-out Xpert MTB/RIF, the UNITAID-funded TBXpert project being managed by the WHO Global TB Programme with the Stop TB Partnership was described, including its interim results in terms of patients detected.

Most high burden countries have policies that include Xpert as the initial diagnostic test for people at risk of drug-resistant TB and for HIV-associated TB. South Africa, Swaziland, Brazil, Moldova now is using Xpert as the initial diagnostic test for all people suspected of having TB. Other countries are now moving beyond the risk groups, though not for all people suspected of having TB; the Philippines tests smear-negative people suspected of having TB with chest X-ray abnormalities, and Tanzania tests all people

suspected of having TB at sites that have a GeneXpert.

In terms of impact, many sites have found that Xpert MTB/RIF results in increases in bacteriologically-positive TB, but studies in Southern Africa, Brazil and Nepal have shown that it does not necessarily increase the number of overall TB cases notified, given frequent clinical diagnoses and empirical treatment. Numbers of rifampicin resistant TB cases detected have increased significantly in many sites, though the overall quantification at global level is challenging given limitations in reporting. Some studies have shown that use of Xpert results in a significant decrease in diagnostic delay and start of treatment, yet few places are able to take advantage of the rapid 2-hour nature of the test. Limited data are available on its impact in terms of morbidity and mortality, and on its cost-effectiveness and impact on patient costs; further research needs were described.

Use of Xpert MTB/RIF for diagnosis of paediatric TB

C.N. Paramasivan (FIND)

Exact burden of childhood TB in India is unknown. Total number of paediatric TB cases in 2013 was 6'391, accounting 5% of all notified TB cases. The challenges existing in diagnosis of TB in children were discussed. Xpert MTB/RIF testing for presumptive paediatric TB cases was piloted in four major Indian cities, in order to assess feasibility of implementation, to evaluate Xpert MTB/RIF performance on different types of paediatric specimens under routine programme

conditions and to assess the diagnostic yield of Xpert MTB/RIF assay on different types of specimens. The intervention has included establishing one Xpert MTB/RIF site in each city in the existing RNTCP reference labs and establishing referral linkages with public and private providers for rapid reporting mechanisms (SMS and e-mail). Number of presumptive paediatric cases tested has grown continuously from April to December 2014.

It was noted that most specimens were transported on the same day of sputum collection and most results reported on the same or next day, median turnaround time for specimen transportation, testing and reporting of result was 1 day. The main outcome of the project is that Xpert MTB/RIF led to additional detection of TB cases in all types of specimens as compared to smear microscopy. However, Xpert MTB/RIF performance was suboptimal in pleural and ascetic fluids.



Moving beyond risk groups for Xpert MTB/RIF testing: The role of chest X-ray as a screening tool

Anja Van't Hoog (Amsterdam Institute for Global Health and Development)

CXR is a mainstay of clinical practice and can be used to select patients for diagnostic testing or direct diagnosis of TB, or as a screening tool (in active case finding, prior to LTBI treatment – to rule out active TB, in presumptive TB patients in clinical settings). CXR in active case finding, as a single screening test is characterized by high sensitivity. CXR screening compared to symptom

screening is characterized by higher sensitivity, greater accuracy, and less heterogeneity. CXR can identify persons with highly suggestive TB abnormalities who are missed by bacteriological tests.

As a conclusion it was noted that triage test can reduce diagnostic costs if high sensitivity (detect all cases that can be detected by the confirmatory test). Specificity and cost are a trade-off. Triage test could increase affordability and presumably access to improved TB diagnosis with Xpert MTB/RIF. The utility of computer assisted reading of digital CXRs as a triage test requires further confirmation.

Private sector Xpert MTB/RIF scale-up: successes and challenges of the TBXpert social business projects

Aamir Khan/Imran Zafar (IRD)

In Pakistan in general and in Karachi in particular, there are multiple private providers who are first reference point for the presumed TB patients in approximately 50% of cases. In Bangladesh and in Indonesia, the private providers account for large part of TB diagnosis and treatment as well. Social business support to major public hospitals to scale up Xpert MTB/RIF testing in Karachi, Dhaka and Jakarta is an innovative way to integrate private providers in TB diagnosis and care, which assures free Xpert testing for TB, along with affordable cost of additional laboratory/instrumental testing, including X-ray, blood-sugar etc.

The scope of activities include: installation of a GeneXpert machine at a designated public hospital, providing reagents, cartridges and maintenance; uninterrupted power supply in Karachi; developing referral network in the surrounding area and conducting verbal screening within public hospital ensuring quality sputum and testing, supporting drug-susceptible patient care and direct linkages with PMDT sites. The MTB positivity rate in presumed TB cases in three sites was 6,9-17,6%, and rifampicin resistance rate - 5,6-7,2%. Except Indonesia the treatment enrolment rate for both rifampicin resistant and sensitive cases was over 80%.

Discussion, Q&A:

Question was asked on high rate of rifampicin-resistance in diagnosed TB cases: except pleural and ascetic fluid specimens (where no rifampicin resistant cases were detected) the rate of rifampicin-resistance comprised 8.3-14.6%. In response, the comment was provided that likely re-treatment cases were included among diagnosed cases, which made rifampicin-resistant cases higher.

It was suggested that no increase in TB notification when Xpert is used, comparing to non-use, may be due to the high frequency of symptomatic treatment provided to patients who previously had their diagnosis based on clinical signs only. Thus Xpert has increased bacteriology confirmation rate only. In the same time, possible increase in TB notification expected after introduction of Xpert ULTRA, which has sensitivity

in SS- TB cases comparable to one of liquid culture.

The issue of ensuring high treatment success rate in diagnosed MDR-TB cases was raised, which encompassed both access and adherence to treatment. According to Pakistani representatives, free care is provided to MDR-TB cases both in private and public sector, in latter with funding from GF.

Session 6: Joint TB and HIV services platforms and opportunities for TB/HIV integration

Chairs: Meg Doherty & Heather Alexander

Session 6: Joint TB and HIV services platforms and opportunities for TB/HIV integration		Chairs: Meg Doherty & Heather Alexander
15:30	Point-of-care viral load platforms and opportunities for TB/HIV integration - Commentaries	Nathan Ford / Mercedes Pérez González Yukari Manabe K.S. Sachdeva
16:00	Discussion	
16:30	MDR-TB in PLHIV: impact and response - Commentaries	Enrico Girardi Alena Skrahina Norbert Ndjeka
17:00	Discussion	
17:30	<i>End of Day 2</i>	
17:40	Stakeholders Roundtable on Xpert MTB/RIF (<i>optional open session to discuss operational and technical updates and challenges with manufacturer</i>)	Moderator: Wayne van Gemert

Point-of-care viral load platforms and opportunities for TB/HIV integration

Nathan Ford and Mercedes Perez Gonzalez;
discussants:

Yukari Manabe and K.S. Sachdeva

The availability of multi-analytic platforms (i.e. diagnostic platform that tests multiple analytes using same assay principle) that provides diagnostic services for HIV and TB is a novel and attractive tool to synergize and coordinate overall TB and HIV services. Integrated diagnostic platforms could improve laboratory and programme efficiencies. At service delivery level, single window laboratory services may translate into better integrated patient-centred care. The deployment of viral load platforms for point-of-care testing capable of detecting TB at ARV centres may significantly reduce loss through referral for TB diagnosis, achieve earlier TB diagnosis and reduce mortality.

Platforms for point-of-care (POC) tests are particularly attractive for their potential for decentralized implementation. Currently WHO

recommends that Xpert MTB/RIF should be used rather than conventional microscopy, culture and DST as the initial diagnostic test for pulmonary and extrapulmonary TB in both adults and children living with HIV.

On the HIV side, a tremendous progress has been made in the scale-up of ART, which now covers over 50% of the eligible in many high burden countries and is looking to reach 15 million. Viral load (VL) monitoring is the gold standard for monitoring treatment and the preferred method to identify treatment failure. The latest UNAIDS Fast Track 90-90-90 targets reflect this focus, in particular in the target relating to 90% virological suppression among PLHIV receiving ART. POC viral load offers significant potential for increasing viral load capacity and strengthening scale-up.

Integrated platforms offer significant advantages in terms of efficiency of procurement, installation, calibration, maintenance, training and EQAS (inter-laboratory comparison). Over time costs of tests may be reduced for both NTP and NACP given the better negotiation power. They, however, entail several challenges as well: instrument downtime will affect both HIV and TB services; the development of the laboratory network will need to be harmonized between TB and HIV programs;

access to services may be adversely impacted due to lack of close collaboration: finally, it may lead to creation of monopolies and may translate into reduced incentive for good customer service.



Core messages:

- ✓ Access to viral load is a key priority for HIV programmes.
- ✓ Though centralized and decentralized platforms will probably co-exist, POC viral load offers significant potential for increasing VL capacity. Choice will depend on context
- ✓ Multi-analyte platforms capable to provide diagnostic testing for TB as well as VL determination for HIV routine monitoring is expected to create buy-in with policy makers for further joint TB and HIV programming and integration of TB and HIV diagnostic services.
- ✓ These platforms may lead to substantial savings not only through better negotiation power for consumables, but also through the optimization of efficiency in procurement, installation, calibration, power stabilization, maintenance, training and EQAS.
- ✓ The risk of competing interests needs to be early recognised and addressed. Dialogue and joint planning may prevent that the increasing volumes of VL monitoring is seen as a threat by TB programs.

MDR-TB in PLHIV: impact and response

Enrico Girardi;

discussants

Alena Skrahina and Norbert Ndjeka

Nosocomial epidemics of MDR/XDR-TB among PLHIV continue to occur. Several systematic

reviews have investigated the association between HIV infection and MDR-TB. The evidence for an association is somehow inconsistent and of limited magnitude (estimated pooled OR 1.24; 95%, 1.04–1.43). However, two important patterns can be identified. First, while an association between acquired drug resistance and HIV infection is very weak, the evidence for the association between primary drug resistance and HIV infection is solid. Second, systematic reviews focusing on Eastern Europe reveal a significant association, while those focusing on sub-Saharan Africa do not. The reasons for the geographical differences are unclear, though they may reflect differences in main key populations driving the HIV epidemic. The high risk of transmission of TB and MDR-TB in health care settings underlines the importance of a programmatic approach to effective infection control measures in all settings where PLHIV congregate. The absence of evidence on the risk of acquired resistance supports current WHO policy on TB treatment in PLHIV.

There is a large body of evidence to support HIV infection consistently and significantly affecting the survival of MDR-TB patients. Information on clinical challenges of MDR-TB management in Eastern Europe (EE) is provided by an international cohort of HIV positive patients consecutively diagnosed with TB enrolled in Europe and Latin America. In this cohort, TB/HIV mortality is higher in EE compared to all remaining regions. Despite the fact that the proportion of MDR-TB cases is significantly higher in EE, a definite TB diagnosis (and DST) is significantly less frequent (47%, compared to 71%). Moreover, the use of combination antiretroviral therapy, at TB diagnosis is significantly less frequent in EE.

These data strongly suggest that high mortality in TB/HIV cases in EE is driven by the high prevalence of MDR-TB and by the insufficient clinical response to this challenge, including failure to timely start ARV. In this setting, only a low proportion of TB cases are treated with knowledge of drug sensitivity. Given an approximate 50% probability of MDR-TB in PLHIV with TB and no DST result, any empirical choice to start a regimen for susceptible TB or MDR-TB will carry a 50% probability of choosing the wrong regimen. Access to rapid diagnosis of TB and MDR-TB in PLHIV is the potential solution and should represent a very high priority of HIV

services in this setting, which underlines the need for integrated TB/HIV services

Core messages:

- ✓ All PLHIV should have access to Xpert MTB/RIF as the initial test for TB diagnosis. In countries with high burden of MDR-TB that lack of access to immediate DST for PLHIV is resulting in mistreatment leading to high fatality and potential amplification of MDR-TB.
- ✓ ARV should be started as soon as possible in PLHIV and MDR-TB
- ✓ The same second line regimens used to treat HIV negative persons are recommended, including the newer drugs bedaquiline and delamanid
- ✓ Current evidence on additive toxicity and drug-drug interactions between second line TB treatment and HIV drugs is very limited. This information may become available from ongoing phase III trials for newer TB drugs, but it can only be derived from enhanced pharmacovigilance and ad-hoc PK studies as far as the older second line TB drugs are concerned.
- ✓ Transmission of MDR TB in health care facilities and other congregate settings is a persistent risk for PLHIV, and this calls for continuous improvement of infection control in health care facilities.

Session 7: Country Experiences in strengthening and aligning diagnosis and treatment

Chairs: Daniel Chin and Enos Masini

Wednesday April 29th

Session 7: Country experiences in strengthening and aligning diagnosis and treatment (1)		Chair: Daniel Chin
09:00	Progress and achievements of the EXPAND-TB Project for the diagnosis of multidrug-resistant TB	Daniel Orozco
09:20	The UNION's experience with implementing a 9-month regimen for the treatment of patients with MDR-TB	Valerie Schwoebel
09:40	The endTB Project: Expanding New Drug Markets for TB	Michael Rich
10:00	Strengthening and aligning diagnosis and treatment of drug-resistant TB in India	K.S. Sachdeva
10:15	Discussion	
10:45	<i>Coffee break</i>	
11:15	Roll-out of new diagnostics and first impressions: experience of Brazil	Draurio Barreira
11:30	Strengthening and aligning diagnosis and treatment of drug-resistant TB in Russian Federation	Irina Vasilyeva
11:45	Strengthening and aligning diagnosis and treatment of drug-resistant TB in Myanmar	Zaw Myint
12:00	Models of care for people with drug-resistant TB: advancements in South Africa	Norbert Ndjeka
12:15	Discussion	
13:00	<i>Lunch</i>	
Session 7: Country experiences in strengthening and aligning diagnosis and treatment (2)		Chair: Enos Masini
14:00	Experience of Ethiopia on the use of Xpert MTB/RIF: impact observed	Andargachew Kumsa / Endale Mengesha
14:15	Moldova: Changing the paradigm of PMDT	Liliana Domente
14:30	Advancements in PMDT and electronic recording and reporting in the Philippines	Celine Garfin
14:45	Strengthening and aligning diagnosis and treatment of drug-resistant TB in Bangladesh	S. M. Mostofa Kamal
15:00	Discussion	
15:30	<i>Coffee break</i>	

Progress and achievements of the EXPAND-TB Project for the diagnosis of multidrug-resistant TB

Daniel Orozco (FIND)

The presentation emphasized that the EXPAND-TB Project, which builds on US\$ 87 million of UNITAID support has aligned itself and its activities with national programmes and also with

the complementary resources from multiple partners for laboratory strengthening. An important achievement of the project is in linking and aligning its interventions with the funding streams from these partners and also with the TBXpert project funded by the UNITAID.

A total of 106,983 MDR-TB cases have been diagnosed by 31st December 2014, which represent 72% of the overall updated project

target. 101 of the planned 103 state-of-the-art central or reference laboratories have been established under EXPAND-TB, effectively harnessing UNITAID support for commodities with support from multiple other donors (notably the Global Fund and USG through USAID and PEPFAR). An overview of MDR-TB cases notified in 2009 - 2014 confirms an important contribution of the EXPAND-TB project to global TB control and an unprecedented expansion of diagnostics and treatment of MDR-TB globally.



The UNION's experience with implementing a 9-month regimen for the treatment of patients with MDR-TB

Valerie Schwoebel (The Union)

Early results of an operational study implementing the 9-month “Bangladesh” regimen in nine African countries are promising with > 80% success rate. However, all culture and DST results as well as data on relapses after treatment are not yet available. Some lessons learnt from this study: the excellent results observed in Bangladesh look to be reproducible in a different environment, DOT is strongly recommended, bacteriological follow up by culture is difficult to implement, surveillance of adverse events is absolutely critical. The Union is in favour of promoting this regimen and will communicate all study results as they become available

The endTB Project: Expanding New Drug Markets for TB

Michael Rich (PIH)

Main objectives of the project are to generate new evidence on safety and efficacy of new drugs and accelerate uptake of new drugs and novel regimens. The project will consist of two parts,

first will implement new regimens in 16 countries enrolling 2600 patients and the second part will be a clinical trial with novel regimens to be performed in 5 countries. The project will be following WHO policies, including strong emphasis on proper patient management and active pharmacovigilance. The clinical trial part of the project will follow a novel regimen development approach that is expected to accelerate development of the several most effective and optimised regimens for MDR-TB treatment.

Strengthening and aligning diagnosis and treatment of drug-resistant TB in India

K.S. Sachdeva (Central TB Department, India)

The progress and achievements of India CTD are impressive both in speed of implementation and the scale and focus on narrowing the gap between diagnosis and treatment of both TB and DR-TB patients. Challenges that are being encountered are numerous but many solutions have been identified and implemented to accelerate implementation. An important step for the national TB programme is the official start of the first national drug resistance survey in 2014.

Discussion, Q&A:

During the discussion, questions from the audience highlighted importance of collecting informed consent from patients enrolled in the framework of the endTB project for using patients' data in the research and discussed options of possible use of new TB medicines either concurrently or for the longer periods than current evidence suggests. Part of the discussion focused on the reasons of changing the regimen duration from 9 to 12 months in the UNION projects in nine countries of Africa and concluded with the need for an additional data was available on the mortality during treatment.

At the end of the discussion, representative from Kyrgyzstan made a strong call to partners and donors to help countries to sustain and expand further the achievements that EXPAND-TB project has helped to secure in countries beneficiaries.

Roll-out of new diagnostics and first impressions: experience of Brazil

Draurio Barreira (NTP manager, Brazil)

Presentation described roll-out of Xpert MTB/RIF in Brazil with objective of replacing smear

microscopy testing. Roll-out began in April 2014 and all sites were equipped by the end of April 2015. First results are encouraging showing the increase in detection of rifampicin resistance, significant reduction in the diagnostic delays leading to better alignment between diagnosis and treatment. Further analysis of the experience will be needed and important for wider expansion.

Strengthening and aligning diagnosis and treatment of drug-resistant TB in Russian Federation

Irina Vasilyeva (NTP manager, Russian Federation)

Dr Vasilyeva presented epidemiological situation with TB in Russian Federation, development of the epidemic of TB and DR-TB over the years and plans of the national TB programme in developing TB diagnostic and DST capacity. Priorities of the Ministry of Health are to improve adherence to treatment, introduce new TB drugs and improve TB/HIV control were also presented.



Strengthening and aligning diagnosis and treatment of drug-resistant TB in Myanmar

Zaw Myint (Ministry of Health, Myanmar)

Dr Zaw Myint talked about the TB and DR-TB burden in the country and steps taken while introducing new TB testing and DST. Recent introduction of liquid culture, LPA and Xpert MTB/RIF testing not only increased the detection of DR-TB cases but also allowed for early diagnosis and improved treatment prognosis. Some regions exhibit variable proportions of DR-TB patients' detected not receiving treatment yet but time trends show shrinking wait lists. The treatment success rates in Myanmar currently fluctuate around 70%.

Models of care for people with drug-resistant TB: advancements in South Africa

Norbert Ndjeka (Ministry of Health, South Africa)

South Africa is making big strides to expand use of molecular diagnostics and replace smear microscopy with Xpert MTB/RIF testing as well as making efforts to decentralise DR-TB treatment. The HIV prevalence being a big challenge for both the TB and HIV control efforts also presents a serious problem for advances in the treatment success rates. This calls for the wider and more aggressive introduction of new TB drugs in a more decentralised approach also reducing the diagnosis to treatment delay and reducing transmission.

Discussion, Q&A:

There was an interest from the audience to the incentives scheme for MDR patients in South Africa. Dr Ndjeka explained that some social support through relevant services is provided not focusing on the MDR-TB patients only. Hospitalized patients receive meals and are helped to find or re-initiate employment after leaving the treatment facility. Community involvement was considered to be very important. When asked about the negative aspects of Xpert implementation in Brazil, Dr Draurio answered that main negative aspect is considered to be the cost of the test itself.

Presenters from Russian Federation and South Africa were asked about their experience with BDQ and plans to expanding use of this new TB drug. In Russian Federation there is an ongoing treatment cohort of several tens of patients and the plans are to use this medicine in all pre-XDR and XDR patients following imminent registration of the drug in the country.

South Africa started to see better treatment outcomes in 2010-11 after introduction of moxifloxacin and clofazimin in MDR regimens and is carefully looking for the outcomes of the BDQ clinical trials, some of them running in SA, to prepare for a wider introduction at the same time being cautious and vigilant due to the drug's safety profile. Preliminary results of BDQ use are encouraging from the 12 sites where initial introduction has started.

Experience of Ethiopia on the use of Xpert MTB/RIF: impact observed

Andargachew Kumsa / Endale Mengesha (Ministry of Health, Ethiopia)

Ethiopia is following a structured route for implementation of Xpert MTB/RIF with development of strategy, the national guideline, the algorithms and multiple, cascading training and sensitization workshops for both laboratory professionals and clinicians. Strengthening of the integrated sample referral system and efforts to improve utilization of the GeneXpert systems are part of the implementation efforts. The impact of Xpert MTB/RIF implementation is clearly visible already with about 4-fold increase in RR-TB cases detection from 2013 to 2014. Need for careful site selection and sensitization of clinicians were among the critical steps to accelerate implementation.

Moldova: Changing the paradigm of PMDT

Liliana Domente (NTP manager, Moldova)

Through rapid implementation of the new TB diagnostics in the country with support of the EXPAND-TB and TB Reach projects the time to lab confirmation of TB has decreased. Rapid Rifampicin susceptibility testing is important as country experiences more than 20% of MDR-TB among new cases and more than 50% among retreatment cases. The paradigm of TB care has started to change with decentralization of the TB testing - 30 Xpert units spread in almost all districts of the country, and also with the changing approach to treatment decreasing the length of hospitalization. Among most prominent challenges are the lack of sufficient experience at the PHC level and resistance from clinicians towards the ambulatory management of DR-TB.

Advancements in PMDT and electronic recording and reporting in the Philippines

Celine Garfin (NTP manager, Philippines)

Philippines had a significant gap between patients diagnosed and those started MDR-TB treatment in 2013 (57% of all diagnosed with MDR-TB started treatment). During the last 6-7 years country has scaled up PMDT and increased the number of MDR-TB patients on treatment.

This scale up coincides with a gradual drop in treatment success rates in this group of patients and several efforts are now being implemented to reverse this trend. Relevant changes are being introduced in several key documents guiding TB control in the country and pave the way for reform in TB care. Decentralization of PMDT coupled with enablers and allowances and the roll-out of electronic information system are considered as key interventions to increase access.

Strengthening and aligning diagnosis and treatment of drug-resistant TB in Bangladesh

Mostafa Kamal (NRL, Bangladesh)

Dr S.M Mostafa Kamal presented the progress with the scale up of PMDT in Bangladesh after implementation of GeneXpert and PMDT in two years regimen. The shorter, 9 - 12 month, regimen which is running under a NGO setting as OR showing promising and comparable results. It needs further verification as an OR under government setting in parallel to in two year regimen.

Discussion, Q&A:

It was noticed by the audience that despite adding diagnostic capacity with 30 Xpert instruments the case finding of the MDR-TB cases in Moldova did not increase. Dr Domente replied that this is related to the fact that access to diagnostic services was already good in the country, however the time to detection has decreased significantly, which is an important development as well.

Session 8: Donor perspectives and strategies to strengthen and align diagnosis and treatment

Chair: K.S. Sachdeva

Session 8: Donor perspectives and strategies to strengthen and align diagnosis and treatment		Chair: K.S. Sachdeva
16:00	Diagnostic network and treatment strengthening strategies in USAID-priority countries	Amy Piatek
16:20	UNITAID's approach to funding innovations in TB diagnosis and treatment	Robert Matiru Janet Ginnard
16:40	Achievements and challenges of the Global Fund's New Funding Model for strengthening TB control and PMDT	Mohammed Yassin
17:00	Discussion	
17:30	<i>End of Day 3</i>	
17:40	Stakeholders Roundtable on DST diagnostic technologies (<i>optional open session to discuss operational and technical updates and challenges with manufacturers</i>)	Moderator: Fuad Mirzayev

Diagnostic Network & Treatment Strengthening Strategies in USAID-Priority Countries

Amy Piatek (USAID)

The presentation provided an overview of the United States Government's Lantos-Hyde Tuberculosis Strategy 2015-2019, including the impact, long-term outcomes (e.g. reduction of TB incidence by 90% and mortality by 95% by 2035), medium-term outcomes (e.g. reduction of TB incidence by 25% by 2019) and objectives. In the USAID's mechanism of support, approximately 85% of the support goes to field and regional level, focusing on the response to local needs, technical assistance, expansion of new approaches and technologies, and Global Drug Facility. The USAID provides approximately 15% of its support to activities at the global level through different technical agencies working on policy and guideline development, operational, implementation research and technical support.

The first objective of the strategy on improved quality patient-centred care, DR-TB and TB-HIV services was highlighted including supporting a comprehensive, high quality diagnostic network

for TB. The USAID supports strengthening overall diagnostic networks at global, national (central), intermediate and peripheral levels; and continues its support to scale-up of Xpert MTB/RIF. The presentation also highlighted the USAID's support to manufacturers on improving quality assurance, reducing price, and strengthening drug management systems for anti-TB drugs. A number of country examples on delivery of care supported by USAID were presented such as community PMDT (Nigeria), mHealth and community PMDT (Bangladesh), evaluation of loss-to-follow-up during the MDR-TB treatment (Philippines), and linking diagnostics, drugs and delivery of care in different settings.

UNITAID's approach to funding innovations in TB diagnosis and treatment

Janet Ginnard (UNITAID)

The presentation described UNITAID's contribution to the global response, addressing global goals and challenges in HIV, Malaria and Tuberculosis. An integrated, market-based approach to diagnosis and treatment of TB was presented. The UNITAID-supported projects in TB

diagnostics, EXPAND-TB and TBxpert, are supporting expanded access to quality TB diagnostics and reduction of the diagnostic price. UNITAID will continue working on defining market opportunity and accelerating market entry for innovative TB diagnostics that address needs – e.g. alignment with identified priorities, a more diversified market, testing closer to the point of care, and diagnostics to support access to new medicines or novel regimens. UNITAID-supported projects in TB medicines include work in improving uptake of paediatric TB medicines, developing new formulations of paediatric FDCs, stabilizing drug supply for second-line TB drugs, and supporting the introduction of new medicines and novel regimens. The newly approved EndTB project aims to accelerate access to new medicines and to develop novel regimens which are shorter and less toxic than the currently available regimens.

Global Fund support for strengthening TB Control and PMDT

Mohamed Yassin (The Global Fund)

The presentation provided an update about the Global Fund's TB Grant Portfolio. Between 2002 and 2014, Global Fund has approved TB grants with a total of \$4.8 billion in 109 country and 1 multi-country programmes. Of this total amount, \$3.8 billion has been disbursed and the annually disbursed amount increased up to over 0.7 billion in 2013. In the Global Fund's New Funding Model (NFM), allocation for TB is 18% of the total funding for all three diseases: HIV, malaria and TB. Between May 2014 and January 2015, concept notes with a total of \$10.3 billion for three diseases were submitted and reviewed by the Technical Review Panel (TRP) through windows 1-5. Many of the concept notes are joint TB and HIV. The NFM shows positive outcomes with rapid iteration with TRP and results in 100% final success rate. Estimated average duration from submission to communication of results reduced from 4 months in round 10 to less than 2.7 months in windows 1 & 2 of the NFM. Results from a survey on GF's funding models also show that 77% of the survey participants found the NFM an improvement compared to the round-based model. Lessons learned from the TRP's review of concept notes were also presented.

Discussion, Q&A:

The discussion raised by the audience was on the strategic investment or mobilization of funds for

TB and the strategic use of funds in countries. Global Fund currently fills the investment gaps in the countries and continues working with the governments and other stakeholders to increase in-country investments. Similarly, USAID focuses on the local capacity building and advocates for more countries' responsibilities in investment.

Regarding human resource development (HRD) strategy, USAID supports countries to advocate, empowers the HRD and addresses specific HR issues that would be adaptable to the countries. Global Fund contributes to the program management including filling HR gaps (e.g. hiring staff). UNITAID makes focused, catalytic investments aimed to fundamentally change commodity markets, but some projects do include funding support for complementary areas.. However, sustainability should be considered by countries to avoid HR problems that may occur when the funds stop. Governments or local agencies take over the HR costs is an important and critical point that needs to be advocated.

The audience also raised discussion about UNITAID's work on paediatric formulations. Through the UNITAID-funded STEP TB project, TB Alliance will bring much-needed child-friendly first-line TB medicines to the market in the coming year. Further work is needed to improve access to paediatric medicines for both DS-TB and DR-TB.



Session 9: Initiatives to strengthen PMDT

Chair: Rohit Sarin

Thursday April 30th

Session 9: Initiatives to strengthen PMDT		Chair: Rohit Sarin
09:00	SWIFT Initiative: rationale, achievements and plans	Jennifer Furin
09:20	RESIST-TB: Achievements and future activities	Grania Brigden
09:40	Discussion	
10:00	GDI patient-centred care taskforce update	Carrie Tudor
10:15	GDI research taskforce update	Agnes Gebhard
10:30	<i>Coffee break</i>	
11:00	GDI infection control subgroup update	Carrie Tudor
11:15	GDI advocacy taskforce update	Dalene von Delft
11:30	Discussion	
12:00	<i>Lunch</i>	

SWIFT Initiative: Rationale achievements and plans

Jennifer Furin (Harvard Medical School)

The SWIFT Response Project was announced on December 18, 2014 and consists of 77 international DR-TB experts from 21 countries. SWIFT stands for Society Working on Implementation to Fight TB and the goal of the group is to rapidly develop implementation tools to ensure optimal use of new TB drugs in order to provide the best possible outcomes for patients and programs. These drugs include bedaquiline, delamanid, linezolid and clofazimine.

Since coming together in December of 2014, the SWIFT Response Project has developed a field guide for new drug implementation, a patient workbook to facilitate better communication between providers and patients, and a training curriculum covering relevant topics for the use of new and re-purposed drugs. The group is also working on developing practical tools for pharmacovigilance and training materials for nurses and treatment supporters and also hosts a monthly webinar to share information and lessons learned on new and repurposed drugs

RESIST-TB: Achievements and future activities

Grania Brigden (MSF)

The presentation was on behalf of RESIST TB group. The RESIST TB stands for Research Excellence to Stop TB Resistance. This is an organization of concerned patients, physicians, research scientists and other stakeholders. The mission of RESIST TB is to promote clinical research in the diagnosis and treatment of drug-resistant tuberculosis and accelerate uptake in the field. Dr. Brigden has shared with the audience the activities of the Expanded Access working group and its projects funded by the Firland foundation. One of these projects will be reviewing the regulatory systems of each of the 27 high MDR-TB countries and determining the process for compassionate use, or any similar pre-approval mechanism to access new drugs, and the 2nd will be surveying providers to gather experiences trying to access investigational drugs. RESIST TB in collaboration with GDI's Research Task Force is completing an exercise in establishing PMDT research priorities. This has entailed reviewing literature and resources to identify research questions in PMDT, surveying stakeholders on the relative importance of these research questions, and drafting a manuscript for publication. It was mentioned that RESIST-TB has been collaborating with TBNet on a manuscript formulating consensus guidelines on the clinical

implications of molecular TB drug susceptibility diagnostics. At the end she announced that two symposia's are submitted to the IUTLD 2015 in Cape Town focusing on pre-approval mechanisms to new TB drugs and another will be on new drugs in the preclinical pipeline.

GDI Patient-centred care task force update

Carrie Tudor (International Council of Nurses)

The presentation has emphasised the objectives of the Patient-centred taskforce, including identifying the gaps and priorities for development of practical tools, addressing the urgent needs regarding access to diagnosis and/or treatment enrolment and assisting programs in moving from hospital-based approach to community based care.

Among other activities undertaken by PCC task force, training of nurses, held in Quezon City in the Philippines from 17-21 November in collaboration with rGLC, WPRO, Philippine NTP and the Philippine Nurses Association held in was highlighted. The training included theoretical input, practical exercises and site visits arranged in collaboration with Philippine NTP Manager. Training has been cascaded to other nurses and health professionals In the nearest future the PCC task force plans to develop a practical tools for assessment, planning and implementation of patient-centred PMDT, to conduct a nurse consultant training in each region starting with AFRO and EURO and advocate ensuring that patient-centred PMDT properly planned for and funded within the PMDT scale-up activities. The PCC task force requests for nurse consultants trained in the Philippines to be included as members of review teams in EURO, AFRO, WPRO and SEARO.

GDI Research Task force update

Agnes Gebhard (KNCV; GDI vice chair)

GDI Research task force shared the audience a prioritized research agenda developed in collaboration with the former Research Subgroup of the MDR-TB Working Group of the Stop-TB Partnership and RESIST-TB. The group initially reviewed the previous agenda and afterwards identified the knowledge gaps which later were translated into research questions. Analyses of results are completed and manuscript development is underway.

In the last quarter of 2014, the research task force has developed an overview of ongoing DR-TB research activities. This overview should be seen as a living document and be updated regularly. At the end, the task force leader announced that a Generic protocol for the shorter treatment regimen for MDR TB patients has been already developed and soon be published at the GDI website.

GDI Advocacy Task force update

Dalene von Delft (Advocacy task force lead, GDI Core Group member)

The advocacy task force update was a recorded presentation reported by Jonathan Smith on behalf of GDI Advocacy task force, led by Dalene von Delft. The presentation covered the broad topics of Human Spirit Project's activities and followed by a novel monitoring and evaluation method jointly developed with the task force leader and human Spirit Project team. The Human Spirit Project is an ongoing collection of individual stories of peoples' personal battles in the tuberculosis epidemic with the purpose to meaningfully change the conversation about TB. Through intimate storytelling, the Human Spirit Project brings to light the many challenges the global community is faced with in the TB epidemic, from patients to policymakers. Currently, HSP has issued three films: "Strength of a woman", "Hear no Evil" and "A bird in the wind". The motivation behind the project is that instead viewing the global burden of TB as one large epidemic viewing it as a collection of individual battles. The project does this through themes of shared values and connections.

GDI infection control subgroup update

Carrie Tudor (International Council of Nurses)

The presentation was made by Dr. Tudor on behalf of Infection Control sub-group established in 2007, which initially was set up under TB/HIV working group and in October 2014 moved to GDI. The TB Infection Prevention and Control Working Group is a group of professionals working in TB dedicated to saving lives worldwide.

The mission of IC subgroup is to provide leadership on the implementation of effective TB infection prevention and control with the following strategic objectives: to advocate and communicate for preventing TB transmission as a strategic priority worldwide; to identify key

partners and work with them collaboratively to achieve our common goals; to broaden the evidence base about TB infection prevention and control, and disseminate to improve practice and to sustain improvement and innovate in TB infection prevention and control through better professional practice. In addition to that, the presenter has outlined the activities conducted in the last years as well as future 2015 plans.

Discussion, Q&A:

The leader of SWIFT project was asked if there is any evidence in using bedaquiline in children with MDR TB. The explanation was that as children were excluded in all clinical trials there is no evidence, however SWIFT is recommending using BDQ in vulnerable population, including children. Besides, it was mentioned that BDQ is much safer to use in pregnant woman than any of the 2nd line anti-TB drugs. GDI Research task force leader emphasised that countries need to develop a systematic approach prior using the new drugs, however some of the participants disagreed with this statement and stated that countries need to do both, develop a system and introduce the new drugs as soon as possible.

PCC task force leader was asked about the future plans and perspectives of the task force and if there is any progress in expanding the role of nurses in PMDT. Dr. Tudor mentioned that despite the several challenges in the countries, especially in regards with the lack of human resources, there are several activities planned within the frame of PCC. It was also noted that the detailed explanation of patient-centred approach and what is meant under this term is clearly reiterated in the updated companion handbook developed by WHO. Besides, Dr. Furin has mentioned that currently SWIFT project is working on developing the manual for nurses on how to use new drugs. The next round of discussion was devoted to the necessity of different types of DOT, including VOT and whether this is really patient-centred. The participants had various concerns related to the daily DOT. It was also noted that none of the e-tools are meant to replace the direct communication with patient; on opposite they need to be implemented in order to strengthen the real patient-oriented approach.



Session 10: Symposium on regional GLI/GDI initiatives

Chair: Philip Onyebujoh

Session 10: Symposium on regional GLI/GDI initiatives		Chair: Philip Onyebujoh
13:00	Regional GLC experiences – panel presentations and discussion (EUR, AFR, WPR, SEAR, AMR, EMR)	Regional GLC
15:00	<i>Coffee break</i>	
15:30	Regional GLI experiences – panel presentations and discussion (EUR, AFR, WPR)	Regional GLI
16:30	Priorities for moving forward the agendas of GLI and GDI: facilitated discussion	Tom Shinnick and Charles Daley
17:00	Closure of the Joint Partners Forum	

Part I: Regional GLC experiences – panel presentations and discussion

GLC EUR update

Andrei Maryandyshev (GLC European region)

The presentation emphasized that the WHO/EURO region bears disproportional burden of MDR-TB, out of 27 high MDR-TB burden countries worldwide, 15 are located in WHO/EURO region. Furthermore TB burden is unequally distributed among the region, with 99.5% of MDR TB cases occurring in 18 high priority countries. Proportion of MDR-TB among new and re-treatment cases in WHO/EURO is 14% and 44% respectively, comparing with 3.5% and 14% worldwide, reaching as high as 35% in new cases in Belarus and 62% in Moldova and Uzbekistan. The mission of rGLC EURO is to achieve a WHO European Region free of drug resistant TB. The Main activities of regional GLC for WHO/EURO region including: technical assistance in PMDT on county level, consultations and collaboration with GF Country Teams, regional and national capacity building.

GLC AFR update

Norbert Njeka (GLC African region)

Main objective for regional GLC for WHO/AFRO region is to monitor the implementation of programmatic management of drug resistant TB programmes in Africa. Among main findings/challenges in countries were mentioned: unknown burden of MDR-TB due to poor / non-existent surveillance systems for DR-TB, need for

laboratory strengthening, human resource challenges, including low health worker awareness and skills to effectively manage DR-TB cases, poor quality of services, miscalculation of the need for SLD, poor infection control practices.

GLC WPR update

Lee B. Reichman (GLC Western Pacific region)

GLC/WPRO experience was highlighted PMDT activities in PNG. In 2008-2014 the country has experienced 4th fold growth in TB cases notification, which however was coupled with high loss to follow up (32% in new cases). MDR among new cases in 2014 has comprised 3.2% whereas in previously treated cases 23%. There are certain achievements in TB control, such as political commitment, quality assured 1st and 2nd line anti TB medicines procured by government from the GDF, DOTS expansion, national TB protocol, PMDT guidelines, and TB/HIV collaborative activities guidelines developed/updated.

The Department of health of PNG invited the rGLC to visit and observe the problem directly. This was done in a mission in May 2015 and strong recommendations were made on strategies to begin to alleviate the problem.

GLC SEAR update

Rohit Sarin (GLC South Eastern Asian region)

SEA Region accounts for almost 30% of the global burden of MDR-TB (an estimated 89,000 out of the global 300 000 cases, with 62 000 of regional cases in India alone). However, of these

only 40, 335 RR-TB and MDR-TB cases detected by the end of 2013. High MDR-TB burden in SEAR: Bangladesh, India, Indonesia, Myanmar. There were key recommendations presented from 6th r-GLC meeting, among them: SEA Countries need to develop a policy for systematic, controlled introduction of new drugs like Bedaquiline in line with WHO guidelines; community PMDT model in Bangladesh to be reviewed considering all dimensions of community engagement and implementation barriers. Modalities and lessons learnt through c-PMDT can be shared with other countries; Generic WHO 2014 PMDT training material to be looked into as per country context for adaptation in the countries; r-GLC secretariat can facilitate the process of using opportunities through newly established WHO collaborating centres.

GLC AMR update

Raimond Armengol (GLC American region)

The Regional GLC of AMR was established in April 2011. The following laboratory/treatment capacity is present in the region for diagnosis of MDR TB: DST for FLD is available in all the GF countries (12), for SLD in 5 countries of the region. 14 of 35 countries in the Region have procured and use Xpert (1,093 Xpert modules and more than 450.000 cartridges – until 2014). Around 7,000 people are estimated to develop RR/MDR-TB in the Americas per year. In 2014, a total of 4,154 MDR-TB cases were estimated and 2,108 detected in the 12 GF countries (51% of the estimates). The following achievements on the PMDT in the region were presented: PMDT Expansion Plan is available in all 12 GF countries; Drug procurement through PAHO's Strategic Fund & GDF is taking place in all 12 countries, updated DR-TB guidelines in 9 countries.



GLC EMRO update

Essam Elmoghazy (GLC Eastern Mediterranean region)

There were presented update on implementation of the work plan 2014-2015. The activities were ongoing in following strategic direction: strengthening planning for expansion of PMDT, HR capacity, laboratory capacity, drug management, filling financing gap, monitoring and OR. Eleven monitoring missions have taken place or in progress in the region since November 2014. The next steps in regional PMDT include rGLC meeting 25-26 May 2015, revision of the structure of the committee.

Discussion, Q&A:

The issue of prioritizing preventing MDR-TB activities over treatment of existing MDR TB cases has been highlighted, thus positioning the treatment of susceptible TB as the most effective means of MDR TB epidemics prevention. There was no disagreement that preventing of MDR TB occurrence is a condition sine qua non for effective tackling MDR TB epidemic. To specify the working relations of rGLCs with countries, it was noted that rGLC secretariat is responsible for processing the requests from countries on technical support and liaising with them. The requests can be channelled through country WHO offices as well as directly to rGLC secretariat.

The regulating role of rGLC AFRO in regarding PMDT activities in the region was inquired. It was noted that r-GLC's role is ensuring availability of technical support rather than regulation. The representatives of several r-GLC (SEARO, AFRO, EURO, WPRO) has stressed continuity as well as holistic approach in the provision of the technical support, aiming at involving the same advisers in conducting follow-up missions as well as involving clinical and laboratory advisers in the same missions.

The representatives of number of r-GLC (SEARO, AFRO, EURO, WPRO) have confirmed availability of funds to continue country support for PMDT activities. It was further noted that considerable variability exists between WHO regional from epidemiological, health systems and cultural perspectives, thus making difficult cross-comparison of their experiences and achievements. There is further variability within the regions down to country levels, which makes it possible to provide extensive assessment for PMDT activities only at country levels.

Part II : Regional GLI experiences – panel presentations and discussion

GLI EUR

Martin van den Boom (GLI European region)

The following achievements in PMDT in the region were presented: In 2013, all notified MDR-TB patients started second-line MDR treatment (including cases detected in previous years). 40% increase in MDR-TB detection since 2009. Increase in use of rapid molecular methods at civil and penitentiary TB diagnostic facilities.. Post 2015 WHO EURO TB action plan includes integrated, patient-centred care and prevention, strengthening European Laboratory Network (ELI), New TB algorithm developed by ELI, Strong collaboration with and excellent support by SRLN.

There has also been a considerable and further reduction of SLD stock-outs in High Priority Countries of the WHO European Region, further decrease of default rate of among new lab-confirmed TB cases and an expansion of the electronic case-based data MDR-TB management system and improvement of countries' capacity in utilizing it.

GLI AFR

Moses Joloba (GLI African region)

The update on status of TB labs in WHO-AFRO region was provided, including the fact that 8,535 labs are linked to national TB programmes for AFB smear microscopy services, 63 labs providing TB culture, 52 labs providing solid or liquid phenotypic DST, approximately 39 labs provide LPA, over 500 GeneXpert systems installed in the region by Sep 2014. It was mentioned, however, that quality of services often unreliable due to poor quality assurance and quality management systems.

GLI WPR

Cornelia Hennig (GLI Western Pacific region)

Misalignment: in 2013, of the 71 000 estimated MDR TB cases in the region, 11 000 (16 %) were notified and 6 900 (62 % of notified) were enrolled into treatment. In the 2011 cohort, the proportion of MDR-TB cases successfully completed treatment was 52%, with 21% loss to follow-up and 10% deaths. Country-by-country analysis and tailored action is necessary towards

universal access to DST, improved alignment and case management.

Seven countries of the region plan to or have introduced the 9 month regimen, and three of them have included new TB drugs (bedaquiline/delamanid) in their treatment regimens. The draft Regional Framework for Action to Implement the END TB strategy, for endorsement by the Regional Committee in October 2015, proposes laboratory strengthening with a strong focus on quality management, accreditation, rapid uptake of new diagnostic tools and a strong focus on patient-centred care responding to the psychosocial, material educational needs of all TB patients.



Discussion, Q&A:

As a challenge it was highlighted the shortage of the clinical laboratories in the countries, implementing PMDT activities, thus limiting possibilities for measuring liver / renal functions, complete blood counts. As an approach to tackle this challenge, the experience of AFRO was highlighted, aiming at building horizontal links, finding common grounds and involving general laboratory networks in TB laboratory strengthening activities.

The role of Ugandan SNL was recognized as critical in success of GLI AFRO activities. The need to ensure continuum of care and further integration between diagnostic and treatment activities was continuously highlighted by multiple speakers. One of practical implications of this collaboration and coordination is tackling problem of initial defaulters. In the same time it was noted that in AFRO region no unique identifiers exist for patients thus limiting possibilities for their tracing.

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