Translating the TB UN High-Level Meeting Commitments into Actions

Jointly organized by:
the WHO Regional Office for Europe, the European Centre for Disease Prevention and Control (ECDC) and KNCV Tuberculosis Foundation (KNCV)

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Wolfheze Workshops 2019

Report
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Abbreviations

aDSM active tuberculosis drug-safety monitoring and management
Bdq bedaquiline
CSO civil society organization
Dlm delamanid
DR-TB drug-resistant tuberculosis
DST drug-susceptibility testing
ECDC European Centre for Disease Prevention and Control
EEA European Economic Area
EECA eastern Europe and central Asia
ERI-TB European Tuberculosis Research Initiative
EU European Union
GDF Global Drug Facility
GTN Global Tuberculosis Network
KNCV KNCV Tuberculosis Foundation
LTBI latent tuberculosis infection
MAF Multisectoral accountability framework
MDR-TB multidrug-resistant tuberculosis
MOH Ministry of Health
NTP national tuberculosis programme
PCC people-centred care
PLHIV people living with HIV
PMDT programmatic management of drug-resistant tuberculosis
rGLC regional Green Light Committee
RR-TB rifampicin-resistant tuberculosis
SLD second-line drug
SOP standard operating procedure
SORT-TB Structured Operational Research and Training Initiative
TB tuberculosis
TORs terms of reference
UNHLM United Nations High-level Meeting
USAID United States Agency for International Development
XDR-TB extensively drug-resistant tuberculosis
Acknowledgements

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Background

The tradition of the Wolfheze movement dates back to 1990 when the first regional meeting on tuberculosis (TB) control was organized in the village of Wolfheze in the Netherlands. Since then, the Wolfheze Workshops have taken place every two years and aim to strengthen TB prevention and care in the WHO European Region. The Wolfheze Workshops are a platform for national TB programme (NTP) managers, health authorities, scientists, representatives from civil society organizations (CSOs) and other partners to share experiences and build consensus on the way forward to end TB.

The central theme of the Wolfheze Workshops 2019 was “Translating the TB UN High-Level Meeting Commitments into Actions”. The focus was on accelerating towards ending TB in the WHO European Region, building on the momentum gained from the United Nations General Assembly High-level Meeting on Ending TB (UNHLM) that took place on 26 September 2018 in New York, United States of America.

In view of the urgent need to combat rising rates of HIV and TB/HIV coinfection in the European Region, and in order to more effectively address this alarming co-epidemic, this year the Wolfheze Workshops began with a joint TB/HIV day on 15 May 2019. The day was planned to unite stakeholders of national TB and HIV programmes and relevant partners in defining collective actions for driving the TB/HIV response in the European Region. Other regional issues, such as the high rates of drug-resistant TB (DR-TB), the fact that a considerable number of countries are in pre-elimination/elimination stage, the generally vertical orientation of disease programmes, and patient stigmatization, were also addressed by several sessions.
Session 1. Opening and Key United Nations High-level Meeting declarations on TB and HIV

Summary
The purpose of the session was to raise and maintain awareness of the various regional and global targets for TB, share experiences and identify options for reviewing regional progress towards them.

Dr Marieke van der Werf (European Centre for Disease Prevention and Control (ECDC)) officially opened the meeting, highlighting the importance of Sustainable Development Goal (SDG) 3.3 and the recent UNHLM in international efforts to tackle TB.

Dr Masoud Dara (WHO Regional Office for Europe) then stressed the significance of bringing stakeholders of the national TB and HIV programmes together in such a meeting for the first time, noting that the WHO Regional Office for Europe has combined their TB, HIV and viral hepatitis programmes to ensure improved collaboration.

Reina Buijs (Directorate-General for International Cooperation, Ministry of Foreign Affairs, Netherlands) addressed delegates, detailing the role that the Netherlands is playing in the fight against TB. She stressed the importance of health system strengthening to ensure long-term sustainability for TB and HIV care, as well as the need to ensure the rights of marginalized groups, who are often the most vulnerable to these conditions. Finally, Ms Buijs detailed the Netherlands’ funding of research and innovation for TB prevention and care, and stated her pride that KNCV Tuberculosis Foundation (KNCV) is at the forefront of tackling the disease worldwide.

Dr Masoud Dara summarized political commitments that have been made on TB in 2000–2018, focusing especially on the UNHLM and the important role this has played in increasing political support for TB prevention and care. He noted that while there have been some improvements in TB detection and treatment, there is still some way to go to meet the targets set by the WHO End TB Strategy, with multidrug-resistant TB (MDR-TB) being a particular challenge. Finally, the United Nations common position on ending HIV, TB and viral hepatitis through intersectoral collaboration, published in 2018, attempts to improve the focus on social determinants of health – factors that are beyond the realm of the health sector itself.

Dr Marieke van der Werf presented the epidemiological situation regarding TB and HIV, specifically in Member States of the European Union (EU)/European Economic Area (EEA). She stressed that while targets are being met in some areas (e.g. diagnostics), progress needs to be accelerated in order to achieve treatment success targets. There are some important areas that countries do not routinely collect data on, namely on catastrophic costs, despite this being an integral part of global and regional targets.

Dr Kitty van Weezenbeek (KNCV) presented on research and development for TB, noting that the research pipeline is as busy as it has been for many years. She urged countries to be flexible to adapt to the rapidly changing tools that are at their disposal, but noted that structures need to be put in place in order to benefit from their use, including active TB drug-safety monitoring and management (aDSM), updated national strategic plans, and advocacy measures to convince politicians of the need for a new technology or drug.
It was noted during the morning session that setting targets is one thing but implementing change is quite another. Monitoring and reviewing whether targets have been achieved is essential, but can be difficult. Biased or incomplete data pose significant challenges, but a balance must be struck to ensure there is no duplication and that the number of indicators is not too burdensome for national programmes. In addition, it was felt that annual reporting on some indicators may be excessive and that rationalizing this to every two years may be appropriate in some cases. The role of CSOs in holding governments and NTPs to account was emphasized. In particular, CSOs can be the most effective groups to stand up for the needs of key vulnerable populations that are often disproportionately affected by both TB and HIV. The recently published Declaration of the Rights of People affected by Tuberculosis – developed by the Stop TB Partnership and TB People – highlights the important role to be played by civil society in advocating for individuals with TB. All parties with an interest in tackling TB should ensure sustained advocacy efforts, even when TB incidence rates fall. The last patients are likely to be the most socially or medically complex to treat and without sustained political commitment, the resources and expertise required to treat them may not be available.

NTPs are regularly faced with updated guidelines or new targets for TB care. This poses some challenge to such programmes and their managers, who must bridge the gap between policy and implementation. Professor Zaza Avaliani described the Georgian process of developing new guidelines at country level based on regional guidance, which then needs to be approved by the Ministry of Health (MOH) and accompanied by appropriate training for health-care workers and clinicians on the ground. In addition, he stressed the importance of coupling each implementation plan with one for monitoring to ensure that the policy is carried out correctly.

In acknowledgement of the fact that many sectors – including the health sector – have a responsibility to contribute to tackling TB, WHO has produced the Multisectoral accountability framework to accelerate progress to end tuberculosis by 2030 (MAF). This was initially recommended in the Moscow Declaration to End TB in 2017, and an initial draft was presented at the UNHLM in September 2018. The final draft of the MAF was presented and endorsed at the Seventy-second World Health Assembly in May 2019, and the WHO Regional Office for Europe is planning to develop and gradually implement a regional adaptation of it.
Session 2. Collaboration between TB and HIV programmes and partners

Summary

Group 1. Integrated collaborative TB/HIV service provision, including for key and vulnerable populations
The group work identified key challenges and proposed solutions.

(i) Challenge: insufficient attention to stigma and its effect on treatment outcomes.
Suggestion: more information campaigns for general and targeted populations.

(ii) Challenge: the need for better collaboration between health personnel providing TB and HIV services and involvement of community organizations in improving quality of care. There is a lack of mechanisms for better integration between services at local level and a certain lack of legal foundation and clear mechanisms for institutionalization of the involvement of community organizations for integrated service delivery.
Suggestion: to have a legal framework, roadmap and mechanisms for integrated service delivery focused on patients’ needs with a clear role for community organizations in service delivery. In addition, joint training of health personnel and community organizations on TB/HIV management and collaboration is also important.

(iii) Challenge: involving local governments in implementation of TB/HIV policies and strategies, and a certain lack of commitment of local governments in the TB/HIV response.
Suggestion: involve local governments to have an impact on TB/HIV policies and strategies and use patient community organizations to advocate for and to be messengers to local authorities.

(iv) Challenge: improving quality of services.
Suggestion: joint training of TB and HIV care providers for better management of drug interactions and side effects of TB and HIV treatment of patients with coinfection and comorbidities.

Group 2. Screening for latent TB infection (LTBI) in people living with HIV (PLHIV)
The group had a consensus that LTBI screening should be conducted for PLHIV, however different approaches should be used in different settings. Evidence on optimal screening intervals is insufficient. Participants raised an ethical question as to whether it is appropriate to screen for TB if no treatment is available.
Main challenges: collaboration and communication between health personnel working in HIV and TB; LTBI is not a notifiable disease; low compliance with LTBI treatment.

Group 3. TB/HIV data linkage and sharing of information
It is important to have arguments for evidence-based interventions for HIV/TB patients but there are several barriers when data is collected and integrated:
- Strict data protection: this is often a barrier to data linkage.
- Security policy: different security policies are used for TB and HIV, so it is hard to operate and respond to requests promptly. In some countries, TB and HIV services are located far away from each other, which contributes to a communication problem.
- Quality of data: sometimes it is technically not possible to integrate different databases.
- Data quality is not optimal: information on social risk factors is insufficient due to poorly collected data. For most countries we have data on diagnosis, however, it is much harder to get data on treatment completion both for HIV and TB.
Suggestions: take out patient identifiers so the data can be used to a much greater extent; have coordination meetings between HIV and TB data collection managers; qualitative data is important to close the quantitative data gaps.

Next steps
The TB/HIV epidemic is growing in the WHO European Region. Better coordination is crucial to ensure integrated people-centred services which meet the need of patients. We need to:

- Prioritize WHO recommendations on HIV/TB and other comorbidities and adopt their implementation in country-specific contexts.
- Prioritize prompt diagnosis and treatment of TB/HIV coinfection, especially in advanced HIV cases.
- Better record data. Sharing data and available, effective and sustainable practices is important to further boost their scale-up.
Session 3. Country achievements on improving TB prevention and care

Summary
Integrated, people-centred care (PCC) and prevention is one of the three pillars of the WHO End TB Strategy. In 2019, five years after the launch of this strategy, countries have taken concrete steps to improve case detection, achieve early diagnosis, and treat and support all people with TB. This session aimed at harnessing country experiences and promoting intercountry collaborations, with a focus on efforts to prevent and reduce TB transmission, as concrete contributions towards TB elimination.

During the plenary presentations, participants were informed about the most recent European guidelines for management of LTBI. Similarly, the Guiding principles to reduce tuberculosis transmission in the WHO European Region were presented.

In addition, lessons learned on how to prioritize activities for ending TB in the Republic of Moldova were shared, providing one country example from the European Region. Among these, the importance of political commitment at national level, coupled with collaborative efforts with local authorities, civil society and nongovernmental organizations were highlighted. Several good practices were presented in describing their country approach to: (i) strengthening health system capacity; (ii) ensuring universal access to TB services (i.e. early diagnosis and appropriate treatment with people-centred approaches); and (iii) promoting integration of health services within and outside the health sector (e.g. an integrated model for TB, HIV and opioid dependence therapy).

Group 1. Implementing programmatic approaches for LTBI management
Participants shared their experiences on national implementation of LTBI management. Through interactive discussion, participants reflected on achievements, such as:
• conducting contact investigation among children consistently;
• implementation of targeted LTBI screening (i.e. for immunosuppressed patients and selected migrant groups);
• selecting LTBI treatment regimen based on the drug-resistance pattern of the source case;
• voluntary reporting of LTBI cases, for surveillance purposes.

They also discussed challenges in relation to communication with target populations, highlighting the need to make terms understandable, particularly when referring to the concept of “latency”. Another challenge mentioned was the lack of accessibility to rifapentine in the European market.

Participants also elaborated on county-specific issues that limit the implementation of LTBI management, for instance:
• the perception of LTBI management as low priority, partly justified by limited resources for TB activities;
• limited access to innovations (for diagnostics and treatment);
• dependence on donor funding;
• the reluctance of health-care workers to initiate LTBI treatment, even for child TB contacts.
**Group 2. Reducing the risk of TB transmission**

Participants brainstormed on the topic of reducing the risk of TB transmission in the European Region. At the end of the three-day event, a new Wolfheze working group on infection control was proposed to elaborate further on this topic.

Discussion then focused upon evidence underlying the threshold duration of exposure required to contract TB. The often-cited 8-hour exposure threshold lacks sufficiently robust evidence to support this recommendation. It was acknowledged that many different factors influence transmission of TB, making it difficult to define an adequate threshold. Participants highlighted the need for a stronger evidence base around the factors that contribute to infectiousness and susceptibility. It was suggested that an evidence-based time threshold, would help in advocacy efforts to reduce TB transmission, for example in prisons. In addition, recent research on bioaerosol production by TB patients was mentioned. The research results suggest that normal tidal breathing – not only coughing – could have a significant bearing on patient infectiousness.

Finally, the analysis of the TB cascade of care in Tajikistan showcased the challenges associated with the identification of “missing patients”. This study, implemented by KNCV as part of the Challenge TB project funded by the United States Agency for International Development (USAID), concluded that in order to capture all TB patients, improved data gathering is required, through ensuring that data is collected from all public health centres, laboratories and TB treatment facilities.

**Group 3. Reaching out to vulnerable populations in low-TB incidence countries** (examples from E-detect TB)

Participants were introduced to the objectives and preliminary results of the E-DETECT TB project (Early detection and integrated management of tuberculosis in Europe). This project aims to reduce the prevalence in communities and prisons and develop and disseminate a screening model for migrants and effective strategies for early diagnosis. Some of the highlighted results included:

- Active case finding among prisoners has been introduced in Romania.
- Screening for LTBI and active TB in migrants in Italy has been improved by moving from a fragmented screening process to establishing a single screening centre.
- The use of different LTBI diagnostics across countries explains differing detection rates.
- The proportion of LTBI treatment initiation varies greatly across the European Region.
- EU/EEA Member State action plans on TB vary greatly and could benefit from alignment.

Thereafter, the discussion focused largely but not exclusively on the screening of migrants. The main outcomes included:

- The implementation of screening for active TB and LTBI varies across the European Region.
- The context for screening varies across countries – for example, regarding migration pattern; migrant housing; funding of screening and treatment; and monitoring of the screening and the treatment outcome.
- Screening methods vary over time and between countries.
- Active TB screening needs to be strengthened.
- The E-detect TB project shows that changes in the model of care can greatly improve the effectiveness of LTBI screening and treatment.
• LTBI screening of specific high-risk groups has been proven to be cost-effective in a modelling study done for the ECDC. This could be used as an argument to achieve the necessary funding. Concern was expressed that the studies showing cost–effectiveness of LTBI screening were biased through an observer effect. A solution over time would be to monitor implemented screening and follow up on the results.

• ECDC LTBI guidance is available, but the implementation is the prerogative of each country, this requires political commitment.

• A challenge expressed by several countries was screening and treatment of transit migrants. LTBI screening and treatment is deemed unfeasible in mobile populations. However, it was noted that future shorter treatment regimens could partly solve this issue. Acceptance of screening and treatment may be jeopardized by migrants who fear expulsion.

• Challenges include tools for screening falling short in identifying cases (i.e. symptom screening) or not being widely available (i.e. X-ray).

• Countries with a high burden and a high influx of asylum seekers can benefit from international collaboration and support to strengthen active case-finding approaches.

Next steps
The group discussion also touched on a few possible next steps:

• The creation of a uniform screening policy across the European Region was suggested, but it was also highlighted that such a policy would then need to be adapted to country-specific policies due to the varying national circumstances.

• Collaborative projects are needed to improve access to TB and LTBI screening and treatment in countries facing a high burden of high-risk migrant populations.

• Development and implementation of pragmatic LTBI monitoring is necessary – to follow up on the commitments made by Member States.
Session 4. Research: European perspective

Summary
Major TB research needs in the European Region and key country achievements were discussed during the plenary session.

WHO shared experience in consistent promotion of TB research both globally and at the regional level. Research is one of the pillars of the WHO End TB Strategy and WHO Member States consistently confirmed their commitment to TB research through a number of declarations and resolutions in 2016–2018. WHO currently aims to put political commitment into action through development of the Global Strategy for TB Research and Innovation.

The Global Strategy for TB Research and Innovation will provide WHO Member States with a framework of interventions to remove barriers to TB research and boost innovation, to help achieve the goals and targets of the End TB Strategy. The main objectives of the Strategy are: (i) to create an enabling environment for TB innovation; (ii) to increase financial investment in TB research and innovation; (iii) to ensure equitable access to the benefits of research; and (iv) to promote and improve approaches to data sharing. The Strategy’s unique features include specific recommendations for countries, global partners, civil society and international agencies, and guidelines for implementation and monitoring progress. The Strategy will be available after the Seventy-third World Health Assembly in May 2020.

The Joint Tuberculosis, HIV and Viral Hepatitis Programme of the WHO Regional Office for Europe in turn is active in the Region in promoting the TB research agenda and supporting countries in TB research uptake. The Tuberculosis Action Plan for the WHO European Region 2016–2020 called for the establishment of the European Tuberculosis Research Initiative (ERI-TB). The Initiative was launched in 2016, connecting more than 100 members across the Region. The strategic objectives of ERI-TB include setting the regional research priority agenda, enhancing collaboration between research partners and building country capacity.

The ERI-TB core group conducted a survey using Delphi methodology to capture and prioritize topical research questions for the Europe Region. The final list included 19 research questions divided into three themes (epidemiological research; innovation and fundamental research; and operational research), that have high relevance and high priority in both high and low TB burden countries. Study findings are now available as a WHO publication, Defining the tuberculosis research agenda for the WHO European Region.

The ERI-TB Secretariat presented their Structured Operational Research Training (SORT-TB) initiative, which aims to catalyse research agenda implementation and build capacity at the country level. The 2018–2019 cohort of the initiative included 12 participants from six eastern European countries, which were endorsed by their MOH and selected on a competitive basis. The short-term goals of the initiative include publication of peer-reviewed manuscripts that enable the influencing of country policies and practices, while the strategic goal is to build in-country capacity and leadership for TB research. Twelve research projects run by participants covered eight strategic research areas defined by ERI-TB. The important findings of the studies included: evidence of the effectiveness of bedaquiline (Bdq)-containing regimens in “real world” settings; a list of independent risk factors for MDR-TB, treatment delays and patients lost to follow-up; and an indication of the high proportion of unadjusted regimens in Georgia.
Success stories of research projects that have the potential to influence policies were presented by Belarus and the Netherlands.

In the panel discussion, KNCV representatives expressed concern regarding the lack of publications based on finished research projects to influence programmatic actions. They also presented enabling and disabling factors for putting research into action (including staff changes, political will, funding etc.). NTP representatives from Armenia, Georgia, Moldova and Ukraine, underlined the growing role of research evidence in their decision-making and prioritization of NTP activities. NTP managers pointed out their move towards research agenda development and capacity-building at national level to enhance the quality, relevance and visibility of research projects in their respective countries. Enhanced collaboration and coordination is needed between national stakeholders (research institutions, civil society groups and patient organizations).

Conclusions
• Enhanced intercountry coordination between counterparts, chaired by WHO and partners, facilitates the utilization of human and financial resources to fill the Region’s TB research gaps more efficiently.
• Countries, under the leadership of NTP managers, should engage in partnership with civil society activists and research counterparts, and involve new stakeholders to boost both research uptake and the usage of evidence; with the same aim, NTPs should support publication of in-country research results in international peer-reviewed journals.
• The regional TB research agenda is a cornerstone for identification and tuning up of TB research priorities at country level.
• TB research financing should be enhanced; WHO urges heads of Member States to commit to allocating funding.

Next steps
• The WHO Regional Office for Europe advises partners to closely follow the development of the WHO Global Strategy for TB Research and Innovation and act proactively to put its recommendations into practice.
• Countries are encouraged to participate in further ERI-TB activities, particularly to delegate applicants for the next round of the SORT-TB course.
• The WHO Regional Office for Europe invites all interested counterparts to join ERI-TB, which serves as a platform for intercountry collaboration.
• TB researchers in the European Region are invited to submit their original research manuscripts for review and potential publication in the upcoming issue of the WHO journal, Public Health Panorama, on elimination of TB research gaps.
Session 5. What is new in MDR-/RR-TB management, treatment policies and guidelines

Summary
In this session WHO consolidated guidelines on drug-resistant tuberculosis treatment and other relevant guidance documents were shared. Countries were invited to share their experiences and discuss barriers as well good practices and possible solutions to programmatic implementation of guidelines for both adults and children.

The WHO consolidated guidelines on drug-resistant tuberculosis treatment (2019) include policy recommendations on treatment regimens for isoniazid-resistant TB, MDR-TB and rifampicin-resistant (RR-TB), including longer and shorter regimens for MDR/RR-TB, culture monitoring of patients on treatment, the timing of antiretroviral therapy in MDR/RR-TB patients infected with HIV, the use of surgery for patients receiving MDR-TB treatment, and optimal models of patient support and care.

A treatment duration of 15–17 months after culture conversion is suggested for most patients, although duration may be modified according to the patient’s response to therapy. For the longer regimens that contain amikacin or streptomycin, an intensive phase of 6–7 months is suggested for most patients; the duration may be modified according to the patient’s response. A fully oral regimen is possible and should become the preferred option for most patients. Access to rapid diagnostic tests, and drug-susceptibility testing (DST) remains crucial for better understanding of which treatment regimen to pursue. All recommended agents are available via the Global Drug Facility (GDF). Kanamycin and capreomycin are no longer recommended for use. A shorter MDR-TB regimen of 9–12 months may be used instead of the longer regimens in patients who have not been previously treated for more than one month with second-line drugs (SLDs) used in the shorter MDR-TB regimen or in whom resistance to fluoroquinolones and second-line injectable agents has been excluded.

A modified shorter MDR-TB regimen is possible under operational research conditions. The following steps are recommended:

- develop an appropriate protocol specifying the eligibility criteria, regimen composition, monitoring schedules etc.;
- get the protocol approved by a national ethics review committee ahead of any patient enrolment;
- include informed consent, adherence to the principles of good clinical practice, aDSM, and regular patient monitoring to assess regimen effectiveness when the treatment delivery takes place;
- solicit advice from the WHO Regional Office for Europe prior to initiating operational research for modified shorter regimens.

Debriefing from the Vienna meeting of the Green Light Committee for the WHO European Region

The WHO Regional Office for Europe held a two-day face-to-face meeting of the Green Light Committee for the WHO European Region (rGLC/Europe) on “Introduction of the new guidelines on treatment of drug-resistant tuberculosis” in Vienna, Austria on 19–20 February 2019. Meeting participants included members of the rGLC/Europe; representatives from the Stop TB Partnership, the GDF, USAID and Unitaid; representatives from NTPs from Armenia, Azerbaijan, Belarus, Bulgaria, Georgia, Kazakhstan, Kyrgyzstan, the Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan; staff
from the WHO Global TB programme and from the WHO Regional Office for Europe Joint Tuberculosis, HIV and Viral Hepatitis Programme and Health Technology and Pharmaceuticals Programme. Based on the discussions of the three-day meeting, a set of recommendations were proposed for WHO and partners. Recommendations for NTPs and partners were as follows:

- NTPs benefiting from rGLC support should specify their precise mission needs (including area of focus) in advance, to ensure that missions are planned and executed according to the needs of the country. NTPs are encouraged to play a stronger role in coordinating targeted missions between WHO, rGLC/Europe consultants and donors. NTPs must provide specific and clear inputs for terms of reference (TORs) for rGLC/Europe consultants developed by the rGLC/Europe Secretariat.

- NTPs and partners should collect, analyse and share with WHO data on shorter treatment regimens, off-label use (i.e. Bdq/delamanid (Dim) use beyond six months), and outcomes of Interferon-Gamma Release Assay (IGRA) testing for preventative treatment, to inform recommendation and policy updates. Experiences should be published (as a paper or as a poster) to inform national protocols and contribute to a growing body of evidence at the global level.

- NTP’s are encouraged to request paediatric formulations of SLDs via the GDF catalogue to stimulate production. rGLC/Europe and the GDF can support countries to make specific calculations for children.

- NTP’s are encouraged to use WHO collaborating centres to engage their technical support in the practical application of new recommendations, and support dialogue with the MOH and physicians.

- Donors and partners, especially the Global Fund to Fight against AIDS, Tuberculosis and Malaria, should consider providing additional funds to procure Bdq and to cover the needs for other drugs in order to adequately respond to demand during the transitional period to national funding of drug procurement.

**Genome sequencing for the surveillance of DR-TB**

Genome sequencing is a valuable tool for surveillance of drug resistance in resource-poor settings and could potentially replace phenotypic testing in drug resistance surveys. Use of genome sequencing for broader surveillance of antimicrobial resistance is encouraged. A comprehensive continuous surveillance system for drug resistance should be established, even in settings with limited laboratory capacity. For drugs with suboptimal sensitivity for genome sequencing, compared with phenotypic testing in the general patient population, the true prevalence of drug resistance can be determined using a relatively simple statistical adjustment. The gaps in the determination of the whole spectrum of resistance-conferring mutations can be bridged by developing global repositories. Genetic DST can be implemented in real-life scenarios (population-based surveillance in low- and middle-income settings). Capacity-building and continuous assistance should be in place.

**Experience from Kyrgyzstan**

The USAID Challenge TB project, implemented by the KNCV branch office in Kyrgyzstan, has introduced shorter and individualized treatment regimens. In 2016, a national plan for the implementation of a shorter MDR-TB regimen and individualized regimens using new anti-TB drugs was adopted. Coordination has been improved between TB services and the Pharmacovigilance Unit of the Department for Drug Procurement and Medical Technology of the MOH, which submits data to the Uppsala Monitoring Centre in Sweden. There is a need for strengthening and improving treatment adherence and expanding access to new DR-TB regimens countrywide.

**Working group sessions**

**Group 1**
Procurement supply chain management – updates from the GDF in light of new guidelines

The GDF is a “one-stop shop” for all products required by TB programmes. All TB programmes are eligible to procure quality-assured TB products from the GDF, at GDF negotiated prices. Adult and child-friendly formulations are available for drug-sensitive TB and DR-TB (group A to C). Rifapentine regimens for LTBI have been initiated in Belarus, Estonia, Georgia and Uzbekistan.

The GDF is ready to supply all medicines and diagnostics when countries decide to implement the changes in DR-TB treatment regimens recommended by WHO.

More than 500 TB diagnostic products and laboratory supplies are available to equip and maintain all levels of laboratories, from microscopy/GeneXpert centres to reference laboratories with culture/DST. Any country can order diagnostics through the GDF, using donor or domestic funding. Clients are able to simply select items from the GDF Diagnostics Ordering List (Excel sheet). Buying through the GDF can allow countries to avoid national distributors that may charge up to eight times more for the same product.

Pure substances (Bdq, Dlm and other first- and second-line TB medicines, including linezolid and clofazimine) are available in the GDF catalogue. The GDF has developed a TB medicines dashboard, which organizes, stores and displays TB medicines information from 13 different sources in one easy-to-access place. Countries are requested to share updated QuanTB files regularly with the GDF as it allows them to produce accurate forecasts for their suppliers to facilitate production planning and to ensure that GDF medicines are provided at the lowest possible, sustainable prices.

In shifting to domestic financing and procurement of TB pharmaceuticals and diagnostics, pooled procurement via the GDF or other mechanisms could be a useful approach.

Procurement and supply planning and transition plans require the use of a standard tool (e.g. QuanTB).

Countries have increased procurement frequency to twice a year through the GDF, which avoids drug expiry and stockouts.

For some countries, the potential wastage of obsolete medicines is a reason for delaying the introduction of new treatment regimens.

The political declaration of the UNHLM encourages all nations to use the GDF.

The GDF package of comprehensive technical assistance and capacity-building on quantification, forecasting, procurement and supply chain management of TB medicines – managed by regional technical advisors and a pool of trained consultants (USAID supported) – is available to countries upon request.

The presentation for this working group session is available here.

Efficient drug management as a result of high-level political support – experience from Estonia

The TB programme is fully funded domestically. The main drugs to relieve side effects of MDR-TB treatment are available free of charge. Management of comorbidities is available (including antiretroviral therapy, treatment of diabetes, methadone substitutional therapy, etc.).

A case-based electronic centralized TB registry is in place and is linked to laboratories, the registry of causes of deaths and the population registry. DST is available for all patients with resistance to first- and second-line TB medicines. TB services are integrated, and patients receive social support.

Since 2007, Estonia has participated in clinical trials with Bdq and Dlm. The country has full capacity for providing sufficient laboratory services and has had experience of programmatic management of DR-TB (PMDT) since 2001.

To get new drugs into the country, Estonia has updated its legislative framework, has established collaboration among stakeholders, (such as the National Institute for Health Development, the Ministry of Social Affairs, the State Agency of Medicines, the Health Insurance Fund, health facilities and the TB Consilium) and procures medicines through tender and the EU legislation system.
In 2015, the Ministry of Social Affairs allocated funds for the procurement of Bdq for the first time, followed by Dlm in 2016. The next round followed in 2018/2019. Since 2016, Estonia has had a policy for using new TB drugs: not to save them only for the most difficult cases, but to include them in other MDR-TB treatment regimens when appropriate.

Estonia takes a people-centred approach using new, more patient-friendly treatment regimens (which use less injectables, have fewer adverse effects, have a shorter treatment duration, have better adherence and achieve a higher cure rate); requiring shorter hospital stays; preferring ambulatory directly observed therapy (DOT) (including home visits and DOT at primary health centres); and offering integrated care with treatment of substance abuse and management of comorbidities.

The presentation for this working group session is available here.

Group 2
Progress and required changes in treatment safety monitoring
The results of the Global Tuberculosis Network (GTN) aDSM project were presented. It included 781 cases from 27 countries as of February 2019, and more than 650 complete data sets from 32 countries in April 2019: Mozambique, Nepal, Eswatini, Somalia, Jordan and Uzbekistan candidate to enter (May 2019). The project is perceived as a feasibility study for the implementation of nationwide aDSM projects managed by NTPs. Strengthening national TB consilia is a priority in the Region, as is ensuring a supranational multilanguage instrument to support management of difficult cases, to be used for second opinions and as an educational tool. The GTN offers the platform and an existing panel of experts (as done by the Pan American Health Organization (PAHO)) to countries of the WHO European Region. The GTN also offers the possibility of increasing the number of experts on the panel and creating a regional track, with a WHO Regional Office for Europe-designated clinical coordinator and mutual collaboration and interlinkages.

Treatment safety monitoring – experience from Kazakhstan
Implementation of aDSM in Kazakhstan was started in June 2018. The aDSM plan is a part of the NTP/Global Fund transition plan. The country has an aDSM core package for all MDR-TB and extensively drug-resistant TB (XDR-TB) patients on new drugs and the short treatment regimen. The policies (a protocol, standard operating procedures (SOPs) and forms) have been adopted and widely used since 2018. The country’s priority is registration of new anti-TB drugs and the allocation of domestic funding to provide access for all and establish a sustainable system for the implementation of PMDT. The aDSM component must be integrated into routine clinical monitoring and PMDT within the national programme. Capacity-building and the routine recording and reporting of adverse events will improve quality of care.

Group 3
Updates on MDR-TB management in children
The session highlighted the following issues on treatment of children and adolescents with TB: (i) avoidance of injectable-containing regimens is particularly desirable, (ii) Bdq is recommended for children over six years, Dlm is recommended for children over three years (the dispersible tablet used in trials is not yet available for programmatic use).

DR-TB treatment duration in children is largely guided by achieving 18—20 months, as many may only be clinically diagnosed or have extrapulmonary disease. Shortening the regimen to less than 18 months may be considered in the case of children without severe disease conditions. The Sentinel Project has developed a guide, Management of multidrug-resistant tuberculosis in children, where regimens for children of different
ages and with different resistance profiles to fluoroquinolones are suggested. Paediatric formulations are available from the GDF.
Countries need to:
- facilitate, advocate and negotiate update of national policies, SOPs, overcome regulatory barriers and address acceptance issues;
- collect and share data on children (disaggregated by weight and age) to estimate the real needs and to contribute to the global evidence.

Use of new drugs for children with DR-TB – experience from Belarus
Belarus is developing paediatric patients’ “evidence-based case studies” to help to increase the global knowledge on use and effectiveness of new anti-TB medicines containing regimens under programmatic conditions. In total 37 children and adolescents were treated with new drugs and preliminary results show a good safety profile, no serious side effects and excellent interim treatment outcomes: 22 were cured (18 treated with Bdq), 0 failed, 0 were lost to follow-up, 0 died, and 15 are still on treatment and continue their regimen as prescribed.
The experience gained and evidence gathered from the paediatric cohort in Belarus can promote further implementation of regimens containing new anti-TB medicines in Belarus and other countries of the WHO Europe Region.
The presentation for this working group session is available here.

Building platforms for rapid countrywide adoption of innovations – experience from Kyrgyzstan
For the country to improve its treatment success rate, the introduction of effective regimens and methods of treatment are a priority. Kyrgyzstan introduced more people-centred care with shorter treatment regimens for new DR-TB patients (9–12 months and 2–3 times less expensive) and individualized treatment regimens for XDR-TB patients (with less adverse events).
The main objective was to create a sustainable programme which is capable of rapid adaptation of innovations country wide. Any innovation can be implemented using a step-by-step approach. This takes time but should not discourage and demotivate managers and health-care workers. Proper preparation will ease implementation. In one year (2017–2018), since all legal and practical steps had already been taken, the country was able to put more than 1000 patients on treatment, across all regions. Preliminary treatment outcomes for 2017 (n=119) are: treatment success (78%), lost to follow-up (16%) and treatment failure (6%). Previous treatment for patients with XDR-TB achieved only 11% cured; with innovations in place (new medicines, regimens, tests and adherence technologies, etc.) it increased to 88% (cohort 2017 n=31).
The country is transitioning to new, effective TB treatment regimens (injectable-free, new anti-TB drugs); expanding coverage and availability of rapid XDR-TB diagnostic methods by scaling up the implementation of the transportation system; developing mechanisms for effective state procurement of prequalified anti-TB medicines and other materials; further expanding the TB case management system in primary health care facilities across the country; and building the capacity of health professionals in using modern approaches to diagnose and treat TB.
The presentation for this working group session is available here.

Conclusions
Session five allowed countries to identify the way forward in updating their treatment policies and accelerate the transition to implementation of the new guidelines.
Next steps
For the WHO Regional Office for Europe/partner organizations:
• Continue to provide technical assistance on updating national policies/action plans on implementation of new regimens for MDR/XDR-TB treatment.

For countries:
• Have a very clear plan for the laboratories to start performing DST with the new drugs.
• Provide programmatic implementation of aDSM countrywide.
• Request paediatric formulations of SLDs via the GDF (the GDF can support countries to make specific calculations for children).
Session 6. Countering stigma and achieving people-centred TB care

Summary
In eastern Europe and central Asia (EECA) stigma against individuals affected by TB continues to be a serious barrier to both detection and effective treatment. During the session, participants shared their experiences on promoting PCC models in countries of the EECA region and shared the stories of TB survivors and their work to support patients and the ongoing fight against stigma. An important element of PCC is collaboration between all care providers including government agencies, civil society and – where they exist – private providers. CSOs have proven to be key players in the provision of quality PCC. Combining medical, social, legal and psychological support allowed a doubling of the success rate of MDR-TB treatment. To promote further involvement of civil society in the delivery of TB services, as well as the sustainability of such services, the mechanisms for social contracting should be available in each country. Social contracting of services is the foundation of the sustainability of the country response to the TB epidemic.

Conclusions
• Interventions to reduce stigma related to TB should target such areas as creating community awareness, patient counselling on problem-solving and emotional skills, preparing culturally sensitive and scientifically evidenced media messages, providing financial support for patients, and enhancing the quality of the health-care services.
• It is necessary to develop cooperation mechanisms between national agencies, the private sector and civil society for implementation of PCC and the provision of comprehensive support.
• Psychosocial and legal support, accompaniment in treatment, and peer-to-peer support are important for better treatment adherence and outcomes.
• Greater political will and support both for NTPs and CSOs is crucial if the speed of implementation of PCC is to increase and to make it sustainable.
• The lack of nationally available funding for CSOs is a problem if their potential roles in PCC are to be made a reality. CSOs must be included in the state grants system.
• Limited number and capacity of human resources are a significant barrier to progress and implementation of PCC on the ground, including the awareness and understanding of PCC by health-care staff (middle and lower level medical workers).
• There is a need to emphasize the benefits of provision of high-quality PCC.
• Effective referral systems between different medical and social care providers are needed to fit the individual needs of patients.

Next steps
To overcome stigma, we need to develop and implement different tools at the national level (photo exhibitions, advertising campaigns, digital tools, etc.). CSOs and communities should be part of the development process.
Experiences of successful PCC models and practices (early detection, contact investigation, treatment, post-treatment re-integration into society) in donor’s projects need to be shared at the national level, with further implementation throughout the country.
Before introducing any new policies or tools, it is necessary to find out the needs of the intended target groups (patients, families, communities etc.) themselves; it is necessary to conduct background research among the community to understand their needs and address identified gaps.
A Wolfheze Workshops working group on PCC should continue its work; however, more involvement of representatives from NTP from EECA countries is needed.
Session 7. Next steps and way forward

Summary
Following a summary of key points and next steps from each of the six preceding sessions of the Workshop, the subject of working groups was discussed. It was decided to continue with the DR-TB (aDSM) and PCC working groups. The TB-HIV working group will soon round up its activities, as previously planned.

A few proposals for new working groups were made:
• TB infection control;
• extrapulmonary TB;
• social determinants of TB;
• diagnostics in TB.

Voting took place with “TB infection control” receiving the most votes, followed by the proposal for a “social determinants” working group. Those who proposed each working group were invited to submit TORs for their proposals within the next month. The working groups will be taken forward if adequate TORs are received.

Country representatives to be part of the organizing committee for the next Wolfheze Workshops were chosen. The meeting was closed by Kitty van Weezenbeek and Masoud Dara, who encouraged delegates to take the momentum gained during this workshop forward into their daily work in an attempt to finally end the TB epidemic.
Annex 1. Programme overview

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<thead>
<tr>
<th>Time</th>
<th>Tuesday 14</th>
<th>Wednesday 15</th>
<th>Thursday 16</th>
<th>Friday 17</th>
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<tbody>
<tr>
<td>8:30–9:00</td>
<td>Registration</td>
<td>Session 1. Key United Nations High-level Meeting declarations on TB and HIV. What’s next in the WHO European Region</td>
<td>Session 3. Country achievements on improving TB prevention and care</td>
<td>Session 6. Countering stigma and achieving people-centred TB care</td>
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<td>9:00–10:30</td>
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<td>Session 1. (continued)</td>
<td>Session 4. Research: European perspective</td>
<td>Session 6 (continued)</td>
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<td>10:30–11:00</td>
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<td>11:00–12:30</td>
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<td>Session 2. Collaboration between TB and HV programmes and partners</td>
<td>Session 5. What is new in MDR-/RR-TB management, treatment policies and guidelines</td>
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<td>12:30–13:30</td>
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<td>13:30–15:00</td>
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<td>Session 2. (continued)</td>
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<td>15:30–17:00</td>
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<td>Session 2 (continued)</td>
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<td>17:00–18:00</td>
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<td>Informal side meetings: TBD</td>
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