

Programmatic Management of Drug Resistant Tuberculosis – r-GLC Mission Report: 2017

Democratic People's Republic of Korea

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11/4/2017

Regional Advisory Committee on MDR-TB SEAR (r-GLC) Secretariat WHO South East Asia Regional Office

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**PMDT r-GLC MISSION REPORT
2017**

Programme: Country: Democratic People’s Republic of Korea

Lead implementing agency:

National Tuberculosis Programme, Ministry of Public Health, Government of DPR
Korea

Inclusive dates of mission:

24 October – 2 November 2017

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Acknowledgments:

- Ministry of Public Health, Government of DPR Korea, Pyongyang
- National TB Programme, Government of DPR Korea, Pyongyang
- WHO Country Office for DPR Korea, Pyongyang and India, New Delhi
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Acknowledgments:

The author extends gratitude to the National Tuberculosis Program (NTP), Ministry of Public Health (MoPH), Government of DPR Korea (GoDPRK) and WHO Representative to DPR Korea and India for their kind support in conducting this mission. Thanks also to NTP staff and officials at the sites visited during the mission for sharing valuable information and contributions to enable comprehensive review of PMDT situation of DPRK.

The author acknowledges the leadership, valuable time and insights shared by Dr Choe Kum Song, Senior Officer of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK on behalf of Dr Choe Tong Chol, NTP manager, Director of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK and his team from Central /Provincial TB Preventive Institutes, National Reference Laboratory, Provincial TB Hospital and TB Sanatoria officials who provided necessary information and directions to the author to focus on progress made since the last mission as well as the recent joint monitoring mission, specific foreseen challenges and shape up the recommendations to address the felt unmet needs of the NTP DPRK for PMDT. Thanks also to Dr Kim Hyon, Chief of TB section – PMU Global Fund, MoPH, GoDPRK for sharing the National Strategic Plan 2018-21 and the Global Fund NFM Phase II proposal 2018-21. Thanks to Dr Murat Sahin, Deputy Representative, UNICEF and his team who graciously discussed the support extended as PR of Global Fund, the challenges and way forward for timely utilization of the balances in current Global Fund grants for introduction of shorter MDR-TB regimen with second line – line probe assay and Bedaquiline in DPRK in collaboration with the WHO Country Office. Special appreciations and acknowledgement to Dr Ri Jun Hyok, Dr Kim Myong Hyok and Dr Ko Jin Hyok from the TB PMU & NRL, Pyongyang, MoPH, GoDPRK for their valuable support, care and time given to the reviewer throughout the mission and sharing information on situation, challenges, potential solutions and way forward for TB and MDR-TB interventions in DPRK.

The author would also like to thank Dr Thushara Fernando - WHO Representative to DPRK for the invitation to conduct the mission with technical support under horizontal collaboration in revision of PMDT guidelines including introduction of shorter MDR-TB regimen; Mr Thinlay – Administrative Officer & Mr Jahid Hasan for providing organizational support; Dr Rezwan Kamar - Medical Officer (TB); Dr O Hyang Song & Dr Jo Mun Hwang - NPO-TB at WHO Country Office in DPRK for discussion on specific action points for WHO country office to support DPRK accelerate its response to combat MDR-TB and Dr Partha Mandal - Technical Officer TB at WHO SEARO for their valuable time and guidance on various issues regarding TB and PMDT situation in DPRK and the way forward.

Abbreviations:

ADR	Adverse drug reaction
aDSM	Active drug safety management and monitoring
AO	Administrative Officer
BDQ	Bedaquiline
BHU	Basic Health Unit
CTPI	Central TB Preventive Institute
cTPI	County TB Preventive Institute
CFK	Christian Friends of Korea
DLM	Delamanid
DPRK	Democratic People's Republic of Korea
MoPH	Ministry of Public Health
DOT	Directly Observed Treatment
DRTB	Drug Resistant Tuberculosis
DST	Drug Susceptibility Testing
DVED	Drug Vaccines and Equipment Division
EQA	External Quality Assurance
EBF	Eugene Bell Foundation
FLD	First Line Drugs
GoDPRK	Government of DPR Korea
GDF	Global Drug Facility
TGF	The Global Fund
GLC	Green Light Committee
HA	Health Assistant
HHD	House-hold Doctors
LPA	Line Probe Assay
LT	Laboratory Technologist
LTBI	Latent TB Infection
MDR-TB	Multi-Drug Resistant Tuberculosis
MoPH	Ministry of Public Health
ND	Newer Drugs
NFM	New Funding Model
NTP	National Tuberculosis Control Programme
NTRL	National TB Reference Laboratory
PMDT	Programmatic Management of Drug Resistant Tuberculosis
PMU	Programme Management Unit
PSM	Procurement supply chain management
PTH	Provincial TB Hospital
SCTS	Specimen collection and transport system
SEAR	South East Asia Region
SLD	Second Line Drugs
SL-LPA	Second Line – Line Probe Assay
SMTR	Shorter MDR-TB Regimen

SNRL	Supranational Reference Laboratory
TBS	TB Sanatorium
TO	Technical Officer
UNICEF	United Nations Children’s Fund
VHW	Voluntary Health Worker
WCO	WHO Country Office
WGS	Whole Genome Sequencing
WHO	World Health Organization
XDR-TB	Extensively Drug Resistant Tuberculosis

I. Executive summary:

Democratic People's Republic of Korea is one of the high TB and MDR-TB burden countries in the South-East Asia Region. TB and MDR-TB has been a major public health problem in DPRK. DPRK initiated PMDT services with external support of Eugene Bell Foundation (EBF) since 2008, technical assistance from WHO Country Office and was complemented by the Global Fund support through UNICEF since 2012. Christian Friends of Korea (CFK) has also been supporting DPRK particularly in laboratory capacity development.

Progress made in past 5 years in scaling up PMDT services has been slow. At the moment, DPRK has covered 109 out of 210 counties in 9 out of 12 provinces with PMDT services under the NTP framework and is currently supported by commodity cum technical support by EBF, CFK and GF-NFM funding through UNICEF as principle recipient and WHO Country Office (WCO) for DPRK as sub recipient.

This is the sixth monitoring mission for Programmatic Management of Drug-Resistant TB (PMDT) component of the National TB Control Program (NTP) of the Government of DPR Korea (GoDPRK) and under horizontal collaboration support through WCO DPRK for revision of PMDT guidelines and the introduction of the shorter MDR-TB treatment. The mission was undertaken on behalf of Regional Green Light Committee (r-GLC) of World Health Organization - South East Asia Region (SEAR) from 24 October – 2 November 2017.

The ten days long mission covered briefing meetings with key officials of TB programme management unit (PMU) under NTP, MoPH, UNICEF and WHO DPRK, visit to key health care facilities like National TB Reference Laboratory (NTRL) at Central TB Preventive Institute (CTPI), Pyongyang city provincial TB preventive institute (PTPI), Moranbong county TB preventive institute (cTPI) and TB Hospital, PTPI and Provincial TB Hospital (PTH) at South Pyongan province, TB PMU, UNICEF (PR for GF) and WHO Country Office of DPRK. During the mission, specific meetings were done with key officials from MoPH, GoDPRK viz. Dr Choe Kum Song, Senior Officer of Department of Communicable Disease, Hepatitis and Tuberculosis (focal person for EBF); the team from TB PMU, UNICEF and WHO DPRK. Representatives from EBF, CFK and Global Fund could not be available for discussion during the mission.

The mission also covered a workshop at Pyongyang with NTP, UNICEF and WHO staff with special focus on the updated WHO PMDT Guidelines – 2016. The workshop covered review and discussion around the revision of DPRK's PMDT guidelines to include options of updated DR-TB diagnostic algorithms including second line LPA, shorter MDR-TB regimen and management of pre XDR/XDR TB patients with Bedaquiline or Moxifloxacin containing regimen and effective management of adverse drug reactions (ADR) including concepts of active drug safety monitoring and management (aDSM).

The objectives of the mission were

- To provide recommendations on **scaling-up of PMDT activities** by assessing the country situation and implementation status of recommendations from last rGLC mission (Nov 16).
- To review country **MDR-TB treatment enrolment plan including capacity** and provide recommendations accordingly.
- To provide a detail **route map for MDR-TB expansion plan considering the introduction of shorten-regimen.**
- To review status of **partners' supports in PMDT implementation in the country and to discuss harmonization of technical support** in line with “End TB Strategy” on PMDT the in-country context.
- **Revision of reporting template for ADSM and provide recommendations** on priority bases with timeframes.

The activities include comprehensive review of services in terms of patient care, programme management, supervision monitoring systems, community engagement, information communication systems for TB/DRTB, interactions with key officials, doctors, staff, specialists, patients, community representatives at the sites visited to analyze the progress made and plans developed for TB and PMDT implementation in light of the last year PMDT mission report, the PMDT expansion plan 2018, the current national PMDT guidelines and the resolve to roll-out the updated WHO PMDT guidelines particularly shorter MDR-TB regimen, Bedaquiline and second line - LPA.

The key observations and actionable recommendations based on country's shared felt needs, observed facts, figures and available evidences from program data and field visits were shared and discussed in details by the author with the key stakeholders of MoPH, UNICEF and WHO DPRK.

Findings/Observation

a) Progress from the last mission:

The last mission was held in November 2016. The progress was assessed based on observations made and interactions with key NTP stakeholders of DPRK. Efforts need to be continued to meet the unmet recommendations below.

SN	Priority Recommendations	Progress
1	Expedite complete geographical coverage of PMDT services with current DST criteria and expand offer of DST to previously treated patients (including relapse) followed by new patients while enhancing investments in diagnostic and treatment capacity	Partly met - ongoing
2	Know your TB and DR-TB epidemiology to prompt local epidemiology guided cost-effective strategies Interim – FL-SL DST to 356 culture positive isolates Conduct and complete National DRS	Not Met
3	Comply with WHO Interim Bedaquiline Guidelines and Policy Implementation Package for newer drug by developing clear national guidelines, get in-country regulatory approvals and build capacity of Sadong TB Sanatorium for ADR management and monitoring.	Partly met - ongoing
4	Revise NTP TB Guidelines with PMDT to align with End TB Strategy and recent WHO PMDT Guidelines 2016 to introduce Shorter MDR regimen and second line LPA in DPRK	Not met
5	Develop NSP 2018-20 and GF NFM Phase II proposal with budgets to aim for universal access to TB care	Met
6	Update the PMDT Expansion plan – 2018 and re-programme the available resources to regularize PMDT services on daily basis and to adjust for revisions anticipated in the PMDT Guidelines.	Partly Met - ongoing
7	Expedite laboratory capacity expansion with rapid molecular DST to facilitate faster expansion of PMDT	Partly Met - ongoing
8	Transition to bottom up specimen collection and transport system from Ri and Dong levels to the labs	Not Met
9	Minimize delay in diagnosis to treatment pathway and regularize PMDT services by addressing PSM issues	Not Met
10	Harness the health system strengthening opportunities with PMDT service expansion	Partly Met - ongoing
11	Plan for a systematic phased decentralization and expansion of PMDT services	Partly Met - ongoing

b) Current status of country PMDT implementation:

PMDT services are implemented periodically since 2008 whenever limited supplies of diagnostics and second line drugs are made available through support from TGF (UNICEF & WHO), EBF and CFK. Till date, MDR-TB detection and treatment initiation has been provided in 109 out of 210 counties through treatment section of 15 cTPI and 8 PTH in 9 out of 12 provinces of DPRK. The diagnosis and treatment services are not regular but are provided at intervals of three months with service interruption in between.

A team of CTPI visits selected TBS out of the designated DR-TB treatment centers on monthly basis to collect specimen from presumptive MDR-TB patients i.e. failures of first line treatment or contacts of MDR-TB patients only and get them to NRL to test mainly on solid culture-DST / GeneXpert or the four provinces with recently installed GeneXpert machines including RRL. In 2017, specimen collection through TGF support have been done only in 62 (30%) of the counties in DPRK. However, since July 2017, MDR-TB diagnostic services are halted due to stock-outs of lab consumables for DST for solid culture as well as GeneXpert due to reasons related to recent sanctions. GeneXpert machines have been sub-optimally utilized due to uninterrupted supply of limited number of cartridges. A line-list of presumptive MDR/RR-TB patients is developed and maintained at all county levels awaiting services.

Treatment initiation is done in quarterly cohorts whenever SLD are supplied by UNICEF (PR of TGF) via GDF on six monthly basis or the non-resident EBF team visits the 12 county TBS under their project area with mobile Xpert-MTB Rif and SLD, tests line-listed presumptive MDR-TB and starts lab confirmed RR-TB patients on MDR-TB treatment. The EBF team visits twice in a year and rest of the time the 10 Xpert machines under their project are not available for routine use. Standard MDR-TB regimen is prescribed after an incomplete set of pre-treatment evaluation by doctors/CTPI/EBF team at TBS/PTH as all investigations are not available at TBS/PTH.

All laboratory confirmed MDR/RR-TB patients are hospitalized for the complete duration of treatment. Patients are provided MDR-TB treatment free of cost, follow up cultures, nutritional support, wages protection and counseling to the patients under NTP DPRK as vertical services. aDSM is limited by lack of lab investigations, equipment and clinical capacity. Specialist and emergency consultation is arranged through nearby county general hospital. Second line drug courses are earmarked for every patient initiated on treatment and no additional patients are initiated on treatment beyond the number of courses supplied. Based on a recently completed operational research on feasibility and cost-effectiveness of three models of care, the MoPH has decided to transition to a model of care with partial hospitalization in intensive phase (IP) till culture conversion occurs and ambulatory care in continuation phase (CP) through house-hold doctors (HHD) in various counties. However, the modalities of decentralization have yet to be clearly defined and operationalized.

In 2016, only 1394 (8%) of previously treated patients (2.6% of notified bacteriologically confirmed TB patients) were tested for RR-TB and 814/935 (87%) lab confirmed RR-TB patients were initiated on standard MDR-TB treatment of 18 month duration. Although, this is appreciably greater than the

previous years, this amounts to treatment coverage of only 18% of 4600 notified and 14% of 5700 incident MDR-TB patients as compared to 87% treatment coverage of 130280 incident drug sensitive TB patients estimated in DPRK. However, the treatment success in the 2014 annual cohort of 212 MDR-TB patients has been reported at 75.6% as confirmed by NTP which is commendable. From Oct 2016 – Sep 2017, 1651 MDR-TB patients (including 1026 MDR-TB patients by EBF) have been initiated on treatment so far. The last patient course was initiated on treatment in September 2017 from the latest supplies of 625 patient courses and currently no earmarked patient course is available in the country. The next supplies of 500 courses are expected to be delivered through TGF source in January 2018. Further, at Sadong TBS, 19 XDR TB patients diagnosed by EBF through Korea Institute of Tuberculosis (KIT), Seoul, South Korea have been initiated on Bedaquiline with optimized background regimen as a pilot since September 2016.

c) Key challenges identified in this mission (In order of priority):

The key challenges identified in the current mission are enlisted below:

- 1) MDR-TB diagnostic services have halted since July '17 due to stock-outs of DST consumables as procurement of WHO (TGF) supported 3 GeneXpert machines and 4000 cartridges not processed by Danahar/Cepheid and UNICEF (TGF) supported import of digital X-ray machines/consumables, lab consumables for solid C-DST and LPA FL/SL DST kits from China ports halted due to sanctions. However, CFK and EBF could bring in lab consumables for liquid culture DST and GeneXpert during their recent visits in 2017.
- 2) Approximately 3 million USD is balance in the current GF grant as provisional savings, primarily due to HR, non-procurement of lab equipment and consumables as well as reduction in unit cost of some equipment.
- 3) Epidemiology of M/XDR TB is unknown except for prevalence of RR-TB and a study published with FQ resistance and XDR rates in a small patient cohort (3).
- 4) Draft PMDT guidelines of DPRK partly updated to align with recent WHO PMDT Guidelines – 2016 were deliberated in a two days' workshop with MoPH, NTP staff and Key partners. Consensus obtained to have an integrated guideline to address all variants of DR-TB with appropriate regimen types guided by DST with focus on decentralization and patient centric care with greater engagement of county/Ri/Dong/HHD systems. Evidence based policy decision taken by MoPH for ambulatory care in CP after culture conversion under supervision of the Ri/Dong and HHD. cTPI remodeling decision is an opportunity to prepare cTPI to manage MDR-TB independently. India's revised PMDT guideline was shared for reference.
- 5) An ambitious NSP 2018-21 and the GF NFM Phase II proposal have been developed. However, few gaps were identified and discussed during the workshop to arrive at a consensus for refining the NSP and GF proposals to address the gaps. PMDT expansion plan is yet to be updated and aligned to the NSP 2018-21. Funding gap exists within the NSP after considering domestic and donor contributions.
- 6) PMDT services yet to be available nationwide on day to day basis (9/12 provinces, 109/210 counties offered DST only to failures of CAT II and contacts of MDR-TB. NSP 2018-21 aims for universal DST to >90% diagnosed TB patients in DPRK by 2021.
- 7) Policy decision taken to introduce Shorter MDR-TB Regimen in DPRK, with an initial plan to start a cohort of 100 patients on pilot basis in 2018 to gain experience and complete transition with

increasing numbers proposed annually up to 2019 with simultaneous management of FQ/SLI resistant and XDR-TB patients with individualized treatment with Bedaquiline if available. However, SL-DST capacity is lacking due to procurement/supply blocks. National regulatory approvals have yet to be obtained for Mfx, Lzd, Cfz, Bdq and Dlm.

- 8) Laboratory Capacity constrains PMDT services and its expansion. NRL staff although trained, are yet to successfully complete the proficiency testing for LPA or Solid C-DST for first and second line drugs. Four RRLs, 8 PTPI labs and ~210 GeneXpert sites are proposed in the NSP 2017-21. An indigenous PCR based technology “Gene Chip – DNA micro-assay test” developed by the Academy of Medical Science of DPRK is being validated at 5 provinces.

d) Conclusion: priority recommendations:

SN	Recommendations (preferably not more than 10)	Responsible Person	agency/	Time frame
1	Pursue highest level advocacy to resolve procurement bottlenecks to resume PMDT services in DPRK	MoPH, NTP, NRL, UNICEF, WHO, GF, GDF, CFK and EBF		Dec 2017
2	Expedite activities or urgently re-programme to utilize the provisional savings in the current TGF grants	NTP, PMU, UNICEF, EBF and WHO		Dec 17
3	Know your DR-TB epidemiology to prompt local epidemiology guided cost-effective strategies	NTP, NRL, SNRL, WHO		Dec 18
4	Complete the draft of PMDT guidelines for DPRK within next 30 days and share with WHO SEARO and the author for inputs and finalization within 2017 after incorporating the decision taken in the workshop	NTP, PMU with TA from WHO		Dec 17
5	Refine the NSP and GF proposal to address the inputs provided during the mission	NTP, PMU, UNICEF, EBF, CFK and WHO		Dec 17
6	Expand PMDT services in stages to achieve universal DST in DPRK by 2021	NTP, PMU, UNICEF, WHO, EBF		Jun 18 - Dec 20
7	Complete preparation to introduce shorter MDR-TB regimen and newer drugs	NTP, PMU, NRL, UNICEF, WHO, EBF		Mar 18
8	Build capacity of Laboratory Network in DPRK	NTP, NRL, CFK, EBF and WHO		Jan '18

The MoPH officials agreed to all of the above recommendations and requested to discuss the following points with UNICEF and WHO that was immediately taken up after the debriefing meeting on 2 November 2017.

- The following quantities can be procured through the GF for preparation of initial phase of introduction of shorter MDR-TB regimen alongside second line LPA and Bedaquiline containing regimen for treatment of pre-XDR / XDR TB from the savings of the current grant.
 - 500 courses of Shorter MDR-TB regimen as an initial implementation phase 1 (instead of a pilot with 100 courses)
 - 500 courses of longer MDR-TB regimen
 - 50 courses of Bdq
 - A complement of ancillary drugs for ADR management
 - 47 Kits of First Line LPA & 7 Kits of Second Line LPA
- UNICEF and WHO to mobilize the necessary documents on clinical trial results, evidences on safety and efficacy, specifications, package inserts etc. as required by the national regulatory authority to fast-track informed regulatory approval for newer drugs like Moxifloxacin, Clofazimine, Linezolid, Bedaquiline and Delamanid.

Detailed quantifications developed by the PMU team were reviewed and inputs incorporated by the author and shared with the UNICEF and WHO team over email on 3 November.

The recommendations were gracefully accepted by the key officials of NTP, MoPH, TB PMU, UNICEF and WHO as the author exercised transparency and openness to suggestions from them to enable refinement, improvisation and ownership for enactment.

The NTP, UNICEF and WHO DPRK also requested the author to continue providing inputs after the mission to finalize the PMDT guidelines including shorter MDR-TB regimen and scale up plans of DPRK.

Detailed report:

A. Introduction/Background

The Democratic People's Republic of Korea (DPRK) is situated in the north eastern part of Asia; spread over 120 thousand square kilometers, 80% of which are mountains. Administratively, DPRK is divided into 12 provinces with 3 major cities viz. Pyongyang, Rason and Nampo. Provinces are divided into cities (districts) and counties. A county is further subdivided into smaller geographic areas called Ri (Ub, Gu, Dong). County town called Urban Cities (districts); on the other hand, consist of administrative areas known as Dong. In big cities, the dongs are grouped into administrative units called districts. The 2008 census placed the total population at 24.76 million; ~61% resides in urban areas.

DPRK is one of the high TB and MDR-TB burden countries in the South-East Asia Region. TB and MDR-TB has been a major public health problem in DPRK. In 1998, the Ministry of Public Health (MoPH) adopted DOTS and was expanded nationwide by 2003. DPRK initiated PMDT services with external support of Eugene Bell Foundation (EBF) in 2008 and technical assistance from WHO Country Office. Since then, EBF, a non-residential international NGO, diagnoses MDR-TB patients using GeneXpert brought into the country during their biannual in-country visits and provide the NTP with Second-Line TB drugs, nutrition supplies and blankets, etc. to support in-patient care in select MDR-TB treatment sites. This effort was further complemented by the Global Fund support through UNICEF (PR) and WHO Country Office for DPRK (SR) since 2012. In 2012, the national PMDT guidelines were last updated through a process of wide stakeholder consultation and expert reviews and further updated in 2015. Since June 2012, identified patients were enrolled on treatment with second line drugs (SLDs) supported through the Global Fund grant. Christian Friends of Korea (CFK) has also been supporting DPRK particularly in laboratory capacity development. In 2017, multiple activities like the joint monitoring mission, development of National Strategic Plan for TB (2018-21) and inclusive country dialogue for development of GF NFM Phase II grant (2018-21) have provided the NTP and in-country partners the opportunity to better understand and arrive at consensus on the most appropriate approaches to maximize the cost-effectiveness of scarce resources for PMDT (Programmatic Management of DR-TB).

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- **Revision of reporting template for ADSM and provide recommendations** on priority bases with timeframes.

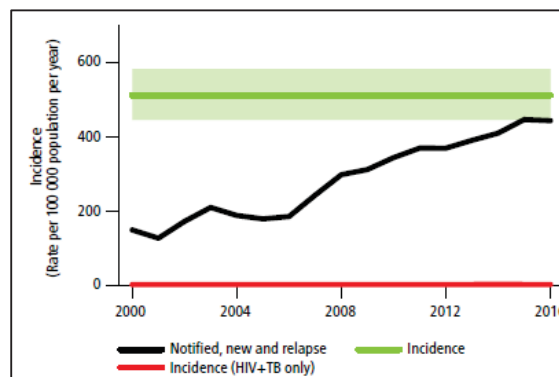
The activities include comprehensive review of services in terms of patient care, programme management, supervision monitoring systems, community engagement, information communication systems for TB/DRTB, interactions with key officials, doctors, staff, specialists, patients, community representatives at the sites visited to analyze the progress made and plans developed for TB and PMDT implementation in light of the last year PMDT mission report, the PMDT expansion plan 2018, the current national PMDT guidelines and the resolve to roll-out the updated WHO PMDT guidelines particularly shorter MDR-TB regimen, Bedaquiline and second line - LPA.

B. Existing TB control program

TB Burden:

DPRK is listed as a high TB and MDR-TB burden country among the updated list of top 30 highest burden countries of the world to be used by WHO during the period 2016–2020 The TB burden and profile of DPRK published in Global TB Report 2017 is annexed with this report. The epidemiological analysis and the national TB prevalence survey (2015-16) conducted by NTP recently were also referred to. The salient observations are as follows:

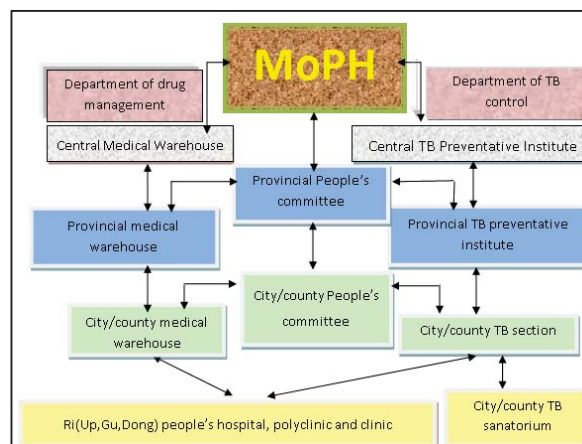
- In 2016, TB mortality is estimated at 43/100,000 population while TB incidence is estimated at 513/100,000 population in DPRK. (1)
- Notification of all forms and all forms of newly notified TB case rate per 100,000 population has increased continuously over the period of 2000-2016 with geographical heterogeneity between provinces. With this impressive increasing trend and 120,323 TB patients notified in 2016 (481/100,000), DPRK has achieved 87% treatment coverage of 130,280 estimated incident TB patients (513/100,000) which is commendable, leaving a treatment gap of ~13% based on the reported estimates.
- The national TB prevalence survey recently conducted by MoPH in DPRK reveal a prevalence of ~641/100000 that would enhance the notification and treatment gap for drug sensitive TB by ~160/100000 when compared to recent prevalence estimates (i.e. existing pool and newly emerging cases per annum). This translates to ~40,000 (25%) TB patients missing from TB notification and treatment in 2016.
- In absence of the private sector, active case finding for TB, regulated supply of quality assured anti-TB drugs through NTP and government ware-houses supply chain system, ambient temperature favorable for maintaining efficacy of drugs in storage conditions, infection control through separation of infectious patients till rendered non-infectious through prompt treatment, sustained high treatment success rates are factors that could prevent emergence and spread of drug-resistance.



NTP & its structure:

In 1998, the Ministry of Public Health (MoPH) adopted DOTS and was expanded nationwide by 2003. The Department of Communicable Disease, Hepatitis and Tuberculosis is in-charge of policy development and planning, organization of TB services, provision of technical support, communications and international partnerships. The TB services are delivered through the general public health system consisting of health facilities in 10 provinces and 2 major cities, 210 counties and over 7,000 dong/ri units, and TB specific institutes at the central and provincial level, and county levels.

At the central level, the Central TB Preventive Institute (CTPI) is the highest technical unit and provides technical support, laboratory and treatment services, training, M & E, routine programme supervision, recording & reporting and research. A central 100-bed hospital attached to CTPI provides clinical services for TB patients. The National TB Reference Laboratory (NTRL) is part of the CTPI and is responsible for external quality



assurance (EQA) for the smear microscopy network, and performance of culture and drug susceptibility testing (DST). The central level works in close collaboration and guidance of MoPH.

At the provincial level, there is a Provincial TB Preventive Institute (PTPI), the Laboratory of the PTPI, and the two Regional TB Reference Laboratories (RRL). The county level is represented by the TB section of the county hospital with a laboratory. There are county sanatoria with TB laboratories. A recent policy decision of investment into remodeling of county hospitals to county TB preventive institutes (cTPI) has been taken by MoPH, GoDPRK where preventive and treatment services will be integrated at the county level. The most peripheral units are the Ri (rural PHC) and Dong (urban) clinics manned by TB doctors and household doctors (HHD). The TB institutes at provincial and city/county levels work in close collaboration and guidance of Provincial and City/County People's committee respectively.

The Central Medical Warehouse (CMW) is the central unit of a parallel department within the MoPH that manages the drug supply chain, with corresponding Provincial Medical Warehouses and County Medical Warehouses.

UNICEF is the principle recipient of the Global Fund grants under the New Funding Model with WHO Country office for DPRK and NTP being the sub-recipients. There exists a coordinator, an officer for monitoring and evaluation and 4 NPOs appointed through UNICEF for grant management. The Global Fund also supports the Project Management Unit (PMU) that is integrated in the NTP and manages grant implementation. The PMU manages both the TB and malaria programs, including procurement supply chain. A PMDT Officer at the PMU provides assistance to the NTP Manager for the PMDT implementation.

While the health infrastructure and workforce is mainly contributed by the GoDPRK, the global fund supports equipment, lab consumables, drugs, trainings, and technical assistance through PMU for drug sensitive and drug resistant TB.

C. Information on M/XDR-TB

Epidemiology of M/XDR TB is largely unknown except for prevalence of RR-TB. Under programmatic settings, a small scale TB DRS with Xpert conducted in one province by the MoPH revealed that MDR-TB is 2.2% in new and 16.3% in previously treated patients. (1) Further, a study published in 2016 revealed 19.1% pre-XDR and 6.7% XDR TB among 194 MDR TB patients enrolled under the EBF project in a small patient cohort (3). This extrapolates to an estimate of an incident 5700 (23/100000) MDR-TB emerging in DPRK annually. The National TB Prevalence survey report shared by the MoPH, DPRK revealed prevalence of 641/100000 population. This will increase the estimates of MDR-TB to about 8000 (32/100000) MDR-TB patients emerging per year, a fourth of whom would be pre-XDR or XDR-TB.

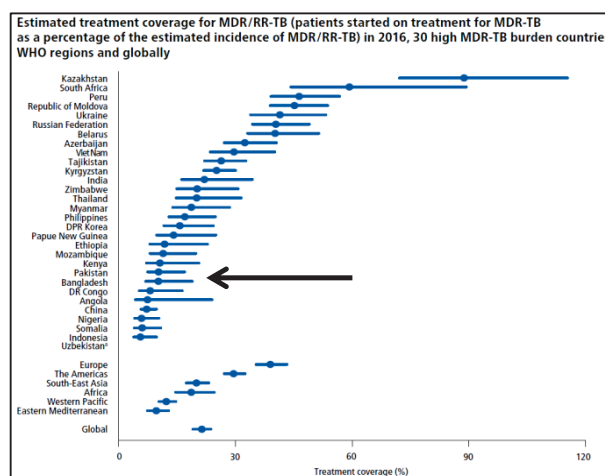
Increasing trend of previously treated patients particularly relapses, estimated TB patients missing from treatment and negligible levels of access to rapid DR-TB diagnosis with prompt appropriate treatment among all notified TB patients, lack of community level infection prevention practices and model of care balancing infection control with access to DR-TB care at decentralized levels could be potential risk factors to promote propagation of drug resistant TB in DPRK.

PMDT services are implemented periodically since 2008 whenever limited supplies of diagnostics and second line drugs are made available through support from TGF (UNICEF & WHO), EBF and CFK.

Till date, MDR-TB detection and treatment initiation has been provided in 109 out of 210 counties through treatment section of 15 cTPI and 8 PTH in 9 out of 12 provinces of DPRK. The diagnosis and treatment services are not regular but are provided at intervals of three months with service interruption in between.

In 2012, the TGF grant commenced and 50 patients received treatment from two PMDT sites in Pyongyang through TGF sources. In 2013, diagnostic services on solid C/DST results were initiated at the NRL after successful proficiency testing for INH (H) and Rifampicin (R) that formed the basis of treatment initiation. Since then, a total of 1457 MDR-TB patients were enrolled on SLD treatment out of which the yearly cohorts of 170, 212, 125, 325, 625 have been enrolled in 2013, 2014, 2015, 2016 and 2017 respectively through TGF source. The last patient course was initiated on treatment in September 2017 from the latest supplies of 625 patient courses and currently no earmarked patient course is available in the country. The next supplies of 500 courses are expected to be delivered through TGF source in January 2018. Based on a recently completed operational research on feasibility and cost-effectiveness of three models of care, the MoPH has decided to transition to a model of care with partial hospitalization in intensive phase (IP) till culture conversion occurs and ambulatory care in continuation phase (CP) through house-hold doctors (HHD) in various counties.

In 2016, only 1394 (8%) of previously treated patients (2.6% of notified bacteriologically confirmed TB patients) were tested for RR-TB and 814/935 (87%) lab confirmed RR-TB patients were initiated on standard MDR-TB treatment of 18 month duration. Although, this is appreciably greater than the previous years, this amounts to treatment coverage of only 18% of 4600 notified and 14% of 5700 incident MDR-TB patients as compared to 87% treatment coverage of 130,000 incident drug sensitive TB patients estimated in DPRK. However, the treatment success in the 2014 annual cohort of 212 MDR-TB patients has been reported at 75.6% as confirmed by NTP which is commendable. From Oct 2016 – Sep 2017, 1651 MDR-TB patients (including 1026 MDR-TB patients by EBF) have been initiated on treatment and drug courses assigned to a patient is completely reserved and not used in part to initiate any other patient.



Over and above this, since 2008, the EBF enrolled 4775 MDR-TB patients on treatment respectively at 9 TB sanatoria and 3 PTHs concentrating around Pyongyang City, South Pyongan province, South Hwanghae province, North Hwanghae province and Nampho city. This includes ~489 and ~537 patients in 2016 & 2017 respectively. Further, at Sadong TBS, 19 XDR TB patients diagnosed by EBF through Korea Institute of Tuberculosis (KIT), Seoul, South Korea have been initiated on Bedaquiline with optimized background regimen as a pilot since September 2016. EBF also provides for nutritional support and warm blankets for DR-TB patients.

Observations:

1. Epidemiology DR-TB is not fully understood:

- While the national DRS now slated to be initiated in 2018, the current PMDT Policy & new national strategic plan are based on a small scale TB DRS with Xpert conducted in one.
 - MDR-TB is 2.2% in new and 16.3% in previously treated patients
 - Further, a study published in 2016 among 194 MDR TB patients enrolled under the EBF project (3) revealed 19.1% pre-XDR and 6.7% XDR TB among MDR TB patients. However, this is not reflected in the national strategic plan.

2. Updating PMDT Guidelines of DPRK

- The MoPH has taken a decision on introduction of shorter MDR TB regimen, second line LPA and Bedaquiline. This is detailed later in the treatment section.
- Draft PMDT guidelines of DPRK partly updated to align with recent WHO PMDT Guidelines – 2016 were deliberated in a two days' workshop with MoPH, NTP staff and Key partners. Consensus obtained to have an integrated guideline with options of diagnostic algorithms with permutation and combinations of various laboratory technologies with DST to at least H, R, Fq, SLI to classify DR-TB patients and design regimen to address all variants of DR-TB with appropriate regimen types guided by DST with focus on decentralization and patient centric care with greater engagement of county/Ri/Dong/HHD systems.
- Evidence based policy decision taken by MoPH for ambulatory care in CP after culture conversion under supervision of the Ri/Dong and HHD. India's revised PMDT guideline was shared for reference. The recent decision of MoPH to remodel cTPI is an opportunity to prepare counties to manage MDR-TB independently. The modalities of decentralization have yet to be clearly defined and operationalized for ambulatory care in continuation phase (CP) through house-hold doctors (HHD) in various counties.

3. PMDT services yet to be available nationwide on day to day basis

- Till date, MDR-TB detection and treatment initiation has been provided in 109 out of 210 counties have offered DST only to failures of CAT II and contacts of MDR-TB through treatment section of 15 cTPI and 8 PTH in 9 out of 12 provinces of DPRK. The diagnosis and treatment services are not regular but are provided at intervals of three months with service interruption in between. This is primarily due to very low investment in capacity building and maintaining uninterrupted supplies of diagnostics and drugs.
- NSP 2018-21 aims for universal DST to >90% diagnosed TB patients in DPRK by 2021.

Recommendations:

1. Know DR-TB epidemiology to prompt local epidemiology guided cost-effective strategies

- Develop protocol, mobilize resources, complete preparation and initiate the National DR survey in DPRK with support from WHO and SNRL Hong Kong for FL & SL DST on MGIT and whole genome sequencing.

- Till such point in time use the available data from initial small scale GeneXpert based DRS conducted in some province and the published study to forecast lab capacity and drug courses requirements.

Responsibility: NTP, NRL, SNRL, WHO

Timelines: December 2018

2. Update the PMDT guidelines of DPRK within 2017:

- Complete the draft of PMDT guidelines for DPRK within next 30 days incorporating the following decision taken in the workshop:
 - i) Reorganize diagnostic and treatment services
 - ii) Propose integrated diagnostic and treatment algorithm with options to address various situation of availability of diagnostics/consumables using WHO endorsed rapid diagnostics to triage patients by resistance to H, R, FQ and SLI to enable treating them with appropriate regimen (standard/individualized including shorter MDR-TB regimen).
 - iii) Decentralize diagnosis and treatment services from province/county and Ri/Dong levels by leveraging on cTPI remodeling for capacity building in LPA/GeneXpert labs, investment in bottom up specimen transport system, DR-TB treatment centers, clinical committees, investigation, ancillary drugs, aDSM system, electronic R&R and re-defining role of Ri/Dong/HHD in MDR-TB services.
 - iv) Clearly define the supply chain management of second-line drugs with stocking norms of reserve drugs at province/county/Ri/Dong levels for ambulatory DOT in continuation phase under supervision of HHD.
- Share the updated version of PMDT guidelines with WHO SEARO and TA for rGLC mission for inputs and finalization within a week.

Responsibility: NTP, PMU with TA from WHO

Timelines: December 2017

3. Expedite complete geographical coverage of PMDT services

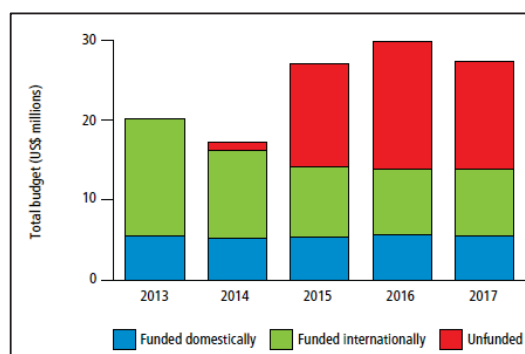
- Aligned and guided by the progress in procurement and supplies of corresponding annual quantities of laboratory consumables (Xpert cartridges, FL-SL LPA kits, solid culture & DST) and second line drugs (including shorter MDR-TB regimen, XDR-TB regimen, Bedaquiline etc.) over the years, expansion of PMDT services to be taken up in the following stages in the specified timelines. This was agreed upon by the MoPH team during the workshop.
 - i) Stage 1: Expand PMDT services to cover remaining 3 provinces and 101 counties with current DST criteria till procurements regularize.
 - ii) Stage 2: Advance in phases to offer DST on day to day basis also to previously treated cases at diagnosis & non-converters in all counties as supplies of lab consumables resume.
 - iii) Stage 3: Advance in phases to offer universal DST also to all diagnosed TB patients in all counties.

Responsibility: NTP, PMU, UNICEF, WHO, EBF

Timelines: Stage 1: Jun 2018; Stage 2: Dec 2019; Stage 3: Dec 2020

D. Government commitment

The MoPH and NTP are committed to implementation of Programmatic Management of Drug Resistant TB (PMDT) and incorporating the WHO recommendations towards ending TB. This commitment translates into an ambitious national strategic plan 2018-21 that aims for universal DST by 2021. However, PMDT service scale-up is severely constrained by lack of resources for investment as well as address procurement and



supply chain bottlenecks for diagnostics and treatment expansion across the country. In 2017, of the total national TB budget of around 27 million USD, only 20% and 30% were reported to be funded by domestic and international funding sources while 49% remained unfunded, the largest funding gap faced by the country in the past five years. This funding gap is exponentially increasing as the domestic and international funding continues to decline since 2014. However, it was learnt during interaction with stakeholders that the government acts humble in completely reporting the expenditures particularly in infrastructure, human resources etc. Among the 9 low income countries out of 30 high burden TB countries, percentage of domestic funding is the highest in DPRK and Government is committed to increase the domestic funds during GF NFM Phase II funding request (2018-2021) to address the funding gap.

The major areas of funding gap identified include diagnostic capacity expansion (equipment, consumables, training, sample transport); treatment capacity (decentralized IC complaint DR-TB treatment centers with aDSM capacity, uninterrupted supply of adequate quantities of quality assured second line drugs), ICT interventions for surveillance and adherence monitoring, patient support and enablers (social protection, nutrition, adherence support, travel support) etc. There are country specific limitations learnt in procurement of certain commodities necessary for scale up of PMDT services, while the government is committed in investment towards building capacity of infrastructure, human resource development and social protection to eliminate catastrophic expenditures etc.

Observations:

1. NSP (2018-21), GF NFM Phase II proposal (2018-21) and PMDT scale up plan:

- The MoPH has recently developed an ambitious NSP (2018-21) and the GF NFM Phase II proposal (2018-21).
- However, few gaps were identified and discussed during the workshop to arrive at a consensus for refining the NSP and GF proposals to address these gaps.
- PMDT expansion plan is yet to be updated and aligned to the NSP (2018-21).
- Funding gap exists within the NSP after considering domestic and donor contributions.

Recommendations:

1. Refine the NSP (2018-21) and GF proposal (2018-21) for the following points:

- Projections of prevalence, incidence, and notification of all forms of TB including MDR-TB need to cover reaching the ~140/100K patients currently missing from notification against estimated ~640/100K prevalent cases. Hence, notification/prevalence needs to increase and stabilize till 2020 before declining.
- Use GeneXpert to enhance yield of case detection among key populations like PLHIV, Children, EP-TB, Sm-ve patients with CXR suggestive of TB.
- Expand the spectrum of Strategy 3 to cover all forms of DR-TB.
- Update projections of DST & treatment courses for 2020-21 to incorporate universal DST to meet the objective of >90% DST coverage in TB patients.
- Add Bdq and drugs to manage PreXDR/XDR-TB from 2018 onwards
- Plan bottom up system for specimen transport initially from county to province and later from Ri/Dong/HHD to county level
- Align NSP (2018-21) with updated PMDT guidelines and expansion plan
- Negotiate with GF for flexibility to re-programme procurements of lab equipment/consumables based on annual assessments of situation and WHO policy updates
- Intensify fund raising (domestic/donor) beyond GF to address funding gap in NSP (2018-21).
- Seek inputs on the PMDT expansion plan after above refinement of NSP(2018-21).

2. GoDPRK to correctly and completely reflect in the annual WHO global TB data collection, the realistic domestic funding contribution made on the TB programme to negotiate for a competitive counterpart international funding to meet the funding gap.

Responsibility: NTP, PMU, UNICEF, EBF, CFK and WHO

Timelines: Dec 2017

E. Partnerships within GoDPRK and with private sector

The general health system under the MoPH is the sole providers of services for TB and DR-TB in DPRK. It was conveyed that private sector do not exist in DPRK.

PMDT implementation commenced in DPRK with partnership through Eugene Bell Foundation since 2008, subsequently with CFK for laboratory strengthening, the Global Fund grant recipients like UNICEF, WHO Country office for DPRK etc. Apart from these there are smaller community level support groups who are engaged for patient care and support for ambulatory patients as well as for active case finding efforts.

Observations:

1. Medical Colleges engagement in PMDT services:

- There are numerous medical colleges across all provinces of DPRK, however, apart from academic activities there were no concrete evidences of their active engagement in PMDT service delivery, patient care, research etc.

Recommendations:

1. Engage Medical Colleges in PMDT services:

- Strategically engage all the departments/specialists of various Medical colleges across DPRK to capitalize on the strengths of each of them as care providers to TB and DR TB patients, referral centers for patients with advanced disease requiring specialist intervention, as training centers and for research.

Responsibility: NTP, PMU with TA from WHO

Timelines: June 2018

F. Advocacy and community engagement

It was learnt from interaction with the programme staff at national, provincial and county levels that advocacy and engagement efforts at the community level was undertaken by the Ri/Dong level staff particularly the HHD while conducting active case finding activities and supervision. This is monitored by the cTPI and PTPI as well as the corresponding people's committees. However, advocacy efforts for fund raising to meet the funding gap requirements after a clear understanding of the strategic plans and budgets developed through a stakeholder consultation process as recommended above.

G. Case finding strategy

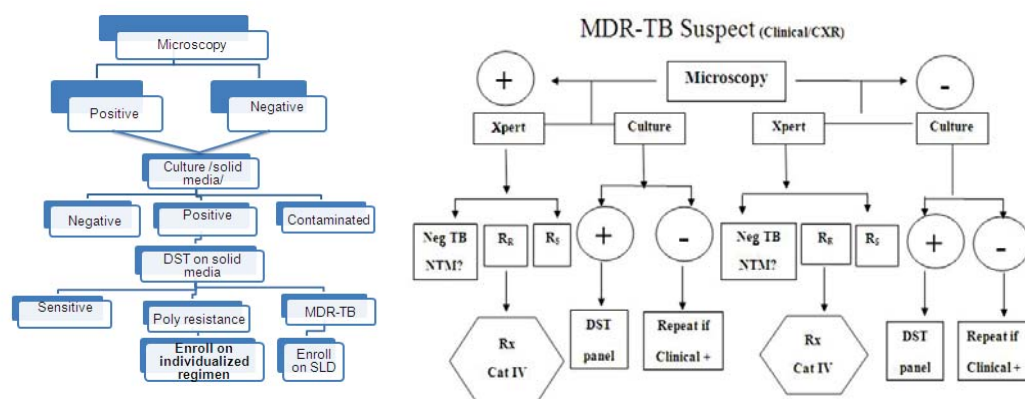
DR-TB diagnosis and treatment services continue to remain episodic i.e. provided at intervals of three months with service interruption in between. It cannot be served on day to day basis unless uninterrupted supplies of diagnostics and drugs could be ensured in the near future.

Although, with government as the sole care provider and active case finding efforts through HHD are undertaken to reach the unreached, DPRK has yet to have a national policy and algorithm indicating a WHO endorsed rapid diagnostic as the initial diagnostic test for all people presumed to have TB and universal access to DST. This is also substantiated by the fact that only half of the pulmonary TB patients notified in 2016 are reported to be bacteriologically confirmed.

Interestingly over the past few years, newly notified pediatric TB case notification rate for the age group of 0-4 has been shown to be at steady level since 2011 compared to an increasing trend in the age group of 5-14 and peaks in the age group of 45-54. Although this could indicate checked transmission among pediatric TB patients and elderly, it may also point to the need for a higher sensitivity diagnostic test like Xpert-MTB-Rif to be clubbed with active case finding efforts to find more patients among these vulnerable and access restricted groups. This would also provide the opportunity of same day and accurate diagnosis of RR-TB along with M-TB among these groups like those identified through active case finding.

For DR-TB case finding, a team of CTPI visits selected TBS out of the designated DR-TB treatment centers on monthly basis to collect specimen from presumptive MDR-TB patients i.e. failures of first line treatment or contacts of MDR-TB patients only and get them to NRL to test mainly on solid

culture-DST / GeneXpert or the four provinces with recently installed GeneXpert machines including RRL. The following diagnostic algorithm is being followed in the PMDT implementing areas of the country:



In 2017, specimen collection through TGF support have been done only in 62 (30%) of the counties in DPRK. From July 2016 to June 2017, only 1052 patients specimen have been tested for DST of whom 640 RR/MDR-TB patients were detected and 625 RR/MDR-TB patients were enrolled on treatment while 15 patients died before treatment initiation. GeneXpert machines have been sub-optimally utilized due to uninterrupted supply of limited number of cartridges. A line-list of presumptive MDR/RR-TB patients is developed and maintained at all county levels awaiting services.

Intermittently, the non-resident EBF team visits the 12 county TBS under their project area with mobile Xpert-MTB Rif and SLD, tests line-listed presumptive MDR-TB and starts lab confirmed RR-TB patients on MDR-TB treatment. The EBF team visits two times in a year and rest of the time the 10 Xpert machines under their project are not available for routine use.

Observations:

1. MDR-TB diagnostic services have halted since July '17:

- MDR-TB diagnostic services have halted since July '17 due to stock-outs of DST consumables as procurement of GF supported 3 GeneXpert machines and 4000 cartridges not processed by Danahar/Cepheid and import of digital X-ray machines/consumables, lab consumables for solid C-DST and LPA FL/SL DST kits from China ports halted due to sanctions.
- However, CFK and EBF could bring in lab consumables for liquid culture DST and GeneXpert during their recent visits in 2017.

2. Sample collection and transport done intermittently by CTPI team

- Sample collection and transport is done by the CTPI team by scheduled monthly visit to the TB sanatorium and PTH on line-listed presumptive DR TB patients (mainly failures of first line treatment).
- This may not be sustainable as the country expands to more DR-TB sites.

- This leads to prolonged waiting period for presumptive MDR TB patients identified at the TB sanatorium.

3. Active case finding (ACF)

- ACF approaches need re-designing with clear delineation of vulnerable groups and the effort is compromised with absence of greater sensitivity diagnostic algorithms with new tools like digital chest-X ray and Xpert-MTB-Rif.

Recommendations:

1. Pursue highest level advocacy to resolve procurement bottlenecks to resume PMDT services in DPRK

- Delegation of WHO, UNICEF and MoPH DPRK visiting Geneva for GF grant negotiation to engage in highest level of advocacy with WHO HQ/SEARO, TGF, GDF and STP to intervene with Danahar/Cepheid & China customs through GDF to support DPRK eliminate the blocks in procurement and supply of diagnostic equipment/consumables on humanitarian grounds to save lives from DR-TB.
- Delegation from DPRK to engage in bilateral dialogue with China and Russia delegation with mediation by WHO at the Ministerial Meeting at Moscow to resolve the import blocks at customs as well as protection to the suppliers.
- MoPH to have a joint meeting with NTP, NRL, UNICEF, WHO, GF, GDF, CFK and EBF to collaborate and complement their capabilities in resolving the procurement and import of laboratory equipment and consumables.

Responsibility: MoPH, NTP, NRL, UNICEF, WHO, GF, GDF, CFK and EBF

Timelines: Nov-Dec 2017

2. Transition to bottom up specimen collection and transport system

- Decentralize the specimen collection at county level microscopy centers of the TB Sanatorium/PTH DR-TB centers to begin with. Once, the diagnostic facilities are decentralized and lab consumables supplies are regularized, the specimen collection centers may be further decentralized to Ri/Dong levels.
- Provide necessary training and three layer packaging material in smaller size boxes (to be designed by NRL) with gel packs for bio safe packaging of specimen collected in cold chain
- Identify a focal person to transport the specimen with travel allowance
- Develop a regular scheduling system in coordination with NRL for transport as and when a presumptive DR TB case is identified.

Responsibility: NTP, NRL, PMU and WHO

Timelines: Feb 18

3. Expand ACF groups:

- The clinically and socially vulnerable groups including children need to be clearly enlisted and defined in the national guidelines to reach the unreached
- Rational cost-effective active case finding approaches need to be re-designed with high sensitivity screening with symptoms and digital chest X-ray and reliable rapid diagnostic tools like Xpert-MTB-Rif for same day confirmation for TB and RR-TB could yield the maximum patients missing from treatment among the above vulnerable groups including children.

Responsibility: NTP, NRL, PMU and WHO

Timelines: Feb 18

H. Laboratory services

Quality assured microscopy centers are established at CTPI/NRL, at all PTPI/PTH and up to all cTPI levels as a three tier system with immediate higher level provides on-site supervision and external quality assurance to the immediate next level of laboratory. The quality of microscopy and the mechanism of quality assurance for smear microscopy were verified during visit to the microscopy center of Pyongyang city and South Pyongan PTPI, Moranbong cTPI. Bacteriological confirmation and follow up of drug sensitive TB is primarily based on smear microscopy across DPRK since the inception of DOTS strategy in 1998.

DR-TB diagnostic services were introduced since 2008 when EBF provided laboratory services by transporting samples to KIT Seoul, South Korea. CFK brought in technical expertise, equipment and consumables including 1 kit each of FL & SL-LPA to build capacity of NRL to conduct quality assured culture and DST for first line drugs as well as establishment of LPA lab under supervision and support of the SNRL Hong Kong.

In 2014, the NRL was unsuccessful in proficiency testing for INH (H) and Rifampicin (R) for solid culture DST through SNRL Hong Kong and was never repeated till date. Solid culture is currently used only for follow up cultures. LPA was last done in May 2016. Five Xpert-MTB-Rif machine (1 at NRL and 4 at RRL or selected PTPI) and 2000 cartridges (1920 for NRL and 20 each for the 4 machines at RRL/PTPI) were procured and supplied with support of WHO DPRK and staff trained jointly by CFK and WHO under periodic monitoring of SNRL Hong Kong. The cartridges exhausted in July 2017. Currently, the NRL is preparing to initiate line probe assay (LPA) pending infrastructure updates (3 clean rooms) and equipment installation to initiate DST for first and second line drugs as well as has initiated proficiency testing for first line and second line drugs (S, H, R, E, O, L, K, A) on solid (C-DST), the drug powders are available in the NRL. Annual maintenance of the laboratory equipment for solid C-DST and LPA as well as air handling units is supported by CFK, it was last done in Nov '16 and is now due.

Since the past few years, EBF brought in 10 Xpert-MTB-Rif machines for primary diagnosis of RR-TB while fresh samples from Sadong TBS are being transported to KIT Seoul for second line DST to FQ

and SLI as part of the Bedaquiline pilot project. Recently, CFK brought few kits of MODS and trained the NRL staff.

Apart from the NRL, one regional reference laboratory at Hamhung City of South Hamgyong province has been upgraded for solid C-DST and initiated solid culture pending proficiency testing for DST while another regional reference laboratory is being developed for solid C-DST at Sariwon City of North Hwanghae province.

Under the NSP 2018-21 & GF NFM Phase II, laboratory expansion has been proposed with 2 RRLs and 10 PTPI level laboratories to cover all provinces with LPA and Solid C-DST. Also, a GeneXpert machine is also proposed for every cTPI level till 2021 to meet the diagnostic demands of DPRK for universal DST.

Observations:

1. Laboratory capacity constrains PMDT services

- NRL has yet to successfully complete proficiency testing for DST in any technology (solid/liquid culture/LPA).
- Four RRLs, 8 PTPI labs and ~210 GeneXpert sites are proposed in the NSP 2018-21.
- An indigenous PCR based technology “Gene Chip – DNA micro-assay test” developed by the Academy of Medical Science of DPRK is being validated at 5 provinces.

Recommendations:

1. Build capacity of Laboratory Network in DPRK:

- NRL to complete proficiency testing in FL/SL-DST on LPA and solid C-DST for first and second line drugs under guidance and support from SNRL Hong Kong.
- NRL to develop and issue guidance document to establish laboratories at PTPI (all technologies) and cTPI levels (GeneXpert); visit for assessment of readiness, undertake proficiency testing for all labs in all technologies and train then in quality assurance mechanisms and lab management systems
- NRL to procure materials, develop SoPs and share it with the PTPI and cTPI for decentralized specimen collection and transport in bio safe environment with training.
- Organize a study tour of focal points for NRL and Academy of Medical Science for validation of in-country Gene-chips for MDR-TB diagnosis and to learn Hong Kong SNRL's indigenous Gene-chips technology to diagnose RR TB.
- SNRL to review the Gene-Chip technology, provide inputs on reducing the manual steps in SoP while maximizing automation, conduct validation with LPA and whole genome sequencing (WGS) and if found reliable, support in getting WHO endorsement.

Responsibility: NTP, NRL, CFK, EBF and WHO

Timelines: Dec 17 – Dec 18

I. Treatment strategy

A line-list of presumptive MDR/RR-TB patients is developed and maintained for the monthly visits for sample collection and testing at NRL by CTPI team. The visit schedules are aligned to the anticipated supplies of next tranche of second line drugs. Treatment initiation is done in quarterly cohorts whenever SLD are supplied by UNICEF (PR of TGF) via GDF or the non-resident EBF team visits the 12 county TBS under their project area on biannual basis with mobile Xpert-MTB Rif and SLD, tests line-listed presumptive MDR-TB and starts lab confirmed RR-TB patients on MDR-TB treatment.

Standard MDR-TB regimen of 18 months duration is prescribed in accordance to WHO PMDT guidelines (2011) after an incomplete set of pre-treatment evaluation by doctors/CTPI/EBF team at TBS/PTH as some investigations like HIV, ECG, Blood sugar, renal function test and pregnancy test are not available at TBS/PTH. The following standard treatment regimens are currently used under NTP PMDT services with subtle differences in regimen composition between EBF and TGF sources:

- MDR/RR-TB regimen: (8) Z Km/Am Lfx Eto/Pto Cs± PAS, (10) Z Lfx Eto Cs
- XDR-TB regimen: the following options are available
 1. Z-Bdq-Lfx-PAS-Lzd-Cfz -Amx/Clv
 2. Z-Mpm-Mfx-PAS-Lzd-Cfz (-Amx/Clv)
 3. Z-Cm-Mfx-PAS-Amx/Clv-Cfz-Lzd
 4. Z-Bdq-Lfx-PAS-Lzd-Cfz –High dose H
 5. Z-OPC-Lfx-PAS-Lzd-Cfz - High dose H

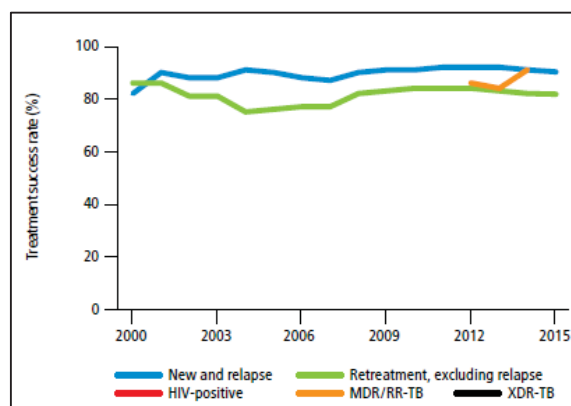
In terms of MDR-TB treatment model, to reach appropriate access to and quality of MDR-TB care with the limited resources, in the end of 2014, MoPH decided to hospitalize all lab confirmed MDR-TB patients for the complete duration of treatment at the PTH in which adequate human resources and infrastructure to deal with MDR-TB patients are available, instead of county TB sanatoria, taking into account the higher capacity of PTHs in program management and patient care. Based on a recently completed operational research on feasibility and cost-effectiveness of three models of care, the MoPH has decided to transition to a model of care with partial hospitalization in intensive phase (IP) till culture conversion occurs and ambulatory care in continuation phase (CP) through household doctors (HHD) in various counties. However, the modalities of decentralization have yet to be clearly defined and operationalized.

Patients are provided MDR-TB treatment free of cost, follow up cultures, nutritional support, wages protection and counseling to the patients under NTP as vertical services. aDSM is limited by lack of lab investigations, equipment and clinical capacity. Specialist and emergency consultation is arranged through nearby provincial or county general hospital. Surgery is conducted only for EP TB patients (non-thoracic sites) wherever surgeons and surgical facilities are available at PTH level. Second line drug courses are earmarked for every patient initiated on treatment and no additional patients are initiated on treatment beyond the number of courses supplied.

In 2016, only 1394 (8%) of previously treated patients (2.6% of notified bacteriologically confirmed TB patients) were tested for RR-TB and 814/935 (87%) lab confirmed RR-TB patients were initiated on standard MDR-TB treatment of 18 month duration. Although, this is appreciably greater than the previous years, this amounts to treatment coverage of only 18% of 4600 notified and 14% of 5700 incident MDR-TB patients as compared to 87% treatment coverage of 130280 incident drug sensitive TB patients estimated in DPRK. However, the treatment success in the 2014 annual cohort of 212 MDR-TB patients has been reported at 75.6% as confirmed by NTP which is commendable. From Oct 2016 – Aug 2017, 1162 MDR-TB patients (including 1026 MDR-TB patients by EBF) have been initiated on treatment. The last patient course was initiated on treatment in August 2017 from the latest supplies of 625 patient courses and currently no earmarked patient course is available in the country. The next supplies of 500 courses are expected to be delivered through TGF source in January 2018. Further, at Sadong TBS, 19 XDR TB patients diagnosed by EBF through Korea Institute of Tuberculosis (KIT), Seoul, South Korea have been initiated on Bedaquiline with optimized background regimen as a pilot since September 2016.

The Central PMDT committee collects and compiles all information from EBF-supported and GF-supported MDR-TB treatment sites. Upon due comparison, the NTP will consider the appropriate way to define the standard MDR-TB management in the country.

Treatment success is consistently above 90% among incident TB patients and above 80% among previously treated TB patients as well as MDR TB patients for the cohorts of 2012 and 2014. In the 2014 annual cohort of 212 MDR-TB patients, commendably, 75.6% as confirmed by NTP were successfully treated. It is claimed that this is mainly due to early detection through active case finding, high DOT compliance and robust regimen. However, with increasing notification of all types of TB patients particularly relapses, the trends of treatment outcomes may decline.



Observations:

1. Policy updates and implementation of treatment strategies for DR-TB:

- Policy decision has been taken to introduce Shorter MDR-TB Regimen in DPRK, starting with an initial cohort of 100 patients on pilot basis in 2018 to gain experience
- Complete transition with increasing numbers is proposed annually up to 2019 with simultaneous management of FQ/SLI resistant and XDR-TB patients with individualized treatment with Bedaquiline if available.
- SL-DST capacity is lacking due to procurement/supply blocks and proficiency tests.
- National regulatory approvals have yet to be obtained for Mfx, Lzd, Cfz, Bdq and Dlm.

Recommendations:

1. Complete preparation to introduce shorter MDR-TB regimen and newer drugs:

- Expedite process to obtain regulatory approvals of drugs new to DPRK by sharing the documentation requirements with UNICEF team to enable them mobilize all documents/evidences/specifications from the manufacturers.
- Prepare NRL/RRLs, provincial, county and Ri/Dong centers of Pyongyang City province (phase I) with all pre-requisite trainings, FL/SL-DST, bio-chemical investigations, ECG, Audiometry, aDSM systems, ancillary drugs for AE/SAE management and revised R&R required for simultaneous introduction of Shorter MDR-TB regimen as well as individualized regimen with/without Bdq for treatment of pre-XDR/XDR-TB triaged using SL-DST (LPA or Solid C-DST) as per the revised PMDT guidelines of DPRK.
- Use learnings from phase I to prepare other provinces/counties in subsequent phases to transition to shorter MDR-TB regimen by 2019 across DPRK.

Responsibility: NTP, PMU, NRL, UNICEF, WHO, EBF

Timelines: Mar 18

J. Program management and coordination

The MoPH coordinates PMDT management including diagnosis and treatment irrespective of funding sources. The MoPH oversees the whole process and funding for MDR-TB management in the country to avoid any duplication of support from different donors.

Observations:

1. PMDT services are centralized in all aspects that contributes to system delays and patient inconveniences

- The following PMDT services were observed to be centralized:
 - i) Sample collection and transport system
 - ii) Drug Susceptibility Testing
 - iii) Pre-treatment evaluation
 - iv) Institutional management of MDR-TB throughout treatment
 - v) Bio-chemical investigation for ADR Monitoring
- With PMDT service expansion in future, decentralization of the above would be necessary for system to cope with the case load

Recommendations:

1. Systematically decentralize PMDT services in all aspects that can minimize system delays and patient inconveniences in the diagnostic treatment pathway

- Enlist facilities up to which decentralization could be feasibly done for each of the above enlisted service delivery components

- Plan for resource mapping, mobilization and capacity building of the concerned facilities where the above services are proposed to be decentralized.
- Strengthen the supervision and monitoring components from the higher to the immediate next level of service delivery to ensure mentoring, troubleshooting and streamlining of services

Responsibility: NTP, PMU and WHO

Timelines: Mar 18

K. Drug management:

First line anti-TB drugs (4FDC) and all second line anti-TB drugs are centrally procured through GDF using the Global Fund grants by UNICEF. The supplies are in 6 monthly tranches. Apart from these, second line drugs are also brought in by the EBF during their episodic services when patients are initiated on treatment at the selected PTH/TBS they serve. There exists no domestic source of funding for drug procurement. Same is the case with procurement and supply of equipment, lab consumables for drug sensitive as well as drug resistant TB diagnosis.

To ensure uninterrupted supply of drugs, the first line drugs (4FDC) are supplied from central to provincial to county warehouses in the form of complete 6 month courses per patients with a stocking norm of 3 months' supply of complete 6 month courses maintained at the provincial and county warehouses. The Ri/Dong household doctors are provided with complete 6 months' supply of 4FDC for every patient diagnosed as TB with an average 15 days to actual treatment initiation from county warehouses via TBS/PTH.

On the contrary, the second line drugs constituting the regimen are supplied from central to county warehouses to TBS/PTH with first supply to cover 6 months of all drugs in the intensive phase per patient followed by 3 monthly supplies of all drugs in continuation phase per patient. The stocking norm for county warehouses is 3 months' supply per patient till end of treatment. Supplies are limited up to the TBS/PTH level as all patients are hospitalized and managed throughout treatment to date. Drugs are supplied in 6 monthly tranches and utilized within one-two months of supplies to initiate MDR/RR-TB patients as per the wait list developed during the monthly sample collection and testing processes. There remains a lean time with no treatment initiation between these supplies in tranches. Drugs earmarked for one patient is not used to initiate treatment of any wait-listed patient. Thus PMDT services are in reality, supply driven and episodic.

Recommendations:

- 1. Once adequate quantities of second line drugs are procured, consider transitioning to a demand driven regular uninterrupted procurement supply chain for diagnostics and drugs to enable early diagnosis and prompt treatment initiation giving equal chance to all presumptive DR-TB patients to receive services as early as possible**
 - Forecast and procure sufficient quantities of second line drug courses to treat the patients of DR-TB diagnosed from all provinces as the numbers increase with the expansion of services to all provinces and the DR testing criteria.

- Transition away from cohort based procurement to consumption based procurement of lab consumables and second-line drugs while maintaining stocking norms for regular supply of 3 monthly stocks per patient at provincial and county level. Stocking norm at Ri/Dong level could be considered along with the policy decision of decentralized ambulatory management of DR-TB patients.
- Consider initiating patients in the wait list with drugs available on shelf for the patients already on treatment (of 18 months duration) keeping a 6 months buffer per patient maintained and adjust the quantification of the next drug order to cover for the remaining months of treatment of existing patients along with the full course of treatment for the next patients. This way, the number of patients put on treatment could be more than the number of patient courses ordered eliminating the waiting list and ensuring regular uninterrupted supplies for existing as well as new patients.
- Consider greater investment in second line drugs forecasted balanced with diagnostics demand through the systematic PMDT scale up planning process with donor funding considering the country specific challenges with domestic funds.

Responsibility: NTP, PMU, UNICEF, TGF and WHO

Timelines: Mar 18

L. Recording and reporting, and data management

DPRK maintains a paper based recording and reporting systems. Paper printouts of forms, registers and quarterly reporting formats for case finding, interim culture conversion and final treatment outcome are sent to the TBS/PTH from CTPI. The reports are sent from TBS/PTH to CTPI through the PTPI concerned in aggregate numbers. The NTP also continues to collect and compile the treatment outcomes data from MDR-TB patient cohorts support by GF and compare the results with data from EBF. Although there is software available at the central level to facilitate data management, this is only for aggregated data and not a case-based web-based data management system.

Observations:

1. TB and DR-TB Surveillance need to be digitalized

- While paper based TB/DR-TB surveillance system with aggregated reporting continues, a new case-based intranet based software is under development to serve epidemiological intelligence to the programme for policy refinements in future.

Recommendations:

1. Nation-wide transition to electronic real-time surveillance system for TB and DR-TB:

- Complete development and field testing of the electronic real-time case based TB data management and patient tracking system to serve as a robust electronic surveillance system for all forms of TB
- Invest for nation-wide implementation of this electronic real-time surveillance system for a dynamic epidemiological intelligence system in country to identify hot-spots, cold-spots,

track migrants and facilitate rational investments in cost-effective strategies to yield maximum outputs within available resources.

Responsibility: NTP, NRL, PMU with TA from WHO

Timelines: June 2018

M. Infection control & health systems

Infection control is an integral part of the PMDT guidelines however, there remains pertinent challenges to infection control posed by need for greater engagement with general health system, the limited access to case finding of infectious pool of patients early from the community and health care facilities described above as well as the climatic conditions demanding specific infection control interventions that could be effective tailored to the country specific needs.

Observations:

1. Health system strengthening opportunities with PMDT service expansion are missed

- Expansion of PMDT services opens opportunities for health system strengthening as follows:
 - i) Infection control interventions for TB are common to and can protect from many airborne infections at various settings. Adequate administrative and personal protective measures observed to be in place at DR-TB centers visited, however, environmental measures to optimize ventilation particularly during cold climates need to be addressed.
 - ii) Pre-treatment evaluation and monitoring adverse events in MDR TB patients particularly with the recommendation of shorter MDR regimen and newer anti-TB drugs require further investment in strengthening the laboratories for bio-chemical investigations at TB sanatorium as well as specific equipment like ECG, audiometer and ophthalmoscope for ADR monitoring.
 - iii) Complex management and the range of adverse effects or drug drug interactions make MDR-TB a multi-systemic venture and require specialist's consultations at regular interval for almost every patient.

Recommendations:

1. Harness the health system strengthening opportunities with PMDT service expansion

- Update the infection control guidelines and integrate the same with the public health systems to become standard operating procedures and integral part of building designs of health facilities.
- Consider training of key architects and engineers involved in the health care facility designing/renovation to be trained in the international course on building designs and environmental measures for airborne infection control.
- Strengthen laboratories at PTH and TB Sanatoria to conduct the complete set of investigations required for pre-treatment evaluation and ADR monitoring
- Equip the DR-TB centers at PTH and TB Sanatoria to monitor ECG, audiometry and ophthalmoscopy for specific ADRs that occur with newer anti-TB drugs

- Establish strong referral network with general hospitals at county and provincial levels for specialist consultation, emergency managements and surgical interventions

Responsibility: NTP, PMU, UNICEF, WHO

Timelines: Jan 18 & ongoing

N. Human resource, Training and Technical support strategy

Sufficient human resources and training for NTP implementation, management and monitoring are provided as well as trained mainly by GoDPRK. This includes functionaries of the various people's committees and TB preventive institutes are central, provincial, county and Ri/Dong clinic levels. External technical support is provided by WHO Country Office for DPRK, CFK for laboratories, UNICEF through TFG for PMU under NTP and EBF external teams.

The recommendations for human resource capacity building are covered in the above relevant sections. The technical assistance need for laboratories is covered in the relevant section above.

The role WHO Country Office DPRK could play in supporting PMDT expansion to universal DST and appropriate treatment by 2021 is proposed below:

- Play a convening role to steer the country dialogue and major initiatives to advance the country towards geographical coverage and phase advancement to universal DST and appropriate treatment with shorter MDR-TB regimen or longer conventional MDR-TB regimen with newer anti-TB drugs.
- Provided Technical Assistance to NTP in the following potential areas:
 1. Epi analysis - National DRS Survey – Protocol Finalization, capacity building, monitoring, data analysis and publication.
 2. Revision of National TB and PMDT Guidelines in line with WHO End TB Strategy and updated PMDT Guidelines – 2016.
 3. Expedite appointment of the Medical Officer for Laboratories through TGF support
 4. Refine the NSP (2018-2021) and GF NFM Phase II proposals (2018-2021) based on recommendations made in the relevant section above.
 5. Capacity building for PMDT expansion and system up-gradation to implement bold policies and strategies enshrined in new guidelines and NSP (2018-2021).
 6. Re-programming current available grants to procure FL-SL LPA, second line drugs for shorter/longer MDR-TB and XDR-TB regimen including Bedaquiline and advocating for above allocation funding if necessary.

O. Supervision and monitoring of the programme

It was informed that the supervision and monitoring functions are aligned to the NTP technical arm hierarchy of CTPI, PTPI, cTPI, County People's hospital and Ri/Dong Poly clinics and HHD. Supervisory visits are regularly conducted from each level to the immediate lower level of services by designated supervisory staff. The corresponding laboratory hierarchy from NRL, to regional, provincial, county level microscopy centers for external quality assurance is also functional. At the community level,

the TB doctors at the Ri/Dong level supervise the household doctors for their functions of active case finding and direct observation of treatment at clinic level followed by home visits of patients who do not show up for their daily FDC for first line treatment. DOT for DR-TB patients are currently done at the TBS/PTH level while patients are managed in the hospital throughout treatment. The treatment support/supervision systems existing for drug sensitive treatment could be capitalized upon for ambulatory DR-TB systems in future with capacity building.

It was informed that the performance review are also conducted in alignment with the NTP technical arm hierarchy of CTPI, PTPI, Country People's hospital and Ri/Dong Poly clinics with the following methodology and frequency:

- At TB Sanatorium/County level – a meeting to review the progress of all indoor patients on treatment with first or second line drugs is conducted on fortnightly basis
- At County Health Committee level – a meeting to review the progress of all ambulatory patients on first line treatment with Ri/Dong Clinics TB doctors and household doctors is conducted on fortnightly basis and a monthly meeting with TBS staff is also conducted to review the case notification and case holding status including reasons for LTFU, ADR management, DOTS implementation.
- At Provincial Health Committee level – a meeting with Chief of County health committee and heads of TBS/PTH to review the progress in PMDT services, programme management, case notification and case holding status including reasons for LTFU, ADR management, DOTS implementation and administrative issues etc. is conducted on a monthly and quarterly basis
- At Central level – a bi-annual review meeting with Directors of PTPIs and Chief of Provincial People's committee is conducted by MoPH/NTP/CTPI to review the progress in PMDT services, programme management, case notification and case holding status and administrative issues etc.

A standard set of supervisory checklists and monitoring indicators exists in the national PMDT guideline that need to be updated in line with the End TB Strategy while revising the national PMDT guidelines recommended earlier.

These processes need to be sustained and strengthened as DPRK heads towards universal access to PMDT services across the country.

P. PMDT plan including funding source (Part of national TB plan or separate)

The MoPH has developed a PMDT expansion plan 2018, however; it needs to be aligned with the NSP 2019-21 as well as the GF NFM Grant phase II. A series of meetings were undertaken with the MoPH team, the TB PMU team, the UNICEF and WHO team to deliberate upon the best way forward to utilize the provisional savings in the current global fund plan, the refinement in the NSP and TGF NFM phase II grant proposal and the need for updating the PMDT guidelines as well as PMDT scale up plan with the NSP. The areas of refinement in the NSP and GF NFM phase II proposal are detailed in the section D above.

Observations:

1. There was an urgent need to utilize the provisional savings from the current GF grants particularly to align it with the need to introduce of shorter MDR-TB regimen.

- Approximately 3 million USD is balance in the current GF grant as provisional savings, primarily due to HR, non-procurement of lab equipment and consumables as well as reduction in unit cost of some equipment.

Recommendations:

1. Expedite activities or urgently re-programme to utilize the provisional savings in the current TGF grants.

- MoPH, NTP, PMU, UNICEF and WHO to identify the potential interventions including diagnostics (FL/SL-LPA), drugs (more shorter regimen and pre-XDR/XDR regimen), investigations, ancillary drugs, ECG machines, audiometry, patient support systems, ICT based adherence monitoring systems, electronic R&R systems, specimen collection and transport, drug supply chain management etc. that can be rapidly implemented to utilize the savings in the current GF grant.
- Also WHO to expedite the appointment of the MO for Laboratory TA.

Responsibility: NTP, PMU, UNICEF, EBF and WHO

Timelines: Dec 17

The mission also covered a workshop at Pyongyang with NTP, UNICEF and WHO staff with special focus on the updated WHO PMDT Guidelines – 2016. The workshop covered review and discussion around the revision of DPRK's PMDT guidelines to include options of updated DR-TB diagnostic algorithms including second line LPA, shorter MDR-TB regimen and management of pre XDR/XDR TB patients with Bedaquiline or Moxifloxacin containing regimen and effective management of adverse drug reactions (ADR) including concepts of active drug safety monitoring and management (aDSM).

The MoPH officials agreed to all of the above recommendations and requested to discuss the following points with UNICEF and WHO that was immediately taken up after the debriefing meeting on 2 November 2017.

- The following quantities can be procured through the GF for preparation of initial phase of introduction of shorter MDR-TB regimen alongside second line LPA and Bedaquiline containing regimen for treatment of pre-XDR / XDR TB from the savings of the current grant.
 - 500 courses of Shorter MDR-TB regimen as an initial implementation phase 1 (instead of a pilot)
 - 500 courses of longer MDR-TB regimen
 - 50 courses of Bdq.
 - A complement of ancillary drugs for ADR management
 - 47 Kits of First Line LPA & 7 Kits of Second Line LPA

- UNICEF and WHO to mobilize the necessary documents on clinical trial results, evidences on safety and efficacy, specifications, package inserts etc. as required by the national regulatory authority to fast-track informed regulatory approval for newer drugs like Moxifloxacin, Clofazimine, Linezolid, Bedaquiline and Delamanid.

Detailed quantifications developed by the PMU team were reviewed and inputs incorporated by the author and shared with the UNICEF and WHO team over email on 3 November.

The recommendations were gracefully accepted by the top brass as the author exercised transparency and openness to suggestions from them to enable refinement, improvisation and ownership for enactment.

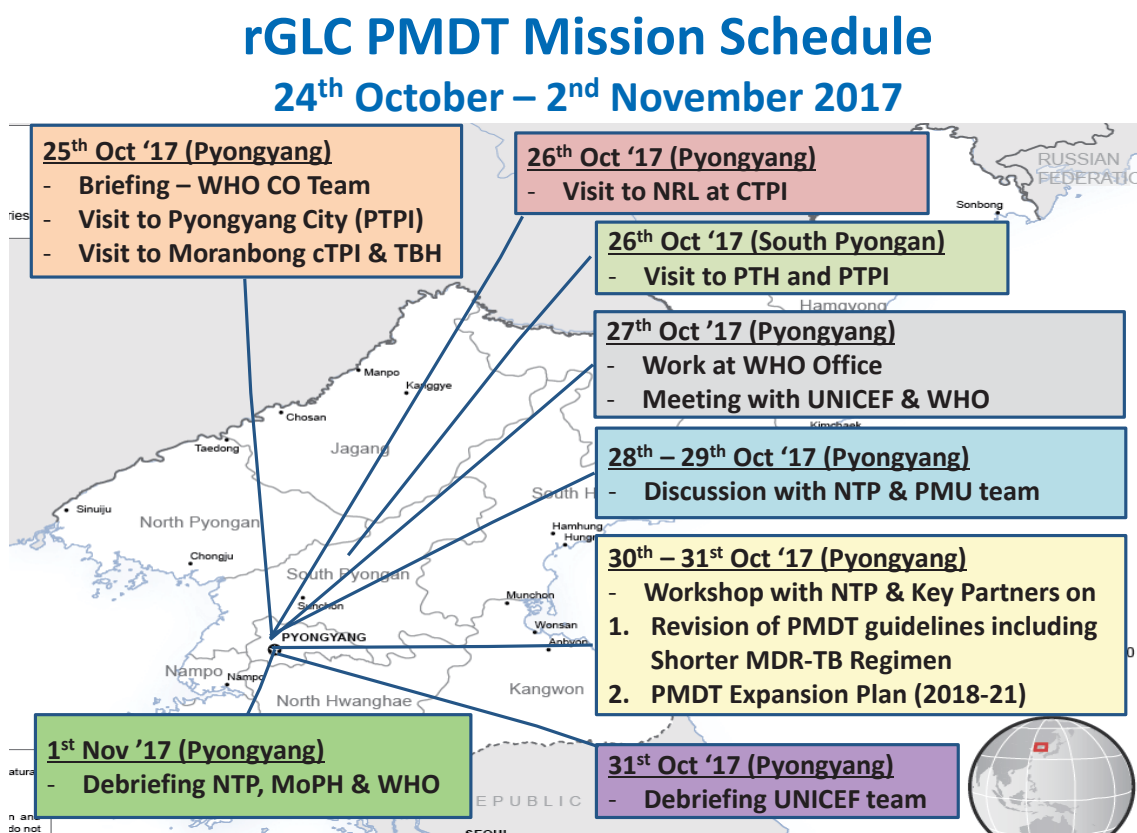
The NTP, UNICEF and WHO DPRK also requested the author to continue providing inputs after the mission to finalize the PMDT guidelines including shorter MDR-TB regimen and scale up plans of DPRK.

Annexure 1 – Terms of Reference (TORS) for technical assistances on MDR-TB management

1. To provide recommendations on scaling-up of PMDT activities by assessing the country situation since the last rGLC mission conducted in November 2016 and review the implementation status of recommendations from last rGLC mission.
2. To review country MDR-TB treatment enrolment plan including capacity of the country programme to adequately manage the proposed patient cohort and the related second line drugs, highlighting the Global Fund supported MDR-TB activities and provide recommendations accordingly.
3. To provide a detail route map for MDR-TB expansion plan considering the introduction of shorten-regimen.
4. To review status of partners' support in PMDT implementation in the country and to discuss harmonization of technical support in line with "End TB Strategy" on PMDT the in-country context.
5. Revision of reporting template for ADSM and provide recommendations on priority basis (not more than 10) with timeframes in the executive summary of the report for implementation and further expansion of PMDT services.

Annexure 2 - Summary of activities (table)

The figure below summarizes the places visited and specific activities undertaken during the mission:



The following stakeholders were met during the mission and technical training on MDR-TB:

At CTPI, NRL, TB PMU MoPH, Pyongyang:

- Dr Hong Sung Il, Global Fund Coordinator, Vice-Director of Department of External Affairs, MoPH, GoDPRK
- Dr Choe Tong Chol, NTP manager, Director of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK
- Dr Choe Kum Song, Senior Officer of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK
- Dr Ri Chol Nam, Researcher of Clinical Research Center, CTPI (Member of central PMDT committee), MoPH, GoDPRK
- Dr O Yong IL, Head of National TB Reference Laboratory(NRL), CTPI, MoPH, GoDPRK
- Dr Ri Chang Son, Lab Doctor, NRL, CTPI, MoPH, GoDPRK
- Dr Kim Pok Nam, Vice-Director of Pyongyang city TB Preventive Institute, MoPH, GoDPRK
- Dr Kim Yong Ae, Member of Pyongyang city PMDT committee, Pyongyang city TB Preventive Institute, MoPH, GoDPRK

- Dr Jo Son Hak, Member of Pyongyang city PMDT committee, Pyongyang city TB Preventive Institute, MoPH, GoDPRK
- Dr Jo Song Nam, Teacher of TB department, Pyongyang Medical College under Kim IL Sung University, MoPH, GoDPRK
- Dr Im Jong Song, Teacher of TB department, Pyongyang Medical College under Kim IL Sung University, MoPH, GoDPRK
- Dr Kim Hyon, TB PMU, Pyongyang, MoPH, GoDPRK
- Dr Choe Song Hwan, TB PMU, Pyongyang, MoPH, GoDPRK
- Dr Yun Yong Hwa, TB PMU, Pyongyang, MoPH, GoDPRK
- Dr Sin Ji Song, TB PMU, Pyongyang, MoPH, GoDPRK
- Dr Ri Jun Hyok, TB PMU, Pyongyang, MoPH, GoDPRK
- Dr Ko Jin Hyok, TB PMU, Pyongyang, MoPH, GoDPRK
- Dr. Kim Myong Hyok, TB PMU, Pyongyang, MoPH, GoDPRK

At WHO Country Office for DPRK, Pyongyang:

- Mr Thinlay – Administrative Officer, WHO DPRK
- Dr Rezwan Kamar – Medical Officer TB, WHO DPRK
- Dr Gagan Singh Sonal - Medical Officer, Malaria, WHO DPRK
- Mr Jahid Hasan – Administrative Team Member, WHO DPRK
- Dr O Hyang Song – National Professional Officer –TB, WHO DPRK
- Dr Jo Mun Hwang – National Professional Officer – TB, WHO DPRK

At UNICEF Country Office for DPRK, Pyongyang

- Mr Murat Sahin – Deputy Representative, Unicef DPRK
- Solongo Dashtseren, Unicef DPRK
- Un Gyong Ha, Unicef DPRK
- Abdurahman Abdo, Unicef DPRK
- Son Il Kim, Unicef DPRK
- Wisam Hazem, Unicef DPRK
- Bakhodir Rahimov, Unicef DPRK

At Pyongyang City TB Preventive Institute:

- Dr Kim Song Ho, Director of Pyongyang city TB Preventive Institute, MoPH, GoDPRK
- Dr Kim Yong Ae, Member of Pyongyang city PMDT committee, Pyongyang city TB Preventive Institute, MoPH, GoDPRK
- Dr Jo Son Hak, Member of Pyongyang city PMDT committee, Pyongyang city TB Preventive Institute, MoPH, GoDPRK
- Kim Sun Ok, Head of Pharmacy, Pyongyang city TB Preventive Institute, MoPH, GoDPRK

At Moranbong County TB Preventive Institute, Pyongyang:

- Ms. Choe Yong Suk, Head of Health Department in Moranbong District People's committee, Pyongyang city, GoDPRK
- Dr Kim Tok Man , Director of Moranbong district TB Preventive Institute, Pyongyang city, MoPH, GoDPRK

- Dr Ri Jong Hyok, Vice-director of Moranbong district TB Preventive Institute, Pyongyang city, MoPH, GoDPRK
- Dr Kim Myong Sin, Head of preventive section, Moranbong district TB Preventive Institute, Pyongyang city, MoPH, GoDPRK
- Dr Pak Jong Chol, PMDT doctor at treatment section of Moranbong district TB Preventive Institute, Pyongyang city, MoPH, GoDPRK

At South Pyongan Provincial TB Institute & Specialized Hospital:

- Dr Ri Gi Chon, Vice-director of South Pyongan Provincial TB Preventive Institute (PTPI), MoPH, GoDPRK
- Dr Kim In Song, Member of Provincial PMDT committee, South Pyongan Provincial TB Preventive Institute (PTPI), MoPH, GoDPRK
- Dr Ra Sung Chol, Director of South Pyongan Provincial TB Specialized Hospital (PTH), MoPH, GoDPRK
- Dr Pak Jong Ik, Vice-Director of South Pyongan Provincial TB Specialized Hospital (PTH), MoPH, GoDPRK
- 2 patients on standard MDR-TB regimen interviewed

Annexure 3 –TB Profile 2016 - DPRK

Democratic People's Republic of Korea

Estimates of TB burden,^a 2016

	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	11 (6.8–16)	43 (27–63)
Mortality (HIV+TB only)	0.051 (0.023–0.089)	0.2 (0.09–0.35)
Incidence (includes HIV+TB)	130 (113–148)	513 (446–584)
Incidence (HIV+TB only)	0.28 (0.14–0.46)	1.1 (0.55–1.8)
Incidence (MDR/RR-TB) ^b	5.7 (3.2–8.1)	22 (13–32)

Estimated TB incidence by age and sex (thousands),^a 2016

	0–14 years	> 14 years	Total
Females	6.9 (5.9–7.8)	27 (23–30)	34 (29–38)
Males	7.7 (6.7–8.7)	89 (77–101)	97 (84–110)
Total	15 (13–17)	116 (100–131)	130 (113–148)

TB case notifications, 2016

Total cases notified	120 323
Total new and relapse	112 606
— % tested with rapid diagnostics at time of diagnosis	
— % with known HIV status	
— % pulmonary	81%
— % bacteriologically confirmed among pulmonary	50%

Universal health coverage and social protection

TB treatment coverage (notified/estimated incidence), 2016	87% (76–99)
TB patients facing catastrophic total costs	
TB case fatality ratio (estimated mortality/estimated incidence), 2016	0.08 (0.05–0.12)

TB/HIV care in new and relapse TB patients, 2016

	Number	(%)
Patients with known HIV status who are HIV-positive	0	
— on antiretroviral therapy		

Drug-resistant TB care, 2016

	New cases	Previously treated cases	Total number ^c
Estimated MDR/RR-TB cases among notified pulmonary TB cases			4 600 (2 300–6 900)
Estimated % of TB cases with MDR/RR-TB	2.2% (0.51–3.9)	16% (5.8–27)	
% notified tested for rifampicin resistance	0%	8%	1 394
MDR/RR-TB cases tested for resistance to second-line drugs			0
Laboratory-confirmed cases			MDR/RR-TB: 935, XDR-TB: 0
Patients started on treatment ^d			MDR/RR-TB: 814, XDR-TB: 19

Treatment success rate and cohort size

	Success	Cohort
New and relapse cases registered in 2015	90%	112 820
Previously treated cases, excluding relapse, registered in 2015	82%	7 882
HIV-positive TB cases registered in 2015		0
MDR/RR-TB cases started on second-line treatment in 2014	91%	212
XDR-TB cases started on second-line treatment in 2014		0

TB preventive treatment, 2016

% of HIV-positive people (newly enrolled in care) on preventive treatment	
% of children (aged < 5) household contacts of bacteriologically-confirmed TB cases on preventive treatment	100% (99–100)

TB financing, 2017

National TB budget (US\$ millions)	27
Funding source:	20% domestic, 30% international, 49% unfunded

Data are as reported to WHO. Estimates of TB and MDR/RR-TB burden are produced by WHO in consultation with countries. Estimates are rounded and totals are computed prior to rounding.

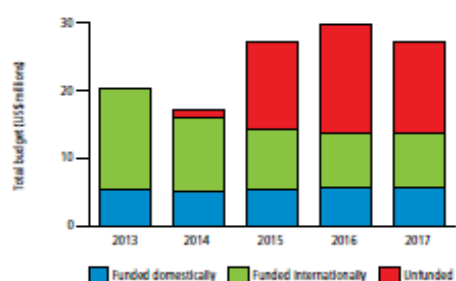
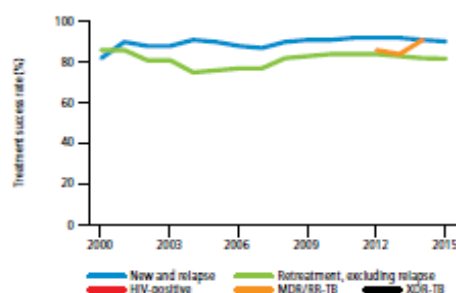
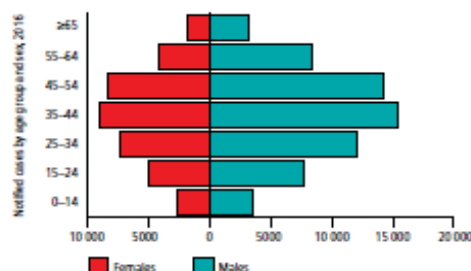
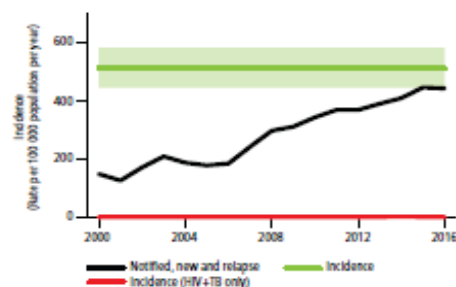
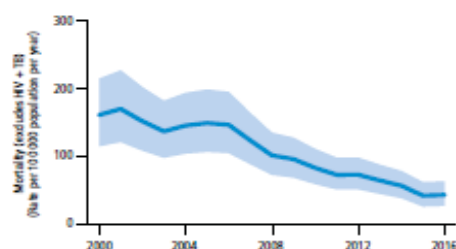
^a Ranges represent uncertainty intervals.

^b MDR is TB resistant to rifampicin and isoniazid; RR is TB resistant to rifampicin.

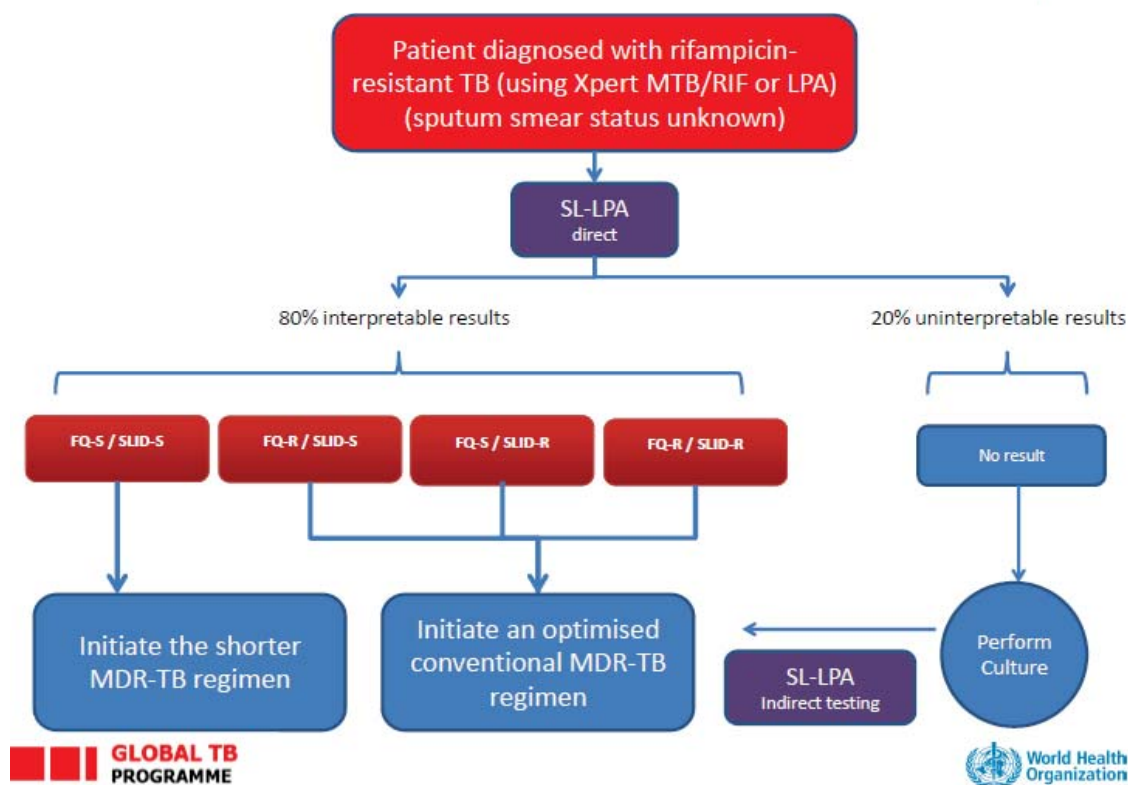
^c Includes cases with unknown previous TB treatment history.

^d Includes patients diagnosed before 2016 and patients who were not laboratory-confirmed.

POPULATION 2016 25 MILLION



Annexure 4 - Proposed Testing Algorithm for DR-TB diagnosis using WHO endorsed rapid diagnostics for DPRK:



Annexure 5 – Summary of PMDT Expansion Plan 2018 for complete geographical coverage in DPRK:

	Baseline (2012)	2013	2014	2015	2016	2017	2018
Number of provinces covered by PMDT	1	1	2	4	6	8	12
Name of provinces covered by PMDT	Pyongyang	Pyongyang	N. Hwanghae	S. Pyongan, N. Pyongan	S. Hamgyong,	N. Hamgyong, Nampho Kangwon	S.Hwanghae, Rason, Ryanggang, Jagang
Culture and DST centers	1 (NRL)	1 (NRL)	1 (NRL)	2 (NRL+1 RRL)	2 (NRL+1 RRL)	3 (NRL+2 RRL)	3 (NRL+2 RRL)
Number of Sanatorium covered by PMDT	2	8	15	15	15	15	18
Number of PTH covered by PMDT				4	6	8	10
Number of MDR-TB patients enrolled in 2 nd -line treatment	50	120	130	250	500	1000	2000
Functioning LPA	NA	1 (NRL)	1 (NRL)	1 (NRL)	1 (NRL)	1 (NRL)	1 (NRL)
Functioning Xpert MTB/RIF	NA	1 (NRL)	1 (NRL)	2 (NRL+1 RRL)	2 (NRL+1 RRL)	3 (NRL+2 RRL)	5 (NRL+ 2RRL+2 PTPI)

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1. World Health Organization, Global TB Report 2017
2. National TB Prevalence Survey Report for DPR Korea (2015-16)
3. Seung KJ, Franke M, Linton SW (2016) Multidrug-Resistant Tuberculosis Treatment in North Korea: Is Scale-Up Possible? PLoS Med 13(8): e1002062. doi:10.1371/journal.pmed.1002062