Programmatic Management of Drug Resistant Tuberculosis – r-GLC Mission Report: 2019 Bhutan

Dr Malik M Parmar (MD),
National Professional Officer – Drug Resistant TB,
WHO Country Office for India, New Delhi

1/31/2019

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

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

PMDT r-GLC MISSION REPORT - 2019

Programme: Country: Bhutan

Lead implementing agency:

National Tuberculosis Programme, Ministry of Health, Department of Public Health, Royal Government of Bhutan

Inclusive dates of mission:

23rd - 30th January 2019

Author:

Dr Malik M Parmar,

National Professional Officer – Drug Resistant TB,

WHO Country Office for India, New Delhi

Acknowledgments:

- Ministry of Health, Royal Government of Bhutan, Thimphu
- National TB Programme, Royal Government of Bhutan, Thimphu
- WHO Bhutan, Thimphu and India, New Delhi
- WHO South East Asia Regional Office, New Delhi

Contents

Acknowledgments:

The author extends gratitude to the National Tuberculosis Control Program (NTCP), Ministry of Health (MoH), Department of Public Health (DoPH), Royal Government of Bhutan (RGoB) and WHO Representative to Bhutan and India for their kind support in conducting this mission.

The author acknowledges the leadership, valuable time and insights shared by Dr Pandup Tshering, Director General, Department of Medical Services; Dr Karma Lhazeen, Director, Department of Public Health and Mr Rixin Jamtsho, Chief Program Officer, Communicable Disease Division (CDD). Special acknowledgements to the leadership, valuable time and insights shared by Mr Chewang Rinzin, Dy. Chief Programme Officer, NTCP Manager - Bhutan along with Mr Ugyen Dendup and Ms Jamyang Pema from his team who provided necessary information on progress made since the last mission, specific foreseen challenges and shape up the recommendations to address the felt unmet needs of the NTCP Bhutan for PMDT. Thanks also to the members of the Technical Advisory Group (TAG) to NTCP Bhutan namely Dr Sonam Wangchuk, Head of and his team from Royal Center of Disease Control (RCDC), Members of Technical Advisory Group viz. Dr Pema Tenzing, Dr Gaki Nima, Dr Tandin Zangpo, Dr. Tashi Choden and others for their time, insights, facilitating national training of medical doctors and pharmacists; and technical deliberations at a TAG meeting around need for systematic interventions for latent TB infection (LTBI), updates in multidrug resistant TB (MDR-TB management), active drug safety management and monitoring (aDSM) and airborne infection control (AIC) in Bhutan.

The author would also like to thank Dr Rui Paulo de Jesus - WHO Representative to Bhutan for the invitation and trust to conduct the mission under horizontal collaboration in revision of TB and PMDT guidelines including introduction of newer injection free regimen; Ms Wangmo Thinley – Administrative Officer for providing organizational support; Ms Sonam Yangchen, National Professional Officer – Communicable Diseases, WHO Bhutan for valuable support, care and time given throughout the mission and sharing information on situation, challenges, potential solutions and way forward for TB and MDR-TB interventions in Bhutan as well as discussion on specific action points for WHO country office to support Bhutan accelerate its response to ending TB. Finally, thanks also to Dr Mukta Sharma – Regional Advisor (TB/HIV/STI/Hepatitis), Dr Partha P Mandal – Technical Officer TB, Dr Vineet Bhatia - Technical Officer MDR-TB at WHO SEARO and Dr Lungten Wangchuk, Medical Officer – Communicable Diseases, WHO Nepal for their valuable time, support and guidance on various issues regarding TB and PMDT situation in Bhutan and the way forward.

Abbreviations and acronyms:

ACF	Active case finding
ADR	Adverse drug reaction
aDSM	Active drug safety management and monitoring
AIDS	Acquired immunodeficiency syndrome
Am	Amikacin
Bdq	Bedaquiline
BHU	Basic Health Unit
Cfz	Clofazimine
Cs	Cycloserine
Dlm	Delamanid
DoPH	Department of Public Health
DOT	Directly Observed Treatment
DOTS	Directly Observed Treatment Short-course
DR-TB	Drug-resistant tuberculosis
DRS	Drug-resistance survey
DST	Drug Susceptibility Testing
DRT	District tuberculosis coordinator
DVED	Drugs, Vaccines and Equipment Division
EPTB	Extra-Pulmonary Tuberculosis
EQA	External quality assurance
FDC	Fixed-Dose Combination
FLD	First line drugs
FYP	Five Year Plan
GDF	Global Drug Facility
GDP	Gross Domestic Product
GF	The Global Fund
GLC	Green Light Committee
GNH	Gross National Happiness
H	Isoniazid
HIV	Human immunodeficiency virus
HRD	Human Resource Development/Division
JDWNRH	Jigme Dorji Wangchuk National Referral Hospital
Lfx	Levofloxacin
LJ	Lowenstein Jensen
LPA	Line probe assay
LT	Laboratory technologist
LTBI	Latent TB infection
MDR-TB	Multi-drug resistant tuberculosis

Mfx	Moxifloxacin
MO	Medical Officer
MoH	Ministry of Health
MSTF	Multi Sectoral Task Force
NACP	National AIDS Control Programme
NGO	Non-governmental organization
NSB	National Statistical Bureau
NSP	New smear Positive Tuberculosis
NTCP	National Tuberculosis Control Programme
NTRL	National TB Reference Laboratory
Ofx	Ofloxacin
P	Rifapentine
PHL	Public Health Laboratory
PMDT	Programmatic Management of Drug Resistant Tuberculosis
PMU	Programme Management Unit
PPE	Personal Protection Equipment
PSM	Procurement supply chain management
R	Rifampicin
RCDC	Royal Center for Disease Control
rGLC	regional Green Light Committee
RGoB	Royal Government of Bhutan
RRH	Regional Referral 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
TAG	Technical Advisory Group
TB	Tuberculosis
TbISS	TB information and surveillance system
VCT	Voluntary Counselling and Testing
VHW	Village Health Worker
WHO	World Health Organization
WCO	WHO Country Office
WGS	Whole Genome Sequencing
WHO	World Health Organization
XDR-TB	Extensively Drug Resistant Tuberculosis

I. Executive summary:

Bhutan is one of the low TB burden countries in the South-East Asia Region. TB has been one of the major public health problems in Bhutan. In 2017, TB and MDR-TB incidence is estimated at 134 and 22 per 100,000 population respectively. Bhutan was awarded Green Light Committee (GLC) approval in 2009 and PMDT was initiated during late 2010. Commendable progress has been made in scaling up PMDT services since then. Now, Bhutan has covered the entire country with PMDT services under the NTCP framework and has applied for GF-NFM funding.

This is the annual monitoring mission for Tuberculosis with focus on Programmatic Management of Drug-Resistant TB (PMDT) component of the National TB Control Program (NTCP) of the Royal Government of Bhutan (RGoB) and under horizontal collaboration support through WCO Bhutan for revision of TB and PMDT guidelines and the introduction of the new WHO recommended injection free oral regimen for MDR-TB. The mission was undertaken on behalf of regional Green Light Committee (r-GLC) of WHO - South East Asia Region (SEAR) from 23 – 30 January 2019.

The objectives of the mission were

- To review follow up actions on recommendations of 2017 rGLC mission;
- To conduct review of progress and plans of PMDT activities;
- To review the implementation of shorter regimen for MDR-TB treatment;
- To undertake training of medical officers/specialists and pharmacists in updated WHO guidelines on TB, MDR-TB and LTBI;
- To provide recommendation on improving quality as well as access to PMDT services in Bhutan.

The mission covered briefing meetings with key officials of MoH, RoGB (DoPH, CPO & NTCP Manager) and WHO Bhutan (WR Bhutan & NPO-CD), visit to key health care facilities like National TB Reference Laboratory (NTRL) at Royal Center for Disease Control (RCDC); Jigme Dorji Wanchuk National Referral Hospital (JDWNRH), TB Unit at JDWNRH; Gidakom Hospital (MDR-TB Treatment Site); District Hospital at Punakha and Wangdue; Thinleygang Basic Health Unit (BHU) level II and Lobeysa Sub-post. An interaction was also held with the Assistant District Health Officer of Wangdue. The author also facilitated a 2 days national training of doctors and pharmacists at Paro and attended a TAG meeting on updating the national guidelines for TB, LTBI, MDR-TB, AIC and aDSM in Bhutan.

The activities include comprehensive review of services in terms of patient care, programme management, supervision monitoring systems, community engagement, information communication systems for TB/DR-TB, interactions with key officials,

specialists, doctors, technicians, staff, 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 PMDT mission report (Oct 2017), the current national strategic plan and national TB guidelines including PMDT, the PMDT expansion plan and the resolve to adoption of the updated WHO treatment guidelines for multi drug-resistant (MDR) and rifampicin-resistant (RR) TB (Dec 2018) and the WHO Guidelines for Latent TB Infection Management.

The mission also covered a deliberation at Thimphu with NTCP manager and his team, specialists from RCDC, JDWNRH and WHO staff with special focus on the WHO treatment guidelines for multi drug-resistant (MDR) and rifampicin-resistant (RR) TB (Dec 2018) to review and discuss around the revision of Bhutan's PMDT guidelines to include options of updated integrated TB and DR-TB diagnostic algorithms complemented by active case finding and infection control in out-patient department through cough corners, inclusion of universal DST through GeneXpert® and second line LPA, injection free MDR-TB regimen with inclusion of newer drugs like Bedaquiline, effective aDSM and AIC measures.

The key observations and actionable recommendations based on country's shared felt needs, observed facts, figures and available evidences from programme data and field visits were shared and discussed in detail by the author with the key stakeholders of NTCP, MoH and WHO Bhutan.

Findings/Observation

a) Progress from the last mission:

The last mission was held in November 2017. The progress was assessed based on observations made and interactions with key NTCP stakeholders of Bhutan.

SN	Priority Recommendations	Progress	Remarks
1	Finalize the updated PMDT guidelines	**Partly met**	Updates needed to align with recent WHO consolidated DR-TB treatment guidelines
2	Ensure that all drugs needed for shorter regimen are part of the country EML	**Met**	
3	Place orders with GDF in consultation with focal point	**Met**	
4	Establish multi-stakeholder high level national initiative in	**Not met**	This has been reiterated during the de-briefing meeting and need to be

	accordance with Delhi Call for Action		followed up through WHO SEARO.
5	Capitalize on the existing momentum and political commitment to mobilize domestic resources – both government and private sector	**Partly met**	This has been reiterated during the de-briefing meeting and need to be followed up through WHO SEARO.
6	Follow-up on pending recommendations made during previous rGLC mission	**Partly met**	This has been reiterated during the de-briefing meeting and need to be followed up through WHO SEARO.

b) Current status of country PMDT implementation:

PMDT services are available in all districts of Bhutan. Diagnosis of DR-TB is offered by RCDC using LPA, liquid/solid culture-DST (BSLIII) to first and second line drugs and 5 GeneXpert® machines. Additionally, 2 regional culture DST laboratories are under consideration to be established and 3 GeneXpert® machines are being considered for procurement by NTCP in 2019. Standard MDR-TB regimen is prescribed after a pre-treatment assessment and all lab confirmed MDR-TB patients are hospitalized at 3 DR-TB centers viz. Gidakom, Gelephu and Mongar MDR-TB treatment centers, till culture conversion followed by ambulatory treatment through family observation with fortnightly/monthly drug dispensing from TB Units and monitoring with random mobile phone calls. JDWNRH assesses patients presenting to or referred to them. Patients are re-admitted to Gidakom site for adverse event management if any. PMDT services are provided free of cost to the patients under NTCP Bhutan well integrated under general health services. Notification of MDR TB patients has increased from 11 (2011) to 60 (2017).

In 2017, only 493 (56%) of the 881 notified TB patients were tested for RR-TB and only 60 lab confirmed RR-TB patients were initiated on standard MDR-TB treatment of 20-month duration (Intensive Phase: 8 Km Lfx Eto Cs Z and Continuation Phase: 12 Lfx Eto Cs Z). This amounts to treatment coverage of 74% of 81 estimated MDR/RR-TB among notified TB patients (881) and 33% of 180 estimated incident MDR-TB patients as compared to 80% treatment coverage of 1100 incident drug sensitive TB patients estimated in Bhutan as per WHO global TB report 2018. However, it is appreciable that the treatment success rate has been consistently above 90% over the past few years with 50 (91%) of the 55 MDR-TB patients from 2016 cohort were successfully treated. The WHO recommended shorter MDR-TB regimen was introduced in March 2018 and Bedaquiline containing longer regimen were introduced in 2019 that were suitable adjusted in accordance to the WHO rapid communication on treatment of MDR/RR-TB (August 2018).

c) Key challenges identified in this mission (by priority):

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

- Although there is an appreciable political commitment expressed with ministerial commitment for ending TB by 2030 in the National Strategic Plan, there is an existing funding gap and shortage of key staff at the NTCP level (only 3 staff).
- National technical and operational guidelines for TB & PMDT need to be updated and aligned with the national strategic plan, End TB Strategy and the recent WHO guidelines for TB prevention, systematic screening, diagnosis, treatment of TB and MDR/RR-TB, aDSM, social support and co-morbidity management particularly malnutrition, smoking and diabetes mellitus etc.
- WHO Bhutan and other partners may need to assess and if needed enhance their organizational capacity to meet the technical assistance demands to support RGoB to end TB within the committed time-frame.
- Although an appreciable digital TB epidemic surveillance system is in use in the form of TB information and surveillance system (TbISS), the epidemiology of M/XDR TB is not clearly understood with only 50% variable testing coverage of universal DST and hence far from nationally representative.
- TB preventive strategies like TB infection control are sub-optimally implemented while Isoniazid (H) prophylactic therapy is limited to people living with HIV (PLHIV) and children <5 years with sub-optimal implementation coverage.
- National TB reference laboratory (NTRL) at RCDC, Thimphu is well established for LPA, Solid/Liquid C-DST however, the proficiency testing for second line drugs on LC-DST is pending; one MGIT 960 and a thermocycler needs repairs; the lab is overburdened for liquid cultures and there is a felt need for 2 additional regional reference laboratories as well as 3 more GeneXpert sites to improve geographical access to enable universal DST.
- Reaching the unreached – health care facilities resort to passive case finding for presumptive TB and presumptive DR-TB (all smear positive, failures and contacts of MDR-TB) while active case finding is conducted by district hospital team and is limited in select vulnerable groups like contacts of TB patients, schools, monasteries and migrant laborers. Only 56% of the 881 notified TB patients were tested with rapid diagnostics at the time of diagnosis in 2017.
- Specimen transportation systems are sub-optimally functional as it takes on an average about 10 days from the time of collection to reach NTRL and GeneXpert sites. This compromises recovery of valid results as well as burdens the NTRL to conduct culture on every specimen received to attempt culture recovery for further processing on LPA and DST, thereby delaying the diagnosis.
- MDR-TB diagnostic and treatment services are centralized leading to delays in access to care with a strategy of long term hospitalization (3-4 months for DR-TB at 3 DR-TB centers and 14 days for DS-TB patients at district hospitals). aDSM system is limited to TAG members. The treatment regimen for drug sensitive and

drug resistant TB need to be aligned with the recent WHO recommendations. National regulatory approvals have yet to be obtained for some of the WHO recommended second line drugs as per the rapid communication like Delamanid (Dlm) and Rifapentine (P).

- Treatment adherence monitoring is relied upon directly observed treatment by a counseled family member with trust, 15 days/1 month dispensing and refill monitoring by TB in-charge at district hospitals.
- A dual system of TbISS and paper-based TB/DR-TB surveillance system with aggregated reporting is in place including QuanTB for drug logistic management. Multiple E/m health software exist that need to be integrated to avoid duplicity of efforts. TbISS need further development and utilized with improving penetration of mobile, social media and internet in the country as well as health information systems under development to serve epidemiological intelligence to the programme for policy refinements in future.
- No clear strategy for TB Free Bhutan including latent TB infection (LTBI) available to this effect. No baseline data available for TB-affected families facing catastrophic costs due to TB.

d) Conclusion: priority recommendations:

The top priority recommendations from the current mission are as follows:

SN	*Recommendations (preferably not more than 10)*	*Responsible agency*	*Time frame*
1	***Execute political commitment:*** *Translate high political commitment into enhanced domestic funding & inter-sectoral/inter-ministerial collaboration with intensive monitoring of a comprehensive strategy for ending TB by 2030. Increase the NTCP staff strength to double or more at the earliest.*	*MoH, NTCP supported by WHO-Bhutan and partners*	*Mar 2019*
2	***Update national TB policy and guidelines:*** *Complete the first draft of updated national guidelines on TB and PMDT guidelines for Bhutan (integrated including Hr TB) within next 90 days and share with WHO SEARO and the author for inputs and finalization within 2019. Conduct a national consultative workshop to deliberate and finalize the guidelines.*	*NTCP supported by WHO-Bhutan*	*June 2019*
3	***Enhance investments in Technical Assistance:*** *WHO Bhutan and other partners to assess and if needed enhance their organizational capacity to meet the technical assistance demands to support RGoB to end TB within the committed time-frame.*	*WHO-Bhutan and other partners based on request from NTCP*	*Aug 2019*

4	***Know your DR-TB epidemic:*** *Expedite coverage of the universal DST to use the RCDC's TbISS more accurately as TB/MDR-TB surveillance system to measure the DR-TB epidemic or conduct periodic national DRS surveys.*	*NTCP, RCDC supported by WHO-Bhutan*	*Dec 2019*
5	***Strengthen TB preventive strategy:*** *Introduce TB preventive package (infection control and LTBI) in conjunction with active case finding among high risk groups through TB care package for BHU, Sub-post and village level as well as at health care facility level.*	*NTCP supported by WHO-Bhutan*	*Nov 2019*
6	***Strengthen DR-TB laboratory network:*** *Expedite proficiency testing of NTRL for second line drugs on LC-DST through SNRL Bangkok, repair of MGIT960 & thermocycler, establishment of 2 additional regional reference laboratories with LPA and liquid culture facilities (MGIT320/manual) and 3 more GeneXpert sites with rational location of the machines at high burden districts to improve geographical access to enable universal DST.*	*NTCP, RCDC supported by WHO-Bhutan*	*GeneXpert – Dec 2019, LPA – Dec 2020*
7	***Reach the unreached:*** *Address the barriers to accessing TB services in Bhutan by introducing a comprehensive TB care package with a standard active case finding strategy for the country along with infection control through cough clinics at all levels of health facilities and at community level (BHU, Sub-post, VHW & NGOs); expand ACF to more vulnerable groups; improve quality of specimen through training; update the diagnostic algorithm for TB, LTBI & DR-TB with investment in capacity building to enable testing all presumptive TB with rapid diagnostics.*	*NTCP, RCDC supported by WHO-Bhutan*	*Dec 2019*
8	***Streamline specimen transport system:*** *Map out bus transport network or utility vans with districts hospitals to streamline shipment of specimen collected within 48 hrs and track with TbISS to enable universal access to TB test and DST.* • *From BHU-II & sub-post to microscopy centers* • *From microscopy centers to GeneXpert* • *From GeneXpert sites to RCDC*	*NTCP, RCDC supported by WHO-Bhutan*	*Dec 2019*

9	***Enhance MDR-TB services:*** *Decentralize MDR-TB diagnostic and treatment services with aDSM systems through network of national, regional and district level DR-TB centers corresponding to diagnostic services; prefer ambulatory care for most patients with counseling and define hospitalization criteria to admit patients; align treatment regimen and transition to the recent WHO recommendations and expedite approvals of national regulatory authorities for some of the WHO recommended second line drugs as per the rapid communication like Dlm and P.*	*NTCP supported by WHO-Bhutan*	*Dec 2019*
10	***Cafeteria approach to adherence monitoring:*** *Introduce a cafeteria approach to strengthen treatment adherence monitoring through* • *Tracers (digital medication monitors), material, psycho-social support, staff education, counsel* • *DOT – health staff or community or family* • *ICT – Video DOT (We Chat/Mobile app) with data pack / missed call/ Pill Boxes*	*NTCP supported by WHO-Bhutan*	*Oct 2019*
11	***Digitalize TB for elimination in Bhutan:*** *Harness the penetration of mobile, social media and internet in Bhutan and further develop TbISS and integrate with various existing software as a complete digital solution to cover e/m health solutions in the whole spectrum of TB services from health education to test request to results to treatment to adherence monitoring to aDSM to GIS mapping to logistic management to e-records and artificial intelligence (AI) for predictive analysis and prompting course correction in the fight to end TB in Bhutan.*	*NTCP supported by WHO-Bhutan*	*Dec 2019*
12	***Switch to end TB mode:*** *Develop a clear comprehensive strategy (prevent, test, treat, rehabilitate) for TB Free Bhutan including LTBI and criteria for TB Free areas with certification and awards. Conduct TB patient cost survey to set a baseline for TB-affected families facing catastrophic cost due to TB. Seek support also from partners, civil societies, multi sector involvement, stakeholders and donors.*	*NTCP supported by WHO-Bhutan*	*Dec 2019*

The NTCP officials agreed to all the above recommendations that were discussed at the debriefing meeting on 30 January 2019. For the revision of the guidelines the following course of action was agreed upon:

- The TAG members and NTCP agreed to develop the first draft of the national integrated TB and DR-TB guidelines with inclusion of LTBI, aDSM and AIC.
- WHO TA will continue the support to NTCP in developing the first draft of the guidelines.
- NTCP to share the first draft with WHO SEARO and the author for further inputs and finalization
- National consultative workshop to be organized with the national experts once the first draft is ready.

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

II. Detailed report:

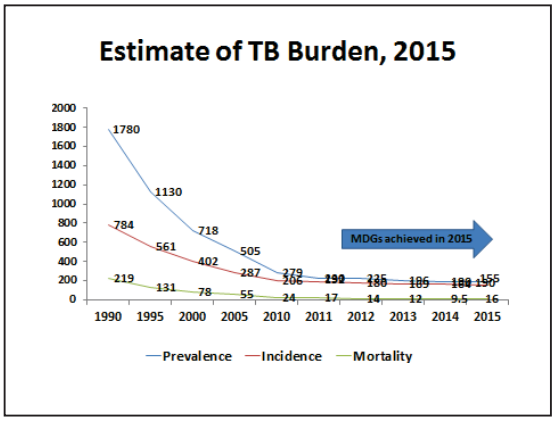
A. Introduction/Background

Bhutan is a mountainous land-locked country situated between the top two high TB burden countries India and China (Tibet Autonomous Region). It has developed high environmental protection standards and promotes the philosophy of Gross National Happiness. The total population as per the report of Population and Housing Census of Bhutan (2017) is 735,553 with the total area of 38,394 sq. km. 62% of population belongs to economically active age group (15-64 years old). 69% of the population lives in rural areas and the population density in the country is 19 persons per sq. km.

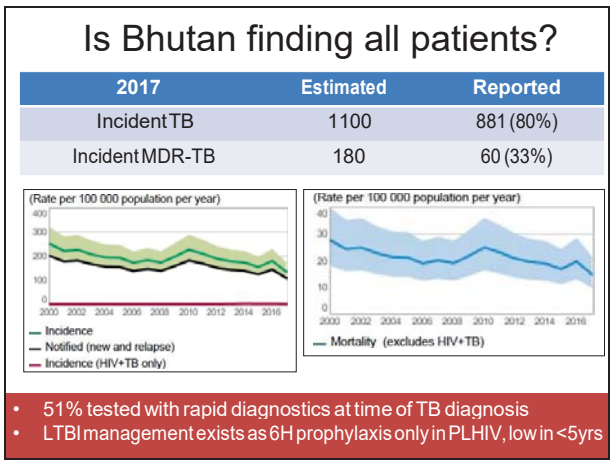
B. Existing TB control program

TB Burden:

Bhutan has achieved the MDG 2015 with a steady declining trend of incidence prevalence and mortality since 1990; however, the decline has slowed down since 2010.



The TB burden and profile of Bhutan submitted for the Global TB Report 2018 is annexed with this report. The epidemiological analysis reported by RCDC through TBISS was also referred to. WHO estimates are based on regional data as a prevalence survey has not been conducted in Bhutan. The salient observations are as follows:



- In 2017, TB incidence is estimated at 134/100,000 population in Bhutan. With 881 TB patients notified in 2017, Bhutan has achieved 80% treatment coverage of 1100 estimated incident TB patients, leaving a treatment gap of ~20%. This translates to 219 TB patients missing from TB notification and treatment in 2017. In contrast, Bhutan has achieved only 33% treatment coverage of 180 incident

MDR-TB patients, leaving a treatment gap of ~67% (~120 MDR-TB patients)

- In 2017, TB killed 15.2 people per 100,000 people (130 per annum) in Bhutan with a declining mortality trend.
- Moreover, only 51% of the notified TB patients were tested with a rapid diagnostic test at the time of diagnosis.
- Eight high burden districts comprising of Chukha, Mongar, Pemagathsel, Samdrup Jonkhar, Samtse, Sarpang, Thimphu and Wangdue account for 80% of all notified TB cases.
- Bhutan has not yet reported the proportion of TB-families facing catastrophic total costs due to TB in 2017 for want of a patient cost survey to be conducted.

The current WHO estimates are based on modeling applied to a declining TB case notification data of NTCP which in turn is based on passive and low sensitivity algorithm for case finding, no data on prevalence survey or inventory studies, significantly low smear negative cases detected over past years, wide variation in access due to hilly terrains throughout Bhutan, second-line DST patterns not known. Thus, there is a felt need to re-estimate burden of TB/DRTB.

Although, RCDC has extended the exceptionally developed a software used for influenza surveillance to deploy an online case based TB information surveillance system (TbISS – www.rcdc.gov.bt) for surveillance of DR TB and patient tracking, it's utilization was suboptimal in the field due to lack of internet connections or non-acceptance by some of the concerned field staff. A national prevalence survey or inventory studies could be options, however, given the investments already made in the TbISS, investing in its further development to serve as a robust online TB & DR-TB surveillance system would be a reasonable affordable and sustainable option to monitor trends of disease burden over time.

NTCP & its structure:

TB services are a part of the comprehensive service package and delivered through a network of facilities in the healthcare delivery system. At the national level, the NTCP is responsible for programming, planning, resource mobilization, monitoring and evaluation. JDWNRH (serves as the national reference hospital) and RCDC (serves as national reference lab and C-DST lab) at Thimphu are premium national institutes supporting NTCP at policy, strategic and service delivery including referral services for TB. Experts from these institutes also serve as members of the National Technical Advisory Group (TAG) for strategic advice on TB guidelines and services as a public health programme.

At the regional level, there are two referral hospitals at Mongar and Gelephu. Both these hospitals are slated to develop regional culture DST laboratories. There are five functional GeneXpert sites and three MDR-TB treatment sites with indoor facility are functional at Gidakom, Gelephu and Mongar Hospital. One more GeneXpert site will be made functional in February 2019 while three more sites are proposed to be established in 2019. At the districts level, District Health Officers/ Chief Medical Officers are responsible for implementing, planning, coordinating, monitoring and evaluating the programme in each district.

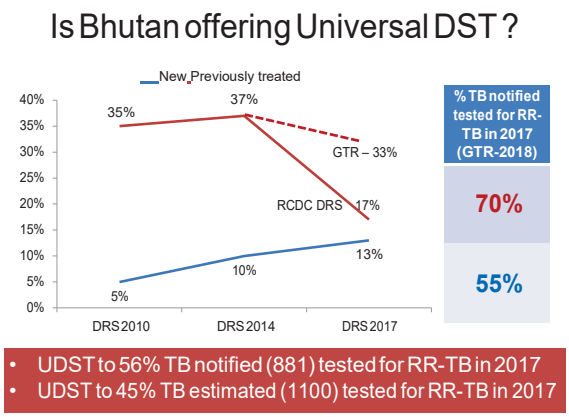
The National Referral, two Regional Referral and 29 District hospitals are responsible for diagnosis (through 37 microscopy centers, 5 GeneXpert sites and NTRL), treatment initiation and monitoring through TB in-charge of the districts. Each district has a TB-in-charge responsible for providing treatment to patients, default tracing, follow-up, reporting of outcomes, community engagement, advocacy communication social mobilization, social welfare linkages for patients and compiling quarterly and annual TB reports for their districts.

The health workers at the Basic Health Units are responsible for the continuation phase of treatment, mobile phone-based follow-up and default tracing, and for sending monthly case holding reports. They are also responsible for referring of TB suspects to the district hospitals for confirmation of diagnosis. PMDT is integrated into the NTCP and delivered as integral part of general health services.

There is no private medical practice in Bhutan. Few private labs exist but do not conduct smear microscopy, while Chest X-Ray is only conducted as part of the structured screening programme for migrant laborers from India for fitness certification required by the national immigration authorities. Anti-TB drugs are regulated and available only through the government health services. Private pharmacies do not sell anti-TB drugs over the counter and was physically verified at Thimphu, Punakha and Wangdue.

While the health infrastructure and workforce are mainly contributed by the RGoB, the Global Fund supports equipment, lab consumables, drugs, trainings, and technical assistance through partners.

C. Information on M/XDR-TB



Epidemiology of MDR-TB in Bhutan is explained through two drug resistance surveys (DRS) that were conducted by the Public Health Laboratory (PHL) in 2010 and 2014 followed by routine DR surveillance through RCDC's TbISS reported on an annual basis. Although an appreciable digital TB epidemic surveillance system is in use in the form of TB information and surveillance system (TbISS), the epidemiology of M/XDR TB is not clearly understood with only 50% variable testing coverage of universal DST mainly due to sub-optimal specimen transportation to 5 GeneXpert sites and hence far from nationally representative. It is also observed that 70% notified previously treated TB cases were tested for RR-TB in 2017 compared to 55% new TB cases.

A declining trend is observed from 2010 to 2017 in the MDR-TB rate among previously treated cases from 35% to 17% as per RCDC's TbISS (although 33% as per Global TB Report 2018) while an increasing trend is observed among new cases from 5% to 13%. Further, the TBISS data also revealed 18.5% and 22.2% any isoniazid (H) resistance among new and previously treated patients in 2017.

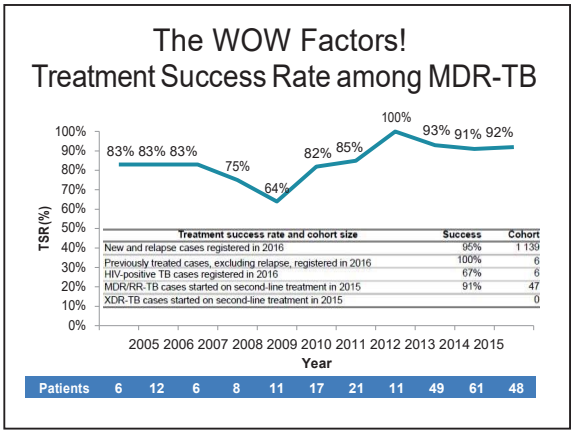
Bhutan was awarded Green Light Committee (GLC) approval in 2009 and PMDT was initiated during late 2010. Bhutan has covered the entire country with PMDT. Diagnosis of DR-TB is offered by RCDC, Thimphu using LPA and liquid/solid culture- DST to first and second line drugs and 5 GeneXpert sites. Standard MDR-TB regimen is prescribed after a pre-treatment assessment and all lab confirmed MDR-TB patients are hospitalized at three MDR-TB treatment sites at Gidakom, Gelephu and Mongar till culture conversion followed by ambulatory treatment through family observation with fortnightly/monthly drug dispensing and monitoring with random mobile phone calls by TB in-charge at districts. JDWNRH assesses patients presenting to or referred to them. Patients are re-admitted to MDR-TB treatment sites for adverse event management if any. PMDT services are provided free of cost to the patients under NTCP Bhutan well integrated under general health services. Notification of MDR TB patients has increased from 11 (2011) to 60 (2017). This amounts to only 33% treatment coverage of 180 incident MDR-TB patients, leaving a treatment gap of 67% (120 MDR-TB patients) in 2017.

TB case detection is a challenge due to passive health seeking behavior of patients and poor-quality specimen collection and transportation to GeneXpert / LPA labs. In addition, delays in diagnostic and treatment services observed primarily due to non-utilization of LPA results for treatment decision, hospitalization policy of 2-4 months until the first culture becomes negative and family observation with mobile phone based follow up of patients with negligible home visits by health workers, inaccessible social protection mechanisms are other challenges observed. Tracking results of SLDST for culture isolates sent to RCDC is delayed.

With negligible levels of private practice, low loss to follow up, non-availability of anti-drugs in the open market, the factors that could probably explain high levels of drug resistance in Bhutan could be as follows:

- Un-acceptable long delays in diagnosis led by delay in specimen shipment and treatment initiation of DR-TB cases augmented by centralized services with accessibility issues in the hilly terrains,
- high levels of H / Poly resistant with cases not differentially diagnosed and treated,
- concerns around quality of directly observed therapy (DOT) and adherence and
- cross-border transmission given that MDR-TB rates are higher in southern districts bordering India as indicated by data from RCDC.

It is appreciable that the treatment success rate has been consistently above 90% over the past few years with 50 (91%) of the 55 MDR-TB patients from 2016 cohort were successfully treated. The WHO recommended shorter MDR-TB regimen was introduced in March 2018 and Bedaquiline containing longer regimen was introduced in 2019 that were suitable adjusted in accordance to the WHO rapid communication on treatment of MDR/RR-TB (August 2018).



Recommendations:

1. Know your DR-TB epidemic:

Expedite coverage of the universal DST to use the RCDC's TBISS more accurately as TB/MDR-TB surveillance system to measure the DR-TB epidemic or conduct periodic national DRS surveys.

Responsibility: NTCP, RCDC supported by WHO-Bhutan
Timelines: December 2019

2. *Establish cross-border patient transfer mechanism:*

Establish a cross-border patient transfer mechanisms through international health regulation mechanisms as well as by exchanging email ids with the bordering Indian states of east, south and west Bhutan to ensure continuity of quality care of TB and MDR-TB patients living on either side of the international border.

Responsibility: NTCP supported by WHO-Bhutan
Timelines: June 2019

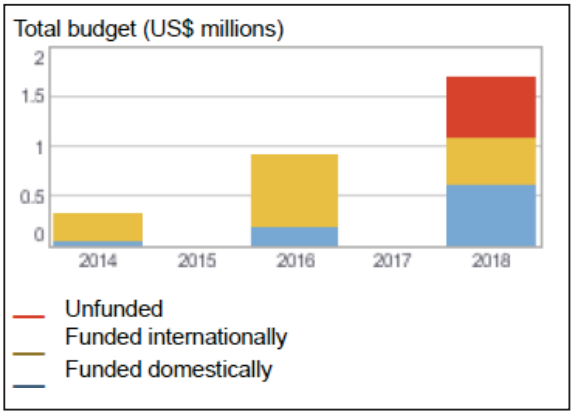
D. Government commitment

The MoH and NTCP 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, aligned to WHO's End TB Strategy that aims for universal DST by 2020.

The WOW Factors!
Strong Political Commitment & Health System

- Ministerial Commitment to End TB by 2030
- Well defined Public Health System from – National – Dzongkhags – Gewog – Chiwog levels
- Health workforce motivated to End TB in Bhutan
- Health care provided free of cost to patients
- Gross National Happiness Commission–for planning and investment
- National Strategic Plan to End TB in place

In 2018, of the total national TB budget of around 1.7 million USD, the domestic funding declined since 2016. However, it was learnt during interaction with stakeholders that the government acts humble in completely reporting the expenditures particularly in infrastructure, human resources etc. and hence, it's giving a picture of greater dependence on international funding. If this is considered, in 2018, the total national TB budget is 1.7 million; of which domestic budget is 0.5 million.



RGoB 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 enhancements in diagnostic

capacity (lab equipment, consumables, training, sample transport); treatment capacity (decentralized IC compliant 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. The government is committed in investment towards building capacity of infrastructure, human resource development and social protection to eliminate catastrophic expenditures etc.

Although there is an appreciable political commitment expressed with ministerial commitment for ending TB by 2030 in the National Strategic Plan, there is an existing funding gap and shortage of key staff at the NTCP level (only 3 staff).

National technical and operational guidelines for TB & PMDT need to be updated and aligned with the national strategic plan, End TB Strategy and the recent WHO guidelines for TB prevention, systematic screening, diagnosis, treatment of TB and MDR/RR-TB, aDSM, social support and co-morbidity management particularly malnutrition, smoking and diabetes mellitus etc.

Recommendations:

1. ***Execute political commitment:***

   Translate high political commitment into enhanced domestic funding & inter-sectoral/inter-ministerial collaboration with intensive monitoring of a comprehensive strategy for ending TB by 2030.
   Increase the NTCP staff strength to double or more at the earliest.

   Responsibility: MoH, NTCP supported by WHO-Bhutan and partners
   Timelines: March 2019

2. ***Update national TB policy and guidelines:***

   Complete the first draft of updated national guidelines on TB and PMDT guidelines for Bhutan (integrated including Hr TB) within next 90 days and share with WHO SEARO and the author for inputs and finalization within 2019. Conduct a national consultative workshop to deliberate and finalize the guidelines.

   Responsibility: NTCP supported by WHO-Bhutan
   Timelines: June 2019

E. Partnerships within RGoB and with private sector

The major technical support for the NTCP is provided by World Health Organization. NTCP has also received technical and commodity assistance from Global Drug Facility (GDF), regional Green light Committee (rGLC), SNRL Bangkok, and independent consultants.

WHO and other partners may need to assess and if needed enhance their organizational capacity to meet the technical assistance demands to support RGoB to end TB within the committed time-frame. The general health system under the MoH is the primary providers of services for TB and DR-TB in Bhutan. In Bhutan, TB medications by legislation are not sold in any private pharmacy or available in any private/faith based or NGO clinics. It is complementing to the NTCP strategies that there were no evidences of TB diagnosis and treatment provided through private practitioners in the districts visited. Although, information was available that doctors of government hospitals may attend to some high-profile cases privately but following NTCP guidelines, however, there was no opportunity to ascertain their TB management practices.

Although Private labs and Chemist exists in Bhutan, neither diagnostic tests nor drugs for TB were available in these private setups visited at Thimphu. Chest X-Rays done as part of the migrant screening programme were used as an opportunity by the fitness certifying doctors to identify probable TB cases for further testing and treatment.

Stringent regulation over sale of anti-TB drugs in private pharmacies was palpable in the districts where the author was denied anti-TB drugs on demand and counselled to visit the nearby government referral hospital with case papers to access TB drugs that are available only through government systems. This is commendable.

Key Observations:

- The NTCP has initiated engagement with private practitioners and this has resulted in the recent referrals, but no formal "Public- Private Mix" or “TB Notification” policy has been developed.

- WHO and other partners may need to assess and if needed enhance their organizational capacity to meet the technical assistance demands to support RGoB to end TB within the committed time-frame.

Recommendations:

1. ***Enhance investments in Technical Assistance:***

WHO Bhutan and other partners to assess and if needed enhance their organizational

capacity to meet the technical assistance demands to support RGoB to end TB within the committed time-frame.

Responsibility: NTCP supported by WHO-Bhutan
Timelines: August 2019

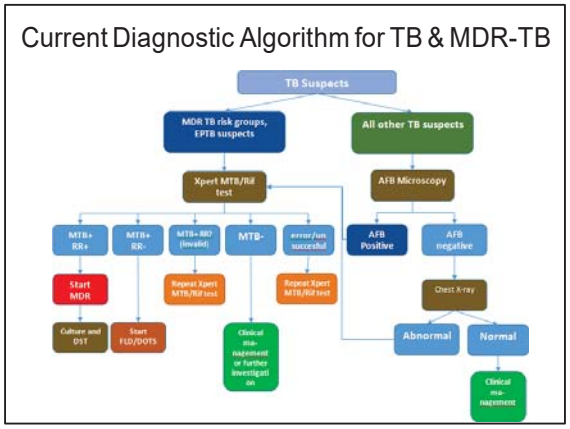
F. Case finding strategy

The potential barriers to accessing health care in Bhutan seems to be challenges with specimen transportation and heavy transportation cost; sub-optimal quality of specimen collected; and long delays in processing the specimen after collection due to transportation delays.

Currently, the following case finding strategies are implemented in Bhutan:

1. Passive case finding for TB and DR-TB:
   - Presumptive TB patients are identified by the staff at the sub-post, BHU-I, BHU-II or district hospital and referred to the nearest microscopy center.
   - For implementation of universal DST, all sputum smear-positive TB patients (new and previously treated), treatment failures and close contacts of confirmed MDR-TB cases having active disease are offered GeneXpert in the 5 sites and their specimen are further sent for phenotypic culture and DST for first line drugs to NRL at RCDC.
   - Specimen transportation systems to NTRL (RCDC) through Bhutan Post transport services or human carriers using bus or utility vehicles of district hospitals are sub- optimally functional as it takes on an average about 10 days from the time of collection to reach NTRL and GeneXpert sites. This compromises recovery of valid results as well as burdens the NTRL to conduct culture on every specimen received to attempt culture recovery for further processing on LPA and DST, thereby delaying the diagnosis.
   - LPA is done on culture isolates of smear positive samples received at NTRL (RCDC). The delays in specimen transport lead to longer cumulative turn-around time resulting from use of combination of technologies (LPA & Solid/Liquid C-DST).
2. Active case finding (ACF) for TB:
   - NTP district team carries out periodic Active Case Finding in vulnerable groups to cover contacts of TB patients, schools, monasteries and migrant laborers.

The diagnostic algorithm used is based on old non-molecular technologies and precludes from meeting the goals of universal DST. Only 56% of the 881 notified TB patients were tested with rapid diagnostics at the time of diagnosis in 2017.



Recommendations:

1. *Reach the unreached:*

Address the barriers to accessing TB services in Bhutan by introducing a comprehensive TB care package with a standard active case finding strategy for the country along with infection control through cough clinics at all levels of health facilities and at community level (BHU, Sub-post, VHW & NGOs); expand ACF to more vulnerable groups; improve quality of specimen through training; update the diagnostic algorithm for TB, LTBI & DR-TB with investment in capacity building to enable testing all presumptive TB with rapid diagnostics. (Annexure 3)

Responsibility: NTCP, RCDC supported by WHO-Bhutan
Timelines: Dec 2019

2. *Streamline specimen transport system:*

Map out bus transport network or utility vans with districts hospitals to streamline shipment of specimen collected within 48 hrs and track with TbISS to enable universal access to TB test and DST.

i) From BHU-II & Sub-post to microscopy centers
ii) From microscopy centers to GeneXpert
iii) From GeneXpert sites to RCDC

Responsibility: NTCP, RCDC supported by WHO-Bhutan
Timelines: December 2019

G.Laboratory services

The National TB Reference Laboratory (NTRL) has a well-equipped and maintained biosafety level III (BSL III) laboratory functioning in the premises of the Royal Center for Disease Control (RCDC), supported by Bangkok Supra-National Reference Laboratory (SNRL). NTRL is proficient in and performing independently genotypic test, Line Probe Assay (LPA) for first and second drugs as well as phenotypic test, culture and DST on solid culture (LJ), liquid culture (MGIT 960) for first line drugs

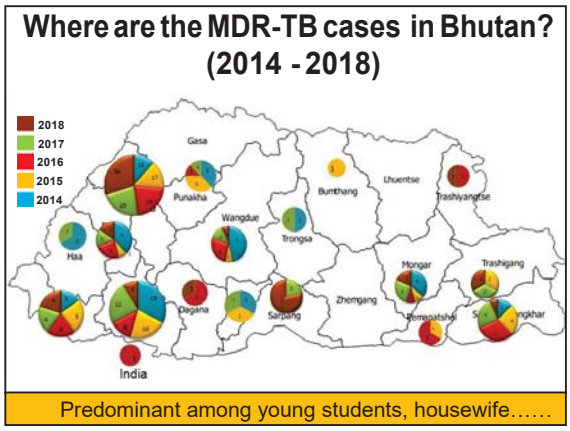
(SHRE) for all specimen received for DST from all over Bhutan. The NTRL is overburdened with LC work as specimens received ~10 days after collection detailed above. It was observed that one MGIT machine and a thermocycler need to be repaired.

An excellent web-based DR TB information surveillance system (TbISS) deployed by RCDC covering whole country and conducts annual drug resistance surveillance.

There are 37 periphery laboratories performing sputum smear microscopy and national external quality assurance system (NEQAS) is in place and conducted by NTRL. Refresher training for less proficient lab technicians based on NEQAS is being conducted by the NTRL on an annual basis. SNRL visits the NRL for QA and technical support on annual basis. The proficiency testing for second line drugs on phenotypic DST is ongoing with SNRL Bangkok.

There are 5 GeneXpert laboratories functional in Bhutan with 1 more laboratory expected to start functioning in February 2019. With the total number of 18 modules among the 6 existing machines, the estimated testing capacity of 12960 per annum would not suffice to conduct universal DST with an estimated testing demand of 15000 tests.

There exists a felt need to establish 2 more regional laboratories with LPA and culture (MGIT – 320 or manual) and 3 GeneXpert laboratories with rational location of these facilities in high MDR- TB burden districts soon to meet the demands of universal DST with better geographical access.



Recommendations:

1. Strengthen DR-TB laboratory network:

Expedite proficiency testing of NTRL for second line drugs on LC-DST through SNRL Bangkok, repair of MGIT960 & thermocycler, establishment of 2 additional regional reference laboratories with LPA and liquid culture facilities (MGIT320/manual) and 3 more GeneXpert sites with rational location of the machines at high burden districts to improve geographical access to enable universal DST.
Consider Next Gen Sequencing and Geo-mapping of TB/MDR-TB patients at RCDC.
Ensure quality improvement as an outcome following NEQAS.
Develop plans and budget for 2 regional labs (LPA, MGIT 320 in BSL 2) and

additional GeneXpert machines and cartridges.

Responsibility: NTCP, RCDC supported by WHO-Bhutan
Timelines: For GeneXpert - December 2019, For LPA December 2020

H. Treatment strategy

Drug sensitive TB patients are hospitalized for treatment initiation for at least 14 days using daily FDCs (as per GDF product line) at dedicated TB wards at NRH/RRH/district hospital/BHU-I level across Bhutan. Hospitalization of MDR-TB patients throughout the intensive phase till the patient is culture converted is mandatory in Bhutan. There is no option of ambulatory treatment initiation even in special situations making it inconvenient particularly for MDR-TB patients as the self-employed patients bear indirect loss of wages or loss of education among students substantiating to the catastrophic economic loss to the family. This policy also demands for more hospital wards and this demand will soon be overwhelming with improvements in Universal DST coverage with additional GeneXpert machines in Bhutan. Patients are discharged on sputum smear conversion and managed by the respective health assistances at BHU I/II level with weekly to monthly dispensing of daily FDCs. Treatment adherence monitoring is relied upon directly observed treatment by a counselled family member with trust, 14 days/1 month dispensing and refill monitoring by TB in charge at district hospitals. The patients are not visited at their homes in Bhutan due to lack of adequate funds for home visits by BHU staff.

All MDR TB patients are put on a standardized regimen aligned to the WHO Guidelines for PMDT. This includes an intensive phase with 5 drugs for 6-9 months (Km, Lfx, Eto, Cs, Z) followed by a continuation phase with the same drugs except the injectable for 18 months (Lfx, Eto, Cs, Z). In 2018, Bhutan rolled out the WHO recommended shorter MDR-TB regimen and quickly adapted the switch from Km to Am soon after the WHO rapid communications were issued. In January 2019, the first patient with MDRFQ (MDR-TB with additional FQ resistance of SL-LPA) was initiated on Bedaquiline containing regimen with interim drug supply support (2 months) from India while the supplies through GDF are expected soon.

Treatment initiation of MDR-TB is centralized to only three MDR-TB treatment sites at JDWNRH Thimphu/Gidakom hospital, regional referral hospitals at Gelephu and Mongar. The medical specialist at JDWNRH & Mongar on behalf of the MDR-TB expert committee enrolls patients after a pre-treatment evaluation; patient is registered at the district level and sent to Gidakom hospital indoor facility for hospitalization throughout the intensive phase of treatment that lasts for 3-4 months depending on the regimen. Indoor facility at Mongar is still under development.

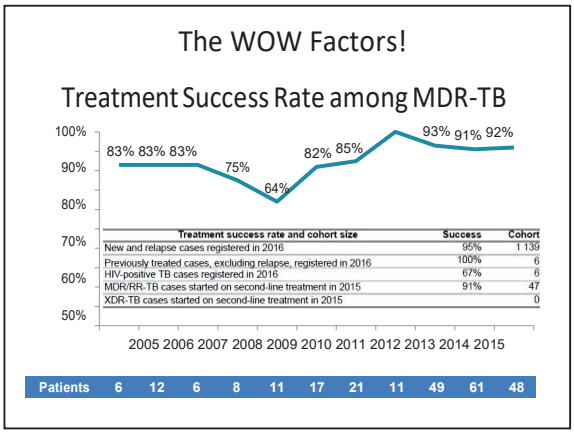
Gidakom & Gelephu are the main admission units for MDR-TB nationally where dedicated chest physician and trained staff manage the patients under guidance of Medical specialist of JDWNRH, Mongar and Gelephu. Recreation and nutrition is being provided to the patients during admission. Patients are also admitted for ADR management while on MDR TB treatment. On discharge, the remaining treatment is organized by the district hospitals.

There is a need for further decentralization of MDR-TB treatment centers at all those districts where GeneXpert is being rationally positioned to balance the diagnostic and treatment capacity and ensure there is no gap in treatment initiation as the country moves towards universal DST. Alternatively, the administrators propose managing drug sensitive and drug resistant TB cases within the same wards earmarked for drug sensitive TB patients that may not be desirable due to risk of cross-transmission of drug resistant TB unless infection control measures are strictly implemented.

Patient education; recording reporting; coordination with referral hospitals and laboratories; drug supply chain management are functions carried out by TB in charge (one of the HA), good recording and regular communication with TB in-charges in the three districts with DR-TB sites, patients compliance on treatment based on mobile phone calls. The health assistants and staff at BHU-I, BHU-II, Sub-posts and village health workers (VHWs) at out-reach clinics (ORCs) are intermittently engaged in treatment support services.

MDR-TB diagnostic and treatment services are centralized leading to delays in access to care with a strategy of long term hospitalization. aDSM system is negligible and limited to TAG members. The treatment regimen for drug resistant TB need to be aligned with the new WHO recommendations i.e. preferably all oral longer regimen for most MDR-TB patients and introduction of regimen for H mono/poly DR-TB. National regulatory approvals have yet to be obtained for some of the WHO recommended second line drugs as per the rapid communication like Delamanid (Dlm) and Rifapentine (P).

Notification of MDR TB patients has increased from 11 (2011) to 60 (2017). This amounts to only 33% treatment coverage of 180 incident MDR-TB patients, leaving a treatment gap of ~67% (~120 MDR-TB patients) in 2017. It is appreciable that the treatment success rate has been consistently above 90% over the past few years with 91% of the 55 MDR-TB patients from 2016 cohort were successfully treated.



Nutritional assessment and supplementation is available for TB and DR-TB patients only during their admission period but there exists no system to continue extending this support for drug sensitive and drug resistant TB patients during their ambulatory care.

Recommendations:

1. ***Enhance MDR-TB services:***

   Decentralize MDR-TB diagnostic and treatment services with aDSM systems through network of national, regional and district level DR-TB centers corresponding to diagnostic services; prefer ambulatory care for most patients with counseling and define hospitalization criteria to admit patients; align treatment regimen and transition to the recent WHO recommendations and expedite approvals of national regulatory authorities for some of the WHO recommended second line drugs as per the rapid communication like Dlm and P. ((Annexure 4)

   Responsibility: NTCP supported by WHO-Bhutan
   Timelines: December 2019

2. ***Cafeteria approach to adherence monitoring:***

   Introduce cafeteria approach to strengthen treatment adherence monitoring through
   - *Tracers (digital medication monitors), material, psycho-social support, staff education, counsel*
   - *Direct observation of treatment (DOT) – health staff or community or family*
   - *Information communication technology (ICT) – Video DOT (We Chat/Mobile app) with data pack / missed call/ Pill Boxes*

   Responsibility: NTCP supported by WHO-Bhutan
   Timelines: October 2019

3. ***Transition from long term hospitalization to ambulatory care:***

   Prefer ambulatory care for most patients with counseling on infection control, adherence and AE reporting.

   Define Hospitalization criteria and admit patients with
   - *advanced diseases – hemoptysis, breathlessness, extensive lung damage*
   - *Medical indication – co-morbidities or derangement of baseline investigations*
   - *psycho-social – substance abuse, alcoholism, homeless*

   Responsibility: NTCP supported by WHO-Bhutan
   Timelines: August 2019

4. ***Expand nutrition assessment and support to all TB patients and their family:***

Establish an intersectoral collaborative mechanism to extend decentralized services for nutritional assessment and supplementation to TB patients and their family.

Collaborate for periodic assessment of BMI and food security for families of TB patients at BHU and Sub-post.

Responsibility: NTCP, other concerned departments supported by WHO-Bhutan and partners
Timelines: September 2019

I. Program management and coordination

The NTCP manager supported with two more colleagues are the only three staff undertaking the program management, supervision, monitoring, and coordination at the national level. There are no other support staffs designated at NTCP at national, regional, district and BHU level.

NTCP services being an integral part of the general health system, the responsibility of programme management and coordination is built into the overall responsibility of the district health officer and medical officers of hospitals and BHUs.

One of the health assistants is designated as TB in-charge in every District/BHU-I level and is responsible for TB programme management, recording reporting, drug supply chain management and mobile/telephone-based monitoring. The MoH coordinates TB and PMDT services irrespective of funding sources through NTCP manager, and district TB-in-charges. The MoH oversees the whole process and funding for MDR-TB management in the country to avoid any duplication of support from different donors.

PMDT services are centralized in all aspects that contributes to system delays and patient inconveniences. With PMDT service expansion in future, decentralization of the above would be necessary for system to cope with the case load. 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 (LFT, RFT, ECG, Audiometry etc.)

Recommendations:

1. ***Strengthen human resources structure to End TB in Bhutan:***

   Undertake upscale re-structuring of the NTCP human resource organogram from national, regional, district to BHU-I and II levels to strengthen programme management, supervision, monitoring and coordination at all levels to align the same with the End TB Strategy, especially to introduce TB preventive services.
   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: MoH and NTCP supported by WHO-Bhutan
   Timelines: December 2019

2. ***Decentralize PMDT services:***

   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. (Annexure 4)

   Responsibility: MoH and NTCP supported by WHO-Bhutan
   Timelines: October 2019

J. Drug management:

Procurement of first line FDC and second line anti-TB drugs as well as equipment & consumables for rapid molecular tests (LPA & GeneXpert) are done by NTCP through GDF using the WHO PQ products.

In 2019, only about 2500 GeneXpert cartridges are likely to be procured through GDF that is far shorter than the expected test demand (15000) if universal DST must be met.

Adequate stocks of first line and second line drugs were available at the national, district and BHU-I level drug stores with reasonably good storage and drug supply chain management practices. Excessive stocks of pediatric FDCs (HR) with near expiry were observed at JDWNRH drug store. Further, there were also shortage of Moxifloxacin and PAS observed.

A second line drug order for 70 MDR-TB patient courses (45 shorter MDR-TB regimen with Am and 25 longer Bedaquiline containing regimen) has been successfully placed through GDF and their supplies have been initiated in 2019. Interim supplies of 2 months

doses of Bedaquiline has been arranged with support from India on loan basis until the supplies of Bedaquiline jars commence in Bhutan through the GDF that is expected by mid-Feb 2019. QuanTB software is used for forecasting while multiple software like TbISS and EBIMS (Electronic Bhutan Inventory Management System) are in use but they do not synchronize with each other.

Recommendations:

1. ***Strengthen drug procurement supply chain management and monitoring:***

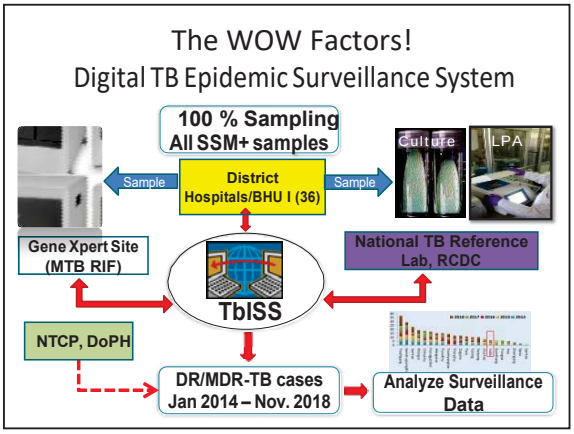
   Substantiate and strengthen capacity at the national level with a focal person for drug and lab logistics supply chain management to

   - procure additional cartridges against the forecasted number of tests (~15000) for universal DST in 2019 and each year subsequently.
   - Follow up with GDF for timely supply of the 70 MDR-TB patient courses including Bedaquiline to enable treatment initiation of patients.
   - closely monitor stock situation to enable timely decision on transferring excessive near expiry stocks to other countries in the region and
   - undertake careful quantification using realistic data guided assumptions for all drugs particularly Pediatric FDCs, Mfx and PAS.

   Responsibility: MoH and NTCP supported by WHO-Bhutan
   Timelines: December 2019

K. Recording and reporting, and data management

A dual system of digital TbISS and paper-based TB/DR-TB surveillance system with aggregated reporting is in place including QuanTB for drug logistic management. It was observed that TbISS is not adequately used by the laboratory staff and TB in-charges for real-time data management and monitoring of the programme either due to training or motivation issues. Multiple E/m health software exist that need to be integrated



to avoid duplicity of efforts. Video DOT (VOT) is being considered under research mode and this could also be potentially integrated to the TbISS for real-time adherence monitoring. TbISS need further development and utilized with improving penetration of mobile, social media and internet in the country as well as health

information systems under development to serve epidemiological intelligence to the programme for policy refinements in future. In discussion with RCDC IT team, TAG and NTCP team, areas for future upgradation of functionalities in TbISS were also explored.

Recommendations:

1. *Digitalize TB for elimination in Bhutan:*

Harness the penetration of mobile, social media and internet in Bhutan and further develop TbISS and integrate with various existing software as a complete digital solution to cover e/m health solutions in the whole spectrum of TB services from health education to test request to results to treatment to adherence monitoring to aDSM to GIS mapping to logistic management to e-records and artificial intelligence (AI) for predictive analysis & prompting course correction in the fight to end TB in Bhutan.

Simultaneously, address internet connectivity issues using mobile services as well as train and encourage all the laboratory staff, TB in-charge and health assistants at district, BHU and Sub-post level to use TbISS fully to make it a real- time surveillance system in its true spirit.

Invest for nation-wide implementation of this electronic real-time surveillance system (TbISS) 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.

Develop TbISS with all essential modules as a complete digital solution to End TB in Bhutan as follows:

- *Rationally remove variables from TB enrollment module*
- *MDR-TB treatment module to be developed – contact tracing, adherence monitoring, aDSM*
- *Data entry up-to SA (BHU) level using TB I/C id or register*
- *Adherence Mobile app with a VDOT/missed call plugged in TBISS Treatment module. Define the specification and programming in consultation with Chief of ICT division.*
- *GIS mapping module*
- *LTBI module – WHO LTBI Care mobile app*
- *Drug Inventory management system integration of TbISS with EBMIS, HMIS, LIS (Polytech 8.3), Bhutan TB Electronic Reporting etc.*

Transition out from the paper-based records to TbISS after completing all essential modules and training of staff up to BHU level.

Responsibility: NTCP supported by WHO-Bhutan
Timelines: December 2019

L. TB Preventive Strategies, Health System and aDSM

The health system hierarchy from national, district and BHU level as well as the strengthened primary health care delivery system through BHU, Sub-post and ORC levels exists as an opportunity for integrating TB care package including the weak aDSM mechanisms and infection control clubbed with community engagement. Pre-treatment evaluation and monitoring adverse events in MDR-TB patients particularly with the recommendation of newer anti-TB drugs require further investment in strengthening the laboratories for bio-chemical investigations and specific equipment like ECG, audiometer and ophthalmoscope for ADR monitoring at national, referral hospitals, district hospitals and BHU-I levels.

There is a national policy for H prophylaxis to PLHIV and children < 5 years, immunosuppressed patients and chronic kidney disease on dialysis with limited implementation using a daily 6H regimen. There is no clear national policy on detection and management of latent TB infection (LTBI) in the country although this is envisaged in the NSP. No clear strategy for TB Free Bhutan including latent TB infection (LTBI) available to this effect. No baseline data available for TB-affected families facing catastrophic costs due to TB.

Infection control is an integral part of the national TB guidelines. IC interventions for TB are common to and can protect from many airborne infections at various settings. Adequate administrative, environmental and personal protective measures were observed to be in place at Gidakom DR-TB center, JDWNRH, District Hospital Punakha & Wangdue and NTRL visited, however, there remain pertinent challenges to implement infection control posed by need for greater engagement with and training of the general health system. Although, the national aDSM committee is the same as the TAG in Bhutan, there is a need for a more robust structure to guide national policy decisions on diagnostics, treatment strategies including clinical management and decentralization of aDSM activities to districts and up to the BHU-I and II levels.

Recommendations:

1. *Design and implement "TB Care Package" including LTBI for Gewog & Chiwog level:*

Develop a comprehensive "TB Care Package" for Gewog & Chiwog level (BHU, Sub-post, ORC level) for implementation and engaging the community to cover at least the following activities and services:

- *i) Mapping vulnerable groups*
- *ii) TB health education including cough etiquette and infection control*
- *iii) Screening (4 symptoms) & referral for LTBI, TB, DR-TB testing*
- *iv) Referral of contacts for screening, chest X-ray and TST/IGRA*
- *v) Specimen collection and transport*
- *vi) Arrange & monitor treatment adherence for LTBI, TB, DR-TB, TB-HIV etc.*
- *vii) Adverse event identification and referral to appropriate level*
- *viii) Assess Nutritional Status – height, weight, mid arm circumference (MAC)*
- *ix) Nutrition and social support*
- *x) Vocational training and employment linkage*

The comprehensive "TB care package" must lead to building system capacity for prevention (infection control & LTBI), detection (active case finding for all forms of TB & DR-TB), treatment (appropriate regimen for all forms of TB & DR-TB) and social protection from catastrophic socio-economic effects of TB (addressing needs for nutritional, co-morbidities, migration, travel enablers, insurances etc.). Use all available tools for implementation through health care system to cover at least low burden districts and effect learning based scale-up to high burden districts. The LTBI strategy should be designed in consultation with the national experts to include at least the following:

- *i) Four symptom (4S) screening, CxR, GeneXpert® among at least house-hold contacts of TB patients: children <5 yrs, PLHIV, adults (annexure 3)*
- *ii) Identification of LTBI – explore availability of TST/IGRA*
- *iii) Treatment of LTBI – explore procurement of Rifapentine and introduction of new 12 weekly regimen (3HP) in risk groups even if TST/IGRA is not available.*
- *iv) Adherence monitoring mechanism*

Responsibility: NTCP, TAG supported by WHO-Bhutan
Timelines: May 2019

2. *Integrate TB Infection Control with active case finding:*

Update the infection control guidelines and integrate its implementation through the public health systems (annexure 3) with the following specific approaches:

i) Community level – through ORCs and engaging Tshogpa and Gup

ii) Health facility OPD – cough corner for infection control and case finding

iii) TB IC in wards –nurses to monitor ventilation, bed spacing, mask electric blankets & disinfection spittoon to patients, restrict visitors, N95 mask to staff

Responsibility: NTCP supported by WHO-Bhutan
Timelines: October 2019

3. *Strengthen and decentralize aDSM system:*

Develop aDSM plan and formats in the guidelines and initiate training, implementation & reporting for aDSM at all levels of health care system.
Strengthen laboratories at national, regional, district and BHU1 levels to conduct the complete set of investigations required for pre-treatment evaluation and ADR monitoring of TB and DR-TB patients. Equip the DR-TB centers at all levels to monitor ECG, audiometry and ophthalmoscopy for specific ADRs that occur with newer anti-TB drugs. Establish strong referral network with national, regional and district level hospitals for specialist consultation, emergency managements and surgical interventions.

Responsibility: NTCP, TAG supported by WHO-Bhutan and partners
Timelines: December 2019

4. *Switch to end TB mode:*

Develop a clear comprehensive strategy (prevent, test, treat, rehabilitate) for TB Free Bhutan including LTBI and criteria for TB Free areas with certification and awards. Conduct TB patient cost survey to set a baseline for TB-affected families facing catastrophic cost due to TB. Seek support also from partners, civil societies, multi sector involvement, stakeholders and donors.

Responsibility: NTCP, TAG supported by WHO-Bhutan and partners
Timelines: August 2019

M. Advocacy and community engagement

Social determinants of TB like loss of wages, catastrophic expenses incurred by families of MDR TB patients, nutritional support, vocational support, psycho-social support are not completely addressed. Engagement of key stakeholders in the community is sub-optimal. Contact with patients is maintained only when they reach the health centers or on mobile phones minimizing compassion, personal touch and dignified care.

Under the Gross National Happiness Commission resources are available through Governors of districts, Kidu Officer, Gewog developmental plan / grant Gups and Tshogpas to address social determinants of health for any disease including TB as part of the developmental agenda. Nutritional support programmes in hospitals can develop specific diet plans for TB patients.

Community level NGO's and self-help groups exist, particularly engaged with HIV, Violence prevention and NCD programmes but not in TB programme although willing to contribute. Such organizations could collaborate and extend social, vocational, nutritional, psychological support to the TB / MDR-TB patient at the community level to promote early case finding, treatment adherence and social determinants of TB. They need mapping, engagement and support from NTCP with basic technical information about the disease and NTCP strategies.

Recommendations:

1. Address social determinants of TB & community engagement in Bhutan:

Address social determinants of TB through inter-sectoral collaboration, harnessing resources available under the Gross National Happiness Commission resources and community engagements through leaders like Dzongdags of districts, Kidu Officer, Gewog developmental plan / grant, Gups and Tshogpas.

Responsibility: NTCP by WHO-Bhutan and partners
Timelines: December 2019

N. Supervision and monitoring of the programme

It was informed that the supervision and monitoring functions are undertaken by NTCP team and district TB in-charges. Supervisory visits are regularly conducted from national level to the districts, BHU and sub-posts by designated national staff. The corresponding laboratory hierarchy from NTRL (RCDC), to regional, district and BHU-I level microscopy centers for external quality assurance is also functional. At the district level, TB in-charge manage the drug stock management, drug dispensing and organization of treatment support directly to the patients, leading to long travel distances and expenses to the patients. At the community level, the BHU-I and sub-post staff are not actively engaged to organize or supervise the functions of active case finding and direct observation of treatment at their level, home visits of patients who do not show up for their daily FDC for first line treatment or MDR-TB ambulatory treatment. It was informed that the annual performance review is also conducted by NTCP to review the progress in TB & PMDT services, programme management, case notification and case holding status and administrative issues etc. These processes need to be sustained and strengthened as Bhutan heads towards universal access to quality TB and PMDT services across the country.

Recommendations:

1. Decentralize supervision and monitoring roles:

Decentralize the role of TB in-charges and engage health assistants at BHU and sub-post level to provide or organize treatment support including adherence monitoring modalities detailed in the section above. Elevate the role of TB in-charges' to a higher level supervisory functions with mobility support to provide supportive supervision and monitoring of the services provided by BHU and sub-post level.
Assign a regional based TB supervision and monitoring officer who is expert in TB and with public health background for a rigorous monitoring and supervision of TB control activity in their region (4-5 officers from the pool) periodically

Responsibility: NTCP by WHO-Bhutan and partners
Timelines: September 2019

O. PMDT plan including funding source

The MoH has developed a PMDT expansion plan within the national strategic plan, however; the national guidelines need to be aligned with the NSP as well as the GF

NFM Grant phase II. The NSP needs to be fully funded through sustained international commitment from donors like GF etc. and enhanced domestic contribution as detailed in section C above.

The mission also covered a two days training of doctors and pharmacists from the district hospitals of all districts of Bhutan on the first two days of the mission at Paro that was facilitated by the author.

The author also facilitated and attended a meeting with the Technical Advisory Group (TAG) for NTCP Bhutan on updating the national guidelines for TB, LTBI, MDR-TB, AIC and aDSM in Bhutan. The recommendations made above cover the areas for updating the national guidelines for TB and PMDT. The TAG and NTCP were of the opinion to have a single integrated national guideline that covers all aspects of TB, LTBI, MDR-TB, AIC, aDSM and other areas of patient support and programmatic aspects. The TAG members agreed to write up the updated sections relevant to their subject expertise in consultation with the NTCP and share the draft write-ups for consolidation at the national level. The NTCP agreed to share the consolidated updated draft of the guidelines for further review and inputs to the WHO SEARO and the author and later organize a national consultative workshop for finalization.

The mission also covered a deliberation at Thimphu with NTCP manager and his team, specialists from RCDC, JDWNRH and WHO staff with special focus on the WHO treatment guidelines for multi drug-resistant (MDR) and rifampicin-resistant (RR) TB (Dec 2018) to review and discuss around the revision of Bhutan's PMDT guidelines to include options of updated integrated TB and DR-TB diagnostic algorithms complemented by active case finding and infection control in out-patient department through cough corners, inclusion of universal DST through GeneXpert® and second line LPA, injection free MDR-TB regimen with inclusion of newer drugs like Bedaquiline, effective aDSM and AIC measures.

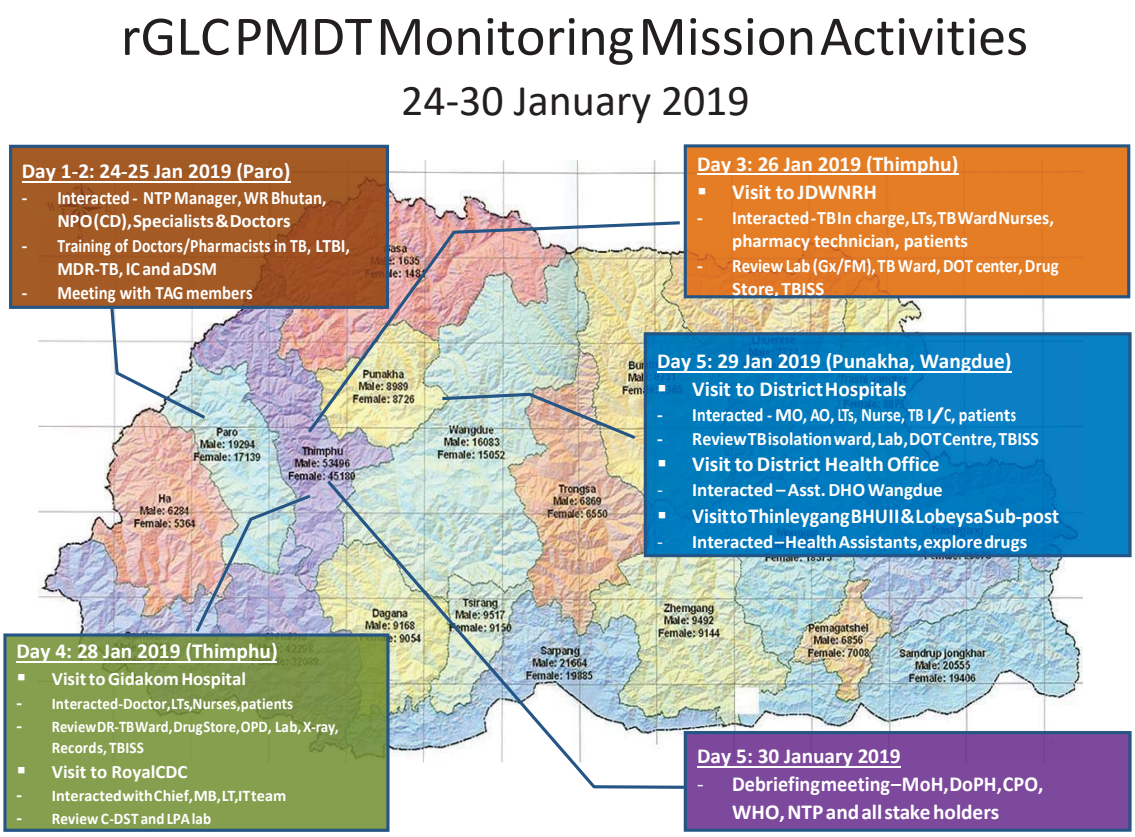
There was a consensus to consider transition from an injectable containing 20-month regimen to an all oral 20-month regimen as per the WHO treatment guidelines for DR-TB (2019). There was willingness to take up regulatory approval for use of newer and repurposed second line drugs like Delamanid and Rifapentine for inclusion in national essential medicine list and procurement adjustments with GDF.

The recommendations were 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 NTCP and WHO Bhutan also requested the author to continue providing inputs after the mission to finalize the PMDT guidelines including longer oral MDR-TB regimen and scale up plans of Bhutan.

Annexure 1 - Summary of activities:

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



Annexure 2 –TB Profile 2017 – Bhutan:

Bhutan

Tuberculosis profile

Population 2017 **<1 million**

Estimates of TB burden*, 2017	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	0.12 (0.076–0.17)	15 (9.4–21)
Mortality (HIV+TB only)	<0.01 (<0.01–<0.01)	0.16 (0.11–0.22)
Incidence (includes HIV+TB)	1.1 (0.83–1.4)	134 (103–169)
Incidence (HIV+TB only)	<0.01 (<0.01–<0.01)	0.77 (0.5–1.1)
Incidence (MDR/RR-TB)**	0.18 (0.12–0.25)	22 (15–31)

Estimated TB incidence by age and sex (thousands)*, 2017

	0-14 years	> 14 years	Total
Females	0.042 (0.027–0.058)	0.35 (0.22–0.48)	0.4 (0.26–0.53)
Males	0.047 (0.03–0.065)	0.64 (0.4–0.87)	0.69 (0.45–0.92)
Total	0.09 (0.065–0.11)	0.99 (0.72–1.3)	1.1 (0.83–1.4)

TB case notifications, 2017	
Total cases notified	881
Total new and relapse	865
- % tested with rapid diagnostics at time of diagnosis	*51%*
- % with known HIV status	*100%*
- % pulmonary	*59%*
- % bacteriologically confirmed among pulmonary	*86%*

Universal health coverage and social protection	
TB treatment coverage (notified/estimated incidence), 2017	80% (63–100)
TB patients facing catastrophic total costs	
TB case fatality ratio (estimated mortality/estimated incidence), 2017	0.11 (0.07–0.17)

TB/HIV care in new and relapse TB patients, 2017	Number	(%)
Patients with known HIV-status who are HIV-positive	5	<1%
- on antiretroviral therapy	*5*	*100%*

Drug-resistant TB care, 2017	New cases	Previously treated cases	Total number***
Estimated MDR/RR-TB cases among notified pulmonary TB cases			81 (57–110)
Estimated % of TB cases with MDR/RR-TB	13% (10–17)	33% (7.5–70)	
% notified tested for rifampicin resistance	55%	70%	493
MDR/RR-TB cases tested for resistance to second-line drugs			0
Laboratory-confirmed cases		MDR/RR-TB: 60, XDR-TB: 0	
Patients started on treatment ****		MDR/RR-TB: 60, XDR-TB: 0	

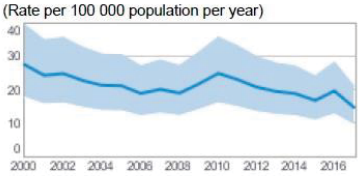
Treatment success rate and cohort size	Success	Cohort
New and relapse cases registered in 2016	95%	1 139
Previously treated cases, excluding relapse, registered in 2016	100%	6
HIV-positive TB cases registered in 2016	67%	6
MDR/RR-TB cases started on second-line treatment in 2015	91%	47
XDR-TB cases started on second-line treatment in 2015		0

TB preventive treatment, 2017
% 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

TB financing, 2018	
National TB budget (US$ millions)	1.7
Funding source: 36% domestic, 28% international, 36% unfunded	

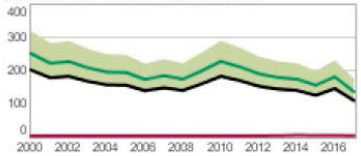
** Ranges represent uncertainty intervals*
*** MDR is TB resistant to rifampicin and isoniazid; RR is TB resistant to rifampicin*
**** Includes cases with unknown previous TB treatment history*
***** Includes patients diagnosed before 2017 and patients who were not laboratory-confirmed*

(Rate per 100 000 population per year)



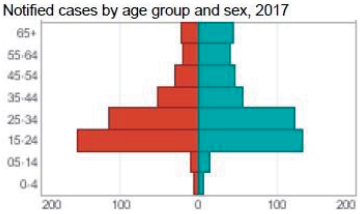
Mortality (excludes HIV+TB)

(Rate per 100 000 population per year)



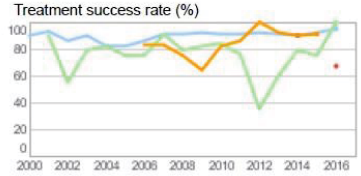
Incidence
Notified (new and relapse)
Incidence (HIV+TB only)

Notified cases by age group and sex, 2017



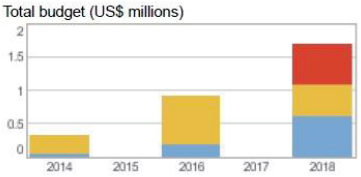
Females Males Incidence

Treatment success rate (%)



New and relapse
Retreatment, excluding relapse
HIV-positive MDR/RR-TB XDR-TB

Total budget (US$ millions)

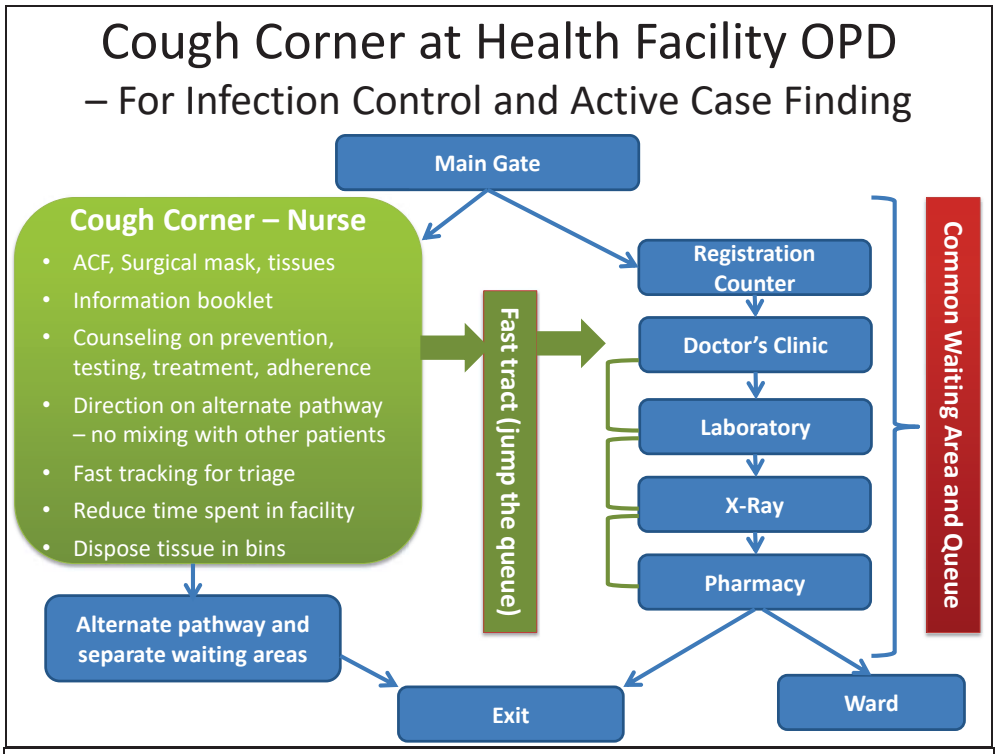


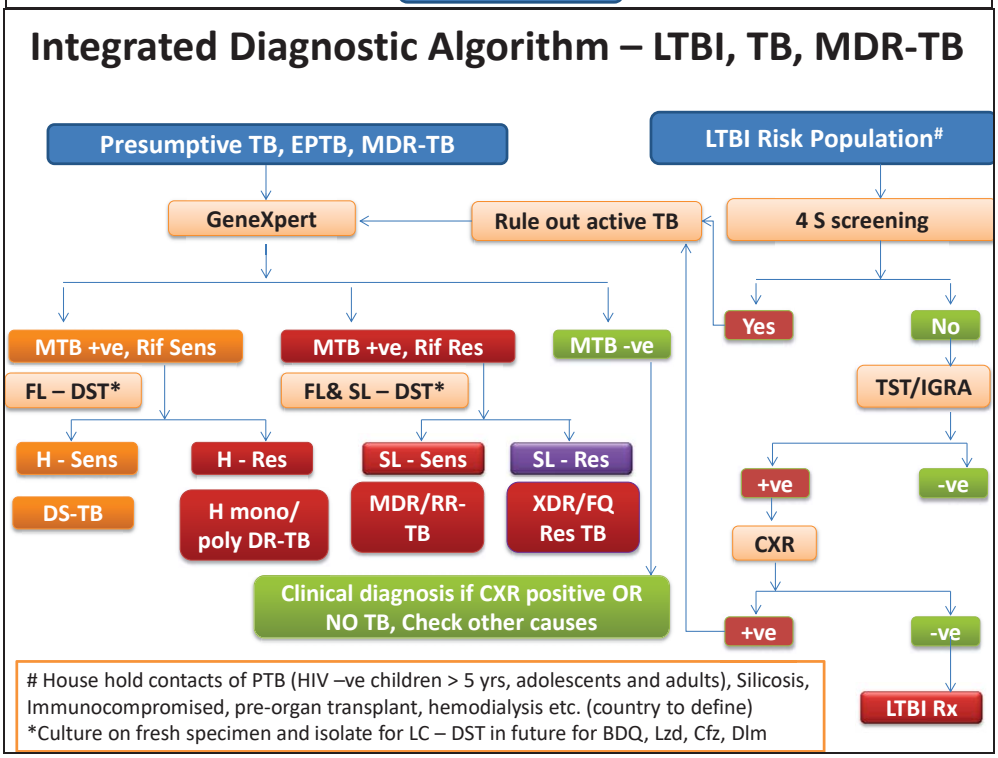
Unfunded
Funded internationally
Funded domestically

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.
Generated: 2019-01-29

Data: www.who.int/tb/data

Annexure 3 - Proposed Active Case Finding with Infection Control in Health Care Facilities; Diagnostic Strategy and Algorithm for Bhutan:





Annexure 4 – Proposed treatment regimen and decentralized model of care:

Drug susceptibility	Proposed Regimen
Drug Sensitive TB	2 HREZ / 4 HRE for all (S in special situations) Baseline FL-LPA to rule out H resistance in R sensitive patients instead of CAT II regimen
H mono/poly DR-TB	6 REZLfx
MDR/RR-TB	Prefer oral longerregimen (6-8 Bdq(6) Lfx Lzd Cfz /12 Lfx Lzd (l)Cfz) Transition out shorter MDR regimen with injections & do OR on oral shorter regimen
XDR / $MDR_{FQ/SLI}$	(6-8 Bdq(6) Lzd Cfz Cs/12 Lzd (l)Cfz Cs) OR Individualized

- Pre-treatment investigation, FU schedule to be updated
- Extension of intensive phase to be based on follow up culture results
- $MDR_{FQ/SLI}$: MDR/RR-TB with additional resistance to FQ or SLI class of drugs