rGLC COUNTRY SUPPORT MISSION REPORT

Country: Thailand

Inclusive dates of mission: 20-21 September 2018

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The programme has agreed with open sharing of this report ☒

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Abbreviations and acronyms

AFB	acid-fast bacilli
AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral drugs
Bdq	Bedaquiline
BoE	Bureau of Epidemiology
BPS	Bureau of Policy & Strategy
BTB	Bureau of Tuberculosis Control
CEM	Cohort Event Monitoring (a method for active pharmacovigilance)
CET	Clinical Expert Team
Cfz	Clofazimine
Cs	Cycloserine
CSMBS	Civil Servant Medical Benefits Scheme
CSO	Civil Society Organization
CXR	Chest X-Ray
DDC	Department of Disease Control
Dlm	Delamanid
DOT	Directly Observed Treatment
DRS	Drug resistance survey
DR-TB	Drug Resistant Tuberculosis
DSM	Direct smear microscopy
DST	Drug Susceptibility Testing
E	Ethambutol
EQA	External Quality Assessment
Eto	Ethionamide
FDC	Fixed Dose Combination
FHI360	Family Health International 360
FLDs	First line anti-TB drugs
GDF	Global Drug Facility
GF/GFATM	The Global Fund to fight AIDS, Tuberculosis, and Malaria
GNI	Gross National Income
GPO	Governmental Pharmaceutical Organization
HAIN	HAIN GenoType MTBDR® plus (line probe assay)
HIV	Human immunodeficiency virus
IC	Infection Control
IPT	Isoniazid Preventive Therapy
Km	Kanamycin
L-J medium	Löwenstein-Jensen medium
LTBI	Latent Tuberculosis infection
LPA	Line-probe assay
MDR(-TB)	Multidrug-resistant (tuberculosis)
Mfx	Moxifloxacin
MoPH	Ministry of Public Health

NEC	National Expert Committee for DR-TB
NFM	New Funding Model (for GFATM grants)
NHSO	National Health Security Office
NRL	National TB Reference Laboratory
NTM	Non-tuberculous mycobacteria
NTP	National Tuberculosis Control Programme
ODPC	Office for Disease Prevention and Control (regional)
Ofx	Ofloxacin
OR	Operational research
PHO	Public health offices (provincial)
PLHIV	People living with HIV
PPD	Purified Protein Derivative (tuberculin skin test)
PR	Principal Recipient (of GFATM)
rGLC	Regional Green Light Committee
RR-TB	Rifampicin-resistant tuberculosis
SAT	Self-administered treatment
SLDs	Second line anti-TB drugs
SMS	Short message service (texting on mobile phones)
SRL	Supranational TB reference laboratory
TAT	Turnaround time
TB	Tuberculosis
TBCM	TB Clinical Management
TUC	Thailand MoPH-US CDC Collaboration
UHC	Universal Health Care scheme
VMI	Vendor-managed inventory
VOT	Virtual (video) observed treatment for TB
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis
Z	Pyrazinamide
ZN	Ziehl-Neelsen

Executive summary

i. TORs of the mission

- Desk review the PMDT progress against the expansion plan as well as against recommendations made in the last mission
- Identify bottlenecks to expansion of diagnostic and treatment services
- Review pharmacovigilance/ aDSM implementation and progress
- Discuss rapid communication by WHO on key changes to guidelines for RR/MDR-TB treatment
- Capacity building for aDSM in the country as part of a Regional workshop

ii. Overall implementation status of PMDT

There has been an improvement in PMDT implementation and various related aspects in past year.

DRUG-RESISTANT TB CARE, 2017			
	NEW CASES	PREVIOUSLY TREATED CASES	TOTAL NUMBER[c]
Estimated MDR/RR-TB cases among notified pulmonary TB cases			2 700 (2 100–3 300)
Estimated % of TB cases with MDR/RR-TB	2.2% (1.5–3)	24% (18–31)	
% notified tested for rifampicin resistance	24%	37%	24 470
MDR/RR-TB cases tested for resistance to second-line drugs			272
Laboratory-confirmed cases			MDR/RR-TB: 1 339, XDR-TB: 7
Patients started on treatment[d]			MDR/RR-TB: 851, XDR-TB: 8

iii. Significant achievements since last visit

- Number of cases screened increased to nearly 4 times over past year
- Laboratory confirmed cases increased from 955 to 1339 between 2016 and 2017
- There has also been a slight improvement in treatment success rate among RR/MDR-TB patients from 58% to 60%, though still below the expected targets of at least 75%. This may also be seen in light of the fact that although 502 cases were reported to be enrolled in 2015, treatment outcome of only 352 cases was reported
- Active case finding for TB and MDR-TB started among high risk groups
- Increasing number of ADRs being reported – around 40 till date through the electronic system

iv. Key challenges identified in this mission

a. Nearly 500 laboratory confirmed cases constituting more than 35% of diagnosed RR/MDR-TB cases not initiated on treatment

b. aDSM needs further strengthening through training and capacity building of those who need to implement it. Specific challenges noted with availability of audiometry and monitoring ototoxicity
c. Transitioning to new regimen will need significant amount of deliberations and trainings in diagnostics as well as treatment services for rapid implementation

v. Priority recommendations of the mission:

Recommendation	Responsible persons/agency	Timeline	Support required to fulfil the recommendation
1. **Case finding**: Country should urgently move towards universal DST for all TB cases and symptomatics from high risk groups. (continuing recommendation from the previous mission)	BTB, DDC, NHSO	Complete coverage by 1st quarter 2019	Planning support may be needed to estimate financial and resource needs
2. **Adoption of all oral regimen**: a. At the time of the mission, CET was supposed to meet in October and adoption of rapid communication was to be discussed b. Develop a transition plan for adoption of new guidelines	BTB, CET	1st quarter 2019	Support on transition planning will be needed
3. **Patient support**: Financial and socio-economic support for all MDR-TB patients should be uniformly available across the country	MoH, DDC, BTB, NHSO	By 4th quarter quarter 2018	For strengthening community engagement in treatment delivery to all MDR-TB cases across country
4. **aDSM –** Follow-up of regional training with further training of peripheral staff in recording and reporting of the adverse events	BTB	Ongoing	Additional budget and technical support may be needed
5. **R&R –** Linking of laboratory information with TBCM	BTB and DDC	Q 1 2019	

vi. Status of priority recommendations of previous mission:

Recommendations	Status
• **Case finding**: Country should urgently move towards universal DST for all TB cases and symptomatic from high risk groups.	• Universal DST guidelines have been developed and there is an increasing number of TB cases being tested for resistance • PMDT trainings being held for MDR centre,
• **Guidelines for shorter regimen** and implementation	• Guidelines for shorter regimen have been developed and incorporated in overall PMDT guidelines. Trainings on guidelines are planned in 2018 • MDR-TB Expert committee met and prepared for the change to new guideline on 7Sep 2018 and plan for next meeting in October 2018
• **Guidelines for XDR-TB**	• The Clinical Expert Team (CET) plays an active role in treatment decision of complicated cases, specifically pre-XDR, XDR-TB, co-morbidities and other complications • Plan for expanding of Regional XDR-TB training and to train doctors on XDR-TB treatment
• **Use of new drugs -** bedaquiline and delamanid	• BTB reportedly has agreed to use of both drugs although only Bedaquiline is registered in the country for use
• **Patient support**: Financial and socio-economic support for all MDR-TB patients should be uniformly available across the country	• Patient support mechanism continue to be the same, though some better coverage and implementation was reported. The following support are available o Socio-economic support from Global Fund (GF) mechanism (if within the GF implementing area) o Ministry of Social Development and Human Security o Tuberculosis Relief Foundation o Social welfare programme of the hospital o Local administration

• **Infection control** and specifically use of personal protective equipment by health staff should be encouraged**.**	• As per govt directive, infection control should be strictly followed in all health facilities • Personal protection measure like the N-95 respirator are being made available • Bamrasnaradura Insititute, DDC, has taken responsibility for capacity building in the country. The institute has trained HCWs in 2017 and M&E by ODPC for Regional and provincial hospitals all over the country.

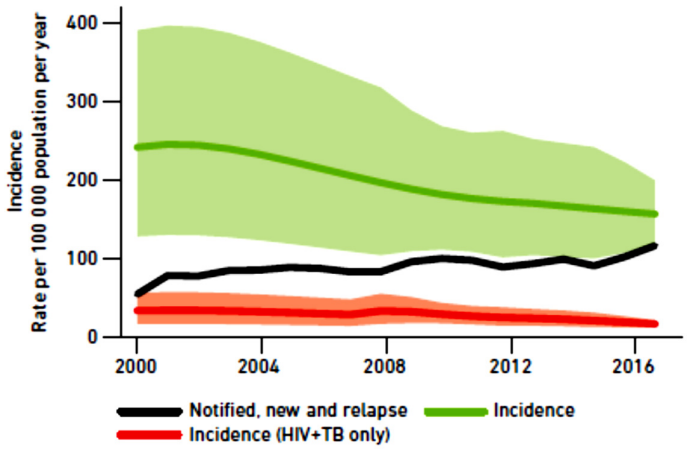
Achieved	
Some progress/ ongoing	
No change	

Detailed report

A. Introduction/Background

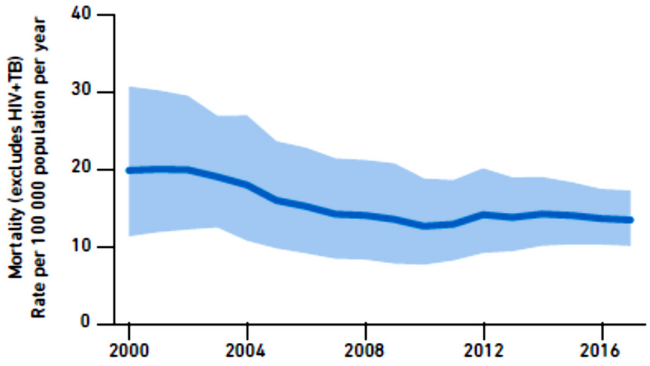
The estimated incidence of TB in 2017 was 156 per 100,000 and estimated mortality, including those dying of TB because of HIV infection, was approx. 16 per 100,000 – a declining trend over past years.

Figure 1: Trend in (estimated) TB incidence and case notification[1]



[1] WHO Global TB Report 2018

Figure 2: Trend in TB mortality[1]



B. Overall DR-TB programme performance

The number of cases screened for drug-resistance increased to nearly 4 times over past year while Laboratory confirmed cases increased from 955 to 1339 between 2016 and 2017.

Table 1: Estimated RR/MDR-TB cases, diagnosis and enrolment in 2017[1]

DRUG-RESISTANT TB CARE, 2017			
	NEW CASES	PREVIOUSLY TREATED CASES	TOTAL NUMBER[c]
Estimated MDR/RR-TB cases among notified pulmonary TB cases			2 700 (2 100–3 300)
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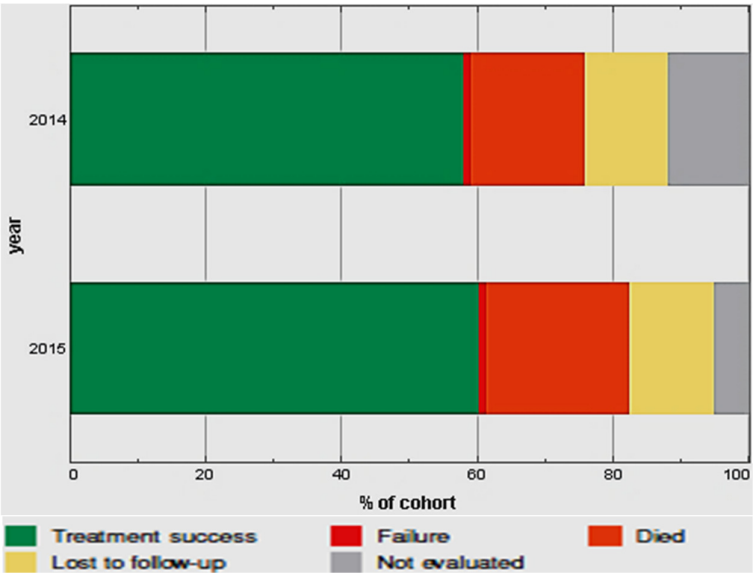
Low enrolment of MDR-TB cases 851/1339 is a cause of concern. It needs to be checked whether this was because of any errors in recoding and reporting.

Figure 3: Treatment success rate for 2014 and 2015 cohorts



There has also been a slight improvement in treatment success rate among RR/MDR-TB patients from 58% to 60%, though still below the expected targets of at least 75%. This may also be seen in light of the fact that although 502 cases were reported to be enrolled in 2015, treatment outcome of only 352 cases was reported

Recommendation

- Reason for low case enrolment of diagnosed cases needs to be analysed. If this is because of discrepancies in recording and reporting, then appropriate correction should be made to the records

C. Case finding strategy

There is a sustained effort to identify TB among key populations as per the national guidelines which includes prisons, elderly with uncontrolled diabetes, PLHIV and migrants. In addition, GeneXpert is being offered for diagnosis of extra-pulmonary TB, however children and other occupational risk groups may also be included in the group that could be offered upfront GeneXpert testing for early and improved diagnosis of TB/MDR TB.

Universal DST at least to Rifampicin should be the 'Standard of Care' in line with the updated WHO targets for ending TB by 2030. Acknowledging that provision of Universal DST will need a considerable quantum of funds for procurement of cartridges for GeneXpert, the country needs to invest in identifying resources from both government and donor partners to meet the needs.

A cost benefit analysis and the modelling exercise clearly shows that use of a highly sensitive TB diagnostic tool especially with the added advantage of Rifampicin resistance detection

will rapidly lead to reduction in the burden of TB and MDR TB and assist in the country reaching the goal of ending TB by 2030.

Screening undertaken in 2017

First line

- GeneXpert 55,960
- LPA 5,102
- Solid culture and DST 4,061
- Liquid culture and DST 3,307

Second line

- LPA 767
- Solid culture and DST 1,950
- Liquid culture and DST Not Done

Recommendation:

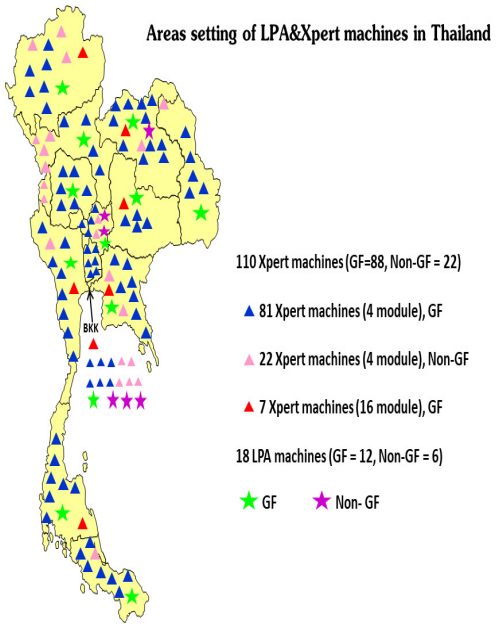
- Country should urgently start undertaking universal DST for all TB cases and symptomatics from high risk groups to achieve the end TB targets

D. Laboratory services and expansion plan

The Molecular facilities both GeneXpert (110) and LPA (18 for first line and 18 for second line) are currently functional. Though both the facilities are available in most ODPCs and a diagnostic algorithm that mainstreams use of GeneXpert for rapid identification of Rifampicin Resistance is available, the TATs for the results range from 8-10 days for GeneXpert and 15-20 days for LPA. In addition, GeneXpert Rifampicin resistant results are being reconfirmed routinely for all groups of patients irrespective of risk groups and likely PPVs.

In addition, some GeneXpert sites are not optimally used mainly attributed to suboptimal referral mechanism, restrictive criteria for testing and an apparent lack of trust molecular platforms for diagnosis of MDR TB.

Figure 4: Distribution of molecular tests across country



EQA for the molecular tests are being undertaken by the NTRL as per GLI norms and standards and is acceptable.

The main functions of the NTRL are training, EQA for all technologies, supervision and monitoring, providing media and reagents to lower level labs, SRL functions and contributing to research agenda of the TB control programme.

It was learnt that usage of GeneXpert is steadily increasing with upto 15,000 tests per month now. However, 10/110 machines are also non-functional due to break-down. Currently it appears that there are funding availablity issues for maintenance of GeneXpert machines.

Recommendations

- Calculations for universal DST and arrangement for corresponding number of cartridges for GeneXpert need to be made. It is estimated that 150,000 cartridges will be needed each year at a cost of about USD 2.3 million
- LPA need not be used for reconfirming all RR -TB cases diagnosed using GeneXpert test. However, in certain low risk cases found to have RR-TB, a repeat GeneXpert or LPA on a new sample may be performed depending on assessed need.
- Arrange funding for dysfunction GeneXpert machine and preferably have a maintenance contract with an agency

E. Treatment strategy

The country has been using standardized longer regimen for treatment of RR/MDR-TB cases. The treatment dosage and regimen in national guidelines is aligned with WHO recommendations.

The country started implementing shorter MDR-TB regimen in 2017 and has expanded their implementation quickly. The use of this regimen is being expanded to 19 sites with more than 100 patients put on treatment this year and there is now an increasing demand in the country for use of this regimen. However, it appears that audiometry monitoring for patients on injectable drugs is a challenge.

The Clinical Expert Team (CET) plays an active role in treatment decision of complicated cases, specifically pre-XDR, XDR-TB, co-morbidities and other complications.

Table 2: Overall enrolment status of patients on second-line drugs

	2018 (till date)	2018 (target)	2019 (plan)
Total patients on second line treatment	524		
Shorter regimen	103 cases	300-500	700
Longer regimen with new and repurposed drugs + XDR	63 cases (2017-2018)		

Table 2: Status of patients on shorter regimen in 2018

Enrollment	On treatment	Intensive	Continuous	Extend	Change to longer regimen
103	**85**	**67**	**17**	**1**	**11**

Treatment delivery (DOT), adherence and social support

Socio-economic support received by patients in various parts of the country are variable with a potential to receive support from

- Global Fund (GF) mechanism (if within the GF implementing area)
- Ministry of Social Development and Human Security for low-income patients
- Thai relief foundation
- Social welfare programme of the hospital
- Local administration

However even where the support is supposed to be provided, its actual availability for patients is variable. As informed by the programme, the socio-economic support received by patients from various sources was as follow

Table 4: Socio economic support received by patients by source (some patients would have received from more than one source)

Type	Government	Foundation from social unit hospital	GF	Tuberculosis relief foundation	Porteck lung foundation	Other (Local agency, other)	Total
1. TB	95	395	-	143	53	1364	2050
2.MDR-TB	54	6	79	29	7	-	175
3. XDR-TB	5	-	17	1	-	5	28
4. Extra-pulmonary	-	-	--	5	-	-	5
Total							2,258

Recommendations

- At the time of the mission, CET was supposed to meet in October and adoption of rapid communication was to be discussed
- Develop a transition plan for adoption of new guidelines
- As in previous report, the socio-economic support availability should be at uniform standards throughout the country

F. Pharmacovigilance/ aDSM

There has been progress in implementation of pharmacovigilance/ aDSM. Guidelines are available and health staff being trained with partner collaborations. A website developed to collect available data (www.thaihpvc.fda.moph.go.th). As per the prescribed policy, pharmacists need to provide monthly report via online system. However, the focus of aDSM for now is shorter regimen and new drugs. ADRs were reported amongst 40 patients in 2017

Figure 5: Number of cases reporting ADR amongst those placed on shorter regimen

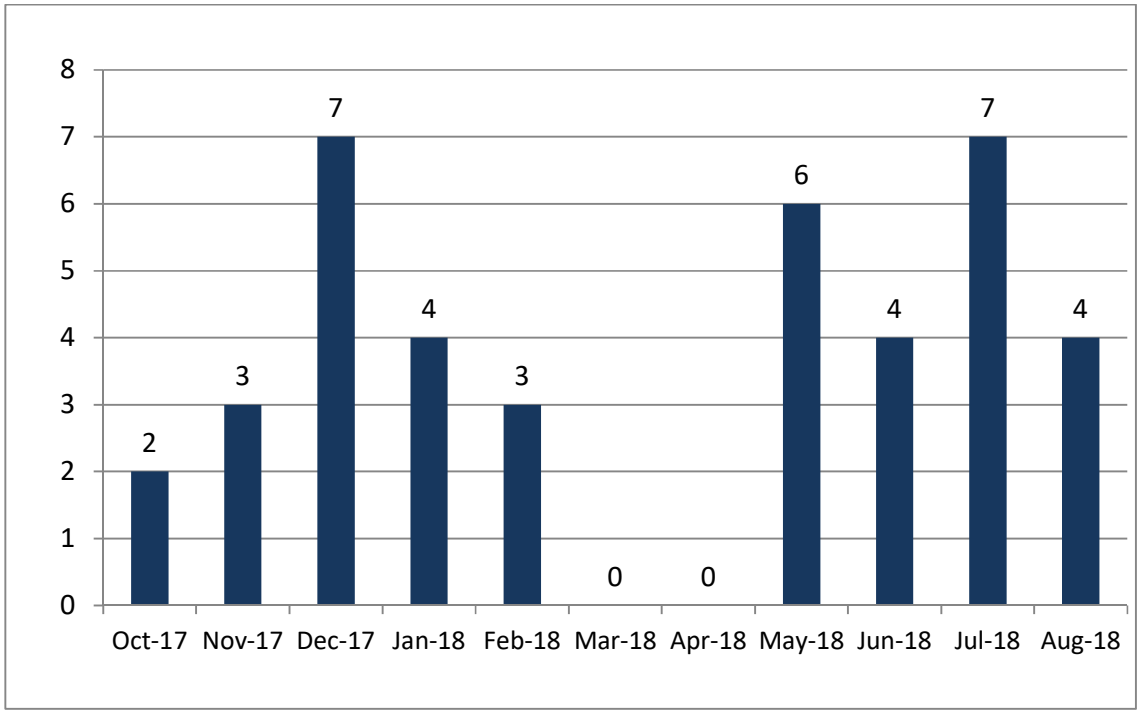
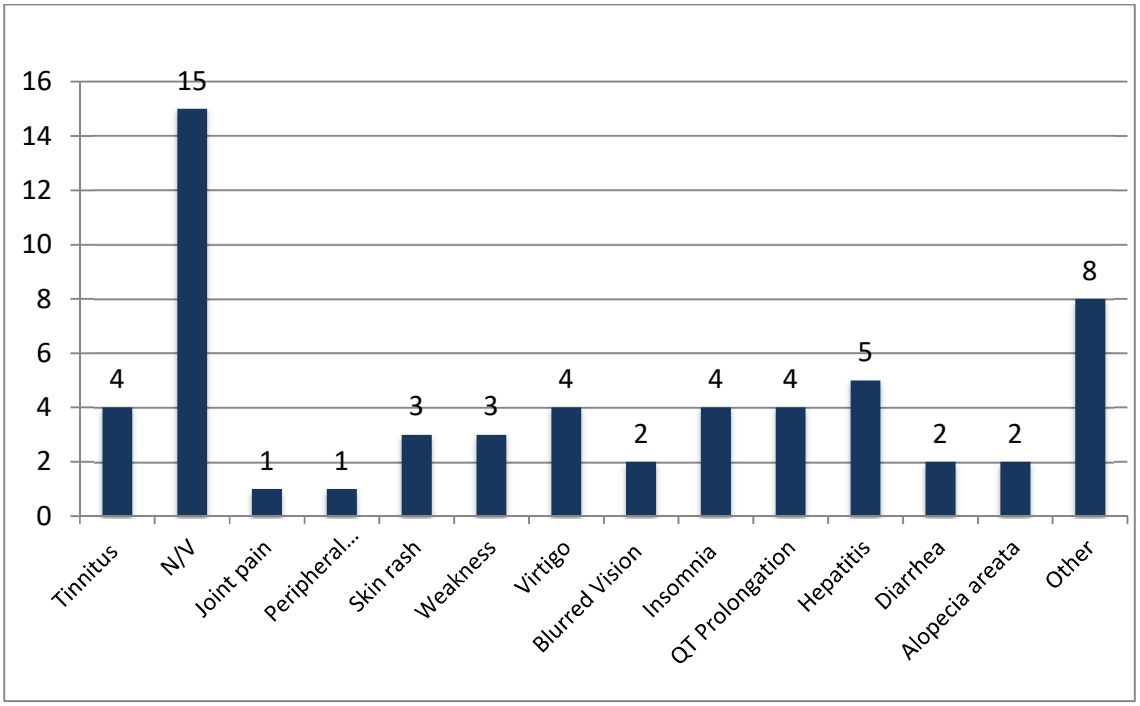


Figure 6: Types of adverse events noted and number of patients



Recommendations

- aDSM should be extended to all patients after introduction of new drugs and novel regimen
- ECG and audiometry testing should be undertaken for all patients. Audiometry is specifically important while using injectable agents
- All health workers should pro-actively monitor adverse events (AEs), using checklist
- AE monitoring should slowly be evolved as practice for all MDR-TB patients

G. Drug management

No stock-outs of second-line drugs were reported in last one year as per discussions. Discussions were held on source of SLDs as this would impact the uptake of new recommendations from WHO on use of SLDs. The source of availablity is summarised in table below

Table 5: Availablity of second-line TB drugs in the country

GROUP	MEDICINES (availablity source)	
Group A:	Levofloxacin OR (NHSO) Moxifloxacin (BTB+GF)	Lfx Mfx
	Bedaquiline (BTB+GF)	Bdq
	Linezolid (BTB+GF)	Lzd

Group B:	Clofazimine (BTB+GF)	Cfz
	Cycloserine OR (NHSO+BTB) Terizidone	Cs Trd
Group C:	Ethambutol (NHSO+BTB)	E
	Delamanid (GF)	Dlm
	Pyrazinamide (NHSO+BTB)	Z
	Imipenem-cilastatin OR Meropenem	Ipm-Cln Mpm
	Amikacin (NHSO+BTB) (OR Streptomycin)	Am (S)
	Ethionamide OR (NHSO+BTB) Prothionamide (GF)	Eto Pto
	p-aminosalicylic acid (NHSO+BTB)	PAS

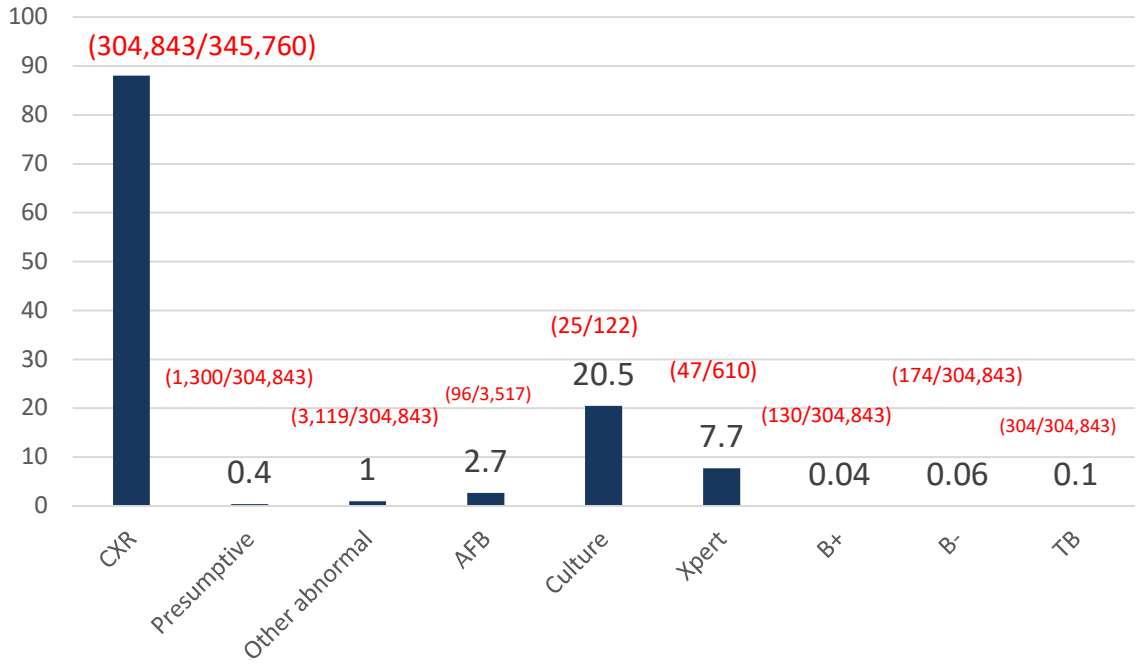
Recommendation

- Assessment of available drugs stocks and how transition impacts the expiry needs to be discussed at the country level.

H. Infection control

Health workers screening is an indicator for extent to which infection control activities are being implemented effectively in the country. It was reported that in 2017, a total of 345,760 health care workers were screened in the country out of whom 130 were found to be bacteriologically confirmed for TB and another 174 were clinically diagnosed – 0.1% TB amongst all screened

Figure 7: Screening of health care workers in the country.



I. Recording and reporting, and data management

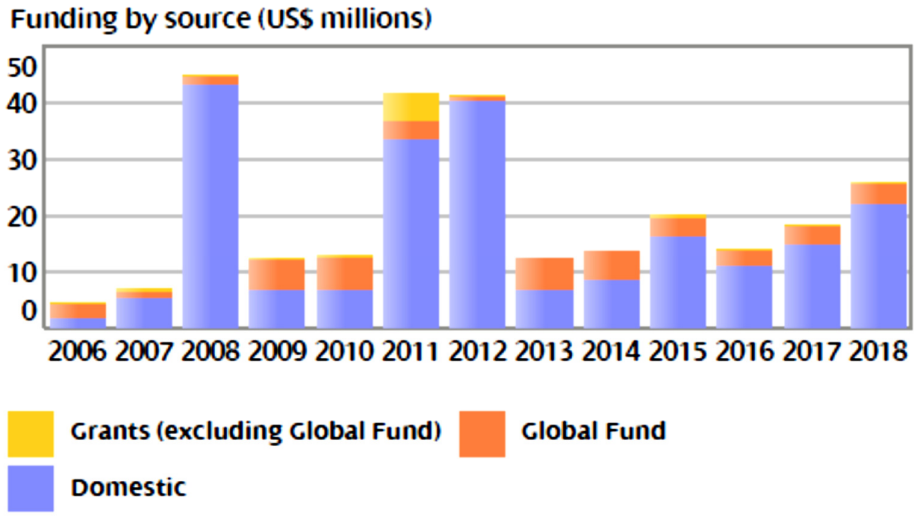
There has been a good progress with TB Case Management (TBCM) online reporting system over last one year. The team was informed that this is now being used by 920 MoPH hospitals and further expanding. Usability of the system for NHSO is also being worked out and there has been an in-principle agreement to use it for NHSO purpose has been reached, which will sort out duplicate reporting needs by the hospitals. Interconnectivity with other systems is also being worked out. For procurement purposes, the TBCM is now linked with Vendor Management Inventory (VMI) system. However, link with Laboratory Information Management System (LIMS) is still not clear. It has been emphasized in earlier reports as well that the two systems need to be linked so that patients diagnosed can be correlated with those started on treatment. Initial loss to follow-up can easily be traced with this linking up allowing for timely action.

Recommendations

- It is reiterated to link LIMS with TBCM to be able to correlate diagnosed cases with those on treatment. This will also reduce discrepancies currently being observed in laboratory reports and programme reports.
- Online aDSM system will also need to be linked with TBCM to improve clinical management of MDR-TB cases as well as capturing essential information on adverse events with use of second-line drugs for the programme and FDA

J. Funding for TB

Trends in TB programme funding as submitted to WHO



There has been a steady increase in domestic funding for TB with a rise from USD 15 million in 2017 to USD 22 million in 2018. Global Fund budget remained almost steady during the two years at about USD 3.4 million. Out of the total budget around USD 5.5 million is allocated for drug-resistant TB – programme costs and drugs

Table 8: TB budget for 2018 as reported to WHO

Budget line item	Budget required [d]	Expected funding [e]	Gap
Laboratory infrastructure, equipment and supplies *Building, maintaining, and renovating TB laboratories, laboratory equipment purchase and maintenance, consummables for all tests (including TB screening for people living with HIV/AIDS), quality assurance, retooling and the transportation of specimens.*	2 946 152	2 946 152	0
National TB Programme staff (central unit staff and subnational TB staff) *Salaries and incentives of those working only on TB activities at central and peripheral levels (for example provincial TB coordinators, district TB coordinators, etc.). Do not include primary health care personnel working on other diseases in addition to TB.*	1 528 138	1 528 138	0
Drug-susceptible TB: drugs *Drugs for patients being treated for drug-susceptible TB. Include children, re-treatment cases and buffer stock.*	9 844 549	9 844 549	0
Drug-susceptible TB: programme costs *The management and supervision of the TB control programme, training, policy development, meetings, visits for supervision, purchase of office equipment/vehicles, construction of buildings for use by programme staff, routine surveillance, advocacy and communication, public-private mix activities, community engagement, active case-finding, infection control, and management of TB drug procurement and distribution.*	5 124 733	5 124 733	0
Drug-resistant TB: drugs *Drugs to treat drug-resistant TB (RR-TB, MDR-TB or XDR-TB). Include drugs to deal with adverse events for RR-/MDR-/XDR-TB patients.*	5 057 765	5 057 765	0
Drug-resistant TB: programme costs *Management of drug-resistant TB services, excluding drugs. Examples are renovation of MDR-TB wards, support for the Green Light Committee, conducting an MDR situation assessment, default and contact tracing, palliative care.*	476 128	476 128	0
Collaborative TB/HIV activities *Collaboration between TB and HIV programmes aimed at reducing the impact of HIV-related TB. Activities include TB/HIV coordinating bodies, joint TB/HIV training and planning, HIV testing for TB patients, HIV surveillance among TB patients, isoniazid preventive therapy (IPT), co-trimoxazole preventive therapy (CPT), joint TB/HIV education/ communication, and antiretroviral treatment for TB patients. TB screening for people living with HIV/AIDS is included under (Lab infrastructure, equipment, and supplies).*	14 672	14 672	0
Patient support *Cash transfers, food packages, transportation vouchers, educational and emotional support to patient or other in-kind benefits given to TB patients.*	205 043	205 043	0
Operational research and surveys *Periodic surveys (prevalence, drug resistance, patient catastrophic cost); routine surveillance (epidemiology review, inventory studies, pharmacovigilance, systematic assessment of the surveillance system); operational research.*	34 349	34 349	0
All other budget lines *Please explain this amount in the "Remarks" box below.*	629 220	629 220	0
Total	**25 860 749**	**25 860 749**	**0**

Annexure 1: Agenda

20 September

Briefing with BTB team

Review of

- progress in PMDT expansion
- progress against recommendations made during last mission
- aDSM implementation status
- patient suport mechanisms

Discussions on rapid communication and next steps in the country

21 September

Review lab expansion status

Review of status of second-line drugs

Review HR status

23 September

Review with facilitators regarding preparations for the aDSM workshop

24-28 September

Regional workshop on strengthening of aDSM capacity (report will be prepared separately)