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

PMDT SUPPORT MISSION REPORT

Country: Bangladesh

Inclusive dates of mission: 16-20 July 2017

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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 immunodeficiency syndrome
CBO	community-based organizations
CPT	co-trimoxazole preventive therapy
DCC	district chest clinic
DCCL	district chest clinic laboratory
DDG-PHS	Deputy Director General of Public Health Services
DGHS	Director General of Health Services
DOTS	directly observed therapy – short course
DRS	drug resistance survey/surveillance
DR-TB	drug-resistant tuberculosis
DST	drug susceptibility testing
DTCO	district TB control officer
EP-TB	extrapulmonary tuberculosis
EQA	external quality assurance
FDC	fixed-dose combination
FLD	First-line (anti-TB) drugs
GDF	Global (TB) Drug Facility
GF	Global Fund (Global Fund to Fight AIDS, Tuberculosis and Malaria)
HRD	human resource development
IC	infection control
IPT	isoniazid preventive therapy
IC	infection control
MDR-TB	multidrug-resistant tuberculosis
M&E	monitoring and evaluation
NGO	nongovernmental organization
NPTCCD	National Programme for Tuberculosis Control and Chest Diseases
NTRL	national TB reference laboratory
PHC	primary health care
PLHIV	persons living with HIV/AIDS
PMDT	programmatic management of drug-resistant tuberculosis
PPM	public-private mix
RDHS	Regional Director of Health Services
RR	rifampicin-resistant
SDG	Sustainable Development Goals
SEAR	South-East Asia Region (of WHO)
SLD	Second-line anti-TB drugs
SOPs	standard operating procedures
TA	technical assistance
TB	Tuberculosis
TWG-TB	Technical Working Group on TB
WHO	World Health Organization
XDR-RB	extensively drug-resistant TB

I. Executive summary

- **TORs of the mission**
  - Discussions and review of progress in PMDT expansion since the last review mission
  - Review of draft SoPs for shorter regimen for MDR-TB
  - Review of existing PMDT guidelines on shorter regimen
  - Review implementation of PMDT and country preparedness for expansion of shorter regimen
  - Discuss findings with NTP and in-country partners
  - Make recommendations based on identified gaps;

- **Progress from the last mission:**
  Since the last mission in 2016 the following achievements have been made.
  - Over 47,000 presumptive MDR patients have been tested and over 900 R-R/MDR patients have been diagnosed and initiated on treatment.
  - There are currently 41 Xpert ® sites all over the country. Another 10 Xpert machines are waiting to be installed.
  - Second line LPA is available and is being used as a rule in test for SLD resistance.
  - Shorter regimen is being scaled up and now covers the Damien Foundation (DF) Hospitals, Rajshahi CDH, NIDCH and is being scaled up to the remaining treatment centers by end of 2017.
  - The hospitalization of RR-/MDR-TB patients has been reduced to 4-6 weeks from the earlier 8 months of the intensive phase.
  - Treatment success is 70% for the 2014 cohort on WHO recommended 20 month regimen and 86% for the 2014 cohort on the shorter regimen.
  - Newer drugs (Bedaquiline and Delamanid) have been introduced through the End TB project for pre-XDR and XDR TB patients since April 2016 and there are currently 114 patients on these newer drugs.
  - USAID supported Challenge TB project, managed by MSH in collaboration with IRD, continues to support the NTP for EQA, maintenance of Xpert ® machines, scaling up of shorter regimen and capacity building.

- **<u>Status of priority recommendations of previous mission:</u>**

Recommendations	Responsible agency/person	Timeline	Status
NTP and partners to ensure timely HR plans as part of project phase out long before project termination to include a handover period for smooth transition to the NTP or to the next project. As application: SIAPS and NTP to have a mutually agreed written handover plan for e-TB Manager, and QuanTB to NTP focal points at the latest 2 months before the closeout in Sept 2016.	MoH – NTP and partners	3rd Q 2016 Jul 2016	There has been discussion between NTP and partners regarding clear transition plan available much in advance to the termination of the projects. In particular, the SIAPS project has been extended till 2019 and the transition plan for the e-TB manager and Quan TB apps has been delayed.

Advocate for increased budget for TB and PMDT and focus resources on essential, high-impact and sustainable approaches, e.g., SLDs, patient-centered care (psycho-social support), community PMDT, etc.	NTP to MOH	3rd Q 2016	The financing through Government of Bangladesh (GoB) has been enhanced from 10% to 31% of the total TB budget. GoB will pay for all first line drugs and HR from 2018 onwards.
Put in place a staff retention program to keep qualified staff in key TB posts for at least 3 years.	MOH	2016	Although there is no written policy, during the discussion with senior administrator it was assured that the retention of key staff retention will be followed in principle.
Carefully discuss the possibility to increase enrolment targets in a phased manner to up to 80% of estimated annual RR-/MDR burden in the expansion plan guided by DRS results	NTP PMDT team and partners	After DRS	The next DRS survey will be initiated in end 2017/early 2018. And the results should be available by mid-2018.The results of the DRS will guide the enrolment targets.
NTRL to maximize collaborative agreement with Antwerp (SRL) and SRL to conduct 1-2 technical assistance visits to the NTRL yearly to develop it to become a proactive central lead in the country's laboratory network, monitoring and supervising other laboratories, including Xpert sites.	NTRL and SRL	3rd Q 2016	There has not been any progress on this.
Ensure that sites and institutions running projects, e.g., IRD for bedaquiline, and the selected Principal Investigator for the new regimen have ample readiness and that the framework for their introduction is established. Reference: WHO – *Intro of Bdq for the treatment of MDR-TB at country level Implementation Plan WHO/HTM/TB2015.11*	NTP	2nd Q 2016	Achieved.
Strengthen SLD procurement planning in light of new drugs and regimens that will be introduced. Equip NTP staff in charge of PSM in forecasting and quantification.	SIAPS and NTP	3rd Q 2016	This is an ongoing process. There has been a considerable improvement in the procurement process for SLDs.
Accelerate finalization of electronic report forms generated by e-TB Manager including those for Detection, Enrolment and Treatment outcomes, and ensure functionality	SIAPS, NTP PMDT Focal Point, NTP e-TB Manager Focal Point	Jun 2016	Ongoing

before end of SIAPS project.			

Achieved	
Some progress/ ongoing	
No change	

Priority recommendations of the mission:

S.No	Recommendation	Responsible persons/ agency	Timeline	Support required to fulfill the recommendation
1	Undertake a workload assessment of the existing Xpert sites and take necessary steps to optimize their use. This can be done by expanding the criteria for presumptive DR-TB; promoting its use for diagnosis of pediatric and extra-pulmonary TB and strengthening the sputum transport mechanism.	NTP	• Dec 2017 for workload analysis and expanding the criteria • 2 Q 2018 for other activities	Support from partners
2	Update the national PMDT guidelines to include the revised diagnostic algorithm, shorter regimen and newer drugs. Develop training material for various cadre staff for implementation of PMDT activities.	NTP	• Dec 2017 for updating the guidelines • Mar 2018 for developing the training material	• Support from partners • External TA may be needed
3	Scale up the shorter regimen and newer drugs with matching expansion of rapid second line DST to ensure accessibility to all diagnosed RR/MDR patients.	NTP	• Dec 2017 for the shorter regimen • Mar 2018 for the newer drugs	Support from partners
4	Set up all elements of aDSM	NTP	Dec 2017	• Support from partners • External TA may be needed
5	The PMDT is funded almost entirely by external sources. The MOH has	NTP and MOH	Ongoing	

	increased its contribution for TB significantly which primarily covers the first line treatment. The MOH should also consider covering some critical components of PMDT.			
6	The affected community groups are an important resource and efforts should be undertaken to identify representatives (individual and groups) from the affected community who are then trained for supporting for advocacy, peer counselling and delivery of PMDT services. This should be a budgeted activity in the national strategic plan which is currently under development.	NTP	Dec 2017	• Support from partners • External TA may be needed
7	Strengthen the supervisory and monitoring functions of the NTRL through provision of adequate HR and enhanced oversight and ownership from the NTP. The NTRL should receive regular technical assistance from the SRL Antwerp lab including 1-2 onsite visits annually.	NTP	Ongoing	• Support from partners
8	Strengthen coordination with partners through regular meetings at least quarterly with definite agenda and discussion points. These meetings should serve as a platform for sharing the project updates, ensuring alignment with the NTP objectives and discussing and resolving challenges faced by the partners. Every project led by partners should have a formal exit plan, prepared by the partner in consultation with NTP, which should get triggered well in advance of the closure of the project ensuring smooth transition and sustainability.	NTP	Ongoing	• Support from partners

II. Detailed report

A. Introduction/Background

The NTP in Bangladesh is implementing PMDT since 2008 using the WHO recommended standard 20-month regimen. Damien Foundation, a major partner in TB control, has been using a 9-month MDR-TB regimen since 2005 and continues to implement this shorter regimen in 26 districts. The last DRS was conducted in 2010-11 with 1.4% MDR-TB among new cases and 28.5% among retreatment cases. The estimated number of DR-TB cases among notified pulmonary TB cases was ~5,100 in 2015.

There has been continuous progress in the enrolment of MDR-TB cases for treatment, which is summarized in the table below.

Year	NIDCH	CDH CTG	CDH, Pabna	CDH, Khulna	CDH, Sylhet	Total	DF	Total
2005-07	-	-	-	-	-	-	242	242
2008	107	-	-	-	-	107	129	236
2009	179	-	-	-	-	179	181	360
2010	183	-	-	-	-	183	154	337
2011	212	41	-	-	-	253	137	390
2012	290	86	-	-	-	376	129	505
2013	330	120	31	14	-	495	191	686
2014	447	123	31	61	-	716	230	946
2015	430	121	26	43	60	680	200	880
2016	461	113	21	60	95	750	168	918
2017 (Jan-Jun)	195	62	12	28	33	330	86	416
Total	**2834**	**666**	**121**	**206**	**188**	**4069**	**1847**	**5916**

Table1: Site wise RR/MDR patient enrolment (2005-2017)

B. Existing TB control program

- **Estimated TB burden:**
  As per the WHO Global TB Report 2016, the TB incidence (including the TB/HIV coinfected) is 225/100,000 population (~362,000 cases), and a mortality rate excluding the coinfected of 45/100,000 (~73,000 cases). Incidence among the TB/HIV co-infected is 0.18/100,000 (~630 cases) with a mortality of 0.14/100,000 (~230 cases). Prevalence and mortality have shown some decline as shown in the **Figure 1.**

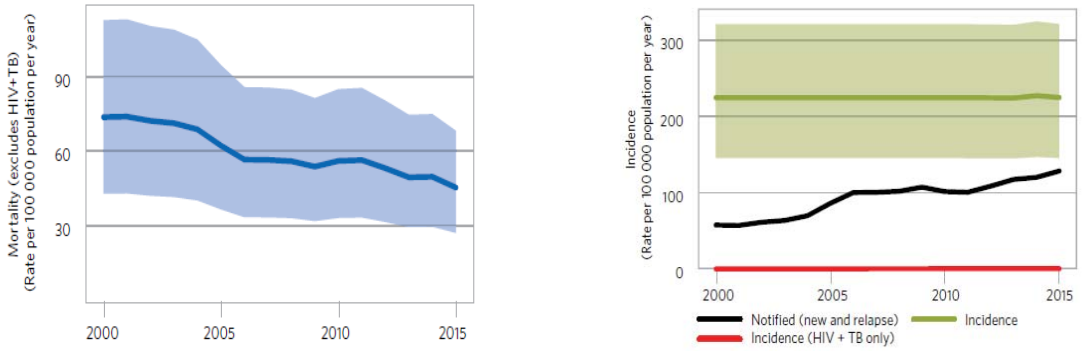


Figure 1: *Mortality and incidence trend (2000-2015) in Bangladesh.*

- **TB case notification and outcomes**:
  DOTSwas introduced in the country in 1993.The notification rate for all TB cases has shown an increasing trend from 2005 to 2015 with a decline in 2010-2011. Case finding efforts have been intensified among smear-negatives, children and remote (hard-to-reach) areas. The notification rate for all forms in 2015 was 138 per 100,000 and NSP was71 per 100,000 **(Figure 2).**

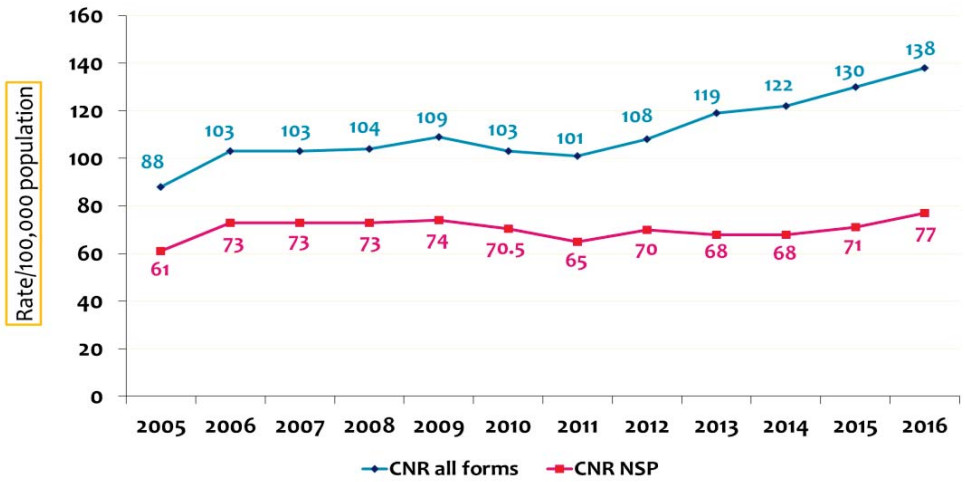


Figure 2: *Case notification rate (2005-2015) in Bangladesh.*

The treatment outcome has been consistently over 90% since 2003 for new and retreatment cases excluding HIV co-infected. The outcome for the 2014 cohort is 94%. (Figure 3)

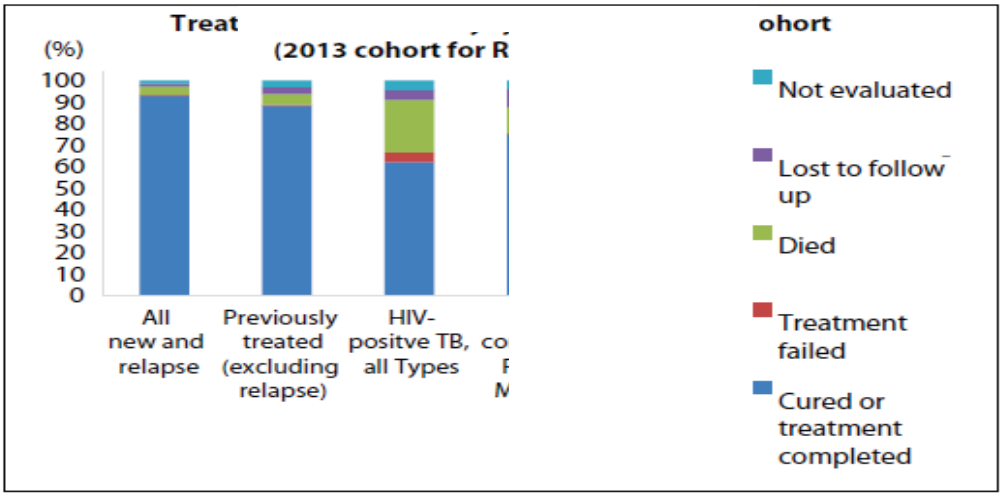


Figure 3: Treatment outcome by type of cases (2014 cohort).

- **NTP structure:**
  Bangladesh is administratively divided into 8 divisions, 64 districts, 490 upazilas, 4,553 unions, 11 city corporations and 323 municipalities. The NTP falls under the Directorate of Mycobacterial Disease Control (MBDC) under the Directorate of General Health Services (DGHS) of the MoH&FW.

The implementation of TB prevention and care services at various levels is undertaken by the staff mentioned below.

- Central level- The Director, Line Director and Program Manager who are entrusted with policy formulation, partners' coordination, technical assistance, procurement, monitoring and supervision, etc.
- Divisional level- The Divisional Director undertakes monitoring and supervision and technical guidance of districts.
- District level- The Civil Surgeon. is responsible for DOTS implementation, monitoring and supervision.
- Upazila level- The Upazila Health and Family Planning Officer (UH&FPO).
- Union/ward and village level- Medical Assistant, Health Assistant and other community health care providers (CHCP).

- **DR-TB burden:**
  - Bangladesh is one of the 30 high MDR-TB burden countries of the world in terms of absolute numbers and rate. Drug Resistance Survey (DRS) done in 2010-2011 by the NTRL, in collaboration with the NTP and WHO, showed a RR/MDR prevalence of 1.6% (95% CI 0.7-2.5) among new TB cases and 29% (95% CI 24-34) among retreatment cases. As per the above prevalence rates the total estimated number of incident RR/MDR cases in 2016 was 9700 and those among the notified pulmonary TB cases was 5200.
  - As per the programme data the prevalence of RR/MDR-TB among various categories of TB patients is significantly lower than the DRS results, as shown in the table below.

Category	Proportion of MDR/RR-TB	
	DRS (2010-11)	**Prog. Data 2016**
Treatment Failures	63.2%	8.6%
Relapses	21.1%	4.8%
Lost to Follow up	13.8%	4.3%
Others	40.8%	0.85%
All Previously Treated Cases	**29%**	**2.8%**
New Cases	**1.6%**	**0.8%**

Table 2: Prevalence of RR/MDR TB - comparison of DRS and programme data

There are no obvious reasons to explain the significant decrease in prevalence and this discordance will be resolved only by the next DRS being planned this year with funding from the ongoing NFM grant.

Recommendation:

- The NTP must expedite the conduct of the next DRS which will provide important update on the burden of DR-TB in the country and guide the future planning of PMDT in the country.

- **Case notification and treatment outcomes among DR-TB patients:**
  - Since 2010 the number of RR/MDR TB cases diagnosed and enrolled on treatment has been increasing consistently with over two fold increase in 2016.

- The gap in diagnosis and enrollment has decreased steadily but significantly from 36% in 2011 to 5% in 2016. The key reasons for non-enrollment (in order of priority) are mortality, reluctance by the patients to start treatment and failure to track the diagnosed patients.

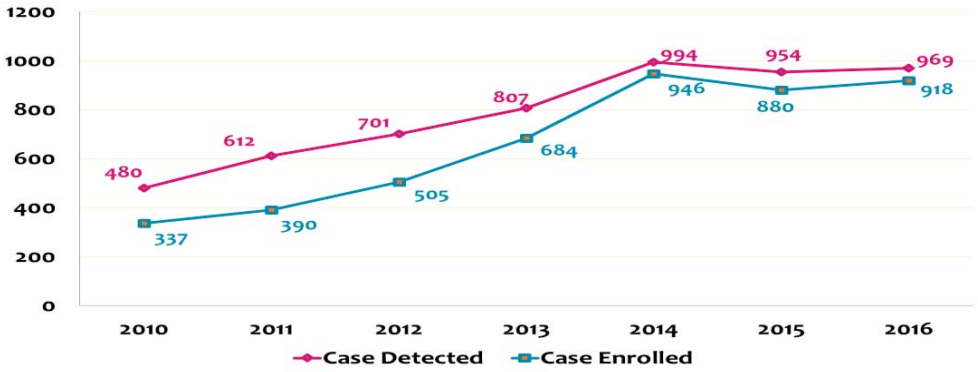


Figure 4: RR/MDR cases diagnosed and enrolled on treatment 2010-16

Recommendation:

- The NTP must undertake necessary steps to address the reasons for non-enrollment. This includes maintaining a line list of all presumptive MDR TB patients with necessary contact details (to track them if they are found to be RR/MDR) and ensuring that their DST is not delayed. Those diagnosed with RR/MDR should be appropriately counselled to alleviate their anxieties and fears related to MDR treatment thus enhancing the acceptance.

- **Treatment outcomes among DR-TB patients**
  - Bangladesh is implementing the 20 month WHO recommended regimen in five of the six DR-TB centres. In the sixth centre managed by Damien Foundation the 9 month shorter regimen is being administered since 2005.The treatment outcomes for the 20 month and 9 month regimens are depicted in figure 5.

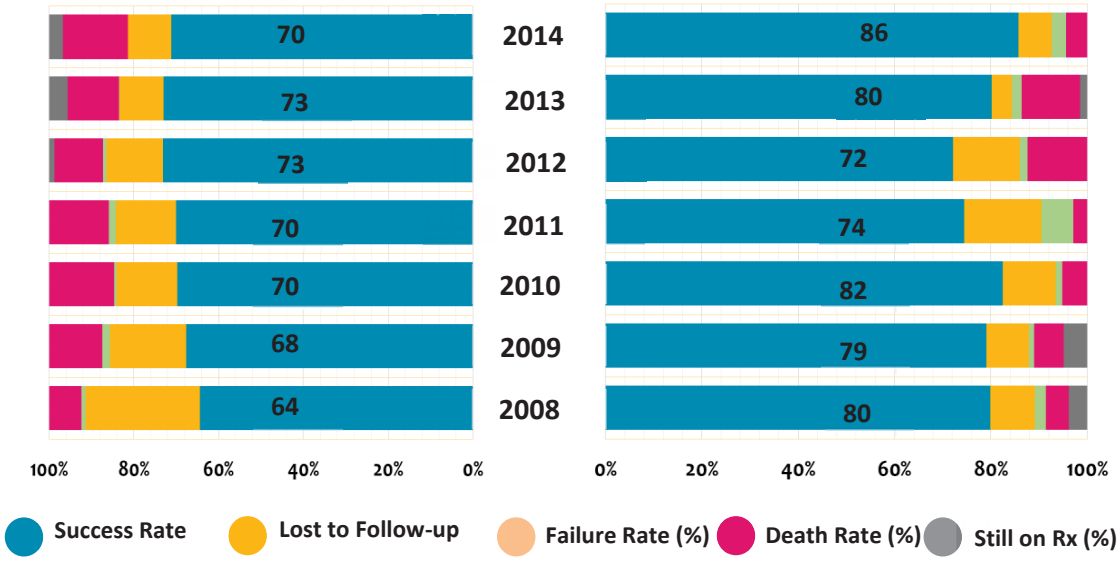


Figure 5: Treatment outcomes of RR/MDR cases 2008-2014 cohorts

C. Political commitment :

- The annual operational plans of the NTP are based on the strategies described in the NSP 2015-2020. Major funding sources are the Global Fund, USAID and MOH. The MOH contributes about 10% of the total TB budget.
- Proportionally, the largest funding amount for implementation of the NSP 2015-2020 is provided through the GF NFM grant, which included a substantial above allocation funding. The Global Fund NFM (Jul 2015-Dec 2017) is the main source of support to PMDT, which is managed by two Principal Recipients (PR), the MOH (NTP) and the Bangladesh Rural Advancement Committee (BRAC). The total NFM budget is over USD 78 million of which 10% is allocated for PMDT. The MOH PMDT portion supports SLDs, laboratory, training, and monitoring & supervision while the BRAC PMDT portion supports the psychosocial aspect of PMDT care, including enablers and incentives for both patients and health workers. For the period 2018-2020 the Global Fund has committed USD 98 million to Bangladesh. The allocation to PMDT is being finalized.
- USAID has been supporting PMDT since 1998 through TB CAP, TB CARE II, and now Challenge TB (CTB), the current flagship global mechanism for implementing USAID's TB strategy covering 2014-2019. CTB covers enablers and incentives for DR-TB patients in 19 districts. The CTB project is transitioning with a focus on urban TB control from October 2017 onwards and will discontinue the socio-economic support for DR-TB patients.

Recommendations:

- The MOH has committed to increasing the contribution from domestic resources from 10% to 31% from 2018. This increased contribution will mainly cover the procurement of FLDs. The MOH needs to increase the domestic contribution further and also plan to support some critical areas under PMDT which is currently completely funded from external sources.
- The withdrawal of the CTB support for PMDT from October 2017 onwards, especially socio-economic support to DR-TB patients, needs to be covered from alternate sources. BRAC is willing to cover this gap in the interim till Dec 2017 from the savings in its current Global Fund grant. The NTP should take this discussion with BRAC on priority. From 2018 this should be budgeted under the next Global Fund grant or domestic budget.

D. Partnerships:

- Bangladesh NTP works closely with multitude of NGOs and other partners. NGOs and local civil society provide screening, referral, and treatment services nationwide, including services in hard to reach areas and underserved population targeting the missing cases.
- Several USAID-funded technical partners provide TB-specific and TB-related technical and implementation inputs in quantification and electronic recording and reporting (SIAPS), CCM functioning (GMS), provision of urban TB services (NHSDP; combined with GF funding of the same network), and a wide range of TB technical areas (Challenge TB).
- The partners provide valuable support to PMDT. However, the sustainability and smooth transition of projects on their completion remains a challenge. This has been observed earlier during transition from TBCARE II to CTB, and from Global Fund R10 to NFM.
- With the revised focus of CTB project, several important activities (described in the section above) related to PMDT will be discontinued from October 2017 which will adversely affect the programme and DR-TB patients.
- Some of the other projects which will close out shortly are End TB project in July 2018 and SIAPSD in 2019.

Recommendations:

- The NTP should have regular meetings with the partners (at least quarterly) with definite agenda and discussion points. These meetings should serve as a platform for sharing the project updates, ensuring alignment with the NTP objectives and discussing and resolving challenges faced by the partners.
- Each project should have a formal exit plan, prepared by the partner in consultation with NTP, which should get triggered well in advance of the closure of the project ensuring smooth transition and sustainability.

E. Advocacy and Community engagement:

- The PMDT services are delivered through a network of community workers through the community approach to PMDT care (cPMDT).
- The involvement of community workers including Health Assistants (HAs), Family Welfare Assistants (FWAs), Community Health Care Provider (CHCP) for PMDT services ensures integration with other health programmes (MCH, Immunisation etc.) thus optimizing resources and ensuring sustainability. The community workers and patients are provided enablers and incentives.
- The engagement of affected community groups (patients and families) in PMDT is sub-optimal.

Recommendations:

- The affected community groups are an important resource for advocacy, peer counselling and delivery of PMDT services. Efforts should be undertaken to identify representatives (individual and groups) from the affected community who are then trained for supporting the aforesaid activities. Sufficient budget should be allocated for this purpose.

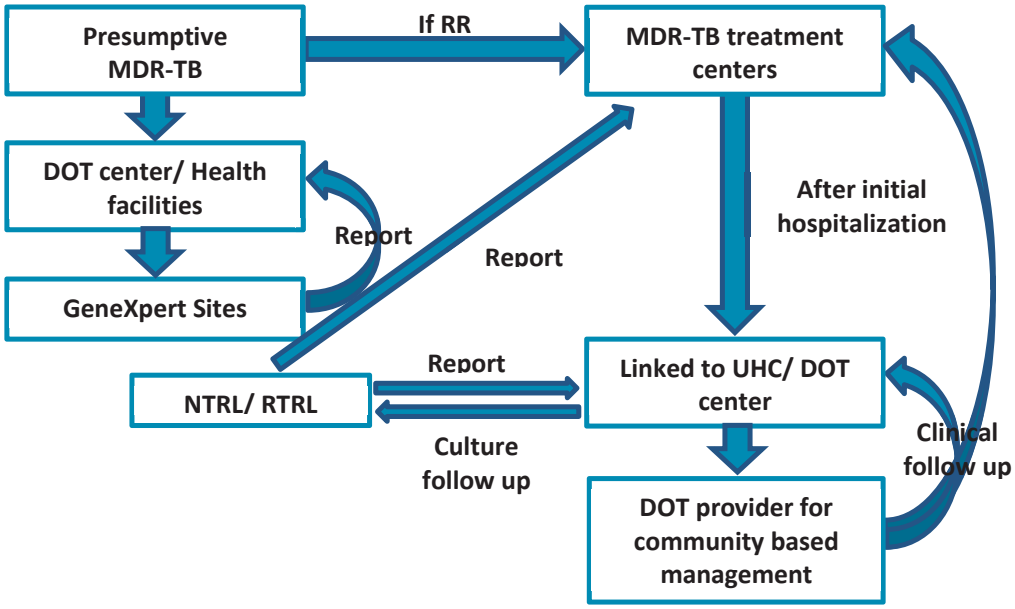
F. Case finding strategy:

- The National PMDT guideline currently prioritises the following risk groups for DST.

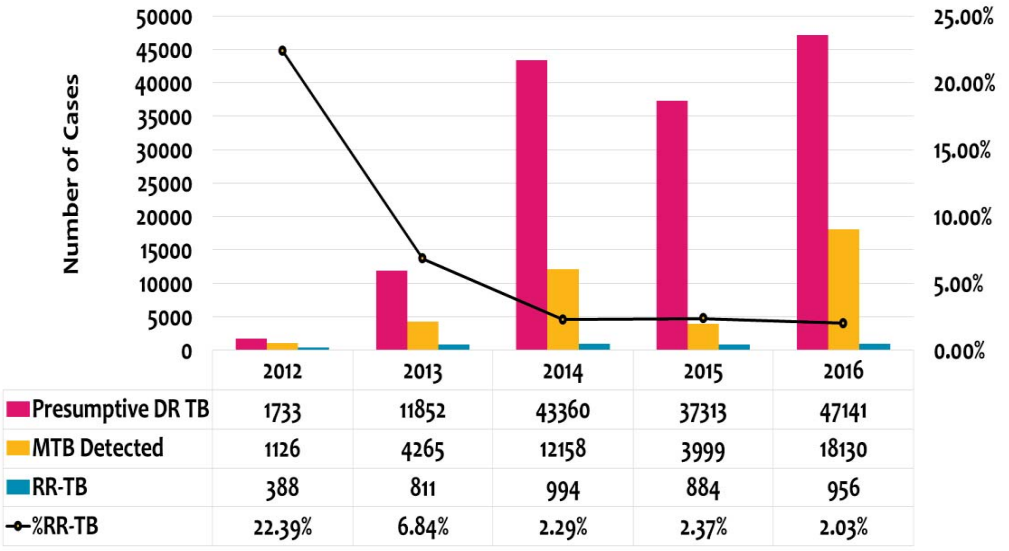
High Risk	○ Failures of Category II ○ Failures of Category I ○ Close contact of MDR TB patient with symptoms
Medium Risk	○ Non converters of Category II ○ Non converters of Category I ○ All relapses (Category I and II) ○ All treatment after loss to follow up (Category I and II) ○ Others: *Any smear negative or extrapulmonary TB patient clinically not improving inspite of treatment as per NTP guidelines*
Low Risk	○ All HIV infected persons

- Presumptive DR-TB registers are maintained and those identified as presumptive MDR TB, as per the above criteria, are subjected to DST. As per guidelines sputum samples of such patients are to be transported to the nearest Xpert site. In the absence of sputum transport facilities patients are referred to the Xpert site for testing which causes avoidable expenditure and inconvenience and also leads to loss in testing.

- The NTRL does Xpert only for smear-negative presumptive DR-TB patients, other than MDR contacts, LPA (HAIN) for smear-positive ones, and culture and DST for symptomatic MDR contacts.
- Those found to be RR/MDR are initiated on treatment at the nearest DR-TB centre where the patient is admitted for pre-treatment evaluation, treatment initiation and monitoring and management of adverse events. The regimen is either 20 month or 9 month (SR) depending on the DR-TB centre. The NIDCH and DF Hospitals are following the SR whereas the other four centres are administering the 20 month regimen. The scale up of the SR is being undertaken and is likely to be completed by end 2017. The RR/MDR patients are subjected to SLDST by LPA available at NTRL. The referral mechanism is depicted in the flow chart below:



- The Xpert machines have increased form 12 in 2012 to 41 in 2016 with additional 10 machines yet to be installed. This has resulted in an exponential increase in Xpert tests from ~1700 in 2012 to ~47000 in 2016 as shown in figure below.



	2012	2013	2014	2015	2016
Presumptive DR TB	1733	11852	43360	37313	47141
MTB Detected	1126	4265	12158	3999	18130
RR-TB	388	811	994	884	956
%RR-TB	22.39%	6.84%	2.29%	2.37%	2.03%

Figure 6: Number and proportion of RR/MDR cases 2012-2016

The proportion of those with RR TB among tested has reduced from 22% to 2% primarily due to the large number of smear negative patients being tested (to diagnose TB) who are not presumptive RR/MDR patients. There was a decline (~15%) in Xpert testing in 2015 due to non-functional Xpert modules/machines and stock out of cartridges. These issues have been addressed with support from CTB and in 2016 the number of Xpert tests done is over 47,000.

- As per the current diagnostic algorithm any new case diagnosed with RR by Xpert is initiated on MDR treatment but the resistance is confirmed by culture and DST.

Recommendations:

- Strengthen the sputum collection and transportation system to avoid referring presumptive DR-TB patients to Xpert sites.
- The diagnostic algorithm followed at NTRL needs to be clarified and revised as per the PMDT guidelines.
- Any new case diagnosed with RR on Xpert is currently being confirmed by culture and DST. As per the WHO guidelines in such cases a repeat Xpert can be done for confirmation. The results of phenotypic DST in such cases if found discordant should be interpreted cautiously as recent evidence shows that phenotypic tests may miss some clinically relevant mutations which are picked up by molecular tests.
- Introduce a policy of testing of all new smear positive new smear negative patients with Xpert. This will lead to an increased detection of primary MDR TB and reduce the transmission of MDR TB

G. Laboratory services and expansion plan

- The country has a laboratory network that is established at National, Regional, District and Peripheral levels.
- **Smear microscopy** is the primary tool for diagnosis of TB in the country. At the end of 2016 there were 1109 microscopy laboratories including with 876 binocular light microscopes and 233 LED fluorescence microscopes (LED-FM) providing services throughout the country. Functional EQA for both ZN and FM microscopy is available.
- **Xpert services** were introduced in 2012 and are being scaled up. At the end of 2016 there are 41 Xpert machines available with another 10 waiting to be installed. Most of the Xpert sites are underutilized. Excluding the NTRL, the other Xpert sites are performing only 3 tests per machine per day. This is due to the limited criteria for presumptive DR-TB and also a weak sputum transportation mechanism. Many Xpert sites were reporting errors due to poor conditions, processing and temperature control. These have been addressed to a large extent through the CTB support which includes recalibration of machines, replacement of modules, re-functionalization of Xpert machines in certain areas, UPS maintenance services and installing Gx Alert 360 for real time monitoring.
- **National and Regional TB Reference Laboratories-** There is one NTRL located in the National Institute of infectious diseases and Chest hospital (NIDCH). The facility is headed by an Assistant Professor and assisted by staff, most of them are adhoc or supported by partners which has the potential risk of interrupting services in case the partners withdraw. The facility has functional solid and liquid culture and performs first and second line LPA. There are 4 RTRLs located in Chittagong, Khulna, Rajashahi and Sylhet. LPA is not available. Khulna and Chittagong don't have liquid culture facility. In addition, Damien Foundation runs a quality assured C&DST laboratory at Netrakona. The NTRL is linked to the WHO SNRL Antwerp.
- An updated laboratory scale up plan for the period 2016-2020 has been prepared. There is a plan to expand the LED-FM, Xpert and LPA services during 2017 and 2018 as per the table below.

Test/service	2016	2017	2018
LED-FM	350	767	1150
GeneXpert	41 (+10)	63	213
LPA	1	5	7

Table 3: Status and plan for diagnostic services 2016-18 as per lab scale-up plan

Recommendations:

- The supervisory and monitoring functions of the NTRL are weak due to shortage of staff and limited capacity to perform on-site evaluations. NTRL should have adequate regular staff with more oversight and ownership from the NTP.
- The NTRL should receive regular technical assistance from the SRL Antwerp lab including 1-2 onsite visits annually.
- Undertake a workload assessment of the existing Xpert sites and take necessary steps to optimize their use. This should be done urgently as more Xpert machines are expected to arrive in the country shortly. The measures to optimise the Xpert use include:
    - Expanding the presumptive DR-TB criteria to include all new smear positive TB patients. This can be initiated in a few districts initially and then expanded in a phased manner while ensuring availability of cartridges and other logistics.
    - Strengthening the sputum transportation mechanisms.
    - Promoting the use of Xpert for diagnosis of pediatric and extra-pulmonary TB. This could be undertaken by engaging pediatricians and other relevant specialists (surgeons, gyanecologists, neurologists etc.) both from the public and private sector and establishing linkages with Xpert sites.
- Plan and establish mechanisms under NTP for continued maintenance of Xpert machines (existing and to be delivered) after CTB support ceases.
- Assess the need and establish additional second line LPA facilities in identified RTRLs to support the ongoing expansion of the shorter regimen.

H. Treatment strategy

- There are currently 6 PMDT sites in the country, five managed by the NTP and one by DF in Rajshahi. The five sites are the NIDCH in Dhaka, and CDHs in Chittagong, Pabna, Khulna and Sylhet.
- 5,500 RR-/MDR-TB patients have been initiated on treatment during 2005 till 2016. The table below shows the actual enrolment numbers from 2005 to 2016.

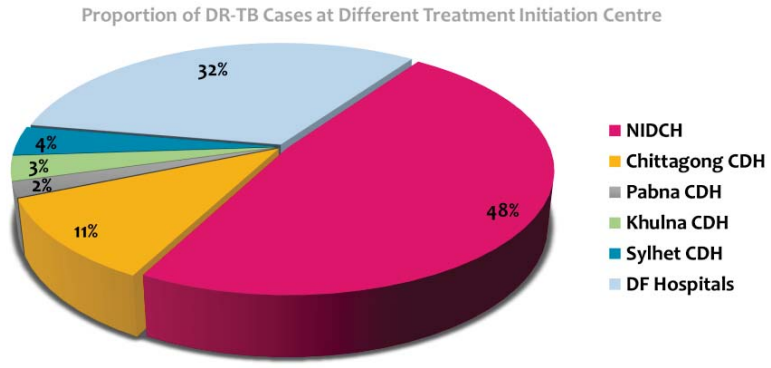
	2005-07	2008	2009	2010	2011	2012	2013	2014	2015	2016
New	242	236	360	337	390	505	686	946	880	918
Cum.		478	838	1175	1565	2070	2756	3702	4582	5500

Table 4: RR/MDR TB enrolment 2005 to 2016

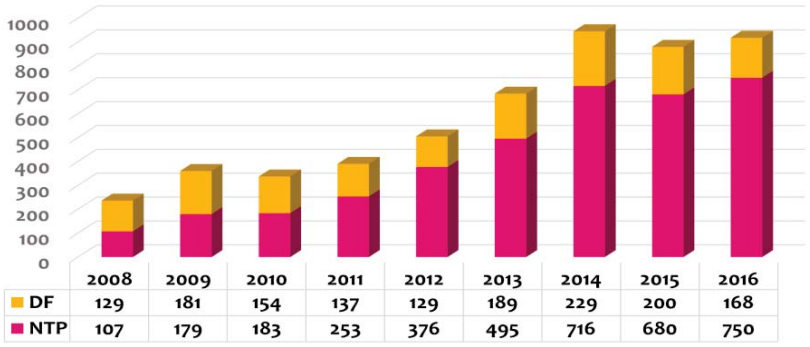
- The proportion of patients enrolled among those diagnosed has increased considerably, from ~70% to ~95% from 2010 to 2016 highlighting the intensive efforts by the programme in following up the diagnosed cases. The gap is now limited to patients who refuse treatment or could not be tracked due to incorrect addresses or migration.

RR/MDR	2010	2011	2012	2013	2014	2015	2016
Diagnosed	480	612	701	807	994	954	969
Enrolled	337	390	505	684	946	880	918
%	70%	64%	72%	85%	95%	92%	95%

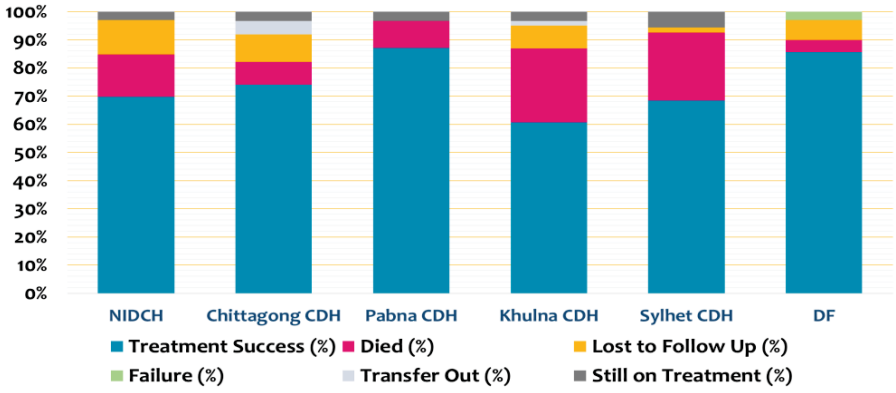
- The proportion of cases enrolled in each PMDT site for the period 2006-16 is depicted in the figure below.



The DF which is implementing the shorter regimen enrolls nearly 200 cases annually.



- The successful treatment outcomes of RR-/MDR-TB cases has been almost steady since 2008. Both the 20 month and 9 month regimens had almost similar outcomes for the 2011 and 2012 (~72%) cohorts. For 2013 and 2014 cohorts the 9 month regimen has shown a much higher success rate ~84% as compared to the 20 month regimen ~72%. This is depicted in the figure 5on page 10 above. The scale up of the shorter regimen has been initiated as detailed in the following section.
- There is a significant variation in the outcomes PMDT site wise as shown in the figure below which depicts the outcomes for the 2014 cohort. The treatment success is lower in Khulna and Sylhet with higher mortality and NIDCH and Chittagong with higher LFU rates.



- **Treatment regimens:**
  - The NTP is following the WHO recommended 20 month regimen since 2008 which includes: **8{Km-Lfx(Ofx)-Eto-Cs-Z/ 12{Lfx(Ofx)-Eto- Cs-Z}**
  - The DF has been using the SR in its area since 2005. The regimen includes: **4{Km-Gfx*-Pto-Cfz-Z-H*-E}/ 5{Gfx-Cfz-Z-E} (* is high dose)**
    Currently, with the non- availability of Gatifloxacin the DF is using levofloxacin in the regimen.
  - Following the WHO's recommendation on implementation of the Shorter Regimen (SR) the NTP has decided to expand the SR across all PMDT sites in a phased manner. The plan and current status is depicted in the table below.

PMDT site	Initiation of SR	No of patients enrolled
NIDCH	April 2017	102
Sylhet CDH	August 2017	-
Khulna CDH	September 2017	-
Chittagong CDH	October 2017	-
Pabna CDH	November 2017	-
Rajshahi CDH (DF)*	2005/Dec 2017	(~1500 since 2005)

The Rajshahi CDH which is under the DF has been implementing the SR under research mode since 2005 and ~1500 patients have been enrolled on treatment. Currently, with the non- availability of Gatifloxacin the DF is using levofloxacin instead in the SR. They have received 250 courses of SR from USAID funding which are likely to last till Dec 2017. Thereafter the DF will be covered by the NTP. Prior to the roll out of the SR the relevant programme staff is being trained with support from CTB using a set of presentations prepared for this purpose.

- **Newer drugs:**
  - Bedaquiline and Delamanid have been introduced through the End TB project in April 2016. The current criteria for the use of newer drugs includes:
    - XDR
    - Pre-XDR
    - Patients with two or more Group 4 drugs (Eto/Pto, Cs, PAS) compromised.
    - Contact of an pre XDR/XDR patient
    - Unable to tolerate MDR drugs
    - Patients who are a "failure" of an MDR-TB regimen
    - Co-morbidities or other condition

    The exclusion criteria are :
    - Baseline ECG QTcF > 500 ms (repeated);
    - History of syncopal episodes, ventricular arrhythmias or severe coronary artery disease or helart failure
    - Children <18 years (Bdq) Dlm 6 – 18 Years can be used
    - Pregnancy and lactation
    - Severe hepatic failure (Bdq)
    - Serum albumin < 2.8 g/dL (Dlm)
    - Patients with central nervous system disorders
  - The End TB project is being implemented at NIDCH with support from IRD, Bangladesh. Dedicated staff has been provided for the project. A strong

pharmacovigilance mechanism has been established with strict cohort event monitoring, rapid identification and management of adverse reactions and regular reporting.

- The first patient was enrolled in April 2016. Total of 252 drug courses (154 Bdq and 98 Dlm) will be available under the project. The enrolment will continue till March 2018.
- Till date 114 patients have been enroled on the newer drugs. This includes 78 on Bdq and 33 on Dlm and 3 on both. The targets vs the actual enrolment is as follows:

Year	Target	Achievement
2016	86	43
2017	128	71
2018	86	

- The number and proportion of patients and their indication for new drugs is listed in the table below.

Indication	Number of patients	%
XDR	9	9
Pre-XDR (FQ)	38	33
Pre-XDR (Inj)	1	1
Contact with a pre XDR/XDR patient	1	1
Unable to tolerate MDR drugs	37	32.4
Co-morbidities or other conditions	28	24.6

- Of the 114 patients on treatment with newer drugs monthly culture results for first three months are available for 80 patients. The results are as follows:

Number	1st Month	%	2nd month	%	3rd month	%
80	58	72.5%	72	90%	78	97.5%

By the end of 3rd month nearly 98% of the patients had become culture negative.

- **Treatment delivery (DOT), adherence and social support**
  - DOT is done by nurses while the patient is admitted in the hospital/PMDT treatment center. Upon discharge, the identified DOT provider (under community PMDT) supervises therapy mostly at the patient's house. In Dhaka city, patients come daily to the urban DOTS center.
  - Social support is provided to patients and community health workers and includes:
    - Nutritional support for enrolled patients- BDT 1500 per month
    - Incentive for DOT Provider- BDT 1800 per month
    - Travel Allowance to the presumptive DR-TB patients and accompanying health workers during ambulatory period for follow-up
    - Cost of ancillary investigations (LFT, RFT etc)
    - Free ancillary drugs

- The social support is provided by NTP, BRAC and CTB in their respective implementation districts. No delay has been reported in disbursement of incentives by patients and DOT providers.

Recommendations:

- The enrolment gap should be reduced further focusing on patients who could not be tracked by taking correct addresses including home addresses if they are migrants and counselling patients (and family members) who are refusing treatment due to various reasons.
- The reasons for higher mortality and loss to follow up rates in identified PMDT sites should be ascertained and addressed. This could be done as operational research to guide programme policy.
- The programme currently has only 6 DR-TB sites where the patients are evaluated and initiated on treatment with 4-6 weeks of admission. Patients across the country have to reach these DR-TB centres which may be inconvenient and also entail significant out of pocket expenditure. The NTP should plan decentralisation of the treatment services by enhancing the number of DR-TB sites in line with the increasing number of patients patients diagnosed with the increase in Xpert sites.
- The PMDT guidelines need to be updated to include the SR and newer drugs.
- Training material should be developed for various cadre of staff who would be involved in implementation of SR and newer drugs.
- The End TB project will enrol limited number of patients (252) and will continue till March 2018. The NTP needs to ensure availability of Bdq and Dlm beyond the End TB project and sustain the mechanisms established by the project for identification and enrolment of eligible patients on newer drugs and monitoring and management of adverse events.
- With the transition in the CTB project from October 2017 the incentives and enablers for DR-TB patients supported by the project will cease. The NTP needs to make an interim arrangement to cover these districts under Global Fund through BRAC or domestic budget.

I. Pharmacovigilance/ aDSM

- Pharmacovigilance is in place for the newer drugs under the End TB project. However, there is no mechanism to actively monitor drug safety and manage adverse events (aDSM) for the SR.
- Ancillary drugs for side effects management are generally available in PMDT sites.

Recommendations:

- The NTP needs to establish mechanism for aDSM ensuring the following key points:
  - aDSM committee to be formed.
  - Data collection tools and SOPs for safety data to be made available
  - Training on staff on aDSM
  - Availability of essential tests like ECG, audiometry and biochemistry tests.
  - Dedicated funding to be made available for aDSM

J. Drug management

- **Central drugstore –**
  - The Central Drug Store in Shyamolee was established with technical assistance by USAID (SIAPS), Global Fund, and the government. It stores both the FLDs and SLDs.
  - There are dedicated staff trained by SIAPS on drug management.
  - All drugs are centrally procured from the Global Drug Facility (GDF) and are therefore quality assured.

- There is inadequate space for storage of SLDs. humidity control is poor and there are signs of seepage and fungal infestation on the walls of the store.

- The stock of SLDs is adequate and there are currently no drugs at risk of expiry.
- SIAPS is USAID-funded assisting PMDT by supporting the NTP to develop a comprehensive supply chain management system to support forecasting, quantification, supply planning, procurement management and distribution of TB commodities. SIAPS has introduced the early warning tool for early detection of expiring drugs or stock outs. This is computerized and updated on the board manually (see photograph below).

Recommendations:

- Ensure good temperature and humidity control in the store. Urgently address seepage and fungal infestation on the walls.
- SIAPS project has been extended till 2019. However, their needs to be a transition plan for sustaining the project by the NTP

K. Recording and reporting, and data management

- **Records and reports:** These are generally complete except for some missing entries as seen in the sites visited.
- **Reporting systems:** There are two different electronic systems in place.
  - e-TB manager is used for both DS and DR-TB. It is a patient-based electronic system and captures all the details including initial and follow-up laboratory results, regimen changes due to side-effects, etc. It automatically generates the reporting formats for national and lower levels. e-TB manager is used at all PMDT sites.
  - DHIS 2 is the national HMIS and is used for all health programmes. It is not a case based system. TB data is aggregated and TB forms 10, 11, and 12 are included in the DHIS2 set up. It has been decided that DHIS 2 will be the main recording and reporting system and there a plan to introduce a case based module in DHIS 2.
  - SIAPS is working on establishing inter-operability of e-TB manager and DHIS2, so that the data from eTB manager can be transferred automatically into DHIS 2 and provide tools and SoPs for local analysis of the patient-based data available in eTB manager.

Recommendations:

- The interoperability of the e-TB manager and DHIS-2 to be completed and case based module to be introduced in DHIS 2 for the DR-TB recording system.
- The data currently being collected should be analyzed at the site and the national level and used for the improvement of the programme. The M&E unit should proactively undertake this process.

L. Infection control

- The infection control measures are weak. Visit to NIDCH showed that most of the windows in the DR-TB ward were closed and the beds were closely placed. The MDR, pre-XDR and XDR patients were frequently admitted in the same ward with a high risk of cross infection.
- Surgical masks for patients and N95 for staff were available and were seen wearing them.
- There is currently no mechanism to triage and fast track presumptive TB patients in OPDs.

Recommendations:

- Airborne infection control practices in general should be followed.
- Triaging of patients in OPD area should be initiated at all PMDT sites.

M. Human resource, Training and Technical support strategy

- The PMDT team at the national level comprises of staff supported by GoB, Global Fund and partners. The key staff include:
    - DR-TB focal point – NTP (GoB)
    - Laboratory focal point – NTP (GoB) supported by staff from NTRL, Global Fund, CTB
    - Treatment- NIDCH, CTB and IRD
    - Drugs- NTP (GoB), SIAPS
    - M&E – NTP (GoB) supported by SIAPS for recording and reporting
- There is significant turnover of staff at all levels. At the NTP there have been frequent changes in key positions including the Line Director and NTP Manager resulting in delayed decisions and implementation.
- With the implementation of the SR and newer drugs there is an urgent need for training of the programme staff at all levels.

Recommendations:

- The GoB should ensure that the key NTP staff should be in place for at least 3 years to ensure that the implementation of activities is not compromised.
- HRD plan based on training needs and skill development for the staff should be prepared.

N. Supervision of the programme

- The national monitoring and evaluation (M&E) plan 2016-2020 lays out the M&E activities at the central, divisional, district, upazilla level and in urban areas. The NTP and its partners have dedicated staff for conducting M&E activities and the central team is expected to visit approximately 3 to 5 districts in every division during the course of a year. The divisional TB consultants are expected to visit approximately 2 to 3 districts in every quarter, again focusing on implementation sites with poor performance shown in quarterly reports. Through the combination of central level- and divisional supervision activities, the NTP expects that every Upazila health complex in the country is visited at least once per year by a higher-level team.

- The supervisory visits by the PMDT team are not integrated with the regular supervisory visits.
- There are no specific SOPs and checklists for PMDT supervisory visits.

Recommendations:

- The supervisory visits need to be integrated. Any supervisory visit should include review of PMDT activities.
- Develop specific SOPs and checklists for PMDT supervisory visits and also ensure that the supervisory reports are compiled and available.

O. PMDT plan including funding source

- As per the PMDT expansion plan (2013-17) 2,300 cases will be treated in 2016 against which only 918 (40%) have been enrolled on treatment. In 2017 the target is 2,650 which will not be achieved.
- The scale up of the shorter regimen as per the expansion plan is as per the table below.

Year	MDR TB cases	Shorter Regimen (DF)	Shorter Regimen (NTP)	Total Shorter Regimen	Total 20 month/ other regimen
2015	1900	250	1400	1650	250
2016	2300	300	1750	2050	250
2017	2650	350	2000	2350	300

- The National Strategic Plan for 2018 to 2022 is under preparation and will be finalised by October 2017.

Annex 1: List of people met during the mission

S.No	Name	Designation	Organisation
1	Dr Rouseli Haq	Director and NTP manager	NTP
2	Dr Nazis Arefin	MO, PMDT focal point	NTP
3	Dr Pronob K Modak	MO, Lab focal point	NTP
4	Dr Mamdoau Diallo	Acting WR	WHO
5	Dr Sabera Sultana	NPO-TB	WHO
6	Dr Mahmudul Hassan	SIAPS	MSH
7	Dr Oscar	Country Director	Challenge TB
8	Dr Kausari Jahan	MDR-TB Advisor	Challenge TB
9	Dr Shayla Islam	MDR-TB Advisor	Challenge TB
10	Dr Tanzir Hossain	Lab Advisor	Challenge TB
11	Dr Hamida	Country Director	IRD
12	Dr. Md. Wahiduzzaman Akhanda	Consultant	IRD
13	Dr Majibur Rehman	National Consultant	NTP
14	Abdul Jalil	Store keeper	NTP
15	Abdul Latif	MDR patient	