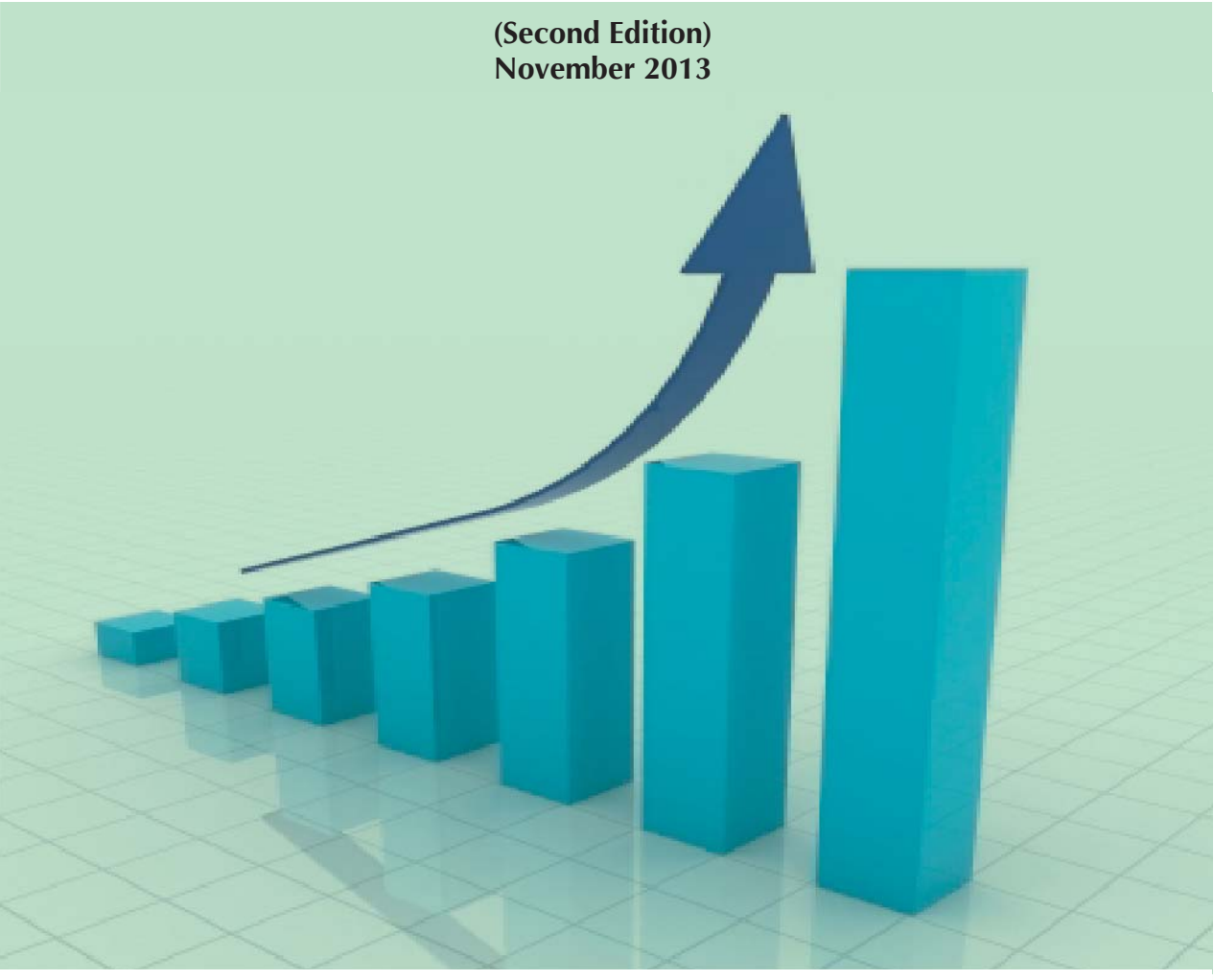
Expansion Plan of Programmatic Management of Drug Resistant TB (PMDT)

2013 to 2017

(Second Edition)
November 2013



National Tuberculosis Control Programme
Directorate General of Health Services
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Abbreviations and Acronyms

AFB	Acid - Fast Bacilli
ADR	Adverse Drug Reaction
ARV	Antiretroviral
AZT	Zidovudine
BMDC	Bangladesh Medical and Dental Council
BMI	Body Mass Index
CDC	Chest Disease Clinic
CDH	Chest Disease Hospital
CHCP	Community Health Care Provider
CPC	Cetylpyridinum chloride
c-PMDT	Community-based Programmatic Management of Drug Resistant TB
CSF	Cerebrospinal Fluid
CT	Computerized Axial Tomography
DM	Diabetes Mellitus
DNA	Deoxyribonucleic acid
DOT	Directly Observed Therapy
DOTS	An Internationally recommended strategy for TB control
DRS	Drug Resistant Survey
DR TB	Drug Resistant Tuberculosis
DST	Drug Susceptibility Testing
ECG	Electrocardiogram
EXPAND-TB	Expanding Access to New Diagnostics for TB. Project funded by UNITAID and implemented by GLI, FIND, WHO and GDF
FWA	Family Welfare Assistant
GDF	Global Drug Facility
GFR	Glomerular Filtration Rate
gGLC	Global Green Light Committee
GLC	Green Light Committee
HA	Health Assistant
HIV	Human Immunodeficiency Virus
HPNSDP	Health, Population and Nutrition Sector Development Programme
IC	Infection Control
INGO	International Non-government Organization
IUATLD	International Union Against Tuberculosis and Lung Disease
LED	Light Emitting Diode
LJ	Lowenstein Jensen
LPA	Line Probe Assay
MDR TB	Multidrug Resistant Tuberculosis
MGIT	Mycobacteria Growth Indicator Tube
MO	Medical Officer
MODCS	Medical Officer for Disease Control and Surveillance
MOTT	Mycobateria Other Than Tuberculosis
MTB	Mycobaterium Tuberculosis
MTB/RIF	Mycobaterium Tuberculosis/Resistance to Rifampicin
NGO	Nongovernmental Organization
NIDCH	National Institute of Diseases of the Chest and Hospital

NTP	National Tuberculosis Control Program
NTRL	National Tuberculosis Reference Laboratory
PCP	Pneumocystis Pneumonia
PCR	Polymerase Chain Reaction
PMDT	Programmatic Management of Drug Resistant Tuberculosis
PO	Program Organizer
QA	Quality Assurance
QC	Quality Control
r-GLC	Regional Green Light Committee
RTRL	Regional Tuberculosis Reference Laboratory
SNRL	Supra National Reference Laboratory (for TB)
SOP	Standard Operating Procedure
SS	Shasthya Shebika
TAG	Technical Advisory Group
TB	Tuberculosis
TLCA	Tuberculosis & Leprosy Control Assistant
TSH	Thyroid Stimulating Hormone
UH&FPO	Upazila Health and Family Planning Officer
UHC	Upazila Health Complex
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNITAID	International facility for the purchase of drugs and laboratory commodities for HIV/AIDS, malaria and tuberculosis
WHO	World Health Organization
WRD	WHO approved Rapid Diagnostic Tools
XDR TB	Extensively Drug Resistant TB
YGH	Yangon General Hospital

Group	Description	Drug	Abbreviation
1	First -line oral anti -tuberculosis drugs	Isoniazid Rifampicin Ethambutol Pyrazinamide Rifabutin	H R E Z Rfb
2	Injectable anti -tuberculosis drugs	Kanamycin Amikacin Capreomycin Streptomycin	Km Amk Cm S
3	Fluoroquinolones	Levofloxacin Moxifloxacin Ofloxacin	Lfx Mfx Ofx
4	Oral bacteriostatic second -line anti -tuberculosis drugs	Ethionamide Prothionamide Cycloserine p-aminosalicylic acid	Eto Pto Cs PAS
5	Anti -tuberculosis drugs with unclear efficacy or unclear role in MDR -TB treatment (not recommended by the WHO for routine use in MDR-TB patients)	Clofazimine Linezolid Amoxicillin/clavulanate	Cfz Lzd Amx/Clv

Executive summary

TB is a major public health concern in Bangladesh. It is listed among the 22 high TB burden and 27 high MDR TB burden countries .

The activities described in the following Programmatic Management of Drug Resistant Tuberculosis (PMDT) Expansion Plan, 2013-2017 facilitate the realization of the following long-term goals in Bangladesh:

1. Nationwide diagnosis of drug resistant tuberculosis (DR TB) in all groups of patients at risk for DR TB especially for M/XDR TB.
2. Diagnosis of DR TB in all HIV/TB co-infected patients.
3. DR TB treatment for all patients diagnosed with DR TB. Treatment to be in accordance with the treatment protocols of the World Health Organization (WHO) using a community-based programmatic approach.
4. Patient treatment support to include palliative care and social support.
5. To transition to a short-course regimen for DR TB in districts beyond the Damian Foundation catchment area, if the required criteria and approval by the WHO can be fulfilled.

The Programmatic Management of Drug Resistant Tuberculosis Expansion Plan 2013-2017 builds upon the existing TB control programme and the National Strategic Plan for TB 2012-2016 . Furthermore it sets forth specific goals and a timeframe for the expansion of the DR TB programme, explains any necessary changes to the existing standard operational procedures and clinical guidelines for DR TB and addresses expansion costs.

When implemented in conjunction with the National Strategic Plan for TB 2012-2016, the PMDT Expansion Plan 2013-2017 aims to ensure that all high risk DR TB patients have access to drug susceptibility testing (DST). In the later years of the plan this would require the availability of 12,000 to 15,000 Xpert MTB/RIF tests for the diagnosis of DR TB. Every patient with documented DR TB will be treated according to the NTP's clinical protocols and offered a community-based option for treatment. Under this plan, a total of 9250 DR TB patients would initiate treatment between 2013 and 2017 (1000, 1400, 1900, 2300, 2650 patients respectively each year).

The PMDT Expansion Plan 2013-2017 provides a nationwide DR TB diagnosis and treatment plan which, if rolled out would cost an estimated cost of 44.7 million USD over a five-year period. The plan relies heavily on funding from the Global Fund for AIDS, TB and Malaria (GFATM) and bilateral donors such as USAID, as well as the Bangladesh MoH with technical support of WHO and other development partners. To ensure the success of the plan it is crucial that ongoing partner support continues and that additional support from the GFATM, bilateral donor agencies, national NGOs and INGOs is secured.

Additionally the PMDT Expansion Plan 2013-2017 provides a roadmap with realistic and obtainable goals for the successful expansion of the DR TB programme in Bangladesh.

Background 1

1.1. Baseline geographic reach

Bangladesh is administratively divided into 7 divisions, 64 districts, 7 metropolitan cities, 483 upazilas (sub-districts) and 4498 unions (Statistical pocket book, Bangladesh 2010) The country is divided into areas where different partnerships collaborate with the NTP to deliver TB services. The primary responsibility of the DR TB programme is shared between the NTP (supported by the GFATM, USAID/TBCARE II and the WHO) and the Damien Foundation (responsible for 28 districts in the north-west area of the country).

At present a community-based approach to DR TB only covers a small percentage of the country compared to that of the drug-susceptible TB programme, which has nationwide community-based coverage. Until DR TB inpatient care can be established in all divisions a patient from any part of the country can be admitted to one of the designated government hospitals. NIDCH in Dhaka and CDH in Chittagong are presently fully operational since 2008 and 2011 respectively. In 2013, CDH Pabna and CDH Khulna also initiated enrollment and management of DR TB patients. There were four pilot districts/areas implementing c-PMDT (Gazipur, Narayanganj, Jessore and Chittagong) as of December 2012 and scalled up in additional 19 Districts and 3 city corporation in 2013.

1.2. TB, MDR TB and XDR TB epidemiology

The estimates of TB incidence and prevalence are detailed in Table 1.1

Table 1.1 - Estimated burden of disease caused by TB, 2011. (Numbers in thousands).

	Population	Mortality			Prevalence			Incidence			HIV + Incident TB cases		
		Best	Low	High	Best	Low	High	Best	Low	High	Best	Low	High
Bangladesh.	150 494	68	29	120	620	300	1100	340	280	400	0.6	0.3	1.0

Ref: Global TB repot 2012

The TB case notifications for year 2011 are provided in Table 1.2

Table 1.2 TB case notifications, 2011

	Total notified	New					Retreatment		New and relapse	History unknown	% New Pulmonary cases smear positive
		Smear positive	Smear neg.	Smear not done	Extra pulmo-nary	Case type unknown	Relapse	Retreatment excl relapse			
Bangladesh	159023	98948	21921	0	27329	0	2701	4665		3459	82

Ref: Global TB repot 2012

Approximately 12% of TB case notifications come from the private sector. The estimated TB case detection rate in Bangladesh is 45% and the success rate of smear positive patients is 92%(1).

At present, MDR TB in Bangladesh is relatively low and XDR TB is rare. However, given the large size of the population, Bangladesh is in the list of 27 priority countries for MDR TB and extensively drug-resistant tuberculosis (XDR TB).

Table 1.3 MDR TB enrolment for treatment 2009-12

Regimen	2009	2010	2011	2012
GLC approved 20-24 Month regimen	179	183	253	376
9 Month regimen (Damien Foundation)	181	154	137	129

In 2010-11, the NTP carried out its first nationwide drug resistance survey (DRS) in new and retreatment TB patients with technical support from WHO (See Table 1.4). Table shows levels of drug resistance (MDR) are low, with 1.4% among new cases and 28.5% among retreatment cases.

Table 1.4 Estimated numbers of MDR TB cases among cases notified, 2010-11

	MDR TB estimates among notified cases.	Confidence interval
% of new TB cases with MDR TB.	1.40%	0.70-2.25
% of retreatment TB cases with MDR TB.	28.50%	24-34
Estimated MDR TB cases among new pulmonary TB cases notified in 2011.	1700	850 - 3000
Estimated MDR TB cases among retreated pulmonary TB cases notified in 2011.	2100	1700-2500
Total estimate among notified cases.	3800	2550-5500

A study conducted in 2005-2006 in a tertiary level hospital (NIDCH) showed that 88% had MDR TB among 96 Category II failures.

Since 2008 till the end of 2013, there are total ten XDR TB diagnosed.

1.3. Collaboration with technical agencies

NTP is implementing drug sensitive TB and drug resistant TB programme in collaboration with GO and NGO partners with the support of different development partners and technical agencies. The majority of activities are implemented directly by the NTP and by groups in the GFATM consortium (of which BRAC is one of the recipient and lead agency of 44 NGOs). The USAID, TBCARE II project is also supporting NTP in implementing both DR TB diagnostic activities and community-based PMDT. The Damien Foundation implements operational research for the care of MDR TB patients, using a short course gatifloxacin-based regimen. WHO working as technical partner of NTP.

The experience of c-PMDT in the 4 districts where it has been implemented is the basis for nationwide expansion.

1.4. Present funding situation

Funding for DR TB activities is largely dependent on external resources and donor agencies. While this is of concern internally it is widely agreed that scaling-up DR TB control in Bangladesh is of national and global interest and as such that external funding is necessary.

The Ministry of Health and Family Welfare (MoHFW) however contributes substantial resources towards the NTP central office which manages the DR TB programme. It supports the initial hospitalization periods and all follow-up care at government Upazila Health Centres (UHCs) and urban or peri-urban TB treatment centers. In short, the MoHFW is committed to the DR TB programme and contributes a sizable portion of the necessary resources annually.

The funding for drug regimens, as of the end of 2012 is detailed in Table 1.5. There is a considerable gap in the number of drug regimens with an identifiable funding source (see Section 3). Furthermore, funding for ancillary drugs, associated costs and care (patient social support, DR TB DOT Provider support and ancillary test , monitoring, medicines to treat adverse drug reactions) are grossly underfunded.

Table 1.5. Drug regimen funding as of 2012

	Year (2012-2013)	Year (2013-2014)	Year (2014-2015)
MDR TB (GFATM).	360	480	600
XDR-TB (GFATM)	5	5	6
MDR TB (*USAID/TBCARE II)	200	0	100
Damien Foundation .	150	200	250
Total	715	685	956

1.5. Major challenges to the PMDT Expansion Plan 2013-2017

The expansion of DR TB diagnosis and treatment activities has three major challenges in the areas of: (1) human resource (HR), (2) diagnosis (case-finding) and treatment capacity (enrollment) and (3) funding (including the supply of drugs and consumables). These three challenges are described briefly in the sections 1.5.1-1.5.3.

1.5.1 Human resource development

Given that each upazila or urban/peri unban DOTS Center is expected to have the capacity to manage DR TB, there is a need to address the human resource gap, especially at field level.

The previous NTP protocols recommend an initial 6 to 8 month hospitalization period, which has resulted in long hospitalizations and long waiting lists to get into the hospital for enrollment. According to the new protocols, patients are to be hospitalized for 1 to 2 months before entering a community-based PMDT programme. Hospital space and staff must adhere to this protocol in each division. In 2012, only two hospitals were able to admit DR TB patients. (NICDH, Dhaka with 120 beds and Chittagong CDH with 32 beds for DR TB).

Ideally, capacity should be increased to have at least one admitting hospital in each division. The doctors, nurses and auxiliary staff associated with these wards require initial training and refresher training in PMDT.

As per National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition and the Standard Operating Procedures of c-PMDT, a UHC/ DOTS Center Outpatient DR TB Team should be set up at each UHC/DOTs center. It will be a considerable challenge to train a team at each center (normally a team consists of 7 to 8 people, see Standard Operating Procedures of c-PMDT for more information on the roles and responsibilities of the team members).

DR TB DOT Providers can be selected from an existing pool of community workers, given their previous training in areas of primary health care and TB.

The selection of DR TB DOT Providers in order of preference is:

1. TB and Leprosy Control Assistant (TLCA);
2. Health Assistants (HAs);
3. Family Welfare Assistants (FWAs);
4. Community Health Care Provider (CHCP).

In circumstances where no DR TB DOT Provider is available from the above four categories, then the DR TB DOT Provider can be selected from:

5. Local Pharmacy holder / Village doctor.
6. Paramedic/Medical assistant (in urban settings);
7. Shasthya Shebika (SS)- an NGO Community Health Volunteer (who can read and write English and Bangla well).

Increased case-finding and diagnosis of DR TB require all health care staff involved in TB care at all levels to be aware of when and how to send DST.

Strong infection control measures should also need to be implemented and maintained at all health facility levels and staffs need to be aware of how to protect themselves from DR TB.

Three training packages have been developed by the NTP in collaboration with USAID TBCARE II project under URC and WHO for training a district or city corporation area to implement PMDT:

1. Training of the medical doctors of GO-NGO. It is a comprehensive training course with duration of five days. This course is designed for the staff of hospitals where patients are enrolled under DR TB regimen and for the supervisors of the implementing partner NGOs.
2. Training of the Outpatient DR TB Team. It is a three-day course, which includes lectures, exercises and case discussions. The training is designed to be a comprehensive training of PMDT for members of the Outpatient DR TB Team.
3. DR TB DOT Provider Training. It is a one-day training course using a Facilitators Guide and Workbook. A DR TB DOT Provider Handbook has also been developed.

1.5.2 Diagnosis and treatment capacity

Diagnostic capacity has developed greatly over the past two years. There are three reference laboratories for culture and DST as of December 2012 under NTP; One at national level in Dhaka and two at regional level, in Chittagong and Rajshahi. Under Damien Foundation there are two reference laboratories for culture and DST. There are 12 Xpert MTB/RIF instruments in Bangladesh as of the end of 2012 (the plans for their placement throughout the country are discussed in Section 3). Using Xpert MTB/RIF as an initial screening test for patients is described in the National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition.

The following groups will be targeted as presumptive DR TB (previously known as DR TB suspects) for drug susceptibility testing (DST):

High Risk:

- Failures of Category II
- Failures of Category I
- Close contact of an MDR TB patient with symptoms

Medium Risk:

- Non converters of Category II (remain positive at month 3)
- Non converters of Category I (remain positive at month 2)
- 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 improved in spite of treatment as per NTP guidelines

Low Risk:

- All HIV infected persons

Note: Ensure proper history taking and quality lab performance including follow up sputum examination for identification of presumptive DR TB as per above groups

Because of increased availability and use of Xpert MTB/RIF instruments, Bangladesh has adequate diagnostic capacity to screen for DR TB. The culture and DST laboratories have the capacity to confirm all RIF-positive Xpert tests, when indicated.

While diagnostic capacity is adequate, the laboratories for ancillary tests (Complete Blood count, serum for potassium, thyroid stimulating hormone, liver function, kidney function and auditory test, Xray etc) which diagnose adverse effects and base line status of the patients are inadquate and will need to be developed.

Treatment capacity will need to be increased with the expansion of the programme, to incorporate shorter hospitalization periods and a move towards c-PMDT. A large number of UHC/Urban DOTS Centers based Outpatient DR TB Team need to be trained to manage DR TB patients at community. The Outpatient DR TB team requires comprehensive training and consistent supervision.

Finally a large number of DR TB DOT Providers have to be trained, given a monthly incentive and supervised in order for community-based treatment programmes to be successful.

1.5.3 Funding

Funding the PMDT Expansion Plan 2013-2017 will be a significant challenge. See Section 5 for secured funding, projected costs and funding gaps.

Organizational structure to be used in the expansion of the PMDT programme 2

2.1. Organizational structure of the DR TB programme

The existing DR TB programme is very well organized at national and local levels and will serve as an excellent foundation for the PMDT Expansion Plan 2013-2017.

Bangladesh received formal GLC approval in August 2006 to treat 700 patients over five years. The first patients were enrolled in August 2008. As of 5 November 2012, 1075 patients have been enrolled on MDR TB treatment, of which 70 patients have been enrolled in the four c-PMDT pilot districts (Gazipur, Narayanganj, Jessore, Chittagong).

The clinical and programmatic protocols and procedures are described in two national guides:

- National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition.
- Standard Operating Procedures: Community-based Programmatic Management of Drug-Resistant Tuberculosis, First Edition.

The NTP coordinates the overall DR TB programme. Treatment begins in the hospital, with a number of hospitals dedicated to DR TB inpatient care. See Table 2.1

Table 2.1 Planned hospital beds for PMDT

Infrastructure	Number of beds for MDR TB functioning as of end 2012	Planned Number of beds for MDR TB for 2013-2017
NIDCH	120	120
Shyamoli	0	150
Chittagong CDH	32	72
Rajshahi CDH	32	32
Sylhet CDH	0	32
Khulna CDH	0	32
Seven segregation hospitals (approximately 10 bed for DR TB in each).	0	70
Damien Foundation (3 Hospitals)	60	60
TOTAL	244	568

Chest disease hospitals and the designated PMDT Committees are responsible to manage patient. After the initial hospitalization period, patients are discharged to the community. Once community-based PMDT is established in an area stable patients can be started on the treatment without hospitalization in consultation with respective PMDT committee.

With the expansion of the programme, the NTP need to be establish a Divisional PMDT Committee at each divition (most commonly lead by a CDH consultant). A full description of the roles and responsibilities of personnel at each level (national, division, district, upazila, DR DOT Provider) is described in detail in the National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition.

For each district, there is a Supervisory Outpatient DR TB Team led by the civil surgeon and CDC consultant. For each district, there is a designated person for the coordination of PMDT programme. Often this is the CDC consultant, NGO district manager working in TB or can be a government district level supervisor.

There are a number of formats for recording and reporting of PMDT, described in the National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition. The information generated from these formats provides the basis to monitor and evaluate the PMDT programme.

An electronic register (not web-based) is kept at the Dhaka NTRL and one at the Chittagong RTRL. NTP has a plan to start web base electronic recording and reporting system for management of DR TB program.

Goals, objectives and targets for expantion of PMDT programme 3

3.1. Goals :

Global targets to reduce the burden of disease caused by TB have been set within the context of the Millennium Development Goals (MDGs) and also by the Stop TB Partnership.

PMDT programme of Bangladesh:

Goal: To reduce morbidity, mortality and transmission of DR TB in Bangladesh. Specific goals to reach the targets are discussed in detail in the following sections.

Objective: "universal access" for quality diagnosis and treatment for all DR TB cases.
Targets: The Bangladesh PMDT programme will focus on three tergets over the next three to five years.

- Detection of more than 70% of the estimated DR TB cases among the notified TB cases.
- To enroll and manage 100% of detected DR TB patients.
- To treat more than 75% of DR TB patients successfully.

These three measures will give an indication of the programme's performance in detecting and treating MDR TB, i.e. reaching the MDGs and the Stop TB Partnership goals and the PMDT Expansion Plan 2013-2017 will serve as a roadmap to accelerate progress towards these goals.

3.2. PMDT Expansion plan targets

This PMDT Expansion Plan 2013-2017 provides year-by year targets for case-finding, MDR TB treatment, and geographic expansion.

3.2.1 Case-finding

The ultimate goal of expanding case-finding strategies is to detect DR TB earlier and to initiate treatment as quickly as possible. Implementing laboratory infrastructural targets can accelerate the process towards achieving these goals. Table 3.1 illustrates the diagnostic laboratories to be developed under the PMDT Expansion Plan 2013-2017. Note that 25 Xpert MTB/RIF instruments from TBCARE II are presently in Bangladesh, which are to be used in 2013. Additional Project (TB REACH) will supply Xpert MTB/RIF as per plan and Mou (up to 25 instruments and 165,000 cartridges), which will arrive gradually in Bangladesh to strengthen PPM. Starting in 2013 and over 3 years they will be placed in the PPM settings and medical school hospitals mostly for TB/DR TB diagnosis.

Table 3.1 - Laboratory expansion

	2013	2014	2015	2016	2017
Xpert instruments (4 module) in Districts	25	44	64	64	64
Xpert instruments (4 module) in city corporations	10	10	11	14	16
Total Xpert (4 module) instruments in country	35	50	75	78	80
Xpert instruments (16 module) at NTRL .	1	1	1	1	1
Number of districts/City Corps* where specimen transportation systems for Xpert and for confirmation culture and DST exist	40/7	64/7	64/7	64/7	64/7
Number of solid culture and DST laboratories		6	6	6	6
Liquid culture (MGIT)	1	1	2	2	2
LPA molecular laboratory	1	1	2	2	2

* In City Corporations the patient goes to the laboratory and the specimen is not transported.

Annex 1 describes the intended placement of the first 25 Xpert MTB/RIF instruments for 2012/13. The placement of additional machines in 2015 and beyond will be determined at a later point.

According to sound modeling techniques, testing all cases of TB for DR TB is cost-effective and more medically efficient (i.e., more lives will be saved). However, it is not feasible to test all TB cases in Bangladesh because it would require more than 160,000 Xpert cartridges on an annual basis, which is feasibly unlikely in the next 5 years.

Table 3.2 estimates the number of Xpert MTB/RIF tests needed to test all presumptive DR TB. While there are nine indications in the National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition, they can be grouped together in four groups. A description of how estimates were made is provided below:

- All previously treated patients before the start of Category II treatment (estimate of tests are based on case notification rates for 2011 of previously treated cases).
- All non-converters - month 2 for Category I treatment and month 3 for category II treatment (since the exact numbers are unknown this is a very rough estimate, which is based on 2% of patients not converting and 20% of those cases being MDR TB cases).
- Close contacts of MDR TB cases that are symptomatic for active TB (this estimate is based on about one contact developing symptoms of TB and requiring an Xpert MTB/RIF test. Many will turn out not to have TB or be MTB negative. Most that are MTB positive will also be RIF positive, close to 80 to 90%. This PMDT Expansion Plan 2013-2107 estimates that about 10% of close contacts that are symptomatic will end up having MDR TB.
- All TB/HIV co-infected patients (estimated at 3% of all HIV cases).

Table 3.2 Annual estimates of Xpert tests needed to fully implement DR TB screening protocols and the estimate of number of Xpert RIF positive cases.

Patient Group	Estimate number of Xpert tests needed with 100% implementation	% with MDR TB (average)	Number of cases positive
Previously treated cases* (relapse, failure, return after default, and others)	7366	28.50%	2099
All non -converters (month 2/3 for Category I treatment and month 3/4 for category II treatment)	2964	20.00%	593
Close contacts of MDR -TB with TB symptoms o r smear positive** (many will be Xpert MTB negative, but those that are Xpert MTB positive will have a high percent of RIF resistance).	2000	Approx imately 10% of those screened will have MDR -TB	200
Screening for TB in all HIV patients / year and screening for MDR -TB in documented TB/HIV patients	2000	1.40%	28
Sub Total	14330		
5% repeat	716		
Totals	15046		2920

*The number of persons requiring retreatment will likely decrease, if non-converters are being tested at month 2/3 and 3/4 of category I and II respectively.
**Calculation based on 2000 patients on treatment with one symptomatic contact for every patient on treatment.

Table 3.2 is based on the assumption that the testing target (100%) is reached. It is however unlikely that any country will reach this target to screen all (100%) patients that comply with the screening criteria.

Table 3.3 sets forth year-by-year targets to continuously increase the percentage of MDR TB screening required for the total number of presumptive DR TB (suspects) and indicates the number of Xpert cartridges that will subsequently be required.

Table 3.3 Annual estimations of Xpert tests needed for MDR TB screening

	2013	2014	2015	2016	2017
Percent of Xpert screening tests implemented	40%	60%	70%	75%	80%
Number of Xpert screening tests implemented	6019	9028	10533	11285	12037
Expected number of RR-TB cases detected(based on an average of 20% percent of Xpert screening for DR TB tests being positive)	1168	1752	2044	2190	2336

The above number of cartridges does not take into consideration Xpert cartridges that are used for indications other than screening for MDR TB, such as to diagnose smear negative TB or to help diagnose TB in people living with HIV. For example, it is estimated that a total of 60,000 Xpert MTB/RIF cartridges will be used in Bangladesh in 2013, of which approximately 8000 will be used for the purpose of MDR TB screening.

Also of note, is that a drug resistance survey (DRS) with Xpert MTB/RIF is planned for 2014 and will use 20,000 cartridges and in 2014-15 a nationwide TB prevalence survey will use 100,000 cartridges.

3.2.2 Number of MDR TB cases treated

The estimated MDR TB burden among notified TB cases is approximately 3800 (1700 new, 2100 retreatment) as per notified cases of 2011. Table 3.4 sets the target number of MDR TB cases to be treated per year and Table 3.5 sets the target number of cases that will be treated with the 2 year MDR TB regimen vs a shorter regimen for MDR TB (either a gatifloxacin- or moxifloxacin-based regimen). Table 3.6 estimates the number of XDR TB cases to be detected and treated.

Table 3.4 Annual predictions of MDR TB cases to be treated

Year	MDR TB cases	Percentage of estimated cases
2013	1000	26%
2014	1400	37%
2015	1900	50%
2016	2300	61%
2017	2650	70%
Total	9250	

Table 3.5 Scale-up of MDR TB treatment based on type of regimen

Year	MDR TB cases	Short regimen for MDR TB by Damien	Short Regimen for MDR by NTP	Total Short Regimen	Total on NTP 2-year regimen/or individualized	% Short Regimen regimen
2013	1000	150	0	150	850	15%
2014	1400	200	450	650	750	46%
2015	1900	250	1400	1650	250	87%
2016	2300	300	1750	2050	250	89%
2017	2650	350	2000	2350	300	89%

Table 3.6 Predicted number of XDR TB cases treated per year

Year	XDR TB cases
2013	10
2014	15
2015	20
2016	20
2017	20

3.2.3 Geographical expansion

The geographic expansion targets are described below in Table 3.7. Annex 1 outlines the intended placement for the first 25 Xpert MTB/RIF instruments.

Table 3.7 Geographic expansion of c-PMDT

	2013	2014	2015	2016	2017
Number of districts with community-based MDR TB	16	40	64	64	64
Number of city corps	3	5	7	7	7

Expanding in a district or city corporation requires the implementation of a number of major activities and decisions including;

- Establishing where the district/city corporation will refer MDR TB patients for the initial hospitalization period,
- Establishing the sputum transport system for Xpert testing and information system to return the results back to the ordering facility,
- Laboratory monitoring, including cultures and monitoring adverse effects,
- Training of Outpatient DR TB Team at each UHC/Urban DOTS Center,
- Establishing a drug management system, including a system to deliver drugs to the district and then onwards to the upazila/DOTS centre,

- Establishing a supervisory system,
- Establishing a system for monitoring and evaluation.

3.2.4 HR development

The importance of HR development derive from the successful implementation of the c-PMDT pilot projects. A designated Outpatient DR TB Team based at the UHC/DOTS Center will serve as the outpatient center for monthly follow-up visits. The Outpatient DR TB Team will refer the patient for hospitalization at the start of treatment and whenever needed. It is expected that an experienced Outpatient DR TB Team will eventually be able to start stable patients on treatment without hospitalization in consultation with respective PMDT committee .

There are two general targets:

1. All staff involved in diagnosing TB and caring for TB patients are trained on: when to presumpt(suspects) DR TB; how to send Xpert MTB/RIF specimens for DST and what procedures to follow, based on the results of the Xpert testing.
2. Establish an Outpatient DR TB Team at each UHC/Urban treatment center responsible for the community-based management of all DR TB cases.

The PMDT Expansion Plan 2013-2017 assumes no new hires for the Outpatient DR TB team, rather it draws from existing staff. Most UHCs will have 0 - 15 patients, and it is thought that existing staff can manage the workload. Each Outpatient DR TB Team HR needs should be considered specifically:

1. Centrally at the NTP.
2. For the initial hospitalization period at treatment initiation center (Hospital).
3. At implementation level (district and UHC level/urban treatment center).
4. In the laboratory.

The HR needs are outlined in Table 3.8 and align with what is in the National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition.

The training needs are extensive with all the UHC and Urban/Peri-urban Outpatient DR TB Teams requiring three days of initial DR TB training with a one-day refresher training course every 6 months should however ensure that the TLCA, as part of their regular duties, allocates time to supervise the community-based DR TB programme, in their catchment area.

The PMDT Expansion Plan 2013-2017 also draws from an existing pool of health care workers to be the DR TB DOT Providers. While the DR TB DOT Provider will be given an additional incentive and transportation allowance, they are not to be considered new hires and in most cases are government employees already within the health system. The PMDT Expansion Plan 2013-2107 assumes the engagement of a District Coordinator in each district implementing c-PMDT. This is often a CDC consultant, an NGO employee, or a government staff.

Table 3.8 Human resource needs at central, regional and laboratory levels .

Central at the NTP Given the size of the scale-up a department at the NTP will be created and dedicated to MDR TB.	• 1 MDR TB Deputy Manager • 2 Physicians (assist with supervision and training) • 1 Training Manager • 1 Administrative Assistant • 1 Accountant • 1 Data Officer
District and UHC/ City Corp and Urban Health complexes. Each District should have a dedicated supervisor/coordinator for all the UHCs/DOTS Centers providing DR TB care. Each UHC will have 7 to 11 people trained, of which there are 8 UHCs per district on average. This would mean training 60-100 people per district/city corporation.	Upazilla Health Complex (UHC) based outpatient DR TB team should be consist of: • Upazila Health and Family Planning Officer (UH&FPO)-Team Leader; • Medical Officer of Disease Control (MODC)-Member Secretary; • Residential Medical Officer (RMO)/Medical Officer (MO) [for back up, if MODC is not available or gets transferred out]; • TB and Leprosy Control Assistant (TLCA). He/she will act as the DR TB DOT Supervisor (and can also be a DR TB DOT Provider if patient lives near-by); • Statistician for medical record keeping; • Medical technologist-Lab (GO/NGO); • Representative from Partner NGO. For Urban/ Peri-Urban Team to consists of: In urban settings, DR TB team should be formed according to respective organogram of the organization. The team leader of the team in the urban areas should be a registered medical doctor under the Bangladesh Medical and Dental Council (BMDC).
Laboratory	**Reference Laboratory:** • As per NTRL and RTRL human resource plans. **DR TB Diagnostic Centers with Xpert:** • 2 Laboratory Technicians pre Xpert center
DR TB DOT Providers The Outpatient DR TB Team to be respoinsible for Training and supervising the DR TB DOT Provider.	DR TB DOT Providers Each DR TB DOT Provider to support between 1-3 patients.

3.2.5 Second-line anti-TB drug supply

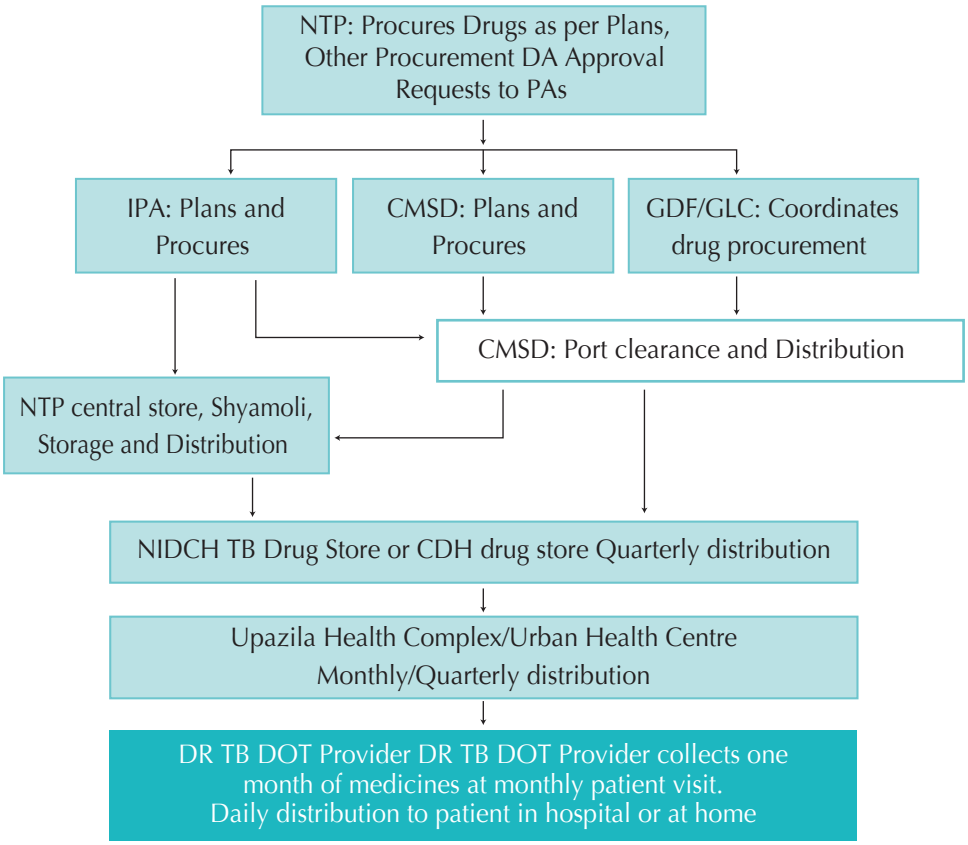
Second-line anti-TB drugs are obtained from the Global Drug Facility (GDF); the WHO Country Office for Bangladesh will continue to provide technical assistance on placing drug orders. Funding for second-line drugs is described in Section 5.

Second-line anti-TB orders will be placed every six months with the GDF. The supply chain for second-line anti-TB drugs will remain as is described in the Operational Manual for DR TB 2nd Edition and as is described in the Procurement and Supply Management Plan for the period from July 2012 to June 2015. The International Procurement Agent (IPA) is responsible for the procurement of goods including health products under the GFATM grant as per approved Bangladesh GFATM work plan. The IPA procurement regulations encourage and ensure transparency and competitiveness in procurement.

The IPA will also adhere to national procurement protocols and regulations (PPR-2008) for the procurement of locally sourced goods. The Central Medical Stores Depot (CMSD) is entrusted by the Government of Bangladesh to conduct procurement for the Ministry of Health & Family Welfare (MoH & FW) and draws from the Government of Bangladesh and other donor funds. Additionally, in procuring good and services in Bangladesh the IPA also adheres to the protocols of the Public Procurement Regulation (PPR-2008).

A more comprehensive representation of the drug procurement organizational structure is illustrated in Figure 1.

Figure 1. Second-line drug supply chain



3.2.6 Monitoring and evaluation

The formats in the National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition shouldl be used and completed by all UHCs and urban/peri-urban treatment centres implementing DR TB activities.

A system for registering all documented DR TB cases in Bangladesh need to be developed. The register will provide following information:

- All RIF positive patients by Xpert.
- Confirmation DST results of RIF positive (when done) by Xpert.
- Any patients found to have MDR TB by conventional DST (even if Xpert is RIF negative or not done).
- The date MDR TB treatment was started for all patients with RIF positive or documented MDR TB by conventional DST methods. If treatment was not started, reason should be indicated in the comments.

Any DST result from an outside non-quality assured laboratory should be repeated at one of the reference laboratories.

A data manager will be positioned in each region. There are plans to turn the electronic register system into a web-based system (to allow access to records via the internet with strict patient confidentiality safeguards). Furthermore, there are plans to implement a mobile telephone system to record DOT visits. Before widespread implementation of the mobile telephone system will be tested and piloted.

Model of care and practical considerations for the implementation of national policy for PMDT 4

The current SOP for c-PMDT (1st Edition) and the National Guidelines and Operational Manual For Programmatic Management of Drug Resistant TB (DR TB) second edition are up to date and are consistent with the WHO 2011 PMDT Guidelines. Both guides will facilitate the scale-up of PMDT activities. This section describes the practical considerations to implementing the PMDT Expansion Plan 2013-2017 and highlights areas that require strengthening and in some cases change.

4.1. Case-finding strategies

To facilitate the case finding / rapid diagnosis of DR TB there are three areas that are key to the success of the goals and targets:

- The use of Xpert MTB/RIF instruments throughout the country to diagnose DR TB.
- The training of all required staff on the protocols of when to screen for drug-resistance with Xpert MTB/RIF.
- A reliable transportation system to transport specimens and return results.
- The performance of second-line DST on all MDR TB patients (this will be particularly important if transitioning to the 9-month regimen).

4.2. The drug regimen and treatment

Building the professional and structural capacity to treat DR TB patients will be built over the 5 years. This includes ensuring that a sufficient number of specialized hospital wards and professional expertise are available during the initial hospitalization period and that Outpatient DR TB Teams who can manage outpatient care and supervise DR TB DOT Providers are in place.

DR TB patients under routine conditions will receive one of two standardized regimens:

1) The NTP approved 2-year regimen
2) A shorter regimen for MDR TB (which at the time of this writing it is undetermined whether it will be a gatifloxacin- or moxifloxacin-based short regimen and whether it will be 9 or 12 months).

(1) The NTP approved 2-year regimen (duration of at least 20 months)

The recommended Standard MDR TB Regimen is as follows:

8{Km-Z-Lfx (Ofx)-Eto-Cs}/12{Lfx (Ofx)-Eto- Cs-Z}

The numbers in front of the drug abbreviations represent the average number of months the drugs are to be given. For exact length of the intensive phase and total treatment lengths depends on sputum culture convertion time.

Table 4.1 Length of Treatment for the Standard MDR TB Regimen

Date of first sustained conversion*	Length of injectable agent	Length of Total treatment for Standard MDR TB regimen
Between month 0 and 4	8 months	20-22 months
Between months 5 and 8	Add 4 months from conversion date	Add 18 months from conversion date

*Date of first negative smear and culture by two consecutive months

Some PAS will have to be ordered for the following situations:

1. The patient's strain tests are resistant to either a fluroquinolone or the injectable agent but not to both or to manage any advers drug reaction.
2. The patient is a contact of a patient who died on a second-line drug regimen or a contact with a known history of resistance to second-line drugs. PAS may be added to strengthen the regimen.
3. The patient cannot tolerate cyscloserine (one of the drugs in the regimen). PAS can be the substitute drug.
4. The patient is pregnant. PAS can be included in the regimen, if approved by a DR TB expert.
5. XDR TB (see below for the XDR TB regimen)

Some capreomycin will have to be ordered for the following situations:

1. For patients with strains test result resistant to kanamycin (or amikacin) or who cannot tolerate kanamycin, capreomycin can be substituted for kanamycin.
2. XDR TB (see below for the XDR TB regimen)

For ordering purposes, approximately 5% of the patients starting the standardized regimens will need regimen adjustments (this does not include XDR TB)

(2) The short-course gatifloxacin- or moxifloxacin-based regimen (duration of 9 to 12 months) WHO recently developed a policy on the shorter course MDR TB regimen and supports its use, provided a number of criteria are in place. Criteria examples include; ethical approval, operational research conditions and the engagement of a monitoring board that is accountable and reports to WHO. For more information see www.who.int/entity/tb/challenges/mdr/short.../index.html. The plan anticipates a gradual increase of patients with MDR TB being placed on the short-course gatifloxacin- or moxifloxacin-based regimen as described in Table 4.1. The

exact scale-up rate of the short-course regimen is hard to predict and as such these approximate target numbers should be considered as preliminary (as more evidence becomes available this could result in accelerating the transition to the short course regimen or abandoning the transition).

This PMDT Expansion Plan 2013-2017 anticipates an increase in the use of the short-course regimen starting July 2013, provided a number of criteria, as indicated below are fulfilled.

1. For areas beyond the Damien Foundation catchment area the regimen is reviewed and approved by the Bangladesh Ethics Board.
2. The drugs are procured in advance and are of a quality, approved by the Bangladesh Regulatory Authorities.
3. Delivery of treatment to be undertaken according to international standards, which assess the effectiveness and safety of the regimen.
4. The establishment of a monitoring system, conducted by an independent board is set up by and reports to WHO.
5. DST of a fluoroquinolone is done at the start of treatment with a short-course MDR TB regimen. This can be in the form of liquid culture or molecular testing such as HAIN. If HAIN is used it will be considered as an initial screening test to be followed up by culture and DST. (Note: patients resistant to a fluoroquinolone should not get the short course regimen, rather an individualized 20 -24 month regimen designed to treat pre-XDR TB or XDR TB).
6. A decision on whether to use moxifoxacin instead of gatifloxacin (to avoid the ADR of dysglycemia) will have to be made by the NTP in consultation with the WHO sponsored independent monitoring board.
7. The willingness to apply the findings of international research on the short-course regimen.

Table 4.1 is the 9-month regimen based on experience from the Damien Foundation. Possible changes to this regimen include moxifloxacin instead of gatifloxacin and a duration extension to 12 months. These changes would be considered, based on experiences from other countries and the recommendations from an independent planning and monitoring board.

Table 4.2 The 9-month regimen used in Damien Foundation catchment area

Duration of treatment (Month)	Drug	Weight in kg		
		25-32	33-50	>50
1-4 (daily) (may be prolonged)	Gatifloxacin* (400 mg)	1	1.5	2
	Z (400 mg)	2.5	4	5
	E (400 mg)	1.5	2	3
	H (300 mg)	1	1.5	2
	Prothionamide (250 mg)	1	2	3
	Clofazimine (250 mg)	1	2	2
	Kanamycin	15 mg/kg	15 mg/kg	15 mg/kg
5th-9th (to 12th) (daily) (5 months fixed)	Gatifloxacin* (400 mg)	1	1.5	2
	Z (400 mg)	2.5	4	5
	E (400 mg)	1.5	2	3
	Clofazimine (50 mg)	1	2	2

*While adverse drug events related to dysglycaemin have been reported in some population, e.g., the elderly, this has not been a major problem in the Bangladesh project. Nonerheless, product availability may become limited and necessitate consideration of an alternative fourth-genetation fluoroquinolone, such as moxifloxacin.

For issoniazid and prothionamide, the highest dosages are given from 55 kg onwards only.

For the treatment of MDR TB, isoniazid is used in a higher dosage than for first- line treatment, thus 300 mg tables are utilized.

Patients aged 45 years and over should receive max. 0.75 g; kanamycin should be given intermittently in case of extension of the intgensive phase; kanamuycin should not be given to pregnant women.

Z = pyrazinamide, E = ethambutol; H = isoniazid

XDR TB will be treated based on past medical history. Drug regimens for XDR TB should be procured based on the predicted number of cases and should include the following drugs:

The Standard XDR TB Regimen

The recommended Standard XDR TB Regimen is as follows:

12(Cm-Z-Mfx-PAS-Cs-Amx/Clv- Lzd -Cfz)/12(Z-Mfx-PAS-Cs-Amx/Clv- Lzd -Cfz)

XDR TB and failures of the Standard MDR TB Regimen should be treated with the above regimen. Ethionamide can be added if there is evidence to suggest it is still susceptible. Additional drugs from Group 4 or 5 and Bedaquiline or other new investigational agent as indicated can also be added under the review by a PMDT committee or an expert in the field of XDR TB treatment. Individualized treatment based on DST results (if possible) is best for management of XDR TB (if possible). The exact regimen (individualized) for all XDR TB patients will be determined by Clinical Management Committee considering DST reports.

The exact recommendations and drugs used to treat XDR TB may vary and the above regimens are to acknowledge that some patients will require individual regimens with costly drug to treat higher levels of drug resistance.

Table 4.3 Length of Treatment for Standard XDR TB Regimen

Date of first sustained conversion*	Length of injectable agent	Length of Total treatment for Standard MDR TB regimen
Between month 0 and 2	12 months	24 months
Between months 3 and 6	Add 10 months from conversion date	Add 22 months from conversion date

4.3. Delivery of care

The model and strategy for the delivery of care is described in the SOP for c-PMDT. Commitment to and the institutionalization of training, refresher training and a supervisory system for the Outpatient DR TB Team and the DR TB DOT Providers, will determine the success of the c-PMDT programme and patient outcomes.

According to the plan and updated protocols all patients will initially be hospitalized. The development and expansion of infrastructural and professional capacity over the next two years will enable this practice. Nonetheless, as the capacity and skill set of Outpatient DR TB Teams develop, it is expected that patients, considered stable, can initiate treatment in the community, i.e. they will not be hospitalized in consultation with the PMDT committee. If in the meantime, hospital waiting lists lengthen, initiating treatment in the community under the DR TB DOT Provider system should be implemented as a back-up strategy.

4.4. Infection control

Infection control measures are described in the recently published guideline "National Guidelines for Tuberculosis Infection Control" Bangladesh in 2011 and will continue to be implemented during the expansion of the programme. All health care providers will periodically be provided with personal N-95 masks, as a protective measure who are exposed to DR TB patients. Clinics and hospitals will be reviewed on a case-by-case basis and an infection control plan will be developed and implemented at each facility, which could have cost implications.

Rapid detection of drug-susceptible and drug-resistant TB and effective treatment are vital to stopping the further transmission of TB and DR TB.

4.5. Adverse drug reaction (ADR) management and monitoring response to therapy

To improve the management of adverse reaction a number of system strengthening initiatives and protocols are to be implemented under the PMDT Expansion Plan 2013-2017:

1. The implementation of an initial enrollment intake form with a monthly encounter paper-based form (this form can also be in electronic format).
2. Electronic improvements to the monitoring of smears and cultures while on treatment.
3. Monthly monitoring of potassium and creatinine while on the injectable agent. Replacement of potassium (and magnesium) as needed.
4. TSH monitoring every three months at minimum for signs of hypothyroidism in patients taking both PAS and ethionamide. Patients receiving only ethionamide can have their TSH checked every six months.
5. Baseline and immediate audiometry implementation for all patients with hearing loss.
6. Provision of ancillary medicines at no cost to all DR TB patients.
7. The measurement of BMI at the start of treatment to calculate and monitor nutritional status and support as needed.

5.1. Estimated total costs

The cost of the PMDT Expansion Plan 2013-2017 is determined by a number of assumptions, which are outlined in Table 5.1. A worksheet is available from the NTP, which has details on all calculated costs.

5.1. Estimated total costs

Assumptions		
1 USD = 80 Tk.		
Length of treatment	24	Months
Incentive for DR TB DOT Provider (travel, phone, incentive) 1800 Taka	23	USD
Patient social support/travel allowance	19	USD
Average cost of one day in hospital (estimate)	15	USD
Average hospitalization in months	56	Days
Cost of NTP approved 2-year regimen	2500	USD
Cost of moxi-based short regimen	2,116	USD
Cost of gati-based short regime	536	USD
Monthly cost of Outpatient DR TB team	864	USD
Cost of doing one Xpert test (including transportation cost, technician cost, electricity…etc.)	12	USD
Average cost of transportation of a specimen (Xpert or culture) includes cost of Falcon tube, CPC and transportation	2.5	USD
Cost of LJ culture per test	20	USD
Cost of MGIT per test	30	USD
Cost of LPA per test	25	USD
Average cost of 3 day MDR TB training	3600	USD
Average cost of 1 day MDR TB refresher	1800	USD
Average number of UHCs in a district	8	
Average number of Urban Centers in Dhaka	24	Urban TB Centre
Average number of Urban centers in a city corporation not including Dhaka	6	Urban TB Centre

Tables 5.2 to 5.10 assist in estimating overall costs, providing insight into the estimated implementation costs of the plan and Table 5.11 estimates the total costs of implementing the PMDT Expansion Plan 2013-2017. The cost per patient is estimated in Table 5.12.

Table 5.2. Total estimated direct costs per patient on NTP approved 2-year regimen.

Component	Average Cost per month (USD)	2 Year Cost amount (USD)	Comments
Second line drugs (cost of injectable averaged over full treatment period)		2,500	For KM-Lfx-Cs-Eto-Z
Ancillary drugs	7	168	
Hospitalization (based on avg. stay = 2 months at 10 USD a day)	Not applicable	840	Government contribution
Transportation for DR TB DOT Supervisor estimated at one supervisor every 2 months at 10 USD per visit.	5	120	
DR TB DOT Provider monthly incentive	23	540	
One time costs for DR TB DOT Provider (mobile phone, storage box, umbrella, torch, bag)	50	50	
Social support and transportation for patient.	19	450	
Sputum smears, Xpert, cultures, and DST and transportation of all tests (assumes one Xpert, culture monthly and then every other month after conversion and one DST test).	See assumptions	452	
Baseline and follow-up investigation costs (liver function test, thyroid function test, blood sugar, kidney function test, X-ray, Blood electrolytes...etc) - first 12 months only.	12	144	
Other/misc costs	5	120	
Total cost per patient for NTP approved 2 -year regimen.		**$5,984**	
Support costs.		**$3,484**	
Drug Costs.		**$2,500**	

Table 5.3 Estimated total direct costs per patient of shorter course MDR TB regimen (Operational Research)

Component	Average cost per month (USD)	9 month amount (USD)	Comments
Second-line drugs (cost of injectable averaged over full treatment)		1,129	Assumes costs of FQ at 1 USD/day, Cfz= .5 USD/day
Ancillary drugs	7	63	
Hospitalization (based on avg stay = 2 months at 10 USD a day)	Not applicable	840	Government Contribution
Transportation for DR TB DOT Supervisor estimated at one supervisor every 2 months at 10 USD each visit	5	25	
DR TB DOT Provider monthly incentive	23	203	
One time costs for DR TB DOT Provider (mobile phone, storage box, umbrella, torch)	50	50	
Social support and transportation for patient	19	169	
Sputum smears, Xpert, cultures, and DST and transportation of all tests (assumes one Xpert, culture monthly and then every other month after conversion and one DST test).	See assumptions	280	
Base line and follow-up investigation cost (liver function test, thyroid function test, blood sugar, kidney function test, X-ray, Blood electrolytes...etc) - first 12 months only	12	72	
Other and misc costs	5	45	
Total cost per patient for moxi-based regimen		**$2,759**	
Support costs		**$1,630**	
Drug costs		**$1,129**	

Table 5.4 Cost of screening 1000 presumptive (suspects) DR TB cases

Component	Cost per unit (USD)	Number	Cost per year to screen 1000 patients (USD)
CPC Tubes and transportation.	2.5	1000	2500
Screening tests using Xpert.	12	1000	12000
Confirmation tests using LJ, MGIT or LPA (assuming all RR-TB needs confirmation) Cost varies for H&R in MGIT = 90USD, LJ= 60, Hain=30 USD. (average take at 60).	60	200	12000
Total			26500

Table 5.5 Infrastructure costs for DR TB facilities**

Infrastructure	One time costs (USD)	Number needed	Total (USD)
NIDCH	20,000	1	20,000
Shyamoli	50,000	1	50,000
Chittagong CDH	20,000	1	20,000
Rajshahi CDH	20,000	1	20,000
Sylhet CDH	20,000	1	20,000
Khulna CDH	50,000	1	50,000
7 Segregation hospital (these are 20 bedded hospitals).	50,000	7	350,000
One room for Xpert at each facility	3,000	80	240,000
CDC (44 facilities)	20,000	44	880,000
Government contribution to general upkeep (management and running of NIDCH, CDHs, 7 segregation hospitals, and 44 CDCs).	Government contribution		
Total Infrastructure (not including government contribution)		100%	1,650,000
Amount of Infrastructure cost in year 1		0%	None
Amount of Infrastructure cost in year 2		33%	550,000
Amount of Infrastructure cost in year 3		33%	550,000
Amount of Infrastructure cost in year 4		33%	550,000
Amount of Infrastructure cost in year 5		0%	None

**NOTE: There is much needed infrastructural improvements to be made and the numbers in Table 5.9 represent the minimum that should be done under the plan. Securing funding for improvements beyond this is strongly encouraged.

Table 5.6 Annual labatory running costs (rough estimates)

Infrastructure	Costs/year (USD)	Remarks
NTRL (Running costs for non-government personnel and maintenance).	150000	
RTRL (Running costs for non-government personnel and maintenance) or culture Lab (Plan to have 6, one in each region).	70000	
NTRL Government contribution.	35000	Government contribution.
RTRL Government contribution.	35000	Government contribution.
Totals	290000	

Table 5.7 Annual training costs/district

Component	District training costs (Initial Training) / year (USD)	Cost of a refresher course (1/year) (USD)
Cost of training an upazila on when to screen for DR TB, how to transport specimens and receive results.	300	150
Three day training (training of Outpatient DR TB Team on DR TB) course. Note, in the GFATM proposal it is only one day. A refresher training course should happen every 6 months.	3,600	1,800
Initial training cost for DR TB DOT Providers (there will be on average one DR TB DOT Provider/ patient and most trainings will be done on a one to one basis. The facilitator will receive 3000 Taka. It assumes an average of 20 patients per district, i.e. 10 DR TB DOT Providers on average).	375	
A refresher training course / 6 months at a district level. 1000 Taka / participant with 15 DR TB DOT Providers / district. 3 Facilitators at district level to receive 1000 Taka per Facilitator for half a day of training.		238
Training costs per hospital (USD)		
Training hospital staff (3 days).	$3,600	$1,800
Training hospital managers (5 days).	$5,000	$2,500

Table 5.8 Estimated PMDT costs over a five-year period, 2013-2017

	2013	2014	2015	2016	2017	
Costs (USD)						**TOTAL (USD)**
Drug costs on NTP approved 2-year regimen.	2,125,000	1,875,000	625,000	625,000	250,000	5,500,000
Support costs on NTP approved 2-year regimen.	2,961,400	2,613,000	871,000	871,000	348,400	7,664,800
Drug costs on moxi- or gati-based short regimen.	169,344	733,824	1,862,784	2,314,368	2,878,848	7,959,168
Support costs on moxi- or gati-based short regimen.	244,538	1,059,663	2,689,913	3,342,013	4,157,138	11,493,263
Cost of screening for DR TB.	159,492	239,239	279,112	299,048	318,985	1,295,876
Running costs of DR TB Outpatient Team.	165,888	323,136	499,392	499,392	499,392	1,987,200
Central NTP management towards DR TB.	48,000	48,000	48,000	48,000	48,000	240,000
Supervisory costs.	149,831	344,611	539,392	539,392	539,392	2,112,617
Infrastructure.	0	550,000	550,000	550,000	0	1,650,000
Laboratory.	605,000	815,000	815,000	815,000	815,000	3,865,000
Training.	114,288	222,488	279,363	168,213	168,213	952,563
TOTAL (USD)	6,742,780	8,823,960	9,058,954	10,071,425	10,023,366	44,720,486

Table 5.12 Estimated total cost per patient

Total patients treated	9250
Cost per patient	4835 USD

In summary, the total estimated cost to implement the PMDT Expansion Plan 2013-2017 over the next five years is 44.7 million USD. The indicated direct patient costs and programme costs are estimates and as such the actual cost of the plan may alter considerably. The costs of the plan assumes a transition from the more costly NTP approved 2 year regimen to the shorter moxifloxacin- or gatifloxacin-based short regimen. If the transition does not occur, the costs of the plan could be an additional 10 to 15 million USD over the five year.

The costs in this section do not try to capture the many financial inputs from the Bangladesh MoH. Neither does the plan calculate the costs of the NTP which has more than 80 government employees or the 100s of MoH staff that will help care for the hospitalized and community-based DR TB patients.

5.2 Funding availability and gaps

The availability of funding for the PMDT Expansion Plan 2013-2017 is partially secured, with major contributions from: 1) GFATM (and its recipients); 2) The Bangladesh Government; 3) USAID TBCARE II; (4) The Damien Foundation and (5) others.

The anticipated funding gap will be estimated on an annual basis by the NTP. There is substantial funding already in place for years 2013 and 2014, which will allow the NTP to make significant progress towards the targets laid out in the expansion plan.

At the time of this writing it is estimated that the GF contribution towards PMDT is over 1.3 million USD in 2013 and over 1.6 million in 2014.

5.3 Resource mobilization

Given the success of the PMDT to date in Bangladesh, donor agencies and partners are convinced that the country is capable of a more extensive scaling-up in the coming 5 years. Mobilizing additional funding is anticipated as the NTP demonstrates initial progress towards target indicators. The Bangladesh MoH, the NTP and collaborating partners have all expressed their full support of the PMDT Expansion Plan 2013-2017 and their commitment to pursue all possible resources to ensure the expansion plan's full implementation.

The WHO Country Office for Bangladesh in consultation with WHO RO-SEAR and WHO HQ will continue to play an important technical role in supporting the NTP to identify and pursue available funding for the PMDT Expansion Plan 2013-2017. Funding opportunities with the GFATM and other bilateral and NGO partners will be explored for years 2015 to 2017.

Work plan and timeline for expansion 6

Table 6.1 proposes a timetable to implement the major activities of the PMDT Expansion Plan 2013-2017. On an annual basis however a more detailed work plan will be drawn up by the NTP, which will outline actual timelines in accordance with funding available.

Table 6.1. Proposed work plan and timeline for expansion activities, 2013-2017

MDR TB Expansion Timeline General Work Plan 2011-2015 - Bangladesh	2013	2014	2015	2016	2017
Activiry Area 1: Publish DR TB Expansion Plan and begin implementation					
Finalization of PMDT Expansion Plan 2013-2017					
Detailed NTP annual work plan in achieving targets in Exp-plan					
Detemine Distrcts/City Corps when and where to expand in 2013-2014					
Detemine Distrcts/City Corps when and where to expand in 2013-2018					
Securing funding for the expansion plan 2013-2016					
Implement the PMDT expansion Plan 2013-2017					
Activtiy Area 2: Implement standard operating and clinical procedures for the manegment of DR TB					
Publish & distribute SOP for c-PMDT and Operational Manual for DR TB					
Implement protocols SOP for c-PMDT and Operational Manual for DR TB					
Activtiy Area 3: Designate sufficient NTP staff for supervision and establish a PMDT coordination committee in each division					
Write job descriptions and desigante PMDT Coordinators					
Desigante NTP staff to focus on PMDT					
Supervisiory tools in place for the PMDT programme					
Activtiy Area 4: Procure second line drugs, ancillary drugs for adverse effects and equipment.					
Order secon line drugs					
Order ancillary drugs (Onec a year)					
N-95 Masks					
Lab Reagents (every 6 months)					
Order Xpert MTB/RIF machines					
Order Xpert Cartidges (every 6 months)					
Order Other equipment supplies					
Activtiy Area 5: Establish and/or mainatain DR TB Treatment Facilities (includes training staff for the facility)					
NTDCH					
Shyamoli					
Chittagong CDH					
Rajshahi CDH					
Sylhet CDH					
Khulna CDH					
Seven segregation hospitals (approximately 10 beds each)	3	7	7	7	7
Activtiy Area 6: Expert MTB/RIF instruments in country					
Xpert (4 module) instruments in country	30	50	76	78	80
Number of solid culture and DST laboratories	4	6	6	6	6
Liquid culture (MGIT)	1	1	2	2	2
LPA molecular laboratory	1	1	2	2	2

MDR TB Expansion Timeline General Work Plan 2011-2015 - Bangladesh																				
	2013				2014				2015				2016				2017			
Activtiy Area 7: Train staff in expansion areas 2013																				
Train NTP DR TB Team																				
Refine and update training materials																				
Train hospital Staff																				
Number of districts with trained in c-PMDT	16				40				61				61				61			
Number of city corps trianed c-PMDT	3				5				6				7				7			
Refresher courses (once a year for all areas)																				

Expected impact of implementation and conclusions 7

Between 2013 and 2017, it is expected that approximately 50,000 TB patients will be screened for rifampicin resistance using Xpert MTB/RIF. During this period, a total of 9250 MDR TB patients will initiate treatment under this plan (1000, 1400, 1900, 2300, 2650 patients respectively each year- Total = 9250).

Without treatment, the majority of these 9250 patients will die after having transmitted MDR TB to their families and communities. Furthermore, a weak or indeed absence of an DR TB programme often stimulates self-treatment and the purchasing of substandard and/or inadequate quantities and combinations of medicines, which can lead to the development and spread of incurable forms of highly resistant TB. Early diagnosis and effective treatment will avert thousands of deaths over time, and by curing the disease patients will prevent the spread of infection to others, leading to a significant decrease in the incidence of DR TB.

The PMDT Expansion Plan 2013-2017 builds on the strengths of the existing TB control programme. It specifies goals for the expansion of the DR TB programme, proposes a timeframe for expansion, explains any necessary changes to be made to the existing standard operational procedures and clinical guidelines for DR TB and provides the roadmap to implement the plan.

If the targets, set forth in this PMDT Expansion Plan 2013-2017 are met by the Bangladesh National Tuberculosis Control Programme the incidence and prevalence rates of DR TB in Bangladesh will decrease. With equally strong DR TB and drug-susceptible TB programmes in place, there is no doubt that Bangladesh can meet the MDGs and the goals of the Stop TB Partnership.

Annex 1

Xpert instrument placement for 2012/13 for MDR TB screening (does not include Xpert Instruments that may be procured in 2013 from TB Reach)

Division	Na me of Center	District coverage	Number of Xpert Machines	Number of notified cases of TB
Dhaka	National TB Reference Lab (NTRL)	Mostly Dhaka CC, Narayangonj, whole country	2	17339
	Shamoly TB clinic	Dhaka CC and district	1	
	Chankharpool TB clinic	Dhaka CC and district	1	
	Tangail TB & Leprosy Hospital	Tangail, Gazipur, Sherpur, Jamalpur	1	3373
	CDC Mymensingh	Mymensingh	1	5808
	CDC B.Baria	Kishorganj, Narshindi, B.Baria	1	3216
	Anontopur TB & Lep Hospital	Netrokona, Sherpur	1	2590
	CDH Faridpur	Faridpur, Rajbari,Madaripur, Gopalgonj, Narail,Madaripur, Sariyatpur	1	1260
Khulna	CDC Khulna	Khulna, Bagerhat, Satkhira	1	2437
	CDC Jessore	Jessore, Narail, Satkhira	1	2360
	CDC Chuadanga	Chuadanga, Jhenaidah, Meherpur, Magura	1	1295
Barishal	CDC Barishal	Barisal, Pirojpur, Jahlokhati	1	2606
	CDC Patuakhali	Patuakhali, Borguna, Bhola	1	1942
Chittagong	RTRL Chittagong	Chittagong, Feni	1	11033
	CDC Rangamati	Rangamati, Khagrachori	1	584
	CDC CoxBazar	Coxbazar, Bandarban	1	2315
	CDC Comilla	Comilla, Feni, Chandpur, Noakhali, Laxmipur	1	5777
Sylhet	CDH Sylhet	Sylhet,Moulivibazar	1	4454
	CDC Sunamganj	Sunamgonj,Habiganj	1	3591
Rangpur	CDC Nilphamari	Nilphamari, Panchagor, Takurgaon	1	1743
	CDC Rangpur	Rangpur, Dinajpur, Kurigram	1	2969
Rajsashi	RTRL Rajshahi	Rajshahi, Chapainobabgonj	1	1822
	CDC Bogra	Bogra, Joypurhat, Gaibandha, Sherpur	1	3644
	CDH Pabna	Pabna, Nator,Sirajgonj	1	1880
			25	

Diagnosis started by Xpert (2012)

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