rGLC COUNTRY SUPPORT MISSION REPORT

Country: Myanmar

Inclusive dates of mission: 04th – 14th July 2018

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MoHS:

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Persons met during the Mission

As per Annexure-1

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Abbreviations and acronyms

aDSM	active TB drug-safety monitoring and management’
BHS	Basic Health Staff
Cfz	Clofazimine
CBTBC	community based TB care
Cs	Cycloserine
Dlm	Delamanid
DR-TB	Drug resistant TB
DST	Drug Susceptibility Testing
Eto	Ethionamide
FLD	First line anti TB drugs
GoM	Government of Myanmar
Gx	GeneXpert
Lfx	Levofloxacin
LPA	Line Probe Assay
Mfx	Moxifloxacin
NSP	National Strategic Plan
NTP	National TB Programme
Ofx	Ofloxacin
Open MRS	Open Medical Record System
PMDT	Programmatic Management of Drug resistant TB
RR- TB	Rifampicin Resistant TB
SDG	Sustainable Development Goals
SLD	Second line anti TB drugs
SL LPA	Second line Line Probe Assay
XDR-TB	Extensively drug resistant TB

I. Executive summary

i) TORs of the mission

Objectives of the PMDT mission

1. To provide technical assistance on multidrug-resistant tuberculosis (MDR-TB), clinical and programmatic management including Pilot project (Shorter Regimen)
2. To provide technical assistance on clinical management of drug-resistant tuberculosis (DR-TB) patients in need of new and repurposed drugs by ward round and clinical workshops
3. To follow up on recommendations made to improve MDR-TB management from the last MDR-TB mission (20th & 30th September 2017)
4. To observe PMDT activities at different levels (Region and District), to provide technical assistance for the improvement of activities
5. To participate in discussions with national DR-TB Expert Committee
6. To review current laboratory capacity and need for expansion in alignment with PMDT expansion plan

Activities

1. The consultants will review all National Guidelines, Manuals, Standard Operational Procedures related to DR-TB before commencing the mission.
2. Monitoring of PMDT activities will include review of laboratory performance, Procurement and Supply Chain Management, clinical activities and recording and reporting. The consultants will also interact and interview with patients, Community Health Workers and staff.
3. Technical assistance will be provided by a clinical expert(s) who will conduct a clinical workshop (Annexure-2).

ii) Findings and observations

[a] *Achievements*

- Myanmar is amongst the thirty high TB burden, high MDR-TB burden and high TB-HIV burden countries in the World and has made considerable progress in PMDT by expanding to all 330 townships since 2016. Patients enrolled on treatment have successively increased from 2,539 in 2016 to 2,666 in the year 2017.

- The laboratory capacity has also been enhanced by microscopy services in 527 centres, with gradual replacement to LED Microscopes. The molecular diagnostics have increased from 5 Gx machines in 2012 to 78 machines till July 2018. The total number of Gx tests done in 2017 was 93,072. The country has a definite plan of providing molecular diagnostics in all districts in a phased manner.

- Phenotypic liquid culture and DST for 1st and 2nd line drugs is being expanded from two sites in Yangon and Mandalay to another site in Taunggyi.

- Criteria for performing Gx have also been expanded to include all TB cases, including those with diabetes mellitus, and presumptive TB cases amongst HIV sero-positive at some sites. This would gradually be scaled up in the entire country, with an intention towards universal DST.

- Procurement of adequate quantities of drugs for MDR-TB patients has been ensured and the delay in starting treatment has been reduced.

- The country continues to maintain a very high treatment success rate of over 80% in MDR-TB patients and this has been made possible by the support and integration of community based TB care (CBTBC) activities with TB partners.

- Country has initiated the shorter treatment regimen and also treatment with new and re-purposed 2nd line drugs on a pilot basis.

- The National Strategic Plan (2016-2020) focuses on early diagnosis, timely and effective treatment, adequate financial and HR support, effective collaboration with partners and communities. The case detection of MDR-TB is proposed to have merely doubled by 2020 while maintaining treatment success rate of over 80%. The country expects that with these interventions the MDR-TB prevalence amongst the new cases would reduce by 20% compared to 2015 baseline.

[b] ***Main challenges***

- Human Resource and capacity limitation at all levels.
- Limited laboratory capacity and infrastructure and inadequate equipment maintenance.
- Sub optimal utilization of Gx at all levels due to poor sputum transport mechanism and poor laboratory networking.
- Over reliance on radiology for the primary diagnosis of TB resulting in over-treatment of primary complex. Instead, Gx should be effectively used as a diagnostic modality in symptomatic children.
- Prevailing sub-optimal external quality assurance mechanisms for laboratories require strengthening
- Recording and reporting primarily manual; electronic systems (Open MRS) needs to be improved and expanded.
- Gap between estimated and diagnosed MDR-TB cases.
- Gap between notified MDR-TB patients and their enrolment for treatment.
- Scale up of shorter MDR-TB regimen (STR).
- Monitoring and supervision needs to be intensified at the National and State level.

- Inappropriate infection control in hospital settings, including TB section in general hospitals and TB hospitals.
- Limited linkage between the NTP and private sector and communities.
- The funding for programme implementation is mainly external.

Priority recommendations of the mission (max 10):

Sl. No.	Recommendation	Responsible persons/agency	Timeline
1	Fill all vacant posts (including Laboratory Technicians) related to programme implementation and management at various levels, and train them on the latest guidelines.	NTP/MoHS/WHO Country Office/ Partners	Initiate in 2nd quarter 2018 and complete within the year
2	Identify the missing TB cases, enhance the case finding through improved sputum transport, actively engaging with partners, improve notification from private sector, target high-risk population and expansion of laboratory services.	NTP/ MMA/Other Partners	Initiate in 2nd quarter 2018 and ongoing
3	Enhance and optimize the laboratory capacity for 1st and 2nd Line DST including use of SL-LPA as initial test for FQ and SL injectable resistance.	NTP/NTRL/ WHO Country Office / Partners	Initiate in 2nd quarter 2018 and ongoing
4	Strengthen patient counseling to reduce diagnostic delays, develop better linkage with the private providers and other partners in order to reduce the gap between diagnosis and treatment.	NTP/MMA/ Other Partners	Initiate in 2nd quarter 2018 and ongoing
5	Scale up shorter MDR-TB Regimen (remove Ethambutol as exclusion criteria) and expand the use of newer and repurposed drugs.	NTP/ DR-TB Expert Committee	Initiate in 2nd quarter 2018 and ongoing
6	Decentralize ART availability and ensure its early initiation, facilitate TB screening amongst PLHIV.	NTP/ National AIDS Control Programme	Initiate in 2nd quarter 2018 and ongoing
7	Ensure funding sustainability beyond 2020	MoHS/NTP/WCO/ In-country Partners	Ongoing

Status of Priority recommendations of previous mission (2017)

Recommendations	Status	Comment
Improve RR/MDR-TB detection through improving access to Gx, strengthening sputum transportation from remote areas, Checking household and workplace contacts and expanding chest X-ray services as an initial screening among high DR-TB risk groups followed by Gx testing.	Ongoing	(i) Gx access improving (ii) Sputum transport needs further strengthening (iii) Contact examination to be strengthened (iv) X-ray services still not improved
Ensure enrollment of maximum MDR-TB patients diagnosed (Reduce the gap between notified & enrolled by <10%)	Ongoing	(i) Gap reduced to 17% but still high, recommendation continues for improvement
Initiate DST guided treatment to all TB patients through testing with Gx and ensuring FL & SL LPA testing for all RR-TB cases	Ongoing	(i) Initiated the process and testing available in two higher functioning laboratories, need to expand further
Improve access to newer drugs following the USAID donation programme	Ongoing	(i) Shorter regimen initiated (ii) Use of new and repurposed drugs initiated (iii) Need to expand and recommendation continues
Initiate Government accountability in electronic data base management at least for MDR-TB	Not done	(i) Recording and reporting largely paper based (ii) In some districts, electronic recording for MDR-TB patients initiated through use of open MRS (iii) Recommendation continues
Ensure continued funding and sustainability of the NTP and implementation of the National TB Strategic Plan	Ongoing	(i) Government budget contributes to one-third of the total budget with most of the components coming from Global Fund (ii) Needs to be prioritized for sustainability

Status of Priority recommendations of previous missions :

Recommendations	Status	Comment
Accelerate the enrolment of MDR-TB patients on treatment to meet the targets for 2016-17	Ongoing	• Expand Gx criteria • Expand MDR-TB centres • Notified DR-TB register (06) for tracking • Patient's education and counselling (encouraging counselling) chapter in DR-TB GL (April 2017) & counselling trainings
Enhance and optimize the laboratory capacity for first and second line DST including use of SL-LPA as initial test for FQ-and SL injectable resistance	Ongoing	• The first BSL-3 Laboratory in State level (TCG in Feb 2017) • SL DST for culture +ve at follow up Month 3 (all pt in PMDT). • SL LPA for all new MDR-TB patients (project TS) who are willing to enroll and preliminarily eligible for STR (Lab screening for STR)
Improve management of patients with MDR-TB and those with second line drug resistance including the programmatic expansion of new drugs, and a plan to use the shorter regimen for eligible patients.	Ongoing	• MDR-TB clinical training • Procurement of audiometers followed by training • Shorter Regimen (Q4 2017) • aDSM multiplying trainings
Ensure continued funding and sustainability of the NTP and implementation of the National TB Strategic Plan	Ongoing	• GF NFM (2018-2020) grant has been approved and signed.

Achieved	
Some progress/ ongoing	
No change	

Progress of recommendations from 2016 MDR-TB Annual Evaluation Meeting (1)

Sl. No.	Recommendations	Status	Comment
1.	To fill up vacant posts in NTP at all levels and Aung San TB Hospital and to provide capacity building (programmatic management and clinical management). To engage all health staff trained for MDR-TB management in PMDT.	Ongoing Ongoing	• Team leaders have been posted & doing TB tasks at their duty station. • Aung San TB Hospital, Deputy MS, Consultant Physician and Assistant Specialist (physician) have been posted • MDR-TB trainings towards clinicians done, S&R ongoing
2.	To strengthen the sputum transportation system from township level and all implementing partners to Gx sites and feedback mechanism of Gx results.	Ongoing	
3.	To maximize the utilization of X-pert testing per existing criteria and to expand the Gx criteria (all smear positive cases at the time of diagnosis and TB-DM co-morbid cases) to all townships.	Ongoing	
4.1	To distribute the updated DR-TB Guideline to all townships, MDR-TB centres, District Hospitals and referral hospitals and to provide trainings based on revised DR-TB guideline.	Done	
4.2	To provide all recording and reporting forms and registers to all townships.	Done	
4.3	Ownership of MDR-TB management including recording and reporting has to be decentralized to Township level.	Ongoing	
5.	To reduce the refusal cases for MDR-TB treatment by encouraging intensive counselling services and pre-enrolment support.	Ongoing	
6.	To encourage the proper and strict DOT (MDR-TB management) by effective	Done	

	utilization of PHS II and community volunteers in addition to the midwives currently working for PMDT.		

Sl. No.	Recommendations	Status	Comment
7.	To distribute the updated Infection Control Guideline and to provide IC trainings to all concerned health staff.	Done	
8.	MDR-TB Shorter Regimen (9-11 months) has to be piloted per Expert DR-TB committee decision.	Ongoing	Pilot Project has been launched in November 2017
9.	MDR-TB Case based recording and reporting system (Open MRS) has to be expanded to a total of 23 MDR-TB centres end of 2017.	Ongoing	
10.	To implement approved National aDSM (active TB Drug Safety Monitoring and Management) plan step by step.	Done	
11.	To conduct a meeting to find ways and means for proper MDR-TB DOT in Yangon Region.	Done	During Yangon Crisis Plan Meetings.

II. Detailed report

A. Introduction/Background (Health care set-up in the country, overall TB and DR-TB burden)

Myanmar with a population of 53 million is amongst the 30 high-burden countries as defined by WHO for TB, MDR-TB and TB/HIV co-infection. WHO estimates (Global Report 2017) the incidence of all forms of TB as 361/100,000 population and TB mortality, excluding TB-HIV, as 47/100,000 population. The current TB incidence is about the same as the earlier incidence rate of 365/100,000 in 2009-10 and there is an overall gap of about 28% in the case detection. The NSP (2016-2020) aims to reduce the TB incidence to 317/100,000 population and TB mortality to 34/100,000 population by the year 2020. Further, the MDR-TB prevalence amongst the new cases is also projected to reduce to 4% from the existing 5% (**Table-1**). The country also projects to increase the notifications to 285/100,000 population while maintaining treatment success rates to over 85% (**Table-2**).

Table-1

NSP (2016-2020) Targets

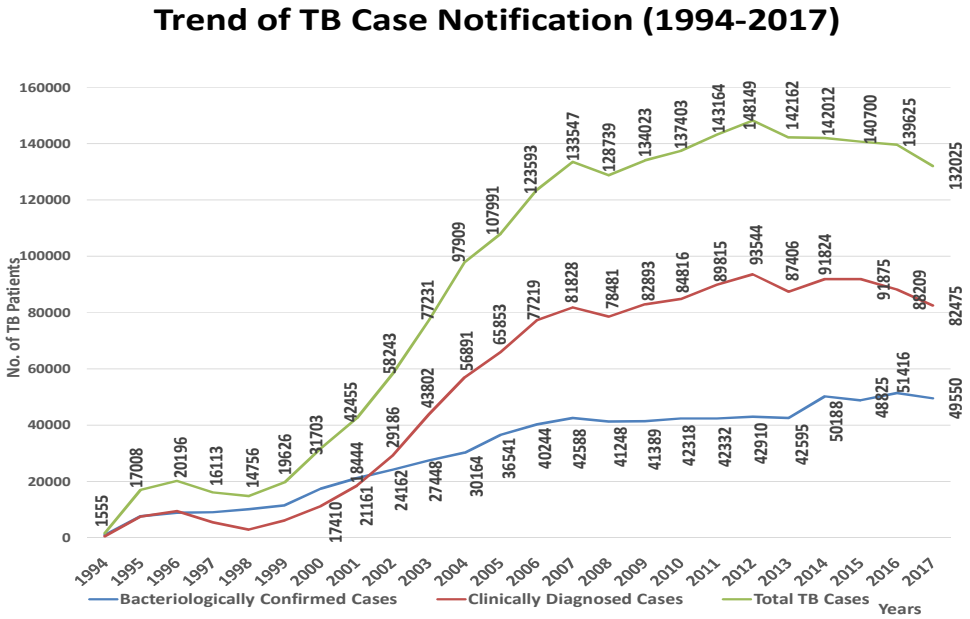
Impact Indicators	Baseline	Targets				
		2016	2017	2018	2019	2020
Reduce the TB incidence by 15% by 2020 compared to 2015 baseline (per 100,000 population)	369	358	348	337	327	317
Reduce the mortality due to TB by 35% by 2020, compared to the 2015 baseline (per 100,000 population)	53	48	45	43	41	34
MDR-TB prevalence among new cases reduction by 20% by 2020, compared to 2015 baseline	5%	4.8%	4.6%	4.4%	4.2%	4%

Table-2

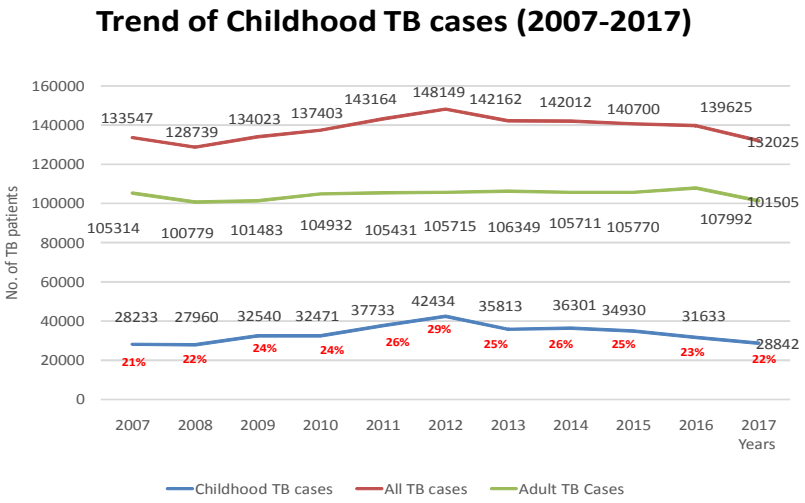
NSP (2016-2020) Targets

Outcome Indicators	Baseline	Targets				
		2016	2017	2018	2019	2020
Case notification rate per 100,000 population (bacteriologically confirmed+ clinically diagnosed)	276	294	292	290	288	285
Case notification rate per 100,000 population (bacteriologically confirmed)	97	106	108	110	112	114
Treatment success rate (bacteriologically confirmed)	85%	≥85%	≥85%	≥85%	≥85%	≥85%
Notification of RR-TB and/or MDR-TB cases	2793	4662	4787	4905	5014	5115
Number of RR-TB and/or MDR-TB cases to be treated	2207	3130	3297	3380	3510	3580
Treatment success rate RR-TB and/or MDR-TB	79%	81%	81%	≥82%	≥82%	≥82%

The graph below shows the trends in TB case notification in Myanmar from 1994 to 2017:



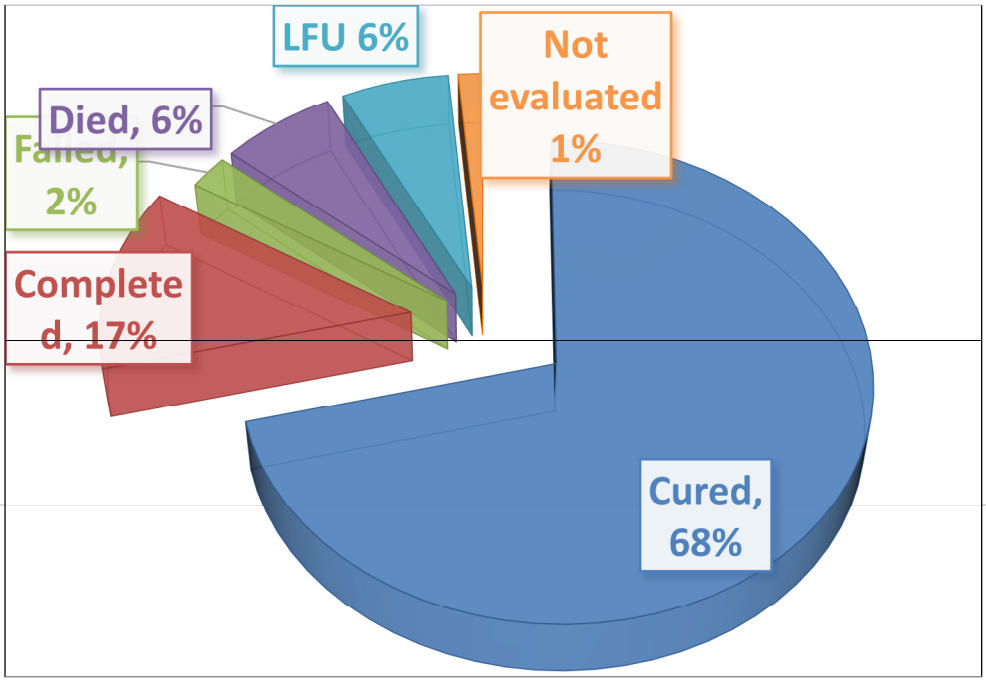
It is also observed that children contribute to 22% of the notification rate. This is primarily due to the clinicians treating primary complex as disease.



The Ministry of Health remains the major provider of comprehensive health care, even though the private sector is also contributing mainly in the larger cities of Myanmar, especially Yangon and Mandalay. PSI Myanmar and MMAPPM TB Project are the key contributors with which the programme is partnering in the effort. The private, for non-profit, run by Community Based Organizations (CBOs) and Faith Based Organizations (FBOs) are also providing ambulatory care though some also provide institutional care. The TB control services are provided through the regional / state and the district/township level hospitals/health centers (330).

Myanmar maintained the treatment success rate for bacteriologically confirmed TB cases for the 2016 cohort at 85% as shown in figure below:

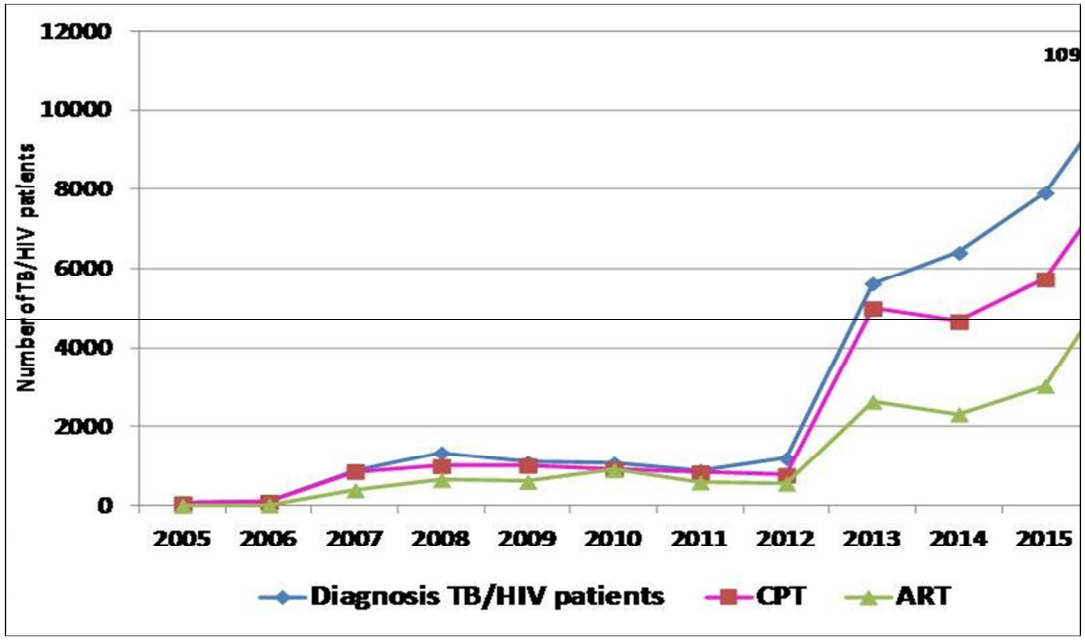
Figure 2: Treatment Outcomes of Bact Confirmed TB Cases (2016 Cohort) (*n*=48,964) (TSR 85%)



The third national TB drug-resistance survey (DRS) 2012-13 showed a prevalence of MDR-TB cases 5.0% among new cases and 27.1% among previously treated cases. As per the WHO Global TB Report 2016, the revised estimate for MDR-TB is ~9,000 annually, including 5,600 amongst new cases and 3,300 amongst previously treated cases.

As per the HIV sentinel surveillance, the prevalence of HIV among new TB patients during 2016 was reported to be 8.5%. The TB-HIV collaborative activities were initiated in 7 townships in 2005 and have expanded to cover 330 townships in 2016. The graph below shows the achievements in the TB-HIV collaborative activities (2005-2017):

Graph 3: Achievements in TB-HIV collaborative activities (2005-2017):



Testing of TB patients for HIV has been improving in Myanmar with a rate of 90% of the 130414 registered cases in the year 2017, of which 9% were HIV positive. Most of these patients (83%) got CPT. However, ART implementation is low at 63% (6371).

The country has developed National Strategic Plan (2016-2020). The key interventions are summarized in the figure below:

Strategic Directions and Key Interventions of National Strategic Plan (2016-2020)

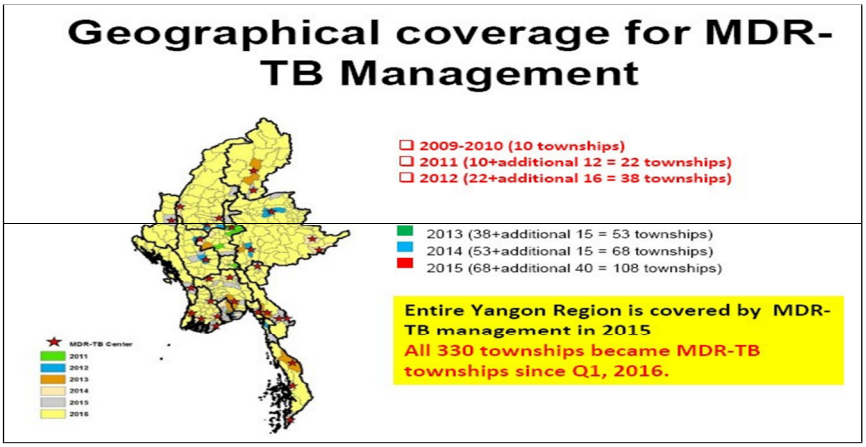
Strategic Direction I: Integrated, Patient-centered Care and Prevention
1.1. Accelerate the appropriate diagnosis of TB
1.2. Identify and treat all forms of TB, among all ages and including drug-resistant and drug-sensitive
1.3. Prevent transmission and the emergence of active TB
1.4. Intensify targeted action(s) to reach marginalized and at-risk populations
1.5. Implement a robust communication strategy, extending from policy makers to patient education
1.6. Engage all care providers, including NGOs and the private sector, in appropriate TB diagnosis and care
1.7. Promote and strengthen community engagement
1.8. Joint TB and HIV programming to enable decentralized and integrated services for TB and HIV

Strategic Direction II: Bold Policies and Supportive Systems
2.1. Secure human and financial resources for implementation of the NSP
2.2. Promote a coordinated and multi-sectoral response and policy development
2.3. Ensure inclusion of TB in UHC and wider economic development plans and activities (social protection)
2.4. Ensure a stable and quality-assured supply of drugs, diagnostic tests and commodities
2.5. Human resources for health

Strategic Direction III: Intensified Research and Innovation
3.1. Implement the prioritized research agenda
3.2. Enhance evidence-based programme monitoring and implementation

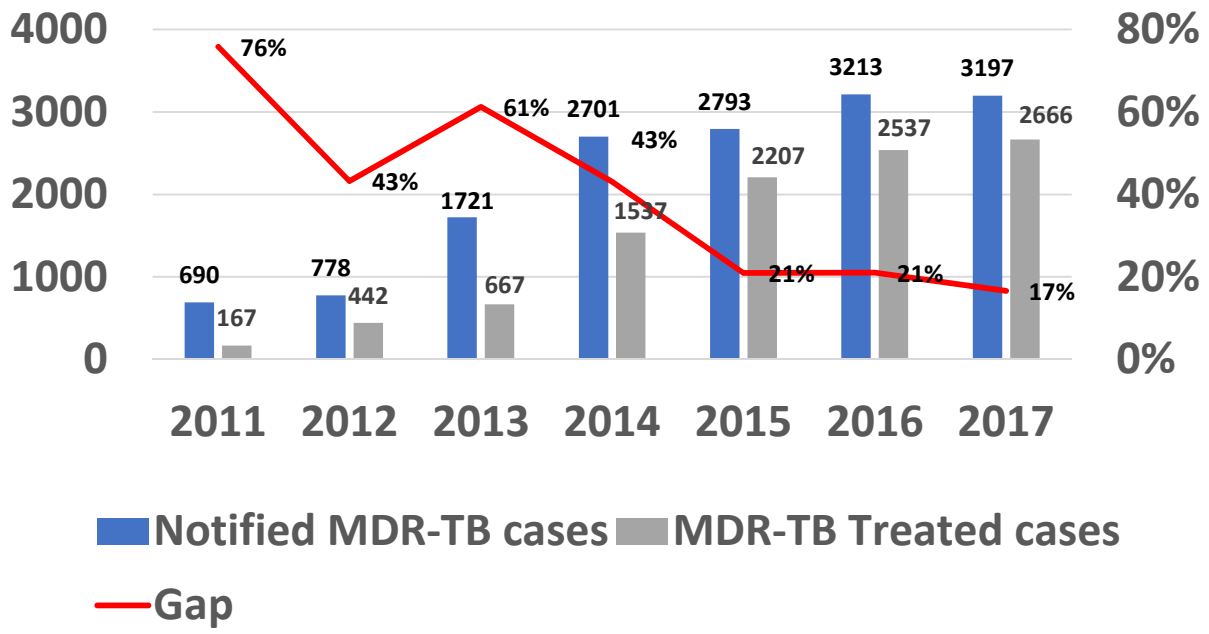
B. Overall programme performance (DR-TB)

The programmatic management of drug resistant TB was initiated in 2011 July after the experience from DOTS Plus pilot project in 5 townships each in Yangon and Mandalay Regions, and has increased to all 330 townships since 1st quarter of 2016.



WHO estimates that MDR/RR TB among the notified pulmonary TB cases to be around 9,000 with a rate of 5.1% in new patients and 27% patients in previously treated cases. The percentage of notified patients tested for rifampicin resistance was 15% in new cases and 63% in previously treated cases making a total of 27,699 for the year 2016. The programme has notified 3197 patients in the year 2017 but put on treatment only 2666. The gap between enrolment and treatment has reduced from 76% in the year 2011 to 17% in 2017. Even though there is a considerable closure of this gap, however, a large proportion of notified patients are still not on treatment.

Comparison of MDR-TB Case Notification and Treatment (2011 - 2017)
Gene-Xpert System



According to health department staff and health care providers, the gap between patients diagnosed and initiated on treatment is often due to patient refusal due to the need for injections, length of treatment, and side effects, and death before treatment initiation, loss to follow-up, and lack of access to care. The program is well aware of this gap, however, and the gap is closing over time.

Yangon region contributes the maximum number of MDR-TB patients. However, with the expansion and decentralization of diagnosis and treatment initiation to district level the contribution of Yangon has decreased during the recent years.

The country has expanded the criteria for Gx testing in an effort to move towards universal DST and ultimately all TB patients are to be tested for drug resistance. In order to achieve this, the capacity for testing through Gx is proposed to be enhanced from currently available 78 machines to 85 machines within this year and make the facility of molecular testing available in all the districts by 2019. In the recent years, it is observed that most of the MDR-TB cases detected are amongst the New MDR-TB suspects or amongst the Relapse. This further strengthens the argument for upfront DST in all TB patients. The treatment success rate (TSR) continue to be high with a success rate of 80% for the cohort of 2015. The TSR of the previous years is as noted below:

Year	No. of patients	TSR
2012	443	79%
2013	667	83%
2014	1495	81%
2015	2174	80%

There are currently 2 accredited culture and DST laboratories at Yangon and Mandalay with facilities for solid, liquid and LPA. These labs are performing DST for first and second line drugs. There is a culture lab in Taunggyi established in 2013 performing culture and it is being upgraded to perform DST.

There currently remains little information available on SLD resistance in the country, and certainly representative data on SLD resistance patterns is lacking. A total of 137 pre-XDR & 74 XDR-TB patients have been identified via various mechanisms between 2014 and Q1 2018. Of all the DR-TB patients detected, 89 have been put on treatment with New and Re-purposed drugs as mentioned in the table below :-

Number of cases treated with New and Re-purposed Drugs				
Year	***XDR***	***Pre-XDR***	***MDR-TB***	***Total***
2014 & 2015	10	--	--	10
2016	8	10	1	19
2017	9	7	9	25
Q1 2018	13	20	2	35
Total	**40**	**37**	**12**	**89**

***Recommendations*:**

- Undertake necessary steps in reducing the enrollment gap by strengthening pre-treatment counseling.

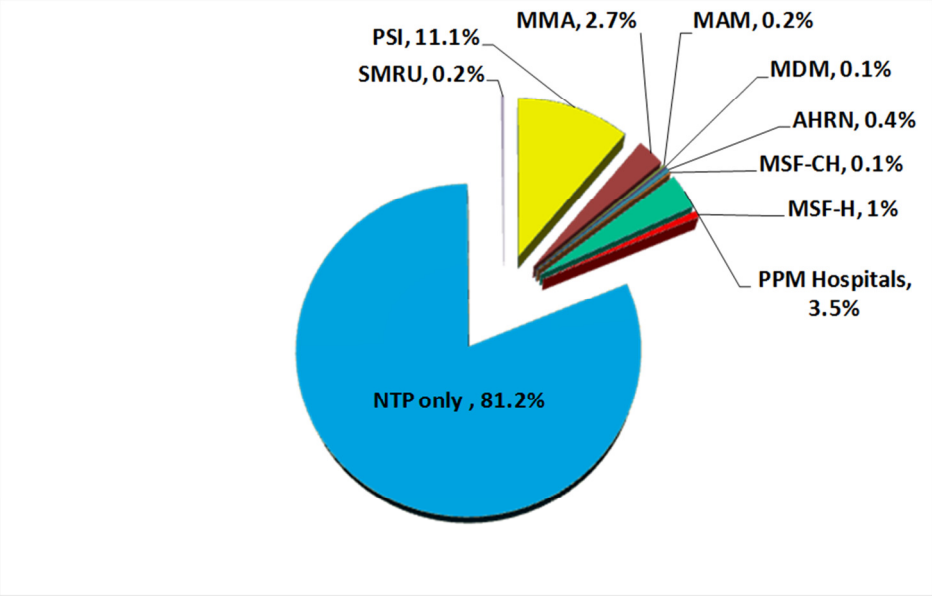
- Accelerate DR-TB detection in order to achieve the enrollment plan through ensuring the adherence to the criteria set for Gx testing and expanding it further and by strengthening contact tracing.

- Mobilize resources and ensure adequate human resources for detection and management of DR-TB patients.

Role of partners in delivery of TB and MDR-TB care

There are many partner organizations, both technical and implementing, that are involved in TB activities in Myanmar. Implementing partners are involved in CBTBC, including case finding activities, sputum collection and transport, DR-TB counseling, and community DOT activities. In total, partners, including the Myanmar Medical Association (MMA) and the Sun Quality Health network of Population Services International (PSI) who are involved in PPM activities contributed 18.8% of total TB cases. This contribution has gone up mainly as a consequence of contribution from MMA and PSI.

Proportion of Total TB cases contributed by NTP only & Other Partners units (Annual 2017) n=132,025



Besides presumptive TB identification and referral, some partners (The Union, MMA) are also engaged in DR-TB patient management (medical doctors working for the

NTP) and in updating individual patient data in open MRS system (The Union, CHAI, MMA).

It was noted that CHAI has been the responsible implementing partner for the open MRS case management system which is discussed below in the reporting and recording section. A coordinator from the Union was present at the Upper Myanmar TB Center and she described the involvement of community volunteers for the provision of DOT, for counseling activities and for sputum collection and transport.

As noted below, partners have been involved with Gx testing in Yangon and four NGOs (MMA, MHAA, PGK and The Union) are involved in CBTBC MDR-TB activities such as patient social and nutritional support and DOT activities, in 84 townships in Upper and Lower Myanmar. To date BHS (Midwives and Public Health Supervisor II) are the chief providers of DOT for DR-TB patients, but, especially with increasing number of MDR/XDR-TB patients being enrolled, they are often overloaded, have other duties and cannot travel to geographically hard to reach areas. This will be a key area where partner organizations can provide support moving forward.

Yangon Partners (Gx Tested in 2017)

	PSI	MMA	MDM	MAM	MSF	Total
Total TB Cases	5222	1004	57	254	276	6813
Gx Tested	1884	596	43	254	276	3053
(%)	(36%) RR+121	59%	75%	100%	100%	45%

Mandalay Community Based TB Care (2017)

Organization	T/S implement	presumptive TB referred	Total TB detected	% detect
MHAA	**6**	2972	447	15%
MCWA	**28**	931	82	9%

Mandalay Partner Activities

No	District	Organization	Activities
1	Mandalay 7 townships, Meikhtilar, Kyaukpadaung, NyaungU, Sintgu, Pyinoolwin, Mogoke, Myingyan ,Ngazun, Natogyi Thaungtha, Mahlaing, Tharzi, Wundwin (20 T/s)	The Union	Patient support Evening DOTS Nutritional support
2	UMTBC, Myingyan, Meikhtilar	The Union	HR support (MDR-TB MO, DA)
3	Yamethin,Pyawbe, Tadaoo, Myittha, Madaya, Sintgaing, Thabeikkyin (7 T/s)	GF	Patient support
4	Kyaukse	MMA	Patient support

MSF-H has been a key partner providing treatment and management for pre-XDR and XDR-TB patients with new and repurposed drugs through the End TB project. However, MSF is transitioning this project to the NTP by the end of 2018 and this role will need to be filled. Involvement and coordination with civil society was not a topic of discussion and appears to be quite weak.

Recommendations:

- Sustain and improve human resources provided by partners.
- Strengthen partnership collaboration including PPM.
- Ensure mandatory notification of TB cases from the private sector.

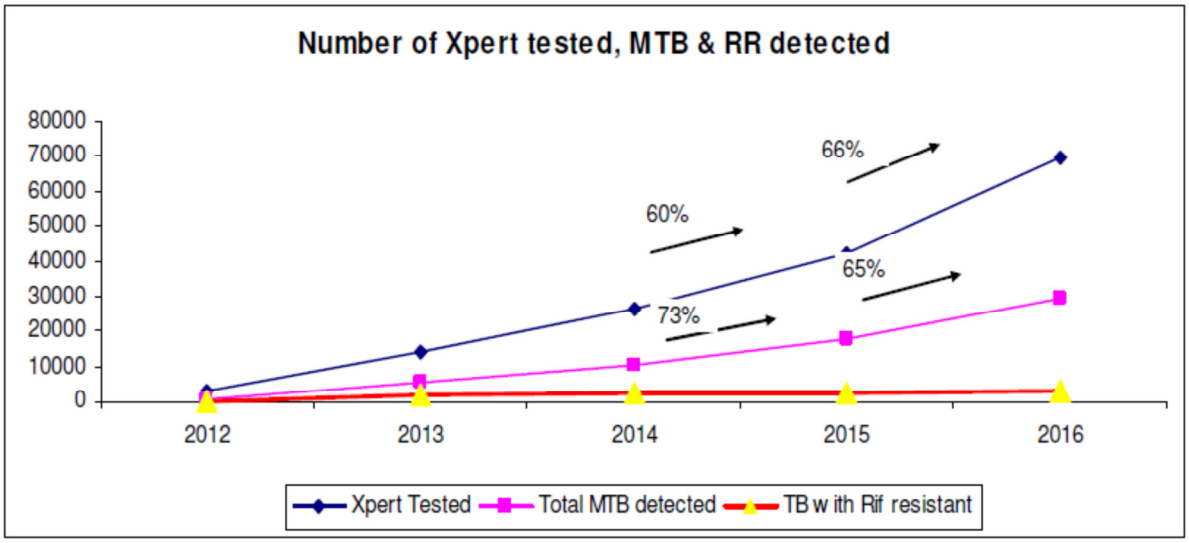
C. Case finding strategy

High MDR-TB burden in Yangon region was noticed after the third DRS and thus Gx testing for all registered TB patients in Yangon Region has started since mid-2015. After that stepwise expansion of Gx criteria was done. The eligibility criteria for Gx are as follows:

1. Retreatment TB cases
2. Close contacts of MDR-TB patients who develop active TB
3. All TB patients and presumptive TB cases living with HIV/AIDS
4. Sputum smear positive at the end of intensive phase (non-converters and positive reverters)
5. TB patients residing in area with high MDR-TB Prevalence (MDR-TB among new TB patients is >10%)
6. TB patients with diabetes mellitus
7. All smear Positive new TB cases
8. Other cases to be considered individually by MDR-TB committee

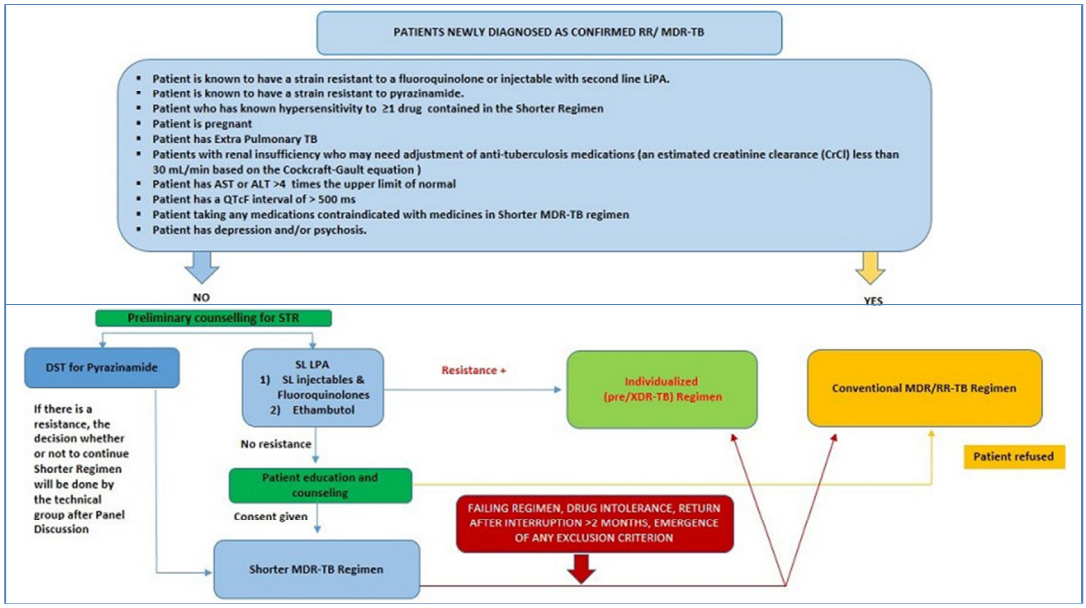
There has been an increase in the number of Gx tests over the years with the increase in number of machines and the expansion in the MDR-TB suspect criteria. Even though the number of tests performed has increased considerably, there is not a proportionate increase in the detection of drug-resistant TB primarily due to the fact that there is a disproportionate increase in the testing of new cases vis-à-vis the other classes mentioned above and we would not expect too much yield of drug resistance from new cases who have no other risk factor.

Graph 6: Number of Gx tested, MTB & Rif resistance detected during last 5 years



The following flow chart has been developed to identify eligible patients for the pilot project of STR for MDR TB:

Figure 1: Algorithm for selection of MDR TB regimen



Recommendations:

- Triaging symptomatic patients with chest X-ray followed by Gx testing for high DR-TB risk groups should be followed.
- Ensure uninterrupted & adequate supply of Gx cartridges and functioning of Gx machines through proper maintenance by mobilizing resources and ensuring funding.
- Monitor & improve referral system to Gx sites from partners in order to improve access to Gx testing.
- Strengthen sputum transportation system from the remote areas in order to improve access to molecular diagnostics.

D. Laboratory services and expansion plan

- **Number of Labs for TB diagnostics.**

Smear Microscopy:

There are 527 Microscopic centers (including 170 LED microscopes), of which 438 (83%) are in Public sector, and 89 (17%) are in Private sector. Even though, EQA smear microscopy is in place at all sites, due to a shortage of human resources, no periodic onsite visits were carried out routinely. Further, most of the technicians (74%) are engaged by NGOs and their sustainability in the programme needs to be ensured.

Gene Xpert sites:

The Gx sites began from 5 machines in 2012 and increased to 78 machines till 2018 in 67 Gx sites.

Report on GeneXpert tests in Myanmar						
	2012 (5) machines	2013 (11) machines	2014 (22) machines	2015 (48) machines	2016 (66) Machines	2017 (73) Machines
Total cases done	3,136	14,246	26,240	41,957	66,237	93,072
MTB not detected	2,303 (73%)	8,895 (62%)	16,089 (61%)	24,265 (58%)	37,056 (56%)	47,225 (51%)
Total MTB detected	833 (27%)	5351 (38%)	10210 (39%)	17692 (42%)	29,172 (44%)	45,837 (49%)
TB with Rif-resistant	259 (9%)	1,689 (12%)	2,631 (10%)	2,719* (6%)	3,213* (5%)	3,175* (3.4%)
TB with No Rif-resistant	556	3435	6986	14215	25,252	41330
TB with Rif-resistant Indeterminate	18	227	534	425	353	457
Proportion "RR+ve" among patients with MTB diagnosed by GXP	31%	32%	26%	16%	11%	7%

The number of Gx tests done has steadily increased from 41,957, 66,237 to 93,072 in 2015, 2016 and 2017 respectively. There is also a decline of Rifampicin resistant cases of 11% in 2016 to 7% in 2017; this may be due to screening of more diagnostic cases, but the number of sites optimally utilizing Gene Xpert remains low.

In addition to this, Partners like PSI, MMA, MDM, MAM, and MSF have performed a total of 3053 Gx tests and of which 121 (3.96%) patients had shown Rif resistance in 2017.

Actual utilization rate of all 73 Gx Machines in 67 sites in 2017 and in 78 machines in 2018 with 2 Runs and 3 runs per day is shown below:

Actual utilization rate	Utilization rate based on 2 Runs/day			Utilization rate based on 3 Runs/day		
	2016	2017	2018	2016	2017	2018
<20%	12	13	8	20	17	17
21-40%	14	14	16	18	23	23
41-60%	14	13	16	6	13	13
61-90%	6	13	13	4	9	8
91% >100%	7	14	15	2	5	6

The majority of the sites were underutilized, being in the range of 20 to 40% utilization from 2016 until 2018. The average number of tests done per machine remained the same from 2016 to 2018 in the range of 4 to 6 specimens per machine.

Workload analysis of Xpert by Region/State (2016 – 2018)

Region/States	Test per day (Average)			Test per Machines (Average)		
	2016	2017	2018	2016	2017	2018
Ayeyarwaddy	19.9	34.9	46.0	4.0	5.8	7.7
Bago	15.2	27.2	33.1	5.1	6.8	8.3
Chin	0.3	1.1	2.2	0.3	0.6	1.1
Kachin	16.7	23.8	23.4	5.6	7.9	7.8
Kayah	1.8	3.5	4.1	1.8	3.5	4.1
Kayin	3.1	7.4	13.0	1.6	3.7	6.5
Magway	7.0	13.3	12.9	3.5	2.7	2.6
Mandalay	52.9	57.5	57.9	4.1	4.4	4.5
Mon	13.1	17.6	20.9	6.6	8.8	7.0
Naypyitaw	4.2	8.0	10.4	2.1	4.0	5.2
Rakhine	4.0	8.0	10.5	1.0	1.6	2.1
Sagaing	8.8	16.1	21.5	2.2	3.2	3.6
Shan (East)	3.7	5.3	7.9	1.9	2.7	4.0
Shan (North)	8.4	2.8	15.6	4.2	0.9	5.2
Shan (South)	6.4	10.5	13.9	2.1	3.5	4.6
Tanintaryi	8.9	9.7	10.5	3.0	3.2	3.5
Yangon	114.3	155.1	186.2	6.7	8.2	9.8
Total	**288.6**	**401.5**	**490**	**4**	**5**	**6**

In Yangon region ,which accounts for more numbers of TB patients, as of now, 28% of registered TB patients were not tested with Gx, and Extra Pulmonary samples and Pediatric patients tested by Gx remains very low. With the recent change in criteria, the number of patients to be tested with Gx is expected to increase in 2018.

EQA for Gx is carried out in 45 Gx sites with the help of JICA. Panel spots were prepared by CDC Atlanta and sent to labs. Out of 45 participating sites, 44 have cleared the proficiency and the remaining one would also have cleared but for the typographic error

- **The number of labs with facilities for testing drug resistance by both phenotypic and genotypic methods and Expansion plan:**

Currently NTRL in Yangon and Upper Myanmar Reference Lab in Mandalay perform Phenotypic culture and DST and Molecular test LPAs for both first and second line drugs.

A new BSL3 lab in addition to previous BSL lab has been built in a new building and equipped with all equipment and facilities to perform Phenotypic Culture and DST including installation of one MGIT and Molecular lab to carry out LPA testing. However, it is lacking in facilities for washing and sterilization and needs a well-ventilated sample reception section. This lab will become functional once permanent electricity connection is provided from the month of August 2018.

A third lab which was performing culture since December 2013 at Taunggyi has been upgraded to BSL3 and LPA facilities with all necessary equipment in May 2018. Due to non-availability of Microbiologist and other laboratory personnel, the lab is yet to be functional.

Workload of NTRL and Mandalay laboratory:

A detailed report of both the laboratories is given as Annexures with their workload, activities undertaken with recommendations.

As per the National policy both the labs test 2 samples for all follow up patients, which needs to be reduced to a single sample aligning with WHO recommendations. This will substantially reduce the workload of both labs, considering the availability of limited human resources, and that only 2 Biosafety cabinets are available at NTRL. Further, transition to liquid culture from solid culture will improve the detection of smear-negative TB and will also reduce the work load of laboratory staff. These two measures of collecting one sample for follow up and using liquid medium will substantially reduce the current turn around time of laboratory results for initiating treatment and patient recruitment.

Recommendations for Laboratory services:

- Field staff needs to be trained in proper sputum collection as most of the samples received are salivary, which contributes for poor culture recovery rates

- Current policy for doing two sputum samples each time during follow up to be modified to single sample as per WHO recommendations.
- Microbiologist and Laboratory Technician positions to be filled up in the new BSL3 lab in Taunggyi which started functioning from May 2018.
- One additional MGIT machine for NTRL and two GT Blots-48 one each for NTRL & Mandalay respectively to be procured to meet the additional work load due to change in criteria
- LPAs for both first line and second line drugs needs to be utilized optimally and nationwide sputum transport mechanism to be strengthened
- Retrain all the staff on Liquid Culture and DST and start performing second line Liquid Culture and DST with no further delay.
- EQA from SNRL, Bangkok which has been discontinued since 2016 to be resumed either from the same or any another laboratory in SNRL network.
- Perform Liquid culture for all follow up samples and discontinue solid culture, this will result in reduced work load of laboratory personal
- Strengthen the EQA of Smear Microscopy and expand LED FM services to more microscopy sites

E. Treatment strategy

PMDT Expansion

PMDT expansion has been rapidly progressing since 2011 and, currently, all 330 townships in the country are able to manage MDR-TB patients. There are two major hospitals that care for MDR-TB patients (Aung San TB Hospital in Lower Myanmar and Patheingyi TB Hospital in Upper Myanmar) and every District has the capability to treat MDR-TB and refer for hospitalization, if necessary. Cumulative PMDT enrolment from mid-2009 to the end of 2017 was 10,414 patients with increasing enrolment every year. Greater than 53% of MDR-TB patients are being diagnosed in Yangon region and, therefore, an MDR-TB crisis situation has been declared in the largest city in Myanmar.

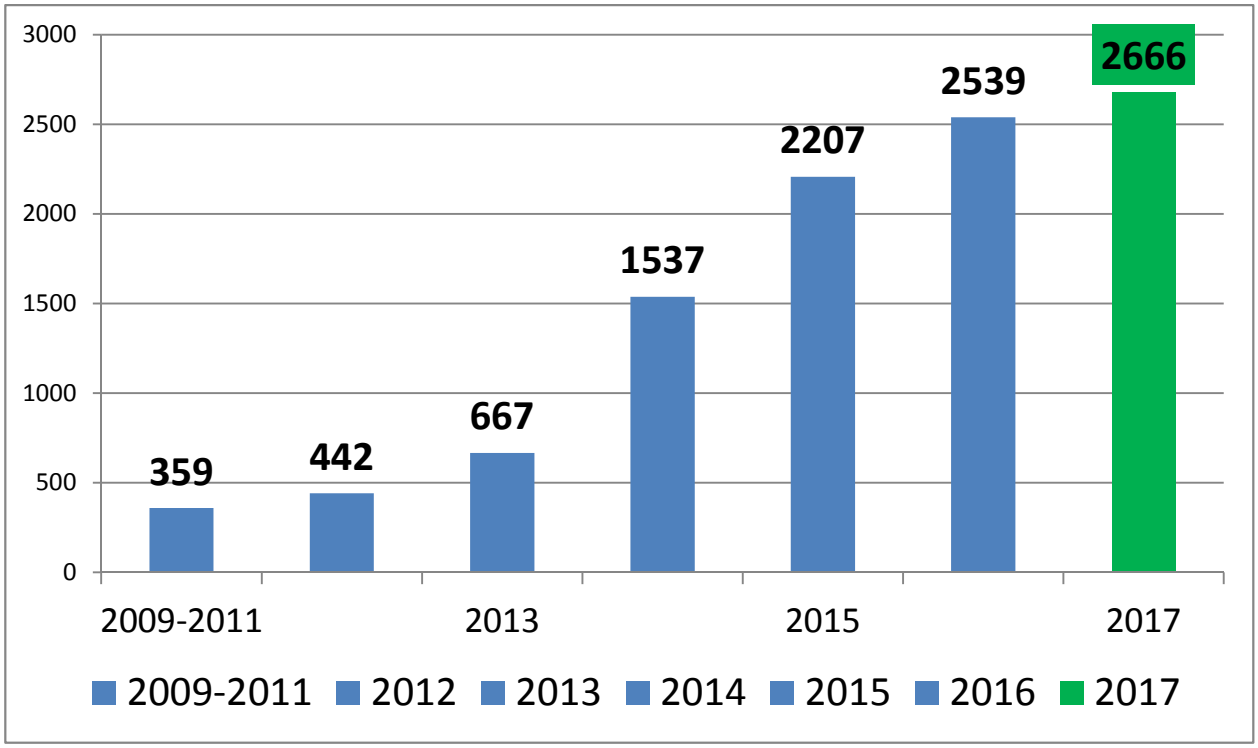
Gap in MDR-TB case detection

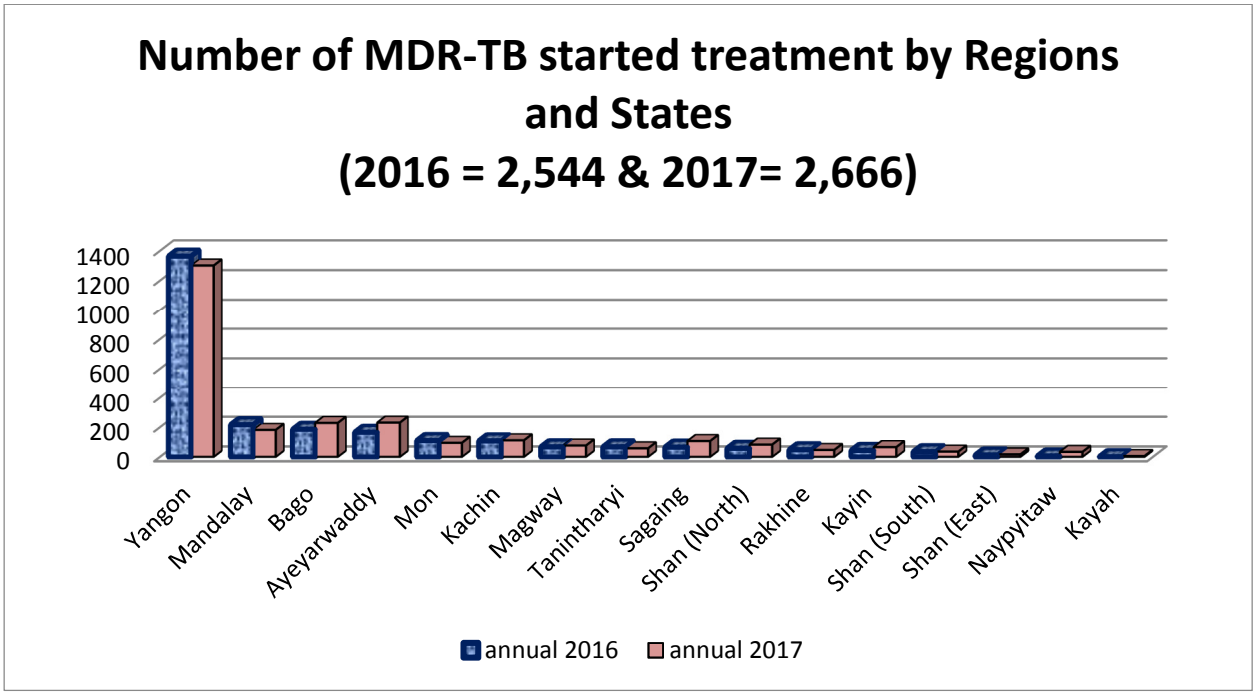
According to the 2016-2020 National Strategic Plan (NSP), the 2017 target for MDR-TB case notification was 4787 cases and the target for MDR-TB cases started on treatment was 3297. The actual numbers of MDR-TB patients notified and started on treatment was 3197 and 2666, respectively, suggesting that MDR-TB case detection and treatment initiation are lagging behind and need to be strengthened. Increased utilization of existing Gx machines and increased implementation of diagnostic services in rural areas (improved sputum collection and transport, greater utilization of chest radiography) as well as urban centers (more Gx testing) is needed. Increase testing of pediatric and extrapulmonary samples by Gx will also improve case detection. Subsequently, expansion of Gx to all TB patients (universal DST) will improve case detection overall (especially given the extremely high proportion of clinically diagnosed cases –

approximately 50% overall) and, specifically, MDR-TB case detection in urban centers such as Yangon.

It is also noted that only 18 pediatric MDR-TB patients were diagnosed in 2017 indicating that MDR-TB is not being adequately diagnosed in the pediatric population, especially pediatric household contacts of infectious MDR-TB patients. Further, appropriate specimens such as gastric aspirates in children under 5 years of age and testing with Gx will improve case detection in children. It was also observed that although HIV-positive patients are receiving symptom screen at ART centers, those who are symptomatic are not being referred properly for TB evaluation (0/4 random symptomatic patients were referred for TB evaluation at the Patheingyi TB Hospital associated ART center). Proper TB evaluation of symptomatic HIV-Positive patients and appropriate evaluation with Gx and chest radiography will be helpful to boost case notification in these special high risk populations.

PMDT Enrollment
(Cumulative enrollment Q3 2009 – Q4 2017 = 10,414 patients)





Delays in treatment initiation

There is also a delay between diagnosis and treatment initiation which might lead to poor patient outcomes and transmission of MDR/XDR-TB in the community. In fact, the high proportion of patients who die before treatment initiation (about 5% of notified cases) and the percentage of new MDR-TB patients (36-47% Q1 2017 through Q1 2018 of enrolled MDR-TB cases) support the theory that delays in treatment initiation are worsening the MDR-TB problem. In Yangon, since 2012, 29/123 pre-XDR-TB patients 10/76 XDR-TB patients expired before treatment initiation. These delays are multifactorial, with delay in sputum culture result and SL LPA result, and delay in drug procurement cited as the biggest contributors. The average wait time to get the culture result for smear-negative patients was 42 days and for smear-positive patients was 25 days. The time from specimen collection for SL LPA to result may be up to two months during which time the patient is often not started on a treatment regimen.

Treatment Regimen

The conventional treatment regimen being used for MDR-TB is **6(Amk Z Lfx Eto Cs ± PAS)/18(Lfx Eto Cs Z ± PAS).** Currently, some patients are still receiving PAS in the treatment regimen, while others are not, seemingly at the discretion of the treating physician. In the latest WHO 2016 PMDT guidelines, PAS has been downgraded to class D3 and is generally not recommended to be part of the conventional treatment regimen. In the last rGLC report, it was also noted that PAS was being used and it was recommended that it not be given due to its lower efficacy and greater potential for ADRs.

The shorter MDR-TB regimen is being implemented in 20 townships in the Yangon Region and in ten townships in the Mandalay Region (with plan to expand to all 28 townships). Implementation started in November of 2017. The regimen is being given for 11 months total with a fixed initiation phase of 6 months followed by a 5 month continuation phase; the injectable is being given 6 days a week and the oral drugs 7 days a week by full DOT. A total of 76 patients have been started on the shorter regimen in Yangon Region and a total of 20 patients in the Mandalay Region. There have been a total of 16 SAEs with four deaths in Yangon Region and one death reported in Mandalay Region among these patients.

Medical criteria for starting the shorter regimen are as follows:

- Newly diagnosed MDR/RR-TB patients per National DR-TB Guideline
- Adults (> 18 yr)
- Regardless of HIV status
- Patient is known not to have a strain resistant to a fluoroquinolone or injectable with second line LPA.
- Patient who signs informed consent to enroll in the shorter MDR-TB regimen
- Patient is willing to use effective contraception if the patient is capable of child-bearing.
- Patient is willing to adhere to the follow-up schedules

Exclusion criteria are as follows:

- Patient is known to have a strain resistant to a fluoroquinolone or injectable with second line LPA.
- Patient is known to have a strain resistant to ethambutol.
- Patient who has known hypersensitivity to ≥1 drug contained in the Shorter Regimen
- Patient is pregnant
- Patient has Extra Pulmonary TB
- Patients with renal insufficiency who may need adjustment of anti-tuberculosis medications
- (an estimated creatinine clearance (CrCl) less than 30 mL/min based on the Cockcraft-Gault equation)
- Patient has AST or ALT >4 times the upper limit of normal
- Patient has a QTcF interval of > 500 ms
- Patient taking any medications contraindicated with medicines in Shorter MDR-TB regimen
- Patient has depression and/or psychosis.

PZA resistance is no longer a criterion for exclusion.

An analysis of isolates from patients evaluated for the shorter regimen from Yangon Region showed that of 229 sputum results from 252 specimens sent to

NTRL, 66 (28.8%) were excluded due to EMB resistance which is not an exclusion criteria per the WHO guidelines. Only 95 patients met criteria for starting the shorter regimen (41.1%) of which 76 were started on the regimen (80%). Of note, the WHO guidelines also recommend that the initiation phase be 4-6 months based on sputum culture conversion.

Including EMB resistance as an exclusion criterion is greatly limiting the number of patients that would otherwise benefit from a shorter treatment regimen and, extending the initiation phase to 6 months for all patients, subjects some patients who are responding well to treatment as evidenced by culture conversion to two additional months of toxic drugs such as the injectable agent.

Regimens for pre-XDR-and XDR-TB treatment, and for MDR-TB patients intolerant to SLDs, approved by the National DR-TB Expert committee include new drugs such as bedaquiline and delamanid and is the following: BDQ/DLM-PAS-PZA-LZD-CFZ-Co/clav(+/-capreomycin). This regimen is being used through the End TB project which is an UNITAID funded joint program between the National TB program, Aung San TB hospital and MSF-Holland which was started in March 2016. MSF-H has enrolled the target 50 patients in the first quarter of 2018, however MSF Myanmar Mission will take more patients (the total number is under negotiation). MSF will take care of their patients until end of treatment. There has been some limited use of Bedaquiline by the NTP also.

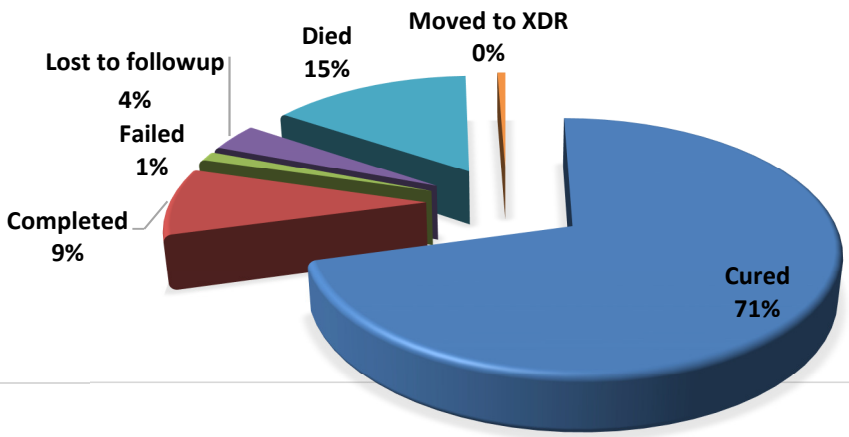
Treatment for HIV/MDR-TB co-infected patients is the same as for HIV-uninfected MDR-TB patients, however, only 56% of co-infected patients (DS and DR) are on ART. This is largely due to the unavailability of ART in decentralized locations which is being addressed by strengthening the network between NTP and NAP centers.

MDR/XDR-TB Outcomes

Treatment success for the 2015 MDR-TB cohort was 80%, however 15% died and 4% were lost to follow-up. Post treatment monitoring should be occurring with one sputum specimen at 3 months post treatment completion and then at 6, 12, 18 and 24 months post treatment completion. It was not clear whether this monitoring for relapse is occurring systematically.

2015 MDR-TB cohort outcome in 2017

TSR=80% (*n*=2180)



Drug Dosages

There has been a problem with QTc interval prolongation noted in patients receiving high-dose moxifloxacin per WHO guidelines as part of the shorter MDR-TB regimen. Many of the patients are under 50 kg, nutritionally deplete and may be prone to greater ADRs with high dose moxifloxacin (600mg and 800 mg daily). Additionally, the newer drugs, bedaquiline and delamanid do not need dose adjustment for weight.

Several drugs are being given twice daily (CS, PAS, Eto), though the guidelines state that they should be given once daily. Twice daily dosage is not optimal for drug delivery for attaining adequate serum levels and for the provision of DOT.

Treatment delivery (DOT)/ adherence and social support for patients

Community based programmatic management of DR-TB is in place with the majority of patients initiating and continuing treatment in the outpatient setting. DOT is provided daily generally by BHS and sometimes by community volunteers who are adequately trained to provide DOT. Hospitalization is reserved for very ill patients, those with co-morbid conditions, and for the management of severe adverse events.

Patient counseling is provided by community volunteers and health care workers at diagnosis and at every visit. Social support is provided at the amount of 30,000 Kyat/month mainly for transportation. There is no systematic provision of nutritional support for patients, but some of the NGOs in some Regions/States do provide such support.

***Recommendations*:**

- Strengthen patient counselling services and reduce diagnostic delays in order to improve enrolment.
- Scale up the shorter MDR-TB regimen (STR) throughout the country
    - Perform second line LPA/Liquid Culture DST in the "0" month for MDR/RR TB patients.
    - Implement SL LPA for all RIF resistant patients for recruitment in STR
    - Start STR at the time of diagnosis of MDR/RR and modify based on second line LPA/DST results.
    - Remove Ethambutol resistance as an exclusion criteria,
    - Review the policy of 6 months treatment with intensive phase (7-drug regimen)
- Modify 20 month conventional MDR-TB treatment regimen to exclude PAS.

- Modify dosage for different second line drugs for weight to mitigate increased adverse drug reactions (ADR).
- Consider giving all medications as single dose except in cases of ADR where twice daily dosage can be given.
- Increase and strengthen the involvement of community volunteers for provision of DOT, especially in urban areas.
- Ensure DOT for DS-TB patients; continue to explore IT models for treatment adherence.
- Follow successfully treated MDR-TB patients at 6 month intervals for 2 years post treatment as per guidelines.
- Expand the use of new drugs in the programme; Bedaquiline and Delamanid should be dosed as per global guidelines.
- Perform operational research to determine the reasons for high mortality among MDR/RR TB patients.

F. Pharmacovigilance/ aDSM

After an aDSM workshop was held in March 2017, a National aDSM (active TB Drugs Safety Monitoring and Management) plan was finalized in June 2017 and a national ToT was held in July 2017. A National Core Committee for aDSM (NCCA) has been created and aDSM is implemented through the End TB Project primarily for patients on new drugs (bedaquiline and delamanid), and is beginning to be implemented for patients who have been started on the shorter MDR-TB regimen. The MSF physician and the TB specialists at ASTH have primarily been involved with aDSM management for patients on new and repurposed drugs. MSF doctors report SAE for End TB patients; since March 2016, reporting has been to the End TB central data base and to the NTP (before NCCA was formed) and to NCCA after it was formed. Starting from January 2018, MoHS doctors report ADRs and SAEs to NCCA (by medical officers, NTP for STR cases in MDR-TB clinics (OPD) and by doctors from 2 TB hospitals for STR and patients on New and/or repurposed drugs).

Since 2016, among 194 patients receiving new and repurposed MDR-TB drugs, there have been 15 deaths and 60 SAEs. The NTP has primarily been responsible for managing SAEs in patients starting the shorter MDR-TB regimen. Since November 2017, when the shorter regimen was implemented, there have been a total of 16 SAEs (nephrotoxicity, QTc prolongation, uncontrolled DM) with four deaths (Arrhythmia, Hepatotoxicity and pneumothorax, RVI) in Yangon and one death in Mandalay among 76 patients in Yangon and 20 patients in Mandalay. There are counselors and a psychiatrist at ASTH and also counselors at the Mandalay TB Hospital who evaluate patients for ADRs and SAEs and refer for physician evaluation if necessary.

Figure 4. Reporting Flow for SAE, Myanmar

aDSM and SAE reports (2016 – 13/6/2018)

	Patients initiated with New & Repurposed Drugs	SAE reports/ events	Number (Death)
2016	19	9	4
2017	40	10	2
Q1 2018	79	16	3
Q2 2018 SAE up to 13 June	56	25	6

There is an NTP form for reporting of SAEs and several patient monitoring tools, including the MDR-TB treatment card and the clinical, bacteriological and laboratory monitoring form. As of yet, a national database for aDSM has not been established and aDSM activities are not standardized for all MDR-TB patients. It is clear from observation that staff at all levels of patient care that there is insufficient training for ADR elicitation and management. One hospitalized patient at ASTH had complete hearing loss and had been admitted for renal failure with an elevated creatinine and a GFR of a 23.5. He was 38 kg and had been on 750 mg Amikacin 6 times weekly for 4-6 months. There had been no audiogram and the patient was only hospitalized when he presented with renal failure. The patient was still on Amikacin at a dose of 500 mg TIW even with the above noted GFR. Another patient at ASTH who had been started on the shorter MDR-TB regimen 2 weeks prior, was admitted with hypokalemia (K+ 2.3), QTc prolongation > 500 milliseconds, and arrhythmia. There was no aDSm form in the chart, but we were told that the SAE had been reported and were shown in a form subsequently. This patient was on high dose moxifloxacin.

During the clinical course case presentation session, there was a case of a patient with QTc prolongation on high dose of moxifloxacin who was hospitalized three times with concomitant hypokalemia and restarted on the same regimen (same dose of moxifloxacin) upon discharge after normalization of the QTc all three times. Finally, she had a run of VT and had to be switched to a conventional regimen. Midwives at the rural health center in Lower Myanmar and other health care professionals in the field at the District Hospitals were not able to answer questions about the common side effects of MDR-TB drugs. There was extremely poor recording of ADRs in patient treatment cards and it was difficult to assess from the review of treatment cards whether patients are having adequate monitoring while on treatment. These examples support the need for greater training and education about aDSM at all levels of provision of TB care and management in Myanmar.

Recommendations:

- Strengthen aDSM for all DR-TB Patients
    - Train all levels of staff for identifying all ADRs and referral whenever required.
    - Ensure proper recording and reporting of ADRs.
    - Perform close ongoing monitoring for early detection of ADRs.
    - Establish a national database for aDSM.

G. Drug management

The current central inventory for Lower Myanmar (Yangon) and Upper Myanmar (Mandalay) appear to be adequate for treatment of patients with the conventional regimen, the shorter regimen (although as the criteria is expanded by dropping EMB resistance as an exclusion criterion, more SLD stock will be required for this

regimen), and for regimens containing new (bedaquiline, delamanid) and repurposed drugs (Linezolid, Clofazamine, Moxifloxacin). UNOPS, the principal recipient (PR) of the Global Fund is responsible for drug procurement from the Global Drug Facility (GDF), while the NTP is responsible for placing orders with UNOPS. NTP has practiced annual quantification and forecasting of all procurement items including Gx cartridge with all partners and UNOPS according to Global Fund request since 2012. The country uses QuanTB for quantification of drugs at the central level, and mSupply at the region/state level. Forecasting of drugs at the central level is based on targets set with Global Fund and the lead time for ordering is at least six months ahead. The Central drug store then distributes drugs to the Upper Myanmar Store (Mandalay) and the Lower Myanmar Store (Yangon) on a quarterly basis. The forecasting of drugs at the Upper and Lower Myanmar stores was less systematic and upon review there was little buffer stock planned for all drugs with the stock being "nil" or close to "nil" at the time of arrival of the next quarter's drugs.

Drugs are subsequently distributed to Regional/State drug stores also on a quarterly basis. The process of drug distribution to State/Regional pharmacists was observed in the Upper Myanmar Store and seemed orderly and well-orchestrated. Drug storage and inventory were commendable, with sufficient space, temperature control and daily monitoring, and observation of first-expiry-first-out in all facility sites visited. At the Upper Myanmar Store, there were several boxes of Rifampicin 150 mg and 300 mg tablets (hundreds of doses) that were three months within expiry. It was explained that there was an over order of loose drugs, and in order to ensure that all of the drug was used, the loose Rifampicin would be used along with loose INH for treating DS patients in the continuation phase (instead of using FDC). It was also observed at the drug store in some sites, that many boxes of Cycloserine had expired. It was explained that there were many side effects reported by patients on CS and, therefore, CS was not being used very much. These situations can be avoided with better planning and a more systematic manner of forecasting drug need.

TB hospitals and township sub-stores collect drugs from Region/State stores and supply to DOT providers on a monthly basis and townships request drug on a quarterly basis. There were no stock-outs of drugs reported at any of the facilities visited except for INH at the ART treatment facility at the Meikhtilar District TB Center in Mandalay where no HIV positive TB patients were treated for latent TB infection with INH from January through June 2017.

Ancillary drugs for management of adverse reactions were available in the facilities and are provided free of charge to all patients in need. These include omeprazole, diclofenac, allopurinol, pyridoxine, levothyroxine, KCl, etc. New drugs such as bedaquiline and delamanid are mainly being used through the END TB Project (MSF, ASTH and NTP) in Lower Myanmar since March 2016. BDQ is used for DR-TB treatment by NTP+ PTG hospital in Mandalay since July 2017 and by NTP/Aung San Hospital in Yangon since Feb 2018. Bedaquiline is being procured by the NTP

through the USAID donation program and the NTP has plans to begin procurement of Delamanid through GDF.

Although there were no instances of Gx cartridge stock-outs, with increased use of existing Gx machines and expansion of the number of Gx machines, there should be a plan to adequately forecast the number of cartridges needed in the future.

***Recommendations*:**

- Ensure that the supply management system be more precise to avoid stock outs and drug expiry.
- Ensure availability of buffer stock at the township level (at least one month).
- Ensure ordering of adequate drug quantities considering additional number of patients to be enrolled based on an increase in coverage and detection of cases.
- Increase the availability of Gx cartridges in view of expanded use of this test in the guidelines.

H. Recording and reporting, and data management

The previous rGLC recommendation to expedite the piloting and roll out of an electronic recording and reporting system for DR-TB and then DS TB, linking program management, treatment facilities, laboratories, drug stores and beneficiaries has not been implemented. Recording and reporting is still largely paper-based and sometimes incomplete. It is difficult to assess the completeness, accuracy and timeliness of reporting in a paper-based system as there is no good way of tracking the process systematically. Not having an electronic surveillance system at the National level makes it extremely difficult to track the epidemiology of DR-TB for purposes of program improvement, to track patients for outcomes monitoring and aDSM, and trouble shoot problems in program management as they arise.

In Lower Myanmar, at the Thaylin District Hospital MDR-TB OPD, use of the Open MRS system for MDR-TB management was observed. It has great potential for MDR-TB case management to ensure adequate treatment and monitoring, but most of the features of the system are not currently being used. For example, reports could be generated to flag when patients need follow-up sputum evaluations and the system could auto-generate a list of these patients weekly, but this function is currently not being used. Using these sorts of functions could decrease the workload of the BHS and other health care workers, aid in the tracking of patients through the system and improve patient outcomes. This system can be expanded throughout the country for MDR-TB case management and tracking and linking with the National TB surveillance system (once implemented). This would greatly improve the ability to monitor the completeness, accuracy and timeliness of reporting.

Mandatory reporting of TB from the private sector is another area that must be addressed. At this time, it is hard to understand the extent of the role played by the private sector in Myanmar as there is no way to track patients who are seen by private sector physicians. We observed, at the Rural Health Center in Upper Myanmar, that symptomatic presumptive TB patients were being referred by the health care worker to follow-up for evaluation, but there was no paper registry to document who was being referred, when and to whom. Therefore, the onus was entirely upon the patient to follow-up with the Public Health sector. Many of these patients may not be able to travel far distances for evaluation or may follow-up with their GP or another private physician. We simply have no way of knowing what is happening to these patients. These patients may be part of the 50,000 missing cases.

Recommendations:

- Establish an electronic surveillance system from the township to the regional/state level to the national level; the current system which is implemented as a pilot should be rapidly expanded.
- Consider expanding the Open MRS system for case management of DR-TB patients
- Keep case records of all patients at the health facility performing monthly monitoring of patients.
- Strengthen the tracking pathway of patients from periphery to diagnostic facility

I. Infection control

The data presented by the NTP manager during the Exit meeting with all stakeholders shows that 36 to 47 % of MDR-TB is occurring among "new" patients and this percentage is increasing over time. This is very worrisome for ongoing transmission of MDR-TB in the community and in the hospitalized settings. Unless there is a great error in eliciting previous treatment history from patients and diagnosis, these are extremely high rates of primary MDR-TB. In order to address infection control, there are three levels of controls – administrative, environmental, and personal protective equipment.

Proportion of registration groups among MDR-TB treatment enrolment (Q1 2017 – Q1 2018)

Enrolment period	New MDR-TB case	Non Converter (IR,RR)	Treatment after LFU (IR,RR)	Treatment after failure of treatment (IR,RR)	Relapse (IR) (RR)	Treatment after MDR-TB treatment	Other*	Total # pt treatment started
Q1 2017	36%	6%	2%	17%	39%	1%	0%	683
Q2 2017	39%	6%	2%	11%	41%	0%	0%	681
Q3 2017	42%	3%	3%	15%	36%	0%	1%	706
Q4 2017	42%	6%	3%	13%	36%	0%	0%	596
Q1 2018	47%	4%	3%	7%	39%	0%	0%	587

Administrative

Within the past few years, a TB-IC assessment has been conducted by an IC expert from KNCV through Challenge TB (CTB). Guidelines have been reviewed and updated, training manual and tools have been drafted and an Expert Committee meeting has been held and a TOT workshop has been done. We were informed that IC trainings are ongoing. We did not observe IC committees at different levels of care and we were not shown any IC policies or procedures at the hospital or clinic level and there was no discussion of such policies or procedures during our site visits to different facilities.

Environmental

In the inpatient facilities visited that house MDR- and XDR-TB patients, there seemed to be relatively good ventilation, except in ASTH the windows were closed in many of the rooms. In ASTH, one ward was noted to have three UV light devices whereas other wards had none. The UV lights were all in the off position and staff had to be reminded to turn them on. In ASTH, patients in the male wards were well segregated by smear status (positive separated from negative) and MDR-TB patients from DS-TB patients, but in there was only one female ward and all different types of patients were housed in that ward. HIV-positive patients were not segregated from HIV-negative patients and it was stated that an XDR–TB ward was being constructed. At the Thaylin District hospital, there were approximately ten TB patients in the General Medical Ward and there was no segregation based on drug resistance or infectiousness. It was stated, however, that an isolation ward was being built for MDR-TB patients. In the Mandalay Upper Myanmar TB Center, there were separate wards for MDR-TB patients, but there were no separate wards in Patheingyi TB Specialist Hospital. All OPDs observed had outdoor waiting areas for smear-positive TB patients, but there was no segregation of DR-TB from DS-TB patients or HIV-positive from HIV-negative patients. At no facility were health care workers aware of the number of air exchanges in their environment. In the township laboratory visited, there appeared to be limited ventilation. There were

fans being used for cooling the environment that were likely not conducive for infection control measures.

Personal Protective Equipment

In most facilities visited, including laboratories, staff was wearing N95 masks; in fact in Thaylin District Hospital, staff in the OPD was wearing their N95 respirators despite the fact that there were no patients present. When this was noted, they removed their masks. At ASTH, the patient visitors were also given N95 respirators, a waste of precious resources. It was also noted that not all staff at ASTH were wearing N95 respirators. At ASTH, we were informed that N95 mask fit testing was happening, but only size large masks were available.

HCW screening

At no facility was there any proactive HCW screening policy or procedure. Symptom screen may be used sporadically, but that was hard to establish. At several facilities, there were reports of HCW who had been diagnosed and treated for MDR-TB.

Recommendations:

- Ensure that adequate administrative controls exist at all medical facilities providing care for TB patients.
- Maintain proper ventilation in all hospital wards and clinics.
- Ensure rational use and monitoring of UV light (effectivity and safety); the light should be functional and put on at all times when patient care is given.
- Ensure the use of PPE (N95 masks) by hospital staff during patient care and the use of surgical masks by patients and family members and give training for proper use.
- Ensure proper segregation of different categories of patients (Sm Pos, Neg MDR, XDR, HIV) both in TB and General hospitals.
- Consider different OP timings for new/DS-TB patients and MDR-TB cases.

J. Human resource, Training and Technical support strategy

The focal point for PMDT in the NTP has additional responsibility of other major programs and hence is not able to provide dedicated input to the NTP. The support of WHO focal point is also linked with the Global Fund Project and sustainability will be an issue on closure of this Global Fund support. There is deficiency of the staff at all levels in the health system. At places, there are vacancies which need to be filled and also post creation in remote areas needs to be considered. In some regions/districts, 40-60% of vacancy exists in key posts such as Medical Officer and Laboratory Staff.

With the expansion and scale up of PMDT services and in the existing model of treatment observation, wherein the DOT Provider visits the house of patients for

administering medication, the strengthening of the peripheral health staff will be essential. There is a continuous need to support the DOT providers to identify side effects and take necessary action. Regular refresher training of DOT providers with close supervision and monitoring will be required to ensure treatment adherence and early diagnosis with management of side effects. This can be done by PMDT staff to the DOT providers.

The other staff in the programme including the Laboratory Technicians, Medical Officers and District Team Leaders needs to be trained and re-trained specially as the programme guidelines have changed considerably.

Recommendations:

- Full-time Focal PMDT person be appointed at the NTP.
- Vacancies in the programme and laboratory services to be filled.
- All staff to be trained/re-trained.

K. Supervision of the programme

The DR-TB committees at the National, Region/State and district/township levels support the supervision and monitoring of PMDT. The central level focal point for PMDT requires training to gather skill on program related supervision and monitoring of district and township site monitoring, especially with all townships now allowed to receive and manage RR-TB patients.

With the expansion of the PMDT services, it is likely that the supervision and monitoring may suffer unless additional human resources (HR) are provided. This is more so from the National to the Regional/State level. The NTP needs to assess the requirement for additional HR, and also review and revise the roles of the DR-TB committees at various levels. This was also recommended during the last mission but has not been addressed.

Recommendations:

- Review and revise the current supervision and monitoring strategy and assess for additional staff need.
- Review and revise the monitoring checklist to ensure all aspects of PMDT monitoring is covered including HR, case finding, treatment, aDSM, drug management, infection control and Recording & Reporting.
- Frequency of supervision at all levels (Centre to Region/State to District to Township) to be enhanced.

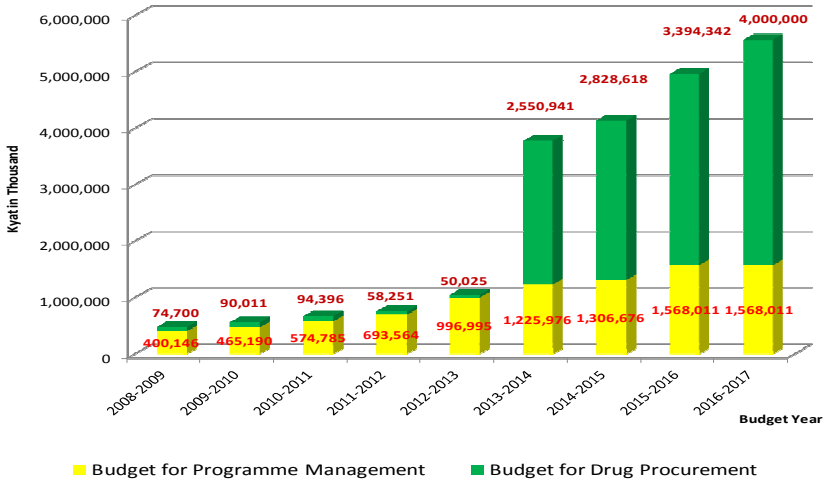
L. PMDT plan including funding source

The current PMDT plan includes enrollment of 2200 patients (including 200 patients on shorter regimen pilot project) under global fund funding and 1200 patients under government funding in 2017. The graph below shows the PMDT plan.

Outcome Indicators	Baseline	Targets				
		2016	2017	2018	2019	2020
Notification of RR-TB and/or MDR-TB cases	2793	4662	4787	4905	5014	5115
Number of RR-TB and/or MDR-TB cases to be treated	2207	3130	3297	3380	3510	3580
Treatment success rate RR-TB and/or MDR-TB	79%	81%	81%	≥82%	≥82%	≥82%

The budget for the NTP has increased gradually over the years with a substantial increase from the year 2013-14 as shown in the figure below :

National Response: Government Budget for NTP (2008-2009 to 2016-2017)



It will be observed that the budget for programme management activity has shown a gradual rise whereas that for drug procurement has increased steeply. This is due to the expenditure on 2nd line drugs.

Further, the Government budget is only contributing one-third of the total budget with most of the component coming from the Global Fund. In order to ensure sustainability post 2020, the Government contribution will need to gradually increase.

Recommendations:

- Continuous monitoring of programme implementation will be required in order to achieve the targets.
- Ensure (and secure) adequate funding

ANNEXURE-1

People met with Mission team

5th July 2018

Central NTP (Yangon Branch), Aung San TB Hospital and National TB Reference Laboratory

Dr Zaw Myint, Senior TB Consultant, Central NTP (Yangon Branch)

Dr Myat Myat Moe, Senior TB Consultant, Central NTP (Yangon Branch)

Dr Thein Myint, Senior TB Consultant, Central NTP (Yangon Branch)

Dr May Thet Naing, Senior TB Consultant, Central NTP (Yangon Branch)

Dr Thandar Hmun, Medical Superintendent, Aung San TB Hospital

Dr Ngway Ngway Win, Deputy Medical Superintendent, Aung San TB Hospital

Dr Mar Mar Htay, Consultant TB Specialist, Aung San TB Hospital

Dr Khin Aye Myint, Consultant TB Specialist (retired), Aung San TB Hospital

Dr Su Hlaing, Specialist Assistant Surgeon, Aung San TB Hospital

Dr Tin Tin Mar, Senior Consultant microbiologist, NTRL

Dr Wint Wint Nyunt, Consultant microbiologist, NTRL

Dr Thynn Lei Swe, Consultant microbiologist, NTRL

Dr Yin Yin, National Technical Officer (MDR-TB), WHO

Dr San San Shein, National Technical Officer (MDR-TB), WHO

Dr May Thu Soe, Medical Officer (MDR-TB), MMA

6th July 2018

Regional Health Department (Yangon Region), Thanlyin District Hospital and TBC, Lat Yat San RHC

Dr Htay Lwin, Deputy Regional Public Health Director

Dr Tin Thitsar Lwin, Deputy Regional Public Health Director

Dr Toe Toe, Medical Superintendent, Thanlyin District Hospital

Dr Win Thein, Physician, Thanlyin District Hospital

Dr Kyi Aye Thet, Physician, Thanlyin District Hospital

Dr Mya Kyae Mone, District Public Health Director, Thanlyin Township

Ms. Lay Nwe, Statistician (NTP)

Dr Nay Lin Aung, MDR-TB doctor, MMA (seconded to NTP)

Ms. Tin Cho Win, MDR-TB nurse, MMA (seconded to NTP)

Mr. Than Win Htike, Lab Technician (NTP)

Mr. Naung Naung Oo, Health Assistant, Lat Yat San Rural Health Center

Daw Yamin Kyi, Midwife, Lat Yat San Rural Health Center

Daw Myint Myint San, Midwife, Lat Yat San Rural Health Center

9th July 2018

MeikHtilar District Hospital and TB center, IHC clinic and NAP clinic

Dr Nyunt Sein, Medical Superintendent, Meikhtilar District Hospital

Dr Aung Kyaw Soe, Physician, Meikhtilar District Hospital

Dr Aye Aye Kyaw, Team Leader (NAP)

Dr Sai Khay Naw Sai, Team Leader (NTP)

Dr Aung Si Thu, Senior Program Coordinator (MDR-TB), The Union

Dr Pyae Phyo Wai, Program Coordinator (MDR-TB), The Union

Dr Than Soe Moe, Medical doctor (HIV), The Union

Dr Aung Khant Kyaw, Medical doctor (HIV), The Union

Mr. Ye Min Htwe, Health Assistant, Shan Tae Rural Health Center

10th July 2018

Regional Health Department, TB OPD, City Private Hospital, Upper Myanmar TB Office, Reference Laboratory (PTG), Patheingyi TB Hospital

Dr Than Than Myint, Regional Health Director

Dr Thin Thin Nwe , Deputy Regional Health Director

Dr Kyi Kyi Sein, Medical Officer, MMA

Dr Nwet Nwet Win, Medical Superintendent, City Hospital (300 bedded private hospital)

Dr Yan Naung Aye, Medical Officer,

Dr Thandar Thwin, Upper Myanmar TB Officer, (NTP)

Dr Htike Htike Ei, Medical Officer (NTP)

Dr Moe Zaw, Senior Medical Superintendent, Patheingyi TB Hospital

Dr Win Tun Oo, Physician, Patheingyi TB Hospital

Dr Khin Moh Moh Aung, Physician, Patheingyi TB Hospital

Dr Moe Thaw Ko, Assistant Surgeon, Patheingyi TB Hospital

Dr Ye Thiha, Assistant Surgeon, Patheingyi TB Hospital

Dr Kyi Kyi Swe, Microbiologist, Reference Laboratory (PTG)

Dr Kaung Myat Tun, NTO, WHO

13th July 2018 (Debriefing Meeting)

Dr Si Thu Aung, NTP Manager

Expert committee members including

Professor Ye Tun (Chairperson)

Dr Si Thu Aung, Director Disease Control/ former NTP Manager (Secretary)

ANNEXURE-2

The Clinical Workshops in Yangon and Mandalay

Morning Session

Introduction by Medical Superintendents of the TB hospitals (DR-TB treatment by new and repurposed drugs in Myanmar)

Presentations by mission consultants

- Understanding mutations and resistance & Updates in TB diagnosis by Dr. L. Prabakaran
- New and repurposed drugs, Shorter Treatment Regimen by Dr. Rohit Sarin
- Management of adverse drug reaction by Dr. Sundari Mase

Afternoon Session

Case presentations and discussion

- 3 cases by mission consultants
- 3 cases by clinicians of TB specialist hospitals (Aung San and PTG)
- Q&A

Summary of Clinical Workshop

- Two workshops were held, one in Yangon on 7 July and the other in Mandalay on 11 July. Attendees were mainly physicians treating TB patients.
- Three presentations were given by the consultants on "Understanding mutations and resistance and Updates in TB diagnosis", "the use of new and repurposed drugs for DR-TB" and "managing adverse drug reactions".
- Cases were presented by the consultants and by Myanmar physicians
- Observations
    - Complicated drug-resistant TB cases were presented for discussion
    - Questions were asked about the diagnosis, treatment and monitoring of DR-TB and about programmatic aspects of DR-TB management
    - Although clinicians were familiar with WHO guidelines and had a basic understanding of DR-TB treatment and management, ongoing clinical consultation for DR-TB cases by an expert in MDR/XDR-TB would be helpful for ensuring better patient care.
- Recommendations
    - Continue weekly or monthly case conferencing for complicated DR-TB patients
    - Include MDR/XDR-TB experts, both within country, and externally as needed

- Provide ongoing training and education for the treatment and management of MDR/XDR TB

Annexure-3

NTRL, Yangon: Salient findings

The staff strength at NTRL consists of one Sr. Consultant Microbiologist, (Dr. Tin Tin Mar) and 3 Consultant Microbiologist (Dr. Wint Wint Nyunt, Dr. Thynn lei swe & Dr. Win Mar Oo). All are Government staff except Dr. Win Mar Oo, recruited through MMA with the support of 3MDG. In addition, three laboratory officers were recently appointed by the Govt. Currently the laboratory has 12 Laboratory Technicians (LTs), {4 from Govt. support and the rest 8 from Partners, WHO (5), MMA (1) & MHAA (2). One Engineer appointed by WHO takes care of the maintenance work of equipment, TB containment facilities and LPA laboratories. Two office and data entry assistants were supported by WHO and MMA respectively. In addition, there are 3 General workers from the Govt.

The laboratory management system is in place. Senior Consultant Microbiologist leads the laboratory activities taking care of supply chain management, Trainings, developing SOPs, attending meetings and EQA activities of Smear Microscopy and Gx, with the support and help provided by other 3 Jr. Microbiologists. Dr. Win Win Nyunt is the designated Quality officer and involved in the Research and DRS activities. Three lab officers are engaged recently are looking after Data management, Store management and supervising laboratory and EQA activities. One of the LTs who received training for three weeks from Georgia is designated as Safety officer. The microbiologists received international training in Solid & Liquid Culture and DST, and LPA; LTs received onsite training from the facilitators of SNRL, Bangkok till 2016 and thereafter from the onsite microbiologist and also recently from Dr. Natalia Shubladze, an international laboratory technical expert from USAID Challenge TB Project. Staff is put on rotation for every 6 months in all sections.

There are seven main sections in the old building namely specimen reception, smear microscopy, washing and sterilization, media preparation, BSL3, LPA laboratories and store. Clear line of authority exists, the Microbiologist is signing off the reports.

ISO 15189: NTRL is preparing for ISO certification using GLI Step wise process towards Accreditation, with the help of partners FHI 360 from Challenge TB Project supported financially by USAID, Challenge TB. They are in the process of completing the phase 3 and planning to go for application by completing the final phase 4 in 2019. Since there is no local accreditation body available in the country, they were in discussion with the donors to decide on a suitable country for application.

Infrastructure:

Existing LPA and BSL3 facilities are in the old building, with all the sections mentioned.

Equipment available:

BSC, Class II (Esco & Baker) -- 2 Nos.
MGIT -1 No.
Refrigerated Centrifuges (Hettich) – 2Nos.
Microliter centrifuge – 1No
Autoclave - 1 for Contaminated materials and 2 for Sterile materials
Inspissators- 2 Nos; Thermocycler-1
Twincubator-2
Scanner (for LPA strip reading).
GT blot-1

Newly constructed laboratory building with 3MDG & Global Fund support is housing BSL3 and LPA Laboratories is equipped with one MGIT Instrument and all other equipment will start functioning by August 2018, after establishing continuous power supply.

However, the new premises lack **washing and sterilization** rooms as well as well -ventilated room for sputum/sample reception area.

Equipment, BSC & BSL3 lab AMC:

Though the equipment were under AMC, the concerned agency is not carrying out maintenance satisfactorily. Centrifuges and BSL3 lab were not certified, 2 BSCs were calibrated and certified recently with the help of Family health International FHI 360 from Challenge TB Project supported financially by USAID.

BSL3 Lab maintenance is done by Natural Green Innovation company (NGI) from Thailand. They provide report for the satisfactory performance/functioning. Lab records the pressure (Gauge) on daily basis. If any problem/break down occurs the WHO supported local engineer rectifies the same with the help of manual or by getting instruction from the agency NGI, in case of major break down, the vendor comes from Thailand for repairing.

Specimen transportation:

Samples from Yangon region were transported on daily basis by Human carrier in NTRL lab vehicle.

Samples collected from other regions and from remote areas are kept in Refrigerators in township labs and sent them in cool boxes carried by Express Buses to Yangon. NTRL person collects the same from the bus station and takes to the lab.

Quality control and assurance:

The general quality assurance: The general quality assurance such as cleaning and waste management is adequate except in washing room and specimen reception area, which requires more attention. SOPs are available in all places.

EQA Smear Microscopy:

External quality control (EQA) for NTRL lab is done through panel testing (PT) twice a year by National Health Lab (NHL).

In all there are 527 microscopic centers out of which 170 sites were having LED microscopes and 2/3rd of the work load is taken care by the LED microscopic sites.

NTRL is responsible for EQA sputum microscopy for 4 districts and 45 Townships, and 73 microscopic centers. The slides collected for Random blinded rechecking (RBRC) on monthly basis is decided by the Microbiologist and the slides are collected by TB coordinators for checking blindly by STLS in Township labs. It gets cross checked by QC coordinator and results conveyed to the microscopic centers by TB officers. Two Senior lab supervisors are performing onsite visits every three months. (EQA) for this lab is done through panel testing (PT) twice a year by National Health Lab (NHL). Quarterly reports sent to NTRL. Microbiologist from NRTL visit annually to the Township labs; recent visit was made by Dr. Thynn Le Swe, NRL Microbiologist, to Rakhine State TB Center and Lab in May2018.

EQA for Gx: EQA for Gx is carried out in 45 Gx sites with the help of donor, Japanese International cooperative agency (JICA). Panel spots were prepared by CDC Atlanta and sent to NTRL through JICA. NTRL distributes panel to the sites and get the consolidated results and share the results with CDC. First two rounds were completed, during the last round all 44 sites passed EQA and one site didn't pass due to typo error. From this year onwards JICA informed NTRL to take over the responsibility of doing EQA in-house by getting the training from CDC.

Work load of NTRL:

NTRL receives 100-120 patient samples in duplicate (around 200 sputum samples/day) on daily basis for smear, LPA and C& DST (both solid and liquid).

Smear: About 200 smears are examined by Auramine staining. Also performs direct smear for EP samples and concentrated smears for culture samples.

LPA work load:

1st Line: A Total of 179 first line LPA tests were performed in 2017, 63 test were performed till 1Q2018

2nd Line LPA: A total of 163 in 2017 and 111 up to 2Q 2018 were done.

2nd line LPA work load was less due to 20 townships alone participated in collecting RR TB Case samples for 2nd line LPA testing but now all the 45 townships participate.

Turnaround time for LPA for STR Patients is 2wks and this delay was due to insufficient availability of cabinets which allow processing of about 200 samples/day.

Solid culture and DST (2017):

A Total of 8031 solid cultures were performed, 60 numbers were positive and 7772 were negative.

A total of 1279 Diagnostics samples were tested of which:

Smear Positive and Culture positive is 271/327 (82%)

Smear Negative and culture positive 17/952 (which includes 50% of EP samples) (2%).

Very low recovery rate of *M.tuberculosis* cultures is attributed to poor sample (salivary) collection.

Follow up MDR TB patients treated with conventional regimen: Solid culture is performed 5 times and liquid culture 6/8 times and no "0" month culture is done.

STR patients: Solid culture is performed 3 times and LC is performed 7 times during treatment.

Solid culture DST for Second line: 103 in 2017 and 34 till 1Q2018

Turnaround time for solid culture reporting is about 2 months, and contamination rate is 3-5%

Liquid culture and DST:

A total of 8058 samples were tested by Liquid culture out of which 88 Nos were positive and 7835 Nos were negative, the contamination rate is 6-8%.

First line LC DST: 48 first line DSTs were performed and 37 numbers till 1Q2018

Second line LC DST was stopped after 2016 due to the lab was not getting EQA Panel testing from SNRL, Bangkok.

EQA: Panel Testing was stopped in 2016, after that in 2017, MSF (Holland) has collected 30 sputum samples on different occasions in duplicate and sent to Antwerp Belgium for comparing 2nd line DST results done by solid method from NTRL and observed 100% concordance with the DST results of NTRL. Results on Sputum samples that were sent in 2018 were not received so far.

Data Entry:

Sputum sample forms were entered in the computer at NTRL and the results were dispatched to the sites on paper-based system, no online entries started for data entry.

Recommendations:

- Field staff needs to be trained in proper sputum collection as most of the samples received are salivary, which contributes for poor culture recovery rates
- 2 additional BSCs in the new lab to be commissioned immediately to meet the turnaround time as laboratory tests were hampered due to problem in having only 2 BSCs
- Current policy for doing two sputum samples each time during follow up to be modified to single sample as per WHO recommendation, this would reduce the work load
- Additional MGIT machine and GT Blot-48 to be procured to meet the additional work load due to change in criteria
- Additional autoclave to be procured for contaminated materials as back up
- EQA from SNRL which has been discontinued from 2016 to be resumed
- Retrain all technical staff on Liquid Culture and DST and start performing second line LC DST
- Microbiologist and LTs position to be filled up in the new BSL3 lab in Taunggyi which started functioning from May2018.
- LPAs for both first line and second line needs to be utilized optimally and sputum transport mechanism to be strengthened
- Gx EQA to be expanded to all the Gx sites
- Light microscopes to be replaced by LED microscopes in phased manner in order of preference in the high volume microscopic centers

Central NTP (Mandalay Branch) Laboratory: Salient findings

Staff strength:

Upper Myanmar laboratory is led by Microbiologist Dr. Kyi Kyi Swe supported by recently appointed 3 Laboratory officers from Govt. 4 lab technicians, two of them from Govt. and two from partners (WHO & Union, 1 each), 5 Grade1 Technicians, 4 Lab cleaners, 1 Lab attendant, one office staff all from Govt. 1 Maintenance Engineer and 1 for Data entry both supported by WHO.

The laboratory management system is in place and preparing for ISO15189 certification is ongoing from 2017 with the support of FHI 360 from Challenge TB project supported financially by USAID using the GLI stepwise approach, completed Phase1 and partially Phase2. Dr. Kyi Kyi Swe, Microbiologist leads the laboratory activities taking care of supply chain management, Trainings, developing SOPs, attending meetings and EQA activities of Smear Microscopy and Gx and installation of new Gx instruments in the region. Microbiologist is signing off the laboratory reports.

The microbiologists received international training in Solid & Liquid Culture and DST, and LPA for two weeks, and one Grade1 Laboratory technician received International training in Germany, Japan and in Thailand. Remaining others were given on the job training by the Microbiologist. All three Laboratory officers recently recruited did not receive training in any of the technologies followed in the lab. Two of the Grade1 laboratory technicians designated as STLS are trained in EQA smear microscopy and takes care of the EQA activities. Accordingly, Random Blinded Re Checking slides are being collected from 58 sites in 28 township laboratories (22FM and 6 ZN) from 7 Districts and 5 Regions supported by Partners (MMA, PSI) and 9 PPM site.

The laboratory has one TB Containment facility for performing C & DST testing, one Molecular laboratory for LPAs testing, Gx laboratory with 2 Instruments with 4 Modules and 1 with 16 Modules. In addition to this, LTs were involved in the DRS activity using Gx Ultra cartridges.

Lab receives sputum specimens in ice boxes maintaining cold chain employing different approaches including human carrier, public transport and also by Air from Kachin state.

EQA for Gx is implemented in 9 out of 11 sites supported by JICA in collaboration with CDC.

IQC: QC is performed for reagent preparation, media preparation and Solid and Liquid DSTs using standard H37Rv strain in each batch.

QA: EQA for LPA and C & DST (both solid and liquid) technologies were in place till 2016 with SNRL, Bangkok and it was discontinued due to absence of communication from the higher lab.

Daily work load:

Diagnosis samples: 5 Patients

Follow up samples: 25 – 30 Patients with 2 samples/patient. A total of 60-75 samples on an average/day

Smear Microscopy is done on direct sputum for Diagnosis samples and concentrated deposit smear examination for follow-up patients.

In addition to this EQA slides are routinely examined.

Gx Laboratory: 30 – 80 samples/day. Av: 40 Tests/day, average 2 runs/day.

Extra Pulmonary samples: Tissue, CSF and Urine samples tested.

LPA 1st Line: It is done only on discordant Gx samples from Newly diagnosed TB patients (low risk) sent from Township and district hospitals. For 2017 and up to **2Q 2018 a total of 196 tests** were done

LPA 2nd Line, started from Nov'17: Performed for patients recruited in STR, **in total 45 tests** were performed.

Solid culture: 3,001 Nos. Contamination rate is around 3 % which is in acceptable limit.
Solid DST (2nd Line): 50 Nos.
Liquid Culture: 3,635 Nos.
LC DST: 1st Line: 102Nos.
2nd Line: 43 Nos.
Contamination rate is around 8% which is in acceptable limits.

Equipment available:

MGIT – 2 Instruments.
BSC - 3 cabinets
Refrigerated Centrifuge: 2
Autoclave – 2 for sterilization and 1 for dirty (8yrs old)
Inspisator:2
GT Blot 20 – 1 (Under Repair)
Twincubator: 1

AMC:
AHU (Negative pressure lab) and all equipment are under Maintenance. All 3 BSCs are certified for performance.

Recommendations:

1. HR to be strengthened: Microbiologist – 1; STLS – 2; LTS - 4
2. Training to be provided for all including 3 laboratory Officers in extended panel of second line drugs in LC DST
3. PT to be resumed with SNRL
4. The following equipment to be procured
   Autoclave for contaminated materials :1
   Twincubator :2 (urgent)
   GT Blot - 48 :1 (urgent)
5. CSF samples to be processed in MGIT

6. Quality of sputum needs to be increased in order to get 2nd line LPA results on time for the STR Patients.
7. Auramine stain (0.1%) sent to Microscopic sites to be supplied once in 2 months as per GLI guidelines.

Meikhtilar District Hospital TB Laboratory: Salient findings:

Meikhtilar TB center situated in the district hospital is headed by Dr. Nyunt Sein and the laboratory performs smear microscopy and Gx under the supervision of team leader Dr. Sai Khay Nom Saing.

Two Laboratory Technicians were posted in the lab each one from Government and from MMA.

Smear microscopy examination is carried out by LED Microscope, with a daily work load of 40-50 slides on average for both diagnosis and follow up. Staining reagents were supplied from Upper Myanmar TB Laboratory once in three months. All the stains were labelled properly, and quality control measures were taken care off. EQA blinded slides were sent to Mandalay lab for rechecking once in a month.

Gx lab has one machine with 4 modules, the average work load being 6 tests/day, all the 4 modules are working and calibrated on 16th October 2017. A total of 1073, 1343 tests were carried out in 2016 and 2017 and 755 tests till 2Q2018; the reports were sent through Gx Alert and the number of invalids reported is less than 5%. Routine maintenance is carried out properly. Biosafety issues were taken care off and the specimens were disposed as per guidelines.

Recommendations:

1. Laboratory needs to receive the EQA results on time
2. The number of Gx tests performed to be increased by strengthening the sputum transport mechanism.
3. Auramine stain (0.1%) needs to be used up to 2 months as per GLI guidelines.

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