Regional Advisory Committee on MDR-TB SEAR (r-GLC) Secretariat

WHO South East Asia Regional Office

PMDT MONITORING REPORT

Country: Nepal

Lead implementing agency: Ministry of Health, Government of Nepal

Inclusive dates of mission: 5 - 11 November 2017

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Contents:

Abbreviations and acronyms

aDSM	Active drug safety monitoring and management
Bdq	Bedaquiline
BNMT	
CHW	Community health worker
Cfz	Clofazimine
Dlm	Delamanid
DOT	Directly observed treatment
DRS	Drug resistance survey
DST	Drug susceptibility testing
DS-TB	Drug-susceptible TB
DR-TB	Drug-resistant TB
EQA	External quality assurance
GDF	Global Drug Facility
GLI	Global Laboratory Initiative
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human immunodeficiency virus
HR	Human resources
HRD	Human resource development
IPT	Isoniazid preventive therapy
IRD	Interactive Research and Development
KNCV	KNCV Tuberculosis Foundation, the Netherlands
Lfx	Levofloxacin
LHLI	LHL International, Norwegian Organisation for Heart and Lung Disease
LPA	Line probe assay
MDR-TB	Multidrug-resistant tuberculosis
Mfx	Moxifloxacin
NATA	Nepal Tuberculosis Association
MOH	Ministry of Health
NTC	National Tuberculosis Centre
NGO	Non-governmental organization
NSP	National Strategic Plan
NTP	National Tuberculosis Program
NRL	National TB Reference Laboratory
PLHIV	People living with HIV/AIDS
PMDT	Programmatic management of drug-resistant TB
PPM	Public–private or public–public mix
QMS	Quality Management System
RR-TB	Rifampicin-resistant TB
RTC	Regional Tuberculosis Centre
SAARC	South Asia Association for Research Coordination
SCI	Save The Children (GFATM subrecipient)
SLD	Second-line drugs
SRLN	Supranational Reference Laboratory Network
STC	Save The Children
STR	Shorter treatment regimen
TB	Tuberculosis
UNITAID	International facility for the purchase of drugs and laboratory commodities for HIV/AIDS, malaria and tuberculosis
USAID	United States Agency for International Development
WHO	World Health Organization
Xpert/MTB/RIF	Rapid TB and MDR-TB diagnostic test based on nucleic acid amplification test
XDR-TB	Extensively drug-resistant tuberculosis

I. Executive summary

i) Progress from last mission

Much progress has been made in the expansion of PMDT, as is laid down in the **PMDT Transition Plan** (July 2017) to introduce new diagnostics, short treatment regimen (STR), using new drugs (Bedaquiline and Delamanid), and including the active Drug Safety Monitoring and Management (aDSM) system.

This plan is an extension of the **National Strategic Plan (NSP)** for Tuberculosis Prevention, Care and Control 2016-2021, where the gains and challenges of TB control, including PMDT, have been articulated. The NSP has been officially endorsed by the Ministry of Health.

The **Drug-resistant Tuberculosis Technical Manual** (clinical guidelines) has been produced in 2017. Also, a **NTP Clinical Manual on TB was** published, incorporating the 2016 WHO recommendations and including a section on Childhood TB and DR-TB.

Inputs from the present rGLC mission were awaited, specifically to get consensus on the diagnostic algorithms, STR and regimen containing new drugs, in order to finalize the Transition Plan and the Technical Manual. Focus of this rGLC mission therefore was on reaching consensus, discuss and observe preparedness at central level and in the field for this transition.

Recommendations from the previous rGLC mission have been addressed, 5 were fully implemented and 6 are still ongoing and approaching implementation. These ongoing recommendations are still to be implemented.

There were also two missions from GLI and SRLN Munich-Gauting specifically looking at laboratory issues. The first mission was conducted to:

- revise/prioritize Laboratory Strategic Plan and recheck/revise projections in line with NSP
- develop of a roadmap for the implementation of the laboratory components of the NSP
- develop infrastructure restructuring for both National Reference Laboratories (NTC and GENETUP/NATA) for quality service delivery
- provide technical assistance to the NTC laboratory team for improving line probe assay diagnostics in order to reduce indeterminate results and cross-contaminations with DNA
- provide technical assistance to GENETUP with further QMS development and the DST in MGIT

A second mission was conducted to:

- introduce QMS to National Reference Laboratory (NRL) at Nepal Tuberculosis Centre (NTC)
- synchronize with the earlier established QMS at National Reference laboratory German-Nepal TB Project (GENTUP)
- develop and implement Standard Operation Procedures (SOP) and forms in GENETUP

Status of Priority recommendations of previous mission (2016)

Recommendation	Responsible persons/ agency	Comments
Establish Treatment/Technical working sub-group in TAG to collect evidences, analyze data and utilize it to formulate policies/SOP for pediatric DR-TB management	NTP and TAG	Ongoing. Recently the pediatric manual (clinical and training) has been developed. Stand-alone SOPs are still to be developed, but the instructions in the manual are clear. Planned Training of regional and provincial Trainer of Trainers (TOTs) is planned to take place before March 2018. The Nepal Pediatric Society is also represented in the TAG
Accelerate and safeguard the process of implementation of mandatory case notification including those from private sectors and endorse strong regulation of over the counter sale of anti-TB drugs	NTP, MOH	Ongoing. The NTP is working on a "TB Act" to formulate mandatory case notification as well as regulation of OTC sale of anti-TB drugs. This Act still needs to be endorsed in Parliament. It is foreseen that it will be tabled this year after the elections, which take place this year.

Actively involve community and civil society to bring the services closer for TB/DR-TB patients as the phasing out of DR-TB (Hostels?) planned in upcoming years	NTP and partners	This activity is planned and the budget is available. In 2018 DR TB patients are going to be treated in the community. Right now 7 DR TB patients are going to be enrolled. The only difference is treatment delivery at home, instead of hostel and clinic, after a short period in hospital.
Review drug orders to adjust transition of shorter regimen and use of newer drug for pre-XDR/XDR patients. Consider early GDF mission for better forecasting and quantifying of drugs use	NTP with support from WHO	Done, as mentioned in the Transition plan. The new drugs still have to be ordered.
Develop clear guidelines, checklists, monitoring indicators for supervision, monitoring and evaluation of PMDT services under NTP for all levels of supervisors and administrators	NTP and TAG	Done
Assign and implement DR-TB focal point at all levels. Develop HR plan that include schedule of training/refreshment course for health staffs that incorporated the latest guidelines/policies e.g. use of new drug, shorter regimen, infection control, pediatric TB, etc.	NTP	Partially done. TB TOTs are identified and training plans are made. aDSM training for TOT is planned to take place immediately following this mission.
Assign IC focal point at all levels to supervise and implement IC measures at all DR-TB health facilities. Review, update and implement the current IC plan according to standard	NTP, MOH	Pending. NTP to review DR TB centres and IC practices. Plans and guidelines exist already since 2013. However, there are limited Human Resources. An IC mission with inventory taking, guideline development and training is planned to take place after March 2018.
The PMDT clinical guidelines will need to be updated to indicate how to use the shorter regimen including modifications to monitoring and reporting	NTP and partners	Done. By end of this mission consensus has been reached over the diagnostic algorithms and treatment regimen. Update of relevant documents, PMDT guidelines and Clinical Manual, will be done immediately following this mission.
Incorporate the use of newer drugs (Bdq and Dlm) in cases of SLD resistance or SLD toxicity to improve treatment outcomes of MDR-TB. Bdq can be the primary new TB drug used in cases of pre-XDR/XDR- TB; however a small amount of Dlm should be available with indications of when to use it. Ensure the pharmacovigilance system in place: at a minimum develop a system consistent with the WHOs recommendations on "active drug safety monitoring and management (aDSM) protocol of reporting of serious adverse events (SAEs). The plan for new TB drugs should be well laid out in the PMDT Expansion Plan	NTP and TAG	Ongoing. Plans to use new regimen and new drugs are laid down in the Transition Plan and Technical Guideline and Clinical Manual. Delamanid importation will be a big hurdle because this drug is not registered in the country, there is no representative of the manufacturer and the quantities required are small.
Consider expansion of Regional labs to intermediate reference laboratory. Strengthen the system of HAIN LPA on SLD for all RR/MDR-TB cases on baseline culture. Consider HAIN LPA for SLD on all smear positive cases of RR-TB to indicate proper DR-TB regimen in a more timely fashion	NTP and partners	There are two reference laboratories, and plans exist to have three more provincial labs to do also DST and LPA. Eventually one laboratory in each province (7) is planned. Triage system using second line LPA

		is agreed upon and already functioning in Kathmandu.
Develop a mechanism to trace patients being referred to other countries (e.g. MoU for cross-border patients)	NTP and other ministries	In 2017 a meeting was held between SAARC, WHO and UNAIDS and IOM. Agreement was reached to use a universal TB card throughout the region. However, treatment regimen differ, no free treatment (for DR TB) in India (low coverage) and patient interrupt treatment.

Achieved	
Progress/ongoing	
No change/pending	

ii) Key challenges identified in this mission in relation to the ToRs

- Implementation of Short Regimen, and longer Bdq containing regimen for pre-XDR and XDR TB patients is taking of slowly. Hampering were the uncertainty about diagnostic algorithms including Second Line Line Probe Assay (SL LPA) for fast triage of patients and regimen design for pre-XDR and XDR patients containing Bdq/Dlm.
- Bdq (and Dlm) is not yet available in the country. Damien Foundation has a cohort of 20 patients ready to be enrolled on the STR, but has to wait for availability of Bdq before starting implementation. Issue is the change in policy of obtaining Bdq free of charge. **NTP Director needs to fill out and sign the Bdq request Annex 1 in order to trigger the GDF procurement process as soon as possible.**
- Active drug safety monitoring and management (aDSM) plans are detailed in recent documents, but still needs to be in place before the roll-out of the STR and use of new drugs. Training of Trainers starts immediately following this mission.
- In the same line, phasing out of Cat II regimen still needs to be done, which depends on the use of new diagnostics including rapid second line drugs testing (patient triage).
- Expansion of PMDT diagnostic and treatment services ("Centres of Excellence") and decentralization of managerial tasks of the NTP to all provinces is planned but uncertainty exists on the new managerial modalities.

iii) Priority recommendations of this mission:

Recommendation	Responsible persons/ agency	Timeline
1. Continue implementing the still ongoing or partially implemented recommendations of the 2016 rGLC mission.	NTP and Partners	**Ongoing**
2. The **PMDT Transition Plan**, after updating with recommended diagnostic algorithms and regimen, including new drugs, should be implemented as planned.	NTP and partners	**Immediately**
3. Revival of **partner coordination** will be essential to streamline support and technical assistance to the NTP, especially in the light of the decentralization process, which is expected to be intensified after the ongoing elections. High turnover of senior management staff in NTC requires dedicated support from partners. PMDT Officers from WHO and partners are needed to support the leadership of the NTC, to maintain and ensure institutional memory, and streamline and coordinate activities and Technical Assistance.	Partners under leadership of WHO	**2018**

Recommendation	Responsible persons/ agency	Timeline
4. **Case finding**: The revised diagnostic algorithm should clearly lead to and visualize the correct DR TB regimen: Short Regimen, conventional regimen and regimen using new drugs. Xpert test to be used as the initial test in high risk groups for DR TB. In areas with restricted access, conventional diagnostic procedures will be followed, but priority for Xpert testing will be given to sputum smear positive cases. Results of the panned Prevalence Survey may be used to target enhanced/active case finding among (DR) TB risk groups and vulnerable populations, other than household contacts and PLHIV.	NTP and partners	**Dec 2018**
5. **Laboratory**: Refer to the recommendations from the recent laboratory missions. Decentralize Xpert sites and FL and SL LPA to all provincial laboratories. NRL to proactively monitor the functional status of Xpert machines and ensure timely repairs, replacement of parts and installation of machines, local maintenance and timely ordering of cartridges. Review Xpert utilization and adjust targets for procurement accordingly.	NTP and partners	**Ongoing**
6. **Treatment**: Start Short Regimen (as pilot) and use of longer regimen with new TB drugs before end 2017, and scale up countrywide by March 2018. Ensure that aDSM is in place, the DR TB Guidelines are updated and finalized, and capacity building done. **NTP Director needs to fill out and sign the Bdq request Annex 1 in order to trigger the GDF procurement process as soon as possible.** Formalise (document) and arrange regular meetings Clinical Expert Team involved in the clinical management of DR TB to discuss the management of individual cases. Cat II regimen should be abolished, and not replaced by a modified Cat II regimen. There is a need for strengthening diagnostic capacity for first line drugs (LPA) in order to diagnose H resistance. Cat II regimen is to be gradually phased out by mid 2018. It is advisable to have a small quantity Dlm available. The NTP Manager should facilitate the importation process using a waiver to facilitate importation. Analyze treatment outcomes of pilot STR and Bdq-containing regimen cohorts, including those on off-label use (Bdq >6 months, children, pregnant, if any) using recommended treatment outcome definitions.	NTP and partners	**Dec 2017** **Immediately**

Recommendation	Responsible persons/ agency	Timeline
7. **Treatment delivery**: Make an inventory of district capacity for ambulatory treatment of DR TB cases, including options for patients for admission to hospital and/or hostel. Intensify training of district staff and community health workers for ambulatory and community based patient care.	NTP and partners	**Ongoing**
8. **aDSM**: Follow the recommendations outlined in the PMDT Transition Plan of 2017. Consider to conduct death audits on all DR TB patients who died, with focus on those using the new and repurposed drugs.	NTP, MOH and partners	**Ongoing**
9. **Recording and Reporting**: Ensure that the new electronic DR TB Patient Tracking and TB Laboratory System is able to provide all information needed to manage DR TB patients including aDSM data. Provide a roadmap with timelines toward full functionality. For next rGLC mission: prepare PMDT programme data in the standard WHO recommended reporting format so that the cascade from presumptive DR TB patients, patients tested, enrolled and their (interim and final) treatment outcomes per treatment regimen, becomes clearly visible.		**Dec 2017** **2018**
10. **Infection Control:** Immediately implement administrative measures at the Regional Centre in Pokhara and Stupa Community Hospital in Kathmandu. Organize an IC mission to review, update and implement the IC plan and roadmap and mainstreaming TB-IC in the existing system, in alignment with current policies (PMDT guidelines, PMDT Expansion plan). In preparation of the planned IC mission, assign IC focal points at national and regional level to supervise infection control measures for DR-TB health facilities	NTP and partners	**Immediately** **2018** **Dec 2017**
11. **Supervision**: Enhance the supervisory visits in the field to include new diagnostics used in PMDT, following the algorithms towards choosing the correct treatment, implementation of the agreed regimen, with new drugs and STR, aDSM (SAE identification and clinical management), interim outcome monitoring including of patients on community DOT, study death analysis, and consistency in paper based and electronic recording and reporting system.	NTP and partners	**Dec 2017**

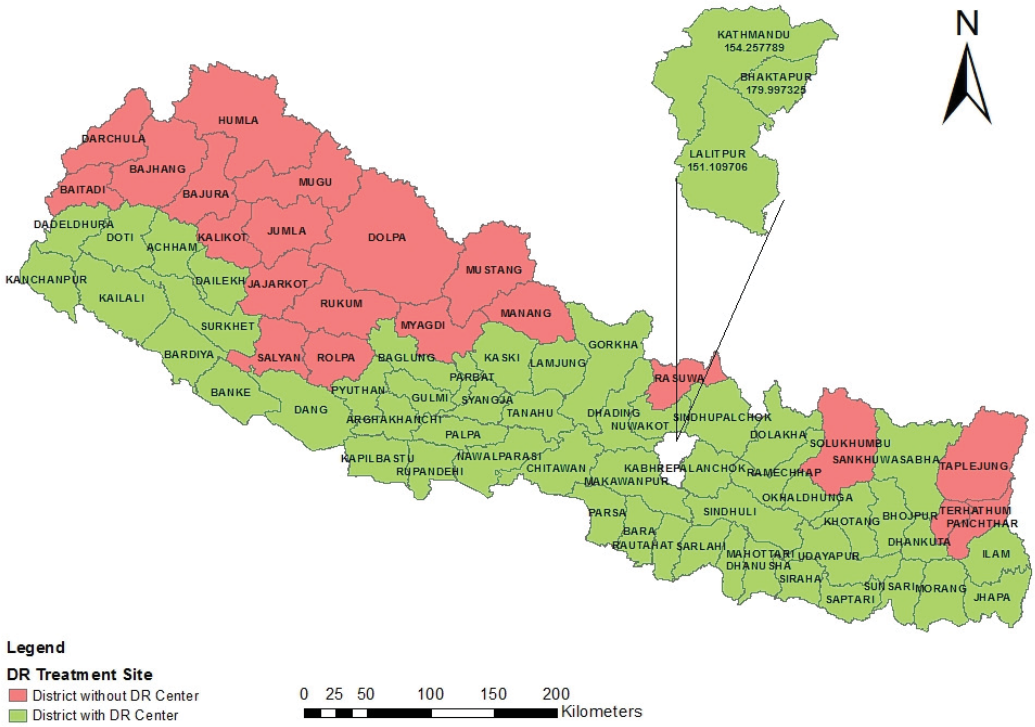
II. Detailed report

A. Introduction/Background

Nepal is a landlocked sovereign state located in South Asia, which is divided into three distinct ecological zones: mountain, hill, and plain (Terai). The hill ecological zone is densely populated with about 44% of country's population. The population of Nepal is approximately 27 million. The country is divided into 14 zones and 75 districts groups into five development regions for administrative purposes: Far-western, Mid-eastern, Western, Central and Eastern. ☐The Terai lies in the southern part of the country where 48% of the population lives. Transportation and communication facilities are more developed in this zone due to its flat terrain. The highest rates of TB burden are located in the most densely populated areas (Terai) in Central Region and other urban areas in Mid-Western Region. ☐

The map in Figure 2 shows that 17% of the districts (the red districts) are not yet covered with PMDT. In these districts <10% of the TB cases are notified annually.

Figure 1. Map of Nepal with coverage of DR TB services in the Districts



B. Existing TB Program

Nepal adopted the directly observed treatment short course (DOTS) strategy in 1996 and reached nationwide coverage since 2001. National Tuberculosis Centre (NTC) is one of the five centres under the Ministry of Health and Population (MoHP) and National Tuberculosis Program (NTP) is one of the priority programs of the Government of Nepal (GoN).

NTP Structure

The NTC is the central body responsible for policy, planning, implementation, monitoring and evaluation of the NTP. The National Strategic Plan is a key instrument to appropriately manage and implement NTP. It highlights the overall aim for the control of TB and clearly defines the goal(s) that needs to be reached as well as the Operational Objectives that should be achieved in the next five-year through strengthening TB control efforts.

NTC has established Program Management Unit (PMU) at the **central** level for overall management of the Global Fund grants. This PMU consists of an overall coordination, finance, monitoring & evaluation, sub recipient management, training, procurement and technical sections for private public partnership and advocacy, communication & social mobilization.

At the **Regional** level, NTP activities are planned and carried out in coordination and cooperation of the Regional Health Directorate. At the Regional level fulltime permanent Regional TB Leprosy

Officers are appointed and are responsible for program implementation, training, monitoring & evaluation and supervision of program activities and drug logistics.

At the **District** level, the District Health Officer/District Public Health Officer is responsible for planning and implementation of NTP activities within the district. Within the district, the basic unit of management for diagnosis and treatment are district hospital and the primary health care centres. Directly Observed Treatment is available at Health Post, Sub Health Post and other health institutions within the district.

PMDT is currently supported under Global Fund National Strategic Application (NSA) grant since July 2010 (Phase 1 – July 2010-July 2012). Current NSA grant has been approved till 18 March 2018 for US$ 10 million.

PMDT in Nepal is being supported extensively by the German-Nepal Tuberculosis Project (GENETUP), National Anti-Tuberculosis Association (NATA) and other NGOs such as Damien Foundation, Save the Children International (SCI), GFATM, KNCV, as well as WHO.

Nepal is also one of the beneficiaries of the UNITAID, under the TB Reach Project that has provided 15 GeneXpert® machines and 56,000 cartridges for their use since 2013. ☐

Nepal is considering a second UNITAID sponsored project, endTB, which would support and facilitate the use of new TB drugs (Bdq and Dlm) in up to 80 patients. ☐

Nepal is now planning to conduct a National Prevalence survey in 2018 when all the preparatory work for the survey has been completed. This will improve the knowledge on epidemiology and extent of TB burden in Nepal, including targets for intensified/active case finding.

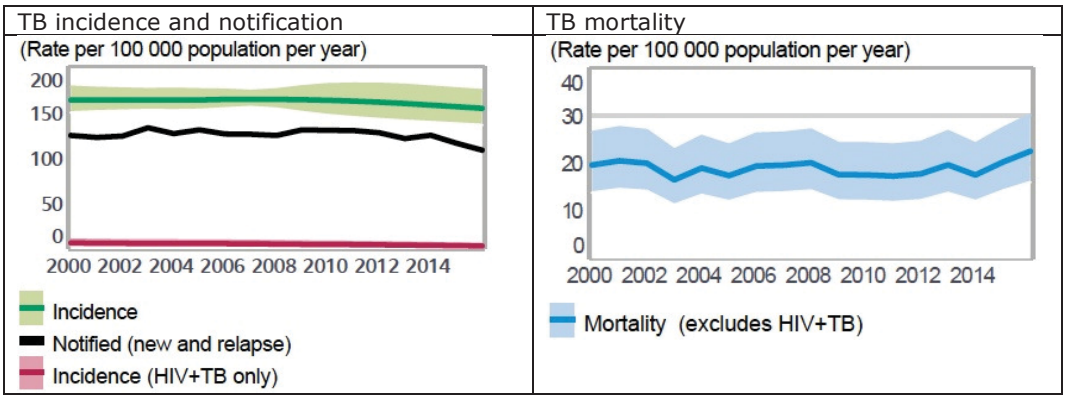
TB Burden and notification

The incidence rate of all forms of TB in 2016 in Nepal is 154 per 100 000 population, with case detection of 79%. Nepal missed the target towards MDGs for 50% reduction of incidence and prevalence compared in 1990, with prevalence rate remain at 215 per 100,000 population in 2014. However Nepal met the target to have halved the mortality of TB cases, with mortality rates 22 per 100 000 population in 2016.

Table 1. TB burden in Nepal (Global TB Report 2017)

2016	Absolute #	Rates (per 100,000)
TB mortality (excluding HIV+TB)	6,500	22
TB mortality (HIV+TB only)	270	0.95
TB incidence	45,000	154 (136-174)
RR-/MDR-TB Incidence	1,500	5.1 (3.1-7.1)
HIV+ TB Incidence	950	3.3 (1.8-5.2)

Figure 2 and 3. Trend of TB incidence, notification and mortality, Nepal, 2016

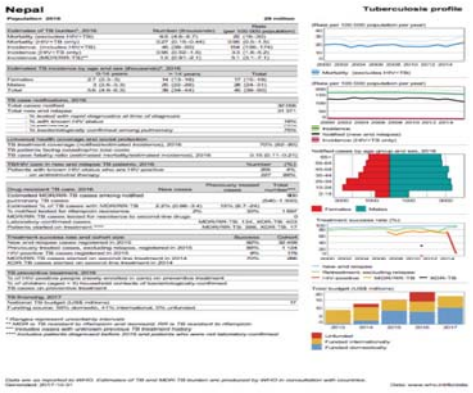


The size and direction of the TB epidemic in Nepal is uncertain, but there is nothing to suggest that incidence is going down and the population has been increasing. The planned Prevalence Survey will determine the size of the TB burden in Nepal. If it follows recent surveys in several other Asian countries, it will show that the TB burden is much bigger than currently thought. Notification rates in the hills and mountains of Nepal are significantly less than those in the terai, making it likely that TB is under-diagnosed in the hills, and particularly in the mountains.

Treatment outcome

Treatment success rate among new pulmonary, bacteriologically confirmed cases remain stable at more than 90% since 2009, while for retreatment cases it has been declining since 2011 from 85% to 74% for 2013 cohort but later increasing again.

Figure 4. Treatment success rate by type of cases, Nepal, 2016



The treatment success rate of bacteriologically positive new and relapse TB cases has remained high, above 90%, for the past several years.

TB/HIV situation

TB/HIV care in new and relapse TB patients in 2016	Number	%
Patients with known HIV status who are HIV positive	255	4%
On ART	227	89%

No further comments.

C. DR-TB situation

Nepal is planning to have a Drug Resistance Survey (DRS), after conducting a national prevalence survey, which has been delayed till 2018. Previous DRS undertaken in 2011-12 conducted by GENETUP in collaboration with WHO estimated the prevalence of MDR-TB to be 2.2% (CI: 1.3 – 3.8) among new cases, 15.4% (CI: 10.1 – 22.7) among previously treated cases. This translates to an expected number of around 1,200 RR/MDR TB cases in Nepal (540 among notified new TB cases and 620 among notified retreatment cases).

An XDR TB survey conducted by GENETUP in 2012 showed that among MDR-TB patients, 28% had Pre-XDR TB and 8% had XDR TB. In 2016 at GENETUP, 40% of 200 MDR-TB samples indicated resistance for FQ. Trend of DR TB case notification is shown in figure 5,m showing an increase in pre-XDR and XDR case notification, probably as a result of better testing capacity with Xpert and SL LPA.

Nepal can be considered a low burden drug resistance country. The numbers of RR/MDR TB cases being diagnosed is slightly increasing and was 379 in 206/17, especially among failures of Cat I and increasingly also primary MDR TB among new cases. Perhaps a high initial Isoniazid resistance plays a role, as well as expansion of testing with Xpert, FL LPA and DST.

So far only passive case finding strategy applied for DR-TB.

The vast majority of MDR-TB patients receive clinic-based DOT (meaning the patient comes to the clinic every day for DOT). Many patients have to move near a treatment or sub-treatment centre to receive their care. To offset the hardship of moving or daily transportation costs, the patients on MDR-TB treatment receive 2,500 NPR per month.

Figure 5. Trend in RR/MDR case notification by tyoe of DR TB, 2016

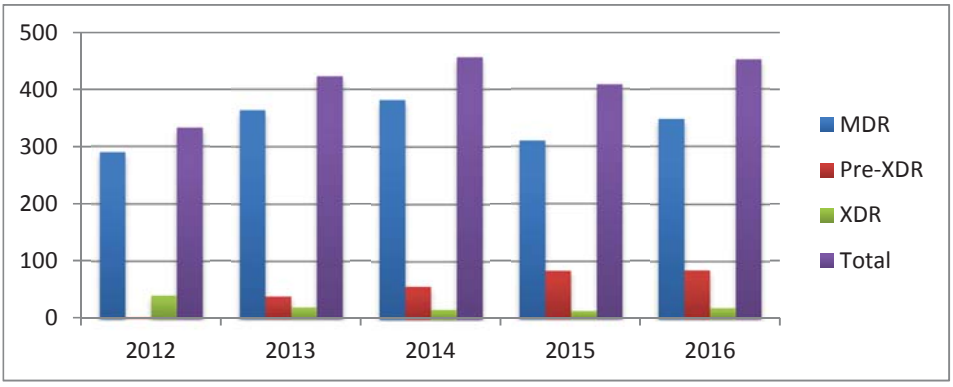
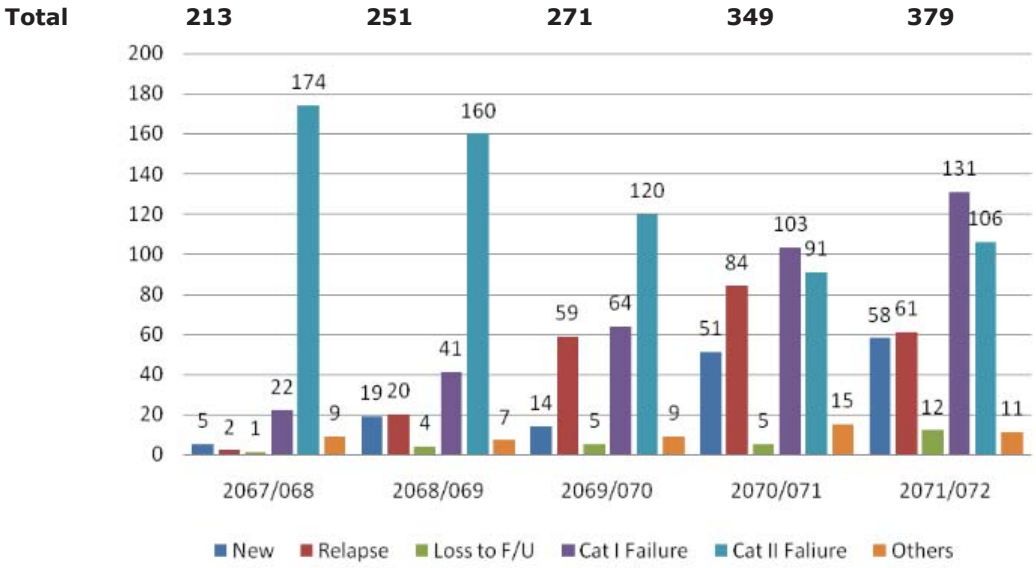
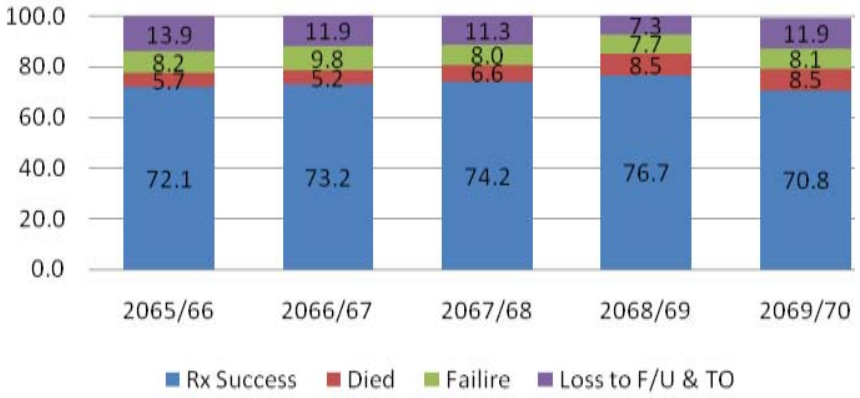


Figure 4. Trend in RR/MDR case notification by risk group*



Treatment outcomes of RR/MDR TB are favourable as compared to global data. However, Loss to Follow up should preferably be less than 10% and mortality less than 5%.

Figure 5. Trend of RR/MDR treatment outcomes*



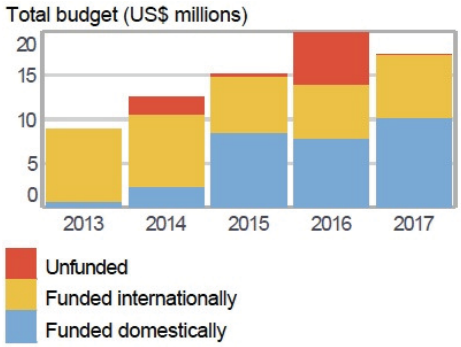
* The data notation in Nepal is different: the year 2071/072 means 2015/2016

D. Government commitment

The NTP is one of the "Priority One" programmes of the Ministry of Health (MoH), Government of Nepal (GoN). It is a comprehensive national programme for TB care and control supported by many national and international stakeholders, including community groups. The National Tuberculosis Centre (NTC) is the central body responsible for policy development, planning, and implementation of the NTP, as well as its monitoring and evaluation.

Despite being a priority health programme, the domestic funding is a small percentage of the total NTP budget, including salaries and infrastructure. About 47% of NTP budget is provided by the Global Fund to fight AIDS, TB and Malaria (GFATM) (Figure 6). LHL International, WHO and National NGOs have also regularly contributed to TB control activities with a relatively modest proportion of the budget. The proportion of unfunded activities has decreased substantially in 2017. The Government of Nepal has used domestic funding to cover 100% first line anti-TB drugs and an increasing proportion (40% - 60%) of second line anti-TB drugs. ☐

Figure 6. Funding of NTP



E. Organisation of PMDT and Partnerships in Nepal

A DR-TB unit was recently established at the National TB Centre (NTC) that is headed by a senior physician consultant and with a PMDT coordinator. The DR-TB Unit is responsible for coordination and implementation of PMDT, including guideline development. In the network, there are a total of 14 PMDT centres that can diagnose, treat and manage DR-TB patients. The PMDT centres are normally linked with a hospital or a health centre. After diagnosis and enrolment on MDR-TB treatment, DR-TB patients are managed by nurses and other health care workers at the sub-treatment centres. Hospital admission is applied for short period of time or patients who need special care. DOT is mainly provided at the health care facilities. Patients on MDR-TB treatment receive some financial support during the treatment. This support should be continued but also simultaneously plan to decentralize / bring services closer to community

Recently, the national PMDT guidelines have been revised that include the updates of current WHO recommendations. In addition, the Clinical Guideline is just to be finalized, following the discussions we had and consensus reached on the diagnostic algorithms, regimens and use of new drugs. It is expected that it will be and approved by the NTC or Ministry of Health. The phase out of the category II regimen for previously treated TB patients has been considered and it was agreed that it will be phased out by July 2018.

Private Sector. No system has been established yet of notification of TB cases from private sector. High resistance to FQ, and the role of private sectors and over the counter availability of anti TB drugs require regulations on this issue. Plans exist to start regulation the OTC issue of TB drugs, as well as mandatory case notification through a TB Act, to be tabled to Parliament. The NTP foresees to address these issues also through the Medical Association and approaching private hospitals, as well as address medical students in their pre-service curriculum.

Multiple external and country-based partners provide assistance to the NTP in TB/DR-TB care, including GENETUP, WHO, Damien Foundation, Save the Children International, LHL International and KNCV. The role of partners will become increasingly important in the light of the decentralization process, which will be apparent following the elections which are taking place at the moment. It is anticipated that existing NTP structure will be phased out without clear view on what will come instead. There is a need to maintain at least a national reference centre (NTC) to manage TB control in Nepal. Partner coordination will remain essential to streamline support and technical assistance to the NTP.

Recommendation:

- Revival of partner coordination (meetings) will be essential to streamline support and technical assistance to the NTP, especially in the light of the decentralization process.

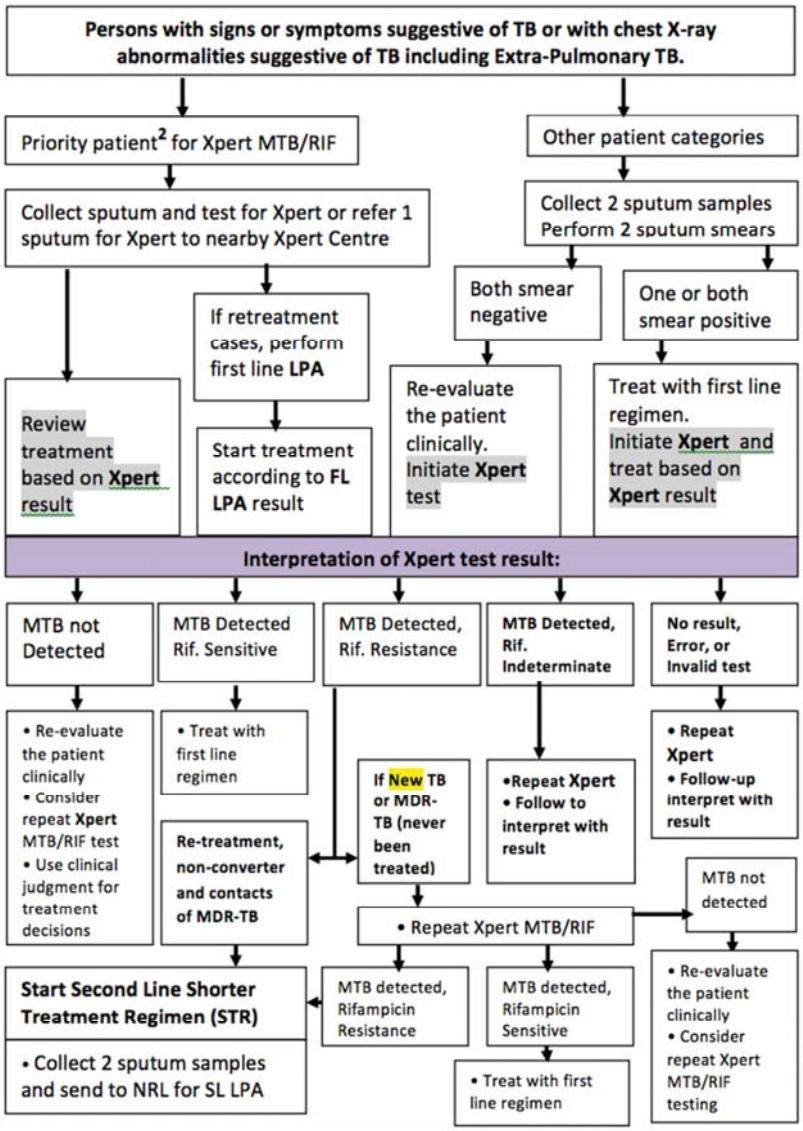
F. Advocacy and community engagement

Refer to treatment delivery (DOTS) below. It appears that there is a huge stigma associated with TB in Nepal. When engaging community DOTS workers for DR TB management, this issue could be addressed in the communities.

G. Case finding strategy

So far only passive case finding strategy applied for DR-TB.

Figure 7. Diagnostic algorithm for presumptive TB, and interpretation of Xpert results

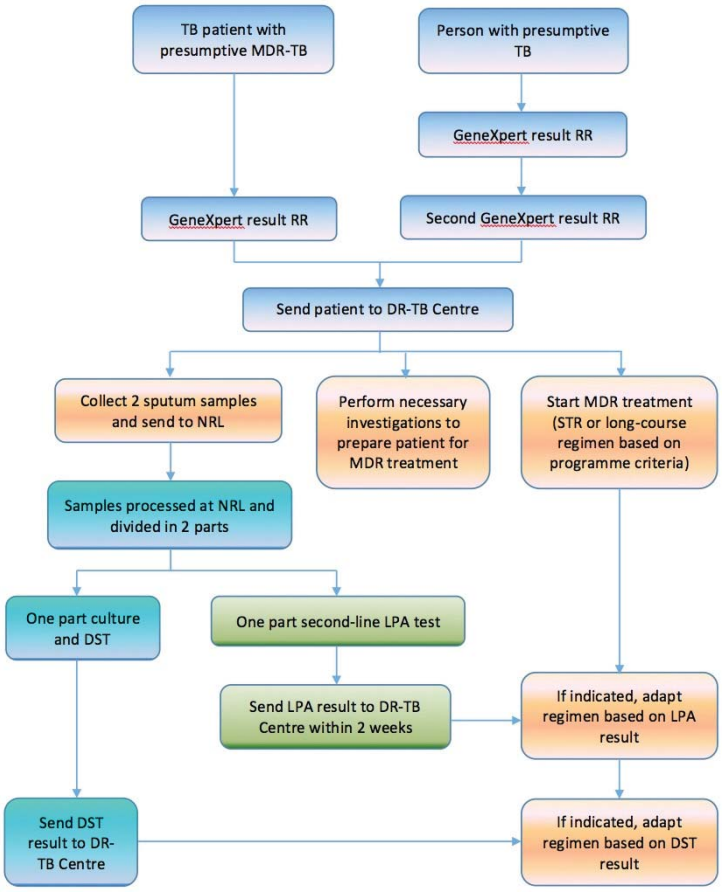


[2] Priority patients include PLHIV, contacts of RR/MDR-TB, lost to follow-up, relapse, failure, non converters (Smear positive at end of the intensive phase of treatment), children, patient live in close (congregate) settings, sample collected through courier system, diabetic, patient whoever has access to Xpert Centre.

This algorithm is slightly different from the one in the Clinical manual. This one mentions the Short Treatment Regimen as a possible outcome of the algorithm. Therefore, the Clinical manual needs to be updated accordingly. In addition, it is advisable that the different regimens, where this algorithm leads to and which is the very purpose of it, are better visible.

The box "Review treatment based on Xpert results" is not clearly understood, as it still concerns a presumptive TB patient, not yet started on treatment. Perhaps what is meant is: initiate treatment based on the Xpert results.

Figure 8. SOP and diagnostic algorithm for using Xpert



In the above diagnostic algorithm it has to be made clear that Persons with presumptive TB are to be divided into two groups, in order to be consistent with the previous algorithm.

Intensified case finding (ICF)
Several projects of active or intensified case finding in Nepal focusing on hill areas, factory workers, private sector, garbage collectors, street children, urban poor in slum areas, refugees, monks, initial defaulters, contacts of TB patients and PLHIV, have shown a disappointing yield, except among TB contacts and PLHIV. Active case finding will therefore be limited to (but at the same time intensified in) those two groups with the highest yields, which offer the best cost-effectiveness and value for money.

Nevertheless, analysis of the planned Prevalence Survey may provide clues for focus intensified case finding on additional risk groups in Nepal.

Recommendations:

- The revised diagnostic algorithm should clearly lead to and visualize the correct DR TB regimen: Short Regimen, longer regimen and regimen using new drugs.

- Xpert test to be used as the initial test in high risk groups for DR TB. In areas with restricted access, conventional diagnostic procedures will be followed, but priority for Xpert testing will be given to sputum smear positive cases.

- Results of the panned Prevalence Survey may be used to target enhanced/active case finding among (DR) TB risk groups and vulnerable populations, other than household contacts and PLHIV.

H. Laboratory

Laboratory issues were recently extensively addressed during two missions from GLI and SRLN from Germany. Their recommendations are here referred to. We observed still not functional MGT machines in both laboratories (in validation stage), as well as not serviced Bio Safety Cabinets level II.

Laboratory network:

Culture and DST: The laboratory network in Nepal continues to expand. There are two reference laboratories for TB (NTC laboratory and GENETUP) with established culture, DST and LPA for first and second-line drugs. Liquid culture by MGIT at the NTC reference laboratory and GENETUP laboratory is in process of validation of results. Three regional laboratories have established solid culture but they are in the process of validating results. There is a plan to set up LPA at these three regional laboratories. The LPA equipment for these 3 laboratories will be procured in July and LPA is expected to be functional by end of 2017.

Xpert MTB/RIF (Xpert): There has been a steady increase in the number of Xpert sites. By end 2017, 60 sites are anticipated from different sources, including those for the Prevalence Survey. Of the existing sites, not all modules have been working. Recently repairs and replacements have been done. At the moment there are 31 Xpert sites with 37 Xpert machines and 113 modules, out of which 30 are in need of repair or replacement. Cepheid provides technical support and supply of modules for replacement as well as solving the Xpert non-functionality problems.

Xpert testing is becoming the more important first diagnostic test for all presumptive TB patients, as reflected in the diagnostic algorithms. There is a need to expand the use of Xpert in the diagnostic algorithm in order to detect more TB as well as DR-TB cases.

Sputum referral system is available via courier from the diagnosis and treatment sites to Xpert sites and reference laboratories for reference laboratory services such as culture, phenotypic DST or LPA.

LPA: Both FL-and SL-LPA are currently done only in 2 laboratories (NTC and GENETUP) but will be expanded to three more sites. At the moment all samples have to be sent by courier to these two laboratories for LPA and DST. The Turn Around Times reported in the two Kathmandu reference laboratories and in the Regional TB Centre in Pokhara were satisfactory. Results are provided by sms or email.

Recommendations:

- Refer to the recommendations from the Laboratory missions
  Decentralize Xpert sites and FL and SL LPA to all provincial laboratories.
  NRL to proactively monitor the functional status of Xpert machines and ensure timely repairs, replacement of parts and installation of machines, local maintenance and timely ordering of cartridges. Review Xpert utilization and adjust targets for procurement accordingly.

I. Treatment strategy

Regimen

During the workshop on the recommended regimen the following issues and concerns about the in Nepal proposed regimen were discussed.

1. Preserving Bdq in case of low level resistance to FQ and resistance to injectable:
   This was not supported, because it would weaken the regimen and could therefore raise some ethical concerns about access to adequate treatment, and prioritizing preserving TB drugs over patient's life. The proposed drug combinations have unclear effectiveness. Finally, x=concerns exist about the country capacity to detect low level FQ resistance.

2. Adding Mpn to the XDR TB regimen:
   Concerns raised include uncertainties about effectiveness of D3 agents, complexity in administering (intra venous administration every 8 hours).There are also limited data/few publications supporting this intervention.
3. Replacing Cs to Eto:
   Concerns were the potential correlation of H resistance and Eto.
4. Adding Mfx and High dose H in case of low level of FQ resistance instead of Lzd and Bdq:
   Concerns included uncertainties about country capacity to detect low level FQ resistance countrywide, the correlation between low level FQ resistance and the high dose of H, and unclear effectiveness of high dose H over Lzd and Bdq combination.

The regimens agreed upon during the one-day workshop are in line with WHO recommendations and are presented in the table below. These are also to be incorporated in the Transition Plan, The PMDT Guideline and the TB Clinical Manual, as well as in all training materials.

Table 2. Recommended DR-TB treatment regimen

Patients subgroups	Regimen
Short Regimen (STR)	6 Km-Mfx-Eto-Cfz-Z-$H_{high\text{-}dose}$-E **/** 5 Mfx-Cfz-Z-E
Standard MDR regimen	8 Km-Mfx-Eto-Cs-Z / 12 Mfx-Eto-Cs-Z
Pre-XDR, resistant to FQs	8 Km-Cs-Lzd-Cfz-Z-Bdq/Dlm(6 months) / 12 Cs-Lzd-Cfz- Z
Pre-XDR, resistant to injectables	8 Lfx-Cs-Lzd -Cfz-Z-Bdq/Dlm(6 months) / 12 Lfx-Cs-Lzd-Cfz-Z
XDR TB	12 Eto-Cs-Lzd-Cfz-Z-Bdq/Dlm(6 months) / 12 Eto-Cs-Lzd-Cfz-Z

When treating DR TB patients with adverse effects, comorbidities, additional resistance patterns, etc. the PMDT Clinical Expert team of the TAG may on a case by case basis decide on modification of the regimen.

Patient management: although a subsection of the TAG is assigned as PMDT working group (9-11 doctors, quorum of 4-5 doctors), in practice this group is meeting only once in 3 to 4 months. Presently individual members (TB Physicians) discuss regularly management difficult DR TB patients. However, it is advisable to have a more former Clinical Expert Team, or Concilium, consisting of all experts involved in the management of DR TB patients, such as clinicians, pharmacist, laboratory technologist, nurse, social worker, etc.. This team should meet on a regular basis (weekly/monthly) to discuss the clinical management of individual cases, also of patients managed in peripheral centres.

Cat II regimen: Reportedly there is a 20% H resistance among retreatment cases and 5% among new TB cases. NTP suggested to modify the Cat II regimen to 3HRZE/5HRE and not using S anymore. However, this regimen was previously recommended by WHO as a first line regimen for countries with high initial H resistance. Soon WHO will recommend another regimen for patients H resistance. For now, the Cat II regimen should not to be replaced by a modified Cat II regimen. It was agreed that existing Cat II regimen will be gradually replaced by mid 2018.

Bdq-containing regimen: Although not an official WHO recommendation, some patients who could not be put on strong regimens due to lack of options and did not yet bacteriologically convert, could be extended to more than 6 months (until 8 months) of Bdq.

Delamanid (Dlm): It is advisable to have a small quantity Dlm available. Importation seems to be difficult because this drug is not registered in the country, there is no representative of the manufacturer in Nepal and the quantities required are small. A possible option for importation would be using a Government waiver.

We observed an issue with ordering Bdq. Previous missions recommended obtaining Bdq under the USAID donation programme. However, recently this policy was changed and orders should be placed (and paid for) through GDF. There is an urgency here because the pilot project by Damian Foundation will guide countrywide implementation of STR and use new drugs.

The team explained the situation by email, which we forwarded to GDF Geneva. The GDF reply: Nepal is a donation-eligible country for the Bdq Donation Program. In order to trigger a new procurement process for the donation, GDF would need the PRF duly filled and signed by the NTP.

The latest version is available at: http://www.stoptb.org/gdf/drugsupply/procurement_forms.asp and the Bedaquiline Annex 1 to be signed by NTP.

Recommendations

- NTP Director needs to fill out and sign the Bdq request Annex 1 in order to trigger the GDF procurement process.
- Start Short Regimen (as pilot) and use of longer regimen with new TB drugs before end 2017, and scale up countrywide by March 2018. Ensure that aDSM is in place, the DR TB Guidelines are updated and finalized, and capacity building done.
- Formalise (document) and arrange regular meetings Clinical Expert Team involved in the clinical management of DR TB to discuss the management of individual cases.
- Cat II regimen should be abolished, and not replaced by a modified Cat II regimen. There is a need for strengthening diagnostic capacity for first line drugs (LPA) in order to diagnose H resistance. Cat II regimen is to be gradually phased out by mid 2018.
- It is advisable to have a small quantity Dlm available. The NTP Manager should facilitate the importation process using a waiver to facilitate importation.
- Analyze treatment outcomes of pilot STR and Bdq-containing regimen cohorts, including those on off-label use (Bdq >6 months, children, pregnant, if any) using recommended treatment outcome definitions.

Treatment delivery (DOT)

Present policy regarding treatment modalities is to focus on ambulatory treatment, following hospital admission for maximum two weeks. There are a number of hostels, or in between homes, for those DR TB patients living too far away for daily DOT at the hospital. These hostels are going to be phased out, although some hostels may still be needed. Patient centeredness includes giving the patient options to be treated at home, in hostel or in hospital. Different levels of capacity of staff to initiate treatment and provide monthly follow up with required tests (chemistry, ECG, etc.) centralized case management will continue to be needed.

In the Regional TB Centre (RTC) in Pokhara there is no laboratory for chemistry and no ECG machine yet, but plans exist to start this service here in the near future. Patient management at the RTC is well done. The experienced staff communicate with patients, and their relatives if needed, by phone and sms text. They also sometimes face cross border issues, for instance with a patient who's the husband resides in India. There is regular communication about difficult cases (XDR) with Dr. Bhabana from GENETUP and patients are also referred to her if necessary.

NTP is in process to involve existing community DOTS workers to also care for DR TB patients. We observed a very experienced and motivated Community DOTS worker (and her son as enthousiast assistant), willing and ready to also take care of DR TB patients. She also plays an important role as screen for presumptive TB and many referred persons by her actually turned out to have TB.

Recommendation

- Make an inventory of district capacity for ambulatory treatment of DR TB cases, including options for patients for admission to hospital and/or hostel. Intensify training of district staff and community health workers for ambulatory and community based patient care.

J. Drug management and Pharmacovigilance/aDSM

Drug and supplies management. As suggested in the previous rGLC report, a GDF mission for better forecasting and quantifying of drugs use is in the Transition Plan and will be conducted in 2018. Therefore detailed analysis of drug and supply management was not included in this mission.

Storage of TB drugs, including second line drugs, is adequate, the temperature is cool and controlled by Air Conditioners. No stock outs were reported. A few years ago some stock had to be discarded due to expiry of the drugs. It concerned 24,000 tablets Eto and 80,000 tablets Cs.

A new drug consignment just had arrived when visiting the store. The present stock position is as mentioned in the table below.

Table 3. Stock position of DR TB drugs in Nepal as per 10 November 2017.

	Medicines	Stock on hand	Expiration date
1	Cm(1000) Capreomycin 1000mg Powder for injection	3.129	28-02-18
		5.012	04-03-18
		10.448	16-03-20
		8128	18-03-20
	Total	**26.717**	
2	Km(1000/4) Kanamycin 1000mg/4ml Solution for injection	**38.450**	31-10-18
3	Amx/Clv acid(875/125) Film coated tablet(s)	**169.764**	31-01-20
4	Cfz(100) Clofazimine 100mg Capsule(s)	10.900	31-03-20
		12.700	30-04-20
		92.900	31-03-21
	Total	**116.500**	
5	Cs(250) Cycloserine 250mg Capsule(s)	255.900	31-12-18
		49.800	31-01-19
		638.800	31-01-21
	Total	**944.500**	
6	Eto(250) Ethionamide 250mg Film coated tablet(s)	154.100	31-07-19
		230.500	31-10-19
		499.500	31-12-20
	Total	**884.100**	
7	Lfx(250) Levofloxacin 250mg Film coated tablet(s)	246.700	30-06-18
		249.700	31-12-19
	Total	**496.400**	
8	Lnz(600) Linezolid 600mg Film coated tablet(s)	3.460	31-05-18
		16.200	31-09-19
	Total	**19.660**	
9	Mfx(400) Moxifloxacin 400mg Film coated tablet(s)	**11.090**	31-08-19
10	PAS (Na 60% w/w) 4000mg Granules/Sachet	34.980	28-02-18
		2.550	31-08-19
		74600	31-03-20
		92225	30-04-20
	Total	**204.355**	
11	Z(400) Pyrazinamide 400mg Film uncoated tablet(s)	3.504	31-08-18
		135.112	31-12-18
		694.848	31-01-19
		146.496	31-09-19
	Total	**704.928**	31-12-19

aDSM is composed of clinical monitoring, clinical management and reporting of Serious Adverse Events (SAE).

Pharmacovigilance is under responsibility of the Department of Drug Administration (DDA) of Nepal. A pharmacovigilance system based on spontaneous reporting exists and it collects data on the drug adverse events from different health care facilities. An online reporting system is available for collection and reporting of the data at the health care facility level. However, the coverage of this system is not yet including TB facilities. The DDA has been working on the expansion of the system to the disease programmes including TB and the DDA is willing to participate and support the establishment of aDSM for MDR-TB.

The organisation of aDSM is addressed in the PMDT Transition Plan and are outlined as follows:

- Core package of aDSM needs to be established for reporting SAEs, and it's components need to be included in the revised PMDT guidelines (e.g. data collection forms, schedules of testing and examinations, coordinating mechanism, M&E)
- Ms Kamala Wagle was appointed by the NTC director to be the focal person for aDSM, who will coordinate aDSM activities
- TB technical advisory group (TAG) will be formalized as the coordinating body for aDSM with the representatives from DDA and at least a cardiologist to be involved in this group.
- NTP was currently working on the development of an electronic/online database for DR-TB. aDSM data need to be included in the database. After setting up the database, linkage with the global database to be established to contribute Nepal aDSM data to the global database

- In all DR-TB treatment centres the laboratory services and clinical examinations required for aDSM (such as EGC, liver function test etc.) should be available or accessible at the nearby health centres or hospitals. NTP's DR-TB unit to assess the availability of or the accessibility to the laboratory and clinical services that are required for aDSM in all the DR-TB treatment centres in advance prior to the start of the implementation of new regimens
- Update the PMDT guidelines with aDSM components
- Set up a referral mechanism that links DR-TB treatment centres with hospital facilities for further management of serious or severe adverse events that may occur during the treatment. Details of this mechanism need to be developed further by NTP DR-TB Unit.

Clinical monitoring and reporting: there is a separate system for collecting information on drug adverse reactions existing in DR-TB treatment centres. All adverse events occurring in MDR-TB patients during treatment are collected through a designed data collection form, which is submitted to the NTC on the monthly basis. The data collection is being implemented by the NATA/GENETUP DR-TB treatment centre.

A special aDSM monitoring and reporting form has been designed, but we were not sure whether it is already in use. A aDSM training of Trainers of Trainers is going to be held immediately after this mission.

Clinical management is outlined in Clinical Manual. In addition, death audits are helpful to learn how DR TB case management using new drugs may be improved. The PMDT team within the TAG should analyse all deaths of DR TB cases, with focus on those using the new and repurposed drugs.

Recommendations:

- Follow the recommendations outlined in the PMDT Transition Plan of 2017.

- Consider to conduct death audits on all DR TB patients who died, with focus on those using the new and repurposed drugs.

K. Recording and reporting, and data management

There are 16 PMDT Recording and Reporting forms and registers, which have been reviewed to accommodate pre-XDR and XDR, use of new drugs and aDSM.

Most of the recording forms are neatly and completely filled out on the Treatment Cards, and in the MDR-TB Register. The patients carry and exact copy of the Treatment Card with them, including a passport picture. We observed that the dosages of medications used for patients were correct.

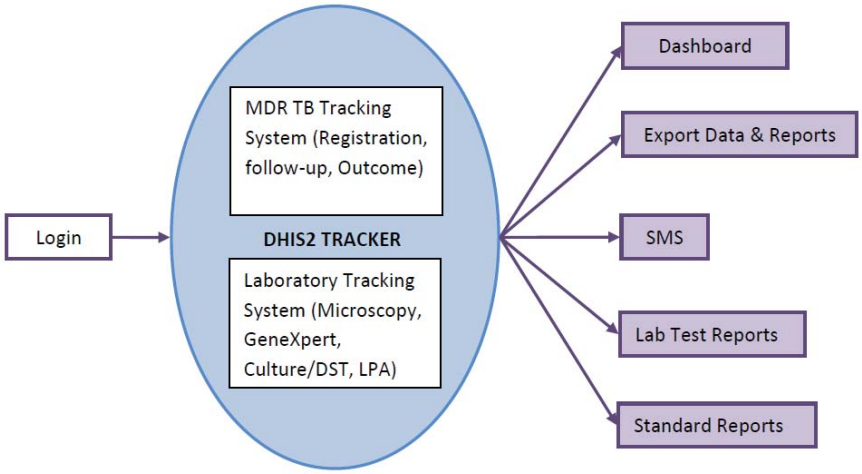
Reports remain paper-based. The existing Open MRS system, called Master ETB register, is used for 6 years. It is a web based application. Till this date Master E-TB register has 6 years tuberculosis data in a central online database. However, the number of registrations in master E-TB register is much less than actual tuberculosis cases (around 50%) and is not functioning satisfactorily. Master E-TB register system had some technical issues on database structure, validation, functionality of viewing statistics and feedback to users. These issues were hindering the recording and reporting process. Thus, ETB has been upgraded, along with feedback mechanism, SMS integration will let user know the progress and possible mistakes and incomplete information.

The DRTB Patient Tracking and TB Laboratory System is a Web-Based Management Information System developed using DHIS2 platform for effective management and monitoring of Multi Drug Resistant (MDR) Tuberculosis (TB) Patient by taking their treatment stage and generate reports for MDR TB management program.

This system also features the complete laboratory information system, including Microscopy, Culture/DST, GeneXpert, and LPA and provides SMS notifications to the patients/DR Focal person of their test results and notification.

As both DRTB Patient Tracking and TB Laboratory System are incorporated within the same system, a patient can be tracked with single system ID within both systems.

Figure 7. DRTB Patient Tracking and TB Laboratory System



In the broader aspect this system is expected to strengthen DHO/DPHO and MDR Treatment Centers to assume responsibility for providing information to the concerned health institutions at districts and higher authority regularly and keep track of updated patient information and also to improve the overall treatment and follow-up procedures of DR patient.

The system is still under development and it is not known when it will be operational. Orientation to the DTLOs and statistical officer is on-going. It is expected that registration will increase rapidly form next quarter onwards.

The SMS notification is very helpful to alert health workers whenever a person within their catchment area is diagnosed with DR TB. It is not clear whether the system allows for aDSM notification and the NTP may whish to ensure that it does.

The challenges for the implementation of this web based system include availability internet and computers, workers skilled in the system, and discrepancies between the system and paper based recording and reporting.

Drug management appears not to be included, and is presently managed by the QuanTB program.

Although reports are available in Xcel sheets it is advisable to have the data presented on day one in the WHO recommended format. This enables fruitful discussions about bottle necks and improvements of the programme.

Recommendation:

- Ensure that the new DR TB Patient Tracking and TB Laboratory System is able to provide all information needed to manage DR TB patients including aDSM data. Provide a roadmap with timelines toward full functionality.
- For next rGLC mission: prepare PMDT programme data in the standard WHO recommended reporting format so that the cascade from presumptive DR TB patients, patients tested, enrolled and their (interim and final) treatment outcomes per treatment regimen, becomes clearly visible.

L. Infection control (IC)

IC is partially addressed in the Clinical Manual, in the PMDT Guidelines, but not in the Transition Plan. It consists a set of recommendations, but no implementation plan.

The NTP is planning an IC mission in 2018 to make an inventory, develop guidelines and SOPs and to train staff who are going to be the IC focal persons in their place of work.

We observed that with relatively simple administrative measures, already a lot could be achieved.

The Regional TB Centre in Pokhara is a large and spacy building with good ventilation. However, the doctor's consultation rooms at the Regional TB Centre are completely enclosed and only have one access door. In the administrative rooms there are rooms with windows. So, either an

exchange of rooms between administration and OPD should be done, or at least an UVGI light should be fitted in the two consultation rooms.

The busy urban TB clinic of Stupa Hospital, where more than 80 patients are seen daily including 7 MDR and 2 Pre-XDR TB patients, has a fan, but a window high on the wall is closed and covered by corrugated iron sheets. Simply removing the sheet could already improve ventilation. The staff was wearing a surgical mask, mostly to protect her from the dust coming from the very busy road.

In both facilities, TB patients are seen in the DOTS clinic though a window with a small opening. Injections are given inside and ventilation within the room seems to be good. No posters were seen with proper cough etiquette pictures or instructions.

We could not observe practices of triage of OPD patients. Posters on the wall are outdated and there were no posters seen explaining cough etiquette to patients.

Sputum collection is done in a special boot outside in the garden. The boot has only one window removed and a small circular opening in the roof. It may be much better to collect sputum just in the open air.

The laboratory at GENETUP premises was recently upgraded to a BSL level 3 laboratory. There is ventilation with negative pressure in the laboratory and positive pressure in the anteroom.

Recommendations:

- Immediately implement administrative measures at the Regional Centre in Pokhara and Stupa Community Hospital in Kathmandu
- Organize an IC mission to review, update and implement the IC plan and roadmap and mainstreaming TB-IC in the existing system, in alignment with current policies (PMDT guidelines, PMDT Expansion plan).
- In preparation of the planned IC mission, assign IC focal points at national and regional level to supervise infection control measures for DR-TB health facilities

M. Human resource, training and technical support strategy

Staff met during this mission from all levels showed a high level of commitment and enthusiasm to take on new innovations.

Reportedly, there are inadequate human resources in microscopy centres.

There is a high turnover of senior management staff. The coming weeks there will be elections in Nepal for central and provincial level. In the federalization process this may have an impact on structure of the NTP, and staffing by dedicated officers.

Recommendation:

- High turnover of senior management staff in NTC requires dedicated support from partners. PMDT Officers from WHO and from NGO's are needed to support the leadership of the NTC, to maintain and ensure institutional memory, and streamline and coordinate activities and Technical Assistance.

N. Supervision of the programme

PMDT is soon expanding with new diagnostics, new drugs and regimens to be rolled out and the NTP needs to expand its supervisory/management capacity. There is low supervision and monitoring from national/regional to the health facilities with PMDT services.

PMDT reviews are regularly undertaken with all DTLOs and RTLOs at national/regional levels. The new guidelines, diagnostic algorithms and new regimens require adaptation of checklists and focus of supervision. Guidelines, checklists, monitoring indicators for supervision have been developed since last rGLC mission.

Recommendation:

- Enhance the supervisory visits in the field to include new diagnostics used in PMDT, following the algorithms towards choosing the correct treatment, implementation of the agreed regimen, with new drugs and STR, aDSM (SAE identification and clinical management), interim outcome monitoring including of patients on community DOT, study death analysis, and consistency in paper based and electronic recording and reporting system.

Annex A. TOR of the mission

In collaboration with the National TB Centre (NTC) and other partners:

- To evaluate the current achievements including implementation of the recommended actions of the previous rGLC mission.
- To assess the implementation of the PMDT activities, including clinical and programmatic management.
- To identify the gaps and the challenges in the implementation of PMDT and adoption of 2016 WHO DR-TB guidelines, specifically transitioning to shorter regimen and new TB drugs.
- To advise on planning for utilization of shorter regimen and new medicines for MDR and XDR TB cases, and for related services including establishing/strengthening pharmacovigilance or aDSM system for use of TB drugs.
- To propose suitable solutions to the NTP for the related work plan and its implementation.

Key issues to be evaluated and reviewed:

- The coordination between the NTP, the supranational reference laboratory, the community and other partners e.g. Save the Children (the Global Fund principal recipient and second-line drug-procurement agency), Damien Foundation, KNCV and WHO.
- The case finding strategies.
- The treatment strategies, administration and follow-up.
- The management system for second-line TB drugs in terms of quantification method, procurement, importation, storage, distribution and delivery to the patients, and scale up plan for enrolment in the next 1 year period, and the plan for procurement of new MDR-TB medicines.
- The current status of laboratory services.
- The infection control strategies.
- The information system and data management.
- The management of side effects of TB and MDR-TB medicines
- The pharmacovigilance system inside MOH and for TB

Expected output:

- Mission report with recommended actions to be submitted to the NTP within 2 weeks following the in-country mission

Annex B. Mission activities

Date	Time	Activity
Sunday 5-11-17		Arrival Kathmandu
Monday 6-11-17	8:45	Briefing with NPO CDC Unit
	11:00	Briefing and Review of progress NTP Director, Unit Chief and concerned staff
		NTC MDR TB clinic, Central Lab, Drug store
		Cohort analysis, review of R&R system
	17:00	Briefing with WR Nepal
Tuesday 7-11-2017		Visit to Western Region, Pokhara Visit to Regional TB Center, District Health Office, Community DOTS volunteer
Wednesday 8-11-2017		Return to Kathmandu Visit GENETUP and Stupa Community Hospital
Thursday 9-11-2017		Discussion and finalization of DR TB Guideline
Friday 10-11-2017	11:00	Debriefing meeting at NTC on mission finding, recommendations and provide advice on technical issues
		Debriefing at WHO (WR+MO+NPO)
Saturday 11-11-2017		Departure

ANNEX C. People met

Date	No	Name	Post	Organization
06-nov-17	1	Dr Kedar Narsing K.C.	Director	National Tuberculosis Centre (NTC)
	2	Dr Naveen Prakash Shah	Pulmonologist (PMDT Unit Chief)	NTC
	3	Mrs Kamala Devi Wagle	Public Health Nurse Officer (PMDT Program Co-ordinator)	NTC
	4	Dr Suvesh Kumar Shrestha	TB Consultant	Save the Children/Global Fund
	5	Dr Sailesh Shrestha	Medical Officer	NTC
	6	Mr Rajendra Basnet	Prog Coordinator	Save the Children/Global Fund
	7	Mr Ratna Bhattarai	Snr M&E Officer	Save the Children/Global Fund
	8	Dr Pramod Bhattarai	MO DR TB	Damien Foundation
	9	Dr Ashish Shrestha	National TB Consultant	WHO
	10	Mr Krishan Adhikari	Lab Technican, Focal Person Xpert	NTC
	11	Birendra Kumar Yadav	BMLT	SCI
	12	Mr Narayan Dahal	Chief Accounts Officer	National TB Center
	13	Dr Shusil Koirala	Country Director Nepal	Damien Foundation
	14	Shyam Kumar Oli	Health Assistant (CB DOT Focal Person)	NTC
	15	Dr Tushar Kanti Ray	TB Consultant	KNCV
	16	Mr Ajudey Prasad Shrestha	Logistics Officer	Save the Children/Global Fund
	17	Sarala Khadka	Logistic Assistant	NTC
	18	Ms. Sarmistha Singh Shrestha	Prog Assistant	WHO

Date	No	Name	Post	Organization
07-nov-17	1	Dr Susmita Jamarkattel	MO	Regional Tuberculosis Centre (RTC)
	2	Arun Kumar Jha	BMLT	RTC
	3	Neeta Gurung	DR Focal Person	RTC
	4	Radha Adhikari	DR Focal Person	RTC
	5	Dinesh Kumar Chapagai	DHO	Kaski District
	6	Basanta Nath Bhattrai	DTLO	Kaski District
	7	Suk Maya BK	CB DOT Provider	Kaski District
	8	Pradeep Sunar	Son of Suk Maya	Kaski District
	9	Bishnu Devi Khadka	CB DOT Provider	Kaski District

Date	No	Name	Post	Organization
08-nov-17	1	Punneshwori Prajapati	DR Focal Person	Stupa Community Hospital
	2	Dr Bhabana Shrestha	Chief GENETUP	GENETUP
	3	Mr Bhagwan Maharjan	BMLT	GENETUP

Date	No	Name	Post	Organization
09-nov-17 and 10-nov-17	1	Dr Naveen Prakash Shah	PMDT Unit Chief	NTC
	2	Mrs Kamala Devi Wagle	PMDT Program Co-ordinator	NTC
	3	Lekh Bahadur Gurung	Program Co-ordinator	BNMT
	4	Dr Pramod Bhattrai	DR TB MO	Damien Foundation
	5	Dr Ashish Shrestha	TB Consultant	WHO
	6	Mr Krishan Adhikari	Lab Technican	NTC
	7	Birendra Kumar Yadav	BMLT	SCI
	8	Namuna Karki	Administrative Officer	
	9	Shyam Kumar Oli	CB DOT Focal Person	NTC
	10	Dr Tushar Kanti Ray	TB Consultant	KNCV
	11	Mr Anil Thapa	PM&E Chief	NTC
	12	Dr Khursid Hyder		WHO
	13	Dr Subash Lakhe		WHO
	14	Dr Ashish Shrestha	TB Consultant	WHO
	15	Dr Jos Vandelaer	WR	WHO
	16	Mr Gokul Misra	Focal person	LHLI
	17	Bijai Maharjan	M&E Focal person	NTC
	18	Sarmistha Singh Shrestha	TB Programme Assistant	WHO

Annex D. TAG Members

N	Position	Organization
1	Senior Consultant Chest Physician (Chair)	NTC
2	Past Director	DG
3	Chief Curative Division	MoH
4	DR TB Medical Officer	Damian Foundation
5	Technical Specialist-TB	SCI
6	Chief	GENETUP / NATA
7	Pediatrician (TB expert)	KMC
8	Pediatrician (TB expert)	Dhulikhel Hospital
9	Director	PAHS
10	Chest Physician	Nepal Army Hosptial
11	Chest Physician	Thorasic Society of Nepal
12	Chair person/rep	KUTH
13	Chest Physician	Dharan Medical College
14	Chest Physician	Patan Hospital
15	Chair person/rep	NCASC
16	Chair person/rep	Nepal pediatric Society
17	Chair person/rep	Nepal Medical Association
18	Chair person/rep	Nepal Orthopedic Association
19	Prof. Consultant chest physician	TUTH
20	Past Director	NTC
21	Consultant Chest Physician	Narayani Sub Regional Hospital
22	Prof. Consultant Chest Physician	Dhangadi
23	Chief Consultant Chest Physician	Ex. Director
24	Chair person/rep	Nepal Gynecology Association
25	Endocrinologist	Nepal Endocrinology society
26	PME Chief	NTC
27	Chair person/rep	Nepal Opthalmic Society
28	Past Director	NTC
29	Past Director	NTC
30	Pharmacologist	Department of Drug Administration/NTC
31	Representatative (Microbiologist)	NPHL
32	Laboratory Incharge	NTC
33	Laboratory Incharge	GENETUP / NATA
34	Training Coordinator	NTC
35	MO	NTC
36	National Consultant - TB	WHO
37	PMDT Program Coordinator	NTC
38	aDSM Coordinator	NTC
39	Consultant Chest Physician (Secretary)	NTC

Annex E. Expansion plan of treatment services (from 2016 report)

Activity	2017	2018	2019	2020
New DR TB treatment centre ("Centre of Excellence")	3	3	3	4
Cumulative	21	24	27	31
New DR TB sub-centre	11	10	11	11
Cumulative	103	113	124	135
DR TB Referral centre with 20-50 bed capacity	5	5	5	5
Hospitals with trained staff for providing DR TB treatment	5	5	5	5
Pilot and expansion of services to Health Posts	7	21	42	49
Hostels (one per region)	5	5	5	5

Annex F. Transition plan Gannt Chart

Activities	Responsible	2017						2018												2019									
		May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
PMDT unit stablishment and strenthening																																	
stablishment of PMDT unit with dedicated HR and its TOR (PMDT unit head, DR TB clinical expert, DR TB programmatic expert, DR TB MnE, aDSM focal point)																																	
Develop the transition plan																																	
Situation assessment, country dialogue & consensus	WHO, NTC, PR, GF & others																																
Finalization of the 1st draft	WHO																																
Providing inputs on budget and SLD quantification	NTC, PR, DFB																																
Review, revision and finalization	NTC, TAG,WHO																																
Submission to the MOH & GF for approval (including budget)	NTC																																
Update the national PMDT guidelines																																	
Assessment of gaps and consensus on the proposed changes	WHO, NTC & others																																
Develop the 1st draft of the updated guidelines	WHO & NTC																																
Review, revision and approval	NTC, TAG, WHO, others																																
Finalization, printing and disseminating																																	
Establish aDSM mechanism																																	
Assign a focal person at NTC																																	
Establish the national coordinating body (TAG+DDA & cardiologist) /Teaching Hospital and Gangalal Hospital	NTC/DR-TB																																
Establish the Treatment center level coordination body (also function as Technical expert group for the treament center which also incorporates aDSM focal point, clinical focal point of the referral sites)	NTC																																
Convene regular TAG meetings (when aDSM discussed)	NTC/DR-TB																																
Print & distribute data collection forms, testing schedules etc.	NTC/DR-TB																																
Develop aDSM electronic database (eTBManager)	NTC/DR-TB, M&E																																
PMDT training for HCWs from 18 treatment centres and 85 sub-centres	NTC																																
Develop Sputum Courier SOP																																	
Conduct assessment on the availability of/accessibility to lab tests/clinical examinations for aDSM	NTC/DR-TB																																
Implementation, monitoring and evaluation in 4 treatment centres	NTC/DR-TB																																
Implementation, monitoring and evaluation in aditional 6 treatment centres	NTC/DR-TB, M&E																																
Implementation, monitoring and evaluation in all treatment centres	NTC/DR-TB, M&E																																
Procure second-line drugs																																	
Quantify drug needs																																	
Request GF funding for SLDs																																	
Place the drug order to GDF (SR, Dm & Bdq)																																	
Review the stock and find solution to address wasted drugs																																	
Capacity building																																	
PMDT training for HCWs from 14 treatment centres	NTC & DF																																
Laboratory training on LPA & DST	NTC/NTRL																																
Train HCWs at 6 Rx centres & corresponding sub-centres on new guidelines (incl. aDSM, SR & new drugs)	NTC/DR-TB																																
Train HCWs at additional 8 Rx centres & sub-centres on new guidelines (incl. aDSM, SR & new drugs)	NTC/DR-TB																																
Train central staff (NTC, DDA, TAG) on aDSM data analysis and causality assessment	NTC/DR-TB																																
TA to facilitate the training workshops (above-mentioned)	NTC, WHO, PR, DF																																
Laboratory preparation																																	
Address the problems of non-functional Xpert modules																																	
Install additional Xpert machines in the peripheral Dx centres																																	
Improve the sputum referral & address lab contamination problem																																	
Improve proficiency of SLD-LPA (NTRLs + regional laboratories)																																	
Implementation of new regimens (shorter & longer)																																	
Implement in 10 PMDT centres																																	
Implement in all PMDT centres in the country																																	