rGLC COUNTRY SUPPORT MISSION REPORT

Country: Indonesia

Inclusive dates of mission: 8 – 12 April 2019

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The programme has agreed with open sharing of this report ☒

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Abbreviations and acronyms

AIDS	Acquired immunodeficiency syndrome
ART	antiretroviral therapy
DOT	Directly observed treatment
DOTS	Directly Observed Treatment Short-course
DRS	Drug resistance survey
DR TB	Drug-resistant tuberculosis
DST	Drug susceptibility testing
GDF	Global TB Drug Facility
GLC	Green Light Committee
GFATM (GF)	Global Fund to fight AIDS, Tuberculosis and Malaria
HIV	human immunodeficiency virus
KALK	Komite Akreditasi Laboratorium Kesehatan (committee for accreditation of laboratories)
KAN	Komite Akreditasi Nasional (national accreditation committee)
KNCV	Royal Netherlands TB Foundation
KOPI TB	Koalisi Organisasi Profesi untuk Penanggulangan TB (coalition of professional organisations for TB control)
LPA	Line Probe Assay
LJ	Lowenstein Jensen
MDG	Millennium Development Goal
MDR-TB	Multidrug-resistant tuberculosis
MICA	Monthly interim cohort analysis
MOH	Ministry of Health
NGO	Non-governmental organization
NTP	National Tuberculosis Programme
NTRL	National TB Reference Laboratory
PDPI	Perhimpunan Dokter Paru Indonesia (Indonesia Pulmonologist Society)
PPM	Public-Private or Public-Public Mix
RSAB	Rumah Sakit Anak dan Bunda (mother and child hospital)
RSUP	Rumah Sakit Umum Pusat (General Hospital)
SEAR	(WHO) South East Asia Region
SLD	Second-line anti-tuberculosis drug
SOP	Standard operating procedures
SRL	Supranational tuberculosis reference laboratory
TB	Tuberculosis
WHO	World Health Organization
XDR-TB	Extensive drug-resistant tuberculosis

Executive summary

i. TORs of the mission

- Discuss transition plan to new WHO guidelines with technical expert group
- Clinical discussion on updated WHO DR TB Guidelines
- Discussion on high loss to follow-up (LFU) before treatment and during treatment and role of treatment support group on DR TB Treatment (Aisyiyah, LKNU, POP TB)
- Discuss actions needed to decrease LFU before treatment and during treatment rate.

ii. Key activities

- TWG meeting along with provincial managers, CSO representatives, partners and clinical expert from South Africa for first two days of the mission
- Site visits: Puskesmas (peripheral health facility) Palmerah and RSAB (mother and child hospital) Harapan Kita
- RSUP (general hospital) Fatmawati and NTP for discussion with IO PPM (project on public-private mix) – PDPI (Indonesia Pulmonologist Society) Pusat and KOPI (Coalition of professional organisations) TB
- Debriefing with WR Indonesia and NTP

iii. Overall implementation status of PMDT compared to targets in NSP and significant achievements in past one year

- Rapid expansion of molecular DST. 815 GeneXpert machines installed as compared to 589 at the time of last mission, another 100 in stores. Around 100 more ordered for this year while the target is to have at least 2023 machines by 2020.
- Expansion of quality assured Culture & Drug Susceptibility Testing laboratory network, quality assured by NRLs, and monitored for Key Performance Indictors by the programme - 21 culture labs and 11 DST labs.
- More than 386,000 patients tested for drug resistance in 2018 and more than 8,800 confirmed with RR/MDR-TB (target for 2018 was 9,000) against 5070 confirmed cases in 2017
- Services have expanded to 188 PMDT treatment centres out of 360 planned in first phase (the final target is to have at least 514 treatment centres).
- Monthly interim cohort analysis (MICA) is introduced and implemented in 6 provinces supported by Challenge-TB and partners to reduce loss to follow-up
- aDSM core package is being implemented in collaboration with National Agency for Drugs and Food Control (NADFC).

iv. Key challenges identified in this mission in relation to the ToRs

- Low enrolment of diagnoses RR/MDR-TB cases (**4,317/ 8,884 cases enrolled in 2018**) apparently because of
    - Slow expansion of treatment services specifically large hospitals

- Non-engagement of CSOs at several places

- High loss to follow-up of those on treatment (~25% for both STR for 2017 cohort and LTR for 2016 cohort) creating risk of development of resistance to second line drugs, specifically repurposed ones like clofazimine. During discussions with community representative, high loss to follow-up was attributed to

    - Adverse events identification and management is not conducive for patients to continue treatment
    - Socio-economic challenges for patients specifically loss of wages (results of another study conducted on the issue are in the narrative)

v. Priority recommendations of the mission:

Recommendation	Responsible persons/agency	Timeline	Support required to fulfil the recommendation
• Reduce loss of patients – before or after start of treatment. – Expand MICA to all provinces with regular review and monitoring of loss to follow-up in each district and province. – Strengthen patient support mechanisms through government mechanisms and CSOs	NTP, Medical services department, partners and CSO	Continuous process till an acceptable level of treatment adherence are reached	
• Hold a high-level coordination meeting with directorate of medical services to ensure rapid engagement of all hospitals as well as ensuring pro-active adverse events monitoring and management (aDSM)	MoH and NTP		
• Multisectoral coordination through high level intervention for TB (national initiative for priority diseases) and establishing accountability.	MoH		
• Advocate for Presidential Decree on TB to accord high priority to the disease at sub-national level with sufficient allocation of resources	MoH		WHO Country office to support the process
• Further dissemination of established screening guidelines – Any patient starting on TB treatment should have a rapid DST done, either at symptomatic stage itself or before start of treatment if diagnosis is based on microscopy	NTP and partners		

Recommendation	Responsible persons/agency	Timeline	Support required to fulfil the recommendation
• Laboratory capacity in the country to be developed for sensitivity testing to new and repurposed drugs	NTP in coordination with laboratories	Q4 2019 – Q12020	WHO-SEARO along with an SNRL
• All oral regimen to be started as longer regimen of first choice by October 2019 with appropriate aDSM	NTP	Q3 2019	

vi. Status of priority recommendations of previous mission:

No	Summary of key recommendations	Responsible agency/person	Time frame	Progress
1.	Accelerate the enrolment of R-R/MDR-TB patients on treatment to achieve the targets for 2018-19. • Reduce the enrolment gap from ~40% to less than 10% by reducing delay between testing and treatment initiation, providing counselling through trained staff/patient support groups to those not willing for treatment and streamlining and expediting baseline evaluation at referral hospitals.	NTP and Partners	For the patients diagnosed in Jan-Mar 19 the enrolment gap should be less than 10%	Jan-Mar 2019 : Confirmed RR/MDR = 1,993 Enrolled = 1,101 Enrollment Rate = 55% MICA is introduced and implemented in 6 provinces supported by CTB. Involvement of Psychologist and peer support after receiving Rif resistant result in some sites
2.	Accelerate the enrolment of R-R/MDR-TB patients on treatment to achieve the targets for 2018-19. • Establish a mechanism for line listing and aggressive tracking and testing of all presumptive DR-TB patients. All districts and provinces should monitor this indicator quarterly.	NTP and Partners	Immediate	TB Diagnosis algorithm using Xpert already in the National guidelines and a follow-up ministerial decree 67/2016. However, variation in implementation in provinces.

No	Summary of key recommendations	Responsible agency/person	Time frame	Progress
	• Scale up Xpert testing (universal DST) of all presumptive TB patients through close monitoring and scaling up sputum transportation services in all districts.		To be completed by March 2019	Regular feedback by NTP M&E and PMDT team. Specimen transportation mechanism in 50 districts in 10 provinces with increase access and utilization. Increase utilization of Xpert 23% last year to 39% now.
3.	Enhance and optimise lab capacity for first and second line DST • Undertake analysis of the Xpert capacity (with availability of 1043 machines by end of 2018), the existing and anticipated workload with the scaling up of universal DST. Simultaneously forecast the requirement of cartridges and ensure adequate supply. • Expedite the establishment and accreditation of the 4 additional LPA labs and ensure that all diagnosed R-R/MDR patients have SL-DST done. Set up sputum transport mechanism from the feeding districts to the SL-DST labs. • Revise the SDP criteria for the liquid DST labs to include INH (0.1, 0.4), Km, Cm and Mfx (0.25 and 1) and train the lab staff as per the recent WHO and	NTP and partners	Complete the analysis and forecasting of cartridge requirement by Dec 2018 By Dec 2018 By Dec 2018	Analysis is done regularly by 1 TO lab, There are 815 Xpert and the national utilisation of Xpert is 39%. Based on these calculation, the cartridges are still sufficient up to Q2 2019. 7 LPA labs available and lab network developed. Drugs selection for DST is in process of updating for adjustment based on the updated WHO guideline

No	Summary of key recommendations	Responsible agency/person	Time frame	Progress
	FIND guideline on critical concentrations.			
4.	Scale up the DR treatment centres (as per the NSP and Ministerial decree) to provide decentralised treatment. This will require: • Expediting the ongoing assessment process • Availability of baseline tests either at the centre or linked with public/private facilities • Availability of funds for minor renovations to ensure infection control • Ensure availability of second line drugs for the shorter regimen and the newer drugs for longer regimen	MoH/NTP / partners	The target of 360 DR Treatment centres should be completed by March 2019	Till March 2019, 187 of 360 (52%) identified hospitals were providing DR TB services. Technical assistance teams have been set up and clinical mentoring team by PMDT TWG provide TA to prioritized hospitals, which have not yet started DR TB services.
5.	Improve treatment success rate from the current ~50% by • Reducing the LFU rates by providing counselling services through trained staff and patients support groups and timely payment of incentives and enablers to DR-TB patients • Reducing the death rates through early diagnosis and treatment initiation • Strengthen the capacity of physicians for clinical management of DR-TB patients through clinical courses, CMEs and regular online discussion using a 'Hub and spoke' model through ECHO or other similar platforms	NTP / PHOs/DHOs/Partners	Ongoing Ongoing Discuss with ECHO or other similar organizers and prepare an implementation plan by Dec 2018.	Outcome Treatment 2016 : SR = 48% LFU = 26% Died = 17% Outcome Treatment 2017 : SR = 17% LFU = 24% Died = 18% On TX = 37% DR TB treatment on Webinar session often done from PMDT hospitals 2 batches of clinical management workshop were conducted on 2018

No	Summary of key recommendations	Responsible agency/person	Time frame	Progress
	• Undertake operational research to document the reasons for LFU and death. This should be a mixed method study (qualitative and quantitative).		Complete the OR by March 2019	Operational research only done at facility-based level
6.	Strengthen aDSM and PV mechanisms in collaboration with NADFC • Sensitisation of the relevant clinical staff on aDSM/PV • Prepare a simple monthly report from all DR Treatment centres to remind and ensure ADRs updated on eTB manager • Bridging/Integration of e-meso and eTB in the interim and SITB finally • Ensure regular quarterly/biannual meetings of the PV Committee for DR-TB		Complete sensitization of relevant staff by Dec 2018 Implement from Oct 2018 onwards Integration with SITB to be completed by mid-2019 Ongoing	On going 5 provinces and 14 districts (1 province in this April) have already conducted workshop of adverse events management and reporting, National committee of TB PV is under development and led by BPOM (Feb 2019) Causality Assessment are done led by BPOM
7.	Urgent action points • There is a high risk of stock out of Xpert cartridges in 4 Q2018 due to non-procurement through the domestic funds. Fast track procurement of cartridges from Global Fund Y2 budget and simultaneously facilitate registration of the supplier in e catalogue. • The calibration of the Xpert machines installed in 2015 and 2016 is overdue.	NTP/WHO	Fast-track procurement of cartridges from Global Fund Y2 budget by Nov 2018 Facilitate registration of the supplier in e	142,130 cartridges were procured using GF funding in June 2018, and 1,149,164 cartridges from APBN in October 2018. There are no stock out of cartridges in Q4 2018. Xpert cartridges are already in the e-catalog (broadcast date March 4, 2019)

No	Summary of key recommendations	Responsible agency/person	Time frame	Progress
	• Include DR-TB patients under BPJS scheme. The calculation has been done and it is about ~10m Rp per patient (excluding diagnostics and drug costs). Prepare a justification note and discuss with National Tariff Commission and BPJS. • Prepare a transition plan for sustaining effective interventions piloted under Challenge TB project.		catalogue by Dec 2018 Complete by Jan 2019. By Nov 2018. Dec 2018	Calibration Done (in Oct 2018) BPJS discussion on going Transition plan from CTB effective intervention is on going
8.	Strengthen monitoring and evaluation • Integration of the various software SITT, eTB Manager, e-meso, EMPATY, ENAM etc. • Plan and undertake regular Grant Monitoring visits from the Central and provincial levels to districts.	NTP and partners	Mid-2019 Ongoing	SITB is on piloting phase Involvement of TWG member in conducting the supervisions
9.	Develop a plan for delivery of community-based DR-TB services (may use the framework given in the report)	NTP and Community groups	Dec 2018	Concept of community-based DR TB services in still in discussion and coordination with stakeholders (DG of Medical services, CSO, etc) Community support mechanism for DR TB consists of: • Health Cadre • Peer Educator • Case manager

Achieved	
Some progress/ ongoing	
No change	

Detailed report

A. Overall DR-TB programme performance

There were about 12,000 estimated MDR/RR TB cases among the notified pulmonary TB cases in 2017. While the number of diagnosed RR/MDR-TB cases has been steadily going up, the enrolment numbers do not seem to be catching up leaving a wide gap between diagnosis and enrolment. The programme also has reported a decreasing treatment success rate among patients on second-line treatment. A major proportion of poor outcomes is contributed by the loss to follow-up.

Figure 1: Case notification and treatment outcome trends for Indonesia

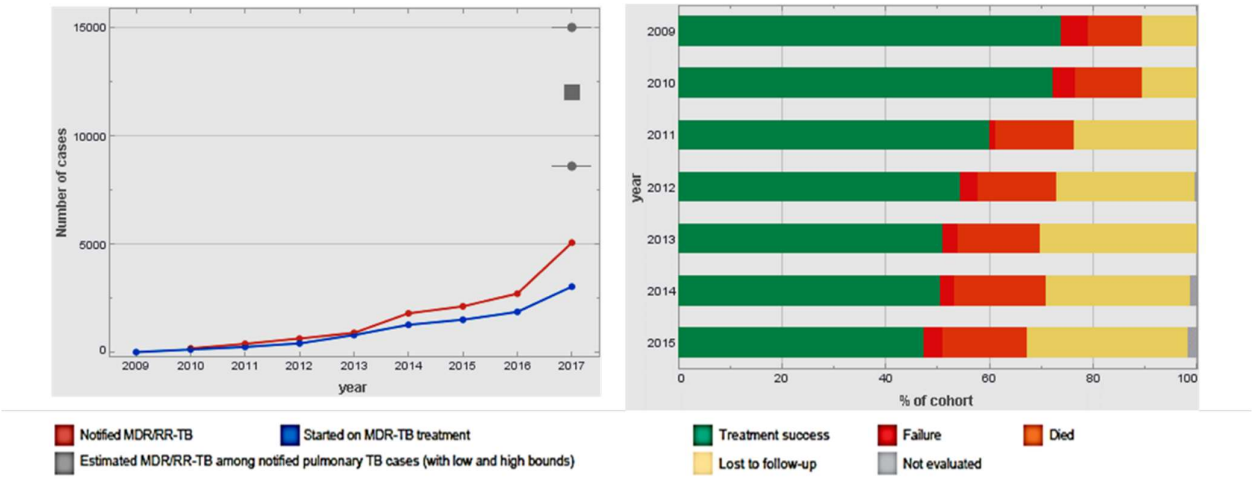


Figure 2: DR TB Progress since 2009 – 2018:

Table 1: Revised DR-TB proportions as per the results of recently concluded DRS

Type of resistance	Proportion (%)	95% CI
RR TB		
New cases	**2.6**	**1.9 – 3.5**
Previously treated	**17.8**	**12.5 – 24.7**
Total	**5.5**	**4.0 – 7.3**
MDR TB		
New cases	**1.4**	**0.9 – 2.2**
Previously treated	**12.4**	**8.0 – 18.7**
Total	**3.5**	**2.4 – 5.1**

Adoption of these results will lead to higher estimates of RR/MDR-TB proportions (and consequent numbers) among the notified pulmonary TB cases

B. Laboratory services

TB services are integrated across the organizational structure into the diagnostic pathology services of Ministry of Health (MOH). Only at the central level, do the National Reference Laboratories (NRL) operate in a vertical mode. The Indonesian TB laboratory network divides into four main levels according to the complexity of the services provided:

- National — National Reference Laboratory
- Provincial — Provincial Reference Laboratory
- Intermediate — Sub-provincial level (intermediate Reference Lab)
- District/sub-district — Health centres and satellite centres

Administratively, the national TB laboratory network is organised under the Directorate of Health Services, whereas the NTP functions under the Director General of Prevention & Disease Control. SRL-Adelaide, Australia provides technical guidance and support to Indonesia for DST Panel Testing of NRL Surabaya, under the WHO-SNRL network. However, there several challenges in this regard.

NTP supports country-wide laboratory network and three designated National Reference Laboratories (NRLs), at the national level. The three designated TB national reference laboratories (as per the Minister of Health through Decree No.1909/MENKES/SK/IX/2011) are: (1) BBLK Surabaya for TB culture and DST, (2) Department of microbiology, faculty of medicine, University of Indonesia, Jakarta for molecular tests, (3) BLK Bandung (West Jawa) for sputum smear microscopy networking. At provincial level, currently, there are 21 TB culture labs. Of which, 11 are capacitated for TB-Drug susceptibility testing (DST). Six more laboratories are in the validation stage for upgradation from culture to DST labs. Six of 11 provincial labs are performing rapid LPA testing for second line molecular DST and additional 4 provincial labs on planning. Except for RSUP Dr Kariadi, all the LPA labs are also TB culture & DST labs. At peripheral level (covering district hospitals and *Puskesmas)*, a network of 792 GeneXpert sites provide diagnosis of RR/MDR TB. At peripheral level at about 7471 sites

distributed across the country, where GeneXpert systems are not installed, sputum microscopy remains the basic TB diagnostic tool. Specimen transport system operates in 62 districts (out of more than 6000) of 10 provinces (out of 34) connecting sputum microscopy sites with GeneXpert sites for RR/MDR-TB diagnosis. Rest of the provinces and districts either use an ad-hoc arrangement for sputum transport, or do not transport sputum to GeneXpert sites, at all, posing challenges to diagnosis and treatment of all incident TB cases in the country.

NTP is guided by a national laboratory action plan (2016-2020) for the expansion of the laboratory network in the country. The plan intends to expand the GeneXpert capacity to 2023 sites by year 2020. NTP along with NTRLs has also developed and follows a certification mechanism of laboratories for Culture and DST, as well as for Line probe assay.

NTP's laboratory team coordinates in laboratory equipment installation, supplies and logistics, to the networked labs. It monitors work-loads of the laboratories, and key quality performance indicators, on quarterly and annual basis. A central team along with partners and NRLs undertakes laboratory on-site support supervisory visits, periodically, as per the laboratory EQA protocol. Many laboratories of the network, at various levels, are certified for quality management systems such as: ISO 15189:2012, and ISO 17025:2017 by KAN (Komite Akreditasi Nasional), and KALK (Komite Akreditasi Laboratorium Kesehatan), Ministry of Health.

Figure 3: TB laboratory network in Indonesia

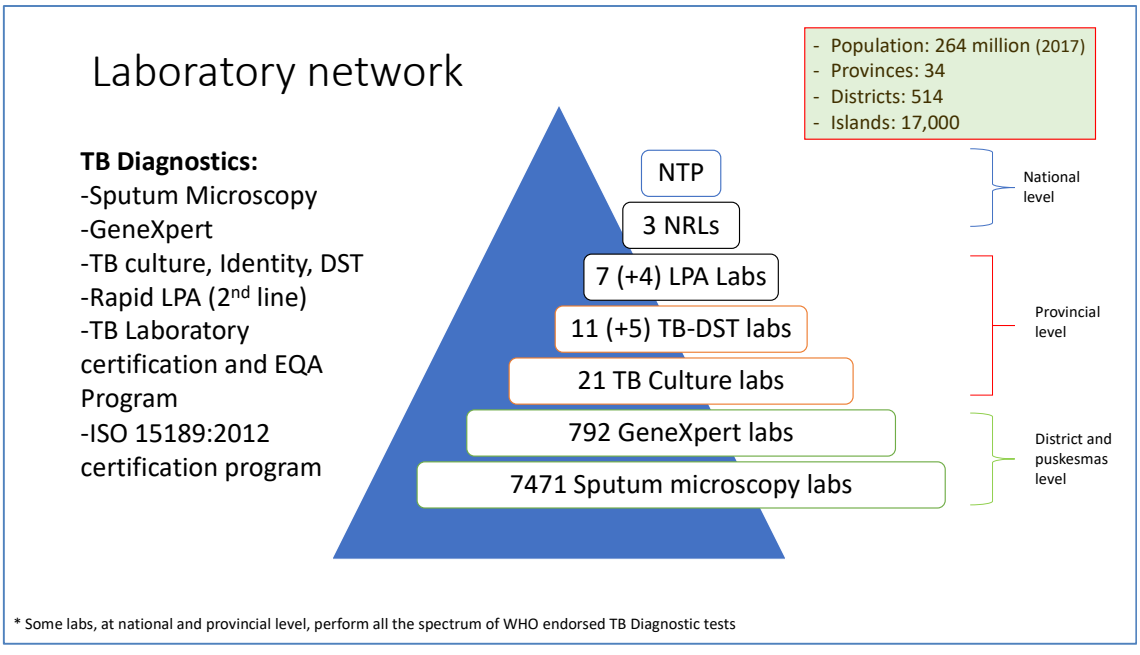


Figure 4: Location of 11 DST Laboratories in 8 Provinces

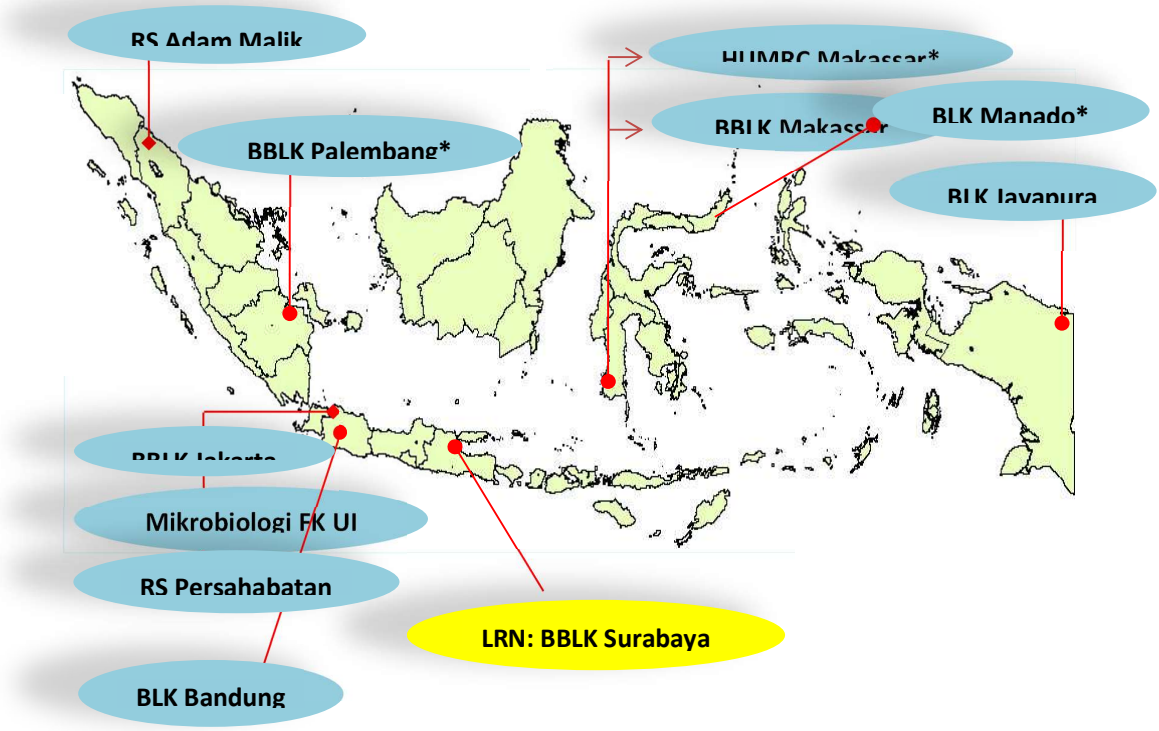
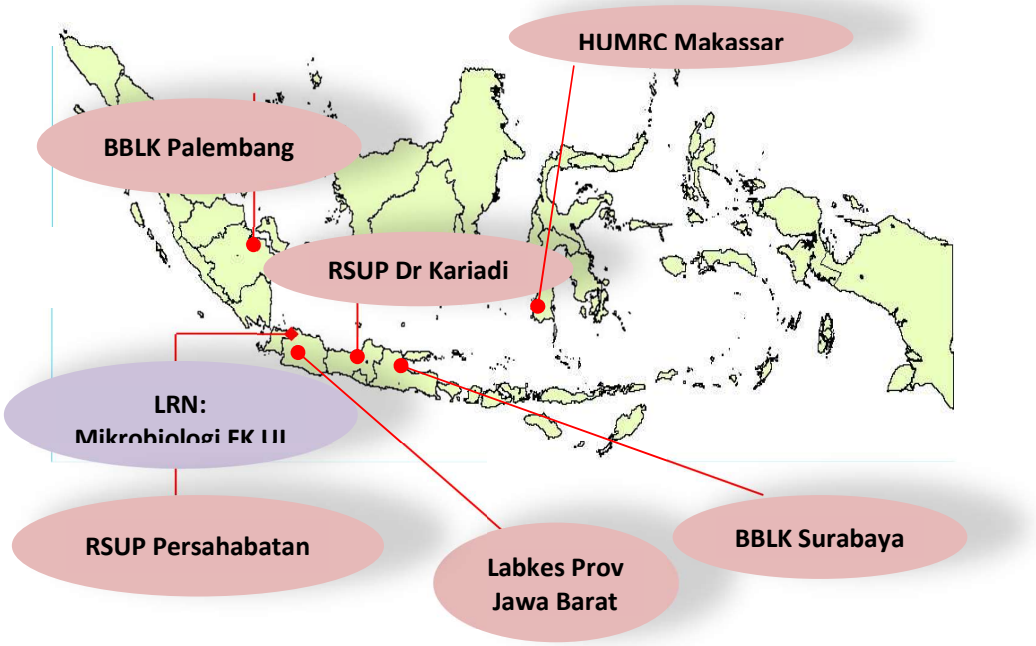


Figure 5: Location of 7 LPA Laboratories in 6 Provinces



Achievements:

- Availability of updated laboratory related policies, guidelines, testing manuals and Standard Operating Procedures, as per WHO guidance.
- Availability of laboratory strategic planning, and partner support for the laboratory expansion.
- Assessment of diagnostic capacity of laboratory network indicates adequacy to meet current needs of the program (diagnostic culture and DST, LPA tests and treatment monitoring tests) although access to services is severely constrained as Indonesia is an archipelago of over 17,000 islands distributed across wide parts of Indian and Pacific Oceans.
- Rapid expansion of GeneXpert network in the past three years: covering all of hospitals, all of district labs, most of sub-district labs, and many peripheral labs:
    - About 792 GeneXpert-sites (815 GeneXpert machines, about 3250 GeneXpert modules).
    - Utilization rates of GeneXpert- reaching up to 50%.
    - Addition 200 GeneXpert machines available to program (100 in the warehouse stores and 100 to be procured in the current financial year). Lab expansion plan intends to acquire about 2000 GeneXpert systems by the year 2020.
    - No major stock-out of cartridges reported in the current year. Sufficient stocks are planned for this year by NTP. MOH is committed to funding Xpert cartridges, and this is highly appreciated
- Expansion of quality assured Culture & Drug Susceptibility Testing laboratory network,
    - Culture and DST labs are quality assured by NRLs and monitored for KPIs by the program (21 culture labs, 11 DST labs). Six more labs are planned for upgradation to liquid culture DST.
- Expansion of rapid Line Probe Assay (LPA) network-
    - Currently, seven laboratories (currently performing 2nd line LPA testing, in routine). Plans to expand 4 more sites.
- Strong NTP laboratory coordination leadership
    - NTP, NTRLs, BBLKs, and Partners. EQA Program for Lab network (C&DST, LPA)
- Initiation of decentralized TB sputum transport network, although this needs scale-up to increase access to diagnostic services
- NTP along with partners and MOH has strengthened the in-country laboratory capacity for Whole Genome Sequencing of *Mycobacterium tuberculosis* isolates under TB Drug resistance surveillance (DRS) study.

Observations:

- Increasing trends in GeneXpert utilization for TB, RR-TB diagnosis, over past two years. 50% utilization of installed capacity of GeneXpert as on Jan 2019. Utilization rates varies among provinces- high in most populated provinces: DKI Jakarta and all provinces of island of Java.
- Recording and reporting:
    - Real-time connectivity solutions for data management of GeneXpert- systems (e.g., Data-to-Care) is under pilot study and need to be implemented across the country. This causes delays in data reporting to central, and provincial unit for supervision and monitoring purposes (especially for prompt follow-up on placing all RR-TB cases under the treatment, as well as for improving laboratory turn-around-times and increasing the access to services).
    - eTB Manager data-management issues:
        - Missing patient registration-data from PMDT sites- delays in laboratory TATs (Turn-Around-Times)

    - No software cross-talk between SITB (software used by all sites for routine TB recording and reporting) and eTB manager (software used by all PMDT sites).
- NTP data suggest that on an average, about 51% of RR-TB patients had phenotypic DST results among all RR-TB patients diagnosed by the program, during 2015-2017 period. Lack of access to reliable specimen transport system is one of the key reasons for this. Similarly, about 25.6% of RR-TB patients among all those diagnosed had rapid SL-LPA results, in 3 and 4th quarter of 2018.
- Currently (starting from 2019), DST labs are providing for phenotypic DST against 5 drugs (Isonizaid (two critical concentrations), Kanamycin, Capreomycin, oflxacin, moxifloxacin (two critical concentrations), as a package. With the proposed changes in treatment regimens, program is planning to develop capacity for phenotypic DST to new anti-TB medicines (as per new proposed treatment regimens): Bedaquiline, Linezolid, Clofazimine, Delamanid and Pyrazinamide
- Bio-safety practices in the TB containment laboratories (Culture and DST) need to be strengthened for PPEs (personal protective equipment), especially for N95 face-mask.
- Enhanced support from SRLs to NRLs of Indonesia remain critical for global laboratory strengthening and control and prevention of drug-resistant tuberculosis in the region. Current support from SRL, Adelaide is very limited, and pertains to only sending PT samples to NRL, Surabaya.

Recommendations

- Develop and implement: a brief plan for all Culture & DST labs with specifics of new drugs & critical concentrations to be tested- with a time-bound plan. Monitor laboratory key performance indicators for the DST of new drugs. As laboratory standardization for DST of new TB drugs is a time-consuming activity (6-9 months), program could start new treatment regimens while NRLs are being capacitated.
- Standardize testing procedures for implementing Phenotypic DST for new drugs, at the minimum, for Bedaquiline, Linezolid, Moxifloxacin, Clofazimine, Delamanid
- Consider extended spectrum DST - with above 5 drugs + Amikacin, Pyrazinamide, and Isoniazid.
- Review and update the procedures and criteria of EQA-Panel Testing for DST by NRL-Surabaya
- Consider addition of strains for evaluating reproducibility of test results as a criterion
- Consider 80% judicial results (for each round) before final accuracy calculations
- Include retraining of staff at NRL Surabaya as an option, in cases where labs fail to achieve expected accuracy in EQA-PT during certification
- Develop 1st Line LPA capacity, as required with adequate linkages to specimen transport from all PMDT sites
- To provide 1st and 2nd line LPA at same time for all RR-TB patients
- Consider developing one of the NRLs (NRL Surabaya) into a WHO GLI centre-of-excellence for TB
    - Enrol with GLI-SRL NETWORK for panel testing rounds administered by SRL, Antwerp (this helps in multiple ways for strengthening certification of multiple phenotypic DST labs (11 labs) developed in the country)
    - Plan and start developing capacity for fulfilling criteria for GLI-Centre of excellence requirements
    - Request support from WHO-Indonesia, and WHO-SEARO

- Consider working closely with DRS-study teams on how to achieve technology- transfer for Next Generation sequencing / Whole Genome Sequencing as replacement to phenotypic DST.

C. Case finding

DR-TB laboratory services are integrated, at various levels, within the decentralized public health structure of Ministry of Health. *Xpert MTB/RIF* is the initial test for diagnosis of tuberculosis (TB) and Rifampicin resistant (RR/MDR)-TB at all laboratories where the GeneXpert systems are installed, supported by ministerial decree 67/2016. Placement of GeneXpert systems is driven by both TB laboratory work-loads, and ease of access to DR-TB services. Laboratories where GeneXpert systems are not installed, smear microscopy remains the initial test, followed by referral of all smear positive specimens to GeneXpert-testing, based the diagnostic algorithm of NTP. For this purpose, a courier-based specimen transport system is currently being implemented across the country. In instances where Rifampicin resistance is detected, the sputum is collected and tested with rapid molecular 2nd line LPA for diagnosis of resistance to quinolones and second line injectable drugs. Simultaneously, sputum is also referred to phenotypic tuberculosis culture and drug sensitivity testing (DST) (liquid culture: MGIT 960 system) for as per a standard testing menu of five drugs with seven concentrations (Kanamycin, Ofloxacin, Moxifloxacin (low and high concentrations), Isoniazid (low and high concentrations), and Capreomycin).

Pilot studies with specimen transport indicate several challenges and remains a trade-off between increasing the laboratory capacity and utilization of existing laboratory capacity. Treatment monitoring for DR-TB is by sputum examination and TB culture (monthly during the intensive phase, and quarterly during the continuation phase)

Although the screening rates are steadily improving, it is observed that there is limited access to universal DST to Rifampicin. About 13.6% of all new and re-treatment patients received DST for Rifampicin, of the total diagnosed, in 2018 (not yet published data). Not all the GeneXpert sites have access to TB diagnosis as ‘initial test’. 51 sites out of 792 sites that perform GeneXpert sites, use Xpert test only for RR/MDR-TB diagnosis.

Table 2: Case finding, screening and enrolment numbers as reported to WHO

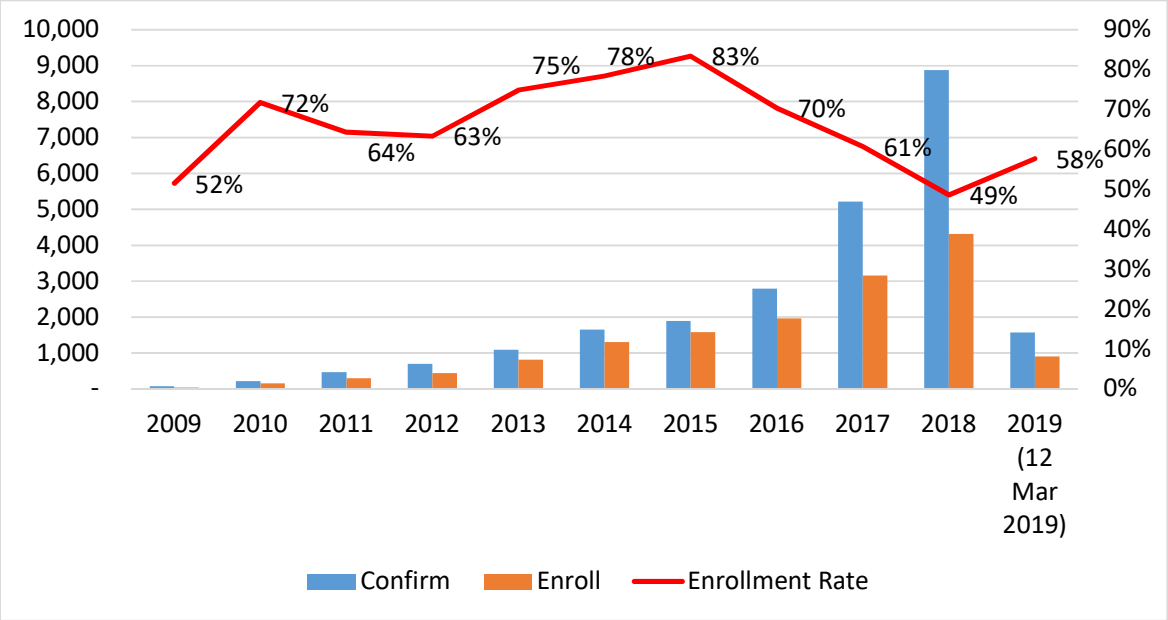
	2009	2010	2011	2012	2013	2014	2015	2016	2017
Notified TB cases	294,732	302,861	321,308	331,424	327,103	324,539	333,562	366,673	446,732
% new TB cases tested for rifampicin resistance		0	0	0	0	1	0	2	16
% previously treated TB cases tested for rifampicin resistance		5	9	13	39	88	79	100	100*
Notified MDR/RR-TB cases		190	408	649	912	1812	2135	2720	5070
Patients started on MDR-TB treatment	20	142	260	426	809	1284	1519	1879	3042
MDR/RR-TB cases in treatment outcome cohort	19	140	260	432	809	1271	1565		
Estimated MDR/RR-TB among notified pulmonary TB cases									12000

*the reported number of those screened for resistance among previously treated cases is more than the number of such cases reported in the same period.

As per the available reports, screening of new cases for resistance improved to 16% for new TB cases while 100% of previously treated cases were tested for resistance (Table 1). The notified RR/MDR-TB cases have also increased to 5070 in 2017 and expected to have further increased to nearly 9,000 in 2018 (unpublished).

Figure 6 below shows trends in enrolment of diagnosed cases. Peaking at 83% in 2015, the enrolment rate has been consistently decreasing reaching 49% in 2018. Initial trends for 2019 show a slight improvement in first quarter but this needs further improvement as well as a watch for the entire year to be sure that sustained improvement is seen over the year.

Figure 6: Trends in case finding and enrolment (includes the unpublished 2018 and 2019 data from the NTP)



Reasons for loss to follow-up before and after initiation of treatment are discussed in subsequent sections.

Recommendations

- Update the National TB diagnostic algorithm per the newly selected DR-TB treatment regimens and need for DST of new TB medicines.
- Improve access to GeneXpert testing for all TB screening and testing facilities: Continue with expansion of specimen transport system; Continue with expansion of GeneXpert sites (as planned).
- Strengthening the systems at provincial, district and peripheral level for ensuring universal access to DST (Rifampicin testing and treatment): Continue monitoring of GeneXpert utilization and strengthening linkage with treatment site to minimize pre-treatment default: implement GeneXpert-electronic connectivity solutions (e.g., DataToCare) for prompt treatment action for all RR TB patients; ensure continuous maintenance/ service/ replacement of defective GeneXpert modules.
-
- Focus on high loss to follow-up (being discussed in next section)
    - Disaggregate data – district wise
    - Analyze CSO engagement and patient support measures

D. Treatment strategy

Patients diagnosed as rifampicin resistant (RR) TB are referred to DR-TB treatment centres for evaluation and treatment initiation. Each DR-TB Treatment centre has a treatment committee which takes decisions regarding the management of the patient. For specialized tests like audiometry, psychiatric evaluation and management of severe adverse events the patients are referred to tertiary centres. Patients coming from other districts are either admitted at the DR-TB centre or need to make their own arrangements for stay. In a few provinces shelters are provided by Aisyiyah Community TB care initiative. After treatment initiation the patient is referred to the nearest health facility (Puskesmas) for domiciliary treatment. The patients are referred to the DR-TB treatment centre for follow-up and for management of adverse reactions or other complications.

Treatment adherence is monitored by the Puskesmas staff. In some districts the adherence is supported by Patient Support groups (PSG) and Community Cadres (CC) who trace those lost to follow-up and counsel them on treatment adherence.

The programme has adopted the shorter treatment regimen (STR) as per the WHO guidelines since Sep 2017. By the time of the mission close to 2500 patients had been initiated on STR. The enrolment for STR has been slow. Additional, about 541 patients have been initiated on bedaquiline treatment so far while around 28 on delamanid.

541 Patients treated with Bedaquiline	2,497 Patients treated with STR	28 Patients treated with Delamanid

Declining treatment success rate among patients initiated on treatment in the country. As can be seen in Figure 7, the major cause of low treatment success rate is high loss to follow-up and deaths among those on treatment.

Figure 7: Treatment success rate among DR-TB patients

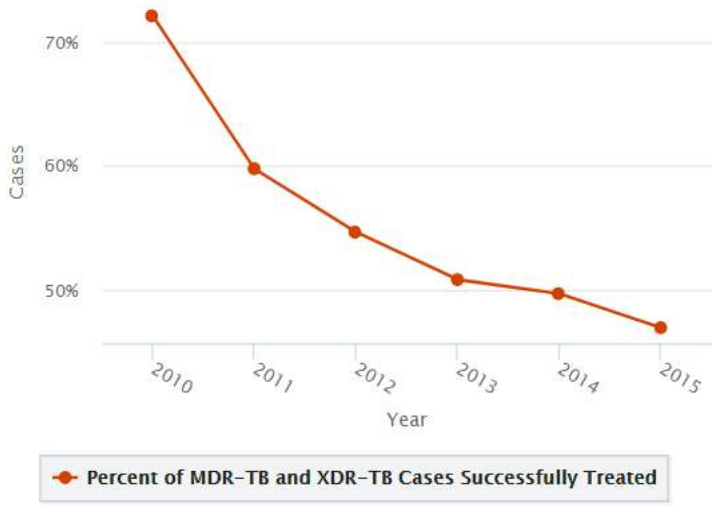
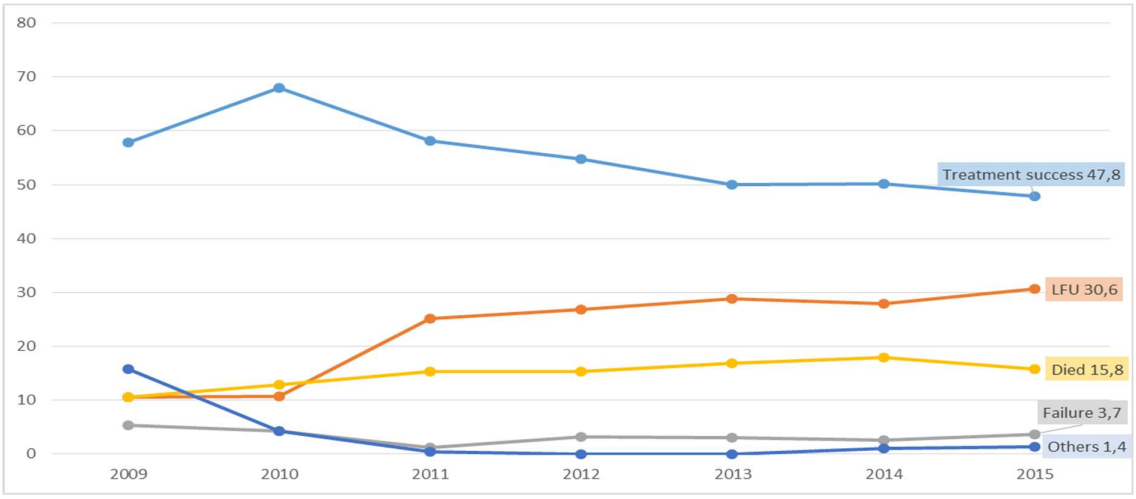
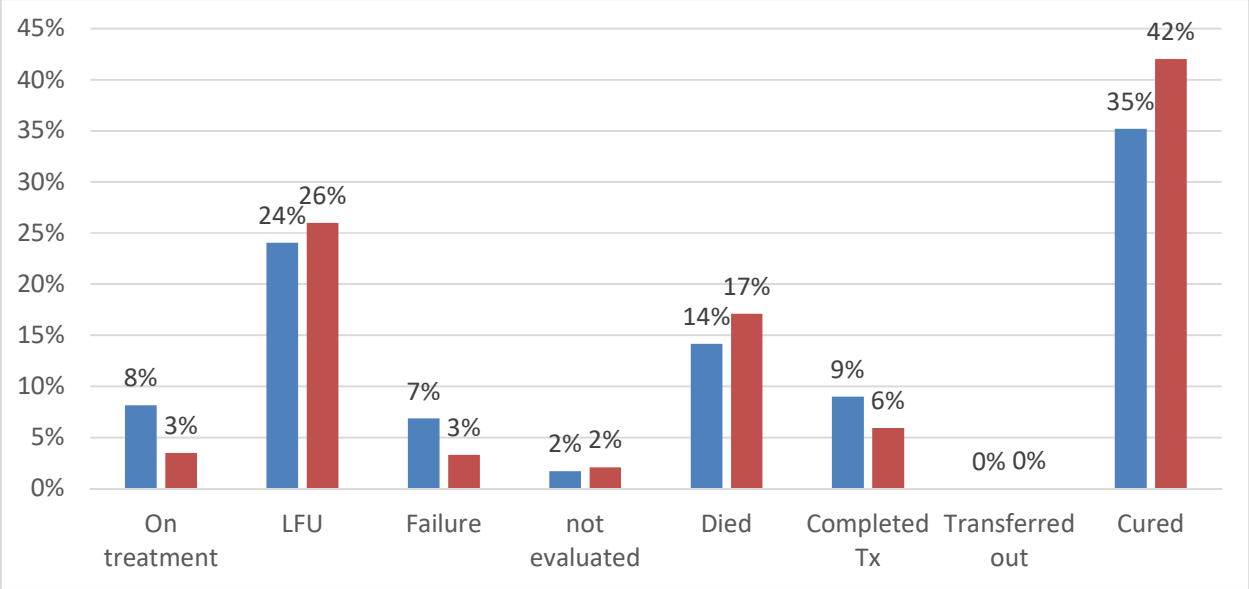


Figure 8: Trends in outcomes of DR-TB patients (by annual cohort till 2015)



Even with use of shorter regimen, the treatment success rates are no better than longer regimen as is seen for the recent cohorts for both groups in Figure 9

Figure 9: Treatment outcome for STR 2017 (blue) & LTR 2016 (red)



As can be seen from the graph above, there are significant instances of loss to follow-up and deaths among patients on STR as well which partly attributed to the fact that no baseline DST. High LFU may lead to development/ amplification of resistance to key drugs like FQ, Cfz used in these regimens.
It is also reported that only 30% treatment centres have audiometry and even when available, high frequency recording is not possible.

The programme plans to start implementing all oral long regimen by October 2019 in accordance with recent updates to WHO guidelines.
The steps being taken for transitioning to new regimen are:

- Preparatory meeting with partners (WHO, rGLC, KNCV CTB, GDF, GF)
- Ongoing discussion with TWG and expert at the national level
- Updated MDR TB guidelines is under development
- Request for BDQ donation has been submitted to GDF (for 3,300 patient)
- Drug calculation is on going
- Speeding up the expansion of culture, DST, LPA facilities and optimise its utility
- Workshop for dissemination to the PHO and MDR Team will be held in September 2019
- Bdq donation has been submitted to GDF and approved (for 3.300 patient)

The treatment regimen under discussion are (with first one being the standard regimen):

1	6 Bdq-Lfx-Lzd-Cfz-Cs-VitB6 / 14 Lfx-Lzd-Cfz-Cs-VitB6
2	6 Bdq-Lfx-Cfz-Cs-E -VitB6/ 14 Lfx-Cfz-Cs-E-VitB6
3	6 Bdq-Lfx-Lzd-Cfz-E / 14 Lfx-Lzd-Cfz-E
4	6 Bdq-Mfx-Lzd-Cfz-E / 14 Mfx-Lzd-Cfz-E
5	6 Bdq-Lzd-Cfz-Cs-E-VitB6 / 14 Lzd-Cfz-Cs-E -VitB6
6	6 Bdq-Lzd-Cfz-Cs-Eto / 14 Lzd-Cfz-Cs-Eto- Vit B6
7	6 Dlm-Lfx-Lzd-Clz-Cs / 14 Lfx-Lzd-Clz-Cs -VitB6
8	20 Lfx-Lzd-Cfz-Cs-Eto -VitB6
9	20 Mfx-Lzd-Cfz-Cs-E -VitB6
10	20 Mfx-Lzd-Cfz-Cs-Z -VitB6
11	6 Lfx-Lzd-Clz-Cs-Amk-VitB6 / 14 Lfx-Lzd-Clz-Cs-VitB6
12	6 Lfx-Lzd-Clz-Cs-S-VitB6 / 14 Lfx-Lzd-Clz-Cs-VitB6
13	6 Lfx-Lzd-Clz-Eto-PAS / 14 Lfx-Lzd-Clz-Eto
14	6 Dlm-Lzd-Clz-Cs-E / 14 Lzd-Clz-Cs-E-Vit B6
15	6 Bdq-Lfx-Cfz-H(Hdose)-Z-E/5 Lfx-Cfz-Z-E
16	9-12 Mfx(Hdose)-Dlm-Cfz-Z

The programme also plans to conduct operational research (OR) on shorter regimen. The mission team was informed that the OR protocol is still in preparation.

Recommendations

- Start all oral longer regimen as standard regimen by October 2019, as planned.
- Baseline DST capacity needs to be strengthened based on new algorithm
- Km may be used for patients already on treatment with the drug under strict watch for early signs of failure but not for new patients starting on second-line regimen (shorter or longer). Use Am where needed
- Develop a minimum package of patient support services to ensure uniformity across country and should be part of NTP policy irrespective of donor availability
- Offer informed choice to patients between shorter and longer regimen
- WHO and partners can support development of protocol
- There needs to be focus on childhood DR-TB as well
- Cat II treatment should be stopped immediately

E. Addressing high loss to follow-up

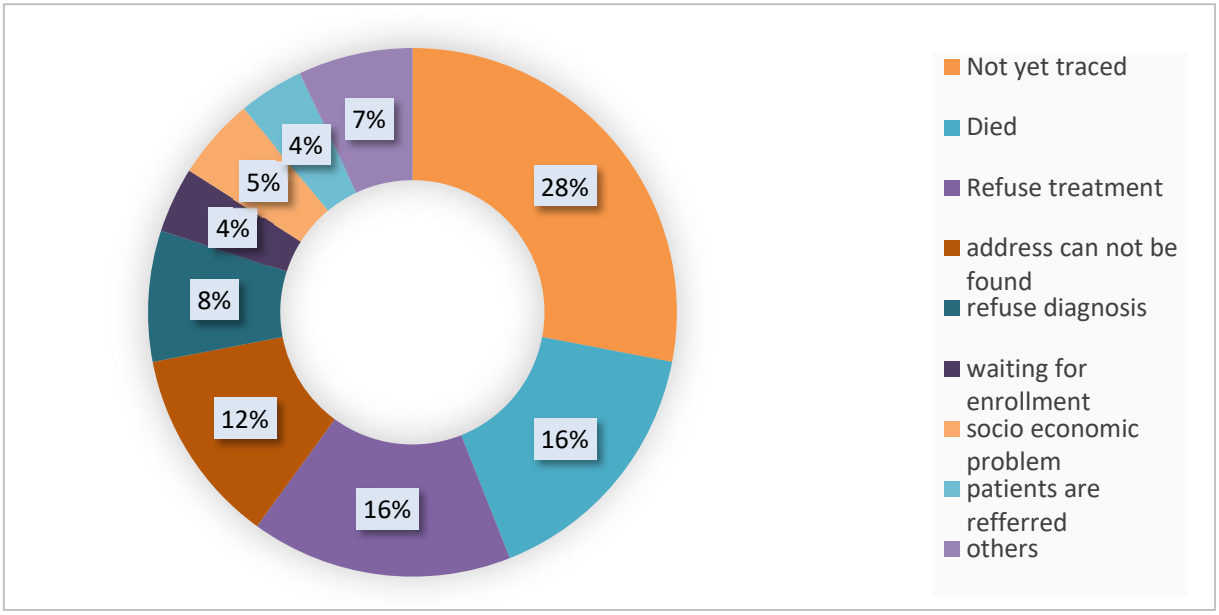
A very high loss to follow-up being reported by the programme before and after start of the treatment, is a cause of concern and was among the main topics of discussion with the programme and community representatives during the mission.

As per the discussions with community representatives during the TWG meeting, high loss to follow-up was attributed to

- Adverse events identification and management is not conducive for patients to continue treatment
- Socio-economic challenges for patients specifically loss of wages

The National TB programme with support of Challenge-TB project and country partners has also done an analysis of reasons of non-enrolment of MDR-TB cases, As per this analysis, the most common reasons (apart from those who were not traced) were refusal from patient and deaths before the start of treatment. Address not being found was also a significant contributor to non-enrolment

Figure 10: Identified reasons of not enrolment (study conducted by NTP/Challenge-TB)



Another aspect explored was the discrepancy n recording and reporting. As also discussed in earlier section, the reported number of those screened for resistance among previously treated cases is more than the number of such cases reported in the same period. This is apparently because of mismatch in reports being generated through two different systems – eTB manager and SITT which are not yet synchronised. Recording and reporting issues probably lead to higher reporting of cases being diagnosed and contribute to the gap between diagnosis and enrolment.

To address some of the issues related to high loss to follow-up, the mission team was informed that the programme has started Monthly Interim Cohort Analysis (MICA) for tackling the problem. MICA is a monthly, district-based activity held by the District Health Office (DHO) aiming to:

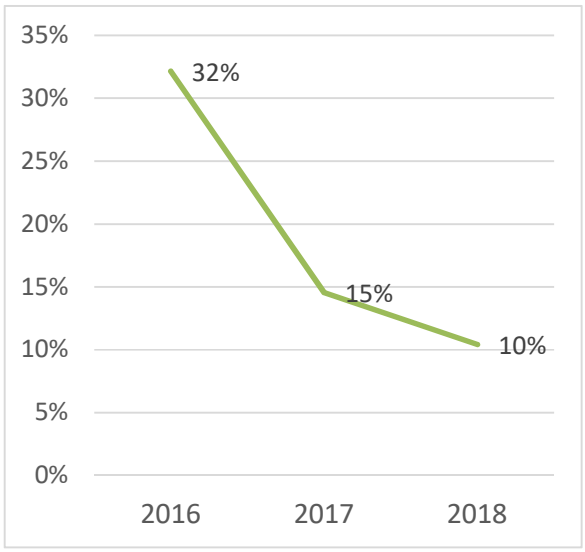
- Ensure all RR-TB patients enrol on treatment
- Ensure all DR-TB patients on treatment finish their treatment successfully
- Ensure patients data and treatment status in eTB manager is updated and validated

As a follow up of MICA, patients not enrolled and LFU are visited by Puskesmas/patients group, reasons of not enrolled/LFU are recorded and reported to DHO. It has been observed that MICA improves communication/coordination between DHO, Puskesmas, and DR-TB treatment sites, patients group. MICA has helped identify challenges related to adherence faced by the patients.

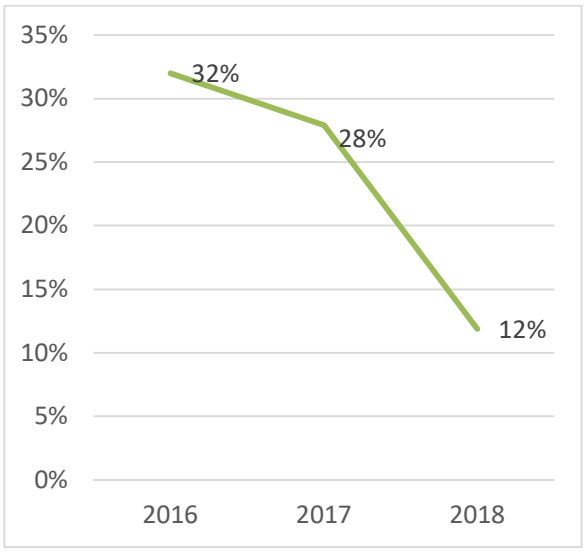
MICA started in 2 CTB supported districts (South Jakarta, N. Jakarta) in March 2017 and is currently done routinely in 16 CTB-supported districts. In Central Java, MICA is done for both DS- and DR-TB. Most of CTB supported districts have plans to continue MICA after CTB ends.

Figure 11: Impact of MICA on Loss to follow-up in some of the provinces

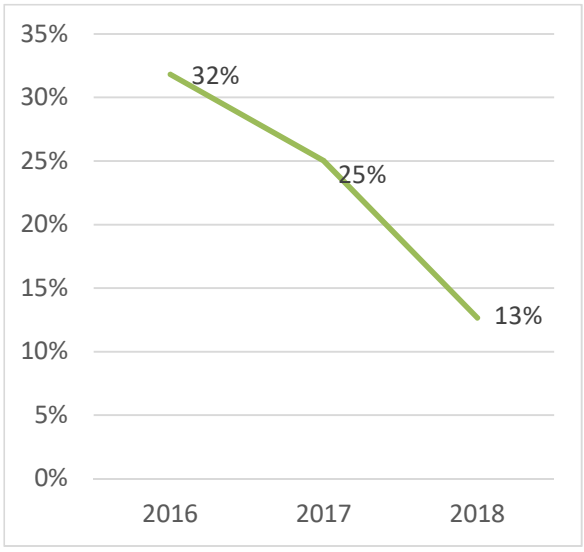
Central Jakarta



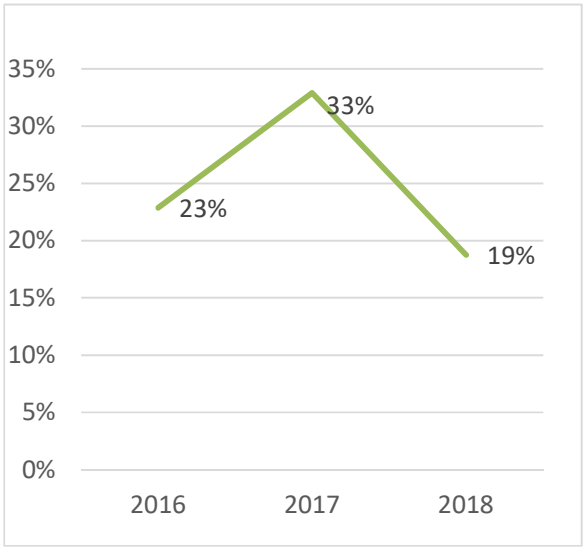
East Jakarta



North Jakarta



South Jakarta



In some districts, MICA has yet to show impacts in improving enrolment rate and reducing LFU.

However, it is clear that rigorous monitoring of enrolments helps reduce loss to follow-up before the start of treatment as well as after the start of the treatment

Recommendations

To address the high loss to follow-up because of adverse events and socio-economic factors, the following programme aspects need to be strengthened.

- Patient education and Counselling
- Local links through community members with District Health Office and social protection schemes
- Strengthening medical management of adverse events
- Ensuring that TB is part of the social protection schemes
- Data triangulation and validation needs to be done during supervisory visits and through MICA.
- Laboratory networking – between the labs and of labs with the programme will help ensure that all diagnosed cases are promptly initiated on treatment
-

F. Treatment coverage and expansion of DR-TB services

As per the Ministerial Decree, it is planned to establish 360 DR-TB Treatment centres in immediate future to service the 34 provinces as per the Ministerial decree issued in 2017. The ultimate target is to have at least 544 such centres. However, till the time of the visit only 188 such centres have been established.

Figure 12: Planned availablity of DR-TB services in the country

100%

Treatment availability for DR TB in Provincial Level

360

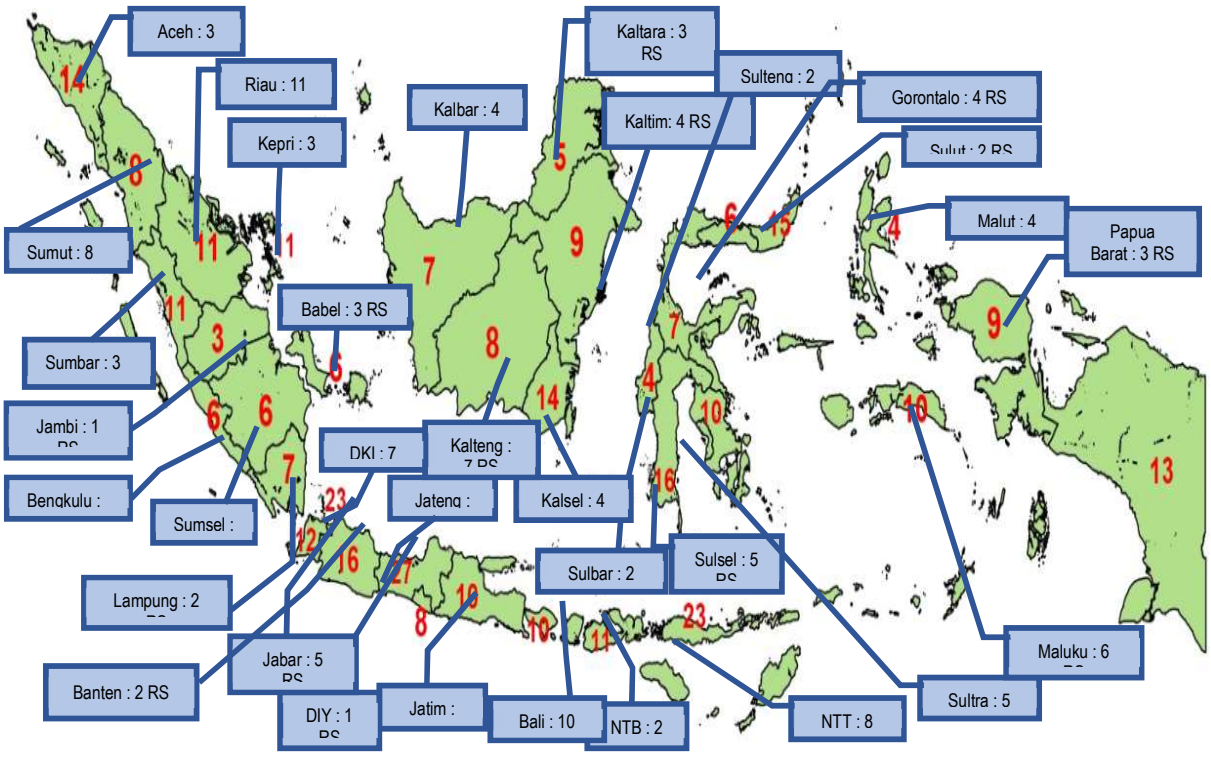
Appointed DR TB referral hospitals

2,304

DR TB satellites

The province wise proposed number of centres (in red) and those presently functional (blue box) are depicted in the Figure 13 below.

Figure 13: Location of DR-TB treatment services vis-à-vis planned in the country



It is clear that expansion of DR-TB treatment services has so far been at much slower pace than planned by the programme. From the visits to the facilities under preparation, it was observed that main reasons for delay in implementation were:

- Hospitals waiting for complete package of services – OPD, Laboratory and in-patient to be launched simultaneously rather than start with existing services.
- Training delays were reported at both Puskesmas and hospitals
- There also appears to be lack of coordination between the national programme and the hospitals because hospitals do not report to the national programme.
- Some funding delays for refurbishment were seen at one of the facilities
- Hospitals that plan to have in-patient facilities wanted proper negative pressure facilities in the wards. However, the location of the wards would promote mixing of patients. Moreover, negative pressure systems are not always well maintained for appropriate functioning.

Recommendations

- Hold a high-level coordination meeting with directorate of medical services to ensure rapid engagement of all hospitals as well as ensuring pro-active adverse events monitoring and management (aDSM) where implementation of services has started.
- Multisectoral coordination through high level intervention for TB (national initiative for priority diseases) and establishing accountability.
- Advocate for Presidential Decree on TB to accord high priority to the disease at sub-national level with sufficient allocation of resources

Specifically, for early engagement of hospitals:

- On-site capacity building of staff to reduce training delays.
- Hospitals who are yet to start services should network with hospitals already implementing for guidance on cases to be initiated on treatment.
- Identify activities that can be started e.g. screening, patient investigations, out-patient services, patient support.

G. Professional bodies' role in expansion of DR-TB services and ensuring quality

KOPI TB is a coalition of multiple professional organization in Indonesia that have commitmen and collaborating to help National TB Programme at national, provincial, and district level through PPM TB network. KOPI TB drives their members to support the activity of PPM TB at district level. Currently 13 professional organizations are engaged in KOPI TB that collaborate to support National TB Program as one group.

Objectives of the coalition

- Increasing the involvement of practitioners – public and private in National TB Program activities
- Ensure that all the members of its organization follow ISTC and National TB Guideline in their daily practice
- Ensure that all treated TB cases are being notified
- Increase the treatment success rate of TB Programme

Planned activities at national level:

1. Mapping of professional organization and members that will be involved;
2. Provide information regarding the formation of central professional organization coalition to its branch;
3. Be resource person for professional organization coalition in provincial level;
4. To support and be involved in the developing of Norms, Standards, Procedures, and Criteria (NPSK);
5. Building action plan and evaluating the professional organization coalition;
6. Undertake supervision and monitoring to provincial and district level;

7. Provide updated information regarding the development of National TB Program to each professional organization.

Provincial level

1. Together with Provincial Municipal Health Office, facilitating the formation of District level coalition;
2. Mapping of professional organization and members that will be involved;
3. Coordinate district level coalition's activity
4. Build action plan and evaluate professional organization coalition;
5. Do supervision and monitoring to district level;
6. Provide updated information regarding the development of National TB Program to each professional organization;
7. On doing its activities, province level professional organization will be facilitated by Provincial Municipal Health Office and related partners;
8. Together with Municipal Health Office and related partners, will act as advocating team to Provincial Government;
9. Act as part of Provincial Trainer Team.

District level

1. As expert practitioner in individual clinical practice, act as part of infectious disease prevention in direct care to patient and give report to information system in district level according to guideline;
2. As expert in hospital, act as motivator, facilitator, and executor in forming the synergistic internal TB service network;
3. Inside DPPM network, act as facilitator in increasing healthcare staff capacity through training, supervision, and clinical mentoring..

Recommendations

For improving engagement of providers in general

- Develop desk reference materials – one page each for:
    - diagnostic algorithm,
    - treatment algorithm and,
    - adverse events identification and management.
- Consider developing a mobile app with all necessary technical materials for the practitioners
- Better use of social media for communicating within National advisory committee and Provincial advisory committee

Recommendations specific for **KOPI TB**

Improving case notification

- Analyse patient pathways and points of loss in the target districts/ hospitals
    - Provider
    - System

    - Patient/ community
- Capacity building of hospitals not yet engaged

Improving treatment adherence and outcomes

- Support patient counselling and education
- Promote pro-active monitoring of adverse events and prompt treatment
- Support NTP in transitioning to all-oral longer regimen and OR for shorter all-oral regimen

Annex 1: Agenda of the mission

Day/Date	Activity	Participants /Notes
Saturday, 6 April 2019 INA TIME – Workshop in Surabaya		
Sunday, 7 April 2019		
Monday, 8 April 2019 - **TWG meeting**		
09.00 – 10.00	Briefing with NTP Manager/PMDT & Lab Team PMDT & Lab situation	NTP
10.00 – 12.00	Panel presentation and discussion : - WHO DR TB Updated guideline 2018, transition plan, what should country do - Experience on all oral regimen in South Africa - Discussion	Dr Vineet Dr Xavier
12.00 – 13.00	LUNCH BREAK	
13.00 – 15.15	Panel: - Draft of Indonesia updated PMDT guideline - Presentation for laboratory networking for the updated guideline, and other lab updates (SL LPA) - Discussion	PMDT Team Lab Team
15.15 – 15.45	Coffee break	
15.45 – 17.00	Presentation for logistic preparation for the updated guideline	Logistic Team
Tuesday, 9 April 2019 – Coordination meeting for reducing loss to follow up before and during treatment		
08.30 – 10.00	Panel Presentation: - PMDT situation, result of STR evaluation - MICA result from 6 provinces, and MICA mechanism	NTP PMDT focal point CTB team
10.00 – 11.00	Panel Presentation and discussion: Challenges of low enrollment of Confirmed Rif res cases and plan of action	DKI

	- Algorithm - Laboratory related - Recording reporting - Community based activity	DI Y Semarang Jakarta Barat
11.00 – 12.00	Panel presentation (@20 minutes): Community support for DR TB reducing initial loss to follow up, discussion and plan of action	NTP ACSM team, Aisyiah, LKNU
12.00 – 13.00	LUNCH Break	
13.00 – 15.15	Discussion	
15.15 – 15.30	Coffee Break	
15.30 – 16.15	Plan of action for reducing initial loss to follow up	
Wednesday, 10 April 2019		
09.00 – 12.00	Visit Puskesmas Palmerah - DOH Present the DR TB situation (MICA result, expansion, etc) in Puskesmas - Meet patients	SuDinkes Kota Jakbar Konsultan GLC Subdit TB
12.00 – 13.00	Lunch and travel	
13.00 – 16.00	Visit to RS Harapan Kita (Assessment and advocacy for starting DR TB treatment)	DG of Medical care Dinkes Prov DKI SuDinkes Kota Jakbar Konsultan GLC Subdit TB
Thursday, 11 April 2019		
08.00 – 11.00	RSUP Fatmawati	DG of Medical care South Jakarta DHO 1 CET/TWG
12.00 – 16.00	Discussion with IO PPM – PDPI Pusat and KOPI TB	KOPI

		PDPI YKI
Friday, 12 April 2019		
08.00 – 08.20	Briefing with WR	
09.00 – 12.00	Coordination meeting with Lab Team	NTP office
13.00 – 15.00	Debriefing with NTP and team	

Laboratory review schedule

Day/Date	Activity	Participants
Sunday, 7 April 2019		
Monday, 8 April 2019 - **TWG meeting**		
09.00 – 10.00	Briefing with NTP Manager/PMDT & Lab Team PMDT & Lab situation	NTP
10.00 – 12.00	Panel presentation and discussion : - WHO DR TB Updated guideline 2018, transition plan, what should country do - Experience on all oral regimen in South Africa - Discussion	Dr Vineet Dr Xavier
12.00 – 13.00	LUNCH BREAK	
13.00 – 15.15	Panel : - Draft of Indonesia updated PMDT guideline - Presentation for laboratory networking for the updated guideline, and other lab updates (SL LPA) - Discussion	PMDT Team Lab Team
15.15 – 15.45	Coffee break	
15.45 – 17.00	Presentation for logistic preparation for the updated guideline	Logistic Team
Tuesday, 9 April 2019 – Coordination meeting for reducing loss to follow up before and during treatment		

08.30 – 10.00	Panel Presentation: - PMDT situation, result of STR evaluation - MICA result from 6 provinces, and MICA mechanism	NTP PMDT focal point CTB team
10.00 – 11.00	Panel Presentation and discussion Challenges of low enrollment of Confirmed Rif res cases and plan of action (@20 minutes): - Algorithm - Laboratory related - Recording reporting - Community based activity	DKI? Jakarta Barat
11.00 – 12.00	Panel presentation (@20 minutes): Community support for DR TB reducing initial loss to follow up, discussion and plan of action	NTP ACSM team, Aisyiah, LKNU
12.00 – 13.00	LUNCH Break	
13.00 – 15.15	Discussion	
15.15 – 15.30	Coffee Break	
15.30 – 16.15	Plan of action for reducing initial loss to follow up	
16.15 – 16.45	Closing ceremony	
Wednesday, 10 April 2019		
08.00 – 16.00	Visit Microbiology Dept FM UI	Subdit TB WHO KNCV PSM – Chemonix
Thursday, 11 April 2019		
08.00 – 16.00	Visit Lab RS Persahabatan	Subdit TB

		WHO KNCV PSM – Chemonix
Friday, 12 April 2019		
09.00 – 12.00	Coordination meeting with PMDT Team	
13.00 – 15.00	Debriefing with NTP and team	