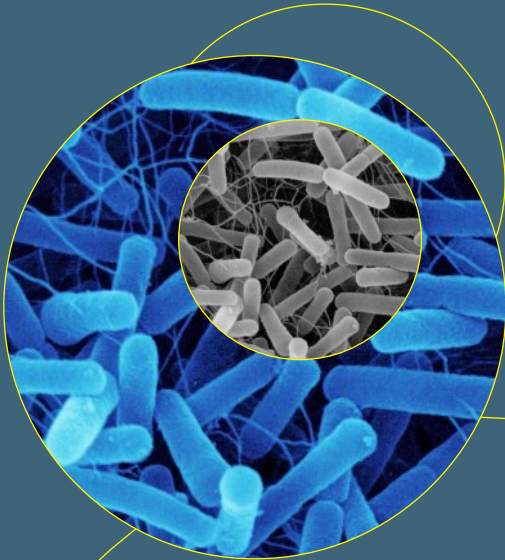
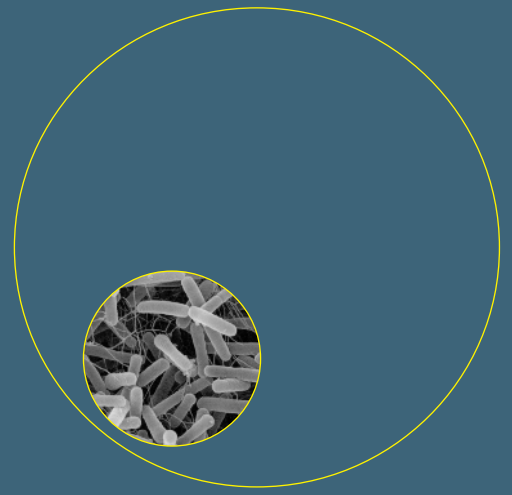




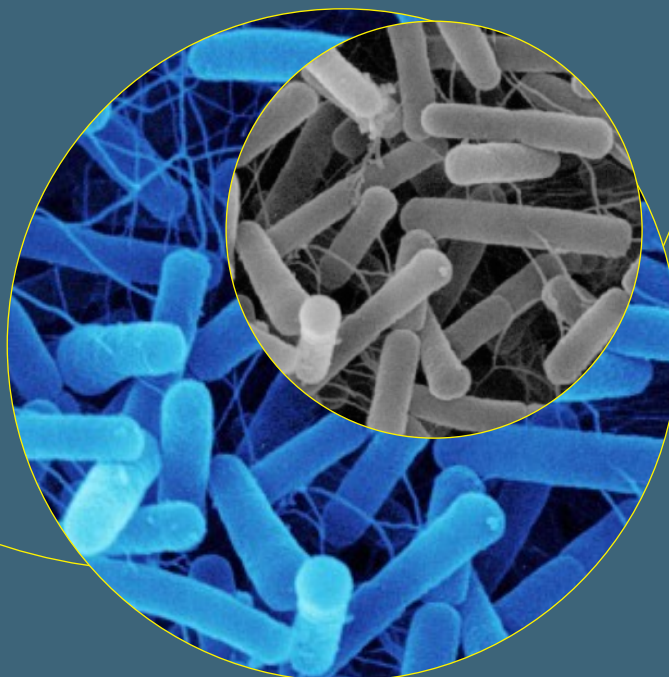
**World Health  
Organization**

Regional Office for South-East Asia



# South-East Asia

Regional response framework for  
**DR-TB** 2017-2021





# Table of Contents

<b>Acronyms and abbreviations</b>	<b>3</b>
<b>Foreword</b>	<b>5</b>
<b>Background</b>	<b>6</b>
The WHO End TB Strategy	7
<b>Progress towards ending drug-resistant TB in the SEA Region</b>	<b>8</b>
<b>Key regional challenges, threats and opportunities</b>	<b>10</b>
Case-finding and diagnosis	10
Patient-centred treatment delivery	11
Health systems	12
Political commitment and financing	12
Research	13
<b>Regional DR-TB response</b>	<b>14</b>
Purpose of the Regional DR-TB Response Framework	14
Vision and goal	14
Objectives	15
<b>Strategic direction 1:</b> Integrated patient-centred care and prevention	15
<b>Strategic direction 2:</b> Bold policies and supportive systems	18
<b>Strategic direction 3:</b> Intensified research and innovation	23
The regional Green Light Committee (rGLC) mechanism	24
<b>Indicators framework for monitoring the DR-TB response in the SEA Region</b>	<b>27</b>
<b>Acknowledgements</b>	<b>31</b>
<b>Annexure 1: Progress in Member States</b>	<b>33</b>
Bangladesh	34
Bhutan	35
Democratic People's Republic of Korea	36
India	37
Indonesia	38
Maldives	39
Myanmar	40
Nepal	41
Sri Lanka	42
Thailand	43
Timor-Leste	44
<b>Annexure 2: Delhi Call for Action to End TB in the South-East Asia Region</b>	<b>45</b>

## South-East Asia Regional response framework for DR-TB, 2017-2021

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# Acronyms and abbreviations

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aDSM	:	active drug safety monitoring and management
CBO	:	community-based organization
CoE	:	centre of excellence
CPT	:	co-trimoxazole preventive therapy
DOTS	:	directly observed therapy, short-course
DR	:	drug resistant
DR-TB	:	drug-resistant tuberculosis
DST	:	drug susceptibility testing
EQA	:	external quality assessment
FLD	:	first-line drug
Global Fund	:	the Global Fund to Fight AIDS, Tuberculosis and Malaria
GDF	:	Global Drug Facility
GDI	:	Global Drug-Resistant Tuberculosis Initiative
INH	:	isoniazid
IQC	:	internal quality control
KNCV	:	Royal Dutch Tuberculosis Association
LF-LAM	:	lateral flow urine lipoarabinomannan assay
LPA	:	line probe assay
MDG	:	Millennium Development Goal
MDR-TB	:	multidrug-resistant tuberculosis
MoH	:	Ministry of Health
MoU	:	memorandum of understanding
NCD	:	noncommunicable disease
NGO	:	nongovernmental organization
NSP	:	National Strategic Plan
NTP	:	National Tuberculosis Control Programme
NTRL	:	national tuberculosis reference laboratory (ies)
OTC	:	over the counter
PMDT	:	programmatic management of drug-resistant tuberculosis

PPM	:	public-private mix
PSM	:	procurement and supply chain management
PV	:	pharmacovigilance
rGLC	:	Regional Green Light Committee
RR-TB	:	rifampicin-resistant tuberculosis
R&R	:	recording & reporting
SDG	:	Sustainable Development Goal
SEA	:	South-East Asia (Region)
SLD	:	second-line drug
SLI	:	second-line injectable
SNRL	:	supranational reference laboratory (ies)
SOP	:	standard operating procedure
STR	:	shorter treatment regimen (for RR/MDR-TB)
TAC	:	technical assistance centre
TB	:	tuberculosis
TWG	:	technical working group
UHC	:	universal health coverage
UNOPS	:	United Nations Office for Project Services
WHO	:	World Health Organization
XDR-TB	:	extensively drug-resistant tuberculosis

# Foreword



It was nearly a decade ago in 2007 when the Sixtieth Regional Committee for South-East Asia (SEA) passed a resolution on tuberculosis that urged Member States “to ensure implementation of interventions to effectively address multidrug-resistant and extensively drug-resistant TB”. The ministerial meeting of high MDR-TB burden countries in Beijing, China in April 2009, and the Sixty-second World Health Assembly, endorsed resolutions urging all Member States to achieve universal access to diagnosis and treatment of MDR-/XDR-TB, and monitor achievement in the sphere of prevention and control of MDR-/XDR-TB.

Since 2009, the number of notified MDR-TB cases in the Region has increased more than 15-fold, from just above 2600 to more than 40 000 in 2016. While this means that significant progress has been made in increasing access to diagnostic and treatment services for drug-resistant TB in the Region, this accounts for less than 20% of the 200 000 new rifampicin resistant and multidrug resistant TB (RR/MDR-TB) cases in 2016 who needed second-line treatment. Treatment success rates among those initiated on treatment in the most recent cohort (2014) was low at 50%. Thus, our efforts have to be multiplied several times more to reach out to all those who need treatment and improve treatment outcomes.

There is a need for a comprehensive approach to addressing the DR-TB burden by preventing the emergence of new MDR-TB cases, as well as through early diagnosis and treatment of existing cases. All sectors will need to be involved to mobilize available resources. While scaling up DR-TB services, health systems would also need to be strengthened in accordance with the needs. Appropriate operational research for diagnosis and models of care will help countries to adapt new tools and technologies to local needs. Treatment of DR-TB takes a long time and generally patients suffer from several side-effects of the drugs. Patient support through psychological, financial and social measures with the engagement of communities and those affected will go a long way in improving treatment adherence and the outcomes of treatment.

The WHO SEA Region, in consultation with several key partners, has developed a response framework to draw a roadmap for regional contribution to achievement of the global targets set forth for DR-TB in the “Ending TB in the South-East Asia Region: Regional Strategic Plan 2016–2020”. The framework will also act as a guiding tool for Member States to develop strategic and operational plans for addressing the issues of RR/MDR-TB, and serve as a reference document and tool of communication for regional priorities to address the challenges related to RR/MDR-TB in the Region.

With the implementation of this response framework, it is expected that the Region would strengthen laboratory capacity by rolling out newer diagnostics, promote universal drug-susceptibility testing, ensure that all patients diagnosed with drug resistance are initiated on appropriate second-line treatment immediately, adopt the latest available evidence and guidelines on DR-TB management, and secure funds for implementing the framework.

The SEA Regional Office of WHO stands committed to supporting all Member States in their efforts to address the problem of DR-TB.

A handwritten signature in black ink, appearing to read 'Poonam Khetrapal Singh'.

**Dr Poonam Khetrapal Singh**  
Regional Director

# Background

The burden of tuberculosis (TB) remains disproportionately high in the WHO South-East Asia (SEA) Region, home to 26% of the world's population. In 2016, an estimated 4.7 million people fell ill with TB in the SEA Region, representing 46% of the total TB incidence globally.

Although the Region experiences relatively low levels (2.8%; range: 2.4–3.1%) of multidrug-resistant (MDR) and rifampicin-resistant (RR) forms of TB among newly detected cases, and 13% (range: 10–15%) among previously treated cases, given the large number of TB cases in the Region, this translates into 117 000 estimated MDR/RR-TB cases among notified pulmonary TB cases each year. Thus in 2016, the Region accounted for more than 30% of the global estimated MDR/RR-TB cases among notified pulmonary TB cases worldwide. Six out of the 30 high TB (and MDR-TB) burden countries are in the SEA Region: Bangladesh, Democratic People's Republic of Korea, India, Indonesia, Myanmar and Thailand (Fig. 1).

**Fig. 1: Global estimated incidence of MDR/RR TB in 2016 for countries with at least 1000 incident cases**



Source: *Global tuberculosis report 2017*. Geneva: World Health Organization; 2017



Even among the high MDR-TB burden countries in the SEA Region, the prevalence and incidence of MDR/RR-TB vary considerably, as do diagnostic and treatment achievements (Table 1).

**Table 1: Estimated proportion of MDR/RR-TB cases, confirmed and treated cases among countries in the SEA Region**

Country	New cases	Retreatment cases	Estimated number among notified pulmonary TB cases n (95% CI)	Laboratory-confirmed cases	Patients started on second-line treatment*
	% (95% CI)	% (95% CI)			
Bangladesh	1.6% (0.59–2.6)	29% (22–36)	5 300 (3 500–7 200)	969	918
Bhutan	11% (8.5–15)	18% (7.7–34)	70 (52–87)	55	55
DPR Korea	2.2% (0.51–3.9)	16% (5.8–27)	4 600 (2 300–6 900)	935	814
India	2.8% (2–3.5)	12% (10–13)	84 000 (72 000–95 000)	37 258	32 914
Indonesia	2.8% (2.2–3.5)	16% (10–20)	11 000 (8 800–13 000)	2 720	1 879
Maldives	1.7% (0.04–9.1)	0% (0–0)	1 (0–4)	1	2
Myanmar	5.1% (3.2–7)	27% (10–44)	9 000 (6 100–12 000)	3 213	2 537
Nepal	2.2% (0.98–3.4)	15% (6.7–24)	900 (540–1 300)	430**	386
Sri Lanka	0.54% (0–1.3)	3.1% (1.6–5.4)	47 (1–93)	23	17
Thailand	2.2% (1.5–2.9)	24% (16–32)	2 800 (2 100–3 500)	955	952
Timor-Leste	2.8% (2.4–3.1)	13% (10–15)	100 (88–110)	6	6
<b>Total</b>	<b>2.8% (2.4 – 3.1)</b>	<b>13% (10 – 15)</b>	<b>117 000 (105 000 – 130 000)</b>	<b>46 269</b>	<b>40 480</b>

Source: *Global tuberculosis report 2017*. Geneva: World Health Organization; 2017.

\*Includes patients diagnosed before 2016 and patients who were not laboratory-confirmed

\*\*Figure corrected after *Global tuberculosis report 2017* was published

## The WHO End TB Strategy

In 2014, the World Health Assembly in its resolution WHA67.1, adopted a new global strategy and targets to end the TB epidemic by 2035. This agenda, which feeds into the WHO End TB Strategy, calls for an integrated approach to ensure inclusive economic and social development, while ensuring peace, security and environmental sustainability.

The End TB Strategy has as its vision a world free of TB, with zero deaths, disease and suffering due to TB. The three pillars of the Strategy are – integrated, patient-centred care and prevention; bold policies and supportive systems; and intensified research and innovation. It is based on the principles of government stewardship and accountability, with monitoring and evaluation; strong coalition with civil society organizations and the community; protection and promotion of human rights, ethics and equity; and adaptation of the Strategy and targets at the country level, with global collaboration.

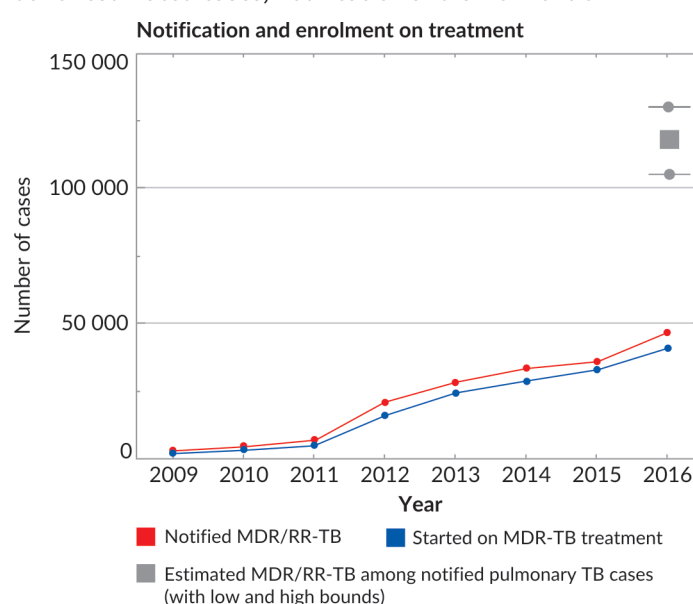
The goal of the Strategy is to move beyond TB “control” to efforts that “end” the global TB epidemic. It is therefore essential to tackle the challenge of drug-resistant (DR) TB, without which the ambitious aim of ending TB cannot be realized.

# Progress towards ending drug-resistant TB in the SEA Region

The SEA Region has made considerable progress in the fight against TB. The Region has achieved the 2015 Millennium Development Goal (MDG) of halting and reversing the incidence of TB. Access to TB care has expanded substantially in the Region. However, challenges remain in relation to universal access to diagnosis and care. These become apparent when we look at the progress in ending DR-TB.

In the SEA Region, only 35 953 out of the 110 000 estimated MDR/RR-TB cases among notified pulmonary TB cases were confirmed by available diagnostic tools, and among those who were diagnosed, 32 648 were started on treatment in 2015 (Fig. 2).

**Fig. 2: Number of estimated cases, notification and enrolment on MDR-TB treatment**



Source: <http://www.who.int/tb/data>

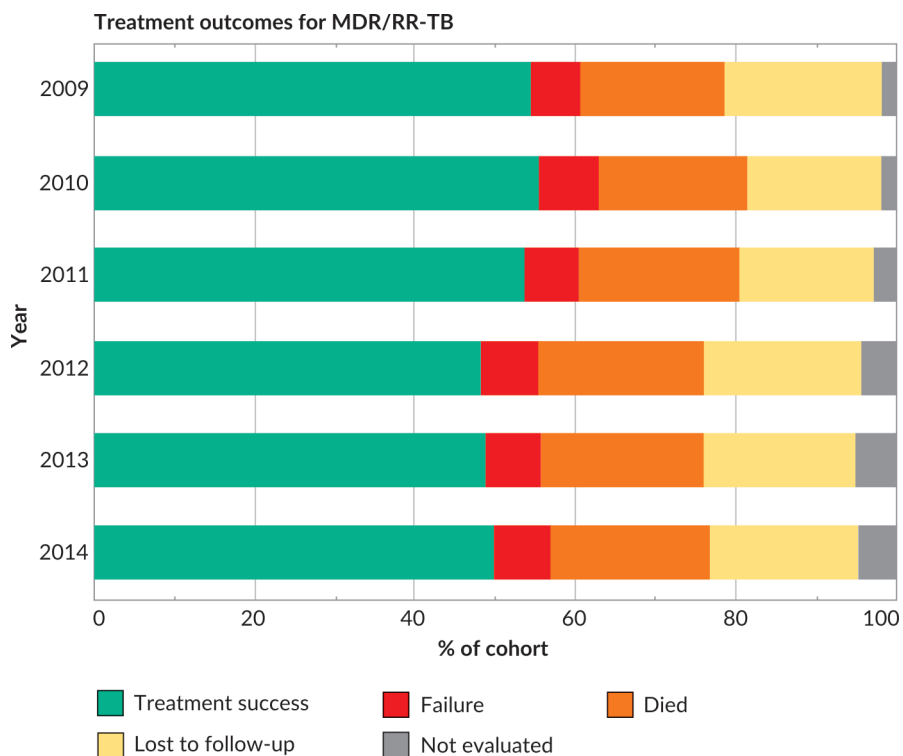
**Table 2: Treatment outcomes for RR/MDR-TB and extensively drug-resistant (XDR)-TB among cases registered in 2014 in Member States of the SEA Region**

Country	RR-/MDR-TB cases started on second-line treatment in 2014		XDR-TB cases started on second-line treatment in 2014	
	Cohort	Treatment success rate	Cohort	Treatment success rate
Bangladesh	946	74%	3	0%
Bhutan	61	90%	0	NA
DPR Korea	212	91%	0	NA
India	22 524	46%	1 262	29%
Indonesia	1271	51%	30	13%
Maldives	0	NA	0	NA
Myanmar	1 497	80%	0	NA
Nepal	286	70%	0	NA
Sri Lanka	13	69%	0	NA
Thailand	414	58%	7	14%
Timor-Leste	3	100%	0	NA
<b>SEA Region total</b>	<b>27 227</b>	<b>50%</b>	<b>1 430</b>	<b>29%</b>

Source: *Global tuberculosis report 2017*. Geneva: World Health Organization; 2017.

Among those with DR-TB, only 49% of those who were diagnosed and started on treatment with second-line drugs (SLDs) were successfully treated (based on the 2013 cohort). This was largely due to high rates of mortality and loss to follow up (Fig. 3).

**Fig. 3: Treatment outcomes of patients diagnosed with MDR/RR-TB in the SEA Region (2009–2014 cohort)**



Source: <http://www.who.int/tb/data>

# Key regional challenges, threats and opportunities

## Case-finding and diagnosis

### Challenges

- In several countries of the Region, private sector providers are not well connected to the national notification system and do not follow national guidelines for the diagnosis of TB.
- In 2015, less than 35% of estimated RR/MDR-TB cases among notified pulmonary TB cases were reportedly diagnosed, and an even lesser proportion was reported to be initiated on second-line treatment within the same year.
- Most countries in the Region have insufficient laboratory capacity to screen all TB cases for drug resistance. Designated laboratories with DST capacity are generally centralized and located at urban centres. Access to laboratory diagnostic services is compounded by a lack of efficient sputum transportation mechanisms. The roll-out of rapid molecular tools has not reached its full potential, largely due to procurement challenges and limited financial resources. Moreover, private sector laboratories are often insufficiently involved in TB diagnosis.
- Laboratory information systems are not always linked with patient management systems. Thus, it is not always possible to verify if anti-TB treatment regimens are appropriate and timely for each and every person diagnosed with DR-TB.

### Threats

- The population at risk exceeds the capacity to screen for the disease.
- Delayed and lack of access to accurate diagnoses results in prolonged infectious periods, ongoing transmission in the community and health facilities (e.g. primary resistance), and inappropriate regimens (i.e. acquired resistance).
- Slow expansion of DST capacity for second-line drugs also means that patients may be on inappropriate regimens, amplifying the existing resistance.

### Opportunities

- Combined laboratory and management monitoring missions by WHO and technical partners provide an opportunity to re-emphasize the need for universal access to DST and aligning these services.
- Projects in some of the countries are exploring mechanisms aligned with vaccine transportation systems while some others are trying courier systems, as per local suitability.
- Domestic and international funding resources are increasingly available for equipment for decentralized molecular testing.

## Patient-centred treatment delivery

### Challenges

- Challenges are faced by programmes in enrolling all diagnosed patients on appropriate treatment, due to stigma, lack of decentralization and lack of treatment capacity.
- The regional treatment success rate among the 2013 cohort of MDR-TB patients (reported in 2015) was low (49%).
- There is a rapidly expanding, and largely unregulated, private sector in several countries. Substantial variation in the quality of services, irrational treatment practices, and limited engagement with the formal TB surveillance systems in this sector have resulted in larger numbers of patients with DR-TB, and the inability to monitor treatment adherence and outcomes.
- Patient-centred care, including DOT, is not strictly followed while administering treatment, even for drug-susceptible TB. Psychosocioeconomic support for patients is insufficient.
- Pharmacovigilance systems to monitor potential antituberculosis drug-related adverse events are weak.

### Threats

- Lack of support for treatment adherence and consequent treatment interruption could lead to prolonged infectiousness and amplification of resistance.
- Insufficient screening for co-morbidities, including HIV infection among DR-TB patients and vice versa, leads to high morbidity and mortality among patients.

### Opportunities

- Engagement of unlinked public and private sector providers, such as laboratories, stand-alone practitioners and general hospitals in recognizing and referring or diagnosing TB and DR-TB, would prevent unnecessary diagnostic delays.
- Systematic follow up of cohorts of diagnosed patients for treatment enrolment could help monitor the early loss to follow up and guide action.
- Countries should organize patient support and counselling starting from the moment of diagnosis, rather than from the moment of treatment enrolment.
- Shorter treatment regimens recommended by WHO could help in improving adherence and treatment outcomes.
- Newer drugs like bedaquiline and delamanid expand the options available for DR-TB cases.
- Civil society within countries can be engaged in patient support and care, specifically in cases of DR-TB and otherwise vulnerable TB patients.

## Health systems

### Challenges

- Although considerable progress has been made in implementing infection control practices, the risk for airborne TB transmission in health-care facilities and congregate settings requires substantial attention and investment in most countries.
- The capacity of national pharmaceutical regulatory authorities to assure the quality of first-line anti-TB drugs (FLDs) and SLDs is limited.
- Pharmacovigilance systems to monitor potential anti-TB drug-related adverse events are weak.
- DR-TB surveillance systems are mostly paper based and not well integrated. In countries where electronic systems exist, there often are considerable difficulties in software and connectivity, hampering full use.
- Mechanisms for drug transportation, storage and stock-keeping are not yet aligned with the needs of PMDT expansion.

### Threats

- DR-TB transmission occurs in institutions, especially at health-care facilities, because of lack of administrative, environmental and respiratory protection controls.
- Transition from the longer regimen to a shorter regimen may lead to drug supply disruptions.
- Insufficient human resources, both in terms of numbers and capacity, may limit the scale up of PMDT.

### Opportunities

- New guidelines on active drug safety monitoring and management (aDSM) make monitoring of adverse events less complicated. Moreover, funding agencies have a greater interest in investing in aDSM because of newer drugs and regimens being introduced.

## Political commitment and financing

### Challenges

- There is heavy dependence on external resources for TB programmes in general, and specifically for components related to PMDT. Most domestic funding allocations are insufficient to meet the burden-driven demand.
- The potential of multisectoral approaches to address the social determinants of TB are not fully realized in most of the countries of the Region.

### Threats

- Some countries of the Region, including those with a relatively low TB burden, have large proportions of drug resistance. Lack of attention and resource allocation for ending TB would lead to possible ignoring of the threat of DR-TB, and its spread could lead to an amplification of the burden of TB as a disease as well as a socioeconomic problem.

- A changing global political scenario may threaten funding commitments from large international donors.

## Opportunities

- The Delhi Call for Action to end TB in the WHO South-East Asia Region. All Member States have committed to accelerating efforts towards ending TB in the Region through establishing an empowered committee in each of the countries to monitor progress towards ending TB, increasing budgetary and human resource allocations, engaging communities, providing patient-centred care and innovative funding mechanisms (details available at Annexure 1).
- “Accelerating efforts towards ending TB” has also been declared as a Flagship Priority of the WHO Regional Office for South-East Asia.
- The recent call by several Member States for achieving the ambitious targets of ending TB even before the timelines of the Sustainable Development Goals shows a renewed commitment towards ending TB.
- The new Global Fund funding model helps governments to develop sustainable plans to increase domestic funding.
- Innovative financing mechanisms need to be explored to plug the remaining gaps.

## Research

### Challenges

- There is limited capacity to conduct research in most countries, and it is considered a lower priority as compared to service delivery.
- Linkage of the NTP with national research institutes is often not strong.
- Investment in research is low in most countries of the Region.
- Implementation of recommendations from research is slow to be adopted and rarely translated into policy and practice.

### Threats

- Weak research methodology, and poorly conducted science often yields conflicting results, which further delays adoption of new technologies and stymies innovation.
- There are competing priorities with service-related activities.

### Opportunities

- Countries with specific research initiatives can coordinate and engage with other countries in the Region to disseminate key findings and develop regional platforms for adaptation.
- Funding availability in programme budgets through donors such as the Global Fund need to be fully utilized.

# Regional DR-TB response

The Regional DR-TB Response Framework tends to align with the Regional Strategic Plan 2016-2010. The overall plan was developed and launched in March 2016 and is available at <http://www.searo.who.int/tb/9789290225058.pdf?ua=1>. The Regional Strategic Plan includes three high-level, overarching indicators, and corresponding regional targets and milestones. The long-term regional targets for reductions in TB cases and deaths by 2030 correspond to the end date of the United Nations' post-2015 Sustainable Development Goals (SDGs) framework, within which targets have been set for 2030.<sup>1</sup> The SDG framework includes the End Strategy 2030 targets for reductions in TB cases and deaths as part of a health-related sub-goal. The corresponding regional milestones are for 2020 – the period covered by this Strategic Plan – and 2025.

## Purpose of the Regional DR-TB Response Framework

- To provide an overview of the planned regional response to MDR/XDR-TB
- To draw a roadmap for regional contribution to achievement of the global targets of ending TB
- To serve as a reference document and tool of communication for regional priorities in addressing the challenges related to MDR/XDR-TB in the Region
- To act as a guidance tool for Member States to prioritize PMDT activities and monitor progress.

## Vision and goal

The goal of this Regional Response Framework is to “End the TB epidemic in the SEA Region by 2035”, by adopting and adapting the vision, milestones and targets as outlined in resolution WHA 67.1, and in alignment with the WHO End TB Strategy.

**Table 3: The Regional Strategy to End TB – three high-level regional indicators and associated targets and milestones**

Indicators	Milestones		Targets	
	2020	2025	SDG 2030	End TB 2035
Percentage reduction in the absolute number of TB deaths (compared with the 2015 baseline, estimated at 780 000)	35%	75%	90%	95%
Percentage reduction in the TB incidence rate (compared with the 2015 baseline, estimated at about 246 cases per 100 000 population)	20%	50%	80%	95%
Percentage of TB patients and their households experiencing catastrophic costs due to TB (level in 2015 unknown)	0%	0%	0%	0%

<sup>1</sup>The SDGs provide a new development framework for 2016–2030, replacing the 2000–2015 Millennium Development Goals (MDGs) framework. For further details, see <https://sustainabledevelopment.un.org/topics/sustainabledevelopmentgoals>.



## Objectives

### The objectives of DR-TB response are:

- To strengthen diagnostic and case-finding capacity toward a policy of universal DST;
- To ensure equitable, patient-centred access to quality-assured anti-TB treatment for all patients with DR-TB using evidence-based regimens and following global treatment guidelines;
- To partner with communities and various stakeholders to establish a comprehensive response to DR-TB, and protect vulnerable and marginalized groups;
- To promote research for continuous improvement in implementing strategies and outreach.

The strategic directions, areas of intervention, and activities to reach the overall goal, vision, objectives and targets to end TB are grouped into the following three strategic directions:

- (1) Integrated patient-centred care and prevention
- (2) Bold policies and supportive systems
- (3) Intensified research and innovation.

Implementation of strategies and interventions under these three strategic directions requires combined efforts and close coordination among the NTP and partners.

## Strategic direction 1: Integrated patient-centred care and prevention

### Strategy 1.1: Early diagnosis of TB, including universal DST for all people with TB

#### Strengthen laboratory capacity in Member States for quality-assured diagnosis

There is an urgent need in the Region for expansion of the network of diagnostic laboratories for TB, including scale up of the use of molecular diagnostic tools for diagnosis of TB and RR-TB as well as second-line LPA (SL-LPA), accessible to patients in the public and private sectors, as well as expansion of the network of culture and phenotypic (second-line) DST diagnostic laboratories for TB with adequate biosafety standards. The network shall strive for universal access to rapid diagnostic tools for the prompt diagnosis of drug resistance among all TB patients.

Individual country development plans shall include internationally recognized standard operating procedures (SOPs), biosafety policies and practices, quality assurance processes, and allocation of sufficient human resources. These priorities shall be incorporated into a national strategic plan, in alignment with country's PMDT expansion plans. Optimal quality of sputum-smear microscopy shall be maintained through internal quality control (IQC) and external quality assessment (EQA) systems.

Rapid diagnostic tools, such as GeneXpert MTB/Rif, and LPA for first- and second-line DST (FL- and SL-LPA), shall be implemented as close to the patient as possible. These rapid diagnostic tools will help to increase the number of patients with confirmed TB, specifically for DR-TB, as well as significantly reduce delays in treatment initiation.

### **Strengthen screening for drug resistance and promoting universal DST**

All health providers, both public and private, should be aware of the risk factors for drug resistance, appropriately screen patients, and eventually refer them for further diagnostic services. Early diagnosis of TB should include the universal availability of FL- and SL-DST. DST should be done for all persons with bacteriologically confirmed TB. In addition, all contacts of DR-TB cases, especially paediatric and immunocompromised persons (i.e. HIV-infected, malnourished and elderly persons, those with diabetes, those using an immunosuppressive agent [antirheumatics, cytostatics, glucocorticoids, opioids]) should be screened for DR-TB using rapid diagnostics. Timely screening and testing can reduce transmission in the community (i.e. primary resistance) and improve the ability to use appropriate, effective regimens, further reducing the chance of acquired resistance.

The above activities need to be complemented by improving awareness and knowledge about DR-TB in the community. All grass-roots workers and health cadres in the community could help in increasing referrals for screening for DR-TB by enhanced awareness about the risk factors. They might also extend their capacity to identify people at high risk for DR-TB and guide them to seek proper diagnosis and treatment in time. In this era of information and communication technologies, the media and communication tools need to be leveraged innovatively to improve awareness and knowledge among the community as well as among health-care providers.

## **Strategy 1.2: Ensure equitable access to quality treatment for people with TB, including those with TB resistant to first-line anti-TB medicines, and provide patient support**

### **Ensure that all patients diagnosed with drug resistance are immediately initiated on appropriate, effective second-line treatment**

Two major programmatic issues that need to be addressed include early initiation of treatment of all patients diagnosed with DR-TB by offering counselling and psychosocial support, and providing appropriate, effective treatment for the right duration while ensuring uninterrupted availability of the needed quality-assured drugs. Many countries witness a high rate of initial loss to follow up (i.e. patients not being initiated on treatment after diagnosis). The long treatment and its side-effects deter patient adherence. Introduction of newer drugs such as bedaquiline and delamanid, as well as shorter regimens for DR-TB, are expected to improve the quality of care, reduce the need for more toxic drugs (e.g. ototoxicity from injections) and improve long-term treatment outcomes of DR-TB patients.

While treating MDR-TB patients, we should not forget children. Primary transmission of DR-TB to children is often observed. Unfortunately, evidence-based trials for paediatric DR-TB regimens have not been conducted. However, the latest WHO DR-TB recommendation suggests that shorter SL regimens might benefit paediatric patients with bacteriologically confirmed results, and they should be afforded the same consideration as adult patients. Future randomized controlled trials and implementation research within programmatic settings are urgently needed to examine the effectiveness of these recommendations.

WHO also has recently released an interim policy on the use of delamanid<sup>2</sup> for children and adolescents to improve the outcomes of DR-TB treatment, particularly those with confirmed resistance or intolerance to either fluoroquinolones or second-line injectable agents. National TB programmes should systematically address the challenges of managing children with TB and DR-TB by formulating child-friendly policies, integrated with maternal and child health services for holistic care.

### **Ensure patient-centred mechanisms and systems for support to all patients in need**

Patient-centred care means providing care that is respectful of and responsive to individual patient preferences, needs, cultural traditions, family situations, social circumstances and lifestyles, and ensuring that patient values guide all clinical decisions. The programme needs to ensure patient-centred mechanisms and systems for social and psychological support to patients in need to ensure effective adherence to ambulatory treatment, as well as follow up after treatment.

Supportive treatment is essential, particularly in the case of DR-TB treatment, where the treatment duration, sophisticated regimen, adverse reactions and psychosocial factors could exhaust the patient's adherence abilities. Support must also help to identify and address factors that may lead to treatment interruption.

Pretreatment counselling should be a part of MDR-TB treatment to help patients understand and prepare for their treatment. Ministries need to develop or modify legislation to minimize patients' financial losses due to the lengthy treatment. They should also provide leave of absence to MDR-TB patients for as long as needed, and facilitate patients' return to jobs or to their education.

Follow up after treatment can and should be taken beyond health facilities to the community level. Current innovations such as e-/m-health have been proven to be effective in supporting treatment adherence and harnessing the strength of family and community. Patient-centred psychosocioeconomic support should be available to all patients, regardless of whether they are treated in the public or the private sector.

### **Establish palliative care for patients with limited treatment options**

Palliative care should be available for patients who have exhausted treatment alternatives. Such support at the end of a patient's life requires a multidisciplinary approach, including sustainable community-based systems, which can be provided even in the patient's home.

National TB programmes, along with other units in the health ministry or NGOs working in palliative care, can facilitate access to services for DR-TB patients. Policies should be updated to ensure that palliative and end-of-life care is in place, along with treatment and expert consultation.

## **Strategy 1.3: Scale up TB–HIV collaborative activities and ensure management of comorbidities**

Considerable implementation of collaborative TB–HIV activities has taken place in most countries of the Region; however, the coverage remains suboptimal. There were 227 000 new TB–HIV coinfections estimated in the Region during 2015. In the same period, 52% of notified TB patients knew their HIV status. Four countries in the Region – India, Indonesia, Myanmar and Thailand – accounted for 98% of the TB–HIV burden in the Region. Member States have to ensure universal HIV counselling and testing for all TB patients, as well the availability of preventive therapy (such as co-trimoxazole preventive therapy [CPT] and isoniazid [INH]) and antiretroviral therapy (ART) among those who are eligible. While most of the collaborative activities have been elaborated in the Regional Strategic Plan

<sup>2</sup>The use of delamanid in the treatment of multidrug-resistant tuberculosis in children and adolescents. Interim policy guidance. Geneva: WHO; 2016 [WHO/HTM/TB/2016.14] ([http://www.who.int/tb/publications/Delamanid\\_interim\\_policy/en/](http://www.who.int/tb/publications/Delamanid_interim_policy/en/), accessed 5 July 2017).

as well as the TB–HIV Response Framework and are applicable to DR-TB patients, some of the key interventions to focus on for PMDT are given below:

### **Ensure access to HIV testing for all DR-TB patients**

Deployment of sensitive and rapid diagnostic tools such as Xpert MTB/Rif at the initial point of care can reduce delay in diagnosis of DR-TB with HIV coinfection, especially in high-burden countries where TB–HIV coinfection is common. A newer approach using urine-based testing with lateral flow urine lipoarabinomannan assay (LF-LAM) has been shown to assist in the screening and diagnosis of active TB in persons with HIV infection with low CD4 counts or those who are seriously ill.

Decentralization of HIV testing services to peripheral health facilities and strengthening provider-initiated testing as well as self-testing are essential to ensure scale up of HIV service coverage among patients with presumptive TB and DR-TB.

### **Scale up screening for DR-TB among people living with HIV, according to international guidelines**

All clients attending HIV testing and service centres should be screened for DR-TB as part of intensified case-finding activities and because of the high risks of morbidity and mortality among undiagnosed cases.

### **Ensure integrated management at primary health-care level of TB comorbidities and noncommunicable diseases of documented risk such as diabetes**

Health conditions and noncommunicable diseases (NCDs) such as diabetes mellitus, drug and alcohol abuse, undernutrition and a range of immune-compromising disorders are risk factors for TB. These comorbidities could affect the response to and outcome of TB treatment.

A national collaborative framework between NCD and communicable disease programmes, including TB, can help to integrate the management of these comorbidities. For example, some countries in the Region have a policy on screening TB patients for diabetes and tobacco smoking.

## **Strategic direction 2: Bold policies and supportive systems**

### **Strategy 2.1: Ensure political commitment with adequate resources and effective management for ending TB and DR-TB**

#### **Adopt the latest available evidence and guidelines on DR-TB management and secure funds for its implementation**

Health systems strengthening and financing needs for the purpose should be planned to secure sufficient funds for health as part of the transition to universal health coverage. This includes funds for the diagnosis and management of DR-TB, and for protecting service users facing or likely to face financial hardship during and after the treatment course.

Some Member States with external funds for specific health programmes are encouraged to include a social security system that reduces patients' out-of-pocket expenditures, or ensure linking of affected people to available social welfare schemes.

## Strategy 2.2: Contribute to strengthening the health system

### Strengthen human resource development through strategic planning and health systems

Effective measures for ending TB means scaling up efforts at ending DR-TB as well, which depends on ongoing hiring, training, deployment and management of health workers.

Inadequate human resources in terms of numbers or capacity to perform needed tasks means an inadequate response of health systems in providing high-quality diagnostic and treatment services for DR-TB, or only small fraction of MDR/XDR-TB cases diagnosed compared with the actual estimated number.

Considering that scaling up DR-TB services requires a more sophisticated approach, Member States need to develop strategic plans for human resource development (HRD) in collaboration and coordination with departments in ministries of health responsible for the Human Resources for Health (HRH) Action Framework. This Framework is designed to assist countries in developing and implementing strategies to achieve an effective and sustainable health workforce.<sup>3</sup> Importantly, this scale up should also include the health services of penitentiary institutions.

### Implement comprehensive infection control measures in health-care facilities<sup>4</sup>

It is important to minimize the risk of transmission of DR-TB within communities. TB infection control requires and complements implementation of core activities to end TB and HIV, and health systems strengthening. It should be part of national infection control policies, in particular, those that target airborne infections.

All health facilities caring for TB patients or people with presumptive TB (whether drug-sensitive or drug-resistant) should implement globally recommended infection control measures, which are based on local epidemiological, climatic and socioeconomic conditions.

### Strengthen the management of anti-TB medicines

Regulation of anti-TB medicines remains an issue, as in some countries anti-TB medicines are readily available over the counter (OTC), often without prescription. With regard to SLDs, fluoroquinolones and second-line injectables are key drugs but often available as OTC drugs. Often, these drugs are also prescribed for chest conditions without ruling out TB. Such a situation drives the high resistance of drugs and contributes to a higher incidence of MDR/XDR-TB. Such practices need to be streamlined and regulated to prevent the development of resistance to SLDs.

The quality of SLDs needs to be assured. Member States need to strengthen collaboration with national drug regulatory authorities in establishing quality control and monitoring systems, and enforcing adherence to common quality assurance standards for TB medicines. The Global Drug Facility (GDF), as an initiative of the Stop TB Partnership hosted in the United Nations Office for Project Services (UNOPS), acts as an operating mechanism to facilitate worldwide, equitable access to TB medicines and diagnostics for both the public and private sectors. The implementation of new drugs such as bedaquiline and delamanid, as well as recent recommendations on shorter treatment regimens for MDR-TB in Member States has been facilitated through a GDF procurement/bundled mechanism.

<sup>3</sup>The HRH Action Framework. In: World Health Organization: health workforce (website) (<https://www.capacityproject.org/framework/>, accessed 5 July 2017).

<sup>4</sup>WHO policy on TB infection control in health-care facilities, congregate settings and households. Geneva: World Health Organization; 2009 [WHO/HTM/TB/2009.419] ([http://apps.who.int/iris/bitstream/10665/44148/1/9789241598323\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44148/1/9789241598323_eng.pdf), accessed 5 July 2017).

## Active TB drug-safety monitoring and management

Active TB drug-safety monitoring and management (aDSM) applies to MDR/XDR-TB patients treated with new medicines, such as bedaquiline or delamanid, repurposed drugs like clofazimine, and MDR-TB patients enrolled in treatment with novel regimens. The safety profile and adverse drug reactions of FLDs and regimens have been well established. The need for aDSM is more for new and repurposed drugs and for shorter treatment regimens due to limited data on adverse events; limited experience in programmatic use, unclear safety in specific patient populations, as well as “off-label” inclusion of some MDR-TB medicines (linezolid, clofazimine).

The overall objectives of aDSM are to manage the risks from drug-related harm and generate standardized aDSM data to inform future policy updates.

As per the essential components of aDSM, patients should undergo active and systematic clinical and laboratory assessment during treatment to detect adverse events (AEs); all AEs detected should be managed in a timely manner, and standardized data should be systematically collected and reported.

Steps to implement aDSM include the following: (1) create a national coordinating mechanism for aDSM; (2) develop a plan for aDSM; (3) define management and supervision roles and responsibilities; (4) create standard data collection materials; (5) train staff to collect data; (6) define schedules and routes for data collection and reporting; (7) consolidate aDSM data electronically; and (8) develop (or use existing) capacity for causality assessment, determine rates and detect signals.

## Strengthen the DR-TB surveillance systems, including the new standards and benchmarks

Drug resistance surveillance data are collected for new (previously untreated) and previously treated TB cases separately, through special surveys or continuous surveillance. When monitoring DR-TB cases in TB programmes, the focus is on those infected with strains showing in vitro resistance to rifampicin (RR-TB). These strains could be mono-, poly-, multi- or extensively drug resistant.

## Strategy 2.3: Improve regulatory frameworks, including the universal health coverage policy

### Achieve universal health coverage and remove financial barriers to diagnosis and care of DR-TB

Universal health coverage and strong social support are basic requirements to ensure that every TB patient is free from the direct and indirect costs of TB. These activities are not the sole responsibility of NTPs. Ideally, collaboration with actors in the health system, e.g. ministries for social protection, NGOs, the private sector and community, should be established. Universal health coverage could be achieved through adequate, fair and sustainable prepayment financing of health care with full geographical coverage, combined with effective service quality assurance, and monitoring and evaluation.<sup>5</sup>

For socially marginalized populations, e.g. those who live in urban slums, mountainous areas, isolated islands or other hard-to-reach areas, even the basic health-care infrastructure for diagnosis and treatment of DR-TB might not be available. Interventions such as mobile diagnostic services or outreach activities clubbed with other health programmes can be organized. On a higher level, policies to address the challenges among marginalized groups such as cross-border migrants, equitable

<sup>5</sup>World Health Report 2010: health systems financing – the path to universal coverage. Geneva: World Health Organization: 2010 (<http://www.who.int/whr/2010/en/>, accessed 5 July 2017).

access to treatment among different genders and various age groups, improvement of infrastructure or transportation need to be instituted by strong leadership from the health sector and related stakeholders in the government.

## **Strategy 2.4: Engage communities, civil society organizations, and all public and private care providers**

### **Actively engage and strengthen the role of communities and civil society organizations in TB activities, including the use of the current e-/m-Health technologies**

The role of civil society organizations (CSOs) becomes critical in establishing, consolidating and scaling up community linkage with essential services, especially in underserved and marginalized population groups, and in difficult-to-reach areas across the country. Countries should explore all possible opportunities to engage CSOs, non-formal and private health-care providers to promote comprehensive coverage and ensure effective TB prevention, early diagnosis and prompt treatment that would prevent drug resistance.

DR-TB patients specifically find it hard to access health facilities for reasons that are often social (stigma, discrimination), economic (transport and other costs) or political (cross-border services, particularly for migrants). To reach the unreached, it is necessary to engage CSOs, specifically CBOs, in integrated, community-based TB services. Some of these organizations work in remote areas with poor and marginalized people, especially women and children. Integrating TB activities such as community-based screening, contact tracing, referrals, treatment adherence support, social and livelihood support and stigma reduction into the work of community health workers and volunteers will help in reaching the unreached.

### **Develop innovative models of public–private and public–public mix approaches for PMDT and allocate resources in the national strategic plans**

Countries have generally experienced the greatest difficulties in engaging unorganized and unregulated private practitioners, qualified and non-qualified, who are often the first points of contact of people seeking care for symptoms of TB. There is considerable scope for engagement of private providers in the management of DR-TB.

Given the size and complexity of the problem, the attention, investments and inputs on the part of national TB programmes in the Region to scaling up even working public–private mix (PPM) models have been largely inadequate. In many countries, public and private hospitals that attract a large number of people with TB do not contribute optimally to the detection and treatment of TB; a large proportion of voluntary health organizations and private providers do not yet collaborate with NTPs and continue to provide uneven care; workplace TB programmes are few and far between; large quantities of TB medicines of questionable quality are sold in private retail pharmacies and investments in scaling up PPM rarely match the actual needs.

Global support in the Region has also led to the development of some innovative models of engaging private providers. Some of these, such as social franchising, have been in place for several years; a newer market-sensitive, social enterprise model has also produced impressive results in some settings. In countries with a large private sector such as India, Indonesia and Myanmar, almost every fifth to every fourth case is notified by private and non-NTP public providers linked through diverse approaches. Some recently established innovative PPM projects in India have shown impressive results; these have used call centres and digital tools to facilitate case notification and treatment adherence among patients in private clinics.



The policies that need to be in place for engagement of all care providers will vary according to the country context. It is also essential to strengthen collaboration with regulatory authorities to enact and/or strictly enforce regulations related to mandatory TB case notification and rational use of TB medicines available in private pharmacies.

The public health strategies to curb DR-TB should be uniform and comprehensive to include those in congregate settings, as these communities usually have higher TB transmission rates. Collaborative TB programmes, including PMDT in prisons, barracks, camps, hostels and other similar congregate settings need to be established and implemented.

## **Strategy 2.5: Address social protection, poverty alleviation and actions on other determinants of tuberculosis**

### **Develop and implement specific mechanisms for social protection of DR-TB-affected patients and their households**

One of the key targets of the End TB Strategy is “No affected families face catastrophic costs due to TB.” Research has shown that despite diagnosis and treatment being provided for free, most individuals have to face high out-of-pocket expenditure on transport, additional medication, nutrition supplementation, etc.

TB has been known as a “disease among the poor”. In the case of DR-TB, the lengthy treatment might further exacerbate the poor financial condition among lower socioeconomic groups.

Social protection could alleviate the burden of income loss and non-medical costs of seeking and staying in care. Policies could include the element of social protection, as suggested in the examples below:

- Schemes for compensating the financial burden associated with illness: cash transfer, food vouchers or packages, social welfare payments, disability pension, sickness insurance;
- Legislation and regulation to protect people with TB from discrimination, such as expulsion from workplaces, health or educational institutions, transport system or housing;
- Instruments to protect and promote human rights, including among vulnerable and different ethnic groups, and genders.

Undernutrition is both an important risk factor for and a consequence of TB, particularly among those with severe drug resistance. It is a common comorbidity among people with active TB and is associated with an increased risk of mortality and poorer treatment outcomes. All individuals with active TB should have their nutritional status assessed and additional support for nutritional care should be provided along with the core treatment.



## Strategic direction 3: Intensified research and innovation

### Strategy 3.1: Implement research to optimize implementation and impact, and promote innovation

#### **Establish centres of excellence for PMDT nationally and regionally to facilitate knowledge exchange, initiate an operational research plan, document evidence/best practices in DR-TB**

Centres of excellence (CoE) or technical assistance centres (TACs) for PMDT will provide ongoing technical support, specifically in high-burden and high-impact countries. Broadly, COEs/TACs could undertake the following activities:

1. Provide technical assistance to the NTP and other implementing agencies within the country to develop comprehensive plans for rapid scale up of PMDT and for implementation of these plans. This would include assistance with development of the national strategic plan (NSP) for ending TB, specifically the PMDT component of the NSP.
2. Train in-country staff using a training-of-trainers methodology to improve the human resource base for the expansion of MDR-TB treatment and management. Provide intensive training to programme managers, physicians, nurses and health workers.
3. Support the NTP in translating and adopting international guidelines and policy documents as and when required.
4. Support the NTP in monitoring PMDT expansion and provide critical inputs for overcoming challenges, including scale up, by involving other relevant health-care sectors.
5. Liaise with the WHO Country Office, technical partners supporting the NTP in the country, CoEs in other countries, and the respective regional Green Light Committee (rGLC) in information exchange and international technical assistance as and when required. The COEs will also support the NTP in organizing annual PMDT monitoring missions.
6. Support and conduct need-based operational research for PMDT expansion.

However, the CoEs/TACs are not expected to duplicate or substitute the work that is already being done by other agencies. While drawing up country-specific terms of reference, care should be taken to ensure the complementary role of CoEs/TACs.

#### **Invest and assist in capacity-building for research training according to the priority areas of Member States and develop an operational research plan to translate the research into action**

Research-enabling environments in which the TB burden is the greatest are urgently required, such as in low- and middle-income countries. It is expected that high TB burden countries in the SEA Region will progressively establish their leadership in TB research by strengthening their own research capacity, whether through domestic funding or external collaboration. This strengthened capacity will contribute to global research efforts to eliminate TB, as well to achieve the End TB Strategy's goals.

Any innovation or new tool or strategy to combat TB must be relevant to the epidemiological situation and health system, and stimulate operational research to ensure its implementation on a wider scale.

The Global Action Framework for TB research has set that by 2020, countries with a high TB burden will have:

- Established a national TB research network;
- Integrated TB research within the NSP;
- Developed a list of national TB research priorities;
- Initiated in-country research training.

To substantially expand TB-related research, each country should develop a comprehensive national TB research plan that is integrated with the NSP to promote and catalyse TB research in the country. The plan should identify research priorities to achieve the 2030/2035 End TB Strategy targets, in alignment with the country's TB burden, research capacity, political and financial resources.

Establishing or strengthening an existing national TB research network is a crucial step towards a national TB research plan. This network should be seen as a partnership between the public and nongovernment sectors and communities, where medical associations or health professionals and researchers from government counterparts (particularly the NTP) collaborate closely with researchers and experts from various disciplines or even other ministries, e.g. Education, Science and Technology.

An effective network also considers the participation of research beneficiaries or end users, in which community and civil society representatives should be actively involved, particularly on the introduction/implementation of new tools to improve their uptake. The network should be as inclusive and multidisciplinary as possible, and address cross-cutting research questions related to TB such as financial (cost analysis study), social determinants of DR-TB treatment (barriers and supportive factors to treatment adherence), etc.

At the regional and national levels, the establishment of CoEs as pioneers or examples for other institutions has been endorsed. These CoEs could accelerate the uptake of new drugs or shorter regimens for MDR-TB (as recommended by WHO), expand laboratory capacity for PMDT to ensure rapid patient triage, provide training, evaluation and data analysis from ongoing surveillance for programme planning, etc.

### **Regional exchange of expertise and learning**

Across the Region, countries have been developing different solutions for the problems they face. While the context of the problem is specific to each country, there are several learning experiences that can serve as solutions to the problem, including the process followed to solve the problem.

Regional meetings provide an opportunity to share experiences and lessons learnt with peers.

## **The regional Green Light Committee (rGLC) mechanism**


The rGLC was established in 2012 with its secretariat housed in the WHO Regional Office under a memorandum of understanding (MoU) with the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) to provide decentralized support to countries for expansion of DR-TB-related services. The rGLC acts as an advisory body performing in accordance with the MoU between the Global Fund and WHO. Its main objective is to provide decentralized monitoring and guidance on new policies and strategies for PMDT interventions in countries of the Region for rapid scale up of DR-TB services. The rGLC in the SEA Region is supporting the implementation of the DR-TB response in Member States, ensuring that country PMDT plans reflect programmatic recommendations on the response to DR-TB, including recording and reporting of the standard indicators selected for the SEA Region.

The rGLC through its secretariat coordinates monitoring missions to countries to assess the progress in implementing services, and undertakes peer review of the monitoring missions' reports. As a follow up to these monitoring missions, the rGLC supports the organization of high-quality technical assistance and resource mobilization for countries in accordance with the PMDT expansion plan.

A total of nine meetings have been held so far. Key recommendations for Member States from the most recent meeting are as follows:

- Quick roll-out of rapid molecular diagnostics for TB and first-line DST for universal access to DST
- Assess the need for SL-LPA and DST, and plan for their introduction/roll-out based on country needs
- Organize consultative meetings along with all relevant stakeholders for discussing a transition to shorter regimen and prepare a transition plan
- Improve access to bedaquiline and delamanid in all countries
- Identify areas needing technical assistance, specifically where external technical assistance is required
- Ensure that aDSM mechanisms are in place, along with introduction of shorter regimen and new drugs





**Indicators framework  
for monitoring  
the DR-TB response  
in the SEA Region**

**(1) Integrated patient-centred care and prevention**

Strategies	Key interventions	Indicator	Baseline		Targets				
			2016	2017	2018	2019	2020	2021	
Early diagnosis of TB, including universal drug susceptibility testing (DST) for all people with TB	Strengthen laboratory capacity in Member States	Number of countries with SL-LPA/DST capacity for all notified rifampicin-resistant TB cases	0	2	4	6	8	10	
	Strengthen screening for drug resistance and promote universal DST	Number of countries where the national policy and diagnostic algorithm indicate universal access to DST	2	3	5	7	11	11	
Ensure equitable access to quality treatment of people with TB, including TB resistant to first-line anti-TB medicines, and provide patient support	Ensure that all patients diagnosed with drug resistance are initiated on appropriate second-line treatment immediately	Number of countries where risk groups are identified for drug-resistance screening	8	11	11	11	11	11	
		Number of countries with a policy of screening all paediatric contacts of DR-TB through rapid DST	2	3	5	7	11	11	
	Number of countries with a treatment success rate of at least 70% among RR/MDR-TB patients initiated on second-line treatment	5	(2013 cohort)	5	6	6	6	8	11
		Number of countries enrolling at least 80% of eligible patients on WHO-recommended shorter MDR-TB regimen	0	1	4	6	8	11	
		Number of countries starting >10% of eligible patients/year on regimens containing bedaquiline or delamanid	NA	2	4	6	8	11	
Establish palliative care for patients with limited treatment options	Number of countries with MDR/XDR-TB patients receiving palliative/end-of-life care	1	1	3	4	6	8		

**(2) Bold policies and supportive systems**

Strategies	Key interventions	Indicator	Baseline		Targets			
			2016	2017	2018	2019	2020	2021
Ensure political commitment with adequate resources and effective management for ending TB and DR-TB	Adopt the latest available evidence and guideline on DR-TB management and secure funds for its implementation	Number of countries that have adopted the most recent update of the WHO DR-TB treatment guidelines	0	6	8	10	11	11
		Number of countries where PMDT expansion plans are fully funded	0	2	4	8	11	11
Contribute to strengthening the health system	Strengthen human resource development through strategic planning and health systems	Number of countries with an HRD plan for PMDT expansion	2	2	6	8	11	11
		Number of countries satisfactorily implementing infection control policies (review mission reports)	0	2	4	6	8	11
Improved regulatory frameworks, including universal health coverage policy	Achieve universal health coverage and remove financial barriers to DR-TB diagnosis and care	Number of countries with a functional aDSM mechanism	No country has all elements in place	4	6	8	11	11
		Number of countries where >90% of diagnosed cases are initiated on treatment within the same year	7 (2015)	8	9	11	11	11
Coverage policy								
Engage communities, civil society organizations and all public and private care providers	Actively engage and strengthen the role of communities, civil society organizations in TB activities, including use of current technologies (e-/m-Health)	Countries with guidelines available for community engagement in service delivery and monitoring of MDR-TB services	3	4	6	8	11	11
		Countries using appropriate technology interventions (like mobile phones) to support treatment adherence	4	5	6	8	11	11

Strategies	Key interventions	Indicator	Baseline		Targets			
			2016	2017	2018	2019	2020	2021
	Develop innovative model of public-private and public-public mix approaches for PMDT and allocate resources in the national strategic plans	Countries with guidelines available for private sector engagement in service delivery and monitoring of MDR-TB services	4	4	6	8	11	11
Address social protection, poverty alleviation and actions on other determinants of tuberculosis	Develop and implement specific mechanisms for social protection of DR-TB-affected patients and their households	Countries with patient support policies for MDR-TB patients – during and after treatment (rehabilitation) incorporated in national guidelines	NA	4	6	8	11	11

### (3) Intensified research and innovation

Strategies	Key interventions	Indicator	Baseline		Targets			
			2016	2017	2018	2019	2020	2021
Undertake research to optimize implementation and impact, and promote innovation	Establish centres of excellence for PMDT nationally and regionally to facilitate knowledge exchange, initiate an operational research plan, document evidence/best practices in managing DR-TB in the Region  Invest and assist in capacity-building for research training according to the priority areas of Member States and develop an operational research plan to translate the research into action	Number of TB high-burden countries with centres of excellence for PMDT  Number of countries with identified research priorities in MDR-TB  Number of countries undertaking research and using the results for policy decisions	0	2	3	4	5	6
			2	4	6	8	10	11
			2	4	6	8	10	11

aDSM: active drug safety monitoring and management; DST: drug susceptibility testing; HRD: human resource development; MDR: multidrug resistant; PMDT: programmatic management of drug-resistant tuberculosis; RR: rifampicin resistant; SL-LPA: second-line line probe assay; XDR: extensively drug resistant



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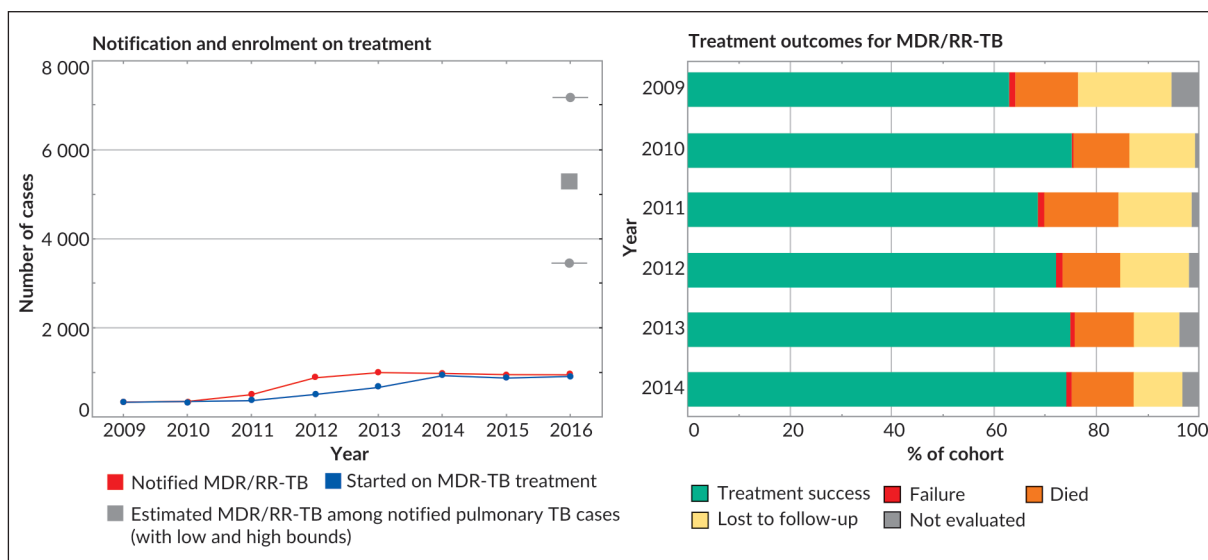
**Annexure 1:  
Progress in  
Member States**

# Bangladesh

## Key challenges in expansion of DR-TB services

- Detection of MDR-TB cases remains low (16% in 2015) due to improper history-taking and slow expansion of GeneXpert.
- A mechanism for transportation of samples is still not established in most districts.
- The number of treatment initiation centres is limited for the intensive phase with functional ECG and audiometry, and other baseline investigations. This shortage is compounded by the national policy requiring treatment in a treatment initiation centre until two consecutive sputum specimens are culture negative, although capacity is insufficient.
- The number of skilled human resources at several MDR-TB treatment sites is insufficient.
- Transition from a 20-month regimen to the shorter 9–12 month regimen on a countrywide basis is taking time.
- Introduction of the new drugs bedaquiline and delamanid has been slow.
- Pharmacovigilance is generally not conducted properly, and the linkage between the national programme and national pharmacovigilance centre is weak.
- Infection control measures are often not fully implemented (e.g. there is a general lack of triage in outpatient waiting areas).

Fig. 4: Bangladesh – DR-TB programme performance, 2009–2016



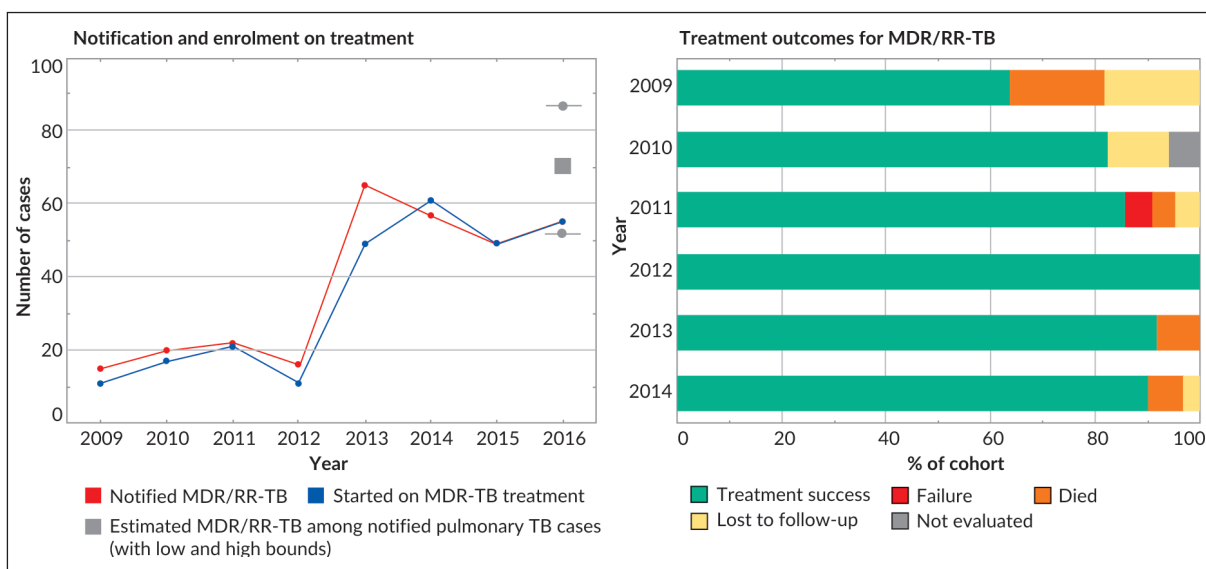
Source: <http://www.who.int/tb/data>

# Bhutan

## Key challenges in expansion of DR-TB services

- There is limited access to WHO-recommended rapid diagnostic tools (e.g. GeneXpert, line probe assays [LPAs]).
- There is a lack of drug susceptibility testing (DST) for SLDs in the country.
- Diagnosis and management of MDR-TB patients is restricted to the capital city.
- Infection control practices are weak.
- Implementation of directly observed treatment, short-course (DOTS) is weak.
- The local epidemiology of DR-TB is not well understood.

Fig. 5: Bhutan – DR-TB programme performance, 2009–2016



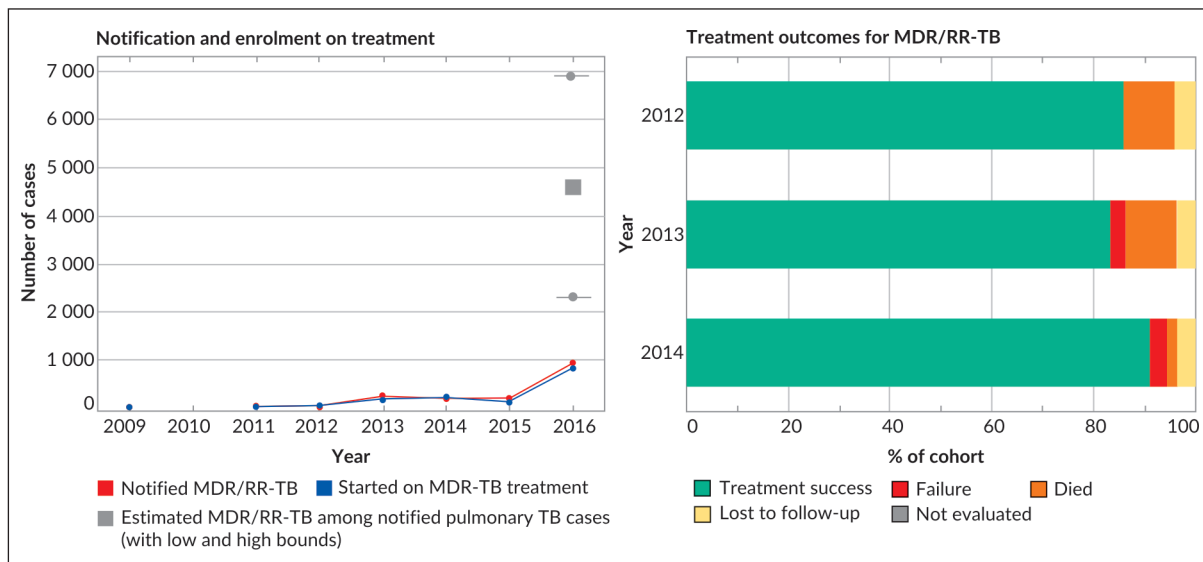
Source: <http://www.who.int/tb/data>

# Democratic People's Republic of Korea

## Key challenges in expansion of DR-TB services

- National coverage of programmatic management of DR-TB (PMDT) services is yet to be fully established (in 7 out of 12 provinces).
- Long delays are observed in diagnosis and treatment initiation due to systemic procurement and supply chain management (PSM) issues.
- PMDT services are completely centralized contributing to delays in diagnosis, treatment initiation and patient inconvenience.
- The local epidemiology of DR-TB is not well understood.
- National estimates of DR-TB prevalence remain unknown, limited to one small survey (~400 isolates from one province).
- National treatment guidelines for both TB and PMDT are not aligned with WHO recommendations.
- Laboratory capacity is limited by the number of laboratories available to undertake the requisite tests and constrains PMDT service expansion.
- Sample collection and transport is done by the Central TB Preventive Institute team during their scheduled monthly visit, which sometimes delays the diagnosis.
- Opportunities to strengthen health systems with PMDT service expansion are missed.

**Fig. 6: DPR Korea – DR-TB programme performance, 2009–2016**



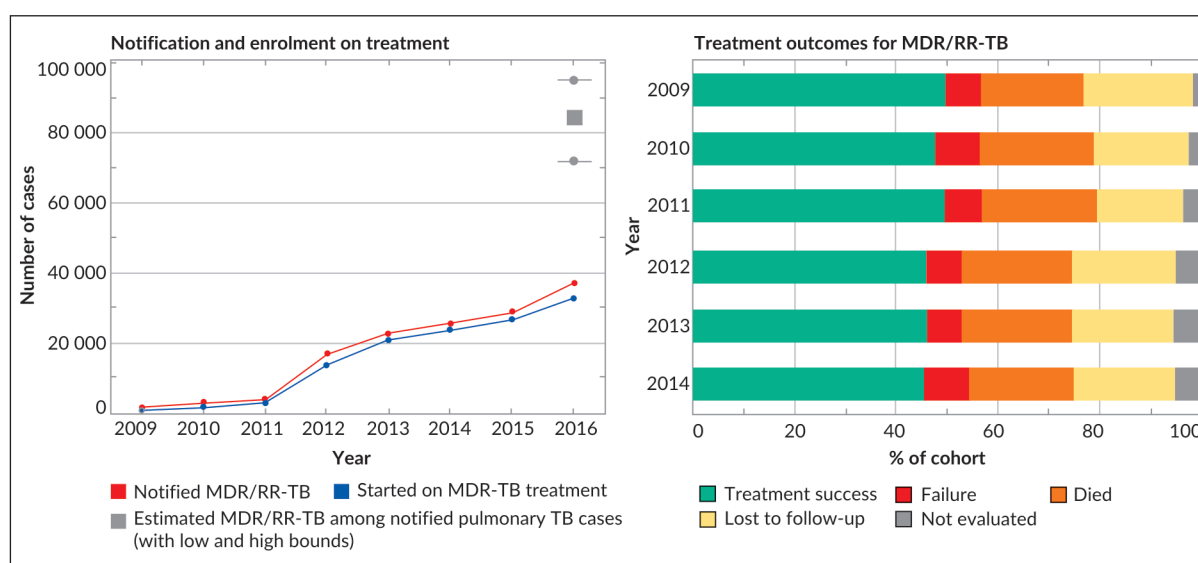
Source: <http://www.who.int/tb/data>

# India

## Key challenges in expansion of DR-TB services

- The enormous population (second most populous country in the world), diversity between states, and even districts, in terms of the population, terrain, level of development, health systems and TB epidemiology pose problems for a uniform centralized approach to ending TB.
- An estimated 170 million people (12%) live in poverty.
- There is considerable variation in DR-TB epidemiology across the country that is not well understood.
- Small, local studies have reported high levels of isoniazid monoresistance among new (11%) and previously treated cases (30%), and an alarming proportion (30%) of MDR-TB cases had baseline fluoroquinolone resistance.
- A substantial proportion of those affected obtain antituberculosis treatment in the largely unregulated private sector.
- Irrational prescription practices for TB and DR-TB continue in the private sector.
- Testing for rifampicin resistance remains suboptimal; approximately 6% of new and 60% of previously treated reported TB cases were tested in 2015.
- Access to rapid molecular diagnostic testing is stymied by a weak national sample transport system, resulting in a long time to treatment initiation in some districts.
- Implementation of airborne infection control measures is limited at all levels of the health service.
- Medical colleges with attached hospitals cater to a large number of TB patients. However, their engagement is suboptimal; not all medical colleges have a DR-TB centre and laboratory.
- Enablers and incentives for patients, families and health-care workers are few, and there was limited awareness of, and linkages to, social support systems for patients and families.

**Fig. 7: India – DR-TB programme performance, 2009–2016**



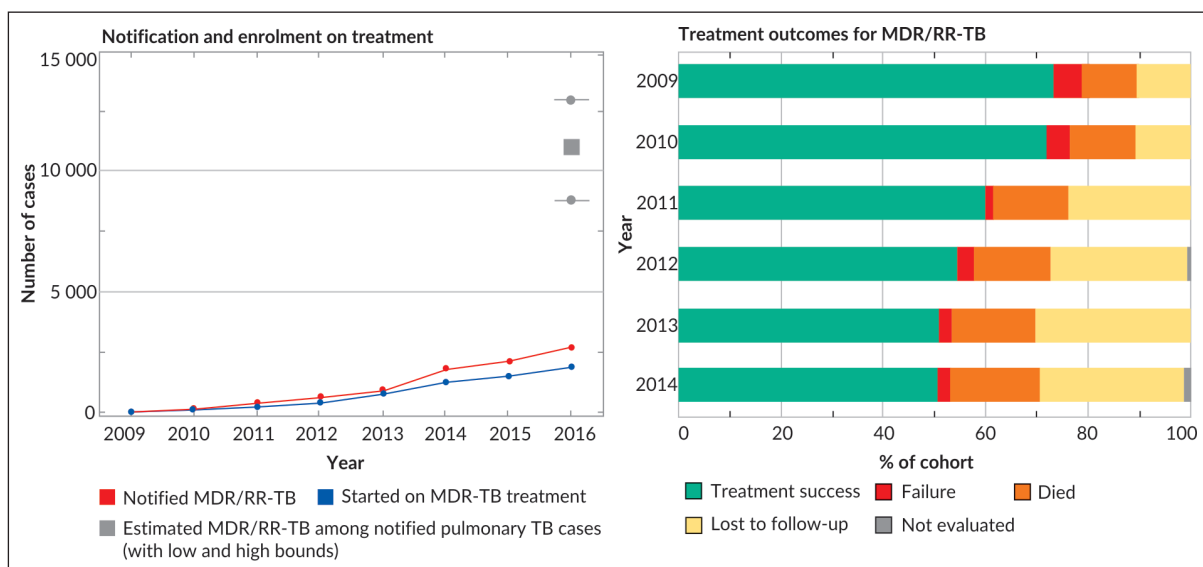
Source: <http://www.who.int/tb/data>

# Indonesia

## Key challenges in expansion of DR-TB services

- The world's largest island country with more than 17 000 islands covering a vast geographical area, including several remote and secluded islands with substantial variations in population, terrain, level of development, health systems and TB epidemiology pose problems for a uniform centralized approach to ending TB.
- Weak basic DOTS in hospitals and a large disconnected private sector are possibly leading to the emergence of drug resistance.
- Overall TB case notification is low (32%); even lower proportions are tested and diagnosed for drug resistance.
- District- and provincial-level leadership and support for the national TB programme is weak.
- Access to rapid molecular diagnostic testing is stymied by a weak national sample transport system, resulting in a long time to treatment initiation in most areas.
- PMDT expansion and decentralization of services is slow.
- Screening for DR-TB focus primarily on previously treated cases, and a very limited number is tested among new pulmonary TB.
- High loss to follow up: initially diagnosed patients not initiated on treatment are around 25% and lost to follow up and during treatment comprise 28%.
- Patient support systems are weak and delayed.
- Follow-up biochemistry tests are variable and adverse effects are not always monitored or treated efficiently.
- Infection control seems to be linked only to treatment of DR-TB cases in most hospitals. It was also noted that infection control measures are often not well planned and are resource intensive.

**Fig. 8: Indonesia – DR-TB programme performance, 2009–2016**



Source: <http://www.who.int/tb/data>

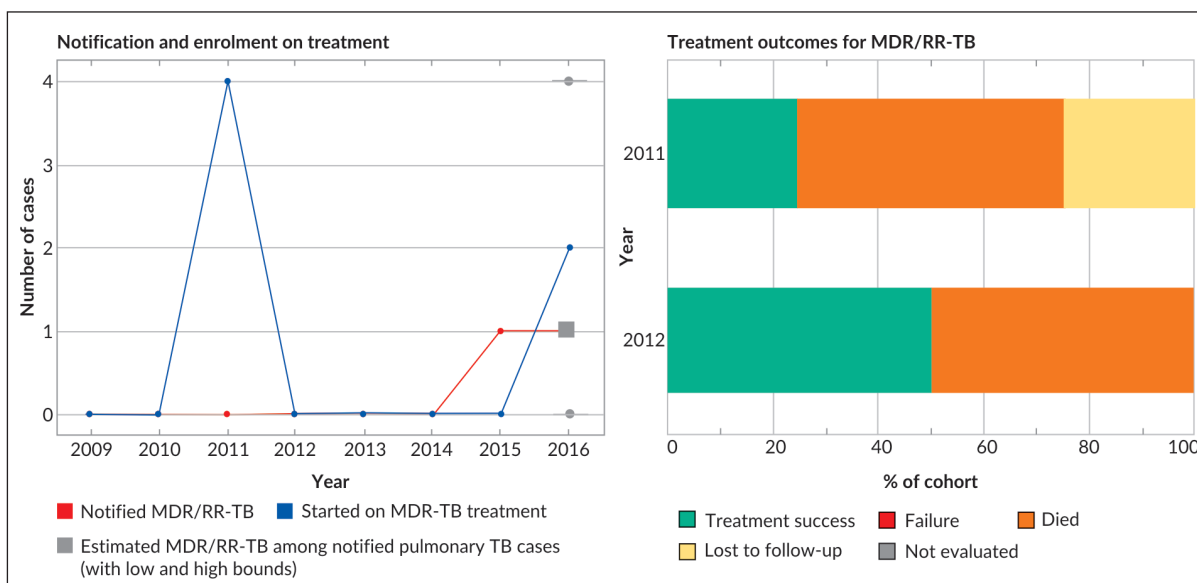


# Maldives

## Key challenges in expansion of DR-TB services

- Central-level capacity to manage, monitor and supervise the programme is weak.
- Diagnosis of DR- and XDR-TB takes a long time because of weak in-country capacity for diagnosis.
- There is no specific DR-TB treatment facility.
- There is social stigma attached to the disease.

Fig. 9: Maldives - DR-TB programme performance, 2009-2016



Source: <http://www.who.int/tb/data>

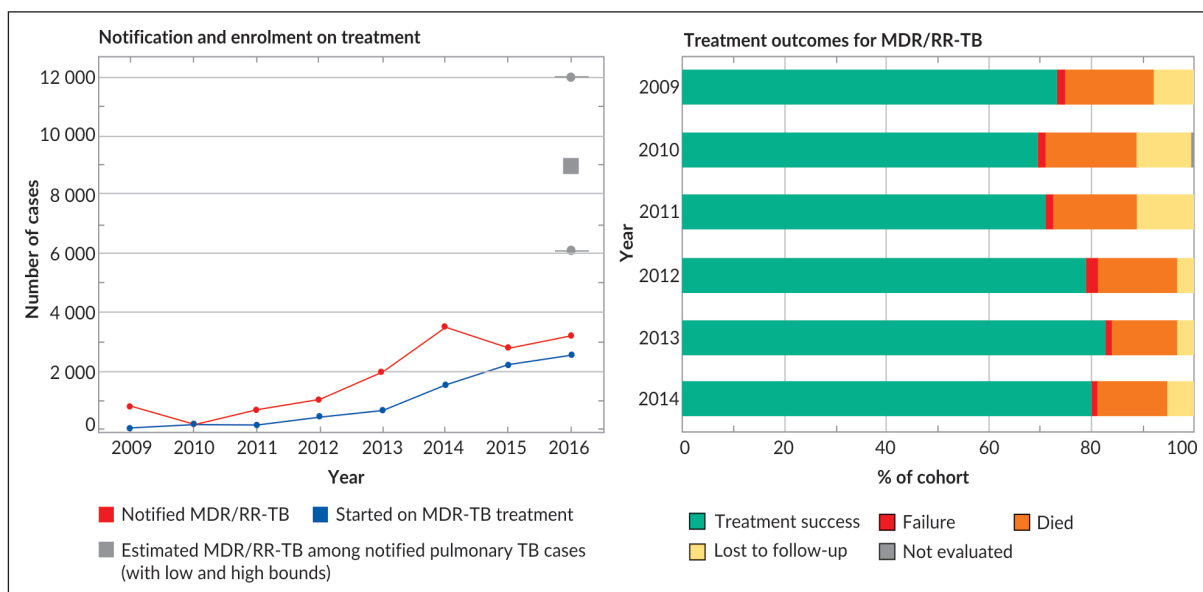
The peak seen because of 4 cases appears prominent because of lower number of cases in the country. This number is contributed by cases diagnosed outside the country but initiated on treatment within the country.

# Myanmar

## Key challenges in expansion of DR-TB services

- The enrolment of MDR-TB patients remains slow and the gap between those diagnosed and enrolled in treatment is still high (21%), though it has reduced.
- Diagnostic capacity for Xpert MTB/RIF remains largely underutilized.
- The proportion of MDR-TB patients tested for SLD resistance remains extremely low.
- Human resources remain a challenge with inadequate key staff (e.g. laboratory technicians, microbiologists, doctors, team leaders, etc.) at the national, state, district and township levels.
- Community volunteers are being used as DOT providers, but this remains limited.
- Infection control measures are not uniformly applied across all health facilities.
- The information system remains paper- and manually based. Piloting of the open medical records system (MRS) has been delayed.
- Despite the increasing contribution from the government, the National TB Control Programme (NTP) still relies heavily on external donors, especially the Global Fund to Fights AIDS, Tuberculosis and Malaria (Global Fund).

**Fig. 10: Myanmar – DR-TB programme performance, 2009–2016**



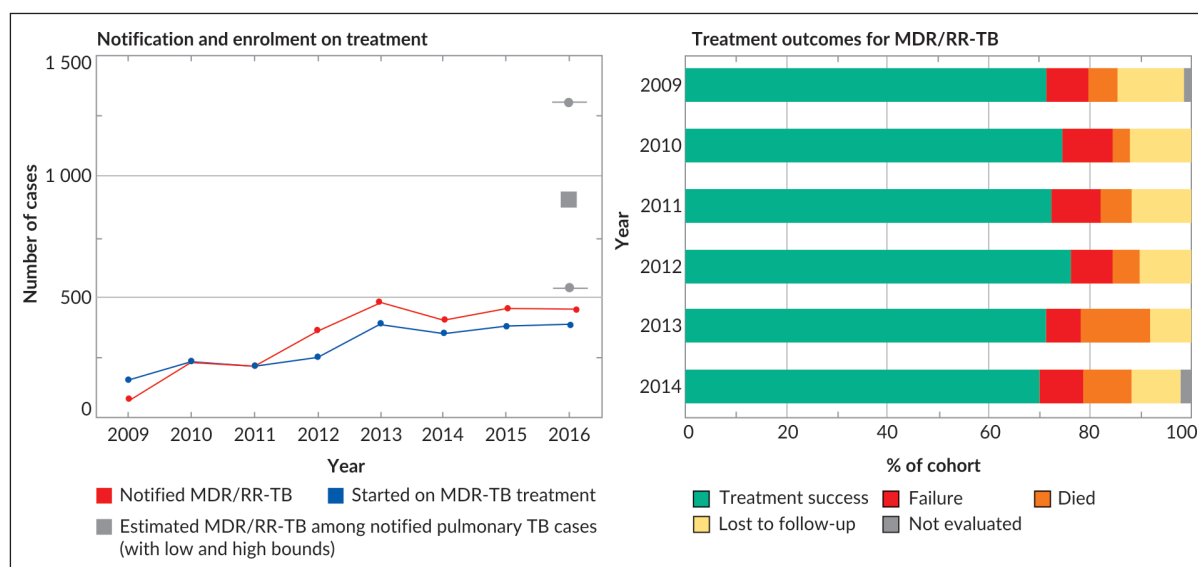
Source: <http://www.who.int/tb/data>

# Nepal

## Key challenges in expansion of DR-TB services

- The true gap between estimated cases and cases being reported to the NTP is not known.
- Regulations and mechanisms to involve the private sector in PMDT are lacking.
- Resistance to fluoroquinolones is high among pre-XDR and XDR-TB cases in the country, as recorded in the German–Nepal TB Project (GENETUP) centre.
- The role of the community and civil society in the PMDT/TB programme is not fully recognized.
- There is a need for capacity-building for DR-TB management at the national and regional levels.
- Poor incentives are given to health staff in the field for the management DR-TB patients.
- There are human resource constraints and old equipment in some laboratories.
- Adverse effects are not routinely recorded in the patients' treatment cards in some health facilities.
- There are dissenting experts' opinions on DR-TB paediatric treatment as no national guidelines have been developed yet.
- There is a lack of infection control measures in many health facilities visited. The recommendation for a designated infection control focal point at the regional and national levels was also stated in the previous mission report.

Fig. 11: Nepal – DR-TB programme performance, 2009–2016



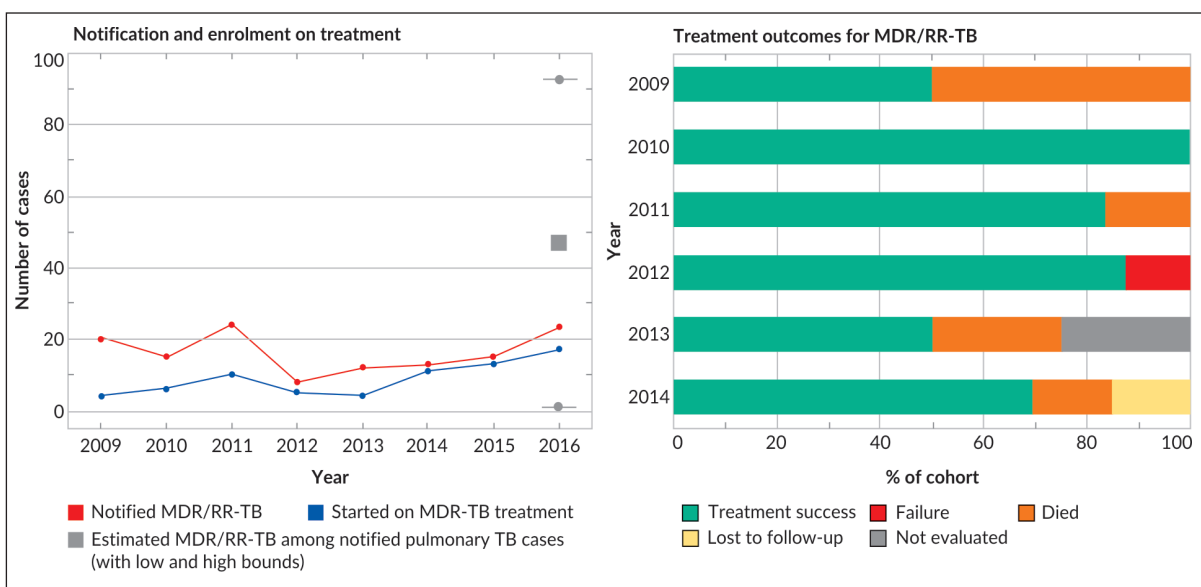
Source: <http://www.who.int/tb/data>

# Sri Lanka

## Key challenges in expansion of DR-TB services

- TB case notification rates for past several years have been static with a very low proportion of retreatment cases among notified TB cases.
- There is wide variation in case notification rates among various districts in the country.
- There is some delay in procurement and roll-out of rapid molecular diagnostics.
- Because the information available is incomplete, there are difficulties in using laboratory data for analysis.
- Teaching hospitals and a growing private sector cater to TB (and MDR-TB) but information flow between the Programme and hospitals is weak.
- Initiation of TB treatment is still centralized to the National Hospital for Respiratory Diseases at Welissera.
- Plans for introduction of a shorter regimen for RR/MDR-TB are not in place yet.
- Proposed additional financial and nutritional support for patients on second-line treatment is still under discussion.
- Infection control practices were inadequate at most places, as was also observed by the previous mission.
- There is very little involvement of nongovernmental organizations (NGOs) and community-based organizations (CBOs) in treatment delivery and care of TB patients, specifically MDR-TB patients.

Fig. 12: Sri Lanka - DR-TB programme performance, 2009-2016



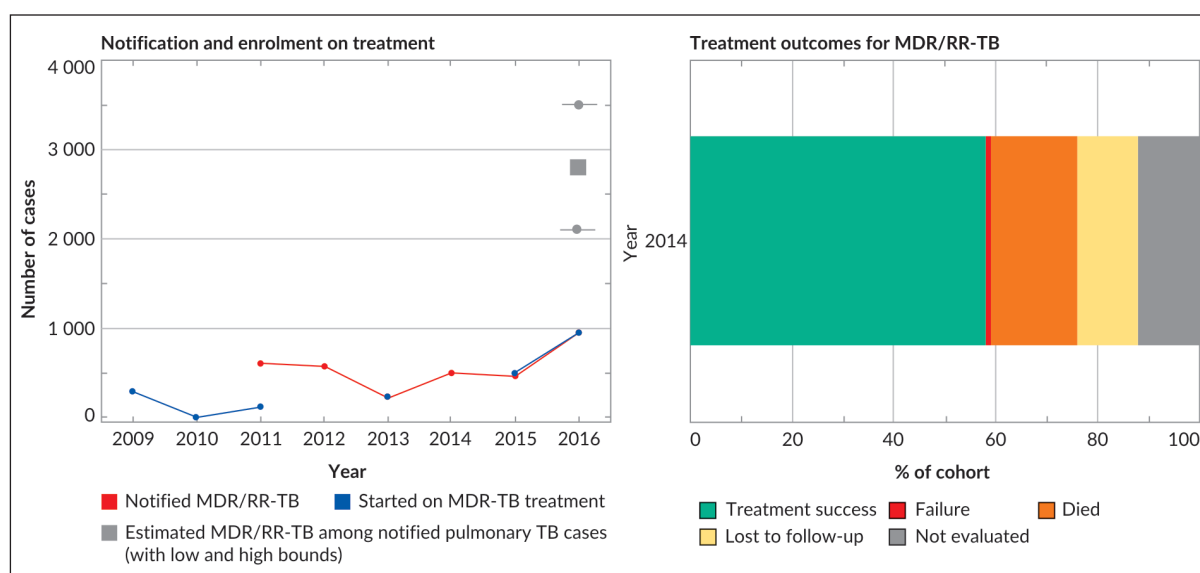
Source: <http://www.who.int/tb/data>

# Thailand

## Key challenges in expansion of DR-TB services

- Only about 20% of estimated RR/MDR-TB patients among notified pulmonary TB cases are being detected and initiated on treatment because of under-notification as well as under diagnosis.
- There is underutilization of available molecular tests, specifically GeneXpert machines and LPA.
- Treatment success rates among patients initiated on SLDs is low.
- Although there is an in-principle agreement to offer financial/material support to RR/MDR-TB patients, enablers through the government system are not always available because of budget issues.
- NGOs and specifically CBOs can play a vital role in complementing MDR-TB services but are not adequately involved.
- Very low treatment success rates are observed among patients on treatment in some of the private sector hospitals because of lack of provision of DOT and no effective mechanism for retrieval of lost patients.
- There are discrepancies in data for PMDT due to multiple reporting channels.
- There are issues with how screening and second-line treatment are provided by hospitals because of policies not being clearly spelt out in guidelines or their misinterpretation by the National Health Security Office (NHSO).

**Fig. 13: Thailand – DR-TB programme performance, 2009–2016**



Source: <http://www.who.int/tb/data>

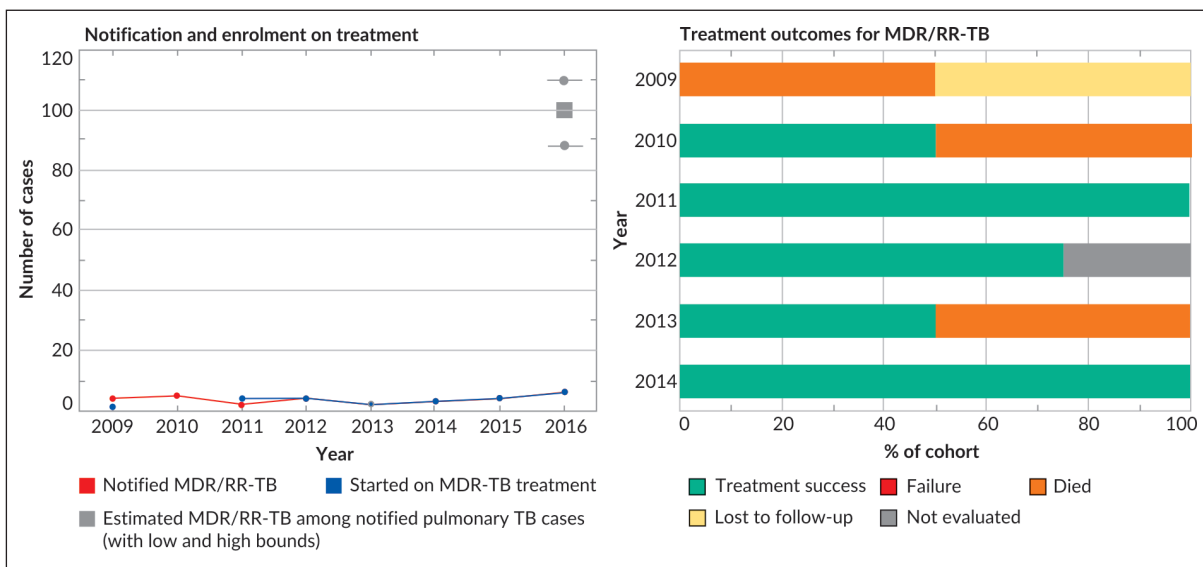
Treatment outcomes were not reported to WHO for earlier years. Hence the figure remains blank.

# Timor-Leste

## Key challenges in expansion of DR-TB services

- Accreditation of the National TB Reference Laboratory (NTRL). Sputum specimens continue to be sent outside the country for culture and DST. This causes considerable delay in getting the right diagnosis.
- Centralization of GeneXpert machines. All three GeneXpert machines are located in or near the capital city of Dili. This makes it difficult for people to access these services from other parts of the country.
- Ad-hoc mechanisms for sputum transportation. There are currently no systems in place for regular sputum collection and transportation. The health system currently relies on health personnel to bring sputum samples to the NTRL for testing.
- Some challenges have also been observed regarding coordination with the Supranational Reference Laboratory (SNRL), specifically with regard to timely specimen transportation.

**Fig. 14: Timor-Leste - DR-TB programme performance, 2009-2016**



Source: <http://www.who.int/tb/data>



**Annexure 2:  
Delhi Call for Action  
to End TB in the  
South-East Asia Region**

In the recently concluded Ministerial Meeting at Delhi on 15–16 March 2017, all Member States of the Region signed the Call for Action for ending TB in the WHO South-East Asia Region. The key commitments in the Call for Action are given below:

- LEAD implementation of the national TB responses in countries – specifically the high-burden countries – by an empowered national initiative that reports to the highest levels of government in Member States, and that includes a multisectoral response and is committed to translating policies into time-bound, result-oriented actions at multiple levels of administration, with ownership and access to real-time monitoring;
- INCREASE budgetary and human resource allocations by governments as well as by their global, domestic and other partners so as to ensure that national TB plans are evidence-informed, fully funded, rationally and effectively used, avoiding wastages;
- ENABLE, using innovative communications, the engagement and literacy of communities and individuals with TB and provide the best possible care to each and every person, including migrants, the aged and other high-risk populations, living with any form of TB, including drug-resistant TB and TB–HIV coinfections, presenting either to the public or the private sector, including general practitioners, while also expediting introduction and expansion of new tools of diagnosis, treatment and prevention as they become available;
- SUPPLEMENT medical care for TB with patient-centred, community-empowering, necessary social and financial protection in a holistic manner through collaborations across and beyond the health sector in every country of the Region;
- WORK jointly with the South-East Asia Regional Office of the World Health Organization and partners to further boost actions in countries, including forming regional research consortiums, mobilizing additional global resources and securing political commitment at the highest levels from countries through the Ministerial Meeting in Moscow, Russia, in November 2017, and at the UN General Assembly Session in 2018, thereby demonstrating regional commitment to end TB; and
- SET UP jointly with the South-East Asia Regional Office of the World Health Organization and partners a Regional Innovation to Implementation (I2I) fund to ensure accelerated sharing of knowledge, including the use of secondary data, intellectual resources and testing innovations to reach out and treat all cases.
- The Regional Director of the WHO South-East Region has accorded a high priority to TB control in the Region, and this is now one of her Flagship Projects.



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## South-East Asia Regional Response Framework for Drug-resistant TB 2017–2021

The WHO South-East Asia (SEA) Region bears a high burden of tuberculosis (TB) and MDR-TB. In 2015, the Region accounted for nearly 200 000 or 35% of the global estimated new RR/MDR-TB cases eligible for treatment. Extensively drug-resistant TB (XDR-TB) has also been reported from six countries of the SEA Region. MDR-TB could potentially replace drug-susceptible TB, and constitutes a threat to global public health security.

In May 2014, the World Health Assembly adopted the End TB strategy. The End TB Strategy has as its vision a world free of TB, with zero deaths, disease and suffering due to TB. Ending TB is not possible without addressing the issues of MDR-TB. The South-East Asia Regional Response Framework for DR-TB 2017–2021 complements the Ending TB in the South-East Asia Region: Regional Strategic Plan 2016–2020” and outlines key strategies for reducing morbidity, mortality and transmission of DR-TB. By fully implementing this Response Framework, the Region will be on track for achieving the overall goal of ending TB. The Plan anticipates that by 2021, all Member States would have fully implemented the WHO guidelines on MDR-TB management and there will be universal access to quality-assured services for all those who need them.



**World Health  
Organization**

Regional Office for South-East Asia