Two years post UN General Assembly High-Level Meeting on the fight against tuberculosis: advances and setbacks in high drug-resistant TB burden countries

Review on the milestones towards the UNHLM drug-resistant TB targets in the 10 highest drug-resistant TB high burden countries

Report of the independent review by the Global drug-resistant TB Initiative
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ABBREVIATIONS AND ACRONYMS

AMR	antimicrobial resistance
Bdq	bedaquiline
DOT	directly observed treatment
DR-TB	drug-resistant tuberculosis
DS-TB	drug-susceptible tuberculosis
DST	drug-susceptibility testing
FQ	fluoroquinolone
HBC	high burden country
HIV	human immunodeficiency virus
LPA	line probe assay
LPA-sl	line probe assay second line
MDR-TB	multidrug-resistant tuberculosis (resistance to at least rifampicin and isoniazid)
MDR/RR-TB	multidrug-resistant or rifampicin-resistant tuberculosis
NSP	national TB strategic plan
NTP	national tuberculosis programme
PMDT	programmatic management of drug-resistant tuberculosis
rGLC	regional MDR-TB advisory committee
RR-TB	rifampicin-resistant tuberculosis
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SDG	Sustainable Development Goal
SLD	second-line drug
TB	tuberculosis
UN	United Nations
UNHLM	United Nations High-Level Meeting on TB
VOT	video directly observed treatment
WHO	World Health Organization
XDR-TB	extensively drug-resistant tuberculosis

1. INTRODUCTION

1.1. The 2018 United Nations High-Level Meeting on TB

Tuberculosis (TB) is the leading cause of death from an infectious disease. An estimated 2 billion people have TB infection, and every year more than 10 million people develop active TB. Also, more than 500 000 people develop drug-resistant TB (DR-TB) every year. The current trend in the decline of TB is not enough to meet the target set in the Sustainable Development Goals (SDGs).

On 26 September 2018, the United Nations (UN) General Assembly held the first-ever high-level meeting on the fight against TB (UNHLM), under the theme "United to end tuberculosis: an urgent global response to a global epidemic". Leaders of all UN Member States committed to "ending the global TB epidemic" by 2030. During the meeting, most of the world's countries endorsed the fact that TB is the top infectious disease killer globally and is a major cause of death related to antimicrobial resistance (AMR). Member States also agreed on the need to accelerate efforts to end TB and reach all affected people with prevention and care, leading to a landmark political declaration listing tangible and specific milestones to be achieved by 2022 *(1)*.

The key targets committed by representatives of states and governments were as follows:

1. 40 million people **treated for TB** from 2018 to 2022, including:
   - ✓ 3.5 million children; and
   - ✓ **1.5 million people with DR-TB, including 115 000 children**.
2. At least 30 million people provided with TB preventive treatment from 2018 to 2022, including:
   - ✓ 6 million people living with HIV; and
   - ✓ 4 million children aged under 5 years and 20 million people in other age groups who are household contacts of people affected by TB.
3. Funding of at least US$ 13 billion per year for universal access to TB prevention, diagnosis, treatment and care by 2022.
4. Funding of at least US$ 2 billion per year for TB research from 2018 to 2022.

These targets build on and are consistent with the milestones for reductions in TB incidence and mortality set for 2020 and 2025 in the End TB Strategy. DR-TB is a significant contributor to mortality caused by TB, and it needs to be addressed urgently to achieve the set milestones and thus also reduce transmission of resistant strains into the community.

The UNHLM culminated in an ambitious political declaration on TB that was endorsed by heads of state; the declaration, with its the three critical components (funding, action and accountability), aimed to strengthen action and investments for the TB response, saving millions of lives. In addition, the relevance and the need to address the challenges of DR-TB was acknowledged as one of the biggest priorities for ending TB, recognizing that the overall TB epidemic is exacerbated by the rise of multidrug-resistant TB (MDR-TB[1]), which is the cause of one third of deaths due to AMR globally.

[1] MDR-TB is defined as TB disease caused by bacilli resistant to at least rifampicin and isoniazid.

The declaration included the need for the UN Secretary-General, with support from the World Health Organization (WHO), to report in 2020 on global and national progress in accelerating efforts to achieve agreed TB goals framed in the 2030 Agenda for Sustainable Development, and on progress and implementation of the UNHLM declaration. This current report is intended to be complementary to the UN progress report that was released in September 2020 *(2)*. It reviews the milestones and progress of high DR-TB burden countries (HBCs) and focuses on the targets related to DR-TB after the resolution and commitment made during the UNHLM. This report aims to assess and document the preparedness and progress made by HBCs to achieve the UNHLM targets for DR-TB control.

1.2. Background and aim

DR-TB[2] diagnosis, prevention and treatment have long been an obstacle course. However, that has changed in recent years, thanks to growing experience and evidence, innovative technology, partnerships and political commitment. The UNHLM was a unique opportunity to achieve international commitment – it opened a distinctive window of opportunity to put TB and its drug-resistant forms high on the international agenda.

The current report was developed in November 2020, half-way through the time frame (2018–2022) for the UNHLM targets. We believe that a review of the achievements in the response to DR-TB and the barriers to reaching the final targets can help to keep alive the spirit of the declaration stemming from the UNHLM, provide a reminder about interim goals and highlight the importance of continued work towards the targets. In addition, interim monitoring of the targets and updating of the UNHLM objectives are part of the declaration itself.

We therefore reviewed the available documentation to assess the level of achievement in different countries, which could then inform progress towards key milestones and highlight barriers to progress internationally. To obtain a representative sample of the MDR-TB or rifampicin-resistant TB (RR-TB) patients around the world, we selected 10 DR-TB HBCs, noting that the relevance and dimensions of the DR-TB problem can be measured in different ways.

To complement the information in the public domain, we approached the national TB programmes (NTPs) of the 10 HBCs with a survey. The aim of the survey was to ascertain the countries' recent preparedness and progress to achieve the DR-TB related UNHLM targets, and to determine potential reasons for slow or no progress and the consequences of the ongoing COVID-19 pandemic.

The final objective was to create and disseminate this report on behalf of the **Global Drug-resistant TB Initiative**. The report is a combination of a DR-TB situation analysis and a comparison within the 10 HBCs in light of the UNHLM commitments.

1.3. TB and DR-TB as a world crisis

TB is currently the world's main infectious disease killer, surpassing HIV and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[3] and DR-TB continues to be a major public health threat. In 2019, WHO estimates that there were about 500 000 new cases of MDR-TB or RR-TB (MDR/RR-TB).

The three countries with the largest share of the global burden of DR-TB are India (27%), China (14%) and the Russian Federation (9%). Globally, 3.4% of new TB cases and 18% of

[2] DR-TB is a broad term that refers to MDR-TB or rifampicin-resistant TB (RR-TB) (MDR/RR-TB), with or without resistance to additional TB drugs.
[3] As of 13 November 2020, it is estimated that 1 296 000 people have died from SARS-CoV-2 globally *(3)*.

previously treated cases had MDR/RR-TB, with the highest proportions (>50% in previously treated cases) being in Eurasian countries.

The political declaration at the UNHLM included commitments to improve the coverage and quality of diagnosis, treatment and care for people with DR-TB. It included specific targets as part of the End TB Strategy *(4)*.

Detection of MDR/RR-TB requires bacteriological confirmation of TB and testing for drug resistance using rapid molecular tests, culture methods or sequencing technologies. Treatment requires a course of second-line drugs (SLDs) for at least 6–9 months (and up to 20 months), supported by counselling and monitoring for adverse events.

Despite some progress in recent years, the reality is that, in 2019, only 206 030 of the estimated 500 000 MDR/RR-TB cases were detected and notified, and only 177 099 of those cases were enrolled on treatment. Thus, in 2019, only about one in three of the estimated 500 000 people who developed MDR/RR-TB were enrolled on treatment.

Patients suffering from TB – particularly those with DR-TB – can be missed along the cascade of care because of gaps in diagnosis and treatment, which translate into lost opportunities for early detection and cure (which could curtail transmission in the community) *(5, 6)*. The most relevant areas of loss along the cascade are detection of drug resistance, enrolment into treatment, and treatment success rates, as outlined below.

1.3.1. Detection of drug resistance among bacteriologically confirmed cases

Increasing the availability of DR-TB diagnosis among high-risk communities or populations is key to diagnosing DR-TB cases. Therefore, increased laboratory capacity is needed. Also, there are significant limitations on confirmation of extensively drug-resistant TB (XDR-TB) or fluoroquinolone (FQ) resistance, which is an integral component for correct allocation for the currently recommended treatment options.

1.3.2. Enrolment into treatment of those diagnosed

Enrolment into treatment depends on the national health care system, which should accommodate patient enrolment. In 2019, 10 countries accounted for 77% of the global gap between treatment enrolments and the estimated number of new cases of MDR/RR-TB; thus, this factor will have a strong influence on progress in closing this gap. These 10 countries were China, India, Indonesia, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation, South Africa and Ukraine. China and India alone accounted for 41% of the global gap.

1.3.3. Treatment success rate

Alongside treatment success rate is the capacity of national health systems to follow up and support patients along the lengthy and unpleasant time during treatment, and the capacity to maintain patients in treatment during the time to cure without relapses. The latest treatment outcome data for people with MDR/RR-TB show a global average treatment success rate of 56%. Examples of MDR-TB HBCs with better treatment success rates (>70%) are Bangladesh, Ethiopia, Kazakhstan and Myanmar.

1.4. The relevance of DR-TB

Many of the SDGs may not be attainable if AMR is not addressed. In 2016, less than 25% of the estimated number of the DR-TB cases were diagnosed and notified, and it was acknowledged that the response to RR-TB, MDR-TB and XDR-TB to date has been insufficient.

The scale of MDR/RR-TB and XDR-TB morbidity and mortality is a key component of the global challenge of AMR, and it could reverse the progress made against TB, especially in low- and middle-income countries. There is a profound gap in access to quality diagnosis, treatment and care for those affected.

The UNHLM declaration also highlights that investments and innovations are urgently needed to fight drug-resistant forms of TB. Countries recognize and admit the need for an urgent response to DR-TB; they have committed to promoting the scaling up of access to diagnosis and treatment of these forms of TB through actions for prevention, diagnosis, treatment, care, and research and development of new products. One of the points in the declaration specifically notes that NTPs may actively contribute to developing national AMR strategies, capacities and plans, and that lessons learned from global, regional and national efforts to combat DR-TB should be used to inform the design and implementation of both global AMR strategies and national action plans.

1.5. The DR-TB HBCs

In the present report, we analyse the baseline and recent achievements of the 10 DR-TB HBCs: Bangladesh, China, India, Indonesia, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation and South Africa.

The Russian Federation does not present an overall extraordinary high burden of TB. However, the important proportion of initial TB cases that are indeed DR-TB cases in the Russian Federation represents the highest DR-TB rate in the world (28 cases/100 000 population) and globally it is in third place in absolute numbers of DR-TB cases (41 000) after India (130 000) and China (66 000). China and India present more total cases but have much lower DR-TB rates (9.6 and 4.6 cases/100 000 population, respectively). These three countries have in common high numbers of patients with DR-TB, but are different in terms of the variables that may be leading to the DR-TB epidemic.

2. METHODOLOGY

This report is mainly an ecological descriptive analysis with information from different sources. It aims to provide a better understanding of the different circumstances driving the DR-TB epidemic and the response to it in the 10 DR-TB HBCs (e.g. targets met and the programme performance and components used to achieve this). Sources of information used in the analysis include national TB strategic plans (NSPs) that focus on the targets of the UNHLM declaration, and country indicators that focus on the targets calculated by the Stop TB Partnership (using available data on those indicators from the last quarter of 2020).

2.1. Key sources of information

During the preparation of the report, information was accessed from various sources and triangulated.

- ✓ We reviewed the **UNHLM declaration** and the **key targets** related to MDR/RR-TB for the selected HBCs *(7)*. As mentioned, the targets are focused on increasing diagnosis of DR-TB and enrolment in treatment.

- ✓ We created a brief **DR-TB epidemic situation analysis** of the selected HBCs using the data from 2018 (the year of the UNHLM) from the WHO *Global TB report 2019 (8)* as the baseline for comparisons among countries (i.e. the starting point to determine whether further trend analysis is necessary). We then used the data from the WHO *Global TB report 2020 (9)* to confirm the level of performance of the targets.

  The UNHLM declaration specifically mentioned that **NSPs** must reflect the key targets, to ensure effective accountability. Therefore, we reviewed the DR-TB component, policies and indicators or targets of each country plan or NSP that endorsed or was aligned to the basic principles of the UNHLM declaration, its programmatic management of DR-TB (PMDT) targets and activities in the years following the UNHLM declaration. In addition, we reviewed NSPs for the existence of clear activities, indicators and targets that could be used to monitor any improvement in DR-TB care, related to three main gaps in the cascade of care:

  – *diagnosis* – there is a need for improvement in laboratory networks and scale-up in molecular testing for DR-TB diagnosis (resistance to rifampicin and FQ);

  – *treatment enrolment* – coordination and specific policies are needed; and

  – *treatment success* – there is a need for activities to improve the quality of the regimens provided, reduce the number of adverse events and the number of cases lost to follow-up, and improve patient-centred care.

- ✓ Some countries were implementing NSPs that were created before the UNHLM declaration; thus, to fine tune the analysis of reviewing the milestones proposed on the UNHLM declaration, we developed a **brief yet comprehensive DR-TB survey** (Annex 1). The survey asked a precise list of standard questions (i.e. the same structured questionnaire was sent to all countries) about the country's level of preparedness to achieve or work towards the UNHLM targets and the performance achieved over the past 2 years, the current status, and barriers to achieving the objectives of the UNHLM declaration (e.g. impact of COVID-19). Initially the survey was sent to each country's WHO TB medical officer, to obtain contacts and facilitate the participation and input of the NTP manager or DR-TB focal point.

2.2. Descriptive analysis

Countries were analysed in terms of similarities and differences in the DR-TB epidemic baseline for 2018, while considering other relevant country circumstances, response to the epidemic (measured in gaps along the DR-TB cascade of care) and subsequent needs. Finally, the level of performance and achievements on the UNHLM targets was analysed, and key information extracted from the NSPs and the survey was used to complement the information from other sources.

In addition to the crude analysis of UNHLM target implementation and the descriptive analysis, a DR-TB cascade-of-care framework was created for each country. The aim of creating the framework was to stress the different weaknesses and strengths in order to establish patterns or potential classifications of a country's needs and key variables in the epidemic dynamics, which could be useful in this study, in further monitoring studies, or in supportive technical assistance or plans.

For the 2018 baseline situation analysis, a *cascade approach* was chosen, both as a summary indicator and as something that could be easily understood and used by policy-makers. This approach highlights key gaps for each country, enabling a focus on improvement towards meeting the UNHLM targets and declaration, and can be applied to all the countries, despite their different profiles and circumstances.

The resulting presentation is structured around the three main points at which patients are lost along the DR-TB cascade of care, and considers the three major gaps (i.e. in diagnosis, enrolment and treatment success). The data presented here are rough estimates based on gross country data; therefore, it was not possible to establish an absolute or precise attributable variable for each outcome and setting. However, the cascade approach can not only provide a view on specific components in PMDT, but can merge the scaling up of access to rapid drug-susceptibility testing (DST), regimens, and the latest evidence-based health technologies and policies (including human rights, and particularly the right to health) in poor and neglected populations *(5, 10)*. Historically, some HBCs have tended to have poor coverage of diagnosis and access to treatment, as well as limited support for successfully completing treatment.

2.3. Country DR-TB performance, UNHLM targets and other variables measured

The UNHLM targets set a value for the number of DR-TB patients to be diagnosed per country per year from 2018 to 2022. In 2018, the Stop TB Partnership used projection models to set specific and bold targets on both categories (number of patients diagnosed and enrolled into treatment) for each specific country; these targets were updated in 2019. The UNHLM declaration mentions that at least 115 000 DR-TB children should be diagnosed and treated between 2018 and 2022, but it does not assign country-specific targets. Questions on the number of DR-TB children diagnosed and treated were part of the survey sent to the countries.

The targets for diagnosis and treatment had been disaggregated to reflect the fact that, in many countries, a significant proportion of diagnosed DR-TB patients do not reach treatment initiation. Treatment success, which is not included in the UNHLM targets, is still a major worldwide gap in PMDT and is fundamental to measuring the real impact of NTPs (i.e. to reduce unnecessary deaths, improve quality of life, reduce disability, reduce transmission of DR-TB in the community and avoid the amplification of resistance patterns). Over the past 10 years, there has been little improvement in treatment success rates, with an overall global success rate of 50% among DR-TB patients (and 57% for 2019).

With few exceptions, the 10 HBCs have had an average treatment success rate of about 50–55%. Therefore, treatment success has been considered in this report, as a way to monitor the positive (or negative) trend of countries towards the UNHLM declaration; in particular, because of the introduction of shorter and less toxic DR-TB regimens in coming years.

3.1. Baseline data on DR-TB by country (2018) – country comparison

All countries were measured and compared using the same summary variables (Table 3.1). The country with the largest estimated number of DR-TB patients annually was India (130 000), followed by China (66 000). The number of DR-TB patients diagnosed is presented according to the overall TB burden, except for those with high rates of DR-TB. The highest rate of DR-TB was that of the Russian Federation, with 28 cases per 100 000 population (i.e. 41 000 incident cases per year). These three countries – China, India and the Russian Federation – accounted for nearly half the global DR-TB burden. Myanmar and South Africa showed disproportionately high rates of DR-TB (21 and 19 per 100 000, respectively); possible reasons for this include challenges in the management of drug-susceptible TB (DS-TB) in the past and high rates of transmission of DR-TB in the community.

We attempted to obtain information on the number of cases of DR-TB in children, but none of the 10 DR-TB HBCs have readily available data in the public domain.

The proportion of DR-TB among new cases was below 5% for all countries, except for China (7%) and the Russian Federation (35%). The proportion of DR-TB among previously treated patients was between 10% and 16% for all countries, again except for China (21%) and the Russian Federation (71%).

Only four countries were measuring FQ resistance among RR-TB patients – currently a key requirement for eligibility to access the short treatment regimens, which in turn is fundamental for expanding services. FQ resistance among RR-TB cases in Bangladesh, the Philippines and South Africa was 5–10%; Pakistan had a level of 37%, whereas less than 10 years ago the figure was only 9%. The situation in Pakistan and possibly in other countries may be rapidly evolving because of unregulated use of FQ for respiratory illness, reduced access to bacteriological diagnosis in the private sector, reduced access to proper health care and over-the-counter sales of FQ.

Information on FQ resistance in key countries with a high proportion of initial rifampicin resistance (e.g. China and the Russian Federation) was not available to the authors of this report.

Table 3.1. *Epidemiological DR-TB profile among the 10 DR-TB HBCs, baseline 2018*

Country	TB cases, incidence estimate	TB rate[a]	DR-TB cases, incidence estimate	DR-TB rate[a]	Number of DR-TB cases in adults diagnosed[b]	Number of DR-TB cases in children diagnosed[a]	Proportion of DR-TB in new cases (%)	DR-TB in previously treated cases (%)	Proportion of FQ resistance among RR-TB cases (%)[c]
Bangladesh	357 000	221	5 900	3.7	1 228	N/A	1.5[d]	N/A	5.6
China	866 000	61	66 000	4.6	14 636	N/A	7.1	21	N/A
India	2 690 000	199	130 000	9.6	58 347	N/A	2.8	14	N/A
Indonesia	845 000	316	24 000	8.8	9 038	N/A	2.4	13	N/A
Myanmar	181 000	338	11 000	21.0	3 479	N/A	4.9	20	N/A
Nigeria	429 000	219	21 000	11.0	2 275	N/A	4.3	15	N/A
Pakistan	562 000	265	28 000	13.0	3 824	N/A	4.2	16	37.0
Philippines	591 000	554	18 000	16.0	7 276	N/A	1.7	16	6.5
Russian Federation	79 000	54	41 000	28.0	27 438	N/A	35.0	71	N/A
South Africa	301 000	520	11 000	19.0	13 199	N/A	3.4	7	9.4

DR-TB: drug-resistant tuberculosis; FQ: fluoroquinolone; HBC: high burden country; N/A: not available; RR-TB: rifampicin-resistant tuberculosis; TB: tuberculosis.
[a] Cases per 100 000 population.
[b] Cases of RR-TB, laboratory confirmed.
[c] The proportions of FQ resistance are estimated by different methods (e.g. surveys, cohorts and studies) and are from different time frames (mainly 2019).
[d] The figures of RR-TB in new and previously treated cases in Bangladesh have varied widely in recent years from the data given in the table (2018) to 0.7% and 11% in 2020.

Source: WHO (2019) *(8)*.

Regarding the performance of the 10 HBCs the profiles were quite varied, depending on the scale of PMDT implementation and laboratory capacity. As an indirect measure, all countries except the Philippines were testing for rifampicin resistance in more than 80% of their previously treated cases. This policy is technically correct, but given that at least half of the DR-TB patients are among the new cases, it is not enough to detect the majority of a country's estimated DR-TB cases. HBCs tend to diagnose only 30% or less of the estimated DR-TB cases, except in the Russian Federation (67%) and South Africa (120%). The high proportion in South Africa reflects a strong political commitment to increasing diagnostic capacity (incident and prevalent cases), through an increasingly decentralized implementation of GeneXpert (a clear advance in comparison with the historical data). For most of the HBCs, the biggest gap in the DR-TB cascade of care is DR-TB diagnosis.

DST of SLDs is being conducted in 70% or more of the RR-TB cases in Bangladesh, Nigeria, Pakistan and the Russian Federation, and in about 30% of RR-TB cases in Indonesia, Myanmar and the Philippines (see Table 3.2; note, there are no data for China).

Table 3.2. *Basic indicators on country DR-TB diagnosis capacity, baseline 2018*

Country	DR-TB cases, incidence estimate	Tested for MDR/RR-TB among previously treated (%)	Laboratory MDR/RR-TB confirmed cases	Gap estimation, laboratory confirmed (%)	Tested for SLD resistance among RR-TB cases (total (%))[a]	Laboratory XDR-TB confirmed cases
Bangladesh	5 900	98	1 228	20.81	853 (69.46)	6
China	66 000	100	14 636	22.17	N/A	430
India	130 000	91	58 347	44.88	38 236 (65.53)	3 400
Indonesia	24 000	127	9 038	37.65	2 526 (27.94)	80
Myanmar	11 000	84	3 479	31.62	927 (26.64)	35
Nigeria	21 000	88	2 275	10.83	1 895 (83.29)	31
Pakistan	28 000	79	3 824	13.65	2 893 (75.65)	95
Philippines	18 000	24	7 276	40.42	2 095 (28.79)	52
Russian Federation	41 000	95	27 438	66.92	24 601 (89.66)	5 112
South Africa	11 000	94	13 199	119.99	7 469 (56.50)	553

DR-TB: drug-resistant tuberculosis; MDR/RR-TB: multidrug-resistant or rifampicin-resistant tuberculosis; N/A: not available; RR-TB: rifampicin-resistant tuberculosis; SLD: second-line drug; XDR-TB: extensively drug-resistant tuberculosis.
[a] With variations, but usually only RR-TB cases enrolled received further resistance investigation.

Source: WHO (2019) *(8)*.

In terms of treatment enrolment, most of the 10 countries miss a significant proportion of patients, but this proportion appears to be lower in those countries with a lower capacity for diagnosis. For example, in 2018, Bangladesh diagnosed only 20% and Nigeria only 11% of the estimated DR-TB cases, although most of those who accessed the programme were placed on treatment (93% and 83%, respectively). In contrast, the Russian Federation diagnosed a higher proportion of the estimated DR-TB cases (67%) and placed nearly all treatment (98%).

The highest proportion of patients lost after diagnosis was seen in Indonesia, where only 46% of the diagnosed patients were treated, followed by China with 61%. This parameter varies widely between countries but, overall, an important proportion of patients who are diagnosed do not get placed onto treatment. This represents a major gap in PMDT among the HBCs.

Provided that DR-TB treatments traditionally last 2 years, obtaining current information on treatment outcomes is challenging. For this analysis, treatment success rates from 2016 were used, on the assumption that (unfortunately) changes in treatment outcomes have been minimal in recent years (but this is expected to change with the use of shorter regimens, new and repurposed drugs, and better individualized approaches).

The highest DR-TB treatment success rates in 2016 were seen in Myanmar (79%), Bangladesh (78%), Nigeria (77%) and Pakistan (64%). These four countries have in common a capacity to diagnose DR-TB, although the few cases that reach the system are placed on treatment and tend to get cured. In the other six countries (covering most of the world's DR-TB burden), the treatment success rates were between 48% and 58% (e.g. India 48%, China 52% and the Russian Federation 54%).

Other variables included in this analysis, which could influence enrolment and treatment success, were a country's level of income, NTP domestic fund, HIV prevalence in TB patients, influence of the private sector and models of care. These variables are discussed below.

In terms of *country level of income*, current figures from the World Bank classification based on gross national income (GNI) per capita indicate that six of the 10 HBCs are considered lower-middle income, whereas China, Indonesia, the Russian Federation and South Africa are considered upper-middle economies *(11)*. In the latter, TB tends to be strongly linked to particular socioeconomically vulnerable groups and to be related to HIV infection.

In parallel, *domestic funding* is less than 25% of the total NTP budget in the lower-middle countries, whereas in the upper-middle economies it ranks from 30% in Indonesia to 100% in the Russian Federation.

We did not have access to country-specific data on *DR-TB/HIV*; however, for South Africa, we extrapolated from DS-TB and found that HIV is apparently a leading force in TB dynamics, with more than 50% of TB cases associated with HIV infection. Levels of HIV are also high among TB patients in Myanmar, Nigeria and the Russian Federation, but are low in the other six HBCs.

Based on information from NSPs, the survey and other sources, the *role of the private sector* tends to be high in Bangladesh, China, India, Indonesia, Pakistan and the Philippines. In those countries, the private sector is usually a first point of contact with services for TB-related symptoms (see Table 3.3).

Table 3.3. *Basic indicators on country DR-TB management and influencing variables, baseline 2018 and 2016 cohort outcomes*

Country	Laboratory RR-TB confirmed cases, 2018	Enrolled on treatment, 2018 – absolute numbers	Enrolment proportion (%)	Private sector influence[a]	HIV estimated[b]	Level of income (World Bank: GNI per capita)[c]	Proportion of domestic funding (%)	Model of care[d]	Cases starting DR-TB, 2016	DR-TB treatment success, 2016 (%)
Bangladesh	1 228	1 147	93.4	Very high	Low	Lower-middle	23	Community	918	78
China	14 636	8 965	61.2	Very high	Low	Upper-middle	92	Hospital based	5 405	52
India	58 347	46 569	79.8	Very high	Low	Lower-middle	77	Community	33 197	48
Indonesia	9 038	4 194	46.4	–	Low	Upper-middle	30	Community	1 905	48
Myanmar	3 479	2 650	76.2	–	Medium–high	Lower-middle	3	Community	2 512	79
Nigeria	2 275	1 895	83.3	–	Medium–high	Lower-middle	8	Community	1 251	77
Pakistan	3 824	3 106	81.2	Very high	Low	Lower-middle	3	Community	2 804	64
Philippines	7 276	6 125	84.2	–	Low	Lower-middle	12	Community	5 071	58
Russian Federation	27 438	27 014	98.0	–	Medium–high	Upper-middle	100	Hospital based	22 593	54
South Africa	13 199	9 558	72.4		Very high	Upper-middle	87	Community	11 159	54

DR-TB: drug-resistant tuberculosis; GNI: gross national income; HIV: human immunodeficiency virus; NSP: national TB strategic plan; RR-TB: rifampicin-resistant tuberculosis; TB: tuberculosis.
[a] Data from NSPs, surveys and other sources.
[b] HIV prevalence in new and relapse TB cases all ages (%), 2018: 0–4.9% low, 5–9.9% medium, 10–19% medium–high, 20–49% high, ≥50% very high.
[c] Level of income economies based on World Bank, GNI per capita 2019 calculations and categories: low income $1035 or less; lower-middle income $1036–4045; upper-middle income $4046–12 535; high income ≥$12 536.
[d] Data from NSPs, surveys and other sources; "hospital based" reflects a centralized system where most of the care and follow-up occurs in hospital, and "community" reflects a system where patients tend to start treatment in a centre for programmatic management of DR-TB, with various methods of follow-up.

3.2. NSP, key achievements and country involvement on the targets

During the process of writing this report, all 10 countries were asked to provide their NSPs; however, only eight countries had NSPs available. Nigeria was working on an updated NSP and the Russian Federation did not have a specific NSP for TB; rather it has a national programme titled "Development of Health" (for 2018–2024), with part of that document being a program for the prevention and control of socially significant infectious diseases, including TB. The Bangladesh NSP that we had access to was published in 2016 and focused primarily on public–private mix activities. South Africa's NSP was part of a wider national strategic plan comprising TB, HIV and sexually transmitted infections (STIs).

Among the eight NSPs available for review, we considered items such as document characteristics; specific information on DR-TB policies; activities and targets, and their relevance to the UNHLM declaration and targets; and mention of clear policies on diagnosis, treatment enrolment and treatment success rates in DR-TB. These data are summarized and presented in Table 3.4.

The length of the plans varied from 10 pages (in the only available NSP from China, from 2017) to 210 pages (in the NSP from Indonesia). All documents articulated a TB strategy for a period of 4–5 years after the year of publication.

Only the NSPs from Indonesia, Myanmar, Pakistan and the Philippines were written after the UNHLM. All four NSPs mention the event and include parts of the declaration.

The NSPs from Indonesia, Myanmar and Pakistan were the only NSPs with a specific section devoted to DR-TB; however, all NSPs mentioned and included relevant information and policies for DR-TB.

Of the eight NSPs reviewed, six (India, Indonesia, Myanmar, Pakistan, the Philippines and South Africa) had specific indicators on DR-TB performance and systems to track progress in DR-TB.

Regarding the targets set during the UNHLM (i.e. number of DR-TB cases diagnosed and treated), these or similar targets were included in the NSPs of India, Indonesia, Myanmar, Pakistan and the Philippines (i.e. in the NSPs written after the UNHLM, plus India). Only the NSP from Indonesia set targets that were the same as those established by the Stop TB Partnership. The indicators set in the NSPs from India and Myanmar were similar to those proposed in the UNHLM, but the NSP targets per year were lower. For Pakistan and the Philippines, the targets set in the NSPs were low, being about half of those in the UNHLM declaration.

An increase in the country's budget was included in the NSPs of India, Indonesia, Myanmar, Pakistan, the Philippines and South Africa. However, it was not possible to measure the DR-TB component per se.

Clear strategies towards reducing the diagnosis gap were specifically mentioned in the policies and targets in the NSPs of India, Indonesia, Myanmar, Pakistan, the Philippines and South Africa. Of the three major gaps in the DR-TB cascade of care, "increase diagnosis" was probably the one most strongly reflected in the NSPs, being mentioned as a core component in the NSPs of India and South Africa.

Strategies towards reduction of the enrolment gap were only specifically included and measured in the NSPs of the Philippines and South Africa.

With the exception of Bangladesh (NSP from 2015 with a main focus on public–private mix), all the NSPs reviewed included specific strategies such as capacity-building, and the use of repurposed and new drugs and shorter regimens.

Table 3.4. *Summary of the NSPs of the 10 DR-TB HBCs*

Country	Year of publication/time frame	No. of pages	Specific section on DR-TB	Specific indicators on DR-TB performance[a]	Inform on systems to track progress on DR-TB	Mention of the UNHLM milestones for DR-TB	Indicators and targets according to the UNHLM	Increase in budget in recent years	Political commitment translated into actions in the NSP	Clear strategies towards reducing the gap for DR-TB		
										Diagnosis	Enrolment	Treatment success
Bangladesh	2016 (2016–2020)	74	No	No	No	Not possible	N/A	Yes	Medium	N/A	N/A	N/A
China	2017 (2016–2020)	10	No	No	No	Not possible	N/A	N/A	N/A	N/A	N/A	N/A
India	2017 (2017–2025)	109	No	Yes	Yes	Not possible	Similar indicator, lower targets	Yes	Medium–high	Yes	Not specific	Yes
Indonesia	Draft 2020 (2020–2024)	211	Yes	Yes	Yes	Yes	Same indicators and targets	Yes	Medium–high	Yes	Not specific	Yes
Myanmar	2020 (2021–2025)	168	Yes	Yes	Yes	Yes	Similar indicator, lower targets	Yes	Medium	Yes	Not specific	Yes
Nigeria	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Pakistan	2020 (2020–2023)	103	Yes	Yes	Yes	Yes	Similar indicators, much lower targets	Yes	Low	Yes	Not specific	Yes
Philippines	2020 (2020–2023)	47	No	Yes	Yes	Yes	Similar indicators, much lower targets	Yes	Medium	Yes	Yes, including targets	Yes
Russian Federation	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
South Africa	2017 (2017-2022) includes HIV and STIs	135	No	Yes	Yes	Not possible	Different targets	Yes	High	Yes	Yes, specific policies[a]	Yes

DR-TB: drug-resistant tuberculosis; DST: drug-susceptibility testing; HBC: high burden country; HIV: human immunodeficiency virus; N/A: information not available or does not apply to any of the indicators considered; NSP: national TB strategic plan; STI: sexually transmitted infection; TB: tuberculosis; UNHLM: United Nations High-Level Meeting on TB.

[a] DR-TB notification, DST done, DR-TB treatment success and milestones.

3.3. PMDT survey

A survey (see Annex 1 for the questionnaire) was sent to the 10 HBCs between September and October 2020, with reminders being sent until 9 November 2020. Responses were obtained from eight of the 10 HBCs (with no response from China and the Russian Federation). These surveys were completed by NTP officials, supported by WHO country staff. The key findings of the survey are summarized in Table 3.5 and commented on below.

3.3.1. Key achievements towards UNHLM declaration objectives and targets

For six countries, the UNHLM declaration happened after the creation of their current NSP and budgets. Therefore, many countries have not yet addressed much of their action plans or funding towards meeting the objectives of the declaration. In contrast, the four countries that developed their NSP after the UNHLM (e.g. Indonesia, Myanmar, Pakistan and the Philippines) did address the UNHLM objectives. Also, most responders considered that the declaration would guide the development of their new NSPs and targets.

All responding countries, except Pakistan, had received increased external funding, and two (India and the Philippines) had received both increased governmental and external funding.

The models of DR-TB care varied from being mainly hospital managed (e.g. China and the Russian Federation), hospital initiated with continuation at decentralized facilities (e.g. Indonesia), centralized PMDT with no involvement of peripheral areas (e.g. Pakistan), fully decentralized without hospital involvement except emergency (e.g. Philippines), or with different options and alternatives (e.g. South Africa). During the 2 years preceding the survey, all countries had expanded their diagnostic capacity and some are moving towards increased decentralization of services (e.g. India, Indonesia, Nigeria and South Africa).

All responding countries:

- ✓ had received at least one monitoring visit from the regional MDR-TB advisory committee (rGLC) in the past 2 years;
- ✓ reported that they were frequently using the short treatment regimen, and had updated their DR-TB guidelines recently or were in the process of doing so;
- ✓ reported having active DR-TB contact tracing activities, although the performance could differ widely within countries; and
- ✓ provided SLDs free of charge (China has a complex system of insurance and reimbursement, where the patient usually has to pay for the SLDs, at least initially).

None of the responding countries reported having stock-outs of DR-TB drugs. These responses can be considered a major achievement in PMDT implementation.

It seems that the UNHLM declaration has helped to revitalize PMDT planning and implementation, moving it towards a clear search for more ambitious targets and an important expansion of diagnosis and treatment capacity, especially in countries with a high level of commitment and internal government funding.

3.3.2. Key challenges and setbacks in moving towards UNHLM declaration objectives and targets

Management of children is a big gap in dealing with DR-TB; an important finding of the survey was the minimal enrolment of children onto DR-TB treatment. South Africa presented the largest proportion, with children making up 6% of their DR-TB cohorts. In most countries,

the proportion of children accounted for less than 3% of the cohorts, with the total number of children on DR-TB treatment being only 1051 in the responding countries for 2019. India was unable to present disaggregated data on children.

The UNHLM target for children being treated for DR-TB is 115 000 during 2018–2022. The current figure of 1051 for the year 2019 represents less than 1% of the target, and thus makes only a small contribution to the 5-year target.

Most responding countries reported having directly observed treatment (DOT), but usually not done by health care workers. Video DOT (VOT) was reported as starting as pilot projects, and there were difficulties in undertaking close clinical follow-up.

The proportion of FQ resistance among MDR/RR-TB cases reported in the survey ranged from 2.5% for the Philippines to 37% for Pakistan. Indonesia, Myanmar and South Africa reported rates of more than 10%; Bangladesh and India reported rates of more than 20%; and Nigeria and Pakistan reported rates of above 30%. There were no clear data on China and the Russian Federation; however, according to rGLC and other consultancy reports, the level of FQ resistance among previously treated or RR-TB cases is likely to be high.

The survey also asked about the capacity to deliver rapid results in FQ resistance through line probe assay second line (LPA-sl). With the exception of South Africa and possibly the Russian Federation (no response to the survey), the capacity is likely to be low or very low for most countries. All responding countries had experienced delays and prolonged turnaround times for results from both culture-based DST and LPA-sl, which hindered clinical decision-making.

FQ resistance and difficulties for prompt diagnosis may have a major impact on current policies regarding short treatment regimens.

Regarding reasons for patients being lost to follow-up, most countries reported the key problem as being the socioeconomic conditions of patients, followed by reduced capacity to follow up cases and, then by distances to DR-TB facilities (making management of side-effects difficult).

Regarding the main barriers for the PMDT implementation, most countries cited reduced funding and inadequate capacity-building or coordination capacity.

3.3.3. COVID-19

All countries surveyed mentioned in their responses the high impact of the COVID-19 pandemic on PMDT activities.

The reasons for the disruption caused by COVID-19 fall into two major groups:

- ✓ Inadequate capacity of NTPs to address DR-TB – among the baseline capacities (which were already suboptimal), there has been a diversion of human resources, economic funds and health facilities, especially laboratories, away from TB to COVID-19. Some countries have experienced important delays in LPA and DST results. At the same time, restrictions on movement during lockdown have made coordination at all levels more difficult.
- ✓ Modification of the health seeking behaviour of patients – in addition to potential coinfection, a range of issues have greatly affected the capacity of patients to access health facilities for diagnosis, treatment and follow-up. These issues include restriction of mobility, fear of infection in health facilities, additional stigma due to COVID-19 and major socioeconomic breakdowns that disproportionately affect vulnerable groups such as TB patients.

Table 3.5. *Key findings of the PMDT survey*

Country	Survey sent	Percentage of children among total DR-TB cases (%)	No. of children enrolled on treatment in 2019	Improvement or changes after the UNHLM	Increase in investment in TB after the UNHLM	Expansion of DR-TB diagnostic capacity since 2018	Expansion and decentralization of treatment since 2018	PMDT sites	Year of most recent rGLC monitoring visit	FQ resistance among MDR/RR-TB patients (%)	LPA-sl capacity sites for RR-TB patients	DR-TB contact tracing activities	Model of care	Year of last DR-TB guidelines	International clinical training	High influence of the private sector	DOT by HCWs/VOT
Bangladesh	Yes	2	24	Few	Yes, increase in external funding	Xpert network scaled up	Yes	9	2018	21.	2	Yes	Hospital initiated and peripheral facility	2020	Yes	No	Yes, by HCW
China	No	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Hospital based	N/A	N/A	Yes	No
India	Yes	N/A	N/A	Yes	Yes, increase in domestic (triple budget) and external funding	Xpert, and DST network scaled up	Yes, x4 PMDT sites since 2018	711	2019	22	54 (considered enough but delays)	Yes	Decentralized	2019	Yes	Yes	Yes
Indonesia	Yes	<1	42	Plan development	Slight increase	Xpert network x2	Yes, x3 PMDT sites since 2018	233	2020	12	7	Yes	Hospital based	Being up dated	No	No	No
Myanmar	Yes	1	35	Not yet but help to plan	Yes, increase in external funding	Slight increase	No	59	2019	12	LPA-sl only for 50% of RR-TB cases	Yes	Ambulatory outpatient care	2020	Yes	Yes, mainly NGOs	Yes, by HCWs

Country	Survey sent	Percentage of children among total DR-TB cases (%)	No. of children enrolled on treatment in 2019	Improvement or changes after the UNHLM	Increase in investment in TB after the UNHLM	Expansion of DR-TB diagnostic capacity since 2018	Expansion and decentralization of treatment since 2018	PMDT sites	Year of most recent rGLC monitoring visit	FQ resistance among MDR/RR-TB patients (%)	LPA-sl capacity sites for RR-TB patients	DR-TB contact tracing activities	Model of care	Year of last DR-TB guidelines	International clinical training	High influence of the private sector	DOT by HCWs/VOT
Nigeria	Yes	3	50	Not yet but help to plan	Yes, increase in external funding	Relative increase	Yes, +16 new PMDT sites	28	2019	34	6 sites, delays	Yes	Ambulatory outpatient care	2017	No	Yes	No
Pakistan	Yes	4	110	Not yet but help to plan	No	Yes, Xpert network	No	33	2020	37	10 sites, delays	Yes	PMDT centralized, ambulatory	2020	No	Yes	No
Philippines	Yes	4	269	Yes	Yes, increase in domestic funding	Yes, Xpert network	Yes, +18 facilities	199	2020	2.	2 sites	Yes	Ambulatory outpatient care	2020	No	Yes	Yes
Russian Federation	No	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Hospital based	N/A	N/A	N/A	N/A
South Africa	Yes	6	521	Received more funds	Increase in external funding	Xpert universal coverage achieved	87% sub-district DR-TB coverture	>206	2018	10–15	Capacity to cover all RR-TB cases	Yes	Patient-centred different options	2020	Yes	No	DOT by HCWs

DOT: directly observed treatment; DR-TB: drug-resistant tuberculosis; DST: drug-susceptibility testing; FQ: fluoroquinolone; HCW: health care worker; LPA-sl: line probe assay second line; MDR/RR-TB: multidrug-resistant or rifampicin-resistant tuberculosis; N/A: not available; NGO: nongovernmental organization; PMDT: programmatic management of drug-resistant tuberculosis; rGLC: regional MDR-TB advisory committee; RR-TB: rifampicin-resistant tuberculosis; TB: tuberculosis; UNHLM: United Nations High-Level Meeting on TB; VOT: video directly observed treatment.

3.4. Level of achievement of the UNHLM targets

After the UNHLM, the Stop TB Partnership developed a set of specific targets for the number of DR-TB patients diagnosed and enrolled on treatment in 2018, and updated these targets in 2019. These targets are precise numbers assigned to each country between 2018 and 2020. In terms of the targets, the values set for 2018–2019 were similar to the numbers of cases diagnosed and treated by each country in the previous years, whereas those for 2020–2021 present a substantial expected increase and those for 2022 present a steady line or decrease.

The country data needed for the targets (DR-TB diagnosed and enrolled on treatment) are included in the annual WHO TB reports. We used the data from the WHO global TB reports from 2019 *(8)* and 2020 *(9)* for the years 2018 and 2019, respectively. We also used information from the survey sent to the HBCs to infer the potential level of achievement during 2020, and the consequences of the COVID-19 pandemic during 2020 and beyond.

Table 3.6 summarizes the 10 HBCs' level of achievement against the UNHLM targets for each year; Annex 3 provides the related country graphs.

3.4.1. Targets for the year 2018

Nine of the 10 HBCs achieved or even surpassed the targets on DR-TB diagnosis for the year 2018; the exception was Pakistan.

Regarding the target of putting patients onto treatment, Bangladesh, Indonesia, Myanmar, Nigeria, the Russian Federation and South Africa achieved 95% or more of the number of patients assigned for each country in 2018. China, India and the Philippines managed to put more than 80% of the number of patients assigned to them onto treatment, while Pakistan achieved 59.5%.

3.4.2. Targets for the year 2019 and trend

For the most part, countries had improved slightly in 2019 compared with 2018, but in some instances they fell away from the targets. Bangladesh, China, India, Indonesia, Nigeria and the Philippines had all increased both diagnosis and enrolments in total numbers, coming close to meeting the targets but with large gaps on enrolment (particularly in Indonesia, where less than 50% of diagnosed cases are enrolled, leaving 5932 untreated cases). China achieved 98% of the diagnosis target and 73% of the treatment enrolment target, meaning that one in four DR-TB patients diagnosed do not receive treatment (representing another 4721 DR-TB patients not treated).

Pakistan did not improve numbers; in fact, it moved further from its targets (Fig. 3.1). Myanmar, the Russian Federation and South Africa remain close to their target numbers but did not improve the total numbers of cases diagnosed and enrolled. Nigeria, despite a modest increase in numbers, has significantly fallen away from both targets, reaching only 63% in diagnosis and 52% on enrolment. Both Myanmar and the Russian Federation diagnosed fewer cases but enrolled more patients – 89% and 80% for Myanmar, and almost 100% on both targets for the Russian Federation (Fig. 3.2).

South Africa exceeded the target for numbers diagnosed, but diagnosed fewer cases than in 2018 and enrolled fewer patients on treatment. Hence, the important gap between diagnosis and treatment enrolment continues, with the country being above target for diagnosis but on only 87% for enrolment.

Pakistan saw reduced numbers diagnosed and enrolled on treatment compared with previous years, and is moving further away from both targets (45% and 35% achievement, respectively).

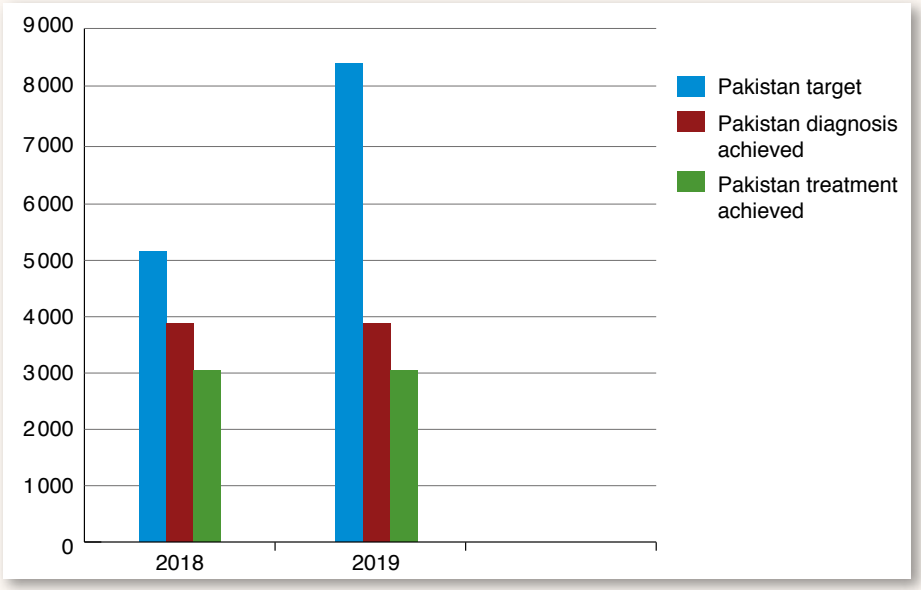
Table 3.6. *UNHLM targets by country and level of achievement during 2018 and 2019 (revised 29 October 2020)*

Country		2018	2019	2020	2021	2022	Cumulative 2018–2022
		Cases / target achieved (%)	Cases / target achieved (%)	Cases / target achieved (%)	Cases / target achieved (%)	Cases / target achieved (%)	
Bangladesh	Target	1 200	1 700	3 600	5 100	5 400	17 000
	Diagnosis achieved	1 228 (102)	1 373 (81)				2 601
	Treatment achieved	1 147 (96)	1 243 243 (73)				2 390
China	Target	10 540	18 520	31 710	44 900	52 270	15 7940
	Diagnosis achieved	14 636 (138)	18 246 (99)				32 882
	Treatment achieved	8 965 (85)	13 525 (74)				22 490
India	Target	53 940	65 390	86 070	11 0210	124 050	439 660
	Diagnosis achieved	58 347 (108)	66 255 (101)				124 602
	Treatment achieved	46 569 (86)	56 569 (87)				103 138
Indonesia	Target	4 200	6 400	14 200	20 500	21 900	67 200
	Diagnosis achieved	9 038 (215)	11 463 (179)				20 501
	Treatment achieved	4 194 (100)	5 531 (86)				9 725
Myanmar	Target	2 700	3 600	7 000	9 700	10 100	33 100
	Diagnosis achieved	3 479 (129)	3 205 (89)				6 684
	Treatment achieved	2 650 (98)	2 892 (80)				5 542
Nigeria	Target	1 900	3 800	10 700	16 300	17 600	50 300
	Diagnosis achieved	2 275 (120)	2 384 (63)				4 659
	Treatment achieved	1 895 (100)	1975 (52)				3 870

Country		2018	2019	2020	2021	2022	Cumulative 2018–2022
		Cases / target achieved (%)	Cases / target achieved (%)	Cases / target achieved (%)	Cases / target achieved (%)	Cases / target achieved (%)	
Pakistan	Target	5 220	8 510	14 450	21 380	26 440	76 000
	Diagnosis achieved	3 824 (73)	3 820 (45)				7 644
	Treatment achieved	3 106 (60)	3 004 (35)				6 110
Philippines	Target	7 170	7 500	12 400	16 300	17 300	60 670
	Diagnosis achieved	7 276 (101)	7 492 (100)				14 768
	Treatment achieved	6 125 (85)	6 169 (82)				12 294
Russian Federation	Target	27 014	27 585	29 297	31 390	32 056	147 342
	Diagnosis achieved	27 438 (102)	27 207 (99)				54 645
	Treatment achieved	27 014 (100)	29 547 (107)				56 561
South Africa	Target	9 750	10 050	10 600	10 090	9 190	49 680
	Diagnosis achieved	13 199 (135)	13 005 (129)				26 204
	Treatment achieved	9 558 (98)	8 743 (87)				18 301

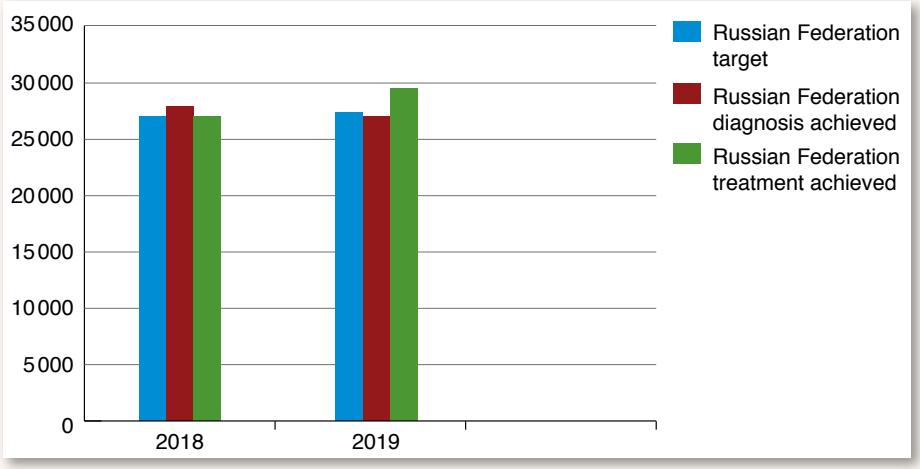
UNHLM: United Nations High-Level Meeting on TB.

Fig. 3.1. *Pakistan UNHLM target achievement and trend for the years 2018 and 2019*



UNHLM: United Nations High-Level Meeting on TB.

Fig. 3.2. *Russian Federation UNHLM target achievement and trend for the years 2018 and 2019*



UNHLM: United Nations High-Level Meeting on TB.

4.1. Countries in context: the 2018 baseline DR-TB cascade of care and other variables

The 10 DR-TB HBCs reviewed represent almost 70% of the global burden of DR-TB. A worldwide assessment of the DR-TB cascade of care in 2015 showed that only 10% of the DR-TB patients in need had a successful treatment outcome. Information from each of the 10 HBCs was analysed to better understand the situation and the complexity of DR-TB. The three gaps measured (diagnosis, enrolment and treatment success) are summary indicators that could be measuring many different variables at the same time. Beyond the targets and the cascade of care, we have analysed and included information from NSPs and a survey on DR-TB, to better understand the DR-TB country circumstances. Precise data on the HBCs concerning the cascade of care for DR-TB are presented in Table 4.1.

The 10 HBC profiles in the cascade of care are summarized in Table 4.2 (precise numbers and proportion of patients remaining in the cascade); relevant graphs are given in Annex 2. Table 4.2 presents and summarizes the proportions of each country on every step of the cascade, to allow quick identification of the main gaps and loss of patients.

Table 4.1. *Cascade of care for DR-TB, with total numbers and proportion in relation to total cases estimated*[a]

Country	DR-TB cases, incidence estimate	Laboratory RR-TB confirmed cases, 2018	Enrolled on treatment, 2018 – absolute numbers	Cases with treatment success according to the 2016 rate[b]	% of cases diagnosed from incidence estimate	% of cases enrolled from incidence estimate	% of cases with treatment success from incidence estimate[b]
Bangla desh	5 900	1 228	1 147	894.66	20.81	19.44	15
China	66 000	14 636	8 965	4 661.80	22.17	13.58	7
India	130 000	58 347	46 569	22 353.12	44.88	35.82	17
Indonesia	24 000	9 038	4 194	2013.12	37.65	17.48	8
Myanmar	11 000	3 479	2 650	2 093.50	31.62	24.09	19
Nigeria	21 000	2 275	1 895	1 459.15	10.83	9.02	7
Pakistan	28 000	3 824	3 106	1987.84	13.65	11.09	7
Philippines	18 000	7 276	6 125	3 552.50	40.42	34.03	20
Russian Federation	41 000	27 438	27 014	14 587.56	66.92	65.89	36
South Africa	11 000	13 199	9 558	5 161.32	119.99	86.89	47

DR-TB: drug-resistant tuberculosis; RR-TB: rifampicin-resistant tuberculosis.
[a] This table and values are those used for the country graphs on the cascade of DR-TB care in Annex 2.
[b] The treatment success is based on the incidence estimate in the 2016 cohort, the most recent rate available at the time of writing this report; that is, treatment success rate is an extrapolation from the 2016 cohort, applied to the 2018 cohorts. Therefore, although it may seem that there have not been significant changes to treatment success rates for more than 15 years, the actual figures from 2018 may well be better than those shown here.

Table 4.2. *Proportion of patients among the 10 DR-TB HBCs achieving the next stage on the cascade of care (highlighting gaps), using baseline 2018 cohorts and treatment outcomes according to 2016 cohorts*

Country	DR-TB cases, incidence estimate	Laboratory confirmation as a % of estimated	Enrolled as a % of diagnosed	Treatment success as a % of enrolled, 2016
Bangladesh	5 900	20.81	93.40	78
China	66 000	22.17	61.25	52
India	130 000	44.88	79.81	48
Indonesia	24 000	37.65	46.40	48
Myanmar	11 000	31.62	76.17	79
Nigeria	21 000	10.83	83.29	77
Pakistan	28 000	13.65	81.22	64
Philippines	18 000	40.42	84.18	58
Russian Federation	41 000	66.92	98.00	54
South Africa	11 000	119.99	72.41	54

DR-TB: drug-resistant tuberculosis; HBC: high burden country.

Following the cascade approach for the year 2018, the proportion of patients successfully treated was still low, and was below 10% in China (7%), Indonesia (8%), Nigeria (7%) and Pakistan (7%) (see Table 4.1). China was low on both diagnosis and treatment success rates. Although Indonesia is apparently substantially increasing its diagnostic capacity, a significant proportion of patients diagnosed are lost during enrolment. In Nigeria and Pakistan, despite good treatment success rates overall, their capacity to diagnose cases is affected by the fact that services are limited and highly centralized. Annex 2 provides graphs for the cascade of care for all 10 HBCs.

South Africa has massively increased local and external funding, with a clear expansion of the capacity for diagnosis and treatment. However, the cascade of care is affected by loss to treatment enrolment and subsequent limited rates of treatment success, although the rate has been improving since 2016 (the rate used as the baseline in this analysis). If support continues during the coming years, the enrolment figures and treatment success rate could increase substantially. The Russian Federation cascade, with high levels of diagnosis and enrolment, is clearly affected by challenging patterns of resistance and possibly loss to follow-up linked to socioeconomic risk factors. Both resistance and loss to follow-up are difficult issues to tackle, needing important support from different angles.

India and the Philippines have demonstrated impressive improvements in both diagnostic capacity and care of those who reach the system. Despite proportions remaining low, important changes are expected if recent improvements in funding, training, decentralization, diagnosis and coordination continue. Bangladesh and Myanmar have high rates of treatment success that offset their limitations in diagnosis.

Despite the initial encouraging results on the UNHLM targets for 2018 and 2019, when we place countries in the context of their actual overall needs and gaps, we are still far from solving the problem in terms of saving lives, reducing disability and suffering, and cutting community transmission. Clearly, there is a need for ambitious targets if we are to achieve

better access to the patients who currently never reach the health systems (diagnosis) and better care of those who have been diagnosed (enrolment and treatment success).

The rest of this section explains the meaning of the different gaps in the cascade of care, and the potential implications for the 10 HBCs.

4.1.1. The diagnosis gap

Investigation of the diagnosis gap helps in understanding the capacity of each country to find the missing DR-TB patients in need of treatment and care. The *numerator* is the total number of cases diagnosed in the country per year and the *denominator* is the number of cases estimated for the country in that same year. The gap between the diagnosed and the estimated represents the potential DR-TB missed from diagnosis. Patients who are not diagnosed can worsen clinically (e.g. have more disability even if they are eventually cured), amplify resistance if managed poorly and continue transmission (eventually dying but after years of community transmission). Extreme examples of the diagnosis gap in the cascade of care are given in Fig. 4.1 for Nigeria and in Fig. 4.2 for South Africa.

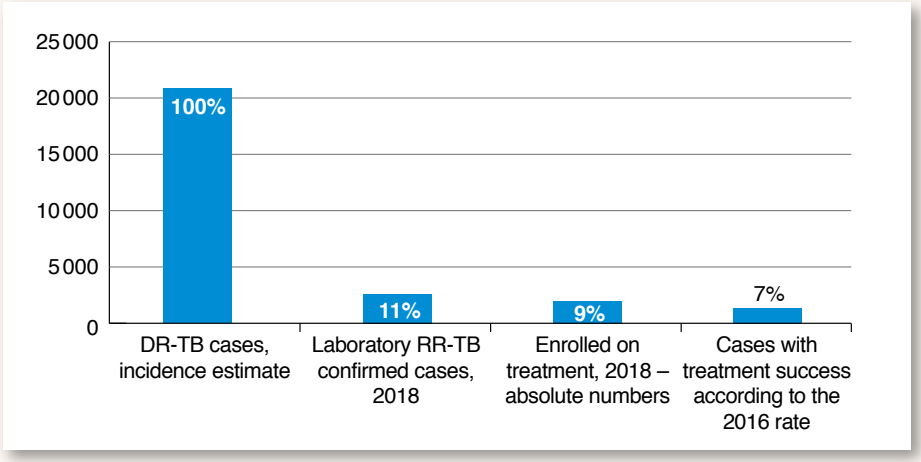
The diagnosis gap measures:

- ✓ the clinical and programmatic capacity of the country and its health system to provide accessible health care for the at-risk population and the country's capacity to detect those cases as presumptive DR-TB patients;
- ✓ the capacity of the laboratory network to cope with the demand and to detect proficiently and timely at least RR-TB; and
- ✓ country and NTP logistics that are essential for streamlining the laboratory workflow and delivery of results (i.e. a referral system for samples, and connectivity tools with peripheral centres or a laboratory information system to facilitate reporting).

The best scenarios in diagnosis for the year 2018 are seen for South Africa (diagnosing 120% of the estimation) and the Russian Federation (diagnosing 67% of the estimation). This reflects an unprecedented investment in DR-TB diagnosis, and improvements in the human resources procedures and capacities for resistance presumption and reference systems. Possible reasons for the excess number of cases diagnosed in South Africa include a downward incidence estimate, diagnosis of incidence and prevalent cases, or other issues related to recording and reporting. Both the Russian Federation and South Africa are upper-middle-income countries, with important national health investment and funding where TB (especially DR-TB) is high on the national health agenda.

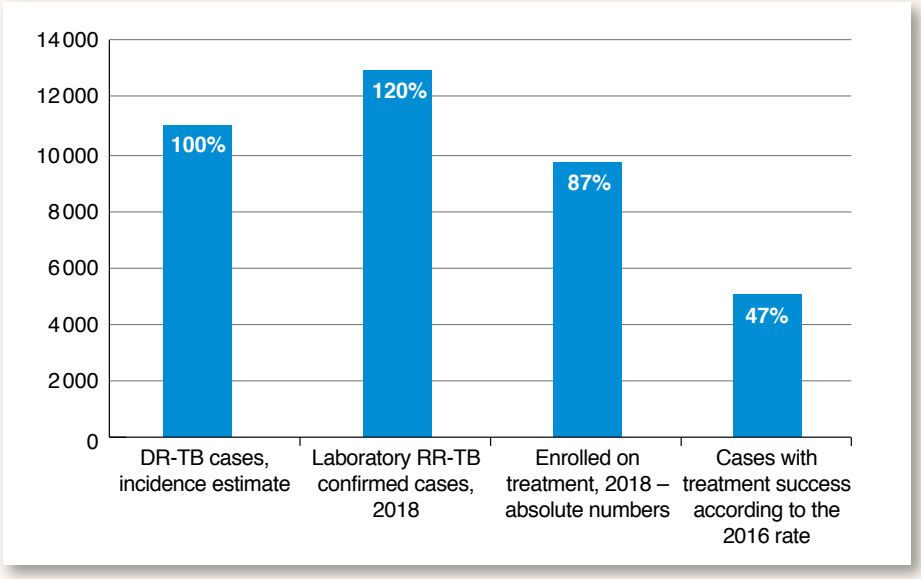
Countries with a lower proportion of DR-TB diagnosis are Nigeria (11%), Pakistan (14%), Bangladesh (21%) and China (22%). All are lower-middle-income countries with important demands on them to strengthen their public health systems and laboratory networks, except for China, which is a upper-middle income country with enormous potential technological, coordination and laboratory capacity. Among the remaining countries, in India, the proportion diagnosed is 45%, which is a great advance on previous years and again reflects the importance of political commitment towards TB diagnosis and of putting bold policies into practice. Similar positive trends were seen in Indonesia and the Philippines, which diagnosed 38% and 40% of estimated DR-TB patients, respectively. Myanmar has remained steady, diagnosing 32% of the estimated DR-TB patients and showing a positive trend in diagnostic capacity.

Fig. 4.1. *Nigeria's DR-TB cascade of care for the year 2018 (treatment success rate estimated from the treatment success rate from 2016, so variations may occur)*



DR-TB: drug-resistant tuberculosis; RR-TB: rifampicin-resistant tuberculosis.

Fig. 4.2. *South Africa's DR-TB cascade of care for the year 2018 (treatment success rate estimated from the treatment success rate from 2016, so variations may occur)*



DR-TB: drug-resistant tuberculosis; RR-TB: rifampicin-resistant tuberculosis.

Reduction of the diagnosis gap entails the creation of strengthened laboratory networks. For low-income or lower-middle-income countries, this can be challenging. However, for those countries with medium or high resources (e.g. China) this gap could be closed more quickly, especially if policies to access vulnerable and risk groups are put in place.

The greatest number of XDR-TB patients was reported by the Russian Federation (5112), followed by India (3400). All other countries reported fewer than 100 cases, except for

South Africa (553) and China (430). Apparently, in 2018 and 2019 there were delays and difficulties in confirming XDR-TB or FQ resistance, which could be fundamental for the current treatment strategies and regimens.

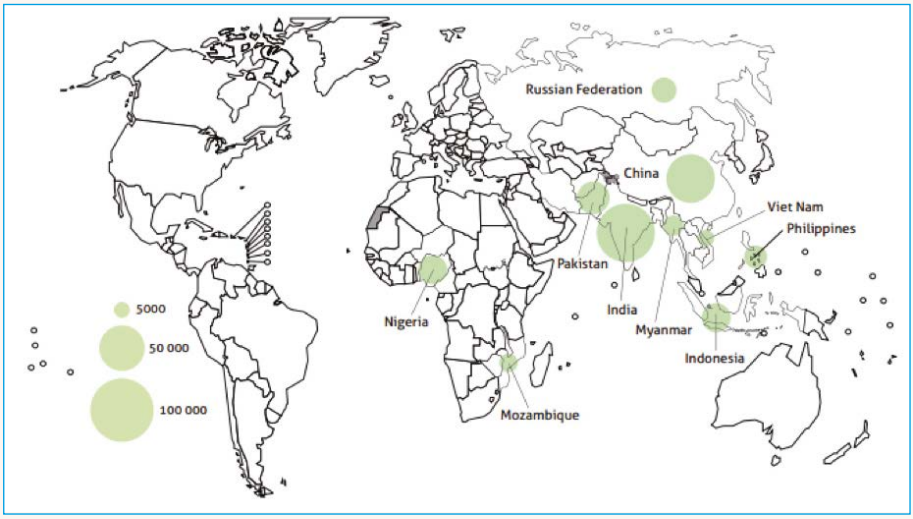
Based on the DR-TB rate (especially RR-TB among new cases), China and the Russian Federation probably have the highest risk of DR-TB community transmission. Thus, if MDR-TB occurs mainly among new cases, strategies for diagnosis need to be strengthened and be different from those in other DR-TB HBCs.

A key gap in diagnosis was the fact that only a limited proportion of children with DR-TB are being diagnosed in the 10 HBCs, reflecting a big gap in this vulnerable population. Solving this issue will need joint clinical and NTP efforts, with expanded diagnosis and laboratory capacity.

4.1.2. The enrolment gap

Investigation of the enrolment gap helps in understanding the capacity of each country and the NTP to make DR-TB treatment available and accessible to patients in need. Fig. 4.3 shows the countries with the highest gaps in DR-TB enrolment during 2019.

Fig. 4.3. *The 10 countries with the largest gap in total numbers between DR-TB diagnosis and treatment initiation in 2018*



DR-TB: drug-resistant tuberculosis.
Source: WHO (2019) *(8)*.

The enrolment gap measures:

- ✓ the overall coordination between laboratories and clinicians in hospitals, health care centres and the private sector, and (to some extent) the efficiency of the NTP;
- ✓ the NTP and health system access to key populations or outreach populations (e.g. those who are poor, are vulnerable or have comorbidities that carry stigma such as addiction and mental health) through health or accessibility policies; and
- ✓ other important secondary variables (e.g. distance to treatment centre, patient payment, poverty, direct and indirect cost, patient-centred policies, and patient empowerment and understanding of decisions).

This gap is probably the one that is most important to improve, because it clearly reflects the quality of the NTP, public–private mix facilities and the country's overall capacity to cope with socioeconomic and clinical barriers that DR-TB patients face. For example, in India, over 80% of people with TB first attend the private sector. There can be substantial diagnostic and notification delays, referral for treatment at the facilities linked to the NTP is not always done, and treatment can be of variable quality depending on the coordination with the NTP. These issues, combined with the absence of drug quality controls, can easily lead to drug resistance.

The countries with the highest enrolments are Bangladesh and the Russian Federation, where only an additional 1% of cases were lost between diagnosis and enrolment. They are followed by Nigeria (2% of cases lost), Pakistan (3% of cases lost) and the Philippines (6% of cases lost). Countries with a lower number of cases diagnosed and an excellent proportion enrolled (e.g. Bangladesh, Nigeria and Pakistan) are probably countries where PMDT remains centralized; that is, they are settings where once patients access care, that care is relatively effective, but not many patients have access to the services. For example, Nigeria has high enrolment and provides SLD DST to 83% of RR-TB patients (second only to the Russian Federation), but this occurs for only a fraction of the overall DR-TB numbers (11% of the estimates).

Decentralization is highly important if countries are to provide patients in need with access to care. However, the complexity of DR-TB management means that, after decentralization, the quality of care may fall. This situation occurred in Pakistan, the Philippines and other countries with big gaps on enrolment that are currently decentralizing care.

In 2018, the greatest proportion of patients lost for treatment after diagnosis, reflecting important deficiencies in patient retention and care, were seen in South Africa (38%), Indonesia (21%), India (19%) and Myanmar (18%).

In Indonesia during 2018, only 46% of the diagnosed RR-TB patients were enrolled on treatment; 4844 diagnosed patients were unable to access treatment, representing a major gap in PMDT (Fig. 4.4). Although the first step should be diagnosis, treatment enrolment needs to run in parallel with diagnosis. Patients lost at this stage are highly vulnerable, and they may receive either no treatment at all or an inappropriate regimen, leading to further resistance and continued community transmission. There is a similar situation in China, even though the total proportions in the cascade losses in enrolment are only 8%. This may seem a small percentage, but for 2018 this equates to only 60% of diagnosed patients receiving treatment, representing 5671 patients who were unable to access treatment. Without further information, we could not explore the reasons for this important gap.

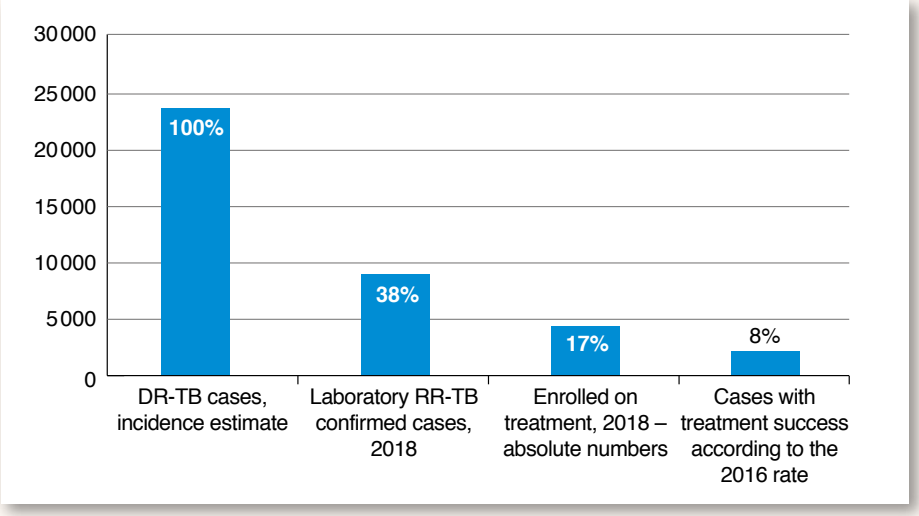
Only two NSPs (of the Philippines and South Africa) considered clear policies and targets to reduce the enrolment gap, which relies particularly on coordination, and decentralization and outreach policies. All such policies could be included in general NTP and health system strengthening. Major barriers to access to care at this point include the role of the private sector, direct or indirect costs for the patient, distance to treatment centres, models of care, and NTP coordination capacity and support.

For countries with long distances between the diagnostic and treatment centres and the place where patients live, or where there is limited universal and free access to primary health care, this gap can be extraordinary challenging. Decentralization of DR-TB management is highly recommended, but requires coordinated clinical training and capacity-building, and supportive supervision with access to case management councils.

As explained above, in addition to lost opportunities, if patients are not enrolled they may receive either no treatment at all or an inappropriate regimen, leading to further resistance and continued community transmission.

According to data, China is at risk of increased DR-TB community transmission, following similar patterns in some Eurasian countries in the past, with access to diagnosis but incomplete access to regimens, clinical monitoring, follow-up or a patient-centred approach.

Fig. 4.4. *Indonesia's DR-TB cascade of care for the year 2018 (treatment success rate estimated from the treatment success rate from 2016, so variations may occur)*



DR-TB: drug-resistant tuberculosis; RR-TB: rifampicin-resistant tuberculosis.

4.1.3. The treatment success gap

Investigation of the treatment success gap helps in understanding the capacity of each country and NTP to effectively manage DR-TB to avoid unnecessary deaths, disability and suffering, while stopping the active transmission of the disease in the community.

The treatment success gap measures:

- ✓ the capacity of the NTP, the laboratory network and clinicians to provide an adequate regimen according to the pattern of resistance;
- ✓ the capacity of the NTP to support the patient along the lengthy process of treatment, providing essential care (e.g. adverse event management) and socioeconomic measures to increase treatment adherence under a framework of patient-centred care;
- ✓ the effectiveness of current DR-TB regimens to cure patients under field conditions;
- ✓ the capacity of the NTP to follow the patient and deal with any problems arising (e.g. side-effects and catastrophic costs) during the long time needed for treatment;
- ✓ laboratory capacity to monitor patients;
- ✓ the lack of socioeconomic, nutritional or psychological support during long-lasting regimens, given that side-effects and low patient empowerment can lead to patients being lost to follow-up; and
- ✓ other variables such as delayed diagnosis; wrong or inappropriate regimen prescriptions (owing to further resistance); other important comorbidities linked to death, side-effects or loss to follow-up; and the potential for severe side-effects linked to death or mild side-effects that, if left unattended, can lead to treatment failure or loss to follow-up.

Changes in treatment success after the UNHLM are difficult to measure in 2020 because the treatment regimens take between 6–9 and 21 months, and there is a lag of 2 years in reports on this indicator. At the time of writing this report, treatment success rates were available for only the 2016 and 2017 patient cohorts. With the implementation of shorter DR-TB regimens and the use of new and repurposed drugs, it is expected that global DR-TB treatment outcomes will improve. However, for the reasons given above, we were unable to evaluate the advantages and disadvantages of the new DR-TB regimens. The same applies to those countries that are implementing a patient-centred approach, although we know that if a programme follows and supports patients through treatment it can cure a higher proportion than a programme that simply introduces an effective regimen.

In most countries, there has been little change in treatment success rates for more than 15 years; therefore, we used the treatment success rates available for the 2016 and 2017 cohorts to calculate the treatment success gap in the cascade of care. Slight changes in the treatment success rate were seen between 2016 and 2017, which could, in part, be attributed to the introduction of short treatment regimens in 2017 in countries such as South Africa. Thus, the treatment success figure is an estimation, and the actual figures from 2018 may well be better than those shown here. For the proposed follow-up and monitoring, this rate could be recalculated in the future.

Table 4.9. *PMDT treatment success rate in the DR-TB cohorts of the 10 HBCs in 2016 and 2017*

	Treatment success rate (%)	
Country	2016	2017
Bangladesh	78	73
China	52	54
India	48	49
Indonesia	48	45
Myanmar	79	79
Nigeria	77	77
Pakistan	64	64
Philippines	58	58
Russian Federation	54	55
South Africa	54	60

DR-TB: drug-resistant tuberculosis; HBC: high burden country; PMDT: programmatic management of drug-resistant tuberculosis.

The highest DR-TB treatment success rates in 2016 were seen in Myanmar (79%), Bangladesh (78%), Nigeria (77%) and Pakistan (64%). Apart from relatively good treatment success rates, all these countries have a low overall DR-TB capacity and centralized DR-TB services. However, if these countries expand their services and the number of patients increases, the rate of treatment success could reduce, unless the expansion is properly funded and quality assured.

Usually, when diagnostic capacity is maximized and countries decentralize care, this is not rapidly followed by an increase in human resources and funding; rather, the quality of care is often reduced, leading to a fall in the overall treatment success rates. Diagnostic and

treatment capacities (including availability of trained and motivated human resources) should increase in parallel.

The countries with the lowest treatment success rates in 2016 were India and Indonesia (both at 48%), followed by China (52%), and the Russian Federation and South Africa (both at 54%). The Philippines is decentralizing but is apparently managing to maintain and increase its historical rates, with a 58% treatment success rate.

The Russian Federation performed quite well in relation to diagnosis and enrolment indicators, but had a relatively low treatment success rate (54%). This may be related to the extensive patterns of resistance present, and TB being linked to important comorbidities and vulnerable or excluded populations.

South Africa has both a high number of missed cases for enrolment and low treatment success rates. The reasons for this could be mixed clinical and programmatic necessities in relation to high rates of HIV coinfection and wide patterns of resistance, although further studies and analysis are needed. South Africa is, however, a country with a rapid uptake of new drugs and regimens for DR-TB, so it will be interesting to observe and explore future trends in treatment success rates.

A particularly important gap in diagnostic capacity that directly implicates and affects TB outcomes is the detection of at least FQ resistance among RR-TB cases. Such resistance appears to be quickly evolving in all HBCs. The currently recommended shorter DR-TB regimens rely heavily on FQ susceptibility, and therefore require access to the short treatment regimens with resultant lower rates of loss to follow-up. If these regimens are used without DST of SLDs, there is a risk of resistance to bedaquiline (Bdq) developing *(12)*. We found data from only four countries on FQ resistance among those with RR-TB. These issues suggest that it might be best to reduce the use of the longer regimens or reduce the use of linezolid because of its high toxicity profile (it can cause permanent disability and even death from lactic acidosis). The Russian Federation was performing better in terms of DST of SLD by testing 90% of its RR-TB patients, followed by Nigeria (83%), Pakistan (76%), Bangladesh (70%) and India (66%). More information is available in Table 3.2.

Indonesia, Myanmar and the Philippines perform DST of SLDs in less than 30% of RR-TB cases. No data were available for China. According to current guidelines, 100% of RR-TB patients should have access to testing for at least FQ resistance. This area certainly needs to be focused on and DST capacity accelerated. Alternatively, current regimens may need to be reinforced in countries with a high proportion of FQ resistance among RR-TB cases. Such data can be crucial for optimal implementation of the current short regimens.

4.2. Patterns of countries according to DR-TB cascade and 2018 data

All countries are different and merit their own in-depth analysis; however, to better understand and compare the PMDT circumstances in the 10 HBCs, an attempt is made here to group the countries analysed into different patterns based on the information obtained from the cascade of care, NSPs and the survey.

Pattern A – low case detection and low treatment success rate (China):

- ✓ PMDT capacities are restricted to hospital and specialized or private centres; drugs and laboratory capacity are available;
- ✓ China is an upper-middle-income country;
- ✓ case detection is low, with 36% of the diagnosed patients lost to treatment enrolment, and a treatment success rate below 50%; there is probably an important association

of DR-TB with socioeconomically vulnerable populations, and barriers to access to care associated with different insurance systems and private health services; and

- ✓ levels of RR-TB in new cases are high, with an important risk of resistance transmission and resistance amplification in the community.

Pattern B – low case detection and high treatment outcomes (Bangladesh, Myanmar, Nigeria and Pakistan):

- ✓ PMDT is probably limited to special centres and is not able to reach patients out of the main cities, but for those who can access it, the system provides relatively good care and outcomes;
- ✓ all are lower-middle-income countries, with limited national budgets, high dependence on external funding, and low HIV rates (except for Nigeria);
- ✓ all have good enrolment rates, except for Myanmar (where 25% of the diagnosed cases are lost); and
- ✓ there is potential for decentralization and the necessary expansion of laboratory capacity; decentralization might be needed, but if there is no extra funding and coordination during decentralization, the reduction in the quality of the services might lead to a reduction in enrolment and treatment outcomes.

Pattern C – moderate case detection and low treatment outcomes (India, Indonesia and the Philippines):

- ✓ all are growing economies, currently with lower-middle-income status (except Indonesia, which is upper-middle);
- ✓ there is a high political commitment to TB care and control, and these countries are decentralizing PMDT services with diagnosis at 40% of the cases but not yet reaching a cure rate of more than 60%;
- ✓ the private sector has a strong influence and there is still high dependence on external funding (except for India); and
- ✓ losses in patient enrolment are especially high in India and Indonesia.

Pattern D – high case detection and poor treatment outcomes (the Russian Federation and South Africa):

- ✓ both are upper-middle -income countries, with high political commitment and interest in TB care and control; expanding DR-TB services and countrywide laboratory networks, leading to high levels of DR-TB diagnosis; and high levels of HIV among DS-TB and possibly DR-TB patients;
- ✓ South Africa is apparently losing nearly 28% of diagnosed cases to enrolment; thus, there is a need for health system strengthening (including recording and reporting) – low treatment success rates are probably related to programme limitations in delivering services (particularly to people living with HIV or socioeconomically vulnerable populations); and
- ✓ the Russian Federation has excellent treatment enrolment, but faces problems in treatment success owing to expanded patterns of resistance; in addition, HIV coinfection and TB are concentrated in marginalized populations with important comorbidities.

Clearly, some countries have great opportunities and economic capacity for improvement. Political commitment, which was an important focus of the UNHLM, is a problem in countries

where domestic funding is limited or in settings where health is mainly managed in the private sector with low involvement of government authorities.

Table 4.10. *Patterns of the 10 DR-TB HBCs*

		Case detection	
		Low	High
Treatment success	Low	China India Indonesia Philippines	Russian Federation South Africa
	High	Bangladesh Myanmar Nigeria Pakistan	

DR-TB: drug-resistant tuberculosis; HBC: high burden country.

4.3. The uncertainty of FQ resistance among the 10 HBCs

Knowing the susceptibility for at least FQ resistance should be a premise for all RR-TB patients starting a short treatment regimen or any RR-TB regimen. FQ and Bdq are the core drugs for the current short treatment regimen. Among the 10 HBCs, the country with the best quality and most consistent data was Pakistan, which presented high levels of FQ resistance (37%) among RR-TB cases. This resistance pattern can be the result of many variables, such as centralized and limited PMDT services, the strong influence of the private service with no bacteriological diagnosis or use of empirical treatments, unregulated use of FQ for the treatment of respiratory infections and no universal access to care. According to country contacts, there is an increase in FQ resistance in rifampicin-susceptible cases and the potential for rapid development of resistance to Bdq in patients under short treatment regimens. This may also be the case in other HBCs under similar conditions, but we do not have reliable laboratory data on FQ resistance in those countries. Our survey of Bangladesh, India and Nigeria found FQ resistance proportions higher than 20% among RR-TB cases, but there were important uncertainties and missing information for the two countries with the highest level of RR-TB in previously treated cases: China and the Russian Federation. Table 4.11 has information on FQ resistance, but there were inconsistencies between the information obtained from the public domain report (for 2018) and the survey (for 2020).

It is clear from the survey that the capacity of countries to test for FQ resistance in all RR-TB cases is very limited, and that LPA-sl capacity, inherent delays in classic DST (liquid or solid), and the logistics of sample transport and referral of information can jeopardize the implementation of current short treatment regimens.

Table 4.11. *Summary of DR-TB, including FQ resistance, among RR-TB cases*

Country	DR-TB cases, incidence estimate	No. of DR-TB cases – adult, diagnosed[a]	Proportion of DR-TB in new cases (%)	DR-TB in previously treated cases (%)	Proportion of FQ resistance among RR-TB cases (%)[b]	Tested for SLDs resistance among RR-TB cases (total (%))[b]	FQ resistance among MDR/ RR-TB cases (%)
Bangladesh	5 900	1 228	1.5	5	5.6	853 (69.46)	21
China	66 000	14 636	7.1	21	N/A	N/A	N/A
India	130 000	58 347	2.8	14	N/A	38 236 (65.53)	22
Indonesia	24 000	9 038	2.4	13	N/A	2 526 (27.94)	12
Myanmar	11 000	3 479	4.9	20	N/A	927 (26.64)	12
Nigeria	21 000	2 275	4.3	15	N/A	1 895 (83.29)	34
Pakistan	28 000	3 824	4.2	16	37	2 893 (75.65)	37
Philippines	18 000	7 276	1.7	16	6.5	2 095 (28.79)	2
Russian Federation	41 000	27 438	35.0	71	N/A	24 601 (89.66)	N/A
South Africa	11 000	13 199	3.4	7	9.4	7 469 (56.50)	10–15

DR-TB: drug-resistant tuberculosis; FQ: fluoroquinolone; MDR/RR-TB: multidrug-resistant or rifampicin-resistant tuberculosis; N/A: not available; RR-TB: rifampicin-resistant tuberculosis; SLD: second-line drug.

[a] Data gathered by survey in 2020.

[b] Data gathered from sources in the public domain from 2018.

4.4. The UNHLM impact and targets according to country data, NSPs and the PMDT survey

For the first time in decades, TB has achieved the international prominence that, as the most deadly of pathogens, it deserves. DR-TB is the leading pathogen for AMR in the world, in terms of patients' suffering and deaths. The UNHLM has been a historical step ahead, with the establishment of clear targets for better DR-TB control guiding and supporting patients.

4.4.1. UNHLM targets for the years 2018 and 2019

As mentioned above, the targets set for 2018 were close to what countries were already obtaining. However, over subsequent years, targets have moved closer to the countries' actual burden estimations.

In terms of *diagnosis* during 2018, most HBCs (except for Pakistan) achieved an important advance in terms of diagnosis, with many obtaining numbers beyond the proposed targets (see Table 3.6 and Annex 3). During 2019, most countries remained close to their targets. Indonesia and South Africa exceeded their targets, probably thanks to expanded laboratory capacity. Conversely, Nigeria and Pakistan lagged, achieving only 63% and 45% of their targets, respectively.

In terms of *treatment enrolment* during 2018, yet again most countries (except for Pakistan) were above 85–95%. Nevertheless, large reductions (>25% of the target) between diagnosis and enrolment were seen for China, Indonesia, Myanmar and South Africa. The clearest example is Indonesia, which in 2018 achieved 215% of the diagnosis target (with 9038 DR-TB cases diagnosed), but enrolled only 100% of the target (i.e. 4194 patients). Hence, 4844 patients were not enrolled on treatment, with more patients lost than included. And despite Indonesia meeting its target for enrolment, this cannot be seen as a good performance; rather, it reflects a need for health system strengthening. On the other hand, despite not achieving any of the proposed targets, Pakistan lost less than 14% of diagnosed patients.

For 2019, most countries achieved more than 80% of the enrolment target figure. However, Nigeria and Pakistan again lagged (achieving 52% and 35% of their targets, respectively), probably because of their reduced capacity to diagnose most DR-TB patients.

We are currently at the half-way point in the time frame of the UNHLM declaration and, overall, the trends compared with the targets appear in a positive light. Most HBCs seem to be following a positive trend in diagnosis and DR-TB care improvement. However, circumstances differ widely between countries (as shown by the examples of Indonesia and Pakistan). For a more accurate country analysis, country-specific in-depth detailed reviews are needed.

For a proper trend analysis, it is important to consider not only the UNHLM targets but also the DR-TB cascade of care analysis and other data sources. Countries with highly centralized services and limited laboratory capacity (e.g. Bangladesh, Myanmar, Nigeria and Pakistan) currently have acceptable cure rates, but will find it difficult to meet the UNHLM targets unless they expand their diagnostic and treatment services. Conversely, countries with expanded laboratory and treatment networks and political commitment (demonstrated by increased government funding), such as India and South Africa, are expected to achieve important improvements in the coming years.

Among the limitations of the UNHLM targets, the following should be considered:

- ✓ The achievement of the current targets represents a massive advance in comparison with the past situation; however, because the targets focus only on diagnosis and treatment enrolment, this is not enough – to see the real impact we need to consider the number of patients cured and without post-treatment disability.

- ✓ The UNHLM declaration has a target of 115 000 children to be diagnosed with DR-TB and enrolled on treatment. However, children currently remain a neglected population in regard to both DS-TB and DR-TB, and there are no specific targets (for number of children diagnosed and enrolled on treatment) per country. Without a specific country target, pursuit of the objective can be challenging. In fact, requesting data on DR-TB in children was included in the survey sent out to the 10 HBCs, but provision of such data was limited.

4.5. UNHLM target estimations for the year 2020

For the proposed targets, 2020 was an inflection point year, where the targets were becoming more ambitious and closer to the DR-TB estimations. In fact, the targets for cases diagnosed and enrolled nearly doubled for seven of the 10 HBCs (Bangladesh, China, Indonesia, Myanmar, Nigeria, Pakistan and the Philippines).

To meet the higher targets, significant investment in laboratory networks and PMDT site expansion is necessary. According to the survey, India and South Africa continue with adequate and increasing government contributions. However, most countries remain highly dependent on external funding, which may or may not increase. Overall, patient services are expanding, but much too slowly to achieve the targets, and especially to cope with the actual DR-TB epidemic.

The COVID-19 pandemic has significantly disrupted TB services and health seeking behaviour, making the targets even less achievable for countries (see Section 4.6, below). The survey results suggested that most countries have been able to maintain the treatment delivery of the patients who were already enrolled before the second quarter of 2020. However, after the second quarter of 2020, notification of diagnosis and treatment enrolment of DR-TB patients severely declined, owing to the pandemic itself and to lockdown policies (e.g. fewer health facilities were open for TB diagnosis, human resources and laboratories were diverted to the COVID-19 response, public transportation was lacking or patients were afraid to attend health facilities). In fact, case notification for the first quarter of 2020 had already been affected because of delays and potential limitations in recording and reporting for TB. DR-TB notifications declined by more than 30%, while treatment enrolment may have declined even more (by up to 40% in some settings). Data were not available from China, where the effects on DR-TB have probably been less severe than in the other HBCs.

An increase in both indicators is expected during the third and fourth quarters of 2020 but it is difficult to evaluate given that it may change with successive waves of COVID-19.

Given the COVID-19 pandemic, putting the declaration back on track is going to be a long and challenging road. TB, and in particular DR-TB, is a lens through which disparities and poverty are amplified, with the disease thriving among the poorest and most vulnerable. The COVID-19 pandemic will also hit these populations hard, and will have a detrimental effect on the countries' economies and health systems. Therefore, unless the momentum of the UNHLM is restored, there is likely to be more stigma, more DR-TB transmission, and less human resources and facilities devoted to TB; also, potential TB funds may be diverted to COVID-19.

It is highly probable that only a few of the HBCs will have achieved the 2020 targets, even in the best scenario. Probably, the trends are going to dip in 2020, and this could potentially affect the overall UNHLM targets and objectives for 2021 and beyond.

4.6. COVID-19 pandemic: an unexpected event with disastrous consequences on TB and DR-TB control

The COVID-19 pandemic and the measures needed to control it have had unprecedented and unexpected consequences, not only for the UNHLM DR-TB targets but for overall world-wide TB care and control. The COVID-19 pandemic will fuel the TB epidemic in several ways:

- ✓ SARS-CoV-2 / TB coinfection – greater morbidity and mortality;
- ✓ measures to control the COVID-19 pandemic:
  - – lockdown – TB activities stopped and movement restricted;
  - – diversion of human resources from TB to COVID-19 during the first and subsequent waves;
  - – diversion of laboratory capacity;
  - – deaths of health care workers; and
  - – stock-out of medications because of disruptions to international trade and movement and heavy control of trans-border trade;
- ✓ world economic crisis – COVID-19-related increase in poverty leading to more TB; and
- ✓ modification of patient health seeking behaviour:
  - – people afraid to seek medical care;
  - – additional stigma;
  - – difficulties in transportation during lockdown; and
  - – impoverishment due to the crisis, and difficulties in attending medical appointments and follow-up, or incapacity to deal with direct or indirect costs related to the disease.

During the second and third quarters of 2020, the COVID-19 pandemic meant that most NTPs were forced to stop or reduce their original plans. Restoring capacity and ensuring the continuity of TB services became a focus of NTPs towards the end of 2020.

All countries responding to the survey mentioned COVID-19 as the most important setback against DS-TB and DR-TB control. The immediate consequences most frequently cited were:

- ✓ reduced DR-TB notification – important diversion of Xpert platforms and laboratory network from TB to COVID-19; and
- ✓ a drastic reduction in DR-TB enrolment.

The impact of COVID-19 on treatment outcomes is still difficult to measure. Countries reported that provision of the medication was generally possible. However, the restriction of movement affected patients' access to DR-TB centres of diagnosis and treatment, which created a lack of DOT, limited clinical follow-up and close monitoring, and limited management of side-effects. In addition, human resources were reallocated from TB to COVID-19 services, and the few staff still providing TB services had to deal with more patients, many of whom had not been seen in months. These factors combined to pose great uncertainties for the treatment outcomes of DR-TB patients in at least the 2019 and 2020 cohorts. An increase in loss to follow-up and possibly treatment failures may appear during this period, despite the efforts of countries towards uptake of better tolerated and safer regimens.

COVID-19 has posed a major challenge in almost all countries for the DR-TB cascade of care, compromising each of the stages of the cascade, with decreases in case finding,

treatment enrolment and treatment success. The capacity of the health systems to provide PMDT services may be able to recover in a matter of months (provided that any subsequent COVID-19 waves are prevented or contained), but the health seeking behaviour of patients may take longer to recover. The first wave of COVID-19 alone is going to interrupt the achievement of the 2020 UNHLM DR-TB targets and will probably continue to have an effect long into the future. Detection and treatment of DR-TB patients are going to be significantly affected by the COVID-19 pandemic in each setting, and will depend on the policies used against COVID-19 (i.e. whether those policies complement or eclipse DR-TB control policies). Interpreting data and validating any improvements in the years to come is going to be challenging.

WHO is clearly aware of the reversal of the progress in recent years in TB control and care. The Stop TB Partnership – in collaboration with Imperial College, Avenir Health and Johns Hopkins University – has presented a mathematical model that shows a range of adverse impacts on TB diagnosis, treatment and mortality rates due to the COVID-19 national lockdowns and gradual restoration measures *(13)*. It is estimated that at least 5 years of progress towards TB elimination could be lost.

According to the models, the COVID-19 pandemic could remain a major public health concern globally at least until 2024 *(14)*. Previous and future lockdown measures will place severe limitations on diagnostic, treatment and prevention services, which is likely to increase the annual number of TB cases and deaths over the next 5 years. Moreover, the poorest and most marginalized people across the world, who already suffer the most from TB (especially DR-TB) and other neglected diseases, are therefore also likely to be the most affected by the COVID-19 pandemic and the international economic crisis ahead *(15-17)*.

It is likely that none of the 10 HBCs will achieve the case notification and enrolment targets for 2020. The targets were already difficult, and results are now likely to be even lower than previous years, being highly impacted by the COVID-19 pandemic and its consequences.

While facing the pandemic, there is clear urgency to restore momentum before the DR-TB epidemic and its patients are further neglected.

4.7. Limitation of the analysis and report

No countries were directly visited during the development of this report. Nevertheless, we believe that the data presented (based on WHO reports, NSPs and contact with countries) are accurate. Some details from countries may have been lost through communication problems, or may be unpublished data or inaccessible data. Therefore, the report should be read as an overall generic report and not as a country-specific report.

The analysis is subject to ecological bias, with most of the information used (at least for the baseline) being from the public domain. The objective was not to produce a perfect report, but one that contained a relevant and informative summary of key findings from the 10 HBCs in terms of a situational analysis for 2018, and the achievements against the UNHLM targets for 2018 and 2019. There is potential for interview bias in the survey sent and response bias in the answers given, but consistency of the responses was checked and compared with the contents of other public domain documents.

Among the 10 HBCs, eight participated in the survey (only China and the Russian Federation did not, and some relevant information may have been lost from these two key settings). The findings from the eight HBCs were considered relevant as the basis for improvements, and to bring clarity to the information available in the public domain (in particular, on specific issues such as DR-TB in children and the impact of the COVID-19 pandemic).

Countries were compared using simple and rapid indicators for description and performance. There are many different epidemiological and socioeconomic circumstances acting as drivers of the DR-TB epidemic and its dynamics. Therefore, the comparisons are purely informative – in-depth analysis for each country should be undertaken to ascertain the precise aspects influencing the results presented.

Owing to the limited data available on XDR-TB patients at the country level, a subanalysis of this crucial population was not undertaken but could be considered for further analysis. Given the current limited evidence, the reduced implementation of DR-TB preventive therapy and the difficulties of obtaining country data on it, such therapy was also omitted from the analysis. Similarly, it was not possible to measure the capacity of access to key populations for DR-TB, as proposed by the End TB Strategy.

Despite the limitations, we believe that, overall, it was useful to monitor the milestones towards the UNHLM DR-TB targets since 2018 and establish a baseline for future comparison. Also, despite the COVID-19 pandemic, it was helpful to orient policies and stimulate public health actions towards the pursuit of the objectives signed by the head of the governments in 2018 at the UNHLM.

5. POTENTIAL FUTURE ACTIONS

1. The information gathered in this report should result in an immediate call to action, to keep and maintain DR-TB activities in countries, despite the COVID-19 pandemic in the HBCs.
2. The findings should be disseminated to raise attention about the need to take clear and bold actions (especially in the current COVID-19 pandemic) to avoid a potential impact on the previous positive trends towards achieving the UNHLM targets in 2020 and beyond. Restoration of the UNHLM spirit and momentum will be crucial for the dynamics of the DR-TB epidemic in the coming years.
3. The Stop TB Partnership should consider establishing a clear target for numbers of children to be diagnosed and treated for DR-TB by country and year, to support the achievement of the global target of 115 000 DR-TB children being diagnosed and enrolled on treatment between 2018 and 2022.
4. Analysis of the DR-TB cascade of care and trends for the 10 HBCs should be considered in 2022 or 2023 for future evaluations of the UNHLM. Progress on reducing the gaps in the cascade can be a crucial indicator.
5. Decentralization of DR-TB services and improvement of laboratory networks are ongoing processes that should be continued and improved in most HBCs, which are not yet able to reach an important proportion of the expected patients.
6. Countries and technical assistance missions should consider, for each country, the reasons behind the potential gaps in the cascade of care (e.g. in diagnosis, enrolment and treatment success). Low levels of enrolment in patients already diagnosed should be a priority area for improvement, followed by mortality, side-effect management, and disability reduction through prompt and correct diagnosis of resistance.
7. Considering the potential high levels of FQ resistance in many countries, access to molecular tests to diagnose such resistance should urgently be accelerated and promoted, to allocate regimens correctly, cure more patients and preserve the effectiveness of current short treatment regimens.
8. The countries that are showing the greatest improvements are generally those that have the greatest political will backing up their efforts. The aforementioned needs should be established and integrated into adequately budgeted NSPs, which are then funded with substantial government contribution.

6. CONCLUSION

Most of the 10 HBCs can be considered to have achieved the UNHLM DR-TB targets for 2018 and 2019. Implementation of the three critical components of the overall UNHLM declaration – funding, action and accountability – has been initiated and is moving in the right direction.

This report presents a general perspective on DR-TB in the 10 HBCs, and will serve as a baseline (2018 – year of the UNHLM, and 2019) for monitoring and evaluation of not only the UNHLM targets for diagnosis and treatment enrolment, but in wider terms the DR-TB cascade of care. This will be useful for different stakeholders (e.g. rGLCs, donors and nongovernmental organizations), decision-makers, health care workers and international technical assistance DR-TB consultants, for overall comparison between countries and within countries over time.

It is clear from the 2018 baseline DR-TB cascade of care that much more is needed, and that most of the DR-TB cases in the 10 HBCs – except the Russian Federation and South Africa – remain without diagnosis and treatment. Even in the settings of those two countries, the treatment enrolment and treatment success rates remain suboptimal. In fact, the 10 HBCs are quite different, and it is not easy to find common patterns or potential policy synergies. We believe that the information gathered in the report, although valuable, should not be taken as a full analysis of any specific country. Despite these limitations (which are typical from ecological analysis and surveys), we believe that this report, with information from three different sources, will be valuable for country and international policy-makers, funders, technical assistants and other relevant actors in DR-TB.

In most of the countries reviewed, the COVID-19 pandemic was reported as representing a significant additional challenge to TB control, with important impacts on DR-TB diagnosis and treatment. The pandemic has seriously jeopardized the achievement of the UNHLM declaration targets and the End TB Strategy goals. This is especially the case given that the consequences of the pandemic are ongoing and the consequences of the earlier lockdowns could continue for 4–5 years owing to difficulties in restoring TB services, effects on the health seeking behaviour of patients, and difficulties in interrupting of TB transmission. In addition to COVID-19, the increasing levels of FQ resistance and the difficulties in obtaining timely susceptibility results can be a challenge to the necessary advance towards a shorter all-oral treatment regimens. Data on DR-TB in children remains scarce, probably reflecting a low level of diagnosis and treatment enrolment in this highly vulnerable population *(18)*.

Even with the improvements reported in 2018 and 2019 in DR-TB after the UNHLM, events in 2020 will clearly result in major setbacks. Targets are going to be missed in 2020 and probably beyond. Governments, NTPs and donors need to be urged to make even greater investment in TB and DR-TB because of the impact of COVID-19. There is a need to revitalize and make visible the problem of DR-TB, to reduce the negative consequences of the COVID-19 pandemic on the DR-TB epidemic.

Compliance with the commitments agreed on in the UNHLM is more important than ever, to cure even more individuals with DR-TB and to reduce community transmission of the most infectious killer and the most prevalent antimicrobial-resistant pathogen.

Box 6.1. Conclusion summary

Most of the 10 DR-TB HBCs can be considered to have achieved the UNHLM DR-TB targets for 2018 and 2019, but all these countries are still far from meeting patients' needs according to the cascade of care.

Increasing levels of FQ resistance and the difficulties in obtaining timely susceptibility results can be a challenge to the necessary advance towards all-oral short treatment regimens in the 10 TB HBCs.

Data on diagnosis and treatment in children are scarce among the 10 HBCs. Unless there is a shift and a new impulse in policies on this vulnerable population, only a fraction of the targets will be achieved.

The COVID-19 pandemic presents a significant additional challenge to TB control, and for DR-TB it jeopardizes the achievement of the UNHLM declaration targets and the End TB Strategy goals.

Revitalizing and making visible the worldwide emergency of DR-TB is now more relevant than ever.

ACKNOWLEDGEMENT OF GLOBAL DRUG INITIATIVE (GDI)

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1. Bangladesh
   WHO: Sabera Sultana, Mya Sapal Ngon, Shah Muhammed Bodrul Hasan
2. China
   NTP: Zhao Yanlin, China NTP Manager
   WHO: Philippe Glaziou
3. India
   NTP: Dr KS Sachdeva, Deputy Director General – Tuberculosis (NTP Manager)
   WHO: Malik Parmar, Avinash Kanchar, Ranjani Ramachandran, Alexandra Vokaty
4. Indonesia
   NTP: Imran Pambudi
   WHO: Shalala Rafayil Ahmadova, Maria Regina Christian, Mikyal Faralina, Charalampos Sismanidis
5. Myanmar
   NTP: Dr Cho Cho San, Dr Thet Naing Oo, Dr Aung Kaung Khant
   WHO: Annemieke Brands, Aye Thida, Mukta Sharma, Partha Pratim Mandal, Fabio Caldas de Mesquita, Kyaw Ko Ko Win
6. Nigeria
   NTP: Dr Victor Babawale, Dr Obioma Cakaniro, Dr Adebola Lawanson,
   WHO: Marek Lalli
7. Pakistan
   NTP: Dr Abdul Ghafoor, Dr Sabira Tahseen
   WHO: Christian Gunneberg
8. Philippines
   NTP: Dr Celine Garfin Dr Mary Rosary Santiago,
9. Russian Federation
   NTP: Dr Irina Vasilyeva
   WHO: Alexei Korobitsyn
10. South Africa
    NTP: Dr Norbert O Ndjeka

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Annex 1. Survey questions: "UNHLM after 2 years: advances and setbacks on DR-TB among the 10 HBCs"

A. DR-TB objectives

1. How many people were diagnosed with DR-TB during 2019 and 2020 (interim if available)? Please sort the answer by *adults* and *children* (<18 years old).

   Adults:

   Children:

2. How many patients were enrolled on DR-TB treatment during 2019 and 2020 (interim if available)? Please sort the answer by adults and children (<18 years old).

   Adults:

   Children:

3. Do you have current figures in DR-TB treatment success rate for the cohorts 2018, 2019 or 2020 (shorter regimens)? Please sort the answer by adults and children (<18 years old).

   Adults:

   Children:

B. Overall PMDT country information

4. Do you think that relevant differences were introduced in the NSP on DR-TB after the UNHLM or in DR-TB practice or PMDT organization? If so, could you kindly describe them with as much detail as possible?
5. After UNHLM, please describe if there were changes in budget or any kind of extra support from the national government or international donors to fund DR-TB activities (diagnosis, patient enrolment or improvement in treatment outcomes).
6. Which ones do you think were the key achievements in your country on DR-TB from 2018–2020?
7. When was the last rGLC monitoring visit to the country? Do you have a report or can we have access to the latest GLC monitoring visit report?
8. Please describe where TB diagnosis is mainly done (hospitals, peripheral medical services, specialized TB centres, private sector, other).
9. Could you briefly describe the country laboratory network? How many GeneXpert devices are available per 100 000 population? How many microscopes per 100 000?
10. Which is the considered current prevalence of FQ resistance among previously treated patients?
11. Is there a functioning LPA network for second-line drugs able to cope with the rifampicin resistance burden? If not, please describe the most recent improvements or obstacles.
12. Are there DR-TB contact tracing activities among children who are contacts of DR-TB patients?
13. Can you describe briefly the country PMDT in terms of hospital based or peripheral centre based? Which is the more frequent model of care?

14. Are there documented medication stock-outs? Do DR-TB patients have to pay out-of-pocket costs for diagnostic tests or medications for DR-TB?
15. Does the country have specific DR-TB guidelines? When were the last updates?
16. Which is the current DR-TB standard regimen?
17. Did key physicians receive any national or international clinical DR-TB training during 2018–2020?
18. Is the private sector a leading force or does it have important influence in the management of DS-TB or DR-TB?
19. Are there DOT or video DOT (VOT) services for DR-TB patients?
20. Which one is the key reason for loss to follow-up: socioeconomic or clinical (or both)? Are there in place socioeconomic policies to support patient adherence? Is there an overall management of side-effects that could be considered as timely or efficient or something to be seriously improved?

C. Barriers in the implementation of the improvements signed by the head of the governments during the UNHLM in 2018

21. Please list any potential administrative barriers (e.g. HR, financing, coordination, other delays or gaps) to the achievements of the UNHLM.
22. Describe specifically and briefly the problems created by the COVID-19 pandemic and its consequences on DR-TB management.

Annex 2. Graphs on countries' DR-TB cascade of care

Treatment success rates for 2018 were estimated from the treatment success rates from 2016, so variations may occur.

Fig. A2.1. *Bangladesh*

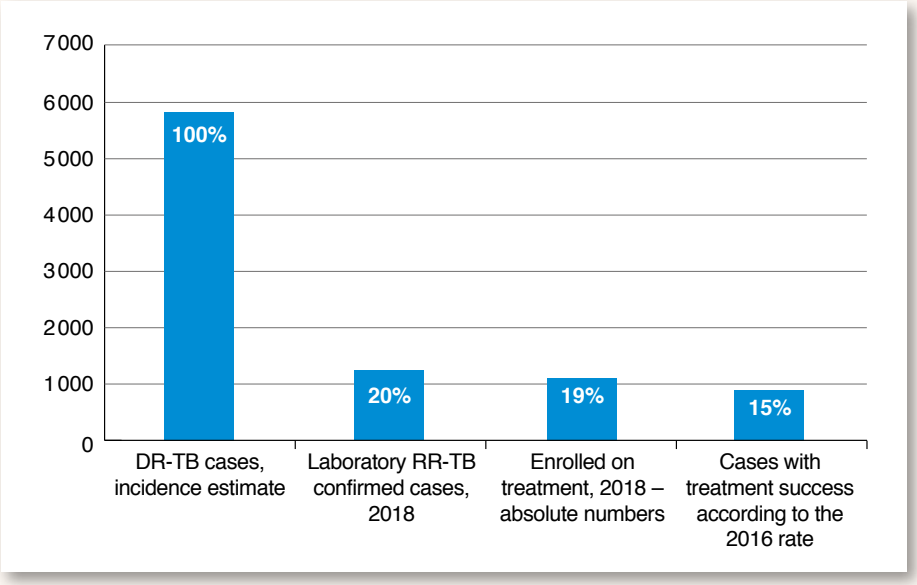


Fig. A2.2. *China*

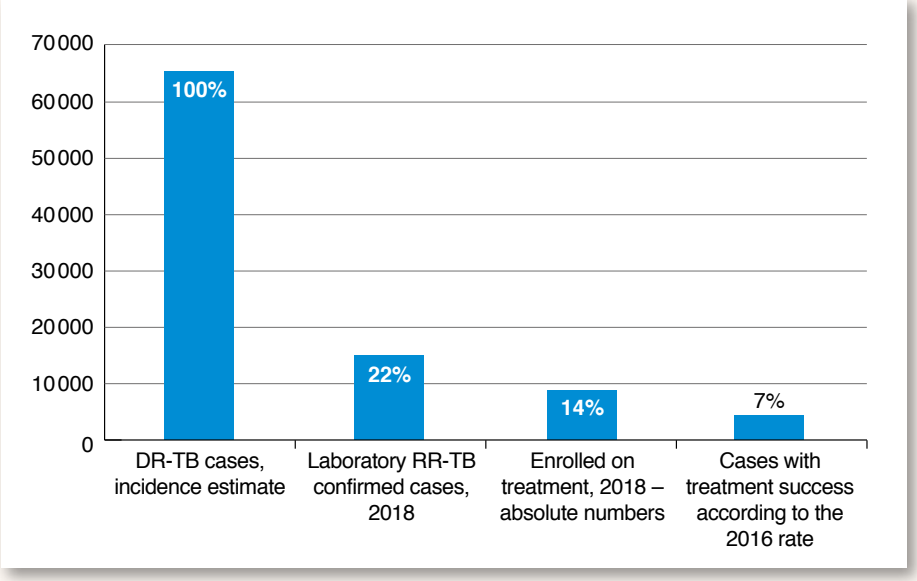


Fig. A2.3 *India*

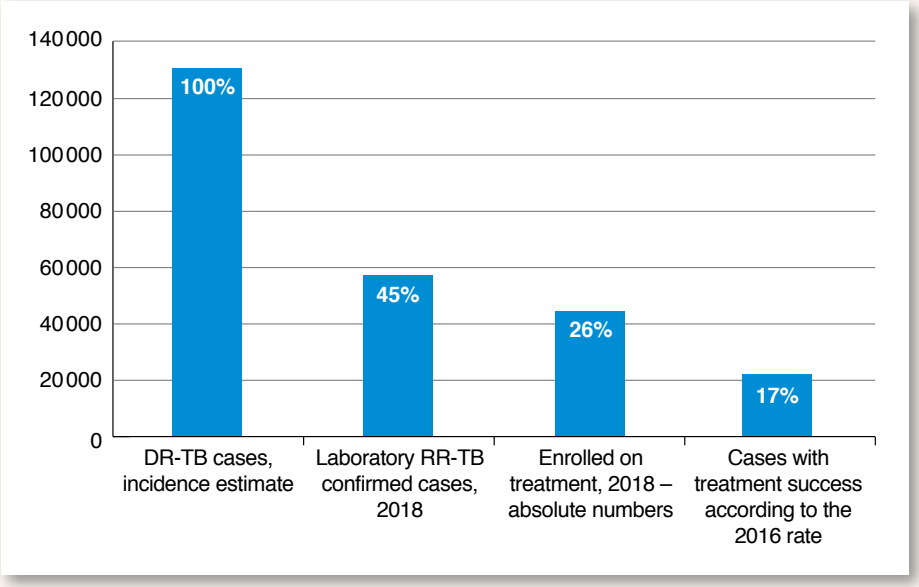


Fig. A2.4 *Indonesia*

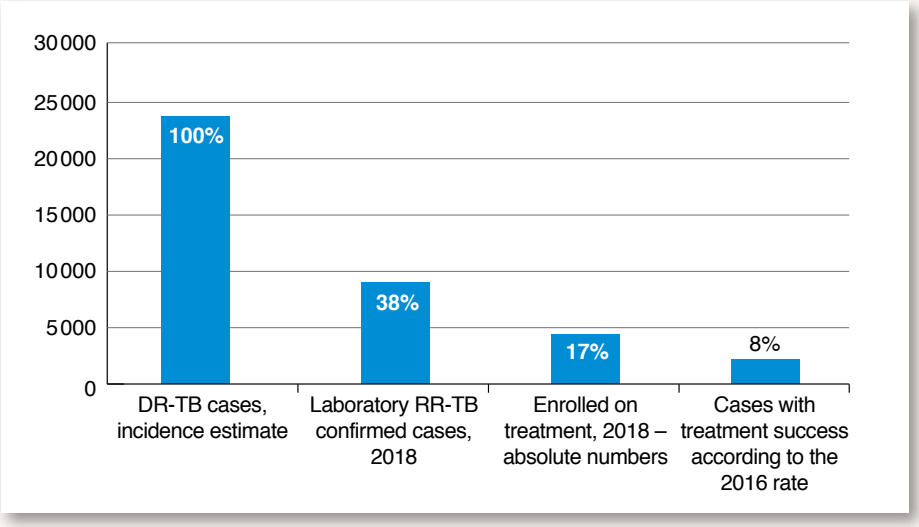


Fig. A2.5 *Myanmar*

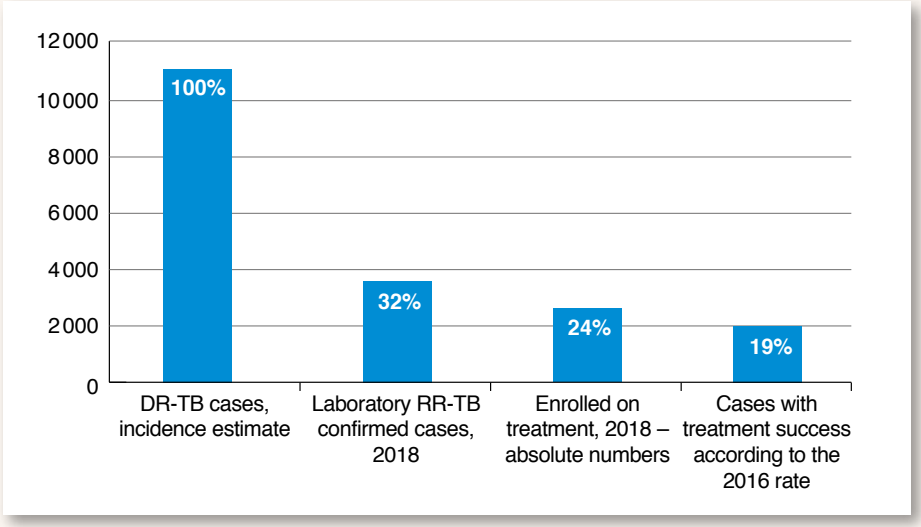


Fig. A2.6 *Nigeria*

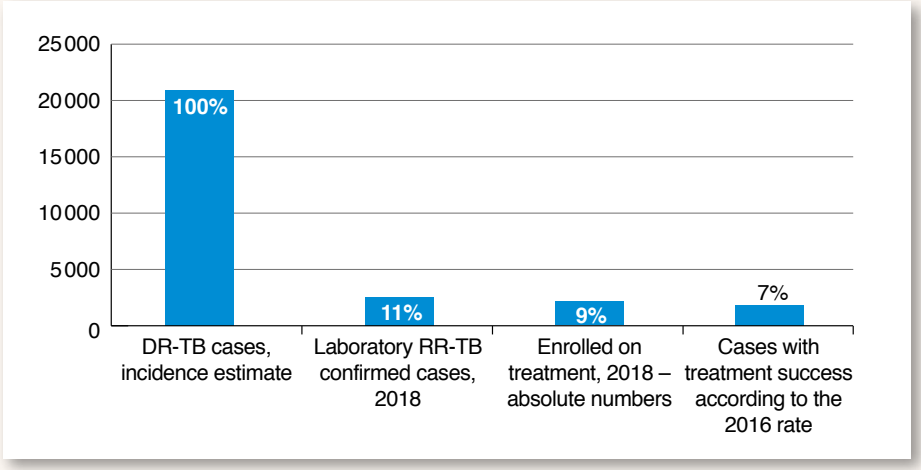


Fig. A2.7 *Pakistan*

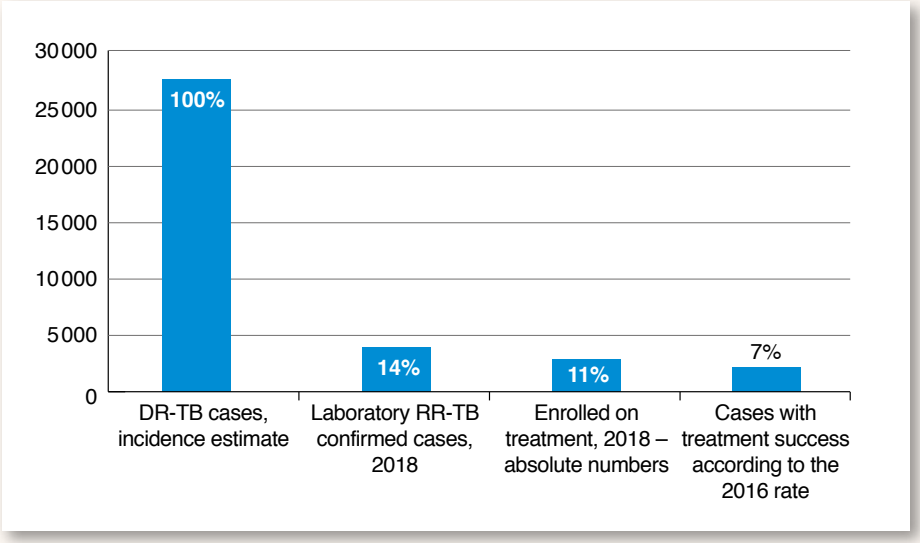


Fig. A2.8 *Philippines*

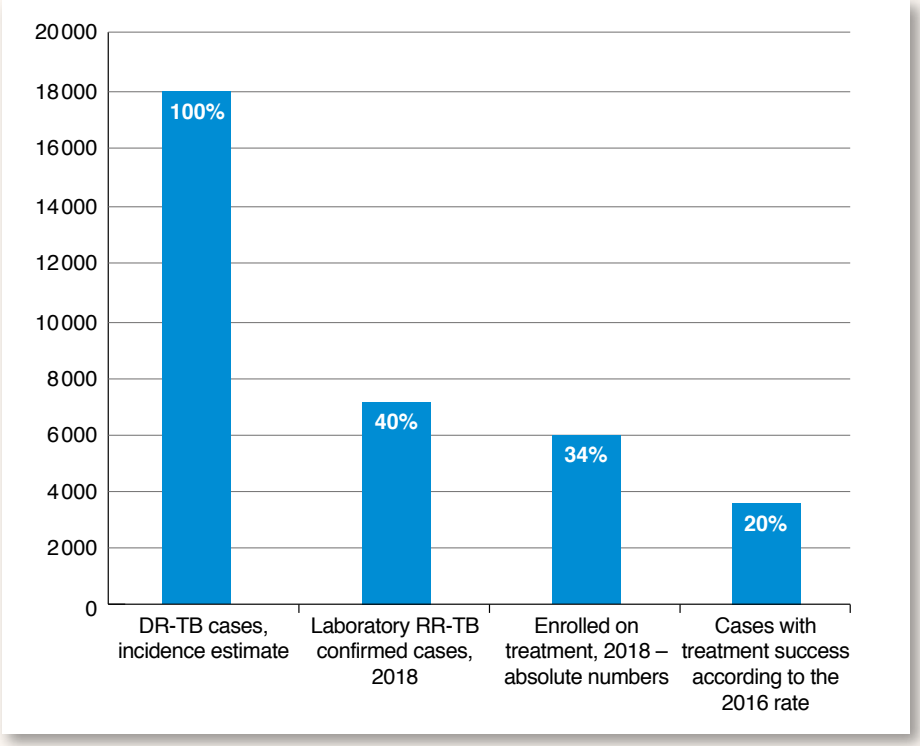


Fig. A2.9 *Russian Federation*

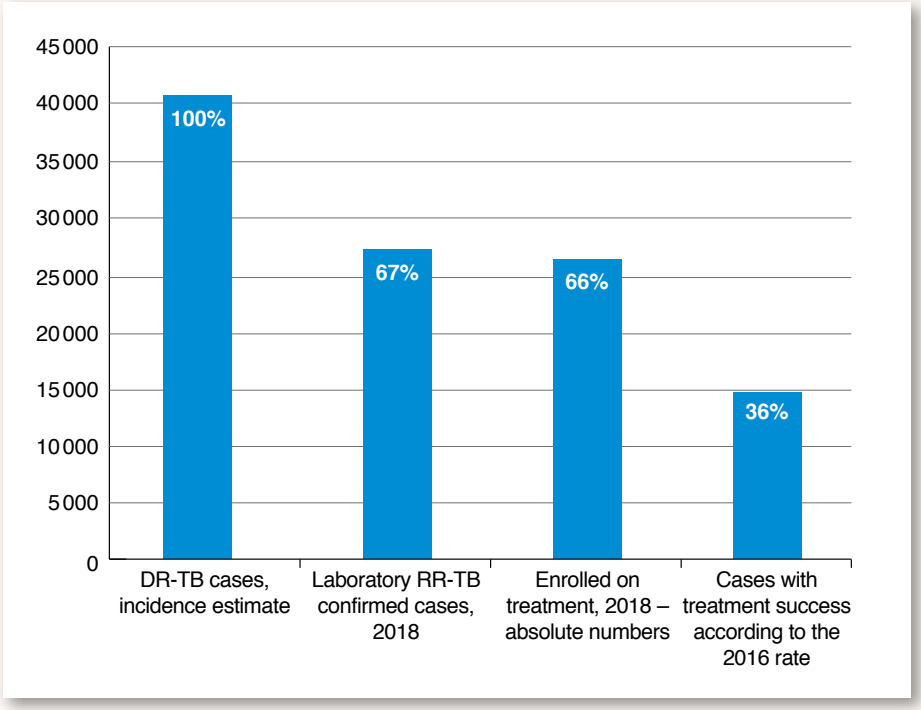
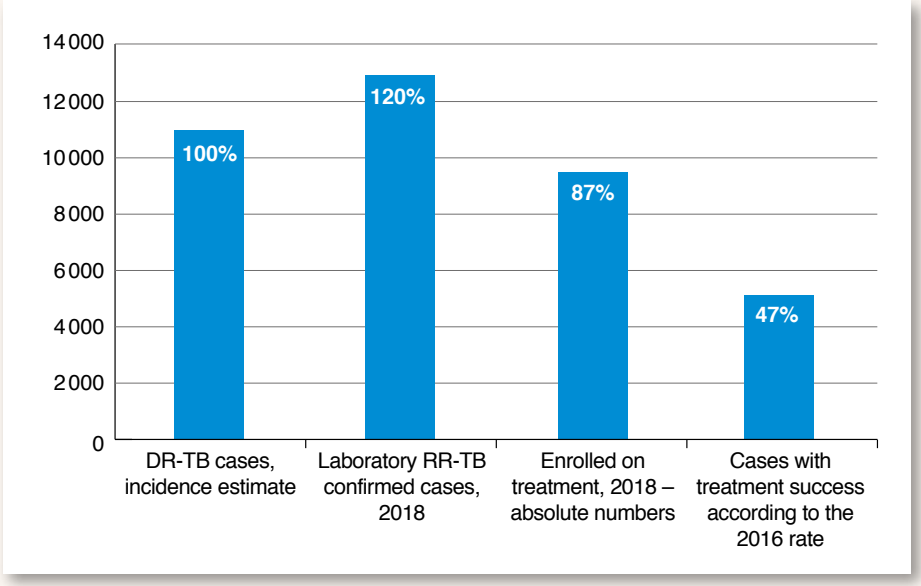


Fig. A2.10 *South Africa*



Annex 3. Level of achievement of the UNHLM targets by country

Fig. A3.1 *Bangladesh*

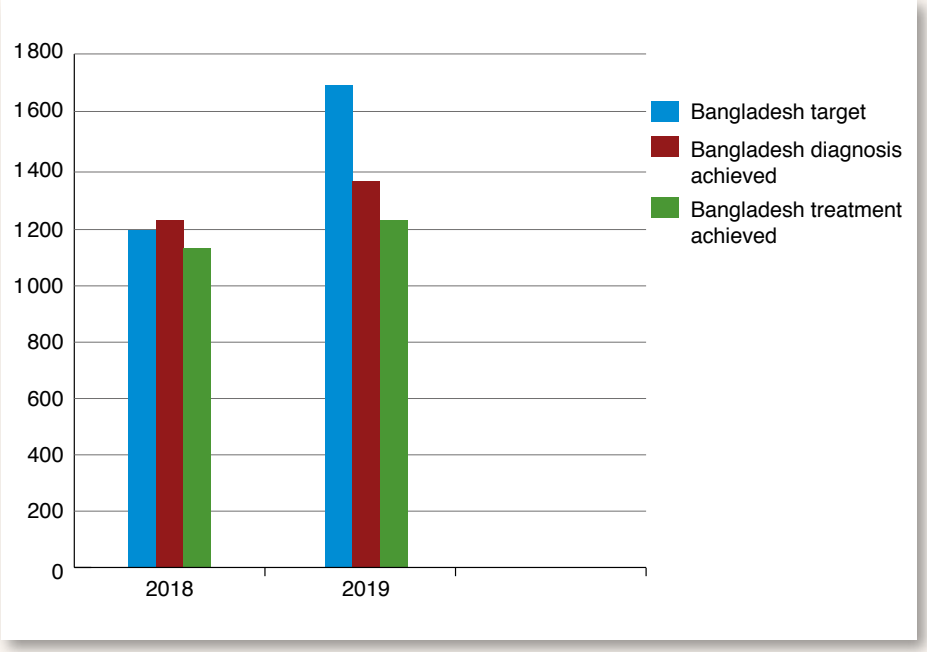


Fig. A3.2 China

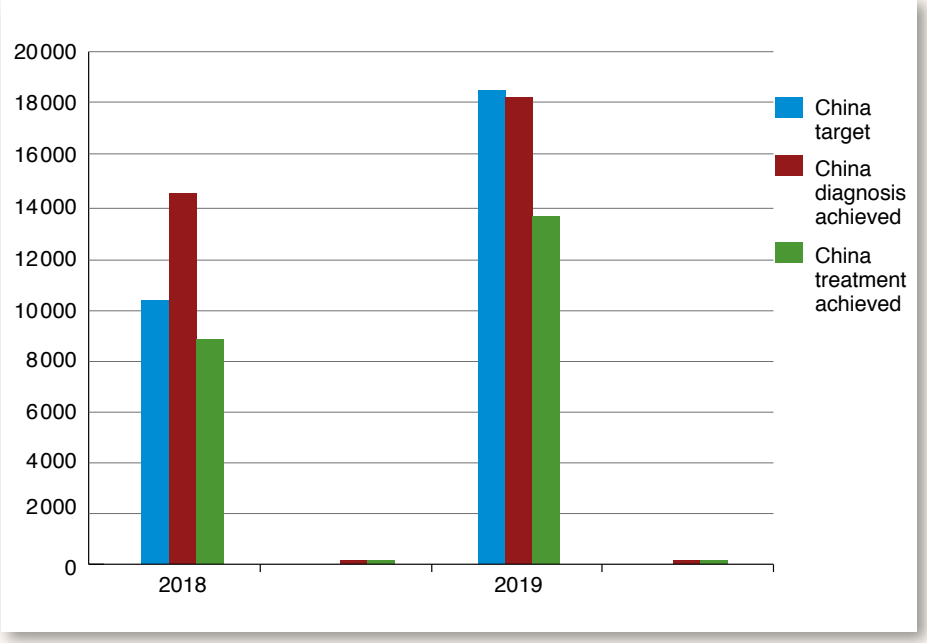


Fig. A3.3 *India*

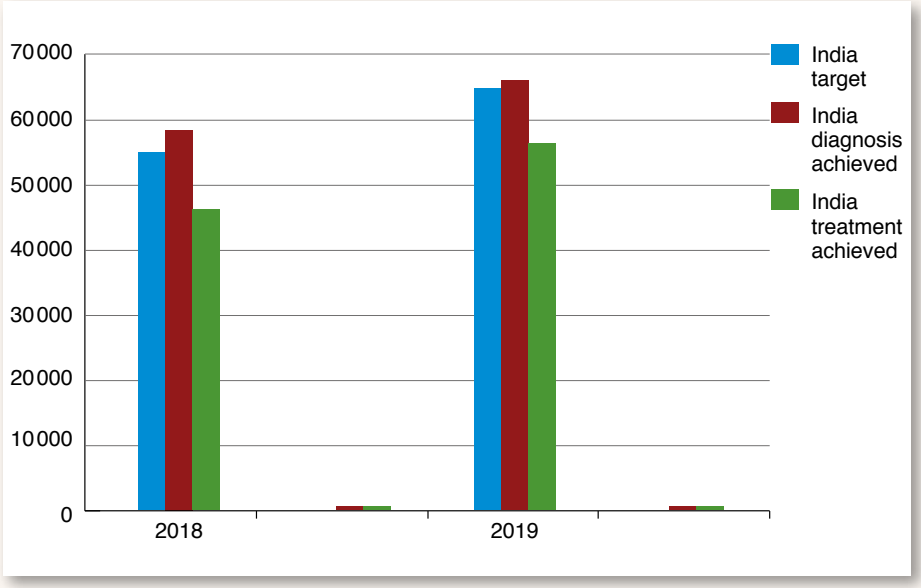


Fig. A3.4 *Indonesia*

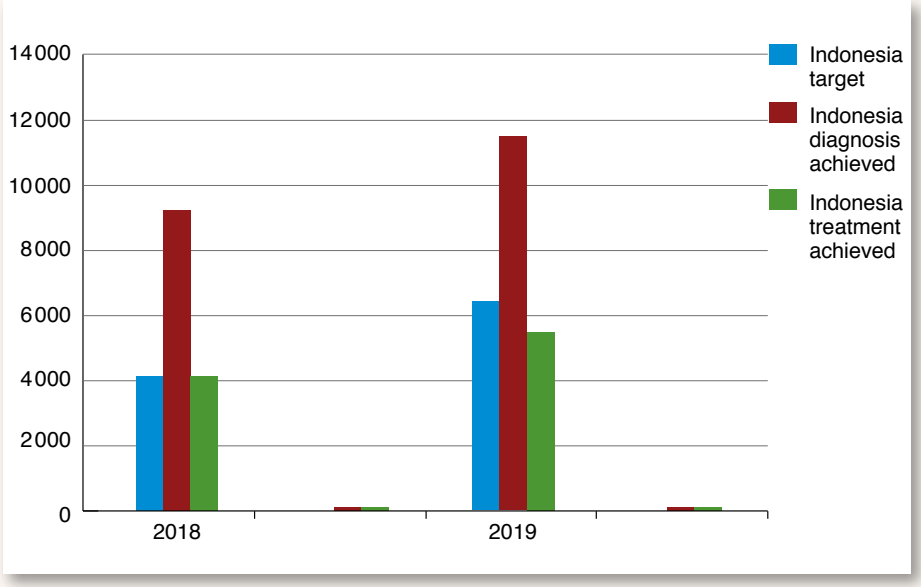


Fig. A3.5 *Myanmar*

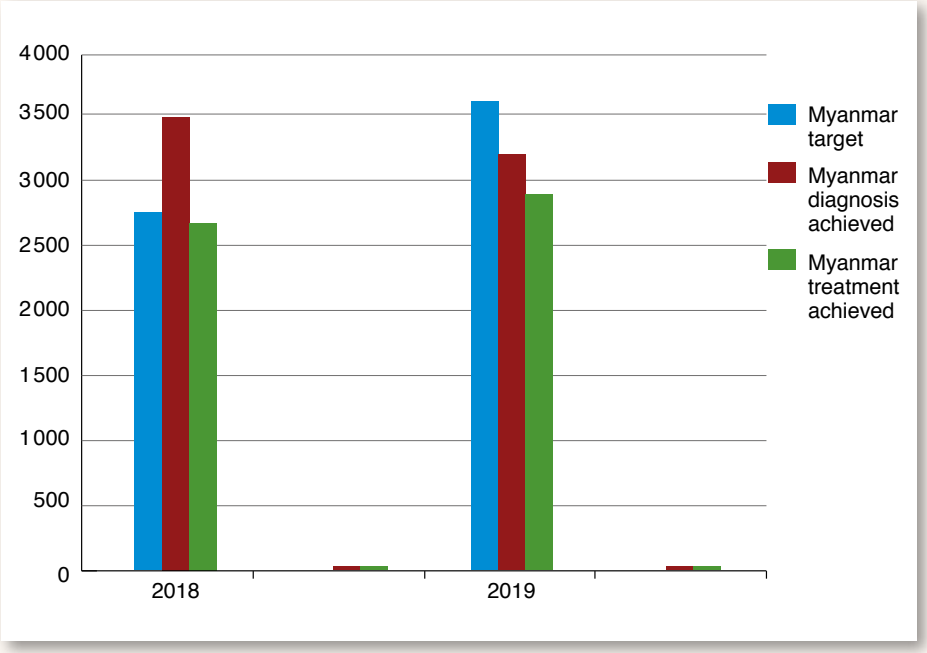


Fig. A3.6 *Nigeria*

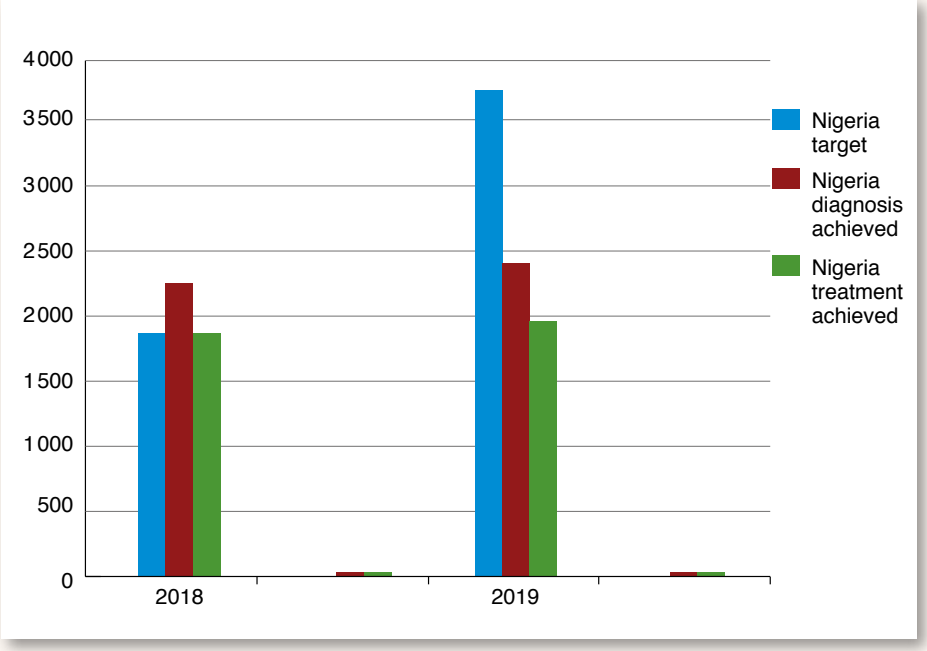


Fig. A3.7 *Pakistan*

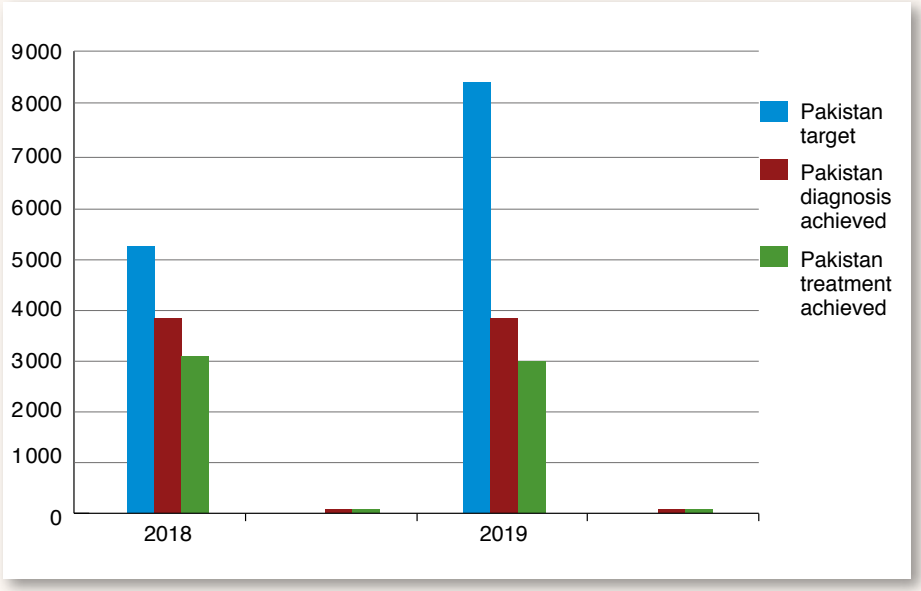


Fig. A3.8 *Philippines*

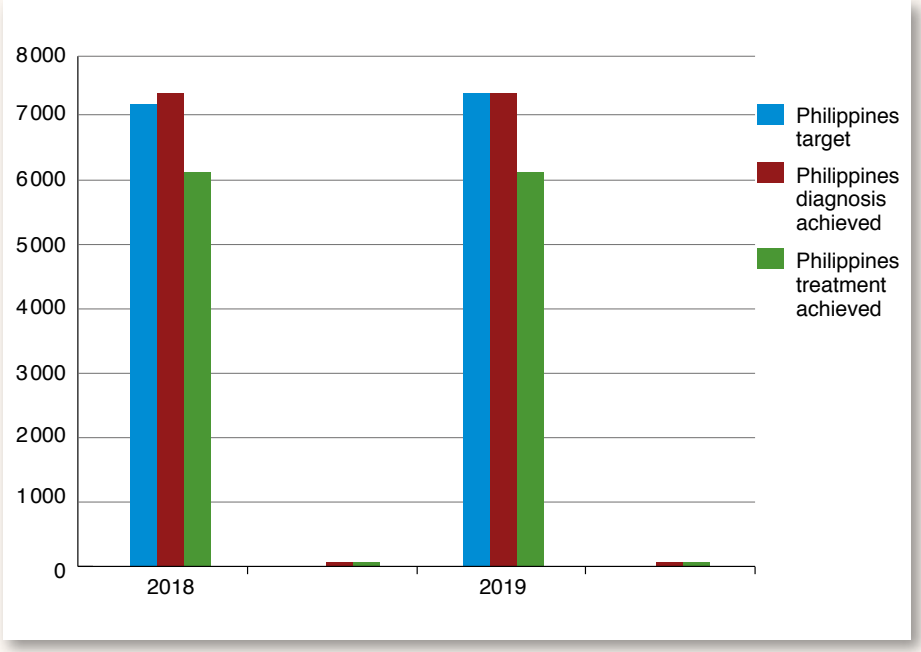


Fig. A3.9 *Russian Federation*

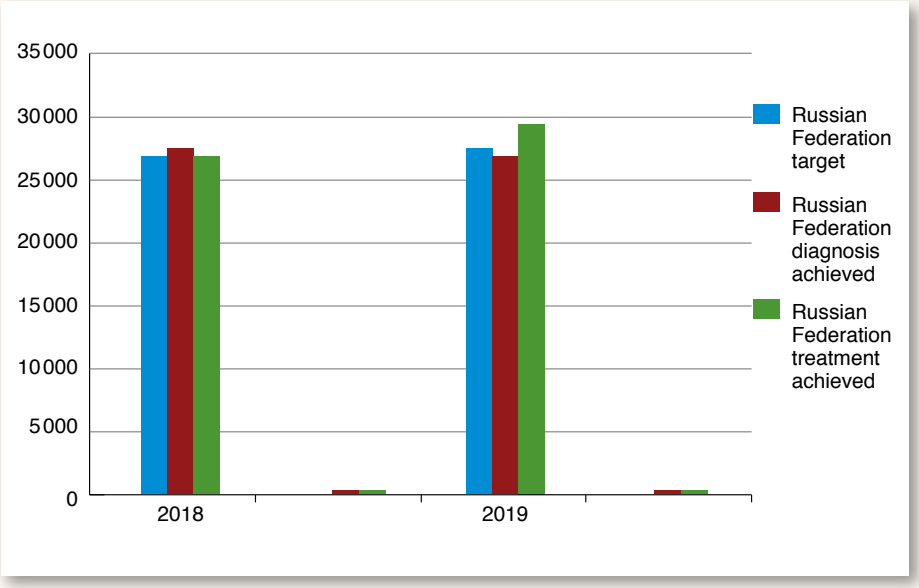
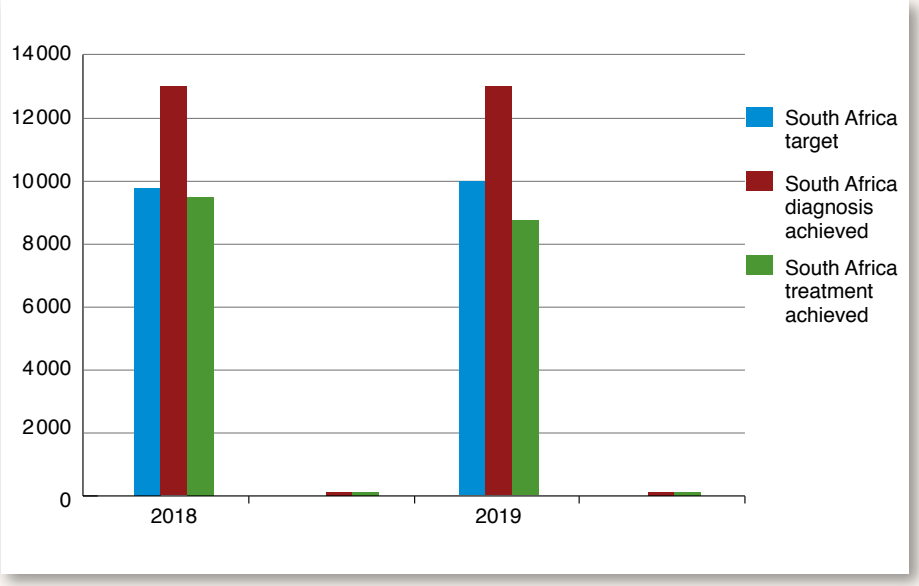


Fig. A3.10 *South Africa*



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Accelerating the response

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