Step Up for TB 2020

Tuberculosis Policies in 37 Countries

A survey of prevention, testing, and treatment policies and practices

MEDECINS SANS FRONTIERES

Stop TB Partnership

MEDECINS SANS FRONTIERES

Médecins Sans Frontières (MSF) is an independent international medical humanitarian organisation that delivers medical care to people affected by armed conflicts, epidemics, natural disasters and exclusion from healthcare. Founded in 1971, MSF has operations in over 70 countries.

MSF has been involved in tuberculosis (TB) care for over 30 years, often working alongside national health authorities to provide treatment in a variety of settings, including conflict zones, urban slums, prisons, refugee camps and rural areas. MSF's first programmes to treat multidrug-resistant TB opened in 1999. MSF has TB treatment projects in 30 countries; it is one of the largest non-governmental providers of treatment for drug-resistant TB.

Largely in response to the inequalities surrounding access to HIV/AIDS treatment between rich and poor countries, MSF launched the Access Campaign in 1999. Its sole purpose has been to push for access to, and the development of, lifesaving and life-prolonging medicines, diagnostics and vaccines for people receiving care from MSF and beyond.

Stop TB Partnership

The Stop TB Partnership is leading the way to a world without TB – a disease that is curable but still kills three people every minute. Founded in 2001, the Partnership's mission is to serve every person who is vulnerable to TB and to ensure that high-quality treatment is available to all who need it.

The Stop TB Partnership's programmes include the Global Drug Facility, which provides quality-assured and affordable TB medicines and diagnostics to countries around the world, and TB REACH, which has helped diagnose and treat over 2 million people with TB by providing small grants to identify and scale up innovative approaches to TB.

The Stop TB Partnership and its nearly 2,000 partners are a collective force that is transforming the fight against TB in more than 110 countries. They include international and technical organisations, government programmes, research and funding agencies, foundations, non-governmental organisations, civil society and community groups, and the private sector.

The Stop TB Partnership operates through a secretariat hosted by the United Nations Office for Project Services (UNOPS) in Geneva, Switzerland, and is governed by a Board that sets strategic direction for the global fight against TB.

Step Up for TB *is dedicated to people affected by TB around the world who are fighting for services, including access to the latest standards in diagnostics and medicines. No one should die of a curable disease for reasons of geography or economic status.*

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EXECUTIVE SUMMARY

Tuberculosis (TB) remains the world's deadliest infectious disease, killing more than 1.4 million people in 2019, despite being curable.[1] But there is hope in the fight against TB. After decades of neglect in implementation, research and development, the TB community has finally seen critical scientific breakthroughs in TB prevention, diagnosis and treatment. At the 2018 United Nations High-Level Meeting on TB (UNHLM), world leaders committed to step up efforts to tackle TB, including rolling out new innovations to diagnose and treat 40 million people with TB disease and 30 million people with latent TB infection (LTBI) by 2022.[2] The availability of new tools and this renewed political commitment have offered a lifeline for people affected by TB and hope for success in the fight against TB.

It is now time for every government to be held accountable for the commitments made and for national policies that will either ensure that critical innovations and tools reach people affected by TB or that leave them behind. This is the 4th edition of this report, which focuses on countries' policies and practices related to 4 key areas of national TB programmes (NTPs): diagnosis, treatment (including models of care), prevention, and medicines procurement policies. Previous editions have shown how the lack of political support and funding hampered the roll-out of new tools.[3] As the COVID-19 pandemic now threatens to set back progress and increase deaths among people with TB, it is even more important that the new opportunities represented by scientific advancements are translated into tangible improvements in the lives of people at risk of TB infection, disease and death.[4]

National policy reforms are the first step toward achieving UNHLM and Sustainable Development Goal (SDG) targets. National policies dictate which healthcare services should be provided to people with signs and symptoms of TB disease; for example, whether they are able to access rapid diagnostic tests, whether they are prescribed the latest and most effective treatments, or whether they are given the psychosocial and material support they need to successfully complete treatment. With science delivering hope in the form of medical tools and other advancements, these policies must be updated rapidly and consistently to keep pace. For their part, the World Health Organization (WHO) should more actively encourage countries to rapidly integrate the most up-to-date science into national policy through WHO guidelines. Doing so can help countries on a path towards meeting not only their UNHLM targets, but also to meeting the Stop TB Partnership's Global Plan to End TB target of an 80% reduction in TB incidence by 2030 (compared to 2015), in line with WHO's End TB Strategy.[5,6]

This *Step Up for TB 2020* report by the Stop TB Partnership and Médecins Sans Frontières (MSF) summarises findings from the 4th survey of national TB policies in the *Step Up for TB* series.[3] This edition presents data on 37 high-burden countries (representing 77% of the global estimated TB incident cases),[1] assessing the extent to which national policies align with international best practices based on WHO guidelines and the latest scientific research. It also reports on some of the barriers to policy adoption and implementation identified by NTPs, although it does not attempt to portray the level of implementation across all policies featured. It offers an insight into the ambitions of governments around the world regarding the care they aim to provide. These ambitions are considered in the context of countries' global commitments and progress in implementation, as reported by WHO.

The results are clear. Survey findings of key diagnosis, treatment, prevention and medicines procurement policies show that too few countries are consistently stepping up to update national policies in a timely manner following the issuance of new WHO guidelines and recommendations. As a result, the products of innovation take far too many years to reach the people who need them, minimising their impact and undermining the delivery of global commitments to reduce unnecessary sickness, deaths and spread of TB.

Diagnosing TB

According to WHO, nearly 1 in 3 people with TB disease is still not diagnosed and notified.[1] Previous editions of this report described the slow roll-out of rapid molecular diagnostics (RMDs) that could help transform the TB response.[3] A decade after these tests first became available, this report finds that more than three-quarters of countries' policies now indicate RMDs as the initial test for all people with symptoms of TB ('RMD-for-All'). However, one-third of responding countries with these policies limit their use to sites which have the RMD installed. Implementation of these policies is also far from comprehensive. As for other essential tests, almost 2 in 3 countries surveyed still do not include in their policies urinary TB lipoarabinomannan (TB LAM) testing for people living with HIV. TB LAM is the only rapid point-of-care TB test available, and there is more than enough evidence of its benefits as a lifesaving point-of-care test.[7,8] Regarding drug susceptibility testing (DST), national policies in the vast majority of countries surveyed indicate universal DST, in line with the 2016 WHO definition.[9] However, updated WHO guidelines on the treatment of drug-resistant TB (DR-TB) require DST to be made available for an expanded set of medicines used in recommended regimens.[10-12] In policy and practice, less than a quarter of countries offer a comprehensive set of DST methods required to ensure people with TB disease are not treated with medicines against which their bacteria are resistant. By stopping short of truly up-to-date diagnostic policies, countries will not be able to reach those people still being missed by health systems, which risks undermining programme effectiveness.

Treating TB

Significant advancements in treatments have given new hope to thousands of people with DR-TB. People with DR-TB previously faced abysmal cure rates of just 57% for multidrug-resistant TB (MDR-TB) and 39% for extensively drug-resistant TB (XDR-TB), as well as months of painful injectables and serious side effects.[1,11,13] As new medicines and treatment options have emerged, WHO guidelines have been updated several times in the last 5 years. More than three-quarters of surveyed countries have revised national policies to include newer, safer, and more effective treatments. Almost all countries now include longer all-oral regimens in their guidelines, and more than half are implementing a modified shorter all-oral DR-TB regimen. Yet alarmingly, almost half of countries report continued use of the most toxic injectable medicines. This report also shows that most countries have yet to adopt more person-centred models of care. In addition to upgrading policies to reflect better regimens, governments must overcome treatment coverage barriers that to date have resulted in only 38% of people with DR-TB started on treatment.[1] With several new treatments expected to come to market in the coming years, national governments must strengthen systems for rapid policy adoption and bringing such innovations to scale.

Preventing TB

TB prevention finally emerged as a priority area through the UNHLM, a major step forward after previous editions of this report highlighted critical neglect of the prevention agenda.[2,3] Since 2017, WHO guidelines on who should receive TB preventive treatment (TPT) have expanded significantly to include all those at heightened risk of TB disease. Science has delivered shorter, more effective TPT regimens, but many countries continue to rely on longer regimens. As this report shows, the majority of national policies still do not include HIV-negative household contacts of all age groups among those who should be systematically provided with TPT. Additionally, almost half of the countries surveyed do not have any high-risk groups beyond people living with HIV and household contacts eligible for TPT. Many countries' national policies are unclear about testing for LTBI prior to the initiation of TPT in some eligible groups. WHO reports have shown recent significant progress in scaling up TPT for people living with HIV, while considerable coverage gaps persist among household contacts, including those under the age of 5.[1] Now that countries have prioritised TB prevention through their UNHLM commitments, they must rapidly update policies and scale up implementation if they are to have any hope of meeting their targets.

Procuring medicines for TB

The successful implementation of these diagnostic, treatment and prevention policies depends upon governments' ability to reliably procure, import and distribute quality-assured medicines and diagnostics. This report's findings on procurement policies are cause for alarm. Based on survey responses and a desk review, almost all high-burden countries are not aligned with the best practices that would uphold the quality of medicines, stabilise supply and ensure affordability. Insufficient national policies increase the risk of stockouts and of diagnostics and medicines of unknown quality entering national programmes. Not only does this jeopardise the lives of people with TB, it also undermines decades of work to stabilise the fragile market for TB medicines. Addressing the barriers to effective, sustainable domestic procurement often requires legislative changes, and countries should urgently prioritise this area of policy reform.

Discussion

Despite these challenges, the *Step Up for TB 2020* report shows the possibility of swiftly turning existing tools and scientific breakthroughs into policies and practices that have the potential to save lives. As demonstrated in some of the examples presented in this report and in the experience of the ongoing COVID-19 pandemic, rapidly adapting and scaling up services is both critical and achievable, especially when governments are proactive and systems are nimble. The TB community does not yet have the perfect set of tools to end TB, and all people affected by TB must be able to access any new tools that do become available as quickly as possible. The critical question is then: at what pace will countries act in order to turn innovation into policy and practice at scale?

The field of TB has historically lacked innovation in medical tools or policies and practices. But, thankfully, this has started to shift. These survey findings indicate that the increased political pressure and attention to TB in recent years has resulted in positive changes.

Countries have been more or less prompt in updating policies regarding innovations in treatment. Countries have been somewhat timely in terms of expanding policies for preventive screenings, but lag behind in expanding access to preventive treatments.

On the other hand, longstanding recommendations to improve diagnosis have moved more slowly. As the entry into care, this is by far the most detrimental gap in the overall response. Another set of enabling policies – policies related to domestic procurement – will determine whether quality of and access to TB medicines will be maintained in the coming years.

It is clear that countries should make relevant policy reforms a central part of their national TB response in order to deliver on their UNHLM commitments and meet Sustainable Development Goals. The range of uptake of 14 key WHO-recommended policies is as low as 15% to as high as 95% among countries surveyed (Executive Summary Dashboard).

The *Step Up for TB 2020* report offers resources to monitor progress and ensure accountability to UNHLM goals. The key policies checklist and dashboard in Annex 1 highlight the successes and opportunities for improvement of national policy responses to TB. The following chapters summarise key findings, present case studies and provide further information. The full *Step Up for TB* dataset, country factsheets and additional advocacy tools can be accessed online.[i]

This report should serve as a call for action. Fundamentally, governments are responsible for updating national policies, and they must now step up for TB. All high-burden countries should ensure full national policy alignment with WHO guidelines by World TB Day 2021, boasting an entirely green dashboard with concrete plans to fully implement every policy. The clock is ticking.

A new way to talk about TB

TB is a continuum between latent TB infection (LTBI) and the deadlier form of active TB disease. In recognition of this, where relevant, this report distinguishes between TB disease and LTBI. This distinction reflects the recent and long-overdue attention by the global TB community to the critical need to prevent progression from latent to active TB through greater testing and treatment of LTBI.

[i] For details visit Stop TB Partnership's website at: www.stoptb.org/suft/, or MSF's website at: www.msfaccess.org/stepupfortb.

Key policies checklist

To meet the commitments of the UNHLM political declaration, every country must adopt and fully implement the following key policies:

DIAGNOSING TB

Rapid molecular TB tests as the initial test for all people who need diagnosis, with specimen referral in place as needed.

Urine-based TB LAM tests for all people living with HIV with signs and symptoms of TB, especially those with advanced HIV or who are critically ill, regardless of CD4 count in both inpatient and outpatient settings.

Comprehensive universal drug susceptibility testing, including: rifampicin and isoniazid resistance for all people starting on treatment; at least fluoroquinolone resistance testing for all people with rifampicin-resistant TB; and drug susceptibility testing methods available in country for rifampicin, isoniazid, fluoroquinolones, bedaquiline, delamanid, linezolid and/or clofazimine, when these drugs are used for routine treatment.

TREATING TB

People-centred TB policies, including decentralised treatment initiation and follow-up at primary healthcare facilities, self-administered therapy as opposed to directly observed therapy where possible, and comprehensive treatment support and adherence counselling.

Injectable-free, all-oral regimens for all children with drug-resistant TB and child-friendly formulations for all.

Injectable-free, all-oral regimens for all eligible people with drug-resistant TB.

Extension beyond 6 months and combination of drug-resistant TB treatments bedaquiline and delamanid allowed.

PREVENTING TB

Shorter TB preventive treatment regimens prioritised for eligible people with latent TB infection, with adequate support to ensure treatment completion.

Systematic screening for active TB disease and testing for latent TB infection among household contacts and provision of TB preventive treatment to those without active TB disease, regardless of age.

ART initiation regardless of CD4 count and universal provision of TB preventive treatment for all people living with HIV.

Inclusive eligibility for TB preventive treatment of vulnerable and at-risk groups.

PROCURING MEDICINES FOR TB

Streamlined regulatory systems and approaches that encourage access to medicines, including mutual recognition between regulatory authorities, domestic registration, collaborative registration procedures and accelerated approval mechanisms.

Full alignment between the national Essential Medicines List and the more recent of either the WHO Essential Medicines List or WHO guidelines, when Essential Medicines List inclusion is a prerequisite for medicines importation, with a plan for regular updates.

Requirement for WHO-prequalified status or approval from an internationally recognised stringent regulatory authority for all TB medicines, whether they are procured from international or domestic manufacturers.

Transparent national tenders, including publication of selection criteria, winning bidder and final price information.

Ability to use international pooled procurement for health products allowed by law, including when domestic funding is used.

EXECUTIVE SUMMARY DASHBOARD

	Diagnosing TB		
Indicator number	1	2	3
Legend: ...: National policies indicate N/A: not applicable Grey: no data **This data consists of two or more individual indicators. "No data" is used when there is "no data" for one or more of the individual indicators considered.*	... a rapid molecular diagnostic (RMD) as the initial test for TB	... urinary TB LAM for routine diagnosis of TB in people living with HIV (PLHIV) and the test is routinely used in both inpatient (IPD) and outpatient (OPD) settings*	... RIF and INH resistance testing for all people starting on treatment; at least FLQ resistance testing for all people with RR-TB; and DST methods available in country for RIF, INH, FLQs, Bdq, Dlm, Lzd, and Cfz, when these medicines are used for routine treatment[a]
Azerbaijan			
Bangladesh			
Belarus			
Brazil			
Cambodia			
CAR			
DPRK			
DRC			
Eswatini			
Ethiopia			
India			
Indonesia			
Kazakhstan			
Kenya			
Kyrgyzstan			
Lesotho			
Liberia			
Malawi			
Mozambique			
Namibia			
Nigeria			
Pakistan			
PNG			
Philippines			
R. Moldova			
Russian Fed.			
Sierra Leone			
South Africa			
Tajikistan			
Thailand			
Uganda			
Ukraine			
UR. Tanzania			
Uzbekistan			
Viet Nam			
Zambia			
Zimbabwe			
Overall uptake (by indicator)	80%	15%	18%

COLUMN LEGEND			
	All presumptive TB	Policy is in place and the test is routinely implemented	All policies in place & DST methods available
	Only risk groups	Policy is in place, but the test is only implemented in IPD settings	All policies at least partially in place and DST methods at least partially available
	NO	There is no policy or the test is not implemented in IPD or OPD settings	One or more policies not in place and/or DST methods not available

(a) Abbreviations: rifampicin (RIF), isoniazid (INH), fluoroquinolone (FLQ), rifampicin-resistant TB (RR-TB), bedaquiline (Bdq), delamanid (Dlm), linezolid (Lzd), clofazamine (Cfz).

	Treating TB and Models of Care			
Indicator number	4	5	6	7
Legend: ...: National policies indicate N/A: not applicable Grey: no data **This data consists of two or more individual indicators. "No data" is used when there is "no data" for one or more of the individual indicators considered.*	... decentralised DR-TB treatment to primary health care (PHC) facility and at home[b]*	... routine use of injectable-free regimens for children with uncomplicated DR-TB	... use of a modified shorter all-oral regimen for eligible adults with DR-TB, either for routine use or operational research[c]	... no limitation to the routine[d], combined use of Bdq and Dlm[e] beyond 6 months*
Azerbaijan				
Bangladesh				
Belarus				
Brazil				N/A [f]
Cambodia				
CAR				N/A [f]
DPRK				
DRC				
Eswatini				
Ethiopia				
India				
Indonesia				
Kazakhstan				
Kenya				
Kyrgyzstan				
Lesotho				
Liberia				
Malawi				
Mozambique				
Namibia				
Nigeria				
Pakistan				
PNG				
Philippines				
R. Moldova				
Russian Fed.				N/A [f]
Sierra Leone				
South Africa				
Tajikistan				
Thailand				
Uganda				
Ukraine				
UR. Tanzania				
Uzbekistan				
Viet Nam				N/A [f]
Zambia				
Zimbabwe				
Overall uptake (by indicator)	22%	72%	61%	20%

COLUMN LEGEND				
	DR-TB treatment initiation and follow-up can be done at a PHC facility and medicines can be taken at home (including injections)	YES	YES	Combined use is allowed without time limits or special approval
	One or more of the above criteria are only partially met	NO	NO	Combined use without time limits is not indicated or allowed, or only allowed with special approval
	One or more of the above criteria are not met			

(b) DR-TB treatment initiation and follow-up can be done at a primary health care (PHC) facility and medicines can be taken at home. **(c)** Modifications to the standardised shorter regimen (beyond the two medicine substitutions allowed by WHO) include replacing the injectable with bedaquiline or other modifications. **(d)** This excludes extensions beyond 6 months upon special approval (e.g. consilia or expert groups); it also excludes countries that allow extensions beyond 6 months, but for specific duration (e.g. 36 weeks). **(e)** Combined use of Bdq and Dlm could be limited to certain groups of patients. **(f)** Bdq and/or Dlm are not indicated in the national policies for routine treatment.

EXECUTIVE SUMMARY DASHBOARD

	Preventing TB			
Indicator number	8	9	10	11
Legend: ...: National policies indicate N/A: not applicable Grey: no data **This data consists of two or more individual indicators. "No data" is used when there is "no data" for one or more of the individual indicators considered.*	... a shorter TB preventive treatment (TPT) regimen (3HP, 3RH, 4R or 1HP)[g]	... household contacts of a person with bacteriologically confirmed DS-TB and DR-TB are investigated for signs and symptoms of TB*	... PLHIV are eligible for TPT	... household contacts of a person with bacteriologically confirmed DS-TB are eligible for TPT, regardless of age*
Azerbaijan				
Bangladesh				
Belarus				
Brazil				
Cambodia				
CAR				
DPRK				
DRC				
Eswatini				
Ethiopia				
India				
Indonesia				
Kazakhstan				
Kenya				
Kyrgyzstan				
Lesotho				
Liberia				
Malawi				
Mozambique				
Namibia				
Nigeria				
Pakistan				
PNG				
Philippines				
R. Moldova				
Russian Fed.				
Sierra Leone				
South Africa				
Tajikistan				
Thailand				
Uganda				
Ukraine				
UR. Tanzania				
Uzbekistan				
Viet Nam				
Zambia				
Zimbabwe				
Overall uptake (by indicator)	65%	78%	95%	51%
COLUMN LEGEND	YES	All household contacts are investigated for signs and symptoms of TB	YES	All DS-TB household contacts are eligible for TPT
	NO	Only household contacts of people with DS-TB or of people with DR-TB are investigated, or investigation is limited based on age	NO	Not all DS-TB household contacts are eligible for TPT
		Household contacts are not investigated for signs and symptoms of TB		

(g) 3HP: 3 months rifapentine plus isoniazid given weekly; 3HR: 3 months of rifampicin plus isoniazid given daily; 4R: 4 months of rifampicin given daily; 1HP: 1 month of rifapentine plus isoniazid given daily.

	Procuring Medicines for TB			
Indicator number	12	13	14	
Legend: ...: National policies indicate N/A: not applicable Grey: no data **This data consists of two or more individual indicators. "No data" is used when there is "no data" for one or more of the individual indicators considered.*	Country is enrolled in the WHO Collaborative Registration Procedure (CRP)[h]	Stringent regulatory authority (SRA)[i] approval and/or WHO Prequalification (PQ)[j] required for importation of TB medicines purchased with domestic funding	SRA and/or WHO PQ quality-assured product status required for procurement of locally manufactured TB medicines	**Overall uptake (by country)**
Azerbaijan			N/A [k]	67%
Bangladesh			N/A [k]	46%
Belarus				31%
Brazil				50%
Cambodia				46%
CAR			N/A [k]	33%
DPRK				50%
DRC			N/A [k]	31%
Eswatini			N/A [k]	75%
Ethiopia				42%
India				29%
Indonesia				43%
Kazakhstan				62%
Kenya				43%
Kyrgyzstan			N/A [k]	46%
Lesotho			N/A [k]	54%
Liberia			N/A [k]	62%
Malawi				60%
Mozambique			N/A [k]	50%
Namibia			N/A [k]	55%
Nigeria				71%
Pakistan			N/A [k]	31%
PNG			N/A [k]	33%
Philippines				50%
R. Moldova				71%
Russian Fed.				64%
Sierra Leone			N/A [k]	45%
South Africa				79%
Tajikistan			N/A [k]	58%
Thailand				82%
Uganda			N/A [k]	62%
Ukraine				79%
UR. Tanzania			N/A [k]	55%
Uzbekistan			N/A [k]	54%
Viet Nam				8%
Zambia				77%
Zimbabwe			N/A [k]	92%
Overall uptake (by indicator)	59%	54%	36%	
COLUMN LEGEND	YES NO	YES Only for some medicines NO	YES Only for some medicines NO	

(h) The CRP accelerates registration through timely sharing of medicine dossiers to national medicines regulatory authorities. Data were collected through a desk review. **(i)** For more information about SRAs see hyperlink (WHO definition of SRA on page 356). **(j)** WHO PQ assesses medicines and active pharmaceutical ingredients to ensure they are safe, appropriate and meeting stringent quality standards. **(k)** TB medicines are not locally manufactured, or locally manufactured TB medicines are not procured.

METHODOLOGY

TB Alert, a TB REACH grantee, provides treatment support to persons with TB identified by the private sector.

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Purpose

The *Step Up for TB 2020* report monitors whether national tuberculosis (TB) policies and practices have been adapted to reflect international guidelines. Governments, advocates and TB-affected communities can use this report to measure and compare countries' progress, including towards political commitments made at the United Nations High-Level Meeting on TB (UNHLM) in 2018, and to help identify priority areas for policy change and advocacy.[2] Previously known as the *Out of Step* report, this 4th edition in the series covers a different, larger set of countries and covers additional policies and practices.[3]

Scope

The *Step Up for TB 2020* report presents the results of a survey of countries' national policies and practices related to 4 key areas of national TB programmes (NTPs): diagnosis, treatment (including models of care), prevention, and medicines procurement policies. Responses were received and included from 37 of 43 countries contacted. All of these countries are included on at least one of the World Health Organization's (WHO) lists of TB, multidrug-resistant TB (MDR-TB) and TB/HIV high-burden countries (together, 'high-burden countries').[14] The 37 countries included in this report are home to 77% of the global estimated TB incident cases and 74% of global estimated rifampicin-resistant cases.[1] They are: Azerbaijan, Bangladesh, Belarus, Brazil, Cambodia, Central African Republic, Democratic People's Republic of Korea, Democratic Republic of the Congo, Eswatini, Ethiopia, India, Indonesia, Kazakhstan, Kenya, Kyrgyzstan, Lesotho, Liberia, Malawi, Mozambique, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, Republic of Moldova, Russian Federation, Sierra Leone, South Africa, Tajikistan, Thailand, Uganda, Ukraine, United Republic of Tanzania, Uzbekistan, Viet Nam, Zambia and Zimbabwe.

Questionnaire development and content

The study team for this report developed a semi-structured questionnaire. Questions targeted the adoption of global guidelines into national policies. Global guidelines included in the survey represent a prioritised list of those policies considered crucial for improving outcomes through the adoption of innovations in prevention, diagnosis and treatment. For selected policies, the survey also assessed future plans, bottlenecks for adoption, and implementation levels as reported by survey respondents.

The questionnaire was divided into 5 sections, covering diagnostics, treatment, models of care, prevention and medicines procurement policies. Technical experts within and outside the study team tested the questionnaire. Once finalised, it was translated into French, Portuguese and Russian and cross-checked by bilingual technical experts.

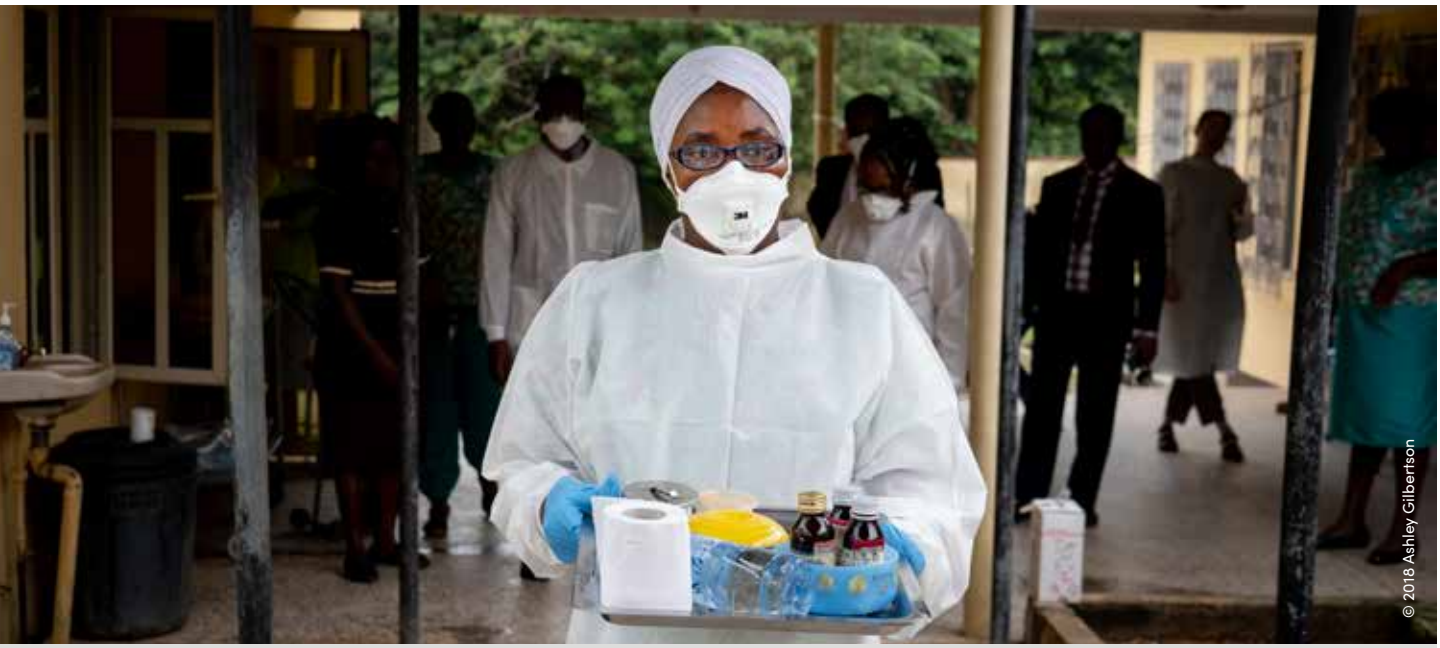
Definitions

International best practice guidelines available as of October 2019 were used as benchmarks, including recommendations found in WHO guidance.

A policy was considered to be adopted by the government at the national level if it was formally legalised through either a published formal written document or a written communication issued and/or circulated by the national government (e.g. Ministry of Health) to national stakeholders with an accompanying statement of guidance or action required.

Only national-level policies in place as of December 2019 were evaluated.[ii] This included guidance issued by NTPs and other official government departments, including HIV programmes and national regulatory authorities. Where implementation status or operational research activities are reported, these were also based on activities happening as of December 2019. Subnational policies or policies implemented by non-governmental actors were not considered national policy unless the NTP had formalised them for the entire country through any of the above criteria.

[ii] For Indonesia and Philippines, policies in place by 9 December 2019 were evaluated. For Ethiopia, policies in place by 16 December 2019 were evaluated. For all other countries, policies in place by 31 December 2019 were evaluated.



Nurse Abosede Serifat Opowu prepares to treat children for drug-resistant tuberculosis at the Government Chest Clinic, Jericho, in Ibadan, Nigeria.

Data collection

Responses to the survey were collected through in-person or telephone interviews with NTP managers or nominated deputies.[iii] Interviews were conducted in English, French, Portuguese or Russian. In 16 countries where Médecins Sans Frontières (MSF) has a project, MSF staff undertook interviews. In the remaining 21 countries, Stop TB Partnership staff or partners led the interviews. All interviewers were trained by the survey team on the questionnaire and methodology, including interpretation of the questions and the national context.

Respondents were informed about the purpose of the survey and formal approval for the publication of responses was sought. Ethical approval was not required as the survey only collected data on national-level policies. Data collection was completed between December 2019 and June 2020.

Additional data on regulatory and procurement policies were collected through a desk review. Data on the WHO Collaborative Registration Procedure (CRP), national Essential Medicines Lists (nEML) and countries that were supported by the Stop TB Partnership Global Drug Facility's (GDF's) paediatric drug-resistant TB (DR-TB) initiative for the introduction of child-friendly formulations are in the public domain.[15-18] Other paediatric DR-TB treatment procurement data were collected through individual communication with NTPs or non-governmental actors. This report also includes country registration information for key quality-assured TB products, which was shared by GDF for the purposes of this report.

[iii] For Cambodia and the Democratic People's Republic of Korea the questionnaire was pre-filled by the study team on the basis of publicly available national guidelines. The pre-filled questionnaire was then shared with the NTP for validation.

Analysis

Once the completed questionnaires were received, they were reviewed for completeness, consistency and quality by MSF and Stop TB Partnership technical staff. They were also cross-checked against available national documents, where possible.

When responses were unclear, incomplete or inconsistent with available national documents, respondents were contacted for further clarification and, where relevant, asked to provide additional evidence. Answers were only excluded if completed survey questionnaires indicated an inconsistent or unclear answer, written evidence from a 2018 or 2019 policy statement did not support the provided answer, and further efforts to clarify with the respondent were unsuccessful.

In this report, survey results are provided for each chapter as both percentages and numbers. If a country did not answer a question or a response was excluded from the analysis, both the numerator and denominator were adjusted.

Each of the following chapters presents a summary of key findings. A dashboard of all key findings and additional findings disaggregated by country can be found in Annex 1. The full survey data set is also available online and includes additional information beyond the data presented in this report.[iv]

Challenges

Towards the end of data collection, the outbreak of the COVID-19 pandemic had a substantial impact on the capacity of NTPs to participate in the study and respond to questions for clarification, resulting in delays to the initial timeline.

In some cases, the study team was not able to secure national policy documents for technical review, especially policies issued by bodies other than the NTP, such as HIV programmes. The nEMLs from Azerbaijan and Sierra Leone were not publicly accessible.

The registration data compiled by GDF is based on information given by suppliers during GDF's last tender beginning 2019, which was then validated by GDF. Where GDF has supported country registrations, additional information has been integrated, but the data have not been systematically updated since early 2019. GDF does not have country registration information for 7 *Step Up for TB* countries (Bangladesh, Central African Republic, Democratic People's Republic of Korea, Lesotho, Papua New Guinea, Russian Federation and Sierra Leone).

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Mainland Hospital, Lagos, Nigeria

[iv] For details visit Stop TB Partnership's website at: www.stoptb.org/suft/, or MSF's website at: www.msfaccess.org/stepupfortb.

DIAGNOSING TB

Boddi Bazar was diagnosed with drug-susceptible tuberculosis in June 2019 from a GeneXpert test. Boddi lives with his family and is seen here during a visit from an MSF outreach team to support his treatment adherence and to refill his medications.

Rapid and accessible TB diagnosis is the entry point to providing treatment and saving lives. In recognition of this, one of the main commitments of the 2018 UNHLM is to provide diagnosis and treatment to 40 million people with TB disease by 2022.[2]

Countries have made notable progress in national diagnostic policy adoption since the 2017 edition of this report.[19] Yet this report finds that many countries are still falling short of adopting international guidelines, and many have yet to implement these policies at scale. More than three-quarters of surveyed countries' national policies indicate the use of rapid molecular diagnostics (RMDs) as the initial test for all people with signs and symptoms of TB, such as Cepheid's Xpert MTB/RIF, Molbio's TrueNat MTB and MTB/RIF, and Eiken Chemical's TB-LAMP. One-third of countries with strong RMD policies still limit these to health facilities where the RMD is physically installed. According to WHO, many countries fall short in scaling up nationwide RMD access, which is reflected in its lower use globally.[1]

Concerningly, this report's findings also show that just over 30% of countries surveyed have lifesaving, urine-based TB lipoarabinomannan (TB LAM) testing for people living with HIV in their policies. Also, more than 80% do not have comprehensive universal drug-susceptibility testing (DST) indicated in their policies and made routinely available.

The result of these national shortcomings is that nearly 1 in 3 people with TB disease is never diagnosed or notified, globally.[1] Still too many who are diagnosed and notified have been tested using slower and less accurate smear microscopy. Unless the policies outlined in this chapter are updated and implemented, millions of people with TB disease will continue to be lost along the diagnostic pathway, and risk being prescribed ineffective treatments or no treatment at all. Millions of others will be diagnosed late, worsening treatment outcomes and spreading disease further.

GRAPHIC 1 Percentage of people with TB diagnosed and notified to WHO in *Step Up for TB* countries (2019)

25% —49%

Central African Republic
Nigeria

50% — 74%

Cambodia
Democratic People's Republic of Korea
Democratic Republic of the Congo
Eswatini
Ethiopia
Indonesia
Kenya
Lesotho
Liberia
Malawi
Namibia
Pakistan
Philippines
South Africa
Tajikistan
United Republic of Tanzania
Uzbekistan
Viet Nam
Zambia
Zimbabwe

75% — 90%

Azerbaijan
Bangladesh
Belarus
Brazil
India
Kyrgyzstan
Papua New Guinea
Republic of Moldova
Sierra Leone
Thailand
Uganda
Ukraine

>90%

Kazakhstan
Russian Federation

Source: World Health Organization, 2020

Key findings

RAPID MOLECULAR DIAGNOSTICS

28/34 (82%) COUNTRIES' policies indicate that a rapid molecular diagnostic is the initial test for all people with signs and symptoms of TB.[v]

17/24 (71%) COUNTRIES' policies do not limit the use of rapid molecular diagnostics to certain facilities, among countries with rapid molecular diagnostics as the initial test for all people with signs and symptoms of TB.

TB LAM

13/37 (35%) COUNTRIES' policies do not require a CD4 count to routinely test people living with HIV who are severely sick or have advanced HIV disease using TB LAM, in line with WHO recommendations; **1/37 (3%)** country policy does require a CD4 count; and **23/37 (62%)** countries do not indicate TB LAM in their policies for routine use.

10/14 (71%) COUNTRIES with policies to routinely test people living with HIV who are severely sick or have advanced HIV disease using TB LAM have implemented this policy and use it in practice.

5/8 (63%) COUNTRIES that have implemented TB LAM for routine use have done so in both inpatient and outpatient settings, while **3/8 (38%)** countries limit routine use of TB LAM to inpatient settings, although the test is also recommended by WHO for outpatients.[vi]

9/13 (69%) COUNTRIES' policies indicate that TB treatment can be initiated based on TB LAM results without a confirmatory test. In the remaining 4 countries, either bacteriological confirmation using another test is required or the policies were not clear.[vii]

DRUG SUSCEPTIBILITY TESTING

31/36 (86%) COUNTRIES' policies indicate rifampicin resistance testing for all people with bacteriologically confirmed TB.

11/36 (31%) COUNTRIES' policies indicate isoniazid resistance testing for all people starting on drug-susceptible TB treatment.

37/37 (100%) COUNTRIES' policies indicate that people with rifampicin-resistant TB are further tested for resistance to at least fluoroquinolones.

10/35 (29%) COUNTRIES have drug susceptibility testing routinely available for the drug-resistant medicines bedaquiline, delamanid, linezolid and/or clofazimine, when these medicines are used in country, according to national TB programmes.

6/33 (18%) COUNTRIES' policies indicate rifampicin and isoniazid resistance for all people starting on treatment; at least fluoroquinolone resistance testing for all people with rifampicin-resistant TB; and drug susceptibility testing methods available in country for rifampicin, isoniazid, fluoroquinolones, bedaquiline, delamanid, linezolid and/or clofazimine, when these drugs are used for routine treatment.

[v] This includes countries with a diagnostic algorithm that screens people with TB symptoms using chest X-rays prior to RMD tests. All countries include Xpert in their RMD policies, either for all people for signs and symptoms of TB disease, or only for selected groups of people. Nigeria's and Thailand's national policies indicate TB-LAMP, and India's policy indicates Truenat, alongside Xpert.

[vi] Among 10 countries that have implemented TB LAM practically, 8 provided a response to the question about the setting in which it is used.

[vii] Among 14 countries that do indicate TB LAM for routine use in their policies, 13 provided a response to the requirement of a bacteriological confirmation.

GRAPHIC 2 Global TB diagnosis gap

Source: World Health Organization, 2020

Rapid molecular diagnostics

A decade after the introduction of the first RMD for TB, finally a majority of responding countries' national policies indicate an RMD as the initial diagnostic test for all people with TB signs and symptoms ('RMD-for-All'). Of the 23 countries surveyed in both the 2017 and 2020 *Step Up for TB* reports, 5 countries that did not have this RMD-for-All policy in place in 2017 have now adopted this best-practice guideline. However, 7/35 (20%) countries restrict RMDs as the initial diagnostic test to certain risk groups, such as those at risk of DR-TB, people living with HIV, children, or people with certain co-morbidities. These countries are now conspicuously out of step (Annex 1). Fortunately, some countries that did not have RMD-for-All policies at the time of the survey have stated that their policies have since been updated to indicate RMD-for-All (for example, India).[viii]

In practice, even in countries with strong policies calling for RMD-for-All, implementation and scale-up of RMDs for routine use remains far too low. Sputum smear microscopy (SSM) remains the most widely used diagnostic tool, with survey respondents reporting on average 10 times as many facilities offering smear microscopy compared to facilities with RMDs.[ix] In 2019, only 28% of all notified incident cases were tested with an RMD according to WHO.[1]

Among the 24 responding countries with RMD-for-All policies, 7 (29%) reported that this policy is limited to only facilities with an RMD installed or facilities that can reach an RMD instrument on the same day.[x] The policies for non-RMD facilities might indicate that only samples from certain risk groups should be referred for RMD testing, which is an unnecessary limitation. Access to RMD testing can be assured through decentralised placement of machines as well as an effective specimen referral system. By not ensuring on-site capacity or routinely transferring samples to locations with RMDs, countries are limiting the impact of these important diagnostic tools.

Countries now have several choices of RMD products, an improvement from the time of the last *Step Up for TB* report in 2017. Cepheid's Xpert MTB/RIF was the first RMD for TB and rifampicin resistance testing, first recommended for use by WHO in 2010 and then recommended as the initial TB test for all adults and children in 2013.[20,21] A competitor's products, Molbio's Truenat MTB and MTB/RIF diagnostic tests, were recommended by WHO in 2020 as initial tests for TB and rifampicin resistance.[22] Since 2016, WHO has recommended that Eiken Chemical's TB-LAMP, a manual molecular assay to detect TB in less than one hour, may be used as an alternative to SSM.[23] According to survey responses, very few countries have included RMDs other than Xpert in national policies. In addition to Xpert, India's policies include Truenat, while Nigeria and Thailand include TB-LAMP in their national policies.[xi]

Key bottlenecks in specimen referral, frequent breakdown of instruments and their modules, slow repair, supply chain interruption, lack of reliable electricity, and the lack of inclusion of private-sector providers continue to hamper scale-up of access to RMDs.[24-29] Price continues to be another barrier, with Xpert MTB/RIF cartridges priced at US$9.98 for the public sector in high-burden countries.[30,31] TB advocates and MSF have called for Cepheid to reduce the price of Xpert cartridges to US$5 per test, inclusive of service and maintenance.[30] This price is based on the estimated cost of manufacturing the cartridge and economies of scale given current volumes. It also better recognizes large public and government subsidies to Cepheid for research, development and selling the cartridge at an initial lower price. Both Molbio's and Cepheid's platforms have applicability beyond TB, and it is essential that manufacturers set affordable prices for instruments, cartridges and maintenance to enable RMD access for all. National policies should be updated accordingly, and manufacturers should make currently available RMD tests more affordable. Furthermore, the need for strengthened research and development to develop an affordable, non-sputum-based, point-of-care, rapid TB diagnostic test remains urgent.[22,32]

[viii] For example, see India's "Rapid response plan to mitigate impact of COVID-19 pandemic on TB epidemic and National TB Elimination Program (NTEP) activities in India-Reg.," available from: https://tbcindia.gov.in/showfile.php?lid=3551

[ix] Country range: 1 to 130 times as many facilities offering SSM compared to RMD, median: 5.

[x] Among 27 countries with policies indicating that an RMD is the initial test for all people with signs and symptoms of TB, answers to a follow-up question could only be accepted from 24 countries.

[xi] Uganda and Zambia do not indicate TB-LAMP in their national policies, but report that TB-LAMP testing is currently routinely available in practice.

Community health screening and testing in Viet Nam

Despite a decade of progress reducing the burden of TB in Viet Nam, a recent national survey revealed that only 57% of people with TB are diagnosed and receive treatment. Recognizing the urgent need to close the gap, the National Strategic Plan includes a strategy to replace smear microscopy with Xpert MTB/RIF and, as an interim measure, require pre-screening with chest X-ray (CXR) where resource constraints impede the scale-up of Xpert MTB/RIF.

However, CXR is also difficult to access in some areas and for hard-to-reach populations. To help address this, the Stop TB Partnership's TB REACH initiative supported a consortium including Interactive Research and Development (IRD) Viet Nam, Friends for International Tuberculosis Relief (FIT) and provincial authorities to implement the Screening With Enhanced diagnostics in Eligible key Population for TB (SWEEP-TB) project. SWEEP-TB provided mobile CXR, TB and LTBI testing and helped demonstrate that mobile radiology can help reduce the TB diagnostic gap.

On the central Vietnamese island of Cu Lao Cham (population: 2,026), SWEEP-TB rolled out a population-wide screening model. Participants underwent symptom screening and CXR followed by Xpert MTB/RIF testing for those with CXR abnormalities, and those without TB disease underwent LTBI testing using tuberculin skin tests (TSTs). People with active TB were linked to care with the NTP, while individuals without TB disease were eligible for LTBI treatment.

Among 1,742 people screened for TB, 10 were diagnosed with TB disease – including 2 people with MDR-TB – and 435 were eligible for TB preventive treatment. Everyone diagnosed with active TB disease and over 90% of those eligible for TB preventive treatment were enrolled onto appropriate treatment.

The project illustrates how replacing smear microscopy with Xpert and using mobile CXR to screen is an effective algorithm for this context.

Ms. Thuy Dong, lead coordinator: "The islanders do not have access to advanced technologies, specialist care or subclinical services. The island doesn't have an X-ray machine. That means that trying to access quality care requires transfer to the mainland, which is expensive at US$20/person. That's why the screening project was so meaningful for the local population! It helped detect the disease early and halt transmission."

A community TB screening event in Cu Lao Cham, Vietnam.

TB LAM

TB is the leading cause of death of people living with HIV, but people living with HIV are more difficult to diagnose with TB disease.[33] However, TB LAM, a urine-based, rapid point-of-care test, offers a simple way to save lives by rapidly detecting TB in people living with HIV.[8,34] WHO first conditionally recommended the use of TB LAM for inpatients in 2015 and updated its policy in 2019 to strongly recommend its use for all people with advanced HIV disease with signs and symptoms of TB, or those who are seriously ill and/or have a low CD4 count.[xii,33] Now, based on growing evidence of its ability to help reduce sickness and death, WHO recommends the test for all people living with HIV with TB symptoms regardless of CD4 count, in both inpatient and outpatient settings.[35] The only commercialised test currently available, Alere Determine LAM, is priced at US$3.50 per test.

Policy adoption, implementation and scale-up of TB LAM has been entirely insufficient. WHO recommends that TB LAM tests should be used routinely for people living with HIV who are severely sick or have advanced HIV disease without requiring a CD4 count. Yet just 13/37 (35%) countries' policies are aligned with this recommendation. One country's policy does require a CD4 count, and the remaining 23 countries do not indicate TB LAM in their policies for routine use. Concerningly, among the 24 countries that do not indicate TB LAM for routine use or that require a CD4 count, 11 are high TB/HIV burden countries. Only 5/22 (23%) responding countries without routine use of TB LAM in national policies reported plans to adopt the policy within the following 12 months, 4 of which are high TB/HIV burden countries. As a result of these shortcomings, people living with HIV will still be unable to access this simple-to-use and affordable TB test in many countries.[36]

Surveyed countries' reasons for not adopting TB LAM policies should serve as a wake-up call for national TB and HIV programmes, donors, technical partners, and advocates alike (Table 1). The most frequently cited reasons for not having TB LAM in national policies are that TB LAM testing is outside of the mandate of NTPs, policy decisions are deferred due to ongoing pilot projects, and lack of funding. In light of new WHO recommendations, NTPs, together with national HIV/AIDS programmes, donors and others providing technical assistance, should address these barriers. Given the evidence that TB LAM can save lives and that more sensitive TB LAM tests are emerging, such as Fujifilm's SILVAMP TB LAM,[37] TB LAM could in the future be used for all people living with HIV. Countries must therefore prioritise TB LAM as a core component of diagnostic services. Otherwise, ensuing delays in TB diagnostic workup and treatment initiation will continue to fail people living with HIV who fall ill with TB disease.[8]

TABLE 1 Reasons for non-adoption of TB LAM in diagnostic policies in 23 countries, as of December 2019

Frequently cited reasons[xiii]	Number of times cited
TB LAM is not within the mandate of the TB programme	5
In-country operational research (OR) or pilots (planning for, ongoing, reviewing results or ongoing OR/pilot-based policy revision)	5
Lack of funding for procurement or implementation	4
National regulations do not allow the use of TB LAM or have delayed the implementation	3
Awaiting a more accurate (sensitivity/specificity) version of TB LAM test	3
TB LAM is not perceived as relevant for the country given the epidemiological context	3

[xii] The WHO recommendation defines a low CD4 count as <200 cells/mm^3 in inpatient settings and <100 cells/mm^3 in outpatient settings.

[xiii] Survey respondents were able to indicate multiple reasons for not having adopted TB LAM in diagnostic policies.

Drug susceptibility testing

Access to universal DST is essential for successfully diagnosing and treating people with DS-TB or DR-TB. The main focus of WHO 'universal DST' recommendations has been that every person with bacteriologically confirmed TB is tested for rifampicin resistance and every person with rifampicin-resistant TB is tested for resistance to at least fluoroquinolones.[9] While the majority of countries (86%) report national policies that indicate all people with bacteriologically confirmed TB are tested for rifampicin resistance, every country should now have this long-standing WHO recommendation included in national policies. Encouragingly, national policies of all countries surveyed indicate DST for fluoroquinolones among people with rifampicin-resistant TB. Nonetheless, implementation remains limited globally. According to WHO, in 2019 only 61% of notified cases were tested for rifampicin resistance.[1] Among those with confirmed rifampicin resistance, 71% were then tested for resistance to fluoroquinolones.[1]

Furthermore, the traditional concept of 'universal DST' as recommended by WHO should be expanded to cover a more comprehensive set of medicines to ensure that people on TB treatment do not receive any medicines to which their TB bacteria are resistant. This is particularly important in light of new WHO treatment guidelines placing greater emphasis on newer medicines and regimens to treat the estimated 1.4 million people who developed isoniazid-resistant TB in 2019, including over 350,000 people whose TB was also rifampicin resistant.[1] A comprehensive universal DST policy should include rifampicin and isoniazid resistance testing for all people starting TB treatment as well as second-line DST for any medicines that are routinely prescribed in country as part of DR-TB treatment regimens, when WHO recommends a DST method.[38] Just 6/33 (18%) responding countries' policies indicate that they are stepping up to a more comprehensive form of universal DST with national policies on rifampicin and isoniazid resistance for all people starting on treatment; at least fluoroquinolone resistance testing for all people with rifampicin-resistant TB; and DST methods available in country for rifampicin, isoniazid, fluoroquinolones, bedaquiline, delamanid, linezolid and/or clofazimine. Those countries are: Azerbaijan, Belarus, Kyrgyzstan, Republic of Moldova, Russian Federation and Tajikistan. With many countries implementing newer regimens (see next chapter, 'Treating TB'), it is unacceptable that so many people with TB disease are being treated without access to appropriate DST.

Comprehensive universal DST must be made a priority in both policy and practice to avoid fueling the DR-TB epidemic. Countries are making progress, and the vast majority of surveyed countries now report the availability of rapid routine second-line DST, such as line probe assay (LPA) technologies. Nonetheless, while currently available RMDs represent a great scientific advancement for TB diagnosis, technologies for rapid DST for medicines such as bedaquiline, delamanid, clofazamine and linezolid are not available yet.[39] For some TB medicines, there is no WHO-recommended method at all.[12,40]

DST remains a complex logistical procedure, often requiring multiple samples and testing methods, specimen transport to central level, and lengthy testing turnaround times. Simpler and more decentralised tests able to detect resistance to multiple medicines at the same time are urgently needed to reduce diagnostic delays and the number of people lost along the diagnostic pathway. There are more tests on the horizon, but in the interim, existing technologies must be made accessible to every person with TB.

Laboratory assistant Iuliia Karbivska is scanning an Xpert MTB/RIF cartridge for use in the GeneXpert machine provided by MSF in the laboratory of the Zhytomyr Regional TB Dispensary in Ukraine.

TREATING TB

Phenduka Mtshali, a patient with drug-resistant tuberculosis, speaks with an MSF field worker at her home in Mbongolwane, a rural area of South Africa's KwaZulu-Natal province which is at the epicentre of South Africa's HIV & TB epidemic.

According to WHO, the treatment success rate for DS-TB is 85%, but just 57% for MDR-TB and 39% for extensively drug-resistant TB (XDR-TB).[1,11] Unsuccessful treatment contributed in part to 1.2 million TB deaths among HIV-negative people and 208,000 deaths among people living with HIV in 2019.[1] If countries are to meet UNHLM goals to treat 40 million people by 2022 – including 3.5 million children with TB disease and 1.5 million people with DR-TB – they will need to step up their efforts to reach people with treatment, provide optimal treatment regimens, and do so in ways that allow people to best fit TB care into their lives.[2,41]

The last decade has delivered significant progress in the development of new, more effective treatments with fewer side effects, fewer pills, and shorter regimens. However, delays integrating new WHO recommendations – including those found in WHO rapid communications – into national policy and practice mean that people with DR-TB continue to miss out on the most effective treatments. Older, outdated and toxic treatment options lead to lower success rates,[12,42,43] threatening the Global Plan to End TB goal of curing 90% of all people diagnosed with TB and DR-TB.[41]

The onus is on governments to ensure all people with TB disease receive optimal treatment. This applies not only to the medicines provided, but also the way in which treatment is delivered. Countries must take steps to better fit treatment into people's lives, in order to reduce the burden on people enrolled in TB care. This includes making treatment more people-centred and available closer to where people live, as well as providing material and psychological support to help manage the physical, social and financial impacts of treatment. These measures are essential to improving treatment completion and success, protecting the rights and dignity of people with TB disease, and averting catastrophic costs.[5] Some key findings from this report indicate positive developments in this direction.

The *Step Up for TB* survey findings also suggest that children with DR-TB in many countries can now benefit from policy changes to eligibility age for treatment with bedaquiline and delamanid. On the other hand, too many countries' policies still indicate unnecessary injectable-containing regimens for children with DR-TB.

While survey results show encouraging signs in countries' adoption of policies related to adult treatments, when it comes to the care of people with TB disease, many are failing to implement innovations in decentralisation of treatment and ensuring an adequate level of treatment support. To reduce unnecessary TB deaths, all countries need to step up and substantially scale up people-centred models of care.

DR-TB treatment regimens

1 Longer all-oral regimen:[xiv] Treatment for MDR-TB/rifampicin-resistant TB (RR-TB) which lasts at least 18 months and is designed using a hierarchy of recommended medicines (preferentially Group A, then B, lastly C),[xv] to include a minimum of 4 TB medicines considered effective based on drug-resistance patterns or patient history.

2 Standardised shorter regimen:[xvi] Treatment for MDR/RR-TB, lasting 9-12 months, which uses a standardised set of medicines, including an injectable agent plus a fluoroquinolone, clofazimine, ethionamide/prothionamide, high-dose isoniazid, pyrazinamide, and ethambutol.

3 Modified shorter all-oral MDR-TB regimen:[xvii] In the context of this report, this definition concerns treatment for MDR/RR-TB with either:

- Modifications to the standardised shorter regimen (beyond the two medicine substitutions allowed by WHO).[xviii] These modifications may include replacing the injectable with bedaquiline, as recommended by WHO in 2020, or other modifications to the standardised shorter regimen recommended by WHO under operational research conditions; or
- A regimen which lasts 6-12 months and is designed using a hierarchy of recommended medicines (preferentially Group A, then B, lastly C), to include a minimum number of TB medicines considered to be effective based on drug-resistance patterns or patient history. This regimen is recommended by WHO under operational research conditions.

4 BPaL regimen: Treatment for people with XDR-TB, intolerant and non-responsive MDR-TB. This regimen lasts 6-9 months and is composed of bedaquiline, pretomanid, and high-dose linezolid. It is currently recommended by WHO for use under operational research conditions.

[xiv] Definitions are based on WHO recommendations as of March 2019, before the shorter all-oral, bedaquiline-containing regimen for MDR/RR-TB was recommended for routine use.

[xv] Group A medicines: bedaquiline, levofloxacin or moxifloxacin and linezolid; Group B medicines: clofazimine and cycloserine or terizidone; Group C: ethambutol, delamanid, pyrazinamide, imipenem-cilastatin or meropenem. Group C also includes the following medicines in select cases: amikacin, streptomycin, ethionamide, prothionamide and *p*-aminosalicylic acid.

[xvi] Definitions are based on WHO recommendations as of March 2019, before the shorter all-oral, bedaquiline-containing regimen for MDR/RR-TB was recommended for routine use.

[xvii] Definitions are based on WHO recommendations as of December 2019, when the shorter all-oral, bedaquiline-containing regimen for MDR/RR-TB was recommended for routine use.

[xviii] The standardised regimen is 4-6 (amikacin/kanamycin/capreomycin)-(moxifloxacin/gatifloxacin/levofloxacin)-(prothionamide/ethionamide)-ethambutol-clofazimine-pyrazinamide- isoniazid (high dose) / 5 (moxifloxacin/gatifloxacin/levofloxacin)-ethambutol-clofazimine-pyrazinamide. The two substitutions allowed by WHO are prothionamide or ethionamide, and moxifloxacin or gemifloxacin or levofloxacin.

Key findings

AMBULATORY CARE

15/36 (42%) COUNTRIES' policies indicate that hospital admission for drug-resistant TB treatment initiation is not required for people who are clinically stable. Still, **14/36 (39%) countries'** policies indicate that hospital admission for drug-resistant TB treatment initiation remains required for certain people, based on criteria other than whether a person is clinically stable.

15/37 (41%) COUNTRIES' policies indicate that drug-resistant TB treatment may be initiated at a primary healthcare facility.

27/36 (75%) COUNTRIES' policies indicate that drug-resistant TB treatment follow-up may be done at a primary healthcare facility.

7/33 (21%) COUNTRIES' policies indicate self-administered therapy as opposed to directly observed therapy for some or all people with drug-susceptible TB.[xix] No country allows selfz-administered therapy for all people with drug-resistant TB, but **3/35 (9%)** countries allow it for some subgroups.

33/37 (89%) COUNTRIES' policies indicate food or transport support is provided to people on drug-resistant TB treatment, of which only **17/33 (52%)** indicate both forms of support are provided to all people on drug-resistant TB treatment.[xx]

OPTIMAL DR-TB TREATMENT FOR CHILDREN

28/37 (76%) COUNTRIES' policies indicate child-friendly second-line medicine formulations for the routine treatment of paediatric drug-resistant TB, and these countries have procured these formulations.[xxi]

32/35 (91%) COUNTRIES' policies indicate that the minimum age for treating children with bedaquiline is 6 years old.[xxii]

29/32 (91%) COUNTRIES' policies indicate that the minimum age for treating children with delamanid is 3 years old.[xxiii]

26/36 (72%) COUNTRIES' policies indicate the routine use of injectable-free, all-oral regimens for children with uncomplicated drug-resistant TB.

OPTIMAL DR-TB TREATMENT FOR ADULTS

29/36 (81%) COUNTRIES have started **(18/29, 62%)** or completed **(11/29, 38%)** implemention of a longer all-oral regimen for the routine treatment of adults with drug-resistant TB.

22/36 (61%) COUNTRIES' policies indicate a modified shorter all-oral regimen for eligible adults with drug-resistant TB for routine use or under operational research. Among these countries, **9/22 (41%)** have started operational research, pilots or implementation for routine use; and **1/22 (5%)** has completed implementation for routine use.

25/37 (67%) COUNTRIES' policies indicate the injectable-containing, standardised shorter regimen for routine treatment of people with DR-TB; a further **3/37 (8%)** countries report using it under operational research or pilot project conditions.

28/37 (76%) COUNTRIES' policies indicate a levofloxacin-containing regimen as the preferred treatment for isoniazid-resistant TB without concomitant rifampicin resistance.

6/35 (17%) and 6/33 (18%) COUNTRIES policies' indicate no limitation of bedaquiline and delamanid use beyond 6 months, respectively.[xxiv]

17/37 (46%) COUNTRIES report still using kanamycin and/or capreomycin in the treatment of drug-resistant TB, against WHO recommendations.

[xix] Self-administered therapy does not include use of adherence tools that require real-time interaction with a healthcare provider, but may include support from family members.

[xx] This includes cash transfers, direct food baskets, vouchers and reimbursement systems.

[xxi] The new paediatric second-line medicine formulation may include one or more of the following: pyrazinamide 150mg dispersible tablet (DT), ethionamide 125mg DT, levofloxacin 100mg DT, moxifloxacin 100mg DT, cycloserine 125mg capsules.

[xxii] Brazil does not indicate bedaquiline in their national policies for routine treatment and Malawi did not provide a response. These countries were not counted in the denominator.

[xxiii] Brazil, Cental African Republic, Russian Federation and Viet Nam do not indicate delamanid in their national policies for routine use, and Malawi did not provide a response. These countries were not counted in the denominator.

[xxiv] Brazil does not indicate bedaquiline in national policies for routine treatment and 1 country was not included in the analysis. These countries were not counted in the denominator for bedaquiline use. Brazil, Central African Republic, Russian Federation, and Viet Nam do not indicate delamanid in their national policies for routine treatment and therefore were not counted in the denominator for delaminid use. Additionally, these findings do not take into account extensions based on consillia approval.

People-centred ambulatory care

Putting people with TB disease at the centre of their treatment is essential to treatment success and one of the most important underlying principles of both the End TB Strategy and the UNHLM.[2,5]

After over 50 years of evidence against the practice, many countries still routinely hospitalise people undergoing TB treatment unnecessarily, particularly those with DR-TB.[19,44] Only 15/36 (42%) countries' policies indicate no requirement for hospital admission for DR-TB treatment initiation of people who are clinically stable. While 14/36 (39%) countries require hospitalisation only for certain people with DR-TB, 7/36 (19%) countries surveyed still require hospitalisation for all. However, person-centred care closer to people's homes is possible, as shown by the 15/37 (41%) countries with policies to initiate DR-TB treatment at primary healthcare facilities (Table 2). It is also encouraging to see more countries (27/36, 75%) with national policies enabling DR-TB treatment follow-up at primary healthcare facilities.

Only 7/33 (21%) countries have national policies that allow self-administered therapy (SAT), as opposed to directly observed therapy (DOT), for some or all people with DS-TB.[xxv] No country allows SAT for all people with DR-TB, but 3/35 (9%) countries have policies that allow SAT for some subgroups. Countries can enable a more person-centred model of care through counselling, digital adherence tools and better medicines delivery models to support treatment completion.[45-48] As countries begin implementing all-oral treatment regimens for DR-TB, such approaches should be implemented more widely. In response to COVID-19, numerous countries have shifted their medicines delivery models to provide multi-month refills closer to home. These countries should recognize the benefits of such person-centred treatment approaches – including SAT with counselling and digital adherence tools – by adopting them in their national policies moving forward.

People with DR-TB require additional support to manage the duration and side effects of treatment, including counselling, nutrition and transport.[5,49] Almost all countries surveyed (33/37, 89%) have national policies that indicate some type of social support (food and/or transport for some or all people with DR-TB). Among them, only 17/33 (52%) indicate both food and transport support for all people on DR-TB treatment. Most countries (32/35, 91%) report major challenges in rolling out these schemes, particularly in relation to funding and implementation (Table 3). Given how critical these interventions are in supporting treatment completion, high-level government support for sufficient budgets and wider reporting of lessons learned from implementation studies are urgently needed.

TABLE 2 Countries decentralising DR-TB treatment initiation to primary healthcare facilities, as of December 2019

Countries
Brazil, Democratic Republic of the Congo, Eswatini, Kazakhstan, Kenya, Kyrgyzstan, Mozambique, Republic of Moldova, Russian Federation, South Africa, Tajikistan, Uganda, Ukraine, United Republic of Tanzania, Zimbabwe

TABLE 3 Challenges in the provision of social support for people with DR-TB in 32 countries, as of December 2019[xxvi]

Frequently cited challenges[xxvii]	Number of times cited
Inconsistent funding or difficulties in releasing funding for social support strategies	22
Implementation challenges, such as distribution of currency, expiry of food supplies, inconsistent reimbursements	14
Poor reporting on the impact of social support service provision	7
Inconsistent availability of a partner to implement social support strategies	6

[xxv] Self-administered therapy does not include use of adherence tools that require real-time interaction with a healthcare provider, but may include support from family members.

[xxvi] Challenges were reported in 32/35 countries that provided a response; 3/35 countries did not report any challenge in the provision of social support.

[xxvii] Survey respondents were able to indicate multiple challenges in the provision of social support for people with DR-TB.

Treating children with DR-TB with child-friendly formulations in Tajikistan

MSF works alongside the NTP in hospitals and TB dispensaries in Dushanbe, Tajikistan and surrounding areas to deliver treatment to children and family members with DR-TB. Children with TB remain a sorely neglected population globally, given that children do not often display obvious symptoms and are difficult to diagnose with sputum-based tests.

Until recently, treatment options for children required either crushing and dividing adult pills that could result in improper dosages, or compounding adult medicines – a task for trained pharmacists.

In mid-2019, the NTP and MSF started treating children with new paediatric formulations, provided by GDF. These were added to MSF's package of care. The medicines are formulated as water-soluble tablets that are easier for children to ingest and simpler for caregivers to prepare and administer.

At the start of July 2020, 39 children began treatment with the new formulations. The NTP has since rolled out the new formulations across the country, and they are expected to feature in the next set of national treatment guidelines.

The new medications are a significant improvement in treatment for children with DR-TB. They also mark another important step in empowering parents and caregivers to take responsibility for treatment outside hospital settings.

Shahlo Uskanova, nurse: "One parent of a child with DR-TB lived in a rented house without a refrigerator so she kept them in a neighbour's fridge.[xxviii] The neighbour kept asking what the drugs were for and the family felt very stigmatised and even moved as a result. The child-friendly pills don't need refrigeration, so things are much easier."

Dr Zulfiya Dusmatova: "We had a child who vomited after taking the medicines, and her mother could not make her take any more medicines because she started crying hysterically or ran away and hid from the mother. This made the mother so anxious – each time the child saw the drugs, she started to cry. Now children can't even see the pills once they are dispersed in the glass – it's much better."

A child receives a compounded TB treatment in Dushanbe, Tajikistan.

[xxviii] The previous syrup formulations had to be kept in a refrigerator and had a short two-week shelf life.

Optimal DR-TB treatment for children

Children are especially vulnerable to TB disease, particularly if they are malnourished and/or HIV positive.[50] In 2019, an estimated 1.2 million children under the age of 15 fell ill with TB disease.[1] Estimates of DR-TB among children range from 25,000 to 32,000 cases per year, but only 8,986 children had access to DR-TB treatment in 2018 and 2019.[1,51] The majority of children with DR-TB are still left undiagnosed and thus untreated, and data on paediatric DR-TB are lacking.[52] There is an urgent need to improve data reporting, particularly on the number of children being treated each year, to have a proper accounting of the number of children that are not being reached.

Fortunately, treatment options for children with DR-TB have improved significantly in recent years. First, paediatric formulations for most second-line medicines came to market in appropriate dosages that are easier to administer in 2017 and 2018. More recently, the US Food and Drug Administration approved paediatric tablets of bedaquiline in May 2020.[53]

In late 2018 the Global Drug Facility (GDF) of the Stop TB Partnership started to provide grants of new paediatric formulations to countries and funded the work of the Sentinel Project on Paediatric Drug-Resistant Tuberculosis, which supported a number of NTPs to become early adopters of these new formulations.[54,55] According to survey findings and a desk review, 28/37 (76%) countries include these formulations in their policies and have procured them.[xxix,18] All countries should follow this example to update their national policy frameworks and procure these new formulations to offer better care to children with DR-TB.

In accordance with the latest WHO guidelines, many countries are adopting policies to make DR-TB medicines more accessible to children. Of responding countries that have bedaquiline and delamanid indicated in their national policies for routine treatment, 32/35 (91%) indicate the use of bedaquiline for children aged 6 and up, and 29/32 (81%) indicate the use of delamanid for children aged 3 and up. Unfortunately, 10/36 (28%) countries still do not indicate injectable-free, all-oral regimens for children with uncomplicated forms of DR-TB. With more than one-quarter of children treated with injectable medicines suffering from irreversible side effects such as hearing loss, policies need to be urgently updated to improve the long-term quality of life for children with DR-TB.[56]

Optimal DR-TB treatment for adults

For decades, no new treatment options were available for people with DR-TB. Treatment regimens included nearly 15,000 pills, 8 months of injections and serious side effects.[57] Finally, scientific advances in recent years have significantly improved therapeutic possibilities for people with DR-TB. WHO guidelines have kept pace accordingly (Table 4). In 2018, WHO first issued guidance recommending all-oral regimens for DR-TB.[11] As results from ongoing research have shown, such regimens have much better treatment outcomes and lower toxicity with reduced side effects.[42,58,59] In June 2019, the WHO Director-General called for countries to transition to all-oral regimens by World TB Day, 24 March 2020.[60]

Encouragingly, a majority of countries (29/36, 81%) have started (18/29, 62%) or completed (11/29, 38%) implementation of a longer all-oral regimen for the routine treatment of adults with DR-TB (Box: DR-TB treatment regimens). In line with December 2019 recommendations, already 22/36 (61%) countries have national policies

Danny Haro, age 6, at his final appointment where he has completed a treatment programme and is free from tuberculosis. His mother Margaret helped him through nine months of treatment, coming to the health centre in Papua New Guinea every month to get the medication.

[xxix] Data on countries that were supported by the Stop TB Partnership Global Drug Facility's paediatric DR-TB initiative for the introduction of child-friendly formulations are in the public domain. Other paediatric DR-TB treatment procurement data were collected through individual communication with NTPs or non-governmental actors.

that include a modified shorter all-oral regimen either for routine use or operational research. Among these 22 countries, 10 (45%) have implemented the regimen for routine use or have started implementing it under operational research, pilot conditions, or for routine use. In contrast, 9/37 (24%) countries reported policies that did not include the standardised shorter regimen for routine treatment of DR-TB, which was first recommended in 2016. Alarmingly, as of December 2019, 17/37 (46%) countries reported still using injectable medicines kanamycin and/or capreomycin in the treatment of DR-TB. WHO explicitly recommends against their use because of severe side effects and unfavourable treatment outcomes.[42,61] Their continued use is unacceptable.

The endTB and other observational studies reported vastly improved treatment outcomes using bedaquiline and delamanid (Box: Treating DR-TB with bedaquiline and delamanid),[69,70] but access to these medicines has remained far too limited. Between July 2015 and December 2019, only 51,098 people (or 11% of those who needed it) accessed bedaquiline and 3,750 accessed delamanid.[71,72] Additionally, among countries that indicate bedaquiline and delamanid for routine treatment in their national policies, only a small minority of countries indicate no limitation of bedaquiline and delamanid use beyond 6 months (6/35 [17%] for bedaquiline, 6/33 [18%] for delamanid) (Table 5).[xxx] Among countries where national policies indicate both bedaquiline and delamanid for routine use, the combined use of these treatments is indicated in 28/32 (88%) countries' policies. However, only 6/26 (23%) allow their combined use beyond 6 months without special approval.[xxxi]

Operational research, including observational studies, builds critical evidence about treatment effectiveness. It also enables countries to make scientific advances accessible as quickly as possible while expanding clinical experience and building systems that allow scaled-up use as soon as broader guidance is issued. A new regimen of bedaquiline-pretomanid-linezolid (BPaL), which showed high treatment success for people with XDR-TB in South Africa, is now recommended in operational research settings.[12,73] Among countries surveyed, 3/36 (8%) are using the BPaL regimen in clinical trials, and 15/36 (42%) have plans to implement its use under operational research or pilot conditions (14/15, 93%), or for routine use (1/15, 7%).[xxxii] As science rapidly advances around DR-TB therapies, this approach of building treatment experience while gathering evidence through operational research continues to be vitally important.

TABLE 4 Key changes to WHO DR-TB treatment recommendations, 2013-2020

Year	WHO guidance updates
2013	Interim policy guidance recommends bedaquiline for DR-TB treatment.[62]
2014	Interim policy guidance recommends delamanid for DR-TB treatment.[63]
2015	Companion DR-TB treatment handbook includes the use of bedaquiline and delamanid.[64]
2016	Guidance recommends standardised shorter regimen to treat DR-TB (the injectable-containing 'Bangladesh regimen').[65] Guidance extends recommendation on delamanid to children and adolescents.[66]
2017	Guidance recommends conditions for expanded combined and extended use of bedaquiline and delamanid.[67]
2018	Rapid communication changes drug groupings, recommends against the use of injectables due to worse outcomes, and recommends first-ever longer all-oral DR-TB treatment regimen. Further guidance issued on isoniazid-resistant TB.[61,68]
2019	Consolidated guidelines on DR-TB treatment issued. Rapid communication recommends shorter all-oral bedaquiline-containing regimen for those eligible and new BPaL regimen under operational research conditions.[10, 11]
2020[xxxiii]	Consolidated guidelines on DR-TB summarises previous updates, confirms safety of extended bedaquiline use and bedaquline-delamanid combination, and recommends more decentralised models of care.[12]

[xxx] 1/36 and 4/37 countries do not include bedaquiline and delamanid in their national policies for routine treatment, respectively.

[xxxi] Among 28 countries with policies indicating combined use of bedaquiline and delamanid, answers to this follow-up question could only be accepted from 26.

[xxxii] This question only concerns the BPaL regimen approved by the US FDA with 1200mg linezolid. Some countries have other trials ongoing at lower doses of linezolid, which were not covered in this survey.

[xxxiii] Note these guidelines were issued after the study window and thus were not used as a baseline against which to judge country policy alignment.

Treating DR-TB with bedaquiline and delamanid

The 2020 WHO guidelines on DR-TB treatment support the safe use of bedaquiline for more than 6 months and the combined use of bedaquiline with delamanid.[xxxiv,12]

Findings from an endTB observational study (a partnership between Partners in Health, MSF, and Interactive Research and Development, with support from Unitaid) support the effectiveness of expanded combined use of these medicines for people who otherwise have limited treatment options. More than 77% of over 1,000 patients who received a longer treatment with bedaquiline and/or delamanid experienced favourable treatment outcomes (cured, treatment completed) with 27 months of follow up. Among this cohort of patients, more than three-quarters of participants had either XDR-TB or pre-XDR-TB.

To improve treatment outcomes and facilitate a prompt update of DR-TB treatment guidelines, countries should explore operational research and systematic data collection on expanded use of bedaquiline and delamanid.[xxxv]

TABLE 5 National policies on bedaquiline extension beyond 6 months, as of December 2019[xxxvi]

Policy	Countries
Bedaquiline extension is allowed beyond 6 months without need for special approval	Democratic People's Republic of Korea, Liberia, Mozambique, Republic of Moldova, South Africa, Ukraine
Bedaquiline extension not indicated, not allowed, or only allowed following special approval	Azerbaijan, Bangladesh, Belarus, Cambodia, Central African Republic, Democratic Republic of the Congo, Eswatini, Ethiopia, India, Indonesia, Kazakhstan, Kenya, Kyrgyzstan, Lesotho, Malawi, Namibia, Nigeria, Pakistan, Papua New Guinea, Russian Federation, Sierra Leone, Tajikistan, Thailand, Uganda, United Republic of Tanzania, Uzbekistan, Viet Nam, Zambia, Zimbabwe
Bedaquiline is not indicated for use in routine treatment	Brazil

GRAPHIC 3 Bedaquiline treatment coverage, 2015 to 2019

who could benefit from bedaquiline received the medicine
between 2015 and 2019

Source: DR-TB STAT, 2019

© Mary Gelman

Ariet, age 4, waits for his cue to take a pill with his mother in the children's ward of National Center of Phthisiology on Tuberculosis Control in Bishkek, Kyrgyzstan.

[xxxiv] Note these guidelines were issued after the study window and thus were not used as a baseline against which to judge country policy alignment.

[xxxv] For further information, visit the endTB website at www.endTB.org and consult the MSF technical brief '*Making the Switch,*' available from: www.msfaccess.org.

[xxxvi] Combined use of bedaquiline and delamanid could be limited to certain groups of people. No data available for Philippines.

PREVENTING TB

Polina, and Andrey, a young couple from Belarus, both had drug-resistant tuberculosis. Together they took part in TB PRACTECAL, a collaborative research project with clinical trials across many affected countries that aims to find better treatments for the disease. In January 2020, both Polina and Andrey completed their treatment successfully.

An estimated one-quarter of the world's population has latent TB infection (LTBI), in which *Mycobacterium tuberculosis* remains dormant due to a robust immune response.[74] A person with LTBI has no clinical symptoms and is not infectious. To help prevent the development of active TB disease, people with LTBI should receive TB preventive treatment (TPT). TPT is an essential part of the End TB Strategy, alongside other preventive measures such as active case finding, infection control and timely treatment for people diagnosed with active TB disease.[5]

At the UNHLM, world leaders committed to providing TPT to at least 30 million people by 2022.[2] This includes 4 million children under the age of 5, 20 million other household contacts and 6 million people living with HIV. This commitment signalled a fundamental shift to prioritise prevention alongside diagnosis and treatment of active TB disease.

This report highlights the variability in TB prevention policies across high-burden countries. Even in countries where policies have been updated to reflect WHO guidelines, implementation of those policies remains limited. Despite an increase in household contacts receiving TPT, countries are not on track to reach their UNHLM targets.[1] This insufficient progress for TB prevention remains a key barrier to reducing TB-related morbidity and mortality.

Even in the face of critical research needs, the tools to prevent TB exist, including for LTBI diagnosis. Shorter TPT regimens represent an important advance as they are easier to complete and can significantly increase coverage of TPT.[75,76] Evidence shows that with available tests and treatment regimens, TPT is feasible in settings with limited resources.[77] Shorter TPT regimens and existing diagnostics to detect LTBI must be brought to scale for all people exposed to TB. TPT should be prioritised for household contacts, people living with HIV and other vulnerable and at-risk groups, including prisoners, healthcare workers, miners, people with silicosis, migrants and people with diabetes. It is up to countries to prevent more active TB disease through ample provision of TPT.

Key findings

TOOLS TO DETECT AND TREAT LATENT TB INFECTION

13/20 (65%) COUNTRIES' policies indicate the tuberculin skin test prior to TB preventive treatment initiation, and **6/18 (33%)** indicate interferon-gamma released assays prior to TB preventive treatment initiation. All countries that indicate interferon-gamma released assays also indicate tuberculin skin test.[xxxvii]

24/37 (65%) COUNTRIES' policies indicate a shorter TB preventive treatment regimen (3HP, 3RH, 4R or 1HP).[xxxviii]

6/11 (55%) and 5/11 (45%) COUNTRIES without shorter TB preventive treatment regimens indicated in national policies reported not having enough time to prepare for implementation and a lack of funding for procurement, respectively, as barriers to policy adoption.

7/35 (20%) COUNTRIES' policies indicate a levofloxacin-containing preventive treatment regimen for contacts of people with drug-resistant TB, while **28/35 (80%)** countries do not indicate any preventive treatment regimen for contacts of people with drug-resistant TB in their policies.

PEOPLE LIVING WITH HIV

36/36 (100%) COUNTRIES' policies indicate that people living with HIV are started on antiretroviral therapy regardless of CD4 count.

34/37 (92%) COUNTRIES' policies indicate that all people living with HIV are screened for signs and symptoms of TB disease at every contact with a health service provider.

35/37 (95%) COUNTRIES' policies indicate people living with HIV are eligible for TB preventive treatment.

HOUSEHOLD CONTACTS

31/37 (84%) COUNTRIES' policies indicate that all household contacts of a person with bacteriologically confirmed drug-susceptible TB are investigated for signs and symptoms of TB disease. Among them, **18/31 (58%)** countries also investigate the household contacts of people with clinically diagnosed drug-susceptible TB.

19/37 (51%) COUNTRIES' policies indicate that household contacts aged 5 years and older of a person with bacteriologically confirmed drug-susceptible TB are eligible for TB preventive treatment.

30/37 (81%) COUNTRIES' policies indicate that all household contacts of a person with bacteriologically confirmed drug-resistant TB are investigated for signs and symptoms of TB disease.

VULNERABLE AND AT-RISK GROUPS

11/37 (30%) COUNTRIES' policies indicate prisoners as an eligible group for TB preventive treatment.

11/37 (30%) COUNTRIES' policies indicate healthcare workers as an eligible group for TB preventive treatment.

14/37 (38%) COUNTRIES' policies indicate miners or people with silicosis as an eligible group for TB preventive treatment.

6/37 (16%) COUNTRIES' policies indicate migrants as an eligible group for TB preventive treatment.

12/37 (32%) COUNTRIES' policies indicate people with diabetes as an eligible group for TB preventive treatment.

[xxxvii] Interferon-gamma release assay (IGRA) is a blood test that diagnoses *Mycobacterium tuberculosis* infection.

[xxxviii] 3HP: 3 months rifapentine plus isoniazid given weekly; 3HR: 3 months of rifampicin plus isoniazid given daily; 4R: 4 months of rifampicin given daily; 1HP: 1 month of rifapentine plus isoniazid given daily.

Tools to detect and treat latent TB infection

WHO recommends TPT for people living with HIV, contacts of people with TB and other people at increased risk of developing TB. In higher TB burden settings, LTBI testing is not mandatory prior to start of TPT for people living with HIV and contacts less than 5 years of age. For contacts 5 years of age or older and other TPT-eligible groups, LTBI testing may be indicated, for which WHO currently recommends either the tuberculin skin test (TST) or the interferon-gamma released assays (IGRA) test.

Currently, 7/20 (35%) countries have policies that do not indicate TST prior to TPT initiation. Among the 13/20 (65%) countries that indicate TST, 6/13 (46%) also indicate IGRA in their national policies.[xxix] In many countries' policies, LTBI testing was generally insufficiently addressed and described. To meet their UNHLM commitments and ensure no person is left behind, countries need to expand LTBI testing capacity. However, limited availability of tests should not be a barrier to scaling up TPT. Countries must update their policies to specify when to use TST or IGRA and to clearly state that while LTBI testing is preferable, it should not be compulsory in order to access TPT, if testing capacity is limited.

Regarding TPT regimens, shorter regimens have fewer side effects and allow people with LTBI to integrate treatment into their daily lives, improving treatment outcomes.[78] WHO recommends 5 different TPT regimens, including 4 rifamycin-based short regimens.[xl,79] The Stop TB Partnership estimates that to reach the UNHLM target, over 6 million people will need to access TPT in 2020, making shorter regimens especially critical.[2]

National policies in 24/37 (65%) countries indicate shorter TPT regimens. The most frequently given reasons for not adopting shorter TPT regimens were not enough time to prepare for implementation and financial reasons (lack of funding for procurement or implementation, or medicines being too expensive) (Table 6). Other studies have found countries report similar challenges to implementing shorter regimens.[80] In a welcome policy change, donors such as the President's Emergency Plan for AIDS Relief (PEPFAR), Unitaid and the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) are actively encouraging countries to switch to and scale up these newer regimens.[81-83] In 2019, these organisations secured a 66% reduction in the price of rifapentine, the most expensive drug used in two shorter regimens recommended by WHO.[84] The lowest price for shorter regimens combining rifapentine and isoniazid now ranges between US$16 and US$26 per person, but without generic competition these prices remain too high for some countries, and not all countries qualify for these lower prices. Uptake has been limited in the absence of political support or technical buy-in from countries that have historically deprioritised prevention using TPT.

WHO recommendations also emphasise that high-risk contacts of people with DR-TB disease should be given the option of levofloxacin-containing TPT after an individualised risk assessment, once active TB disease has been ruled out.[79] Yet only 7/35 (20%) countries included this option in their national policies. Only one country in Eastern Europe and Central Asia indicates TPT for DR-TB contacts in its national policy, despite the region having 9 DR-TB high-burden countries. It is critical that people at high risk of developing DR-TB are offered the best possible standard of prevention and care.

TABLE 6 Reasons for not including a shorter TPT regimen in policy in 11 countries, as of December 2019

Frequently cited reasons[xli]	Number of times cited
Not enough time to prepare for implementation	6
Lack of funding for procurement	5
Lack of funding for implementation	4
Medicines are too expensive	3
Not aware of WHO recommendation for shorter regimens	2
National procurement and import regulations are prohibitive	1
Not aware of shorter regimens	1
Other reasons: no local evidence on the safety and cost effectiveness	1

[xxix] Out of 37 country responses, only 20 responses could be included due to a mistake in the interview process.

[xl] The 5 recommended TPT regimens are: 1 month of rifapentine plus isoniazid given daily (1HP); 3 months rifapentine plus isoniazid given weekly (3HP); 3 months of rifampicin plus isoniazid given daily (3HR); 4 months of rifampicin given daily (4R); and 6-36 months of isoniazid given daily (IPT). 1HP, 3HP, 3HR and 4R qualify as 'shorter regimens.' 1HP was added to the list of recommended TPT regimens in early 2020.

[xli] Survey respondents were able to indicate multiple reasons for not having including a shorter TPT regimen in policy.

People living with HIV

HIV is the strongest known risk factor for LTBI developing into active TB disease. A person with HIV and LTBI is 20 times more likely to develop active TB disease than an HIV-negative person with LTBI.[85] TB disease is the most frequent cause of AIDS-related deaths worldwide.[1] The End TB Strategy aims to reduce TB-related deaths among people living with HIV by 75% by 2020 compared to 2015 rates, a commitment reaffirmed by world leaders at the 2016 UN High-Level Meeting on HIV/AIDS.[2,5]

WHO recommends that people living with HIV receive life-long antiretroviral therapy (ART) regardless of their CD4 count, are screened for signs of symptoms of TB during every contact with a healthcare provider, and are universally provided TPT as part of a comprehensive package of HIV care.[79,86,87] By rapidly enrolling people living with HIV on ART and providing TPT, most people living with HIV can remain TB-free.[75,88,89]

In line with the previous *Step Up for TB* survey findings in 2017, the vast majority of countries surveyed integrated these recommendations into their national policies. All countries' policies indicate that people living with HIV are started on ART regardless of CD4 count. Nearly all countries' policies indicate TB screenings for all people living with HIV and indicate people living with HIV are eligible for TPT (92% and 95%, respectively).

Thanks to increasing global ART coverage (67% as of December 2019), TB-related deaths among people living with HIV dropped by 58% between 2005 and 2018, according to UNAIDS.[90] Still, the rate of TB-related deaths among people living with HIV is not decreasing quickly enough, making access to TPT even more important. WHO data show that the number of people living with HIV receiving TPT increased from 1.8 million in 2018 to 3.5 million in 2019. Just 3 countries – India, South Africa and the United Republic of Tanzania – accounted for 57% of all people living with HIV started on TPT in 2019.[1] This means that the specific UNHLM target of TPT coverage for people living with HIV is within reach. According to WHO, 2019 coverage of TPT among people living with HIV on ART was 50% across 62 countries for which this information could be calculated.[1]

Fortunately, countries can make progress quickly when there is political commitment. In 2018, the government of Uganda launched a 100-day surge plan with the support of USAID and PEPFAR, reaching 25% of all people living with HIV with TPT in a single year.[91,92] This example demonstrates what can be achieved with high-level political support, a clear and timebound implementation plan, and coordination with healthcare providers and community groups. Countries striving to achieve similar results can look to Uganda as a blueprint, while Uganda could build on this model by using a similar approach to reach other vulnerable groups.

Household contacts

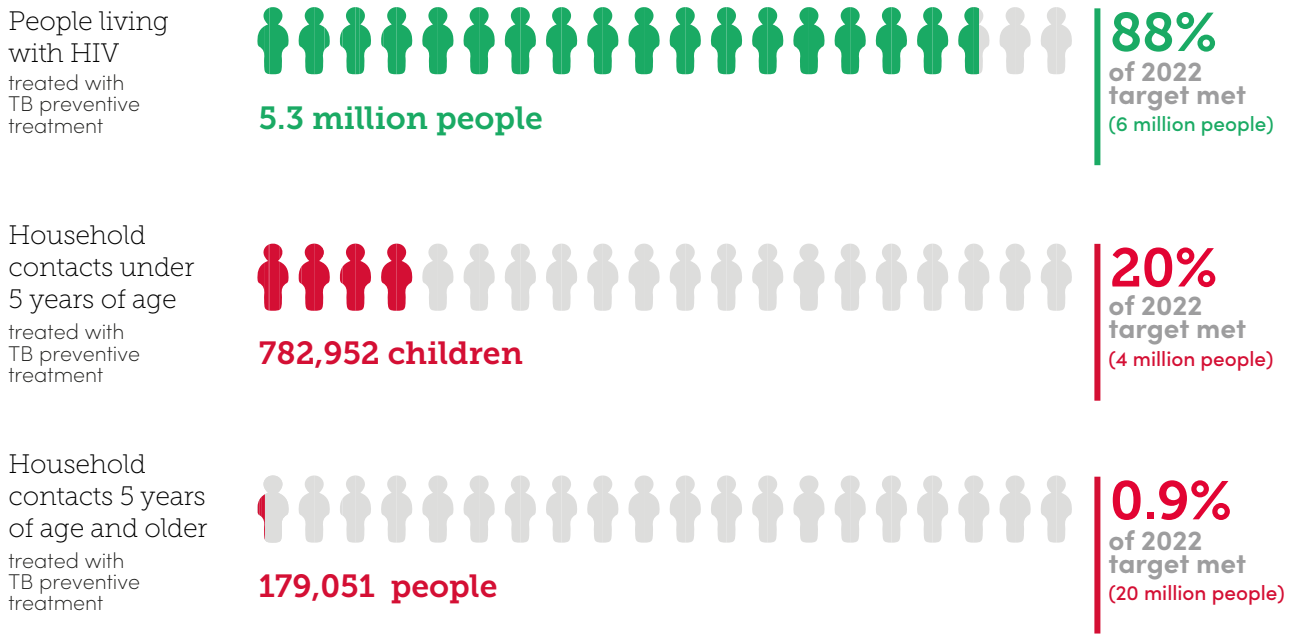
Two-thirds of the at least 30 million people meant to receive TPT by 2022 are household contacts of people with TB disease.[2] WHO has long recommended that TPT be provided to all household contacts under the age of 5. While policy adoption is widespread among countries surveyed, global implementation has remained entirely insufficient (see infographic). In 2018, WHO expanded its guidance, calling for all household contacts to be systematically screened and provided with TPT, regardless of age.[87]

The Global Plan to End TB aims for 100% coverage of contact tracing and TB screening among all household contacts of people with bacteriologically confirmed pulmonary TB disease by 2022.[41] Most (31/37, 84%) countries policies' indicate that all household contacts of a person with bacteriologically confirmed DS-TB should be investigated for signs and symptoms of TB disease. However, contacts aged 5 years and older are only eligible for TPT in the policies of 19/37 (51%) countries.

A tuberculin skin test is administered in Vietnam.

Over three-quarters (30/37, 81%) of countries surveyed include household contacts of people with bacteriologically confirmed DR-TB in their policies for investigation of signs and symptoms of TB. Notably, many countries' policies (15/37, 40%) do not indicate contact tracing for household contacts of people clinically diagnosed with DS-TB, despite TB transmission still being possible.[93] This policy restriction thus risks missing a significant proportion of household contacts at risk of developing TB disease.

GRAPHIC 4 TB preventive treatment: 2018-2019 coverage versus UNHLM 2022 targets



Source: World Health Organizations, 2020.

Vulnerable and at-risk groups

Vulnerable and at-risk groups are more likely to be exposed to TB and to develop active TB disease because of where they live or work, or the co-morbidities they have.[79] As a result, the highest rates of TB are often concentrated among these populations, even as TB incidence is gradually reduced in the general population. WHO identifies a number of at-risk populations who should be eligible for TPT and recommends countries adopt dedicated programmes for comprehensive TPT provision.[79] In order to reach many of these vulnerable and at-risk groups, it is also important to scale up testing of LTBI.

Countries have made insufficient progress recognizing vulnerable and at-risk groups who should receive TPT. People in prisons face risks of TB disease and LTBI that are 23 and 26 times higher than the general population, respectively.[94] However, only 11/37 (30%) countries have national policies in place that identify prisoners as a group eligible for TPT. The same number of countries define healthcare workers as eligible for TPT.

Miners and people with silicosis can also face disproportionately high rates of TB.[95,96] For example, in South Africa the TB incidence rate among miners is 10 times the WHO threshold for a health emergency.[97] However, only 14/37 (38%) of survey countries have policies indicating miners or people with silicosis are eligible for TPT, including South Africa. Failing to provide LTBI testing and TPT to the most vulnerable people puts them at unacceptable risk of active TB disease.

As governments continue to tackle the TB epidemic, they must place vulnerable and at-risk communities at the heart of their programmes. Given the urgent need to scale up TPT among these groups, countries should be as inclusive as possible for their context when defining national TPT policies. This enables clinicians to test and offer TPT to locally identified high-risk groups. People-centred TPT care should include decentralised TPT distribution and adapted models of care to ensure that no one is left behind.

TB preventive treatment for prisoners in Malawi

In Chichiri, a district in Malawi, MSF worked with the Ministry of Health and Prison Health Services to provide a comprehensive package of TB and HIV care for the incarcerated population there. High HIV prevalence, poor living and nutritional conditions, overcrowding and lack of ventilation all contribute to the extremely high rates of LTBI and TB disease in the prison.

In 2019, a pilot project was launched, which included intensified screening to rule out active TB and detect LTBI among people in prison. It also included provision of treatment for active TB as well as for TPT upon project enrolment, and then mass screenings every 6 months, and finally screening once again upon an individual's release from the prison.

Previously, only people living with HIV with no active TB disease were started on TPT with isoniazid. The pilot brought two TPT innovations: fixed-dose combination (FDC) of cotrimoxazole-isoniazid-pyridoxine for people living with HIV, thereby greatly reducing the pill burden, and 3HP for those who were HIV-negative and had a positive tuberculin skin test.[xlii]

During the pilot, 325 people living with HIV started the FDC treatment and an additional 671 people in the prison (more than 95% of those eligible) started 3HP, with 70% of people completing the course while in prison. Counselling, with support from inmate peer educators, was a clear factor in adherence and treatment completion.

The pilot demonstrated that TPT is feasible in prison settings and should be adopted and brought to scale elsewhere, along with intensified screening. Still, improving living conditions that contribute to poor health and TB for people in prison must remain a priority.

Dr Patrick Mangochi, Deputy Medical Coordinator for MSF Malawi: "For people living with TB or those at risk of TB, this project provided a number of benefits. Not the least of which was providing intensified screening and provision of treatment actually within the prison, rather than offsite.

"If people in prison are told about the services and the associated benefits, they are very willing to accept and even play a role in service provision. Once people understand the disease, they are very incentivised to protect not only themselves, but also everyone around them. Oftentimes they would express that that they are their 'brothers' keepers'."

Prisoners in Maula prison in Lilongwe, Malawi, live in extremely overcrowded conditions that fuel the spread of TB and other infectious diseases. MSF carried out a pilot project in the prison to offer TB preventive treatment.

[xlii] 3HP: 3 months rifapentine plus isoniazid given weekly.

PROCURING MEDICINES FOR TB

A pharmacist stands outside a pharmacy in Hyderabad, India.

© Stop TB Partnership

The ability of countries to successfully treat TB relies on their ability to procure quality-assured, affordable TB medicines. Many countries have used the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), which provides 69% of all international funding for TB programmes globally,[98] and other donors' funding to purchase TB medicines through the Stop TB Partnership's Global Drug Facility (GDF).[99] In addition to helping source and secure quality-assured, life-saving treatment for millions of people with TB, GDF's approach also improves fragile market dynamics for TB medicines. This approach includes pooled procurement and in-country support to introduce new tools and prevent stockouts. This has helped increase the number of suppliers, reduce prices and incentivize adherence to WHO quality standards. For this reason, the UNHLM political declaration encourages countries to use pooled procurement, such as the GDF, for the procurement of TB medicines.[2]

However, the benefits realized over the last two decades of pooled procurement are at risk as countries shift to buying more medical products without donor support.[100] The Global Fund's Sustainability, Transition and Co-Financing policy requires all recipient countries to gradually increase their co-financing commitments.[101] Many countries choose to fulfil these requirements

through increasing domestic procurement of TB medicines. This can present challenges because national procurement laws frequently apply different standards to domestic procurement compared to what donor-funded procurement requires. For example, the Global Fund requires that medicines meet WHO quality-assurance standards whereas many countries do not. Furthermore, GDF's pooled procurement mechanism secures lower prices and better terms as compared to those obtained by individual countries procuring on their own. Pooled procurement mechanisms can achieve this by leveraging large volumes and by applying risk-sharing approaches, such as facilitating packaging in multiple languages and reducing transaction costs between multiple clients and suppliers. Regardless of the level of Global Fund and GDF support that countries receive, their national policies are important for ensuring sustainable, affordable access to quality-assured TB medicines.

In addition to seeking survey responses, a desk review was conducted to assess countries' regulatory policies and procurement practices. Findings were reviewed to identify gaps that should be addressed at country level to ensure sustained supply of affordable, quality-assured medicines when support from donors, including the Global Fund, is dramatically reduced or ends.

Key findings

SUPPLY

16/30 (53%) COUNTRIES have domestically registered at least one WHO-recommended fixed-dose combination for adults with drug-susceptible TB that is WHO pre-qualified or registered by a stringent regulatory authority. Even fewer countries have domestic registrations in place for quality-assured paediatric fixed-dose drug-susceptible TB combinations, most drug-resistant TB medicines for adults, any drug-resistant TB medicines for children, or medicines for latent TB infection (Table 7).

12/35 (34%) COUNTRIES have all WHO Group A and B drug-resistant TB medicines listed on their national Essential Medicines List.[xliii,xliv]

22/37 (59%) COUNTRIES are enrolled in the WHO Collaborative Registration Procedure. Among them, only **14/22 (64%)** have used it to register at least one TB medicine.

30/37 (81%) COUNTRIES allow early access mechanisms for TB medicines by law.

QUALITY

21/36 (58%) COUNTRIES require a WHO and/or US Centers for Disease Control and Prevention recommendation for the importation of TB medicines.

14/26 (54%) COUNTRIES require internationally recognised stringent regulatory approval and/or WHO prequalified status for the importation of TB medicines purchased with domestic funding, while **1/26 (4%)** does so only for first-line TB medicines.

5/14 (36%) COUNTRIES require stringent regulatory approval and/or WHO prequalified status when procuring domestically manufactured medicines, while **1/14 (7%)** does so only for first-line TB medicines.

TRANSPARENCY

15/25 (60%) COUNTRIES provide transparency for national tenders for TB medicines, including publication of selection criteria, winning bidder and final price information.[xlv]

ALIGNMENT WITH BEST PRACTICES

23/35 (66%) COUNTRIES have both the 4-medicine (rifampicin 150mg/isoniazid 75mg/pyrazinamide 400mg/ethambutol 275mg) and 2-medicine (rifampicin 150mg/isoniazid 75mg) fixed-dose combinations to treat drug-susceptible TB listed on their national Essential Medicines List.[xlvi]

6/22 (27%) COUNTRIES enrolled in the WHO Collaborative Registration Procedure have used it to register the 4-medicine (rifampicin 150mg/isoniazid 75mg/pyrazinamide 400mg/ethambutol 275mg) or 2-medicine (rifampicin 150mg/isoniazid 75mg) fixed-dose combinations to treat drug-susceptible TB.

[xliii] National Essential Medicine Lists are not available for Azerbaijan and Sierra Leone.

[xliv] Group A medicines include bedaquiline, linezolid, and levofloxacin or moxifloxacin. Group B medicines include clofazimine and cycloserine or terizidone.

[xlv] Some answers from respondents could not be verified against national policy documents.

[xlvi] National Essential Medicine Lists are not available for Azerbaijan and Sierra Leone.

The results are cause for alarm: almost all surveyed high-burden countries are not prepared to reliably procure quality-assured, affordable TB medicines. People affected by TB are already experiencing the consequences of the Global Fund 'procurement cliff' as countries shift from Global Fund-supported procurement to national procurement.[102] NTPs, national regulatory authorities (NRAs), donors and technical assistance providers should urgently put in place the systems, policies and legal frameworks to better ensure a sustained supply of quality-assured, affordable TB medicines. Without such steps, countries risk failing to meet their UNHLM commitments and undoing decades of improvements to stabilise and consolidate the TB medicines market. The consequence would be additional loss of life for people with TB.

© Oksana Parafeniuk

Medication being prepared by a Ministry of Health nurse before being distributed to patients at the Zhytomyr Regional TB Dispensary in Ukraine.

Supply

According to most countries' laws, medicines must meet a number of prerequisites for purchasing or importation. This may include domestic registration of the medicines and their inclusion on the national Essential Medicines List (nEML).[103] When procuring through GDF or other international procurement mechanisms, waivers to these prerequisites are often granted. However, as countries begin to procure independently, not meeting these criteria can generate challenges. This report shows that only a minority of countries have the core set of WHO-recommended quality-assured TB medicines registered domestically (Table 7). Similarly, most countries do not have all of the WHO-recommended TB medicines included on their nEMLs.

In too many instances a country is not considered an attractive enough market to entice companies to file for national registration of a medicine. To address this and other regulatory challenges, WHO launched the Collaborative Registration Procedure (CRP) in 2012.[15,104] It enables countries with limited regulatory capacity to utilise the assessments and inspections done by WHO through the WHO Prequalification Programme or by an internationally recognised stringent regulatory authority (SRA) in order to formally register a medicine within 90 days.[xlvii,15,105] However, while 22/37 (59%) countries surveyed are enrolled in the CRP, only 14/22 (64%) have used the CRP to register a TB medicine. To avoid jeopardising access to life-saving treatments and to limit the workload of NRAs, countries should urgently prioritise use of the CRP, given its clear benefits in facilitating and streamlining registration.

In parallel with registration, national laws should also include early-access mechanisms, such as compassionate use, named-patient basis or clinical access programmes. These mechanisms enable importation of non-registered medicines, including new medicines in the final stages of clinical development before they are registered. Countries that used these mechanisms to access bedaquiline and delamanid scaled up coverage more rapidly once they were recommended for routine use.[106] Unfortunately, 7/37 (19%) survey countries still do not allow early access by law. With the TB treatment pipeline more robust than in previous years, countries should urgently update national laws to enable early access and benefit from future scientific breakthroughs in a timely manner.[107]

[xlvii] According to WHO, an internationally recognised SRA is a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), an ICH observer, or a regulatory authority associated with an ICH member through a legally binding, mutual recognition agreement. For more information: https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex11.pdf.

TABLE 7 Countries with domestic registration for WHO-prequalified (PQ) or SRA-approved medicines, as of December 2019

Treatment	Medicines	Number (%) of countries that registered a WHO PQ or SRA approved medicine *
DS-TB medicines for adults	Rifampicin 150mg/isoniazid 75mg/ pyrazinamide 400mg/ethambutol 275mg	14/30 (47%)
	Rifampicin 150mg/isoniazid 75mg	16/30 (53%)
DS-TB medicines for children	Rifampicin 75mg/isoniazid 50mg dispersible tablet	9/30 (30%)
DR-TB medicines for adults	Bedaquiline (100mg)	9/30 (30%)
	Levofloxacin (250mg)	13/30 (43%)
	Linezolid (600mg)	14/30 (47%)
DR-TB medicines for children	Levofloxacin (100mg dispersible tablet)	1/30 (3%)
LTBI medicines for adults	Rifapentine (150mg)	5/30 (17%)
	Isoniazid (300mg)	14/30 (47%)

*Data were available only for 30 of the countries surveyed

Quality

Countries should regularly update their national treatment guidelines for TB to be aligned with WHO clinical guidelines. Countries should also require that any TB medicines imported for programmatic use are recommended by WHO. Yet this critical coherence between international guidelines and national importation rules is a reality in just over half (21/36, 58%) of responding survey countries.

Pharmaceutical quality is another important prerequisite for TB medicines imported or purchased on the national market. Substandard medicines threaten the lives of those who take them by failing to effectively treat TB infections.[108] They also result in poor control of communicable diseases and, in the case of antibiotics, drug resistance can develop.[109,110] In the Eastern Europe and Central Asia region alone, WHO reported 11% of sampled TB medicines failed to meet expected quality standards, in a 2011 report.[111] In contrast, among WHO-prequalified samples and those supplied through GDF, zero samples failed to meet quality standards, indicating that these mechanisms effectively assure the quality of TB medicines.[111]

TB medicines should therefore be quality assured, through WHO prequalification or approval by an internationally recognised SRA. As the survey findings show, many high-burden countries do not require medicines procured with national budgets to meet these standards. When procuring medicines from international suppliers using national budgets, 14/26 (54%) responding countries require compliance with WHO quality standards. When procuring from domestic manufacturers, only 5/14 (36%) apply this requirement.

As a result, GDF reports that 35 low- and middle-income countries purchased TB medicines of unknown quality over a 24-month period (Box: Domestic procurement and supply challenges).[112] Governments requiring WHO prequalification or SRA approval will encourage manufacturers to improve compliance with WHO quality standards and help to protect the lives of people with TB. This will additionally prevent further fragmentation of the TB medicines market, as non-quality-assured medicines will not be able to undercut quality-assured products by offering lower prices.

Domestic procurement and supply challenges

The Global Drug Facility (GDF) monitors domestic procurement and supply of TB medicines in a range of low- and middle-income countries. Between 2017 and 2019, GDF observed alarming problems with supply of TB medicines under domestic procurement in dozens of countries in Africa, Asia, Eastern Europe and Central Asia, and Latin America, including Global Fund-eligible countries that use domestic procurement to meet co-financing requirements.[112] During this time, 35 countries procured medicines of unknown quality, 25 countries experienced stockouts, 16 experienced failed government tenders and 10 procured medicines not recommended by WHO guidelines.

The consequences for people with TB in these countries are the risks of not receiving quality-assured treatments. In the context of increasing donor withdrawal from procurement support and rising co-financing required from countries, more countries and people with TB risk being exposed to these issues.

To address these challenges, all countries need strong national regulatory and procurement systems and enabling policies and legal frameworks. Without these systems and frameworks in place, countries will face otherwise preventable difficulties providing the sustained supply of quality-assured, affordable TB medicines needed to scale up TB care and meet the UNHLM commitments.

Transparency

Countries can use a number of strategies to secure affordable prices for TB medicines. The experience of the last 20 years of scaling up HIV and TB medicines shows that fostering generic competition and leveraging volumes are among the most effective in lowering the price of medicines.[113–115] Lower volume national tenders draw interest from fewer suppliers or, in some cases, no suppliers at all. This means countries have less power when negotiating the price of a medicine with a manufacturer. Research shows that low- and middle-income countries can pay as much as 20 to 30 times the minimum international reference price for quality-assured basic generic medicines.[116]

The call to pharmaceutical corporations for transparency in the pricing of medicines is growing, including a resolution at the 72nd World Health Assembly, which could aid in countries' negotiation of prices and pursuit of generic competition.[113,114,117–119] As noted in the resolution, "The availability of comparable price information may facilitate efforts towards affordable and equitable access to health products." Furthermore, since 1999, WHO has recommended that governments publish the selection criteria, winning bidder and final price information of national tenders.[117] The publication of this information allows external monitoring of the procurement processes and pricing trends. When the products purchased by a government do not meet WHO quality standards, clinicians and TB-affected communities must be aware of the potential implications on their treatment and have the right to hold their governments to account for providing quality care.

Of the 25 countries for which survey data were available, only 15 (60%) are following WHO's long-standing recommendations. As more high-burden countries shift to domestic procurement for TB medicines, many are already paying much higher prices, with significant implications on stretched national health budgets.[102,116] It is in the interest of all countries to institute transparent procurement policies to maintain equitable access to lifesaving TB medicines.

Alignment with best practices

Reports of stockouts, failed tenders and non-quality-assured products are increasing, and countries need to improve preparedness for domestic procurement.[102] Currently no comprehensive best-practice guidance exists on effective domestic procurement policies. WHO's most recent guidelines were published in 1999, before the formation of the GDF, the Global Fund and other key health bodies.[117]

Despite this, countries should follow current long-established recommendations when procuring medical products. These include many of the policies and practices outlined above, including transparent tenders; ensuring regulatory and procurement systems enable access to quality-assured medicines (mutual regulatory recognition, WHO CRP, waivers); and regularly updating their nEMLs. Almost all high-burden countries have not adopted all of these recommendations in their national policies.

One alarming sign relates to the regulatory arrangements for quality-assured fixed-dose combinations (FDCs) to treat DS-TB in adults. These FDCs have been prescribed to people with DS-TB worldwide for years and are essential to reducing the risk of resistance development, yet this report highlights the poor rate of local registration of quality-assured versions. As FDCs for DS-TB are the first medicines that many countries source through domestic procurement, this is a worrying indication of the regulatory status of other TB medicines, like those for DR-TB or LTBI (Table 7).

Given the fragility of the TB medicines market, and further complications posed by issues like packaging requirements and limited international supply of active pharmaceutical ingredients, the UNHLM declaration encourages countries to make use of international pooled procurement mechanisms, such as the GDF. In countries with local manufacturing capacities, this could be an interim step at least until the local production of TB medicines becomes compliant with WHO quality standards. Additional technical assistance, targeted funding and mitigation strategies while shifting from Global Fund support are needed to adapt national procurement laws accordingly and get in-country TB medicines production ready to compete on the international market.[102]

© Ashley Gilbertson for Stop TB's GDF

Nurse Akanji Adebimpe replenishes stocks of Stop TB treatment kits at the government chest clinic, Jericho, in Ibadan, Nigeria.

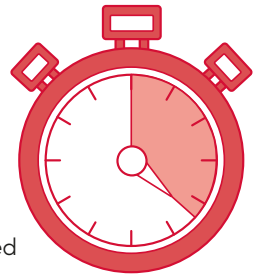
CONCLUSION

In 2018, 193 governments committed to stepping up the fight against TB at the first UN High-Level Meeting on TB (UNHLM). Two years later, this *Step Up for TB 2020* report, as part of an accountability effort to monitor progress towards these goals, shows that many high-burden countries have yet to introduce much-needed policy reforms. Countries only have two years left to deliver on the targets set at the UNHLM. This is still achievable if policies are rapidly updated and implemented at scale.

There is hope in the fight against TB. To deliver change, countries must now step up and ensure full policy alignment with WHO guidelines by the next World TB Day, 24 March 2021. The findings of this report can be used to evaluate national policy alignment, including by civil society and communities affected by TB, to determine national, regional and global priorities and to drive forward concrete policy reform and implementation of these policies to scale. Ultimately, countries' successes will be measured in the pace of action and in lives saved; with two years to go, there is no time to waste.

GRAPHIC 5 No time to waste to avert TB deaths

In 2019,
a person died of TB
every 22 seconds*



Governments should act fast to adopt and scale up recommended TB policies to save lives.

* Counting deaths among HIV-negative people and people living with HIV.

Source: World Health Organizations, 2020.

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Emmanuel spoke about his experience of ambulatory TB treatment and care at a celebration of World TB Day 2020 in Makeni Government Hospital, Bombali District, Sierra Leone.

Additional Resources

DASHBOARDS AND COUNTRY FACTSHEETS

In addition to the key policies dashboards included in the Executive Summary and Annex 1, the full *Step Up for TB* data set is available online alongside individual country factsheets. To access additional *Step Up for TB* tools, visit:

www.stoptb.org/suft/ or
www.msfaccess.org/stepupfortb

ADVOCACY TOOLS

Key advocacy materials, such as sample letters and social media tiles, are also available online. Advocates are encouraged to make use of these when using the *Step Up for TB* report to hold their government to account for delivering on their UNHLM commitments. To access additional *Step Up for TB* tools, visit:

www.stoptb.org/suft/ or
www.msfaccess.org/stepupfortb

MORE INFORMATION FROM MSF

MSF has produced technical briefs, issue briefs and reports on many of the topics discussed in this report. They are regularly updated and include helpful background information, research findings and recommendations. To access these materials, visit:

www.msfaccess.org

GLOBAL PLAN TO END TB

The Global Plan to End TB 2018–2022 is a costed plan and roadmap for a concerted response to TB, aligned with the UNHLM political declaration. Among other things, it provides an estimate of the resources needed to achieve the UNHLM targets and detailed programmatic recommendations for different country settings. To access the Global Plan, visit:

www.stoptb.org

ABBREVIATIONS

ART	Antiretroviral therapy
BPaL	Bedaquiline-pretomanid-linezolid (DR-TB treatment regimen)
DOT	Directly observed therapy
DR-TB	Drug-resistant tuberculosis
DS-TB	Drug-susceptible tuberculosis
EECA	Eastern Europe and Central Asia
EML	Essential Medicines List
FDC	Fixed-dose combination
GDF	Global Drug Facility
IGRA	Interferon-gamma release assay
HIV	Human immunodeficiency virus
LPA	Line probe assay
LTBI	Latent TB infection
MDR-TB	Multidrug-resistant tuberculosis
MSF	Médecins Sans Frontières
NRA	National regulatory authority
NTP	National TB programme
PEPFAR	President's Emergency Plan for AIDS Relief
PQ	Prequalification
RMD	Rapid molecular diagnostic
RR-TB	Rifampicin-resistant tuberculosis
SAT	Self-administered therapy
SRA	Stringent regulatory authority
TB	Tuberculosis
TB LAM	Lateral flow urinary TB lipoarabinomannan test
TPT	TB preventive treatment
TST	Tuberculin skin test
UNHLM	2018 UN High-Level Meeting on TB
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

GLOSSARY

Antiretroviral therapy: Antiretroviral therapy (ART) is used to treat HIV. The standard of care is a combination of medicines that target different steps in the virus lifecycle to prevent it from replicating and to prevent the development of drug resistance. ART dramatically reduces mortality and morbidity rates among HIV-positive people and improves their quality of life.

CD4 count: Testing done in people who are HIV-positive to measure the number of CD4 T-cells in a sample of blood; this number indicates the status of a person's immune system.

Co-financing: Co-financing refers to national governments investing in donor-funded health programmes with their domestic budget. Donors like the Global Fund have co-financing policies that require recipient countries to gradually increase their co-financing commitment over time in order to remain eligible to receive donor funding.

Compassionate use: The terms "compassionate use", "expanded access" or "special access" refer to programmes intended to provide potentially life-saving experimental treatments to people suffering from a disease for which no satisfactory authorised therapy exists and/or to people who cannot enter a clinical trial. Compassionate use refers to programmes that make medicinal products available either on a named-patient basis or to cohorts of patients. Compassionate use needs to be framed within a national legislation that established the conditions under which the medicine is made available.

Consilium: A group of several experts to confer and give advice on the treatment of people with DR-TB. In some countries, the use of some medicines or the "off label" use of medicines requires special approval from a consilium or similar expert group.

Drug-susceptible TB: When a given drug is effective (meaning it kills bacteria or prevents them from reproducing) against a type of virus or bacteria. This means that the drug can help to clear infections (although TB and many other infections need to be treated with more than one drug). TB strains that are susceptible to all first-line drugs are called drug-susceptible or drug-sensitive.

Drug-resistant TB: A broad term to encompass all forms of drug-resistant TB, including isoniazid-resistant, rifampicin-resistant (RR), multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

Essential Medicines List: A list of the minimum medicine needs for a basic healthcare system. The EML includes the most effective, safe, and cost-effective medicines for priority conditions. WHO updates its EML every 2 years. The WHO EML serves as a model for national EMLs.

Extensively drug-resistant TB: see XDR-TB.

First-line medicines: The first medicines used to treat a disease. In the case of TB, the following medicines are considered first-line medicines: isoniazid, rifampicin, ethambutol and pyrazinamide. These medicines are highly effective in treating drug-susceptible TB.

Fixed-dose combination: A combination of more than one medicine in a single tablet. The combination of medicines reduces the risk of the development of resistance to any of the single components in the medicine regimen, as well as making the treatment easier to take.

Latent TB infection: TB infection in which *Mycobacterium tuberculosis* remains dormant due to a robust immune response. A person with latent TB infection has no clinical symptoms and is not infectious.

Line probe assay: A line probe assay is a type of drug susceptibility test that uses polymerase chain reaction (PCR) and reverse hybridization methods to rapidly detect mutations associated with drug resistance. They are suitable for use at laboratories with the capacity, infrastructure and biosafety to conduct molecular testing.

Multidrug-resistant TB: MDR-TB is resistant to at least isoniazid and rifampicin, the two most powerful first-line antibiotics used for TB treatment.

Mycobacteria: Types of bacteria of the genus *Mycobacterium* that cause disease, including TB and leprosy.

M. tuberculosis: *Mycobacterium tuberculosis* is a pathogenic bacterial species of the genus *Mycobacterium* and the causative agent of most cases of TB; it was first discovered in 1882 by Robert Koch.

Operational research: Operational research is applied research that aims to generate the evidence needed to support effective and sustained adoption of innovations within a health system. By implementing new innovations in operational research settings, additional evidence of their effectiveness and how to implement them for maximum impact can be generated.

People-centred care: A people-centred approach to care considers the needs, perspectives and individual experiences of people affected by TB, while respecting their rights to be informed and receive the best quality care based on individual needs. It requires the establishment of mutual trust and partnership between the person affected and the care provider, and creates opportunities for people to provide input into and participate in the planning and management of their own care. People-centred care improves treatment outcomes while respecting human dignity.

Point-of-care testing: When diagnosis is carried out as close as possible to where patient care is provided. The driving notion behind point-of-care testing is for the test to be as convenient as possible and give immediate results, leading to the prompt initiation of treatment.

Pooled procurement: Pooled procurement is a process whereby several buyers consolidate their purchases into a single transaction with a manufacturer. By pooling their orders, they are able to negotiate better prices. The Stop TB Partnership's Global Drug Facility is a pooled procurement mechanism that has worked to increase access to affordable, quality-assured TB medicines and to stabilise the fragile TB drug market by consolidating and forecasting demand and providing technical assistance.

Pulmonary TB: Form of TB where *M. tuberculosis* bacteria infect the lungs.

Rapid molecular diagnostics (RMDs): Rapid molecular tests that detect the DNA of *M. tuberculosis.* RMDs such as GeneXpert and Truenat are able to detect TB from a sputum sample in a matter of hours and are also able to test for resistance to rifampicin.

Silicosis: Silicosis is a progressive interstitial lung disease, which can develop in people whose occupations expose them to dust with silica, such as mining. For more information, see: https://www.who.int/bulletin/volumes/94/10/15-163550/en/

Second-line medicines: Second-line medicines are used to treat TB in people who have forms of TB that are resistant to first-line medicines.

Second-line drug susceptibility testing (DST): Testing for resistance to medicines used to treat drug-resistant TB.

Smear-positive pulmonary TB: An individual whose sputum is positive for acid-fast bacilli by smear microscopy.

Smear-negative pulmonary TB: An individual whose sputum is negative for acid-fast bacilli by smear microscopy. The diagnosis can be made either with other bacteriological methods such as culture or attending to the clinical symptoms.

Stringent regulatory authority (SRA): According to WHO, an internationally recognised SRA is a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), an ICH observer, or a regulatory authority associated with an ICH member through a legally binding, mutual recognition agreement. For more information, see: https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex11.pdf

TB REACH: TB REACH is a multilateral funding mechanism established in 2010 with the leadership of Global Affairs Canada. TB REACH provides grants to partners for testing innovative approaches and technologies aimed at increasing the number of people diagnosed and treated for TB, decreasing the time to appropriate treatment and improving treatment success rates. It combines fast-track, results-based financing and rigorous, external monitoring and evaluation (M&E) to produce results, so other donor agencies and/or national governments can scale up successful approaches and maximise their own investments. Its most recent call for proposals was launched with support from the US Agency for International Development (USAID).

Universal DST: WHO recommendations on DST have traditionally been that every person with bacteriologically confirmed TB is tested for rifampicin resistance and every person with rifampicin-resistant TB is tested for resistance to at least fluoroquinolone and second-line injectable medicines. However, there are other drug susceptibility tests that should be included to help ensure that people on TB treatment do not receive any medicines to which they are resistant. See universal DST, comprehensive.

Universal DST, comprehensive: A comprehensive universal DST policy should include: rifampicin and isoniazid resistance testing for all people starting TB treatment; at least fluoroquinolone resistance testing for all people with rifampicin-resistant TB; and DST methods available in country for rifampicin, isoniazid, fluoroquinolones, bedaquiline, delamanid, linezolid and/or clofazimine, when these drugs are used for routine treatment.

WHO Prequalification (PQ) Programme: The Prequalification Programme, set up in 2001, is a service provided by WHO to facilitate access to medicines that meet the unified standards of quality, safety and efficacy for HIV/AIDS, malaria and TB. For more information, see: http://apps.who.int/prequal/

WHO Collaborative Registration Procedure: The Collaborative Registration Procedure, launched in 2012, enables countries with limited regulatory capacity to utilise the assessments and inspections done by WHO through the WHO Prequalification Programme or by an internationally recognised stringent regulatory authority to formally register a medicine within 90 days.

XDR-TB (extensively drug-resistant TB): XDR-TB is an MDR-TB strain with additional resistance to a fluoroquinolone and an injectable drug.

ANNEX 1: DASHBOARD

S. Thangkhoshin Hookip lives in Churachandpur, India and has MDR-TB. Every day MSF nurses visit him to administer an injection and watch him take all the daily medicines he needs (15 pills in total). This home-based treatment normally lasts for two years.

© Jan-Joseph Stok

DIAGNOSING TB

Legend:
...: National policies indicate
N/A: not applicable
Grey: no data

	Rapid Molecular Diagnostics (RMD)					Urinary TB LAM	
	... an RMD as the initial test for TB	... limits to the use of an RMD to certain facilities as the initial test for TB	... all children are eligible for an RMD as the initial test for TB	No. facilities with routine RMD testing services per 1000 estimated incident cases	No. facilities offering routine Xpert MTB/RIF, Truenat, TB-LAMP testing and/or other RMD[a]	... urinary TB LAM for routine diagnosis of TB in people living with HIV (PLHIV)	... PLHIV who are severely sick or have advanced HIV disease are eligible for urinary TB LAM, regardless of CD4 counts
Azerbaijan				2.5	15		N/A
Bangladesh				0.5	191		N/A
Belarus				9.3	26		N/A
Brazil				2.1	206		N/A
Cambodia		N/A		1.4	64		N/A
CAR				0.3	8		
DPRK				0.2	23		N/A
DRC		N/A		0.5	130		N/A
Eswatini				7.6	32		
Ethiopia				2.0	313		N/A
India		N/A		0.6	Xpert MTB/RIF: 1195, Truenat: 350		N/A
Indonesia				1.0	878		N/A
Kazakhstan				9.6	125		N/A
Kenya				1.4	189		
Kyrgyzstan				3.4	24		
Lesotho				2.4	34		N/A
Liberia				1.2	18		N/A
Malawi		N/A		2.9	79		
Mozambique				1.7	184		N/A
Namibia				2.8	34		
Nigeria				0.9	395		
Pakistan		N/A		0.6	361		N/A
PNG				1.3	49		
Philippines		N/A		0.8	491		N/A
R. Moldova				17.8	57		N/A
Russian Fed.				4.1	Xpert MTB/RIF: 153, Other RMD[b]: 144		N/A
Sierra Leone				0.6	14		N/A
South Africa				0.5	176		
Tajikistan				5.8	45		
Thailand				1.4	Xpert MTB/RIF: 150, TB-LAMP: 2		N/A
Uganda				2.7	Xpert MTB/RIF: 236, TB-LAMP: 5		
Ukraine				3.9	134		
UR. Tanzania				1.6	219		N/A
Uzbekistan				2.3	51		N/A
Viet Nam		N/A		0.7	126		N/A
Zambia				5.0	Xpert MTB/RIF: 295, TB-LAMP: 20		
Zimbabwe				4.7	137		
Overall uptake (by indicator)	80%	71%	97%	-	-	39%	92%

COLUMN LEGEND							
	All presumptive TB	NO	All presumptive TB	-	-	YES	YES
	Only risk groups	YES	Only risk groups	-	-	Adoption planned in next 12 months and/or used in operational research	NO
	NO		NO	-	-	Not in policies, operational research, or planned in the future	

(a) Figures for Xpert MTB/RIF unless otherwise specified. **(b)** The rapid RT-PCR method developed in Russia.

DIAGNOSING TB

Legend: ...: National policies indicate N/A: not applicable Grey: no data	*(cont.)* Urinary TB LAM		Drug susceptibility testing (DST)				
	Urinary TB LAM is implemented for routine use in inpatient (IPD) and outpatient (OPD) settings	... TB treatment can be initiated based on urinary TB LAM without a confirmatory test	... rifampicin (RIF)-resistance testing for all bacteriologically confirmed TB cases	... isoniazid (INH)-resistance testing for patients starting on DS-TB treatment	... people with rifampicin-resistant TB (RR-TB) are further tested for resistance to at least fluoroquinolones (FLQs)	... use of the "traditional universal DST"	DST is routinely available for bedaquiline (Bdq), delamanid (Dlm), linezolid (Lzd) and/or clofazimine (Cfz), when these medicines are used for routine treatment
Azerbaijan	N/A	N/A					
Bangladesh	N/A	N/A					
Belarus	N/A	N/A					
Brazil	N/A	N/A					
Cambodia	N/A	N/A					
CAR		c					
DPRK	N/A	N/A					
DRC	N/A	N/A					
Eswatini							
Ethiopia	N/A	N/A					
India	N/A	N/A					
Indonesia	N/A	N/A					
Kazakhstan	N/A	N/A					
Kenya							
Kyrgyzstan							
Lesotho	N/A	N/A					
Liberia	N/A	N/A					d
Malawi							
Mozambique	N/A	N/A					
Namibia							
Nigeria							
Pakistan	N/A	N/A					
PNG		c					
Philippines	N/A	N/A					
R. Moldova	N/A	N/A					
Russian Fed.	N/A	N/A					
Sierra Leone	N/A	N/A					
South Africa							
Tajikistan							
Thailand	N/A	N/A					
Uganda							
Ukraine		c					
UR. Tanzania	N/A	N/A					
Uzbekistan	N/A	N/A					
Viet Nam	N/A	N/A					
Zambia							
Zimbabwe							
Overall uptake (by indicator)	42%	90%	86%	31%	100%	86%	29%

COLUMN LEGEND							
	Both OPD and IPD	YES	YES	YES	YES	YES	DST for all drugs that are used for treatment
	Only IPD	NO	Select groups/ locations only	Select groups only	Select groups/ locations only	One or both policy components for select groups/locations only	DST available for at least one but not all drugs used for treatment
	Not implemented		NO	NO	NO	One or both policy components not indicated	DST not available for any of the drugs used for treatment

(c) Policies reported as unclear. **(d)** It was not possible to confirm the country response.

Legend: ...: National policies indicate N/A: not applicable Grey: no data	*(cont.)* Drug susceptibility testing (DST) ... RIF and INH resistance testing for all people starting on treatment; at least FLQ resistance testing for all people with RR-TB; and DST methods available in country for RIF, INH, FLQs, Bdq, Dlm, Lzd, and Cfz, when these medicines are used for routine treatment	Treatment monitoring ... monthly sputum culture during the full duration of DR-TB treatment[e]	Overall uptake (by country)
Azerbaijan			82%
Bangladesh			50%
Belarus			100%
Brazil			64%
Cambodia			50%
CAR			31%
DPRK			75%
DRC			30%
Eswatini			86%
Ethiopia			55%
India			50%
Indonesia			56%
Kazakhstan			70%
Kenya			71%
Kyrgyzstan			93%
Lesotho			64%
Liberia			70%
Malawi			27%
Mozambique			55%
Namibia			77%
Nigeria			67%
Pakistan			60%
PNG			38%
Philippines			44%
R. Moldova			91%
Russian Fed.			82%
Sierra Leone			67%
South Africa			86%
Tajikistan			71%
Thailand			38%
Uganda			77%
Ukraine			85%
UR. Tanzania			40%
Uzbekistan			64%
Viet Nam			44%
Zambia			64%
Zimbabwe			79%
Overall uptake (by indicator)	18%	67%	

COLUMN LEGEND		
	All policies in place & DST methods available	Yes, monthly and full duration
	All policies at least partially in place and DST methods at least partially available	Should receive culture for follow-up of treatment, but not monthly and/or not for the full duration of treatment
	One or more policies not in place and/or DST methods not available	No culture follow-up

(e) Irrespective of whether long or short regimen.

TREATING TB

Legend: ...: National policies indicate; N/A: not applicable; Grey: no data	Paediatric TB						
	... the fixed-dose combination (FDC) rifampicin-isoniazid-pyrazinamide (RHZ) to treat paediatric DS-TB	Paediatric RHZ FDC is routinely used for DS-TB treatment	... child-friendly formulations of second-line medicines for routine treatment of paediatric DR-TB[a]	Country procured the child-friendly formulations of second-line medicines[a]	... the minimum age for treating children with bedaquiline (Bdq) is 6 years of age	... the minimum age for treating children with delamanid (Dlm) is 3 years of age	... routine use of injectable-free regimens for children with uncomplicated DR-TB
Azerbaijan							
Bangladesh							
Belarus							
Brazil					N/A [b]	N/A [c]	
Cambodia							
CAR						N/A [c]	
DPRK							
DRC							
Eswatini							
Ethiopia							
India							
Indonesia							
Kazakhstan							
Kenya							
Kyrgyzstan							
Lesotho							
Liberia							
Malawi							
Mozambique							
Namibia							
Nigeria							
Pakistan							
PNG							
Philippines							
R. Moldova							
Russian Fed.						N/A [c]	
Sierra Leone							
South Africa							
Tajikistan							
Thailand							
Uganda							
Ukraine							
UR. Tanzania							
Uzbekistan							
Viet Nam						N/A [c]	
Zambia							
Zimbabwe							
Overall uptake (by indicator)	97%	89%	76%	92%	91%	91%	72%

COLUMN LEGEND							
	YES	YES	YES	YES	YES		YES
	NO	FDC ordered but not yet routinely used	NO	NO	Age limits are not specified in the national policies		NO
		NO			Age limits higher than WHO recommends		

(a) The new pediatric second-line drug formulations may include one or more of the following: Pyrazinamide 150 mg DT, Ethionamide 125 mg DT, Levofloxacin 100 mg DT, Moxifloxacin 100 mg DT, Cycloserine 125 mg capsules. **(b)** Bdq not indicated in the national policies for routine treatment. **(c)** Dlm not indicated in the national policies for routine treatment.

Legend: ...: National policies indicate N/A: not applicable Grey: no data	DR-TB treatment composition	Longer all-oral DR-TB treatment regimen		Modified shorter all-oral DR-TB[e] treatment regimen	
	Status of policy adoption of the WHO DR-TB guidelines as of end December 2019[d]	... use of a longer all-oral regimen for adults with DR-TB, either for routine use or operational research (OR)	A longer all-oral regimen for the treatment of adults with DR-TB has been implemented for routine use	... use of a modified shorter all-oral regimen for eligible adults with DR-TB, either for routine use or OR	Implementation status of the modified shorter all-oral regimen for treating adults with DR-TB
Azerbaijan					
Bangladesh					
Belarus					
Brazil					
Cambodia					
CAR					
DPRK					
DRC					
Eswatini					
Ethiopia					
India					
Indonesia					
Kazakhstan					
Kenya					
Kyrgyzstan					
Lesotho					
Liberia					
Malawi					
Mozambique					
Namibia					
Nigeria					
Pakistan					
PNG					
Philippines					
R. Moldova					
Russian Fed.					
Sierra Leone					
South Africa					
Tajikistan					
Thailand					
Uganda					
Ukraine					
UR. Tanzania					
Uzbekistan					
Viet Nam					
Zambia					
Zimbabwe					
Overall uptake (by indicator)	81%	92%	81%	61%	36%

COLUMN LEGEND				
National policies are updated	YES	Implemented for routine use	YES	Started or completed (OR or routine use)
National policies not updated, but transition plan developed	NO	Started implementation for routine use	NO	Planned but not started (OR or routine use)
National policies not updated, no strategic/transition plan has been developed		Planned but not started implementation for routine use		Not planned and not started (OR or routine use)
		Implementation for routine use not planned or started		

(d) This concerns the WHO consolidated DR-TB guidelines first issued in December 2018 (final version published in March 2019). This does not concern implementation of the Rapid Communication issued in December 2019. **(e)** Modifications to the standardised shorter regimen (beyond the two medicine substitutions allowed by WHO) include replacing the injectable with bedaquiline or other modifications.

TREATING TB

Legend: ...: National policies indicate N/A: not applicable Grey: no data	Standardised shorter DR-TB treatment regimen[f]		Bedaquiline-pretomanid-linezolid (BPaL)[g]	Mono-INH resistant TB	Duration of Bdq and Dlm	
	... standardised shorter regimen for the routine treatment of eligible adults with DR-TB	... amikacin (Am) as the preferred injectable agent in the standardised shorter regimen	Status of implementing BPaL at country level	... a levofloxacin-containing regimen as the preferred treatment for Hr-TB without concomitant RR-TB	... no limitation to Bdq use beyond 6 months[j]	... no limitation to Dlm use beyond 6 months[j]
Azerbaijan	NO	N/A				
Bangladesh	YES					
Belarus	NO	N/A				
Brazil	NO	N/A			N/A [k]	N/A [l]
Cambodia	YES					
CAR	YES					N/A [l]
DPRK	YES					
DRC	YES					
Eswatini	YES			[i]		
Ethiopia	YES					
India	YES					
Indonesia	YES					
Kazakhstan	YES					
Kenya	NO	N/A				
Kyrgyzstan	YES					
Lesotho	NO	N/A				
Liberia	NO	N/A	[h]			
Malawi	YES					
Mozambique	NO	N/A				
Namibia	YES					
Nigeria	YES					
Pakistan	YES					
PNG	YES					
Philippines	YES					
R. Moldova	PARTIAL NO	N/A				
Ruassian Fed.	PARTIAL NO	N/A				N/A [l]
Sierra Leone	YES					
South Africa	NO	N/A				
Tajikistan	YES					
Thailand	YES					
Uganda	YES					
Ukraine	YES					
UR. Tanzania	YES					
Uzbekistan	YES					
Viet Nam	YES					N/A [l]
Zambia	PARTIAL NO	N/A				
Zimbabwe	NO	N/A				
Overall uptake (by indicator)	68%	83%	8%	76%	17%	18%

COLUMN LEGEND				
	YES	Clinical trials ongoing and/or routine use has started and/or OR or pilot has started	YES	Extension allowed without time limits or special approval
	NO	OR or pilot planned but not started and/or routine use is planned but not started	NO	Extension without time limits is not indicated or allowed, or only allowed with special approval
		OR or pilot and/or routine use not planned in the coming 12 months		

(f) The standardized shorter regimen includes 4-6 (Am/Kan/Cm)-(Mfx/Gfx/Lfx)-(Pto/Eto) -Cfz-Z-INH(high) / 5 Mfx-Cfz-Z-E, also known as the "Bangladesh regimen". **(g)** In December 2019, WHO recommended use of BPaL under operational research conditions. This question only concerns the BPaL regimen approved by the US-FDA with 1200 mg Lnz. Some countries have trials ongoing at lower dose of Lnz, which has not been covered in this survey. **(h)** Operational research or pilot is planned but not started, but implementation for routine use is not planned in the coming 12 months. **(i)** According to the drug resistance survey (DRS) results, the country decided to exclude Lfx in the regimen because of unknown susceptibility of rifampicin. **(j)** This excludes extensions beyond 6 months upon special approval (e.g. consilia or expert groups); it also excludes countries that allow extensions beyond 6 months, but for specific duration (e.g. 36 weeks). *(continued next page)*

Legend: ...: National policies indicate N/A: not applicable Grey: no data	Combination of Bdq and Dlm		Injectables	Overall uptake (by country)
	... combined use of Bdq and Dlm for routine DR-TB treatment	... no limitation to the combined use of Bdq and Dlm[m] beyond 6 months[j]	Kanamycin (Km) and/or capreomycin (Cm) are no longer used routinely	
Azerbaijan				65%
Bangladesh				76%
Belarus				53%
Brazil	N/A [k] [l]	N/A [k] [l]		14%
Cambodia				65%
CAR	N/A [l]	N/A [l]		24%
DPRK				74%
DRC				71%
Eswatini				71%
Ethiopia				65%
India		N/A [n]		50%
Indonesia				60%
Kazakhstan				57%
Kenya		N/A [n]		58%
Kyrgyzstan				62%
Lesotho				63%
Liberia				90%
Malawi				78%
Mozambique		N/A [n]		76%
Namibia				60%
Nigeria				71%
Pakistan				81%
PNG		N/A [n]		58%
Philippines				74%
R. Moldova				75%
Ruassian Fed.	N/A [l]	N/A [l]		60%
Sierra Leone				67%
South Africa				90%
Tajikistan				71%
Thailand				74%
Uganda				80%
Ukraine				86%
UR. Tanzania				67%
Uzbekistan				65%
Viet Nam	N/A [l]	N/A [l]		50%
Zambia				75%
Zimbabwe				75%
Overall uptake (by indicator)	88%	23%	54%	

COLUMN LEGEND			
	Combined use is allowed for routine DR-TB treatment	Combined use is allowed without time limits or special approval	Neither Cm or Km routinely used
	Combined use is allowed under OR	Combined use without time limits is not indicated or allowed, or only allowed	Cm and/or Km routinely used
	Combined use not indicated		

(k) Bdq not indicated in the national policies for routine treatment. **(l)** Dlm not indicated in the national policies for routine treatment. **(m)** Combined use of Bdq and Dlm could be limited to certain groups of patients. **(n)** Bdq and Dlm (combination) not indicated for use in national policy for routine treatment.

TREATING TB — MODELS OF CARE

Legend: ...: National policies indicate N/A: not applicable Grey: no data	Treatment initiation		Decentralisation			People-centered care
	... hospitalisation for DS-TB treatment initiation is not required for people who are clinically stable	... hospitalisation for DR-TB treatment initiation is not required for people who are clinically stable	... DR-TB treatment can be initiated at a primary health care (PHC) facility	Lowest health care level where DR-TB treatment can be initiated	... DR-TB treatment follow-up can be done at a PHC facility	... daily DR-TB medicines, including injections, can be taken at home
Azerbaijan				Scientific Research Institute on Lung Diseases		
Bangladesh				PMDT[a] facility (secondary & tertiary)		
Belarus				PMDT facility (tertiary)		
Brazil				N/A		
Cambodia				PMDT facility (secondary & tertiary)		
CAR				Secondary level facilities		
DRPK				PMDT facilities (provincial level)		
DRC				N/A		
Eswatini				N/A		
Ethiopia				Secondary level facilities		
India				PMDT facilities (district level)		
Indonesia				Hospital (secondary & tertiary level)		
Kazakhstan				N/A		
Kenya				N/A		
Kyrgyzstan				N/A		
Lesotho				Central level health facility (tertiary level)		
Liberia				Hospital		
Malawi				District and central hospital		
Mozambique				N/A		
Namibia				Secondary level hospitals (district)		
Nigeria				Secondary level facilities		
Pakistan				PMDT facility (tertiary level)		
PNG				PMDT facility (provincial level)		
Philippines				Secondary level		
R. Moldova				N/A		
Russian Fed.				N/A		
Sierra Leone				Secondary level		
South Africa				N/A		
Tajikistan				N/A		
Thailand				Secondary level		
Uganda				N/A		
Ukraine				N/A		
UR. Tanzania				N/A		
Uzbekistan				District TB clinics and wards		
Viet Nam				PMDT facility (tertiary level)		
Zambia				Secondary (district) & tertiary level hospitals		
Zimbabwe				N/A		
Overall uptake (by indicator)	73%	42%	41%	-	75%	57%
COLUMN LEGEND	NOT REQUIRED	NOT REQUIRED	YES	-	YES	YES
	Only for select groups/people			-	Only for select people/specific circumstances	
	REQUIRED	REQUIRED	NO	-	NO	NO

(a) Programmatic management of drug-resistant TB (PMDT).

Legend: ...: National policies indicate N/A: not applicable Grey: no data	*(cont.)* **People-centered care**		**Social support**	**Overall uptake (by country)**
	... people with DS-TB can take their daily TB medicines as self-administered therapy (SAT)[b]	... people with DR-TB can take their daily TB medicines as SAT[b]	... food and transport support is provided to all people on DR-TB treatment[c]	
Azerbaijan				38%
Bangladesh				50%
Belarus				0%
Brazil				50%
Cambodia				38%
CAR				25%
DRPK				13%
DRC				25%
Eswatini				63%
Ethiopia				63%
India				63%
Indonesia				25%
Kazakhstan				38%
Kenya				75%
Kyrgyzstan				63%
Lesotho				50%
Liberia				17%
Malawi				50%
Mozambique				38%
Namibia				38%
Nigeria				38%
Pakistan				50%
PNG				25%
Philippines				50%
R. Moldova				67%
Russian Fed.				38%
Sierra Leone				25%
South Africa				75%
Tajikistan				25%
Thailand				17%
Uganda				71%
Ukraine				63%
UR. Tanzania				63%
Uzbekistan				0%
Viet Nam				25%
Zambia				57%
Zimbabwe				75%
Overall uptake (by indicator)	3%	0%	46%	
COLUMN LEGEND	YES	YES	Food and transport provided	
	Only under specific circumstances	Only under specific circumstances	Food and/or transport provided for some or all people with DR-TB	
	NO	NO	No food or transport support provided	

(b) Self-administered therapy does not include use of adherence tools that require real-time interaction with a healthcare provider, but may include support from family members.
(c) This includes cash transfers, direct food baskets, vouchers and reimbursement systems.

PREVENTING TB

Legend: ...: National policies indicate N/A: not applicable Grey: no data	Regimen for latent tuberculosis infection (LTBI) treatment	LTBI regimen for DR-TB contacts	HIV test and treat	TB signs and symptoms screening			
	... a shorter TB preventive treatment (TPT) regimen (3HP, 3RH, 4R or 1HP)[a]	... a levofloxacin-containing preventive regimen for contacts of people with DR-TB	... people living with HIV (PLHIV) receive ARV treatment regardless of CD4 count	... PLHIV are screened for signs and symptoms of TB at every healthcare visit	... household contacts of a person with bacteriologically confirmed DS-TB are investigated for signs and symptoms of TB	... household contacts of a person with clinically diagnosed DS-TB are investigated for signs and symptoms of TB	... household contacts of a person with bacteriologically confirmed DR-TB are investigated for signs and symptoms of TB
Azerbaijan							
Bangladesh							
Belarus							
Brazil							
Cambodia							
CAR							
DPRK							
DRC							
Eswatini							
Ethiopia							
India							
Indonesia							
Kazakhstan							
Kenya							
Kyrgyzstan							
Lesotho							
Liberia							
Malawi				[b]			
Mozambique							
Namibia							
Nigeria							
Pakistan							
PNG							
Philippines							
R. Moldova							
Russian Fed.							
Sierra Leone							
South Africa							
Tajikistan							
Thailand							
Uganda							
Ukraine							
UR. Tanzania							
Uzbekistan							
Viet Nam							
Zambia							
Zimbabwe							
Overall uptake (by indicator)	65%	20%	100%	92%	84%	49%	81%

COLUMN LEGEND					
	YES	YES	YES	All PLHIV	All household contacts
	NO	NO	NO	Only PLHIV age <5 or PLHIV ≥5	Only household contacts age <5 or ≥5
				No PLHIV screened	No contacts investigated

(a) 3HP: 3 months rifapentine plus isoniazid given weekly; 3HR: 3 months of rifampicin plus isoniazid given daily; 4R: 4 months of rifampicin given daily; 1HP: 1 month of rifapentine plus isoniazid given daily **(b)** It was not possible to confirm the country response.

Legend: ...: National policies indicate N/A: not applicable Grey: no data	*(cont.)* TB signs and symptoms screening		Eligible groups for TPT as indicated in national policies:				
	... household contacts of a person with clinically diagnosed DR-TB are investigated for signs and symptoms of TB	... screening of signs and symptoms of TB for all diabetics at every healthcare visit	PLHIV	Household contacts (<5 years) of bacteriologically confirmed DS-TB	Household contacts (5 years and above) of bacteriologically confirmed DS-TB	Household contacts of clinically diagnosed DS-TB	Prisoners
Azerbaijan							
Bangladesh							
Belarus							
Brazil							
Cambodia							
CAR							
DPRK							
DRC							
Eswatini							
Ethiopia							
India							
Indonesia							
Kazakhstan							
Kenya							
Kyrgyzstan							
Lesotho							
Liberia							
Malawi							
Mozambique							
Namibia							
Nigeria							
Pakistan							
PNG							
Philippines							
R. Moldova							
Russian Fed.							
Sierra Leone							
South Africa							
Tajikistan							
Thailand							
Uganda							
Ukraine							
UR. Tanzania							
Uzbekistan							
Viet Nam							
Zambia							
Zimbabwe							
Overall uptake (by indicator)	62%	61%	95%	100%	51%	19%	30%
COLUMN LEGEND	All household contacts	YES	YES	YES	YES	YES	YES
	Only household contacts age <5 or ≥5	NO	NO	NO	NO	NO	NO
	No contacts investigated						

PREVENTING TB

Legend: ...: National policies indicate N/A: not applicable Grey: no data	*(cont.)* Eligible groups for TPT as indicated in national policies:					Overall uptake (by country)
	Health care workers	Miners or people with silicosis	Migrants	People with diabetes	People receiving dialysis	
Azerbaijan	YES	YES	YES	NO	YES	68%
Bangladesh	NO	NO	NO	NO	NO	32%
Belarus	NO	NO	NO	NO	NO	26%
Brazil	YES	YES	YES	YES	YES	89%
Cambodia	NO	NO	NO	NO	NO	47%
CAR	NO	NO	NO	NO	NO	47%
DPRK	YES	YES	YES	YES	YES	72%
DRC	NO	NO	NO	NO	NO	21%
Eswatini	YES	YES	YES	NO	YES	89%
Ethiopia	NO	NO	NO	NO	NO	53%
India	YES	YES	YES	YES	YES	84%
Indonesia	NO	NO	NO	YES	YES	79%
Kazakhstan	NO	YES	YES	NO	YES	74%
Kenya	YES	NO	NO	NO	NO	53%
Kyrgyzstan	YES	YES	YES	YES	YES	53%
Lesotho	YES	YES	YES	YES	NO	84%
Liberia	YES	NO	NO	NO	NO	47%
Malawi	NO	NO	NO	NO	NO	44%
Mozambique	NO	NO	NO	NO	NO	53%
Namibia	NO	NO	NO	YES	NO	53%
Nigeria	YES	NO	NO	NO	NO	63%
Pakistan	NO	YES	YES	NO	YES	37%
PNG	NO	NO	NO	NO	NO	37%
Philippines	NO	NO	NO	NO	NO	42%
R. Moldova	NO	YES	YES	NO	YES	79%
Russian Fed.	NO	YES	YES	YES	YES	83%
Sierra Leone	NO	NO	NO	NO	NO	33%
South Africa	NO	YES	YES	YES	NO	68%
Tajikistan	NO	NO	NO	YES	NO	58%
Thailand	NO	NO	NO	NO	NO	61%
Uganda	NO	NO	NO	NO	NO	32%
Ukraine	NO	YES	YES	NO	YES	84%
UR. Tanzania	NO	NO	NO	NO	NO	42%
Uzbekistan	NO	NO	NO	YES	YES	58%
Viet Nam	NO	NO	NO	NO	NO	21%
Zambia	YES	YES	YES	YES	YES	84%
Zimbabwe	NO	NO	NO	NO	YES	68%
Overall uptake (by indicator)	30%	38%	38%	32%	41%	
COLUMN LEGEND	YES	YES	YES	YES	YES	
	NO	NO	NO	NO	NO	

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Luisa Ure, in Papua New Guinea, says of her nearly 3-year TB treatment: "The treatment was very hard in the beginning. There are so many pills to take, I could only swallow one by one. It was difficult to stick to the treatment."

PROCURING MEDICINES FOR TB

Legend: ...: National policies indicate; N/A: not applicable; Grey: no data	Early access	Medicine procurement			Transparency
	Early access mechanisms for TB medicines allowed by law	WHO and/or US-CDC[a] recommendation required for importation of TB medicines	Stringent regulatory authority (SRA)[b] approval and/or WHO Prequalification (PQ)[c] required for importation of TB medicines purchased with domestic funding	SRA and/or WHO PQ quality-assured product status required for procurement of locally manufactured TB medicines	Transparency required for national tenders for TB medicines (elements: publication of selection criteria, winning bidder & final price)[e]
Azerbaijan				N/A [d]	
Bangladesh				N/A [d]	
Belarus					
Brazil					
Cambodia					
CAR				N/A [d]	
DPRK					
DRC				N/A [d]	
Eswatini				N/A [d]	
Ethiopia					
India					
Indonesia					
Kazakhstan					
Kenya					
Kyrgyzstan				N/A [d]	
Lesotho				N/A [d]	
Liberia				N/A [d]	
Malawi					
Mozambique				N/A [d]	
Namibia				N/A [d]	
Nigeria					
Pakistan				N/A [d]	
PNG				N/A [d]	
Philippines					
R. Moldova					
Russian Fed.					
Sierra Leone				N/A [d]	
South Africa					
Tajikistan				N/A [d]	
Thailand					
Uganda				N/A [d]	
Ukraine					
UR. Tanzania				N/A [d]	
Uzbekistan				N/A [d]	
Viet Nam					
Zambia					
Zimbabwe				N/A [d]	
Overall uptake (by indicator)	81%	58%	54%	36%	60%

COLUMN LEGEND					
	YES	YES	YES	YES	All three elements fulfilled
	NO	Only for some medicines			Only one or two elements fulfilled
		NO	NO	NO	No elements fulfilled

(a) United States Centers for Disease Control and Prevention (US-CDC). **(b)** For more information about SRAs see hyperlink (WHO definition of SRA on page 356) **(c)** WHO PQ assesses medicines and active pharmaceutical ingredients to ensure they are safe, appropriate and meeting stringent quality standards. **(d)** TB medicines are not locally manufactured, or locally manufactured TB medicines are not procured. **(e)** Some answers from respondents could not be verified against national policy documents.

Legend: ...: National policies indicate N/A: not applicable Grey: no data	WHO Collaborative Registration Procedure (CRP)[f]			National Essential Medicines List (nEML)[g]		Overall uptake (by country)
	Country is enrolled in WHO CRP	Use of WHO CRP to register at least one TB medicine	Rifampin-isoniazid-pyrazinamide-ethambutol (RHZE) (150/75/400/275) or rifampin-isoniazid (RH) (150/75) registered through the WHO CRP for the treatment of DS-TB	All WHO Group A and B DR-TB medicines[h] are listed on the nEML	RHZE (150/75/400/275) and RH (150/75) to treat DS-TB are listed on the nEML	
Azerbaijan						60%
Bangladesh		N/A	N/A			43%
Belarus						20%
Brazil		N/A	N/A			50%
Cambodia		N/A	N/A			71%
CAR		N/A	N/A			0%
DPRK		N/A	N/A			38%
DRC						67%
Eswatini		N/A	N/A			60%
Ethiopia						50%
India		N/A	N/A			13%
Indonesia		N/A	N/A			25%
Kazakhstan						38%
Kenya						70%
Kyrgyzstan						67%
Lesotho		N/A	N/A			29%
Liberia		N/A	N/A			50%
Malawi						75%
Mozambique						89%
Namibia						67%
Nigeria						70%
Pakistan						63%
PNG		N/A	N/A			17%
Philippines						75%
R. Moldova		N/A	N/A			63%
Russian Fed.		N/A	N/A			17%
Sierra Leone						50%
South Africa						40%
Tajikistan		N/A	N/A			80%
Thailand						70%
Uganda						88%
Ukraine						60%
UR. Tanzania						100%
Uzbekistan						75%
Viet Nam		N/A	N/A			43%
Zambia						89%
Zimbabwe						63%
Overall uptake (by indicator)	59%	64%	27%	34%	66%	
COLUMN LEGEND	YES	YES	YES	YES	YES	
	NO	NO	NO	NO	NO	

(f) The CRP accelerates registration through timely sharing of medicine dossiers to national medicines regulatory authorities. Data were collected through a desk review. **(g)** Data were collected through a desk review of nEMLs available online or shared by the respondents; nEMLs were not available for two countries. **(h)** Group A: levofloxacin or moxifloxacin; bedaquiline; linezolid. Group B: clofazimine; cycloserine or terizidone.

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