



THE PARADIGM

SHIFT →

Global Plan to End TB: 2018-2022

Paradigm Shift

noun [c]

“a time when the usual and accepted way of doing or thinking about something changes completely”



The Paradigm Shift 2018-2022

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Global Health Campus
Chemin du Pommier 40
1218 Le Grand-Saconnex
Geneva, Switzerland

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US\$ 77.8 BILLION NEEDED TO REACH THE UNITED NATIONS TB TARGETS

Five-year period: 2018-2022



(US\$ Billion)

- TB Prevention and Care
- R&D of new diagnostics, drugs and vaccine
- Basic science research

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ACKNOWLEDGMENTS

The Stop TB Partnership acknowledges with gratitude everyone's contribution to the Global Plan to End TB 2018–2022. Hundreds of people contributed to the formulation of this Global Plan through various channels, including two online consultations. We thank each of them for their enthusiastic feedback and support. The global health community will implement this plan together.

Global Plan Task Force:

Paula I Fujiwara (Chair), Katherine Floyd, Blessina Kumar, David Lewinsohn, David Mametja, Thokozile B Nkhoma, Aaron Oxley, KS Sachdeva, Cheri Vincent, Eliud Wandwalo and Richard White.

Alternate Members of Task Force:

Sevim Ahmedov, Philippe Glaziou, Janika Hauser, Rachael Hore, Mukadi YaDiul and Mohammed A Yassin.

Secretariat to the Global Plan Task Force:

Mohammed Anouar, Lucica Ditiu, Suvanand Sahu and Shinichi Takenaka.

Others from Stop Partnership Secretariat

Sara Gonzalez Andino, Ramón H. Crespo, Jacob Creswell, Jacqueline Huh, Brian Kaiser, Amera Khan, James Malar, Kadiria Malkoc, Enos Masini, Andrei Mosneaga, Sreenivas Nair, Gregory Paton, Nina Saouter (with the support of Diana Schwalb), Viorel Soltan and Brenda Waning.

Special thanks go to

- Paul M Jensen for the drafting and editing work
- Carel Pretorius, Avenir Health, for the modelling work
- David Dowdy, Johns Hopkins Bloomberg School of Public Health, for the “cost of inaction” modelling work

Sincere thanks also go to

the leadership and members of the New Tools Working Groups consisting of the Working Group on New TB Diagnostics, Working Group on New TB Drugs and Working Group on New TB Vaccines.

Stop TB Partnership Board members:

Nazira Abdula, Timur Abdullaev, Farhana Amanullah, Elzhan A Birtanov, Erika Arthun, Pierre Blais, Sara Boiten, Joanne Carter, Lucica Ditiu, Osagie Emmanuel Ehanire, Paula I Fujiwara, Moin Karim, Yosuke Kita, David Lewinsohn, Susan Maloney, Luiz Henrique Mandetta, Lelio Marmora, Ren Minghui, Aaron Motsoaledi, Thokozile B Nkhoma, Austin Obiefuna, Aaron Oxley, Peter Sands, Miriam Schneidman, Adrian Thomas, Stéphanie Seydoux, Harsh Vardhan, Cheri Vincent and Kitty van Weezenbeek.

This document would not have been possible to develop without the support of the Bill & Melinda Gates Foundation, USAID and the Global Fund to Fight AIDS, Tuberculosis and Malaria.

ABBREVIATIONS & ACRONYMS

aDSM

Active drug-safety monitoring

AI

Artificial intelligence

AMR

Antimicrobial resistance

BRICS

Brazil, Russian Federation, India, China, South Africa

CBM

Community-based monitoring

COE

Challenging operating environment

CRG

Community, rights and gender

CSO

Civil society organization

CSR

Corporate social responsibility

CSS

Community systems strengthening

DALY

Disability-adjusted life year

DAT

Digital adherence technology

DR-TB

Drug-resistant tuberculosis

DST

Drug susceptibility testing

DS-TB

Drug-susceptible tuberculosis

FBO

Faith-based organization

FDA

U.S. Food and Drug Administration

GCP

Good Clinical Practice

GDF

Global Drug Facility

GERD

Gross domestic expenditure on research and development

GNI

Gross national income

LAM

Lipoarabinomannan

LMIC

Low- and middle-income country

MAF-TB

Multisectoral Accountability Framework to Accelerate Progress to Eliminate Tuberculosis by 2030

MDR-TB

Multidrug-resistant tuberculosis

NGO

Nongovernmental organization

NGS

Next-generation sequencing

NHP

Nonhuman primate

NTP

National tuberculosis programme

OECD

Organisation for Economic Co-operation and Development

PDP

Product development partnership

POC

Point-of-care

PPM

Public-private mix

R&D

Research and development

ROI

Return on investment

RR-TB

Rifampicin-resistant tuberculosis

SADC

Southern African Development Community

SDG

Sustainable Development Goal

SHI

Social health insurance

TB

Tuberculosis

TIME

TB Impact and Model Estimate

TPP

Target product profile

UHC

Universal Health Coverage

UN

United Nations

UNHLM

United Nations High-Level Meeting

WHO

World Health Organization

XDR-TB

Extensively drug-resistant tuberculosis

GLOSSARY

Active TB disease

an illness in which TB bacteria are multiplying in different parts of the body. The symptoms of active TB disease include cough, weakness, weight loss, fever, loss of appetite and night sweats. A person with active TB disease may be infectious and spread TB to others. In the Global Plan, “people with TB” or “people ill with TB” refers to those who have active TB disease

Antibiotic

a drug used to treat bacterial infections. Anti-TB drugs are also antibiotics. Antibiotics have no effect on viral infections.

Antimicrobial resistance (AMR)

the ability of a microorganism to withstand the effects of antibiotics. Antibiotic resistance typically evolves when a random mutation of the microorganism develops, making it less susceptible to the effects of a particular drug.

BCG

the Bacillus Calmette–Guérin TB vaccine is named after the French scientists who developed it, Calmette and Guérin. BCG provides adolescents and adults with little protection against TB, but it is often given to infants and small children in countries where TB is common, as it can prevent some of the most severe forms of TB in children.

Case detection

when a person’s TB is diagnosed and reported within the national surveillance system. Although the term “case” is used widely in public health to refer to an instance of disease, it should be used with sensitivity in health care settings to avoid dehumanizing people. A person is not a case, but a fellow human being. Individuals seeking or receiving care for TB may find it demeaning if they overhear a health worker describing them as a “case”.

Contact

a person who has spent time with a person with infectious TB.

Close contact

a person who has had prolonged, frequent or intense contact with a person with infectious TB. This group includes people who live together or spend a great deal of time together in close proximity. Close contacts, or household contacts, are more likely to become infected with *M. tuberculosis* than contacts who see the person with TB less often.

Community systems

are the structures, mechanisms, processes and actors through which communities act on the challenges and needs that they face. They are made up of different types of entities: community members, formal and informal community organizations and networks, and other civil society organizations. Such systems are usually less formalized and less clearly defined than health systems. Entities that make up community systems have close links with communities; therefore, they are in a position to better understand the issues faced by those who are most affected and to find smart solutions.

Community systems strengthening

refers to initiatives that contribute to the development and/or strengthening of community-based organizations in order to increase knowledge of and access to improved health service delivery. It usually includes capacity-building of infrastructure and systems, partnership building, and the development of sustainable financing solutions.

Culture

a test to see whether there are TB bacteria in an individual’s sputum/phlegm or other body fluids. This test can take two to four weeks in most laboratories.

Drug-resistant tuberculosis

disease caused by a strain of TB bacteria that is resistant to the most commonly used anti-TB drugs.

Extensively drug-resistant tuberculosis

disease caused by a strain of TB bacteria that is resistant to isoniazid and rifampicin (the two most commonly used anti-TB drugs), as well as a fluoroquinolone and at least one of the three injectable second-line drugs (amikacin, kanamycin, capreomycin).

Extrapulmonary TB

TB disease in any part of the body other than the lungs (for example, pleura, kidney, spine, brain or lymph nodes).

Gender-sensitive

gender-sensitive policies, programmes or training modules recognize that both women and men are actors within a society, that they are constrained in different and often unequal ways, and that consequently they may have divergent and sometimes conflicting perceptions, needs, interests and priorities.

Multidrug-resistant tuberculosis

disease caused by a strain of TB bacteria that is resistant to at least isoniazid and rifampicin (the two most commonly used anti-TB drugs).

Mycobacterium tuberculosis

the bacterium that causes TB infection and TB disease.

Nutritional support

aims at ensuring adequate nutrition and includes assessment of the dietary intake, nutritional status and food security of the individual or household; offering nutrition education and counselling on how to ensure a balanced diet, mitigate side effects of treatment and infections, and ensure access to clean water; and providing food supplements or micronutrient supplementation where necessary.

OECD

Organisation for Economic Co-operation and Development (OECD) brings together 30 member countries sharing a commitment to democratic government and the market economy.

People-centred approach to TB care

a people-centred approach considers the needs, perspectives and individual experiences of people affected by TB, while respecting their right 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. A people-centred approach improves treatment outcomes, while respecting human dignity.

People affected by TB

this term encompasses people ill with TB and their family members, dependents, communities and health care workers who may be involved in caregiving or are otherwise affected by the illness.

People with TB

this term encompasses people who are ill with active TB. The term “people (or person) with TB” recognizes that people with TB should not be defined solely by their condition. The term may be preferable to the word “patient” in certain contexts (e.g., non-medical and community settings).

TB Preventive therapy (TPT)

medicines that prevent TB infection from progressing to active TB disease.

Southern African Development Community (SADC)

is an intergovernmental organization headquartered in Gaborone, Botswana. Its goal is to further socioeconomic cooperation and integration as well as political and security cooperation among 15 southern African states. It complements the role of the African Union.

Sputum

phlegm coughed up from deep inside the lungs. Sputum is examined for TB bacteria using smear microscopy, culture or molecular tests.

Stigma

is derived from the Greek meaning “a mark or a stain”. Stigma can be described as a dynamic process of devaluation that significantly discredits an individual in the eyes of others. Within particular cultures or settings, certain attributes are seized upon and defined by others as discreditable or unworthy. When stigma is acted upon, the result is discrimination that may take the form of actions or omissions.

TB disease

an illness in which TB bacteria multiply and attack a part of the body, usually the lungs. The symptoms of active TB disease include weakness, weight loss, fever, loss of appetite and night sweats. Other symptoms of TB disease depend on where in the body the bacteria are growing. If TB disease is in the lungs (pulmonary TB), the symptoms may include a bad cough, pain in the chest and coughing up blood. A person with pulmonary TB disease may be infectious and spread TB bacteria to others.

TB infection

also called latent TB infection. It is a condition in which TB bacteria are alive but inactive in the body. People with TB infection have no symptoms; they do not feel sick, cannot spread TB bacteria to others, and usually test positive for infection – positive to a tuberculin skin test or a special test called IGRA (interferon gamma release assay). In the Global Plan, people referred to as “infected with TB” are people having such latent TB infection.

TB prevention and care

the efforts of health care workers to provide TB services to the communities they serve. These terms are preferred over “TB control”, which may create the perception that TB experts are in full control of all aspects of prevention, treatment and care of people with TB. It is useful to examine the term “control” critically so as to avoid neglecting resources and capacities of communities and people affected by TB.

Sustainable Development Goals (SDGs)

provide a shared blueprint for peace and prosperity for people and the planet, now and into the future. The 2030 Agenda for Sustainable Development was adopted by all United Nations Member States in 2015, and at its heart are the 17 Sustainable Development Goals (SDGs), which are an urgent call for action by all countries – developed and developing – in a global partnership. The global health community thrives to achieve SDG 3: ensure healthy lives and promote well-being for all at all ages.

Universal Health Coverage (UHC)

means that all people have access to the health services they need, when and where they need them, without financial hardship.

UNHLM on TB

the first High-Level Meeting on TB held by UN Member States at the UN General Assembly in New York on 26 September 2018. The meeting resulted in a Political Declaration endorsed by heads of state and government outlining the key commitments that must be met for the world to end the TB epidemic by 2030, as called for in the UN Sustainable Development Goals. In 2023, UN Member States will convene a follow-up High-Level Meeting for a comprehensive review of their progress.

For more information on suggested language and usage for tuberculosis communications, please access the Stop TB Partnership Language Guide:

http://www.stoptb.org/assets/documents/resources/publications/acsm/LanguageGuide_ForWeb20131110.pdf

FOREWORD

Since the Global Plan to End TB 2016–2020 was released, the TB community has seen the beginning of a seismic paradigm shift. Ambitions have been raised, the TB community has become increasingly unified, and governments have been pressed to fill the gap between ambition and reality. The Stop TB Partnership called for action at the highest political levels, resulting in the UN High-Level Meeting (UNHLM) on TB in September 2018 and a Political Declaration endorsed by world leaders that included a set of ambitious targets.

It had been widely acknowledged that the biggest gap in the fight against TB was political will. It's what ensures TB diagnostics, medicines and new innovations reach the people who need them the most. It's the key to increasing TB funding to the US\$ 15 billion a year needed to reach the UNHLM funding targets. The leadership of heads of state and government is what translates political declarations and targets into lives saved.

Another turning point was the overdue realization that we will only succeed with the full partnership and collaboration of people affected by TB. This requires an approach that is grounded in human rights and Universal Health Coverage, and that includes communities in every area of decision-making as full partners in the planning, implementation and monitoring of the TB response. While we still have much work to do to make this a reality, this approach is beginning to transform the TB response.

And we have evidence that the paradigm shift set out in the Global Plan is starting to work. The WHO Global TB Report 2019 shows that 7 million people affected by TB were reached with TB diagnosis and treatment in 2018 – an increase of 600,000 people over the previous year and the largest ever annual increase. We are overcoming the persistent barriers many people face in accessing health services, aided by a strategic initiative by the Global Fund, the Stop TB Partnership, WHO and partners to support

country programmes to accelerate progress in finding people with TB.

For this 2018–2022 Global Plan update, a Task Force of the world's leading experts came together with people affected by TB, civil society and communities. Supported by two public consultations, the Plan sets out the steps needed to get on track to end TB.

Reaching the targets of the UNHLM Political Declaration is the driving force of this update, headlined by the overarching goal to diagnose and treat 40 million people with TB by 2022. The Stop TB Partnership has translated the UNHLM on TB targets to national level so that every country knows where the finish line is.

This Global Plan 2018–2022 should be owned by every single stakeholder, partner and country programme. The Stop TB Partnership, along with its more than 2,000 partners, aims to build on these bold foundations by calling to shift TB prevention and care to the community level in order to ensure we reach the most vulnerable populations, including migrants, miners, children, and people affected by HIV, and continue to bring the best possible prevention, treatment and care to where it's needed most.

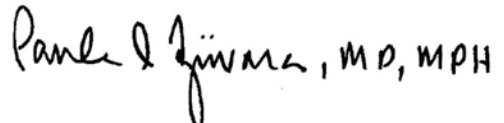
This updated Plan represents our chance to get on track to end TB by 2030. As the Stop TB Partnership Board Leadership, Executive Director of the Secretariat, and Chair of the

Global Plan Task Force, we are committed to mobilizing every potential resource, every ounce of energy and every dollar necessary until we live in a world where no one dies from TB.

The TB community is united and determined to see this fight through to the end. History also tells us that bold and audacious steps offer the greatest chance for success. For TB, that is the only hope.



Dr. Luiz Henrique Mandetta
Chair, Stop TB Partnership Board,
and Minister of Health of Brazil



Dr. Paula I Fujiwara
Chair, Task Force of the Global Plan to
End TB 2018–2022, and Scientific Director,
International Union Against Tuberculosis and
Lung Disease



Dr. Joanne Carter
Vice-Chair, Stop TB Partnership Board,
and Executive Director, RESULTS and RESULTS
Educational Fund



Dr. Lucica Ditiu
Executive Director
Stop TB Partnership secretariat



EXECUTIVE SUMMARY

The 'Global Plan to End TB 2018–2022: The Paradigm Shift' is a costed plan and roadmap for a concerted response to tuberculosis (TB), aligned with the United Nations (UN) Political Declaration on TB. It provides an estimate of the resources needed to achieve the targets and commitments set at the UN High-Level Meeting (UNHLM) on TB in September 2018.

Following the UNHLM on TB, the Stop TB Partnership Board requested the development of an update to the 'Global Plan to End TB 2016–2020' (launched in December 2015) under the guidance of the Global Plan Task Force. The 'Global Plan to End TB 2016–2020' introduced an overhaul of the 'business-as-usual' approach to TB – a paradigm shift. This ambitious update calls for an even more determined push to accelerate the scale-up of TB care and prevention, and to increase investments in the research and development (R&D) of new tools, so that no one is left behind.

The Global Plan is centred on strong political leadership to achieve the country shares of the global TB targets agreed in the UN Political Declaration on TB. It highlights the need for a rights-based, people-centred approach, accelerated innovation in care delivery, the introduction of new tools, substantial investment in R&D and a strong country response.

TB is the world's leading cause of death from a single infectious agent. In 2018, an estimated 10 million people became ill with TB and an estimated 1.5 million died.¹ Drug-resistant (DR-) TB affected approximately half a million new people in 2018, presenting a public health crisis and health security risk in many countries. Yet, only an estimated one in three people with DR-TB are being treated today. A further challenge is the

more than 3 million people with TB each year who are not diagnosed and, as a result, are left behind without effective treatment and care.

The global rate of decline in the number of people becoming sick with TB each year – a 2% decline from 2017 to 2018 – falls far short of the pace of progress needed to end the TB epidemic by 2030, as envisioned by the World Health Organization's (WHO) End TB Strategy. Without a clear investment plan and a paradigm shift in how TB is addressed, the world will not meet the UNHLM targets or the Sustainable Development Goal (SDG) to end TB by 2030.

The world has a short window of opportunity to get on track to end TB.

The world must unite around a newly energized effort to end TB.

¹ Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

THE UN POLITICAL DECLARATION ON TB NOT ONLY ARTICULATES A CRUCIAL COMMITMENT TO IMPLEMENTING A RIGHTS-BASED RESPONSE TO TB GLOBALLY, BUT ALSO SETS OUT SPECIFIC TARGETS FOR UN MEMBER STATES TO ACHIEVE BY 2022:

1 SUCCESSFULLY TREAT 40 MILLION PEOPLE WITH TB, including 3.5 million children (under 15 years of age).

2 SUCCESSFULLY TREAT 1.5 MILLION PEOPLE WITH DR-TB, including 115,000 children.

3 PROVIDE TB PREVENTIVE THERAPY FOR AT LEAST 30 MILLION PEOPLE, including 4 million children under the age of 5, 20 million other household contacts of people affected by TB, and 6 million people living with HIV.

4 INCREASE GLOBAL INVESTMENT for TB prevention, diagnosis, treatment and care to US\$ 13 billion annually.

5 INCREASE GLOBAL INVESTMENT FOR TB R&D to US\$ 2 billion annually.

6 MEMBER STATES ALSO COMMITTED TO TAKING CONCRETE ACTIONS necessary to achieve these targets, including working to end TB stigma and all forms of discrimination, and developing integrated, people-centred, community-based and gender-responsive health services based on human rights.

The Global Plan estimates that between 2018 and 2022 a total of US\$ 77.8 billion is needed, according to the following breakdown:

- ✦ A total of US\$ 65 billion is needed for providing TB prevention and care.
- ✦ A total of US\$ 12.8 billion is needed for R&D of new tools and basic science research, which consists of:
 - at least US\$ 10.8 billion needed for R&D of new TB diagnostics, medicines and at least one vaccine, at an average of US\$ 2.16 billion per year; and
 - a total of US\$ 2 billion needed for basic science research related to TB, at an average of US\$ 400 million per year.

Each chapter of the Global Plan to End TB 2018–2022 begins with a summary of the issues and priority actions for national governments and other key stakeholders.



CHAPTER 1 lays out five fundamental shifts that are needed to realize a paradigm shift in the global approach to TB. While the actions called for remain very much in line with the previous edition of the Global Plan, they have been reframed to align with the new UNHLM on TB commitments. This chapter describes the Global Plan people-centred targets called the 90-(90)-90 targets. This chapter also includes new recommendations for ensuring accountability for action. Specifically, it calls for governments and TB stakeholders to implement the elements of the WHO Multisectoral Accountability Framework to Accelerate Progress to End Tuberculosis by 2030 (MAF-TB).



CHAPTER 2 provides updated TB Impact and

Model Estimate (TIME) results showing how countries can make annual progress towards achieving the UNHLM on TB treatment and prevention targets. It also proposes “investment packages”, i.e., packages of priority interventions that countries should invest in to scale up progress to achieve the TB treatment and prevention targets. The updated modelling shows that reaching the targets to provide TB treatment to 40 million people and TB preventive therapy to 30 million will result in getting the world on track to end TB by 2030, albeit with the 2020 milestones for incidence and mortality achieved by 2021 – a year later than originally envisioned. This Global Plan update provides model treatment and prevention targets for nine different country settings. Indicative targets for individual countries can be found on the Stop TB Partnership website: <http://www.stoptb.org/resources/countrytargets>



CHAPTER 3 provides a blueprint for reaching key populations – people who are vulnerable, marginalized, underserved or at-risk of TB infection and illness – with TB care and services. This Global Plan update describes how key populations can be meaningfully engaged and empowered to participate in TB governance and decision-making. It calls for action to fulfil the UNHLM on TB commitments to promote and support an end to stigma and all forms of discrimination, and to enact policies and practices that will improve outreach to key populations, including removing any laws, policies and programmes that discriminate against people with TB. This chapter provides recommendations for specific actions that can be taken to engage and support specific key populations.



CHAPTER 4 lays out approaches and best practices for engaging partners, with a focus on

TB affected communities, community-based organizations, academics and the private sector. Community-based organizations must play a key role in the planning and provision of TB care at the local level, as they are ideally placed to help increase TB awareness, reach those who may be missed, provide social support, reduce stigma, monitor and evaluate programmes, and serve other vital roles. This chapter lays out approaches for advancing both community-based and community-led efforts. The chapter also lays out approaches for partnering with the private sector, including health-product manufacturers, actors within private health care systems, industries outside the health sector, academics and labour unions.



CHAPTER 5 focuses on approaches for addressing TB within the context of universal health coverage (UHC) and applying renewed strategies involving socioeconomic actions. The chapter calls for UN Member States to fulfil the commitment they made at the 2019 UNHLM on UHC to address TB through comprehensive approaches and integrated service delivery, leaving no one behind. Socioeconomic actions require going beyond biomedical interventions to engage a much broader array of stakeholders and allies, including those working in social welfare, labour, housing, urban regeneration, agriculture and justice, as well as cultural leaders and traditional healers.



CHAPTER 6 identifies priorities for advancing R&D and ensuring access to new TB tools with a focus on new diagnostics, medicines and vaccines. The Global Plan recognizes that when it comes to TB R&D, we cannot afford business as usual. New modelling included within the chapter shows the cost of delay in investment in R&D for new tools. This chapter calls on UN Member

States to fulfil their commitment to closing the TB R&D funding gap by mobilizing an increase in funding from approximately US\$ 700 million in 2017 to over US\$ 2 billion annually by 2022. The chapter also provides an updated, costed framework to guide new investment in TB R&D in line with the forthcoming WHO Global Strategy for TB Research and Development. In addition to this funding support, global investment in basic science research also needs to increase to an estimated US\$ 400 million per year. The chapter describes a new fair-shares framework through which countries can fill the TB R&D funding gap. Model “off-the-shelf” research projects are included for the first time. These projects could be initiated quickly to contribute significantly to the development of new diagnostics, medicines and vaccines. The chapter also lays out the rationale and priorities for advancing basic science research, optimizing the delivery of new tools through operational research, putting new digital tools to use, and creating an overall enabling environment for R&D. To ensure access to new tools, the chapter concludes with an updated review of advocacy priorities, best practices for community engagement, and established rights-based access principles.



CHAPTER 7 provides an updated plan through which UN Member States should fulfil their commitment to increase financing for TB prevention and care to US\$ 13 billion annually and increase TB R&D financing to more than US\$ 2 billion annually. This chapter provides new projections of the annual resources needed to achieve the global UNHLM on TB treatment and prevention targets. Resource needs for TB prevention and care are presented by country income group, WHO Region, Global Plan country setting, Global Fund eligibility and BRICS membership. Individual country resource needs for TB prevention and care are available at <http://www.stoptb.org/resources/countrytargets>. The updated investment scenarios are designed to put countries on track to reach those treatment and prevention targets and to advance the R&D pipeline in order to end the TB epidemic by 2030. Updated calculations project that countries will save US\$ 44 for every US dollar invested in Global Plan activities, with a net global economic benefit of US\$ 711 billion for full implementation.

BY FINANCING THE GLOBAL PLAN'S INVESTMENT SCENARIO (2018–2022):

- 1** countries will reach the UNHLM treatment targets set for 2022;
 - 2** the End TB Strategy 2020 milestones will be achieved a year later, in 2021;
 - 3** the world will be on track to achieve the 2025 milestones and the SDG target of ending TB by 2030;
 - 4** 40 million people will be treated for TB, including 3.5 million children and 1.5 million people with DR-TB, and over 30 million people will receive TB preventive therapy, leading to 1.5 million fewer deaths due to TB and 48 million disability-adjusted life years (DALYs) averted.
 - 5** New tools from R&D will be on the horizon for the final battle to end TB by 2030. A 5-year delay in increasing funding for TB R&D – the cost of inaction – would lead to approximately 2 million additional people dying and an additional 13.9 million people developing TB.
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INTRODUCTION

Tuberculosis (TB), an airborne communicable disease caused by the *bacterium Mycobacterium tuberculosis*, is the world's leading cause of death from a single infectious agent.

In 2018, an estimated 10 million people became ill with TB and an estimated 1.5 million died.¹ Drug-resistant (DR-) TB affected approximately half a million new people in 2018, presenting a public health crisis and health security risk in many countries. Yet, only an estimated one in three people with DR-TB are being treated today. A further challenge is the more than 3 million people with TB each year who are not diagnosed and, as a result, are left behind without effective treatment and care.

From 2017 to 2018, there was a 2% decline in the number of people who became sick with TB, but this falls far short of the pace of progress needed to fulfil the aims of the UN Sustainable Development Goals (SDGs) and the World Health Organization's (WHO) End TB Strategy (Box 0.1). While there have been some important areas of progress, significantly more resources are needed to ensure that people have access to quality TB prevention and care using the best tools available, and to invest in the kind of innovation that is essential for developing modern diagnostics, vaccines and treatment regimens. At the current rate of progress, the world will not end TB until the end of the century.

We must get the global TB effort on track.

In September 2018, the United Nations General Assembly convened the first-ever UN High-Level Meeting (UNHLM) on TB. This watershed event was attended by more than 1,000 people, including 16 heads of state and more

than 100 ministers and country leaders.² The meeting produced a Political Declaration on the Fight Against TB³, which was adopted by the UN General Assembly. The Political Declaration established targets and commitments to be achieved by 2022 in order to reach the SDGs of ending the TB epidemic by 2030. The Political Declaration serves as a vital and unprecedented commitment to implementing a rights-based response to TB globally, spurring countries into action at the highest political level.

The UNHLM and the accompanying Political Declaration were the outcomes of coordinated advocacy and high-level political action. In September 2016, the Stop TB Partnership Board, championed by its then Chair Dr. Aaron Motsoaledi (South Africa's Health Minister at the time), called for a UNHLM on TB, recognizing the extraordinary need for action by heads of state. In November the following year, WHO convened a Global Ministerial Conference on Ending TB. The conference took place in the Russian Federation and was addressed by President Vladimir Putin. This conference produced the Moscow Declaration to End TB.⁴ At an event preceding the Stop TB Partnership Board Meeting in Delhi, India in March 2018, Prime

¹ Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

² UNHLM on TB key targets and commitments. Geneva: Stop TB Partnership; 2019. http://www.stoptb.org/global/advocacy/unhlm_targets.asp

³ Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. https://www.un.org/en/ga/search/view_doc.asp?symbol=A/RES/73/3

⁴ Moscow Declaration to End TB. Geneva: World Health Organization; 2017. https://www.who.int/tb/features_archive/Online_Consultation_MinisterialConferenceDeclaration/en/

Minister Narendra Modi made a speech calling for accelerated efforts to end TB. He also committed to ending the disease in India in 2025, ahead of the global target. In June 2018, an Interactive Civil Society Hearing was held to capture community expectations and concerns, many of which were incorporated into the final Political Declaration. In the months leading up to the UNHLM on TB, civil society and affected communities from around the world advocated for concrete treatment and prevention targets, among other policy commitments, that were adopted in the UNHLM Political Declaration on TB.

Despite the urgent challenges, there is hope for ending TB. In recent years, research and development (R&D) has led to the introduction of a new diagnostic test that has reduced the time it takes to test for resistance to a key antibiotic. In addition, the first new DR-TB medicines in a generation have been introduced, and new vaccine research has reached its most promising stage in decades. The Global Fund to Fight AIDS, Tuberculosis and Malaria has raised US\$ 14 billion in funding commitments from donors for 2020–2022. Since the previous edition of the Global Plan, we have seen renewed drive to achieve shared progress on global health goals, for example, in the strengthened global effort to achieve Universal Health Coverage (UHC) and the collaboration of leading health institutions in the Global Action Plan for Healthy Lives and Well-being for All. We have also seen TB survivors and affected communities become increasingly organized, establishing new global norms and expectations through the 2019 Declaration of the Rights of People Affected by Tuberculosis⁵, along with the TB Survivors Statement⁶, which calls on all TB stakeholders to “do nothing about us without us.”

We must continue to build on this momentum to end TB.

This updated Global Plan to End TB 2018–2022 reflects the progress made over the last five years and is intended to support the achievement of the UNHLM commitments set for 2022. By implementing the Global Plan’s priority actions and mobilizing the needed funding, national governments and TB programmes, backed by stronger worldwide advocacy, can put us on track to end TB by 2030, in line with the SDGs.

BOX 0.1: WHO’S END TB STRATEGY

The End TB Strategy¹, adopted by the World Health Assembly in 2014, is a 20-year strategy to end the global TB epidemic. The strategy draws on the opportunities presented by the SDGs, especially those goals aimed at achieving UHC and social protection from disease. The End TB Strategy has established targets to reduce TB deaths by 95% and reduce the number of people who develop TB every year by 90% by 2035 (compared to 2015 levels), and to ensure that no family is burdened with catastrophic expenses due to TB. To stay on track towards achieving the strategy’s aims, interim milestones have been set for 2020, 2025 and 2030. The Global Plan supplements WHO’s End TB Strategy and aligns with the SDGs by providing recommendations for how national governments and other stakeholders can prioritize actions to end the TB epidemic, as envisioned by the End TB Strategy.

Stakeholders in all countries must play a greater role in ending TB. As more than half of the world’s people with TB and two-thirds of the world’s people with DR-TB are believed to be in Brazil, Russian Federation, India, China and South Africa (BRICS) and in other emerging economies, increased and sustained commitment, especially by the BRICS countries, will be crucial for meeting the global milestones set by the End TB Strategy.

5 Declaration of the Rights of People Affected by Tuberculosis. Geneva: Stop TB Partnership; 2019. <http://www.stoptb.org/assets/documents/communities/FINAL%20Declaration%20on%20the%20Right%20of%20People%20Affected%20by%20TB%2013.05.2019.pdf>

6 Survivors Statement, presented in the Opening Ceremony of the 50th Union World Conference on Lung Health by survivor Nandita Venkatesan. Paris: International Union Against Tuberculosis and Lung Disease; 2019. <https://hyderabad.worldlunghealth.org/2019/11/survivors-statement/>

1 The End TB Strategy. World Health Organization; 2015. https://www.who.int/tb/strategy/End_TB_Strategy.pdf?ua=1

FIGURE 0.1: SUMMARY OF KEY UNHLM ON TB TARGETS AND COMMITMENTS

UN MEMBER STATES COMMITTED TO FULFILLING THE FOLLOWING KEY TARGETS BY 2022:

- | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>1 Successfully treat 40 million people with TB, including 3.5 million children (under 15 years of age).</p> <p>2 Successfully treat 1.5 million people with DR-TB, including 115,000 children.</p> <p>3 Provide TB preventive therapy for at least 30 million people, including 4 million children under the age of 5, 20 million other household contacts of people affected by TB, and 6 million people living with HIV.</p> <p>4 Increase global investment in TB prevention, diagnosis, treatment and care to US\$ 13 billion annually.</p> <p>5 Increase global investment in TB R&D to US\$ 2 billion annually.</p> | <p>6 Promote and support an end to stigma and all forms of discrimination.</p> <p>7 Develop integrated, people-centred, community-based and gender-responsive health services based on human rights.</p> <p>8 Deliver, as soon as possible, new, safe, effective, equitable, affordable and available vaccines.</p> <p>9 Continue to develop and implement the elements of the new Multisectoral Accountability Framework.</p> <p>10 Provide a progress report in 2020 and a comprehensive review by heads of state and government at a High-Level Meeting in 2023.</p> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

TO THIS END, COUNTRIES SHOULD FULFIL THEIR UNHLM COMMITMENT TO ENGAGE WITH ALL RELEVANT STAKEHOLDERS – AND LEAVE NO ONE BEHIND – ESPECIALLY IN THOSE SECTORS EXPLICITLY IDENTIFIED WITHIN THE POLITICAL DECLARATION:

Health and nutrition	Finance	Labour
Social protection	Education	Science and technology
Justice	Agriculture	Environment
Housing	Trade	Development

FIGURE 0.2: TIMELINE FOR ACTION



BOX 0.2:

TB AND THE SUSTAINABLE DEVELOPMENT GOALS

The 17 SDGs constitute the overarching focus of global priorities for development cooperation and will guide national priorities in most countries over the next decade. Ending the TB epidemic by 2030 is one of the targets under Goal 3, which is to “ensure healthy lives and promote well-being for all at all ages.”

The SDGs will be achieved only if they are addressed comprehensively, understanding the clear links between the goals and how progress towards one goal will aid progress towards others. While ending the TB epidemic is closely linked to achieving a number of SDGs, incorporating appropriate TB responses into efforts to meet some of the other SDGs will accelerate the end of TB.

There are multiple links between TB, poverty and food security (Goals 1 & 2). Preventing lost work hours due to TB globally will add US\$ 12 billion to achieving sustainable economic growth, and full and productive employment (Goal 8). Goal 17 calls for strengthening domestic resource mobilization and finding additional financial resources from multiple sources. It also calls on developed countries to fully implement their commitments to provide official development assistance, including the commitment to devote 0.7% of gross national income (GNI) for this purpose. As economies grow, associated improvements in both living conditions (Goal 11) and equal rights to health care treatment (Goal 16) will help slow the spread of TB. When the world strengthens enforceable legislation for the promotion of gender equality (Goal 5) and reduces inequalities by eliminating discriminatory practices (Goal 10), people will be able to access TB diagnosis and care more easily, especially in cases where financial inequity, family responsibilities and cultural barriers may have prevented them from receiving care in the past. Combating climate change (Goal 13) could mitigate the need for large numbers of people to migrate in response to a changing climate (i.e., into crowded urban environments that are favourable to TB transmission), forestalling negative population-level changes in nutrition and other potential outcomes.¹

1 The Lancet Infectious Diseases. Climate change: the role of the infectious disease community. *Lancet Infect Dis.* 2017;17(12):1219. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(17\)30645-X/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30645-X/fulltext)





1.A PARADIGM SHIFT IN THE FIGHT AGAINST TB



SUMMARY

The goal of the Global Plan is to provide a costed blueprint for actions that countries should take to fulfil the targets and commitments in the Political Declaration of the UNHLM on TB and to get on track to end TB as outlined in the WHO's End TB Strategy and the SDGs.

To accomplish this, we must significantly step up the fight against TB. In September 2018, the UNHLM on TB produced the first-ever UN Political Declaration on TB, which establishes a political and policy agenda for achieving the aims of the End TB Strategy and the SDGs. As part of a renewed effort to end the epidemic, the Political Declaration contains numerous specific targets and actions that governments have

committed to achieving by 2022. We now need an inclusive, multisectoral effort and full investment in order to fulfil the Political Declaration's people-centred commitments over the next few years, with the ultimate goal of ending TB. The Global Plan's updated modelling shows that if the UNHLM prevention and treatment commitments are fulfilled by 2022, the world will come on course to end TB.

THE GLOBAL PLAN FOCUSES ON THREE PEOPLE-CENTRED TARGETS CALLED THE 90-(90)-90 TARGETS:

1 Reach at least 90% of all people who need TB treatment and prevention.

2 Reach at least 90% of people in key populations.

3 Achieve at least 90% treatment success among people diagnosed with TB or who are eligible for preventive therapy.¹

¹ These targets were inspired by both the UNAIDS 90-90-90 treatment targets and the Communiqué of the 4th Meeting of BRICS Health Ministers in December 2014, which urged the BRICS nations to aspire to three 90% targets for their countries' TB activities by 2020. Communiqué of the IV Meeting of BRICS Health Ministers, Brasilia, 5 December 2014. Brasilia: Ministry of External Relations of Brazil; 2014. <http://www.brics.utoronto.ca/docs/141205-health.html>

PRIORITY ACTIONS

To end TB, with the active engagement and involvement of TB survivors, affected communities, broader civil society, the private sector and international partners, national governments must:

✦ Publicly champion country efforts to end TB and mobilize all necessary resources to achieve the 90-(90)-90 targets and fulfil

the UNHLM commitments, including national shares of global treatment and prevention targets for reaching both adults and children

with drug-susceptible (DS-) and drug-resistant (DR-) TB.

✦ Carry out the five fundamental changes identified in the Global Plan to effect the paradigm shift that is critical to ending TB:

1. Exhibit inclusive, multisectoral and accountable leadership that includes a strong commitment to regular reporting and review of progress.
2. Transform the TB response to be equitable, rights-based and people-centred, with proactive efforts to reach key populations.
3. Accelerate R&D and advance innovation in TB programmes and interventions.

4. Ensure TB programmes and activities are supported by strong health systems that leave no one behind.

5. Invest the funds necessary to end TB, using all available new and innovative funding streams.

✦ Disaggregate TB data to allow for monitoring progress among adults, children, men, women and key populations.

✦ Establish and sustain a global, multisectoral mechanism for ensuring accountability for fulfilling UNHLM commitments.

People-centred global targets: 90-(90)-90

We must step up the fight and get on track to end TB. Today, only around 50% of those who become ill with TB are cured. Achieving the Global Plan's targets will address this unacceptable gap in TB care.

The HIV UNHLM Political Declaration of 2016² recognizes the TB 90-(90)-90 targets, and the TB UNHLM Political Declaration³ builds further on the targets by specifically including commitments for finding and treating TB in adults and children. Impact modelling shows that

achieving the 90-(90)-90 targets and fulfilling the UNHLM commitments by 2022 will set the world on course to meet the 2025 incidence and mortality milestones of the End TB Strategy. The 90-(90)-90 targets are explained below (see Figure 1.1).

2 Resolution adopted by the General Assembly on 8 June 2016. A/Res/70/266. Political Declaration on HIV and AIDS: on the fast track to accelerating the fight against HIV and to ending the AIDS epidemic by 2030. New York: United Nations General Assembly; 2016. https://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf

3 Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmonTBDeclaration.pdf>

FIGURE 1.1: THE 90-(90)-90 TARGETS

THE GLOBAL PLAN ARTICULATES THESE AS THE 90-(90)-90 TARGETS:



TARGET 1: Reach 90% of people in need of TB treatment and prevention

By improving the rates at which people are diagnosed and treated, countries can reduce the spread of the disease and drive down incidence. This requires early detection and prompt treatment of 90% of people with TB (both DS- and DR-TB) and 90% of people who require preventive therapy.⁴

Proactively reaching out to people who are at risk of TB and providing systematic screening, diagnosis and appropriate care – an approach commonly known as active case finding – is essential to reaching the millions of people who go without access to TB services. While the best approaches to active case finding will be determined by local contexts, emerging best practices include supporting community-based outreach efforts; strengthening health systems to be able

to better provide TB services; integrating TB screening with other health interventions (e.g., HIV, diabetes, nutrition); optimizing the use of existing tools and resources; scaling up successful active case finding pilots; and ensuring government financing and support for active case finding.⁵

A much stronger focus on prevention is also essential to end TB. People at risk of TB have a right to receive preventive therapy, and people should be tested and treated for TB infection with strict adherence to human rights and the strongest ethical considerations. In 2018, WHO updated its TB prevention guidelines to recommend an overall more aggressive effort to deliver care to people who would benefit from

4 Preventive therapy treats TB infection before it progresses to TB disease.

5 Best practices on TB case finding and treatment: reflections and lessons from West and Central Africa and beyond. Geneva: The Global Fund to Fight AIDS, Tuberculosis and Malaria; 2018. https://www.theglobalfund.org/media/8273/core_wca-tb-best-practices_technicalbrief_en.pdf?u=637066545900000000

TB prevention.⁶ Groups who are most urgently in need of prevention include those with TB infection who are most likely to progress to active TB disease, for example, people living with HIV, infants, children and adults who are household contacts of someone diagnosed with TB, and patients with silicosis or other health conditions that put them at high risk. These at-risk groups should receive systematic screening for TB and be provided with preventive therapy.

TARGET 2: Reach 90% of people in need of treatment and prevention among vulnerable, underserved, at-risk populations

Target 2 is a subset of Target 1 (hence the parentheses). Equity and human rights demand a special effort to reach these populations. (Chapter 3 describes key population groups.) Targeting the most vulnerable populations constitutes good public health and economic policy. The purpose of Target 2 is also to provide treatment and care through affordable programmes that protect patients and their families from the often catastrophic costs associated with having TB. The Global Plan recommends that each national TB programme (NTP) work with communities affected by TB to define its key populations, to plan and implement appropriate services, and to measure, report on and review progress towards reaching these populations.

TARGET 3: Achieve at least a 90% treatment success rate among all people diagnosed with TB and among all those eligible for TB preventive therapy

This includes all people diagnosed with DS-TB or DR-TB, or who are eligible for preventive therapy. Currently, in many settings, a large number of people who are diagnosed with TB do not start on treatment and might not even be notified of their status. The Global Plan urges TB programmes to adopt the new approach of notifying all people diagnosed with TB infec-

tion or disease of their status; ensuring full and proper treatment for all in need, including contacts of people with active TB who are eligible for preventive therapy; being accountable for the outcomes of treatment; and reporting all outcomes nationally, disaggregated by age and key population. To achieve this target, countries will need to provide comprehensive support that ensures continuity of care and helps people with TB complete a full course of quality-assured treatment.

**BOX 1.1:
FIND. TREAT. ALL. #ENDTB**

To scale up the response to achieve the 90-(90)-90 targets and reach universal access to TB prevention and care, WHO, the Stop TB Partnership, and the Global Fund to Fight AIDS, Tuberculosis and Malaria have launched a joint initiative: FIND. TREAT. ALL. #ENDTB. The initiative involves civil society, affected communities and development financing partners, all of whom are asked to join in the effort with concrete commitments to reach all adults, children and adolescents living with TB disease (DS- and DR-TB) and TB infection. In the short-term, the priority of the initiative is to enable access to care for the millions who miss out on quality TB care each year.¹

1 Joint Initiative "FIND. TREAT. ALL. #ENDTB" [Website]. Geneva: World Health Organization; 2019. <https://www.who.int/tb/joint-initiative/en/>

6 Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva: World Health Organization; 2018. <https://apps.who.int/iris/bitstream/handle/10665/260233/9789241550239-eng.pdf?sequence=1>

The Paradigm Shift

In line with the UNHLM Political Declaration on TB, the Global Plan identifies five fundamental changes that must be implemented as part of the paradigm shift needed to end TB. Implementing these shifts will help accelerate countries' progress towards achieving the 90-(90)-90 targets.⁷

⁷ The previous edition of the Global Plan identified eight fundamental changes that must be made to produce the paradigm shift needed to end TB. While the aims remain the same, these changes have been revised in the current edition to align with the key commitments made in the UNHLM Political Declaration on TB.

1. Exhibit inclusive, multisectoral and accountable leadership that includes a strong commitment to regular reporting and review of progress.

All stakeholders need to adopt the mindset that our goal is to end TB. Progress as dramatic as that envisioned in the End TB Strategy can only be achieved once a country's leadership announces to its population – and its public health services – that TB will be fought on a long-term campaign basis, similar to HIV or even polio, and that it will dedicate the resources

needed to end TB in the country. High-level national leadership should also institute systems of accountability for ending TB in line with commitments (see below for a more detailed discussion of accountability for ending TB).

Collectively, within the UNHLM Political Declaration on TB, governments committed to providing:

COMMITMENT 1

diagnosis and treatment with the aim of successfully treating 40 million people, including 3.5 million children, for TB by 2022;

COMMITMENT 2

diagnosis and treatment with the aim of successfully treating 1.5 million people, including 115,000 children, for DR-TB by 2022;

COMMITMENT 3

preventive therapy for at least 30 million people, including 4 million children under 5 years of age, 20 million other household contacts of people affected by TB, and 6 million people living with HIV, by 2022.

Fulfilling these commitments is critical for ending TB and will require the mobilization of a broad spectrum of government officials – heads of state and government, members of parliament, mayors, and community administrators – to work with civil society organizations (CSOs) and individual citizens in a long-term effort to diagnose, treat and prevent TB. This effort will demand political commitment and coordination at the highest levels that tie together government ministries, especially ministries of finance and labour. It will also require effective alliances between government, civil society, affected

communities and the private sector for action on poverty, social protection, justice and labour reform. Furthermore, this will require greater South-South collaboration on capacity-building in countries, human resources with the right skillsets and technical capacities, and people to design and implement strategic regional initiatives.

2. Transform the TB response to be equitable, rights-based and people-centred, with proactive efforts to reach key populations.

A human-rights-based approach to TB is grounded in international, regional and domestic law. These laws establish the rights of all people everywhere to attain the highest standard of health, to be free from discrimination, and to enjoy privacy, freedom of movement, and

the benefits of scientific progress, among others. Human rights law also establishes the legal obligations of governments and private actors.

In order to implement a human-rights-based approach to TB, countries should:

- 1** Prohibit discrimination against people with TB;
- 2** Empower people to know their TB status, and establish legal rights to access TB testing and treatment, including the elimination of financial and physical barriers to treatment and care;
- 3** Ensure the participation of people affected by TB in health policy decision-making processes;
- 4** Establish mechanisms to address the rights of people with TB and ensure their implementation;
- 5** Protect the privacy of people with TB.

A gender-based approach to TB aims at addressing the social, legal, cultural and biological issues that underpin gender inequality and contribute to poor health outcomes. It encourages gender-responsive investments to prevent new cases of TB and to strengthen the response to fulfil the right to health of women and girls, men and boys, and people of all genders, in all their diversity.

Wherever applicable, these protections should be included in constitutional law or legislation. If this is not possible, they should be incorporated as legal rights in national and local TB policies.

People with TB and the groups that represent them must be at the heart of the paradigm shift towards an equitable, rights-based, people-centred approach. Affected communities

must be included in every area of decision-making, serving on boards of organizations and institutions that provide care, and sharing their experience and knowledge as equal and valuable partners in all TB forums. The community must also be resourced and empowered to form caucuses, to choose its own representatives, and to interact with the media.

People with TB and their communities must also be partners in the design and planning of strategies to end TB, and given a key role in monitoring and evaluation, especially at the point of need. New tools, including social media, social auditing and social observatories, which are key to knowledge-sharing at the community level, have the potential to be used strategically alongside traditional forms of epidemiological surveillance.

3. Accelerate R&D and advance innovation in TB programmes and interventions.

The paradigm shift requires new medicines, diagnostics and vaccines, and for TB programmes to be equipped to end TB as an epi-

demic. National governments and research funders need to prioritize TB R&D and take steps to create an enabling environment for further

progress. Programmes must be equipped to rapidly and efficiently roll out any new medicines, diagnostics and vaccines that reach the market in order to ensure equitable access to new TB tools.

National authorities responsible for the fight against TB need to be empowered to undertake necessary policy changes, allocate resources and implement activities that will have an impact. Programmes should respond to the needs of local settings, identifying TB hotspots and areas that will require more intensive efforts, such as areas with high levels of poverty.

TB programmes must focus not only on saving lives, but also on stopping transmission through

early case detection and stronger prevention via a targeted approach to serve communities at high risk. TB programmes should be equipped to leave behind the past approach of slowly scaling up pilot projects in favour of a more rapid scale-up of DS- and DR-TB treatment and care. To do so, programmes will need to look for innovative approaches to service delivery, embracing the use of social media and mHealth. Local programmes also need to be empowered to find innovative solutions to identify and treat vulnerable groups. These efforts will require high-quality data collection, real-time monitoring, and private sector expertise.

4. Ensure TB programmes and activities are supported by strong health systems that leave no one behind.

Strong health systems are essential for closing the gaps in the provision of TB diagnosis, treatment and prevention. The fragmentation of TB activities and the low political priority often given to TB programmes within country health systems must end, as must the separation of programmes for tackling different forms of TB and coinfections with specific diseases. Instead, TB programmes should be coordinated with HIV/AIDS and maternal and child health programmes, and TB care should be delivered through primary health care in the context of UHC and new health financing models. Governments should invest in community-based systems, involving TB survivors, affected communities and community leaders in the design of people-centred programmes that provide local access to TB care and services for all.

Efforts to tackle TB should also include interventions to provide care and services for extrapulmonary TB and for zoonotic TB, embracing the One Health approach. This approach recognizes that the health of humans is connected to the health of animals and the environment. There is an urgent need to increase the human resources available to end TB, and to improve

the collection and analysis of data to better inform and correct programming.

Medical interventions alone will not be enough to end TB. Non-medical actions and investments, such as efforts to improve housing and sanitation, reduce poverty and strengthen social safety nets (e.g., UHC, disability insurance and workplace protections for people with TB) and programmes to eliminate catastrophic costs for people and families affected by TB, will drive down the numbers of people becoming ill and dying from TB. Planning for and investing in such non-medical activities cannot wait, as these normally take several years to implement and to have an impact on TB incidence.

5. Invest the funds necessary to end TB, using all available new and innovative funding streams.

Ending TB requires a sustained increase in domestic, donor and innovative funding for TB programmes and TB R&D, with significant front-loaded investments in the period of the Global Plan (see Chapter 7 on resource needs). In the UNHLM Political Declaration on TB, national governments committed to mobilizing at least US\$ 13 billion annually to support TB care. Significant changes should also be made to the way funds are raised and deployed to include increased investment in community-based systems.

TB programmes must make a compelling business case for increased and frontloaded budgets and then make efficient use of resources, prioritizing investments and pooling resources with other programmes. Innovative financing approaches, including better use of incentives,

present an opportunity to increase TB resources. Results-based financing approaches are being rolled out in numerous countries and are beginning to generate positive results by providing financial incentives to providers and facilities for specific results attained. TB programmes must be part of such initiatives.

In addition to continuing to strengthen the public-sector response to TB, TB programmes should engage business sector and private sector health providers as partners, harnessing companies' consumer-driven approaches and embracing their ability to meet demands for key services through social business models. As social health insurance initiatives and innovative, blended finance mechanisms are scaled up, TB programmes need to proactively align and integrate with these initiatives.

The economic case for ending TB

The economic case for ending TB is compelling. An analysis conducted by KPMG projected that if the status quo continues, the deaths caused by TB will cost the global economy US\$ 983 billion between 2015 and 2030.⁸ TB treatment, however, is low-cost and highly effective. On average, effective treatment may give an individual in the middle of his or her productive life about 20 additional years of life, resulting in substantial economic and health returns.⁹

The High-Level Panel for the UN's SDGs has estimated that an investment of US\$ 1 in TB care yields a return of US\$ 30.¹⁰ Other studies have put the return as high as US\$ 115 for each dollar

invested.¹¹ The economic benefits of ending TB outweigh the costs, making TB efforts a critical piece of the sustainable development agenda.

The Global Plan's investment packages propose interventions tailored to have the greatest impact and provide the maximum return on investment (ROI) for the particular setting. The investment packages selected for the different settings are described in detail in Chapter 2.

8 Global economic impact of tuberculosis: a report for the Global TB Caucus. Zurich: KPMG; 2017. https://docs.wixstatic.com/ugd/309c93_bf9baa1398334a8aa1ff19cb083b129e.pdf?index=true

9 Vassal A. Tuberculosis perspective paper: benefits and costs of the education targets for the post-2015 development agenda. Tewksbury: Copenhagen Consensus Center; 2014. <http://www.copenhagenconsensus.com/publication/post-2015-consensus-health-perspective-tuberculosis-vassal>

10 Report of the Secretary-General's High-Level Panel of Eminent Persons on the Post-2015 Development Agenda. New York: United Nations Secretary-General; 2015. <https://www.un.org/sg/en/management/beyond2015.shtml>

11 Goodchild M, Sahu S, Wares F, et al. A cost-benefit analysis of scaling up tuberculosis control in India. *Int J Tuberc Lung Dis*. 2011;15:358–62.

Measuring progress

The Stop TB Partnership will measure progress towards the 90–(90)–90 targets, along with the milestones for R&D and funding goals set out in the Global Plan. The first report was published in 2017 and served as a baseline, using the then-latest data available from 2015.¹²

Based on 2018 data reported by national governments to WHO, only 68% of the estimated number of people with TB globally and 30% of those with DR-TB were diagnosed and started on treatment. Coverage among children was even lower. The vast majority of people eligible for TB preventive therapy did not access it; only 27% of eligible children under 5 received TB preventive therapy. The number of household contacts over the age of 5 who received preventive therapy actually decreased by 30% from 2017 to 2018. Huge data gaps still exist that need to be filled in order to understand the accessibility and outcomes of TB care and services among key populations. Overall, the treatment success rate for DS-TB was 80%; for DR-TB, it was 55% globally.¹³

Moving forward, governments should disaggregate data to enable monitoring of progress among adults, children, men, women and key populations. The Global Plan recommends that national governments, in collaboration with civil society, adopt additional process-oriented targets as needed to track and publicly report on progress against elements related to the paradigm shift, as described in the next section. Such elements include the number of people tested for TB, community systems, key populations and private sector care.

¹² The tuberculosis report for heads of state and governments. Geneva: Stop TB Partnership; 2017. http://www.stoptb.org/assets/documents/resources/publications/acsm/909090_PDF_LR.pdf

¹³ Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

BOX 1.2:

SOUTH AFRICA: THE PARADIGM SHIFT IN PROGRESS

Some countries are already showing that a paradigm shift is possible. South Africa, a country with one of the world's highest rates of TB, has embarked on a broad, multi-year campaign to dramatically drive down its TB rates.

In the last few years, South Africa has taken many bold steps, some of which are outlined below:

- South Africa is the first country to have completely replaced microscopy with rapid molecular testing with GeneXpert as the initial diagnostic tool for TB. This shift has also ensured that the drug resistance status of every person is identified at the time of diagnosis, enabling prompt initiation of the correct treatment regimen.
- The country was the first to scale up the new TB medicine bedaquiline for most people diagnosed with rifampicin-resistant (RR-) TB. This will dramatically reduce the use of injectable medicines in the country in line with international best practice.
- The country has been the fastest to scale up TB preventive therapy. Although the coverage is not yet adequate, South Africa alone was responsible for about 40% of the global TB preventive therapy numbers in 2017.
- The country has already largely integrated its HIV and TB care, seeking to ensure that every individual diagnosed with HIV is also tested and, if necessary, treated for active TB or given TB preventive therapy, using modern tools. South Africa has been at the forefront of screening among key population groups, taking bold steps to learn from such experiences and set up a quality improvement system for efficient and targeted awareness and screening programmes.
- With its infrastructure and research capacity, the country is also playing a critical role in the R&D of new, more effective tools to prevent, diagnose and treat TB. South African researchers are making major contributions to the global efforts in new tool development, from early-stage research through to large-scale clinical trials.

The rapid strides taken by South Africa have been possible for a number of reasons. But, one of the critical reasons has been the high political commitment of the government, driven by the Health Minister and supported by the President, Vice President and the Parliament.

Accountability for fulfilling TB commitments

UNHLM commitments to accountability

Underpinning their operational commitments to mobilize an urgent response to TB, UN Member States promised to take steps to foster accountability for fulfilling those commitments. The Global Plan urges Member States to fulfil all of the accountability commitments they endorsed in the UN Political Declaration on TB.

These include commitments to taking high-level action, establishing monitoring and reporting systems and procedures, and reviewing progress with respect to global, regional and national TB efforts.

The Political Declaration also requested that the UN Secretary-General, in close collaboration with the WHO Director-General, promote collaboration among all stakeholders to end the TB epidemic and implement the Political Declaration, together with Member States and relevant entities, including funds, programmes, specialized UN agencies, UN regional commissions, the Stop TB Partnership, Unitaaid and the Global Fund.

Essential for accountability: the TB Multisectoral Accountability Framework

Ensuring accountability is a complex endeavour. In order to provide a common framework for discussing accountability, and to help identify where the TB response needs to strengthen its attention and focus, WHO was asked to develop an accountability framework in conjunction with partners. Endorsed globally at the highest political levels, the WHO Multisectoral Accountability Framework to Accelerate Progress to End Tuberculosis by 2030 (MAF-TB)¹⁴ is the essential framework for ensuring that TB commitments lead to measurable progress

BOX 1.3:

INDIA: AMBITIOUS POLITICAL COMMITMENT TO END TB¹

Home to one in four people with TB worldwide, India has recently changed the trajectory of progress on TB in the country. In a historic speech on 13 March 2018, Prime Minister Narendra Modi articulated a vision of ending TB in India by 2025, ahead of the SDG targets. This commitment has since led to several unprecedented steps:

- An ambitious National Strategic Plan was developed and commitment was made to fully fund it.
- Three to four times more funding for TB was allocated from the domestic budget.
- Several steps were taken to improve TB care and the notification of TB diagnosed in the private sector. In the last few years, the private sector has notified hundreds of thousands of TB patients who have received diagnosis and treatment, leading to significant increases in TB case detection and notification in the country. In 2018, 300,000 more TB cases were notified than in 2017.
- India is the only country so far to have implemented a live web-based information system where TB notifications are available in the public domain in real time, by state and by district. This system, called "Nikshay"², serves as a patient management and tracking system that connects laboratories, treatment sites, private sector providers, and public health functions such as notification and contact investigation.
- People on TB treatment are eligible to receive direct cash transfers to their accounts on a monthly basis to be used for nutrition and social support.
- The Prime Minister's Office, Health Minister, Chief Ministers of States and Members of Parliament have been involved in monitoring the TB response through simple people-centred targets set for each state and district.

The ambitious steps India is taking to end TB provide a practical model for other countries to adapt within their own context.

14 Multisectoral accountability framework to accelerate progress to end tuberculosis by 2030. Geneva: World Health Organization; 2019. <https://www.who.int/tb/publications/MultisectoralAccountability/en/>

1 Nadda JP. India's leadership to end tuberculosis. *Lancet*. 2019;393(10178):P1270-2. doi:10.1016/S0140-6736(19)30487-8

2 Nikshay dashboard. <https://reports.nikshay.in/>

that ends TB. National delegations participating in the Global Ministerial Conference on Ending TB in the SDG Era called for the development of the MAF-TB, which was then developed by the WHO Secretariat in consultation with UN Member States and TB stakeholders.¹⁵ The UN General Assembly welcomed the draft MAF-TB in 2018, and the WHO Secretariat finalized the MAF-TB in April 2019.

The MAF-TB provides an overview and structure of the components and mechanisms that make up a comprehensive and effective approach to accountability, as well as the relationships between them. The framework can and should be adapted to suit the needs of the various contexts in which it is being implemented. The

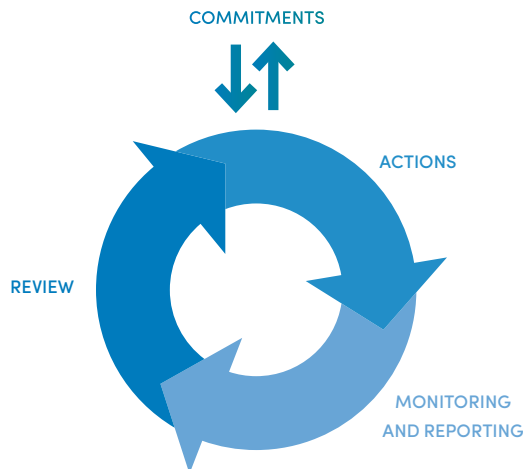
framework is multisectoral, involving sectors of the economy and the government that relate to the broader effort to fulfil TB commitments: health and nutrition, finance, labour, social protection, education, science and technology, justice, agriculture, the environment, housing, trade and development.

The essential components of the MAF-TB are: commitments, actions, monitoring and reporting, and review, where monitoring and reporting are used to track progress and outcomes towards fulfilling commitments, and review is used to assess results and recommend future actions. (Figure 1.2). These components are described in detail within the MAF-TB document.¹⁶

15 Moscow Declaration to End TB. Geneva: World Health Organization; 2017. https://www.who.int/tb/features_archive/Online_Consultation_MinisterialConferenceDeclaration/en/

16 Multisectoral accountability framework to accelerate progress to end tuberculosis by 2030. Geneva: World Health Organization; 2019. <https://www.who.int/tb/publications/MultisectoralAccountability/en/>

FIGURE 1.2: ESSENTIAL COMPONENTS OF THE MAF-TB



Putting accountability into action

Various stakeholders need to take urgent steps to ensure accountability for fulfilling commitments to end TB. These steps need to be taken at the global level as well as at national and regional levels.

Critically, there is a need for a global, multi-sectoral mechanism for reviewing international progress towards fulfilling commitments. Governments, affected communities, broader

civil society, donors and partners all have a mutual stake in promoting accountability in order to ensure that commitments are fulfilled and targets are met.

WITH ACTIVE PARTICIPATION FROM AFFECTED COMMUNITIES AND BROADER CIVIL SOCIETY, NATIONAL GOVERNMENTS SHOULD TAKE THE FOLLOWING STEPS:

STEP 1

Update, fund and implement national TB strategic plans, policies and legislation, as needed, to fulfil TB commitments, including national fair shares of global TB treatment and prevention commitments, as well as funding commitments.

STEP 2

Establish national multisectoral accountability frameworks for guiding actions, monitoring and reporting, and ensuring national high-level review of progress towards fulfilling TB commitments.

STEP 3

Publish annual monitoring reports on national TB efforts that include up-to-date information on TB epidemiology, NTP performance, and a comprehensive analysis of TB financing trends.

STEP 4

Use these monitoring reports as the basis for high-level national review, engaging key stakeholders in high-level review mechanisms.

Regional bodies and country blocs should establish high-level review mechanisms to periodically review regional and country-bloc progress towards fulfilling TB commitments.

Multilateral health, development and financing agencies should update strategic and operational plans to account for new activities to be implemented in order to support national governments and key stakeholders to fulfil TB commitments in both high-burden and donor countries.

Donors should support national CSOs in their efforts to hold national governments accountable for fulfilling TB commitments. They should also support civil society in establishing and maintaining regional coalitions of nongovernmental organizations (NGOs), survivor and community groups

for the purposes of knowledge-sharing and advocacy, focused on promoting government accountability for fulfilling TB commitments.

BOX 1.4:

COMMITMENTS TO ACCOUNTABILITY ENDORSED BY UN MEMBER STATES IN THE POLITICAL DECLARATION ON TB

HIGH-LEVEL ACTIONS:

- Develop or strengthen, as appropriate, national TB strategic plans to include all necessary measures to deliver the commitments in the Political Declaration.
- Promote TB as part of national strategic planning and budgeting for health.
- Establish and promote regional efforts and collaboration both to set ambitious targets and to generate resources.

MONITORING AND REPORTING:

- Strengthen national capacity for data collection, analysis and use for monitoring and review purposes.
- Request the Secretary-General, with the support of WHO, to provide a progress report in 2020 on global and national progress, across sectors, in accelerating efforts to achieve the agreed TB goals within the context of achieving the SDGs, including reporting on implementation of the TB Political Declaration at national, regional and global levels.

REVIEW:

- Conduct high-level national review of progress, preferably under the direction of the head of state or government, with active involvement of civil society and affected communities, parliamentarians, local governments, academia, the private sector and other stakeholders within and beyond the health sector.
- Use existing regional intergovernmental institutions to review progress, share lessons and strengthen collective capacity to end TB.
- Strengthen linkages between TB elimination and relevant SDG targets, including towards achieving UHC, through established SDG review processes, including the high-level political forum on sustainable development.
- Use the Secretary-General's 2020 progress report to inform preparations for a comprehensive review by heads of state and government at a follow-up UNHLM in 2023.^{1,2}

1 Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmontbDeclaration.pdf>

2 A full treatment of accountability can be found in the UN Political Declaration, paragraphs 4, 22, 23, 48, 49, 50, 51, 52 and 53.



2.IMPACT MODELING AND A DIFFERENTIATED RESPONSE



SUMMARY

This Global Plan update continues to use the TB Impact and Model Estimates (TIME) approach from the 2016–2020 Plan. This modelling tool provides realistic scenarios through which countries should scale up TB treatment and prevention services annually (from 2018 to 2022) in order to reach the TB treatment and prevention targets laid out in the UN Political Declaration on TB.

Results of the modelling are presented with reference to country groups based on income status, Global Fund eligibility, Global Plan country setting, WHO region and separately for BRICS, so

that countries can prioritize different packages of TB investments depending on their specific contexts. This Global Plan update presents investment packages for nine different country settings.

PRIORITY ACTIONS

Epidemiological modelling shows that achieving the UNHLM on TB prevention and treatment targets will enable the world to get on track to end TB by 2030, achieving the 2020 End TB Strategy milestones by the year 2021. All countries should therefore plan to achieve their share of the global UNHLM targets. Indicative UNHLM targets for individual countries are available on the Stop TB Partnership website at <http://www.stoptb.org/resources/countrytargets/>.

1 The Global Plan is a call to action for countries to meet the UNHLM targets by 2022 or sooner, thereby preventing at least 1.5 million deaths. To ensure scale-up and to maximize impact, countries should invest in intervention packages that are tailored to the needs of their settings, as laid out in the Global Plan.

2 Country governments should see the Global Plan's investment packages as a starting point for developing detailed national strategic plans for ending TB. Those national plans should be multisectoral and include measures for strengthening the private sector's role in ending TB, especially in country settings where significant numbers of people seek care from private providers.

Modelling the UNHLM on TB treatment and prevention targets

The Global Plan 2016–2020 modelled the impact of achieving the 90–(90)–90 targets as part of an accelerated global response to the TB epidemic. However, the actual progress made in the global TB response has not kept pace with the Global Plan. As a result, the world is not on course to achieve the 2020 milestones of the End TB Strategy.

Recognizing this slow progress and the need for high-level political commitment, the UNHLM on TB has set ambitious prevention and treatment targets to be achieved by 2022 in order for the

world to catch up and get on track to reach the End TB Strategy milestones. (See the Introduction for a full breakdown of key UNHLM targets.)

THESE TARGETS INCLUDE:

- 1 successfully treating 40 million people with TB, including 3.5 million children;
- 2 successfully treating 1.5 million people with DR-TB, including 115,000 children;

- 3 providing TB preventive therapy for at least 30 million people, including 4 million children under the age of 5, 20 million other household contacts of people affected by TB, and at least 6 million people living with HIV.

The Global Plan 2018–2022 modelling has been updated to determine the estimated epidemiological impact of achieving these targets.

The TB Impact and Model Estimates (TIME) approach¹ was used to predict the impact of scaling up to the TB prevention and treatment targets established in the UN Political Declaration on TB. Country-specific models were calibrated to WHO data on incidence and mortality estimates in 29 countries. These countries repre-

sent a range of contexts and are home to 80% of the world's people with TB. The estimated impact of the Global Plan 2018–2022 in these countries was then applied to WHO epidemiological trends for an additional 142 countries², by assigning to each country a TIME-modelled country in the same context or group.

The modelling methods and assumptions are described in [Annex 1](#).

1 Houben R, Lalli M, Sumner T, et al. TIME Impact: a new user-friendly tuberculosis (TB) model to inform TB policy decisions. *BMC Med.* 2016;14(56). doi:10.1186/s12916-016-0608-4

2 The 142 countries comprise a Global Plan result set determined by the intersection of the WHO Global TB Programme country-level data and the UNAIDS country-level Spectrum AIM/EPP files. Spectrum AIM/EPP is the software used by UNAIDS to produce country-level estimates of HIV burden and resource needs.

Modelling results

The Global Plan’s modelling shows that business as usual will surely miss the 2020 milestone and will not end TB, but the implementation of the Global Plan will lead to a sharper decline in incidence which will put the world on track for ending TB (Figure 2.1).

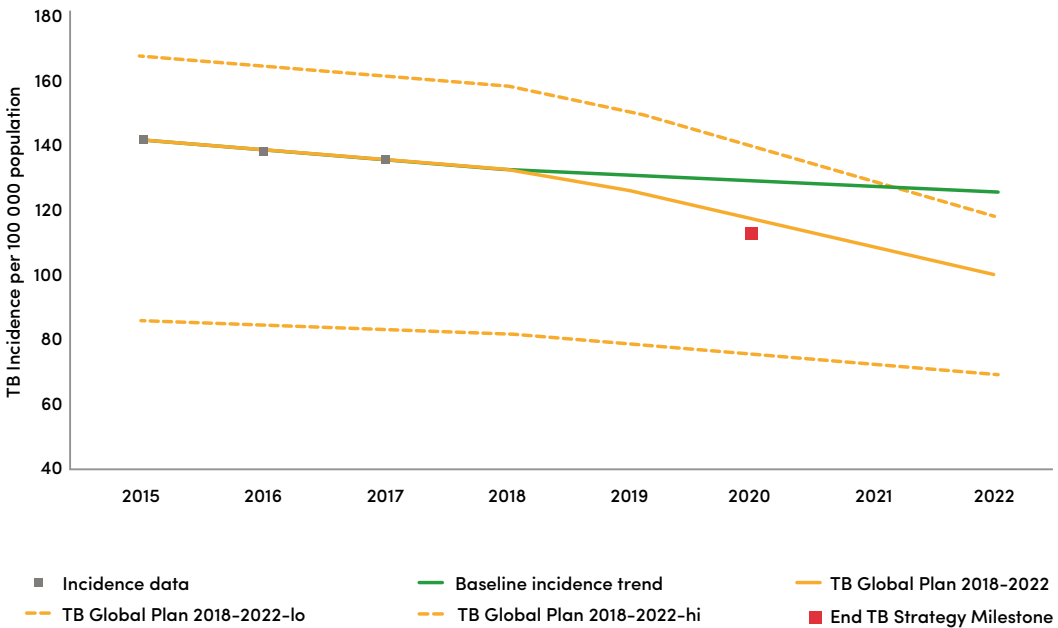
Figures 2.2 and 2.3 show the cumulative UNHLM on TB targets by year and by the nine country settings. Figures 2.4 and 2.5 show that achieving these treatment targets will result in getting on track to end TB by 2030, albeit with the 2020 incidence and mortality milestones achieved a year later in 2021. Achieving the targets will lead to an estimated 1.5 million lives saved during the period 2018–2022.

UNHLM on TB targets by WHO region, income status and country group

Tables 2.1a–2.1d show the projections of the

numbers of people who need to receive treatment for TB – including children (0–14 years) and those in need of treatment for multidrug-resistant (MDR-) TB – and TB preventive therapy. These projections are disaggregated by country group. It should be noted that the scale-up of TB notification targets happens against the background of reducing TB incidence; as a result, some countries may show a flattening of the scale-up curve and even a decline towards 2022. In addition, in the spirit of the UNHLM commitments, the TB preventive therapy targets should be interpreted as the floor and not the ceiling; therefore, countries should make efforts to exceed these targets.

FIGURE 2.1: IMPACT ON INCIDENCE OF TB



■ Notification-target
 ■ Notification (1-14 years)
 ■ Notification MDR

FIGURE 2.2: CUMULATIVE UNHLM ON TB TARGETS BY YEAR

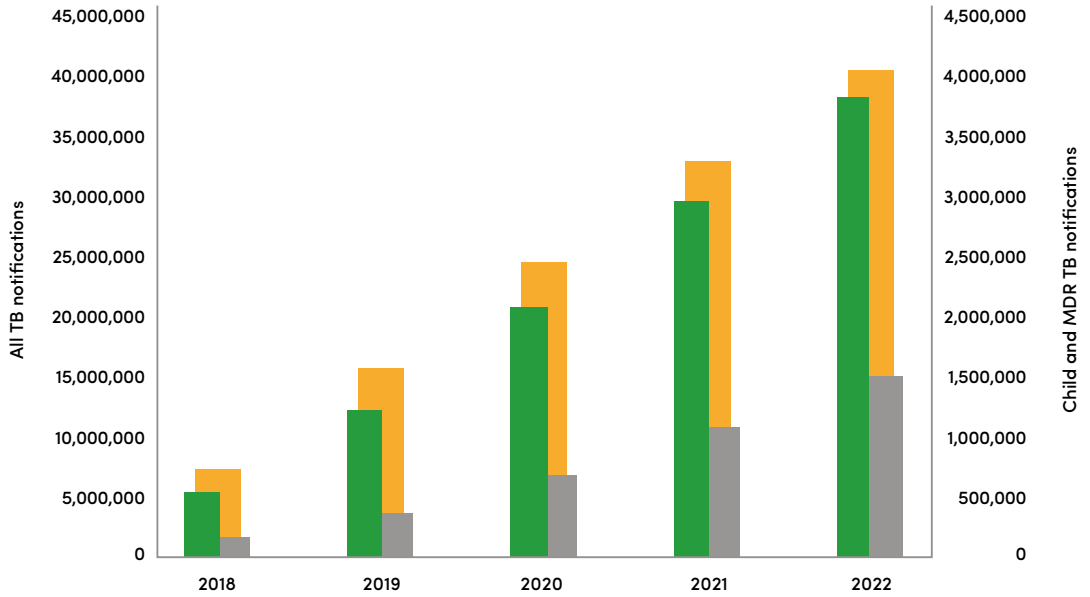


FIGURE 2.3: CUMULATIVE UNHLM ON TB TARGETS BY COUNTRY SETTINGS

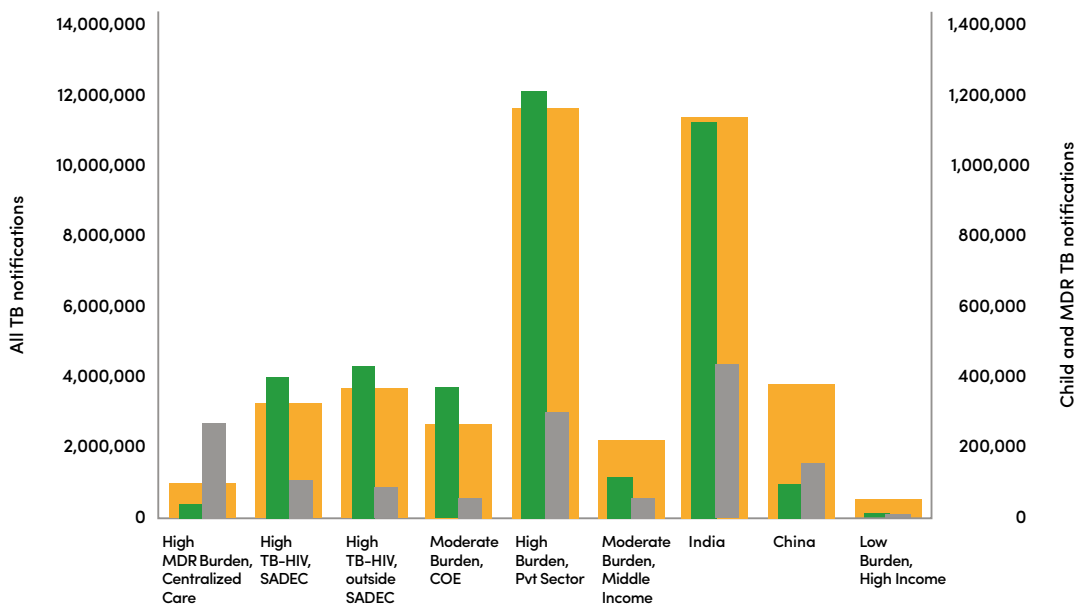


FIGURE 2.4: IMPACT ON INCIDENCE OF REACHING UNHLM ON TB TREATMENT TARGETS



FIGURE 2.5: IMPACT ON TB MORTALITY (IN HIV-NEGATIVE INDIVIDUALS) OF REACHING UNHLM ON TB TARGETS

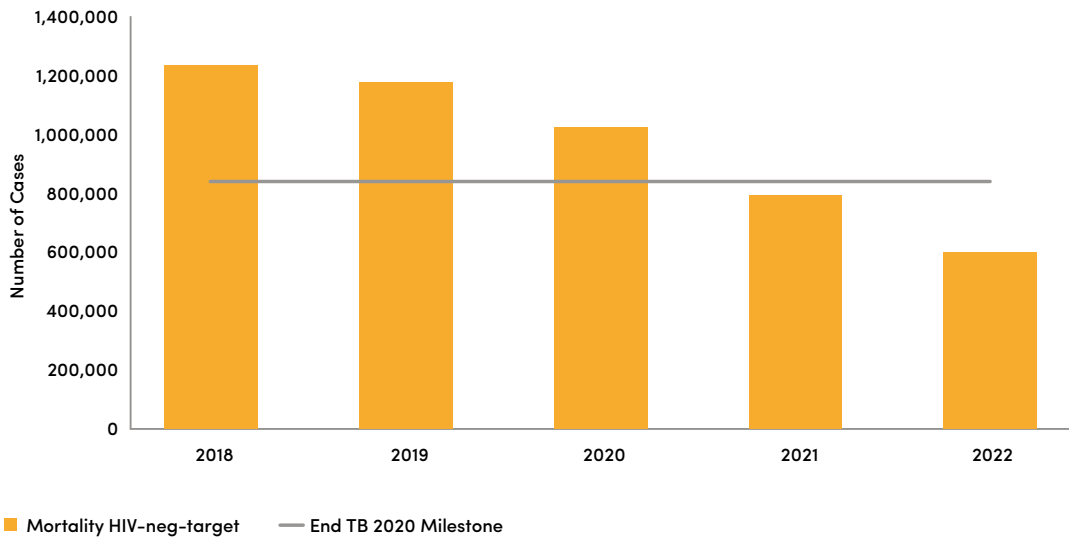


TABLE 2.1.A: PROJECTION OF NUMBERS OF PEOPLE ON TREATMENT BY INCOME STATUS, GLOBAL FUND ELIGIBILITY, GLOBAL PLAN COUNTRY SETTING, WHO REGION AND BRICS MEMBERSHIP

	2018	2019	2020	2021	2022	Total
TB NOTIFICATION TARGETS – TOTAL						
GLOBAL TOTAL						
Total (Global, including OECD countries)	7,266,564	8,471,030	8,700,110	8,257,682	7,733,123	40,428,508
Total (Global, excluding OECD countries)	7,125,765	8,332,480	8,570,469	8,137,500	7,622,250	39,788,464
BY INCOME STATUS						
Low income	918,600	1,080,100	1,266,000	1,216,400	1,146,800	5,627,900
Lower middle income	4,638,545	5,617,524	5,738,920	5,454,794	5,103,074	26,552,857
Upper middle income	1,588,340	1,655,907	1,585,828	1,485,833	1,390,746	7,706,655
High income	121,020	117,436	109,304	100,608	92,466	540,835
GLOBAL FUND ELIGIBLE COUNTRIES, BY INCOME STATUS						
Low income	918,600	1,080,100	1,266,000	1,216,400	1,146,800	5,627,900
Lower middle income	4,635,345	5,614,024	5,735,720	5,451,894	5,100,374	26,537,357
Upper middle income	475,907	514,157	503,441	465,237	430,518	2,389,261
Total	6,029,872	7,208,302	7,505,181	7,133,549	6,677,709	34,554,613
GLOBAL PLAN COUNTRY SETTING						
High MDR Burden	214,450	205,850	195,050	185,450	179,050	979,850
High TB/HIV, SADC	575,100	650,400	725,300	688,800	638,300	3,277,900
High TB/HIV, non-SADC	531,550	666,000	850,400	848,000	799,700	3,695,650
Moderate Burden, COE	431,500	513,580	599,450	579,200	554,300	2,678,030
High Burden, Private Sector	1,988,400	2,445,200	2,563,000	2,430,000	2,270,900	11,697,500
Moderate Burden, Middle Income	428,740	460,050	464,241	441,033	415,825	2,209,889
India	2,155,900	2,572,200	2,404,900	2,245,600	2,092,600	11,471,200
China	806,000	827,150	776,850	728,000	679,900	3,817,900
Low Burden, High Income	126,095	121,453	112,147	103,673	95,403	558,771
WHO REGION						
EMR	538,620	618,011	706,007	668,964	631,021	3,162,624
AFR	1,403,366	1,672,617	1,999,215	1,945,311	1,827,209	8,847,718
AMR	249,900	268,379	266,646	253,408	237,985	1,276,317
EUR	270,377	260,230	245,506	232,097	222,312	1,230,522
WPR	1,441,561	1,514,543	1,514,286	1,446,252	1,352,945	7,269,588
SEAR	3,362,740	4,137,250	3,968,450	3,711,650	3,461,650	18,641,740
BRICS						
Total	3,390,500	3,841,900	3,602,300	3,362,300	3,134,600	17,331,600

TABLE 2.1.B: PROJECTION OF NUMBERS OF CHILDREN (AGES 0–14) ON TREATMENT BY INCOME STATUS, GLOBAL FUND ELIGIBILITY, GLOBAL PLAN COUNTRY SETTING, WHO REGION AND BRICS MEMBERSHIP

	2018	2019	2020	2021	2022	Total
TB NOTIFICATION TARGETS – CHILDREN (AGES 0–14)						
GLOBAL TOTAL						
Total (Global, including OECD countries)	538,433	680,890	853,199	894,549	868,829	3,835,901
Total (Global, excluding OECD countries)	534,796	676,933	849,312	890,922	865,475	3,817,438
BY INCOME STATUS						
Low income	101,786	127,897	166,450	171,550	164,000	731,683
Lower middle income	392,142	497,169	617,703	650,277	633,856	2,791,148
Upper middle income	41,894	53,066	66,348	70,410	68,867	300,584
High income	2,606	2,754	2,692	2,306	2,101	12,459
GLOBAL FUND ELIGIBLE COUNTRIES, BY INCOME STATUS						
Low income	101,786	127,897	166,450	171,550	164,000	731,683
Lower middle income	391,942	496,969	617,503	650,077	633,656	2,790,148
Upper middle income	26,127	30,045	33,212	32,686	31,221	153,292
Total	519,986	655,062	817,336	854,483	829,027	3,675,894
GLOBAL PLAN COUNTRY SETTING						
High MDR Burden	7,587	7,688	7,870	7,646	7,390	38,180
High TB/HIV, SADC	51,700	66,400	92,600	98,700	95,600	405,000
High TB/HIV, non-SADC	46,988	65,608	99,812	112,810	110,009	435,227
Moderate Burden, COE	57,260	69,176	84,648	83,980	79,218	374,282
High Burden, Private Sector	206,227	230,928	264,627	263,525	254,623	1,219,929
Moderate Burden, Middle Income	18,630	21,900	25,429	26,166	25,161	117,286
India	140,000	202,700	251,900	271,000	265,800	1,131,400
China	6,522	12,823	22,824	27,622	28,120	97,911
Low Burden, High Income	3,123	3,242	3,061	2,690	2,512	14,629
WHO REGION						
EMR	71,073	81,690	94,959	90,278	84,614	422,614
AFR	128,800	170,222	243,127	263,025	254,523	1,059,695
AMR	10,967	12,534	13,458	13,497	12,793	63,249
EUR	9,738	9,972	10,009	9,543	9,126	48,388
WPR	69,023	82,238	99,614	104,178	100,346	455,399
SEAR	248,833	324,235	392,032	414,029	407,427	1,786,556
BRICS						
Total	169,650	240,780	300,180	322,400	316,000	1,349,010

TABLE 2.1.C: PROJECTION OF NUMBERS OF PEOPLE ON MDR-TB TREATMENT BY INCOME STATUS, GLOBAL FUND ELIGIBILITY, GLOBAL PLAN COUNTRY SETTING, WHO REGION AND BRICS MEMBERSHIP

	2018	2019	2020	2021	2022	Total
MDR-TB NOTIFICATION TARGETS						
GLOBAL TOTAL						
Total (Global, including OECD countries)	171,305	209,009	302,554	392,538	429,483	1,504,889
Total (Global, excluding OECD countries)	168,797	206,329	299,147	388,439	425,453	1,488,165
BY INCOME STATUS						
Low income	8,690	12,331	24,025	34,392	37,324	116,762
Lower middle income	97,468	121,637	183,089	243,068	269,173	914,436
Upper middle income	62,906	72,704	92,714	111,921	119,911	460,155
High income	2,239	2,334	2,723	3,154	3,073	13,523
GLOBAL FUND ELIGIBLE COUNTRIES, BY INCOME STATUS						
Low income	8,690	12,331	24,025	34,392	37,324	116,762
Lower middle income	97,449	121,615	183,052	243,024	269,131	914,271
Upper middle income	23,432	24,200	27,612	30,435	30,358	136,038
Total	129,619	158,196	234,753	307,919	336,878	1,167,300
GLOBAL PLAN COUNTRY SETTING						
High MDR Burden	49,520	50,984	54,432	58,567	59,969	273,471
High TB/HIV, SADC	14,284	16,664	23,079	27,754	28,924	110,705
High TB/HIV, non-SADC	4,821	7,752	18,320	27,012	28,880	86,786
Moderate Burden, COE	2,926	4,905	12,252	18,192	19,438	57,713
High Burden, Private Sector	25,655	33,883	60,749	85,972	95,959	302,218
Moderate Burden, Middle Income	6,693	7,825	12,311	15,783	15,969	58,582
India	53,940	65,390	86,070	110,210	124,050	439,660
China	10,593	18,585	31,788	44,989	52,346	158,301
Low Burden, High Income	2,034	2,164	2,663	3,160	3,063	13,084
WHO REGION						
EMR	6,702	10,959	20,283	29,836	35,471	103,250
AFR	20,564	26,798	47,405	63,781	67,364	225,913
AMR	4,686	5,248	7,624	9,354	9,523	36,435
EUR	51,117	52,612	56,276	60,500	61,845	282,350
WPR	23,276	32,808	53,836	73,937	83,600	267,456
SEAR	64,960	80,584	117,130	155,130	171,681	589,485
BRICS						
Total	101,994	122,491	159,377	198,690	219,666	802,218

TABLE 2.1.D: PROJECTION OF NUMBERS OF PEOPLE ON TB PREVENTIVE THERAPY BY INCOME STATUS, GLOBAL FUND ELIGIBILITY, GLOBAL PLAN COUNTRY SETTING, WHO REGION AND BRICS MEMBERSHIP

	2018	2019	2020	2021	2022	Total
TB PREVENTIVE THERAPY TARGETS						
GLOBAL TOTAL						
Total (Global, including OECD countries)	3,641,200	4,143,200	6,541,400	9,048,600	10,481,500	33,855,900
Total (Global, excluding OECD countries)	3,545,000	4,143,200	6,541,300	9,048,500	10,481,400	33,759,400
BY INCOME STATUS						
Low income	952,700	777,100	1,210,800	1,613,900	1,817,700	6,372,200
Lower middle income	1,676,700	2,158,300	3,666,900	5,305,800	6,286,800	19,094,500
Upper middle income	928,200	1,093,100	1,520,000	1,926,700	2,164,000	7,632,000
High income	83,500	114,700	143,700	202,200	213,000	757,100
GLOBAL FUND ELIGIBLE COUNTRIES, BY INCOME STATUS						
Low income	952,700	777,100	1,210,800	1,613,900	1,817,700	6,372,200
Lower middle income	1,676,200	2,157,400	3,665,500	5,304,000	6,284,700	19,087,800
Upper middle income	612,000	601,700	774,000	869,100	902,000	3,758,800
Total	3,240,900	3,536,200	5,650,300	7,787,000	9,004,300	29,218,700
GLOBAL PLAN COUNTRY SETTING						
High MDR Burden	201,000	274,200	364,200	473,500	558,700	1,871,600
High TB/HIV, SADC	1,229,900	968,600	1,241,000	1,480,600	1,526,600	6,446,700
High TB/HIV, non-SADC	479,500	752,500	1,170,900	1,447,300	1,620,200	5,470,400
Moderate Burden, COE	242,300	257,800	472,500	653,500	777,900	2,404,000
High Burden, Private Sector	346,600	643,500	1,249,600	1,928,300	2,347,900	6,515,900
Moderate Burden, Middle Income	132,400	199,900	314,300	443,100	514,900	1,604,600
India	801,100	719,600	1,225,400	1,867,000	2,252,900	6,866,000
China	111,100	192,000	328,000	503,300	611,500	1,745,900
Low Burden, High Income	97,300	135,200	175,400	252,100	270,800	930,800
WHO REGION						
EMR	120,100	217,000	437,700	662,200	805,400	2,242,400
AFR	1,916,300	1,926,300	2,799,100	3,461,900	3,785,500	13,889,100
AMR	140,200	199,500	276,700	382,700	421,700	1,420,800
EUR	234,500	320,300	423,400	560,900	653,700	2,192,800
WPR	212,500	362,500	656,500	1,024,400	1,243,000	3,498,900
SEAR	1,017,500	1,117,700	1,947,900	2,956,600	3,572,200	10,611,900
BRICS						
Total	1,568,000	1,577,400	2,407,500	3,334,600	3,899,500	12,787,000

Country settings

The Global Plan provides sets of recommended actions – “investment packages” – designed to achieve the 90-(90)-90 targets. These investment packages are tailored to the local characteristics of the TB epidemic, as well as to the health system constraints and socioeconomic situations in various country settings.

Similarities exist between countries within a particular region or between countries with similar histories, socioeconomic conditions or health system constraints. As a result, countries are grouped into different “settings”.³ Countries can

be associated with the characteristics of more than one setting, and provinces within a single country can fit into different settings. The method for defining each setting is explained in Annex 2.

³ Country settings are not meant to form any alternative to existing formal groupings in public health, such as WHO regions, etc. Nor are they meant to form classifications for funding allocations or any other operational decisions.

FIGURE 2.6: NINE COUNTRY SETTINGS

- 1 EASTERN EUROPEAN AND CENTRAL ASIAN SETTINGS** that have a high proportion of drug-resistant TB and a hospital-based care delivery system
- 2 SOUTHERN AND CENTRAL AFRICAN SETTINGS** where HIV and mining are key drivers of the epidemic
- 3 AFRICAN SETTINGS** with moderate to high HIV where mining is not a significant issue
- 4 SETTINGS WITH SEVERELY UNDER-RESOURCED HEALTH SYSTEMS** or country settings with challenging operating environments (COE)
- 5 SETTINGS WITH A HIGH TO MODERATE BURDEN OF TB** with a large proportion in private sector care
- 6 MIDDLE-INCOME COUNTRY SETTINGS** with a moderate TB burden
- 7 INDIA SETTING**
- 8 CHINA SETTING**
- 9 LOW-BURDEN SETTINGS** and country settings on the verge of eliminating TB

Setting 1:

EASTERN EUROPEAN AND CENTRAL ASIAN SETTINGS THAT HAVE A HIGH PROPORTION OF DR-TB

While the TB incidence and notifications in these countries have declined substantially over the past decade, the proportion of DR-TB is very high, with resistance also to second-line medicines. Traditionally, most people with TB are hospitalized, and the typically long duration of hospital stays and insufficient infection control in hospitals create conditions that promote the further spread and amplification of drug resistance. This TB care delivery model is also expensive and results in sub-standard treatment outcomes. Key populations, such as seasonal labour migrants and prisoners, face the most significant barriers in accessing services including preventive therapy.

Strengthening the performance of health systems with regard to TB will foster people-centred TB services and improve TB outcomes. Countries in this setting should ensure universal coverage with modern rapid diagnostics at all levels, implement the new medicines and treatment regimens for DR-TB, and intensify treatment support, including treatment of comorbidities, active drug-safety monitoring (aDSM), management of adverse events and appropriate

adherence support. TB prevention needs to be scaled up, including preventive therapy for adult contacts of people with DS-TB and for all contacts of people with DR-TB. Systemic measures are needed to promote effective and efficient resource allocation and provider payment mechanisms in order to address the special needs of key population groups and upgrade TB information systems.

PROPOSED INVESTMENT PACKAGE:

- 1 Roll out rapid molecular diagnostics as the initial test for DS- and DR-TB at all levels of care.
- 2 Increase the coverage and improve the quality of rapid culture and drug susceptibility testing (DST) investigations at referral laboratories.
- 3 Ensure universal access to quality treatment of DR-TB, with a special emphasis on children and adolescents.
- 4 Ensure appropriate support for treatment adherence, including the use of digital tools.
- 5 Strengthen the monitoring of people with TB on treatment, and the management of comorbidities, adverse events and pharmacovigilance.
- 6 Upgrade and enhance TB information systems.
- 7 Ensure effective TB infection control at all levels of TB care.
- 8 Enable effective and efficient health financing and allocation mechanisms and people-centred TB care delivery systems.
- 9 Address the special needs of key populations, with a special emphasis on prisoners and migrants.
- 10 Scale up the coverage and improve the quality of contact investigation, testing for TB infection and preventive therapy, with a special focus on adult household and other close contacts and providing preventive therapy for contacts of people with DR-TB.

Setting 2:

SOUTHERN AND CENTRAL AFRICAN SETTINGS WHERE HIV AND MINING ARE KEY DRIVERS OF THE EPIDEMIC

The TB epidemic in these countries is fuelled by the HIV epidemic, with 50–80% of people with TB also living with HIV. HIV prevention and care has scaled up rapidly in the last several years, which is one of the reasons TB has declined more quickly in this country setting than it has globally. The mining industries in this country setting, however – including both large-scale mining operations and smaller-scale “artisanal” mines – pose significant challenges.

Mining-related silicosis is a risk factor for TB, and labour migration across international borders complicates the provision of proper TB treatment and care. There is strong political commitment at the highest level of the Southern African Development Community (SADC) countries to address mining-related TB, and a regional proj-

ect on TB and mining has been implemented in the last few years. These should be seen as initial steps towards a much more robust effort to protect mine workers from TB, while providing quality TB care and support for individuals and mining communities affected by TB.

PROPOSED INVESTMENT PACKAGE:

- 1 Rapidly scale up molecular diagnostics as the initial test for DS- and DR-TB.
 - 2 Strengthen culture and DST at referral laboratories, laboratory quality assurance and specimen transportation.
 - 3 Improve management of HIV-associated TB and other comorbidities.
 - 4 Roll out active TB case finding for people living with HIV and contacts of people with TB.
 - 5 Provide testing for TB infection and preventive therapy for people living with HIV, and child and adult contacts of people with TB.
 - 6 Address the special needs of key populations (prisoners, mobile populations, miners and others).
 - 7 Further strengthen information systems and make them web-based live systems to improve TB data and programming.
 - 8 Increase access to DR-TB treatment for adults, children and adolescents.
 - 9 Strengthen community-based interventions and civil society involvement, including treatment support incentives and enablers.
 - 10 Improve treatment monitoring, management of adverse events and pharmacovigilance/aDSM.
 - 11 Invest in human resources development for TB care.
 - 12 Remove human rights and gender-related barriers to accessing TB services.
-

Setting 3:

AFRICAN SETTINGS WITH MODERATE TO HIGH HIV WHERE MINING IS NOT A SIGNIFICANT ISSUE

This setting is similar to Setting 2, in that, HIV fuels the TB epidemic in these countries, but mining activities have a comparatively smaller impact on the TB situation.

PROPOSED INVESTMENT PACKAGE:

- 1 Roll out molecular diagnostics as the initial test for DS- and DR-TB, and strengthen the system for specimen transportation.
 - 2 Scale up active TB case finding and contact investigation.
 - 3 Increase access to treatment of DS- and DR-TB for adults, children and adolescents, improving treatment monitoring, management of adverse events and pharmacovigilance/aDSM.
 - 4 Provide testing for TB infection and preventive therapy for adult household and other close contacts of people with TB, including children and people living with HIV.
 - 5 Improve TB/HIV case finding and diagnosis with management of HIV-associated TB and other comorbidities.
 - 6 Strengthen community-based interventions and civil society involvement, and remove human rights and gender-related barriers to accessing TB services.
 - 7 Strengthen information systems to improve TB data and programming, and make these systems electronic and web-based.
 - 8 Accelerate engagement of private providers to close gaps in TB care.
 - 9 Strengthen culture and DST at referral laboratories with laboratory quality assurance.
 - 10 Address the special needs of key populations (prisoners, mobile populations and others), including treatment support incentives and enablers.
 - 11 Strengthen procurement and supply chain management (PSM) systems.
-

Setting 4:

SETTINGS WITH SEVERELY UNDER-RESOURCED HEALTH SYSTEMS OR COUNTRY SETTINGS WITH CHALLENGING OPERATING ENVIRONMENTS (COES)

These countries face ongoing conflicts that have severely weakened the health care system and displaced populations, posing significant security-related barriers to the provision of TB care. While it may not be feasible to expect rapid scale-up in these countries over the next few years, it is possible to create a foundation for sustained scale-up through targeted actions and innovative solutions, while achieving short-term impact.

PROPOSED INVESTMENT PACKAGE:

- 1 Strengthen specimen transportation systems with innovative technology and approaches.
 - 2 Address the special needs of key populations, such as prisoners, internally displaced populations and refugees, and improve active TB case finding in these populations.
 - 3 Increase access to DS- and DR-TB treatment for adults, children and adolescents.
 - 4 Improve community-based interventions and civil society involvement, including for treatment support incentives and enablers.
 - 5 Remove human rights and gender-related barriers to accessing TB services.
 - 6 Roll out molecular diagnostics for DS- and DR-TB.
 - 7 Improve TB information systems with innovative technology and approaches.
 - 8 Establish delivery models for preventive therapy in adult household and other close contacts of people with TB.
 - 9 Strengthen information, communication and social mobilization.
-

Setting 5:

SETTINGS WITH A HIGH TO MODERATE BURDEN OF TB WITH A LARGE PROPORTION OF PEOPLE WHO SEEK CARE IN THE PRIVATE HEALTH CARE SECTOR

These are primarily high TB burden countries in Asia where people with TB tend to be largely seen by private providers. In some situations, these countries also have public hospitals that are not linked to the NTP or notification system. As a result, many people seeking care are diagnosed and treated in the private health care system with varying quality of care and with essentially no treatment support systems. Most people seeking care in the private sector incur substantial out-of-pocket expenses.

Innovative models of engagement with the private sector are required. Greater progress can be made by establishing business models that improve private health sector care, develop user-friendly systems for universal TB notifica-

tion, and create and strengthen partnerships to provide support to people with TB, including the elimination of catastrophic out-of-pocket TB expenses.

PROPOSED INVESTMENT PACKAGE:

- 1 Strengthen engagement with private sector health care providers to ensure that they provide quality-assured treatment and care for all people with TB who seek care in the private sector.
 - 2 Strengthen active TB case finding and contact investigation.
 - 3 Roll out molecular diagnostics as the initial test for DS- and DR-TB, and strengthen the specimen transportation system.
 - 4 Improve culture and DST at referral laboratories and laboratory quality assurance.
 - 5 Scale up treatment for people with DR-TB, including children and adolescents
 - 6 Strengthen information systems for TB, including digital solutions for online notification.
 - 7 Ensure treatment completion by strengthening financial and psychosocial support for people with TB.
 - 8 Provide testing for TB infection and preventive therapy for household and other close contacts of people with TB.
 - 9 Engage all stakeholders in high-level advocacy and strategic planning that pursues innovative health financing solutions to close funding gaps.
 - 10 Strengthen human resources for TB care using innovative strategies and tools.
 - 11 Promote community-based interventions and civil society involvement for improved TB care, including activities for community mobilization and eradication of stigma and discrimination.
-

Setting 6:

MIDDLE-INCOME COUNTRY SETTINGS WITH A MODERATE TB BURDEN

These predominantly Asian and Latin American countries have moderate levels of TB and have the resources to address most of the investment needs for scale-up. Although these countries have social support schemes focused on poor and marginalized groups, these key populations continue to face barriers in accessing health care, leading to delayed diagnosis and catastrophic expenses for individuals and families.

PROPOSED INVESTMENT PACKAGE:

- 1** Strengthen TB diagnostics with rapid roll-out of molecular diagnostics as the initial test for DS- and DR-TB, and improve culture and DST at referral laboratories with laboratory quality assurance.
 - 2** Strengthen active TB case finding and contact investigation.
 - 3** Provide TB preventive therapy for child, adolescent and adult contacts of people with TB, as well as for people living with HIV and other at-risk groups.
 - 4** Address the special needs of key populations (prisoners, mobile populations, miners and others).
 - 5** Strengthen DR-TB treatment in adults and children.
 - 6** Enhance TB information systems.
 - 7** Promote community-based interventions, civil society involvement and high-level advocacy.
 - 8** Engage the private sector to provide quality-assured TB care.
-

Setting 7:

INDIA

India is home to one in four people living with TB and has the largest NTP in the world. As a result, the country must be considered its own setting. To a great extent, the progress made in India will determine global progress against TB.

While India's private sector is usually the first point of contact for people seeking health care, people with TB frequently seek care by going back and forth between the public and the private sectors. Accordingly, India needs to invest further in the public health infrastructure and improve and sustain the quality of TB services that are provided across both the public and private sectors.

Several groundbreaking innovations and research studies conducted in India have shaped the global response to TB. However, given its strong economic growth, the country should invest more resources in its public health sector.

TB's impact varies within the country, severely and disproportionately impacting the urban poor and certain population groups, such as tribal and indigenous peoples. This variation demands a differentiated approach across states, urban and rural hotspots, and key populations.

There is a very high level of political commitment in India. Prime Minister Narendra Modi has issued an official call to end TB in the country by 2025 – five years ahead of the global target. This political will needs to translate into sustained rapid scale-up of comprehensive services to end TB.

PROPOSED INVESTMENT PACKAGE:

- 1 Scale up engagement with private health care providers to ensure quality care for all people with TB.
- 2 Roll out molecular diagnostics as the initial test for DS- and DR-TB, and improve culture and DST at referral laboratories with laboratory quality assurance.
- 3 Scale up active TB case finding and contact investigation.
- 4 Strengthen digital real-time TB information systems for efficient TB surveillance systems.
- 5 Strengthen the provision of DR-TB treatment for adults, children and adolescents, with greater access to new medicines.
- 6 Provide testing for TB infection and preventive therapy for household contacts of TB, including for adults, children and other high-risk groups.
- 7 Strengthen human resources for TB care through innovative strategic approaches, including the purchase of services and public-private partnership models.
- 8 Increase access to DS-TB treatment for adults, children and adolescents.
- 9 Expand and maintain treatment support systems – incentives and enablers – including for financial and nutritional support and for digital treatment support technologies.
- 10 Invest in research and innovation for new tools, vaccines, diagnostics, and drug regimens.

Setting 8:

CHINA

As a high TB burden country with the domestic resources and capacity to address the TB epidemic, China must also be considered separately. Nearly all TB funding in China comes from domestic sources. The country has conducted several prevalence surveys that demonstrate declining levels of TB.

This decline has been attributed mainly to high levels of case detection and treatment success, as well as rapid socioeconomic development. Linking hospitals to the public health system via electronic notification systems, coupled with good governance in the health system, has massively increased the proportion of TB that is notified.

While China appears to have high levels of health coverage, TB diagnosis and quality TB care are too often out of reach for the poor and other marginalized populations due to user fees and other costs for accessing care. Treatment coverage of DR-TB in China is also far below the global average.

PROPOSED INVESTMENT PACKAGE:

- 1** Rapidly roll out molecular diagnostics as the initial test for DS- and DR-TB.
 - 2** Scale up DST and DR-TB treatment for adults, children and adolescents.
 - 3** Improve early diagnosis among key populations through routine contact investigation and active case finding.
 - 4** Provide testing for TB infection and preventive therapy for adult and child household contacts of people with TB and for other key populations (the elderly, prisoners, mobile populations, and others).
 - 5** Address the special needs of key populations through active case finding and treatment support, including incentives and enablers and psychosocial support.
 - 6** Invest in TB research and innovation for new diagnostic, treatment and prevention tools.
 - 7** Address financial losses incurred by poor people with TB through financial support strategies.
-

Setting 9:

LOW-BURDEN SETTINGS AND COUNTRY SETTINGS ON THE VERGE OF ELIMINATING TB

These are low-burden, high-income countries that have already reached or are close to reaching the goal of ending TB. These countries should now target TB elimination, i.e., reducing the incidence to 1 per million population. In these countries, TB is concentrated among the most vulnerable populations, such as migrants, the poor and other marginalized groups. Although the unit cost of managing TB in these countries is high, they have the capacity to adequately fund TB care.

These countries include Organisation for Economic Co-operation and Development (OECD) Development Assistance Committee (DAC) countries, which have the capacity to contribute more to the global effort to end TB. These

resource contributions should be increased and contributed to established multilateral mechanisms (e.g., the Global Fund, the Global Drug Facility, Unitaid) and R&D institutions.

PROPOSED INVESTMENT PACKAGE:

- 1 Support active case finding and comprehensive care among key populations.
 - 2 Support routine contact investigation.
 - 3 Provide testing for TB infection and preventive therapy for all contacts of people with TB in household and other settings.
 - 4 Address the special needs of key populations (migrants, people living in poverty and other marginalized groups).
 - 5 Strengthen high-level advocacy and national strategic planning, engaging all stakeholders.
 - 6 Increase contributions to the global TB effort, including through multilateral financing mechanisms.
 - 7 Invest in TB research and innovation for new diagnostic, treatment and prevention tools.
-



3.REACHING KEY POPULATIONS



SUMMARY

Reaching key populations – people who are vulnerable, marginalized, underserved or at risk of TB infection and illness – will be essential for ending TB. It is imperative from both an epidemiological and an equity and human rights perspective that we strive to protect people in key populations; provide them with care; understand the social, political, legal and economic barriers they face in accessing the TB prevention, diagnosis, treatment, care and support services they need; and involve them as priority stakeholders and equal partners in the fight against the disease.

To reach TB key populations, they must be meaningfully engaged and empowered to participate in TB governance and decision-making. If TB programmes are to understand the lived experience of TB, they must facilitate the meaningful participation of the representatives of key populations, on behalf of the constituencies they represent, in all TB policy, programme and governance discussions and decisions. Indeed, a significant aspect of reaching these populations is investing in building the capacity and coordination of TB key populations in advocacy,

treatment literacy, peer support, monitoring and evaluation, programme design, procurement and human rights – which together can contribute to creating a care-enabling environment for those most vulnerable. Therefore, such efforts must receive increased priority. These actions will help to find and treat the 3.3 million missing people with TB who go undiagnosed or unreported to public health systems each year in a way that is not only more effective, but is also human-rights-based, gender-sensitive and people-centred.

PRIORITY ACTIONS

Governments:

- ⊕ Set an operational target of reaching at least 90% of people with TB in key populations through improved access to services, systematic screening where required, and new active case finding approaches, and providing all people in need with effective and affordable treatment.
- ⊕ Fulfil the UN High Level Meeting (UNHLM) commitments to remove any laws, policies and programmes that discriminate against people with TB.
- ⊕ Promote and support an end to stigma and all forms of discrimination, and enact policies and practices that improve outreach, education and care. Governments can use the stigma assessment tools developed by the Stop TB Partnership and other partners.
- ⊕ Extend support for key populations, improve quality of information, and ensure TB care and support is provided in safe environments free from stigma and discrimination.

- ✦ Integrate the UNHLM on TB commitments related to key populations into national TB strategies and guidelines; and develop and implement multisectoral plans for outreach and service provision for specific key populations.
- ✦ Using community, rights and gender (CRG) assessment tools, assess which populations are vulnerable to TB along with the barriers that prevent access to care, and carry out targeted outreach accordingly. Report on progress in TB with data disaggregated by key population, following clear policies that ensure privacy and protect human rights.
- ✦ Implement gender-sensitive policies and programming across all aspects of TB programmes, with particular consideration for both disease prevalence and access to services.
- ✦ Facilitate the involvement of TB survivors and key populations in all levels of policymaking and programmatic design in order to ensure that TB services are people-centred and meet the expressed needs of affected communities; and invest in networks and organizations of TB survivors to build the required capacity to effectively engage in TB governance.

Technical partners:

- ✦ Provide countries with frameworks for prioritization, action and monitoring progress in improving access to TB services for key population groups; and support the meaningful engagement of these populations through investment and capacity-building monitoring and advocacy, particularly in terms of TB and treatment literacy, monitoring and evaluation, and human rights.

Mining companies:

- ✦ Implement strong infection control policies and provide workplace health and safety programmes that greatly reduce workplace

exposure to silica dust, and provide routine TB screening, prevention and a system to ensure that mine workers with TB and their families receive appropriate quality care and support services.

Prisons and detention centres:

- ✦ Provide routine TB screening, diagnosis and access to appropriate quality TB care for prisoners, other people in detention and staff working in those facilities.
- ✦ Ensure continuity of care for incarcerated persons released back into the general population during the course of receiving TB treatment or preventive therapy.
- ✦ Reduce overcrowding and malnutrition, and address the limited ventilation in prisons and detention facilities.

Advocates:

- ✦ Work to ensure that the human rights of people affected by TB are upheld with regard to TB prevention, treatment and care.
- ✦ Support the growth and cultivation of global, regional and national networks of TB survivors and members of affected communities, and partner with them in advocacy activities at every opportunity.
- ✦ Prioritize the investment in networks of TB survivors and affected communities so that they can effectively contribute in a coordinated manner as decision makers, service providers, monitors of programmes and advocates.
- ✦ Engage in all relevant elements of the MAF-TB, including holding governments accountable for taking action to fulfil the UNHLM on TB commitments, reporting on progress and reviewing outcomes.
- ✦ Advocate for participation of TB affected

communities, including those from key populations, within decision-making bodies and processes, as promised within the UN Political Declaration on TB.

Reaching key populations is an equity and human rights imperative

It is unacceptable that nearly half of the world's people cannot afford or access quality health care, live in unhealthy environments, or are malnourished. We have a collective responsibility to support key populations who face higher risks associated with TB, to provide them with a cure, and to empower them to be both leaders and equal partners in the fight against the disease. Reaching key populations is critical to fulfilling the promise of the SDGs, which is to leave no one behind.

The UN Political Declaration on TB further commits UN Member States to leave no one behind in the effort to end TB. But, as the UN Committee for Development Policy has acknowledged, leaving no one behind is “seldom disputed in principle, but the complexity of its practical implementation is often insufficiently acknowledged”.¹ This reality is why it is so essential to take proactive, concrete actions to reach key populations who are at higher risk of TB.

Key populations are those who experience increased impact from TB and decreased access to services. Stigma, discrimination, violence and harassment, restrictive laws and policies, and criminalization of behaviours or practices place key populations at greater risk of TB and make it more difficult for them to access services.² Key populations vary depending on the setting. To reach key populations, they must be empowered as decision makers in the TB response. Acknowledging their unique role in having lived experience of TB can help to inform the removal of social, political, legal, gender, economic or cultural barriers

to access; extend support for people with TB – including through peer support networks; increase the quality of information; and ensure that TB care is provided in safe environments free from stigma and discrimination, where privacy is upheld.

As discussed in Chapter 4, key population groups and affected communities themselves can take leadership roles in providing many of these services. For this to happen, governments should assess which populations are vulnerable to TB, where they are concentrated geographically, and what barriers stand in the way of them accessing care. Governments should then carry out targeted outreach accordingly, using the available CRG tools developed for addressing TB in key populations. Rights-based policy and legislative frameworks also must be in place, backed by adequate funding.

The UN Political Declaration on TB aligns with numerous international legal frameworks in committing to protect and promote the right to the enjoyment of the highest attainable standard of physical and mental health. Specifically, governments committed to removing discriminatory laws, policies and programmes against people with TB; to promoting and supporting an end to stigma and all forms of discrimination; and to enacting policies and practices that improve outreach, education and care.

1 Leaving no one behind. UN Committee for Development Policy. New York: United Nations; 2018. https://sustainabledevelopment.un.org/content/documents/2754713_July_PM_2_Leaving_no_one_behind_Summary_from_UN_Committee_for_Development_Policy.pdf

2 Key populations [Website]. Geneva: The Global Fund to Fight AIDS, Tuberculosis and Malaria; 2019. <https://www.theglobalfund.org/en/key-populations/>

These actions are critical to fulfilling another commitment within the Political Declaration: finding the 3.3 million missing people with TB who go undiagnosed or unreported to public health systems each year.³ This is the aim of **FIND. TREAT. ALL. #ENDTB.**, a joint initiative of WHO, Stop TB Partnership and the Global Fund to engage TB affected communities, civil society and development financing partners in addressing the barriers preventing millions from accessing quality-assured TB care and support each year.⁴

The Global Plan recommends that countries set a separate operational target of reaching at least 90% of those they would define as key populations by improving access to services, conducting systematic screening⁵ where required, implementing active, new and innovative case-finding methods, and providing all people who require it with effective and affordable treatment.

Countries are encouraged to report on their progress with respect to TB using data that are disaggregated by key population. Technical partners are encouraged to provide countries with frameworks for prioritization, action and monitoring progress in improving access to TB services for key population groups.

Examples of successful interventions that have been implemented to reach key populations can be found in a compendium of case studies from the Stop TB Partnership's TB REACH programme.⁶ TB REACH has also included strong examples of support for key populations within the field guides made available through the

Global Fund Strategic Initiative to Find the Missing People with TB.⁷

TB and gender

Gender disparities in TB present huge challenges in providing access to services. Worldwide, men are much likelier than women to contract and die from TB, with approximately 6 million adult men contracting TB and 840,000 dying from the disease in 2017, compared to 3.2 million adult women who suffered nearly half a million deaths.⁸ At the same time, TB has a grave impact on women during reproduction and in pregnancy. TB is still the leading infectious killer among women globally. Women are also more likely to provide care for people who are sick with TB, placing them at risk of exposure in caregiving situations.

Improving access to TB services for all demands a gender-sensitive approach. People of different genders are affected differently by TB, are subject to varying levels of stigma, and face different barriers to access as a result of both power and economic inequalities. Gender impacts levels of stigma and heightens the risk of infection and disease in many settings. Socioeconomic and stigma-related barriers can be addressed through quality gender-responsive programming across the care cascade and promotion of gender equality through TB programmes that empower women and girls. In some situations, legal support is necessary to ensure that people from key populations can access care and prevention and remain free from unjust policies and practices such as involuntary isolation and discrimination.⁹

3 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

4 Joint Initiative "FIND. TREAT. ALL. #ENDTB" [Website]. Geneva: World Health Organization; 2019. <https://www.who.int/tb/joint-initiative/en/>

5 For guidance, see WHO's guidelines on systematic screening for active TB at: <http://www.who.int/tb/tbscreening/en/>

6 Improving tuberculosis case detection: a compendium of TB REACH case studies, lessons learnt and a monitoring and evaluation framework. Geneva: Stop TB Partnership; 2014. http://www.stoptb.org/assets/documents/resources/publications/technical/TB_Case_Studies.pdf

7 The Strategic Initiative to Find the Missing People with TB [Website]. Geneva: Stop TB Partnership; 2018. <https://stoptb-strategicinitiative.org/>

8 Tuberculosis in women. Geneva: World Health Organization; 2018. <https://www.who.int/tb/areas-of-work/population-groups/gender/en/>

9 Tuberculosis, gender and human rights. Geneva: The Global Fund to Fight AIDS, Tuberculosis and Malaria; 2017. https://www.theglobalfund.org/media/6349/core_thumanrightsgenderequality_technicalbrief_en.pdf

A PARADIGM SHIFT TOWARDS A HUMAN-RIGHTS-BASED APPROACH TO TB

The UN Political Declaration on TB calls for transforming the TB response to be rights-based. The promotion and protection of the human rights of people affected by TB is a legal, ethical and moral imperative, and is of crucial importance if the response to the epidemic is to be effective in bringing relief to affected individuals and communities.

A human-rights-based response to TB is critical, as it can contribute to overcoming barriers to accessing TB education, prevention, diagnosis, treatment, care and support services. There is a range of human rights considerations relevant for TB interventions. These include ensuring access to safe, quality, affordable medicines and diagnostics; freedom from stigma and discrimination; privacy; liberty; participation of TB survivors; dignity; gender equity; assembly; access to scientific progress (see Chapter 6 for discussion on access strategies for new TB tools); and realizing the highest attainable standard of health.

These are the rights of all people, but particular attention needs to be given to realizing the rights of those who are most vulnerable and marginalized, including the urban and rural poor, people living with HIV, people who use drugs, children, migrants, refugees, indigenous peoples, miners and people deprived of liberty. Through human-rights-based, gender-sensitive and people-centred TB interventions, social, political, cultural, legal and economic barriers to accessing TB services can be overcome and the effectiveness of TB interventions can be significantly enhanced.

LEGAL FRAMEWORKS AND PRECEDENTS FOR ENSURING THE RIGHTS OF PEOPLE WITH TB

The Declaration of the Rights of People Affected by Tuberculosis¹ builds on the Universal Declaration of Human Rights², stating that people with TB have the right to life; the right to dignity; the right to the highest attainable standard of physical and mental health; and the right to freedom from torture and other cruel, inhuman or degrading

treatment, among other rights. Under international and regional human rights law, states have legal obligations to respect, protect and fulfil those rights. Non-state actors also have responsibilities to respect the human rights of people affected by TB. There are legal precedents that have compelled states to provide TB care and support to people affected by TB. Judgments by the European Court of Human Rights, for example, have required states to provide TB care for children in state custody. And, in 2007, Argentina's Supreme Court ruled that the state was obligated, under human rights treaties and national and provincial constitutions, to provide TB care for members of the Toba indigenous community.³ Support is needed to help key populations access legal support when systems of justice must be engaged in order to gain access to TB care.

HUMAN RIGHTS AND TB PREVENTION

The UN Political Declaration on TB also committed to prevent TB by providing 30 million people with TB preventive therapy, including 4 million children under the age of 5, 20 million other household contacts of people affected by TB, and 6 million people living with HIV. Reaching 30 million people with preventive therapy will require a paradigm shift in how health systems view the rights of people who are exposed to TB. Health systems must recognize and act to honour people's right to know their TB status (i.e., whether they are living with TB infection). This will provide the foundation for supporting activities that proactively reach people at risk of TB with access to evaluation and quality-assured preventive therapy. In Uganda, for example, in a piloted approach called DETECT Child TB, child household contacts of adults diagnosed with TB were routinely evaluated for TB through decentralized services provided by health workers within the community. Using this approach, 74% of children under 5 received TB preventive therapy compared to the 27% of children under 5 who received TB preventive therapy worldwide in 2017.^{4,5} Improved methods are needed to test for TB infection, especially in key populations at risk of being repeatedly exposed to TB (e.g., health workers).

1 Declaration of the Rights of People Affected by Tuberculosis. Geneva: Stop TB Partnership; 2019. <http://www.stoptb.org/assets/documents/communities/FINAL%20Declaration%20on%20the%20Right%20of%20People%20Affected%20by%20TB%2013.05.2019.pdf>

2 Universal Declaration of Human Rights. Paris: United Nations General Assembly; 1948. <https://www.un.org/en/universal-declaration-human-rights/>

3 Silent epidemic: a call to action against child tuberculosis. Paris: International Union Against Tuberculosis and Lung Disease; 2017. <https://childtb.theunion.org/wp-content/uploads/2018/08/Silent-Epidemic.pdf>

4 Zawedde-Muyanja A, Nakanwagi A, Dongo J, et al. Decentralisation of child tuberculosis services increases case finding and uptake of preventive therapy in Uganda. *Int J Tuberc Lung Dis*. 2018;22(11):1314–21. doi:10.5588/ijtld.18.0025

5 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

TB stigma

Eradicating stigma is essential to reaching the millions of missing people who develop TB and go without care and support. This effort goes hand in hand with more targeted efforts to reach key populations with services. People with TB report facing stigma even from their own family members, friends and colleagues. This stigma often leads them to take measures to hide their diagnosis from others. People with TB can also experience self-stigma, wherein a person internalizes attitudes of shame, disgust or even guilt associated with TB. The stigma associated with TB creates a profound social and cultural barrier that makes it more difficult for people with TB to openly seek the care and support they need and to complete their TB treatment.¹⁰ For these reasons, it is important that affected communities measure stigma, lead the conversation on TB stigma and spearhead efforts to educate the public about what TB is actually like for those who experience it. This act of owning one's own story and sharing it with others can create understanding that reduces TB stigma.

To assist governments in taking action to dispel TB stigma, the Stop TB Partnership – with support from USAID and in collaboration with the Global and Regional Community Networks, health care workers from the Global Coalition of TB Activists, human rights experts from Northwestern Pritzker School of Law, and technical partners such as WHO and KNCV – has developed TB stigma assessment tools¹¹ that countries can use to assess the types, levels, causes and impact of TB stigma, and to develop recommendations to combat stigma.¹²

10 Women & stigma: conversations of resilience in the war against TB. Amsterdam: Global Coalition of TB Activists; 2018. <http://www.tbonline.info/media/uploads/documents/women-and-stigma-full-book.pdf>

11 TB stigma assessment: implementation handbook. Geneva: Stop TB Partnership; 2019. <http://www.stoptb.org/assets/documents/communities/STP%20TB%20Stigma%20Assessment%20Implementation%20Handbook.pdf>

12 TB stigma measurement guidance. The Hague: Challenge TB; 2018. https://www.challengefb.org/publications/tools/ua/TB_Stigma_Measurement_Guidance.pdf

Key population groups

Recognizing the higher prevalence of TB among men, the UN Political Declaration on TB acknowledges specific key populations that are vulnerable or in situations that make them vulnerable to TB, including women and children, indigenous peoples, health care workers, migrants, refugees, prisoners, miners and others exposed to silica, the urban and rural poor, underserved populations, undernourished people, individuals who face food insecurity, ethnic minorities, people and communities at risk of exposure to bovine TB, people living with diabetes, people with mental and physical disabilities, people with alcohol use disorders and people who use tobacco. People within key population groups are at greater risk of TB because of increased exposure, limited access to quality-assured TB services, or biological or behavioural factors (Table 3.1). People in one category can also be part of the other groups. A mine worker, for example, might live in a community with little access to health care and might be living with HIV. He might also smoke and/or have diabetes. He might also pass TB to other family members.

Children and adolescents

In 2018, an estimated over 1 million children under 15 years of age developed TB and 233,000 died of the disease.¹³ Approximately 80% of these deaths were among children under 5. Children with TB often come from families that are poor, have not received information or education about the disease, and live in communities with limited access to health services. Even if children have access to health services, the health services or facilities often lack the tools and expertise to diagnose TB in children. The most commonly used diagnostic tools are not appropriate for use in children because they require sputum to be collected and children have difficulty producing sputum. Child contacts of adults with TB should be routinely screened

13 Dodd PJ, Yuen CW, Sismanidis C, et al. The global burden of tuberculosis mortality in children: a mathematical modelling study. *Lancet Glob Health*. 2017;5(9):e898–906. doi:10.1016/S2214-109X(17)30289-9

TABLE 3.1. KEY POPULATIONS FOR TB

People who have
INCREASED EXPOSURE
to TB
due to where they
live or work

Prisoners, sex workers, miners, hospital visitors,
health care workers and community health workers

PEOPLE WHO:

- ✦ live in urban slums
- ✦ live in poorly ventilated or dusty conditions
- ✦ are contacts of individuals with TB, including children
- ✦ work in environments that are overcrowded
- ✦ work in hospitals or are health care professionals
- ✦ are in contact with or live with livestock

People who have
LIMITED ACCESS TO QUALITY TB SERVICES

Migrant workers, women in settings with gender disparity, children, refugees or internally displaced people, illegal miners, and undocumented migrants

PEOPLE WHO:

- ✦ are from tribal populations or indigenous peoples
- ✦ are homeless
- ✦ live in hard-to-reach areas
- ✦ live in homes for the elderly
- ✦ have mental or physical disabilities
- ✦ face legal barriers to access care
- ✦ are lesbian, gay, bisexual or transgender

People at
INCREASED RISK
of TB because
of biological or
behavioural factors
that compromise
immune function

PEOPLE WHO:

- ✦ live with HIV
- ✦ have diabetes or silicosis
- ✦ undergo immunosuppressive therapy
- ✦ are undernourished
- ✦ use tobacco
- ✦ suffer from alcohol-use disorders
- ✦ inject drugs

and provided TB preventive therapy or treatment as appropriate; however, there are huge gaps in service delivery, and in 2017, over 75% of children eligible for TB preventive therapy worldwide did not receive it.¹⁴

Children from impoverished communities also face a much higher risk of malnutrition and wasting, both in utero when their mothers are

malnourished and after birth.¹⁵ Infants and children under 5 are the most challenging to diagnose and are the most likely to die from TB. In fact, a greater proportion of TB is missed in children than in adults.

For all of these reasons, the UN Political Declaration on TB has a target of reaching 3.5 million children with TB treatment and 115,000 children with MDR-TB treatment between 2018

14 Roadmap towards ending TB in children and adolescents. Geneva: World Health Organization; 2018. <https://www.who.int/iris/bitstream/handle/10665/274374/9789241514668-eng.pdf>

15 Odone A, Houben RMG, White RG, et al. The effect of diabetes and undernutrition trends on reaching 2035 global tuberculosis targets. *Lancet Diabetes Endocrinol.* 2014;2:754–64. doi:10.1016/S2213-8587(14)70164-0

and 2022. Given the fact that there are currently no global data, or national-level data in many countries, on the numbers of children accessing MDR-TB treatment, surveillance systems to monitor MDR-TB among children must urgently be established.

Childhood TB must be a cross-cutting national health priority and not the sole responsibility of NTPs. It should be addressed in collaboration with child health services, as care for sick children is primarily sought through paediatric services, and as part of overall efforts to scale up maternal and child health services. Health care workers and paediatricians in both public and private sectors should report all children diagnosed with TB to NTPs. In turn, NTPs must report treatment outcomes for these children.

Adolescents (10–19 years) also face particular challenges. Adolescents with TB often present with infectious disease typically seen in adults, which leads to a high risk of transmission in schools and other places where adolescents gather. Fears of stigma and challenges associated with peer-pressure, the risk of HIV, and behavioural risks arising from the use of alcohol and tobacco also present risks for adolescents. Adolescents need friendly health services, relevant psychosocial support, and treatment and care that causes minimal disruption to their education. To better understand how the TB epidemic impacts adolescents ages 10–14 and 15–19, countries should disaggregate TB data into these different age groups.¹⁶

Tackling TB in children and adolescents will require a focus on mothers, too. Women living with HIV – who are more likely to have TB – need assistance and care from the health system in order to reduce the possibility of passing infections to their children.¹⁷ Thus, TB should be integrated at the primary care level in maternal and child health programmes through antenatal and postnatal clinics.

The Roadmap Towards Ending TB in Children and Adolescents (Figure 3.1) sets the goal of reaching zero TB deaths among children worldwide. It describes key actions and an urgent need for enhanced investments in order to ensure that this goal is met.¹⁸

18 Roadmap towards ending TB in children and adolescents. Geneva: World Health Organization; 2018 <https://www.who.int/iris/bitstream/handle/10665/274374/9789241514668-eng.pdf>

BOX 3.2: RESULTS OF STOP TB PARTNERSHIP/ GDF'S NEW TOOL LAUNCHPAD ON PAEDIATRIC DR-TB

In 2018, the Stop TB Partnership's Global Drug Facility (GDF) launched its Paediatric DR-TB Initiative to catalyse the introduction and scale-up of child-friendly formulations of medicines to treat DR-TB. The initiative, partially funded by the Government of Japan, provided technical assistance (from the Sentinel Project on Drug-Resistant TB in Children and implementers such as KNCV and Partners in Health) and procurement support to introduce six child-friendly formulations in 17 early-adopter countries. The initiative expanded in 2019, with additional support from the United States and Japan, to include more than 50 countries and three more formulations that had become available or were newly recommended. Having child-friendly formulations available is one step in increasing the number of children with DR-TB who are treated and reaching the UNHLM targets of treating 115,000 children for DR-TB by 2022.

<http://www.stoptb.org/gdf/pedsDRTBinitiative.asp>

People living with HIV

TB is the most common cause of death in people living with HIV.¹⁹ High rates of TB and HIV coinfection are a major challenge to driving down TB incidence in many countries. According to WHO's most recent data, an estimated 880,000 people worldwide living with HIV became sick with TB in

16 Roadmap towards ending TB in children and adolescents. Geneva: World Health Organization; 2018. [y](#)

17 Gupta, A, Bhosale, R, Kinikar, A, et al. Maternal tuberculosis: a risk factor for mother-to-child transmission of human immunodeficiency virus. *J Infect Dis.* 2011;203:358–63. doi:10.1093/infdis/jiq064

19 Pawlowski A, Jansson M, Skold M, et al. Tuberculosis and HIV co-infection. *PLoS Pathog.* 2012;8:e1002464. doi:10.1371/journal.ppat.1002464

FIGURE 3.1: ROADMAP TOWARDS ENDING TB IN CHILDREN AND ADOLESCENTS



Source: Roadmap towards ending TB in children and adolescents. Geneva: World Health Organization; 2018

2017.²⁰ Among people with TB infection,²¹ people living with HIV are up to 27 times more likely to develop TB disease,²² but the risk is significantly lower for those who access HIV treatment. It is also more difficult to screen people with HIV for TB based on symptoms. Like people with TB, people living with HIV are often subject to stigma and discrimination, which can prevent them from accessing services.

TB and HIV coinfection is particularly acute in Africa, where 84% of all HIV-associated TB deaths occurred in 2017.²³ There is also an urgent need to tackle both diseases in an integrated manner in countries outside of Africa. Data show that Eastern Europe is seeing rising rates of both HIV prevalence and DR-TB.

The UN Political Declaration on TB includes a target for providing more than 6 million people living with HIV with preventive TB therapy by 2022. The Global Plan echoes this target and calls for countries to find at least 90% of all people with TB in the population that require treatment (including those living with HIV) and place them on appropriate therapy (including TB treatment and preventive therapy for people living with HIV).

The UN Political Declaration on HIV²⁴ commits to working towards the target of reducing TB-related deaths among people living with HIV by 75% by 2020, and commits to the 90-(90)-90 targets of the Stop TB Partnership's Global Plan to End TB.

Reaching these targets will require an accelerated

integration of TB and HIV services, and strong leadership and political commitment to carry out the interventions recommended by WHO and UNAIDS for jointly addressing HIV and TB.²⁵

Health workers

The world has an estimated 59 million health workers.²⁶ TB remains a significant occupational risk for health workers in low-income and lower middle-income countries, and in some institutions in high-income countries. This means that health systems need to ensure that health workers are protected from the risk of infection. The risk is particularly high in situations where there is increased exposure to TB and inadequate infection control measures.²⁷ Health workers in primary health care facilities – who are predominantly women – are at risk of acquiring TB from patients that they care for and at increased risk of developing TB.²⁸ Laboratory workers also face a risk of TB infection from exposure to infected specimens.

Efforts to prevent TB acquired in health care settings (hospitals, primary health care facilities and other community-based facilities) should focus on, in order of priority, primary prevention through administrative controls, engineering controls, and respiratory protection for health workers.^{29,30} These efforts should be augmented with secondary prevention measures, including periodic TB screening, and treatment and care for both TB infection and

20 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

21 Latent TB Infection: updated and consolidated guidelines for programmatic management. Geneva: World Health Organization; 2018. <https://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/>

22 TB and HIV [Website]. Geneva: World Health Organization. <https://www.who.int/tb/areas-of-work/tb-hiv/en/>

23 HIV-associated tuberculosis: achievements in 2017. Geneva: World Health Organization; 2017. https://www.who.int/tb/areas-of-work/tb-hiv/tbhiv_factsheet.pdf?ua=1

24 Resolution adopted by the General Assembly on 8 June 2016. A/Res/70/266. Political Declaration on HIV and AIDS: on the fast track to accelerating the fight against HIV and to ending the AIDS epidemic by 2030. New York: United Nations General Assembly; 2016. https://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf

25 WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders. Geneva: World Health Organization; 2012. https://www.who.int/tb/publications/2012/tb_hiv_policy_9789241503006/en/

26 Joseph B, Joseph M. The health of the healthcare workers. *Indian J Occup Environ Med.* 2016;20(2):71–2. doi:10.41003/0019-5278.197518

27 Menzies, D, Joshi, R, Pai, M. Risk of tuberculosis infection and disease associated with work in health care settings. *Int J Tuberc Lung Dis.* 2007;11(6):593–605.

28 Claessens MM, van Schalkwyk C, du Toit E, et al. Tuberculosis in health care workers and infection control measures at primary health care facilities in South Africa. *PLoS One.* 2013;8(10):e76272. doi:10.1371/journal.pone.0076272

29 Including carefully screening patients for TB symptoms and separating people thought to potentially be sick with TB from others within the health facilities, rapid patient diagnosis and treatment, and periodic screening of health workers for TB.

30 Engineering controls reduce the presence of TB bacilli in the air. Common methods are ventilation, opening windows and, in mild environments, placing waiting rooms outside.

active disease in health workers. Workplace protections are essential for protecting health workers in cases where they are diagnosed with TB. Health workers should also be protected from the costs associated with occupational TB exposure. In low-income settings, these measures are often poorly implemented and resourced, if at all.

Mine workers

As an industry, mining is a major driver of TB in countries with weak occupational regulations and lax enforcement. The working environment in mines is extremely favourable for the spread of TB. Risk factors include high prevalence of silicosis (a severe pulmonary disease caused by exposure to silica dust), high temperatures and humidity in mine shafts, crowded working and living conditions, high rates of HIV infection, and tobacco and alcohol use.³¹ Mine workers in southern and central Africa are often migrants, who face unique complications when it comes to accessing health care. Since migrants make up a significant portion of the labour forces of mining companies, it also means that when mine workers are sick with TB and cannot access quality, continual care, TB spreads to the workers' home communities in other parts of the country or across national borders.

The world's 10 largest mining companies alone employed nearly 1 million people in 2019,³² while small-scale and "artisanal" mining involves 40 million people.³³ The mining industry has a responsibility to enact and enforce strong workforce TB policies and practices. National TB strategies must directly address the role of mining activities in the epidemic, as well as the responsibility of mining companies to ensure safe and healthy work

environments.³⁴ South Africa has taken the lead by introducing mandatory TB screening for mine workers and, together with nine other southern African nations, is currently implementing a Global Fund Regional Grant for addressing TB in miners.³⁵ Fifteen southern African countries have pledged to improve treatment and care for current and former mine workers with TB and their families.³⁶ Similar initiatives are needed in other regions, particularly in Asia and South America.

Other methods to tackle TB among mine workers³⁷ should include reducing silica dust, providing better housing, improving cross-border care, tracing contacts, and screening for HIV. Greater investments are needed in particular to regulate and reduce silica dust exposure in both large- and small-scale mining in line with the UN Political Declaration on TB commitment to reduce "silica dust exposures in mining, construction and other dusty workplaces".³⁸

Prisoners and other people whose freedom of movement is restricted

More than 11 million people worldwide are held in penal institutions.³⁹ The conditions in many prisons fuel the spread of TB. In sub-Saharan Africa, for example, some prisons have rates of TB that are up to 1,000 times higher than in the general

31 Stuckler D, Steele S, Lurie M, et al. Dying for gold: the effects of mineral mining on HIV, tuberculosis, silicosis, and occupational diseases in southern Africa. *Int J Health Serv.* 2013;43:639–49. doi:10.2190/HS.43.4.c

32 Leading mining companies worldwide based on number of employees in 2019. Hamburg: Statista; 2019. <https://www.statista.com/statistics/726584/largest-mining-companies-worldwide-by-employment/>

33 State of the artisanal and small-scale mining sector 2019. Washington, DC: World Bank; 2019. <https://delvedatabase.org/uploads/resources/Delve-2019-State-of-the-Artisanal-and-Small-Scale-Mining-Sector.pdf>

34 Stuckler D, Basu S, McKee M, et al. Mining and risk of tuberculosis in sub-Saharan Africa. *Am J Public Health.* 2011;101(3):524–30. doi:10.2105/AJPH.2009.175646

35 Global Fund regional grant to support the southern Africa TB in the Mining Sector Initiative [News story]. Geneva: Stop TB Partnership; 2016. http://www.stoptb.org/news/stories/2016/ns16_003.asp

36 Baleta A. Southern African declaration targets TB in mining sector. *Lancet.* 2012;380(9849):1217–8. doi:10.1016/S0140-6736(12)61698-5

37 RESULTS UK, AIDS Rights Alliance of Southern Africa. Tuberculosis in South Africa's gold mines: a united call to action. London: RESULTS UK; 2013. <http://results.org.uk/sites/default/files/TB%20in%20South%20Africa's%20Mines%20-%20A%20call%20to%20action.pdf>

38 Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmonTBDDeclaration.pdf>

39 Walmsley R. World prison population list, 12th ed. London: Institute for Criminal Policy Research; 2018. https://www.prison-studies.org/sites/default/files/resources/downloads/wppl_12.pdf

population.⁴⁰ In Brazil, a population-based study showed that over half of TB strains circulating in the population could be traced back to prisons.⁴¹ A 2017 systematic review showed that all studies suggested high rates of MDR-TB in prison populations in post-Soviet states.⁴² As institutional settings, prisons can also contribute to the development and spread of DR-TB, as incoming and outgoing prisoners are unlikely to complete a full treatment course without targeted support.

Addressing TB in prisons will require significant collaboration among the health and judicial sectors and the research community to map the scale of drug resistance within prisons and devise innovative ways to prevent transmission. Linking the health care provided inside and outside prisons is vital to ensuring continuous TB care.

Special approaches to TB are also required for groups living in refugee camps and relocation camps. Approaches to providing TB in these situations should be based on international best practices and be responsive to local conditions.⁴³

Migrants

Migrants are an increasing share of the world's population – 258 million in 2017 up from 220 million in 2010.⁴⁴ Certain migrants are particularly vulnerable to TB.⁴⁵ These include populations that often have poor access to health services, pos-

sibly because they are living in an area illegally, because of differences in language or ethnicity, and/or because of a lack of awareness of entitlement to health services. Undocumented migrants face particular difficulties in accessing care. Even when migrants can access treatment, the need to move for employment or the threat of forced displacement often results in disrupted TB treatment, increasing the likelihood that drug resistance will emerge.

As both a public health and a human rights imperative, policies should allow people to access TB diagnosis and treatment regardless of immigration status.⁴⁶ Similarly, immigration and labour policies should ensure that a person is not excluded from consideration for recruitment or retention based on his or her TB status.

Health care workers must be sensitized to migrants' needs, especially the potential for TB and HIV coinfection and DR-TB. Continuity of care is particularly important in migrant populations, and the development of cross-border referral systems with contact-tracing and information sharing will be important for harmonizing treatment protocols across borders along migration corridors. This will require not only collaboration between health actors, but also collaboration between government ministries on migration policy.

People who use drugs and/or misuse alcohol

Drug use has been linked to a higher incidence of both latent TB infection and active TB disease.⁴⁷ The increased risk of infection is due in part to the physiological effects of drug use, especially opiates, which lead to compromised immunity. People who use drugs are also at increased risk of delayed treatment-seeking, and increased risk

40 Biadglegne F, Rodloff AC, Sack U. Review of the prevalence and drug resistance of tuberculosis in prisons: a hidden epidemic. *Epidemiol Infect.* 2015;143:887–900. doi:10.1017/S095026881400288X

41 Sacchi FP, Praca RM, Tatará MB, et al. Prisons as reservoir for community transmission of tuberculosis, Brazil. *Emerg Infect Dis.* 2015;21:452–5. doi:10.3201/eid2103.140896

42 Droznin M, Johnson A, Johnson A. Multidrug resistant tuberculosis in prisons located in former Soviet countries: a systematic review. *PLoS One.* 2017;12(3):e0174373. doi:10.1371/journal.pone.0174373

43 Tuberculosis care and control in refugee and displaced populations. Geneva: World Health Organization. 2007. https://www.who.int/iris/bitstream/handle/10665/43661/9789241595421_eng.pdf;jsessionid=D7CAA855D4364F425CF5E5DE0FB19E8E?sequence=1

44 International migration report 2017: highlights. New York: United Nations, Department of Economic and Social Affairs, Population Division; 2017. https://www.un.org/en/development/desa/population/migration/publications/migrationreport/docs/MigrationReport2017_Highlights.pdf

45 World Health Organization, International Organization for Migration. Tuberculosis prevention and care for migrants. Grand-Saconnex: International Organization for Migration; 2014. <https://tbandmigration.iom.int/publication/tuberculosis-prevention-and-care-migrants>

46 Plan to Stop TB in 18 high-priority countries in the WHO European Region, 2007–2015. Copenhagen: World Health Organization Regional Office for Europe; 2007. <http://www.euro.who.int/en/publications/abstracts/plan-to-stop-tb-in-18-high-priority-countries-in-the-who-european-region,-20072015>

47 Deiss RG, Rodwell TC, Garfein RS. Tuberculosis and illicit drug use: review and update. *Clin Infect Dis.* 2009;48:72–82. doi:10.1086/594126

of sickness and mortality. Opiates may suppress tell-tale TB symptoms such as persistent cough. People who use drugs are at risk for a variety of environmental and behavioural factors that tend to coexist with drug use, such as homelessness, tobacco and alcohol use, imprisonment, and risk of HIV and hepatitis C from infected needles.⁴⁸

The effects of drug use and alcohol misuse can also mean that people do not access health services at critical junctures, such as for TB diagnosis and treatment immediately after HIV diagnosis. Even when people who use drugs or misuse alcohol do have access to TB care, they may face challenges in completing a complicated or lengthy TB drug regimen. People who use drugs or misuse alcohol are also at increased risk of facing stigma and discrimination from health care workers.

Integrating TB treatment with services for people who use drugs or misuse alcohol can help reach the most vulnerable, so long as TB treatment continues after rehabilitation. Psychosocial support and day hospitals could greatly increase the rate of treatment success.⁴⁹ Because close contacts are at higher risk, TB infection can often spread among groups of people who use drugs together. Therefore, interventions targeting these populations must include TB preventive therapy. A harm reduction approach is critical for providing rights-based TB care for people who use drugs, including the provision of medically assisted therapy for people with opioid-use disorders.

The elderly

The elderly are the largest group of people living with TB infection, particularly in developed countries. Those 65 years and older are more vulnerable to TB – and more at risk of TB infection converting to TB disease – partly because immunity diminishes with age. Certain medicines taken

for common noncommunicable diseases affecting the elderly heighten the risk of TB infection converting to TB disease. Studies have found a higher frequency of underlying illnesses, more adverse reactions to medicines, and higher mortality in elderly TB patients.⁵⁰

Clinical features may be atypical, and older adults with pulmonary TB are more likely to have non-specific symptoms.⁵¹ Special attention is also needed because treatment outcomes are usually poor in older people with TB. Diagnosis is difficult and TB is frequently overlooked, often detected only at autopsy.⁵²

People living with diabetes

Experts estimate 15.3% prevalence of diabetes among people with active TB worldwide. WHO found diabetes to be an underlying factor for 790,000 people who developed TB in 2017.⁵³ By weakening the immune system, diabetes raises the risk of developing TB by two to three times.⁵⁴ The association between these diseases is of great concern, since diabetes rates are rising sharply in many low- and middle-income countries (LMICs) with a high TB burden.

There are a number of ways to jointly tackle TB and diabetes. In January 2019, the International Union Against Tuberculosis and Lung Disease (The Union) published a new technical guide for the co-management of diabetes mellitus/TB, developed in partnership with the World Diabetes

48 Grenfell P, Baptista Leite R, et al. Tuberculosis, injecting drug use and integrated HIV-TB care: a review of the literature. *Drug Alcohol Depend.* 2013;129:180–209. doi:10.1016/j.drugalcdep.2012.11.013

49 Figueroa-Munoz JI, Ramon-Pardo P. Tuberculosis control in vulnerable groups. *Bull World Health Organ.* 2008;86:733–5. <https://www.who.int/bulletin/volumes/86/9/06-038737/en/>

50 Rajagopalan S. Tuberculosis and aging: a global health problem. *Clin Infect Dis.* 2001;33(7):1034–9.

51 Lee JH, Han DH, Song JW, et al. Diagnostic and therapeutic problems of pulmonary tuberculosis in elderly patients. *J Korean Med Sci.* 2005;20(5):784–9.

52 Rajagopalan S, Yoshikawa TT. Tuberculosis in the elderly. *Zeitschrift für Gerontologie und Geriatrie.* 2000;33(5):374–80. doi:10.1007/s003910070

53 Noubiap JJ, Nansseu JR, Nyaga UF, et al. Global prevalence of diabetes in active tuberculosis: a systematic review and meta-analysis of data from 2.3 million patients with tuberculosis. *Lancet Glob Health.* 2019;7(4):PE448–E460. doi:10.1016/S2214-109X(18)30487-X

54 Marais BJ, Lonnroth K, Lawn SD, et al. Tuberculosis comorbidity with communicable and non-communicable diseases: integrating health services and control efforts. *Lancet Infect Dis.* 2013;13:436–48. doi:10.1016/S1473-3099(13)70015-X

Foundation.⁵⁵ This guide provides essential information for frontline health professionals for the management and care of people with both diabetes mellitus and TB.

People diagnosed with diabetes should be considered for systematic screening in high TB burden settings.⁵⁶ People with TB diagnosed with diabetes could be managed under the TB programme in order to ensure coherent disease management. They could then be referred to diabetes programmes after completing their TB treatment.⁵⁷

Community health workers whose role is to reach out to TB patients can be trained in blood glucose testing to ensure dual care. Information on TB should also be provided to diabetes treatment centres so that health care workers are able to identify when to refer people for TB investigation. Procurement and delivery systems used for TB medicines could be used for insulin, which can be prohibitively expensive; supply of insulin is often unreliable in LMICs.

There are opportunities for the prevention of both diseases, since levels of hyperglycaemia associated with pre-diabetes appear to correlate with a higher risk for TB.⁵⁸ Efforts to integrate diabetes and TB care should not remain separate from those to address HIV and TB jointly. All the risk factors for TB should be approached holistically in order to maximize resources.

People who smoke tobacco and/or are exposed to air pollution

Tobacco smoking (and passive smoking) and indoor air pollution from burning biomass fuels in poorly ventilated kitchens and homes are major risk factors for TB.⁵⁹ An estimated 830,000 of people diagnosed with TB worldwide in 2017 were linked to tobacco smoking.⁶⁰ This is especially concerning, since smoking and burning fuels indoors are highly prevalent practices in countries where TB is common. These practices increase the risks of becoming infected with TB, developing active TB disease, experiencing poor treatment outcomes, and relapsing.⁶¹ Reducing the number of people who smoke and reducing indoor air pollution are key interventions for ending TB. Because tobacco smoking is such a high risk factor for TB, smoking cessation support could form part of TB-related counselling and care on initial diagnosis.

It is also plausible that exposure to outdoor or ambient air pollution can suppress immunity and make people more vulnerable to TB. At this point, however, data are limited on the potential relationship between ambient air pollution and TB, with the studies that do exist showing mixed results. Given that ambient air pollution is the leading environmental risk factor for disease globally, there is a need for further research on its potential effects on TB.⁶²

People affected by malnutrition

In 2017, an estimated 1.9 million people developed TB where malnutrition was the attributed under-

55 Yan L, Harries AD, Kumar AMV, et al. Management of diabetes mellitus-tuberculosis: a guide to the essential practice. Paris: International Union Against Tuberculosis and Lung Disease; 2019. <https://www.theunion.org/what-we-do/publications/technical/management-of-diabetes-mellitus-tuberculosis-a-guide-to-the-essential-practice>

56 Collaborative framework for care and control of diabetes. Geneva: World Health Organization; 2011. <https://www.who.int/tb/publications/tb-diabetes-framework/en/>

57 Sullivan T, Ben Amor Y. The co-management of tuberculosis and diabetes: challenges and opportunities in the developing world. *PLoS Med.* 2012;9:e1001269. doi:10.1371/journal.pmed.1001269

58 Viswanathan V, Kumpatla S, Aravindalochanan V, et al. Prevalence of diabetes and pre-diabetes and associated risk factors among tuberculosis patients in India. *PLoS One.* 2012;7:e41367. doi:10.1371/journal.pone.0041367

59 Lin HH, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. *PLoS Med.* 2007;4:e20.

60 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

61 Improving tuberculosis case detection: a compendium of TB REACH case studies, lessons learnt and a monitoring and evaluation framework. Geneva: Stop TB Partnership; 2014. http://www.stoptb.org/assets/documents/resources/publications/technical/TB_Case_Studies.pdf

62 Popovic I, Magalhaes R, Ge E, et al. A systematic literature review and critical appraisal of epidemiological studies on outdoor air pollution and tuberculosis outcomes. *Environmental Res.* 2019;170:33–45. doi:10.1016/j.envres.2018.12.011

lying cause.⁶³ Malnutrition and TB are strongly linked, with undernutrition reducing immune defences against TB and encouraging the transition from latent infection to active disease. TB can also impair the body's ability to absorb nutrients and micronutrients, which in turn leads to malnutrition and wasting.

In March 2018, India's Prime Minister Narendra Modi announced that his country would allocate US\$ 100 million through 2025 to ensure adequate nutritional support for people living with TB through direct cash transfers.⁶⁴ This is a first step that should be evaluated and built upon in India and in other countries. Many of the people who are already at high risk of TB infection, such as impoverished people living in crowded, unsanitary housing, are also likely to be undernourished. The association between undernutrition and TB is so strong that people who are overweight have even lower incidence of TB than people of a healthy weight (although obesity increases risk factors for diabetes and other metabolic diseases).

Ensuring food security for the general population is an important component of preventing TB. There is also some evidence that tailored nutritional support during TB care can help patients adhere to treatment, especially those with DR-TB.⁶⁵ WHO has provided relevant guidance.⁶⁶ To make nutritional support a reality, interdepartmental efforts from other ministries, including those responsible for social welfare, finance, food and agriculture, will be vital. These efforts should be monitored and reviewed as part of a country's implementation of the MAF-TB.

People affected by zoonotic TB

Zoonotic TB in humans, caused by *Mycobacterium bovis* (the bacterium that causes bovine TB), is mostly acquired from domestic animals and their products. Consumers of unpasteurized milk or untreated animal products from infected animals, people living in rural communities in which bovine TB is endemic, cattle herders, dairy workers, and workers who come in contact with infected animals or animal products are all at a higher risk of contracting zoonotic TB.

An estimated 147,000 people developed zoonotic TB in 2016, and 12,500 died due to the disease.⁶⁷ But, this estimate is very uncertain; the true scale of how many people are affected by zoonotic TB is unknown due to the lack of adequate diagnostic tests for *M. bovis*; furthermore, its measurement is complicated by a lack of routine surveillance. This is especially concerning in developing regions in which bovine TB is endemic and sociocultural practices increase the risk of transmission of *M. bovis* to humans.

As articulated in WHO's Roadmap for Zoonotic Tuberculosis,⁶⁸ efforts to prevent and care for people with zoonotic TB must be cross-sectoral and multidisciplinary, following the One Health approach. The One Health approach addresses both human health and veterinary sectors in responding to disease, given that animals and humans share the same environment. In the context of TB, it requires the development of diagnostic tools, strengthening of surveillance systems and data quality, and assessment of the economic impact of *M. bovis*.^{69,70}

63 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

64 We in India are working towards eliminating TB by 2025: PM Modi. 13 March 2018. <https://www.narendramodi.in/text-of-pm-s-address-at-the-inaugural-session-of-end-tb-summit-539297>

65 Sinclair D, Abba K, Grobler L, Sudarsanam TD. Nutritional supplements for people being treated for active tuberculosis. *Cochrane Database Syst Rev.* 2011;9(11):CD006086. doi:10.1002/14651858.CD006086

66 Nutritional care and support for patients with tuberculosis: guideline. Geneva: World

Health Organization; 2013. https://www.who.int/tb/publications/nutcare_support_patients_with_tb/en/

67 Zoonotic tuberculosis. Geneva: World Health Organization; 2017. <https://www.who.int/tb/zoonoticTB.pdf>

68 Roadmap for zoonotic tuberculosis. Geneva: World Health Organization; 2017. https://www.who.int/tb/publications/2017/zoonotic_TB/en/

69 Muller B, Dürr S, Alonso S., et al. Zoonotic *Mycobacterium bovis*-induced tuberculosis in humans. *Emerging Infect Dis.* 2013;19:899–908. doi:10.3201/eid1906.120543

70 Cosivi O, Grange JM, Daborn CJ, et al. Zoonotic tuberculosis due to *Mycobacterium bovis* in developing countries. *Emerging Infect Dis.* 1998;4:59–70. doi:10.3201/eid401.980108



4. KEY COLLABORATING PARTNERS: CIVIL SOCIETY, COMMUNITIES, AND THE PRIVATE SECTOR



SUMMARY

To find and treat all people with TB and achieve the End TB Strategy milestones, countries must engage with civil society, community organizations and the private sector as partners at all stages of planning and implementing the response to TB.

Civil society and community-based organizations must play a key role in the planning and provision of TB care by increasing awareness; contributing to active case finding; improving access to care; encouraging and supporting people with TB during the course of treatment; providing psychosocial support and reducing stigma; monitoring programmes; facilitating community engagement in R&D; and engaging in advocacy. The private sector also has an

important role to play in providing, developing and partnering to deliver quality and affordable TB care, new tools, resources and expertise. Investments are required to strengthen health and community systems and public–private partnerships. A change in mindset, along with an enabling environment, is needed in order to meaningfully engage with communities and unlock the full potential of the private sector.

PRIORITY ACTIONS

NTPs:

- ⊕ Strengthen community health systems so that quality-assured TB care and support can be accessed locally.
- ⊕ Engage civil society and TB affected communities from the start in designing and planning TB programmes and interventions, involving them as active partners in the implementation, monitoring and review of TB services.
- ⊕ Partner with the private sector and labour unions towards scaling up access to TB care, establishing workplace TB policies and initiatives, and improving community outreach.
- ⊕ Invest in public–private partnership models

to ensure that people accessing care for TB in the private sector receive good quality services and are notified.

Donors and impact investors:

- ⊕ Increase funding for civil society and community organizations as part of efforts to end TB.
- ⊕ Provide funding for global coordination of advocacy in partnership with TB affected communities, with the aim of ensuring accountability for fulfilling the UNHLM on TB commitments.

Private industry and businesses:

- ✦ Adopt non-discriminatory recruitment and retention policies, promote infection-free and safe workplaces, and provide staff and their families with good-quality and affordable TB diagnostic, treatment and notification services.
- ✦ Partner with NTPs, TB organizations and community organizations in corporate social responsibility (CSR) initiatives.

Civil society and communities as key partners in the response to TB

The UNHLM on TB helped shift the focus of the global approach to TB away from “controlling” the epidemic towards *ending* the epidemic.

Historically, “controlling” TB has entailed a top-down approach, whereas ending TB is radically different. Ending TB embraces an approach that empowers TB survivors, affected communities and broader civil society as partners, because they are ideally positioned to help identify and overcome the social, political, cultural, legal, gender and economic barriers to accessing TB services, care and support. They are also in the unique position of being experts on the lived experience of TB. They know the side effects, the stigma and discrimination, the isolation, the economic, physical and psychological burden, and, for many, the lifelong legacy of the disease.

Civil society and community-based organizations, including patient-based organizations, NGOs, faith-based organizations (FBOs), youth groups and community volunteers, are also fundamental partners in the drive towards universal access to TB care and services. Community health workers and TB survivor peer-support networks provide vital support to health systems in many resource-poor countries, as they can help reach communities that are hardest to reach. Furthermore, many serve as a voice for the most vulnerable, advocating for the needs of TB patients and advising on interventions that are feasible in their specific setting. Without their

active involvement in the planning, implementation and monitoring of TB programmes, the result is often top-down disease programmes that may be aligned with global and national strategies, but nevertheless remain inefficient because they lack an understanding of the local context and community-level dynamics; or they fail to uphold the rights of the people they are meant to serve because the affected communities are not engaged as partners.

These principles – that TB affected communities are not just recipients of services but active agents in the TB response, that TB patients are people first and patients second, and that the community remains even as governments, policies, guidelines and donor priorities may shift – has seen the increased emergence of TB survivors and TB affected communities claiming their place as equal partners in all aspects of the TB response.

Ensuring meaningful community engagement and coordination

As core partners in international and national TB activities, TB affected communities should be brought on board at the start of the planning process before new TB interventions or initiatives are designed. TB programmes should include Civil Society Organizations (CSOs) in core activities, inviting them to attend key meetings, such as those for strategy-setting and programme review, and to sit on scientific boards. The ultimate aim should be well designed TB services that are owned and sustained by communities, working in collaboration with the government and other stakeholders.

The Global Plan recommends a variety of ways in which communities should be more deeply engaged in the various aspects of the TB response. Communities should be involved in the response to end TB through both community-based efforts and community-led efforts. Community-based efforts are those that are carried out locally in settings outside of the formal health care system. Community-led efforts are those that are managed, governed or carried out by members of the community. Both community-based and community-led efforts should link to the formal health system.¹

A key challenge in engaging communities and civil society has historically been the relatively few individuals and networks committed to ending TB, and a lack of coordination with and within civil society. The result has been the voices of civil society and communities not being heard and thus not having an impact on national and global planning. This is changing, however. Networks of TB survivors, such as TBpeople, TB Proof and We Are TB, have grown organically in recent years, adding to community coalitions such as the Global Coalition of TB Activists (GCTA), the Global TB Community Advisory Board (TB CAB) and the TB Europe Coalition (TBEC). There is a need to further enroll and build the capacity of TB survivors to engage in advocacy and other elements of the TB response through participation in organized networks, forums, and national,

regional and global groups; direct resource contributions to survivor-led organizations and coalitions; partnerships with stakeholder organizations; training; and other forms of support and collaboration.

The TB community could further build its capacity by working even more closely with the HIV community. High rates of TB and HIV coinfection necessitate integrated approaches in key regions, especially in Africa. This integration is crucial down to the community level. The TB community should also engage more with other advocacy constituencies that offer the potential for collaboration. This includes FBOs, legal clinics, human rights organizations, anti-poverty and microcredit networks, and women and youth networks. These endeavours will require significant increases in funding from advocacy donors, alongside increased action on the part of governments to include the communities affected by TB within decision-making bodies and processes.

In all cases, NTPs should periodically evaluate progress in engaging with CSOs and affected communities and assess the impact it has on the fight against TB. This will help programmes to direct resources where they are shown to be most effective. WHO tracks and reports on two key indicators related to community involvement in providing TB care and services: the contribution of community referrals to TB case notifications and the treatment success rate for people who benefited from any form of community treatment support. For 2018, however, only 56 countries reported progress on the

¹ Technical brief: community systems strengthening. Geneva: Global Fund to Fight AIDS, Tuberculosis and Malaria; 2019. https://www.theglobalfund.org/media/4790/core_communitysystems_technicalbrief_en.pdf

first indicator, together reporting that 27% of TB notifications were attributed to community referrals. Only 38 countries reported data on the second indicator, showing that the treatment success rate for people receiving community support was 87%. Community contributions to TB notifications and treatment success should be routinely monitored and reported nationally.

Community systems strengthening

Community systems strengthening (CSS) is a useful approach to planning engagement with civil society and affected communities, particularly to help TB programmes fulfil their commitments to human rights and gender equity.² CSS refers to supporting the development of informed, capable, coordinated and sustainable structures, mechanisms, processes and actors through which community members, organizations and groups interact, coordinate and deliver their responses to the challenges and needs of their communities.³ By considering communities and their role as part of the larger health system, CSS enables an analysis of the different facets of that system, how they are interconnected, and what aspects need to be strengthened. With the necessary skills and resources, communities can help health systems to determine the needs of people with TB, advocate for better services, and hold donors and governments accountable.

While civil society is broadly active in global and national decision-making forums, civil society's participation at subnational and local levels varies more widely. To build effective community systems and to meaningfully engage TB survivors and TB key affected populations at all levels, a number of elements are required:

MOBILIZATION: TB survivors must be mobilized, engaged and supported for coordination.

Efforts are required to bring those who have survived this experience together and to ensure that this mobilization is sustainable. Leveraging the support of established CSOs is critical in the process of building or strengthening networks.

CAPACITY-BUILDING: Community organizations hold critical knowledge about the health needs of and what interventions are feasible for their communities. While TB survivors, civil society and community representatives often have abundant grassroots expertise, they might need capacity-building and support, for example, to meaningfully participate at high-level meetings; engage with international organizations and governments; conduct outreach to the news media; or engage in processes through which policies are shaped. Performing these function requires support for enhancing scientific literacy, developing capacity to counsel and support peers, and developing the advocacy skills needed to hold governments accountable for acting on, reporting on and reviewing their commitments.

ENABLING ENVIRONMENT: TB survivors must have a seat at the decision-making table. While telling the story of their lived experience of TB can be compelling, it is their role as catalysts of programmes and policies that must be further advanced. For this to be effective, representatives of TB affected communities must develop a constituency that they consult and report back to. They must also be given the time and resources to prepare and strategize on key decision points, ensuring that the voice of TB communities resonates through every TB discussion at every level.

FINANCIAL INVESTMENT: Community systems for meaningful engagement must receive the investment they need to become sustainable. They are not a luxury or a side note. As highlighted in the UN Political Declaration on TB, TB affected communities and civil society are a critical element of the TB response that is beginning to emerge. Their participation can be a game changer for national programmes and millions of people impacted by TB every year.

2 Technical brief: community systems strengthening. Geneva: Global Fund to Fight AIDS, Tuberculosis and Malaria; 2019. https://www.theglobalfund.org/media/4790/core_communitysystems_technicalbrief_en.pdf

3 Ibid

To hold national governments accountable for fulfilling their need to “develop integrated, people-centred, community-based and gender-responsive health services based on human rights”, advocacy capacity-building should include training on the use of human rights impact assessment tools. Such tools can enable communities to anticipate and respond to the potential human

rights impacts of government, trade, and national and corporate policies related to TB.

The Global Fund has produced a technical brief on CSS that goes into further detail about its benefits and approaches with respect to TB.⁴

4 Ibid

BOX 4.1:

CIVIL SOCIETY NETWORKS AT GLOBAL AND REGIONAL LEVELS

“TB survivor” refers to any person with TB or who has had TB. “TB affected community” or “community of people affected by TB” refers to any person with TB or who has had TB, as well as their family members, social contacts and caregivers. In addition, “TB affected community” refers to TB key populations, including children, health care workers, indigenous peoples, people living with HIV, people who use drugs, prisoners, miners, mobile and migrant populations, and the urban and rural poor. Networks of people affected by TB, TB survivors and civil society now exist at the global, regional, national and subnational levels, but further efforts are needed to strengthen these networks and ensure their active role in planning, implementing and monitoring the TB response, as well as in demand creation for the best quality of TB services for all.

THE MOBILIZATION OF TB AFFECTED COMMUNITIES HAS MATERIALIZED IN DIFFERENT WAYS.

At the national level, efforts are being led by organizations and networks, for example:

- Club des Amis Damien in the Democratic Republic of the Congo
- TB Proof in South Africa
- We Are TB in the United States

At the regional level, there are networks of TB affected communities and civil societies, for example:

- Asia-Pacific Coalition of TB Activists (ACT Asia-Pacific!)
- Africa Coalition on Tuberculosis (ACT!) in Anglophone Africa
- Americas TB Coalition in Latin America and the Caribbean
- Dynamics of Francophone Africa’s Response to TB (DRAF TB) in Francophone Africa
- TB Europe Coalition (TBEC) in Europe and Central Asia

Globally there are two networks:

- Global Coalition of TB Activists (GCTA), which has been leading advocacy efforts focusing on the stigma faced by people affected by TB
- TBpeople, which led the development of the Declaration of the Rights of People Affected by Tuberculosis in 2018–19.

In addition to patient networks, there is the Global TB Community Advisory Board (TB CAB). This is a group of research-literate community activists who advise product developers and institutions conducting clinical trials for new TB medicines, regimens, diagnostics and vaccines, providing input on study design, early access, regulatory approval, post-marketing and implementation strategies.

Nationally and globally allied, coordinated networks were crucial in securing the key commitments of the UN Political Declaration on TB, and remain essential partners in the effort to ensure national and global accountability for action to end TB.

With community-based networks, groups and coalitions existing in many regions, there is need now for continued coordination at the global level in order to promote knowledge-sharing and joint activities, and elevate experiences from the grassroots level to inform global policymaking and advocacy, with a focus on ensuring government accountability for fulfilling the UNHLM on TB commitments. Donor support for such work is critical.

Advancing community-based and community-led efforts

COMMUNITY-BASED CARE AND SUPPORT:

The UN Political Declaration on TB affirmed that people with TB need integrated care and support, including from the community. This includes psychosocial, nutritional and socio-economic support for successful treatment, and the reduction of stigma and discrimination. In response, UN Member States committed to *“developing community-based health services through approaches that protect and promote equity, ethics, gender equality and human rights in addressing tuberculosis by focusing on prevention, diagnosis, treatment and care, including socioeconomic and psychosocial support, based on individual needs, that reduce stigma, and integrated care for related health conditions, such as HIV and AIDS, undernutrition, mental health, non-communicable diseases including diabetes and chronic lung disease, and tobacco use, harmful use of alcohol and other substance abuse, including drug injection, with access to existing and new tools.”*⁵

In fulfilling this commitment, it is important to improve the accessibility of community-based TB care and services for both active TB and TB infection. People with TB also often have needs that must be met over the course of their lifetimes, even after the completion of successful TB treatment. This includes care for TB comorbidities (e.g., HIV, diabetes), for underlying factors in the development of TB (e.g., exposure to silica dust, malnutrition, tobacco use), for other conditions that are risk factors for TB (e.g., treatment for Crohn’s disease or rheumatoid arthritis), and for impaired lung function that can persist far beyond the completion of TB treatment.

ENGAGING COMMUNITY HEALTH WORKERS TO RAISE AWARENESS AND REACH THE UNREACHED:

Community health workers play an important role in reaching people who are missed by health systems, helping to fulfil governments’ commitments to “leave no person behind.” Through community outreach and educational programmes, community health workers encourage people who have TB symptoms to contact a health care worker or visit a health facility. When people are not able to travel, community workers can also help to transport sputum samples to the nearest health facility for diagnosis. Community health workers can also aid in the conduct of TB contact investigations, identifying household members who need to be screened and who are eligible for TB prevention, diagnosis and care. In fact, TB diagnosis is often delayed as people who are sick with TB shop around for diagnosis and treatment, leading to unnecessary out-of-pocket expenses. This out-of-pocket spending before receiving a reliable diagnosis is a major factor contributing to the catastrophic costs associated with TB. Encouraging people with TB symptoms to seek appropriate medical care relies on the trust and peer-to-peer relationship that a community representative can bring (Box 4.2).⁶

The participation of existing community health workers in such active case-finding initiatives has improved case detection and treatment outcomes.⁷ However, their role has yet to be maximized. One way to work with community health workers to actively identify persons in need of TB screening and care is to integrate TB community outreach with HIV, maternal and child health or other outreach programmes.

Gender is an important dimension of the community-based response to TB, and community health workers who provide services are often best prepared to conduct outreach to particular

5 Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmonTBDeclaration.pdf>

6 Yassin M A, Datiko DG, Tulloch O, et al. Innovative community-based approaches doubled tuberculosis case notification and improve treatment outcome in southern Ethiopia. PLoS One. 2013;8(5):e63174. doi:10.1371/journal.pone.0063174

7 Ibid

communities or key populations when they can respond to the gender-based needs of people receiving care and services, for example, sex workers, adolescent boys, adolescent girls, and mine workers.

Work performed by community health workers should be integrated into the service delivery of health facilities, both at the local level and the level of policy and strategy. Social media and social audit mechanisms should be more widely used to enable patients, CSOs and community members to contribute to improving services and monitoring progress. For example, WHO's ENGAGE-TB Approach, developed in 2012, offers guidance to NTPs on how to effectively work with NGOs and CSOs that are not already working on TB.⁸

COMMUNITY-BASED MONITORING (CBM):

Communities must be empowered to be watchdogs in the TB response, making sure all other stakeholders are realizing their commitments as the rights of people affected by TB are being promoted and protected. To this end, community-based monitoring (CBM) can help to bridge the gap between the health system and the community.

CBM in TB is an intervention, driven by local information and community needs, that aims to increase accountability in the TB response so that essential, quality and timely TB care and support services are available, accessible and acceptable to all, especially to those who are vulnerable, underserved or at risk of TB. By engaging people with TB and TB affected communities to provide feedback and report barriers that inhibit access to services, CBM can improve the responsiveness and equity of TB care and support services, inform the design of TB programmatic interventions and policy decisions, and evaluate the TB response. CBM can help to reach the unreached by generating

information that can be used to close the gap in the number of people lacking access to TB care. It also facilitates public participation and strengthens local decision-making on issues that are important to both the community and the TB response, including complex social, economic and human rights issues that result in millions of people with TB being missed by health systems each year.

Since 2017, the Stop TB Partnership, with support from USAID and the Global Fund, has developed a community-monitoring framework and digital solution platform called OneImpact to facilitate CBM of the TB response. OneImpact is currently supporting eight countries to implement the intervention.⁹

ENGAGING TRADITIONAL HEALERS:

Community-based systems can play a transformative role by linking informal providers with formal health systems. A major challenge in TB care is that many people with symptoms in low-resource, high-burden countries first seek care from traditional healers or pharmacists, rather than from public health clinics or hospitals. TB programmes need to more actively reach out to these traditional healers and pharmacists and work with them to provide referrals to health centres.

PROVIDING PSYCHOSOCIAL SUPPORT, SOCIAL PROTECTION AND PALLIATIVE CARE:

Completing TB treatment can be challenging. The treatment is lengthy and inevitably has side effects, making counselling and support a critical part of comprehensive TB care. Community members, who may have had TB themselves, can help to ensure that TB patients receive the psychosocial support they need to successfully complete TB treatment.

It can be expensive to travel to clinics to access treatment, especially for people living in remote areas. In addition, having to travel means that people with TB might lose income in the process

8 ENGAGE-TB Approach: Operational guidance: integrating community-based tuberculosis activities into the work of nongovernmental and other civil society organizations. Geneva: World Health Organization; 2012. https://www.who.int/tb/publications/2012/engage_tb_policy/en/

9 OneImpact [Website]. Geneva: Stop TB Partnership; 2019. <https://stoptbpartnershiponeimpact.org>

BOX 4.2:

ETHIOPIA'S HEALTH EXTENSION WORKERS

Since 2003, the Government of Ethiopia has been implementing a health extension worker (HEW) programme, which has helped to achieve significant improvements across a range of health priorities.¹ Studies have shown that HEWs have helped to substantially improve access to TB care and services, as well as treatment success. In Ethiopia's rural Sidama Zone, for example, HEWs were trained to work in their communities to identify people with TB symptoms, collect sputum samples, and prepare slides in the field for testing before being transported to the laboratory for staining and reading. More than 1,000

HEWs collected sputum samples from more than 200,000 people with TB symptoms and identified more than 17,500 people with smear-positive TB. This intervention doubled the number of people put on treatment in a zone of more than 3 million people. In addition, the HEWs provided treatment support, with treatment success rates improving from 76% to 95% between 2010 and 2015.² Ethiopia has since achieved a national TB treatment success rate of 96% for new cases of TB, as of 2017, which is significantly higher than the global average of 85%.³

1 Assefa Y, Gelaw YA, Hill PS, et al. Community health extension program of Ethiopia, 2003–2018: successes and challenges toward universal coverage for primary healthcare services. *Global Health*. 2019;15(1):24. doi:10.1186/s12992-019-0470-1

2 Datiko D, Yassin M, Theobald S, et al. Health extension workers improve tuberculosis case finding and treatment outcome in Ethiopia: a large-scale implementation study. *BMJ Glob Health*. 2017;2(4): e000390.

3 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

of seeking treatment. Community members can help to ensure that people with TB are linked with social protection schemes, such as food vouchers or conditional cash vouchers for treatment support.

FBOs of all religions are also a vital resource for community-based care. These groups, along with other community-based workers, can help to provide palliative care to people with TB at home – a service that is beyond the capacity of most health systems.

ROLE OF COMMUNITIES IN ERADICATING STIGMA:

There is still considerable stigma surrounding TB. Eradicating this stigma is a crucial component of encouraging people to seek care and supporting them throughout the course of TB treatment. For many people affected by TB, the greatest challenge they face is stigma. Stigma can come from family members, the surrounding community, coworkers or health care workers. It can even include self-stigma, wherein people with TB internalize feelings of shame or guilt for having TB.

In the UN Political Declaration on TB, national governments committed to “*promote and sup-*

port an end to stigma and all forms of discrimination, including by removing discriminatory laws, policies and programmes against people with tuberculosis, and through the protection and promotion of human rights and dignity, as well as policies and practices which improve outreach, education and care”.¹⁰ In response, NTPs and partners should invest in targeted interventions for eradicating stigma, designed and implemented in coordination with TB survivors, affected communities, and cultural leaders and influencers. Since stigma is rooted in social and cultural perceptions, including gender, education campaigns in communities will be important, in addition to laws and policies, for helping to break down misconceptions and biases that lead to stigma and discrimination. The more that communities are meaningfully engaged and the more that TB survivors are empowered to advocate, engage in TB decision-making processes and assume leadership roles in TB efforts, the more stigma will diminish.

10 Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmonTBDDeclaration.pdf>

Where discriminatory laws remain, advocacy for law reform will be crucial. In all cases, social media and other digital platforms can play an important role in eliminating stigma, and identifying and overcoming other social barriers to accessing TB services and care.

ENGAGING COMMUNITIES IN RESEARCH:

Engaging TB affected communities in all aspects of research – from early-stage research to the design of clinical trials and the delivery and large-scale uptake of successful innovations – will help to make communities equal partners in the fight against TB. All researchers and sponsors should develop community engagement plans and take steps to include affected communities, patient groups and civil society in TB R&D. In fact, community members themselves are organized and ready to advise research institutions on how to optimize their engagement with communities for research purposes (Box 4.3).¹¹ Chapter 6 of the Global Plan addresses community engagement in research in more detail.

PROVIDING FUNDING SUPPORT FOR COMMUNITY CAPACITY-BUILDING AND CIVIL-SOCIETY-LED ADVOCACY:

Consistent, sustained investment in CSS is vital to realizing the full potential of communities in the fight against TB. With increased financial support for community-based and community-led interventions, as well as for civil-society-led advocacy and accountability efforts, we can mobilize the resources necessary for achieving UNHLM on TB targets for treatment, prevention and R&D. Without additional investment in communities and civil society, we will maintain a status quo of slow progress, and we will remain off track for meeting the global TB targets. Donors and impact investors should consider funding civil society and community organizations as part of their effort to end TB. Resource needs are discussed in detail in Chapter 7.

BOX 4.3:

PARTNERING WITH PARLIAMENTARY CHAMPIONS TO END TB

Since the UN Political Declaration was endorsed by heads of state, members of parliament (MPs) around the world have mobilized to take the outcomes of the declaration back to national parliaments for implementation.

Parliamentarians are holding governments accountable through the creation of national TB caucuses, which are independent networks of MPs within the countries. These caucuses are a powerful channel through which to raise awareness on TB and consequently on the UNHLM targets. In many countries, CSOs are serving as focal points for policy advocacy. These national structures create important opportunities for coordinating advocacy and government engagement internationally and regionally.

With the support of the Global TB Caucus (GTBC), in 2019, national caucuses were launched in Brazil, Denmark, Eswatini, Paraguay, Romania and Chad, bringing the total to 50 caucuses worldwide. MPs from 93 countries reported taking parliamentary action on the UNHLM targets in 2019.

The Global TB Caucus is an international network of over 2,500 MPs in over 150 countries who work to build the political will to end TB. The Global TB Caucus focuses on supporting decision makers who are engaged on TB and prepared to take meaningful actions, such as engaging ministers of health or deploying parliamentary processes to advocate for greater investments in TB.

MPs secured budget increases in several countries, including the Netherlands, where The Hon. Anne Kuik worked closely with KNCV to secure an additional US\$ 5.5 million during budget negotiations for global implementation of new TB diagnostics. In Kenya, The Hon. Stephen Mule successfully raised nearly US\$ 2 million for the national TB budget.

At the global level, the Global TB Caucus brings MPs together to share their experiences at summits, including the African TB Summit in August 2019, which brought together over 40 MPs from the region. This cooperation encourages MPs to work at a regional level within political platforms such as APEC, AU, G7 and G20 to bring TB forward on the international agenda.

¹¹ Good Participatory Practice: guidelines for TB drug trials. Dublin: Critical Path Institute; 2012. <https://www.cptrinitiative.org/downloads/resources/GPP-TB%20Oct1%202012%20FINAL.pdf>

Partnering with the academic community

Academic experts have always played an essential role in the global TB response, from conducting research and educating the next generations of leaders, to influencing technical guidelines and providing sources of expert advice to government officials and policymakers. Contributions from the academic community are particularly important for advancing all manner of TB research. The role of the academic community in research is discussed in more detail in Chapter 6.

An important need for strengthening partnership with the academic community is in advocacy. Academics can share data-driven evidence with other TB stakeholders, including policymakers and the news media, which can be used in the course of setting policies, mobilizing resources, and developing public health interventions, among other things.

One model for academic involvement in advocacy is the network of academics in the United Kingdom, which organized in order to advocate for support for the UNHLM on TB from the UK Government. More than 130 academics in the United Kingdom, including the leaders of prominent universities and academic organizations, sent a co-signed letter to then-Prime Minister Theresa May urging her participation in the UNHLM. They then used the opportunity to gain media attention for the UNHLM.¹²

Effectively involving greater numbers of academic experts in advocacy will require providing new training and coaching opportunities in the areas of strategic communications and media engagement. It will also require efforts to network more academic experts with advocates and to provide academic experts with opportunities for engaging policymakers and the media. In doing so, academics can share expert insight to influence TB policy and public health practice. Likewise, there is a need to strengthen the scientific literacy of advocates and activists, so that more advocates can make effective advocacy use of the new research the academic community produces on a regular basis. In an ideal scenario, every new piece of academic research produced on TB should be evaluated for its potential use for advocacy, then distilled and shared with advocates and influencers who are in relevant positions to be able to translate important new research into real-world impact.

¹² May urged to join global talks on TB. The Sunday Times, 4 August 2018. <https://www.thetimes.co.uk/article/may-urged-to-join-global-talks-on-tb-hsf39jsn2>

Partnering with the private sector

Partnering with the private sector is critical to ending TB. In the context of ending TB, the private health sector encompasses the following stakeholders.

Partnering with private sector health product manufacturers

Commercial manufacturers, including manufacturers of laboratory equipment and vaccines, contribute directly to the R&D of new tools, and the production and supply of diagnostics and

medicines to meet the needs of TB programmes and people with and affected by TB worldwide. Public-private partnerships with such companies are essential for fast-tracking the development of new tools, as well as for making medicines, diagnostics and vaccines affordable and accessible to people with TB. In 2019, for example, Unitaid, the

Global Fund and Sanofi announced an agreement through which the price of the medicine rifapentine – a medicine critical for achieving the target of providing 40 million people TB preventive therapy by 2022 – was reduced by nearly 70%.

As new TB diagnostics, medicines and vaccines are developed, such partnerships will play a key role in providing access for people with TB and in ensuring a steady supply to match demand, especially during the rapid scale-up of services.

Partnering with the private health care system

One of the top priorities for reaching the UNHLM on TB target to treat 30 million people for TB by 2022 is to ensure that people can receive quality-assured TB diagnosis (including rapid DST), treatment and care where they seek care. People in many countries prefer private sector health care because of its ease of access and the perception of higher quality. In a number of countries in Asia, a substantial proportion of people with symptoms of TB, including the poor, seek care first at private clinics. A priority then is to ensure that the TB care provided in the private health sector is actually of high quality. Furthermore, in most country settings, only a small proportion of the patients

diagnosed and treated for TB by private providers are referred or notified to NTPs. There is therefore great potential to make the private health system a true partner in TB care and prevention and to address case notification gaps. Modelling published by the Lancet Commission on TB suggests that optimizing the engagement of private sector health providers could avert 8 million TB deaths between 2019 and 2045 in India alone.¹³

NTPs face major constraints in their efforts to engage with the private sector to scale up TB care, chiefly due to a lack of funding or capacity. Successful projects have addressed these challenges by investing in private intermediary agencies and creating social business models for the provision of quality TB care. Such models have not derailed the business models of private health care providers, but have worked with them synergistically to improve quality, affordability and public health responsibilities. The use of digital health tools and innovative voucher-based reimbursement systems has also contributed greatly to the success of these projects.

13 Reid M, Arinaminpathy N, Bloom A, et al. Building a tuberculosis-free world: The Lancet Commission on Tuberculosis. *Lancet*. 2019;393(10178):1331–84. [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(19\)30024-8.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(19)30024-8.pdf)

COUNTRIES SHOULD WORK TO SECURE ADEQUATE RESOURCES TO IMPLEMENT AND SCALE UP AN APPROPRIATE MIX OF THE FOLLOWING PRIVATE HEALTH SECTOR ENGAGEMENT STRATEGIES:

- a** Share the burden of engaging numerous independent private practitioners among private “intermediary organizations” that can establish and scale up social franchising and social business models; NGOs with the capacity and skills to work with private practitioners; and professional societies and associations.
- b** Optimize and expand engagement with large hospitals, academic institutions and NGOs.
- c** Mobilize and support corporate and business sector health services in order to initiate and expand workplace TB programmes to serve workers, their families and communities.
- d** Engage communities and civil society to seek care from and promote private providers offering high-quality TB care.
- e** Enforce mandatory TB case notification through simplified and user-friendly digital tools, the rational use of TB medicines, and certification and accreditation systems to identify and incentivize collaborating providers.

It is also important for national authorities and international donors to recognize that, in a number of settings, people have more confidence in the private health sector. Investments should therefore be made to strengthen both public and private sectors to help scale up good-quality, affordable TB care in both sectors.

One way to increase this kind of investment is to strengthen public-private mix (PPM) approaches to scaling up access to TB care and services. PPM refers to engagement by the NTP with private sector providers of TB care, such as private individual and institutional providers, the corporate or business sector, mission hospitals, NGOs and FBOs.¹⁴ In 2018, WHO's Global TB Programme, the Stop TB Partnership's Public-Private Mix Working Group and international partner agencies released a new roadmap for pursuing a PPM approach.¹⁵ A companion document provides a landscape analysis of current efforts and challenges involved in engaging with private providers to expand access to TB care and services.¹⁶

Investment in public-private partnership approaches to strengthening private sector TB care is important for all countries. The Global Plan highlights this need particularly in two of the nine settings: Setting 6 (middle-income country settings with a moderate TB burden) and Setting 7 (India). Even in countries where most TB treatment is handled by the public sector, engagement with the private sector is still required for referrals and early TB diagnosis and treatment. The consequent reduction in diagnostic delay could have a major impact on reducing TB transmission.

Partnering with industry outside the health sector

Private industry is needed in the fight to end TB in two ways: by ensuring their workplaces follow best practices for preventing TB transmission and for providing TB care and support to staff and their families, and by undertaking CSR activities. TB predominantly affects people in their most productive years, and certain industries in particular (e.g., mining, health care) have rates of TB transmission that are significantly higher than average. Industries and businesses, especially those that are labour-intensive, need to adopt non-discriminatory recruitment and retention policies, promote infection-free and safe workplaces, and provide staff and their families with good-quality, affordable TB diagnostic, treatment and notification services. NTPs and TB organizations can partner with businesses to provide staff training and to assist in the development of workplace TB programmes, establishing links between those programmes and the health system.

Partnering with labour unions

NTPs should work with labour unions to create and enforce workplace provisions that reduce the risk of exposure to TB and provide access to care and support for those affected by TB, including for TB prevention. This is especially important for industries where workers are at high risk of TB, such as the health care and mining sectors. Unions can help to put in place strong workplace programmes, advocate for national laws and policies that eliminate discrimination of people with TB, ensure safe environments with regard to TB, and enforce best practices and human-rights-based policies with regard to migration and treatment of foreign workers.

Focusing CSR activities on TB

Efforts to end TB should engage corporate CSR initiatives. This is an important area for further engagement between TB programmes, their

14 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

15 Public-private mix (PPM) for TB prevention and care [Website]. Geneva: World Health Organization; 2019. <https://www.who.int/tb/areas-of-work/public-private-mix/en/>

16 Engaging private health care providers in TB care and prevention: a landscape analysis. Geneva: World Health Organization; 2018. <https://www.who.int/tb/publications/2018/PPMlandscape/en/>

stakeholders, and businesses. Financial and in-kind contributions from the private sector are critical to progress in many areas, particularly in innovation, the use of information technology, and logistics management. Businesses with products and services that reach large populations may provide opportunities for public education and community outreach. Co-branding partnerships with the health sector could help

raise TB awareness and eradicate stigma. Businesses could work with NTPs to help create TB-free districts or cities, or to fund feasibility studies for impact bonds or other innovative interventions. In all cases, CSR initiatives should be adequately financed to achieve their aims. They should also be needs-based, results-driven, and respect and promote the rights of communities affected by TB.

Supporting national multisectoral platforms

A national platform is a voluntary alliance between organizations drawn from the public, civil society and private/business sectors that commit to working collaboratively towards the goal of ending TB. All partners contribute from their core competencies, share risks and responsibilities, and benefit by achieving mutual and shared goals.

A national platform contributes to the implementation of the national TB strategic plan by harnessing the contributions of all stakeholders, in close collaboration with the country's NTP. For this reason, the platform's main focus is decided by the partners on a case-by-case basis and will vary depending on the country context. Examples of priorities range from advocacy and resource mobilization to the coordination of service delivery.¹⁷ National platforms should also play a key role in conducting coordinated advocacy and in implementing various elements of a national Multisectoral Accountability Framework, with the aim of ensuring country-wide accountability for fulfilling TB commitments and achieving TB targets.

¹⁷ National platforms [Website]. Geneva: Stop TB Partnership. <http://www.stoptb.org/countries/partnerships/>



5. UNIVERSAL HEALTH COVERAGE AND SOCIOECONOMIC ACTIONS IN TB



SUMMARY

New strategies focusing on socioeconomic actions are required to achieve the 90-(90)-90 targets and end TB. Ministries and agencies across government, beyond the ministries of health and the public health sector, must collaborate in order to have maximum impact on the TB epidemic.

UHC, underpinned by the availability of TB care and services provided through primary health care, must be at the heart of such strategies, with the goal of making TB programmes high-quality, affordable and accessible to all, leaving no one behind. At the same time, countries can build on the public health infrastructure currently in place

through TB programmes as a strategy for pursuing UHC. People affected by TB need the support of social protection policies and programmes to help them recover from sickness and manage any disability or loss of function resulting from TB, without having to suffer catastrophic financial loss or other avoidable hardships.

PRIORITY ACTIONS

Governments:

- ✦ Fulfil commitments made in the UN Political Declaration on UHC, including the commitment to strengthen efforts to address TB by advancing comprehensive approaches and integrated service delivery, ensuring no one is left behind.
- ✦ Invest in and implement non-medical interventions in parallel to medical services, including TB community education, social protection, poverty alleviation and improved housing.
- ✦ Assess barriers to accessing TB services and address them in national UHC agendas. Ensure TB services are included within social benefit packages.
- ✦ Create a multisectoral response at the national level; consider establishing a national TB coor-

dination council that mobilizes support from across sectors and promotes accountability for fulfilling TB commitments.

- ✦ Implement patient cost surveys to understand the drivers of TB patient costs and use findings to improve financial and social protection policies.

Advocates:

- ✦ Equip parliamentarians and decision makers with evidence showing how focusing on TB will also improve performance in tackling other national priorities, including other UN SDGs (see Introduction for discussion on related SDGs).

- ✦ Engage and enroll new potential allies outside of the traditional TB community, including those working in social welfare, labour, housing, urban regeneration, agriculture, judiciary, legal and law enforcement, and other relevant sectors, as well as cultural leaders and traditional healers.

Health programmes:

- ✦ Ensure health care staff treating people with TB understand social protection policies and the associated programmes for which people with TB are eligible.
- ✦ In the course of pursuing UHC, ensure the right balance of integrating TB care into primary health care and maintaining specialized TB managerial functions.
- ✦ Ensure operational research is used to guide and improve the implementation of social protection programmes.

Researchers:

- ✦ Strengthen the body of evidence showing the links between socioeconomic actions and progress made against TB.

Even though free TB diagnosis and treatment are at the heart of global TB efforts, individuals and families affected by TB often still struggle with other associated costs, including non-medical costs related to accessing TB care, such as travel expenses and the opportunity cost of missing work. These costs can be catastrophic, and even though TB diagnosis and treatment is almost always provided for free in the public health sector, TB programmes do not often compensate people for these other expenses. When the costs become too great, it creates a powerful disincentive that prevents people from accessing TB care. On a population level, the high costs associated with TB suppresses access to care, creating a barrier that stands in the way of ending the disease.

Ending TB requires a holistic approach that incorporates a broad range of medical and non-medical interventions carried out across a range of sectors. Compared with older approaches to “controlling” TB, the End TB Strategy has increased the focus on poverty alleviation and social protection as critical pieces of a holistic, multisectoral effort. Combined with urban regeneration, these interventions have the potential to enhance prevention, improve access to care and prevent TB-related catastrophic costs.

In addition to investing in further improvements in the accessibility and quality of TB care and services provided through public health systems, implementing these measures will require greater involvement of the private sector, civil society and community health workers. However, the need for non-medical interventions means that a greater range of non-medical actors must be engaged. Planning and investing to end TB is not solely the task of health ministries, but also of other ministries and government agencies, including those responsible for social welfare, finance, labour, housing and urban regeneration, agriculture and others. Engaging finance ministries – with NTPs and advocates from across sectors participating strategically in national budget processes – is crucial to seeing more resources flow towards a multisectoral TB response.

Improving medical services: UHC

TB and UHC efforts go hand in hand; in 2018, roughly 40% of people with TB did not have access to appropriate treatment. In fact, given the huge global burden of TB, expanding TB efforts provides an important pathway towards UHC and the potential to strengthen health systems by building on health infrastructure originally established for the purposes of delivering TB care. At the same time, the global push towards achieving UHC provides an opportunity for TB services to scale up, become more affordable and accessible, and improve in quality. For these reasons, social protection and UHC are core components of the End TB Strategy. Pillar Two of the strategy seeks to ensure that health and social sector policies work jointly to address the social determinants of TB.

After years of neglect, UHC is once again high on political agendas. In September 2019, the UN General Assembly convened a UNHLM on UHC. The resulting Political Declaration on UHC¹, endorsed by the UN General Assembly, reaffirmed the commitments made in the UN Political

Declaration on TB. The UHC Declaration also committed to strengthening efforts to address TB by advancing comprehensive approaches and integrated service delivery, ensuring no one is left behind.

It is critical that TB programmes seize the opportunity created by this high-level political attention on both TB and UHC, and actively engage in efforts to secure greater access to TB care through national efforts to achieve UHC. Depending on the country context, in order to be part of the UHC and health insurance initiative, TB programmes may need to restructure their budgets, service delivery mechanisms and data collection methods.

Health care financing has become a prominent aspect of global efforts towards UHC, and health insurance schemes are increasingly being rolled out in many low-income countries. However, many people at risk of TB lack health insurance coverage. Even while TB care and treatment remains free in the public sector, efforts should be made to include people at risk of TB within national health insurance schemes. As discussed in Chapter 4, community health workers can help reach the “missed” millions of people in need of TB care by reaching out to communities, tracing contacts of people impacted by TB, and educating family members. The capacity of health facilities must be strengthened to provide TB care and services for greater numbers of people in need.

BOX 5.1:

KEY TB COMMITMENTS IN THE UN POLITICAL DECLARATION ON UHC

Reaffirm the strong commitments made through the political declarations adopted at the High-level Meetings on ending AIDS, on tackling antimicrobial resistance, on ending tuberculosis, and on the prevention and control of non-communicable diseases, as well as the General Assembly resolutions entitled “Consolidating gains and accelerating efforts to control and eliminate malaria in developing countries, particularly in Africa, by 2030”.

Strengthen efforts to address communicable diseases, including HIV/AIDS, tuberculosis, malaria and hepatitis as part of universal health coverage and to ensure that the fragile gains are sustained and expanded by advancing comprehensive approaches and integrated service delivery and ensuring that no one is left behind¹.

¹ Political Declaration of the High-level Meeting on Universal Health Coverage “Universal health coverage: moving together to build a healthier world”. New York: United Nations General Assembly; 2019. <https://www.un.org/pga/73/wp-content/uploads/sites/53/2019/07/FINAL-draft-UHC-Political-Declaration.pdf>

BOX 5.2: WHAT IS UHC?

UHC is defined as ensuring that all people can use the health services they need, that these services are of sufficient quality to be effective, and that the use of these services does not expose the user to financial hardship.¹ SDG 3 ensures healthy lives and promotes well-being for all at all ages. This goal focuses on achieving UHC, which includes financial risk protection, access to quality essential health care services, and access to safe, effective, quality and affordable essential medicines and vaccines for all. As it relates to TB, UHC means providing access to quality-assured care and services for DS-TB, DR-TB, TB infection and zoonotic TB for people of all ages, leaving no one behind.

1 What is universal coverage? [Website]. Geneva: World Health Organization; 2019. http://www.who.int/health_financing/universal_coverage_definition/en/.

Integrating TB into poverty alleviation and social protection activities

There is an extensively documented, strong positive correlation between poverty and TB across all age groups. A new review of children's susceptibility to TB described the relationship between paediatric TB and poverty as "overwhelming", with poverty being the leading factor putting children at risk of being exposed to TB, being infected, developing disease and experiencing poor outcomes.² A recent statistical modelling exercise conducted by experts from WHO, the London School of Hygiene & Tropical Medicine and other universities found that ending extreme poverty and expanding social protection coverage would result in an 84.3% reduction in TB incidence by 2035.³

In addition to the direct health costs of seeking TB care, many households also incur significant related expenses, including costs for travel, food and childcare, and loss of income. These costs can be catastrophic for families, as their spending on health care can exceed 40% of their disposable income.⁴ Income loss accounts for, on average, 60% of the costs incurred by people with TB, with 25% attributed to direct costs associated with tests, medicines and hospitalization.⁵ Addressing these costs and

eliminating catastrophic spending is critical to ending TB, especially since the disease disproportionately affects families who are impoverished and malnourished.

Evidence shows how social protections, particularly those focused on treatment adherence, can improve TB outcomes and operational results.⁶ Many social protection programmes have used conditional cash transfers to incentivize participation. This model has been employed to improve public health in many LMICs, notably in Brazil and more recently in India (see Box 5.4: India's National Direct Cash Transfer Programme).

2 Roy R, Whittaker E, Seddon J, et al. Children and *Mycobacterium tuberculosis*: a review of susceptibility and protection. *Lancet Infect Dis.* 2019;19(3):e96–108. doi:10.1016/S1473-3099(18)30157-9

3 Carter D, Glaziou P, Lönnroth K, et al.. The impact of social protection and poverty elimination on global tuberculosis incidence: a statistical modelling analysis of Sustainable Development Goal 1. *Lancet Glob Health* 2018;6:e514–22. doi:10.1016/S2214-109X(18)30195-5

4 Xu K, Evans DB, Kawabata K. Household catastrophic health expenditure: a multicountry analysis. *Lancet.* 2003;362:111–7. doi:10.1016/S0140-6736(03)13861-5

5 Eliminating the financial hardship of TB. Geneva: World Health Organization; 2013. http://www.who.int/tb/publications/UHC_SP_factsheet.pdf

6 Boccia D, Hargreaves J, Lönnroth K, et al. Cash transfer and microfinance interventions for tuberculosis control: review of the impact evidence and policy implications. *Int J Tuberc Lung Dis.* 2011;15:S37–49. doi:10.5588/ijtld.10.0438

BOX 5.3:

WHAT IS SOCIAL PROTECTION – AND WHAT HAVE GOVERNMENTS COMMITTED TO DO ABOUT IT?

Social protection includes public actions that address poverty, economic shocks and social vulnerability, taking into account the relationship between exclusion and poverty. Through income or in-kind support and programmes designed to increase access to services, social protection helps to realize people's rights.¹

Under the umbrella of social protection is social support, which includes various strategies for supporting people throughout the course of their TB care. Examples of common social support strategies for TB include:

- **PATIENT SUPPORT:** supporting people to complete a full course of treatment;
- **FINANCIAL SUPPORT:** stipends or reimbursements to defray out-of-pocket costs or provide nutritional support during treatment;
- **HEALTH EDUCATION:** providing reminders to renew medications; helping to develop coping methods during treatment;
- **PSYCHOLOGICAL SUPPORT:** helping to relieve the psychological burden of experiencing TB through empathy, trust-building and caring.

By endorsing the UN Political Declaration on UHC, governments have committed to “*stop the rise and reverse the trend of catastrophic out-of-pocket health expenditure by providing measures to assure financial risk protection and eliminate impoverishment due to health-related expenses by 2030, with special emphasis on the poor as well as those who are vulnerable or in vulnerable situations*”²

By endorsing the UN Political Declaration on the Fight Against TB, governments have also committed to enabling and pursuing multisectoral collaboration in order to:

- provide **SOCIAL PROTECTION** for children affected by TB, as well as for their caregivers;
- strengthen support and capacity-building in countries that have **SOCIAL PROTECTION** systems with limited resources;
- help developing countries raise domestic revenues, and provide bilateral financial support towards achieving UHC and **SOCIAL PROTECTION** strategies.³

1 UNICEF social inclusion, policy and budgeting [Website]. New York: UNICEF. <https://www.unicef.org/socialpolicy/>

2 Political Declaration of the High-level Meeting on Universal Health Coverage “Universal health coverage: moving together to build a healthier world”. New York: United Nations General Assembly; 2019. <https://www.un.org/pga/73/wp-content/uploads/sites/53/2019/07/FINAL-draft-UHC-Political-Declaration.pdf>

3 Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmonTBDeclaration.pdf>

Social protection efforts require support from health systems and other sectors. Nutritional programmes should collaborate with the World Food Programme and national agencies responsible for food and nutrition. Cash transfer programmes for the poor that often exist under social welfare ministries need to be made accessible to people with TB. Additional operational research can demonstrate impact and identify more effective means of implementing social protection activities.⁷

In order to maximize collective efforts towards achieving the health-related SDGs, in 2018, 11 of the world's largest international health and development agencies developed a framework for collaboration: The Global Action Plan for Healthy Lives and Well-being for All⁸. This framework is built on three strategic approaches: Align. Accelerate. Account. To learn more about how the world's health organizations are working together to accelerate progress towards ending TB and achieving UHC, go to: <https://apps.who.int/iris/handle/10665/311667>

7 Lutge E, Lewin S, Volmink J, et al. Economic support to improve tuberculosis treatment outcomes in South Africa: a pragmatic cluster-randomized controlled trial. *Trials*. 2013;14:154. doi:10.1186/1745-6215-14-154

8 Towards a global action plan for healthy lives and well-being for all: uniting to accelerate progress towards the health-related SDGs. Geneva: World Health Organization; 2018. <https://www.who.int/iris/handle/10665/311667>

Countries are encouraged to undertake an assessment of barriers to accessing TB services and to address them in their UHC agenda. WHO has developed a handbook for conducting TB patient cost surveys that countries can use to assess the drivers of costs for TB patients and their families.⁹ Survey findings can then be used to improve financial and social protection policies for families affected by TB. Health care staff who care for people with TB should be aware of social protection policies and programmes, such as disability grants, for which people with TB are eligible. In addition, given TB's public health significance as an airborne communicable disease, TB care and services should be included in social benefit packages.

9 Tuberculosis patient cost surveys: a handbook. Geneva: World Health Organization; 2017. https://www.who.int/tb/publications/patient_cost_surveys/en/

Likewise, countries should apply findings from research on social protection in order to develop and optimize social protection interventions for people affected by TB. The SPARKS (Social Protection Action Research and Knowledge Sharing) interdisciplinary research network evaluates the effects of social protection strategies on health, economic and wider outcomes. SPARKS network members have produced original research on catastrophic health costs, cash transfer programmes, social policy, government social protection interventions and related issues in Brazil, India, South Africa, Viet Nam and other country contexts.¹⁰

10 SPARKS Network reports and publications. Stockholm: SPARKS Network Secretariat; 2018. <https://sparksnetwork.ki.se/news-and-events/publications/>

Addressing antimicrobial resistance within the context of UHC

The UN General Assembly, G20, G7, BRICS, and Asia-Pacific Economic Cooperation bloc, as well as ministers from countries across South-East Asia and the African Union have all issued communiqués identifying antimicrobial resistance (AMR) as a critical threat to global health security and economic prosperity, pledging action in response. DR-TB alone causes almost one-third of all deaths from resistant pathogens, making the effort to end TB the cornerstone of the response to AMR and a crucial piece of the global health security agenda.¹¹

Achieving universal access to TB care, while providing people with TB and their families with the social support they need to adhere to quality treatment and prevention, is essential to solving the AMR challenge. DR-TB has a chance to develop any time a person with TB receives inadequate, substandard or incomplete treatment. Unfortunately, the living conditions common in low-income settings – especially urban

environments where communities lack access to nutrition and quality health care – tend to make it challenging to complete TB treatment, leading to the emergence of drug resistance.¹² Today, due to the vast numbers of people who have received such care, the ongoing spread of resistant TB strains is responsible for most new instances of people developing MDR-TB and extensively drug-resistant (XDR-) TB. MDR-TB

11 Tuberculosis – the cornerstone of the AMR threat. London: TB Europe Coalition; 2017. http://www.tbcoalition.eu/wp-content/uploads/2015/03/AMR_brochure_spreads.pdf

12 Lange C, Chesov D, Heyckendorf J, et al. Drug-resistant tuberculosis: an update on disease burden, diagnosis and treatment. *Respirology*. 2018;23:656-73. doi:10.1111/resp.13304

infection in particular has become a significant burden. A recent modelling exercise estimates that three in every 1,000 people globally are living with MDR-TB infection, with the prevalence around 10 times higher among people under 15 years of age.¹³

13 Knight GM, McQuaid CF, Dodd PJ, et al. Global burden of latent multidrug-resistant tuberculosis: trends and estimates based on mathematical modelling. *Lancet Infect Dis.* 2019;19:903–12. doi:10.1016/S1473-3099(19)30307-X

Ensuring that every person affected by TB has access to the proper treatment and is supported to complete that treatment is essential to ending TB and stopping the danger to global health security posed by TB drug resistance. R&D of new tools for diagnosing, preventing and treating TB is also critical and will be discussed in Chapter 6.

Improving the urban environment

Over the coming decades, the majority of the world's population growth is set to occur in urban areas. In many low-income countries, and even in many middle-income ones, urban areas have grown rapidly, but without much planning or resources. This has left the poorest to live in slums. For an airborne disease such as TB that is fuelled by overcrowding, poor ventilation, inadequate sanitation and undernutrition, this development trend has significant implications.

Urban development strategies that improve the physical environment and reduce overcrowding therefore have the potential to make a significant impact in the fight against TB.¹⁴ Health

care facilities that are well located in relation to housing could enable better links to health services. Improving urban living conditions would also greatly benefit efforts to tackle other diseases such as diarrhoea and pneumonia that are caused by overcrowding and poor water and sanitation.

14 Hargreaves JR, Boccia D, Evans CA, et al. The social determinants of tuberculosis: from evidence to action. *Am J Public Health.* 2011;4:654–62. doi:10.2105/AJPH.2010.199505

Legal resources

Numerous legally binding treaties, conventions and national constitutions guarantee people the right to the highest attainable standard of health. In cases where governments have not adequately safeguarded that right, people have used litigation and the courts to force governments to uphold their rights to access essential health services, their rights to be free from discrimination and other rights.

In some contexts, litigation can be an important accountability tool for people affected by TB.¹⁵

The University of Chicago School of Law in the United States and the Global Drug-Resistant TB Initiative have compiled a valuable compendium of case law focused on TB and human rights that includes summaries of court cases

15 McBroom. Litigation as TB rights advocacy. *Health Hum Rights.* 2016;18(1):69–84.

from a variety of country contexts pertaining to various TB-related issues, including inhuman and degrading treatment, compensation, compulsory isolation, employment discrimination, negligence, right to privacy and other issues.¹⁶

16 Tuberculosis, human rights and the law. 1st ed. Chicago: International Human Rights Clinic, University of Chicago Law School; 2017. [http://www.stoptb.org/assets/documents/communities/TB%20Human%20Rights%20and%20the%20Law%20Case%20Compendium%20\(First%20Edition\).pdf](http://www.stoptb.org/assets/documents/communities/TB%20Human%20Rights%20and%20the%20Law%20Case%20Compendium%20(First%20Edition).pdf)

Creating an enabling environment: political will and policymaking

Advocacy is key to raising the profile of TB and ensuring accountability for action across all relevant sectors. Engaging and enrolling allies from across sectors, and creating a broad-based, influential constituency that can help drive the response needed to end TB requires a major shift in mindset both within and outside of the community of people working on TB. TB is an urgent societal challenge, and the TB community cannot face it alone.

BOX 5.4:

INDIA'S NATIONAL DIRECT CASH TRANSFER PROGRAMME

In March 2018, the Government of India instituted a direct cash transfer system for people with TB. The cash transfer programme is one of several social protection and support measures included within the National Strategic Plan for TB Elimination in India 2017–2025. The programme called “Nikshay Poshan Yojana” (NPY) provides direct cash transfers of INR 500 (approximately US\$ 8) monthly to the bank accounts of people with TB or their close family relatives, to be used for nutritional support.

Direct Benefit Transfer (DBT) is a mechanism that can enable targeted and transparent delivery of benefits to citizens through the use of technology. For TB, DBT has been implemented through four schemes within India's NTP:

- Nikshay Poshan Yojana (NPY)
- Honoraria to treatment supporters
- Transportation support to people with TB living in tribal areas
- Financial incentives for TB notification and successful treatment outcomes, provided to private health providers and those who make referrals for TB care

Once the bank account details and unique identity number of a person with TB are processed in Nikshay – the electronic online TB notification system – the information is further linked to the Public Finance Management System (PFMS), which credits the funds to the designated bank account. The same approach is used for treatment supporters and for private providers.

From April 2018 to March 2019, more than 1.5 million beneficiaries received financial benefits of more than US\$ 36 million through the NPY, while treatment supporters, people with TB from tribal areas and private providers were collectively provided US\$ 3 million. Funding for these financial services is supported through India's national TB budget, with funds provided through a loan from the World Bank.

For more details see:

<https://tbcindia.gov.in/WriteReadData/India%20TB%20Report%202019.pdf>

[https://tbcindia.gov.in/index1.](https://tbcindia.gov.in/index1.php?lang=1&level=1&sublinkid=4802&lid=3316)

[php?lang=1&level=1&sublinkid=4802&lid=3316](https://tbcindia.gov.in/index1.php?lang=1&level=1&sublinkid=4802&lid=3316)

BOX 5.5:

PRESERVING THE CAPACITY TO END TB: LEARNING FROM HISTORY

In 2002, an analysis of the history of WHO policies and guidance going back to 1948¹ found that policy approaches had shifted several times over the decades from vertical, TB-specific approaches towards increased integration of TB care within general outpatient services. The integration of managerial functions specific to TB followed, driven by the rationale that integration of these specialized functions (e.g., TB training, supervision, logistics and communications) would make their implementation more efficient and cost-effective. The health reform process of the 1980s led to further integration of what had previously been the specialized functions of dedicated TB programmes.

As a result, NTPs were essentially dismantled in many countries. This dismantling led to a decline in the available TB expertise, weakened support for TB research and produced large resources gaps – just as the HIV pandemic began driving a new epidemic of TB. The need for an urgent TB response led countries to rebuild their TB

programmes throughout the 1990s, a decade that also saw international adoption of DOTS (directly observed treatment, short-course) as the standard TB response strategy. After 2000, countries began once again to integrate TB services and functions with other areas of the health system.

In reviewing this history, the lesson that emerges is that neither vertical approaches nor excessive integration of TB functions are completely successful. Nor are specialized and integrated approaches mutually exclusive. Instead, the best chance of ending TB is through a mixed approach that continues to maintain specialized functions in some capacities (such as for planning, training, disease monitoring, and assessment), integrates service delivery within primary health care, enrolls stakeholders from beyond the health sector in efforts to end TB, and relies on effective advocacy to keep TB high on national political and policy agendas.

1 Raviglione MC, Pio A. Evolution of WHO policies for tuberculosis control, 1948–2001. *Lancet*. 2002;359:775–80. doi:10.1016/S0140-6736(02)07880-7

When it comes to overseeing multisectoral policymaking for TB that also aligns with national UHC and AMR strategies, one way to ensure the better integration of TB with other programmes is for countries to set up a TB coordination council at the national level, similar to a national AIDS board, and to work more closely with existing national health committees. National councils can engage ministries outside of the health ministry, ensuring that, for example, the ministry of finance is engaged in creating budgetary space; housing is engaged in addressing urban crowding and revising building codes as needed to allow for adequate ventilation; and justice is engaged in upholding the rights of people affected by TB.

NTP managers are not the best positioned to lead coordinated efforts across several departments and ministries. However, with adequate resources and high-level political support, NTP managers can effectively advise other programmes on how to incorporate TB into their activities. Political will needs to come from a consortium of ministers and high-ranking government officials, even if they need to be spurred

into action by advocates, TB survivors, affected communities and their allies, and business and cultural leaders.

The way the argument is framed is also key. Focusing on TB will also improve performance towards achieving other UN SDGs. And social protection interventions are likely to impact multiple diseases simultaneously, making their implementation more valuable and cost-effective.

As TB risk factors are diverse, policy approaches should contain a mix of TB-specific approaches (i.e., interventions that directly reach people with TB and aim to influence a particular TB indicator) and TB-sensitive approaches (i.e., interventions that reach people who are at risk of TB and can indirectly reduce their vulnerability, such as better housing and ventilation, or agricultural policies aimed at improving nutrition).

Better data on the links between TB and socio-economic actions should be collected in order to equip decision makers and parliamentarians with the evidence to change policy and allocate

resources for social protection. Addressing TB will require major systemic changes in regulatory capacity (to ensure the rational use of medicines and infection control, among other issues), health care financing (through improved health insurance schemes), and boosting the capacity of health care systems to ensure UHC.

BOX 5.6:

JAPAN: EXPANDING TB CARE AS A PATHWAY TO UHC

In 1961, Japan achieved UHC. In the 1950s, TB was the largest killer, popularly known as the “national disease”. TB was so prevalent that more than 20% of total medical expenditures were allocated to TB.

In 1951, the national TB Prevention Act was enacted, after which the Ministry of Health and Welfare launched a massive campaign against TB through public health systems strengthening, which resulted in a 25% decline in the number of people with TB by 1958.¹ TB care was rapidly expanded by:

- collectively engaging the national government, together with the private sector, community and individuals;
- creating a dedicated TB budget within national health insurance programmes, which was used to expand coverage of TB care and services;
- engaging the participation of local authorities in the national TB campaign.²

The infrastructure, systems and processes put in place during the course of Japan’s TB campaign created the opportunities for Japan to achieve UHC.

1 Jimba M, Fujimura MS, Ong KIC. How can we avoid making universal health coverage a white elephant? *Lancet*. 2019;393(10189):2394. doi:10.1016/S0140-6736(19)30213-2

2 Takemi K. Proposal for a T-shaped approach to health system strengthening. *Health Syst Reform*. 2016;2(2):8–10. doi:10.1080/23288604.2015.1123339





6. NEW TOOLS



SUMMARY

While we can accelerate progress, we cannot actually end the TB epidemic with the tools that we have today. Increased investment in new diagnostics, treatment regimens and vaccines is urgently needed, along with greater investment in basic science research. Advancing operational research is also critical for testing the practical utility of approved therapies and interventions, addressing barriers to access as new tools are approved, and introducing and scaling up access to new tools in the most efficient and effective way possible.

In the last five years, there has been exciting progress in the development of new tools, including positive results from two Phase IIb vaccine clinical efficacy trials published in 2018; the emergence of new rapid molecular TB tests and technologies that are showing great promise for drug-resistance testing; and a new medicine approved by the U.S. Food and Drug Administration (FDA) for treating XDR-TB.

To build on this progress and continue to advance TB R&D of improved vaccines, medicines and diagnostics, the world's governments have committed to increasing funding for TB R&D from roughly US\$ 700 million annually to over US\$ 2 billion annually. In addition to this funding support, global investment in basic science research also needs to increase to an estimated US\$ 400 million per year in order to understand the most promising approaches to

new tools R&D. Delaying this investment by even one year could result in 4.8 million additional people developing TB and 670,000 additional people dying from the disease, leading to an additional US\$ 5.1 billion in TB treatment costs alone.

Closing the R&D funding gap and creating a research-enabling environment is going to take concerted advocacy, with greater involvement of TB researchers, TB survivors and affected communities working together to hold governments accountable for fulfilling their commitments. Engaging communities affected by TB at all stages of the research process –including in research that identifies and helps to overcome the social, legal, political and economic hurdles in the way of developing and providing access to new tools – is vital to the ultimate success of any research initiative.

PRIORITY ACTIONS

Carrying out the following actions will require a collaborative effort on the part of national governments, public and private research institutions, biopharmaceutical companies, the philanthropic and financial sectors, civil society and affected communities. Advocacy will remain critical to ensuring accountability for these actions.

- Devote more than US\$ 2 billion annually to TB R&D to close the over US\$ 1.3 billion annual TB R&D funding gap. New funding should be used to increase support for research institutions, partnerships and collaborations, including product development partnerships (PDPs), the BRICS TB Research Network, and innovative funding mechanisms and incentives. Table 6.1 summarized the funding needs for TB R&D for medicines, diagnostics, vaccines and basic science research.

TABLE 6.1: SUMMARY OF FUNDING NEEDS FOR TB R&D (US\$ MILLION)*

Tool	Total Funding Need 2018–2022
Medicines	6,800
Diagnostics	916
Vaccines	3,067
Basic Science Research	2
Total	12,783
Annual funding need:	2,557

*Does not include funding for roll-out

- Accelerate the development and use of new tools. R&D priorities include:

⊕ Diagnostics:

- Develop rapid and affordable non-sputum-based tests for diagnosis or triage.
- Develop accurate DST for critical medicines.
- Improve tools for detecting TB infection and testing for risk of progression to active disease.

⊕ Medicines:

- Increase the number of new candidates

with novel mechanisms of action in the clinical pipeline.

- Advance the development of new treatment regimens that will be superior to current regimens.
- Focus on treatment-shortening strategies for both TB disease and TB infection.

⊕ Vaccines:

- Accelerate the late-stage development of vaccine candidates, including late-stage evaluation of the M72/AS01E vaccine candidate, and work with countries to prepare for successful licensure and roll-out.
- Accelerate the development of next-generation vaccine candidates to ensure highly effective vaccines for all affected populations.
- Evaluate novel TB vaccine concepts and investigate mechanisms and correlates of vaccine-induced protection.

- Invest US\$ 400 million in basic science research in order to better understand the most promising approaches to discovering new TB diagnostics, medicines and vaccines.

- Create an enabling environment for TB R&D by:

⊕ developing, funding and implementing national TB R&D strategies;

⊕ increasing research centre capacity for conducting clinical trials in high TB and MDR-TB burden countries;

⊕ streamlining and harmonizing regulatory processes from clinical development to regulatory submission and regional approval, and building country capacity

to evaluate new tools that have already been tested and shown to be safe and effective in other countries;

- ✦ investing in and sustaining a talented field of TB researchers;
 - ✦ supporting operational research in order to understand how to optimally implement new tools within specific country and local contexts.
5. Optimize access to new tools through comprehensive access strategies developed for new medicines, diagnostics and vaccines, aided by operational research that identifies and helps to overcome social, political, legal and economic barriers to access.
 6. Advocate effectively; strengthen community systems, research literacy, and the meaningful engagement of TB affected communities in research; and include advocates and members of TB affected communities in decision-making structures and scientific forums.

ADVANCING THE TB RESEARCH AGENDA

When it comes to investing in TB R&D, we cannot afford business as usual. Without new medicines, diagnostics and effective vaccines, we will not achieve the steep reductions in incidence and mortality that we need, and millions more people will die from the disease. Country governments should support TB R&D by developing and funding national plans for TB research, or by integrating TB into national health research agendas. R&D efforts should be needs-driven, evidence-based and guided by the core principles of affordability, efficiency, equity and collaboration.

The following section lays out priorities for essential investments in new TB tools, projected impacts of new investments, and highlights of the R&D progress achieved in the last five years.

Strategic frameworks for the R&D of new TB tools

TABLE 6.2: NEW MEDICINES STRATEGIC FRAMEWORK 2018–2022

Vision:

To develop shorter, more effective medicines and regimens for all age groups and populations affected by TB

Goals:

Introduction of a new regimen with a shorter duration (2–4 months) and containing three or four new medicines with no pre-existing resistance to treat both DS- and DR-TB. Introduction of shorter duration regimens to prevent TB.

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
Sustaining the pipeline through basic discovery for TB medicines	New clinical candidates entering Phase I	Accelerate screening and optimization of new chemical entities; validate biomarkers; develop animal models that are more predictive of clinical efficacy; identify new drug targets	1,400
Maintaining trial site capacity	Increase the number of Good Clinical Practice/Good Laboratory Practice (GCP/GLP) compliant sites available for TB drug trials	Identify, maintain and provide training at GCP/GLP compliant sites	400
Developing a shorter regimen for DS-TB	Complete Phase III of a 2–4 month regimen for DS-TB and, where possible, a universal regimen for all active TB	Conduct trials: pK studies, Phase I, Phase II (EBA, SSSC, drug-interaction studies), and Phase III to advance two to three new shorter regimens	2,000
Developing a safe, higher efficacy and shorter regimen for MDR-TB	Complete Phase III of a shorter regimen for MDR-TB	Conduct trials: pK studies, Phase I, Phase II, and Phase III to advance two to three new shorter regimens	800
Improving treatment for children in parallel to efforts in adults	Complete formulation and clinical testing in children in conjunction with any new regimen advancing in adults	Include children in trials as early as possible for new regimens; develop safe, reliable and user-friendly regimens for all forms of TB in children early in the development process; conduct drug-interaction studies, where regulatory requirements necessitate such studies in children	200
Developing a safer, high-efficacy regimen for TB infection	Complete Phase III of a safer, high-efficacy regimen for TB infection	Conduct Phase III trials of new regimens for TB infection with the aim of a shorter duration of treatment	120
Ensuring adoption of new TB medicines and regimens at country level	Patients access newly approved medicines and regimens, especially in high-burden countries	Include new medicines and regimens in national policies and guidelines; implement mechanisms to expedite regulatory processes in countries; engage key stakeholders; conduct extensive training of health providers	700
Engaging community and civil society in the entire process of drug development and access	Community and civil society are represented in all decision-making processes and forums along the drug discovery and development pipeline	Include community and civil society representatives in advisory committees, protocol and study design, scientific networks and other forums related to TB drug development	90
TOTAL FUNDING REQUIRED			5,710

TABLE 6.3: NEW DIAGNOSTICS STRATEGIC FRAMEWORK 2018–2022

Vision:

To achieve early and universal diagnosis of all people with all forms of TB to foster progress towards TB elimination, by making appropriate and affordable diagnostic solutions available in the right setting and ensuring that diagnostic results are linked to treatment, and provide the basis for continuous drug resistance surveillance

Goals:

Development of new diagnostic tools and accompanying solutions to:

1. Improve TB case detection through accurate tests, enabling patient-centred use at all levels of the health care system, for all populations, including children and those living with HIV, key populations including vulnerable groups, migrants, underserved groups, and develop innovative diagnostic strategies that ensure better outreach to people with TB.
2. Enable timely and effective treatment to reduce mortality and ongoing transmission, and prevent antimicrobial resistance by rapidly and simply detecting resistance to existing and future drugs.
3. Develop novel tests to enable rapid DST and treatment monitoring/test of cure to detect insufficient treatment sooner.
4. Reliably identify individuals at risk of progression from latent TB infection to active TB disease in order to introduce targeted preventive therapy and cut transmission.

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
Ensuring the availability of critical knowledge to enable the development of new diagnostic tools and solutions	Undertake discovery science and build/improve capacity for such discovery research to identify and validate new markers	Support consortia on biomarker discovery using different platforms and approaches targeting: <ol style="list-style-type: none"> a. detection of active TB at point of care b. identification and characterization of mutations c. progression to active disease d. treatment monitoring e. validation of promising biomarkers f. maintenance of a biomarker database 	194.5
	Ensure increased access to clinical reference materials that are critical for the development and validation of new TB diagnostics	Engage in specimen collection, maintenance and expansion of repositories, data management and quality assurance/quality control for: <ol style="list-style-type: none"> a. specimen bank b. strain bank c. paediatric specimen bank d. extrapulmonary TB specimen bank e. specimen bank for treatment monitoring f. data repository for chest X-ray images 	32
	Support assessment of <i>M. tuberculosis</i> genetic variants and their clinical relevance to inform the development of molecular tests for the detection of DR-TB	Develop and maintain a centralized repository of global genomic and clinically relevant data; review for quality and standardization. <ol style="list-style-type: none"> a. Develop a database housing sequence and associated metadata from <i>M. tuberculosis</i> complex and use the data to validate mutations associated with resistance to TB medicines. b. Support contribution of relevant sequencing data by a large number of groups to ensure geographical diversity. c. Maintain the database to sustain efforts. 	31.5

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
	Increase efficiency of the early development pipeline and support decisions before large-scale trials	Conduct studies for evaluation/demonstration studies planned under objective 3 in order to assess potential impact and help plan those studies in the most effective way	25
	Undertake research and consultations to support development of eHealth solutions	Define patient charter/ethical criteria, and build consensus on patient identifiers	1.5
Total Objective 1 – Addressing knowledge gaps			284.5
Developing a portfolio of new diagnostic tools coupled with a package of accompanying solutions to ensure that results translate into patient treatment	Develop tests and solutions for the diagnosis of active TB at the point of care in all patient populations, including children and people living with HIV	Support test development, technical and clinical validation during development of: <ul style="list-style-type: none"> a. smear-replacement tests and solutions b. biomarker-based non-sputum tests and solutions c. triage referral tests and solutions 	142.5
	Develop tests and solutions for detection of drug resistance	Support test development, technical and clinical validation during development of: <ul style="list-style-type: none"> a. next-generation DST at peripheral levels b. DST for new and repurposed medicines and new drug regimens including MIC testing where relevant c. next-generation sequencing (NGS) directly from sputum 	60.5
	Develop tests and solutions for predicting the risk of disease progression	Endorse and revise target product profiles (TPPs). Conduct test development, and technical and clinical validation during development, including validation and qualification of immune activation biomarkers	33
	Develop tests to support syndromic approaches to help differentiate between pathogens and reduce antibiotic overtreatment	Validate and qualify suitable biomarkers for syndromic tests for patients with respiratory symptoms on first visit to primary health care services in order to help differentiate between pathogens, providing a clinically actionable answer	29
	Develop tests and solutions for treatment monitoring/ test of cure	Develop a TPP. Conduct test development, and technical and clinical validation during development, including molecular candidates, and validate and qualify suitable biomarkers	9
	Develop eHealth and connectivity solutions to facilitate patient access to tests listed above	Endorse and revise TPPs. Integrate connectivity in diagnostic technologies, and develop eHealth applications and aggregation platforms	8
	Total Objective 2 – Development of a portfolio of new tests and solutions		

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
Evaluating the portfolio of new diagnostic tools and solutions, including new detection strategies, as well as alternative approaches to case finding, optimized use, and innovative delivery mechanisms; demonstrating patient benefit and predicting likely impact within the entire health system	Conduct evaluation in clinical trials and demonstration studies for new tests and solutions identified above, as well as for syndromic approaches	Carry out the following: <ul style="list-style-type: none"> a. Evaluation tests for active TB and for DST (MDR-/XDR-TB) b. Demonstration studies of TB tests and DST c. Demonstration studies of tests targeting paediatric TB d. Demonstration studies of tests targeting extrapulmonary TB e. Evaluation and demonstration of syndromic approaches f. Demonstration studies of eHealth solutions and platform for connected diagnostics 	94.5
	Predict patient impact from the use of improved diagnostics on TB detection rate, transmission and mortality	<ul style="list-style-type: none"> a. Develop mathematical modelling b. Conduct impact and cost-effectiveness studies to evaluate new technologies and innovative strategies/approaches 	70
	Conduct market analysis and estimate potential for new diagnostics	Update and expand existing market assessments	2
Total Objective 3 – Evaluation, demonstration and impact			166.5
Ensuring that fully validated new diagnostic tools and solutions are widely available and appropriately used in endemic countries	Roll out new tools and solutions	Procure devices and consumables for the roll-out of at least one new technology to support the detection of active TB in 90% of new cases and drug resistance in 100% of cases in high-risk groups	2,300
	Strengthen laboratory capacity for appropriate scale-up of new tools	<ul style="list-style-type: none"> a. Training (coordination, development of tools, sessions, training supervisors, specimen transfer) b. Quality assurance and accompanying measures c. Ongoing assistance d. Training assistance for supply management aspects 	228
	Ensure patient-centred diagnosis and decentralization of testing	<ul style="list-style-type: none"> a. Diagnostic referral system (sample transportation, results delivery to patients/clinic, follow-up with patients) b. m/eHealth solutions/transmission of results c. Incentive systems for patients to compensate for time required for diagnosis 	77
	Integrate TB/HIV laboratory services (TB testing in HIV settings), as well as screening for comorbidities such as hepatitis	Conduct demonstration projects and operational research on how the viral load test could be used as a predictor to screen for TB	24

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
	Ensure private sector integration	<ul style="list-style-type: none"> a. Incentives for the private sector to use endorsed tools b. Laboratory strengthening and external quality assurance for tools in use in the private sector c. Scale-up of models such as IPAQT and JEET 	23
	Maintain speed of national policy change and in-country regulation processes	<ul style="list-style-type: none"> a. Harmonize regulatory processes in problematic countries: China, Russian Federation, Brazil to some extent b. Support national policy change and adoption (local cost-effectiveness and validation studies) 	33
	Sensitize stakeholders (NTPs, ministries of health, technical, procurement and funding agencies, patient community representatives)	Coordinate with advocacy groups; organize workshops with NTPs, ministries of health, technical procurement and funding agencies, and patient representatives	10
	Conduct operational research on how best to deliver diagnostic services in routine programmatic settings to ensure a patient-centred approach, and to estimate costs and resources used by NTPs	Conduct studies covering different test categories and scenarios, as well as different settings, i.e., low/high MDR, low/high HIV, different geographies, TB infection test & treat target groups, strategies for contact-tracing	30
	Scale up manufacturing and other market interventions to bring price down	Invest in commercialization and successful scale-up	75
	Introduce new drug DST and DST for additional group C drugs in countries	Introduce appropriate testing strategies and protocols, and external quality assurance for phenotypic testing and molecular detection, including DST for new drugs, revision of critical concentration when necessary, and gathering the necessary knowledge to design and implement next-generation targeted sequencing	34
	Expand sequencing capacity in countries as of 2022	Implement capacity to perform NGS at reference laboratory level, and provide training and support in data analysis. Establish a mechanism to use the supranational reference laboratory capacity as the main driver to provide this training and long-term support	20
Total Objective 4 – Availability and appropriate use of new tests (inc. roll-out)			2,854
Without roll-out			73
TOTAL FUNDING REQUIRED			3,587 (with roll-out) 806 (without roll-out)

TABLE 6.4: NEW VACCINES STRATEGIC FRAMEWORK 2018–2022

Vision:

To develop new, more effective vaccines that will safely prevent TB in all age groups and populations

Goals:

Development of new diagnostic tools and accompanying solutions to:

1. Prevent TB disease and interrupt transmission through the development of new vaccines to prevent infection, progression, reactivation and/or reinfection
2. Incorporate and consider access strategies throughout the TB vaccine development process
3. Further strengthen community engagement in TB vaccine R&D

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
Continuing to advance the clinical pipeline of TB vaccine candidates	Advance candidate and candidate concepts through clinical trials, utilizing portfolio management and common stage-gating criteria	Initiate Phase III trial of M72/AS01E vaccine candidate	1,250
		Continue to support vaccine candidates through the clinical pipeline and initiate new Phase I/IIa/IIb trials on vaccine candidates that meet criteria	
	Explore and implement novel Phase II clinical trial designs to identify the most promising vaccines as early as possible in development and optimize use of resources	Conduct trials using prevention of infection and prevention of recurrence study designs	75
	Ensure sufficient capacity to support large-scale clinical trials	Scale up manufacturing to support large-scale (Phase IIb/III) clinical trials	500
		Expand clinical trial and laboratory capacity in different regions to conduct clinical trials at GCP standards	
	Conduct studies to assess prevalence and incidence of relevant TB vaccine trial endpoints in populations to be involved in clinical efficacy trials	Conduct incidence and prevalence of TB infection studies; incidence of disease studies; and cross-sectional prevalence of disease studies in multiple regions	25
Total Objective 1 – Clinical pipeline			1,850
Enhancing knowledge through experimental medicine	Develop and test a human challenge model to speed TB vaccine R&D	Support a consortium to advance the human challenge model through development and preclinical phase, and initiate clinical phase	40
		Conduct NHP challenge studies to determine correlates of protective immunity	150
	Complete human studies in parallel with nonhuman primate (NHP) challenge studies in order to learn about protective immune responses	Compare results from NHP studies with those in human efficacy trials (and back-translate for model verification)	
	Test key hypotheses about protective immune responses	Conduct multiple experimental medicine studies to test different hypotheses	100
Total Objective 2 – Experimental medicine			290

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
Increasing emphasis on early-stage and discovery research	Identify immune correlates of protection and disease Identify novel vaccine targets	Identify immune mechanisms and correlates through preclinical comprehensive host response analysis	60
		Integrate biomarker discovery into all Phase IIb and Phase III studies	100
		Explore different mechanisms of protective immunity (e.g., mucosal, alternate cellular targets, innate immunity, and humoral immunity)	40
	Investigate new approaches to mount an effective response	Conduct studies of unconventional immune cells Conduct studies of humoral immunity Improve formulation and antigen delivery through adjuvant and vector development (Note: robust and scalable) Ensure more optimal delivery, e.g. by exploring unconventional routes of vaccine delivery	100
Total Objective 3 – Early-stage and discovery research			300
Improving animal models	Develop and optimize fit-for-purpose animal models to also allow assessment of vaccine efficacy in immunologically primed and/or latently infected individuals or under conditions of coinfection or comorbidity in order to find signals of prevention of infection and/or recurrence of disease or blockade of natural transmission	Enhance the infrastructure and diversity of the portfolio of modalities for preclinical stage and priority gating of candidates; qualify and verify models by benchmarking against clinical signals	150
Total Objective 4 – Animal models			150
Improving preclinical and clinical readouts	Standardize reagents, harmonize assays and benchmark relevant signals by forward- as well as back-translation/ verification between preclinic and clinic	Gather stakeholder input and come to consensus on path forward	1
		Continue to expand on programmes to provide reagents to laboratories and research facilities	30
		Develop necessary assays based on stakeholder consensus	40
Total Objective 5 – Reagents and assays			71
Laying the groundwork for adolescent and adult vaccination campaigns	Conduct strategic access and implementation research	Study cost-of-goods, TB cost-effectiveness, full value proposition, health economic assessment, country vaccine readiness, and vaccine landscape	12
Total Objective 6 – Conduct strategic access research			12

Objective	Milestone	Major Activities	Funding Required 2018–2022 (US\$ Millions)
Engaging communities in TB vaccine R&D	Strengthen community engagement in research	Ensure that clinical trials have community advisory/engagement plans and involve community representatives in the design, conduct and dissemination of research	90
		Vaccine developers actively engage community stakeholders in the R&D process from early-stage research to clinical trials and licensure	
Total Objective 7 – Community engagement			90
TOTAL FUNDING REQUIRED			2,763

Progress in the R&D of new tools

Significant progress has been made in the development of new tools since the last Global Plan was published in 2015. These advances have been made possible mostly through sustained research funding to academic, non-profit organizations, and government-supported laboratories, alongside private sector contributions to research pipelines. Key milestones and progress for new tools are summarized below.

BOX 6.1:

THE NEW 1HP REGIMEN SHORTENS TB PREVENTIVE THERAPY TO ONE MONTH

No TB elimination scenario is realistic without a major advance in TB prevention. Yet, with the notable exception of South Africa, TB prevention has been a persistently neglected aspect of TB care in high-burden countries. The neglect of TB prevention as a core strategy must end.

In addition to exciting advances in TB vaccine development, research on TB prevention has led to the recent development of effective regimens that are shorter in duration and easier for people living with TB infection to complete. The shortest prevention regimen available

today is 1HP, a daily dose of rifapentine and isoniazid taken for four weeks. A Phase III clinical trial involving 3,000 participants over the age of 13, all of whom were living with HIV, found that 1HP performed just as well as nine months of isoniazid, which has long been the standard for TB preventive therapy.¹ One of the key challenges to overcome in scaling up access to shorter TB preventive regimens is in ensuring the equitable availability and affordability of rifapentine in all countries.

1 Swindells S, Ramchandani R, Gupta A, et al. One month of rifapentine plus isoniazid to prevent HIV-related tuberculosis. *N Engl J Med*. 2019;380:1001–11. doi:10.1056/NEJMoa1806808

New vaccines

- ✦ TB vaccine research is at its most promising stage in decades. As of August 2019, at least 14 candidates are in clinical trials, seven of which are being tested in Phase IIb or Phase III trials; numerous other candidates are in preclinical and earlier stages of development.¹
- ✦ Results from a Phase IIb efficacy trial of vaccine candidate M72/AS01E demonstrated for the first time that a vaccine can protect adolescents and adults with latent TB infection from developing active TB disease.
- ✦ Results from the first Phase IIb TB vaccine clinical trial using a prevention of infection trial design indicated that BCG revaccination may protect high-risk, uninfected populations from TB infection.
- ✦ Novel vaccine candidates CMV-TB and intravenous and mucosal BCG demonstrated unprecedented protection in NHP models.
- ✦ Elucidating the roles of trained innate immunity and mucosal immunity has enhanced our understanding of host protective immune responses (how vaccines might induce protection).
- ✦ Good Participatory Practice guidelines for TB vaccine trials were launched in 2017, and an active network of community engagement leads at clinical trial sites has been developed.

1 Global tuberculosis report 2019. Geneva: World Health Organization; 2019. https://www.who.int/tb/publications/global_report/en/

New medicines

- ✦ In 2016, WHO published new guidelines for a standardized, shorter course treatment for MDR-TB.²

2 WHO treatment guidelines for drug-resistant tuberculosis. 2016 update. Geneva: World Health Organization; 2016. <https://apps.who.int/iris/bitstream/10665/250125/1/9789241549639-eng.pdf>

BOX 6.2:

THE POTENTIAL OF FUJILAM AS A POC DIAGNOSTIC TEST

Fujifilm's SILVAMP TB LAM, or FujiLAM, is the first of a new generation of LAM tests for detecting TB. Testing is done using a urine sample, which is easy to collect from people of all ages. Lipoarabinomannan, or LAM, is a molecule produced by TB bacteria to help them colonize the body by deactivating the white blood cells produced by the immune system. FujiLAM is not the only diagnostic test that detects the presence of LAM, but it has been shown to be significantly better at detecting LAM than the LAM test previously recommended by WHO for diagnosing TB in people living with HIV. In a comparison study published in 2019, FujiLAM was 70% effective at detecting LAM versus 42% for the previously recommended LAM test, compared to a reference standard using the sputum-based Xpert MTB/RIF test.¹ Test results take less than an hour, and the test can be used by health care workers with minimal training. No complex instruments are involved.

Further testing is needed to assess FujiLAM's potential as a POC diagnostic test for TB. The test's greatest potential is in serving individuals who have difficulty producing sputum, particularly children, health facility inpatients and people living with HIV who are more severely ill. Looking forward, the introduction of a LAM test that is just as sensitive as currently available sputum-based tests would be transformative for TB diagnosis.

1 Broger T, Sossen B, du Toit E., et al. Novel lipoarabinomannan point-of-care tuberculosis test for people with HIV: a diagnostic accuracy study. *Lancet Infect Dis.* 2019;19(8):852–61. doi:10.1016/S1473-3099(19)300001-5

- ✦ At least eight new chemical entities have been advanced into early advanced pre-clinical and clinical development.
- ✦ Dozens of new essential drug targets have been identified and are being explored.
- ✦ One new medicine, pretomanid, has been approved by the U.S. FDA for use in combination with bedaquiline and linezolid for treatment-intolerant or treatment non-responsive MDR-TB and XDR-TB.
- ✦ Promising results from a Phase III trial indicated that a one-month treatment of

rifapentine and isoniazid was noninferior to nine months of isoniazid for the treatment of TB infection in people living with HIV.

New diagnostics

- ✦ By 2020, it is expected that up to 18 diagnostic products may be sufficiently advanced to undergo review by WHO.
- ✦ In 2019, for the first time, WHO published a Model List of Essential In Vitro Diagnostics. This landmark development signals the vital importance of linking use of medicines with diagnostic tests to advance the UHC agenda.
- ✦ The Fujifilm SILVAMP TB LAM test has shown promise, following an encouraging diagnostic accuracy evaluation study. This test is one

of several next-generation TB LAM tests that are being developed for broader use in the general population, regardless of HIV status, and for use in children. Research in this field has evolved, and there is growing recognition that LAM is detectable in all TB patients, potentially allowing for a true point-of-care (POC) diagnostic test for all.

- ✦ Indian company Molbio Diagnostics has developed a machine called Truenat™, which uses nucleic acid amplification technology (NAAT) to identify TB, as well as to detect resistance to rifampicin, the most commonly used TB medicine. Cartridge-based (CB-) NAAT is widely used in India and has transformed TB diagnosis by reducing the time-to-result from months to hours, allowing patients to start treatment without delay.

BOX 6.3:

THE M72 VACCINE TRIAL ADVANCES VACCINE RESEARCH

Currently, there is no TB vaccine approved for use in adults living with TB infection. But, in a Phase IIb clinical trial, the M72/AS01E vaccine – more commonly known as M72 – safely provided protection for 50% of 3,573 adults who were already infected with *M. tuberculosis*. In this case, protection means that the vaccine prevented those adults living with TB infection from developing active TB disease. Modelling shows that a vaccine providing this level of protection has the potential to avert tens of millions of new TB cases and prevent millions of deaths. Further evaluation is needed to define the potential impact with more precision. The trial results showed that it is possible to develop a new vaccine that improves the body's ability to control TB infection and prevent people from getting active TB disease.¹ Given the sheer numbers of people living with TB infection, such a vaccine has the potential to provide a widespread public health benefit and be transformational in TB prevention.

The M72 Phase IIb clinical trial was conducted in Kenya, South Africa and Zambia among HIV-negative adults. The study was sponsored by GSK and conducted in partnership with Aeras/IAVI with funding from the Bill & Melinda

Gates Foundation, the Department for International Development (DFID) in the UK, the Directorate General for International Cooperation in the Netherlands, and the Australian Agency for International Development. Additional investment is needed to advance the M72 vaccine towards licensure and implementation through further research and testing.

The results of the M72 Phase IIb trial mark a watershed moment in the development of new, more effective vaccines to prevent TB, and late-stage evaluation of this vaccine candidate must be supported. However, it is likely that more than one vaccine will be necessary to end the TB epidemic, as vaccine protection will likely vary among different ages, populations (e.g., those with or without coinfections, different host genetics) and stages of infection. We must continue to improve vaccine efficacy and explore alternative routes of administration. Therefore, it is imperative to continue to invest in the development of other candidates in the clinic, a robust preclinical pipeline, and early-stage research on innovative approaches to vaccine development.

¹ Tuberculosis research funding trends 2005–2017. New York: Treatment Action Group; 2018. <http://www.treatmentactiongroup.org/content/tbrd2018?eType=EmailBlastContent&eld=-Zdac4161-dc99-43a2-9447-4d18aeb4c8ac-overlay-context=content/tbrd2018>

BOX 6.4:

THE WHO GLOBAL STRATEGY FOR TB RESEARCH AND DEVELOPMENT

As this Global Plan update went to press, WHO was in the process of following through on the 71st World Health Assembly's call to develop a new Global Strategy for TB Research and Development. The strategy is intended to be an overarching guidance document with a set of evidence-based recommendations. Its main goal is to provide all UN Member States with a framework of interventions aimed at removing barriers in TB research and innovation. The strategy's target audience is primarily ministries of health, science and technology, finance and education. In the spirit of fast-tracking efforts to end TB, the strategy also makes the case for a unified and aligned response in which key relevant national and international partners and TB affected communities undertake the investments and partnerships necessary for accelerating innovation.

THE STRATEGY HAS FOUR OBJECTIVES:

1. Create an enabling environment for TB research and innovation.
2. Increase financial investments in TB research and innovation.
3. Promote and improve approaches to data sharing.
4. Ensure equitable access to the benefits of research and innovation.

This Global Plan update complements the new Global Strategy for TB Research and Development by providing a framework that identifies specific priority areas for TB R&D, including proposed "off-the-shelf" research projects that can be initiated with available funding, as well as a framework through which countries can close the current US\$ 1.3 billion R&D funding gap.

✦ NGS refers to sequencing technologies that can rapidly process millions of DNA sequences in parallel to decode the genome of a person or bacterium in order to find genetic mutations that are associated with drug resistance. This means that a comprehensive drug-resistance profile can be effectively identified for accurate diagnosis and management of DR-TB. In the last three years, NGS has been successfully used for surveillance of drug resistance in TB, and in 2018, WHO published a technical guide on the use of NGS technologies for DR-TB detection.³

3 Technical guide on next-generation sequencing technologies for the detection of mutations associated with drug resistance in *Mycobacterium tuberculosis* complex. Geneva: World Health Organization; 2018. https://www.who.int/tb/publications/2018/WHO_technical_guide_nextgen_sequencing/en/

Priority “off the shelf” research projects

The Stop TB Partnership’s Working Groups on New TB Vaccines, New TB Diagnostics, and New TB Drugs (together, the New Tools Working Groups) have identified the following “off the shelf” research projects that research funders can support. These projects are highlighted because they would significantly advance the state of TB R&D and could be initiated quickly.

FIGURE 6.1: OFF-THE-SHELF RESEARCH PROJECTS: DIAGNOSTICS

TITLE: DECENTRALIZED NEXT-GENERATION SEQUENCING (NGS) FOR AFFORDABLE, SCALABLE AND RAPID TB DRUG-SUSCEPTIBILITY TESTING (DST)

RATIONALE: NGS refers to sequencing technologies that can rapidly process millions of DNA sequences in parallel, to decode the genome of a person or bacterium and find genetic mutations that are associated with drug resistance – which means that a comprehensive drug resistance profile can be effectively identified for accurate diagnosis and management of drug resistant TB. It is a technique that is already well-established to inform personalized treatment decisions in oncology.

THE PROJECT: Decentralized NGS based solutions below the reference level i.e. bringing NGS workflows closer to the patient. This will involve late stage development of decentralized products/platforms or workflows along with validation and clinical evaluation.

INVESTIGATORS: A team-based approach that integrates academia and industry.

ESTIMATED COST: US\$25 M

TITLE: A TEST THAT PREDICTS PROGRESSION FROM INFECTION TO TB DISEASE (INCIPIENT TB TEST)

RATIONALE: An ideal test of TB disease progression would differentiate the various stages from infection to active TB, and may detect the presence or absence of incipient TB (defined as the prolonged asymptomatic phase of early disease during which pathology evolves, prior to the clinical presentation of active disease). Current commercially available diagnostic tests—the tuberculin skin test and IFN- γ release assays—are insufficient in their ability to predict which infected individuals will progress to disease, due to the fact that they detect a memory immune response.

THE PROJECT: A large clinical trial using a test aligned with the WHO TPP for incipient TB in an at risk population where trial participants are stratified for treatment based on incipient TB test score.

INVESTIGATORS: Clinical trial experts.

ESTIMATED COST: US\$40 M

TITLE: A BIOMARKER BASED TEST

RATIONALE: A more sensitive point-of-care non sputum-based test to replace smear microscopy for detecting pulmonary TB that is easy to perform and has limited operational requirements.

THE PROJECT: Developing a next-generation biomarker based test for broader use in the general population independent of their HIV status, and for use in children.

INVESTIGATORS: Product developers, academia and clinical trial experts.

ESTIMATED COST: US\$10 M

FIGURE 6.2: OFF-THE-SHELF RESEARCH PROJECTS: MEDICINES

TITLE: MONITORING AND PHARMACOVIGILANCE FOR THE INTRODUCTION OF NEW TB MEDICINES

RATIONALE: To assure that we can appropriately treat patients and detect the emergence of resistance to new TB medicines, and that practical approaches to the development of standardized, laboratory and POC DST can be implemented. These are critical to properly design clinical trials and to create surveillance systems at the country level.

INVESTIGATORS: Experts from sponsoring companies or not-for-profit PDPs working with diagnostic experts and hospital-based laboratorians to develop DST data for single drugs and combinations of drugs.

ESTIMATED COST:
US\$50 M

THE PROJECT: Support R&D of agar, liquid-based assays, or newer technologies to rapidly assess effective plasma concentrations of drugs and develop data for resistance monitoring in affected countries.

TITLE: PRECLINICAL TESTING OF NEW DRUG COMBINATIONS TO DETERMINE OPTIMAL SYNERGY IN NEW REGIMEN DEVELOPMENT

RATIONALE: With the increasing number of new candidate compounds, identifying the optimal dosages and combinations for regimen development will require careful assessment of efficacy in preclinical tests prior to evaluations in humans.

INVESTIGATORS: A consortium of scientists with drug testing expertise in test tube and animal models of infection working with regulatory agencies to define useful combinations.

ESTIMATED COST:
US\$60 M

THE PROJECT: Form a collaboration among drug developers to share information and organize laboratory evaluations based on prior testing data to compare combination effects.

TITLE: EVALUATION OF NEW REGIMENS FOR SHORTENING THERAPY IN BOTH DS- AND DR-TB

RATIONALE: A coordinated network of clinical trial sites throughout the world should be established for systematic conduct of Phase II/III efficacy trials of new regimens with shorter durations of therapy. This would support promising combination treatments evaluated in a systematic fashion without duplication of effort.

INVESTIGATORS: Physicians, health care workers, statisticians, data centres, hospital laboratories, and regulatory agencies working in a cooperative framework to advance new medicines.

ESTIMATED COST:
US\$200 M

THE PROJECT: A network of clinical investigators with trial sites throughout the globe working in a concerted fashion to test newer ideas for treatment.

FIGURE 6.3 OFF-THE-SHELF RESEARCH PROJECTS: VACCINES

TITLE: DEVELOP AND REFINE PRECLINICAL MODELS THAT REFLECT THE FULL SPECTRUM OF MTB INFECTION

RATIONALE: The use of animal models in preclinical evaluation of potential vaccine candidates is a necessary and important step to determining if a vaccine candidate may be effective in humans, before entering human clinical trials. However, although the most commonly used animal models for TB simulate the control of infection once established, they fail to model many aspects of human infection. More refined, “fit for purpose” animal models that better reflect Mtb infection and progression to disease in humans are needed to support and accelerate preclinical and early stage vaccine development and advance the most promising candidates into human trials.

THE PROJECT: Develop animal models that better predict vaccine effect in humans and develop the necessary tools to enable both evaluation of novel vaccines and identification of correlates of protection.

INVESTIGATORS: A multi-team approach with investigators who have the ability to coalesce different talents and skills.

ESTIMATED COST: US\$100 M

TITLE: DEVELOPING CONTROLLED HUMAN CHALLENGE MODELS FOR TB VACCINE EFFICACY EVALUATION

RATIONALE: Controlled human challenge models, which involve intentionally infecting healthy adult volunteers with weakened strains of a pathogen to assess a vaccine’s ability to protect against it, have been pivotal in accelerating vaccine development for other major infectious diseases, such as malaria, RSV and influenza, as they enable early, small-scale human testing of a vaccine’s protective ability before commencing lengthy, expensive, large-scale clinical trials. A controlled human challenge model for TB would be a valuable addition to the toolbox to establish the conditions for safe infectious challenging of humans for surrogate vaccine efficacy evaluation.

THE PROJECT: Develop the tools for controlled human challenge tests, including safe mycobacterial reporter strains and experimental medicine protocols for infectious challenge, follow up and readout of bacterial replication/persistence in the context of investigational human vaccination.

INVESTIGATORS: Multi-disciplinary team approach to include vaccinologists, clinical TB experts, molecular bacteriology, and human immunology.

ESTIMATED COST: US\$40 M

TITLE: LAYING THE EPIDEMIOLOGICAL FRAMEWORK TO PREPARE FOR LATE STAGE TB VACCINE DEVELOPMENT

RATIONALE: Late stage vaccine evaluation requires populations in which ongoing Mtb transmission and disease occurs at a frequency that would allow for the design of cost-effective efficacy trials. To properly design and size efficacy trials, accurate estimates of TB infection and disease incidence and prevalence in the target populations are necessary. The conduct of these epidemiologic studies also helps to enhance site capacity and prepare sites and staff for the conduct of subsequent efficacy trials according to high Good Clinical Practice and regulatory standards.

THE PROJECT: Conduct cross-sectional incidence and prevalence of TB and HIV infection and TB disease studies at up to 40 clinical sites in Southeast Asia, Eastern Europe, South America and Sub-Saharan Africa to ensure capacity for design and conduct of TB vaccine efficacy trials.

INVESTIGATORS: A consortium of investigators with epidemiological expertise, and country level support, working in collaboration with vaccine trial sponsors and clinical operations staff.

ESTIMATED COST: US\$25 M

Basic science research

M. tuberculosis is the pathogen that causes TB. The mechanisms by which *M. tuberculosis* causes human infection are still incompletely understood.⁴ In order to understand the most promising approaches to discovering new TB diagnostics, medicines and vaccines, researchers would benefit greatly from understanding more about the TB bacillus, how it interacts with a living body, and how the body mobilizes a protective immune response.

Some of the most urgent areas for basic science research include understanding more about how TB infection progresses to disease, how to predict the risk and stages of disease progression based on biomarkers,⁵ and how to more reliably and easily know when a person has been cured through treatment. Advancing TB basic science also requires support for new infrastructure, including biorepositories, i.e., physical facilities for storing, along with the means for collecting, processing and distributing, specimens that are used for scientific research.

The Global Plan estimates that US\$ 400 million is needed annually to significantly advance TB basic science research, which is in addition to the over US\$ 2 billion needed annually to advance TB R&D pipelines. Basic science research is typically conducted by academic institutions, industry and public-private partnerships, which rely in a large part on public funding. Funds dedicated to basic science will promote innovation, advance our knowledge of TB and enhance our ability to develop new tools to prevent, diagnose and treat it. Moreover, adequate research funding will have the added benefit of attracting and retaining a new generation of scientists to the field of TB research.

4 Grundner C. To fight tuberculosis, fund basic research. PLoS Biol. 2018;16(9):e3000037. doi:10.1371/journal.pbio.3000037

5 A biomarker is a measurable substance inside the body that reliably indicates the presence of TB infection and/or TB disease. LAM, discussed earlier in the chapter, is an example of a TB biomarker.

Paediatrics and key populations

Advancing a research agenda designed to meet the specific needs of children is critical to ending the paediatric TB epidemic. Research efforts directed towards TB in children have focused mostly on finding out how to apply existing tools to diagnose, treat and prevent paediatric TB. However, children have needs that differ from those of adults. For example, children have difficulty producing sputum, making them poor candidates for diagnosis using the rapid diagnostic test Xpert MTB/RIF, which tests sputum. The Stop TB Partnership Child & Adolescent TB Working Group and Treatment Action Group have laid out a detailed list of research priorities for child TB.⁶ Priority investments in R&D include:

PREVENTION: Identify new, shorter and simpler preventive regimens; develop a new vaccine for

infants, children and adolescents that improves on the current BCG vaccine.

6 Treatment Action Group, Stop TB Partnership Child & Adolescent TB Working Group. Research priorities for paediatric tuberculosis. New York: Treatment Action Group; 2018. http://www.treatmentactiongroup.org/sites/default/files/Paediatric_TB_ResearchPriorities_10_8_18_Web.pdf

DIAGNOSIS: Develop novel tests that are not invasive and can be used at the point of care.

TREATMENT: Evaluate the safety and efficacy of new TB medicines in children and adolescents to determine optimal dosing; identify treatment regimens that are shorter and simpler than those currently available; and ensure that TB treatment regimens are available in child-friendly formulations.

Additional research is needed to understand some of the basic characteristics of TB as it affects infants, children and adolescents, including the immune response to infection and associated biomarkers (regular changes that occur

in the body that can be reliably measured and that indicate TB infection and TB disease) that can inform the development of new tools.

It is also important to include other key populations, such as people living with HIV, pregnant women, the elderly, people with or at risk of diabetes, people who are immunocompromised, and at-risk populations such as health care workers, miners, household contacts, prisoners, and others in the R&D of new tools. (Key populations are addressed in more detail in Chapter 3.)

CREATING A RESEARCH-ENABLING ENVIRONMENT

Increase support for research institutions, partnerships and collaborations

It is critical that research institutions be supported to advance TB innovation. Below are examples of institutions and initiatives that are key to accelerating the R&D of new TB tools. Each entity carries out its work through multisectoral collaboration.

PDPs: Product development partnerships (PDPs) remain critical to advancing R&D for new TB tools. PDPs, a type of public-private partnership, are not-for-profit organizations that work through collaborations with private-sector manufacturers, governments, NGOs and academia, and typically pool resources and technical expertise to develop and commercialize new tools. PDPs are especially important for developing new TB tools because traditional market incentives are not powerful enough to drive innovation for TB.

Key TB research entities that operate through a PDP model include the TB Alliance (focused on advancing the research pipeline for new TB medicines), FIND (focused on innovative new diagnostics), IAVI and the Tuberculosis Vaccine Initiative (TBVI) (both focused on new vaccines). While not a PDP, the Critical Path Institute is a public-private

partnership that aims to accelerate the pace and reduce the costs of developing new medical products, including through collaborations such as TB-PACTS, a data platform that curates TB clinical trial data, standardizes them, and makes them publicly available to qualified researchers.⁷

RESEARCH CONSORTIA: The TB Trials Consortium (TBTC) is a collaboration of researchers from the US Centers for Disease Control and Prevention, public health departments in other countries, and various medical centres. TBTC partners conduct clinical, laboratory and epidemiologic research concerning the diagnosis, clinical management, and prevention of TB infection and disease. The

⁷ TB-Platform for Aggregation of Clinical TB Studies [Website]. Dublin: Critical Path Institute. <https://critical-path.org/programs/dcc/projects/tuberculosis/tb-platform-for-aggregation-of-clinical-tb-studies-tb-pacts/>

AIDS Clinical Trials Group (ACTG) supports the largest network of researchers conducting clinical trials in the world, including research sites in resource-limited settings. Research conducted by ACTG partners includes important studies on the use of TB tools in people living with HIV.

BRICS TUBERCULOSIS RESEARCH NETWORK:

BRICS countries have emerged as key global actors in TB innovation. Between 2007 and 2016, the average annual increase in TB research publications from the BRICS countries was nearly double the annual increase in TB research publications across all countries. In 2016, 31% of all TB research publications had a first author from a BRICS country.⁸ The BRICS TB Research Network was established to further develop the base of TB R&D being carried out across Brazil, Russian Federation, India, China and South Africa, and to accelerate the best use of both existing and new interventions in TB care and prevention. The international collaboration builds on new national TB research initiatives, including India's TB Research Consortium, Brazil's National TB Research Strategy, and new TB activities being carried out by South Africa's Strategic Health Innovation Partnerships. With 38% of global TB deaths occurring in the five BRICS countries, the BRICS TB Research Network will need to play a growing role in the discovery and dissemination of new TB tools, both individually and as international collaborators.

THE MEDICINES PATENT POOL (MPP): The MPP is a UN-backed public health organization established to improve access to affordable, quality-assured medicines in LMICs through public health-oriented licensing that covers medicines for HIV, HCV, TB, and other patented essential medicines. The MPP is a potential avenue for public health licensing of existing and new TB medicines. The new licenses, which cover any valid patent and pending patent application, are non-exclusive, sublicensable, worldwide and royalty-free, and allow access to preclinical and clinical (Phase I and Phase IIa) study data and results.

THE LIFE PRIZE: The Life Prize is a concept for collaborative R&D that, when applied to TB innovation, is designed to accelerate the introduction of new TB treatment options. The ultimate aim of The Life Prize is to identify a new TB treatment regimen that can be used to treat all forms of TB, including DR-TB, in one month or less. The Life Prize concept envisions the licensing of promising molecules from commercial manufacturers and other research institutions, and making that pool of molecules available to research institutions that will test them in treatment combinations. The Life Prize also envisions creating a new way of rewarding investment in TB R&D by providing three types of funding and financial incentives:

- Prize funding for research institutions that enter new drug candidates that fulfil pre-defined criteria into clinical trials
- Grant funding to finance the clinical testing of new treatment regimens with the potential to treat all forms of TB
- Funding for the fair licensing of intellectual property and clinical data in order to permit open, collaborative research

In this way, The Life Prize concept envisions reducing the risks and substantial costs that research institutions face with the traditional approach to R&D. To promote access, the concept model also provides a way to separate the cost of investment in R&D from the price and volume of medicine sales in order to facilitate equitable and affordable access. In the UN Political Declaration on the Fight against TB, UN Member States noted The Life Prize as a research platform through which research collaboration for TB can be strengthened.

⁸ Global investments in tuberculosis research and development: past, present and future. Geneva: World Health Organization; 2017. https://www.who.int/tb/publications/2017/Global_Investments_in_Tuberculosis_Research_Investment/en/

Increase site capacity for conducting clinical trials

The most promising new tools for ending TB in LMICs will be those that have been demonstrated to work well in those environments. This requires testing new tools in the environments where they will be most widely used. The challenge, however, is that there is limited capacity in LMICs to conduct the number of necessary clinical trials, particularly as new vaccines, medicines and diagnostics enter larger, late-stage trials.

Barriers typically include a lack of financial and human capacity, ethical and regulatory system obstacles, lack of research environments, including lack of physical research infrastructure, operational barriers and competing demands.⁹

To address these challenges, research funders should work to promote investigator-driven research by local researchers in LMICs, while LMIC governments should invest in strengthening domestic research capacities. Stronger international collaboration is critical to supporting and creating new systems for conducting clinical trials in LMICs.¹⁰ The European and Developing Countries Clinical Trials Partnership

(EDCTP), for example, supports partnerships between European and African institutions and researchers in collaboration with the pharmaceutical industry and like-minded organizations in order to accelerate the clinical development of new or improved interventions to prevent or treat HIV/AIDS, TB, malaria and other poverty-related infectious diseases.

Communities in which clinical trials will be conducted must be fully engaged, as laid out in the Good Participatory Practice Guidelines for TB Drug Trials and the Good Participatory Practice Guidelines for TB Vaccine Research 2017.^{11,12}

9 Alemayhu C, Mitchell G, Nikles J. Barriers for conducting clinical trials in developing countries: a systematic review. *Int J Equity Health*. 2018;17:37. doi:10.1186/s12939-018-0748-6

10 Alemayhu C, Mitchell G, Nikles J. Barriers for conducting clinical trials in developing countries: a systematic review. *Int J Equity Health*. 2018;17:37. doi:10.1186/s12939-018-0748-6

11 Good Participatory Practice: guidelines for TB vaccine research. Rockville: AERAS; 2017. http://www.aeras.org/img/uploads/attachments/1015/good_participatory_practice_for_tb_vaccine_research.pdf

12 Good Participatory Practice: guidelines for TB drug trials. Dublin: Critical Path Institute; 2012. <https://www.cprinitiative.org/downloads/resources/GPP-TB%20Oct1%202012%20FINAL.pdf>

Ensure an efficient and predictable regulatory and policy environment

A frequent obstacle to accessing new tools is the lack of transparency in the national registration process. In the case of medicines, for example, there is often no forum for interaction or discussion between the drug sponsor applicant, regulatory authorities, and communities in terms of the registration process. The present lack of regulatory harmonization has resulted in staggered, country-by-country approval procedures for new tools, resulting in deadly delays.

Country governments should build their capacity to evaluate new tools that have already been tested in other countries, allowing those that are shown to be safe and effective to be imported

for use. WHO-issued guidance can support and expedite country policy-setting and adoption, particularly in countries without rapid regulatory processes. One other potential solution is

to help expedite TB research by streamlining and harmonizing regulatory processes from clinical development to regulatory submission and regional approval.

Sustain a talented field of TB researchers

Ensuring long-term success in TB R&D requires nurturing the field of TB research itself by incentivizing and strengthening the capacity of researchers to focus their efforts on TB innovation, from basic science research through to translational research and clinical trials. Specific efforts should be made to support and increase research in high TB burden countries. The UNESCO eAtlas of Research and Experimental Development (<http://on.unesco.org/RD-map>) provides a visualization of the number of researchers overall per country, demonstrating the disparity in the numbers of researchers in high-income, middle-income and low-income countries.

Training the next generation of young investigators is a top priority – a need that has traditionally been filled by mechanisms such as Wellcome Trust fellowships, National Institutes of Health (NIH) support at the pre- and post-doctoral level, and European Union funding. However, as is apparent from the UNESCO eAtlas, these initiatives alone are not likely to fill this void. Both governmental and nongovernmental funders must recognize this need, and provide support to train and sustain the next generation of researchers. This should include proactive career support and career development activities, providing explicit opportunities for networking and presenting research in local, regional and global research forums.

Partnerships like TDR – a joint effort by UNICEF, UNDP, the World Bank and WHO – provide a model for supporting the training of TB researchers who are working to improve TB care at the systems level in LMICs. Through the Structured Operational Research and Training Initiative (SORT IT) – a global operational research partnership led by TDR in collaboration with the The Union and Médecins Sans Frontières (MSF) – researchers are trained to conduct operational research on their countries' priority challenges, build sustainable operational research capacity, and make evidence-informed decisions

for improving TB programme performance.¹³ Participants perform classroom work, develop a research protocol and application for ethics review, receive training in data management and analysis, design a data analysis plan, write and submit a paper to a peer-reviewed journal, and in some cases develop a policy brief or presentation for policymakers and other stakeholders.¹⁴

Another project, ADVANCE, supported by USAID, is a multi-partner research initiative that increases the involvement of African and Indian researchers in all stages of HIV vaccine R&D.¹⁵ New initiatives along the lines of SORT IT and ADVANCE, applied to TB basic science research and clinical research, would help to ensure the long-term capacity for innovation in all areas of TB research.

13 SORT IT [Website]. Geneva: World Health Organization. <https://www.who.int/tdr/capacity/strengthening/sort/en/>

14 Viney K, Bissell K, Hill P. Building operational research capacity in Papua New Guinea and the Pacific Islands. PHA. 2019;9(S1):S3. doi:10.5888/pha.19.0039

15 Accelerating the development of vaccines and new technologies to combat the AIDS epidemic (ADVANCE). Washington, DC: USAID; 2016. <https://www.usaid.gov/sites/default/files/documents/1864/USAID-ADVANCE-Brief2-508.pdf>

Investing in new tools

TB R&D funding needs

Both public research institutions and commercial developers are investing too little in TB R&D, which is slowing the advancement of the new tools needed to end TB. In the UN Political Declaration on TB, UN Member States recognized the “lack of sufficient and sustainable financing” for TB research and innovation. In response, they committed to “mobilize sufficient and sustainable financing, with the aim of increasing overall global investments to US\$ 2 billion in order to close the estimated US\$ 1.3 billion gap in funding annually for tuberculosis research”.¹⁶

Table 6.4 shows annual TB funding needs for the R&D of new TB medicines, diagnos-

tics and vaccines from 2018 to 2022, including “catch-up” amounts based on the funding gaps in 2016 and 2017. The projected total funding required for 2018–2022 is US\$ 6.8 billion for new medicines development, US\$ 916 million for new diagnostics and US\$ 3.1 billion for new vaccines, totalling US\$ 10.8 billion for the five-year period, or US\$ 2.16 billion annually. These figures do not include the resources needed to roll out new tools, nor do they include the resources needed for basic science research or the operational research required to identify the most effective ways of implementing new tools in various national contexts.¹⁷

¹⁶ Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmontbdeclaration.pdf>

¹⁷ A fuller treatment of recent TB R&D funding trends, including analysis of funding for basic research, operational research, and paediatric TB research, is found in the annual Tuberculosis research funding trends reports produced by Treatment Action Group and the Stop TB Partnership.

TABLE 6.5: ANNUAL FUNDING NEEDS FOR TB R&D (US\$ MILLION)*

Tool	Total Needed 2018–2022	Annualized (per year funding)	Gap 2016/2017	Total Funding Need 2018–2022 + Gap
Medicines	5,710	1,142	1,090	6,800
Diagnostics	806	161	110	916
Vaccines	2,763	553	304	3,067
Total	9,279	1,856	1,504	10,783
Annual funding need:				2,157

*Does not include funding for roll-out

A “fair shares” framework for closing the TB R&D funding gap

The TB R&D funding gap could be filled quickly if countries with the greatest capacity to invest and countries with the most benefit to gain from new TB tools devoted just a small fraction of each of their total gross domestic expenditure on R&D (GERD) to TB. In 2017, only three of the 32 countries reporting more than US\$ 100,000 in TB R&D funding – South Africa, New Zealand and the Philippines – met their fair share of TB R&D funding, considered 0.1% of their overall GERD.¹⁸ If 62 countries – those that make up the G20, plus countries that WHO classifies as having a high TB burden, plus a grouping of the world’s wealthiest countries that are not included in either of the other groups – devoted at least 0.1% of their GERD to TB R&D, they would close the annual funding gap for TB R&D.¹⁹ These so-called fair-share funding targets are considered a minimum of what countries should invest in TB R&D. The GERD framework is one proposal for fulfilling the UN Political Declaration on TB commitment to close the TB R&D funding gap, “ensuring that all countries contribute appropriately to R&D.”

18 Tuberculosis research funding trends 2005–2017. New York: Treatment Action Group; 2018. http://www.treatmentactiongroup.org/content/tbrd2018?eType=EmailBlast-Content&eld=7dac4161-dc99-43a2-9447-4d18aeb4c8ac_-_overlay-context=content/tbrd2018

19 Investing in R&D to end TB: a global priority. New York: Treatment Action Group; 2017. http://treatmentactiongroup.org/sites/default/files/Funding%20target%20brief_final_31Oct.pdf

Innovative financing approaches

In keeping with their commitment, UN Member States should mobilize sufficient and sustainable funding for TB research and innovation by engaging innovative financing mechanisms as one of the means to mobilize new resources. Developing new, innovative sources of funding is critical to diversifying the funding base for TB R&D, as the funding currently available relies heavily on a small number of countries and funding agencies.²⁰

In 2017, Unitaid became the world’s third largest multilateral funder of TB R&D and the fifth largest funder overall.²¹ Unitaid funds late-stage development and addresses market barriers to accelerate the introduction of new tools. The main source of Unitaid’s funding comes from an innovative financing mechanism: a small tax on airline tickets purchased in 10 countries.²² UN Member States have also recognized The Life Prize as a promising innovative financing concept for TB R&D.

The Stop TB Partnership’s Accelerator for Impact (a4i) is a public-sector blended finance impact investment fund to support the next generation of people-centred innovations for TB and global health.

20 Tuberculosis research funding trends 2005–2017. New York: Treatment Action Group; 2018. http://www.treatmentactiongroup.org/content/tbrd2018?eType=EmailBlast-Content&eld=7dac4161-dc99-43a2-9447-4d18aeb4c8ac_-_overlay-context=content/tbrd2018

21 Ibid

22 Cameroon, Chile, Congo, France, Guinea, Madagascar, Mali, Mauritius, Niger, Republic of Korea.

THE FUND WILL FOCUS ON:

- 1 Pivoting the care model to become more digitalized, virtual and on-demand in order to make it as convenient as possible for people to access and receive quality, affordable care;
- 2 Catalysing the rapid roll-out of new TB and global health innovations; and
- 3 Unlocking new funding and capital from both public and private sector investors.

Innovative financing mechanisms hold significant untapped potential for advancing TB R&D. It is now up to national governments, multilateral institutions, and the philanthropic, corporate and financial sectors to partner together and deliver new solutions that harness that potential.

The cost of inaction: what is the result of underfunding R&D?

One way to conceptualize the importance of up-front investment in new tools is to estimate the cost of inaction.²³ In other words, what will the negative consequences be if the world fails to fill the funding gap for TB R&D?

Even using conservative assumptions (see below), the estimated cost of inaction would be tremendous (Figure 6.3).

²³ This inaction is defined as the cost of future TB treatment and lost productivity that would accrue if the world achieved the 2020 milestones of the End TB Strategy by 2022, but failed to make the necessary investments in new tools between 2020 and 2025.

BY 2030, A FIVE-YEAR DELAY IN INVESTMENT IN R&D FOR NEW TOOLS WOULD RESULT IN:

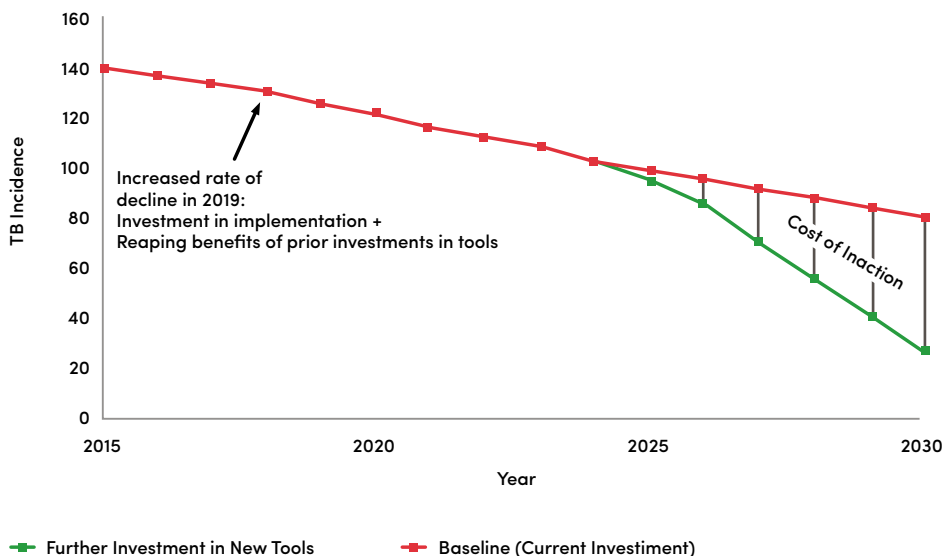
- 1 13.9 million additional people becoming sick with TB
- 2 2 million additional TB deaths
- 3 49.8 million DALYs suffered as a consequence of TB (75.1 million without discounting)
- 4 US\$ 14.2 billion in additional costs for TB treatments alone (US\$ 21.6 billion without discounting)
- 5 US\$ 172 billion in lost productivity (US\$ 259 billion without discounting).²⁴

²⁴ Each disability-adjusted life year (DALY) is valued at per-capita GNI in this scenario.

Thus, the total cost of inaction on TB R&D is estimated to be more than US\$ 185 billion in additional treatment costs and lost productivity. These costs are expected to increase even further beyond 2030. Even a one-year delay in investment after 2020 would carry a tremendous cost: 4.8 million additional people having TB; 670,000 additional TB-related

deaths; US\$ 5.1 billion in added TB treatment costs (US\$ 7.5 billion without discounting); 17.3 million additional DALYs (25.2 million without discounting); and an additional US\$ 60 billion (US\$ 87 billion without discounting) in lost productivity.

FIGURE 6.4: PROJECTED NUMBERS OF PEOPLE DEVELOPING TB WITH NEW TOOLS VERSUS WITHOUT NEW TOOLS



THE COST OF INACTION WAS CALCULATED BASED ON THE FOLLOWING ASSUMPTIONS:

- 1** The annual percentage declines in TB incidence and mortality that were achieved to reach the 2020 milestones by 2022 without new tools would continue through to 2030.
- 2** Five years after the additional investment in new tools (in 2020), the decline in incidence and mortality would increase steadily and to a degree sufficient to achieve the 2030 milestones. The impact of new tools would therefore be only slowly realized over time – with greater impact in 2030 than in 2025.
- 3** The cost of TB treatment would not increase above 2018 levels.
- 4** A 5% annual discount rate was applied to all costs and DALYs, thereby reducing the value of future savings in costs and productivity (although undiscounted costs and outcomes are also presented).
- 5** Health utility losses from TB were assumed to scale with TB mortality, and a standardized conversion was made of 35 years of life lost (YLL) per TB death and 0.35 years of life with disability (YLD) per TB case (the ratios estimated by the 2017 Global Burden of Disease study).²⁵

²⁵ GBD results tool [Data tool]. Seattle: Institute for Health Metrics and Evaluation. <http://ghdx.healthdata.org/gbd-results-tool>

Advocating for new TB tools

Accelerating the pace of TB innovation is going to take stronger, more coordinated advocacy. Using the Global Plan and the WHO Global Strategy for TB Research and Innovation, advocates – including TB researchers, civil society, affected communities and survivors – can join together in advocating for more resources and better policies that are needed to close the US\$ 1.3 billion TB R&D funding gap, create an enabling environment for developing new tools, and ensure equitable access to the benefits of TB research and innovation.

Advocacy is key to making an evidence-based case for governments to get more deeply involved in inherently risky research and to steer resources towards efforts that have the greatest potential for ending the epidemic in high-burden countries; for meeting the needs of patients and TB affected communities; and for creating clear and reliable pathways for new tools to enter into widespread use. Government ministries and national legislatures remain the most important primary audiences for advocacy; the following actions will help to nurture a TB research advocacy coalition that is better prepared to engage these entities.

Strengthening research literacy among affected communities and advocates

Just as it is critical to nurture the next generation of researchers, it is also important to nurture research advocates who can work with the research community to mobilize R&D funding and help create an enabling environment for TB innovation. As part of this process, it is critical to build the research literacy of TB survivors and affected communities as well as global health advocates. Strengthening advocacy for new TB tools requires more routine knowledge-sharing and coordination between the TB research and advocacy communities. Research literacy training opportunities and materials need to be provided to civil society and affected communities so that they are informed, educated and engaged throughout the research process. New research studies need to be routinely shared with advocates who can help translate findings and recommendations into advocacy messages and to share important studies with decision makers

and the news media. Advocacy funders should consider additional grantmaking that supports strategic communications and advocacy training for TB researchers, as well as scientific literacy training for TB advocates and survivors.

Strengthen the research community's role in advocacy

Scientists can speak credibly not only about new research findings, but also about the barriers and opportunities they face in TB innovation. Scientists within communities of practice should work together more proactively, taking advantage of such forums as the Stop TB Partnership's New Tools Working Groups and the membership structure of The Union, for example, in order to advocate for research funding and for the policy change needed to create enabling environments for research. With larger cadres of advocacy-savvy TB researchers, advocacy organizations can find more opportunities to enroll researchers in advocacy campaigns and policymaker outreach.

Engage TB survivors as partners in advocacy

Community-driven advocacy has become an important way to increase investment in scientific research and access to new tools, and to progress the advancement of human rights in the TB response, particularly for the most vulnerable, underserved and at-risk populations.

Community advocates play a critical role in research. They are uniquely placed to document, monitor and analyse the intersectionality between social determinants of health

and effective TB responses. Their increased engagement stems from community demands for self-determination and meaningful participation in the TB response.

One model for community advocates' engagement in research is through community-based participatory research (CBPR). This model is grounded in principles of collaborative and equitable community engagement in research and shared ownership of research issues, processes and products.

Global community networks (e.g., Global Coalition of TB Activists, TBpeople) and regional community networks (e.g., ACT Asia-Pacific!, ACT!, DRAF TB, TBEC, We Are TB) have doubled since 2016. Their advocacy was instrumental in securing the targets and commitments of the UN Political Declaration on TB, including the commitments to mobilize sufficient and sustainable financing for R&D and deliver as soon as possible new, safe, effective, equitable, affordable, available vaccines; POC and child-friendly diagnostics; DST; and safer, shorter and more treatment regimens for adults, adolescents and children for all forms of TB disease and infection. TBpeople is partnering with the Stop TB

Partnership and McGill University to demand TB innovation, while re-imagining approaches to TB care for all.

Engage parliamentarians

Members of parliament (especially those sitting on relevant committees responsible for budgeting, health, regulatory, science and technology research, even national defence) must be better educated about the need for new TB tools and the commitments their governments have made to support TB research through the UN Political Declaration on TB. The Global TB Caucus provides the TB research and advocacy communities with an entry point to parliamentary engagement in more than 130 countries.

Expand advocacy efforts beyond ministries of health

Ministries outside of health, including finance, science and technology, labour and regulatory committees, are essential to creating budgetary space and defining the rules and regulations that create a research-enabling environment. Therefore, these actors should be routinely engaged by advocates.

Applying best practices to community engagement throughout the R&D process

Meaningfully engaging TB affected communities is essential to ensuring access to new TB tools. Research institutions should follow best practices for engaging TB affected communities within all research activities and within decision-making bodies and forums. The International Ethical Guidelines for Health-related Research Involving Humans establishes universal principles for engaging communities in research activities, advising that:

“Researchers, sponsors, health authorities and relevant institutions should engage potential participants and communities in a meaningful participatory process that involves them in an early and sustained manner in the design, development, implementation, design of the

informed consent process and monitoring of research, and in the dissemination of its results.”²⁶

²⁶ International ethical guidelines for health-related research involving humans. Geneva: Council for International Organizations of Medical Sciences; 2016. <https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf>

Specifically related to TB, research institutions should consult the Good Participatory Practice Guidelines for TB Vaccine Research and Good Participatory Practice Guidelines for TB Drug Trials, which help to facilitate effective engagement with affected communities and stakeholders at all stages of the research process.^{27,28}

Engaging communities in research also fulfils a key guideline in WHO's *Ethics Guidance for the Implementation of the End TB Strategy*: "Community members should have the opportunity to participate in research beyond their role as potential trial participants. This participation should extend throughout each stage of the research process, from the design and conduct of studies to the dissemination of results."²⁹

Community participants should be from the geographic area where the research is being conducted. They can be a subpopulation among the participants recruited and can include groups within the broader society who have a stake in the outcomes of the research. In the context of geographic areas are communities of people affected by TB, including people with TB, TB survivors and representatives of TB key affected populations such as the urban poor, undocumented migrants, people living with HIV, people who use drugs, and people in prisons. These groups must be engaged and their capacity strengthened as a priority in all aspects of research activities, ensuring that this engagement is human-rights-based, gender-sensitive and people-centred.

Communities should be consulted early in the research process, before a study is even initiated, to inform the research design. Community engagement should then remain ongoing

through established modes of communication between researchers and community members.

There are several established models of effective community engagement in TB research. One of the most common models involves the establishment of community advisory boards (CABs) by research networks and institutions. CABs work to ensure community voices, needs and priorities are reflected at each stage of the research process, from designing studies and conducting trials to disseminating results and working to translate results into policy change.³⁰

Engaging with communities in all aspects of R&D also creates new groups of informed advocates who can effectively communicate the benefits of TB R&D to governments, regulatory authorities, funders and other institutions. People affected by TB, particularly TB survivors, must be engaged as experts in this space.

TB affected communities can play a key role in monitoring the outputs of research, helping to ensure that the benefits of scientific progress are accessible to all people, free from stigma and discrimination, irrespective of how they individually identify or where they live. TB affected communities can also champion enhanced research on the successes and benefits of TB community-based service delivery, advocacy and monitoring for social accountability.

30 DeLuca A, Lessem E, Wegener D, et al. The evolving role of tuberculosis advocacy. *Lancet Respir Med*. 2014;2(4):258–9. doi:10.1016/S2213-2600(14)70035-9

27 Good Participatory Practice: guidelines for TB vaccine research. Rockville: AERAS; 2017. http://www.aeras.org/img/uploads/attachments/1015/good_participatory_practice_for_tb_vaccine_research.pdf

28 Good Participatory Practice: guidelines for TB drug trials. Dublin: Critical Path Institute; 2012. <https://www.cptrinitiative.org/downloads/resources/GPP-TB%20Oct11%202012%20FINAL.pdf>

29 Ethics guidance for the implementation of the End TB Strategy. Geneva: World Health Organization; 2017. <https://www.who.int/tb/publications/2017/ethics-guidance/en/>

ROLLING OUT AND OPTIMIZING ACCESS TO NEW TB TOOLS

Any time lost between the licensure of a new tool and getting it to people in need leads to unnecessary suffering and loss of life. With proper planning and a strategic, evidence-based approach to access and optimization of use, countries can get the most value and benefit from the use of new tools. The following section lays out activities that national governments should undertake to scale up access and understand the most effective ways of deploying new tools within the health system.

Applying access principles to the delivery of new TB tools

The Universal Declaration of Human Rights and the International Covenant on Economic, Social and Cultural Rights uphold the rights of people to enjoy the benefits of scientific progress and its applications. In keeping with these rights, the accessibility of new TB tools needs to be considered from the outset of the R&D process.

The accessibility of new tools is intimately tied to how R&D is financed and conducted, including incentive strategies, policies of research funders, governance of research institutions, and the values, norms and standards that guide R&D. As the UN Political Declaration on TB states, TB R&D should be “needs-driven, evidence-based, and guided by the principles of affordability, effectiveness, efficiency and equity”.³¹ These principles should guide R&D from the earliest point in the R&D process.

While there are important areas of progress, TB R&D has long been underfunded. Given TB’s public health significance as an airborne communicable disease that is responsible for more deaths than any other single infectious agent, where discrimination is both a cause and a consequence of the disease, and where large numbers of people in poor and marginalized populations are chiefly affected, states have an

obligation to promote the development of new diagnostics, treatment regimens and vaccines, including through robust international cooperation, and to ensure access for all.³²

The UN Committee on Economic, Social and Cultural Rights has defined the right to health to include the availability, accessibility, acceptability and quality of health-related goods and services, where:

³² World Health Organization, Office of the United Nations High Commissioner for Human Rights. The right to health: Factsheet No. 31. Geneva: Office of the United Nations High Commissioner for Human Rights; 2008. <https://www.ohchr.org/Documents/Publications/Factsheet31.pdf>

- ⊕ availability requires making health goods and services available in sufficient quantity;
- ⊕ accessibility involves four elements, all of which require attention be paid to how they impact key populations: non-discrimination, physical accessibility, affordability and access to information;
- ⊕ acceptability requires all health facilities, goods and services to be respectful of

³¹ Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. United to end tuberculosis: an urgent global response to a global epidemic. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. New York: United Nations General Assembly; 2018. <https://www.who.int/tb/unhlmonTBDDeclaration.pdf>

medical ethics and culturally appropriate, sensitive to sex and life-cycle requirements, as well as designed to respect confidentiality while improving the health status of people;

- ✦ quality requires goods and services to be scientifically and medically appropriate and of good quality.³³

It is essential that all stakeholders involved in promoting and carrying out TB R&D design and implement their activities in ways that respect, protect and ensure these rights-based principles at every stage in the R&D process, including the delivery of new tools.

33 General comment no. 14, The right to the highest attainable standard of health (article 12 of the International Covenant on Economic, Social and Cultural Rights. Geneva: UN Committee on Economic, Social and Cultural Rights; 2000. <http://docstore.ohchr.org/SelfServices/FilesHandler.ashx?enc=4slQ6QSmIBEDzFEovLCuWIAVC1NkPsgUedPIF1vfP-MJ2c7ey6PAz2gaojTzDjmC0y%2B9t%2BsAtGDNzdEqA6SuP2r-0w%2F6sVBGTpvTSCbiOr4XVFTqhQY65auTFbQRPWNDxL>

BOX 6.5:

ENSURING COUNTRY READINESS TO DELIVER NEW TB VACCINES FOR ADOLESCENTS AND ADULTS

New TB vaccines developed for adolescents and adults are most likely to have the greatest overall impact of any new tool on the global epidemic, but access presents a significant challenge. Without adequate planning and investment, the kinds of new campaigns and programmes that would be needed to roll out a new and widely used TB vaccine could take decades to implement, and the challenges surrounding widespread adolescent and adult vaccination are complex.

Assessing and addressing the gaps in programmes and systems that could hinder the roll-out of a new vaccine requires comprehensive “strategic access” operational research. Various aspects of this research include evaluating cost-of-goods, pricing criteria, TPP cost-effectiveness, country vaccine readiness, and the vaccine landscape. It will also be important to understand the programmatic suitability for prequalification (PSPQ) early in the devel-

opment process, so that licensed products are likely to be preapproved for procurement by multilateral institutions like Gavi and UNICEF.

It will also be important to identify and advocate for programmatic approaches that could best reach adolescents and adults, such as potentially administering a TB vaccine through the same platform used for administering the human papillomavirus vaccine to young teenagers, and in line with a ‘life course’ vision of the future of immunization programmes.

Global access to new TB vaccines must integrate evidence, technology, policy, funding and politics, with end-users, communities, physicians and NTPs actively engaged in the process. These activities will help to ensure the alignment and smooth transition of new vaccines from R&D to worldwide markets in order to achieve maximum benefit for individuals and optimized impact on the epidemic.

Expanding the use of operational research

Operational research involves a wide range of research activities that are used to investigate strategies, interventions, tools and knowledge that can improve the performance of health systems and programmes.³⁴ Despite improvements in recent years, large implementation gaps still exist in the delivery of quality-assured, people-centred TB care. Scaling up country-level capacity for operational research is essential to close those gaps and to reach universal access to TB prevention, diagnosis and treatment. Operational research is also necessary to understand how best to introduce and scale up new tools within various populations, and how best to combine medical care with social-service support in order to achieve the best treatment outcomes and better address the underlying factors that put people and communities at risk of TB.³⁵

Research funders should allocate specific funding for operational research, directing it as a priority towards initiatives that will build the evidence base for closing implementation gaps in LMICs.

To be sustainable, operational research capacity needs to be more routinely embedded within NTPs, with resources allocated through annual budgets.

34 Zachariah R, Harries AD, Ishikawa N, et al. Operational research in low-income countries: what, why, and how? *Lancet Infect Dis* 2009;9(11):711–7. doi:10.1016/S1473–3099(09)70229–4

35 Global strategy for TB research and innovation. Geneva: World Health Organization; in press.

KEY PRIORITIES FOR OPERATIONAL RESEARCH INCLUDE:

KEY PRIORITY 1

understanding how TB tools are used in local contexts, informing early-stage planning for the introduction of new tools in order to reduce delays between licensure and effective use;

KEY PRIORITY 2

understanding how to most efficiently and effectively conduct active case finding, an approach by which health systems proactively reach out to people at risk of TB and see that people receive screening, diagnosis and appropriate care and support;

KEY PRIORITY 3

improving access to treatment, care and psychosocial support, including assessing, monitoring and overcoming social, legal, political and economic barriers to access, for both DS- and DR-TB;

KEY PRIORITY 4

understanding how public and private sectors can coordinate and collaborate to improve all aspects of accessing and delivering TB care and support;

KEY PRIORITY 5

optimizing TB infection control in order to reduce transmission;

KEY PRIORITY 6

improving methods for conducting disease surveillance, monitoring and evaluation of TB programmes;³⁶

KEY PRIORITY 7

understanding the role that TB affected communities and TB survivors can play throughout and beyond the TB cascade of care, including in TB service delivery.

36 Global investments in tuberculosis research and development: past, present and future. Geneva: World Health Organization; 2017. https://www.who.int/tb/publications/2017/Global_Investments_in_Tuberculosis_Research_Investment/en/

Digital health and precision medicine

Digital health solutions have the potential to improve treatment support and the quality of TB care, while reducing costs and ensuring that quality-assured TB care and support services are available, accessible and acceptable to all. Access to the Internet and to smartphones is still relatively limited in many areas with high TB burden, but mobile phones with SMS capability are common.³⁷ New digital tools can help to improve TB treatment adherence and support in a way that is less burdensome for people with TB, and engage affected communities to monitor the TB response.

At the systems level, new digital tools, such as India's Nikshay platform, can help improve systems for patient registration and record-keeping, laboratory test orders, epidemiological surveillance and the movement of patient care from one health provider to another, among other functions. Other digital applications can help improve medicine forecasting and provide e-education for health professionals, people with TB and communities impacted by TB.³⁸

The potential for improving TB care through digital technology, when used in the context of comprehensive care and support, is still largely untapped. However, one digital tool, the Stop TB Partnership's Onelmpact, is facilitating community-based monitoring (CBM) by engaging people affected by TB to report barriers to accessing quality and timely TB care and support services in order to strengthen the TB monitoring and evaluation system and response to people's needs. To promote the scale-up of digital tools for TB care, WHO has recently worked to collect evidence from digital health pilot projects, develop TPPs for digital tools, and provide recommendations regarding how best to implement and pay for digital health tools for the purpose of ending TB.^{39,40}

Precision medicine can also help to improve both clinical treatment and care for individuals, as well as the public health response to TB. New advances in whole genome sequencing and interpretation have the potential to eventually replace traditional DST, which only tests for a limited number of resistance mutations and requires several weeks to deliver results. Interpretation can be aided by clinical decision support systems, which are computer systems that assist clinicians in a number of ways to provide optimized care for individuals based on their specific needs.⁴¹

Artificial intelligence (AI) is not new, but has gained traction in health care in the last decade due in part to advances in deep learning neural networks. Neural networks have been used for speech recognition with great success, and have been increasingly used in the health care field for different applications in image recognition. AI for image recognition has a number of potential applications in TB, specifically for reading chest X-rays and in other areas where reading is done by humans. TB REACH has supported a significant number of the early studies using AI to read chest X-rays. Recent developments include a published study examining multiple deep learning reading applications at multiple sites.⁴² This study showed that three different deep learning applications outperformed experienced human readers. There are multiple benefits of using AI to read

37 Yoeli E, Rathauer J, Bhanot S, et al. Digital health support in treatment for tuberculosis. *N Engl J Med*. 2019;381:966–87. doi:10.1056/NEJMc1806550

38 Digital health in the TB response: scaling up the TB response through information and communication technologies. Geneva: World Health Organization; 2015. <http://www9.who.int/tb/publications/eHealth-tb/en/>

39 Digital health in TB care and control [Website]. Geneva: World Health Organization. <https://www.who.int/tb/areas-of-work/digital-health/en/>

40 Handbook for the use of digital technologies to support tuberculosis medication adherence. Geneva: World Health Organization; 2018. https://www.who.int/tb/publications/2018/TB_medication_adherence_handbook_2018/en/

41 Temesgen Z, Cirillo D, Raviglione M. Precision medicine and public health interventions: tuberculosis as a model? *Lancet Pub Health*. 2019;4(8):e374. doi:10.1016/S2468-2667(19)30130-6

42 Qin ZZ, Sander MS, Rai B, et al. Using artificial intelligence to read chest radiographs for tuberculosis detection: a multi-site evaluation of the diagnostic accuracy of three deep learning systems. *Scientific Reports*. 2019;9:15000. doi:10.1038/s41598-019-51503-3

chest X-rays, including the ability to standardize scoring, savings on the costs of GeneXpert testing, and improved detection when using chest X-ray as a triage test. Using AI to read chest X-rays can be especially helpful in places where there is a lack of trained human readers and high screening throughputs.

AI can help to classify other data as well, including sounds. Additional applications of AI that could help the TB response are being devel-

oped, including electric remote cough monitors, automated reading of microscopic examinations, and use of AI to identify 'hotspots' for TB screening campaigns or to help health care workers recognize people receiving TB treatment who may need specialized attention and support. The vast amount of data that are generated from TB programmes will assist in the development of new AI applications and uses in the TB response.

TABLE 6.6: SUMMARY OF TARGET PRODUCT PROFILES FOR TB DIGITAL TOOLS¹

Function	TPP: short description
Patient care	1. Video observed treatment (VOT) via mobiles 2. eHealth portal for TB patients
Surveillance & monitoring	3. Graphic dashboards for TB 4. eNotify TB 5. ePV for TB
Laboratory information systems	6. TB diagnostic device connectivity
eLearning	7. Patient information platform on TB and smoking cessation 8. Web-based training for health care professionals on TB and smoking cessation 9. Clinical decision support systems for TB and tobacco care

¹ Target product profiles and priority digital health products for TB [Website]. Geneva: World Health Organization. <https://www.who.int/tb/areas-of-work/digital-health/target-product-profiles/en/>

As applications for digital health tools continue to expand, as access to information and communications technologies continue to grow in LMICs, and as AI becomes more capable, operational research will continue to be essential in order to understand how best to apply digital tools to support people with TB and improve the quality of care. Concerns remain that digital technology has the potential to replace human contact, or even be misappropriated for uses

that overstep the purposes of improving support and quality of care by violating people's rights to privacy and autonomy. Therefore, it will remain essential to seek input from people with TB and survivors in the course of designing digital health applications. Adhering to ethical standards will also remain critical in the course of navigating issues of privacy, oversight, accountability, public trust, data governance and management in the application of digital health tools.

BOX 6.6:

TB REACH DIGITAL ADHERENCE TECHNOLOGY (DAT) PROJECTS

In Wave 6, TB REACH, with support from the Bill & Melinda Gates Foundation, funded 13 projects that focus on the use of digital adherence technologies (DATs) to enhance treatment support and improve treatment outcomes. These projects are being implemented in 12 countries, supporting various populations and settings, and using varying DAT tools such as 99DOTS, evriMED, SureAdhere (video observed technology, or VOT), and other locally developed technologies. The 13 TB REACH DAT projects provide a unique opportunity to understand the use and implementation of DATs for TB treatment across different

settings and contexts. Lessons learned from these projects will help to close the global evidence gap in understanding the impact of these tools on treatment outcomes, as well as any challenges and opportunities related to their use among people with TB, health care providers and TB programmes.

More information is available at:

<http://www.stoptb.org/global/awards/tbreach/wave-6DAT.asp>



7.RESOURCE NEEDS



SUMMARY

Increased investment in TB continues to be urgently needed. By fulfilling their UNHLM on TB commitments to invest at least US\$ 13 billion annually in TB prevention and care and to increase funding for TB R&D to over US\$ 2 billion annually, governments can put the world on track to end TB.

BY FINANCING THE GLOBAL PLAN'S INVESTMENT SCENARIO (2018–2022):

- | | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>1 Countries will reach the UNHLM treatment targets set for 2022.</p> <p>2 The End TB Strategy milestone of 2020 will be achieved a year later, in 2021.</p> | <p>3 The world will be on track to achieve the 2025 milestones.</p> <p>4 New tools from R&D will be on the horizon for the final battle to end TB by 2030.</p> |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
-

Financing TB prevention and care: The Return on Investment (ROI) in TB prevention and care is US\$ 44 for every dollar spent. Meeting the full resource needs for TB care and prevention for 2018–2022 will lead to 40 million people being treated for TB, including 3.5 million children and 1.5 million people with DR-TB, and over 30 million people receiving TB preventive therapy. This will lead to 1.5 million fewer deaths due to TB and 48 million DALYs averted.

Financing TB R&D of new tools: Having new tools is essential to ending TB. Fully meeting the resource needs for TB R&D will lead to the development of the new diagnostics, new medicines and effective vaccine needed to end the TB epi-

demic. A five-year delay in increasing funding for TB R&D – the cost of inaction – would lead to approximately 2 million additional people dying and an additional 13.9 million people developing TB. (See Chapter 6 for a more detailed discussion on the cost of inaction.)

While the bulk of these investments should come from domestic resources and international donors, the mobilization of alternative funding sources – private sector funding, blended financing, loan buydowns, social health insurance, philanthropy from high-net-worth individuals, social impact bonds, micro levies or taxes, and pooled donor trusts – could dramatically accelerate the pace of scale-up.

PRIORITY ACTIONS

The following priority actions need to be taken to close the gap in funding for TB prevention and care.

Governments:

- ✦ Heads of state and governments of all high TB burden countries must mobilize an increase in domestic funding for TB.
- ✦ BRICS and upper-middle-income countries should increase their domestic resources for TB to fully meet the increased funding needs to achieve the UNHLM treatment targets.
- ✦ Following the full replenishment of the Global Fund, governments must use all available tools to maximize funds for TB from the Global Fund to meet the ambitious UNHLM targets, which includes full disbursement of country allocations, expansion of catalytic funding and prioritization of portfolio optimization.
- ✦ Countries should explore financing a share of the expansion of TB services through cost savings within existing TB budgets: by decentralizing TB care, sharply reducing the number of people with TB who are hospitalized and reducing hospitalization times. Seek ways to improve the efficiency of TB programme implementation without reducing quality.
- ✦ Additional external funding needs to be mobilized and made available to low-income countries and select lower-middle-income countries who have limited fiscal space to increase their domestic budgets.
- ✦ Governments should develop investment cases for TB at country level using modelling and costing projections to inform national strategic plans, advocacy for resource mobilization and resource allocations.
- ✦ NTPs and partners must tap the full potential of social health insurance schemes, innovative funding and impact financing for TB.

Development partners:

- ✦ The World Bank and other development banks must ensure that all instruments available for loans and grants to high TB burden countries are considered during negotiations on credit agreements in order to make funds available for TB, including blended finance mechanisms and loan buydowns.
- ✦ Partners and advocates should engage with strategically important high-burden middle-income countries to double or triple their domestic budgets for TB.

Closing the TB R&D funding gap requires the following urgent actions:

- ✦ The global community must recognize that funding for TB R&D is a shared responsibility. Countries should contribute at least 0.1% of their GERD to TB.
- ✦ As home to half of the world's people with TB and with strong R&D capacity, BRICS countries should substantially increase their funding for TB R&D.
- ✦ Increase support for TB R&D from pooled funding mechanisms such as the European and Developing Countries Clinical Trials Partnership and the Global Health Innovative Technology Fund.
- ✦ Innovative financing mechanisms, private sector funding and start-up financing mechanisms must be engaged to promote and fund new tools development.

Investment requirements to achieve the UNHLM targets

A significant increase in resources both for current interventions and for the development of new tools is needed in order to reach the targets that governments committed to at the UNHLM on TB. The returns on this investment will be dramatic, both in human and in economic terms.

Between 2018 and 2022, a total of US\$ 77.8 billion is needed with the following breakdown:

- ✦ A total of US\$ 65 billion is needed for providing TB prevention and care.
- ✦ A total of US\$ 12.8 billion is needed for R&D of new tools and basic science research, which consists of:
 - at least US\$ 10.8 billion needed for R&D of new TB diagnostics, medicines and at least one vaccine, at an average of US\$ 2.16 billion per annum; and

- a total of US\$ 2 billion needed for research in basic science related to TB, at an average of US\$ 400 million per year.

Details on the funding for TB prevention and care are presented below. Details on research funding are presented in Chapter 6.

Figure 7.1 shows the resource needs at the global level for TB prevention and care, the available funding if the current trend of funding continues without further increase, and the resulting funding gap.

FIGURE 7.1: RESOURCE NEEDS FOR TB PREVENTION AND CARE AT GLOBAL LEVEL (US\$ BILLION)

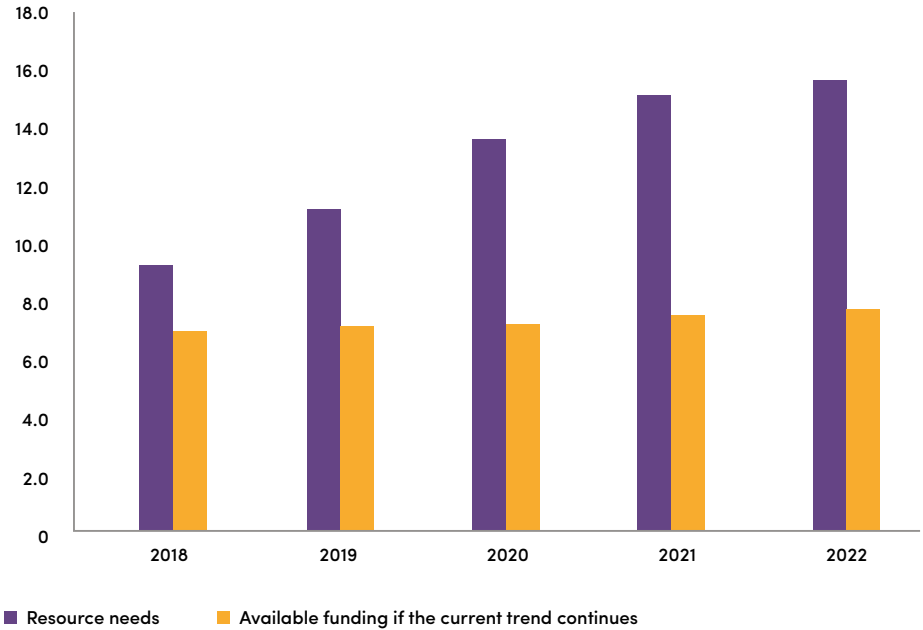


TABLE 7.1: RESOURCE NEEDS FOR TB PREVENTION AND CARE (US\$ BILLIONS)

	2018	2019	2020	2021	2022	Total
GLOBAL TOTAL						
Total (Global, including OECD countries)	9.24	11.18	13.64	15.15	15.61	64.82
Total (Global, excluding OECD countries)	8.54	10.48	12.97	14.51	15.00	61.50
BY INCOME STATUS						
Low income	0.87	1.13	1.60	1.85	1.95	7.38
Lower-middle income	3.20	4.35	5.88	6.86	7.19	27.48
Upper-middle income	4.51	5.05	5.55	5.86	5.92	26.90
High income	0.66	0.65	0.61	0.58	0.55	3.05
GLOBAL FUND ELIGIBLE COUNTRIES, BY INCOME STATUS						
Low income	0.87	1.13	1.60	1.85	1.95	7.38
Lower-middle income	3.20	4.35	5.87	6.85	7.19	27.46
Upper-middle income	1.57	1.82	1.96	2.00	2.04	9.39
Total	5.64	7.30	9.43	10.70	11.17	44.24
GLOBAL PLAN COUNTRY SETTINGS						
High MDR Burden	2.53	2.74	2.97	3.16	3.21	14.60
High TB/HIV, SADC	0.86	1.09	1.37	1.50	1.56	6.38
High TB/HIV, non SADC	0.84	1.20	1.90	2.23	2.33	8.49
Moderate Burden, COE	0.31	0.42	0.62	0.73	0.77	2.84
High Burden, Private Sector	1.15	1.66	2.32	2.80	3.01	10.94
Moderate Burden, Middle Income	0.89	1.03	1.12	1.16	1.15	5.34
India	0.88	1.14	1.31	1.45	1.50	6.27
China	1.02	1.13	1.25	1.33	1.31	6.04
Low Burden, High Income	0.77	0.79	0.79	0.79	0.76	3.91
GLOBAL PLAN COUNTRY SETTINGS						
EMR	0.28	0.43	0.75	0.97	1.06	3.49
AFR	1.97	2.65	3.79	4.35	4.55	17.30
AMR	0.71	0.82	0.88	0.91	0.91	4.23
EUR	2.85	3.05	3.27	3.44	3.48	16.10
WPR	1.86	2.09	2.39	2.58	2.58	11.50
SEAR	1.56	2.14	2.56	2.89	3.04	12.20
BRICS (BRA, CHN, IND, RUS, ZAF)						
Total	3.96	4.60	5.18	5.60	5.71	25.05

Table 7.1 shows the annual resource needs (2018–2022) for TB prevention and care to reach the UNHLM treatment targets for 2022 and to put the world on track to end TB. Resource needs are shown for the world as a whole, as well as for different groups of countries. Breaking down the global resource needs, US\$ 61 bil-

lion is needed in non-OECD countries, while US\$ 44 billion is needed in countries eligible for Global Fund financing over the 2018–2022 period. Resource needs for individual countries are available here

(<http://stoptb.org/resources/countrytargets/>).

FIGURE 7.2: COST CATEGORIES OF FUNDING NEEDS FOR TB PREVENTION AND CARE, 2018–2022

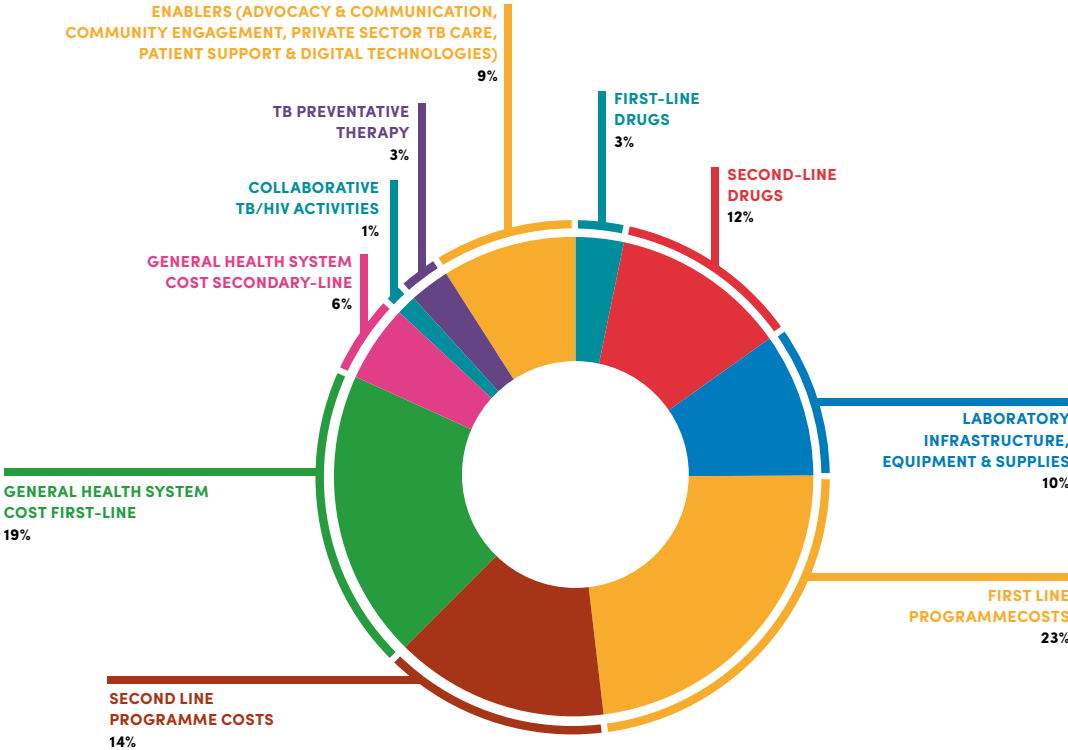
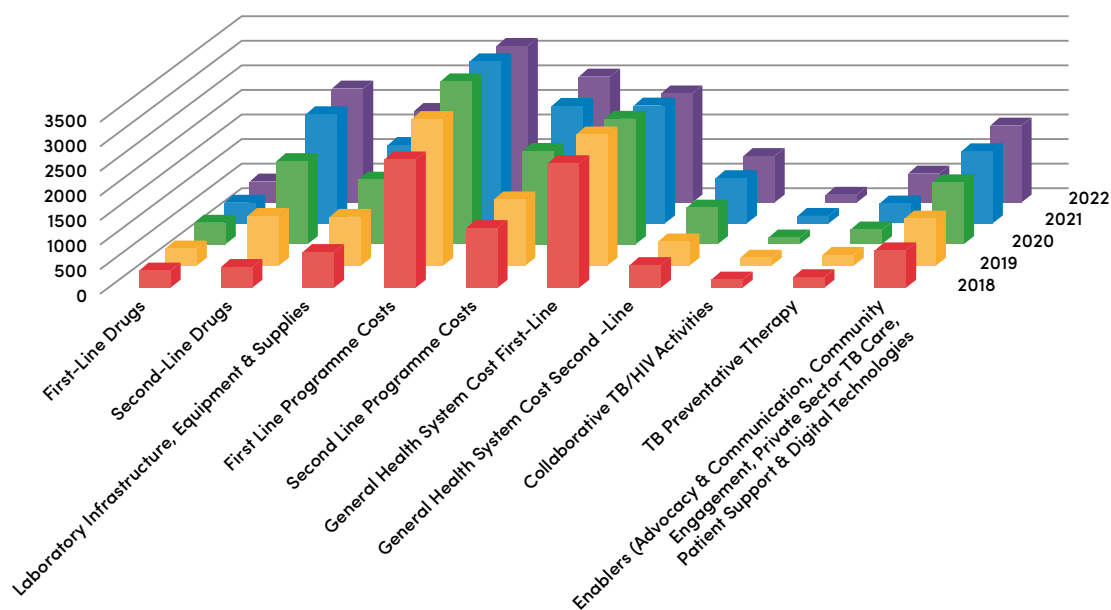


Figure 7.2 shows the disaggregation of total funding needs for TB prevention and care for 2018–2022 by cost category, and Figure 7.3 shows the cost categories by year.

FIGURE 7.3: COST CATEGORIES OF FUNDING NEEDS FOR 2018–2022, IN US\$ MILLION



First-line programme costs include management and supervision, TB programme human resources, training, policy development, meetings, purchase of office equipment/vehicles, construction of buildings for NTPs, routine surveillance, advocacy and communications, PPM activities, community engagement, active case finding, infection control, and management of TB medicine procurement and distribution.

Second-line programme costs include management of DR-TB services, renovation of MDR-TB wards, Green Light Committee-related activities, loss-to-follow-up and contact tracing, and palliative care.

The general health system cost categories (both first- and second-line) include hospital outpatient consultations, hospitalization and ambulatory care costs, together with distribution costs related to TB commodities. These costs are often not included in NTP budgets, but are covered from health system budgets.

TB/HIV collaboration includes TB/HIV coordinating bodies, joint training and planning, HIV testing for people with TB, and joint TB/HIV information and education.

The TB preventive therapy cost category includes medicines for all on preventive therapy, but TB infection testing for only a proportion of contacts over 5 years of age. It is assumed that older isoniazid-based regimens will gradually be replaced by newer rifampentine-based regimens. The cost of contact investigation and exclusion of active TB before starting preventive therapy is not included here, as these activities are already included under first-line programme costs and TB/HIV collaboration. Similarly, human resources costs for TB preventive therapy are included under first- and second-line programme costs.

The enablers cost category includes activities that provide an enabling environment for rapid scale-up of TB prevention and care. These

enablers include advocacy and communications, community systems strengthening and engagement, private sector TB care, patient support and protection, and digital technologies. Although several countries include some of these activities under the programme costs category, they are insufficiently budgeted for. Therefore, the proportion of budget for these enablers was based on best practice country examples applied to other countries, or to countries in similar settings (e.g., private sector TB care was applied to only countries with a large private sector TB care).

The annual estimated resource needs increase from 2018 to 2022 because of the scale-up of the numbers of people to be diagnosed and treated, and because several unit cost categories are expected to grow as described in Annex 1. Laboratories comprise the fastest growing unit cost category due to anticipated changes in diagnostic technologies and the anticipated greater numbers of people to receive TB testing.

Costing approach and limitations

Resource needs were estimated from WHO's TB financial database, which includes budgets reported from over 100 countries, and health system costs estimated independently by WHO. From these data, unit costs were derived for cost categories, adjusted for future trends based on expert opinion, and applied to the treatment scale-up targets from the TIME model. Unit costs were imputed for countries that did not report to WHO, using learner algorithms as part of the modelling exercise. The detailed methodology for estimating the resource needs for reaching the UNHLM targets is presented in Annex 1.

The costing approach is subject to certain limitations. The manner in which the different cost categories are bundled together and reported by WHO is a constraint that does not allow cost categories to be broken down in other ways. Furthermore, the costing for the period 2018–2022 does not factor in the introduction of future new diagnostics or medicines that are currently not available.

Governments should carry out country-level modelling of the TB epidemic and develop detailed costing projections to inform national strategic plans and investment cases for ending TB. NTPs and TB advocates can use these national strategic plans and investment cases to advocate for increased TB funding, aligned with national budgeting processes, as well as for donor engagement.

The Global Plan recommends more robust collection of financial data from NTPs, national health accounts, and international development partners, along with increased investment in tracking and improving unit costs, costs of new interventions, and domestic investments. In addition, the different cost categories should be disaggregated at the point of data collection for a better understanding of the financial implications.

What will the Global Plan achieve?

Patients treated, lives saved and progress towards ending TB

Meeting the full resource needs for TB care and prevention for 2018–2022 will lead to:

- ⊕ 40 million people treated for TB, including
 - 3.5 million children
 - 1.5 million people with DR-TB
- ⊕ more than 30 million people receiving TB preventive therapy
- ⊕ 1.5 million fewer deaths due to TB
- ⊕ 48 million DALYs averted (see Annex 1 for details on DALYs averted).

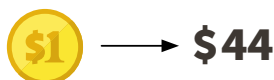
New diagnostics, medicines and a vaccine in time to end TB

Fully meeting the resource needs for developing new tools will lead to the development of the new diagnostics, new medicines and effective vaccine needed to end the TB epidemic.

Delaying an increase in funding for TB R&D by five years will lead to approximately:

- ⊕ 2 million additional people dying from TB
- ⊕ 13.9 million additional people developing TB
- ⊕ 49.8 million DALYs lost as a consequence of TB (75.1 million without discounting)
- ⊕ US\$ 14.2 billion in additional costs for TB treatments alone (US\$ 21.6 billion without discounting)
- ⊕ US\$ 172 billion in lost productivity (US\$ 259 billion without discounting).

(See Chapter 6 for additional discussion on the cost of inaction.)



Return on investment (ROI)

When a TB programme provides people with effective prevention and treatment, preventing death and disability, they receive supplemental economic benefits. First, it is possible that the prevention of TB may save household expenditures on health care. Second, when TB is prevented (or effectively treated), household members are able to continue or resume productive work.

An ROI analysis was performed for the Global Plan 2018–2022, based on the methodology of the Lancet Commission on Investing in Health¹, but

adapted to new guidelines for benefit–cost analysis following the work with the Global Fund to estimate the ROI of the new replenishment cycle 2020–2022. The methodology is described in Annex 1.

Table 7.2 summarizes the net economic benefit and ROI for every US\$ invested in Global Plan activities by country group and income status.

The ROI is US\$ 43.7 for every dollar spent on TB prevention and care as proposed in the Global Plan 2018–2022. The net economic benefit of the investment is estimated at US\$ 711 billion.

An ROI of 1:44 makes TB prevention and care scale-up under the Global Plan 2018–2022 one of the best investments under the SDGs.

¹ Jamison DT, Summers LH, Alleyne G, et al. Global health 2035: a world converging within a generation. The Lancet Commissions. 2013;382(9908):1898–955. <https://www.thelancet.com/action/showPdf?pii=S0140-6736%2813%2962105-4>

TABLE 7.2: ROI AND NET ECONOMIC BENEFIT OF IMPLEMENTING THE GLOBAL PLAN 2018–2022

ROI (per US\$ invested) relative to BAU	Net Benefit, 2018–2022 (in US\$ millions)	ROI, 2018–2022, for every US\$ invested
Global	711,000	43.7
BY COUNTRY GROUP		
High MDR Burden	18,000	8.2
High TB/HIV, SADC	86,000	48.3
High TB/HIV, outside SADC	62,000	16.5
Moderate Burden, COE	3,000	2.9
High Burden, Private Sector	177,000	40.4
Moderate Burden, Middle Income	33,000	55.4
India	204,000	184.4
China	66,000	58.7
Low Burden, High Income	2,000	632.4
BY INCOME STATUS		
Low income	39,000	12.7
Lower-middle income	308,000	36.0
Upper-middle income	269,000	96.1
High income	95,000	57.8

BOX 7.1: INVESTING IN TB CARE YIELDS LONG-TERM HEALTH SYSTEMS GAINS

Investments in TB strengthen health systems for the long term, increasing their ability to fight other diseases and outbreaks. Health systems strengthening can be achieved in several ways.

First, investing in early and effective TB diagnosis builds lasting diagnostic, laboratory and case finding capacity in the health system. TB symptoms are not specific and occur in multiple diseases. Therefore, tools such as microscopes and X-rays have manifold uses beyond TB. Efforts to improve early TB case finding, therefore, can positively impact the early detection of other conditions, particularly those affecting the lungs.

TB laboratory networks are known for establishing standardization and quality assurance processes that can positively impact the quality of public health laboratories across the board. The Global Plan calls for the integration of TB laboratory and diagnostics into health systems and improved access through specimen transportation. It envisages well integrated TB programmes as a conduit for strengthening health systems for early disease diagnosis.

Second, investments that strengthen contact investigation for TB will create a system that can be reliably called upon during infectious disease outbreaks, such as for

Ebola, which demand the rapid mobilization of both health facilities and communities to conduct extensive contact investigations.

Third, fighting TB requires investment in airborne infection control practices. Such investment builds the capacity of health systems to quickly respond to other airborne infection outbreaks, such as influenza and respiratory syndromes.

Fourth, as TB treatment requires lengthy interaction with patients and communities, TB investments can strengthen overall engagement with these communities to the benefit of other health programmes.

Fifth, TB treatment demands strong and reliable medicine supply chain systems. Further improvements to these systems and greater integration of these systems into the wider health systems of countries directly benefit health systems seeking to improve supply chains for other diseases.

Finally, costs besides commodity-based or direct costs make up a large proportion of the costs. These costs involve laboratory strengthening, the improvement of health system components, and human resources development – all of which have the potential to make a lasting, positive impact on the overall strength of health systems.¹

1 Harries A, Jensen P, Zachariah R, et al. How health systems in sub-Saharan Africa can benefit from tuberculosis and other infectious disease programmes. *Int J Tuberc Lung Dis.* 2009;13(10):1194–9.

Sources of funding for the Global Plan

The “global public goods”² nature of most TB investments makes it a priority for funding with a wide societal benefit. In fact, investment in TB yields one of the best ROIs among all SDG targets.³ The Copenhagen Consensus Center estimates that every dollar invested in TB yields US\$ 43 in economic benefit. The Global Plan investment scenario gives a similar ROI of US\$ 44 per dollar invested, as described above. In its January 2019 meeting, the Stop TB Partnership Board issued a Call for Action.⁴

2 “Global public goods” are defined as those goods that are both “non-rival” (i.e., anyone can consume the good without affecting the utility derived from its consumption) and “non-excludable” (i.e., once the good is produced, no one can be prevented from enjoying it). The World Bank Group A to Z. Washington, DC: World Bank; 2015. https://elibrary.worldbank.org/doi/10.1596/978-1-4648-0484-7_global_public_goods

3 Post-2015 Consensus: what are the smartest targets for the post-2015 development agenda? Tewksbury: Copenhagen Consensus Center; 2015. <https://www.copenhagenconsensus.com/post-2015-consensus>

4 The Stop TB Partnership Board calls for a dramatic increase in funding for TB. Geneva: Stop TB Partnership; 2019. http://www.stoptb.org/news/stories/2019/nsi9_005.asp

RECOGNIZING THE NEED FOR INCREASED RESOURCES AND THE SERIOUS FUNDING GAP, TO REACH THE UNHLM ON TB TARGETS FOR 2022, THE BOARD CALLED FOR:

- 1 the full replenishment of the Global Fund and use of all available tools to maximize funds for TB to meet the ambitious UNHLM targets; this includes full disbursement of country allocations, expansion of catalytic funding, prioritization of portfolio optimization, etc.;
 - 2 heads of governments of all high TB burden countries to increase domestic funding for TB, and the Stop TB Partnership and its partners to engage with strategically important high-burden middle-income countries to double or triple their domestic budgets for TB;
 - 3 the World Bank and other development banks to ensure that all instruments available for loans and grants to high TB burden countries are considered during negotiations on credit agreements, including blended finance mechanisms, in order to make funds available for TB;
 - 4 the Stop TB Partnership to work with partners to tap the full potential of social health insurance schemes, innovative funding and impact financing for TB;
 - 5 recognition by the global community that funding for TB R&D is a shared responsibility; as such, the Board supports the proposal to develop specific R&D targets for TB for each country, recognizing that different countries might choose to support local or regional research initiatives;
 - 6 the Stop TB Partnership to form a “TB Finance Task Team” to work on traditional and innovative options available to increase funding for TB, particularly in the context of UHC, in order to identify opportunities and provide strategic guidance to the Board and Secretariat for resource mobilization for the global TB response.
-

There are three broad sources of funding for implementation and research: domestic funding, external funding and innovative financing.

Domestic financing

For high-income countries, BRICS countries and upper-middle-income countries, nearly all TB investments should flow from domestic resources. The Russian Federation and other Eastern European countries may be able to finance a significant share of the expansion of TB services through cost savings within historical TB budgets by continuing the current trend of people-centred TB care, reducing the number of patients that are hospitalized, and reducing hospitalization times. Other middle-income, high-burden countries could rationalize their TB activities by better integrating TB care into general health services. However, a paradigm

shift focused on ending TB will only be possible if countries are prepared to dedicate special budget lines, as South Africa has done. India has recently quadrupled its domestic budget for TB, driven by high-level political commitment and the vision of the Prime Minister to end TB in the country by 2025, five years ahead of the global target. Such dramatic increases (doubling, tripling or quadrupling) in domestic budgets for TB are needed in several middle-income and high TB burden countries.

The economic realities are very different in low-income countries. Most of the high-burden countries in this subset remain heavily dependent on external financing for their TB programmes. Moreover, large parts of TB budgets currently go unfunded. These countries will need increased external funding support, including grants and loans at concessionary rates from development banks.

In order to determine the right blend of funding sources to finance the efforts outlined by the Global Plan, each country's circumstances must be taken into account. Circumstances vary widely. It is important to track increases in domestic funding through better systems of financial reporting from countries, especially through national health accounts where they exist. Inter-government coordination mechanisms, such as the African Union, should also play a role in advocating and monitoring increased domestic funding for TB.

Increasing the efficiency of domestic TB programmes

The choices facing TB policymakers and programme implementers are daunting because of a persistently high burden of disease, limited resources, and the need to compare emerging technologies with cheaper (but older and less effective) approaches.

This challenge requires a shift towards allocative efficiency, i.e., the maximization of health outcomes using the most cost-effective mix of health interventions, delivered to target populations in the highest priority areas via streamlined service delivery. Procurement of medicines and diagnostics is one area where domestic budgets can be made more efficient by procuring quality-assured products at good prices from the Stop TB Partnership's GDF. The UN Political Declaration on TB therefore encourages all countries to use GDF.

The Global Plan urges countries to use analytical approaches that incorporate data on the cost and effectiveness of interventions in real-world applications in order to estimate how the burden of TB can be addressed using available resources. It also encourages countries to seek ways to improve the efficiency of TB programme implementation without reducing quality.

Setting up social contracting mechanisms for funding local NGOs from government domestic funds is essential to ensure that civil society is

engaged in increasing the efficiency and reach of the TB response in the country. Social contracting can lead to substantial improvements in access, quality of services, equity and impact.

Social health insurance (SHI)

Social health insurance (SHI) is a mechanism by which funds within countries can be raised and pooled to finance health services.⁵ In European SHI systems, employees and their employers contribute to a package of services available to the insured and his or her dependents. Many governments also subsidize these systems to ensure sustainability.

These contribution programmes are designed to ensure that wealthier people contribute more than the poor, and that the sick do not pay more than the healthy. In addition, some governments have extended coverage to people who cannot pay, such as the poor and unemployed, by meeting or subsidizing their contributions.

This approach has benefits in the context of TB. As SHI schemes generally charge higher rates for coverage to wealthier people (who are less likely to have TB) and often provide free coverage to poorer people (who are more likely to have TB), SHI mechanisms can help to reduce health inequalities, avoid catastrophic costs for people with TB, and redistribute funds towards TB – increasing the overall levels of funding available for expanding access to TB care and services.

A number of countries are planning to introduce and/or scale up SHI as part of their efforts to attain UHC. TB programmes must seize the opportunity to include TB care in the package of coverage provided by SHI. To the extent possible, all forms of TB managed by both public and private health systems should be brought under

5 Doetinchem O, Carrin G, Evans D. Thinking of introducing social health insurance? Ten questions. Technical brief for policy-makers, Number 4/2009. Geneva: World Health Organization; 2009. https://www.who.int/health_financing/documents/cov-pb_e_09_04-10qshi/en/

the coverage of SHI schemes. Efforts should also be made to ensure that SHI schemes are inclusive and provide coverage to key populations, such as migrants.

For financing UHC, several countries are changing their health financing mechanisms by introducing strategic purchasing of services and a range of provider payment mechanisms with or without SHI. TB programmes need to take active part in these discussions in order to benefit from such health financing approaches.

International financing

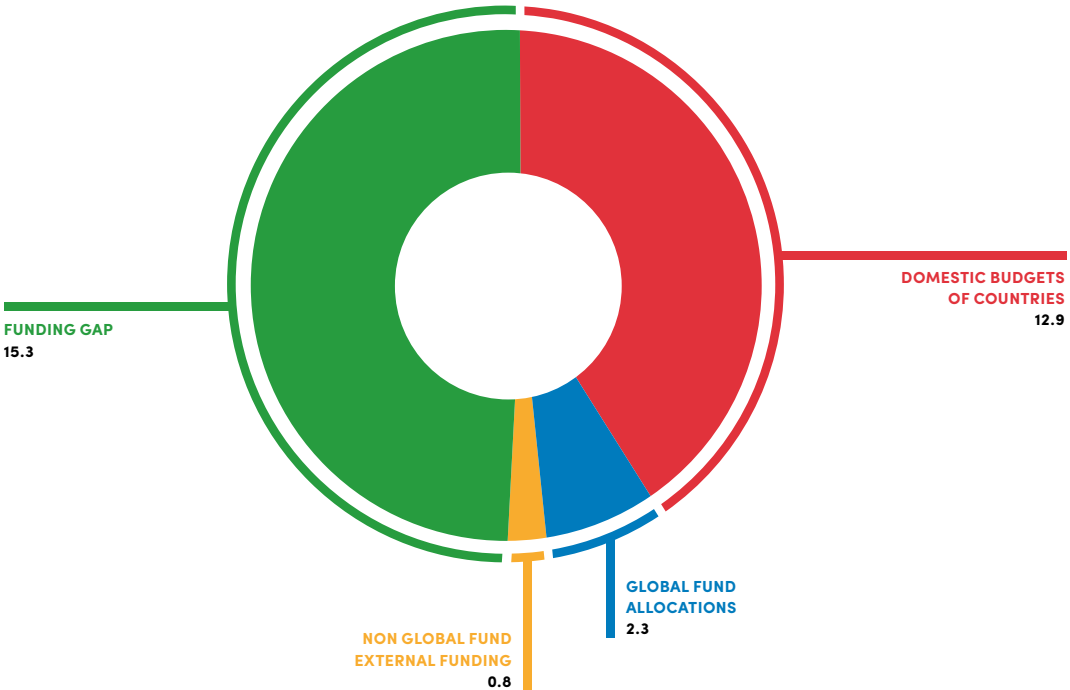
Figure 7.4 provides an illustration of the need for increased international funding in Global Fund-eligible countries. It shows the funds that are

anticipated from domestic sources, the Global Fund, and other external sources, as well as the additional funding that countries will require over and above these sources.

Given that the figures for domestic funding are based on the optimistic forecast scenarios prepared by the Global Fund, it is clear that there is a significant and increasing need for additional contributions from the Global Fund and other international sources. Without such additional funding, the 2022 targets will not be met.

For Global Fund-eligible countries, the total resource need for the Global Fund funding cycle 2020–2022 is US\$ 31.3 billion. The optimistic scenario of increased domestic funding, along with continued external funding at current levels, will provide up to US\$ 16 billion, which leaves an

FIGURE 7.4: US\$ 31.3 BILLION NEEDED IN GLOBAL FUND-ELIGIBLE COUNTRIES DURING 2020–2022: POSSIBLE SOURCES AND GAPS



additional funding requirement of US\$ 15.3 billion that needs to be mobilized.

Loans from development banks, including loan buydowns and converting debt into grants

The World Bank and other regional development banks provide loans to countries, which, if used smartly, can make substantial resources available for TB. Such loans have been used by countries to fund TB programmes for several years. More recently, innovative approaches have been used to blend loans and grants from different sources, making borrowing more attractive to countries. One such approach is to use grants from the Global Fund, bilateral donors or private sector to pay for the interest on loans from the World Bank or regional development banks. This is often referred to as “loan buydown.” For example, the Government of India accessed a World Bank loan of US\$ 500 billion for its TB programme, and the interest amounting to about US\$ 40 million was paid by the Global Fund. In low-income countries, another approach of converting loans into grants could also be implemented.

High-net-worth individuals and the Giving Pledge

The Giving Pledge is a commitment by the world’s wealthiest individuals and families to dedicate the majority of their wealth to philanthropy. As of 2019, 204 people have pledged for a total of over US\$ 500 billion. This is a hitherto untapped source of funding for TB.

Innovative financing

Global health has a strong track record of developing innovative financing mechanisms. While still primarily backed by traditional donors, the Global Fund and Unitaid, for example, have developed innovative approaches to mobilizing, pooling, channelling, allocating and implement-

ing resources to direct large amounts of funding rapidly to LMICs.⁶

These mechanisms will continue to play a key role in the fight against TB. The Global Fund alone contributes nearly 70% of international financing.⁷ But, there is a need to cultivate funding from non-traditional donors.

Impact bonds

One instrument that may have the potential to secure additional funding is the impact bond. This is a financial scheme whereby investors pay in advance for interventions in order to achieve agreed-upon results. Then, they work with delivery organizations to ensure that those results are achieved. Outcome funders (governments and/or donors) make payments to investors if the interventions succeed, with the degree of returns linked to the level of success of the results achieved. In this sense, impact bonds are like other results-based approaches, but with up-front capital. This ensures finance at affordable rates for service providers. There are two main types of impact bonds: social impact bonds (SIBs), which are typically implemented on the scale of a city or district, and development impact bonds (DIBs), which are typically implemented on the scale of a country or significant region of a country.

In the context of TB programming, impact bonds could encourage investors to provide up-front capital to support the efforts of various service providers to improve TB diagnosis and treatment in high-burden communities.

These activities would have both social and financial benefits. The social impact would be generated from the reduced burden of disease

6 Atun R, Knaul FM, Akachi Y, et al. Innovative financing for health: what is truly innovative? *Lancet*. 2012;380(9858):2044–9. doi:10.1016/S0140-6736(12)61460-3

7 Dieleman J, Murray CJL, Haakenstad A. Financing global health 2014: shifts in funding as the MDG era closes. Seattle: Institute for Health Metrics and Evaluation; 2015. <http://www.healthdata.org/policy-report/financing-global-health-2014-shifts-funding-mdg-era-closes>

and the increased productivity of a population with fewer active TB cases. Governments and companies providing TB care (e.g., in mining communities) would realize financial benefits through the reduced costs incurred in treating patients. The government would also benefit from the increased tax revenues generated from a more economically productive population. These savings would form part of the capital that would be paid back to investors.⁸

Blended finance

Blended finance is another framework that has the potential to increase the funding available for TB programmes and R&D. As the name suggests, this approach facilitates the blending of public and private capital to finance development goals.

Its principal aim is to unlock investment from the private sector. Typically, clinical trials for new tools (e.g., TB tests) constitute a high-risk activity with no guaranteed financial returns for a company. Blended finance seeks to reduce that risk by providing public sector and philanthropic funding to defray programme costs – such as technical support for study and intervention design – that a company would not be able to meet. The approach therefore has the potential to leverage private sector investment, innovation and expertise for projects that would otherwise be left on the shelf.

Micro levies/taxes

Taxes and micro levies on consumer goods can also generate resources for global health. The most cited example is a small tax on airline ticket purchases. Started in 2006 in France, the tax has now spread to Cameroon, Chile, Congo, Madagascar, Mali, Mauritius, Niger and Republic of Korea. The funds raised support Unitaid in purchasing treatments for HIV, TB and

malaria. From a tax of around US\$1 for an economy-class ticket and US\$ 40 for a business-class seat, as of 2019, Unitaid manages a health project portfolio of US\$ 1.3 billion.⁹ There remain numerous other opportunities in the areas of extractive industry, processing, consumption and finance where such taxes could be levied.

Pooled donor trusts

Donor-based trusts are pooled funds that distribute grants to organizations to meet defined social outcomes. Their main feature involves a multi-donor approach, which aims at better coordinating the funding for programmes, while raising awareness for issues that need additional attention.

Trusts can help to simplify the grantmaking process and maximize impact. For example, the Power of Nutrition is an independent charitable foundation founded in 2015 with US\$ 150 million contributed by the UK Government (DFID) and the Children's Investment Fund Foundation, followed by additional founding contributions made by UBS Optimus Foundation, with the World Bank and UNICEF serving as implementing partners. The foundation works to increase the efficiency of funding for undernutrition and other specific health goals related to stunting and wasting. The fund requires countries to provide matching capital for efforts to tackle the issues.

Corporate social responsibility (CSR)

CSR is a mechanism for businesses to be socially responsible by contributing to the society in which they operate for social, health and environment issues. Large corporations and businesses operating in high TB burden countries need to be engaged and encouraged to invest in TB. In recent years, oil companies in Nigeria (Agbami Partners) have built, equipped and

8 Innovative financing for global health R&D. Santa Monica: Milken Institute; 2012. <http://assets.milkeninstitute.org/assets/Publication/InnovationLab/PDF/IL-Global-Health-Report.pdf>

9 Annual report 2018–2019. Geneva: Unitaid; 2019. <https://unitaid.org/annual-report-18-19/>

donated TB clinics to the government. There has also been recent progress in India¹⁰ and Indonesia¹¹ in increasing corporate sector funding for innovations in TB.

10 Tuberculosis projects. Mumbai: India Health Fund; 2019. <http://www.indiahealthfund.org/tuberculosis-centre/tuberculosis-projects/>

11 Innovative investment in Indonesia Health Fund. Geneva: Global Fund to Fight AIDS, Tuberculosis and Malaria; 2019. <https://www.theglobalfund.org/en/news/2014-04-09-innovative-investment-in-indonesia-health-fund/>

Meeting the financing needs for R&D

The urgent need to fund TB R&D

The TB epidemic cannot end with the tools available today. Countries can achieve dramatic gains by scaling up to meet the UN HLM targets. However, after 2025, existing tools will have a diminishing impact and will no longer be sufficient to bend the epidemic curve of TB steeply enough to meet the milestones of the End TB Strategy. Every day the epidemic continues, the human and economic costs only increase. To avert these costs, it is imperative that we urgently and rapidly scale up investments in new diagnostics, drug regimens and vaccines today. Delaying that investment by even one year could result in billions of dollars in additional treatment costs alone. TB R&D, access and optimization of new TB tools are discussed in detail in Chapter 6.

There is a huge gap in the financing for R&D of new tools to fight TB. In 2017, a total of US\$ 772 million was invested in TB R&D, just 38.6% of the US\$ 2 billion annual funding target.¹² This shortfall in funding means researchers must limit their projects to fit within a constrained funding environment, stifling the creativity, innovation and

experimentation needed for the development of new diagnostics, medicines and vaccines. Crucially, insufficient resources limit the number of researchers willing to enter or stay in the field of TB R&D.

Diversifying the funding base for TB R&D

Maintaining current partnerships and diversifying the funding base with new donors, investors and private sector actors are priorities.

These efforts must increase. Government, public sector and philanthropic donors, particularly the Bill & Melinda Gates Foundation, have provided essential funding for TB R&D. Some pharmaceutical industry partners have also invested resources and expertise.

However, expanding investments from BRICS countries – countries that account for nearly half of all TB and have significant research infrastructure and capacity – would provide a major boost. The establishment of the BRICS New Development Bank (NDB), with its US\$ 50 billion in capital, represents one such opportunity for BRICS investment in TB R&D.

A number of additional funding sources exist, including pooled funding mechanisms such

12 Tuberculosis research funding trends 2005–2017. New York: Treatment Action Group; 2018. <http://www.treatmentactiongroup.org/content/tbrd2018?eType=EmailBlast-Content&id=7dac4161-dc99-43a2-9447-4d18aeb4c8ac-overlay-context=content/tbrd2018>

as the European and Developing Countries Clinical Trials Partnership and the Global Health Innovative Technology Fund. It is imperative that these initiatives be strengthened, supplemented and adequately coordinated.

The complexities, costs and risks of TB R&D will require multiple funding platforms and partners, and a combination of push and pull mechanisms. Push mechanisms, such as traditional grants, finance R&D activities up-front, reducing the risk to researchers and developers. Pull mechanisms incentivize private sector investment in R&D. In 2007, for example, the U.S. FDA introduced the priority review voucher, granted to companies that discover drugs for neglected diseases. These vouchers can then be sold on the secondary market.¹³ For diagnostics, expanding the market through widespread implementation of existing solutions, while at the same time making new tools more affordable, would help to drive a virtuous cycle of demand creation. (See Chapter 6 for a more detailed discussion of TB R&D financing needs.)

¹³ Noor W. Placing value on FDA's priority review vouchers. *In Vivo*. 2009;27(8):1–8.

ANNEX 1 ESTIMATING THE COST AND IMPACT OF THE GLOBAL PLAN TO END TB: 2018–2022¹

¹ Document prepared by Carel Pretorius, Avenir Health

OVERVIEW

This document details the methodology developed for modelling the cost and impact of the Global Plan to End TB: 2018–2022.

The strategy is based on the 90–(90)–90 targets set in the Global Plan to End TB: 2016–2020, adding the specific targets from the UNHLM on TB: to treat 40 million people with TB between 2018 and 2022, including 3.5 million children and 1.5 million people with MDR-TB, and to provide TB preventive therapy to over at-least 30 million people. These targets are the result of a series of meetings and declarations at the UN General Assembly in New York aimed at ending TB.²

The impact modelling methods can be summarized as a framework for adjusting trends in key TB indicators, such as TB incidence, mortality and notification, to reflect the epidemiological impact of the programmatic implementation of the Global Plan to End TB: 2018–2022.

Simulations for TB were performed using the Impact component of the TB Impact Model and Estimates (TIME) model³, a dynamic compartmental TB model developed in the open-source Spectrum suite.

The method for estimating the resource needs associated with implementing the Global Plan 2018–2022 can be described as a framework for estimating unit costs of key budget categories, such as first- and second-line medicines, laboratory costs and programme management, from budget data reported to WHO. Missing data for countries that reported some or no financing data were imputed from the dataset using a multivariate statistical method. Notification trends were applied to the unit cost estimates and then used to project resource needs for the Global Plan 2018–2022. Unit cost increases were derived from the modelling steering group recommendations, based on the implementation of new guidelines and best practices. Without these unit cost increases, overall resource needs should decrease as incidence reductions lead to notification reductions, as projected to happen before 2022.

2 Note that these targets used simple, non-dynamical-model-based calculations that preceded this analysis.

3 Houben R, Lalli M, Sumner T, et al. TIME Impact: a new user-friendly tuberculosis (TB) model to inform TB policy decisions. *BMC Med.* 2016;14(1):56. doi:10.1186/s12916-016-0608-4

THE GLOBAL PLAN 2018–2022: UNHLM TARGETS

Treatment targets

Several modelling decisions were made in order to model the UNHLM targets using the TIME model. The first deals with the overall notification objectives.

To achieve the UNHLM notification target of 40 million by 2022, we simply increased the screening rate in TIME linearly⁴ from the base year (2017) values to a value that would achieve 40 million cumulative cases treated by 2022. The same final screening rate was applied to all countries, meaning that there would be a corresponding mix of impacts.⁵ There is no way to further specify country allocations in terms of their contribution to the 40 million. It should be further noted that impact in any country was constrained to not exceed 10% in any year – a constraint suggested during technical consultations with WHO and agreed by other partners of the steering group.

The relative distribution of paediatric TB among all patients resulted in 3.7 million children with TB notified and treated without any adjustments.

The MDR-TB target of 1.5 million was achieved through an overall approach of increasing the DST coverage from 2017 levels among notified cases to 100% of the MDR-TB burden, expressed relative to notifications. Thus, an assumption was made that the uncovering of MDR-TB is tied to the scale-up of notifications in general.

TB preventive therapy targets

The Global Plan 2018–2022 has a greater focus on preventive therapy targets than the Global Plan 2016–2022. The updated Plan calls for 100% coverage of contact-tracing in the household (HH) of all bacteriologically positive cases by 2022. We extended the definition of index cases beyond the definition used in the UN Political Declaration on TB to include 15% of smear-negative cases, following suggestions of the steering group.⁶

Furthermore, it was assumed that all people newly starting on antiretroviral therapy (ART) would receive preventive therapy, as well as 15% of people already on ART in 2018. This would taper over time to 0% of patients already on ART by 2022. Estimates for the distribution of active TB and latent TB in adults and children in HHs of index cases were based on Fox et al. 2013⁷. HH size estimates and the percentage of HH under 5 years of age were based on DHS data where available; a global average was used where such DHS data were not available (HH size of five and 15% of HH under the age of 5).

The result of these assumptions is the provision of preventive

4 All scale-up patterns were linear in the updated Global Plan analysis, unlike the s-shaped patterns used in the 2016–2020 Global Plan analysis.

5 The mix of screening rates would guarantee a mix of impacts, but there are many other model-based factors contributing to the mix of impact factors.

6 The degree of the extension of preventive therapy was provided by the steering group.

7 Fox GJ, Barry SE, Britton WJ, et al. Contact investigation for tuberculosis: a systematic review and meta-analysis. *Eur Respir J.* 2013;41:140–56. doi:10.1183/09031936.00070812

therapy to about 33 million people between 2018 and 2022, including 7 million children, 16 million adults and 10 million people living with HIV on ART.

Other targets

Other elements of the Global Plan 2018–2022 strategy were specified directly as inputs in TIME. Treatment success was specified separately for non-MDR- and MDR-TB, and separately for HIV-negative and HIV-positive not on ART or on ART. Most of the significant programme elements implied by “100% linkage to appropriate care” were directly implemented in TIME: 100% of notified TB/HIV cases not receiving ART were linked to ART.

MODELLING THE EPIDEMIOLOGICAL IMPACT OF THE GLOBAL PLAN 2018–2022

TB countries and country groups/contexts

Epidemiological impact was estimated by applying the TIME modelling framework to capture the potential impact of the Global Plan 2018–2022. The model was calibrated to the WHO Global TB Programme (GTB) data from 29 countries. These countries represent a range of contexts and 80% of the global TB burden. The estimated impact of the Global Plan 2018–2022 strategy in these countries was then applied to GTB epidemiological trends for an additional 142 countries⁸, by assigning to each country a TIME-modelled country in the same context or group.

TB contexts or groups were determined using statistical analysis of a multivariate dataset. The variables represented TB burden (cases and deaths), HIV burden, TB/HIV burden and aspects of socioeconomic standing (e.g., GDP per capita, Human Development Index, Fragile State Index), TB service delivery (e.g., TB treatment success) and general health systems financing (e.g., per capita health expenditure).

The group corresponding to countries with a high degree of private sector involvement in TB diagnosis and treatment was further used in the resource needs exercise. For these countries, a markup was added to projected budgets to cover commitments countries have made to strengthen public–private mix (PPM) activities.

GTB epidemiological data and trends

The Global Plan TB burden analysis relied strongly on incidence and notification data reported to WHO GTB in 2017.

A cubic spline regression approach was used to project

baseline trends through incidence and notification data. The trends thus obtained form the basis of the counterfactual to trends under the Global Plan 2018–2022 strategy should it be fully implemented within the 2018–2022 timeframe.

The projected TB incidence trends were used together with the reported TB/HIV data to disaggregate the total number of TB incident cases into three assumed components: HIV-negative, HIV-positive not on ART, and HIV-positive on ART, as outlined in Pretorius et al. 2014⁹. This disaggregation method was also based on cubic-spline regression, combining data from GTB and UNAIDS at country level.

The CD4 information and ART status information used in the HIV disaggregation method were drawn from the UNAIDS dataset. The TB/HIV data came from three sources that countries report to GTB: nationwide representative HIV serological surveys among a sample of reported TB cases, data from HIV sentinel groups, and results from routine testing of TB patients where testing coverage of newly reported cases is high.

TB mortality is affected by a complex relationship between active TB disease and many clinical variables. We approximated these variables in a simple functional relationship between incidence and case fatality ratios (CFRs). The eight categories of CFRs (HIV-negative, HIV-positive not on ART, HIV-positive on ART <6m, and HIV-positive on ART ≥6m, by notification status) were both clinically relevant and possible to estimate from available data. Using this approach, TB mortality was calculated as a product of incidence and CFRs.

The TIME model

TIME has been used by TB policy makers and NTPs to develop strategic responses to TB and produce projections that inform funding applications. The model has been used in many TB settings, including in countries where TB is driven by HIV and/or by weak health systems, in countries with high MDR-TB burden and in countries where TB programmes depend on a high level of private sector involvement. The estimates component of TIME was used by GTB to produce estimates for TB/HIV burden for the WHO Global TB Report.

The TIME model reflects key aspects of the natural history of TB, including primary and latent infection, reinfection and reactivation of latent TB. Smear positivity, negativity and smear conversion are explicitly handled in the model. TIME also accounts for the characteristics of paediatric TB, treatment history and drug resistance. It has an additional structure for HIV/ART that mimics the structure of the Spectrum AIDS Impact Model (AIM) module so that it can directly use the HIV programmatic data. TIME includes two generic strains by resistance status: susceptible and resistant to treatment. Resistance can be acquired during treatment or upon transmission at rates that distinguish it from the susceptible TB type in the model.

⁸ The 142 countries comprise a Global Plan result set determined by the intersection of the GTB country-level data and UNAIDS country-level Spectrum AIM/EPP files. Spectrum AIM/EPP is the software used by UNAIDS to produce country-level estimates of HIV burden and resource needs.

⁹ Pretorius C, Glaziou P, Dodd PJ, et al. Using the TIME model in Spectrum to estimate tuberculosis-HIV incidence and mortality. *AIDS*. 2014;28 Suppl 4:S477–87. doi:10.1097/QAD.0000000000000484

Epidemiological impact of the UNHLM targets

Figure 2.1 in Chapter 2 illustrates the modelled situation with respect to TB cases. The dots show data on the total number of cases and a baseline trend through these data. The assumption underlying the baseline was no further scale-up of interventions post-2017, resulting in a gradual decrease in cases. The red line shows the impact of the Global Plan 2018–2022 and the red square indicates the End TB target for cases, which is a 20% reduction on 2015 estimates by 2020.

Table 1 shows TB cases from 2018 to 2022 in WHO regions, Global Fund-eligible countries and cases globally.

UNHLM targets by WHO region, income status and country group

Tables 2.1 in Chapter 2 show the projections of volumes of patients in terms of notifications, notifications in children (ages 0–14), MDR-TB notifications and TB preventive therapy.

These projected targets at the global level closely match the UNHLM on TB targets.

TABLE 1: TB CASES BY WHO REGION

Region	TB CASES					Total
	2018	2019	2020	2021	2022	
EMR	796,800	772,300	730,400	687,200	643,000	3,629,700
AFR	2,436,500	2,319,800	2,173,100	2,031,400	1,892,600	10,853,400
AMR	287,700	282,400	269,400	255,200	239,700	1,334,400
EUR	257,500	244,900	230,600	217,900	208,300	1,159,200
WPR	1,823,400	1,764,600	1,659,200	1,555,800	1,453,000	8,256,000
SEAR	4,357,700	4,183,600	3,920,800	3,666,800	3,419,700	19,548,600
Global Fund Eligible	8,694,000	8,350,800	7,839,500	7,340,700	6,851,500	39,076,500
Global	9,959,474	9,567,640	8,983,464	8,414,228	7,856,295	44,781,101

MODELLING THE FINANCIAL NEEDS OF THE GLOBAL PLAN 2018–2022

GTB financing data for TB programmes

The costing method is based on WHO's financing database, to which more than 100 countries report financing data and from which unit costs were derived. These unit costs were based on notifications and applied to notification trends to estimate future needs.

It must be noted that costing methods that depend on the WHO TB financing data will be subject to the known and unknown limitations of the data, such as completeness and accuracy, as well as the way cost categories are aggregated. Nevertheless, the WHO TB database represents a detailed and complete financial reference database that has been routinely used in similar costing work for global TB costing and funding projections.

The first step in estimating the resource needs for the Global Plan 2018–2022 was to make a choice between using expenditure and using budget data. Expenditures are capped by funding realities, while budgets are based on national TB

strategic plans. As such, budgets are aspirational and typically include requests for improved diagnostic tools, equipment, and programme implementation structures. In effect, budgets are based on the types of TB programme improvements that are required in order to achieve the ambitious targets set out by the Global Plan. However, the information available does not allow for direct mapping between the budgets reported to WHO and TB programme elements implied by the Global Plan.

A decision was made to base unit costs in our analysis on reported budget data. Furthermore, we used 2016 data, which seemed to be more complete than the 2017 data, which we received perhaps at a time when they were being further processed. The cost categories we used are listed in Table 3 below.

In addition to these cost categories, WHO made available hospitalization and ambulatory care cost estimates. While costs resulting from TB patient health utilization (i.e., hospitalization and ambulatory care) do not typically represent a direct cost to the TB programme, these are significant costs that are related to TB case management and that need to be planned for, even if these costs accrue under another health

budget. These costs include patient in-day and out-day costs. To estimate these costs at country level, WHO uses estimates for average per-day hospitalization costs drawn from the Choice database and frequency of visit information reported as part of the WHO finance questionnaire.

Imputing missing unit cost data

For all of the services considered, only about 50% of the countries in the analysis had complete unit cost data, i.e., data in all categories. We used a learner algorithm¹⁰ to impute the missing unit costs. The training sets consisted of data from countries reporting non-zero unit costs, excluding China and India. The variables included in the original models were: total TB notifications, new HIV-positive notifications, confirmed RR- and MDR-TB, TB mortality excluding HIV, mortality among people living with HIV, TB incidence, TB incidence among people living with HIV, population size, population of people living with HIV, annual AIDS deaths, total need for ART, GDP per capita, Human Development Index, Fragile State Index, and health expenditures. The candidate algorithms were elastic net, random forest, support vector machine, boost, step AIC and step forward. The set of models selected was used to predict the unit costs in all the countries. To obtain uncertainty ranges, we repeated this process 200 times. At each iteration, the training set was sampled with replacement. The median of the simulations obtained for countries with missing data was used to impute the missing data, and the 95% uncertainty bounds were derived using the percentile method.

There are naturally many challenges in imputing missing data, including not knowing if the data are really missing or are perhaps reported in another category. Other than expert opinion, which resolved these questions in some instances, we had no other information to determine if and where that might be the case.

As an overall check, our base year (2016 in the case of financing data) budget estimate was US\$ 6.5 billion as opposed to US\$ 6 billion among countries that reported data, i.e., a 9% increase in expected budgets resulting from our imputation of what we assumed to be missing data.

Trends in unit costs

The costing steering group provided projected distributions and cost increases of different drug regimens, and insights into how the implementation of new guidelines is expected to influence resource needs.

Treatment

We applied these distributions of regimen types (long and short-course regimens in the case of second-line medicines, both of which are expected to double in cost, and assuming

10% requiring isoniazid-resistant TB treatment, i.e., adding fluoroquinolones, in the case of first-line medicines), both at base year and at the eventual expected distribution.

This method led to an annual increase in first-line medicine costs of 4.5% and a one-time increase of 110% for second-line medicines in 2019.¹¹ These annual increases are an applied component of first-line and second-line medicines that corresponds directly to medicine costs. (There are also other expenditures in these categories including buffer stock and distribution, and upfront procurement costs.)

MDR-TB case management

We assumed a 5% increase in the MDR-TB case management unit cost category for the increased monitoring of MDR-TB treatment and side effects, based partly on an assessment of budget increases for South Africa between 2015 and 2017 (6% annual unit cost increase). Although new MDR-TB patient guidelines call for more patient support, which argues for a bigger increase in the unit cost for MDR-TB case management, patient support mechanisms were added separately under enabling activities and so this aspect of MDR-TB cost increases was kept moderate.

Labs

For laboratory unit cost increases, we used South Africa as a model country in terms of budgeting and investing in the expansion of the use of X-ray for screening and GeneXpert for primary diagnosis. This gave a 17.8% annual increase in the unit cost for labs. We also used a spreadsheet calculation, which produced an estimate of an annual increase of (conservatively) 50% for this implementation.¹² We assumed an estimate of 25% for the annual increase in laboratory-related unit costs.

Preventive therapy

We made assumptions about the distribution of cases on a rifampentine-based regimen and less expensive regimens. We assumed that large demand and volumes will lead to a decrease in unit costs. We did not add costs to help ensure adherence and completion of the preventive course. The cost of ruling out active TB and other related costs for contact investigation are covered under programme costs and lab costs.

Hospitalization and ambulatory care

These costs include patient in-day and out-day costs as reported in the WHO financial database. In order to estimate these costs at country level, WHO uses estimates for average per-day hospitalization costs drawn from the Choice database and frequency of visit information reported as part

10 Sinisi SE, Polley EC, Petersen ML, et al. Super learning: an application to the prediction of HIV-1 drug resistance. *Stat Appl Genet Mol Biol.* 2007;6:7. doi:10.2202/1544-6115.1240

11 This 110% increase is based on expected short- and long-term price increases for second-line medicines and budgetary adjustments already underway.

12 This workbook used the unit cost from the One Health Model to estimate the cost of transitioning a diagnostic programme from the dominant clinical use of smear microscopy to the use of X-ray and GeneXpert by 2022. The method also accounted for equipping new laboratories for population densities according to WHO guidelines.

of the WHO finance questionnaire.

The increased use of non-injectable second-line medicines is expected to lead to a decrease in the number of hospitalization days for DR-TB patients by 2022. We assumed that countries with more hospitalization than the average, which we estimated to be 75 days, would decrease hospitalization to reach 75 days by 2022. We also assumed there would be no change in the annual unit cost for hospitalization of first-line patients.

Programme support costs

We assumed there would be no increase in overall programme management unit costs. There is little evidence in the budget data over the last few years to justify an increase in programme management costs.

Table 3 summarizes the unit cost increases used in the analysis.

Enabling activities

It is recognized that there has been a lack of investment in key enabling activities. The steering group agreed to uniformly increase projected budgets to include fixed percentages for specific 'enabling' activities, including advocacy and communications, PPM activities and community engagement.

We used detailed budgets from a few countries, such as India, Philippines, Georgia and Tajikistan, that were judged to be representative in terms of budgeting for enabling activities, in order to estimate the size of enabling cost categories, direct patient support, mobile technologies, community engagement, advocacy and communications, and PPM activities, relative to the total budgets (see Table 4). Country budgets were then adjusted to maintain the relative size of these estimates from 2018 through 2022. The country group classifications of the Global Plan 2016–2020 were used to assign PPM costs to countries with high private sector involvement.

TABLE 2: FIELDS AND DESCRIPTIONS FROM WHO FINANCING DATABASE

Database field	Name	Description
Budget_lab	Laboratory infrastructure, equipment and supplies	Building, maintaining and renovating TB laboratories, laboratory equipment purchase and maintenance, consumables for all tests (including TB screening for people living with HIV/AIDS), quality assurance, retooling and the transportation of specimens
Budget_staff	NTP staff (central unit staff and subnational TB staff)	Salaries and incentives for those working only on TB activities at central and peripheral levels (for example, provincial TB coordinators, district TB coordinators, etc.); does not include primary health care personnel working on other diseases in addition to TB
Budget_fld	DS-TB: medicines	Medicines for patients being treated for DS-TB, including children, re-treatment cases and buffer stock
Budget_prog	DS-TB: programme costs	Management and supervision of the TB programme, training, policy development, meetings, visits for supervision, purchase of office equipment/vehicles, construction of buildings for use by programme staff, routine surveillance, advocacy and communication, PPM activities, community engagement, active case finding, infection control, and management of TB medicine procurement and distribution
Budget_slid	DR-TB: medicines	Medicines to treat DR-TB (RR-TB, MDR-TB or XDR-TB), including medicines to deal with adverse events for RR-/MDR-/XDR-TB patients
Budget_mdrmtg	DR-TB: programme costs	Management of DR-TB services, excluding medicines, for example, renovation of MDR-TB wards, support for the Green Light Committee, conducting an MDR-TB situation assessment, loss-to-follow-up and contact tracing, palliative care
Budget_tbhiv	Collaborative TB/HIV activities	Collaboration between TB and HIV programmes aimed at reducing the impact of HIV-related TB; activities include TB/HIV coordinating bodies, joint TB/HIV training and planning, HIV testing for people with TB, HIV surveillance among people with TB, co-trimoxazole preventive therapy (CPT), joint TB/HIV education/communication, and ART for people with TB; TB screening for people living with HIV/AIDS is included under Lab infrastructure, equipment, and supplies
Budget_patsup	Patient support	Cash transfers, food packages, transportation vouchers, educational and emotional support or other in-kind benefits given to people with TB
Budget_orsrvy	Operational research and surveys	Periodic surveys (prevalence, drug resistance, patient catastrophic cost); routine surveillance (epidemiology review, inventory studies, pharmacovigilance, systematic assessment of the surveillance system); operational research
Budget_oth	All other budget lines	

TABLE 3: ESTIMATED ANNUAL UNIT COST INCREASES

Unit Cost Description	Increase Reached by 2022	Comment
Programme Support	0.0%	No data
First-Line Medicines	4.5%	Implementation of new guidelines
Second-Line Medicines	110%	Implementation of new guidelines. One-off increase in 2019.
MDR-Case Management	5.0%	Based on analysis of South Africa budget
Labs	25.0%	Based on analysis of South Africa budget
TB/HIV	0.0%	Preventive therapy handled separately
Health Services non-MDR	0.0%	Not estimated, but expected to decrease
Health Services MDR	0.0%	Country-specific decreases estimated

TABLE 4: ENABLING ACTIVITIES ADDED TO BUDGETS. PS-PATIENT SUPPORT, MT-MOBILE TECHNOLOGIES, CSO-COMMUNITY ORGANIZATION, ADV & COM-ADVOCACY AND COMMUNICATIONS

Country group	PS	MT /ICT	CSO	Adv &Com	PPM activities	Total
	Mark-up ranges for enabling activities					
	5.0%–8.0%	1.0%	2.5%–3.0%	1.0%–2.0%	2.0%–9.0%	
High MDR Burden, Centralized Care	5.0%	1.0%	2.5%	1.0%	0.0%	9.5%
High TB/HIV, SADC	5.0%	1.0%	2.5%	1.0%	0.0%	9.5%
High TB/HIV, outside SADC	5.0%	1.0%	2.5%	1.0%	0.0%	9.5%
Moderate Burden, COE	5.0%	1.0%	2.5%	1.0%	0.0%	9.5%
High Burden, Pvt Sector	5.0%	1.0%	2.5%	1.0%	8.0%	17.5%
Moderate Burden, Middle Income	5.0%	1.0%	2.5%	1.0%	0.0%	9.5%
Low Burden, High Income	5.0%	1.0%	2.5%	1.0%	0.0%	9.5%

Nigeria, South Africa, Kenya and United Republic of Tanzania – countries previously classified under the ‘high HIV’ groups – were added to this ‘PPM’ group.

No markups for enablers were added to the budgets of high-income, low-burden countries.

No markups for enablers were added to health systems costs (i.e., mostly hospitalization costs), since these costs are not borne by NTPs.

Resource needs results

Table 7.1 in Chapter 7 shows the financial needs required to implement the Global Plan 2018–2022 by income status, Global Fund eligibility, Global Plan country group, WHO region and BRICS membership, as well as globally. Resource needs will increase substantially from around US\$ 9.2 billion in 2018 to about US\$ 15.6 billion by 2022 should the Global Plan 2018–2022 be fully implemented. A total of US\$ 64.8 billion will be needed for the period 2018–2022, averaging US\$ 13 billion per annum.

Table 5 shows the average patient care costs for non-MDR and MDR-TB cases. These estimates include drug costs, general health system costs and programme support costs.

Excluding enablers, which are difficult to separate according to MDR status, the average cost to treat non-MDR patients is about US\$ 1,050, while the average cost for MDR patients is US\$ 15,500. In Global Fund-eligible countries, these figures are US\$ 860 and US\$ 12,700, respectively. The average MDR patient cost in the WHO European Region, which generally has a high degree of centralized patient care, can be as high as US\$ 32,000.

Note that there is an expected increase in the global patient care cost for non-MDR patients over the 2018 to 2022 period. For MDR-TB, while there is also an expected drug cost increase, the cost per patient is somewhat offset by the expected drop in hospitalization costs; consequently, the cost per MDR patient treated for the 2018–2022 period stays relatively stable.

RETURN ON INVESTMENT

A return-on-investment (ROI) analysis was performed using the Global Plan 2016–2022 method, i.e., the methodology of the Lancet Commission on Investing in Health (Jamison et al. 2013¹³), but adapted to new guidelines for benefit–cost analysis following work with the Global Fund to estimate the ROI of the new replenishment cycle.

An adjusted value of a statistical life (VSL) calculation was used to calculate country- and year-specific VSLs:

$$VSL_{it} = \left(VLSY_{USA} * \left(\frac{GDP_{it}}{GDP_{USA}} \right)^e \right) \quad t = 2018, 2019, \dots, 2022,$$

where VSL_{*i*} is the value for country *i* in year *t*, VLS_{USA} is calculated using the Jamison et al. (2013) estimate of VSL for the United States of US\$ 9.4 million divided by an assumed remaining life expectancy of 40 years; GDP_{*i*} is the purchasing-power-parity (ppp) adjusted gross domestic product (GDP) per capita of country *i* in year *t* in international dollars, which was obtained from the April 2018 World Economic Outlook; GDP_{USA} is the ppp adjusted GDP per capita of the United States (estimated at US\$ 57,815 for 2018); *e* is an estimate of income elasticity of 1.5.

To calculate the net-benefit (or return) relative to a business-as-usual scenario, the total number of deaths averted by the Global Plan was multiplied by the country-year-specific VSLs, subtracting the additional costs of the Global Plan 2018–2022:

$$\text{Net-Benefit} = (\text{Deaths_BAU} - \text{Death_GP})_c * VSL_c - (\text{Cost_GP} - \text{Cost_BAU})_c$$

where *c* = country. ROI is given by:

$$\text{ROI} = \text{Net-Benefit} / (\text{Cost_GP} - \text{Cost_BAU})_c$$

Deaths and costs were discounted to present values in 2018 by applying a discount factor of 3%. Only HIV-negative deaths were considered, as most of the benefits in HIV-positive deaths averted are expected to result from ART expansion within HIV programmes, which is mostly not a cost to NTPs.

Results are presented in Table 7.2 in Chapter 7, showing a global net benefit of ~ US\$ 711 billion and an ROI of approximately 1:44 by 2022 (a US\$ 1 investment yields US\$ 44 in return) if investments are continued to maintain the high coverage implied by the implementation of the Global Plan 2018–2022. It should be noted that much of the unmet need lies in low-income countries; for those countries, the ROI is expected to be significantly lower: 1:13.

An ROI of 1:27 was estimated in the past for the ‘standard’ scale-up scenario of the Global Plan 2016–2020. The ROI of the ‘accelerated’ Global Plan 2016–2020 was estimated at 1:85. The ROI estimate for the Global Plan 2018–2022, which has elements of the accelerated scale-up along with additional ‘enabling costs’, falls between the previous ROI estimates – closer to the ROI of the standard investment Global Plan 2016–2020.

13 Jamison DT, Summers LH, Alleyne G, et al. Global health 2035: a world converging within a generation. The Lancet Commissions. 2013;382(9908):1898–955. doi:10.1016/S0140-6736(13)62105-4

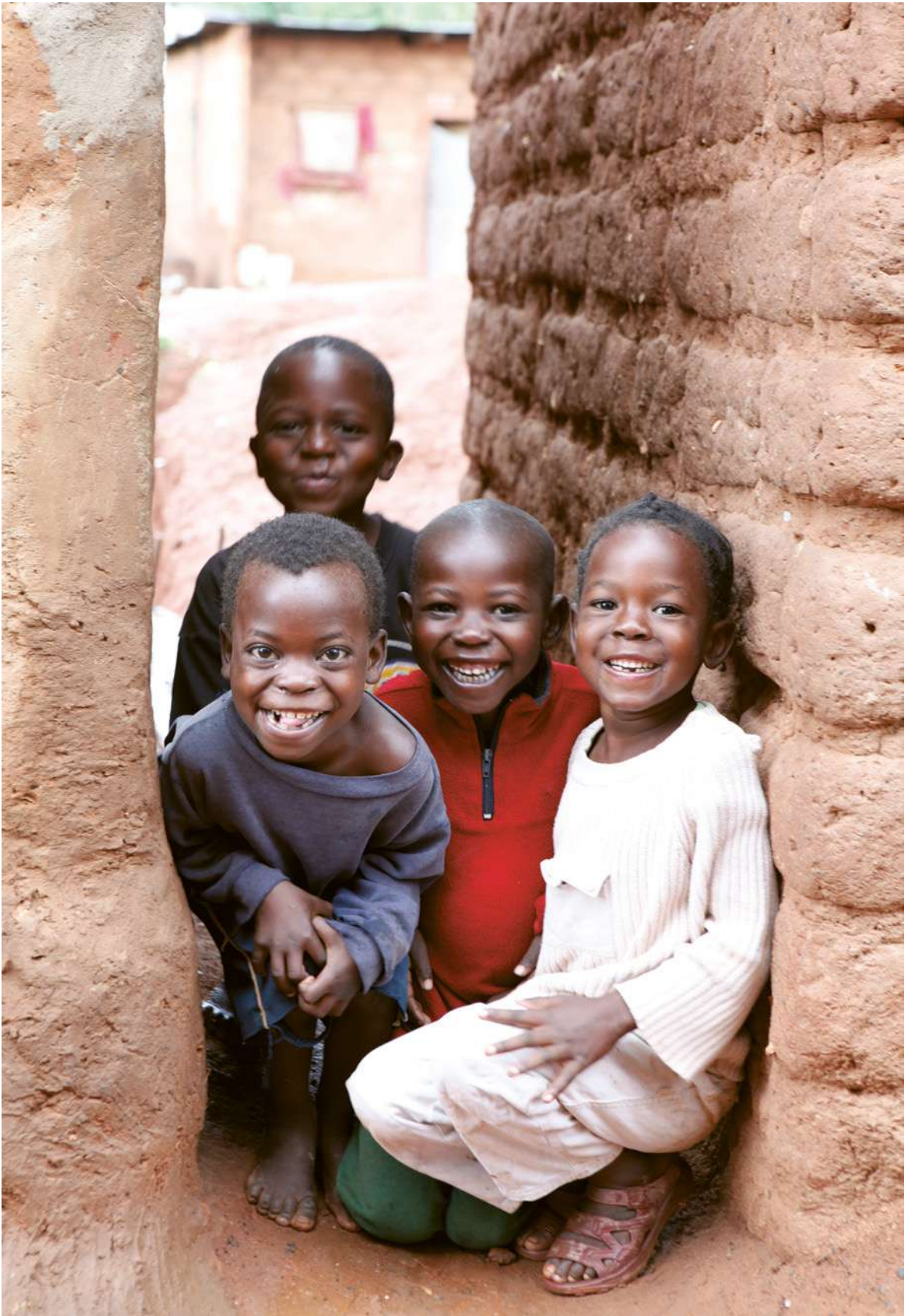
TABLE 5: COST PER NON-MDR AND MDR PATIENTS TREATED, BY INCOME STATUS, GLOBAL FUND ELIGIBILITY, GLOBAL PLAN COUNTRY GROUP, WHO REGION AND BRICS MEMBERSHIP

	2018	2019	2020	2021	2022	Total
COST PER PATIENT TREATED: NON-MDR (USD)						
GLOBAL TOTAL						
Total (Global, including OECD countries)	990.00	970.00	1,060.00	1,160.00	1,270.00	1,090.00
Total (Global, excluding OECD countries)	910.00	910.00	1,000.00	1,100.00	1,210.00	1,020.00
BY INCOME STATUS						
Low income	830.00	850.00	910.00	990.00	1,110.00	940.00
Lower middle income	580.00	600.00	710.00	800.00	900.00	710.00
Upper middle income	1,970.00	2,040.00	2,190.00	2,340.00	2,510.00	2,190.00
High income	5,790.00	5,850.00	5,920.00	6,020.00	6,110.00	5,930.00
GLOBAL FUND ELIGIBLE COUNTRIES, BY INCOME STATUS						
Low income	830.00	850.00	910.00	990.00	1,110.00	940.00
Lower middle income	580.00	600.00	710.00	800.00	900.00	710.00
Upper middle income	2,680.00	2,790.00	3,060.00	3,380.00	3,760.00	3,110.00
Total	780.00	800.00	900.00	1,010.00	1,130.00	920.00
GLOBAL PLAN COUNTRY SETTING						
High MDR Burden, Centralized Care	6,540.00	6,810.00	7,410.00	8,050.00	8,480.00	7,360.00
High TB/HIV, SADC	1,320.00	1,370.00	1,450.00	1,600.00	1,800.00	1,510.00
High TB/HIV, non-SADC	1,460.00	1,620.00	1,900.00	2,160.00	2,410.00	1,950.00
Moderate Burden, COE	680.00	700.00	760.00	820.00	920.00	780.00
High Burden, Private Sector	480.00	510.00	560.00	630.00	720.00	580.00
Moderate Burden, Middle Income	1,890.00	1,990.00	2,060.00	2,170.00	2,300.00	2,080.00
India	330.00	340.00	370.00	400.00	450.00	370.00
China	1,240.00	1,260.00	1,310.00	1,350.00	1,410.00	1,310.00
Low Burden, High Income	4,660.00	4,640.00	4,720.00	4,840.00	4,980.00	4,760.00
WHO REGION						
EMR	430.00	460.00	500.00	560.00	650.00	520.00
AFR	1,270.00	1,360.00	1,520.00	1,710.00	1,910.00	1,570.00
AMR	2,590.00	2,680.00	2,780.00	2,910.00	3,080.00	2,800.00
EUR	6,270.00	6,480.00	6,940.00	7,430.00	7,790.00	6,910.00
WPR	1,210.00	1,210.00	1,230.00	1,280.00	1,350.00	1,250.00
SEAR	400.00	410.00	460.00	500.00	570.00	470.00
BRICS (BRA,CHN,IND,RUS,SAF)						
Total	780.00	760.00	810.00	870.00	950.00	830.00

	2018	2019	2020	2021	2022	Total
COST PER PATIENT TREATED: MDR (USD)						
GLOBAL TOTAL						
Total (Global, including OECD countries)	14,680.00	16,920.00	15,550.00	15,200.00	15,430.00	15,500.00
Total (Global, excluding OECD countries)	14,620.00	16,850.00	15,490.00	15,140.00	15,370.00	15,440.00
BY INCOME STATUS						
Low income	14,460.00	19,520.00	19,190.00	19,360.00	19,700.00	19,110.00
Lower middle income	6,730.00	9,670.00	10,330.00	10,620.00	10,830.00	10,140.00
Upper middle income	26,680.00	28,630.00	25,170.00	24,240.00	24,900.00	25,570.00
High income	21,650.00	27,510.00	26,940.00	26,420.00	26,650.00	25,890.00
GLOBAL FUND ELIGIBLE COUNTRIES, BY INCOME STATUS						
Low income	14,460.00	19,520.00	19,190.00	19,360.00	19,700.00	19,110.00
Lower middle income	6,730.00	9,660.00	10,330.00	10,620.00	10,830.00	10,140.00
Upper middle income	13,990.00	17,480.00	17,140.00	17,270.00	17,310.00	16,700.00
Total	8,630.00	11,680.00	11,950.00	12,130.00	12,330.00	11,740.00
GLOBAL PLAN COUNTRY SETTING						
High MDR Burden, Centralized Care	30,010.00	33,930.00	34,410.00	35,180.00	36,290.00	34,140.00
High TB/HIV, SADC	8,750.00	13,800.00	15,190.00	15,940.00	16,280.00	14,670.00
High TB/HIV, non-SADC	13,580.00	17,620.00	16,980.00	16,960.00	17,180.00	16,910.00
Moderate Burden, COE	15,790.00	18,610.00	18,000.00	18,140.00	18,390.00	18,110.00
High Burden, Private Sector	9,780.00	14,490.00	15,250.00	15,660.00	15,980.00	15,120.00
Moderate Burden, Middle Income	13,080.00	17,080.00	16,280.00	15,930.00	15,920.00	15,830.00
India	3,660.00	5,060.00	5,090.00	5,120.00	5,140.00	4,950.00
China	7,140.00	9,000.00	9,030.00	9,100.00	9,150.00	9,020.00
Low Burden, High Income	18,660.00	25,090.00	28,720.00	31,010.00	32,120.00	28,110.00
WHO REGION						
EMR	12,400.00	19,520.00	19,920.00	20,190.00	20,580.00	19,850.00
AFR	10,860.00	16,060.00	17,250.00	17,900.00	18,240.00	17,030.00
AMR	16,570.00	21,970.00	21,410.00	21,310.00	21,140.00	20,790.00
EUR	29,540.00	33,500.00	33,970.00	34,730.00	35,880.00	33,700.00
WPR	9,380.00	11,700.00	11,200.00	11,220.00	11,380.00	11,190.00
SEAR	4,520.00	6,410.00	6,760.00	6,920.00	7,050.00	6,620.00
BRICS (BRA,CHN,IND,RUS,SAF)						
Total	15,640.00	16,730.00	14,410.00	13,630.00	13,880.00	14,510.00

TABLE 6: RESOURCE NEEDS (US\$ BILLIONS), BY COST CATEGORY, INCLUDING ENABLERS

RESOURCE NEEDS (US\$ BILLIONS)						
Cost Category	2018	2019	2020	2021	2022	Total
First-Line Medicines	339.1	404.9	444.8	436.2	422.3	2,047.2
Second-Line Medicines	408.7	1,010.6	1,689.9	2,215.1	2,295.5	7,619.7
Laboratory Infrastructure, Equipment and Supplies	705.3	1,000.3	1,312.5	1,566.7	1,833.8	6,418.7
First-Line Programme Costs	2,560.8	2,947.8	3,276.6	3,258.5	3,147.5	15,191.2
Second-Line Programme Costs	1,191.0	1,346.1	1,891.2	2,364.9	2,527.4	9,320.7
First-Line General Health System	2,489.4	2,640.4	2,540.8	2,362.9	2,200.5	12,234.0
Second-Line General Health System	445.6	494.7	751.1	931.0	925.1	3,547.7
Collaborative TB/HIV Activities	155.8	156.6	157.5	158.2	158.6	786.7
Preventive Therapy	206.5	217.7	316.3	399.8	565.2	1,705.6
Enablers	741.7	960.6	1,263.9	1,454.1	1,530.4	5,950.7
Total	9,244.0	11,179.7	13,644.7	15,147.4	15,606.4	64,822.2



ANNEX 2
INVESTMENT PACKAGES
BY COUNTRY SETTING

Country settings were identified in the Global Plan 2016–2020 through a process of grouping countries based on their TB epidemiology, geopolitical situation, health system, income, etc. To group countries, a quantitative principal component analysis (PCA) was conducted using 27 parameters, supplemented with expert opinion.¹ The updated Global Plan 2018–2022 makes no changes to the country settings.

The Global Plan’s investment packages are groups of interventions, tailored to the country settings, which propose how investments are to be prioritized in order to achieve the UNHLM on TB targets and be on track to end or eliminate TB. These investment packages include investments in interventions that are needed, but are currently either not implemented or need to be massively scaled up.

Selection process for intervention and investment packages for each setting

The following steps were used for this purpose:

1. Create the Scoring Matrix of interventions.

All possible interventions were listed based on earlier work

done for the Global Fund TB Modular framework. There were 35 interventions in four areas: Case Finding and Diagnosis; Treatment and Case Management; Prevention; and Enabling Environment and Systems. A Scoring Matrix was created to identify investment packages for nine country settings.

2. Rate interventions in each country setting using the Scoring Matrix.

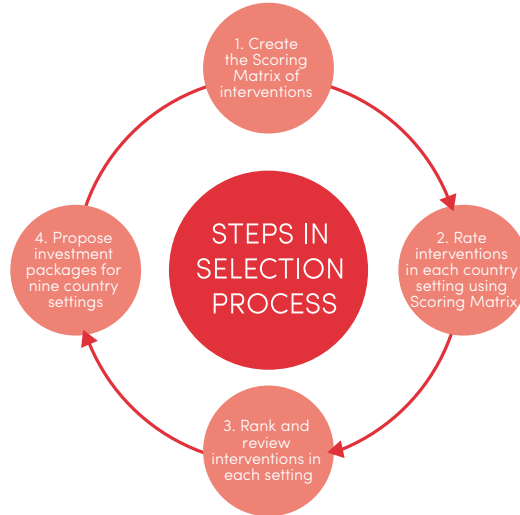
Six TB experts with diverse experience at country level and global level independently scored interventions for each setting.

3. Rank and review interventions in each country setting.

Aggregated scores from the experts were used to rank interventions from high to low score for each setting, and a consensus was developed using the Delphi technique.

4. Propose the investment packages for nine country settings.

¹ Annexes to the Global Plan to End TB 2016–2020. Geneva: Stop TB Partnership; 2015. <http://www.stoptb.org/assets/documents/global/plan/plan2/Annexes.pdf>



SCORING MATRIX FOR INVESTMENT PACKAGES

1. Case Finding and Diagnosis

Intervention	Description
1.1. Roll-out of molecular diagnostics as initial test for TB and RR-TB	At peripheral service delivery level; Xpert MTB/RIF for now, but also other technologies that will be endorsed in the near future.
1.2. Specimen transportation	It is suggested to have specimen referral (transportation) as a separate Intervention aimed at increasing access to both rapid molecular tests (Xpert, LPA) and culture-based tests.
1.3. Culture and DST at referral laboratories and laboratory quality assurance	Ensuring universal DST for first-line and second-line medicines, using rapid techniques at referral level. Includes also genome sequencing as applicable in the near future.
1.4. Active TB case finding	Includes community and facility-based case finding and special groups at risk (i.e., prisoners, miners, etc.); mobile diagnostic units, community mobilization and people-friendly support systems; specific strategies aimed at diagnosis among children and women, etc.
1.5. TB/HIV case finding and diagnosis	Includes both i) TB screening among people living with HIV and use of specific diagnostics for people living with HIV like TB LAM, and ii) HIV testing and counselling among people with TB.
1.6. Contact investigation	It is suggested to include contact investigation separately to emphasize the importance of scaling up this Intervention for finding active TB cases (including adult contacts), while testing and preventive therapy for TB infection are included under the Prevention module below.
1.7. Other relevant tools and activities, case finding and diagnosis	Chest X-ray, digital X-ray, computer-aided diagnosis, other activities related to this Module that do not fall strictly under the above Interventions.

2. Treatment and Case Management

Intervention	Description
2.1. Treatment of DS-TB in adults	Includes procurement of first-line medicines, but also other relevant activities (technical assistance, training, etc.) that do not fall under the other Interventions in this Module.
2.2. Treatment of DS-TB in children and adolescents	Same as for Intervention 2.1 above, but for children 0–14 years of age and adolescents 15–17 years of age.
2.3. Treatment of DR-TB cases in adults	Includes procurement of second-line medicines, but also other relevant activities (technical assistance, training, etc.) that do not fall under other Interventions in this Module.
2.4. Treatment of DR-TB in children and adolescents	Same as for Interventions 2.3 above, but for children 0–14 years of age and adolescents 15–17 years of age.
2.5. Patient support: incentives and enablers	Monetary incentives, food packages, transportation enablers and other incentives (for all types of TB cases).
2.6. Patient support: video-observed treatment and other digital adherence technologies	All kinds of 'innovative' digital technologies for TB – important to develop and monitor.
2.7. Patient support: other activities	Psychosocial assistance, peer support, nutritional and livelihood support, rehabilitation and other adherence support not categorized under the above two Interventions.
2.8. Treatment monitoring, management of adverse events and pharmacovigilance/aDSM	It is proposed to separate this Intervention in order to emphasize the importance of clinical monitoring and aDSM (especially in DR-TB cases), although it also relates to the next Intervention.
2.9. Management of HIV-associated TB and other comorbidities	See the remark above. Includes antiretroviral therapy, but also management of other comorbidities such as hepatitis, diabetes, etc.
2.10. Other activities, treatment and case management	Other activities related to this Module that do not fall strictly under any of the above Interventions.

3. Prevention

Intervention	Description
3.1. Testing and preventive therapy for TB infection in children	Includes medicines with appropriate regimens and monitoring for treatment completion, technical assistance, training and other needs.
3.2. Testing and preventive therapy for TB infection in people living with HIV	Same as for Intervention 3.1 above.
3.3. Testing and preventive therapy for TB infection in adult household and other close contacts of TB patients	Same as for Intervention 3.1 above.
3.4. Testing and preventive therapy for TB infection in other at-risk groups	Same as for Intervention 3.1 above.
3.5. Preventive therapy for contacts of people with DR-TB	Same as for Intervention 3.1 above.
3.6. Infection control	It is proposed to include infection control under the Prevention module. Includes infection control in inpatient and outpatient/community settings, health worker surveillance for TB, etc.
3.7. Other activities, prevention	Other activities related to this Module that do not fall strictly under any of the above Interventions.

4. Enabling Environment and Systems

Intervention	Description
4.1. High-level advocacy, strategic planning and engaging all stakeholders	Support to country-level multisectoral and intersectoral engagement to end TB, including nationwide national strategic plans and regional/subnational plans.
4.2. Information, communication and social mobilization	Includes information/education activities for the general public, as well as for different special target audiences.
4.3. Health financing and service delivery for TB	Includes health system reform and development initiatives that are relevant for improving TB prevention and care as part of UHC (related to health financing schemes, resource allocation, provider payment mechanisms, enabling people- and patient-centred models for delivering TB services).
4.4. Human resources development for TB care	Includes all types of human resources for health (HRH) initiatives that have an impact on TB prevention and care (e.g., medical education reforms, task-shifting, engaging other providers, involving primary health care providers, various capacity-building activities, etc.).
4.5. Community-based interventions and civil society involvement	Broader scope initiatives and projects that enable effective participation of community actors and civil society in TB prevention and care. Note: specific projects targeting, for example, CSO support for adherence of DR-TB patients, may also be considered under Interventions 2.2–2.4 above.
4.6. Addressing special needs of key populations (prisoners, mobile populations, miners and others)	Includes specific activities that focus on the listed groups (e.g., social support to ex-miners with TB and their families; different TB prevention and care activities in cross-border migrants, etc.).
4.7. Removing human rights and gender-related barriers to accessing TB services	Activities that address stigma and discrimination reduction, human rights and legal literacy, legal services, monitoring and reform of laws and policies, training of law makers, sensitization of health care providers on human rights and medical ethics, etc.
4.8. Engaging private health care providers	PPM activities that may cross-cut case finding, treatment, prevention and other aspects of TB care. Also includes management systems and tools needed for effective PPM TB implementation and monitoring, which require separate budget such as interphase agencies, digital systems for notification and monitoring, incentives, etc., as well as certain eligible patient costs.
4.9. Procurement and supply management (PSM) systems	Covers various aspects of PSM for medicines and health products relevant to TB, with special attention in view of transition from donor funding.
4.10. TB information systems	Strengthening TB information systems that provide for effective oversight, monitoring and evaluation of TB interventions at national and subnational levels, as well as international data exchanges, including real-time case-based TB surveillance with or without integration into the general health management information system (HMIS).
4.11. Other activities, enabling environment and systems	All other activities related to this Module that do not fall strictly under any of the above Interventions.



Stop  Partnership

Global Health Campus
Chemin du Pommier 40
1218 Le Grand-Saconnex
Geneva, Switzerland

www.stoptb.org