Global Plan to End TB: 2023-2030
DRAFT FOR STOP TB PARTNERSHIP COORDINATING BOARD

13 May, 2022

Executive Summary

The Global Plan to End TB, 2023-2030 (Global Plan) is a plan for ending tuberculosis (TB) as a public health challenge by 2030—the year by which governments around the world have committed to achieving the United Nations Sustainable Development Goals. It provides the most detailed costing estimates of any Global Plan to date. This Global Plan builds on the previous edition, *Paradigm Shift*, which laid out priority actions from 2018-2022 that were informed by global commitments endorsed by member states at the 2018 United Nations High Level Meeting (UNHLM) on Tuberculosis.

This Global Plan anticipates the priority actions that will be necessary in the wake of the COVID-19 pandemic and informs follow-up commitments to be made at a second UNHLM on TB in 2023.

The numbers of people diagnosed with TB plummeted during the COVID-19 pandemic, reversing progress against TB by several years and injecting greater urgency to global TB efforts. Though the pandemic severely disrupted these efforts, it also created a new sense of what can be achieved through mobilization of political will and financial and human resources. The discovery and roll-out of the first COVID-19 vaccines in less than one year was unprecedented, while global distribution has been woefully inequitable—an experience that provides critical lessons for TB vaccine development and access.

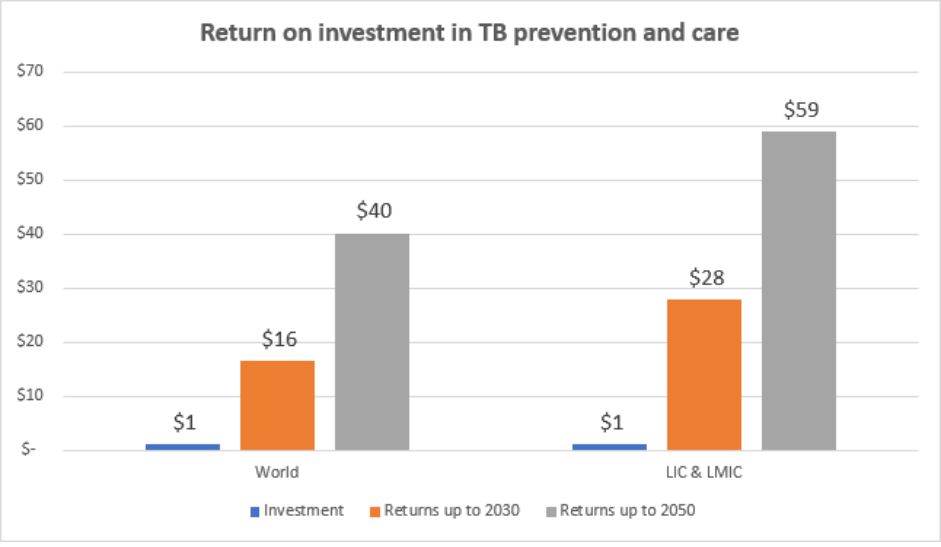
Like previous editions, this Global Plan emphasizes the need for a rights-based, people-centred approach to ending TB. It increases the focus on prevention as a public health priority alongside universal access to TB care and support, an accelerated approach to TB research and development, and the introduction and scale-up of new TB tools. For the first time, this edition anticipates that comprehensive interventions will include the development and use of a new TB vaccine. Implementing the Global Plan will require a stronger, sustained commitment to partnerships that involve participation from a variety of sectors as well as TB survivors and members of affected communities.

To aid country-level decision-making, this edition of the Global Plan provides guidance for investing in a comprehensive package of interventions. These "investment packages" are based on new impact modeling and financial estimates, which project that ending TB is feasible by 2030 with significant new inputs that support implementation at scale. This modeling also contributed to the investment case for the 7th replenishment of the Global Fund to Fight AIDS, Tuberculosis and Malaria in 2022.

Return on investment

The Global Plan is an investment in both human life and economic productivity. Implementing the priority actions recommended by the Global Plan would deliver a return of US$ 40 for every dollar invested.

Figure A. Return on investment in TB prevention and care

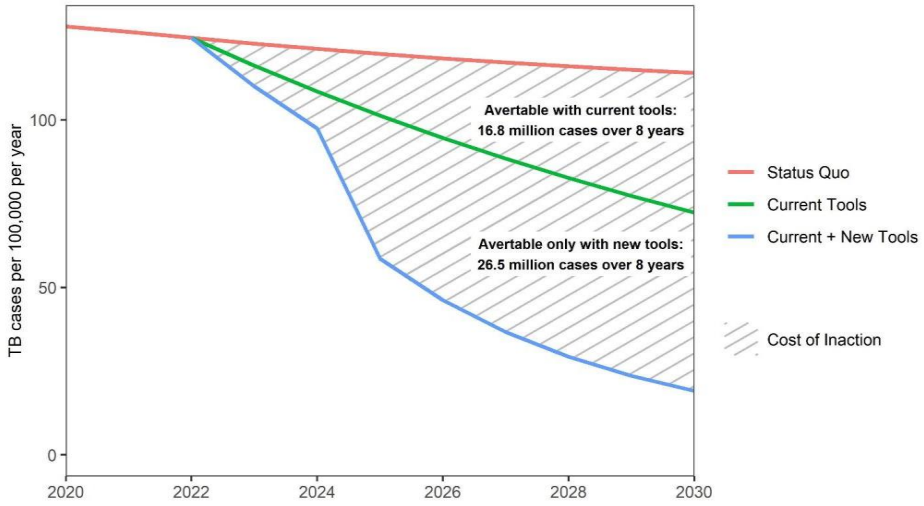


The cost of inaction

Delaying or failing to implement the Global Plan would result in immense human and economic loss. If the status quo were to continue from 2023 through 2030, an additional 43 million people would develop TB, leading to 6.6 million additional TB deaths and a global economic cost of US$ 1 trillion. Humanity would lose a projected 234 million disability-adjusted life years (DALYs).

To avert this scenario will require a substantial and rapid scaling up of public health interventions using currently available tools (i.e., treatment regimens, diagnostics) and an increase in investment in TB research and development for new tools.

Figure B: The potential human cost of failing to implement the Global Plan 2023-2030.



Resource Needs

This edition of the Global Plan projects that between 2023 and 2030, US$ 249.98 billion will need to be mobilized from all sources—governments, philanthropy, the private sector, and innovative sources of financing. This includes US$ 157.2 billion, averaging US$ 19.65 billion per annum, for TB prevention and care, and an additional amount of US$ 52.6 billion for vaccination once a new vaccine is available. This increase is driven by the need to make up for lost progress due to COVID-19, to accelerate the development and introduction of new TB tools—including at least one new vaccine—and to make up for financing gaps in prior years.

An additional US$ 40.18 billion is needed to accelerate the development of new TB medicines and treatment regimens, diagnostics, and vaccines, which includes US$ 800 million annually to support basic science research.

Table A: Resources needed for TB prevention, care and support (USD billions)

	2023	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**
Diagnosis	4.8	5.7	7.1	8.0	7.4	7.0	7.0	7.2	54.1
Treatment	0.9	1.0	1.1	1.1	0.8	0.6	0.5	0.5	6.5

Prevention	0.7	0.8	1.0	1.1	1.2	1.4	1.5	1.7	9.3
Vaccination	0.0	0.0	0.0	0.0	12.4	12.8	13.4	14.0	52.6
Health Systems	1.9	2.2	2.8	3.1	2.7	2.4	2.4	2.5	20.0
Enablers	2.3	2.5	3.0	3.2	3.0	2.9	3.0	3.1	22.9
Program Costs	5.2	5.3	5.4	5.5	5.6	5.7	5.8	5.9	44.4
Total	**15.7**	**17.6**	**20.3**	**21.9**	**33.1**	**32.8**	**33.6**	**34.9**	**209.8**

Table B. Resources needed to accelerate research and development of new TB tools, 2023-2030

New Tool	Investment needed (US$ billions)
Medicines	16.06
Diagnostics	7.72
Vaccines	10.00
Basic science	6.4
Total	**40.18**

Projected Impact

Modeling projects the following impact objectives and targets will be met if the Global Plan 2023-2030 is fully funded and implemented.

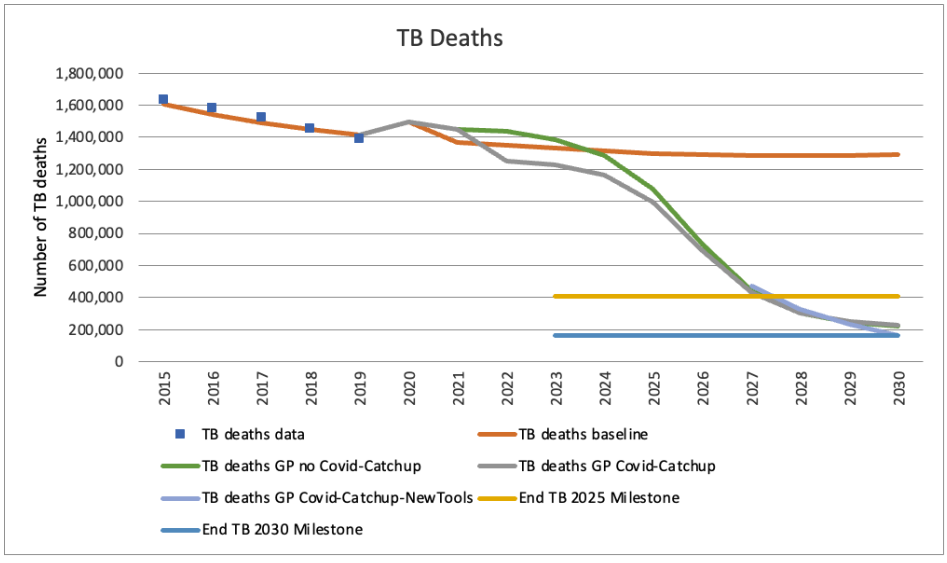
- At least 95% of people with TB will receive a diagnosis
- All high-risk and key and vulnerable populations will be able to access periodic screening
- 50 million people will access appropriate TB treatment, including 3.7 million children and 2.2 million people with drug-resistant TB

- 35 million people will access TB preventive treatment
- At least one new TB vaccine will be introduced for widespread use by 2026

These and other interventions would lead to:

- A 80% decline in the number of people who develop TB annually per 100 00 population by 2030 (compared to 2015)
- A 90% decline in the number of people who die from TB annually by 2030, compared to 2015 (Figure 2)

Figure C: Projected TB deaths in various Global Plan implementation scenarios.



This edition of the Global Plan was developed by a writing team working in collaboration with the Global Plan Task Force and a team of epidemiological and financial modelers, with input gathered from the international community through a series of public regional and global consultations. There are nine chapters.

Chapter 1 provides the international context that informs the Global Plan. Chapters 2 through 9 provide priorities for action.

Chapter 2. Ending TB through comprehensive investment packages implemented at scale

Priority actions:

- Invest in a comprehensive investment package
- Scale up interventions to achieve key objectives and targets

Chapter 3. Scaling up TB care

Priority actions:

- Re-imagine TB care, delivering services through a people-centered approach
- Scale-up the use of modern diagnostics
- Find the missing people with TB
- Expand early diagnosis, including at sub-clinical stages
- Develop and implement public communications strategies to raise TB awareness and promote early health-seeking
- Integrate TB screening and testing into other health services, with a focus on services that address common comorbidities or risk groups, depending on local epidemiological context.
- Provide support that enables people receiving TB care to complete a full course of treatment without an undue burden on them and their families, while avoiding catastrophic costs.
- Strengthen procurement systems and supply chains

Chapter 4. Scaling up TB prevention

Priority actions:

- Implement Airborne Infection Prevention and Control (AIPC) measures in health care settings and high-risk indoor places where people congregate
- Provide TB preventive treatment (TPT) for those living with TB infection and who are at higher risk of progression to active TB disease
- Deploy effective vaccines once such vaccines are officially recommended and available.
- Address TB risk factors and social determinants

Chapter 5. Partnering with key stakeholders: communities and the private sector

Priority actions:

- Increase funding support for engaging TB-affected communities in the TB response at least fourfold
- Support community-based and home-based models for delivering TB prevention and care
- Scale up public-private mix (PPM) approaches to improve the quality of TB care, reduce out-of-pocket expenses and improve data reporting in the private health sector
- Support a multi-sectoral TB response through stronger partnerships

Chapter 6. Ending TB through Universal Health Coverage, Pandemic Preparedness and Response, and Socioeconomic Actions

Priority actions:

- Expand access to TB services through UHC initiatives
- Position the TB response at the center of Pandemic Preparedness and Response efforts
- Invest in poverty alleviation and sustainable development

Chapter 7. Human Rights, Stigma, Gender, Key & Vulnerable Populations

Priority actions:

- Position universal human rights as the foundation of the TB response
- Eliminate TB-related stigma and discrimination
- Ensure TB interventions are gender-responsive
- Prioritize, reach, and involve key and vulnerable populations

Chapter 8. Research and develop new TB tools

Priority actions

- Invest, at minimum, US$ 4 billion annually to accelerate the research and development of new TB diagnostics, medicines, and vaccines. Resources need to be mobilized from governments and philanthropies, increased engagement with the private sector, and new approaches to innovative and sustainable financing.
- Develop a new TB vaccine by 2025
- Accelerate the development of new tools to prevent, diagnose, and treat TB by identifying innovative product-development pathways and improving collaboration among actors in product development

- Invest at least US$ 800 million annually in basic science research
- Expand the use of operational research
- Develop and implement digital tools
- Create an enabling environment for TB R&D
- Apply best practices in community engagement throughout the R&D process
- Apply access principles in rolling out and optimizing the use of new tools
- Strengthen advocacy for TB innovation

Chapter 9. Resource Needs & Return on Investment

Priority actions:

- Mobilize US$209.8 billion in total funding from 2023 through 2030–an average of US$26.22 billion per year–from domestic, international, and innovative funding sources to support the scale-up of TB prevention and care and the implementation of a new TB vaccine. This includes an average of US$ 19.65 billion per year for TB care and prevention from 2023 through 2030, plus US$ 52.6 billion in total for the implementation of a new vaccine from 2026 through 2030.
- Mobilize US$40.18 billion in funding for TB between 2023 and 2030 for TB R&D and basic science research through a more diversified funding base

Modeling projects a strong return on investing in the Global Plan. In line with previous analyses of the economic benefits of TB care and prevention, every US$ dollar invested in implementing the Global Plan will deliver US $40 in economic return, accounting for benefits projected to accrue through 2050. Low- and middle-income countries will see an even greater return, with US $59 in economic benefits for every dollar invested.

Ch 1. Introduction

COVID-19 changed the world. The TB response must adapt to a new reality, but also embrace new possibilities.

The pandemic started impacting high TB burden countries by early 2020. TB services in most countries experienced significant disruptions due to:

- COVID-19-related lockdowns and restrictions decreased people's mobility and access to TB diagnosis, treatment and care.
- TB services at all levels of the health system were curtailed or stopped completely, as the sudden increase in the demand for COVID-19 testing and care overwhelmed health systems.
- Human and financial resources, technical expertise, laboratory and treatment equipment that were previously used for TB programmes were shifted to the COVID-19 response.
- People became reluctant to go to health facilities out of fear of catching the virus.
- New and/or the exacerbation of existing human rights and gender related barriers to services.

TB diagnoses and notifications plummeted. The first observations came from India. Other countries followed.

In May 2020, a modeling study predicted that the impacts of COVID-19 would cause increases in the numbers of people developing and dying from TB– enough so to reverse years of declines in TB incidence and mortality. Data from countries and reported by WHO in 2021 confirmed that COVID-19 had indeed reversed global TB progress by several years.

Because of the devastation caused by the pandemic, most political leaders suddenly saw public health as a top priority. World leaders spent an enormous amount of time and effort to protect lives and livelihoods. This resulted in a massive public health response.

- Screening and testing were made available at an unprecedented scale, using modern technology developed in a few weeks or months, with access points both within and outside the health system, with rapid notification of results.
- Countries quickly scaled up genome sequencing capacity—even those not known for having strong laboratory infrastructure.
- Real-time COVID-19 data were made available—even in countries that struggle to provide timely reporting for other health programs.

- Vaccines were developed and administered in less than a year.
- Digital technology was adopted at a large scale and provided a host of solutions.

Some of the things deemed as impossible in TB responses now seem increasingly possible after the COVID-19 experience.

Global TB Goals and Commitments

Sustainable Development Goals

Despite the pandemic, the global commitment to end tuberculosis (TB) by 2030 has remained unchanged. This commitment is enshrined in the Sustainable Development Goals (SDGs), which the UN adopted in 2015. SDG Goal 3, Target 3.3 calls for an end to the TB epidemic, measured by a decline in the rate of people who develop the disease each year.

SDG target 3.3 directly commits to end TB. But several other SDGs contribute to ending TB. These include targets to achieve universal health coverage (target 3.8), ending hunger and malnutrition (targets 2.1 & 2.2), eradicating extreme poverty and reducing poverty in all forms (targets 1.1 & 1.2), strengthening social protection systems (target 1.3), and a number of targets under the goal of reducing inequalities and making cities and settlements safe.

WHO End TB Strategy

In 2014, the 67th World Health Assembly endorsed the WHO End TB Strategy. It established objectives that are necessary to end TB by 2030. Using 2015 as a baseline, the strategy aims to reach the following two targets by 2030:

- Reduce the global TB incidence rate by 80%
- Reduce the number of TB deaths by 90% worldwide

UN High Level Meeting and other commitments

Recognizing the world's slow progress towards ending TB, in 2018 the UN General Assembly held its first-ever High-Level Meeting (UNHLM) on TB. The outcome was a political declaration in which commitments to the SDGs and End TB Strategy were reaffirmed. The political declaration also established specific commitments for expanding TB prevention, care, research and funding, while placing human rights at the foundation of the global TB response. The political declaration set global targets to be achieved by 2022. The purpose was to put the world on track to achieve the goal of ending TB by 2030. At the beginning of 2022, however, the world was largely off-track to

meeting the ambitious UNHLM targets and commitments. Another UNHLM is planned for 2023.

In addition to global targets and commitments, TB-related commitments have been made from time to time by groups of countries that together share a substantial burden of TB and have an ambition to act against TB jointly and decisively. Such groups of countries include the BRICS, the G20 and WHO SEAR countries. Such political declarations serve the purpose of keeping the fight against TB high on the political agenda at national and international levels.

The goal to end TB by 2030 is ambitious–even more so as a consequence of COVID-19. But the pandemic also demonstrated that countries–governments, civil society and the private sector, together–are capable of mobilizing robust responses to public health crises. The Global Plan's modeling projects that countries can end TB by 2030 if they mobilize responses that are proportional to the need, with investments in interventions that will create impact in their various settings. Now more than ever, investment and action are critical.

Ch 2. Ending TB through comprehensive investment packages implemented at scale

Priority actions:

- Invest in comprehensive investment packages of TB interventions.
- Scale up interventions to achieve key objectives and targets.

Globally, TB incidence and mortality has been only slowly declining over the last decade, with COVID-19 leading to an increase in TB deaths.

We have proven approaches and tools to, diagnose, treat, and prevent TB, which must be optimized and scaled up. At the same time, thanks to research and development efforts, new tools—and improved versions of existing tools—are expected to become available during the next few years.

Some parts of the world have shown that TB can be reduced substantially if all tools and approaches are applied comprehensively and at scale. Unfortunately, in many high TB burden countries these tools have been applied inconsistently or without a systematic approach, mainly due to a lack of resources. This has led to limited gains and missed opportunities to halt transmission.

Invest in comprehensive investment packages of TB interventions

The Global Plan calls for countries to invest in a comprehensive package of interventions that can end TB. A comprehensive investment package is a set of high-level interventions strategically needed to end TB. While not an exhaustive list of detailed interventions and activities, it is comprehensive because it covers the categories of interventions needed to end TB:

- Early diagnosis
- Treatment and care
- Prevention
- Systems and enablers
- Research and development
- Resource mobilization

Depending on their specific, local needs, different settings should focus relatively more on some interventions than others while still maintaining a comprehensive approach to investment. It is essential to not neglect investment in any category. Types of interventions must be prioritized depending on epidemiological context (Table 1).

Table 1. Comprehensive Investment Packages for Ending TB by 2030

Early diagnosis (Chapter 3)
Scale up modern point-of-care diagnostics and universal drug susceptibility testing, aided and supported by: - robust diagnostic networks - integration of TB screening and testing within other health and nutritional services - x-ray for TB screening, enhanced by AI-powered computer-aided detection - electronic connectivity systems for timely reporting and linkage to treatment
Detect TB as early as possible, in subclinical stages, by implementing active case finding. Prioritize outreach to: - close contacts of people with TB - people living with underlying risk factors - key populations - health workers - people exposed to silica dust - populations with poor access to health services
Care and support (Chapter 3)
Provide people-centred care for all adults, children and adolescents with TB and DR-TB, using the latest approved treatment regimens, with comprehensive clinical monitoring and management of comorbidities and underlying conditions.
Provide mental health evaluation, care and support during and post-treatment.
Provide evaluation and care for post-TB disease, preventing TB recurrence.
Integrate TB care and support into othe relevant health and nutrition programs with a focus on underlying conditions such as nutrition, HIV, diabetes, tobacco cessation and alcohol use disorder.
Expand and maintain support systems that include: - psychosocial support - incentives and enablers - digital adherence support technologies
Provide care that is human rights-affirming, free of stigma and discrimination, and gender-responsive.
Prevention (Chapter 4)
Scale up TB infection testing in line with a "test and treat" strategy, prioritizing key populations and communities that will benefit the most from TB preventive therapy.

Provide universal access to TB preventive therapy for: - child, adolescent and adult contacts of people with TB - people living with HIV - key populations depending on epidemiological context
Implement airborne infection prevention and control measures across the health system and ensure laws, policies and regulations for congregate settings and confined public spaces implement standards and best practices for airborne infection prevention.
Apply a One Health approach, collaborating with food safety authorities to prevent transmission of zoonotic TB in populations at risk of acquiring bovine TB.
Develop a vaccine implementation readiness plan
When new vaccines become available, introduce and scale up vaccination to reach target population coverage
Systems and enablers (Chapters 5-7)
Ensure that the TB response is equitable, human rights based, gender responsive and free of stigma and discrimination, addressing the needs of key populations.
Enagage affected communities in planning, implementation, monitoring and governance bodies involved in the TB response, providing fair compensation for their service where appropriate.
Invest in community health systems including human resources, capacity building and necessary tools and approaches to bring people-centred care to the community level.
Address the needs of key populations.
Strengthen policies, engagement, support and supply chains to private health providers, ensuring that all people with TB who seek care in the private health sector receive affordable, quality-assured care.
Transition TB information systems from paper-based to digital, enabling real-time notification and efficient surveillance systems that aid more effective decision-making.
Strengthen human resources for TB, including formalizing the roles of community health workers.
TB research and development (Chapter 8)
Invest in identifying innovative produce-development pathways and increasing collaboration among key stakeholders in product development
Nurture and support growth in the field of TB researchers

Build clinical trial capacity, including in LMICS and LICS
Apply access principles and best practices in community engagement
Invest in advocacy that improves science literacy among advocates and affected communities, builds advocacy skills among the TB scientific community, and promotes regular communication and collaboration between advocates, scientists and affected communities.
Resource mobilization (Chapter 9)
Intensify outreach to diversify the base of funding sources and enroll new partners in the TB response.
Invest in advocacy and strategic communications to mobilize resources and political will for full implementation of the Global Plan.

Scale up interventions to achieve key objectives and targets

To carry out the WHO End TB Strategy and achieve the SDG of ending TB by 2030, this updated Global Plan sets the following targets based on impact modeling (see below). The priority actions presented by this Global Plan need to be implemented to achieve these achieve these objectives and targets.

Deliver early diagnosis and TB treatment and care (Chapter 3)

Each year millions of people with TB go without a diagnosis, denying them access to life-saving TB care. When people are diagnosed, they commonly receive a late diagnosis and/or a diagnosis with old tools that provide too little information to select an appropriate treatment regimen.

At the same time, prevalence surveys have shown that about half of people with laboratory-confirmed active TB disease may not have symptoms or might not report symptoms. This is known as “subclinical TB.” This suggests that many people with active TB disease are not seeking diagnosis and care.

Thanks to recent investments in innovation, TB treatment is becoming shorter and safer. Yet many people are denied access to appropriate treatment using the best regimens available. Delays are also common between the time when people are diagnosed with TB and when they start treatment.

Objectives:

- Reduce TB transmission by actively searching out proactively bringing timely TB services to those in need, including those who have not come into contact with the healthcare system.
- Ensure universal access to appropriate treatment that is initiated immediately following accurate diagnosis.

Targets to achieve by 2030:

- Find and diagnose at least 95% of people with TB, including drug-susceptible and DR-TB in adults and children.
- More than 90% of pulmonary TB should be diagnosed by rapid molecular tests and more than 90% of bacteriologically identified TB strains should have a drug sensitivity test (DST) before initiating treatment.
- Deliver treatment to 50 million people from 2023-2030, including 3.7 million children and 2.2 million people with RR-TB or MDR-TB
- Initiate appropriate treatment for all people diagnosed with TB
- Achieve at least 90% treatment success for all forms of TB

Prevent TB transmission, infection and disease (Chapter 4)

Prevention is closely linked with detection and treatment, because early diagnosis and effective treatment prevent the spread of infection. A comprehensive approach to prevention requires protecting people from TB exposure and preventing TB infection from progressing to active disease, and expanding understanding and support for preventing TB recurrence and other long-term adverse health effects that can result from TB.

Objectives:

- Prevent exposure to TB.
- For people who have been exposed, prevent TB infection from progressing into active TB disease, and prevent recurrence of TB and post-TB disease (i.e., TB-related sequelae).

Targets to achieve by 2030:

- Provide TB preventive treatment (TPT) to 100% of eligible TB contacts
- Provide TPT to 100% of PLHIV
- Provide TPT to 35 million people at risk of TB
- A least one new TB vaccine recommended for use in 2025 and rolled out in 2026
- Achieve at least 60% target population coverage with a new vaccine by 2030

Implement enablers & strengthen systems (Chapters 5-7)

The tools needed to detect, treat and prevent TB will only reach all people in need when surrounding health systems function well and underpinned by a human rights approach that values the rights of all people equally. TB programmes need to provide support that enables people receiving TB care to complete a full course of treatment without an undue burden on them and their families, while avoiding catastrophic costs. At the same time, a people-centred approach recognizes that medical interventions are necessary but not sufficient, and that to end TB will require interventions that extend beyond the health sector.

Objective: Invest in interventions that enable and make detection, treatment, and prevention interventions impactful and equitable.

Targets to achieve by 2030:

- At least 90% of countries have a Communities, Rights and Gender (CRG) action plan, budget line and monitoring mechanism
- At least 90% of countries have identified Key and Vulnerable Populations in their national TB plans, proposes specific actions, have budget line and a monitoring mechanism
- At least 90% of countries anticipating implementing a new TB vaccine have a vaccine readiness plan

Accelerate research and development of new TB tools (Chapter 8)

The Global Plan's modeling shows that new diagnostics, medicines, and vaccines are essential to ending TB by 2030. The research and development pipelines for new TB tools are more promising than at any point in recent history, but a lack of funding for R&D is a critical barrier to moving candidates to market. Funding for TB R&D has fallen far short of the need. COVID-19 provides key lessons for what is possible to achieve in innovation with funding backed by political will and facilitated by efficient regulatory approval processes.

Objective: Accelerate the research and development of new TB tools needed to end TB.

Target to achieve by 2030: Achieve the goals and objectives set by the Global Plan's strategic frameworks for vaccines, diagnostics and medicines.

Chapter 9: Mobilize resources to implement the Global Plan (Chapter 9)

The Global Plan presents priority actions representing contributions from all sectors involved in the global TB response. The single biggest barrier to implementing the Global Plan and ending TB is a shortfall in resources. The Global Plan's projected funding needs are in line with what modeling shows is needed to compensate for progress lost during the COVID-19 pandemic and accelerate a decline in incidence and death in order to reach the global goal of ending TB by 2030.

Objective: Mobilize resources from a diversified base of domestic, international and innovative financing sources, using advocacy and strategic communications to enroll new partners in fully implementing the Global Plan.

Targets to achieve by 2030:

- Mobilize $209.8 billion for TB programs and enabling interventions from 2023-2030[9]
- Mobilize $33.8 billion for R&D for new TB medicines, diagnostics and vaccines from 2023-2030.
- Mobilize at least $6.4 billion for TB basic science research

Milestones:[1]

- 2023-2027: deliver TB treatment to 38.6 million people, including 2.8 million children and 1.7 million people with RR-TB or MDR-TB
- 2028-2030: deliver TB treatment to 11.4 million people, including 0.9 million children and 0.5 million people with RR-TB or MDR-TB
- 2023-2027: deliver TPT to 16 million people
- 2028-2030: deliver TPT to 19 million people

Modeling the Global Plan's impact

The Global Plan conducted epidemiologic modeling to answer the question: What interventions are needed to end TB by 2030? This chapter presents key findings from this modeling. It provides guidance for how countries can take actions that reduce TB incidence, mortality, notifications and create greater impact as determined by key indicators.

The full modeling report is available in Annex 1.

Key findings:

[1] Targets for 2027-2030 will have to be revised if 2023-2027 targets are not met.

- A comprehensive approach to diagnosis, treatment and prevention is needed at scale.
- Diagnosing people earlier—even at the subclinical stage—is critical. This requires using active case finding and screening all household contacts of people diagnosed with TB.
- Improvements in diagnosis and treatment of TB are needed through a variety of interventions, but these measures alone are not enough to end TB.
- Preventive therapy needs to be massively scaled up.
- We can achieve important progress with currently available tools, but new tools are essential for making the necessary strides.
- Ultimately, to end TB, a new vaccine is necessary to extend the benefits of prevention much more widely and more durably than is currently possible with preventive therapy.

Changes in modeling from the previous approach

For past Global Plans (2016-2020 and 2018-2022), modelers relied strongly on national TB budget and expenditure reports submitted by countries to WHO to derive unit costs and estimate resource needs. This Global Plan uses what is called a "normative approach," where anticipated implementation of tools (e.g. diagnostics, medicines) and services (e.g. patient support) are made consistent with WHO guidelines. This approach allowed for projecting more detailed cost needs.[2]

[2] In particular, unit costs in previous Global Plans could only be estimated in broad categories. For example, costs could be estimated related to diagnosis or treatment or collaborative HIV-TB activities, without a clear relationship between guidelines and costs in different program areas (e.g. screening, diagnosis, monitoring, prevention) or types of people receiving care (e.g., depending on age, pulmonary vs extrapulmonary TB, MDR/RR status, HIV status or other variables). Following the recommendations of a technical working group, a "normative ingredients-based approach" was developed to cost all direct services (i.e. at the point of care) within a representative sample of nine types of algorithms for screening, treatment and prevention, which are tailored to the guidelines for different types of patients receiving care. The guidelines are based on WHO recommendations, with greater detail in some elements (e.g., timing of an intervention's roll-out).

Figure 1: Global TB cases, impact by 2030, with or without a catch-up effort in 2022, and with or without new tools rolled out in 2026.

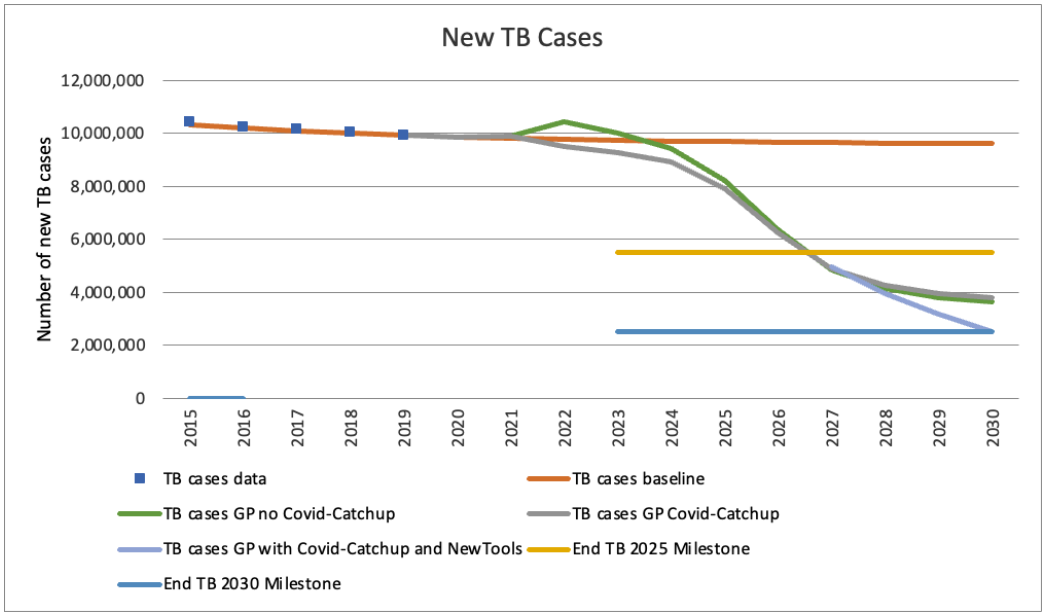


Figure 2: Global TB deaths, impact by 2030, with or without a catch-up effort in 2022, and with or without new tools rolled out in 2026.

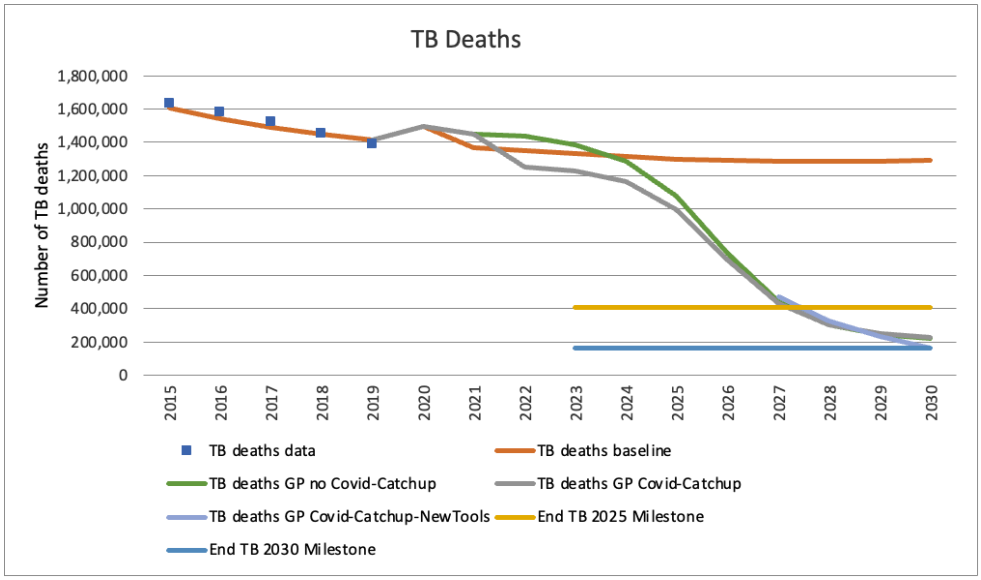


Table 2. Model projections for TB incidence rates and deaths, 2023-2030

Incidence rate (per 100,000 population)									
Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**2023-2030**
GLOBAL TOTAL									
Total (Global, including OECD countries	116.4	111.1	97.8	76.4	59.3	51.1	47.2	44.9	75.0
Total (Global, excluding OECD countries)	137.5	131.2	115.3	90.0	69.7	60.1	55.4	52.6	88.2
BY INCOME STATUS									
Low income	169.3	157.1	132.5	98.4	73.5	62.3	56.4	52.6	97.9
Lower middle income	193.0	184.8	163.4	127.9	98.9	84.7	77.7	73.4	124.3
Upper middle income	57.4	54.5	47.9	37.9	30.1	26.6	25.1	24.3	37.9
High income	8.8	7.8	6.9	5.6	4.5	4.0	3.8	3.7	5.6
GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	1.9	2.1	2.4	2.6	2.5	2.5	2.5	2.6	19.3

Lower middle income	8.2	9.3	11.0	12.0	11.2	10.7	10.7	11.0	84.0
Upper middle income	1.4	1.5	1.7	1.8	1.7	1.7	1.8	1.8	13.4
All GFATM countries	11.5	13.0	15.1	16.3	15.5	14.9	15.0	15.5	116.7
GLOBAL PLAN COUNTRY SETTING									
Moderate Burden, COE[3]	170.3	160.3	133.1	91.6	62.7	51.4	45.8	42.3	92.0
Low Burden, High Income	11.7	10.5	9.3	7.5	6.1	5.4	5.1	5.0	7.6
Moderate Burden, Middle Income	50.7	49.0	41.7	32.4	23.9	19.2	16.9	15.5	30.9
High Burden, Private Sector	160.1	154.0	136.8	107.5	83.7	72.4	67.0	63.9	105.0
High MDR burden, Centralized Care	50.5	48.7	43.6	36.0	29.7	26.6	25.1	24.1	35.6
High TB-HIV, SADC[4]	230.9	185.9	148.2	118.3	98.6	86.9	79.4	74.2	124.8
High TB-HIV, outside SADC	124.9	117.5	102.7	80.7	64.3	56.7	52.6	49.8	79.7
WHO REGION									

[3] Council of Europe

[4] Southern African Development Community

EMR	107.6	103.7	91.5	70.8	54.7	47.1	43.3	40.9	69.1
AFR	182.4	166.3	141.9	109.4	85.7	74.7	68.7	64.5	109.4
AMR	26.9	26.0	22.2	17.2	12.7	10.3	9.1	8.4	16.5
EUR	23.0	21.8	19.5	16.0	13.2	11.8	11.1	10.7	15.9
WPR	87.7	84.5	74.4	57.5	44.5	38.9	36.6	35.4	57.4
SEA	195.3	188.7	168.1	132.0	101.6	86.5	79.2	75.0	127.5
BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	108.5	105.0	94.7	75.6	58.8	50.7	47.1	45.2	73.0

TB Deaths (per 100,000 population)

Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**2023-2030**
GLOBAL TOTAL									
Total (Global, including OECD countries	15.4	14.5	12.3	8.5	5.2	3.6	3.0	2.7	8.0
Total (Global, excluding OECD countries)	18.3	17.2	14.6	10.1	6.2	4.3	3.5	3.1	9.5

BY INCOME STATUS									
Low income	24.8	22.2	17.7	11.4	6.6	4.4	3.6	3.3	11.3
Lower middle income	27.1	25.7	21.9	15.3	9.5	6.6	5.3	4.7	14.3
Upper middle income	5.3	5.0	4.2	2.8	1.7	1.2	1.0	0.9	2.7
High income	0.9	0.8	0.7	0.5	0.3	0.2	0.2	0.2	0.5
GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	24.8	22.2	17.7	11.4	6.6	4.4	3.6	3.3	11.3
Lower middle income	27.1	25.7	21.9	15.3	9.5	6.6	5.3	4.7	14.3
Upper middle income	26.1	25.1	21.5	14.7	8.9	6.3	5.4	5.0	14.0
All GFATM eligible countries	26.6	25.0	21.1	14.5	8.9	6.2	5.0	4.5	13.7
WHO REGION									
EMR	9.1	8.7	7.3	4.9	2.9	1.9	1.6	1.5	4.6
AFR	37.6	34.5	28.2	18.5	10.9	7.6	6.4	5.8	18.1
AMR	2.0	1.7	1.3	0.8	0.4	0.3	0.2	0.2	0.9
EUR	2.2	2.1	1.7	1.2	0.8	0.5	0.4	0.3	1.2

WPR	4.1	3.8	3.2	2.1	1.2	0.9	0.7	0.7	2.1
SEA	28.1	26.9	23.2	16.6	10.5	7.3	5.8	5.1	15.3
BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	15.5	15.2	13.4	9.9	6.4	4.4	3.5	3.1	8.9

TB Case Notifications

Table 3 shows overall TB case notification targets, case notification targets for children under 15, and case notification targets for people with MDR/RR-TB. Top-line TB case notification targets are:

- 50.0 million people with TB in the period 2023-2030 and 38.6 million in the first 5 years (2023-2027)
- 3.7 million children with TB in the period 2023-2030 and 2.8 million in the first 5 years (2023-2027)
- 2.2 million people with MDR/RR-TB in the period 2023-2030 and 1.7 million in the first 5 years (2023-2027)

Table 3: TB notifications (all ages, children under 15 and MDR/RR TB), 2023-2030

TB Notifications (all ages, millions)									
Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**
GLOBAL TOTAL									
Total (Global, including OECD countries	7.8	8.0	8.7	8.2	6.0	4.6	3.9	3.6	50.7

Total (Global, excluding OECD countries)	7.6	7.8	8.6	8.1	6.0	4.5	3.9	3.6	50.1
BY INCOME STATUS									
Low income	1.0	1.0	1.1	1.0	0.7	0.6	0.5	0.5	6.4
Lower middle income	5.3	5.4	6.0	5.6	4.2	3.1	2.7	2.5	34.8
Upper middle income	1.4	1.4	1.6	1.5	1.1	0.8	0.7	0.7	9.1
High income	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.5
GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	1.9	2.1	2.4	2.6	2.5	2.5	2.5	2.6	19.3
Lower middle income	8.2	9.3	11.0	12.0	11.2	10.7	10.7	11.0	84.0
Upper middle income	1.4	1.5	1.7	1.8	1.7	1.7	1.8	1.8	13.4
All GFATM countries	11.5	13.0	15.1	16.3	15.5	14.9	15.0	15.5	116.7
WHO REGION									
EMR	0.5	0.5	0.5	0.5	0.4	0.3	0.3	0.2	3.1
AFR	1.4	1.5	1.8	1.9	1.4	1.1	1.0	1.0	11.2

AMR	0.2	0.2	0.3	0.2	0.2	0.1	0.1	0.1	1.5
EUR	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.1	1.0
WPR	1.4	1.4	1.5	1.4	1.0	0.7	0.6	0.6	8.5
SEA	4.0	4.1	4.5	4.1	3.0	2.2	1.8	1.7	25.5
BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	3.7	3.7	4.0	3.8	2.8	2.1	1.7	1.6	23.5

TB Notifications (people under 15, millions)									
Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**
GLOBAL TOTAL									
Total (Global, including OECD countries	0.57	0.59	0.64	0.59	0.44	0.33	0.29	0.27	3.72
Total (Global, excluding OECD countries)	0.56	0.59	0.64	0.59	0.44	0.33	0.29	0.27	3.70
BY INCOME STATUS									
Low income	0.11	0.11	0.11	0.10	0.07	0.06	0.05	0.05	0.65
Lower middle income	0.42	0.45	0.49	0.46	0.33	0.25	0.22	0.20	2.82
Upper middle income	0.03	0.04	0.04	0.04	0.03	0.02	0.02	0.02	0.23
High income	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01

GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	0.11	0.11	0.11	0.10	0.07	0.06	0.05	0.05	0.65
Lower middle income	0.42	0.45	0.49	0.46	0.33	0.25	0.22	0.20	2.82
Upper middle income	0.02	0.02	0.02	0.02	0.02	0.01	0.01	0.01	0.14
Total	0.55	0.57	0.62	0.58	0.42	0.33	0.28	0.26	3.61
WHO REGION									
EMR	0.06	0.06	0.07	0.07	0.05	0.04	0.03	0.03	0.42
AFR	0.13	0.14	0.15	0.16	0.12	0.10	0.09	0.08	0.96
AMR	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0.00	0.06
EUR	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.03
WPR	0.06	0.06	0.06	0.05	0.04	0.03	0.03	0.02	0.36
SEA	0.29	0.31	0.34	0.31	0.22	0.16	0.14	0.12	1.89

BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	0.19	0.18	0.20	0.19	0.14	0.10	0.09	0.08	1.16
MDR/RR TB (thousands)									
Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**
GLOBAL TOTAL									
Total (Global, including OECD countries	350.7	346.1	373.4	345.3	256.0	193.7	165.9	153.3	2,184.5
Total (Global, excluding OECD countries)	256.6	243.9	259.0	239.1	183.3	139.6	118.8	109.0	1,549.4
BY INCOME STATUS									
Low income	14.5	14.2	15.1	14.0	10.7	8.4	7.4	6.9	91.1
Lower middle income	31.9	31.8	36.4	38.3	30.2	24.5	22.2	21.1	236.4
Upper middle income	207.7	195.3	204.3	183.9	140.1	105.0	87.9	79.8	1,204.1
High income	96.7	104.8	117.6	109.1	74.9	55.8	48.5	45.6	652.9
GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									

Low income	14.5	14.2	15.1	14.0	10.7	8.4	7.4	6.9	91.1
Lower middle income	30.6	30.6	35.3	37.4	29.6	24.0	21.7	20.6	229.8
Upper middle income	25.3	25.6	27.7	26.8	20.8	16.8	15.1	14.3	172.4
All GFATM eligible countries	70.4	70.4	78.0	78.2	61.1	49.2	44.1	41.8	493.3
WHO REGION									
EMR	141.9	139.9	155.8	152.1	114.8	84.7	69.8	62.8	921.8
AFR	20.1	18.3	18.3	15.2	11.8	9.2	8.0	7.5	108.5
AMR	73.2	77.1	89.8	88.6	62.8	47.3	41.5	39.2	519.6
EUR	91.6	87.9	86.3	68.3	50.4	39.7	35.3	33.2	492.6
WPR	15.5	14.6	14.5	12.4	9.5	7.5	6.5	6.1	86.7
SEA	8.4	8.3	8.7	8.6	6.6	5.3	4.8	4.5	55.3
BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	2.5	2.5	2.9	2.4	1.9	1.4	1.1	1.0	15.7

TB Prevention

Table 3 shows overall targets for providing TB preventive therapy (TBP) to eligible contacts of people diagnosed with TB, PLHIV, and other risk groups. Top-line TPT targets are:

- 35 million people at risk in the period 2023-2030 and 26 million in the first 5 years (2023-2027)
- 21 million contacts in the period 2023-2030 and 16 million in the first 5 years (2023-2027)

Table 4: TB preventive treatment TPT (adults, children U15 and PLHIV in ART cohorts), 2023-2030

TB Prevention, Adults (millions)									
Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**
GLOBAL TOTAL									
Total (Global, including OECD countries	3.0	3.1	3.5	3.4	2.6	2.0	1.7	1.6	20.8
Total (Global, excluding OECD countries)	3.0	3.1	3.5	3.4	2.5	2.0	1.7	1.6	20.7
BY INCOME STATUS									
Low income	0.4	0.5	0.5	0.5	0.4	0.3	0.3	0.2	3.0
Lower middle income	2.0	2.1	2.3	2.3	1.7	1.3	1.1	1.1	14.0
Upper middle income	0.5	0.6	0.6	0.6	0.4	0.3	0.3	0.3	3.7
High income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	0.4	0.5	0.5	0.5	0.4	0.3	0.3	0.2	3.0
Lower middle income	2.0	2.1	2.3	2.3	1.7	1.3	1.1	1.1	14.0
Upper middle income	0.2	0.2	0.3	0.2	0.2	0.2	0.1	0.1	1.6
All GFATM eligible countries	2.7	2.8	3.1	3.0	2.3	1.8	1.5	1.4	18.6
WHO REGION									
EMR	0.2	0.2	0.2	0.2	0.2	0.1	0.1	0.1	1.4
AFR	0.7	0.8	0.9	1.0	0.8	0.6	0.6	0.5	5.9
AMR	0.1	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.7
EUR	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2
WPR	0.4	0.4	0.5	0.5	0.3	0.2	0.2	0.2	2.8
SEA	1.5	1.6	1.7	1.6	1.2	0.9	0.7	0.7	9.8
BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	1.4	1.4	1.5	1.5	1.1	0.8	0.7	0.6	9.1

TB Prevention, Children 0-14 years (millions)									
Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**

GLOBAL TOTAL									
Total (Global, including OECD countries	1.12	1.15	1.28	1.26	0.94	0.72	0.62	0.57	7.65
Total (Global, excluding OECD countries)	1.11	1.15	1.28	1.26	0.94	0.71	0.61	0.57	7.63
BY INCOME STATUS									
Low income	0.27	0.27	0.29	0.28	0.21	0.16	0.14	0.13	1.73
Lower middle income	0.72	0.75	0.85	0.85	0.64	0.49	0.42	0.38	5.09
Upper middle income	0.13	0.13	0.14	0.13	0.10	0.07	0.06	0.06	0.82
High income	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	0.27	0.27	0.29	0.28	0.21	0.16	0.14	0.13	1.73
Lower middle income	0.72	0.75	0.84	0.85	0.64	0.48	0.42	0.38	5.08
Upper middle income	0.06	0.06	0.06	0.06	0.04	0.04	0.03	0.03	0.37
All GFATM eligible countries	1.05	1.08	1.20	1.18	0.88	0.68	0.58	0.54	7.19

WHO REGION									
EMR	0.10	0.10	0.11	0.10	0.08	0.06	0.05	0.05	0.66
AFR	0.39	0.42	0.50	0.56	0.42	0.33	0.30	0.28	3.20
AMR	0.03	0.03	0.03	0.03	0.02	0.02	0.01	0.01	0.18
EUR	0.01	0.01	0.01	0.01	0.01	0.00	0.00	0.00	0.06
WPR	0.12	0.12	0.12	0.11	0.08	0.06	0.05	0.05	0.70
SEA	0.46	0.47	0.50	0.46	0.33	0.24	0.20	0.18	2.85
BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	0.39	0.38	0.41	0.39	0.29	0.21	0.17	0.16	2.40

TB Prevention, PLHIV (millions)									
Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**
GLOBAL TOTAL									
Total (Global, including OECD countries	0.93	1.02	1.09	0.66	0.63	0.64	0.65	0.66	6.27
Total (Global, excluding OECD countries)	0.91	1.01	1.08	0.65	0.62	0.63	0.64	0.65	6.19

BY INCOME STATUS									
Low income	0.27	0.29	0.31	0.22	0.21	0.22	0.22	0.23	1.97
Lower middle income	0.36	0.41	0.44	0.27	0.25	0.26	0.26	0.27	2.52
Upper middle income	0.29	0.31	0.33	0.17	0.16	0.16	0.16	0.16	1.72
High income	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.06
GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	0.27	0.29	0.31	0.22	0.21	0.22	0.22	0.23	1.97
Lower middle income	0.36	0.41	0.44	0.27	0.25	0.26	0.26	0.27	2.52
Upper middle income	0.21	0.24	0.25	0.10	0.09	0.09	0.09	0.09	1.15
All GFATM countries	0.84	0.93	1.00	0.58	0.56	0.56	0.57	0.58	5.63
WHO REGION									
EMR	0.03	0.03	0.04	0.02	0.01	0.01	0.02	0.02	0.17
AFR	0.67	0.72	0.76	0.46	0.44	0.45	0.46	0.47	4.44

AMR	0.06	0.07	0.07	0.06	0.06	0.06	0.06	0.06	0.50
EUR	0.01	0.03	0.04	0.02	0.02	0.02	0.02	0.02	0.19
WPR	0.06	0.06	0.07	0.05	0.05	0.05	0.05	0.05	0.44
SEA	0.09	0.10	0.11	0.05	0.04	0.04	0.04	0.04	0.53
BRICS (BRA,CHN,IND,RUS,ZAF)									
Total	0.25	0.28	0.29	0.14	0.13	0.13	0.13	0.13	1.49

Supplementary modeling: Indonesia, Kenya, Ukraine and Uzbekistan[5]

To supplement the analysis provided by the TIME model, the Global Plan presents additional modeling analyses in four focal countries: Indonesia, Kenya, Ukraine and Uzbekistan. This supplemental modeling provides some understanding of the combinations of interventions that are necessary to meet the End TB goals in these contrasting settings. These four countries were chosen in order to capture important features of TB epidemiology today:

- The strong role of a fragmented private healthcare sector in managing TB in many South- and South-East Asian countries (Indonesia)
- The role of HIV coinfection as a key driver of TB incidence (Kenya)
- The substantial burden of rifampicin-resistant TB in many countries in Central and Eastern Europe, and elsewhere (Ukraine, Uzbekistan)

[5] Supplemental modeling for Ukraine was conducted prior to invasion and the outbreak of war in February 2022. While this modeling scenario was no longer valid for Ukraine by the time the Global Plan was finalized, the modeling case study remains in the Global Plan to illustrate the impact modeled for this type of epidemiological setting and an additional country Uzbekistan was added to the modelling.

Three distinct models simulate the TB epidemiology in each of the three countries. This tailored approach allowed for modeling different combinations of interventions while accounting for disruptions to TB services arising from the COVID-19 .

Improving diagnosis and care is important in all three countries. At the same time, the modeling emphasizes how important it is to tailor intervention priorities to local settings.

Rolling out an effective vaccine will be necessary to meet the End TB goals in all three settings, although each country will require a different minimum level of vaccination coverage. The model assumes a new vaccine is licensed in 2025, with distribution starting in 2026 and scaled up over three years to achieve the vaccination coverage rate included in each country model.

Until a new vaccine is available, it remains critical to bring high-quality TB services to as many people as possible. This means 1) bringing case detection and treatment outcomes in the private sector up to the same level of quality found in the public sector, and 2) scaling up active case finding. The models project that in Indonesia and Ukraine, case finding will need to be extended to finding people with subclinical TB.

Indonesia

Figure 3 shows model projections for TB incidence in Indonesia. The model projects a temporary decrease in incidence in 2020, because lockdowns against COVID-19 are likely to have the effect of reducing TB incidence in the short term. In the longer term, however, the model projects that service disruptions would lead to a substantial increase in TB incidence.

The model projects that Indonesia could end TB by 2030 if the following interventions were scaled up in a linear fashion from 2022 through 2025, and maintained thereafter:

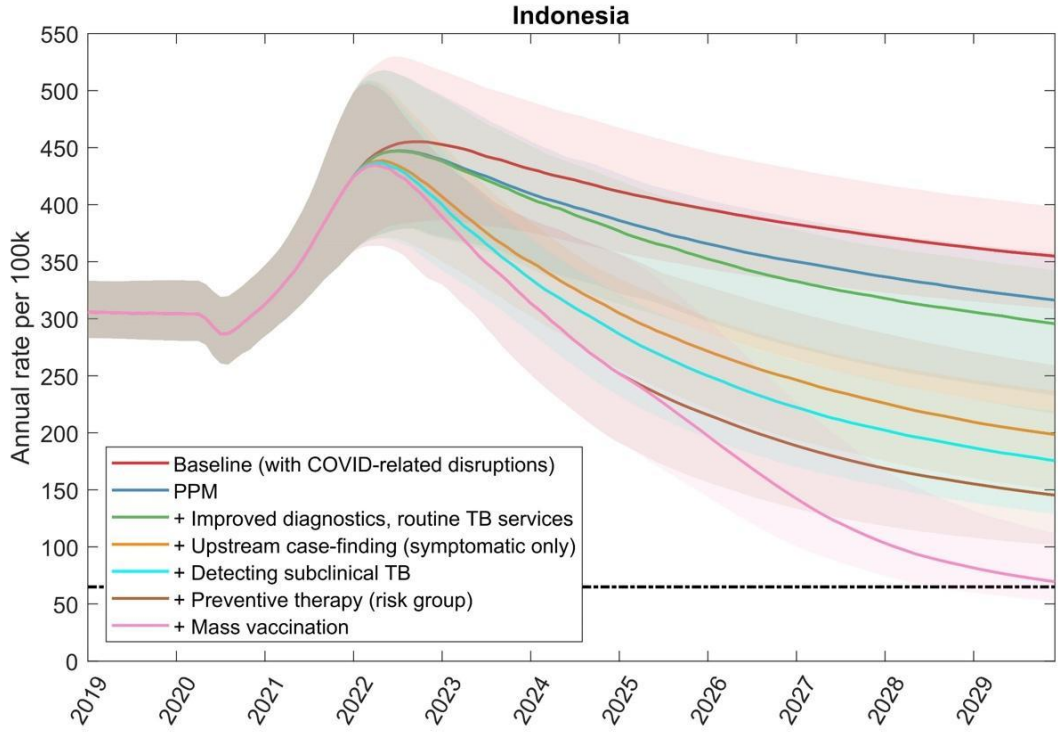
- Care delivered through a mix of public- and private-sector effort (PPM)
- Improved TB diagnosis
- Active finding of people living with symptomatic TB (active case-finding, plus creating demand for existing TB services)
- Detection of sub-clinical TB
- Preventive therapy focusing on at-risk groups

- Mass vaccination with a new TB vaccine

An important intervention to note is the detection of subclinical TB. Previous Global Plans have not emphasized this intervention. The model shows the important role that detecting subclinical TB can play, in the TB response. It is important to ending TB in Indonesia by 2030.

In addition to its direct impact, PPM indirectly enables other interventions. For example, PPM enhances the impact of preventive therapy by increasing the number of people with TB who are reported to the TB programme, and whose contacts can benefit from preventive therapy. Overall, coordination of TB services across the healthcare system—whether in the public or private sectors—will be critical for meeting the End TB goals.

Figure 3. Projected impact of comprehensive TB interventions in Indonesia, 2019-2030.



It will not be possible to meet the End TB goals by 2030 without a new TB vaccine. Shown here is a coverage scenario where 65% of people living with TB

infection receive a post-exposure vaccine with 60% efficacy, from 2025 onwards.

Kenya

Figure 4 and Figure 5 show model projections for TB incidence in Kenya. In Figure 2 the model projects that Kenya could reach the End TB goal to reduce incidence if the following interventions were scaled up in a linear fashion from 2022 through 2025, and maintained thereafter:

- Improved TB diagnosis
- Active finding of people living with symptomatic TB (active case-finding, plus creating demand for existing TB services)
- Preventive therapy focusing on at-risk groups
- Mass vaccination with a new TB vaccine

Acting case-finding (plus care-seeking generated by creating more demand for TB services) has an important role in reducing TB incidence. However, the model projects that it is possible to meet the End TB goals in Kenya without extending case detection to subclinical TB. This is partly because preventive therapy has a stronger effect in Kenya than in other countries modeled. Because HIV is a driver of TB epidemiology in Kenya, the uptake of preventive therapy among PLHIV will play a critical role in reaching the End TB goals.

So will a new TB vaccine. Vaccine coverage does not need to be as high as in Indonesia to meet the End TB goals. The model scenario depicted in Figure 2 shows 40% coverage (versus 60% in Indonesia). Again, the strong role played by preventive therapy in PLHIV brings the End TB goals within closer reach In Kenya than it does in other settings.

In practice, Kenya has begun implementing case-finding for subclinical TB. The model in Figure 5 projects that actively detecting subclinical TB can also reduce incidence and make it possible to reach the End TB goals with reduced (33%) vaccine coverage.

Figure 4. Projected impact of comprehensive TB interventions in Kenya, without detecting subclinical TB, 2019-2030.

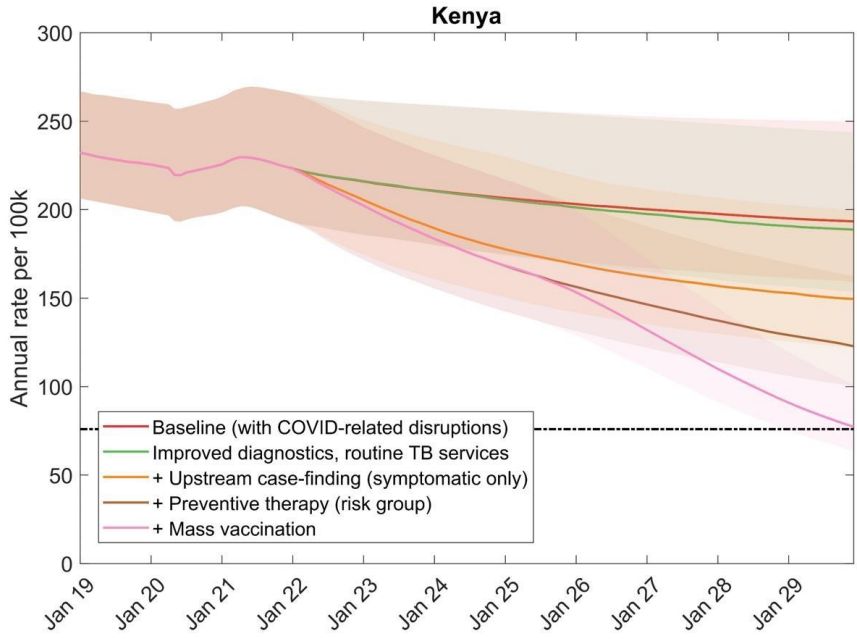
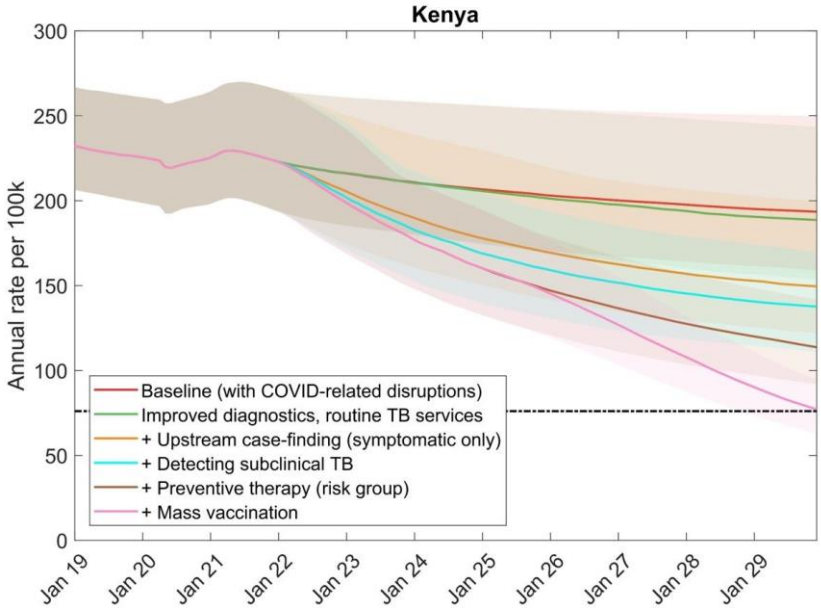


Figure 5. Projected impact of comprehensive TB interventions in Kenya, with detecting subclinical TB, 2019-2030.



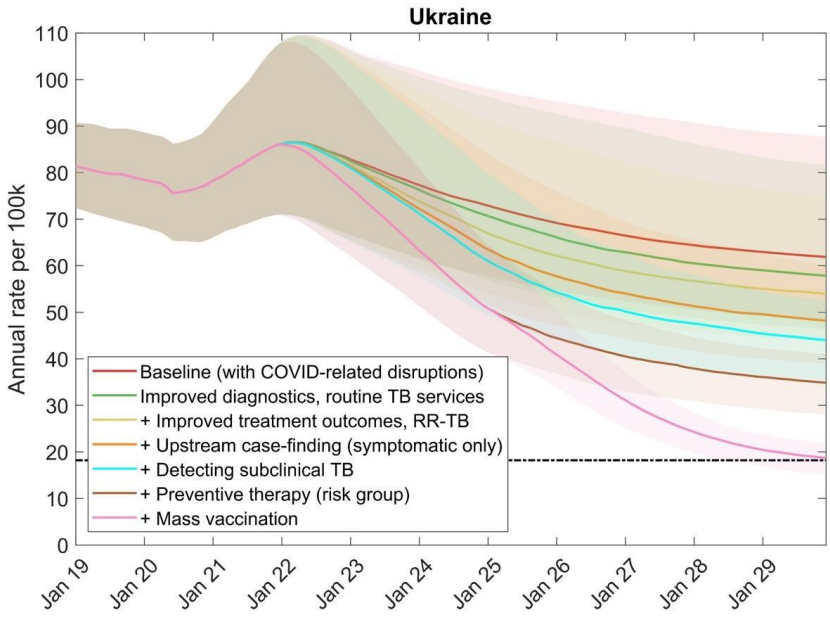
Ukraine

Figure 6 shows model projections for TB incidence in Ukraine. The model projects that Ukraine could reach the End TB goal to reduce incidence if the following interventions were scaled up in a linear fashion from 2022 through 2025 and maintained thereafter:

- Improved TB diagnosis
- Improved treatment outcomes for rifampicin-resistant TB
- Active finding of people living with symptomatic TB (active case-finding, plus creating demand for existing TB services)
- Detection of sub-clinical TB
- Preventive therapy focusing on at-risk groups
- Mass vaccination with a new TB vaccine

Given the burden of rifampicin-resistant TB (RR-TB) in Ukraine, the model projects that improving care for people with RR-TB would contribute significantly to reducing incidence and is necessary to achieving the 2030 End TB goals. This would need to involve using molecular diagnostics on a wide scale (facilitating the early recognition of RR-TB) and improving second-line treatment outcomes. A new vaccine is also critical, and the country would need to achieve 70% vaccine coverage.

Figure 6. Projected impact of comprehensive TB interventions in Ukraine.



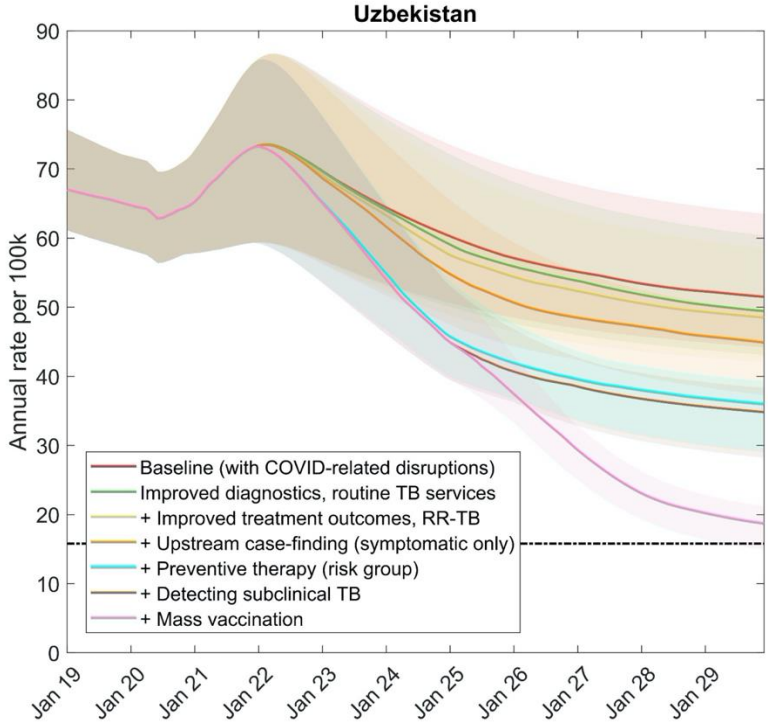
Uzbekistan

Figure 7 shows that Uzbekistan can reach the End TB goal to reduce incidence if the following interventions were scaled up in a linear fashion from 2023 through 2025 and maintained thereafter:

- Use of improved diagnostics
- Improved treatment outcomes for drug-susceptible and rifampicin-resistant TB
- Upstream case-finding of symptomatic TB
- Detection of subclinical TB

Starting in 2026, the roll-out of a post-TB-exposure vaccine with at least 60% efficacy and that reaches at least 65% of people with TB infection would decrease incidence further in line with the End TB goal.

Figure 7. Projected impact of comprehensive TB interventions in Uzbekistan, 2019-2030.



See Annex 2 for supplemental modeling methodology and further analysis.

Ch 3. TB Diagnosis and Care

Priority actions

- Re-imagine TB care, delivering quality services through a people-centered approach.
- Scale-up the use of modern diagnostics
- Find the missing people with TB
- Expand early diagnosis, including at sub-clinical stages
- Develop and implement public communications strategies to raise TB awareness and promote early health-seeking.
- Integrate TB screening and testing into other health services, with a focus on services that address common comorbidities or risk groups, depending on local epidemiological context.
- Provide support that enables people receiving TB care to complete a full course of treatment without an undue burden on them and their families, while avoiding catastrophic costs.
- Strengthen procurement systems and supply chains.
- Expand the use of real-time digital TB surveillance systems

Re-imagine TB care, delivering quality services through a people-centered approach.

People-centered care organizes the delivery of health services around the needs and expectations of people and communities. It prioritizes meeting those needs and expectations of people at all stages of their lives. And it balances the rights of people with TB with their responsibilities and capacity as stakeholders in the health system.[6] The delivery of patient-centred care should also be guided by principles of equity, inclusion, and gender-responsiveness (see Chapter 7).

Reimagining TB care means globally embracing a people-centered approach. The TB-REP[7] Scientific Working Group defines people-centered TB care as *"an*

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[6] *A people-centred model of tuberculosis care. A blueprint for Eastern European and Central Asian countries.* First edition (WHO, 2017); https://www.euro.who.int/__data/assets/pdf_file/0004/342373/TB_Content_WHO_PRO_eng_final.pdf

[7] TB-REP is a is a multi-country, multi-partner program funded by the Global Fund and implemented by the Centre for Health Policies and Studies as the principal recipient jointly with WHO Regional Office for Europe, TB Europe Coalition (TBEC), TBpeople,

efficient and integrated set of affordable, accessible and acceptable health services, provided in a supportive environment to prevent, diagnose and treat TB." In other words, people-centered TB care not only ensures effectiveness and safety of services, it also ensures that people with TB get the right care, at the right time, by the right team, and in the right place.

Done properly, people-centered TB care closes the gaps in the care cascade, creating a seamless experience from initial care seeking all the way through to successful treatment and appropriate care for post-TB disease. People-centred TB care is based on the most recent evidence-based clinical standards. Just as importantly, people-centred TB care delivers convenient services with high satisfaction to both the person with TB and the provider(s) of care.

When designing a people-centered approach to TB care, programmes should ensure that:

- TB survivors are meaningfully engaged and their priorities incorporated throughout the design process
- TB services are as convenient for people to access as possible, including for the most marginalized and vulnerable populations
- The service model meets persons with TB and their families' needs and expectations
- Underlying factors are addressed in the context of care (e.g., comorbidities, nutrition status, alcohol or tobacco use)
- Services, tasks and responsibilities are defined for each setting and within different facilities, while recognizing the need for flexibility to respond to the needs of individuas with TB
- Functioning referral systems are in place across various settings and facilities
- A robust data-reporting system is in place to monitor performance, including diagnostic delay, loss to follow-up and the quality of services from the user perspective
- Any technology is used in ways that connect people to the health system, not alienate them from it
- People in TB care and their families are protected from catastrophic financial expenses

Deliver people-centred care in the community

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the Global TB Caucus, in partnership with national TB programs and civil society organizations.

Delivering people-centered TB care is only feasible by strengthening the delivery of TB care at the community level, supplementing care made available at higher levels of the health system.

Community-based and ambulatory care[8] typically leads to better TB outcomes compared with hospital-based or inpatient care. WHO recommends that TB care be provided mainly in community-based and ambulatory settings as long as certain criteria are met with regard to the person's clinical condition, the presence of infection control measures, and the availability of adequate treatment support. There also needs to be a back-up plan in cases where a person with TB does need inpatient care.

Civil society organizations with a direct presence in local communities play important roles in ensuring TB care is people-centered, especially by:

- Strengthening community involvement in all aspects of the TB response
- Supporting people who are in TB care to complete treatment
- Delivering psychosocial support to people who are in TB care and their families
- Creating and maintaining community awareness of TB
- Monitoring the availability, accessibility, acceptability and quality of TB services
- Eliminating TB stigma, discrimination and other human rights related barriers to TB services

Funded with resources from the state or other sources, social contracting is one model that helps civil society organizations be more sustainably involved in providing some TB services.

Use technology to deliver people-centred care

Re-imagining TB care also requires moving beyond traditional "brick-and-mortar" approaches to using all available means of delivering care that are efficient, high quality and convenient. Convenient care means it is available

[8] Care delivered in a setting where a person is not admitted to a hospital.

within the community and even within people's homes, including in remote areas.

Innovations in digital health make it more feasible than ever to deliver this level of convenience. (Chapter 8 discusses priorities for developing new digital solutions.) Examples include:

- Digital/video-enabled health consultations and treatment support
- Real-time case notifications and disease monitoring
- Mobile app-based information-sharing and communication
- E-learning

Out of necessity, the use of these innovations skyrocketed during the COVID-19 pandemic. Solutions were often tailored to meet local needs. As a result, the technology infrastructure, the regulatory environment, and users' familiarity with digital health tools—which have applicability across disease areas—are far more advanced today than they ever were before.

Ensuring the widespread use of these innovations is critical to delivering care at a scale necessary to end TB. It is equally important to ensure that technology is not used in such a way that creates new "digital divides" that create technological barriers to care and worsen health inequities.

Provide care for post-TB disease

Research shows that up to 70% of people who are cured of TB disease will continue to experience other health challenges as a consequence of having had TB. Medical experts have begun to recognize post TB lung disease (PTLD) as a health condition that requires attention on both the individual and population levels. PTLD refers to a spectrum of different disorders that can affect various parts of the pulmonary system, leading to higher risks of developing TB disease again and shortened life expectancy. Relatively little research has been conducted on PTLD, and no studies had been conducted on PTLD in children as of 2021.[9]

The first set of clinical guidelines for providing care for PTLD were published in 2021.[10] They provide guidance for:

[9] https://pubmed.ncbi.nlm.nih.gov/33401266/

[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8504493/

1. assessing patients for PTLD when they reach the end of TB treatment
2. identifying people with PTLD who should receive pulmonary rehabilitation (PR)
3. tailoring a PR programme to meet the needs of people and local communities
4. evaluating the effectiveness of PR
5. conducting education and counseling
6. addressing PTLD in a public health context

The Global Plan urges TB programmes to follow these guidelines in planning and implementing programming that provides care for PTLD and addresses PTLD at a population level.

People who have been cured of TB can also experience other health effects.[11] Rates of cardiovascular disease are higher in people who have had TB. Anxiety and depression are also commonly experienced by people with TB. And people who have completed second-line treatment for drug-resistant TB often face hearing loss. TB programmes should plan and implement approaches for identifying these conditions and providing appropriate care and support that continues after TB treatment is completed.

Strengthen the TB workforce

There is an urgent need to increase human resources available to end TB. Health workforce development includes all types of human resources for health (HRH) initiatives that have an impact on TB care and prevention, including medical education reforms, task-shifting, training primary health care providers to deliver people-centred TB care.

Wherever possible, the roles of community health workers should be formalized. Community health workers have long been a crucial part of the TB response. They are essential to delivering community-based TB care. However, the TB response continues to be stymied by unpaid labour provided by community health workers. With proper investment, community health workers can have a significant impact. A project funded by Stop TB's TB REACH initiative in Ethiopia found twice as many people with TB in a 15-month period than the previous 15 months, simply by employing community health workers

[11] https://pubmed.ncbi.nlm.nih.gov/31753065/

and professionalizing their roles within the health system.[12] This model has been replicated throughout Ethiopia and in other countries.

Ensure a continuum of care in challenging operating environments

Conflict and natural disasters weaken health systems and displace populations, causing significant breakdowns in the provision of TB care. With a record number of refugees around the world today, ensuring access to TB care for refugees and internally displaced people is a critical challenge. Refugees and internally displaced people, facing urgent needs to secure the basic provisions that sustain life, face a higher risk of contracting and dying from infectious diseases. Lack of access to healthcare, while a number of other factors including crowded housing, undernutrition, stress, and unmanaged co-morbidities, increase the risk of developing TB. Breaks in the continuum of care can lead to the emergence and spread of DR-TB. At the same time, conflict can actually contribute to the spread of TB. These challenges make TB one of the most common causes of death among refugees.[13]

Implementing a comprehensive approach to TB care that involves cross-border collaboration, establishment and safeguarding of humanitarian corridors and supply chains, targeted funding, political solutions, and advocacy and communications is critical to creating and maintaining a continuum of care in such environments.

Box: The Stop TB Partnership's Re-imagining TB Care Initiative

Given the challenges of delivering TB care, the Stop TB Partnership's Re-imagining TB Care initiative has tested assumptions about *when*, *where*, and *how* TB care and services are accessed and delivered. Its aim is to identify solutions for scaling up early, local access to care, using digital solutions.[14]

[12] Ethiopian Community Health Workers Help Double the Number Of Vulnerable People Provided With TB Care: https://www.stoptb.org/news/ethiopian-community-health-workers-help-double-number-of-vulnerable-people-provided-with-tb

[13] https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00104-7/fulltext

[14] https://stoptb.org/assets/documents/about/cb/meetings/34/34-06%20Accelerating%20New%20TB%20Tools%20and%20Approaches/34-6.12_Re-imagining%20TB%20Care_Background%20paper.pdf

To this end, the Re-Imagining TB Care Initiative has developed a background paper that lays out guiding principles, goals and objectives for delivering people-centred TB care. Programmes can use this resource to help them identify which solutions are most promising for scaling up access to people-centered TB care within their local contexts.

Scale up the use of modern diagnostics

Universally replace sputum microscopy with rapid molecular diagnostics as the initial diagnostic test

Rapid and accessible TB diagnosis is the first step in providing effective treatment and saving lives. Many countries today still rely on sputum microscopy as the initial diagnostic test for TB. Rapid molecular tests need to replace sputum microscopy as the initial diagnostic test.

Diagnostic testing also needs to move to the point of care. This will make testing more accessible and will reduce the time it takes for people to obtain their test results and start treatment. There are multiple molecular tests recommended by WHO that can be used to expand access to diagnosis through their implementation at different levels of the health system. Technologies that test for multiple diseases at one time provide even greater opportunities. They can improve system efficiencies, save costs, provide a better user experience, and ultimately help improve quality of care.

Use complementary technologies and methods to improve rapid TB detection

Use urine-based LAM tests for testing TB in PLHIV

TB is the leading cause of death of people living with HIV, but it's more difficult to diagnose people living with HIV using sputum. TB LAM, a urine-based, rapid point-of-care test, offers a simple way to detect TB in people living with HIV (PLHIV). WHO recommends the test for all PLHIV with TB symptoms regardless of their CD4 count, in both inpatient and outpatient healthcare settings. TB LAM should be added to diagnostic algorithms,[15] to be used in addition to rapid molecular tests that use sputum.

Use stool to test for TB in children

[15] https://www.who.int/publications/i/item/9789240029415

Detecting TB in children has historically been challenging because of how difficult it can be for children to produce a sputum sample. In 2020, WHO recommended using stool to test for TB in children, using rapid molecular tests.[16] This is an easy and pain-free method for rapidly testing for TB in children. It should be universally implemented.

Use CAD to screen for TB disease

A chest x-ray can rapidly identify people who should receive diagnostic testing for TB. It can also reduce the number of symptomatic people requiring rapid molecular tests, along with those associated costs. Computer-aided detection (CAD) tools use artificial intelligence (AI) to read chest x-rays for signs of TB and issue findings. These findings are then used for screening and triage.

CAD overcomes some of the main limitations of a chest x-ray, providing accurate, rapid results with no inter- or intra-reader variability. Recommended by WHO for use either alongside or in place of human readers, CAD can increase access to chest X-ray and thereby TB care in regions where few or no human x-ray readers are available.[17] Coupled with lightweight portable X-ray systems, the technology makes screening for TB feasible even in remote locations.

Use more routine and comprehensive drug susceptibility testing

Access to universal drug susceptibility testing (DST) is essential for successfully diagnosing and treating people with drug-resistant TB. DST needs to become more routine and comprehensive, so that no person receives medications to which their TB organism is resistant. This is especially important in light of WHO treatment guidelines that emphasize using newer medicines and treatment regimens for treating people with rifampicin-resistant and isoniazid-resistant TB. DST lab capacity and specimen referral networks need to be built to achieve this.

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[16] https://www.who.int/publications/i/item/9789240033450

[17] chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/viewer.html?pdfurl=https%3A%2F%2Fapps.who.int%2Firis%2Fbitstream%2Fhandle%2F10665%2F340256%2F9789240022614-eng.pdf&clen=3321323&chunk=true

Technology for identifying drug resistance is evolving. Next-generation genomic sequencing (NGS) will allow health systems to quickly detect resistance to a wide profile of medicines. Evidence continues to be collected on the use of NGS, and the catalog of clinically relevant mutations in TB bacilli continues to grow. WHO is expected to issue recommendations on using NGS to guide clinical treatment decisions in 2023.

Build capacity for testing for TB infection

Countries must not only build capacity for active TB disease. They must also address the massive reservoir of TB infection. TB infection may eventually become TB disease, and an approach that focuses only on testing people when they have TB symptoms will result in continued spread of TB.

Because the tuberculin skin test (TST) can show a false-positive result in people who have received the BCG vaccine, it has limited use in countries with high vaccination rates. Interferon-Gamma Release Assays (IGRAs) and next-generation skin tests are more specific than TST and should replace their use. WHO recommends multiple IGRAs, and has evaluated antigen-based skin tests and found them to be accurate, acceptable, feasible, and cost-effective alternatives to tuberculin skin tests and IGRAs.[18]

Strengthen diagnostic systems to meet higher demand for testing

Scaling up modern diagnostics involves more than adopting new technologies. The effort must consider the entire diagnostic network, installing new testing sites and replacing old tests in the right places to ensure people's access. Increasing access means testing networks need to be able to meet higher demand. This requires having robust specimen referral systems, sufficient human resources, supervision and quality assurance, appropriate infrastructure and electricity, and comprehensive service and maintenance plans for all equipment. WHO provides guidance for programmes on implementing diagnostics networks.[19]

Find the missing people with TB

[18] https://www.who.int/publications/i/item/WHO-UCN-TB-2022.1

[19] WHO. Operational Handbook
https://www.who.int/publications/i/item/9789240030589

TB can be diagnosed, treated and cured. And yet a large proportion of people developing TB are unable to access good quality diagnosis and treatment. Such individuals are often referred to as the “missing people” with TB. During the period 2015-2020, worldwide an estimated 3 to 4 million people with TB went without a diagnosis or were treated in the private sector without being accounted for in national data. The large number of people who are missing from TB care is one of the main reasons that TB incidence and mortality has been declining so slowly in recent years.

At the 2018 UN High Level Meeting on TB, UN member states issued a political declaration committing to reduce the numbers of missing people with TB and to scale up TB treatment to reach all people with TB by 2022. Significant progress was made by countries during 2018 and 2019, but the COVID-19 pandemic created a major setback starting in 2020.

The Global Plan recommends that, at minimum, 95% of people developing TB each year need to be diagnosed and treated, and that no one should be left behind. To find the missing people with TB, different approaches will be needed depending on the local setting. Some of the most effective approaches include:

- Active TB case finding
- Eliminating barriers to health services, including barriers related to human rights, gender and stigma
- Engaging with the private health care sector to diagnose TB, provide appropriate care and notify cases to national TB programmes
- Finding the missing people with TB also means ensuring that people everywhere have access to modern TB diagnostics. Old TB diagnostics such as sputum microscopy should not be used for diagnosing TB because it fails to detect 40% of TB and cannot detect drug resistance.

Countries are implementing a number of interventions to find the missing people with TB. TB REACH projects are designed specifically to find and diagnose more people with TB. And a Global Fund strategic initiative for finding the missing people with TB has provided a platform for implementers from different countries to learn from each other.

Expand early diagnosis, including at sub-clinical stages

The Global Plan's modeling shows the importance of early diagnosis in reducing transmission and incidence of TB. (See Chapter 2.) Numerous studies have identified delays in diagnosing people who have TB symptoms. Prevalence surveys have consistently found that about half of people with laboratory-confirmed TB do not report symptoms or are asymptomatic, referred to as "sub-clinical TB."[20]

Knowing this, the Global Plan recommends that high TB burden countries should invest significantly more resources in TB screening and active case finding aimed to detect TB early and to initiate early treatment. Populations with high rates of TB should be periodically screened for TB, regardless of symptoms.

Sub-clinical TB can be diagnosed by X-ray followed by bacteriological confirmation. X-ray is an excellent tool to screen people for pulmonary TB, as it is more sensitive than symptom-based (i.e., clinical) screening. X-ray technology has improved in recent years. Modern X-rays are digital, highly portable, and produce high-resolution digital images, allowing X-rays to be deployed in mobile vans and in communities.

Artificial intelligence (AI) solutions are also improving and becoming more available. AI can read X-ray images faster and better than trained human radiologists. Ultra-portable digital X-rays with computer aided reading of results should be used by countries to screen people for pulmonary TB in populations with high rates of TB.

Several initiatives have demonstrated the value of population-level TB screening followed by confirmatory molecular tests in those with abnormal X-rays. Stop TB Partnership's TB REACH initiative has supported several projects that have demonstrated the value of such screening.[21] Large-scale screening of populations have been undertaken by several national TB programmes, such as India, Viet Nam, Cambodia and others.

Population-level TB screening and active case finding are cost-effective interventions. Costs can be further reduced by conducting multi-disease

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[20] https://pubmed.ncbi.nlm.nih.gov/32936877/

[21] https://www.thelancet.com/journals/landig/article/PIIS2589-7500(21)00116-3/fulltext

screenings, such as for TB along with COVID-19, lung cancer, diabetes, use of tobacco and other conditions.

New tools could further facilitate population-level screening, testing and diagnosis of subclinical TB. The Global Plan calls for funding and fast tracking the research and development of biomarker-based tests for diagnosing subclinical TB.

Develop and implement public communications strategies to raise TB awareness and promote early health-seeking.

Raising TB awareness and motivating people to seek care is essential to finding the missing people with TB and helping all people with TB receive an early diagnosis. This requires countries to develop and implement communications strategies for public education and behavior change. The following are basic elements that should be included when developing a communications strategy.

Set goals

Communications goals should always serve and complement TB program goals. Analyzing TB response needs, gaps and opportunities within domestic and regional settings will help determine goals. Analyzing the strengths and weaknesses in communications capacity will show where goals are realistic and where capacity needs to be strengthened in order to achieve them. Each activity should be undertaken with a clear purpose and desired outcome in line with communications goals, with quantifiable targets for measuring impact. Examples of types of goals include:

- Improving basic knowledge about TB among key vulnerable populations or the general public in TB-affected countries.
- Improving awareness about where to receive screening or testing.
- Increasing numbers of people with TB who seek testing.
- Improving knowledge among health workers about what to do when people seek TB testing or care.
- Educating government officials about TB and the TB response.
- Building empowered and capacitated networks of people affected by TB to help reach, engage and support TB key vulnerable populations.

Identify audiences

Identifying key audiences, and understanding their values and motivations, is a critical starting point in developing communications strategies. It is also critical to understand literacy and languages spoken by audiences, and to produce communications that audiences easily understand. Priority audiences might include key populations, health workers, government officials, news media and strategic partners.

Develop messaging

Messaging should be positive and educate audiences about solutions. It should be culturally appropriate. Messaging that motivates audiences to seek care early should emphasize that TB is preventable and curable. Ideally, messaging should be developed and tested with representatives of audiences.

Engage partners

Identify partners who share the same or complementary goals and who are willing to contribute to developing or implementing communications strategies. Partners can bring more visibility and add credibility to messaging. Partners should be engaged based on their credibility, reliability and connection with key audiences. When it will help to achieve goals, communications efforts should be coordinated with partners at sub-national, national, regional, and global levels. Partners can come from many places, such as:

- TB survivors and champions
- Government offices
- Non-governmental organizations
- Businesses and corporations
- Faith communities
- News media
- Celebrity ambassadors
- Social media influencers

Identify tactics, tools and communications channels

Tactics are categories of actions that can help achieve communications goals. Tools are tangible assets used to implement tactics. Channels are ways through which people communicate or receive information.

Common tactics:

- Educating health workers
- Educating people seeking care
- Community outreach
- Disseminating messages through media channels
- Making official announcements
- Working with public-facing leaders and influencers to share messages with their audiences
- Sensitizing judiciaries, law and policy makers
- Public demonstrations
- Webinars, live online chats
- Townhall/community meetings

Common tools used for communications:

- Brochures, pamphlets, signs, banners
- Advertisements
- Press releases, prepared statements
- Websites
- Social media platforms
- SMS/text messaging platforms
- Webinar platforms
- Television, radio and podcast programs
- News editorials and Op-Eds
- By-line articles
- Talking points and written speeches
- Letters
- Plays and skits

Common tools used for planning and project management:

- Work plans
- Editorial calendars
- Checklists
- Project management software applications

Common communications channels:

- News media (television, radio, print, digital)
- Advertising (including content marketing)
- Social media (including blogs)

- Newsletters
- Email
- Telephone
- SMS/text messaging apps
- Word of mouth

Develop and implement campaigns

Any one tactic on its own will have limited effect. The most effective approach to raising awareness is to implement a variety of tactics through a planned campaign. In a campaign, tactics are implemented in a coordinated way, with the effect of each tactic reinforcing others. Tactics are used to communicate with specific audiences, through communications channels that are chosen based on which ones audiences are known to use. Thoughtful planning is key to successful campaigns.

To raise awareness and encourage early health-care seeking among key vulnerable populations, a campaign might involve:

- Educating health workers about TB and incentivize them to educate people seeking care about common symptoms and where to access testing
- Displaying educational signs at health facilities
- Conducting community outreach that includes a skit
- Publishing an Op-Ed by a TB survivor in local or national news media, which is used to earn interviews with local or national media
- Coordinate partners to share TB messages through social media and SMS
- Get local radio stations to run public service announcements
- Work with local faith leaders to share messages with fellow adherents
- Use social media to amplify all the above activities

Measure and evaluate impact

The success of any campaign depends on achieving goals to increase the numbers of the right people seeking care. In areas where campaigns are implemented, measurable outcomes should be increased numbers of people:

- screened for TB
- diagnosed with TB
- diagnosed with sub-clinical TB

- initiating TB treatment

Integrate TB screening and testing into other health services, with a focus on services that address common comorbidities or risk groups, depending on local epidemiological context.

Innovative approaches are needed to find the missing people with TB and ensure they receive a diagnosis and care. At the population level, these approaches need to be linked with co-morbid conditions to regain momentum to end TB.

A systematic review looking at integrated TB and NCD services found higher levels of integration conferred more benefits to patients in terms of managing TB and NCDs.[22] A systematic review looking at the integration of HIV with other health services found that overall, the strategy led to improved health and health-system outcomes.[23] Integrating TB care with tobacco cessation services has also been recognized as a critical service for people with TB and HIV who use tobacco.[24]

Integrated Service Delivery (ISD) combines multiple interrelated health services in one interaction. By addressing multiple health issues simultaneously, ISD promotes convenience in ways that align with the goal of delivering people-centered care. If used widely, this approach has the potential to accelerate the finding of missing persons with TB while addressing other health conditions that contribute to TB morbidity and mortality (i.e., HIV, diabetes, malnutrition, tobacco use, and COVID-19).

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[22] Foo CD, Shrestha P, Wang L, Du Q, García Basteiro AL, Abdullah AS, et al. (2022) Integrating tuberculosis and noncommunicable diseases care in low- and middle-income countries (LMICs): A systematic review. PLoS Med 19(1): e1003899. https://doi.org/10.1371/journal.pmed.1003899

[23] Bulstra CA, Hontelez JAC, Otto M, Stepanova A, Lamontagne E, Yakusik A, et al.(2021) Integrating HIV services and other health services: A systematic review and meta-analysis. PLoS Med 18(11): e1003836. https://doi.org/10.1371/journal.pmed.1003836

[24] Jackson-Morris, Angela & Fujiwara, Paula & Pevzner, E.. (2015). Clearing the smoke around the TB-HIV syndemic: Smoking as a critical issue for TB and HIV treatment and care. The International Journal of Tuberculosis and Lung Disease. 19. 10.5588/ijtld.14.0813.

ISD can also contribute to progress towards universal health care coverage, and it aligns with the global move towards One Health, a multidisciplinary approach that links the health of humans, other animals and the environment through collaborative, multisectoral, and transdisciplinary initiatives to combat diseases. The One Health approach aims to improve Global Health Security and strengthen health systems (see Chapter 6).

ISD can be initiated from TB services by incorporating screening for other diseases. For example, chest x-rays taken to diagnose TB can be used to screen for lung cancer, COPD and other conditions. Similarly, TB screening can be added to vaccination campaigns.

There are different ways to coordinate services using an ISD approach, including:

- Diagnosis and referral to other health facilities/providers
- Active follow-up
- Providing care for multiple health conditions at the same facility on the same day

Several initiatives have integrated other health conditions into their TB screening platforms, including:

- Joint TB and COVID-19 screening
- TB screening conducted through COVID-19 vaccination campaigns
- Joint screening of TB and other diseases such as diabetes, silicosis, other airborne infections, lung malignancy and mental health conditions
- TB screening integrated with tobacco-use counseling and cessation support
- Integrated sample transportation systems
- Community health workers trained to provide services for multiple health priorities

ISD can also be combined with other initiatives, such as active case finding campaigns, immunization campaigns, and reproductive, newborn and child health services. Interventions focused on engaging private providers for ISD can also help more people with TB receive an early diagnosis and access care.

Mobile vans with digital portable or handheld x-ray machines and portable laboratory equipment can be more widely used where appropriate to access

communities and key vulnerable populations. To mobilize communities to participate in these campaigns, interventions use various media for outreach and awareness.

Achieve universal access to the most effective TB treatment regimens

TB has a high rate of mortality without treatment. Studies of the natural history of TB disease in the absence of treatment with anti-TB drugs (conducted before drug treatments became available) found that about 70% of individuals with sputum smear-positive pulmonary TB died within 10 years of being diagnosed, as did about 20% of people with culture-positive (but smear-negative) pulmonary TB.

Improve treatment effectiveness through development of new drug regimens

Efforts are needed to improve TB treatment effectiveness. Effective TB treatment, including for drug-resistant TB, relies on the use of several antibiotics administered in combination without interruption for several months. With research funding needs only partially met, some progress has been made in recent years to identify more efficacious, safer medicines and shorter treatment regimens. The development of new regimens using repurposed medicines such as linezolid, clofazimine and rifapentine is on a more positive course than in years past.

That said, continued new drug development is needed to make TB treatment regimens more people-centered by making them shorter, safer, more effective, and less costly—especially regimens for treating drug-resistant TB.

See Chapter 8 for discussion of TB R&D priorities.

Achieve universal access to all-oral regimens for treating drug-resistant TB.

Drug-resistant TB (DR-TB) is a global public health crisis. DR-TB is harder to treat than drug-susceptible TB and presents major challenges for patients, health care workers and health care services. Globally, almost 15% of people with MDR/RR-TB die from the disease, and 26% of those deaths are in people with extensively drug-resistant TB (XDR-TB). Continued community transmission in many parts of the world, combined with resistance that is becoming more enhanced, is weakening global health security and undermining progress against TB.

Shorter, all-oral (i.e., no injections) DR-TB treatment regimens are urgently needed. Current drug regimens used to treat DR-TB are far from satisfactory. Compared with treatments for drug-susceptible TB forms, these regimens require a longer course of treatment, the use of more toxic medicines, and an exponential increase in the ingestion of pills. Many people receiving care for DR-TB experience significant adverse events and have poorer treatment outcomes.

Continue to develop evidence-based recommendations for improving the effectiveness of treatment for drug-resistant TB.

Especially as new drugs are developed, there is a critical need for the continual development of evidence-based policy recommendations to guide the treatment and care of people with drug-resistant TB. These recommendations need to better outline a comprehensive care path that people should take after being identified by the health system and referred for DR-TB treatment.

Provide support that enables people receiving TB care to complete a full course of treatment without an undue burden on them and their families, while avoiding catastrophic costs.

In addition to better treatment regimens, people-centered TB care should include:

- Psychosocial support that helps people with TB complete a full course of treatment
- Humane forms of treatment support
- Monitoring and management of adverse events/drug reactions
- Clinical monitoring and management of comorbidities (e.g., HIV, hepatitis and non-communicable diseases)
- Support that fulfills the various non-medical needs of people with TB, including respect for human rights, privacy/confidentiality, and a stigma- and discrimination-free environment

Psychosocial support is often essential for people to complete TB treatment without experiencing hardship or even trauma. Psychosocial support is a critical part of people-centered care. It improves TB treatment outcomes, as it makes it easier to receive care for the whole duration of treatment. Family members, civil society and nongovernmental organizations and community members are key facilitators of psychosocial support.

For years, this kind of support has more or less been a standard part of TB care in high-income countries. It includes:

- Psychological support, including patient and family education, counseling sessions or peer-group support
- Material support, which minimizes or eliminates indirect costs incurred by patients that create a barrier to accessing and continuing care. Material support often comes in the form of:
    - Financial assistance, such as bonuses, transport subsidies, housing incentives or living allowances
    - Food assistance, such as meals, food baskets, food supplements or food vouchers

People receiving TB care should receive regular treatment assistance and support, whether at home or in another adequate ambulatory facility. This should be accompanied by appropriate infection control measures, including preventive treatment for other household members.

Treatment support can be delivered in line with people's circumstances (such as at the workplace, school, health post, primary care center, drug/alcohol dependence treatment center or outreach program). After care is established and infectiousness is no longer a risk, it is critical that whenever possible, people in care remain fully integrated in their community and their routine lives, enabling them to engage normally with the environment they are accustomed to.

Strengthen procurement systems and supply chains

Reliable and efficient system for procurement, supply chain and distribution of health products for TB is essential. Procurement and supply systems in countries must be nimble enough to support the introduction of new medicines, treatment regimen and diagnostics.

The number of TB diagnostics and medicines—including new formulations of existing medicines—has grown in recent years. Thanks to investments in innovation, WHO recommends new medicines and new diagnostics at regular intervals. More new diagnostics, medicines, vaccines and other technologies are expected before 2030. These new products will need efficient regulatory approval and systems for procurement and distribution.

During the COVID-19 pandemic, countries gained considerable experience in rapidly procuring new diagnostics, vaccines and therapeutics. TB programmes must learn from this experience and prepare for the introduction of new TB medicines and diagnostics as soon as they are available.

During the pandemic there were also significant shifts in the way medicines were distributed to people for screening or care at home. The pandemic induced 'stay-home' services led to important shifts towards strengthening home-based and community-based services, which are likely to last and develop further. Such services will need health products to be distributed to the communities and homes of people.

In several high TB burden countries, the private health care sector provides TB care to a substantial proportion of people with TB. National TB Programmes in such countries must ensure that the private health care sector has access to the latest TB diagnostics and medicines, and that people get these services at affordable prices. Where quality can be assured, national TB programmes also have the option to outsource certain services (e.g., laboratory services) to the private sector using smart contracting mechanisms.

Box: The Global Drug Facility
Recognizing its advantages, the 2018 UN political declaration on TB encouraged all countries to utilize the Stop TB Partnership Global Drug Facility (GDF) for procuring TB medicines, diagnostics and related services. The GDF offers countries a platform for procuring quality-assured medicines and diagnostics at reduced prices. GDF is a one-stop bundled procurement and supply mechanism providing a unique package of services that combine strategic procurement of TB products and coordination of market activities, with technical assistance and capacity-building for TB programmes.

Expand the use of real-time digital TB surveillance systems

TB surveillance involves the continuous and systematic collection, analysis and reporting of data related to TB infection and TB disease in a population. Digital surveillance should capture data on the complete cascade of TB screening, diagnosis, treatment and care of both TB infection and active disease.

Real-time, digital TB surveillance systems make data available in more timely fashion compared with traditional surveillance approaches and provides more granular views of TB trends, from local to national levels. They also enable

regular data analysis that supports adaptive responses to TB trends, allowing programs to target resources toward specific geographic areas or toward population groups in need of services. LMICs in particular stand to benefit from transitioning from paper-based to digital TB surveillance systems. Programs must adhere to high standards of digital privacy and data security when implementing digital surveillance systems.

New digital tools are making digital TB surveillance more feasible than ever before, and improving the use of real-time digital TB surveillance is a key priority for operational research (see Chapter 8).

WHO is expected to publish new guidance for the implementation of digital TB surveillance systems in 2022.[25]

[25] https://www.who.int/publications/digital/global-tuberculosis-report-2021/featured-topics/case-based-surveillance

Ch 4. Prevention

As described in Chapter 2, prevention is a critical part of a comprehensive package of interventions to end TB and needs significant new investment to scale up.

Priority actions:

- Address TB risk factors and social determinants
- Provide TB preventive treatment (TPT) for those living with TB infection and who are at higher risk of progression to active TB disease.
- Implement Airborne Infection Prevention and Control (AIPC) measures in health care settings and high-risk indoor places where people congregate.
- Prepare for successful global roll-out of effective vaccines once such vaccines are officially recommended and available.

Address TB risk factors and social determinants

The most common underlying, health-related risk factors for TB are:

- undernutrition
- HIV/AIDS
- smoking tobacco
- alcohol use disorders
- diabetes mellitus

These five risk factors can each be prevented or managed in line with the relevant Sustainable Development Goals. Progress against these five risk factors will contribute immensely toward ending TB. To prevent TB among people who live with common underlying risk factors, TB programmes should coordinate or integrate services with programmes for nutrition, HIV, smoking tobacco, alcohol misuse, diabetes, and COVID-19.

TB is also driven by social determinants, chiefly poverty, poor living conditions, stigma and discrimination, and conditions that fail to protect and promote human and gender rights. Closely related to poverty, undernutrition is the biggest risk factor for TB globally. It is the primary contributor to TB incidence in all regions except Europe (where the leading risk factor is alcohol misuse).

Prevent TB through a multisectoral approach

Addressing TB risk factors requires a multisectoral approach that extends beyond the health sector and encompasses the broader development agenda. Most countries have created programmes and initiatives to address at least some TB risk factors and social determinants, including poverty, substandard housing, and workplace health initiatives (e.g., for mine workers).

High rates of TB or TB risk factors within communities are often indicators that should lead governments to include such populations under existing programmes or create new programmes as needed. To address underlying risk factors and social determinants of TB, governments should pursue an all-of-government approach that aligns, coordinates or integrates TB programme activities with those of other government programmes and initiatives.

National TB programmes should address the interplay between TB and undernutrition as a priority. Nutritional support must be provided with the dual objective of improving treatment outcomes and decreasing mortality in people with TB, as well as reducing incidence of TB among contacts and undernourished communities. Countries should follow international guidelines and best practices on TB and nutrition and be aware of new evidence emerging through research. India, for example, has begun to provide nutrition support packages as a part of TB care.

While HIV is the leading driver of TB in certain regions, particularly in sub-Saharan Africa, HIV is a significant underlying risk factor in all countries affected by TB. Collaborative programmes between TB and HIV activities have been implemented in most countries. Countries must build on this progress by addressing remaining gaps and challenges in these programmes.

Chapter 7 presents an agenda for addressing stigma and discrimination, implementing a gender-sensitive TB response, eliminating TB stigma, and reaching key and vulnerable populations.

Strengthen collaboration among health and social programmes

Preventing or addressing TB risk factors will require collaboration among TB programmes, other health programmes, development initiatives and communities. TB programmes must reach out to these programmes and initiatives to ensure that communities are no longer exposed to the same risk

factors they have been exposed to in the past, disrupting the cycle of TB and reducing the risk of TB relapse. For example, TB programmes can do this by:

- Including people with TB, their families, and immediate communities in relevant programmes and initiatives, including poverty alleviation policies, cash transfers, nutritional support programmes, social security benefits, urban housing initiatives, and compensation schemes.
- Partnering with programmes for other health-related risk factors to form a bi-directional partnership that benefits all programmes. This can include bidirectional screening and testing for TB and diabetes, TB and HIV, TB and nutritional status, TB and smoking tobacco, or other respiratory conditions such as TB and COVID-19. TB should also be made part of relevant multi-disease screening and testing initiatives.
- Populations and communities experiencing high rates of TB are included in national and international development programmes.
- Settings known for congregation and crowding, such as prisons or urban apartments, have policies in place for airborne infection prevention and TB prevention and care.
- Encouraging or incentivizing the addition or enlargement of windows in housing design practices.
- Preventing food-borne TB transmission from animals infected with *Mycobacterium bovis*, which also causes TB disease and is transmitted by infected dairy products. Which requires coordinating with food safety programmes in areas where raw milk, cheese and/or blood are commonly consumed (see below)
- Incorporating TB screening and prevention practices within workplace health and safety policies and programmes.
- Including TB anti-stigma content within diversity, equity and inclusion programmes.

TB programmes and their national- and international-level partners must advocate and invest in this multi-sectoral approach. A strong commitment to partnerships will ensure that programme goals are acted upon through a whole-of-government and whole-of-society approach and monitored through the SDG framework.

Prevent transmission of zoonotic TB using a One Health approach

A historically neglected area of the TB response, zoonotic TB refers to strains of TB that are transmitted from non-human animals to humans. Most zoonotic TB in humans is caused by *M.bovis*, transmitted from cattle. Bovine TB primarily affects key and vulnerable communities that are at risk of TB from eating meat, drinking milk, or drinking blood sourced from cattle with TB. These food products can be made safe through cooking or pasteurization.

At the population level, zoonotic TB can be addressed through a One Health approach. One Health recognizes and implements interventions informed by the interconnection between humans, other animals (in the case of TB, mostly cattle) and the environment.[26]

WHO, the FAO, OIE and the UN Environmental Program (UNEP) have joined together to create a "Quadripartite" tasked with advancing One Health priorities. A One Health joint plan of action is expected in 2022, which will provide strategic guidance that countries can use to address zoonotic TB.

Key to addressing zoonotic TB in humans is preventing transmission from cattle, the main reservoir of infection with relevance for people. TB programmes in countries with communities that are at risk of bovine TB should develop policies and interventions for preventing transmission in line with a One Health approach. TB programmes should work with food safety authorities to develop and implement interventions that support communities to eliminate risks of food-borne TB transmission.

Relevant TB programmes should consult the Roadmap For Zoonotic Tuberculosis to learn more about challenges and solutions.[27]

Provide TB preventive treatment (TPT) for those living with TB infection and who are at higher risk of progression to active TB disease.

An estimated one in four people worldwide are living with TB infection (i.e., *Mycobacterium tuberculosis* (Mtb) bacteria are contained in a dormant state within the body, and the person is not currently sick). People infected with Mtb have a 5-10% life-time risk of developing active TB disease. People are at

[26] Coronaviruses, which cause COVID-19, are another example of a zoonotic pathogen that requires a One Health approach in order to protect human populations from future pandemics.

[27] https://theunion.org/technical-publications/roadmap-for-zoonotic-tuberculosis

greater risk of progressing to active TB disease most recently after infection. For people with comorbidities and/or weakened immunity caused by diabetes, malnutrition, or other conditions, the risk of TB infection developing into TB disease is substantially higher.

Expand access to TB infection testing and to TB preventive treatment (TPT)

TPT reduces the risk of developing active TB disease by as much as 60%, making it a key intervention for stopping TB transmission.

Expanding access to TPT requires:

- making TPT available to all who test positive for TB infection
- contact tracing followed by routine screening of vulnerable contacts and at-risk groups
- access to accurate diagnosis of TB disease and TB infection
- sufficient TPT drug and ancillary supplies
- reliable supply chains

Governments should have a policy that clearly identifies groups eligible for TPT, TB infection testing options, TPT regimen options, and a system for monitoring results.

At minimum, TPT should be available to those who are at highest risk of developing active TB disease. These groups include:

- All contacts of people diagnosed with bacteriologically confirmed TB
- People living with HIV (PLHIV)
- Frontline health workers
- People with silicosis
- Immigrants from high TB burden countries
- Incarcerated persons
- Persons living or working in crowded conditionssil

Research and development (R&D) can play a vital role in harnessing the full potential of TPT. Already, new technologies, such as IGRA blood tests and IGRA-based skin tests, are expected to expand the number of people recommended to receive TPT and accurately select those who will benefit from TPT. Countries should scale up a “test-and-treat” approach for TPT as infection testing technology advances and allows for more decentralized testing.

Having a vaccine that prevents TB infection from progressing to active TB disease would be a paradigm-shifting tool. When a new vaccine is shown to provide protection from TB disease that is similar to or better than TPT, vaccination should become the primary prevention tool and TPT should be reserved as a preventive for people who are ineligible for vaccination. The Global Plan anticipates having at least one TB vaccine available for use by 2025.

Strengthen contact-tracing and TB disease monitoring capabilities using digital technologies

Improving capabilities for contact tracing and disease monitoring are needed to expand access to quality care. To best improve these capabilities, countries should invest in digital-technology-based contact-tracing systems for TB at the community level. Where possible, countries can build on the capabilities that were further developed in response to COVID-19.

This investment would help:

- expand access to TB screening, early TB diagnosis and treatment—including both TPT and treatment for active TB disease
- improve country Pandemic Preparedness and Response (PPR) capabilities, making them more resilient to future airborne pandemics
- enable countries to more easily share data with key stakeholders, including civil society and technical agencies that assist TB efforts and ensure accountability–a function made difficult by current data systems

To build capabilities for TB monitoring and contact tracing, countries need to:

- Enact a standard-of-care policy indicating that all household contacts and other close contacts of people with TB should be traced, screened for TB disease and infection, and made eligible for TPT as appropriate.
- Deploy digital tools to assist health workers in health facilities and community-based programmes.
- Invest in accurate, high-quality data systems.
- Hire and retain sufficient human resources to carry out TB monitoring and contact tracing.

Implement Airborne Infection Prevention and Control measures in health care settings and high-risk indoor places where people congregate.

TB spreads through airborne aerosols, which makes airborne infection control measures critical to preventing transmission. Airborne infection prevention and control (AIPC) has always been a part of the TB response framework, but implementation has mostly been confined to laboratory and clinical settings. And even in these settings, AIPC principles have not been applied consistently, with implementation prioritizing hospital- or health facility-acquired infection.

The COVID-19 pandemic has focused the world on the threat posed by airborne pathogens. All health facilities should apply best practices for AIPC. Beyond the health system, places where people congregate also need to take all possible AIPC measures. Countries and national TB programmes should pursue TB infection prevention and control as part of a comprehensive AIPC approach rather than as a TB-specific initiative. Scaling up AIPC is especially important for LMICS, where progress in implementing measures has lagged.[28]

Taking these steps would aid the response to TB and all other airborne infections. They would also increase the likelihood that health facilities could 1) continue functioning during outbreaks of airborne infections and 2) help prevent the community transmission that fuels pandemics.

Scaling up AIPC measures requires action in three areas:

- Administrative measures
- Environmental measures
- Personal respiratory protection

Administrative measures

- Develop high, medium, and low airborne transmission risk zoning, signage, and precaution strategies in health care and congregate settings.
- Decongest health facilities by building systems for specimen transport and supply of medicines to people at their residence, especially for TB and other diseases requiring chronic care.
- Ensure reliable supply-chains for AIPC supplies, equipment, and services.

[28] https://www.who.int/publications/m/item/global-report-on-infection-prevention-and-control

- Triage for prompt diagnosis and treatment of people attending health facilities based on signs and symptoms of diseases spread through the airborne route.
- Develop affordable, easy-to-use, and sensitive rapid point-of-care (POC) testing for TB and other respiratory and/or airborne pathogens, including identification and drug-susceptibility testing for all (primary) health care facilities.
- Provide education for health care workers and the general public on universal masking and personal respiratory protection use.
- Where needed, institute systems for certifying filtering masks/respirators that are now available on the market.

National AIPC standards for health facilities and other buildings should be developed or updated in order to help advance these measures. Priority changes include:

- Update architecture design parameters to include:
    - Risk-based zoning
    - Analysis of existing ventilation (natural, mechanical or mixed) and its maintenance
    - Maximized natural ventilation
    - Airborne isolation (for people confirmed or presumed to have TB or other airborne infections)
- Update ventilation standards for various public places (e.g., schools, places of worship, cinemas, restaurants) to include:
    - Allowance for recirculation of treated/disinfected air
    - Minimum requirements for air changes per hour (ACH)
    - Consideration of whether and how the building could be used for airborne pandemic response needs
- Promote upper-room ultraviolet germicidal irradiation (UVGI) system minimum requirements (e.g., total UV-C output, beam parameters, certification etc.)
- Invest in structural changes to health facilities as needed to meet AIPC standards

Environmental measures

- Maximize natural ventilation wherever and whenever possible
- Build airborne isolation capabilities in health care facilities

- Promote single-pass mechanical ventilation (HVAC) for health care facilities with at least 12 ACH (air changes per hour) for high airborne transmission risk areas.
- Revise standards for recirculation of treated/disinfected air in HVAC for health care and public buildings.
- Use professionally designed and maintained Upper-Room UVGI systems as an alternative, supplement, and/or backup for ventilation in health care and indoor congregate settings
- Limit recirculating air conditioning use in crowded and high-risk settings unless it is used for air-mixing where upper-room UVGI is used
- Room air purifiers/cleaners
- Filtering masks for public and commercial use

Personal respiratory protection

- Ensure universal masking for high-risk indoor events/situations
- Ensure mandatory masking for all people being diagnosed or treated for TB and other respiratory infections.
- Provide certified face respirators (i.e., FFP2, N95, or equivalent certification) respirators for health care workers and other persons in high-risk settings.

Global partners with capacity, including the Stop TB Partnership Working Group on AIPC, should provide technical assistance to countries to help guide implementation of AIPC measures.
Countries have an opportunity to build on COVID-related public awareness and adaptations in people's behavior in ways that can reduce the risk of TB transmission in the community. They should use communications campaigns to promote evidence-based behaviors including:

- Social distancing
- Self-isolation when infectious
- Masking
- Cough etiquette

Implementing these measures will require investments from the health system, urban development agencies and authorities in charge of congregate settings. The Global Plan resource needs estimates (see Chapter 9) include costing for implementing AIPC in health care facilities managed by TB programmes, but does not include costing for implementing AIPC in the

general health system or in congregate settings that do not receive resources from TB programmes.[29]

Prepare for successful global roll-out of new effective vaccines once such vaccines are officially recommended and available.

The Global Plan's modeling projects that new and effective vaccines are needed to end TB (see Chapter 2). Vaccines are an essential part of the WHO End TB Strategy for the post-2025 period.[30]

Among the scientific community, the aim is to develop vaccines that:

- are at least 50% efficacious in preventing pulmonary TB disease in adolescents and adults and at least 80% efficacious in infants.[31] For the purpose of this Global Plan, modeling is based on a post-infection vaccine that is 60% efficacious in adolescents and adults.
- confer long-term immunity
- achieve high coverage in adolescents and adults (see Chapter 8)

TB advocates have called for a new effective TB vaccine for use by 2025. This is possible if funding for new TB vaccine R&D is made available immediately, and if the scientific R&D process is fast-tracked using the same approaches used for COVID-19 vaccine development.

Box: Limitations of the BCG vaccine

The BCG vaccine was first deployed in 1921 and ever since has been the only TB vaccine available. In most high TB burden countries, BCG is given to children in the first days or weeks of life as part of the country's childhood immunization programme. Coverage is relatively high in most countries where the vaccine is used.

BCG protects against severe forms of childhood TB that are associated with high mortality, but the vaccine in its current form and dosage has little to no effect on protecting adolescents and adults from developing TB disease.

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[29] Additional resources:
WHO Core Components for Infection Prevention and Control Programs

[30] https://www.who.int/tb/End_TB_brochure.pdf

[31] https://www.who.int/publications/i/item/WHO-IVB-18.06

Several TB vaccine candidates are in development that have the potential to provide pre- and post-infection protection for all age groups, particularly adults and adolescents. (See Chapter 8 for details.)

A novel TB vaccine is likely to come to market within the timeframe of this Global Plan. Assuming the vaccine is effective, to deliver impact it must also be:

- Affordable
- Widely available
- Integrated in health systems in high TB burden settings
- Accepted by at-risk populations

Delivering new TB vaccines to adults and adolescents

Adults and adolescents will be prioritized for a new TB vaccine, because evidence shows vaccination of these populations would achieve the most impact on reducing TB transmission and would prevent TB in infants and children by reducing their risk of exposure.[32] Unique challenges must be overcome to ensure broad and timely vaccination of adult and adolescent populations, which fall outside of standard immunization infrastructure. Only 9% of countries in SEARO and 11% in AFRO– the regions with the highest and second highest TB burdens—have adult vaccination programmes (Williams, 2020).

Lessons learned from introducing the human papillomavirus (HPV) vaccine point to difficulties in delivering vaccines to older populations. Almost a decade after launch, HPV immunization programmes reached only 6% of girls, adolescents and young adult women aged 10–20 years (Bruni et al., 2016). Despite the historically slow roll out of vaccines to adolescents and adults in low-and middle-income countries, COVID-19 has shown that where political will and sufficient resources exist, it is possible to introduce and scale-up access to a new vaccine in adolescents and adults much faster.

Administering a new TB vaccine will require identifying the pathways for overcoming historic challenges and delivering the vaccine to the highest-risk adult and adolescent populations. As part of this work, it will be critical to:

[32] https://spiral.imperial.ac.uk/handle/10044/1/26504

- prepare adequately for new TB vaccines
- mobilize communities and advocate
- Invest adequate resources in vaccine roll-out and scale-up
- promptly make vaccines available
- work with partners to maximize vaccine access and uptake
- ensure equitable access to vaccines
- apply learnings from COVID-19 vaccination campaigns

Prepare adequately for new TB vaccines

Countries should begin preparing now to introduce TB vaccines in order to achieve high vaccine coverage. Having a well-functioning system for delivering infant and child vaccines is not a strong predictor of country readiness to deliver adult and adolescent vaccines (World Bank, 2021).
Preparation will require:

- Engaging with stakeholders early: Early engagement with key stakeholders involved in vaccine financing and policy development—including WHO, the Product Development for Vaccines Advisory Committee (PDVAC), the Strategic Advisory Group of Experts (SAGE) on Immunization, Gavi, national programme heads, and end users from affected communities—will help facilitate vaccine policy adoption, procurement, and introduction.
- Country-specific data and projections: Data will be important to inform introduction planning, including:
    - In-depth country-specific value proposition analyses
    - Epidemiological data at country and subnational level
    - Modeling to define vaccine development investment caes and country-specific vaccine use cases
- Assessingments of programme costs, benefits, and budget impacts can help decision makers:
    - formulate national TB vaccine policies
    - determine screening algorithms
- Developing vaccine implementation plans: Preparatory work is needed to develop vaccine implementation plans that prioritize high-risk groups, are people-centred, and define the generic public health system requirements to deliver a new TB vaccine, based on a thorough assessment. Plans must be sure to include:
    - vaccine use cases that clarify when TB vaccines should be used versus other existing biomedical prevention options (e.g., TB preventive treatment)
    - financial and procurement processes

    - development of training materials and implementation aids
    - delivery strategies
    - positioning of ancillary supplies
    - awareness-raising and demand generation
    - vaccine safety and impact monitoring
- Engaging with stakeholders: Early engagement with key stakeholders involved in vaccine financing and policy development—including WHO, the Product Development for Vaccines Advisory Committee (PDVAC), the Strategic Advisory Group of Experts (SAGE) on Immunization, Gavi, and national programme heads—will help facilitate vaccine policy adoption, procurement, and introduction.

Mobilize communities and advocate

Maximizing high coverage of new TB vaccines will require a clear understanding of behavioral factors and perceptions that influence vaccine uptake. TB programmes have faced hesitancy surrounding TPT, arising from concerns about its benefits versus side effects in healthy individuals. And anti-vaccination sentiment during the COVID-19 pandemic heightened vaccine hesitancy in some settings.

Health education and communication campaigns that provide accurate, evidence-based information will be needed to generate demand and acceptance of vaccines. As part of these efforts, vaccine hesitancy needs to be proactively addressed. Mass-media campaigns, engagement of locally trusted leaders, civil society mobilization, and robust community engagement efforts are needed to address misinformation and mobilize demand. Community engagement efforts must reach key and vulnerable populations. (See Chapter 7 for details on reaching key and vulnerable populations and Chapter 8 for details on advocacy for vaccines and other new tools.)

Resources needed for bringing new TB vaccines to market simply will not materialize without effective advocacy. As a priority, advocacy is needed to mobilize resources for TB vaccine R&D and implementation. More advocates are needed who are trained to understand the science underlying TB vaccines. Related to that, scientific progress in TB vaccine development needs to become more visible and used to build policy champions for TB prevention. Advocates are critical to ensuring that TB prevention interventions reflect the best available scientific evidence.

Invest adequate resources in vaccine roll-out and scale-up

Adequate funding must be mobilized to support the manufacturing, procurement and distribution of vaccines, especially in high-burden settings.

This is the first Global Plan to estimate costs for rolling out new TB vaccines.[33] Global costs to implement a new vaccine are projected to average US$13.15 billion annually from 2027 through 2030, totaling US$52.6 billion. Modeled cost estimates include costs to scale up the use of a two-dose TB vaccine, reaching at least 60% of adults and adolescents by 2028, and to maintain 60% coverage or more after that. The cost of vaccine dose units, and the operational cost for vaccine delivery, have been informed by the experience of rolling out COVID-19 vaccines. (See Chapter 2 for vaccine impact modeling and Chapter 9 for costing details.)

In order for governments and multilateral initiatives (e.g., Gavi) to mobilize resources for implementing new TB vaccines, those vaccines need to be affordable and demonstrate value for money. Determining the incremental costs and cost-effectiveness of new TB vaccines within various implementation scenarios will be important for securing sustainable financing. Government financing will be critical: while 80% of TB incidence is in low- and lower middle-income countries, many TB-affected countries are not eligible or will be transitioning from Gavi support in the coming years.

Private-sector companies provided only 2% of available financing for vaccines research in 2020 (TAG, 2021), highlighting the lack of commercial interest in this neglected market. While there is a potentially large market for new TB vaccines in high-burden countries, the lack of a market in high-income countries–and therefore the prospect of lower profits–could disincentivize commercial actors from entering the TB vaccine market.

This means that market-shaping interventions will be critical to securing early investments in production capacity, helping to ensure that once a new vaccine is licensed, supply is adequate to meet demand.[34] Such market-shaping interventions could include:

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[33] Previous Global Plans included only the costs of vaccine R&D.

[34] Market-shaping interventions commonly aim to reduce costs, distribute risk, or provide new information into the market. For key concepts involved in market shaping interventions see https://www.usaid.gov/sites/default/files/documents/1864/healthymarkets_primer.pdf

- advance market commitments, where governments, in advance of regularly approval, contract with manufacturers to bulk-purchase vaccines once they are approved for use
- directly providing public funding to scale up manufacturing capacity
- tech transfer, where knowledge and technology needed to manufacture vaccines is shared with other manufacturing partners

Any public financial support that is provided to private-sector partners must require those partners to adhere to principles of equitable allocation and timely availability in high-burden settings.

Promptly make vaccines available

Innovations in the ways that research is conducted and vaccine candidates are approved could speed the time it takes for new vaccines to reach the market.

Conducting clinical trials and demonstration studies in the communities or regions where new TB vaccines will be implemented, using best practices for community engagement, can build confidence and support among communities and governments for eventual vaccine licensure and roll-out. While having broad geographic representation in clinical trials is important, different countries have different requirements for conducting trials. Product developers spend significant amounts of time complying with varying national requirements in order to conduct clinical trials in different countries. Agreeing on uniform clinical trial requirements across countries could help expedite clinical development and licensure pathways for new vaccines (and other tools).

Regulatory authorities should explore the suitability of applying existing expedited approval pathways to new TB vaccines in ways that accelerate access while maintaining evidentiary rigor. Uniform expectations and formats required for review submissions would help product developers more efficiently generate the necessary data and more rapidly file for licensure in multiple countries (Marks, 2021). Joint review and mutual recognition platforms, such as EU Medicines for All (EU-M4All), Collaborative Registration Pathways, and the forthcoming African Medicines Agency, can allow trusted regulatory partners to share the burden of regulatory review, which could further expedite critical decision-making and speed up access to new TB vaccines.

Ensuring timely vaccine availability will require prompt filing for registration of new vaccines in high-burden countries. Manufacturers should engage with regulators from priority countries early in the product development lifecycle, including with platforms such as the African Vaccine Regulatory Forum (AVAREF) and the WHO prequalification team.

Work with partners to maximize vaccine access and uptake

Countries can find different avenues for making new vaccines accessible and acceptable by collaborating with a wide range of stakeholders. Governments should focus on:

- Strengthening linkages between TB programmes, public health authorities responsible for vaccination, routine childhood immunization programmes, and private sector health providers.

- Integrating TB vaccination within complementary health and social programmes, including:
    - HIV treatment and prevention services
    - sexual and reproductive health care services
    - providers of chronic care for comorbidities, such as diabetes, smoking and malnutrition
    - COVID-19 vaccination programmes

- Exploring opportunities to use non-traditional and decentralized approaches for delivering vaccines delivery—including those deployed for COVID-19 vaccine roll-out, such as:
    - mobile units
    - schools
    - sporting events
    - other community-based sites *(Peltzer et al, 2021).*

Ensure equitable access to vaccines

Global commitment to equitable, affordable and sustainable access to new TB vaccines is essential. Given the likelihood that a phase 3 trial will involve unprecedented levels of public funding from many governments, as well as philanthropic dollars, the final product of research must be treated as a global public good and made equitably available to all who may benefit from it, in keeping with the commitment by UN member states in the TB political declaration to approach TB research and development (WHO, 2021).

Apply learnings from COVID-19 vaccination campaigns

After new vaccines are introduced in high-income countries, low- and middle-income countries have typically had to wait a decade before receiving access to them. This has been the case even with financing and market-shaping interventions. (Yellow House, 2021).

The COVID-19 pandemic highlighted global challenges in deploying adult or adolescent vaccines, including:

- lack of country preparedness
- lack of vaccination access points
- weak diagnostic capacity
- lack of purchase financing in many countries
- weak demand in the face of misinformation and vaccine hesitancy (Africa CDC, 2021)
- inequity in vaccine implementation

However, a tremendous surge of resources and political will contributed to the development and authorization of COVID-19 vaccines in the unprecedented time of less than a year.

Governments collectively mobilized $104 billion to fund research and development (R&D) of COVID-19 vaccines and therapeutics in the first 11 months of the pandemic. This included funds mobilized through advanced market commitments, which helped to incentivize and de-risk commercial investments in R&D. (See Chapter 9 for discussion of advanced market commitments and other forms of innovative financing.) That is 113 times more than the $915 million invested by all funders on TB research in 2020.[35] Lessons learned from this historic achievement should be used to accelerate the development and implementation of TB vaccines. These lessons include:

- Mobilizing political will is critical
- R&D can be accelerated through innovative clinical trial designs, including the use of adaptive study designs; advancing vaccine candidates in late-stage trials; and conducting different phages studies in parallel
- Manufacturing capacity must be built in parallel with clinical development, inlcuding in high TB-burden countries

[35] https://www.treatmentactiongroup.org/resources/tbrd-report/tbrd-report-2021/

- Data sharing, technology transfer, and public health-oriented approaches to intellectual property management should be built into advanced market purchase commitments and other funding agreements
- Expedited regulatory pathways for TB vaccines should be pursued, while maintaining evidentiary rigor
- Use of non-traditional, decentralized, and people-centered pathways can expand accessibility of vaccines

Ch 5. Key Stakeholders: Communities and the Private Sector

Priority actions

- Increase funding support for engaging TB-affected communities in the TB response at least fourfold
- Support community-based and home-based models for delivering TB prevention and care
- Scale up public-private mix (PPM) approaches to improve the quality of TB care and data reporting in the private health sector.
- Support a multi-sectoral TB response through stronger partnerships

Ending TB requires that governments engage with communities and the private sector as partners in the TB response.

Civil society and community-based organizations must play a key role in the planning and delivery of TB care. They are ideally positioned to contribute to the TB response in numerous ways, including:

- improving TB awareness
- providing support to people in care
- reducing stigma
- Informing the design of people-centred TB services
- facilitating community engagement in research and development (R&D) of new TB tools
- advocating for TB resources, policies and interventions
- promoting government accountability for reaching targets and fulfilling commitments

Partnering with the private health sector is especially critical to:

- expanding access to people-centered care
- improving quality of care
- finding people with TB
- improving TB reporting and surveillance
- implementing new TB tools

Increase funding support for engaging TB-affected communities in the TB response at least fourfold

A community is shaped by the shared experiences through which its members are connected to one another. TB-affected communities include people who have lived with TB, as well as their families, friends, social supports, and members of key and vulnerable populations (see Chapter 7 for discussion of key and vulnerable populations).[36]

In recent decades, the TB response has focused on maximizing TB case detection, notification, and treatment. The social aspects of the disease have been overlooked, and so Communities, Rights and Gender (CRG) initiatives have suffered from insufficient attention and chronic underinvestment.

The 2018 UN Political Declaration on TB and the 2020 UN Secretary General's Progress Update Report both acknowledge a long overdue need to engage affected communities in the TB response. This is an ethical and programmatic priority. The overall funding needed to implement the Global Plan represents a fourfold increase over currently available funding. Given the historically low levels of investment in community engagement, governments should quadruple their baseline budgets for community-led activities.

At a minimum, countries should follow WHO operational guidance for integrating community-based activities into TB prevention and care.[37] But to fully acknowledge and respond to the socioeconomic and psychosocial implications of TB, support for communities must extend beyond health systems. Community-led responses, such as human rights and gender programs and community-led social accountability, are vital to ensure everyone affected by TB can access quality TB services, no matter who and where they are. These people-centered initiatives led by TB-affected communities often fall outside of the formal health sector, go largely unsupported, and must be scaled up.

A person who has lived with a disease is a distinct kind of expert. Yet TB survivors and members of affected communities often lack status as partners in the TB response. Engaging TB survivors and affected communities is not merely a matter of providing a seat at a table within decision-making fora. Community organizations must be engaged in the design, implementation,

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[36] Declaration of the Rights of People Affected by Tuberculosis: https://www.tbpeople.org.uk/declaration

[37] ENGAGE-TB Approach: Operational Guidance https://www.who.int/publications/i/item/9789241504508

monitoring, review and governance of TB programs. Ensuring this level of participation requires resources to empower community organizations to:

- engage in formal processes involved in the TB response
- coordinate with other partners
- ensure good governance
- engage in advocacy and communications
- compensate community members and partner organizations to engage in south-to-south learning

Box: Meaningfully engaging communities in national TB planning

A study conducted by TBPeople in 2021, with support from the Global Fund, assessed the meaningful engagement of TB-affected communities in the development of National TB Strategic Plans. It identified "a huge gap in access to information and lack of capacity, which prevent communities from being meaningfully engaged in the development, implementation and monitoring of national strategies."[38] Many survey participants indicated that while they were invited by their health ministries and other partners to participate in discussions around NSP development, community participation often felt tokenistic. While the report noted significant progress in community engagement over the previous five years, that progress was most evident in countries that received funding from the Global Fund or other international donors for its national TB program.

Support community-based and home-based models for delivering TB prevention and care

Community-based health care includes any type of care provided to people in community facilities and in home-based settings. It is delivered by a workforce at the community level comprised of health workers, both lay and professional, formal and informal, and paid and volunteer. It also includes support and supervisory staff. Because it provides people with flexible options for receiving care and support, home-based care is people-centred. In line with a people-centred approach, countries should explore how to best

[38] Meaningful Engagement Of the Communities Of People Affected By Tuberculosis In the Development Of National Strategic Plans On Tuberculosis https://www.tbpeople.org.uk/_files/ugd/0210c3_ab5cbadbffa5435dbb98fe02e6c2dd5c.pdf

implement home-based TB care, telemedicine, and a differentiated service delivery[39] approach as options for people in addition to facility-based care.

Box: Common services that can be provided through community health systems

- Promoting awareness, behavior change, and community mobilization.
- Reducing stigma and discrimination around disease.
- Screening for TB and TB-related illness (e.g. HIV counseling and testing; diabetes screening), through home visits.
- Facilitating access to diagnostic services (e.g. sputum or specimen collection and transport).
- Providing TB prevention measures (e.g. preventive treatment, TB infection control, and BCG vaccination).
- Referring community members for diagnosis of TB and related diseases.
- Initiating treatment and monitoring for TB and co-morbidities.
- Providing peer support and individual follow-up for people receiving care.
- Supporting socioeconomic interventions (e.g. food supplementation and income generation).
- Providing home-based care for TB and related diseases.
- Leading community advocacy.

Pursue community-based active TB case finding

Active case finding helps eliminate barriers to health services. This results in earlier diagnosis, an earlier initiation of care, and reduced transmission. Active case finding has proven to have a positive impact on TB incidence, prevalence, and mortality, as well as lead to cost-saving for countries. It also helps raise community awareness and reduce TB stigma. Community-based programs are ideally positioned to carry out active case finding because of how close they are to where people live, work and socialize. Countries can use the guide

[39] Differentiated Service Delivery (DSD) is an approach used to provide people-centred HIV care. UNAIDS defines DSD as "a client-centred approach that simplifies and adapts HIV services across the cascade, in ways that both serve the needs of people living with HIV better and reduce unnecessary burdens on the health system."

Finding Missing People with TB in Communities as a resource for expanding community-based active case finding.[40]

In contrast, the old approach of passive diagnosing people with TB—in which those with TB symptoms self-present at health facilities for testing and diagnosis—is inexpensive and requires less effort from the health system. But putting the burden of seeking care on people who may or may not be aware of TB signs and symptoms, rather than the health system, has led to delayed diagnosis, delayed care, worse health outcomes, and continued TB transmission. Multiple TB prevalence surveys have shown that large numbers of people with TB are often not aware that they have TB. Many do not have symptoms or do not consider minor symptoms to require professional care. In recent years, the evidence has become clear that passive testing alone will not reduce TB incidence enough to end it.

Budget adequately for community-based health systems

Adequate resources are required for effective community health systems. Though some level of volunteerism can be expected, for sustained actions, resources including human resources, capacity building, management costs, procurement, and logistics should be included in national TB program budgets. Funding for community organizations should be appropriately reflected in TB programme budgets, and where they do not already exist, TB programmes should develop financial systems for funding or compensating community organizations.

Scale up public-private mix (PPM) approaches to improve the quality of TB care and data reporting in the private health sector.

Of the approximately 3 million "missing people" with TB (i.e., the difference between the number of reported TB diagnoses and the total number of people estimated to develop TB in a given year), more than half are believed to be in seven countries with robust private health sectors: Bangladesh, India, Indonesia, Myanmar, Nigeria, Philippines, Pakistan. These are countries where Public-Private Mix (PPM) approaches are a priority.

In recent years, countries have pioneered a number of PPM approaches for engaging private health care providers. Some countries have begun gradually

[40] https://stoptb-strategicinitiative.org/elearning/wp-content/uploads/2019/04/STBFG_03.pdf

taking PPM approaches to scale, despite persistent challenges in moving from donor to domestic funding for TB activities. Success in these and other countries can serve as an example for other countries to craft effective engagement strategies. Table 6 provides examples of these approaches.

Table 6. Examples of PPM approaches in high-burden countries

Country	Approach
Bangladesh, India, Myanmar, Pakistan	Engagement led by highly effective NGOs that act as intermediaries between private health care providers and NTPs
India	Has ambitious targets, allocates substantial budgets, strong political support for engaging private health care providers
Indonesia, Philippines	Expanded focus from engaging small numbers of high-volume private hospitals to increasing engagement of primary care providers and increasing efforts to leverage social health insurance schemes
Indonesia	Public health system directly engages private health care providers with the support of professional associations

WHO has produced a detailed landscape analysis of approaches for engaging private health care providers in the TB response, which can serve as a useful resource for countries.[41]

A number of digital applications are becoming more available and can help countries improve data reporting and quality of TB care in the private health sector, including:

- Digital registration systems
- Digital vouchers for drugs and diagnostics
- Digital treatment support technologies
- Digital x-rays

[41] Engaging Private Health Care Providers In TB Care and Prevention: A Landscape Analysis, 2nd edition: https://apps.who.int/iris/bitstream/handle/10665/351023/9789240027039-eng.pdf?sequence=1&isAllowed=y

- Digitally delivered incentive payments provided to people with TB and to health providers
- Artificial intelligence-based tools

See Chapter 8 for discussion on the development and implementation of digital tools.

Social health insurance (SHI) funds health services through pooled contributions from individuals. SHI is one of the main ways of financing health services, and some countries are using SHI schemes as a strategy for reaching universal health coverage. Where they exist, SHI schemes provide an opportunity to improve the quality of TB care in the private sector.

To be successful, TB programmes must be adequately funded to support PPM approaches. To support and scale-up PPM approaches, governments should:

- Budget for private-sector engagement implemented at scale.
- Reduce costs for private-sector facilities that treat TB, to prevent catastrophic out-of-pocket costs from being passed to people with TB. One way to reduce such costs is removing taxes on all TB-related essential products.
- Provide TB tools and supplies, including software and digital connectivity, to assist private sector facilities.
- Establish transparent and reliable funding mechanisms for supporting private health sector engagement.

Engage private industry in efforts to end TB

Private industry, including those outside of the health sector should play a bigger role in ending TB. In fact, industry has an interest in leading certain areas of the TB efforts. TB predominantly affects people in their most economically productive years, and certain industries in particular—such as mining, where workers are in poorly ventilated spaces and exposed to silica dust—have high rates of their workforce affected by TB. Other companies, especially labour-intensive industries can be impacted by TB when they have operations located in countries or communities affected by TB.

Industries should contribute to ending TB by:

- ensuring their workplaces follow best practices for preventing TB transmission and providing TB care and support to staff and their families
- supporting TB prevention and care through corporate social responsibility (CSR) or environment, social and governance (ESG) activities
- adopt non-discriminatory recruitment and retention policies
- promote infection-free and safe workplaces
- participating in public TB campaigns

TB programmes and TB advocates 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. Ending Workplace TB is an example of a global initiative for TB-free workplaces.

Support a multi-sectoral TB response through stronger partnerships

A country-level partnership platform is a voluntary alliance among governments and stakeholders across civil society–often including private-sector health facilities, academia, professional associations and affected communities–committed to working together to achieve objectives necessary for ending TB. Partners understand that TB impacts them all on some level, and that they share responsibilities–and experience the benefits–of helping end the disease. They contribute their core competencies to the effort, understanding that they benefit when TB declines in their country. In addition to strategic planners and implementers, partnerships should include TB champions, celebrities, and/or opinion leaders who raise the public profile of TB and influence decision-making.

Partnerships can be used to design and implement virtually any part of the TB response, in line with the aims of TB programs. Because partnerships involve stakeholders from outside of government, they are especially important for designing and implementing national Multisectoral Accountability Frameworks. This includes stakeholders directly responsible for carrying out interventions.

A partnership platform's aims are decided by its members and should be determined by the country context. Examples include:

- Providing technical assistance

- Mobilizing resources
- Driving advocacy and communications
- Integrating human and gender rights into national TB policies and programs
- Improving access to comprehensive TB services
- Promoting innovation and new approaches in the national TB response

The benefits of establishing a country-level platform include:

- Innovation and strategic alliance
- Multisectoral participation
- Increased resources
- Proactive leadership
- Social change
- Technical support

Ch 6. Ending TB through Universal Health Coverage, Pandemic Preparedness and Response, and Socioeconomic Actions

Priority actions

- Expand access to TB services through UHC initiatives
- Position the TB response at the center of Pandemic Preparedness and Response efforts
- Invest in poverty alleviation and sustainable development

Expand access to TB services through UHC initiatives

Universal Health Coverage (UHC) is essential for ensuring access to TB care and prevention. Where people lack health coverage, they face a far more difficult challenge accessing TB diagnosis and care. Where social safety nets are weak or absent, people with TB often face the added challenge of losing income or economic opportunities. Achieving UHC is so critical to ending TB that the WHO End TB Strategy requires countries to "move with urgency" toward UHC and ensure that no affected people or families face catastrophic costs.

In adopting the Sustainable Development Goals, all countries committed to achieving UHC by 2030 (Figure 8). The COVID-19 pandemic pushed millions of people into poverty, adding urgency to the goal of reaching UHC and further exposing the need for resilient health systems that meet the needs of all people.

UHC means:

- All people can use the promotive, preventive, curative, rehabilitative and palliative health services they need
- Those services are of high enough quality to be effective
- Use of those services does not expose people to financial hardship[42]

Fig. 8. Key areas of commitment to universal health coverage[43]

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[42] Universal health coverage (UHC). Fact sheets. Geneva: World Health Organization; 1 April 2021 (https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc), accessed 14 November 2021).

[43] United Nations high-level meeting on universal health coverage in 2019. Key targets, commitments and actions. Geneva: UHC2030; 2020

Countries must expand access to the full range of high-quality TB services in line with the End TB Strategy. There are steps that countries can take that will have a significant impact on people's ability to conveniently access TB services.

Expand delivery of TB services through primary care

Expanding primary health care is the most important step that countries can take toward achieving universal health coverage. Primary health care is the cornerstone of a sustainable, people-centered, community-based, and integrated TB service delivery system. Expanding primary health care requires strengthening referral systems between primary and other levels of care, and strengthening PPM approaches. (See Chapter 3 for discussion of community-based care and Chapter 5 for discussion of PPM approaches.)

Integrate and coordinate delivery of TB services within services for other comorbid and underlying health conditions

Large numbers of people who develop TB have one or more common underlying conditions. Countries can expand access to TB services and help identify people with TB early by integrating TB services within care for its five most important risk factors—HIV/AIDS, diabetes, undernutrition, tobacco use, alcohol use disorder—as well as other health services as appropriate, such as hepatitis or COVID-19. Coordination should take place at both strategic and programmatic levels. See, for example, frameworks for coordinating TB-HIV

(https://www.uhc2030.org/fileadmin/uploads/uhc2030/Documents/UN_HLM/UHC_key_targets_actions_commitments_15_Nov_2019__1_.pdf)

activities,[44] TB-diabetes activities, and TB and tobacco cessation.[45] (See Chapter 3 for discussion of coordinating and integrating TB care with other health programs and services.)

Scale up active case finding and outreach to key and vulnerable populations

These efforts are foundational to finding the missing people with TB, ensuring people are diagnosed as early as possible, and preventing further TB transmission. Reaching key and vulnerable populations is critical to a TB response that is human-rights based and equitable.

Integrate mental health services into TB care

There is a bi-directional link between TB and mental health. Having TB can lead to mental health challenges that stem from causes such as stigma, social rejection, and an inability to work. The main mental health conditions that affect people with TB are depression, anxiety and alcohol use disorder. TB can also potentially be exacerbated when mental health conditions lead to inflammation or suppression of the immune system, which can heighten one's risk of developing TB. The adverse effects of some medicines used to treat TB can also lead to or worsen mental health conditions. Given the links between TB and mental health conditions, people with TB should receive mental health screening as a routine and early part of care, using established and validated screening methods, and provided appropriate support. To integrate mental health services into TB care at scale will require education and training for health workers, advocacy from the TB community, and operational research to understand how mental health services can be most effectively integrated into TB care in various settings.[46]

Improve resource allocation through better TB information systems.

TB data collection should be integrated within public health surveillance and data systems. They should support real-time, reliable and accurate data

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[44] WHO Policy On TB/HIV Collaborative Activities. https://apps.who.int/iris/bitstream/handle/10665/44789/9789241503006_eng.pdf;sequence=1

[45] Collaborative Framework for Care and Control of Tuberculosis and Diabetes. https://www.ncbi.nlm.nih.gov/books/NBK310838/

[46] https://www.usaid.gov/sites/default/files/documents/TB_and_Mental_Health_USAID_REPORT_FINALTRACKED_EDITS_AG_508c_1.pdf

collection. Data should be disaggregated by income, sex, age, race, ethnicity, migratory status, disability, geographical location and other characteristics required to identify gaps in access to essential TB services and to enable real-time intervention. Many countries set up advanced data collection capabilities for monitoring COVID-19. These capabilities should be adapted to use for TB.

Improve the quality of TB services

Having access to services only matter if those services are of sufficient quality to be effective. All healthcare providers need to follow authoritative clinical standards for TB care. Health provider noncompliance with clinical standards prevents people with TB from receiving the quality services they need.

The Global Plan recommends the following ways to efficiently improve the quality of TB services:

- Strengthen health-worker recruitment, education and training. All health workers responsible for delivering TB services—including primary health care providers, health care providers in the private sector, community health workers, and lab personnel—need to know how to properly diagnose, treat and care for people with TB.

- Ensure access to quality-assured TB tools. Quality care begins with affordable, safe, and effective TB tools. Diagnostic networks in many countries need to be upgraded with modern diagnostic tools. Countries can ensure the quality of TB medicines by procuring from the Global Drug Facility as recommended in the UN Political Declaration on Global TB. Countries can also increase access to quality-assured TB tools by strengthening procurement and supply management systems in order to mitigate the risk of product stock-outs.

- Expand access to support services to all people in need. Providing routine holistic support as a part of TB care (e.g., nutritional support, psychosocial support, cash benefits etc.) is a part of providing quality people-centred TB care. When expanding support services, countries should prioritize vulnerable groups who face the biggest barriers to accessing and completing care and who have experienced the worst health outcomes.

- Invest in digital tools. Digital tools can empower both people affected by TB and TB service providers, making the delivery of TB care more people-centered and cost-effective. See Chapter 8 for discussion on the development and implementation of digital tools in the TB response.

Eliminate catastrophic costs associated with accessing TB services

Countries can eliminate catastrophic costs associated with accessing TB services by taking complementary steps at two levels: ensuring adequate financing for the TB response, and reducing costs associated with accessing TB services.[47]

- Ensure adequate financing for the TB response. Progress in reducing the burden of TB disease requires adequate and sustained funding for TB diagnostic, treatment and prevention services. Countries should pursue funding for UHC through increased domestic resources plus external resources where necessary. Taxation and innovative financing should be used to improve the sustainability of financing wherever possible.

- Reduce costs associated with accessing TB services. One way to reduce costs of TB services is to include TB services within national essential health service packages. Most countries identify a package of essential health services that people can access at no or minimal cost. TB services should be included, given its significance as a disease of public health concern. Similarly, TB services should be included within social health insurance schemes. (See Chapter 5 for discussion of social health insurance.) Another way is to include coverage for TB services within risk-protection schemes. People seeking TB care should qualify for national or subnational risk protection schemes, such as those that provide cash transfers or in-kind support, income replacement, food and nutrition support, and other forms of social support.

Box. Catastrophic costs faced by people and families affected by TB[48]

[47] Eliminating the financial hardship of TB. https://www.who.int/tb/publications/UHC_SP_factsheet.pdf?ua=1

[48] Global tuberculosis report 2021, WHO, https://www.who.int/publications/i/item/9789240037021

Given the importance of UHC to targets for reductions in TB incidence and mortality, the End TB Strategy included a third target that no persons with TB and their households face total costs that are catastrophic. The definition of catastrophic used for this TB-specific indicator is total costs (comprising direct medical expenditures, non-medical expenditures and income losses) above 20% of household income.

Since 2015, a total of 25 countries have completed a national survey of costs faced by TB patients and their households, of which 23 (including 14 of the 30 high TB burden countries and one of the three global TB watchlist countries) have reported results. The percentage facing catastrophic costs ranged from 13% (95% confidence interval [CI]: 10–17%) in El Salvador to 92% (95% CI: 86–97%) in Solomon Islands; the pooled average, weighted for each country's number of notified cases, was 47% (95% CI: 33–61%) (Figure 9 and Figure 10).

In countries that reported disaggregated data, the pooled average was considerably higher for drug-resistant TB. Survey results are being used to inform approaches to health financing, service delivery and social protection that will reduce these costs.

Figure 9. Estimates of the percentage of TB patients and their households facing catastrophic costs, national surveys implemented 2016-2020.

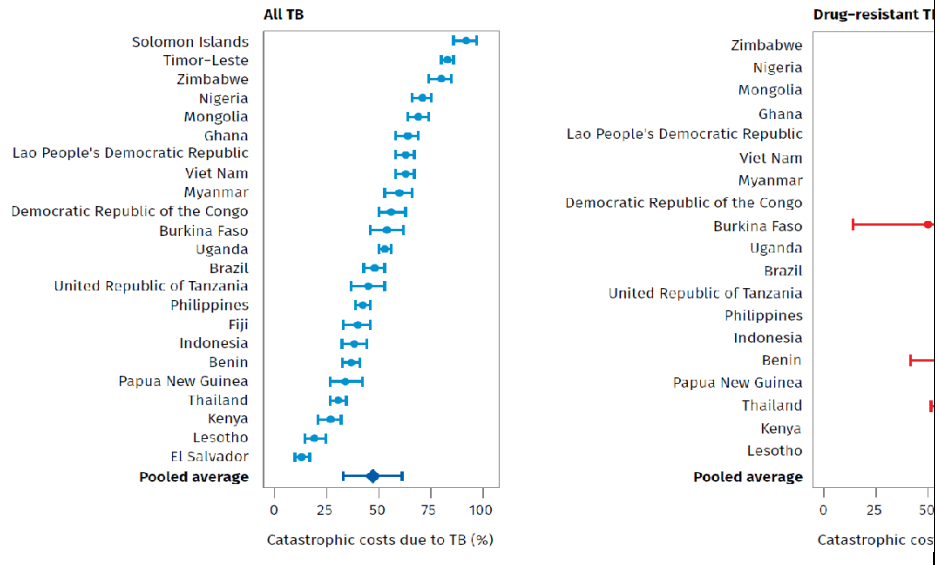
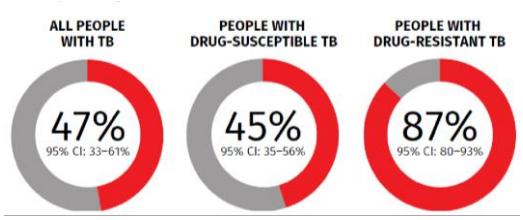


Figure 10. Average percentage of people with TB and their households facing catastrophic costs in 23 national surveys completed since 2015.



Promote accountability through multisectoral accountability frameworks (MAFs)

Political will is critical to achieving UHC, which means that governments must be held accountable for taking action in line with their commitments. Inadequate political leadership and financial constraints remain the major obstacles to equitable progress toward UHC. The Global Plan calls on national governments to provide the overall stewardship to keep TB elimination high on the development agenda through political commitment, investments and oversight. At the same time, TB stakeholders must work together to hold governments accountable for fulfilling their commitments.

Given that social and economic determinants, and not just health determinants, drive the TB epidemic, countries should institute accountability frameworks that involve multiple relevant sectors beyond the health sector. Multisectoral Accountability Frameworks (MAFs) provide a structured way to engage all relevant TB stakeholders—including civil society and affected communities, the private sector and academia—in decision-making, monitoring, review, and remedial actions needed to achieve objectives for UHC and TB.

Position the TB response at the center of Pandemic Preparedness and Response efforts

The world was unprepared for the COVID-19 pandemic. As a result, COVID-19 created enormous but preventable disruptions to nearly every facet of life for most of the world's people. To avoid a repeat scenario, governments have begun investing more in Pandemic Preparedness and Response (PPR).

TB elimination efforts should be positioned at the center of PPR. Practically speaking, this means that TB elimination programs should both contribute to and receive support from PPR efforts.

The reasoning is clear. Highly transmissible disease pathogens that are airborne or spread through droplets have the greatest potential to seed another global pandemic. Because TB and COVID-19 are similar in several ways–they spread through airborne transmission and require a similar set of public health interventions–many countries used their TB infrastructure and related human resources to respond to the COVID-19 emergency. Human resources were re-assigned, while hospitals, laboratories and diagnostic equipment used for TB were redesignated for the COVID-19 response. TB programs were centers of expertise on many interventions needed for COVID-19, such as airborne infection control, contact tracing, appropriate use of quarantine and isolation, and respiratory care. If governments had been fully meeting their commitments to support TB elimination at the time that COVID-19 emerged, countries would have been better prepared to respond.

Instead, TB programs were severely under-resourced when the pandemic hit. This left countries, especially high-TB-burden countries, with significantly less capacity to respond to COVID-19. It also meant repurposing TB programs to fight COVID-19 disrupted TB services, adversely impacting TB elimination efforts.

Adding investments to strengthen the infrastructure and capacity of TB programs will help preemptively develop surge capacity to fight any new respiratory infection of pandemic potential. Smart investments under PPR will help the fight against TB and at the same time prepare the world to face the next airborne-disease pandemic. The capacity to eliminate TB is so closely linked with PPR that monitoring progress in TB should be part of the monitoring of state of preparedness to fight any new respiratory infection. Investments that have dual benefits for TB elimination and PPR should be considered TBE-PPR (Table 7).

Table 7. Areas of investment in TBE-PPR

Detection and Care
Scaling up diagnostic capacity with a focus on multiplex molecular testing platforms for respiratory pathogens provided at point-of-care and unconventional access points, e.g., mobile diagnostic units

X-ray screening, including the use of AI to read images in areas facing shortages of radiologists.
Digital health tools (e.g., AI-based CADs, DATs)
Systems for contact tracing, including human resources, technology and infrastructure needed to do this activity in community and at scale
Respiratory care infrastructure (e.g., human resources, hospital beds, equipment, supply, surge capacity, private-sector care)
Community systems strengthening for delivery of community care as well as for community-led systems for monitoring of services, gaps and barriers
Prevention
Airborne/droplet infection prevention and control (AIPC) implemented across the health system, congregate settings and public spaces
Surveillance
Genome sequencing
Real-time data surveillance and analysis with public-facing dashboards that report against key indicators (e.g., ILI/SARI, testing information, positive case numbers, variants, deaths and other outcomes)
Research and development
Fast-track treatment and vaccine research

While WHO, the G20 and other initiatives[49] have created political momentum for PPR at the global level, high-level recommendations need to be adapted to country contexts. To enable this adaptation, TB programs in high TB burden countries must communicate with their counterparts in the government ministries responsible for PPR, including ministries of health, public affairs, defense, and agriculture, working together to ensure that PPR plans and investments are built on the country's TB response. The targeted areas of investment in Table TK can serve as a guide for action. Global partners working

[49] COVID-19: make it the last pandemic. The Independent Panel for Pandemic Preparedness & Response: https://theindependentpanel.org/wp-content/uploads/2021/05/COVID-19-Make-it-the-Last-Pandemic_final.pdf

on TB must continue to advocate to WHO, G7, G20 and the donor community to position TB elimination at the center of PPR.

Achieving UHC through global health security and AMR efforts

Closely related to PPR, global health security has emerged as an important construct in public health in response to growing recognition that communicable diseases in any one part of the world can easily spread to other areas, with worldwide public health implications. The UN General Assembly, G20, G7, BRICS, and Asia-Pacific Economic Cooperation bloc, and ministers from countries across South-East Asia and the African Union have identified antimicrobial resistance (AMR) as a critical threat to global health security and economic prosperity, pledging action in response. In 2018, the UN General Assembly recognized drug-resistant TB as a critical challenge, and that the grave risks to individuals and public health caused by DR-TB are cause for alarm

Achieving universal access to TB care, while providing people with TB and their families with the social support they need to complete a full regimen of appropriate TB treatment or TB preventive therapy, is essential to preventing AMR in TB. Drug-resistant TB runs a risk of emerging any time a person with TB receives inadequate, substandard or incomplete treatment. Where people with TB lack people-centred care and adequate support—such as nutritional, psychosocial, or mental health support—the risks are greater that treatment will be interrupted and resistance will emerge. Preventing the emergence of TB resistance is also a priority among mobile populations such as refugees, internally displaced people and migrant workers, where breakdowns in the continuum of care can lead to treatment interruptions.

While the emergence of new instances of TB resistance are critical to prevent, due to a lack of action, DR-TB has spread to the point where most people with resistant forms of TB acquired it through airborne transmission. The challenges posed by the global spread of DR-TB affected all countries. Even the wealthiest countries that are close to eliminating TB can and are impacted even when small numbers of people become sick with DR-TB.[50] An addition to the overall burden of TB globally, the ongoing spread of DR-TB combined with shortfalls in investment to develop new TB treatment regimens, makes TB a global health security risk.

[50] https://www.healthaffairs.org/doi/10.1377/hlthaff.2018.0894?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

Ensuring universal access to TB prevention, care and support is essential to ending TB and stopping the danger to global health security posed by TB drug resistance. Given the high-level political attention given to global health security—particularly in light of COVID-19 and renewed understanding of the risks posed by airborne respiratory pandemics—TB programmes should work to incorporate their goals into health security agendas. Budgets allocated for health security and antimicrobial resistance (AMR) can serve as sources of funding for TB activities, helping to bring TB budgets in line with the demonstrated need. Global health security and AMR initiatives can also provide critical sources of funding TB research and development, helping to develop new TB treatment regimens—including a potential pan-TB regimen that can treat all forms of TB—and new vaccines that can prevent future emergence of DR-TB.

Invest in poverty alleviation and sustainable development

Compared with approaches to "controlling" TB that were followed in previous decades, the End TB Strategy increased the focus on poverty alleviation and social protection as critical pieces of a holistic, multisectoral effort. Combined with sustainable development efforts, these interventions have the potential to enhance prevention, improve access to care and prevent TB-related catastrophic costs.

Given the number of social determinants that drive the TB epidemic (see Chapter 4), the TB response must engage a broader range of non-medical actors. 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 planning, 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.

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 fueled by overcrowding, poor ventilation, inadequate sanitation and undernutrition, this development trend has significant implications.

Sustainable development strategies that improve living standards have the potential to make a significant impact in the fight against TB.[51] 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.

[51] 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

Ch 7. Human Rights, Stigma, Gender, Key & Vulnerable Populations

Priority actions:

- Position universal human rights as the foundation of the TB response
- Eliminate TB-related stigma and discrimination
- Ensure TB interventions are gender-responsive
- Prioritize, reach, and involve key and vulnerable populations

Recognizing the powerful social dynamics underpinning the TB epidemic, this chapter provides guidance for implementing a TB response that is rooted in universal rights, eliminates TB stigma, is gender-sensitive, and reaches key vulnerable populations. This approach is critical to reaching people and communities affected by TB.

Social and cultural factors heavily influence people's TB risk and vulnerability, and their ability to access TB prevention, care, and support. These factors relate to a person's identity and a wide range of other determinants, including:

- stigma and discrimination
- gender
- socio-economic status
- legal and class status
- nutritional status
- housing status
- access to education
- access to information
- language (including language spoken and use of stigmatizing language)
- surrounding cultural norms

Because these social factors play a huge role in driving the TB epidemic, it is critical that TB responses extend beyond the health system and include broader interventions that:

- address socio-economic factors that increase one's risk of and vulnerability to TB and/or influence health-seeking behavior
- remove legal, cultural, human rights and gender-related barriers to prevention, care, and support
- create an enabling environment for TB prevention, care, and support

- strengthen community systems, measured by indicators[52]

Understanding the need for such an approach, TB-affected communities and civil society have called for a global TB response that is "right-based, equitable, and stigma-free, with communities at the centre."[53]

There is also a consensus among leaders that the TB response needs to be grounded in human rights and address the epidemic's social and cultural dynamics. For example, the 2018 UN political declaration on TB, building on the End TB Strategy, committed governments to pursuing "an equitable, human rights-based" TB response. The UN Secretary General also identified the need to "promote human rights and combat stigma and discrimination" as one of ten priority actions needed to accelerate the TB response and reach global TB targets.[54]

Position universal human rights as the foundation of the TB response

The End TB Strategy demonstrates the long-held understanding that there is a connection between TB and human rights. How to operationalize a human rights-based TB response, however, has taken much longer to understand.[55]

Since the UN HLM on TB in 2018, the TB community has made significant progress in articulating exactly how human rights must inform the global TB response, most notably in the *Declaration of the rights of people affected by TB.* This landmark document lays out how the TB response must abide by and promote universal human rights.[56]

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[52] https://stoptb.org/assets/documents/about/cb/meetings/33/33-06%20Civil%20Society%20and%20Communities/33-6.1%20STP%20UNHLM%20CRG%20Report_17%20Nov%202020.pdf

[53] https://stoptb.org/assets/documents/communities/A%20Deadly%20Divide_%20TB%20Commitments%20vs.%20TB%20Realities_Call%20to%20Action.pdf

[54] https://www.who.int/news/item/21-10-2020-un-secretary-general-outlines-priority-recommendations-to-accelerate-the-tb-response-and-reach-targets

[55] https://stoptb.org/assets/documents/communities/NairobyTBStrategyFINAL.pdf

[56] https://stoptb.org/assets/documents/communities/FINAL%20Declaration%20on%20the%20Right%20of%20People%20Affected%20by%20TB%2013.05.2019.pdf

Grassroots communities, civil society, TB policy makers and program implementers can find specific guidance for operationalizing human rights, building capacity and increasing sensitization to communities, rights and gender (CRG) issues.[57,58] Tools are also available to help document and understand how various human rights- and gender-related barriers are impeding efforts of national TB programs.[59]

National TB programs, civil society, and theTB-affected community should jointly assess how social factors are being addressed and/or are impeding progress against TB. They should also jointly assess how human rights, gender and key and vulnerable populations are reflected or prioritized within laws and guidelines.[60]

Community-led monitoring

Communities can and should play a leadership role in monitoring certain aspects of the TB response. As part of the commitment to human rights and social accountability, community-led monitoring (CLM) has become a critical part of the TB response within countries. CLM is a process that promotes accountability for the success of health and social programs. The process involves people who have the most at stake—users of services—in monitoring access to and quality of services, and working with health or social programs to improve them.

CLM is based on routine, systematic oversight of local and national health and social systems, using consultations with community members to identify service gaps and areas for improvement. Insights gained through CLM are also

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57 https://stoptb.org/assets/documents/communities/The%20Right%20To%20Breathe%20-%20Human%20rights%20training%20for%20people%20with%20&%20affected%20by%20TB.pdf

58 https://stoptb.org/assets/documents/communities/Activating%20A%20Human%20Rights%20Based%20Tuberculosis%20Response_Policy%20Brief%20(2020).pdf

59 https://stoptb.org/assets/documents/communities/TB%20CRG%20Country-Level%20Assessment%20Protocol%20Template_DRAFT.pdf

60 https://www.hhrjournal.org/2021/12/building-the-evidence-for-a-rights-based-people-centered-gender-transformative-tuberculosis-response-an-analysis-of-the-stop-tb-partnership-community-rights-and-gender-tuberculosis-assessment/

used to inform advocacy and policy change that benefits TB-affected communities.

CLM can contribute to the collection and disaggregation of age, gender, and key and vulnerable population data. It can capacitate and empower TB affected communities and civil society while providing added critical value to national TB, HIV, COVID-19 and other health responses. [61]

It is critical that CLM tools, including virtual tools, are developed and implemented in a way that promotes and protects the rights (including rights to security, privacy and confidentiality) of people affected by TB. Those rights should be enshrined as appropriate in relevant legislation, policies, and guidelines (e.g., in consumer, data and health laws and policies).

Table 8. Actions for integrating human rights into the local TB response

Planning
Conduct a TB CRG Assessment, develop a costed national TB CRG Action Plan, fund and implement the national costed TB CRG Action Plan
Engagement
Formalize engagement and sensitization of TB and human rights in TB policy and implementation among judges, lawyers, law enforcement, legal aid service providers and law schools.
Invest in TB survivor networks to coordinate and meaningfully engage and participate in all components of the TB response as they impact the constituencies they represent.
Capacity building

[61] https://stoptbpartnershiponeimpact.org/

Conduct capacity building and sensitization training for TB survivors and civil society on human rights-based programming, advocacy and remedies.
Sensitize health care workers in public and private sectors on the need to incorporate a human rights-based approach to TB in their work.
Develop and implement a comprehensive curriculum to advance TB affected community and civil society literacy in TB, TB diagnosis, TB tools and technologies, TB treatment, TB care, TB data, TB financing and TB research.
Monitoring
Periodically conduct a TB legal and human rights score card analysis
Adapt and implement real time community-led monitoring for social accountability of human rights and gender related barriers to TB and social protection services.
Fund TB survivors and civil society to monitor, document and report human rights violations of abuses among people with TB and to advocate, including through litigation, law and policy reform.
Advocacy
Review and reform social protection systems accessible and inclusive for people affected by TB including support for income, nutrition, shelter, mental health and legal aid.

Utilize legal resources to uphold people's right to health

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 safe- guarded 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.[62] 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 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.[63]

Eliminate TB-related stigma and discrimination

All people with TB is equal before the law and entitled to be free from all forms of discrimination. States have obligations to eliminate discrimination, embodied in legal conventions such as the Convention on the Elimination of All forms of Discrimination against Women and the International Convention on the Elimination of All Forms of Racial Discrimination.[64]

TB CRG assessments have identified TB-related stigma and discrimination as the leading barriers to TB prevention, diagnosis, and care.[65] Assessments have also found that sigma and discrimination are most severe when multiple vulnerabilities intersect, including gender and key/vulnerable population status.

Stigma and discrimination can manifest through direct acts or omissions of actions. They can also manifest through language and body language, where people with TB are described with negative connotations or even blame (e.g.

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

[63] 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%20 Compendium%20(First%20Edition).pdf

[64] https://stoptb.org/assets/documents/communities/FINAL%20Declaration%20on%20the%20Right%20of%20People%20Affected%20by%20TB%2013.05.2019.pdf

[65] https://www.hhrjournal.org/2021/12/building-the-evidence-for-a-rights-based-people-centered-gender-transformative-tuberculosis-response-an-analysis-of-the-stop-tb-partnership-community-rights-and-gender-tuberculosis-assessment/

use of terms such as “defaulter” or “TB suspect”). Such language is unnecessary and inexcusable when alternative language exists that positively engages and helps empower people affected by TB.[66]

As a first step to eliminating TB-related stigma and discrimination, programs need to understand how and why stigma and discrimination manifest, where they manifest, and the impact experienced by people who may need access to health services. As a priority, this includes understanding how stigma and discrimination relates to gender and impacts key and vulnerable populations.

Programs must then develop and implement evidence-based interventions that bring about the end of TB-related stigma and discrimination. These interventions need to be monitored and reviewed to ensure that they have the intended impact. While eliminating TB stigma is a priority, more rigorous evaluation needs to be applied to understand the most effective approaches.[67]

Efforts to identify, measure and mitigate TB stigma and discrimination have been advanced by many partners, including KNCV[68], GCTA[69], TB Proof[70] and the Stop TB Partnership. The TB Stigma Measurement Assessment tool[71] is one example. Programs can adapt the tool and use it to collect data on:

- Anticipated stigma, self-stigma, enacted stigma (i.e., stigma directly experienced) and observed stigma among people diagnosed with TB
- Secondary TB stigma, stigma directly experienced, and stigma observed by family members and by primary carers of people diagnosed with TB
- Perceived TB stigma against people diagnosed with TB in communities and stigma observed by the community

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[66] Link to new language guidance

[67] https://pubmed.ncbi.nlm.nih.gov/29025489/

[68] https://www.kncvtbc.org/en/tb-stigma/

[69] https://gctacommunity.org/?page_id=7293&v=7d31e0da1ab9

[70] https://tbproof.org/unmaskstigma-campaign/#:~:text=The%20%23UnmaskStigma%20Campaign%20aims%20to,communities%20regarding%20TB%20and%20HIV.

[71] https://stoptb.org/assets/documents/communities/STP%20TB%20Stigma%20Assessment%20Implementation%20Handbook.pdf

- Perceived TB stigma against people diagnosed with TB in health care settings and stigma against health care workers
- Structural stigma (any existing laws/policies, the enforcement of those laws/policies and the corresponding media coverage that could harm or protect people diagnosed with TB)

This tool was used to create the first TB CRG indicators, which include:

- % People diagnosed with TB reporting that self-stigma inhibited them from seeking and accessing TB services
- % People diagnosed with TB reporting that stigma in their community/neighborhood inhibited them from seeking and accessing TB services
- % People diagnosed with TB reporting that stigma in a health care setting inhibited them from seeking and accessing TB services[72]

Table 9. Actions for eliminating TB stigma and discrimination

Planning and implementation
Conduct a TB Stigma Assessment, incorporate the findings into a costed national TB CRG Action Plan, fund and implement the national costed TB CRG Action Plan
Education and training
Sensitize policy makers, health service providers and media partners regarding language that stigmatizes or disempowers people with TB as well as the effects of using such language; train people to use language that supports and empowers people with TB.
Ensure communication and information campaigns avoid stigmatizing language and focus on use of language that empowers people with TB and TB survivors.
Policymaking

[72] Link to Global Fund Performance Framework

Develop legal and policy protections and remedies for people affected by TB to be free from stigma and discrimination in health care settings, law enforcement, employment and the community.
Advocacy and strategic communications
Promote legal and policy protections for health care workers to mitigate their experience from stigma and discrimination.
Develop high level communications campaigns, supported by high profile champions and supporters, that demystifies and normalizes the experience of having TB.
Monitoring and evaluation
Develop and incorporate TB stigma indicators into monitoring and evaluation frameworks and as a priority in national strategic plans.
Adapt and implement real-time community-led monitoring for social accountability of stigma and discrimination in health care settings, employment settings and community settings.
Funding in to support TB survivors, civil society and TB key and vulnerable populations to build evidence of stigma and discrimination, of effective mitigation strategies and approaches, including advocacy, litigation, law and policy reform.

Ensure TB interventions are gender-sensitive and -transformative

In order to identify and overcome gender-related barriers to TB services, there is a need for gender-sensitive TB engagement, leadership, programming and policies. The Sustainable Development Goals (in particular SDG 5), which recognize that gender equality is key to development, support a gender-sensitive approach to TB elimination.

Globally, TB rates are higher in men than in women.[73] Men and boys also account for a larger share of TB mortality. Evidence suggests that cultural and socio-economic factors play a large role in determining TB risk and disease.[74] Men are often more mobile and can also be more affected as a result of their greater tendency to use substances, inclusive of cigarettes, alcohol and drugs.[75] Generally, though far from a universal rule, men often take longer to access TB care compared to women.

While certain behavioral and industrial risks are weighted towards men, there are also risks that are weighted towards women. HIV, which is more prevalent in women than in men, increases the risk of TB more than ten-fold. Yet this does not seem to translate to proportional increases in women with TB, or notably different treatment outcomes to those found elsewhere in countries where this has been explored. Malnutrition, the leading underlying risk factor for TB disease, is more common in women than men.[76] While women are documented to generally have better health-seeking behaviours, they are more likely to experience cultural and socio-economic challenges that delay or block their access to TB care.

An analysis of TB CRG Assessments from 20 countries found that patriarchal norms negatively impact women's access to TB services and increase their vulnerability to infection and disease. Also, that women and girls affected by TB face more frequent and intense stigma and discrimination than men, sometimes leading to abuse, gender-based violence or abandonment.[77] Based

[73] The notable exception is Afghanistan, where women are consistently shown to experience higher rates of TB.

[74] https://stoptb.org/assets/documents/global/awards/tbreach/TB-REACH_Gender2021-web.pdf

[75] https://stoptb.org/assets/documents/global/awards/tbreach/TB-REACH_Gender2021-web.pdf

[76] https://www.fao.org/3/al184e/al184e00.pdf

[77] https://www.hhrjournal.org/2021/12/building-the-evidence-for-a-rights-based-people-centered-gender-transformative-tuberculosis-response-an-analysis-of-the-stop-tb-partnership-community-rights-and-gender-tuberculosis-assessment/

on these findings, a gender investment package[78] must respond to the unique challenges faced by women and girls.

The TB response has too often reinforced societal gender discrimination. This can happen in several ways, such as lower wages for women in the health workforce, exclusion or stigmatization of gender-diverse people, and information, education and communication (IEC) materials that reinforce patriarchal gender roles.[79]

A global network of women, in their diversity, who are affected by TB, has been formed to champion women's empowerment and a gender sensitive TB response.[80] It is critical then that the TB responses increasingly integrate gender sensitivity and for this transition to be driven by TB-affected communities.

Very little is known about TB epidemiology of gender-diverse people and communities, though the data do demonstrate that TB epidemics might be concentrated in communities that are stigmatized and marginalized because of their gender nonconformity. When India's national TB program began tracking TB among transgender people in 2018, TB notifications among this group were 426/100,000 , compared to 134/100,000 in women and 211/100,000 in men, indicating a high TB burden in this population.[81]

Table 10. Actions that contribute to a comprehensive gender-sensitive TB response

Education and capacity building

78 https://stoptb.org/assets/documents/communities/TB%20Gender%20Investment%20Package.pdf

79 https://stoptb.org/assets/documents/global/awards/tbreach/TB-REACH_Gender2021-web.pdf

80 https://stoptb.org/assets/documents/communities/TB%20Women%20Strategic%20Plan%202021-2025.pdf

81 https://stoptb.org/assets/documents/global/awards/tbreach/TB-REACH_Gender2021-web.pdf

Conduct capacity building and sensitization training among TB survivors and civil society on gender sensitive programming, advocacy and remedies as well as women's empowerment.
Sensitize health care workers in public and private sectors on the need to incorporate a gender sensitive approach to TB in their work
Programme management
Implement gender-sensitive policies and programming across all aspects of TB programmes, with particular consideration for both disease prevalence, leadership, women's empowerment and access to services.
Update databases to reflect diverse gender identities
Develop a policy in advance of gender equity that includes gender representation and pay equity in the TB workforce, facility based service quality, stigma reduction and remedies and community based case finding.
Review and reform social protection systems accessible irrespective of gender identity including support for income, nutrition, shelter, mental health and legal aid.
Monitoring and evaluation
Adapt and implement real time Community Led Monitoring for social accountability of gender related barriers to TB services with data disaggregated gender.
Conduct qualitative and quantitative operational research to generate evidence-base for the effectiveness of a human rights-based and gender-responsive approach to TB, especially among TB key and vulnerable populations.
Adovacy and strategic communications

Develop TB communication and information materials that are empowering and inclusive for women and gender diverse people and ideally are developed with input from that audience.
Funding advocacy, monitoring and accountability through women-led TB survivor and civil society organizations

Prioritize, reach, and involve key and vulnerable populations

Reaching key and vulnerable 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 programmes:

- prioritize ending TB among key and vulnerable populations
- ensure key and vulnerable populations have convenient access to TB prevention and care, including through primary care and integrated health services (e.g., TB-HIV, TB-diabetes, TB and tobacco cessation)
- understand the social, political, legal and economic barriers key and vulnerable populations face in accessing TB services
- involve key and vulnerable populations as priority stakeholders and equal partners in the fight against TB
- coordinate and collaborate with other programs and ministries focused on gender, rights and development

Figure 11: key and vulnerable populations

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 TB patients, including children
- work in environents that are overcrowded
- work in hospitals or are health care professionals

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 groups
- are homeless
- live in hard-to-reach areas
- live in homes for the elderly
- have mental or phyiscal disabilities
- face legal barriers to access care
- are lesbian, gay, bisexual or transgender

People at **INCREASED RISK** to 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

If TB programmes are to understand the lived experience of TB, they must facilitate the meaningful participation of the representatives of key and vulnerable populations, on behalf of the constituencies they represent, in all TB policy, programme and governance discussions and decisions. A significant aspect of reaching key and vulnerable populations is investing more in capacity building and providing avenues for their participation in a wide range of TB activities, including:

- programme design, monitoring and evaluation
- peer support
- treatment literacy
- research and development
- advocacy
- human rights interventions

An analysis of the first 20 countries to prioritize TB key and vulnerable populations revealed a list of 26 different key and vulnerable population groups [TK need to present in table or visual form]. Programs can find information on many of these specific key and vulnerable populations in a series of briefs and investment packages, which can be used as resources for prioritizing keykey and vulnerable populations and developing relevant interventions.[82] The Global Plan recommends carrying out these exercises as a part of a broader CRG assessment (see above).

In 2022, a TB key and vulnerable population size estimation tool will be available for countries to better understand and prioritize key and vulnerable populations and to develop and tailor interventions and allocate resources to the respective needs of those populations. This tool will also be integrated into the TB CRG Assessment Protocol.[83]

Table 11. Actions for prioritizing and reaching key and vulnerable populations

Planning
Conduct national TB key and vulnerable population prioritization exercises and to conduct size estimations of the prioritized TB key and vulnerable populations.
In partnership with TB key and vulnerable populations, develop and prioritize interventions for prioritized TB key and vulnerable populations that are culturally and linguistically appropriate, and where possible, TB survivor and key and vulnerable population-led.
Policymaking
Review and reform social protection systems accessible and inclusive for TB key and vulnerable populations including support for income, nutrition, shelter, mental health and legal aid.

[82] TB Key and vulnerable population briefs (hyperlinked) - Prisoners; Mobile Populations People who use drugs; Children; indigenous peoples; People living with HIV; health care workers; urban poor; rural populations; miners

[83] https://stoptb.org/assets/documents/communities/TB%20CRG%20Country-Level%20Assessment%20Protocol%20Template_DRAFT.pdf

Engagement
Support the participation of TB survivors and key and vulnerable populations as meaningful partners in TB research and development initiatives
Advocacy and strategic communications
Invest in networks and organizations of TB survivors and key and vulnerable populations to build the required capacity to effectively engage in TB governance, advocacy, accountability, demand generation, law and policy reform and service delivery.
Fund advocacy and engagement of TB key and vulnerable populations.
Facilitate the meaningful engagement and participation of TB survivors and key and vulnerable populations in all levels of policymaking and programmatic design to ensure that TB services are rights-based, gender-sensitive and people-centered and meet the expressed needs of key and vulnerable populations.
Monitoring and operational research
Adapt and implement real time community-led monitoring for social accountability with data disaggregated by age, gender, key and vulnerable population status.
Conduct operational research exploring the identification, mitigation and overcoming of human rights related barriers to accessing services for TB key and vulnerable populations, and to nuance findings and interventions to address gender in this context.

Box: Challenge Facility for Civil Society

The Challenge Facility for Civil Society (CFCS), a Stop TB Partnership initiative, exposed an immense need for more resources for CRG interventions. The CFCS provides grants to TB-affected community and civil society organizations working to ensure that the TB response is rights-based, gender-transformative, people-centered, and accountable. Because of the high demand for CRG support, on average the facility was able to meet only 15-20% of the requested funding need within its first three rounds of grantmaking.

Affected communities and their allies in civil society have called on donors to close this funding gap.[84]

[84] *Deadly Divide: TB Commitments vs. TB Realities,* https://stoptb.org/assets/documents/communities/The%20Deadly%20Divide_TB%20Commitments%20vs%20TB%20Realities%20FINAL%20HLM%20Report.pdf

Ch 8. Accelerating Development of New TB tools

Priority actions

- Invest, at minimum, US$ 4.22 billion annually to accelerate the research and development of new TB diagnostics, medicines, and vaccines. Resources need to be mobilized from governments and philanthropies, increased engagement with the private sector, and new approaches to innovative and sustainable financing.

- Accelerate the development of new tools to prevent, diagnose, and treat TB by identifying innovative product-development pathways and improving collaboration among actors in product development. Research priorities include:
    - Vaccines:
        - Develop a new TB vaccine by 2025.
        - Diversify and broaden the pipeline of next generation TB vaccine candidates by expanding research on *Mtb* immunology and basic mycobacteriology, and develop animal models that better reflect human infection and disease.
        - Provide resources and support to efficiently move a diverse range of vaccine concepts from the lab to the clinic.
        - Significantly accelerate clinical development of vaccine candidates and ensure sufficient financing, resources, and capacity to advance multiple promising candidates through efficacy trials and licensure without delay.
        - Conduct research on correlates of vaccine-induced protection during vaccine efficacy trials to inform vaccine design and expedite clinical trials of future vaccine candidates.
        - Work with countries and affected communities to prepare for successful licensure and roll-out of new TB vaccines once licensed (see Chapter 4).
    - Diagnostics:
        - Develop rapid, affordable, tests for diagnosis or triage that do not rely exclusively on sputum and are used at the point of care.

        - Develop accurate DST for critical medicines, including through sequencing-based tests and strategies for early detection of resistance to the drugs used in regimens.
        - Improve tools for detecting TB infection (i.e., latent TB), subclinical TB and testing for risk of progression to active disease.
        - Develop and harness artificial intelligence (AI) and machine learning-based tests.
    - Medicines:
        - Increase and advance the number of novel drug candidates in the clinical pipeline.
        - Advance the development of new treatment regimens that will be superior to current regimens for drug-sensitive and drug-resistant forms of TB.
        - Focus on treatment-shortening strategies for both TB disease and TB infection.
- Invest at least US$ 800 million per year in basic science research.
- Expand the use of operational research.
- Develop and implement digital tools.
- Create an enabling environment for TB R&D.
- Apply best practices in community engagement throughout the R&D process.
- Apply access principles in rolling out and optimizing the use of new tools.
- Strengthen advocacy for TB R&D.

Invest, at minimum, US$ 4.22 billion annually to accelerate the research and development of new diagnostics, medicines, and vaccines.

Investments in science and technology are crucial to tackling any disease and are an absolute necessity to reach goals of elimination of disease. For TB, a disease that primarily affects the developing world, funding has always fallen short of meeting the basic required levels needed to support research and development needs.

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 get sick or die from the disease. After years of under-investment, developing these tools will require commitment and funding from governments, the private sector, and philanthropic organizations that is on par

with the urgent need for innovation. It will also require a radically transformed approach to accelerating promising medicine, diagnostic and vaccine candidates through the development pathway. R&D efforts should be needs-driven, evidence-based and guided by the core principles of affordability, efficiency, equity and collaboration.

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 global investments to US$ 2 billion per year in order to close the estimated US$1.3 billion gap in funding annually for tuberculosis research."[85] For a few reasons, TB R&D resource needs have since increased to a minimum of US$ 4 billion annually.

First, investments in TB R&D have consistently fallen short of the need. In 2020, governments collectively invested only US$642 million in TB R&D (of a total US$915 from all funding sources). Adjusted for inflation, total investment in TB R&D was flat between 2018 and 2020.[86] The commercial pharmaceutical sector also invested very little in TB R&D, including almost nothing for vaccines. In contrast to their support for a COVID-19 vaccine, multilateral funders such as Gavi, CEPI, and the multilateral development banks have not yet contributed significant resources to support TB R&D (TAG, 2021). As a consequence, TB R&D continues to suffer from a lack of funding.

Second, funding needs are projected to increase as certain promising product candidates need to be tested in Phase 3 clinical trials, which are larger and more costly to implement than earlier phase trials. This is the first Global Plan to cost out Phase 3 vaccine trials.

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[85] 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

[86] Stop TB Partnership, Treatment Action Group. Tuberculosis Research Funding Trends, 2005-2020. chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/viewer.html?pdfurl=https%3A%2F%2Fwww.treatmentactiongroup.org%2Fwp-content%2Fuploads%2F2021%2F12%2Ftb_funding_2021.pdf&clen=4388568&chunk=true

Table 12 shows annual TB funding needs for the R&D of new TB medicines, diagnostics and vaccines from 2023-2030.

Table 12. Resources needed for TB R&D, 2023-2030

Tool	Investment needed (US$ billions)
Medicines	16.06
Diagnostics	7.72
Vaccines	10.00
Total	33.78

US$ 40.18 billion is needed to accelerate the research and development of new TB medicines and treatment regimens, diagnostics, and vaccines–which from 2023-2030. This includes US$ 800 million annually for basic science research.

While the figure includes R&D resource needs for new vaccines, the roll-out of a new vaccine is costed separately and expected to begin in 2026. (See Chapter 9 for detailed discussion of TB financing. See Chapter 4 for details on vaccine implementation.) The Global Plan urges countries to increase investment in operational research required to identify the most effective ways of implementing new tools in various national contexts.[87]

The resource needs for TB R&D are greater than the US$2 billion funding needed in prior years. The increased need reflects the lack of investment in prior years and includes the costs of carrying out large-scale Phase 3 vaccine trials–a cost that reflects advances in vaccine R&D in recent years. Costed priorities are presented in R&D strategic frameworks for diagnostics, medicines and vaccines below. See Chapter 9 for a discussion of mobilizing resources for TB R&D.

Apply lessons from the development and distribution of previous innovations

[87] A fuller treatment of recent TB R&D funding trends, including analysis of funding for basic research, operational research, and child TB research, is found in the annual Tuberculosis research funding trends reports produced by Treatment Action Group and the Stop TB Partnership.

Investments, partnerships, and global multisectoral efforts translated to remarkable impact in creating effective therapies for HIV, and, more recently, COVID-19. Advocacy, a sense of urgency, political will as well as substantial public and private investments proved critical to see these impressive results.

The response to COVID-19 involved unprecedented scientific innovation. The introduction of multiple vaccines in rapid time showed what is possible to achieve with a critical mass of resources and political will.

Working together, governments, the private sector and philanthropy identified new approaches and pathways to development, which allowed them to move quickly through the R&D and regulatory processes and introduce new products in record time. At the same time, the global community failed to ensure that new vaccines were distributed equitably around the world. High-income countries amassed large vaccine stocks and quickly achieved relatively high rates of vaccine coverage, while low-income countries faced challenges acquiring vaccine stock and distributing vaccines efficiently, leading to relatively low rates of vaccine coverage during the same time period.

The global TB R&D community must learn and leverage as much as possible from the COVID-19 response in order to transform the approach to advancing new TB medicines, diagnostics and vaccines.

The urgency is even greater now than in the past, considering the pandemic's impact on TB R&D, which include the diversion of resources (human, financial and infrastructure) and delays in TB research activities. With immense resources invested in COVID-19, scientists today face even less incentive to develop careers in TB research. New resources are critically needed to rebuild TB R&D capacity and safeguard TB innovation from potential future disruptions.

Accelerate the development of new tools to prevent, diagnose, and treat TB by identifying innovative product-development pathways and increasing collaboration among key stakeholders in product development.

The following section lays out strategic frameworks for accelerating the research and development of new TB vaccines, diagnostics and medicines.

New Vaccines R&D

Vision: To develop new, more effective vaccines that will directly and safely prevent TB in all age groups and populations and are affordable and accessible to those who most need them.

Goals:

1. Develop new TB vaccines that prevent TB infection, TB disease, and/or recurrence of TB disease following successful treatment of TB, thereby interrupting TB transmission
2. Incorporate the goal of equitable accessibility throughout the TB vaccine R&D process
3. Strengthen community engagement in TB vaccine R&D

Table 13a. Strategic framework adapted from the Roadmap for Research and Development of New TB Vaccines, published by EDCTP and AIGHD, April 2021.

Objective 1: Diversify the TB Vaccine Pipeline to increase probability of success in developing effective, new TB vaccines			
Priority	**Key Actions**	**Comments**	**Funding Required (US$ millions)**
Mechanisms and biomarkers of protection	Conduct observational clinical studies combining pathogenesis and immunology, making use of systems biology, epidemiology and modelling	Identify components of the host-pathogen interaction associated with clearance, progression to disease and subclinical disease; identify biomarkers and biosignatures of natural protection.	1000
	Study the role of non-conventional, cellular immunity, antibody responses and trained innate immunity in natural and vaccine-induced protective responses	Explore cellular responses through class-I restricted CD8+ T cells, Th17 cells and MAIT cells; B- cell and antibody responses including Fc-mediated antibody effector functions; and innate immune responses through unconventionally restricted T cells and epigenetic reprogramming of monocytes and natural killer cells. Investigate their role in human immune responses to *M. tuberculosis.*	
	Identify biomarkers and biosignatures that correlate with vaccine-induced protection	Based on data and biological samples from trials that have shown protection signals; through targeted approaches to detect cellular and/or humoral immune responses and unbiased approaches including transcriptional profiling of blood cells and mycobacterial growth inhibition assays.	
Undertake novel approaches to vaccine discovery	Develop new vaccine concepts that induce a broad diversity of potentially protective immune responses	Explore candidates that generate non-conventional cellular immunity, protective antibody responses and trained innate immunity.	
	Study mucosal immune responses	Understand the determinants of protective immune responses in the lung parenchyma and mucosa, and how these can be inferred by systemic responses.	
	Discover antigens that are protective in humans	Identify Mtb expressed proteins, peptides and non-protein antigens that can be recognized by the human host immune	

		system, applying IFN-γ as well as non-IFN-γ based screening approaches, including by genome-wide strategies.	
Develop and apply improved vaccine formulations and delivery platforms	Study the effects on vaccination outcomes of adjuvants, vaccine platforms and lineage of the Mtb challenge strain	Amongst others through experimental medicine studies.	200
	Explore new routes of vaccine administration	Including aerosol and intravenous approaches, amongst others through experimental medicine studies.	
	Study how vaccines can direct immune responses to the lungs	Evaluate the capacity of different formulations and delivery platforms to induce mucosal immune responses.	
Establish a Controlled human infection model	Develop a controlled human infection model for immunobiology studies	To inform basic knowledge gaps, as well as for proof-of-principle studies to inform down- selection of candidates, platforms and routes of administration. Participant safety, sensitivity and ethical issues will be critical to address.	50
Advance promising vaccine candidates from early preclinical to clinical developmen t	Conduct the necessary studies for IND or equivalent regulatory submission	To provide development partners, funders and regulators with sufficient evidence of safety (including necessary toxicology studies) and intended biological activity (e.g., immunogenicity; protection in pre-clinical challenge models) to support and enable advancement into phase 1 clinical studies.	550

Table 13b. Priorities and actions to accelerate clinical development of new TB vaccines: animal models

Objective 2: Optimize and standardize animal models for understanding TB mechanisms of protection and accelerating vaccine development			
R&D priority	**Key actions**	**Comments**	
Optimized animal models	Develop *fit for purpose* animal models	Back-translate into immunogenicity, infection and disease animal models the results/findings from adolescent/adult and paediatric trials, ideally using the exact same product as in humans, and from clinical studies of disease progression and subclinical disease.	735
	Develop animal models to provide insight into the relation between prevention of Mtb infection (POI) and prevention of TB disease (POD)	Leverage results from human trials with PoI and, ideally, both PoI and PoD endpoints, as well as from clinical studies of clearance and disease progression to optimize animal models.	
	Develop immune compromised animal models that can predict/replicate findings in specific human target populations	Back-translate into disease animal models the results that will emerge from clinical trials including those in all age groups and immune compromised humans.	
Comparison of vaccine candidates within and across animal models	Standardize and harmonize animal models	Including harmonization and standardization of challenge strain selection; definition of protection outcomes, including the use of imaging and scoring gross pathology specimens. Identify priorities for future experimental directions, e.g., assessing aerosolized delivery of vaccines.	
	Perform head-to-head testing of candidate vaccines	In independent laboratories using the standardized models that best predict protection in humans.	

Table 13c: Priorities and actions to accelerate clinical development of new tuberculosis vaccines: clinical trials

Priority 3: Advance candidates through clinical trials			
R&D priority	**Key actions**	**Comments**	**Total $ incomplete costing**
Conduct clinical trials utilizing portfolio management and common stage-gating criteria	Implement Phase 3 trials of vaccine candidates that meet criteria to advance to licensure. and policy recommendations		6500
	Continue to support vaccine candidates through the clinical pipeline and initiate new Phase I/IIa/IIb trials using PoI, PoR, and POD endpoints	Bias toward selection of PoD endpoint in adolescent /adult population considering likely disproportionate effect on reducing spread of Mtb (as compared to PoI or PoR approaches or studies in infants and young children)	
	Include safety trials or safety assessments for people living with HIV in clinical trial planning and implementation		
Ensure adequate Clinical Trial site capacity in high TB burden regions to conduct global regulatory standard human	Make inventory of clinical trial site capacity	Identify potential sites beyond the existing ones; assess quality and suitability in terms of existing technical and laboratory infrastructure.	
	Collect epidemiological data in sites considered for phase II/III trials	In various parts of the world, as a continuous process: age-stratified data on TB incidence; age- stratified incidence/prevalence of latent TB infection; Mtb lineage distribution; data on special populations such as people living with HIV and other populations considered for vaccine trials.	
	Develop vaccine trial sites, including sustainable human capacity	Develop infrastructure and human capacity, including mentorship and support of junior investigators, in diverse geographic locations to take account of potential variation in efficacy and safety due to heterogeneity in host and bacteriological genetic background.	

trials of novel vaccines	Study potential barriers to trial acceptance	Social science research of barriers to participating in TB vaccine trials and completing follow-up, including TB-associated stigma, other stigma, and social barriers; compile best practices from successful vaccine trial sites.	
	Promote community engagement in TB vaccine trials	Integrate Community engagement into all phase II or phase III studies sponsors and developers should start developing plans for community engagement before phase I studies start.	
Trial endpoints	Define standardized PoD trial endpoints that better capture the various TB disease states in diverse target populations	Standardize definition of laboratory-confirmed pulmonary TB; develop clinical endpoints representative of subclinical TB if established as a substantial contributor to TB transmission; improve bacteriological confirmation of TB disease in neonates and infants and people living with HIV; improve bacteriological confirmation of extrapulmonary disease.	8
	Define and develop better PoI trial endpoints	Define an endpoint for Mtb infection for establishing PoI; this endpoint should differentiate Mtb infection from vaccine-induced immune response.	
	Quantify the clinical translation of PoI into PoD	Analyse existing and new observational data; include secondary PoI endpoints in phase III PoD trials, considering that this quantification may be different for different types of vaccines.	
Correlates of protection (CoPs)	Collect biospecimens for identifying CoPs	In planned and ongoing phase IIb and phase III trials.	800
	Identify CoPs for TB disease	From phase IIb and phase III trials that have shown protection: analyse data and putative CoP values from individual trials and, if possible, from meta-analyses of several trials.	
	Validate CoPs for TB disease	Validate putative CoP identified by back-translation of trial results in terms of vaccine-induced response and clinical protection in immunogenicity studies, new trials with a clinical PoD endpoint and potentially controlled human infection models. Validate identified COP in PWHIV to enable immuno-bridging studies	
Trial harmonization and design	Harmonize clinical trial protocols	Define an agnostic trial “shell” of standardized outcomes, inclusion criteria and measurements for clinical trials for different vaccine types. This would also address secondary endpoints; inclusion criteria for people living with HIV infection or diabetes; and standardized measurements over time.	7

	Evaluate and develop new models for TB vaccine clinical trials with increased time-and cost-efficiency	Phase I: explore innovative trial designs that provide information on the local human immune response. Phase IIb/III: efficacy trials within contact investigations, active case finding programs and high-risk populations; adaptive trial designs for evaluating the safety, immunogenicity and efficacy of different vaccine types.	
Improve 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; continue to expand on programs to provide reagents to laboratories and research facilities; develop necessary assays based on stakeholder consensus	150

Table 13d. Priorities and actions to ensure public health impact: epidemiology and modelling

R&D priority	Key actions	Comments	
Country-specific data and projections	Conduct in-depth country-specific value proposition analyses	Assess value drivers for new TB vaccines across different countries and stakeholders considering preferred delivery strategies; efficacy relative to safety; manufacturing, strain standardization and price; willingness to pay; and cost of delivery.	
	Collect epidemiological data at country and subnational level	To inform economic and impact modelling related to country decisions on introduction of new TB vaccines and market volumes: (sub)national TB disease and infection prevalence including in specific risk groups (people living with HIV, elderly); identify potential target groups for vaccination based on contribution to transmission; map *M. tuberculosis* genotypic variation.	
	Modelling to define vaccine development investment cases and country-specific vaccine use cases	Modelling of implementation scenarios, the epidemiological impact, cost-effectiveness and budget impact in consultation with countries for vaccines that are close to market introduction, using transmission and economic modelling as well as other quantitative approaches.	
Post-licensure studies	Develop valid approaches for real-life vaccine scale-up studies	Develop designs and validated tools for establishing real-world effectiveness, safety and public health impact following introduction; establish and/or support post-licensure registries making use of existing expertise from introduction of other vaccines; strengthen surveillance systems for collection of baseline epidemiologic data.	
	Conduct post-licensure evaluations of vaccine effectiveness, impact and safety	Real-world post-licensure studies and surveillance to establish effectiveness across various subpopulations (e.g., people living with HIV) and Mtb lineages; effectiveness and safety when given concurrently with other vaccines; safety in subpopulations (e.g., pregnant women); impact on TB disease incidence; non-specific health effects for vaccines replacing BCG.	

Abbreviations: BCG - Bacille Calmette-Guérin, Mtb - *Mycobacterium tuberculosis,* R&D - research and development, TB - tuberculosis.

Table 13e. Priorities and actions to ensure public health impact: research to ensure optimal implementation

R&D priority	Key actions	Comments	
Health system conditions for vaccine introduction	Define the generic public health system requirements to deliver a new TB vaccine	For a vaccine for adolescents and adults: determine in different countries the feasibility of various strategies including vaccination campaigns; conditions for immunization programs to implement these strategies; requirements for optimizing access for different population groups; integration of TB vaccination within and beyond national TB programmes; and approaches to measuring vaccine uptake in adolescents/adults. For a vaccine for neonates and infants: determine the fit in the Expanded Programme on Immunization and required timing with regard to other vaccinations.	
	Conduct pre- and post-introduction assessments of country immunization programmes	Assess the pre-introduction country-specific readiness of immunization programmes and health systems to handle, store and administer the new TB vaccine (considering its characteristics, particularly for delivery to adolescents and adults), to monitor vaccine coverage and adverse events, and to communicate adverse events.	
Barriers and enablers of vaccine uptake	Assess drivers of acceptability and uptake of new TB vaccines in various settings	Social and behavioural research to determine across countries and settings decision makers' and public and health workers' perceptions around new vaccines, related to dosing, safety concerns, religious concerns, gender, use with other vaccines versus specialized programmes, and for immunotherapeutic vaccines, integration with TB treatment.	

Abbreviations: R&D - research and development, TB - tuberculosis.

Table 14: Priorities and actions with regard to enabling conditions for tuberculosis vaccine development

Enabling priority	Actions
Funding	
Attract new investments in TB vaccine R&D	Develop a comprehensive global value proposition for TB vaccines that encompasses vaccine characteristics, use case, societal value, business case, investment case, and health and micro/macro-economic impact assessment.
	Broaden the funding base with governments, charitable funders and donors. Mobilize domestic R&D funding from large countries' governments; get specific donors involved that could contribute to funding downstream aspects of TB vaccine R&D; engage with the HIV and antimicrobial resistance communities.
	Attract new entrants in TB vaccine R&D. Involve actors, technologies, models and knowledge from outside the TB vaccine research field; funders should promote such involvement in their funding programmes, e.g., in the specification of calls and eligibility criteria.
Innovate financing for TB vaccine R&D	Create collaborations or partnerships for joint funding of trials with mechanisms for pooling resources between R&D funders, governments and industry with selection procedures that are product and country agnostic, and strict norms for what the funding will be used for and under which conditions.
	Customize calls to the clinical development pathway through options for their flexibility long term funding (e.g., ten years, with intermediate go/no-go decisions) allowing consortia to adopt a long-term R&D perspective for a specific candidate or approach.
Create mechanisms that attract investment in early stages of development	Reduce commercial uncertainty by providing incentives for stronger engagement from industry and other vaccine developers through grant funding and advance market commitments with a clearly defined path to commercialization, including production of a successful candidate.
	Ensure that intellectual property can be used efficiently, openly, and equitably to facilitate TB vaccine R&D in ways that promote collaboration among universities, biotech and pharmaceutical companies, and government funders.
Open science	

Promote timely and open access of data, specimens and results	Funders and product development partnerships should require registration of all animal and human studies, open access publication of both positive and negative results, data-sharing and posting in open access databases as condition for funding and/or consortium membership.
	Biospecimens collected in clinical studies should be made available based on peer review, overseen by an access committee. Access to biospecimens should not be granted on first-come first-serve basis but to researchers with the most innovative ideas and approaches.
	Establish publicly searchable patent databases for TB vaccine research (as exist for drug development) to promote the diffusion of knowledge by facilitating access to the information disclosed in a patent, including antigens, adjuvants, platforms, and processes.
Create a mechanism for coordinating open science in TB	Establish a platform for data sharing, starting with data from clinical studies, including generic protocols for contextual data (e.g., for what purpose was the data collected); proper use (e.g., ethical rules, privacy regulations) and acknowledgement of original collectors/contributors of the data in secondary use and publications.
	Develop and coordinate systems and procedures needed for efficient data and specimen sharing across the field of TB research and across TB research funders.
Stakeholder engagement	
Create a supportive environment for TB vaccines	Raise political commitment for new TB vaccines to ensure new political commitment at country level and continue high level commitments making sure that existing commitments and defined targets are met, based on clear communication about the need, efficacy and safety for new TB vaccines towards policy makers, including the risk-benefit and cost-benefit analysis of a new TB vaccine.

	Advocate for development and uptake of new TB vaccines with vaccine developers and the public through positive messaging about opportunities and actions in vaccine development.
	Harmonize and fast-track regulatory review and local approval of vaccine trial protocols based on the example of AVAREF; establish NITAGs in countries that do not have them and strengthen their capacity; fast-track regulatory approval of TB vaccines.
	Create innovative incentives by forecasting demands from countries and engaging multilateral funders, including GAVI, GFATM, Unitaid and CEPI in offering novel financing mechanisms.
Overcome barriers to delivery and uptake	Engage with end-user communities to address stigma, vaccine hesitancy and adherence; provide and communicate a convincing rationale for (high-risk) target groups to be vaccinated; involve end-user communities in the research process; build resilient information systems to counter vaccine related misinformation and disinformation.
	Develop approaches to community-level delivery (e.g., through community health workers) to address gaps in access to vaccination; educate healthcare networks, the medical community and the general public about TB vaccine introduction through targeted, country-specific approaches.
Promote TB vaccine and research literacy	Create a global program for community engagement and training for new TB vaccines; develop mechanisms for engaging community representatives in TB vaccine development; engage and educate community representatives who can speak to policy makers to invest in the development and introduction of new vaccines; support community engagement in TB vaccine clinical trials.

	Foster strategic and reciprocal partnerships between vaccine scientists/sponsors and representatives of civil society and TB affected communities to support the involvement of all parties in advocacy for new TB vaccines.

The End TB Strategy calls for a new effective TB vaccine for use by 2025. It is likely that more than one vaccine will be necessary to meet the needs of different populations and different regions. This is possible if funding for new TB vaccine R&D is made available immediately, and if the scientific R&D process is fast-tracked using the same approaches used for COVID-19 vaccine development.

Scientific advances, particularly in the past five years, have demonstrated the feasibility of developing new vaccines to prevent TB infection and to prevent TB disease. These advances included positive results from two Phase 2b clinical trials. However, while these results were published nearly five years ago, phase III studies have not yet started due primarily to chronically inadequate resources.

The successful development and licensure of at least one new TB vaccine by 2025 will require a transformation in the vaccine development pathway, including:

- Accelerating clinical development pathways, including streamlining the design and reducing the duration of efficacy trials while meeting regulatory requirements for licensure.
- Developing animal models that reflect relevant human outcomes (i.e. resistance to infection) and are 'fit-for-purpose' to prioritize vaccine candidates for human testing
- Evaluating novel vaccine technology platforms (e.g. mRNA) for TB and identifying human-protective antigens.
- Developing innovative financing models and public-private partnerships that will enable the rapid development and deployment of vaccines once efficacy has been established.
- Investing in scale-up of manufacturing and preparing the supply chain to ensure ample supply and rapid distribution of vaccines once licensed.

Roadmap for the Research and Development of New Tuberculosis Vaccines

In April 2021 the European & Developing Countries Clinical Trials Partnership (EDCTP) and the Amsterdam Institute for Global Health and Development (AIGHD) launched a Global roadmap for research and development of tuberculosis vaccines (Global Roadmap). The Global Roadmap identifies key barriers to TB vaccine R&D and implementation, ways to overcome them, and a shared set of priorities to guide TB vaccine R&D activities. The Global Plan's

strategic framework for TB vaccine R&D has been adapted to align with this Global Roadmap, and funding requirements were applied to these research priorities and activities. More details and information about these activities and priorities can be found in the Global Roadmap.

Recognizing that people with HIV are at high risk for TB infection and disease and that they tend to have a less robust immunological response to vaccination, a Roadmap for Developing TB Vaccines for People with HIV has been developed. This Roadmap seeks to accelerate development of TB vaccines for PLHIV by addressing gaps and unanswered questions regarding priority vaccine indications, clinical trial design, measures of safety, immunogenicity, and efficacy considerations for people with HIV.

New diagnostics R&D

Vision: To ensure that all people with TB can access a convenient, accurate, rapid TB diagnosis.

Goals:

1. Develop rapid, affordable, tests for diagnosis or triage that do not rely on sputum and are used at the point of care.
2. Develop accurate drug sensitivity tests for critical medicines, including through sequencing-based tests and strategies for early detection of resistance to the drugs used in regimens.
3. Improve tools for detecting TB infection (i.e., latent TB), subclinical TB and testing for risk of progression to active disease.
4. Develop and harness artificial intelligence (AI) and machine learning-based tests.

Objectives:

1. Ensure expanded and equitable access to critical knowledge and resources that enable the development of new diagnostic tools.
2. Develop and evaluate a diverse portfolio of new tests and solutions.
3. Demonstrate patient benefit and predict impact within the entire health system.
4. Ensure that WHO approved diagnostics are made available and appropriately used in relevant countries.

The last decade has seen a scaling up of automated diagnostic technologies that have been replacing sputum smear microscopy as the standard test in many parts of the world. The Global Plan calls for building on this progress to

further develop and introduce the widespread use of diagnostics based on biomarkers such as urine or blood that can work for all people (e.g., infants and children), for both pulmonary and extrapulmonary TB, and used wherever people seek and receive care.

To create a more enabling environment for implementing the new TB diagnostics strategic framework, in addition to new financing, developers need better access to biobanks, better access to data (including through open access arrangements), and stronger collaborations with academic research institutes. Public policy and regulatory environments that support the efficient approval and widespread uptake of new diagnostics would further help to create incentives for investment in new TB diagnostics R&D.

Table 15: R&D strategic framework for new TB diagnostics

New Diagnostics Strategic Framework 2023 – 2030

Objective	Milestone	Major activities	Funding required 2023 – 2030 (US$ millions)
Objective 1			417.15

Ensure expanded and equitable access to critical knowledge and resources that enable the development of new diagnostic tools	Increase access to reference materials and digital repositories that are critical for the discovery, development and validation of new TB diagnostics	a. Facilitate sample storage and database maintenance within country of collection, reducing the need for import/export permits b. Ensure that international biobanks and digital repositories collaborate and have centralized, open-access mechanisms and dashboards so requestors can obtain samples from anywhere c. Promote highest quality in biobanking and database curation to ensure global representativeness, relevance and integrity. In compliance with patient rights, data protection laws and FAIR Data Principles[1]	62.54

	Integrate biomarker discovery and validation in well powered trials and studies collecting high quality data	a. Undertake research to identify and validate new non-sputum-based biomarkers and diagnostic concepts addressing high priority use cases, including pediatric TB, EPTB, HIV, subclinical TB, preventing relapse, and to guide personalized medicine in TB.	316.4
	Support assessment of MTB genetic variants to inform the development of molecular tests for the detection of drug-resistant TB	a. Expand the global knowledgebase and repositories with genomic, phenotypic, and associated metadata from MTBC samples, review for quality and standardization b. Support contributions of sequencing datasets by diverse groups (National TB Programs, academics, consortia, etc.) to expand and maintain a catalog of mutations	16

		associated with resistance to anti-TB drugs and that is updated periodically to ensure standardized and accurate interpretation of data	
	Undertake research and consultations to support the development of person-centered diagnostic tools and solutions	a. Definition of patient charter/ethical criteria, and consensus-building on appropriate patient data utilization and data protection protocols b. Include end users (people who have experienced TB, health workers, lab technicians etc.) from conceptualization, design, evaluation, and implementation of diagnostic tools and solutions, taking into account	16.71

		social and gender factors c. Evaluate alternate, minimally-invasive or non-invasive, easy-to-collect or self-collected specimen methods	
	Disseminate knowledge on diagnostic tools and solutions	a. Develop clearer guidelines for validation studies for new diagnostics b. Update target product profiles (TPPs) c. Develop and promote online country-specific platforms for knowledge sharing on diagnostic development, ongoing accuracy trials, and implementation research, including massive online open courses (MOOCs) and in-	5.5

		country “TB think-tanks”	
Objective 2			1,6214.47

Develop and evaluate a diverse portfolio of new tests and solutions	Develop fit-for-purpose diagnostics for testing strategies addressing the major diagnostic gaps in TB	Develop tests and solutions for the following: a. Fast and affordable tests to determine risk of developing active TB disease in infected, at-risk populations b. Improved TB screening tools c. Simple and affordable point-of-care diagnostics for TB detection in all patients, including EPTB, PLHIV and pediatric TB d. New tools that are based on easy-to-obtain non-sputum samples e. High-throughput centralized diagnostics f. Early detection of subclinical TB disease g. Detection of drug resistance, including both pDST and gDST sequencing-based strategies	848.93

		h. Treatment monitoring and tests of cure i. Multi-disease platforms and tests to differentiate between pathogens, reduce antibiotic overuse, and improve self-isolation strategies j. Digital diagnostics for relevant use cases listed above	
	Conduct accuracy trials for new tests and evaluate their clinical performance in trials to guide global policy and country uptake	Carry out accuracy trials and evaluation studies for the tools a-j listed above	612.54

	Ensure that any diagnostic is a connected diagnostic, so that surveillance, reporting, and linkage to care is automated	a. Support development of standardized digital data collection tools suitable for multiple settings and transition away from paper-based data collection b. Strengthen and centralize national TB surveillance systems using digital tools and applications c. Incorporate connectivity elements such as digital readers/QR codes in the design of novel TB diagnostics to make the reporting of results digital d. Improve the timeliness of reporting diagnostic results to patients using digital tools and applications	160
Objective 3			566.08

Demonstrate patient benefit and predict impact within the entire health system	Predict patient and health system impact from the use of new diagnostics and solutions to improve TB detection, reduce transmission, and prevent mortality	a. Demonstrate impact of new diagnostic tools on patient important outcomes, through pragmatic implementation trials in relevant countries and settings b. Use diagnostic network optimization (DNO) and modeling to estimate the likely impact and cost-effectiveness of new technologies and innovative diagnostic strategies c. Conduct qualitative studies on end users (people who have experienced TB, health workers, lab technicians etc.) values and preferences, quality of care, and health system utilization	549.08

	Conduct market analysis and estimate the potential of new diagnostics	Update and expand existing market assessments	4
	Work with companies and regulatory bodies to streamline the process of regulation, WHO prequalification, and national and international approval	a. Quality assurance and post market surveillance b. Support and streamline processes for WHO prequalification and national regulatory processes	13
Objective 4			5,115.12
Ensure that WHO approved diagnostic are made available and appropriately used in relevant countries	Roll out tools and solutions, supporting transition away from smear microscopy for TB diagnosis	Procure devices and consumables for the rollout of WHO approved molecular tools and innovative solutions (new and existing) for rollout in high-burden countries	4,158

	Effectively integrate diagnostic tools within the health system, including within the private sector	a. Empower countries to develop fit-for-purpose models using DNO to optimize the placement and integration of diagnostic tools based on country contexts b. Integrate TB diagnostic services with diagnostic services for communicable and non-communicable diseases c. Incentivize the private sector, including pharmacies, medical clinics, and hospitals, to use WHO endorsed tools d. Strengthen information technology (IT) capacity to implement more advanced diagnostic technologies that use AI	526.5

		e. Strengthen laboratory capacity for appropriate scale-up of new tools via: i. Training (coordination, development of tools, sessions, training supervisors, reference specimen transfer) ii. Empowering in-country partners (e.g., Supranational Reference Laboratories, Centers of Excellence) to support introduction of new tools in-country and promote operational research iii. External quality assurance and accompanying measures for tools being used iv. Ongoing external and within-country assistance, including for supply	

		management aspects	

	Ensure patient-centered diagnosis and decentralization of testing where appropriate[1]	a. Include people with TB in decision-making/policies regarding TB diagnostics b. Develop patient-centered solutions for effective, rapid sample collection and transportation c. Ensure that proper services are in place to link patients to care following their diagnosis	48
	Support rapid policy change at the country-level for implementation and facilitate in-country regulatory processes	a. Support country-specific policy change and regulatory processes (local cost-effectiveness and validation studies) b. Harmonize regulatory processes in high-burden countries with stringent regulatory systems and difficult markets to penetrate	59.62

	Sensitize stakeholders about diagnostic uptake and national diagnostic algorithms	Coordinate with advocacy groups and civil societies to organize workshops with NTPs, ministries of health, technical procurement and funding agencies, medical associations (pharmacy, chest physicians etc.), and patient representatives	35
	Scale up manufacturing and other market interventions to bring price down	a. Invest in commercialization and successful scale-up, including local diagnostic start-ups and companies to create lower-cost, innovative diagnostic solutions b. Support local manufacturers to improve scale-up c. Conduct market interventions to reduce the price of diagnostic products (e.g., pool procurement mechanisms, advanced market	264

		commitment, volume guarantee, demand forecasting, demand generation, cost of goods sold (COGS), optimization, new channels etc.)	
	Expand next generation sequencing capacity in countries by 2030 and establish hubs for genomic drug resistance surveillance	a. Build capacity and sustainable infrastructure, and provide training and support in genomics and bioinformatics to implement next generation sequencing approaches for genomic surveillance of drug-resistant TB at the reference laboratory level b. Reinforce the mechanism to use the supranational reference laboratory network and WHO	24

		collaborating centers as the main driver to provide training, study guidance, and long-term support	
TOTAL			7,719.82

[1]Guiding principles that make data findable, accessible, interoperable, and reusable (FAIR Data Principles)

[1]"Automated device for sputum collection and Mtb DNA isolation at the sites of patient's residence is necessary to facilitate sample collection for the centralized diagnostics using high throughput Mtb DNA sequencing, especially in poor resource settings"

New medicines R&D

Vision: Develop shorter, more effective, and safe medicines and regimens for all age groups and populations affected by TB

Goals:

1. Introduce shorter treatment regimens (less than 4 months) for treating all forms of TB using three or four new medicines with no cross-resistance to existing medicines
2. Introduce shorter regimens for TB preventive therapy

Objectives:

1. Sustain the pipeline through basic discovery for TB medicines
2. Increase trial site capacity

3. Introduce shorter regimens for DS-TB and, where appropriate, evaluate as potential universal regimens
4. Develop a safe, higher efficacy and shorter (4 months) regimen for MDR-TB
5. Improve TB treatment for children
6. Develop a safer, high-efficacy regimen for TB infection
7. Ensure adoption of new TB medicines and regimens at country level
8. Engage community and civil society in the entire process of medicine development and access

Currently available treatment regimens, while improved in recent years, still require several months of treatment with multiple antibiotics. Treatment regimens for active TB are long and complex for both people with TB and for health systems to administer. Antimicrobial resistance (AMR) is also a widespread challenge that is limiting the effectiveness of currently available regimens and will always be a looming risk factor for treatment regimens that are long and complex, as incomplete or inappropriate treatment accelerates the emergence of drug resistance.

To create a more enabling environment for implementing the new TB medicines strategic framework, developers need more financing mechanisms for advancing drug candidates from Phase 1 to Phase 2 trials without delays, more drug candidates brought together from diverse sources, and more consortia or collaborations that evaluate new regiments in late-stage clinical trials. Such consortia could play a key role in evaluating new regimens for potential to serve as universal TB treatment regimens. Having better preclinical and translational models could help developers make better predictions about which early-stage drug candidates have the most potential for human benefit, reducing time and costs of R&D by helping to better steer efforts toward the most promising candidates. Having more innovative financing mechanisms for funding distribution of new treatment regimens would help to create stronger incentives for investing in R&D for new TB medicines.

Table 15: New medicines R&D strategic framework

Objective	**Milestone**	**Major Activities**	**Funding Required 2023–2030** (US$ Millions)

Sustain the pipeline through basic discovery for TB medicines	One new clinical candidate entering Phase I each year	Accelerate screening and optimization of new chemical entities; validate biomarkers of treatment outcomes; develop in vitro and animal models that are more predictive of clinical efficacy; identify new drug targets	3,500
Increase 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 develop new GCP/ GLP compliant sites, including clinical trial sites, clinical laboratory, pharmacy, and biospecimen storage capacity	900
Introduce shorter regimens for DS-TB and, where appropriate, evaluate as potential universal regimens	Complete Phase III trials of a shorter than 4-month regimen for DS-TB and assess regimens for all forms of active TB.	Conduct trials: pharmacokinetics studies, Phase I, Phase II (early bactericidal activity, serial sputum colony counting, drug-interaction studies), and Phase III to advance two to three new treatment-shortening regimens	7,200

Develop a safe, higher efficacy and shorter (4 months) 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 treatment-shortening regimens	2,000
Improve TB treatment for children	Complete formulation development and clinical testing in children	Include children in trials as early as possible for new regimens; develop safe, reliable and user- friendly regimens for all forms of child TB early in the development process; conduct drug-interaction studies	430
Develop 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 with high efficacy and safety	330
Ensure adoption of new TB medicines and regimens at country level	Enhanced access of patients to 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	1,500

		countries; engage key stakeholders; conduct extensive training of health providers	
Engage community and civil society in the entire process of medicine development and access	TB-affected community and civil society members have been recruited to all decision-making processes and forums along the medicine discovery and development pipeline	Include TB-affected community and civil society representatives, and specifically high risk populations, in advisory committees, protocol and study design, scientific networks and other forums related to TB drug development to ensure adequate drug access.	200
TOTAL FUNDING REQUIRED			16,060

Meeting the unique needs of children and adolescents

Research efforts directed towards TB in children and adolescents have focused mostly on finding out how to better apply existing tools. However, children and adolescents have needs that differ from those of adults. For example, children have a hard time producing sputum, making them poor candidates for diagnosis using tests that require sputum collection (e.g., the rapid diagnostic test Xpert MTB/RIF).

Treatment Action Group and the Stop TB Partnership Child & Adolescent TB Working Group and Treatment Action Group have laid out a detailed agenda for child and adolescent TB R&D.[88] Priorities include:

[88] Treatment Action Group, Stop TB Partnership Child & Adolescent TB Working Group. Research priorities for paediatric tuberculosis. New York: Treatment Action Group; 2018.

Prevention: Identify new, shorter, and simpler preventive regimens; develop a new vaccine for infants, children and adolescents that improves on the current BCG vaccine.

Diagnosis: Develop novel tests that are not invasive, do not rely on sputum, 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.

Basic science research: Research is needed to better understand how TB affects infants, children, and adolescents, including the immune response to infection and associated biomarkers that can inform the development of new tools.

Invest at least US$ 800 million annually in basic science research.

Scientists still do not fully understand how *M. tuberculosis* causes infection.[89] The world would especially benefit from understanding more about how the TB bacillus interacts with the body, and how the body mobilizes a protective immune response. Gaining this understanding would help drive innovation and enhance the ability to develop new tools to prevent, diagnose and treat TB.

Basic science research is typically conducted by academic institutions, industry and public–private partnerships, which rely in a large part on public funding. At least US$ 800 million is needed annually to advance TB basic science research.[90] This funding should be used to address priorities such as:

- Undertaking research to understand:
  - how TB infection progresses to disease

http://www.treatmentactiongroup.org/sites/default/files/Paediatric_TB_ResearchPriorities_10_8_18_ Web.pdf

[89] Grundner C. To fight tuberculosis, fund basic research. PLoS Biol. 2018;16(9):e3000037. doi:10.1371/journal.pbio.3000037

[90] In addition to the US$ 2 billion minimum needed annually to advance TB R&D pipelines.

    - how to predict the risk and stages of disease progression based on biomarkers[91]
    - how to more easily and reliably know when a person has been cured through treatment
- R&D infrastructure, including biorepositories (i.e., facilities for collecting, storing, processing and distributing specimens used for scientific research)[92]
- Developing and sustaining a larger field of TB researchers
- Improving collaboration between researchers and research centers

Expand the use of operational research

Operational research involves a wide range of research activities used to investigate strategies, interventions, tools and knowledge that can improve the performance of health systems and programmes.[93] Despite improvements in recent years, large implementation gaps still exist in the delivery of TB care that is quality-assured and people-centred. 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.[94]

Research funders should allocate specific funding for operational research, directing it as a priority towards initiatives that will build the evidence base for informing decisions that can close implementation gaps in LMICs.

To be sustainable, operational research capacity needs to be more routinely embedded within NTPs, with dedicated operational research professionals and resources allocated through annual budgets.

Key priorities for operational research:

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[91] 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.

[92] A biorepository is a facility for the long-term storage and conservation of biological specimens

[93] 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

[94] Global strategy for TB research and innovation. Geneva: World Health Organization; in press.

1. understand 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

2. understand 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

3. improve 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

4. improve access and equity for hard-to-reach populations in LMICs, which is critical to achieving UHC

5. understand how public and private sectors can coordinate and collaborate to improve all aspects of accessing and delivering TB care and support

6. optimize TB infection control in order to reduce transmission

7. improve methods for conducting disease surveillance (including real-time digital surveillance), monitoring and evaluation of TB programmes[95]

8. understand the role that TB affected communities and TB survivors can play throughout and beyond the TB cascade of care, including in TB service delivery

Box: SORT-IT

TDR—a joint effort by UNICEF, UNDP, the World Bank and WHO—provides a model for supporting the training of TB researchers who are working to improve TB care at the health systems level in LMICs. Through the Structured Operational Research and Training IniTiative (SORT IT)—a global operational research partnership led by TDR in and implemented with over 60 partners—researchers are trained to conduct operational research according to country priorities, build sustainable operational research capacity, and make evidence-informed decisions for improving TB programme

[95] 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/

performance.[96] 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 acquire the skills and tools for improved communication of research findings (for research uptake) for policymakers and stakeholders.[97,98]

Develop and implement digital tools.

Digital health refers to using a mix of digital technologies and software applications to transform health services. They can be applied to a wide range of healthcare issues, processes and functions in order to improve physical and mental well-being at the individual and population levels (Table TK).*Scale up the use of digital health tools*

Scaling up digital health has many potential benefits:

- Makes health services more efficient
- Reduces capacity constraints in the health workforce
- Reduces costs for health systems and for people
- Improves people's access to the health system
- Reduces health inequities
- Improves health outcomes and well-being

Scaling up digital health in low and middle-income countries (LMICs), especially, would help address staffing and resource constraints that have historically made it difficult both to deliver and to access TB care. Though access to the Internet, smartphones, and other forms of technology is still relatively limited in LMICs, mobile "feature" phones (i.e., phones that lack the advanced functionality of smartphones but can make calls, send text messages, and access some simple Internet features through a text-based interface) are extremely common. These phones can be used for digital health.

Box: Common types of digital health tools

[96] SORT IT [Website]. Geneva: World Health Organization. https://www.who.int/tdr/capacity/strengthening/sort/en/

[97] 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

[98] WHO. Communicating research findings with a KISS. https://tdr.who.int/newsroom/news/item/21-06-2021-communicating-research-findings-with-a-kiss

- **Electronic Health Records (EHR), also known as Electronic Patient Records (EPR).** These are software solutions that replace paper records with digital records. They can also facilitate digital transactions.
- **Telecare, also known as telehealth.** This refers to the delivery of healthcare (e.g., consultation, treatment monitoring and support) remotely using telecommunications technology.
- **Digital medical electronics.** These include a wide range of devices that can be used both inside or outside of a person's body. Common applications include medical imaging (e.g., digital chest x-rays) and electronic sensors (including sensors that can be ingested or implanted to monitor bodily functions).
- **Mobile devices, services and apps.** These are solutions that monitor and share health information using mobile technology. Devices are wearable. Apps appear on mobile phones.
- **Health analytics and bioinformatics.** These use powerful computing technology to analyse large amounts of data. Health analytics tends to focus on helping health program managers understand trends in real time, which helps them make better decisions that improve health care delivery and better manage disease in a population. Bioinformatics uses technology to collect and analyse large quantities of biological data, such as genomic information.
- **Digital adherence tools.** These are digital tools that support people with TB to complete a full course of appropriate treatment in a people-centred way. They can use video chat where video communication technology is available and can be appropriately organized and operated by health care providers and people receiving care. Mobile technology can also be used, including text messages or telephone calls, to provide ongoing treatment adherence support.

If scaled up, the digital health tools that would be especially helpful for ending TB include:

- Computer-aided detection (CAD):[99] CAD is an image-based diagnostic tool. CAD is powered by software that uses artificial intelligence (AI) to read chest x-rays for signs of TB and provide an output that can be used for screening and triage.
- Diagnostics connectivity solutions: Diagnostic connectivity provides the ability for diagnostic instruments to remotely share data, allowing for instant reporting of results to clinicians and databases, real-time epidemiological surveillance, and real-time monitoring of diagnostic supplies.

[99] https://www.stoptb.org/ai-powered-computer-aided-detection-cad-software/cad-and-ultra-portable-x-ray-practical-guides

- Telemedicine that connects TB specialists with people who need care for remote consultations and treatment monitoring and support.
- Remote adherence technologies that support people with TB to complete treatment.

Table 16. Applications of digital health solutions at different levels of the health system.

Health system level	Applications		
Population health	Disease surveillance and forecasting Population health risk management Intervention selection and targeting Communicating health information to the public or key populations Incentivizing people to seek health services		
Individual health	*Diagnosis*	*Treatment*	*Prevention*
	Image-based diagnosis Whole genome sequencing Screening and triage, including self-screening Monitoring health or diagnostics data, including self-monitoring	Digital adherence support Drug 3D printing Personalized treatment Telehealth	Identifying vaccine candidates Predicting risk of disease progression
	Managing referrals between points of service Providing health-education content to patients and families		
Health system	Real-world, real-time data collection Transmitting data/medical information to healthcare providers Detecting drug resistance Providing training content to healthcare providers Capacity planning and management Quality assurance Delivering supplies by drone		
Pharmaceutical and insurance	Drug discovery Supply chain management Monitoring inventories Real-world evidence collection and analysis Adaptive trial design Remotely monitoring clinical trials		

industries	

Provide guidance for scaling up implementation of digital health tools

TB programs need to know what tools to procure and implement, where, and how. They need to know how to prioritize, how to operationalize, and how to optimize solutions. This is a complex undertaking that poses numerous challenges. Governments and technical agencies need to provide clear, up-to-date guidance for innovators, implementers and policymakers to aid them in developing, operationalizing and providing an enabling environment for digital health.

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 designing digital health applications. Adhering to ethical standards will also remain critical in navigating issues of privacy, oversight, accountability, public trust, data governance and management in the application of digital health tools.

Develop strategies for integrating digital health tools into national TB programs

With effective guidance, national TB programs would be better positioned to develop strategies for integrating digital health in their TB elimination efforts. These strategies are essential for prioritizing which tools to invest in and where, and for coordinating governments, innovators, implementers and end users in the integration process. Countries will have more technical resources that can be used for strategy development as WHO works to strengthen the evidence base for digital health in the fight against TB, evolves its guidance in line with advancements in digital health tools, provides technical assistance to countries, and supports digital health policy development.

Create a research-enabling environment

Accelerating TB R&D requires changes in the surrounding research environment that can enable major leaps in innovation. Enabling TB R&D requires improving:

- support and incentive structures for researchers, including in LMICs
- data-, information-, and sample/material-sharing practices
- support for research centers and research collaborations
- capacity to conduct clinical trials, especially in LMICs
- regulations and policies that underpin R&D and product approval
- strengthening advocacy for TB innovation

Develop and sustain a talented field of TB researchers

Ensuring long-term success in TB R&D will require nurturing and incentivizing researchers to focus their efforts on TB innovation, from basic science through translational research and clinical trials.

Training the next generation of scientific investigators is a priority traditionally supported by mechanisms such as Wellcome Trust fellowships, National Institutes of Health (NIH) support at the pre- and post-doctoral levels, and European Union funding. These initiatives are critical but insufficient to fill the void.

Both governmental and nongovernmental funders must recognize the urgent need to train and sustain the next generation of researchers, and special efforts should be made to support and strengthen the capacity of researchers in high TB burden LMICs. Support should include financial investment, proactive career support and career development activities, as well as additional opportunities for training, networking and presenting research in local, regional and global forums. These efforts should be particularly aimed at graduate, post-graduate (doctoral), and junior faculty early-career researchers. Two model initiatives are SORT-IT for operational research and ADVANCE for HIV research (see Box below).

The COVID-19 pandemic has had multiple impacts on this collective investment in early career TB researchers. Firstly, resources in the form of grants and early research opportunities, which previously focused on TB and other infectious diseases have been diverted to prioritize COVID-19 research. Many TB scientists were diverted to assist with COVID-19 solutions using TB research infrastructure, including access to human cohorts and nonhuman primates, clinical operations, supply chain for lab reagents, and biosafety level 3 facilities. Furthermore, students considering careers in infectious disease research have been attracted to study COVID-19 by its higher profile and the enormous resources devoted to it, which makes it more difficult to recruit early trainees to study TB.

The lockdowns and travel restrictions imposed by COVID-19 and inequitable global vaccine access have also dramatically decreased access to conferences and

networking opportunities for early career investigators, impacting their ability to showcase their work to other investigators in the field, which would previously have led to collaborations and opportunities for employment and career advancement. The focus now should shift toward repurposing the expanded COVID-19 research infrastructure to other infectious diseases, particularly a high-priority respiratory disease such as TB.

Box. ADVANCE
Supported by USAID, ADVANCE (Accelerating the Development of Vaccines and New Technologies to Combat the AIDS Epidemic) is a multi-partner research initiative that increases the involvement of African and Indian researchers in all stages of HIV vaccine R&D.[100] 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.

Support Open Science and Information Sharing

The Roadmap for TB Vaccine Research and Development and the WHO Global Strategy for Research & Innovation identify the importance of open science and information to the R&D process. The WHO Global Strategy notes that "Sharing high-quality data…fosters scientific progress, promotes discovery…, improves future data collection methods… and allows for the analysis of similar data from multiple sources, which can subsequently inform national and global policy-making in a cost-effective and timely manner." Key actions to promote open science identified in the Roadmap are outlined in Table X.

Table 17. Key Actions to Promote Open Science, Roadmap for Research & Development of New TB Vaccines

Promote timely and open access of data, specimens and results	Funders and product development partnerships should require registration of all animal and human studies, open access publication of both positive and negative results, data-sharing and posting in open

[100] 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

	access databases as condition for funding and/or consortium membership.
	Biospecimens collected in clinical studies should be made available based on peer review, overseen by an access committee. Access to biospecimens should not be granted on first-come first-serve basis but to researchers with the most innovative ideas and approaches.
	Establish publicly searchable patent databases for TB vaccine research (as exist for drug development) to promote the diffusion of knowledge by facilitating access to the information disclosed in a patent, including antigens, adjuvants, platforms, and processes.
Create a mechanism for coordinating open science in TB	Establish a platform for data sharing, starting with data from clinical studies, including generic protocols for contextual data (e.g., for what purpose was the data collected); proper use (e.g., ethical rules, privacy regulations) and acknowledgement of original collectors/contributors of the data in secondary use and publications.
	Develop and coordinate systems and procedures needed for efficient data and specimen sharing across the field of TB research and across TB research funders.

Increase collaboration in the development of new tools

Below are examples of institutions, partnerships and collaborations that are key to accelerating the R&D of new TB tools. Each entity carries out its work through multisectoral collaboration. 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 they combine the expertise and resources from multiple sectors and help to overcome weak market incentives for developing new tools.

Table 18. Key TB R&D entities

Entity	Model	Focus
TB Alliance	PDP	medicines/treatment regimens R&D
Foundation for Innovative New Diagnostics (FIND)	PDP	diagnostics R&D
International AIDS Vaccine Initiative (IAVI)	PDP	vaccines R&D
TB Vaccines Initiative (TBVI)	PDP	vaccines
TB Trials Consortium	government consortium	clinical, laboratory, epidemiological research

AIDS Clinical Trials Group (ACTG)	network	TB-HIV clinical trials
Medicines Patent Pool	UN-associated organization	licensing
BRICS TB Research Network	government network	basic research, R&D, clinical trials, operational research
European and Developing Countries Clinical Trials Partnership (EDCTP)	partnership between non-profit, government and private sectors	R&D
UNITE4TB	government-sponsored consortium	treatment regimens Phase 2 clinical research
European Regimen Accelerator for TB (ERA4TB)	public-private partnership	medicines/treatment regimens R&D
Pan-African Consortium for the Evaluation of Antituberculosis Antibiotics (PANAcea)	government and EDCTP-sponsored consortium	treatment regimens clinical research
PAN-TB	philanthropic-nonprofit-private-sector consortium	medicines/treatment regimens R&D

EU-PEARL	public-private partnership	clinical research platforms

Increase site capacity for conducting clinical trials in LMICs

The most promising new tools for ending TB will be those that have been demonstrated to work well in countries and settings with the highest burden of TB. This requires testing new tools in the environments where they will be most widely used and will have the greatest impact. As new diagnostics, medicines, and vaccines enter late-stage trials, investment in the development of trial site and laboratory capacity is becoming increasingly urgent. This includes investing in physical infrastructure to ensure appropriate laboratory capacity is available for large-scale trials, and in human capacity and training to ensure that trials are conducted in accordance with Good Clinical Practice, Good Participatory Practice and Good Laboratory Practice standards.

Clinical trial capacity must be developed and enhanced in multiple regions, as the efficacy of any new tool might vary in different populations and regions. A new tool's licensure and acceptance for use can also be affected by where it was tested.

Existing clinical trial sites should be used for TB research wherever possible. Sites should be developed with an aim toward sustaining their capacity over the long term, providing continued opportunities for trained staff, and utilizing the developed infrastructure for other disease areas.

Barriers to conducting trials in LMICs include:

- a lack of financial and human resources
- ethical and regulatory system obstacles
- lack of physical research infrastructure
- operational barriers
- competing demands.[101]

Addressing these challenges requires steps to be taken together:

[101] 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

- LMIC governments should invest in strengthening domestic research capacities.
- All partners should work together to strengthen international collaboration with the aim to improve or create new systems for conducting clinical trials in LMICs.[102]
- Research funders should promote investigator-driven research by local researchers in LMICs.
- Research organizations should strengthen their engagement of affected communities in trial design and execution as laid out in the Good Participatory Practice Guidelines for TB Drug Trials and the Good Participatory Practice Guidelines for TB Vaccine Research 2017.[103,104]

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. When registering medicines, for example, there is often no forum for interaction between the drug sponsor applicant, regulatory authorities, and communities. 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 of new tools, 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.

Apply access principles in rolling out and optimizing the use of new tools

Any time lost between the licensure of a new tool and people in need being able to use it leads to unnecessary suffering and loss of life. With proper planning and a strategic,

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[102] 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

[103] Good Participatory Practice: guidelines for TB vaccine research. Rockville: AERAS; 2017. http://www.aeras.org/img/uploads/ attachments/1015/good_participatory_practice_for_tb_vac- cine_research.pdf

[104] 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

evidence-based approach to access and optimization of use, people can get the most value and benefit from 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.

The Universal Declaration of Human Rights, the International Covenant on Economic, Social and Cultural Rights, and the Declaration of the Rights of People Affected by Tuberculosis 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".[105] 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.[106]

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:

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[105] 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

[106] 26 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 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.[107]

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.

Apply best practices in community engagement throughout the R&D process

Researchers and research institutions must embrace the involvement of communities as a standard part of the R&D process. Best practices should be followed for engaging TB-affected communities within all research activities and within decision-making bodies and fora. 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,

[107] General comment no. 14, The right to the highest attain- able 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=4slQ6QSmlBEDzFEovLCuW1AVC1NkPsgUedPlF1vfP-MJ2c7ey6PAz2qaojTzDJmC0y%2B9t%2BsAtGDNzdEqA6SuP2r-0w%2F6sVBGTpvTSCbiOr4XVFTqhQY65auTFbQRPWNDxL

development, implementation, design of the informed consent process and monitoring of research, and in the dissemination of its results."[108]

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.[109] [110]

Engaging communities in research also fulfills 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."[111]

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. Key populations are discussed in Chapter 7.

These groups must be engaged and their capacity strengthened as a priority in all aspects of research activities. Community engagement must be 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

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[108] 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

[109] 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

[110] 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

[111] 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/

should then remain ongoing through established modes of communication between researchers and community members.

Engaging with communities in all aspects of R&D also creates new groups of informed people who can advocate for TB R&D. 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.

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.

Box. Models of community engagement in research

Community Advisory Boards (CABs): Research entities can establish CABs to ensure that 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.[112]

Community-based participatory research (CBPR): In the CBPR model, community members and researchers collaborate on all aspects of a research project, and community members work with scientists as equal partners. The CBPR model is grounded in principles of collaborative and equitable community engagement in research and shared ownership of research issues, processes and products.

Strengthen advocacy for TB R&D

[112] 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

Implementing the priority actions above will only be possible with powerful advocacy. Informed by the Global Plan and the WHO Global Strategy for TB Research and Innovation, TB researchers, civil society, affected communities and survivors must work together to advocate for R&D funding, for the actions that contribute to a research-enabling environment, and for equitable access to the products and benefits created through innovation.

Priorities for strengthening advocacy for TB R&D include improving research literacy among the advocacy community, deepening the research community's involvement in advocacy, and strengthening collaboration between researchers and advocates.

Improve scientific literacy among the advocacy community

Research literacy means understanding and being able to effectively communicate key concepts, processes and goals being pursued in TB R&D. Wherever research literacy is lacking, TB advocates will be limited in their capacity to affect change.

Better research literacy training opportunities and supporting tools need to be developed and made accessible for advocates across civil society. They should support advocates in three areas:

- Developing an understanding of key concepts in TB R&D, so they can effectively track developments in TB R&D
- Developing skills to communicate about TB R&D issues, so they can translate R&D priorities into effective messages
- Understanding the landscape of TB R&D community (i.e., research institutions, policymaking processes, regulatory bodies), so they can identify and pursue effective advocacy strategies

Deepen the research community's involvement in advocacy

Likewise, advocacy funders and research institutions should support initiatives that support researchers to become more effective advocates for the TB R&D agenda. Scientists can speak credibly not only about new research findings, but also have important insights about barriers and opportunities in TB innovation. There are challenges, however, that need to be overcome to involve researchers in advocacy, particularly when it comes to communications habits and ability to navigate the advocacy landscape. Priorities for deepening the research community's involvement in advocacy include:

providing more advocacy and strategic communication training opportunities for TB researchers
strengthening relationships with TB advocates and coalitions
elevating the visibility of TB research

Scientific researchers are typically trained to communicate with other scientists, creating challenges when it comes to communicating with advocates, policymakers, the news media and other stakeholders who are not scientists. This communications gap can create a significant barrier for advocacy, undermining progress in TB R&D.

Research scientists have also typically not been trained in advocacy strategy and tactics and lack familiarity with the advocacy landscape. It can be difficult to know where or how to become involved in advocacy, even when members of the research community want to.

However, with larger cadres of advocacy-savvy TB researchers, advocacy organizations can find more opportunities to enroll researchers in advocacy campaigns and policymaker outreach. Research studies and key insights from the research community can be routinely shared with advocates who can help translate findings and recommendations into advocacy messages to share important studies with decision-makers and key influencers such as the news media.

Better advocacy training opportunities and supporting tools need to be developed and made accessible for members of the R&D community. They should support researchers in four areas:

- Developing knowledge of common advocacy strategies and tactics
- Building strategic communications skills, such as media training, Op-Ed writing and public speaking
- Translating research findings and insights into action and impact
- Building collaborative relationships with professional TB advocates and advocacy coalitions

Strengthen collaboration between researchers and advocates

Researchers and advocates can both become more effective when they work together. When advocates build science-literacy skills, and when researchers

develop strong advocacy skills, it equips both to communicate with each other and work more effectively together.

Advocates are well placed to help build greater visibility around important research studies and scientific advances, because advocates maintain relationships with journalists, policymakers and organizational leaders. Likewise, researchers can add value to advocacy efforts by providing expert scientific perspectives that complement the policy knowledge and lived experience of advocates and affected communities.

To work together effectively, researchers and advocates need to communicate early and often. When researchers communicate proactively with advocates about their work–such as by alerting advocates in advance of new studies being published–they provide advocates with new information they can use to earn media coverage, publish Op-Eds, engage grassroots campaign networks, or secure meetings with decisionmakers–all of which are essential to advocating for resources and policies needed to accelerate the development of new TB tools. To enable regular communication, advocates and members of affected communities should be included in research decision-making structures and scientific forums.

Ch 9. Resource Needs, Return on Investment, and Cost of Inaction

Resource needs for TB care and prevention

Priority actions:

- Mobilize US$209.8 billion in funding between 2023 and 2030. Of which US$ 157.2 billion, averaging US$ 19.65 billion per annum, is for TB prevention and care, and an additional amount of US$ 52.6 billion for vaccination once a new vaccine is available.
- Mobilize US$40.18 billion in funding between 2023 and 2030 for TB R&D and basic science research.
- Diversify the funding base for TB implementation and R&D.
- Mobilize resources through stronger TB advocacy and strategic communications

The Global Plan conducted modeling that projects the costs of implementing interventions at this scale. Modelers costed 54 interventions, each with an annual unit cost in US dollars. The costing model includes interventions using tools available as of 2022, plus new tools that are projected to be introduced and have a significant impact on TB trends. In a key change from previous Global Plans, the model includes the cost of diagnosing sub-clinical TB at scale as well as the cost of implementing an effective new vaccine.

The costing methodology for this Global Plan improves on the methodology used in previous Global Plans. Internationally recommended normative approaches for TB prevention and care were costed using unit costs derived from the 'ValueTB' database, literature review, GDF catalog, and expert opinion. Using WHO data, programme-level and health systems costs were also used. Finally, enablers were costed by using mark-up percentages mainly derived from best-practice country budgets. (Annex TK includes details on the costing methodology and data sources.)

Mobilize US$209.8 billion in funding between 2023 and 2030. Of which US$ 157.2 billion, averaging US$ 19.65 billion per annum, is for TB prevention and care, and an additional amount of US$ 52.6 billion for vaccination once a new vaccine is available.

The Global Plan urges TB programs, with the support of their governments, to plan program budgets in line with the full expression of need for TB

interventions and research and development aligned with the global goal to end TB by 2030.

An average of US$26.2 billion is required per year to implement the Global Plan from 2023 through 2030, not including resources needed to accelerate TB R&D (see below for R&D resource needs). Average annual costs are Table 1 provides a breakdown of major cost categories per year, totaling $US209.8 billion from 2023 through 2030. Figure 1 presents these resource needs in graph form.

Major cost categories include scaling up TB diagnosis, treatment, prevention, and the implementation of a new TB vaccine in 2026. These interventions will need to be supported by activities needed to strengthen health systems and fund enablers, along with associated programme costs. Diagnosis, treatment and vaccination costs are direct costs for providing TB services at the health facility level. Programme costs are additional costs that are necessary for administering national TB programs. Enabling activities include:

- Direct patient support
- Advocacy and communications
- Communities, Rights and Gender interventions
- Public-private mix activities

Global costs for all cost categories excluding vaccination are projected to average US$19.65 billion per year, totalling US$157.2 billion. Global costs to implement a new vaccine are projected to average US$13.15 billion annually from 2027 through 2030, totaling US$52.6 billion.

Table 19 shows the annual and total financing needs required to implement the Global Plan, not including the costs of R&D. Costs are broken out to show what they are based on various country categories, including income status, Global Fund eligibility status, epidemiological context, WHO region, and BRICS membership. As the figures show, resource needs are required to increase from around $15.7 billion USD per year in 2023 to US$34.9 billion annually. A significant increase in funding required from 2027 onwards anticipates the need to support large-scale implementation of a new TB vaccine.

Table 19: Resource Needs by cost category (USD billions)

	2023	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**

Diagnosis	4.8	5.7	7.1	8.0	7.4	7.0	7.0	7.2	54.1
Treatment	0.9	1.0	1.1	1.1	0.8	0.6	0.5	0.5	6.5
Prevention	0.7	0.8	1.0	1.1	1.2	1.4	1.5	1.7	9.3
Vaccination	0.0	0.0	0.0	0.0	12.4	12.8	13.4	14.0	52.6
Health Systems	1.9	2.2	2.8	3.1	2.7	2.4	2.4	2.5	20.0
Enablers	2.3	2.5	3.0	3.2	3.0	2.9	3.0	3.1	22.9
Program Costs	5.2	5.3	5.4	5.5	5.6	5.7	5.8	5.9	44.4
Total	**15.7**	**17.6**	**20.3**	**21.9**	**33.1**	**32.8**	**33.6**	**34.9**	**209.8**

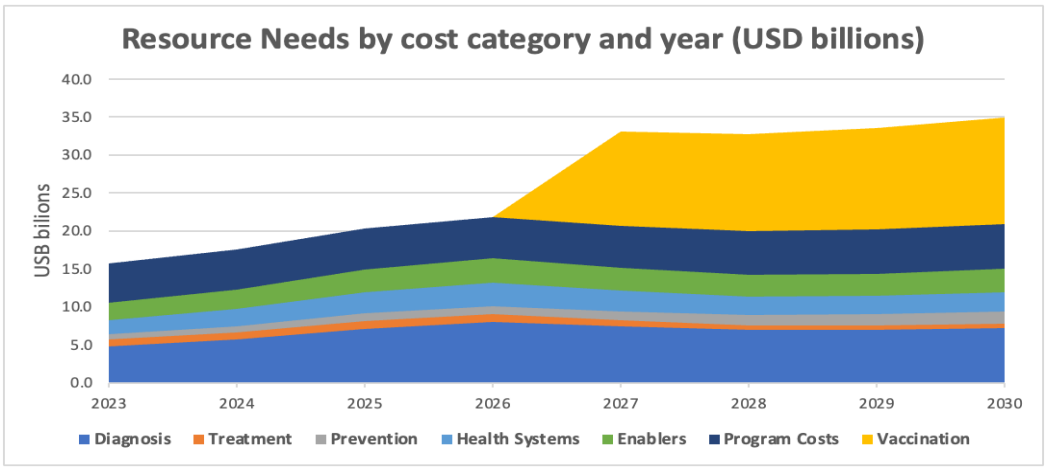
Table 20: Resource Needs, by Income Status, TGF eligibility, Global Plan country group, WHO region and BRICS membership (in US$ billions)

Country category	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**Total**
GLOBAL TOTAL									
Total (Global, including OECD countries	15.7	17.6	20.3	21.9	33.1	32.8	33.6	34.9	209.8

Total (Global, excluding OECD countries)	15.2	17.0	19.7	21.2	30.3	30.0	30.6	31.8	195.9
BY INCOME STATUS									
Low income	1.8	2.1	2.3	2.5	3.5	3.6	3.7	3.9	23.4
Lower middle income	8.5	9.7	11.4	12.5	16.7	16.4	16.7	17.3	109.1
Upper middle income	4.9	5.3	6.0	6.4	10.4	10.4	10.7	11.1	65.2
High income	0.4	0.5	0.5	0.5	2.4	2.4	2.6	2.7	12.1
GFATM ELIGIBLE COUNTRIES, BY INCOME STATUS									
Low income	1.8	2.1	2.3	2.5	3.5	3.6	3.7	3.9	23.4
Lower middle income	8.5	9.7	11.4	12.5	16.7	16.4	16.6	17.2	109.0
Upper middle income	1.5	1.6	1.8	1.8	2.4	2.4	2.4	2.5	16.4
Total	11.8	13.3	15.5	16.8	22.6	22.3	22.7	23.6	148.7

WHO REGION									
EMR	0.8	0.8	1.0	1.1	2.1	2.1	2.2	2.3	12.3
AFR	4.7	5.2	6.0	6.8	8.4	8.5	8.8	9.2	57.6
AMR	0.8	0.8	0.9	1.0	2.6	2.6	2.7	2.9	14.4
EUR	1.5	1.4	1.4	1.3	2.8	2.8	2.9	3.0	17.2
WPR	3.1	3.5	4.1	4.4	7.3	7.2	7.4	7.7	44.6
SEA	4.9	5.7	6.8	7.3	9.9	9.6	9.6	9.9	63.8
BRICS (BRA,CHN,IND,RUS, ZAF)									
Total	6.8	7.5	8.6	9.3	14.0	13.7	13.9	14.3	88.1

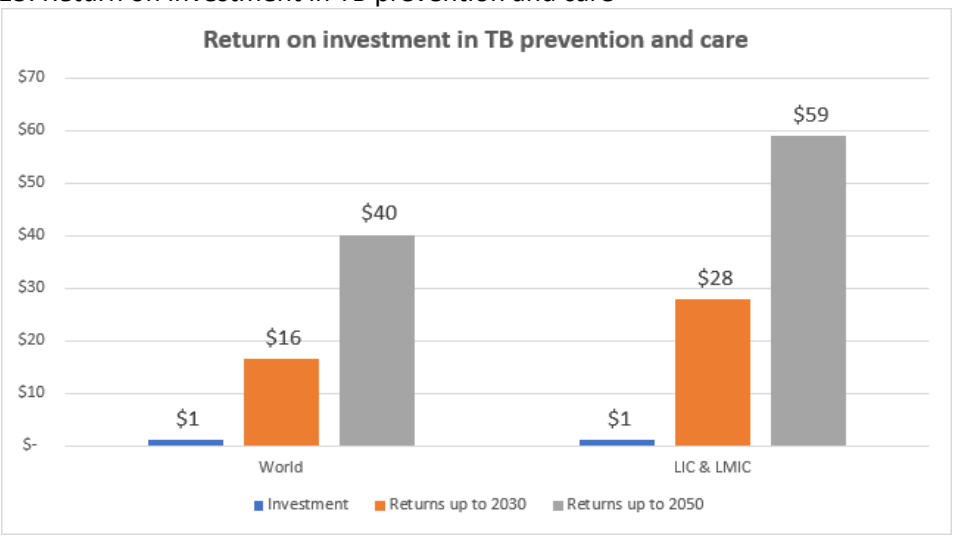
Figure 12. Resource Needs by cost category (USD billions)



Return on Investment

Investing in the TB response provides a global public good. In fact, the work to end TB yields one of the best returns on investment among all of the SDG targets. Fully implementing the Global Plan will yield a return on investment (ROI) of US$ 40 per dollar invested, accounting for economic returns projected to accrue through 2050. Low- and middle-income countries will see an even greater return, with US $59 in economic benefits for every dollar invested. The rationale for projecting ROI through 2050 is to account for long-term projected economic returns of mass TB screening and TB vaccination campaigns that the Global Plan recommends to be implemented between 2023 and 2030.

Figure 13. Return on investment in TB prevention and care



Mobilize US$40.18 billion in funding for TB between 2023 and 2030 for TB R&D and basic science research.

The Global Plan's modeling shows innovation is essential to eliminating TB. Existing tools will have a diminishing impact after 2025 and will no longer be sufficient to bend the incidence curve steeply enough to end the epidemic by 2030.

As Chapter 8 details, R&D of new TB medicines, diagnostics and vaccines is projected to require $33.8 billion from 2023-2030 in order to end TB. Basic science research will require at least an additional $6.4 billion.

The human and economic costs of TB only increase every day the epidemic continues. It is crucial to immediately increase investment in new diagnostics, drug regimens and vaccines in order to avoid these costs. Even if current interventions were fully implemented, a four-year delay in investments in R&D for new tools would still result in millions of additional TB deaths and billions of dollars in additional treatment costs alone (see "Cost of Inaction" later in this section (see Chapter 8).

The massive gap in financing for TB R&D places at risk the whole effort to eliminate TB. In 2020, total TB R&D investment was less than half of the US$ 2 billion needed for that year.[113] This shortfall forces researchers to delay or even halt the advancement of promising candidates and extends research timelines, stifling the creativity, innovation and experimentation needed for the development of new diagnostics, medicines and vaccines. Crucially, the limited resources available for TB research creates disincentives for researchers to enter or stay in the field.

Governments, philanthropic donors (particularly the Bill & Melinda Gates Foundation), and some pharmaceutical industry partners have provided essential funding for TB R&D. In mobilizing new resources, the priority is to keep current TB R&D partners and funders engaged while diversifying the funding base with new donors, investors and private-sector actors.

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[113] https://www.treatmentactiongroup.org/wp-content/uploads/2021/12/tb_funding_2021.pdf

When it comes to allocating resources, the complexities, costs and risks of TB R&D will require multiple funding platforms 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.

The BRICS countries—countries that account for nearly half of the world's TB incidence and have substantial research infrastructure and capacity—have the power to inject significant new resources into the BRICS TB Research Network. Other partners, such as the European and Developing Countries Clinical Trials Partnership[114] and the Japan-based Global Health Innovative Technology Fund,[115] should be further strengthened to increase their capacity for supporting TB R&D. There is opportunity to coordinate efforts strategically among R&D partners globally, with the aim of advancing TB R&D objectives. For example, partners should explore building on the success of pooled funds and replicating the approach for TB R&D.

Given the need to greatly increase funding for TB R&D, potential for a TB R&D fund that brings together multiple donors or entities to pool funding, coordinate efforts and resources, and share risks must also be fully explored. An ad-hoc expert group convened by Stop TB Partnership will be a valuable first step in addressing the desirability, feasibility, institutional mechanism and scope of such a fund.

Box: A "fair shares" framework for closing the TB R&D funding gap

In the 2018 UN Political Declaration on TB, governments committed to closing the TB R&D funding gap by "ensuring that all countries contribute appropriately to R&D." One approach to ensuring all countries contribute appropriately is to establish an expectation that countries with the greatest capacity to invest and countries with the most benefit to gain from new TB tools each devote an equal proportion, or "fair share" of their total gross domestic expenditures on R&D (GERD) to TB R&D. The TB R&D funding gap could be closed quickly and equitably if governments followed this approach. In 2020, only one government–the United Kingdom–invested more than 0.1% of its GERD in TB R&D, meaning governments have substantial room to

[114] https://ec.europa.eu/info/research-and-innovation/research-area/health-research-and-innovation/edctp_en

[115] https://www.ghitfund.org/

increase funding for TB R&D within the context of their overall R&D expenditures.[116]

Box: TB R&D Innovative Financing Partners

UNITAID
Unitaid is one of the largest sources of innovative financing for TB R&D.[117] Unitaid funds late-stage development TB medicines and diagnostics, is an important source of funding for R&D for pediatric TB, and addresses market barriers to accelerate the introduction of new tools. Unitaid is also one of the world's largest funders of TB operational research. The main source of Unitaid's initial funding came from a small tax on airline tickets purchased in 10 countries.[118]

a4i
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. The fund focuses on:

1. Pivoting the TB care model to become more digitalized, virtual and on-demand in order to make it as 2. convenient as possible for people to access and receive quality, affordable care.
3. Catalysing the rapid roll-out of new TB and global health innovations Unlocking new funding and capital from both public and private sector investors.

The cost of inaction

One way to conceptualize the importance of up-front investment in new tools is to estimate the cost of inaction.[119] In other words, what will the negative

[116] https://www.treatmentactiongroup.org/resources/tbrd-report/tbrd-report-2021/

[117] Tuberculosis research funding trends 2005–2017. New York: Treatment Action Group; 2018. http://www.treatmen-tactiongroup.org/content/tbrd2018?eType=EmailBlast- Content&eId=7dac4161-dc99-43a2-9447-4d18aeb4c8ac-overlay-context=content/tbrd2018

[118] Cameroon, Chile, Congo, France, Guinea, Madagascar, Mali, Mauritius, Niger, Republic of Korea.

[119] 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

consequences be if the world fails to fully fund implementation of the Global Plan?

Using even conservative assumptions, the estimated cost of inaction would be tremendous (Figure XXTK). Over eight years (2023-2030), the total cost of inaction is expected to result in an additional 43 million people developing TB, with 6.6 million additional TB deaths and a global economic cost of US$ 1 trillion. Humanity would lose a projected 234 million disability-adjusted life years (DALYs). (See Appendix TK for discussion of methodology and assumptions.) The global community can avoid these consequences by investing in a rapid scaling up of public health interventions using currently available tools (i.e., treatment regimens, diagnostics) and accelerating the research and development of new TB tools.

These figures break down as follows:

By 2030, failure to fully scale up current interventions in line with the Global Plan would result in:

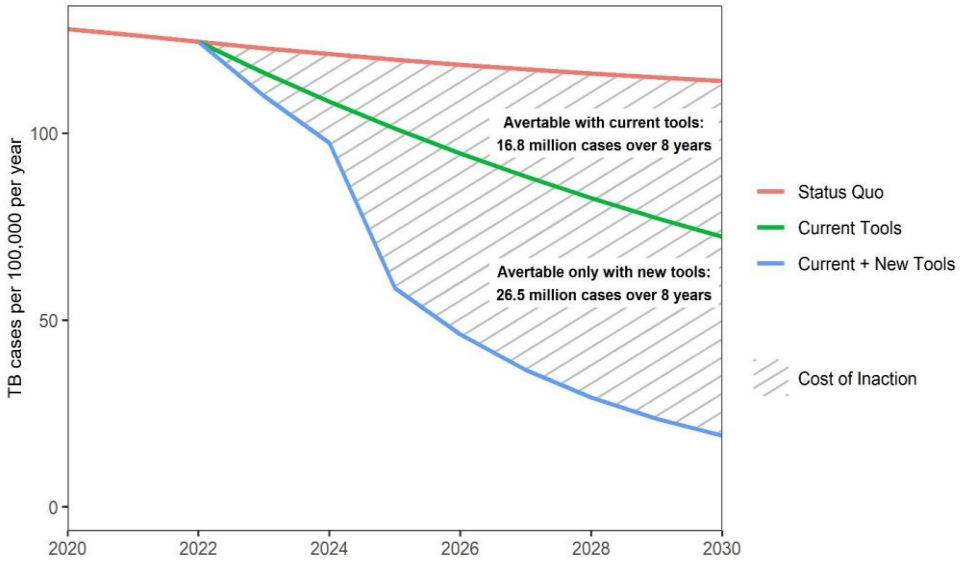
- 16.8 million additional people sick with TB
- 3.8 million additional TB deaths
- 133 million incremental TB-attributable DALYs
- $20 billion in TB treatment costs
- $645 billion in lost productivity

This impact represents the ceiling of what can be achieved without new tools. Even if current interventions were fully implemented, a four-year delay in investment in R&D for new tools would still result in (US$):

- 26.5 million additional people sick with TB
- 2.8 million additional TB deaths
- 101 million incremental TB-attributable DALYs
- $31 billion in TB treatment costs
- $487 billion in lost productivity

Figure 14: The potential human cost of failing to implement the Global Plan 2023-2030.

2022, but failed to make the necessary investments in new tools between 2020 and 2025.



Diversify the base of funding for TB implementation and R&D.

Implementing the Global Plan is going to take increased support from current partners plus the nurturing of a range of new partners. There are three broad sources of funding for implementation and research and development–domestic funding, international funding, and innovative financing–each with multiple mechanisms for mobilizing resources, representing an even larger pool of potential new partners for the TB community to nurture.

Table 21. Sources of TB funding and potential mechanisms

Type of funding source	Funding mechanisms	Key partners
Domestic sources	National and subnational budgets, social health insurance, increased TB programme efficiencies	Ministry of health, ministry of finance, national and subnational TB programmes, HIV programmes, health insurers, social protection programmes
International/Multilateral	International financing mechanisms, development banks, corporate social responsibility, private philanthropy, product development partnerships	WHO, Stop TB Partnership, Global Fund, UNICEF, BRICS TB Research Network, European and Developing Countries Clinical Trials Partnership,

		Global Health Innovative Technology Fund, World Bank, InterAmerican Development Bank, Asian Development Bank, Bill & Melinda Gates Foundation, Children's Investment Fund Foundation, TB Alliance, FIND, TBVI, IAVI, pharmaceutical companies, biotech companies, the Giving Pledge
Innovative finance	Impact bonds, blended finance, micro-levies, taxes, pooled donor trusts, corporate social responsibility	Stop TB Partnership, Unitaid, HEAL Fund, Wellcome Trust, Bamboo Capital Partners, UBS Optimus Foundation, Agbami Partners, India Health Fund

Mobilizing domestic funding

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 people with TB that are hospitalized, and reducing hospitalization times. Other middle-income, high-burden countries could expand care cost-effectively by further integrating TB care into general health services.

However, scaling up to a comprehensive response will only be possible if countries dedicate specific budget lines to TB and increase these budget lines. South Africa, India and Indonesia are examples of countries that have done this and have the potential to do more. In recent years, India quadrupled its domestic budget for TB and Indonesia tripled its domestic budget, driven in both cases by high-level political commitment. Such dramatic increases are needed in several middle-income and high TB burden countries.

The economic realities are very different in low-income countries (LICs). TB programmes in most LICs depend on external financing. Meanwhile, large parts of TB budgets currently go unfunded. Programmes in these countries

need increased funding through a variety of sources, including grants and concessionary loans from development banks.

To determine how to finance the efforts outlined by the Global Plan, each country's circumstances must be considered. 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 play a role in advocacy and monitoring domestic funding for TB.

Increasing the efficiency of TB programmes

It is not enough to increase funding. Funding also needs to be allocated and used more efficiently. The goal should be to streamline delivery of the most cost-effective interventions to target populations in the highest priority areas. As TB nears elimination, resources should support and enable shifts in strategy. The challenge is to improve efficiency without sacrificing access, quality of programs or quality of care.

Examples of actions countries can take to make programmes more efficient include:

- Invest in a comprehensive strategy for TB elimination (see Chapter 2).
- Use data analytics to guide resources toward interventions that will have the most impact.
- Invest in newer technologies for screening and diagnosis.
- Procure medicines and other products from the Global Drug Facility.
- Use social contracting with local NGOs to deliver people-centred services within communities.

Covering TB service costs with social health insurance

Social health insurance (SHI) is a mechanism by which funds within countries can be raised and pooled to finance health services.[120] In a number of country SHI programmes, employees and their employers contribute to a package of services available to the insured and their dependents. Many governments subsidize SHI programmes to ensure sustainability.

[120] 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/

Contribution requirements are progressive in SHI programmes. Higher income people contribute more than people with low incomes, and people living with illness do not pay more than people who are healthier. Some governments have extended insurance coverage for people with little or no income by meeting or subsidizing their contributions. The SHI approach can help mobilize significant resources for TB elimination, while promoting equity in the health system and helping people avoid catastrophic costs.

TB programmes must seize the opportunity to include TB care in the package of coverage provided by SHI. SHI programmes should provide coverage for all TB services delivered by both public and private health systems. Efforts should also be made to ensure that SHI schemes are inclusive and provide coverage to key populations, such as migrants. For financing UHC, wherever governments introduce 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 include TB services within such health financing approaches.

International funding

Official development assistance and multilateral funding will remain critical sources of international funding for TB efforts–and critical targets for advocacy. Goal 17 of the Sustainable Development Goals calls on developed countries to fully implement their commitment to devote 0.7% of gross national income (GNI) for official development assistance (ODA). Advocating for increasing ODA for TB prevention, care and R&D–either through bilateral programs or for multilateral efforts–is a vital priority in line with this goal.

The Global Fund remains the single largest international source of funding for TB efforts and will remain a vital source of financing for the foreseeable future. Because the majority of funding contributions to the Global Fund come from governments, advocacy is critical to ensuring that the Global Fund remains fully funded and able to meet country demands for support. For Global Fund-eligible countries, the total resource needs for the 2024-2026 Global Fund replenishment cycle is US$15.2 billion per year. Even in a scenario of full replenishment of the Global Fund, however, eligible countries will be left with significant gaps in their national TB budgets based on actual funding needs.

TB kills more people than HIV and malaria put together, and yet the Global Fund has historically provided the lowest proportion (18%) of its resources to

TB. For the 2023-2025 funding cycle, the Global Fund will allocate marginally more resources to TB contingent upon an unprecedented higher level of Global Fund replenishment. Advocacy efforts by TB stakeholders for more equitable distribution of funds between the three diseases in the portfolio of Global Fund has not met with success. The Global Plan therefore calls for new external financing instruments for TB care and prevention, without which TB cannot be ended in LICs and LMICs.

Loans from development banks, including loan buydowns, blended loan-grant financing and converting debt into grants

The World Bank and other regional development banks provide loans that can make substantial resources available for TB elimination. Some TB programs have used these kinds of loans for several years.

More recently, innovative approaches have been used to blend loans and grants from different sources, making borrowing more attractive and less expensive to countries. One such approach is to use grants from the Global Fund, bilateral donors or the private sector to pay down interest on loans from the World Bank or regional development banks. This is called a "loan buydown." For example, the Government of India accessed a World Bank loan of US$ 400 million for its TB programme, and the interest amounting to about US$ 40 million was paid by the Global Fund.[121]

Another approach is to incentivize countries to access loans from development banks by blending loans with grants provided by other donors. For example, the Asian Development Bank and the Government of Japan have a mechanism through which countries can access blended loan and grant financing.

A "debt swap" is another approach of converting loans into grants. For example, Indonesia did this through an agreement with Germany.[122]

It is critical that TB programmes communicate their resource needs to their country's Health and Finance Ministers, so that those needs can be raised in discussions with the World Bank and regional development banks when discussing the country's broader development financing needs.

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[121] https://www.worldbank.org/en/news/press-release/2019/06/27/tuberculosis-india-world-bank-loan

[122] https://www.theglobalfund.org/en/news/2021-04-14-indonesia-germany-and-global-fund-sign-new-debt-swap-agreement-to-fight-tb/

Private philanthropy

Private philanthropy is a largely untapped source of TB financing. Opportunities for pursuing private philanthropy have opened up as a result of the 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 has been an untapped source of funding for TB.

Innovative financing

Global health has a strong track record of developing innovative financing mechanisms. The Global Fund and Unitaid, for example, have developed innovative approaches to mobilizing, pooling, channeling, allocating and implementing resources to direct large amounts of funding rapidly to LMICs and LICs.[123] These innovative financing mechanisms have potential to play an even bigger role in the fight against TB.

Innovative financing mechanisms already being explored in global health R&D must continue to be assessed to determine their suitability for supporting TB R&D, including matching funding schemes, public-backed bonds to raise TB R&D capital, advance market commitments (for new TB vaccines) or competitive programs seeking to fund the most promising R&D leads. One type of pull mechanism that could be replicated is the U.S. FDA's Tropical Disease Priority Review Voucher Program.[124] The FDA grants these vouchers to companies that work on discovering drugs for neglected diseases. A company holding a voucher can receive expedited regulatory review for new drug candidates. The vouchers are valuable and can be sold on the secondary market.[125]

Impact bonds

Impact bonds are a financial scheme where investors pay in advance for interventions, with an agreement to achieve specific results. Investors then

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[123] 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

[124] https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/tropical-disease-priority-review-voucher-program

[125] Noor W. Placing value on FDA's priority review vouchers. In Vivo. 2009;27(8):1–8.

work with delivery organizations to ensure those results are achieved. As part of the arrangement, outcome funders (i.e., governments and/or donors) agree to pay the investors if the interventions succeed.

In this sense, impact bonds are similar to other results-based approaches, but with capital provided up front. 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, treatment and prevention in high-burden communities.

These activities would have both social and financial benefits. The social impact would be generated from the reduced incidence of TB and the increased productivity of a population. 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.[126]

Blended finance

Blended finance is an approach where governments help to free up investment from the commercial sector by providing guarantees that lower the risk involved in making those investments. This approach is especially suited for LMICs and emerging markets where higher risk has limited the availability of resources from commercial finance.

The Stop TB Partnership has entered into an agreement with Bamboo Capital Partners to co-launch the HEAL fund, a blended finance fund to deploy both public and private sector capital to innovators developing health technologies that can address TB and other communicable and non-communicable diseases

[126] Innovative financing for global health R&D. Santa Monica: Milken Institute; 2012. http://assets1c.milkeninstitute.org/assets/Publication/InnovationLab/PDF/FIL-Global-Health-Report.pdf

in LICs and emerging markets, and to provide the necessary product roll-out support.[127]

Micro levies/taxes

The most cited example of a micro levy for TB is a small tax on airline ticket purchases. Started in 2006 in France, the tax is now collected from airline tickets purchased in Cameroon, Chile, Congo, Madagascar, Mali, Mauritius, Niger and the Republic of Korea. The funds raised support Unitaid in purchasing treatments for HIV, TB and malaria. Supported in part through a tax of around US$ 1 for an economy-class ticket and US$ 40 for a business-class seat, Unitaid helps countries introduce and scale up the use of innovative health technologies and solutions (see Box). There are numerous other areas where micro levies could be established, particularly in areas involving extractive industries and the financial sector.

Pooled donor trusts

Pooled donor trusts distribute grants to organizations to meet defined social outcomes. Their main feature involves a multi-donor approach, which aims at better coordinating funding for programmes, while raising awareness for issues that need national or global 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 in order to receive support.

Corporate social responsibility (CSR)

CSR is a mechanism for businesses to be socially responsible by contributing to social, health and environmental causes in areas where they operate. Large corporations and businesses operating in high TB burden countries need to be

[127] https://pro.stoptb.org/news/stop-tb-partnership-and-bamboo-capital-partners-to-re-imagine-tb-care-deploying-blended-finance

engaged and encouraged to invest in TB. In the past, oil companies in Nigeria (Agbami Partners) have built, equipped and donated TB clinics to the government. Corporations in India (e.g., the India Health Fund established by Tata Trusts) and Indonesia have also increased their support for TB elimination through CSR initiatives.

Mobilize action through stronger TB advocacy and strategic communications

As COVID-19 demonstrated, policy makers will make resources available for global public health when they understand the matter is an urgent priority for their populations. Governments have likewise made historic commitments to end TB. Holding governments accountable for investing the resources necessary to fulfill those commitments is going to take a much stronger advocacy effort driven by TB survivors and affected communities; civil society coalitions of advocates, scientists and public health experts; and their allies.

Expand the presence of advocates focused on TB resource mobilization

Funders who are interested in supporting efforts to end TB can multiply the impact of their resources by funding more advocates to mobilize TB resources from governments, multilateral institutions and other sources. There are established TB advocacy coalitions devoted to mobilizing TB resources from key donor countries and from governments of high-TB-burden countries–but there is space to replicate these approaches in many other countries. Advocates focused on mobilizing TB resources closely track TB and national research budgets and funding allocations year to year. This can be a complex task that sometimes requires getting governments to establish new approaches to budgeting or to identifying and quantifying funds that are used to support TB interventions and R&D. Successful approaches show that by developing relationships with finance officials inside of governments and institutions, advocates can monitor TB resource flows, providing critical information that informs advocacy.

Engage more TB survivors and affected communities as advocacy leaders

People directly affected by TB have lived experience and are an essential kind of expert who is vital to TB advocacy. TB survivors can fulfill a role in TB advocacy that no one else can: they can ground the TB narrative in human, experiential terms that others can understand and relate to on a deep emotional level.

TB survivors and affected communities have assumed a more prominent role in TB advocacy in recent years, working as partners with full-time TB advocates, public health experts and members of the scientific community. Supporting the growth and capacity of TB patient networks is especially critical to communicating more persuasively with policymakers, building greater TB awareness among the general public, and holding governments accountable for fulfilling TB commitments.

Broaden engagement with government officials

Members of parliament (especially those sitting on relevant committees responsible for budgeting, health, regulatory, science and technology research, even national defense) 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. Advocates can partner with the Global TB Caucus, which provides the TB advocacy and research communities with an entry point to parliamentary engagement in more than 130 countries.

TB advocacy has for a long time focused on advocating for ministries of health to prioritize TB. Other ministries need to be engaged with equal focus, including finance, science and technology, labour and regulatory committees, which are essential to mobilizing resources, supporting programmes and initiatives that reach communities with TB services, addressing underlying determinants, and seeing governments adopt and scale up the use of new TB tools and technologies.

Increase TB's visibility in the news media

Earning coverage of TB issues in the news media is one of the most important ways of maintaining a sense of urgency surrounding the need to end TB. More opportunities need to be made available for TB survivors and affected communities, research scientists and public health experts to receive training on how to effectively communicate with the news media. Media engagement should be explored routinely in the lead up to the publication of important new research studies, policy reports and other key moments, such as scientific conferences and policy events where TB is on the agenda. Opinion media provides additional opportunities for communicating newsworthy insights that can inform the TB response.

Improving advanced coordination between advocates, researchers, TB survivors and affected communities can help to ensure that earned media coverage of TB is used effectively for advocacy purposes. Sharing media coverage with policymakers at all levels is an effective way of disseminating insights and keeping them up-to-date on progress and challenges in the TB response.

See Chapter 8 for discussion of advocacy needed to accelerate TB R&D.