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ARTICLE

One Million Lives Saved Per Year: A Cost–Benefit Analysis of the Global Plan to End Tuberculosis, 2023–2030 and Beyond

Carel Pretorius[1], Nimalan Arinaminpathy[2,3], Sandip Mandal[1], Suvanand Sahu[4], Madhukar Pai[5], Roland Mathiasson[6] and Brad Wong[6,7]

[1]Avenir Health, Glastonbury, USA
[2]MRC Centre for Global Infectious Disease Analysis, School of Public Health, Imperial College London, London, UK
[3]The Jameel Institute, School of Public Health, Imperial College London, London, UK
[4]Stop TB Partnership, Geneva, Switzerland
[5]Epidemiology & Global Health, McGill University, Montreal, Canada
[6]Copenhagen Consensus Center, Tewksbury, USA
[7]Mettalytics, South Golden Beach, Australia
Corresponding author: Brad Wong; Email: brad@copenhagenconsensus.com

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Abstract

This report presents a cost–benefit analysis of increased spending on tuberculosis (TB) using impacts and costs drawn from the Global Plan to End Tuberculosis, 2023–2030. The analysis indicates that the return on TB spending is substantial with a centrally estimated benefit–cost ratio (BCR) of 46, meaning every US$ 1 invested in TB yields US$ 46 in benefits. Alternative specifications using different baselines, interventions, cost profiles, and discount rates still yield robustly high BCRs, in the range of 28–84. This report also shows that TB investment would avert substantial mortality, estimated at 27.3 million averted deaths over the 28-year period between 2023 and 2050 inclusive: almost 1 million averted deaths per year on average. Accounting for all estimated direct and indirect costs, the cost per averted death is slightly over US$ 2000. Interventions to address TB represent exceptional value-for-money.

1. Introduction

Decades of effort and resources have seen the burden of tuberculosis (TB) fall steadily across low- and lower–middle-income countries (LLMCs).[1] From 1990 to 2019, the incidence of TB in these countries fell from 285 cases per 100,000 to 176 cases per 100,000, while deaths

[1] Unless otherwise stated, figures with respect to incidence, funding, and intervention parameters are for low- and lower–middle-income countries.

fell from 63 per 100,000 to 46 per 100,000 (IHME, 2021). Despite these steady improvements, TB remained the world's most deadly infectious disease before the COVID-19 pandemic. Emerging evidence from 2020 and 2021 indicates that COVID-19 has worsened the burden of TB across LLMCs (Stop TB Partnership, 2022). The number of people with undiagnosed and untreated TB went up, with an 18% decrease in TB notification between 2019 and 2020, from 7.1 million to 5.8 million. There was partial recovery in 2021, to 6.4 million TB notifications. As a result, deaths from TB increased in 2020, and deaths as well as incidence increased in 2021, reversing declining trends in both deaths and incidence observed over the previous years (WHO, 2022*b*).

Interventions to address TB have consistently yielded very high benefit–cost ratios[2] (BCRs) in Copenhagen Consensus' previous global- and country-level projects. For example, the central BCR for the *Post-2015 Consensus* project was 43 (Vassall, 2014). In India, interventions to address TB yielded BCRs more than 100 (Arinaminpathy, 2018*a*, *b*). For Ghana, BCRs ranged from 38 for active case finding to 190 for adherence counseling (Rudman *et al.,* 2020).

The underlying logic for these extremely high BCRs can be straightforwardly explained: TB has a high mortality rate if untreated and spreads easily to others via the airborne route. The WHO reports that 45% of those who contract TB will die if untreated, which rises to almost 100% over a long disease period if the person also has HIV/AIDS (WHO, 2022*b*). Treatment is effective and inexpensive, with the median cost for a standard regimen of 6 months treatment for drug-susceptible TB equaling US$ 300–500 in LLMCs (Siapka *et al.,* 2020).[3] Moreover, treatment acts as prevention, potentially stopping 5–15 onward infections per year (WHO, 2022*b*).

Relative to a hypothetical scenario where there is no treatment, providing US$ 500 of TB medicines to avoid a 45% chance of death for the individual plus one onward infection would yield a BCR of approximately 300 at the value-of-statistical-life used in the *Halftime SDG Series.* Of course, treatment cannot avert infections that occur before diagnosis, and there are additional costs for diagnosis, case finding, adherence incentives, and patient costs. In addition, a realistic counterfactual is unlikely to be the absence of treatment. Nevertheless, this stylized example shows that the maximum BCR for TB treatment is very large, and there is ample room to add more costs or to lower incremental benefits and still yield a very large return on investment.

Congruent with the aims of the *Halftime SDG Series*, the purpose of this report is to estimate the BCR of a substantial, marginal increase in spending to address TB for LLMCs. To do this, we would ideally draw from a global model that generates incremental costs and impacts of various intervention combinations to not only estimate BCRs but also identify the highest returning package among a set of plausible options. Unfortunately, no such optimization model exists for TB at a global scale.

The most recent global modeling exercise for TB is that conducted for *The Global Plan to End TB, 2023–2030*, hereafter the *Global Plan* (Stop TB Partnership, 2022). The *Global Plan* provides aspirational scenarios to reduce the number of TB deaths and the TB incidence by 90% and 80%, respectively, by 2030 relative to 2015 in line with the UN's Sustainable Development Goals. The *Global Plan*, commissioned by the Stop TB partnership, is a collaborative and inclusive document, developed with the input of numerous partners (including the Copenhagen Consensus), stakeholders, and experts over the course of almost

[2] Benefit–cost ratio = Net present value of benefits/net present value of costs

[3] Siapka *et al.* (2020) include numerous studies where patients were provided treatment in in-patient settings. The costs therefore might represent values on the upper end of a potential range.

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2 years. The plan calls for scaling up existing tools for addressing TB—such as molecular diagnostics and approaches for early case finding—as well as funding and deploying innovations, such as digital adherence tools and a new vaccine over the period 2023 to 2030. The *Global Plan* reports that US$ 250 billion in funding would be required between 2023 and 2030 to implement the plan, leading to 6.6 million averted deaths and 234 million averted disability-adjusted-life-years (DALYs).

The current analysis takes the *Global Plan* modeling as the starting point to conduct benefit–cost analysis for the *Halftime SDG Series.* While it was not constructed as an optimization exercise, it can provide insight into a plausible range of BCRs for increased funding to TB. We report the results of funding the entire *Global Plan*, and an alternative scenario where insufficient resources prevent developing and deploying a new vaccine. The primary baseline used to assess marginal benefits and costs is one where TB burden follows the steady downward trajectory prior to the COVID-19 pandemic, without any assumed disruption in TB notifications and treatment after 2022. This baseline assumes TB services have recovered fully during 2022 and reverted to pre-pandemic trends. We also demonstrate how results change using a "disruption" baseline that models a pathway where reduced notifications during the pandemic are not reversed. In this case, TB incidence reaches a new, higher level and grows rapidly. Following the rest of the *Halftime SDG Series*, we focus on results in LLMCs. While the *Global Plan* has a focus on the period 2023–2030, we model all results out to 2050 to capture the full impacts of the interventions.

In our main specification (*Global Plan* with no vaccine funding compared to the standard baseline), an extra US$ 4.4 billion is required in 2023, with incremental costs peaking in 2027 at US$ 7.1 billion. Thereafter, incremental resources needed fall with reductions in TB incidence. In 2030, incremental costs total US$ 5.2 billion, and in 2050, an extra US$ 2.6 billion is required. Importantly, these costs include health system costs and substantial markups beyond patient costs such as program costs and enablers, meaning they are likely to represent long-term resource needs.

With this funding, incremental averted cases and deaths are 370,000 and 85,000, respectively, in the first year and continue rising over time. By 2030, LLMCs see 4.5 million fewer cases and 906,000 fewer deaths compared to a standard baseline (Figures 1 and 2). By 2050, there are 8.0 million fewer incremental cases and 1.4 million fewer incremental deaths. The BCR of the main specification (*Global Plan* with no vaccine funding scenario compared to standard baseline) is 46. The BCR of the *Global Plan* with no vaccine funding compared to a disruption baseline is higher at 71. The full *Global Plan* BCR, with new vaccines compared to a standard baseline, is lower at 37.[4] Other sensitivity analyses are conducted with BCRs ranging from 28 to 84. In all specifications, the BCRs place TB spending as one of the highest returning investments in global health and development. In our preferred specification, 27 million deaths are averted over a 28-year period, making TB investments one of the most consequential in reducing human death and suffering of all the *Halftime SDG Series* analyses.

2. The Global Plan to End TB, 2023–2030

The *Global Plan* is a collaborative document that was developed over 2021 and 2022. The aim of the plan was to identify and model interventions that would end TB as a public health

[4] The results reported in this study differ slightly from the *Global Plan* due to differences in the time-period considered, and this study focuses on low and lower-middle-income countries only.

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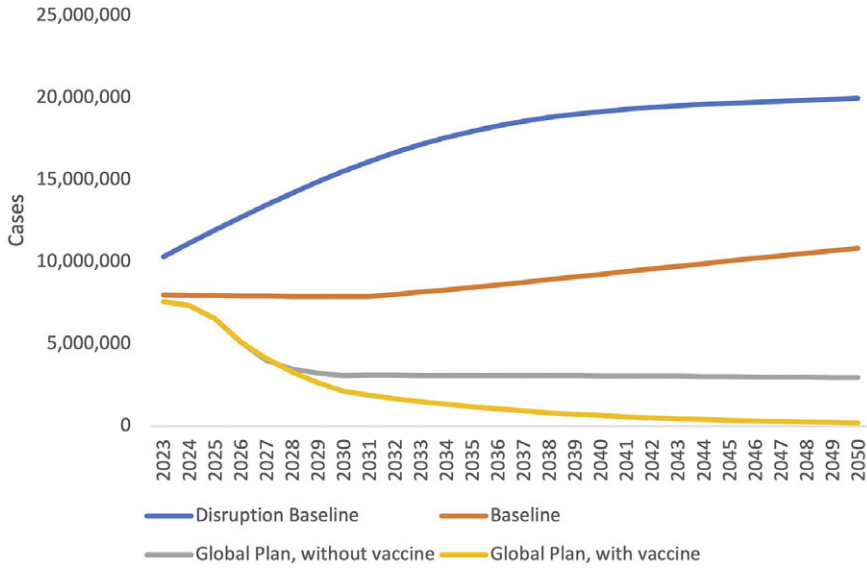

Figure 1. *TB cases under baseline and Global Plan scenarios.*

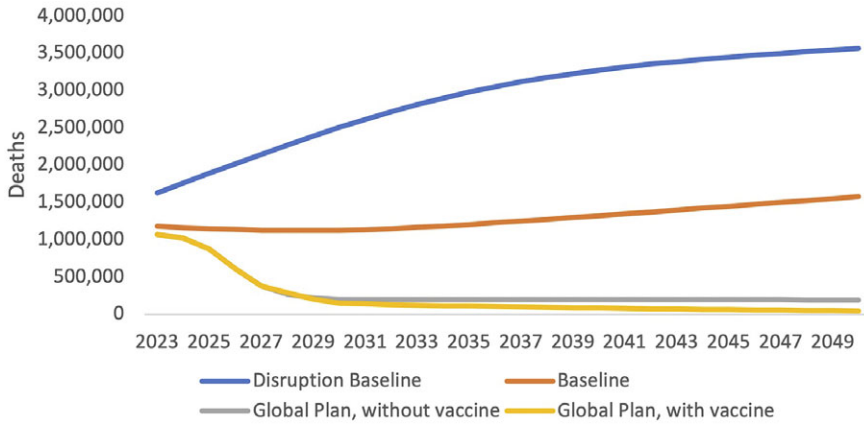

Figure 2. *TB deaths under baseline and Global Plan scenarios.*

challenge by 2030, defined as a reduction in number of TB deaths and TB incidence per 100,000 by 90% and 80%, respectively, relative to 2015.

The *Global Plan* calls for a series of major activities, each with multiple interventions:

1. *Scaling up TB diagnosis and care* such as modern diagnostics, integration of screening and testing with other health services, expanding screening for early detection of TB, and support for patients to avoid catastrophic costs.
2. *Scaling up TB prevention* such as preventative treatment for contacts and those living with HIV, airborne infection prevention and control, addressing risk factors for TB, and deploying a new vaccine.

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3. *Partnering with key stakeholders: the community and private sector*, including supporting community-based and home-based models for delivering TB prevention and care, and scaling up public–private mix approaches to improve the quality of TB care.
4. *Ending TB through universal health coverage, pandemic preparedness and response, and socioeconomic actions* including expanding access to TB services through universal health coverage initiatives and positioning the TB response at the center of pandemic preparedness and response efforts.
5. *Considering human rights, stigma, gender, and key and vulnerable populations including* positioning universal human rights as the foundation of the TB response, eliminating TB-related stigma and discrimination, and ensuring that TB interventions are gender sensitive and gender transformative.
6. *Accelerating development of new TB tools* including investing, at minimum, US$ 5 billion annually to accelerate the R&D of new TB diagnostics, medicines, and vaccines, developing a new TB vaccine by 2025, and investing at least US$ 800 million annually in basic science research.

A full list of interventions can be found in the *Global Plan.* The total undiscounted funding requirement is reported as US$ 250 billion across 2023 to 2030 with approximately US$ 210 billion for service delivery and US$ 40 billion for R&D.

With these interventions, epidemiological modeling projects that the *Global Plan* would drive down cases and deaths with a particularly rapid decrease between 2025 and 2028. Across 2023–2030, the *Global Plan* predicts 43 million averted cases, 6.6 million averted deaths, and 234 million averted DALYs.

3. Description of scenarios and modeled impacts[5]

3.1. Baseline scenarios

Two baseline scenarios were adopted for this analysis. The need for two baseline scenarios reflects uncertainty over the expected short- and long-term impacts of potential disruptions to TB care brought about by the COVID-19 pandemic and the speed of recovery from these disruptions.

The first baseline, or the "standard baseline," reflects historical experience with TB prior to the COVID-19 pandemic. The disruptions that occurred during the pandemic are assumed to be reversed. Assumed spending in the baseline is relatively constant, ranging between a narrow band of US$ 6.3 to US$ 6.9 billion (constant US$ 2020) between 2023 and 2050. This somewhat reflects historical trends of TB spending over recent years (sources: IHME (2021) and *Global Plan*, WHO (2022*a*, *b*). Figures are reported in constant 2020 US$.).[6] In

[5] In this section, we report the methods and results of the baseline and intervention scenarios that were drawn from the prior analysis conducted for the *Global Plan.* For the purposes of the benefit–cost analysis, these were taken as given.

[6] Estimated historical spending in low- and lower–middle-income countries is the sum of relevant country TB budgets from WHO (2022*a*, *b*) plus out-of-pocket (OOP) expenditures from IHME visualizer Financing Global Health (IHME, 2021). The intervention scenarios include payments to cover direct patient costs, and therefore, a fairer comparison against historical government budgets requires the addition of OOP expenditures. Last, intervention scenarios also include above patient costs that are not included in the historical spending data.

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the short run, TB incidence follows the slow, almost flat trajectory seen since the mid-2010s. Annual absolute changes in incidence are no greater than 0.25% per year, up to 2030. However, with a growing population, funding is unable to keep TB incidence at a steady state, and TB cases and deaths begin to increase steadily until 2050. In 2050, there are an expected 10.8 million cases and 1.6 million deaths (Figures 1 and 2).

In the second baseline, known as the "disruption baseline," TB service delivery fails to recover to pre-COVID levels. Under this assumption, the model predicts that in 2023, cases are 30% higher than in the standard baseline, around 10.3 million, with deaths at 1.6 million. Due to insufficient service provision, TB cannot be contained, leading to a rapid rise in incidence and TB mortality. By 2030, cases are at 15.5 million with 2.5 million deaths. By 2050, cases are at 20.0 million with 3.6 million deaths. This scenario requires reduced funding being made available to overcome the TB burden. This baseline can be construed as a plausible "worst-case scenario" for TB until the middle of the century.

In this report, we focus more on results using the standard baseline. We also report comparisons to the disruption baseline.

3.2. Intervention scenarios

Two intervention scenarios are considered in this report. The first scenario includes all the elements of the *Global Plan*, except the new vaccine. This implies the use of existing tools, and some new, to-be-developed tools such as improved diagnostics and medicines. The second scenario includes vaccine research and deployment.

The intervention scenarios were constructed to ensure key targets were met. These include

(i) At least 95% of people with TB will receive a TB diagnosis.
(ii) All high-risk and key and vulnerable populations will be able to access periodic screening.
(iii) 50 million people will access appropriate TB treatment, including 4.7 million children and 3.32 million people with drug-resistant (DR-) TB. 35 million people will access TB preventive treatment (TPT).
(iv) At least one new TB vaccine will be introduced for widespread use by 2026 (vaccine scenario only).

The TB Impact and Estimates (TIME) model (Houben *et al.,* 2016) and supplementary modeling work were used to estimate the epidemiological impact of meeting the above targets for each country.

Regarding screening and treatment, screening rates were increased in an S-shaped curve starting in 2023 and ending in 2030. Existing tools were explicitly modeled in TIME predominantly using X-ray screening and rapid molecular tests, generating a sensitivity and specificity of 84.8% and 99.7%, respectively, for systematic screening of household contacts and high-risk groups. For people with HIV who are newly enrolled on antiretroviral therapy (ART) and those who are already on ART, sensitivity was set at 72% and 65% and specificity at 98% and 97%, respectively. Treatment success was increased in the model from 2019 levels (carried to 2023) to 90% by 2030.

The *Global Plan 2023–2030* continues the focus of the previous *Global Plan 2018–2022* on TPT, calling for 100% coverage of contact tracing (for finding TB and offering TPT) in the household of all people diagnosed with bacteriologically positive TB by 2022 and

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onward. Furthermore, it is assumed that all new people taking ART for HIV/AIDS and those already on ART and eligible for TPT will receive TPT. Estimates for the distribution of active and latent TB in adults and children in households of index cases were based on Fox *et al.* (2013). Household size estimates and the percentage of the household under 5 years of age were based on demographic health surveys where available, and a global average was used where not (household size of five and 15% of household members under the age of 5). ART cohort sizes were estimated using the Spectrum AIM model used annually to produce estimates for the *UNAIDS Annual Global Report* on the AIDS pandemic, among other purposes.

The TIME model does not directly model the finding and treatment of subclinical TB or TB prevention through large-scale vaccine programs. Insights into the additional impact of these "new" tools, when added to a program implementing existing tools at full scale, were obtained via supplementary modeling work. This supplementary modeling conducted more detailed analysis of intervention combinations in four focus countries: Indonesia, Ukraine, Uzbekistan, and Kenya, to provide estimates of impacts from new tools. The results suggest that these tools can lead to the achievement of the 2030 impact milestones.[7] Coverage scales up gradually reaching 30% for treating subclinical TB and 60% for a post-exposure TB vaccine by 2030.

The epidemiological impacts in terms of incident cases and deaths from each scenario are depicted in Figures 1 and 2, respectively. The *Global Plan* sees a rapid decrease in both cases and deaths over the 8 years from 2023 to 2030. In 2030, cases are expected to fall to 2.1 million (with vaccine) or 3.1 million (without vaccine). Deaths are expected to fall substantially to 145,000 (with vaccine) or 197,000 (without vaccine) in the same year. From 2030 to 2050; the incidence and mortality profile of the *Global Plan* without vaccine essentially stays in a steady state. The *Global Plan* with vaccine continues a gradual reduction of incident cases and deaths such that in 2050 cases are predicted to be 196,000 with 46,000 deaths.

4. Cost–benefit analysis

The analysis covers the period 2023–2050 with all figures reported in 2020 US$. The analysis assumes a discount rate of 8% following standardized assumptions across the *Halftime SDG Series.* Impacts of different discount rate are assessed in sensitivity analyses. Costs and benefits were estimated at a country level and then aggregated to calculate global and regional values.

4.1. Costs of service delivery

In a departure from previous *Global Plan* exercises, the 2023–2030 *Global Plan* adopts a "normative approach" to TB treatment, meaning that the projected implementation of tools (e.g., diagnostics, medicines) and services (e.g., patient support) is consistent with current and anticipated international guidelines. This approach has allowed for more detailed and complete projections of resource needs with service delivery costs estimated using a bottom-up, ingredients-based approach. Seven types of costs were estimated: diagnosis, treatment,

[7] See *Global Plan* appendix for full details of the supplementary modeling work.

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prevention, health systems, enablers, programs costs, and vaccination costs, with methods differing by type of cost.

Diagnosis, treatment, and prevention costs were estimated by first establishing common TB services including case finding, diagnosis, and treatment. The services are:

(i) Passive case finding, pulmonary TB
(ii) Passive case finding, extrapulmonary TB
(iii) Systematic screening, household and close contacts
(iv) Systematic screening, preventative treatment for household and close contacts
(v) Systematic screening, people living with HIV
(vi) Systematic screening, other key and vulnerable population groups
(vii) Detection of drug resistance and comorbidities (for all patients diagnosed through passive and systemic screening)
(viii) TB treatment regimens and services, 6-month regimen consisting of isoniazid, rifampin, pyrazinamide and ethambutol for two months and then isoniazid plus rifampin for four months (2HRZE/4HR).
(ix) TB treatment regimens and services, 4-month regimen consisting of rifapentine-moxifloxacin regimen for the treatment of drug-susceptible pulmonary TB. (RPT-Mox)
(x) TB treatment regimens and services, rifampicin-susceptible, isoniazid-resistant TB
(xi) TB treatment regimens and services, all-oral shorter regimen
(xii) TB treatment regimens and services, Bedaquiline + Pretomanid + Linezolid (BPaL) regimen
(xiii) TB treatment regimens and services, 18–24-month drug-resistant TB regimen
(xiv) TB treatment regimens and services, delamanid-based regimen (children only)

Next, the primary cost drivers of each service were established including composite interventions (e.g., clinical assessment, X-ray, sputum transportation, etc.), the staff time required to deliver the service, and health system costs for in-patient and out-patient care. Fifty-four separate interventions were identified and costed as part of this exercise. Moreover, service profiles varied according to age, pulmonary status, HIV status, MDR status, and passive versus active TB of patients. Detailed descriptions of these service profiles are reported in the *Global Plan* appendix (Stop TB Partnership, 2022).

Unit costs for the 54 interventions were sourced from the Value TB project (Sweeney *et al.,* 2021). Detailed data were available for five countries: Ethiopia, Georgia, India, Kenya, and Philippines. Unit cost data were then extrapolated to other countries by first determining how much of each profile represented tradeable goods, non-tradeable goods, and labor. The share of tradeable goods was converted using market exchange rates or directly sourced from the latest prices available in relevant procurement catalogues. Non-tradeable goods were transferred to target countries using purchasing-power parity exchange rates. Labor costs were converted using ratios of GDP per capita between the target and reference country (Serje *et al.,* 2018).

For the cost transfer approach:

(i) Georgia was used as a reference for upper–middle-income TB burden countries.
(ii) India was used as a reference for lower–middle-income high TB burden countries in South Asia.

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(iii) The Philippines was used as a reference for middle-income high TB burden countries in the Western Pacific Region.
(iv) Kenya was used as a reference for middle-income high TB burden countries in Africa.
(v) Ethiopia was used as a reference for lower-income high TB burden countries.

Once unit costs were established for each country, costs were applied to expected coverage levels under the intervention scenarios. If costs were unavailable from Value TB (primarily treatment costs), a constant parameter value was assumed for all countries sourced from procurement catalogues such as Stop TB Partnership's Global Drug Facility.[8] Assumptions used in the costing analysis and the methodological approach for each assumption are presented in Table 1.

Health systems costs represent facility-level costs required for in- and out-patient visits across each intervention. Unit costs were sourced from WHO-CHOICE database and are applied to requirements for each service as detailed in the *Global Plan* appendix (Stop TB Partnership, 2022).

Enablers comprise specific "enabling" activities, including direct patient support (5%), advocacy and communications (1%), community rights and gender activities (6%), and public–private management (12% for countries with a high degree of private healthcare sector presence). Enabling costs were estimated as percentage markups on prevention, diagnosis, treatment, and health system costs and were based on the detailed budgets of the Democratic Republic of the Congo, Georgia, India, Philippines, and Tajikistan, which were judged to be representative in terms of budgeting for enabling activities.

Program costs consist of above patient level costs and were also estimated as a percentage mark up on direct services costs. The markup value was based on average expenditure data reported to the WHO and is equal to 70%.

Lastly, *vaccination* costs are assumed to equal US$ 6 per dose (US$ 4 for vaccination and US$ 2 for delivery), requiring two doses per person.

4.2. *Total costs of the* Global Plan

The cost profile of the two different baseline scenarios and two different intervention scenarios is presented in Figure 3.[9]

The baseline requires spending of US$ 6.5 billion over the period of analysis. The disruption baseline assumes US$ 3.0–3.3 billion in spending every year.

The two intervention scenario cost profiles require substantial increases in spending US$ 10.4 billion initially, rising to US$ 12.7 billion by 2026. In 2027, when the new vaccine is assumed to be ready and deployed, the costs for the *Global Plan* with vaccine rise sharply for 4 years to around US$ 18-US$ 19 billion, reflecting the initial rollout to an unvaccinated population. From 2031 onwards, both profiles decline gradually, although they are still several billion dollars more

[8] Not all countries procure drugs through standard international catalogues. For example, the South African government has its own procurement process that results in different drug prices from international catalogues. It is beyond the scope of this paper to consider each country's unique drug procurement process.

[9] Figures differ from those reported in the *Global Plan* because this study considers only low and lower-middle-income countries. Moreover, *Global Plan* figures are reported in nominal US$ while this study reports figures in constant 2020 US$.

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Table 1. *Unit cost values used across 54 interventions in TB modeling in US$.*

Intervention	Method	25th percentile	Median	75th percentile
Sputum smear microscopy (Ziehl-Neelsen or LED Fluorescence Microscopy)	Value TB	2	4.8	16.4
Chest radiography	Value TB	1.4	4.4	31.1
Molecular WHO-recommended diagnostic test	Value TB	14.5	18.9	25.1
Clinical assessment	Value TB	0.1	7.1	85.2
Liquid culture	Value TB	24.2	83.1	303.8
Line Probe Assay-First Line Drugs	Value TB	7.9	55.4	86.5
Urinary lipoarabinomannan test	Value TB	4.1	5.8	13.1
Sputum collection and transportation	Value TB	1.5	3.4	8.3
Computed tomography (CT) scan	Value TB	5.5	25.9	64.3
Serum Glutamic Pyruvate Transaminase test	Value TB	0.6	8.7	37.1
Serum Glutamic Oxaloacetic Transaminase test	Value TB	0.6	8.7	37.1
Renal function test	Value TB	1.6	20.3	97.7
Tuberculin skin tests	Value TB	0.9	3.8	10
Interferon Gamma Release Assay test	Value TB	8.5	17.8	61.8
Diabetes test	Value TB	0.6	2.4	7.1
HIV test	Value TB	2.4	3.9	8.6
Patient counseling	Value TB	0.4	2.1	20.3
Digital adherence technologies/Directly observed therapy	Value TB	0.4	2.1	20.3
Sputum smear microscopy at the end of intensive phase and the end of treatment	Value TB	2	4.8	16.4
Liver function tests	Value TB	2.2	26.5	122.8
Post-TB treatment follow-up for TB disease every 6 months up to 2 years	Value TB	0.4	2.1	20.3
Sputum culture (monthly)	Value TB	7.4	13.2	112.7
Sputum smear microscopy (monthly)	Value TB	2	4.8	16.4
Computer-assisted detection	Constant	1.1	1.1	1.1
Portable digital X-ray	Value TB	1.1	3.5	27.7
Xpert MTB/XDR	Value TB	34.5	68.1	74.1
Line Probe Assay - Second Line Drugs	Constant	63.3	63.3	63.3
Targeted genome sequencing	Constant	63.3	63.3	63.3
Fine needle aspiration cytology	Value TB	0.7	4.1	13.6
Biopsy	Value TB	0.7	22.8	115.8
Ultrasound	Value TB	0.7	4.1	13.6
Gastric aspiration	Value TB	0.7	4.1	13.6

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Table 1. *Continued*

Intervention	Method	25th percentile	Median	75th percentile
C-Reactive Protein test	Value TB	2.9	18.1	83.6
Electrocardiogram	Value TB	1.1	3.5	27.7
Sputum transportation	Constant	10.5	10.5	10.5
2HRZE/4HR (adult)	Constant	45.3	45.3	45.3
2HRZE/4HR (pediatric)	Constant	22.7	22.7	22.7
4 RPT-Mox (adult)	Constant	245.7	245.7	245.7
4 RPT-Mox (pediatric)	Constant	122.9	122.9	122.9
Short all-oral Bedaquiline regimen (9–12 months) Adult	Constant	738.2	738.2	738.2
Long regimen for Drug Resistant-TB (18–20 months) Adult	Constant	1054.5	1054.5	1054.5
Long regimen for Drug Resistant-TB (18–20 months), contains delamanid, Adult	Constant	2003.6	2003.6	2003.6
Bedaquiline + Pretomanid + Linezolid (BPaL) regimen, adult	Constant	949.1	949.1	949.1
Modified BPaL regimen, adult	Constant	949.1	949.1	949.1
Delamanid-based regimen (pediatric)	Constant	949.1	949.1	949.1
Digital adherence (Smart Medication Container)	Constant	9.4	9.4	9.4
3 HP (adult)	Constant	15.8	15.8	15.8
3 HR (pediatric)	Constant	15.8	15.8	15.8
Treatment for isoniazid-monoresistant tuberculosis(adult)	Constant	45.3	45.3	45.3
Treatment for isoniazid-monoresistant tuberculosis (pediatric)	Constant	22.7	22.7	22.7
Inpatient care (for severe adverse drug reactions)	WHO	<1	48.0	1031.7

Note: "Value TB" means that the parameter was converted from the Value TB database using the transfer method described in the text. "Constant" means that a single parameter was used for all countries. "WHO" means that the figures were sourced from the WHO CHOICE model.2HRZE/4HR describes the treatment regimen containing isoniazid, rifampin, pyrazinamide and ethambutol for two months/isoniazid plus rifampin for four months. 4 RPT-Mox describes the four-month rifapentine-moxifloxacin regimen for the treatment of drug-susceptible pulmonary TB. 3 HP describes the regimen for treatment of latent TB infection, consisting of weekly doses of isoniazid and rifapentine for three months.

than baseline spending. The vaccine plan is slightly more expensive than the non-vaccine plan after 2031 to account for vaccinating the new cohorts of unvaccinated Figure 3.

4.3. Benefits

In this cost-benefit analysis, only averted deaths are incorporated as benefits, not averted cases. In a previous cos-benefit analysis, we note that averted mortality comprised nearly all of the benefits (Rudman *et al.,* 2020). Averted mortality is valued using a standardized

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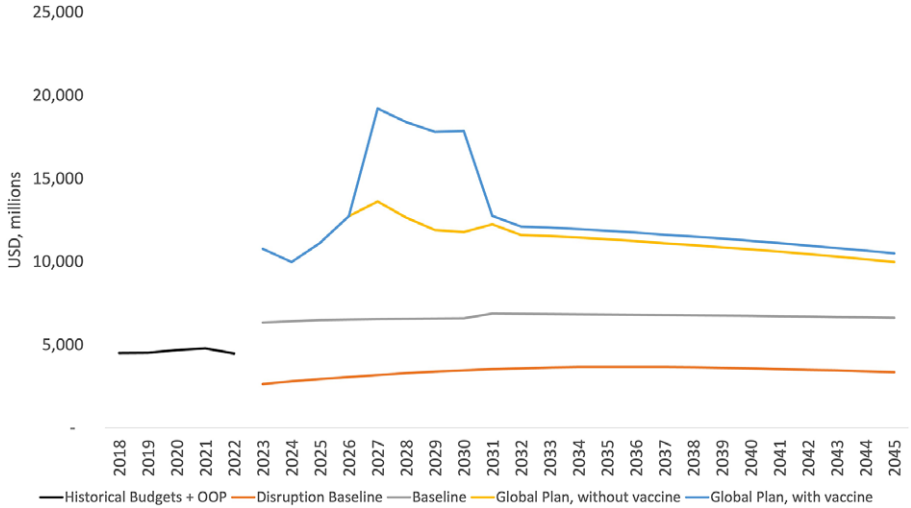

Figure 3. *Cost profile of baseline and intervention scenarios, LLMCs. Sources: IHME (2021) and* Global Plan*, WHO (2022a, b). Figures are reported in constant 2020 US$. OOP = out of pocket expenses*

approach across all *Halftime SDG* papers that follow the recommendations of Robinson *et al.* (2019). Moreover, we do not include other important but difficult to quantify benefits related to promoting partnerships, the reduction of stigma associated with TB, and spillover research benefits beyond the TB sector.

To estimate the value of averted mortality, we take a reference value for the U.S. VSL of US$ 9.4 million (2015 dollars), representing approximately 160 times income as measured by income per capita PPP. This is transferred to the entire low- and lower–middle-income population via the ratio of GDP per capita, using an income elasticity of 1.5.

To estimate these values, we take the population-weighted PPP GDP per capita figure in 2020 US$ for the group of LLMCs and the United States of America and estimate the VSL at time $t = 0$, 2020.

$$VSL_t = \left(\frac{PPP\ GDP\ pc_{LLMC,t}}{PPP\ GDP\ pc_{USA,t}}\right)^{e-1} * 160 * GDP\ pc_{LLMC,t}$$

Following Cropper *et al.* (2019), we estimate each subsequent VSL in the time series according to the following formula:

$$VSL_{t+1} = VSL_t * (1+g_t)^e$$

where g_t is the real GDP per capita growth rate between period t and $t + 1$ (SSP Database, IIASA GDP Model, Scenario SSP2_v9_130219) and $e = 1.5$.

The GDP growth in this group of countries outpaces the population growth, so that the VSL grows rapidly over time. In constant 2020 US$ values, the benefit of an averted death is US$ 98,700 (2020), US$ 149,800 (2025), US$ 212,000 (2030), US$ 276,300 (2035), US$ 338,100 (2040), US$ 396,800 (2045), and US$ 456,000 (2050).

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Table 2. *Benefits, costs, and BCRs of the Global Plan, 2023–2050.*

	Incremental costs (millions, 2020 US$)	Incremental benefits (millions, 2020 US$)	BCR	Cases averted (millions)	Deaths averted (millions)	Cost per death averted
Relative to standard baseline						
Global Plan without vaccines	56,391	2,595,230	46.0	148.8	27.3	2063
Global Plan with vaccines	74,607	2,789,179	37.4	195.9	29.6	2520
Relative to disruption baseline						
Global Plan without vaccines	96,150	6,822,452	71.0	378.7	72.4	1328
Global Plan with vaccines	114,366	7,016,400	61.4	425.7	74.7	1532

Note: Incremental costs and benefits are discounted at 8%. BCR = benefit-cost ratio

4.4. Cost–benefit analysis results

Results of the cost–benefit analysis are presented in Table 2. We present incremental costs, incremental benefits, and BCRs for both scenarios relative to the two baselines. In all specifications, BCRs are high, and the number of averted deaths is large.

In the main specification (without vaccines, standard baseline), incremental costs equal US $ 56.4 billion over 2023–2050 while incremental benefits are a substantial US$ 2,595 billion. The BCR is 46.0. Deaths averted are estimated at 27.3 million over 28 years, at a cost per death averted of US$ 2063. With vaccines, estimated costs are 32% higher, while benefits are 7% higher. The BCR is 37.4 with a cost per death averted of US$ 2520. Comparisons to disruption baseline yield higher costs and substantially higher benefits. BCRs are 71.0 and 61.4 without and with vaccine development and deployment, respectively.

4.5. Sensitivity analyses

In this section, we generate several alternative specifications of costs and benefits to test the sensitivity of results against the underlying assumptions.

We consider four sensitivity analyses:

(i) Including the costs of R&D into the analysis
(ii) Reducing the *Global Plan*'s costs beyond 2035 for the vaccine scenario
(iii) Increasing the discount rate to 12%
(iv) Decreasing the discount rate to 5%

Results of these sensitivity analyses are presented in Table 3. Across all analyses, BCRs remain very high, ranging between 28 and 84.

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Table 3. *Benefit–cost ratios from sensitivity analyses.*

	Main scenarios	Including R&D costs	Lower intervention spending beyond 2035 for vaccine scenario	Discount rate = 12%	Discount rate = 5%
Relative to standard baseline					
Global Plan without vaccines	46.0	34.0	n/a	36.6	55.4
Global Plan with vaccines	37.4	27.7	46.3	29.4	45.6
Relative to disruption baseline					
Global Plan without vaccines	71.0	58.8	n/a	57.5	83.9
Global Plan with vaccines	61.4	49.9	70.1	49.4	73.2

4.6. Including the costs of R&D

The Global Plan includes a substantial funding request for the costs of R&D. We have chosen not to include these costs in the main cost-benefit analysis under the assumption that the costs of R&D will be embedded in the price of the new tools. Including R&D costs likely represents double counting of costs, in the same way that including, for example, the cost of pharmaceutical companies' marketing or employee wages in addition to the price of the new tools would represent double counting. Nevertheless, given that R&D is specifically highlighted in the *Global Plan*, we demonstrate the impact on BCRs from including R&D costs.

Note that the benefits of R&D include an improvement in the efficiency and/or effectiveness of TB management. These have been incorporated into the impact calculations noted previously.

Costs of R&D for TB were estimated by the Stop TB Partnership New Tools Working Group and reported in the *Global Plan.* Total R&D costs for vaccines, diagnostics, treatments, and basic research are estimated at almost US$ 40 billion over the period 2023–2030 (Figure 4).

The *Global Plan* does not specify the time profile of these investments. Moreover, these costs require attribution to LLMCs and our two main scenarios (with and without vaccines). While most TB R&D costs will likely be borne by high-income countries, we attribute these to LLMCs for the purpose of sensitivity analysis and on the basis that these will likely come from budgets earmarked for global health. For the purposes of the cost-benefit analysis, we assume that:

(i) All R&D costs are incurred equally over 4 years in 2023, 2024, 2025, and 2026. This ensures all necessary technologies are ready for deployment in 2027, the first year in which vaccines are included as part of the activity profile.
(ii) Half of the basic research costs and all medicines and diagnosis R&D costs are attributed to the *Global Plan* scenario without vaccines.
(iii) Of these R&D costs, the relevant share for LLMCs is based on their expected case numbers as a share of global case numbers over the period 2027–2050. This equals 83%.

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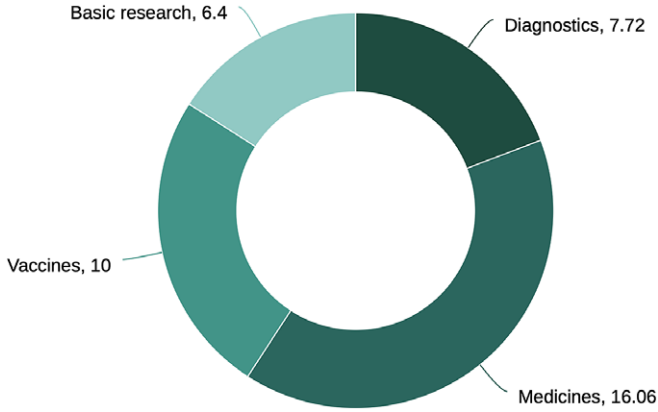

Figure 4. *R&D costs for TB over the period 2023–2030, billions of US$. Source: Global Plan to End TB 2023–2030.*

(iv) Half of the basic research costs and all vaccine R&D costs are attributed to vaccines scenario.

(v) Of the global vaccine R&D costs, costs are apportioned to LLMCs based on their share of global population in 2025–2030 as estimated by the UN. This is done on the basis that vaccine activity and service delivery is highly tied to population. The share attributed to LLMCs is 53%.

Including R&D costs reduces the BCRs by 17–26% depending on the combination of baseline and intervention scenarios. The BCR of our preferred specification (*Global Plan* without vaccines against standard baseline) is 34.0 with R&D costs included.

4.7. Lower intervention spending beyond 2035 for the vaccine scenario

In the *Global Plan*'s vaccine scenario, cases and deaths fall to very low levels by 2030. However, funding requirements remain high, more than US$ 9 billion annually. While the funding requirements per case are relatively stable for the baseline and without vaccine intervention scenario across the outer years, 2035–2050,[10] the *Global Plan* with vaccine scenario sees an increase in the cost per case from US$ 11,334 in 2035, rising to US$ 48,625 in 2050.

This potentially overestimates the required funding for that scenario. Therefore, we consider an alternative scenario where the cost per case is fixed at US$ 11,334 across the entire period 2035–2050. The new cost profile for this sensitivity analysis is presented in Figure 5. Costs fall with incidence such that counterfactual costs in the standard baseline are higher after 2041.

[10] Cost per case (total annual funding requirements divided by number of incident cases) beyond 2035 is relatively constant and declines for each scenario. For the disruption baseline, cost per case starts at $187 in 2034 and falls to $156 in 2050. For the standard baseline 2035 = US$ 729, while 2050 = US $600 per case. For the *Global Plan* without vaccine, 2035 = US$ 3,513 and 2050 = US$ 3,074. However, for the *Global Plan* with vaccine 2035 = US$ 11,334 while 2050 = US$ 48,625.

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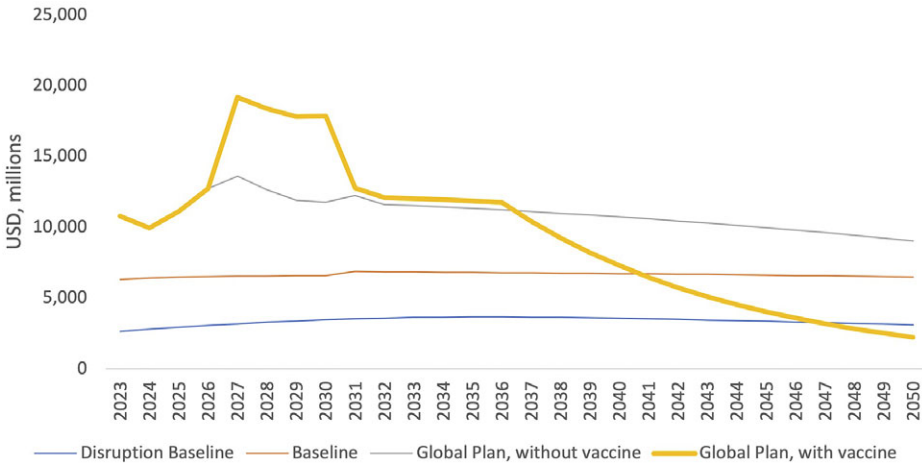

Figure 5. *Alternative cost profile for Global Plan with vaccine scenario.*

The BCR of this scenario is 46.3 compared to the standard baseline (Table 3), essentially the same BCR as the *Global Plan* without vaccine (46.0). Compared to the disruption baseline, the BCR with the new cost profile is 70.1.

4.8. Changing discount rates

As a final sensitivity analysis, we alter the discount rate to 5% and 12%. As expected, the BCR of our preferred specification rises with the lower discount rate to 55.4 and falls with the higher discount rate to 36.6.

5. Discussion and conclusion

This report conducts a cost–benefit analysis of increased spending on TB using impacts and costs drawn from the *Global Plan.* The analysis indicates that the return on TB spending is substantial with a centrally estimated BCR of 46.0. Alternative specifications using different baselines, interventions, cost profiles, and discount rates still yield very high BCRs, in the range of 28–84. This report also shows that TB investment would avoid substantial mortality, estimated at 27.3 million averted deaths over the 28-year period between 2023 and 2050 inclusive, an average of roughly 1 million averted deaths per year. Under the costing assumptions used in this paper, the cost per averted death is slightly over US$ 2000. Interventions to address TB represent exceptional value-for-money.

Investments in TB are expected to be equity enhancing insofar as more lives would be saved in poorer countries than in wealthier countries. Moreover, funding will be provided by a combination of international donor and domestic governments, via taxation, while beneficiaries are more likely to be the lower end of the income distribution. Therefore, TB investments are likely to represent transfers from more wealthy individuals to less wealthy individuals within and across countries.

Note that against either baseline, new vaccine deployment has a lower BCR than the intervention without vaccines. This implies that the incremental BCR of just vaccines is

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lower than the BCR of the scenario without vaccine. This is partly driven by the high cost of the vaccine, requiring delivery to almost the entire population, as well as the fact that in the *Global Plan*, vaccine delivery was modeled as the last intervention after several interventions were already scaled. This means that in the modeled results, there are mechanistically fewer deaths and cases to avert from deploying the vaccine. The results do not provide insight into the BCR of a hypothetical scenario where a new vaccine is deployed in the absence of the other interventions.

The main limitation of this analysis is that we could only consider scenarios developed under the *Global Plan* exercise. That effort was not designed to optimize based on BCR, even if the resulting BCRs are substantial. Rather it was designed to focus on the combination of interventions that can end TB by 2030. The supplementary modeling done for the *Global Plan* showed that unless all interventions are deployed in a comprehensive manner it will not be possible to end TB by 2030 and reach the SDG target. A more nuanced analysis would consider different combinations of interventions, for example, comparing improvements in diagnostics only versus incentives to improve patient adherence versus existing tools plus a vaccine. The scenarios present in the *Global Plan* are aspirational targets envisaging substantially more comprehensive TB services than have been delivered historically. In addition, a more flexible model would ideally identify optimal packages under different levels of funding. This latter approach would be especially useful since budgets for TB have remained relatively constant in recent years, despite requests for more funding. To the best of our knowledge, an optimization model at a global scale is unavailable and the evidence base for assessing the impacts of TB spending at a global scale is relatively limited. The development of such a model as a priority research effort would be helpful to further optimize TB spending.

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Competing interest. The authors declare none.

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