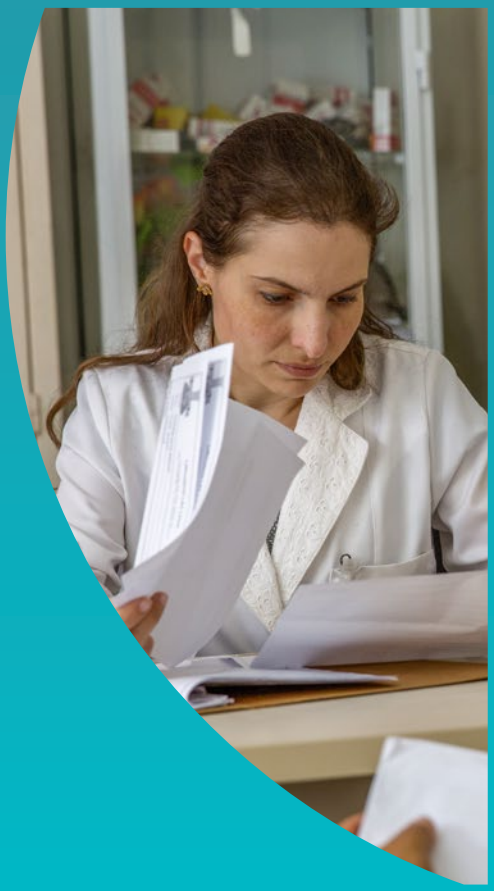
Funding a tuberculosis-free future

an investment case for screening and preventive treatment



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Funding a tuberculosis-free future: an investment case for screening and preventive treatment

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Introduction

Tuberculosis (TB) remains one of the leading causes of death from an infectious agent despite being preventable and treatable. Worldwide in 2022, an estimated 10.6 million people fell ill with TB and 1.3 million people died from it, mostly in low- and middle-income countries *(1)*.

The World Health Organization (WHO) End TB Strategy has the vision of making the world free from TB – that is, with zero deaths, disease and suffering from the disease – and ending the global TB epidemic by 2035. The End TB Strategy aims at reducing, by 2035, the number of TB deaths by 95% and the incidence of TB by 90% compared with 2015. To achieve these targets, countries should strive to achieve 90% coverage for both TB treatment and TB preventive treatment (TPT) *(2, 3)*.

Therefore, in 2023 countries set ambitious new targets at the second UN High-Level Meeting on the Fight Against TB in 2023, aiming to treat 45 million people between 2023 and 2027, including 4.5 million children and 1.5 million people with drug-resistant TB *(4)*. Countries also committed to treat 45 million people with TPT, including 30 million household contacts of people with TB, covering children and 15 million people living with HIV. There is also a commitment to pay particular attention to people who are vulnerable or in vulnerable situations, including those who live in remote geographical regions. Moreover, countries aiming to eliminate TB as a public health problem should be able to bring down TB incidence to <1 TB case per 1 million population by 2050 or earlier.

Ending the global TB epidemic requires translating the commitments made at the 2023 UN High-Level Meeting into action. This includes increasing investments in TB screening and TPT. The investment case presented here examines in detail the costs and benefits of TB screening plus TPT in four countries – Brazil, Georgia, Kenya and South Africa – and these may serve as examples for other settings with a similar epidemiological context. The results of the assessment show that relatively modest investments can achieve significant health and economic benefits in all four countries.

This investment case provides strong economic arguments for policy-makers and advocates to raise awareness among the public and government of the true costs of TB and the benefits of screening and prevention. The findings of the investment case should encourage governments and donors to increase funding for accelerated implementation of TB screening plus TPT in key risk populations.

Investing now in screening and preventive treatment for TB means that by 2050

fewer people will develop TB

Brazil	Georgia	Kenya	South Africa
485 000	10 000	1.4 million	1.4 million
-18%	-24%	-44%	-33%

many lives will be saved

Brazil	Georgia	Kenya	South Africa
52 000	970	235 000	276 000
-23%	-33%	-52%	-40%

equating to large numbers of years of life saved

Brazil	Georgia	Kenya	South Africa
1.9 million	37 000	9.3 million	10.2 million
-22%	-33%	-53%	-42%

This requires investment to scale up TB screening and preventive treatment

Additional annual investment per capita required from 2024 to 2050

Brazil	Georgia	Kenya	South Africa
US$ 0.28	US$ 0.57	US$ 0.49	US$ 1.11

Investing in TB screening and preventive treatment offers a substantial societal return for each dollar invested

Societal return on investment (ROI) of investing in TB screening plus TPT, by 2050

Brazil	Georgia	Kenya	South Africa
11:1	4:1	27:1	39:1

TB screening plus TPT offers a substantial return on investment.

The role of screening in ending TB

TB screening is defined as the systematic identification of people at risk for TB disease, in a pre-determined target group, by assessing symptoms and using tests, examinations, or other procedures that can be applied rapidly**.**

TB screening plays an important role in addressing the case detection gap and in finding the "missing millions". Globally in 2022, 7.5 million people were newly diagnosed with and treated for TB, but an estimated 10.6 million people developed TB that year *(1)*. This means that more than 3 million people with TB (29%) were not diagnosed or reported to WHO in 2022 alone.

TB screening helps to bring health services closer to people, thereby removing some barriers to diagnosis and treatment *(5, 6)*. It is an important strategy to reach those who are most vulnerable and have the least access to care, which is particularly important because TB disproportionately affects the poorest and most vulnerable populations.

TB screening can improve treatment outcomes by detecting people with earlier disease. It can also reduce costs for patients, including the risk of catastrophic costs.

TB screening helps to improve TB epidemiology at the community level. By detecting more people with TB, it reduces the prevalence and transmission of TB, and thus lowers incidence in the following years.

TB screening to exclude TB is the essential first step in initiating TPT among those who are at high risk, and integrating the two steps leads to important gains in efficiency.

The role of preventive treatment in ending TB

TPT is a proven and effective intervention to avert the development of TB disease among those exposed, reducing their risk by about 60–90% when compared with people who do not get TPT.

TPT given to people at the highest risk of progressing from TB infection to disease, remains a critical intervention to bring down incidence by 2035 to the levels envisaged by the End TB Strategy *(3, 7, 8)*.

TPT for people at risk, combined with active TB case-finding and treatment, is the most effective public health intervention to reduce incidence in the absence of an effective TB vaccine.

TB screening saves lives, and the additional impact of TB preventive treatment is substantial.

Modelling innovations in TB screening and preventive treatment

Reaching people at highest risk of TB disease

Screening and TPT should reach the people at greatest risk of developing TB disease. Aligned with WHO recommendations, the populations targeted for TB screening and TPT in the modelling analysis were: (i) people living with HIV, (ii) household contacts of TB patients and (iii) a priority population, defined uniquely for each of the four countries. In Brazil, the priority population was persons deprived of liberty (i.e. prisoners); in Georgia, it was persons accessing care for injection drug use; while in Kenya and South Africa, it was persons living in high-incidence communities. It was assumed that the priority populations were screened for 3 consecutive years (2024–2026), after which the intervention was stopped. For more detail about the country-specific interventions, please see *(9)*.

The model

A compartmental age-stratified dynamic transmission model for TB was used to evaluate the reductions in incidence and mortality achieved by 2050 with a package of TB screening and TPT interventions compared with the current practice of diagnosing and treating TB disease and infection. The package of interventions incorporated feasible levels of coverage of currently available and recommended diagnostics and treatments.

Calculating health and economic impacts

To demonstrate health impact, the cumulative numbers of TB episodes and deaths averted between 2024 and 2050 were calculated for a scenario in which the TB screening and TPT interventions were scaled up starting in 2024 compared with a status quo scenario. The number of lives saved and episodes of TB disease avoided, and the healthy life-years gained were then translated into the economic and social benefits that would have been lost in a business-as-usual scenario in which no new or additional action was taken. The results presented are not discounted.

Screening for TB disease

Screening with the latest recommended strategies using digital, portable or ultraportable chest radiography, computer-aided detection (CAD), molecular diagnostics and tests for C-reactive protein (CRP) were modelled with the intention to balance sensitivity and specificity (Table 1). Among all people living with HIV who are on antiretroviral therapy (ART), screening for TB disease is repeated annually. For all people living with HIV who are not diagnosed with TB disease, TPT is offered once, without testing for TB infection.

TB preventive treatment

The use of shorter, rifamycin-based TPT regimens was modelled. A 3-month regimen of daily isoniazid plus rifampicin (3HR) was used for child contacts and children living with HIV who are younger than 2 years. For contacts and people living with HIV who are 2 years or older, a 3-month regimen of weekly isoniazid plus rifapentine (3HP) was modelled.

Tests for TB infection

The use of a tuberculin skin test (TST) was modelled for household contacts aged 5 years and older because it requires fewer resources than interferon-γ release assays (IGRAs) and is likely to be more familiar to practitioners in resource-constrained settings.

Table 1. TB screening and preventive treatment interventions included in the model

Population	Age group (years)	TB disease screening[a]				TB skin test	TPT		Coverage
		Symptoms	CRP	CXR	CAD	TST	3HR	3HP	
People living with HIV on ART	0–4	1					<2 years	2–4 years	90%
	≥5	1						✓	
People newly diagnosed with HIV not yet on ART	0–4	1					<2 years	2–4 years	90%
	5–9	1						✓	
	≥10	1	2					✓	
Household contacts	0–4	1		1			<2 years	2–4 years	90%
	≥5	1		1		✓		✓	50%
High-risk population	0–14	No intervention							0%
	≥15	1		1	1				60%

ART: antiretroviral therapy; CAD: computer-aided detection; CRP: C-reactive protein; CXR: chest X-ray; TPT: TB preventive treatment; TST: tuberculin skin test; 3HP: weekly isoniazid plus rifapentine; 3HR: daily isoniazid plus rifampicin.

[a] Numbers indicate the order of tests (1 = first test done; 2 = second test done if previous test positive); in all screening algorithms, the Xpert MTB/RIF Ultra (Cepheid) was used as the diagnostic confirmatory test.

The burden and costs of TB

The global burden and costs of TB are large. The modelling showed that should the status quo be maintained, between 2024 and 2050, over 10 million people will develop TB and more than 1.3 million people will die from TB in the four countries studied. TB also leads to a substantial loss of life-years, from 109 000 in Georgia to 24 million in South Africa. Many of these would have been productive life-years because people are often young when they die of TB, at an average age of 37 years.

TB has high costs for society. Only a small proportion of these costs are direct health system costs (ranging from 1.7% in South Africa to 7.8% in Kenya). The majority are costs to patients and to society (Table 2).

Table 2. Societal costs of TB, by country

	Brazil	Georgia	Kenya	South Africa
Total societal cost of TB between 2024 and 2050	US$ 81.2 billion	US$ 830 million	US$ 41 billion	US$ 167.1 billion
Average annual cost to society	US$ 3.01 billion	US$ 30.7 million	US$ 1.52 billion	US$ 6.19 billion
Proportion of country GDP in 2024	0.16%	0.12%	1.34%	1.53%

TB screening saves lives, and the additional impact of TB preventive treatment is substantial

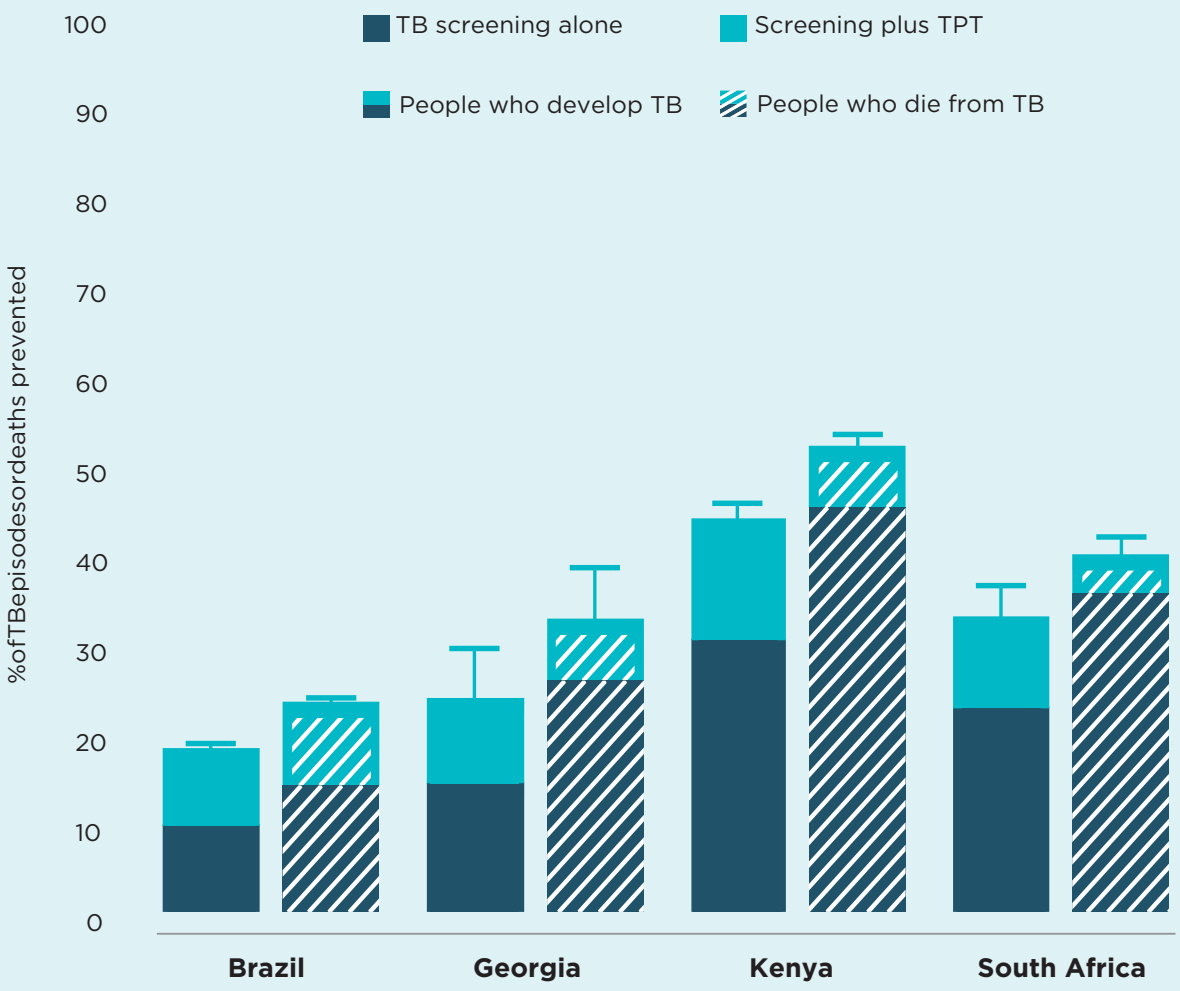
In all four countries, many episodes of TB can be prevented and lives saved by investing in TB screening (Table 3, Fig. 1). Adding TPT to screening for TB disease creates efficiencies and maximizes health and financial gains. Integrating TPT with TB screening prevents a substantial number of additional TB episodes as well as saving many more lives.

Table 3. Contribution of TB screening plus TPT to the impact of the intervention, by country, 2024–2050

Impact[a]	Brazil	Georgia	Kenya	South Africa
TB screening alone				
TB episodes prevented	255 000 (–10%)	6 000 (–14%)	949 000 (–30%)	992 000 (–23%)
Lives saved	32 000 (–14%)	770 (–26%)	205 000 (–45%)	249 000 (–36%)
Total impact of screening plus TPT				
TB episodes prevented	485 000 (–18%)	10 000 (–24%)	1.4 million (–44%)	1.4 million (–33%)
Lives saved	52 000 (–23%)	970 (–33%)	235 000 (–52%)	276 000 (–40%)
Life-years saved	1.9 million (–22%)	37 000 (–33%)	9.3 million (–53%)	10.2 million (-42%)

TPT: TB preventive treatment. [a] Values are no. (% reduction).

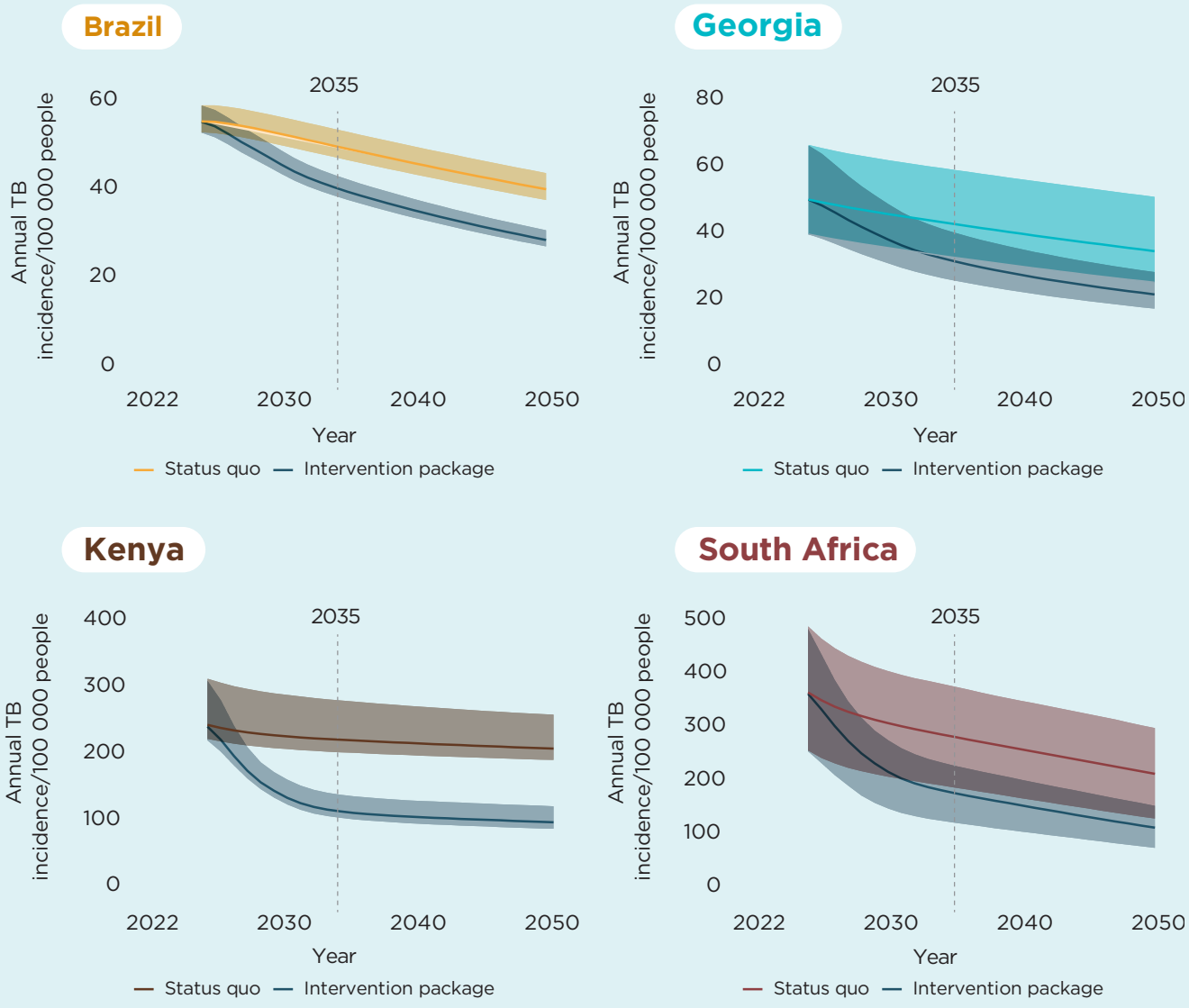
Fig. 1. Proportion of TB episodes and deaths prevented with TB screening and TB preventive treatment (TPT)



TB screening plus preventive treatment leads to large reductions in national TB incidence

In all four countries, TB screening plus TPT leads to a substantial reduction in national TB incidence (Fig. 2). With full implementation of the package, the reduction in national TB incidence would range from 29% to 54%. In the three countries with high HIV prevalence – Brazil, Kenya and South Africa – scaling up TB screening plus TPT among people living with HIV leads to a drop of 8% to 27% in TB incidence by 2050, while bigger gains can be achieved with broader-based interventions in high-burden countries. TB screening plus TPT can make a substantial contribution towards reaching the End TB targets.

Fig. 2. Projected reductions in annual TB incidence in four countries, 2024–2050



How much investment is needed?

This analysis shows that an additional investment of between US$ 0.28 and US$ 1.11 per capita per year could deliver a package of screening plus TPT that will reduce the burden of TB (Fig. 3). Per capita health system costs are higher during the period when interventions are scaled up (2024–2030), but decrease over time to below US$ 0.50 per capita by 2050. The calculation takes into account the human and capital resources needed to fully implement the screening and preventive treatment interventions.

Fig. 3. Investments needed to scale up TB screening plus preventive treatment

Total health care cost of scaling up TB screening and preventive treatment (in US$)

Brazil	Georgia	Kenya	South Africa
1.6 billion	59 million	0.7 billion	1.77 billion

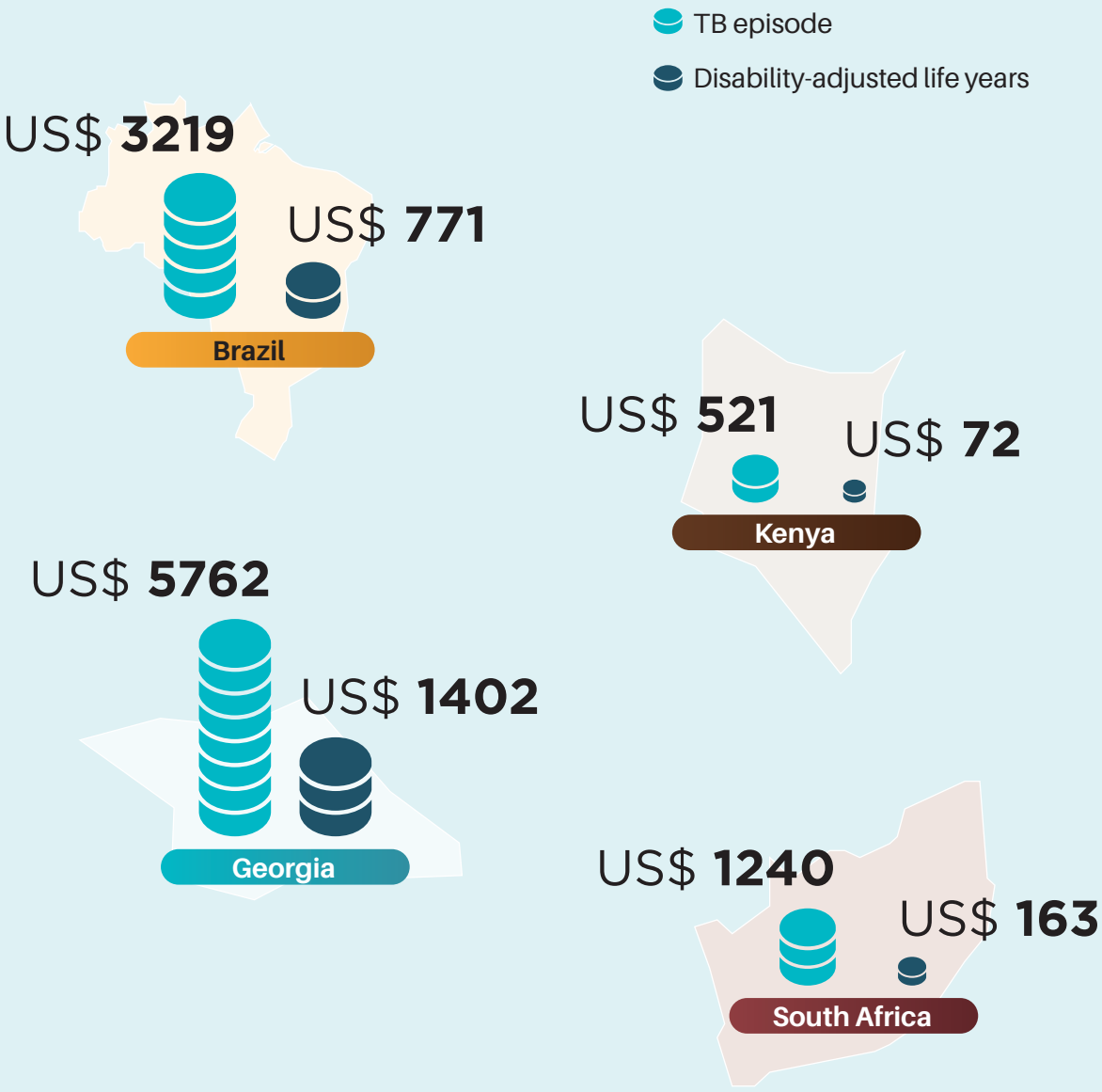
Average cost per capita per year (in US$)

Brazil	Georgia	Kenya	South Africa
0.28	0.57	0.49	1.11

TB screening plus preventive treatment is cost-effective

From the health system perspective, the costs per TB episode prevented are modest, and the costs per disability-adjusted life-year (DALY) averted are well below conventional willingness-to-pay thresholds (Fig. 4).[1] From a societal perspective, the intervention package was cost-saving in all four countries.

Fig. 4. Incremental health system cost per TB episode and DALY averted (US$)

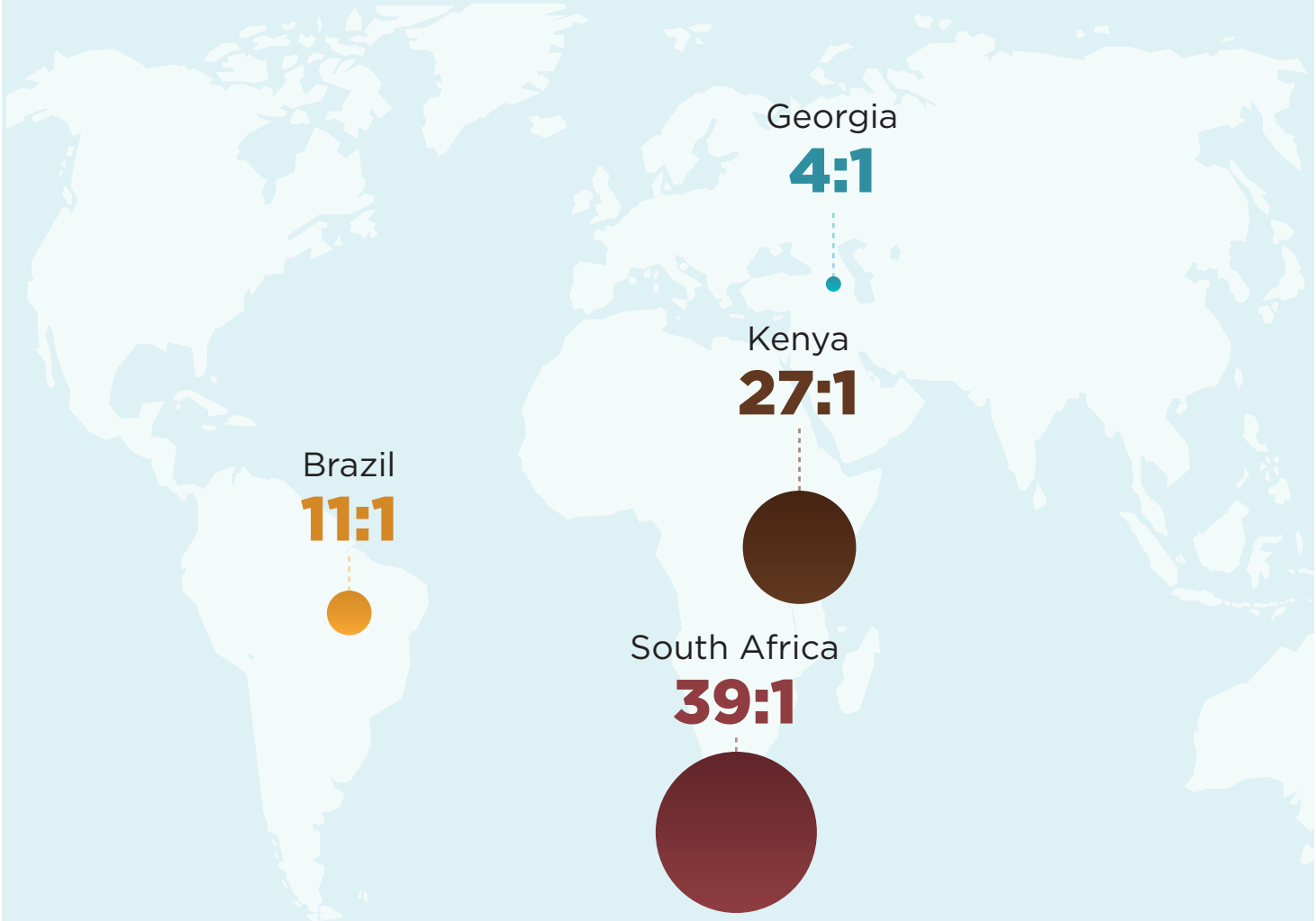


[1] To determine cost-effectiveness, country-specific willingness-to-pay thresholds per DALY averted were used. These thresholds were US$ 13 644 for Brazil, US$ 1 603 for Georgia, US$ 1 002 for Kenya, and US$ 4 834 for South Africa (all in 2023 US$).

TB screening plus preventive treatment offers a substantial societal return on investment and reduces the cost of TB to society

The societal return on investment (ROI) varied between countries, from US$ 4 to US$ 39 gained for every dollar invested (Fig. 5).

Fig. 5. The societal return of investing in TB screening plus TPT

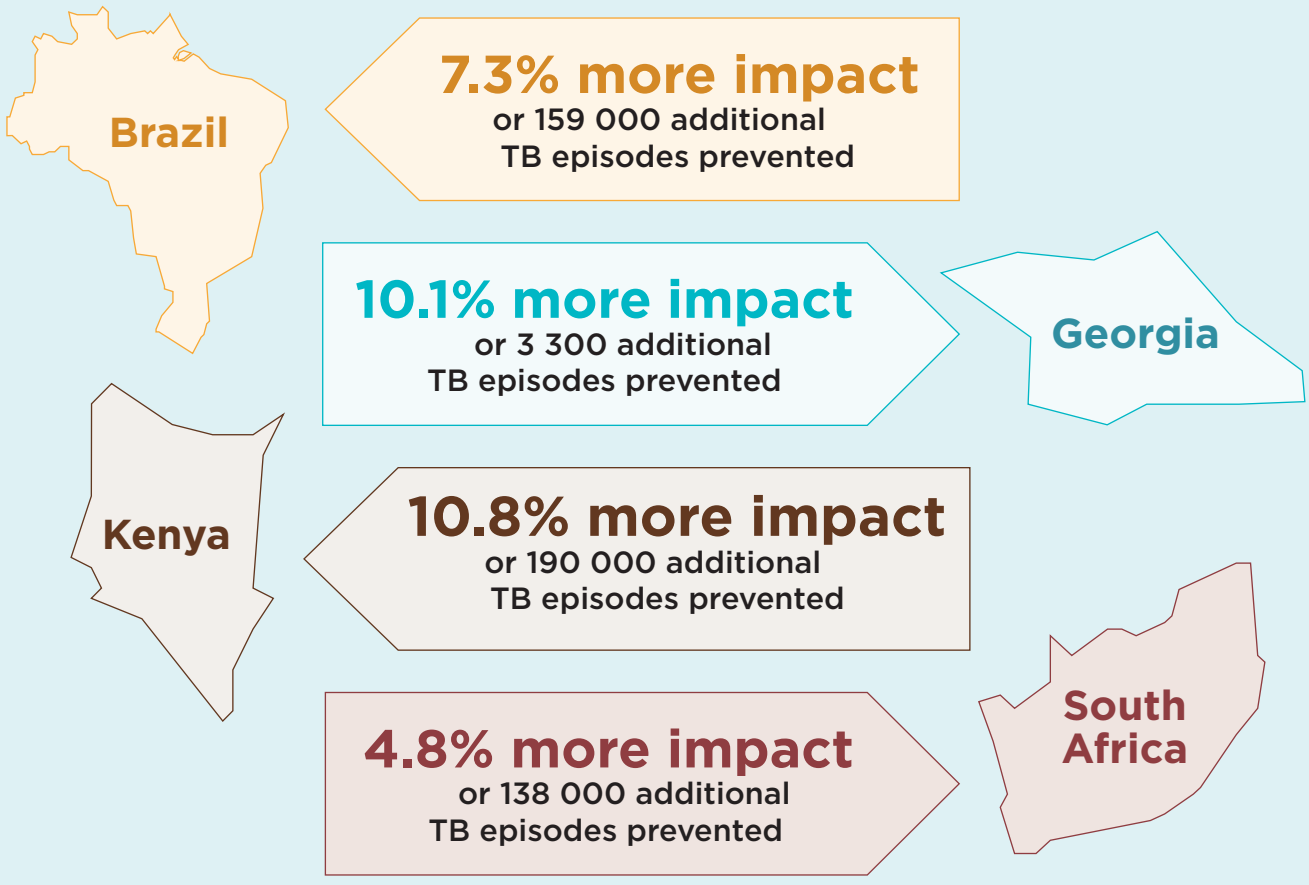


The way forward

Governments and donors at all levels should see implementing TB screening plus TPT as a key investment in public health and an opportunity to strengthen health systems and provide universal health coverage. TB screening plus TPT is essential to achieving the End TB targets while also helping to address the health needs of the poorest and most vulnerable populations.

While the results presented in this investment case are already impressive, more gains could be made by further scaling up the proposed interventions, by repeating interventions in the high-risk population beyond a third year, by looking for other synergistic programme actions in diagnosis and treatment, and by investing in an enhanced package of TB screening plus TPT. An ambitious enhanced package, reaching nearly all individuals belonging to the priority groups and utilizing technologies that could foreseeably be broadly recommended in the near future (e.g. 1HP [i.e. 1 month of daily isoniazid and rifapentine], CAD for younger populations, antigen-based skin tests) would magnify the impact of the interventions (Fig. 6).

Fig. 6. More impact from an enhanced package of interventions



Ending the TB epidemic requires allocating sufficient investments to TB screening plus TPT. Investing in TB screening plus TPT can prevent large numbers of people from developing TB, save lives and lead to significant societal ROIs. Targeting priority high-risk groups relevant to the local epidemiology and achieving high coverage of TB screening and TPT are essential to ensuring lasting impact. Greater investments in better screening tools, shorter TPT regimens, new skin tests for TB infection and enhanced coverage can result in large societal ROIs.

References

1. Global tuberculosis report 2023. Geneva: World Health Organization; 2023 (https://www.who.int/publications/i/item/9789240083851, accessed 11 March 2024).

2. Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's new End TB Strategy. Lancet. 2015;385:1799-801. doi:10.1016/S0140-6736(15)60570-0.

3. The End TB Strategy [website]. Geneva: World Health Organization; 2021 (https://www.who.int/teams/global-tuberculosis-programme/the-end-tb-strategy, accessed 11 March 2024).

4. UN General Assembly High-level Meeting on the fight against tuberculosis, 2023 [website]. Geneva: World Health Organization; 2023 (https://www.who.int/activities/preparing-for-the-un-high-level-meeting-on-the-fight-against-tuberculosis--2023, accessed 11 March 2024)

5. WHO consolidated guidelines on tuberculosis. Module 2: screening – systematic screening for tuberculosis disease. Geneva: World Health Organization; 2021 (https://www.who.int/publications/i/item/9789240022676, accessed 11 March 2024).

6. WHO operational handbook on tuberculosis. Module 2: screening – systematic screening for tuberculosis disease. Geneva: World Health Organization; 2021 (https://www.who.int/publications/i/item/9789240022614, accessed 11 March 2024).

7. WHO consolidated guidelines on tuberculosis. Module 1: prevention – tuberculosis preventive treatment. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/9789240001503, accessed 11 March 2024).

8. WHO operational handbook on tuberculosis. Module 1: prevention – tuberculosis preventive treatment. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/9789240002906, accessed 11 March 2024).

9. Vesga JF, Salaheldin Mohamed M, Shanda M, Jabbour E, Lomtadze N, Kubjane M, et al. The return on investment of scaling tuberculosis screening and preventive treatment: a modelling study in Brazil, Georgia, Kenya, and South Africa (https://www.medrxiv.org/content/10.1101/2024.03.12.24303930v1, accessed 15 March 2024).

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