

Technical brief

Towards a proposal for a novel TB vaccine R&D financing initiative

Background document for the engagement series on late-stage TB vaccine financing

Original brief: October 2024

Revised brief: June 2025

Note

This brief outlines key considerations and tentative recommendations towards a new financing initiative for TB vaccines R&D, with a focus on late-stage candidates. It is designed to provide background information to help stimulate debate during the workshop series on late-stage TB vaccine R&D financing R&D. The original brief was drafted for the first workshop in the series at the World Health Summit in Berlin, Germany in October 2024. The current version has been revised ahead of the regional workshop at the 12th EDCTP Forum in Kigali, Rwanda on June 19, 2025. We welcome comments and critique. The contents of this paper and the outputs of the workshop series, which includes engagement with a range of key stakeholders, will inform the development of a validated proposal for late-stage TB vaccine R&D financing.

A new financing initiative for TB vaccine R&D: why now?

Tuberculosis (TB) is the world's deadliest infectious disease. Amid already constrained financial support for essential TB services and rising levels of drug resistance, 1.25 million people died from TB disease in 2023 and 10.8 million people fell ill.¹ Nearly 90% of the global TB burden occurs among populations in low- and middle-income countries (LMICs), whose risk of developing and dying from TB is exacerbated by undernutrition, overcrowding, and inadequate water, sanitation and hygiene services.² Multiple new TB vaccines that work across all age groups, particularly among adolescents and adults who are most at risk of developing and spreading TB, are critical to eliminate TB and meet the 2030 End TB targets.³ New TB vaccines will also help prevent the spread of drug resistant TB, thus mitigating the growing global health and security threat of antimicrobial resistance (AMR).

The investment case for new TB vaccines is well established, especially concerning adults and adolescents. New TB vaccines could avert up to 76 million cases and save up to 8.5 million lives over 25 years, while being cost-saving in almost all high burden countries (HBCs), with returns on investments of up to US\$372 billion and generating up to \$3 trillion in economic growth globally.⁴ Universally accessible TB vaccines will prevent disease, curb transmission, combat the spread of drug resistance, contribute to sustainable pandemic preparedness and response (PPR) infrastructure, fight health inequalities, and return up to \$7 for every \$1 invested in their delivery over 25 years.⁵

The TB vaccine development pipeline shows more promise today than ever before: at least 16 candidates are in the clinical pipeline, including two novel candidates, M72 AS01/E and MTBVAC, that entered late-stage efficacy trials in adolescents and adults in 2024, and several more in preclinical development, with new partnerships and plans in development to ensure they will be affordably and equitably accessible once available.⁶

Notwithstanding the scientific challenges to developing new TB vaccines, chronic and severe shortfalls in research and development (R&D) investments remain a key obstacle to efficiently advancing TB vaccine candidates through the pipeline. At current resource levels, it is not possible to test sufficient numbers of candidates at the necessary scale and pace to deliver the multiple vaccines required to meet the varying needs of people vulnerable to developing TB disease (e.g., diverse target populations, indications of use, and health system requirements, and heterogeneous demands).

Despite repeated, ambitious high-level political commitments, including pledges to invest \$5 billion annually in TB R&D by 2027 and deliver new TB vaccines by as early as 2028, annual funding for TB vaccines only exceeded \$145 million for the first time in 2023 with \$230 million of investments reported.⁷ This welcome but insufficient increase, relative to an estimated annual need of \$1.25 billion, was due to an increase in philanthropic spending by 47% compared to 2022, largely driven by a \$550 million investment from the Gates Foundation and Wellcome in the Phase 3 trial of M72/AS01E.⁸ Philanthropies are now outspending governments in TB vaccine R&D.

We cannot depend solely on philanthropic funding to conduct pivotal efficacy trials. Overall, funding depends on limited and unpredictable public and philanthropic funding, with persistent financing gaps and a lack of sustainable funding streams preventing the uninterrupted progress of candidates through the pipeline, particularly in late-stage trials. The global health architecture, however, has changed dramatically in the first six months of 2025 due to sharp spending cuts by the U.S. government, alongside significant cuts announced by other major global health R&D funders (including 25% from Belgium, 37% from France, 30% from the Netherlands, and 40% from the U.K.). These shifts together signal a highly uncertain funding landscape for global health R&D at large, including for TB vaccines.

New TB vaccines are within reach — but only with greatly increased and sustained investments.^a Preliminary estimates using an adapted Portfolio-to-Impact (P2I) model suggest we need \$500-1000 million to fill the clinical development funding gap to bring at least one novel candidate to licensure in the next 10-15 years.^{9,10} The momentum generated by recent initiatives, such as the WHO TB Vaccine Accelerator Council, present strategic opportunities to mobilize high level political support and investments. Coordinated and joint financing that supports diversified funding streams, innovative and custom funding mechanisms, and the incentivization of novel partners, could overcome the funding shortfalls and galvanize the necessary political leadership and action across the entire R&D to implementation continuum.

TB Vaccine Pipeline

Vaccine candidates under clinical development

There are 16 vaccine candidates in the pipeline as of May 2025, of which 8 are in active trials. The candidates are placed under the phase which corresponds to the most advanced ongoing or completed trial.



Information reported by vaccine sponsors or found in clinical trial registries or other public sources
Institutions listed are vaccine sponsors and development partners

Additional information, including the full list of clinical trials for each candidate, can be accessed via the QR code or at newtbvaccines.org/tb-vaccine-pipeline/

Last update: 29 May 2025

Limited funding streams

The top eight funders of TB vaccine research invested 94% (\$213.9 million) of all financing in 2023 (Figure 1). The Gates Foundation and the U.S. National Institutes of Health (NIH) were the largest funders, contributing 37% and 33% respectively of total funds in 2023.⁷ Open Philanthropy and Wellcome were the third and fourth largest funders, investing approximately 8% and 6% of total funds respectively in 2023. Importantly, TB vaccine research is not addressed by existing multilateral and global health funding mechanisms, be it the Global Fund for Aids, Tuberculosis and Malaria, Gavi, the global vaccine alliance, CEPI, or the World Bank's Pandemic Fund.¹¹

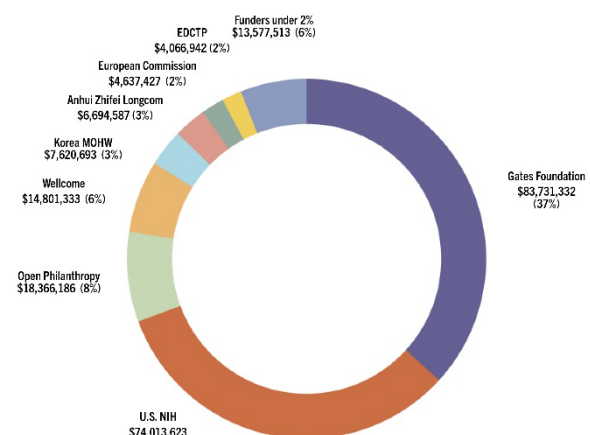


Figure 1. The top TB vaccine R&D funders in 2023⁷

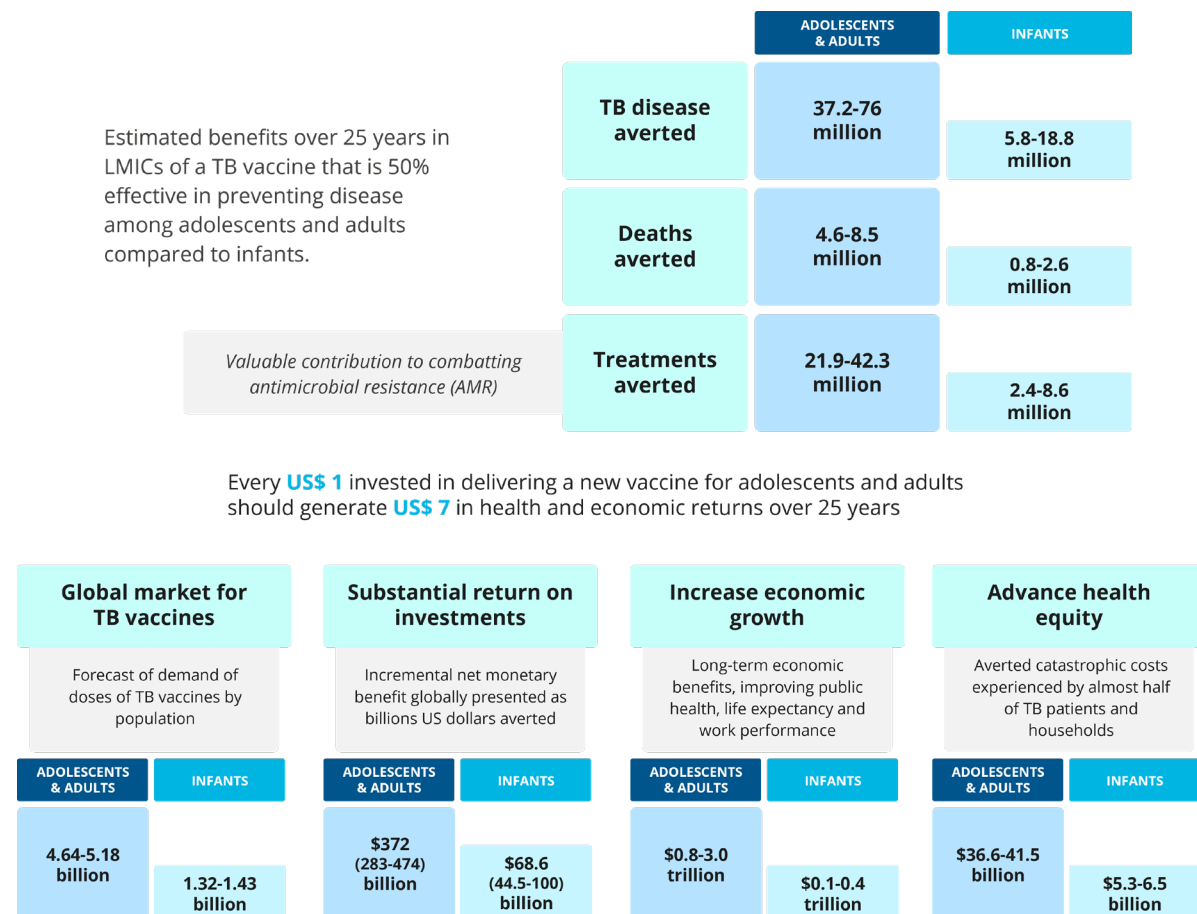
^aIt is estimated that governments must invest 0.15% of their total research expenditure in TB research to meet their fair share of the \$5 billion target.²⁹

Estimating the portfolio funding needs

To estimate the amount of funding needed to achieve a desired outcome – defined as at least one new TB vaccine licensed – based on the current clinical pipeline, we applied the adapted Portfolio to Impact model proposed by Young, et al.^{9,10} This model allows for establishing cost estimates for supporting product portfolios towards the launch of new products based on assumptions including complexity of the products being developed and related success rates of trials (phase 1-3) and estimated costs per trial. Assuming that all TB vaccine candidates in the clinical pipeline are complex vaccines, except M72, which was designated a simple vaccine given established proof of concept in a previous phase 2b trial, the model suggests that \$500-1000 million is needed to fill the funding gap for clinical development activities to bring at least one novel candidate to licensure in the next 10-15 years. Given the limitations of the model, especially when applied to just one product category for one disease, the values used in the model will need to be further refined.

Estimating the market and impact of future TB vaccines

No detailed analyses are available on the markets and impact of and demand for specific TB vaccines. Efforts are underway to map these for a number of TB vaccine candidates in late-stage development, including M72 AS01/E and MTBVAC. Furthermore, in June 2024, the Gavi board approved the inclusion of TB vaccines in its Vaccine Investment Strategy (VIS) for the next strategic period, 2026-2030 – this strategy will include health impact, value for money, and economic impact analyses for TB vaccines in Gavi-eligible markets.¹² The WHO TB vaccine investment case, published in 2023, outlines the potential health and economic impact of vaccines that meet the WHO preferred product characteristics for 105 low- and middle-income countries, which account for 93% of the global TB burden.⁵ The main findings are summarized below.



A novel TB vaccine R&D financing initiative

The limited funding for TB vaccine R&D to date consists almost exclusively of grant funding. Such funding has been tremendously valuable in cultivating the clinical pipeline today, but it is too limited, too fragmented, and too short in duration to support vaccine candidates through late-stage development – leading to significant delays between phases of clinical development.²⁴ There have been instances of loan-based financing for TB vaccine development, for example the support of the European Investment Bank (EIB) to the Serum Institute India to support the development of VPM1002, through a mechanism previously supported by EIB, InnovFin.¹³ TB vaccine development has not yet benefited from pull financing mechanisms, even though some could be well suited to support late-stage development. The value and limitations of pull-based financing to support late-stage R&D has been reviewed in various reports, including a recent publication by DSW which provides a helpful overview of various pull mechanism to support R&D for neglected diseases, including TB.¹⁴ Options such as Advanced-Market or Pooled-Procurement Mechanisms as well as Development Impact Bonds, individually or in combination, could be explored, though their ability to support and de-risk R&D is untested. Further guidance on the applicability and value of pulled financing mechanisms to support late-stage TB vaccine development, considering the estimated market and public health impact of such vaccines, will be needed.

Generating substantial new funding or financing for TB vaccine R&D, especially in support of late-stage development, may need to encompass a mix of funding mechanisms, both pull and push, such as grants, loans, investments, or bonds. Cohesion in such a mix of funds will be essential, requiring substantial funder-investor coordination.

In terms of pooled funding mechanisms, several proposals for global biomedical R&D funds have been published over the last decade. These proposals posit that a range of financing mechanisms can be implemented in tandem, with a diverse range of funders, including MICs, to mobilize significant annual investments for global health R&D of up to \$2 billion.^{15–17} While these proposal have not been implemented to date, they illustrate the potential for diverse funders to pool resources and de-risk individual investments. A number of funds have however been launched in recent years to address specific disease areas, including malaria, polio, and AMR.^{18–20} These initiatives have mobilized pooled funds of billions of dollars to support the development and deployment of new technologies against major global health challenges, coordinating the support of diverse public sector, philanthropic, and private funders in novel public-private partnerships.

Elsewhere, the Global Health Innovative Technology (GHIT) Fund, launched in 2013, represented the first public-private partnership fund to involve a national government, a United Nations agency, a consortium of pharmaceutical and diagnostic companies, and an international philanthropic foundation.²¹ The Global Health Investment Fund (GHIF), launched in 2012, mobilised a \$108 million social impact fund through sponsorship by the Gates Foundation with the support of JP Morgan Chase, that invested in 12 companied developing biomedical innovations targeting diseases disproportionately affecting people living in LMICs. The fund's portfolio companies have successfully commercialized more than a dozen products delivered to over 100 million people.²² Meanwhile CEPI, founded in 2017, is leading the mobilization of multilateral investments in a range of emerging infectious diseases and invested millions of dollars in COVID-19 vaccine development. Inspiration can be drawn from these initiatives in the design of a novel financing initiative for TB vaccine R&D.

A joint approach of complementary financing mechanisms

No single country or entity can meet the funding shortfall alone. While the potential market for TB vaccines is large, it is considered insufficiently predictable and lacks attractive returns on investment as it is concentrated in LMICs. Market forces alone will not bring TB vaccine R&D to fruition.^{23,24}

A joint financing approach presents a strategic opportunity to mobilize resources for TB vaccine R&D by efficiently leveraging a range of complementary financing mechanisms.²⁵ Such an initiative could mitigate risks associated with R&D, address market failures constraining TB vaccine research, and overcome the limitations of traditional grant funding.

The mechanisms and investments in the initiative can be tailored to a country's economic and research capacities and disease burden to ensure that high-income countries and high burden middle-income countries (MICs) can both optimize their contributions.¹¹ As a co-investor, MICs could receive a range of economic benefits, including volume guarantees and discounted or preferential prices for the marketed product.²⁶ Further, a high return on investment in R&D in LMICs has been well documented, including support for clinical trial infrastructure, production capacity for new health products, and prevention and treatment of diseases beyond the initial disease area of investment.^{26,27}

Potential impact of a joint TB vaccine R&D financing initiative

An innovative financing approach could accelerate TB vaccine R&D, supporting the pathway for their implementation, and generating impact across a number of key areas over the next 10-15 years:

1. Accelerate TB vaccine R&D by supporting a portfolio of candidates for which well-defined plans exist to achieve licensure, broad supply and equitable access, as verified by expert technical panels. With the aim to bring at least three late-stage products through efficacy trials to deliver at least one candidate to licensure. Robust and independent transparency and accountability mechanisms should be enacted in tandem to ensure success and credibility of the initiative.
2. Provide coordinated and sustainable funding by implementing complementary financing mechanisms, in turn strengthening the R&D capacity and infrastructure to bring about new TB vaccines. Such an approach, once validated, could also be leveraged to support other areas of TB R&D, or late-stage vaccine development for other existing or future global health threats.
3. Deliver measurable public health and socioeconomic impact by bringing novel vaccines to market this decade, helping reach the WHO End TB targets by 2030.
4. Ensure that funding is contingent on access conditionalities aimed at securing equitable, affordable, sufficient, timely, and sustainable access for all countries that seek to benefit.
5. Support coordinated and harmonized regulatory and market access pathways, facilitating entry of at least one novel TB vaccine into the market during the lifespan of the fund.
6. Galvanize political leadership and accountability with a coalition of the willing championing the initiative's launch, aligned with the WHO TB Vaccine Accelerator Council's priorities and strategy.²⁸

Conclusion

A novel financing initiative for TB vaccine R&D can help secure the funding and resources needed to deliver new TB vaccines this decade, saving millions of lives and billions of dollars. By implementing a range of complementary financing mechanisms to support a portfolio of candidates, funding partners can effectively mitigate the risk of individual investments and maximize the potential return on investment in economic output and public health and societal impact.

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