

# An investment case for new tuberculosis vaccines: advocacy insights

Thursday, January 19, 2023

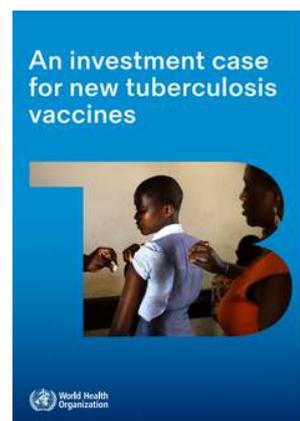
During the first meeting of the year, we were joined by Richard White and Rebecca Clark from the TB Modelling Group at London School of Hygiene and Tropical Medicine and Allison Portnoy from the Harvard T.H. Chan School of Public Health as they presented on the recently published 'An investment case for new tuberculosis vaccines'. The presentation was followed by a Q&A as we explored how this work can be best used for TB vaccine advocacy. Key takeaways included the need to clearly articulate the urgency in both accelerating the research and development of new TB vaccines and maximizing the speed of their eventual rollout.

## What is 'An investment case for new tuberculosis vaccines'?

This document summarizes the results of the WHO-commissioned full value proposition for new tuberculosis (TB) vaccines. The assessment was commissioned to provide early evidence for national and global decision-makers involved in TB vaccine development and implementation, who include stakeholders involved in vaccine research, financing, regulation and policy-making, manufacturing, introduction and procurement. The goal is to accelerate development of effective vaccines against TB and their rapid introduction into countries.

Click [here](#) to learn more

Published: December 2022



## Key takeaways from the report

The investment case estimates that, over 25 years in low- and middle-income countries (LMICs), a vaccine that is 50% effective in preventing disease among adolescents and adults could avert up to 76 million new TB cases, 8.5 million deaths, 42 million courses of antibiotic treatment and US\$41.5 billion in costs faced by TB affected households, especially for the poorest and most vulnerable. A vaccine that is 75% effective could avert up to 110 million new TB cases and 12.3 million deaths.

Vaccine products for both infants and adolescents/adults were estimated to be cost-effective from a societal perspective compared to a 1x per-capita GDP threshold in a majority of countries, including all high TB-burden countries, and cost-saving in 44-55% of countries. The study further suggests that every \$1 invested in a 50% effective vaccine could generate an economic return of \$7 in terms of averted health costs and increased productivity over 25 years.

	VACCINE FOR ADOLESCENTS AND ADULTS	VACCINE FOR INFANTS
<b>TB DISEASE AVERTED</b>	<b>37.2-76 million</b>	<b>5.8-18.8 million</b>
<b>DEATHS AVERTED</b>	<b>4.6-8.5 million</b>	<b>0.8-2.6 million</b>
<b>CUMULATIVE TREATMENTS AVERTED</b>	<b>21.9-42.3 million</b>	<b>2.4-8.6 million</b>
<b>COSTS AVERTED BY TB-AFFECTED HOUSEHOLDS</b>	<b>US\$ 36.6-41.5 billion</b>	<b>US\$ 5.3-6.5 billion</b>

*Estimated benefits over 25 years in low- and middle-income countries of a TB vaccine that is 50% effective in preventing disease among adolescents and adults compared to in infants*



### What do the percentage GDP thresholds mean?

The per-capita GDP/DALY-averted thresholds used in the models refer to defined thresholds of what a country is willing to pay for health in a population, including specific thresholds depending on country income level (i.e., middle-income-country). Per-capita GDP/DALY-averted is commonly used as a proxy for societal willingness-to-pay in LMIC settings, which do not have defined thresholds. For the model, multiple per-capita GDP/DALY-averted thresholds were used, including lower thresholds, thresholds reflecting country-level health opportunity costs, and a \$100/DALY-averted 'best buy' threshold to combine willingness, feasibility, and affordability.

<sup>1</sup> In other words, the marginal productivity of healthcare expenditure representing the opportunity cost of committing expenditure to a specific intervention in terms of health. See the following papers for more information:

- Ochalek J, Lomas J, Claxton K. [Estimating health opportunity costs in low-income and middle-income countries: a novel approach and evidence from cross-country data](#). *BMJ Glob Health*. 2018;3(6):e000964.
- Ochalek J, Claxton K, Lomas J, Thompson HM. [Valuing health outcomes: developing better defaults based on health opportunity costs](#). *Expert Review of Pharmacoeconomics & Outcomes Research*. 2021;21(4):729-736.

### Is the estimate that every \$1 invested could generate \$7 in economic return calculated at the point of introduction of a new vaccine, excluding the costs of getting there, i.e., R&D costs?

It is based on the one-time cost of introduction including training and social mobilization as well as ongoing delivery costs. Further, this value takes into account the averted costs for drug-susceptible and drug-resistant TB diagnosis and treatment and the costs incurred for antiretroviral therapy. This estimate does not include investments in R&D or new infrastructure and delivery platforms that may be needed.

### Given that a one-time mass campaign results in the greatest benefit, should we focus on advocating for a one-time campaign or is it more reasonable to push for multiple small campaigns?

There is a high upfront cost of a one-time campaign but bigger returns. If we advocate for a one-time campaign, we will need to push for fulfilling roll out in a few funding cycles. In short, the quicker we can get a vaccine out, the bigger the impact will be. However, delays in funding the R&D of new TB vaccines will delay the rollout. Thus, there could be a trade off by investing more funding now to ensure a vaccine is available sooner, which possibly may reduce the feasibility of a one-time campaign.

### There are estimated absolute gains in GDP of US\$1.6 trillion by 2080 for a vaccine targeting adolescents and adults. Can we calculate a crude estimate of the return on investment (ROI) of developing a TB vaccine by dividing the estimated gain of \$1.6 trillion by the estimated budget to develop a vaccine?

This can be done, but as suggested it will be a crude estimate. The methodology should be highlighted in a footnote if used. This may also include the cost for introduction.

- A comment from the audience also noted that advocacy messaging should also emphasize that there would be other benefits of investing in R&D beyond TB.
- A second comment requested disaggregated estimates for up to 2050 or other key milestones.

### How can we make the urgency clear with key stakeholders?

It's important to highlight the tradeoff of both not implementing accelerated scale up and not accelerating the development of new TB vaccines. For every year of delay, cases and deaths that could have been prevented will occur, and some health and economic benefits are lost. Further, health equity and financial risk protection analysis can give powerful messaging in terms of out-of-pocket expenditure and catastrophic costs to TB-affected households. Not only are we averting TB disease and deaths, but also catastrophic costs experienced by the poorest households.

- *Cost of inaction data for South Africa and India based on a model estimating impact by 2050 will be published in 2023. Please contact Richard White ([richard.white@lshtm.ac.uk](mailto:richard.white@lshtm.ac.uk)) and Rebecca Clark ([rebecca.clark@lshtm.ac.uk](mailto:rebecca.clark@lshtm.ac.uk)) if you would like to receive the papers when ready.*
- *There was a request for additional analysis on the impact of each year of delay, if possible, including by country (e.g. China, India, South Africa) for engagement with specific country governments and stakeholders.*
- *An offline comment noted that for R&D, a one-year delay in a clinical trial does not necessarily equate to a one-year delay in bringing a vaccine to market. A one-year delay in a clinical trial can lead to a multiple year delay in reaching the market due to impacts on trial site preparation, enrollment, and community engagement, among others.*

### It is unlikely that we will have a vaccine available by 2025. What are some of the specific advocacy asks considering this?

The greatest impediment to access is not yet having a new TB vaccine licensed. Phase III trials are extraordinarily expensive (in excess of US\$400-\$600 million) and the field is hindered by significant delays such as has been seen with the M72/AS01E candidate. It is important to advocate for the avoidance of delays that happen if a vaccine candidate obtains a signal of efficacy at Phase IIb and call for the de-risking of seamlessly moving to a Phase III trial. Is there some fund or pooled funding mechanism that can be leveraged to advance directly into Ph III?

As the modeling showed, introducing as quickly as we have done so for COVID, would likely save ~50% more lives than introducing at the same rate that other new (non-COVID) vaccines have been introduced in LMICs historically.

Further, the delay to Phase III trials is extremely frustrating but it is also frustrating how long they take. We should be encouraging funders to try and complete the trials more quickly. This is feasible but we need to ensure that we have a large enough number of people in high TB incidence areas.

### How much has the analysis of the funding need for TB vaccine R&D (i.e., in the Global Plan 2023-2030) and for introduction once licensed taken into account the upfront costs needed to accelerate research activities?

We need to consider how quickly we need these funds. Do we need an equal amount each year or do we need higher upfront investments to be able to accelerate research, whether through innovation or scale-up?

For vaccine rollout, the [Global Plan 2023-2030](#) estimates that \$52.6 billion will be needed to support large-scale implementation of a new TB vaccine from 2027-2030. This increases from \$12.4 billion in 2027 to \$14.0 billion in 2030 (see p144 for more).

**How can we bring governments to be committed to such investment cases? Further, catastrophic expenditure is defined as 20% or more of a household's annual income in the majority of low-income countries. Is the threshold used in the investment case specific to this level or also applicable to MICs as well?**

Have a message that matters to a Minister of Finance, not just a Minister of Health. Ministers of Finance should be interested in the catastrophic costs averted as a key outcome of financial risk. The 20% threshold was used across all the countries in the analysis, as recommended by WHO in the Global TB report. It is important to note that the value of 20% of a household's annual income differs by each country setting and incorporates a distribution of income levels.

**Other considerations and comments shared:**

- *How can we link dollar investments to existing mechanisms (e.g., Global Fund, Financial Intermediary Fund)?*
- *It may be more proactive and positive using COVID vaccine delivery as an example, including in the need for huge cohorts for trials.*

**Publications**

Portnoy A, Clark RA, Quaife M, Weerasuriya CK, Mukandavire C, Bakker R, et al. (2023) **The cost and cost-effectiveness of novel tuberculosis vaccines in low- and middle-income countries: A modeling study.** PLoS Med 20(1): e1004155.  
<https://doi.org/10.1371/journal.pmed.1004155>

**Pre-prints**

Clark RA, Mukandavire C, Portnoy A, Weerasuriya CK, Deol A, Scarponi D, et al. (Oct 2022) **The impact of alternative delivery strategies for novel tuberculosis vaccines in low- and middle-income countries: a modelling study.**  
medRxiv 2022.04.16.22273762;  
<https://doi.org/10.1101/2022.04.16.22273762>  
*[accepted at Lancet Global Health, publication expected in coming months]*

Portnoy A, Clark RA, Weerasuriya CK, Mukandavire C, Quaife M, Bakker R, et al. (Oct 2022) **The potential impact of novel tuberculosis vaccines on health equity and financial protection in low- and middle-income countries.**  
medRxiv 2022.10.29.22281678;  
<https://doi.org/10.1101/2022.10.29.22281678>

Portnoy A, Arcand JL, Clark RA, Weerasuriya CK, Mukandavire C, Bakker R, et al. (Nov 2022) **The potential impact of novel tuberculosis vaccine introduction on economic growth in low- and middle-income countries.** medRxiv 2022.11.23.22282690;  
<https://doi.org/10.1101/2022.11.23.22282690>

