The urgent need for a TB vaccine

Translating **science** into **global** health impact

A vaccine is necessary to end the TB pandemic. IAVI and partners continue to make strides to reach this goal.

A global public health emergency

Tuberculosis (TB), declared a public health emergency by the World Health Organization (WHO) in 1993, remains a major global health threat. Before COVID-19, TB killed more people than any other single infectious disease. As the COVID-19 pandemic has waned, TB once again kills more people —approximately 1.3 million per year, more than 3,560 people every day — than any other infectious disease in much of the world. Additionally, TB is one of the main drivers of the growing global antimicrobial resistance crisis, with multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) both on the rise. These forms of drug-resistant TB are very difficult and expensive to treat and carry an increased risk of treatment failure and death than for drug-sensitive TB.

TB is primarily a disease of poverty. More than 90% of people who fall ill with TB live in developing and emerging economies, imposing an enormous socio-economic burden on patients, families, and communities. In 2014, the WHO adopted an End TB Strategy, calling for a reduction in TB deaths of 35% by 2020 and 75% by 2025, as compared to 2015. (WHO End TB Strategy, 2014.) Tragically, we are nowhere near achieving these goals, as the net reduction in TB deaths between 2015 and 2021 reached only 5.9%. These goals will only be achievable through the introduction of vaccines capable of preventing the development of TB disease in adolescents and adults, among whom most disease and transmission occurs.

Limited impact of existing vaccine

The only available TB vaccine is the more than 100 years old bacillus Calmette-Guérin (BCG). BCG is effective in protecting infants and young children against developing severe TB disease, such as TB meningitis and miliary TB. Although a recent South Africa-based study suggested that BCG revaccination may reduce the chance of becoming infected with Mycobacterium tuberculosis (M.tb), the germ that causes TB. among adolescents without evidence of prior M.tb infection, BCG generally offers variable and mostly poor protection against TB disease in the lungs in adolescents and adults. New vaccines capable of preventing TB disease in adolescents and adults are essential in stopping the ongoing TB epidemic.

TB by the numbers

10.6 million
people developed TB disease in 2022

1.3 million
people died of TB disease in 2022

25% of people
globally may be infected with TB

$1.25 billion
annual funding need for TB vaccine R&D

710,200 new TB cases
among people living with HIV in 2022

Sources available at iavi.org/fact-sheets-sources

TB R&D shortfall

TB R&D has been chronically underfunded in relation to the impact of TB upon global health. At the United Nations High-Level Meeting on TB in 2023, world leaders pledged to deliver US$5 billion per year for TB research by 2027. The Global Plan to End TB 2023-2030 projects that an annual investment of $1.25 billion will be needed for TB vaccine R&D if we are to have a chance of reaching the End TB targets: decreasing TB mortality by 90% and decreasing new cases of TB by 80% in 2030 as compared to 2015 rates. Despite these commitments, annual investments in TB research only exceeded $1 billion for the first time in 2021, while funding for TB

vaccines has never exceeded $145 million per year, greatly hindering the development of new, desperately needed TB vaccines.

TB vaccine development is at a critical juncture

We are just now making breakthroughs in clinical efficacy trials, animal models, and new candidates that will inform the next generation of research and clinical development; for the first time in history, three new TB vaccines are either in Phase III efficacy trials or soon will be if sufficient funding is made available to conduct these complex, expensive trials. If these advances are slowed, the world is likely to lose 10-20 years of progress toward a successful vaccine. We need to accelerate the development of TB vaccines by removing financial obstacles to conducting Phase III licensure studies; supporting research and development of new, even more promising TB vaccine strategies; testing TB vaccines in broader populations; and developing strategies to ensure prompt and equitable access to future TB vaccines.

New TB vaccines on the horizon

Recent results from clinical trials provide hope that new, effective TB vaccines can be licensed and utilized globally in the coming decade if appropriate investments are made in clinical trials to assess vaccine safety and efficacy, and to ensure that these vaccines, once licensed, will be accessible to those most at risk of developing and spreading TB. Moreover, there are ongoing efforts to broaden the diversity of immune responses through innovative and emerging platforms, such as mRNA approaches, and improved protein-adjuvant combinations. Funders must invest in all phases of research and develop a plan for access to bring the first of a new generation of safe and effective TB vaccines to the people who need them most. As the pipeline progresses, so do the resources needed, with the late development stage requiring up to 70% of the estimated R&D budget.

The impact of COVID-19 on TB

Modeling from STOP TB Partnership finds that the COVID-19 pandemic may have set back the fight against TB by up to 12 years, with conservative estimates suggesting an additional 6.3 million people will fall ill with TB and an additional 1.4 million people will die of TB between 2021-2025.

Global TB vaccine pipeline

Overall pipeline

14 trials
whole-cell, subunit, viral-vector, and mRNA candidates in all phases

Late-phase efficacy trials

8 trials
whole-cell and subunit in Phase II proof-of-concept to Phase III

Candidates supported by IAVI

MTBVAC* and **mRNA-encoded TB antigens**

* Trials in adults and adolescents. Biofabri is leading clinical development of the candidate in infants (currently in a Phase III trial).

IAVI gratefully acknowledges the generous support provided by the following major funders:

Biomedical Advanced Research and Development Authority (BARDA) | Foundation for the National Institutes of Health | National Institute of Allergy and Infectious Diseases | amfAR, The Foundation for AIDS Research | Broadway Cares/Equity Fights AIDS | The City of New York, Economic Development Corporation | Congressionally Directed Medical Research Program (DoD) | GSK | The Hearst Foundations | Keith Haring Foundation | Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the USA and Canada)

And many other generous individuals and partners around the world

As of January 2024