The urgent need for a TB vaccine

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 1.6 million per year, more than 4,100 people every day — than any other infectious disease in much of the world. This is more people than die every year of HIV/AIDS and malaria, combined. Additionally, TB is one of the major contributors to the global burden of antimicrobial resistance, 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 with them increased risk of treatment failure and death than for drug-sensitive TB.

TB is primarily a disease of poverty. More than 90% of TB cases occur 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 2020 reached only 5.9%. These goals only will be achievable through the introduction of vaccines capable of preventing the development of TB disease in adolescents and adults, the primary spreaders of Mycobacterium tuberculosis (M.tb), the germ that causes TB.

Limited impact of existing vaccine

There is only one TB vaccine, bacillus Calmette-Guérin (BCG), which is over 100 years old. The vaccine is effective in protecting infants and young children against developing severe tuberculosis disease, such as TB meningitis and miliary TB. Although a recent South Africa-based study suggested that BCG revaccination of adolescents absent evidence of prior infection with M.tb may reduce the chance of becoming infected with M.tb, BCG generally offers variable and mostly poor protection against lung TB disease in adolescents and adults. New vaccines capable of preventing TB disease in adolescents and adults are essential in stopping the ongoing TB epidemic.

TB R&D shortfall

TB R&D has been chronically underfunded in relation to the impact of TB upon global health, even though it causes more deaths than HIV/AIDS and malaria combined. At the United Nations High-Level Meeting to End TB in 2018, world leaders pledged to deliver at least $2 billion per year for TB research, of which $550 million was earmarked for TB vaccine R&D. Despite these commitments, TB research is impeded by an annual $1.1 billion shortfall, while funding for TB vaccines has never exceeded $120 million per year, greatly hindering the development of new, desperately needed TB vaccines.

Sources available at iavi.org/fact-sheets-sources
The Global Plan to End TB 2023-2035 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 of TB death and disease.

**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

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<tr>
<th>Overall pipeline</th>
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<tr>
<td><strong>11 trials</strong></td>
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<td>whole-cell, subunit, and viral-vector candidates in all phases</td>
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<th>Late-phase efficacy trials</th>
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<td><strong>9 trials</strong></td>
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<td>whole-cell and subunit in Phase II proof-of-concept to Phase III</td>
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**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).

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