The urgent need for a TB vaccine

A vaccine is necessary to end the TB epidemic. 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. Today, more than 4,000 die of TB every day. 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. TB is primarily a disease of poverty, with over 90% of TB cases occurring in developing and emerging economies and imposing an enormous socio-economic burden on patients, families, and communities. It has become clear that we are far off course to reach the WHO goal to end TB by 2035. This cannot be achieved without new vaccines, diagnostics, and drugs.

Limited impact of existing vaccine

There is only one TB vaccine, bacillus Calmette-Guérin (BCG), which is nearly 100 years old. The vaccine has efficacy in protection against severe tuberculosis disease, such as TB meningitis and miliary TB, in infants and young children, but offers variable and mostly poor protection against lung disease in adolescents and adults. The latter populations are responsible for spreading TB in the community. To interrupt transmission, new and more effective vaccines that target adolescents and adults are therefore needed.

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. The Declaration of the 2018 UN High-Level Meeting on Ending TB included the Stop TB Partnership’s call for TB R&D investment to be increased to meet the funding shortfall of $1.1 billion, while also noting the importance of developing new and effective vaccines. Meanwhile, the WHO has concluded that “targets for 2035 cannot be met without intensified R&D.”
**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. If these advances are slowed, the world is likely to lose 10-20 years of progress toward a successful vaccine. We now need to accelerate the development of TB vaccines: we need to confirm the results of the recent studies, test TB vaccines in broader populations, plan for licensure trials, and develop roadmaps to ensure prompt and equitable access to future TB vaccines.

**New TB vaccines on the horizon**

Recent significant trial results suggest new effective TB vaccines can be developed in the coming decade if appropriate investments are made. Moreover, there are ongoing efforts across the TB research community to broaden the diversity of immune responses through innovative and emerging platforms, such as mRNA and DNA approaches, antibody-mediated protection, 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.

**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 over the next five years.

**Why do we need a vaccine to end the TB epidemic?**

- Vaccines typically provide long-lasting protection.
- Vaccines could eliminate adherence and stigma problems associated with TB treatment.
- Vaccines would reduce the incidence of MDR- and XDR-TB.
- Vaccines that prevent TB transmission would have a significant impact on the epidemic.

**Global TB vaccine pipeline**

<table>
<thead>
<tr>
<th>Pipeline Type</th>
<th>Number of Trials</th>
<th>Phase(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall pipeline</td>
<td>15+</td>
<td>whole-cell, subunit, and viral-vector candidates in all phases</td>
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<tr>
<td>Late-phase efficacy trials</td>
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<td>whole-cell and subunit in Phase II proof-of-concept to Phase III</td>
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<tr>
<td>IAVI clinical trial collaborations</td>
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<td>whole-cell and subunit in Phases II and III</td>
</tr>
</tbody>
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**IAVI gratefully acknowledges the generous support provided by the following major funders:**

[IAVI's acknowledgment list includes various organizations and entities that support TB research and development.]

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As of April 2022