

## Time to invest in tuberculosis research and disease control



World TB Day on March 24, 2023, marks another year of both progress and setbacks for tuberculosis research and control efforts. The COVID-19 pandemic continues to impact tuberculosis case detection, treatment, and prevention, which has led to millions of missed cases. However, the promise of vaccines and continued developments in the diagnosis and treatment of tuberculosis are important steps towards the WHO End TB Strategy goals of an 80% drop in new cases and 90% drop in people dying from tuberculosis by 2030.

Kogieleum Naidoo and Rubeshan Perumal summarise advances in tuberculosis control over the past decade and highlight the pressing need for strategies to reduce tuberculosis incidence and mortality—not least, strategies to reduce latent infection, duration of infectiousness, and risk of community transmission. A key goal for disease prevention is the rollout of an effective vaccine. On Dec 8, 2022, WHO published the results of an assessment that highlights the potential health and economic benefits of investing in tuberculosis vaccine development and implementation. WHO estimates that if adolescents and adults were given a vaccine that was 50% effective at preventing tuberculosis, over 25 years it would reduce new tuberculosis cases by 76 million and deaths by 8.5 million.

In January, 2023, WHO announced plans to establish a TB Vaccine Accelerator council, which will facilitate the licensing and use of effective, novel tuberculosis vaccines. The council will encourage collaboration between funders, global health agencies, and governments to overcome barriers in tuberculosis vaccine development. This focus on tuberculosis vaccines comes at a crucial time. Currently, the only licensed tuberculosis vaccine is the 1921 BCG vaccine, which can protect young children against severe forms of tuberculosis, but offers inadequate protection to adolescents and adults. However, at least 16 vaccines are under development, and if any of these proves to be effective, successful implementation will require adequate investment and support.

The question remains of how to reach the populations most at risk of infection and tuberculosis disease progression with a safe, effective vaccine. Molebogeng Rangaka and colleagues discuss how future vaccine trial designs might fulfil the ethical duty of researchers to provide tuberculosis preventive treatment (TPT) to

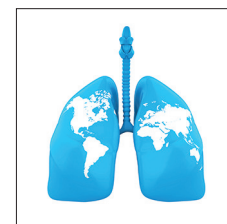
participants—reflecting the expanded WHO recommendations for those eligible for TPT—and include the high-risk populations most likely to benefit from new vaccines.

TPT is evolving to include shorter, safer regimens as an alternative to 6–9 months of isoniazid monotherapy. The next step is to determine which of these shorter-course regimens is optimal. Nicholas Winters and colleagues indirectly compared a 3-month isoniazid-rifampentine regimen (3HP) with 4 months of rifampicin (4R) in an individual patient data network meta-analysis. They found that a higher proportion of participants who received 3HP administered as directly observed therapy completed treatment. However, participants receiving 3HP also had a higher proportion of adverse events. There was no difference between 3HP and 4R in terms of tuberculosis prevention. These results will help clinicians to weigh the benefits of these two shorter TPT regimens. Naidoo and Perumal emphasise that TPT strategies should focus on the “dynamic, multistate, bidirectional spectrum of latent incipient, subclinical, and clinically active tuberculosis” rather than considering tuberculosis as a dichotomy of latent infection and active disease, and rapid phenotypic drug-susceptibility profiling could support the rollout of new drugs.

In addition to the End TB Strategy goals of reducing tuberculosis cases and deaths, an important aim is to protect families from the huge financial costs related to tuberculosis. If vaccines are successfully implemented, a dramatic decrease in the number of courses of antibiotics required could save households billions of dollars. According to the WHO assessment, for every \$1 invested in a vaccine that is only 50% effective, there would be an economic return of \$7 in terms of averted health costs and increased productivity. Shorter treatment regimens could also lead to reduced costs for families that do need treatment.

In the wake of the COVID-19 pandemic, substantial investment is needed to support high-quality tuberculosis research, to strengthen local health-care services and promote equitable access to care across all populations at risk, and to ensure effective implementation of new treatments that come to market. Momentum must not be lost if we are to see meaningful progress in reducing the burden of tuberculosis disease by World TB Day 2024.

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For more on **World TB Day 2023** see <https://www.who.int/campaigns/world-tb-day/2023>

For more on **missed tuberculosis cases** see *News Lancet Respir Med* 2022; 10: e112

For the **10<sup>th</sup> Anniversary Round-up from Naidoo and Perumal** see *Online/Comment* [https://doi.org/10.1016/S2213-2600\(23\)00090-5](https://doi.org/10.1016/S2213-2600(23)00090-5)

For the **WHO investment case for tuberculosis vaccines** see <https://www.who.int/publications/i/item/9789240064690>

For more on the **WHO TB Vaccine Accelerator council** see <https://www.who.int/news/item/17-01-2023-who-announces-plans-to-establish-a-tb-vaccine-accelerator-council>

For the **article by Rangaka and colleagues** see *Online/Personal View* [https://doi.org/10.1016/S2213-2600\(23\)00084-X](https://doi.org/10.1016/S2213-2600(23)00084-X)

For the **meta-analysis by Winters and colleagues** see *Online/Articles* [https://doi.org/10.1016/S2213-2600\(23\)00096-6](https://doi.org/10.1016/S2213-2600(23)00096-6)

For more on **progression and regression along the spectrum of tuberculosis disease** see *Online/Review* [https://doi.org/10.1016/S2213-2600\(23\)00097-8](https://doi.org/10.1016/S2213-2600(23)00097-8)