Ending the TB pandemic: the urgency of a new and improved TB vaccine and the World Health Organization's TB Vaccine Accelerator Council

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WHO's decision to establish a council to accelerate TB vaccine development is crucial in tackling the global TB epidemic. 10 million new cases and 1.4 million deaths in 2020 alone highlights the urgency for improved vaccines. https://bit.ly/3PtXZfR

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Abstract

We support the World Health Organization (WHO) recent decision to create a council to accelerate the development of a tuberculosis (TB) vaccine. With over 10 million new cases and 1.4 million deaths in 2020 alone, new and improved vaccines are urgently needed. Recent advancements in TB vaccine research offer hope, but a lack of funding, coordination and understanding of immune responses have impeded progress. A TB Vaccine Accelerator Council aims to bring together resources and expertise to overcome these obstacles and speed up development. Support and investment in research are crucial to ultimately eradicate TB and achieve the WHO goal of ending TB by 2035.

Introduction

We write in support of the World Health Organization (WHO) recent decision to establish a Tuberculosis (TB) Vaccine Accelerator Council (TB VAC) as announced on 17 January 2023 [1]. The goal of the council is to speed up the process of ending TB. According to WHO, the new council will bring together key stakeholders, that include representatives from governments, academia, the private sector and civil society to accelerate the development, testing and roll-out of new TB vaccines. TB poses a significant burden with 10 million new cases and 1.4 million deaths reported in 2020 [2]. This figure increased to about 10.6 million new TB cases and 1.6 million TB deaths in 2021 [3]. Despite the availability of the bacille Calmette–Guérin (BCG) vaccine for nearly a century, its effectiveness is limited, and new, improved vaccines are urgently needed. The history of TB vaccine development has been marked by both progress and failures. The BCG vaccine was first developed in 1921 and is the only licensed vaccine for TB. Notwithstanding, the effectiveness of the BCG vaccine varies widely depending on the population and setting. BCG provides protection against severe forms of childhood TB. However, it has poor protection against adult pulmonary TB, necessitating the need for new vaccine candidates that can offer better protection against all forms of TB, and the priority for improved methods that could enhance the evaluation of vaccine efficacy. This viewpoint emphasises the imperative of the newly established TB VAC in addressing these challenges. By fostering collaboration, innovation and inclusivity, the TB VAC will play a crucial role in overcoming barriers, promoting equitable access, and driving progress in TB vaccine research and development (table 1).

Why is a TB Vaccine Accelerator Council necessary?

TB is a highly infectious disease caused by *Mycobacterium tuberculosis* and transmitted through respiratory droplets. The estimated reproductive number of *Mycobacterium* ranges from 0.4 to 7.2, emphasising the urgency for effective TB preventive measures. Moreover, the emergence of drug-resistant

TABLE 1 SWOT (strengths, weaknesses, opportunities and threats) analysis: creation of a Tuberculosis (TB) Vaccine Accelerator Council (TB VAC)

Strengths
TB VAC will address and proactively tackle the adverse impact of COVID-19 on TB services
TB VAC encourages global collaboration among funders, global health agencies, the private sector and governments
TB VAC is getting high-level support from eminent global health leaders, such as Dr Tedros Adhanom Ghebreyesus, the Director-General of the World Health Organization
Weaknesses
TB VAC will need to find solutions for the complex scientific and technical challenges related to vaccine efficacy, safety and immunological responses
TB VAC requires huge resources and adequate funding for successful establishment and day-to-day operation
Navigating the time-consuming and challenging regulatory and approval processes for vaccine development can be difficult
Achieving sufficient manufacturing capacity and a robust supply chain for TB vaccines can be challenging
Inadequate skilled researchers, laboratories and infrastructure may impact progress
Access to target populations: the logistics of reaching and vaccinating affected populations, particularly in low-income and middle-income countries could be enormous
Opportunities
Improved TB prevention: development of effective vaccines to reduce global TB cases including drug-resistant cases and deaths
Global health impact: potential to significantly impact global health by accelerating TB vaccine development
Threats
Insufficient funding: inadequate financial resources could impede the successful establishment and operation of the TB VAC
Scientific challenges: overcoming scientific bottlenecks related to vaccine efficacy, safety, and immunological responses

TB strains, such as multidrug-resistant TB and extensively drug-resistant TB, creates a major threat to TB control, and necessitates the development of new vaccines to address the health and economic burden associated with drug resistance [2, 4]. Recent advances in TB vaccine development have shown promise for new approaches such as subunit and adjuvanted vaccines [5]. These scientific advances have also enhanced the understanding of protective immune responses against *M. tuberculosis*, although this has not led to development of a definitive TB vaccine. A TB VAC will harness all the necessary resources and expertise needed to accelerate the development and implementation of new TB vaccines. The WHO's proposed TB VAC aims to tackle the barriers hindering TB vaccine development in the past. Examples of these barriers include lack of funding, coordination, and understanding of the immunological mechanisms that protect against TB [6]. By creating a platform for collaboration and coordination among researchers, policymakers and funders, the TB VAC will address these obstacles and accelerate the development of new and effective TB vaccines [7]. The new TB VAC will also play a critical role in coordinating the efforts of various stakeholders to tackle the complex challenges involved in developing new TB vaccines.

History of TB vaccine development: recent advances, successes and failures

Historically, TB vaccine development has faced challenges due to factors such as limited understanding of protective immune responses, the complexity of the disease and inadequate research funding. There has been unprecedented global attention on coronavirus disease 2019 (COVID-19) vaccine development; by contrast, efforts to develop TB vaccines have lagged behind, with 16 candidates currently in the pipeline. However, recent progress in TB vaccine research, including the identification of new candidates like MVA85A and H56, and the exploration of innovative approaches such as combination vaccines and adjuvants, provides renewed hope for an effective TB vaccine [5]. These novel findings facilitated additional insights into the protective immune responses against *M. tuberculosis* (including exploration of mRNA vaccines against new strains of TB) and paved the way for novel strategies that could enhance vaccine efficacy [4, 8, 9]. A deeper understanding of the challenges of developing new TB vaccines could facilitate identification of new vaccine targets that are crucial for successful TB vaccine development [6, 10, 11]. Interestingly, the economic benefits of developing effective TB vaccines are enormous. A modelling study by Portnoy *et al*. [12] observed that a vaccine with 50% efficacy could avert approximately 76 million TB cases, 8.5 million deaths, and 42 million courses of antibiotic treatment among young people and adults above 25 years of age. The study underscored the cost-effectiveness of novel TB vaccines, which can lead to substantial savings in healthcare costs and productivity losses.

Investing in TB vaccine development is not only a public health imperative but also an economically sound decision.

Adapting lessons from the COVID-19 pandemic for TB vaccine development

Vaccines against COVID-19 were developed in less than a year, while TB, a disease that has been prevalent for decades, still lacks effective vaccines. Vaccines have been a game-changer in the fight against COVID-19 and can have a similar impact on TB if developed quickly and effectively. The COVID-19 pandemic has provided valuable lessons for accelerating the development of vaccines for other diseases such as TB [12]. Very strong public–private partnerships can be pivotal in the development of TB vaccines and other tools for diagnosis and treatment. In addition to vaccine development, it is essential to strengthen healthcare infrastructure, enhance laboratory capacity and improve access to quality diagnostics and anti-TB drugs. The involvement of the private sector, academia, civil society and international organisations is vital for driving innovation, securing funding and facilitating technology transfer. Lessons learned from the COVID-19 pandemic highlight the importance of public–private partnerships in accelerating vaccine production.

Innovative pathways: advancing TB vaccine development and equitable access for low- and middle-income countries

Low- and middle-income countries (LMICs) bear a significant burden of TB and must be actively involved in the development and implementation process. Engaging these countries in research, clinical trials and implementation programmes will ensure that vaccines are tailored to their specific needs and can be effectively delivered in resource-constrained settings. In addition, equitable access to new TB vaccines is crucial for LMICs. There must be established mechanisms to ensure affordable pricing, fair distribution and sustainable financing. The involvement of LMICs in the development and implementation process will help to address their unique challenges, make vaccines affordable and enhance community acceptance. Also, future paths for TB vaccine development should focus on innovative strategies such as antigen design to enhance the immune response. Exploring novel vaccine platforms, including mRNA vaccines and combination vaccines that stimulate a broader immune response, can also fast-track the development timeline.

In conclusion, the TB VAC, coupled with a holistic approach that encapsulates improved access to diagnostics and treatment, collaboration, equitable access and innovative strategies, offers hope in TB elimination. By learning from the lessons of COVID-19, engaging LMICs, and investing in research and development, we can pave the way for effective TB control worldwide and ultimately achieve the goal of ending the TB pandemic by 2035. Strong international collaborations, data sharing, research transparency and standardisation of protocols will be crucial to optimise the operations of the TB VAC.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of Jhpiego Nigeria, Johns Hopkins University or APIN Public Health Initiatives.

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