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Editorial

World Tuberculosis Day 2024 theme "Yes! We can end TB" can be made a reality through concerted global efforts that advance detection, diagnosis, and treatment of tuberculosis infection and disease

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Every year, World Tuberculosis (TB) Day is commemorated on March 24 and is targeted at raising public and political awareness of TB, a preventable and treatable disease. World TB Day commemorates the day in 1882 when Professor Robert Koch announced his discovery of the microbial cause of TB, the TB bacillus, *Mycobacterium tuberculosis*.

Despite effective TB treatment being available for over 65 years, TB today causes 1.3 million deaths yearly, mostly in low- and middle-income countries. Drug-resistant TB is the leading cause of death owing to antimicrobial resistant disease in the world today and is a growing global health security threat, with hundreds of thousands of people affected every year [1]. It is in this dismal global situation that "Yes! We can end TB!" is the World Health Organization (WHO) and STOP TB Partnership's theme for World TB Day [1]. This theme remains the same as that of World TB Day 2023 to emphasize and deliver a message of hope to those who continue to be affected. Critical to highlight on this day will be the provision of the required global funding to enable faster uptake of new WHO management recommendations for finding, diagnosing,

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and effectively treating infections and all cases of clinical TB using new and updated WHO recommendations and guidelines [2–5].

Although global efforts to combat TB have saved an estimated 75 million lives since 2000, the COVID-19 pandemic, coupled with conflicts across Europe, Africa, and the Middle East [6,7] and poor socioeconomic conditions, have reversed years of progress that was being made by global efforts to control and eventually end TB. The deteriorating global economic situation, with rising cost of living and reduction of budgets for national health programs, has disproportionately affected the poorest and disadvantaged, the very populations who are most affected by TB. Moreover, access to available WHO-recommended TB diagnostics and treatment regimens remains a major challenge, especially in low- and middle-income countries, where 80% of the annual TB caseload occurs.

The United Nations General Assembly (UNGA) convened its second High-Level Meeting (HLM) on the fight against TB on September 22, 2023 to revisit the global targets established for 2018-2022 during the first meeting and to develop new targets up to 2027. Member states at the meeting endorsed a political declaration that reaffirms global commitments to end TB by 2030. The targets of the first United Nations HLM sought to treat at least 40 million individuals with TB worldwide from 2018 to 2022, addressing the TB needs of 3.5 million children, providing treatment for 1.5 million individuals with drug-resistant TB, and initiating TB preventive treatment (TPT) for at least 30 million people. The new global targets for 2023-2027 are more ambitious [1]. These include achieving 90% of patients having access to quality-assured diagnosis and treatment, 90% of individuals at risk of developing disease having access to TPT, 100% of people with TB having access to health and social benefits packages, raising 22 billion US$ for research, and developing a new vaccine against TB.

In this special *International Journal of Infectious Diseases* issue to commemorate World TB Day, we present nine reports covering several of these aspects. We discuss several prevention issues. Prevention starts with vaccines [8]. There have been no new TB vaccines available since the introduction of the bacille Calmette–Guerin vaccine over a century ago. Encouragingly, several promising TB vaccine candidates are currently being evaluated in phase II and III clinical trials [8]. In parallel, we describe the immunology approaches to design vaccines and immune diagnostic tests for TB [9]. The screening strategies are reported in terms of political commitments, as the Prevention and Systematic Screening Initiative, which is a new approach to technical assistance, focused on prevention and systematic screening, to end TB in the WHO European Region by 2030 [10,11]. Screening procedures and TPT are also discussed, with a focus on persons moving from high- to low-TB endemic countries [12]. This highlights the importance of identifying persons with TB infection and ensuring they receive TPT to prevent the re-activation of latent TB infection (LTBI) toward TB disease, leading to further transmission. In addition to screening migrants, South Korea developed a highly successful program for LTBI screening. This intervention has contributed to an annual 5.2% reduction in TB incidence between 2011 and 2016 through the screening of community workers, including daycare centers for children, kindergarten, and schools [13].

Although TB mainly affects the lungs, it can also affect other organs. When people with pulmonary TB cough, sneeze, or spit, TB bacilli are propelled and spread through the air and respiratory droplets. A person in close contact needs to inhale only a few mycobacteria to become infected. About a quarter of the global population (around 2 billion people) is estimated to have an immune response against TB and are likely to have TB infection. Most people with LTBI will not go on to develop TB disease and some will clear the infection. People showing an immune response against TB bacteria have a 5-10% lifetime risk of falling ill with TB disease during their whole life span. Those with compromised immune systems, such as people living with HIV, malnutrition, or diabetes, or using tumor necrosis factor inhibitor therapies or tobacco, have a higher risk of falling ill [14,15]. Screening is done by standardized interferon-γ release assays and skin tests [16–18], the new one based on the intradermal inoculation of ESAT-6 and CFP-10, which are *M. tuberculosis*-specific antigens compared with those included in the tuberculin skin test [16–18]. The challenges of these new skin tests are also covered here [19].

Finally, we report an overview of experimental non-sputum diagnostic and biomarkers assays for TB disease detection and progression to disease. Non-sputum tests can be very important for diagnosing extra-pulmonary TB or pulmonary TB in those unable to expectorate, such as children, or in immunocompromised subjects where the sputum *M. tuberculosis* load can be very low. A test based on the Actiphage technology to detect *M. tuberculosis* DNA in the blood is described [20] as useful for TB diagnosis and identifying those with TB infection that may progress to TB disease [21,22]. An alternative and potentially complementary approach for the detection of progressors to TB disease is by measuring host inflammation [23]. Host immune responses can be measured by a proteomic and transcriptomic assessment that can detect increasing immune activation associated with TB disease progression several months before the onset of clinical disease [24,25]. The potential importance of new methodologies for defining the latency stage of TB infection based on the detection of *M. tuberculosis* DNA in $CD34^+$ cells in the blood of subjects with TB infection is discussed [26,27]. These methodologies could help to better understand TB pathogenesis and may allow specific targeting of the patients who require TPT.

Conclusion

To achieve global TB control and eventually elimination, we need several actions: increased investments to accelerate the promising new TB vaccines pipeline, implementation of new immune strategies for better vaccine design, new therapies and/or therapy regimens, new diagnostic tests, implementation of prevention through screening using standardized old and new diagnostic tests for TB infection detection [28], implementation of the non-sputum diagnostic tests for TB disease, and implementation of tests for the identification of those progressing toward TB disease to better target those needing therapy.

In the current dialogue on getting available TB interventions rolled out, it is critical to note that when Professor Robert Koch first announced the discovery of *M. tuberculosis*, TB was an epidemic ravaging all of Europe and the United States, and it was causing the death of one in every seven people in the community. It is, thus, a blight on the conscience of all political leaders and governments that 142 years after this brilliant discovery, TB continues to be the cause of the disease in 10 million people annually [1]. The global community must reflect on the historical, social, philosophical, and political factors that led to a failure in TB control for the past century. The rates of TB in Europe and the United States started to decline well before the advent of TB drugs and this was attributable to improved housing conditions, living standards, and nutrition [29,30]. However, such improvements are not universally accessible, and TB remains an epidemic of injustice and a paradigm for health inequality. Re-establishment of the political commitments at the UNGA-HLM in 2017 is required to bring TB control efforts back on track to achieve the WHO and STOP TB 2025 targets. Governments in low- and medium-income countries must invest more in TB control efforts and link them to the WHO Sustainable Development Goals of reducing poverty, poor housing, and malnutrition. Only then can we say “Yes! We can end TB.”

Declarations of competing interest

Delia Goletti is on the scientific board of PBD Biotech. The remaining authors have no competing interest to declare.

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Author contributions

DG wrote the first draft; AZ, SAA and EP revised the first draft; all the authors revised the second draft and added their comments and modifications. All the authors approved the final version.

Transparency Declaration

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