



REVIEW ARTICLE

# Decoding the WHO Global Tuberculosis Report 2024: A Critical Analysis of Global and Chinese Key Data

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## Abstract

The World Health Organization (WHO) “Global Tuberculosis Report 2024” underscores the ongoing challenges and progress in the global fight against tuberculosis (TB). Despite a slowdown in the annual increase in TB cases and a decline in TB-related deaths, the disease remains a significant public health threat with 10.8 million new cases reported in 2023. The report reveals a persistently high burden of TB, especially in low- and middle-income countries, and highlights the escalating issue of drug-resistant TB. The report also emphasizes the critical need for increased funding, improved diagnostics, and more effective TB treatment regimens. The impact of the COVID-19 pandemic on TB control has been substantial, disrupting healthcare services and exacerbating existing challenges. This paper provides an in-depth interpretation of the report, analyzes global TB trends, updates the status of drug-resistant TB, discusses the intersection between TB and HIV, and summarizes the implications of the pandemic on TB control efforts. The report concludes with a call for intensified global action, including increased investment in research and innovation, to achieve the United Nations’ Sustainable Development Goals related to TB control. The stakes are high, but with concerted efforts, the goal of ending the TB epidemic is within reach.

**Key words:** Tuberculosis, Drug-resistant TB, Diagnostics and treatment, HIV co-infection, Sustainable development goals, End TB strategy

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## INTRODUCTION

The World Health Organization (WHO) released the “Global Tuberculosis Report 2024” on 29 October 2024 [1]. The report provides a comprehensive review of the progress and challenges in global tuberculosis (TB) control, serving as a critical reference for governments and international organizations in formulating future TB prevention and control strategies. The

report encompasses the latest data from 2023, reflecting the current state of the global TB epidemic and the impact on public health.

There were 10.8 million new TB cases globally in 2023 according to the “Global Tuberculosis Report 2024” with an incidence of 134 per 100,000 population [1]. Among these new cases, 662,000 (6.1%) were co-infected with HIV and 400,000 (3.7%) were patients with

multidrug-resistant (MDR) or rifampicin-resistant (RR) TB. The rate of multidrug-resistant/rifampicin-resistant TB (MDR/RR-TB) was 3.2% among new cases and 16% among previously treated cases. The global number of TB mortalities reached 1.25 million in 2023, making TB the leading cause of death from a single infectious disease globally with the number of deaths nearly twice the number of HIV/AIDS-associated deaths. These data underscore the persistent and severe nature of the TB epidemic and the urgent need for more effective control measures. Despite significant progress in TB control over recent years, these advances have been insufficient to address the global TB challenge.

This paper aims to provide a detailed interpretation of the “Global Tuberculosis Report 2024” to examine the current state of TB control, the challenges faced, and the opportunities for improvement. In our analysis we compiled a detailed interpretation of the WHO report and extracted key data points essential for understanding the global TB landscape. The original data was accessed from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/data>) for any data not explicitly mentioned in the report. GraphPad Prism software was utilized for data analysis and visualization to ensure accuracy and clarity in the findings. All data were independently verified by at least two experts to maintain the highest standards of reliability and validity in the research.

It is hoped that this interpretation will offer valuable insights for policymakers, researchers, and public health professionals to aid them in better understanding the characteristics of the TB epidemic and the socioeconomic impact. Additionally, this paper will focus on the control of drug-resistant tuberculosis (DR TB), particularly the specific challenges and response measures in China. We aim to propose concrete recommendations for the further optimization and development of global TB control strategies based on these analyses, thereby contributing to the achievement of the TB-related targets outlined in the United Nations 2030 Agenda for Sustainable Development Goals (SDGs) [2,3].

## TB BURDEN AND EPIDEMIC TREND ANALYSIS

### Global TB case estimates and incidence vary significantly

The recently published Global TB Report for 2024, which compiled data from 215 countries and regions, revealed that an estimated 10.8 million individuals were affected by TB worldwide in 2023 (Table 1) [1]. The TB incidence, defined as new cases per 100,000 population, was 134 in the same year. This report provides an in-depth analysis of the global trends in TB case estimates and incidence from 2010–2023 (Fig 1). There has been a noticeable deceleration in the annual increase of TB cases with a trend towards stabilization. The total number of estimated incident TB cases showed a slight downward trend during this period with the lowest figures recorded in 2020. The global TB incidence had an annual decrease of approximately 2% between 2010 and 2020 (Fig 1). While progress has been made in TB spread, success has been incremental. The advent of the SARS-CoV-2 pandemic led to significant disruptions in the diagnostic, preventive, and treatment systems for TB and other infectious diseases, particularly during the peak pandemic years of 2020 and 2021 [4]. The number of reported TB incident cases worldwide was estimated to be 10.1 million in 2020, increasing to 10.4 million in 2021, 10.7 million in 2022, and 10.8 million in 2023. The global TB incidence is projected to increase by 4.6% from 2020 to 2023, rising from 129 in 2020 to 134 in 2023. Furthermore, the number of newly diagnosed TB cases worldwide is expected to reach a new peak in 2023. The gap between the overall TB incidence and the number of newly diagnosed cases is narrowing. The global pandemic has set back progress in combating TB by several years. The sustained increase in subsequent years reflects the ongoing impact of disruptions to TB care and service delivery during the pandemic. The net reduction in the global TB incidence was 8.3% from 2015–2023. The 2025 milestone of the End TB Strategy, which aims for a 50% reduction from 2015–2025, remains a significant challenge. However, the rate of increase has slowed significantly to 0.2% between

**TABLE 1** | Estimates of TB burden globally.

| Items                                                                      | Number                             | Rate per 100,000 population* |
|----------------------------------------------------------------------------|------------------------------------|------------------------------|
| Total TB incidence, 2023                                                   | 10,800,000 (10,100,000–11,700,000) | 134 (125–145)                |
| TB incidence in people living with HIV, 2023                               | 662,000 (589,000–739,000)          | 8.2 (7.3–9.2)                |
| Multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) incidence, 2023 | 400,000 (360,000–440,000)          | 5 (4.5–5.5)                  |
| TB deaths in HIV-negative people, 2023                                     | 1,090,000 (977,000–1,200,000)      | 13 (12–15)                   |
| TB deaths in people with HIV, 2023                                         | 161,000 (132,000–193,000)          | 2 (1.6–2.4)                  |

\*Estimates of TB burden are produced by the WHO in consultation with countries. Ranges represent uncertainty intervals. The original data obtained from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/data>).

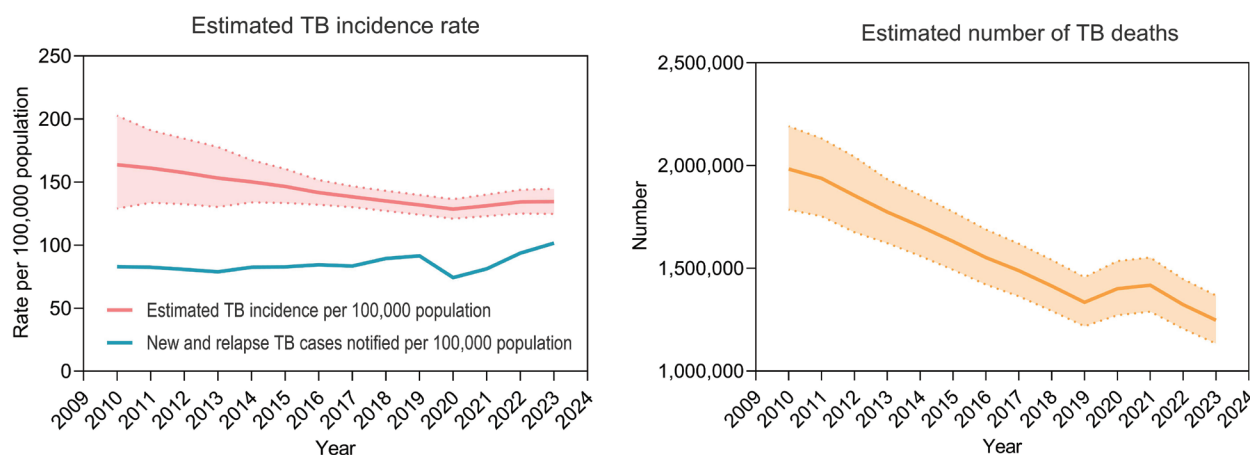


**FIGURE 1** | Estimated TB incidence and deaths from 2010–2023. The original data obtained from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/data>).

2022 and 2023, indicating a potential plateau, which is an encouraging sign of progress.

The prevalence of TB varies considerably at the regional level. In 2023 most individuals who developed TB were in the WHO regions of Southeast Asia (45%), Africa (24%), and the Western Pacific (17%), with smaller proportions in the Eastern Mediterranean (8.6%), the Americas (3.2%), and Europe (2.1%). Furthermore, the extent of decline in the global TB incidence rate since 2015 has considerable variation. Some WHO regions have made progress towards the 2025 milestones for reductions in the TB incidence. The WHO African and European regions have shown significant advances, exceeding the initial targets set by the End TB Strategy. The most substantial decline was observed in the WHO European region, with a net reduction of 27% by 2023. The decline was significant between 2015 and 2020, after which the decline flattened from 2021–2023. The WHO African region was the only region to show a continuous decline in the incidence of TB each year since 2010, with a net reduction of 24% by 2023. In contrast, the incidence of TB continued to increase in 2023 in 2 WHO regions (the Americas and the Western Pacific). The estimated net increase for the former reached 20% by 2023 compared to 2015, which is a cause for concern. The ranking of the 8 countries with the highest disease burden has remained unchanged for the last 3 years. These eight countries account for more than two-thirds of all estimated incident cases worldwide. The countries with the highest incidence are India (26%), Indonesia (10%), China (6.8%), the Philippines (6.8%), Pakistan (6.3%), Nigeria (4.6%), Bangladesh (3.5%), and the Democratic Republic of the Congo (3.1%). Additionally, India and the Philippines are among the 39 countries where the TB incidence in 2023 was >5% higher than 2015.

Of the 10.8 million individuals who fell ill with TB in 2023, 88% were adults and 12% were children and young adolescents (0–14 years of age). A breakdown of the TB burden by age and gender reveals that adult men (≥15 years of age) bear the greatest burden with an estimated 6.0

million cases, followed by adult women (≥15 years of age) with an estimated 3.6 million cases (Fig 2). It is estimated that 1.3 million cases occurred among children and young adolescents. Due to challenges associated with an accurate diagnosis, there are significant gaps in case detection and reporting, particularly among children <5 years of age. Moreover, in this age group <50% of the estimated cases were notified.

### TB-related mortality continues to decline globally

It has been estimated that 1.25 million TB-associated deaths occurred worldwide in 2023, including 161,000 and 1.09 million individuals with and without HIV, respectively. The estimated global number of deaths caused by TB has exhibited a decline over the past two consecutive years (1.32 million in 2022 and 1.42 million in 2021; Fig 1). It is noteworthy that the overall trend in deaths caused by TB has consistently declined since 2010 (except for 2020 and 2021), during which the global pandemic of COVID-19 occurred. The most recent data indicated that the number of TB-associated deaths has declined to below the pre-pandemic level of 1.34 million in 2019, suggesting a reversal of the disruptions to TB management during the pandemic years. Nevertheless, the most recent data on the leading causes of mortality in 2023 are currently unavailable. Since the publication of the 2023 Global TB Report, the WHO has released updated estimates of all-cause and cause-specific mortality extending to 2021. These estimates indicate that TB is the 10<sup>th</sup> leading cause of death worldwide. It seems reasonable to posit that TB has reclaimed its status as the leading infectious disease killer. The measurement of annual mortality rates enables evaluation of our health system efficacy and the allocation of resources to the areas of greatest need. TB will continue to represent a significant global public health concern in the coming years.

### TB burden and epidemic trends in China

China is classified within the critical junction of three global high-burden lists for TB, HIV-associated TB, and

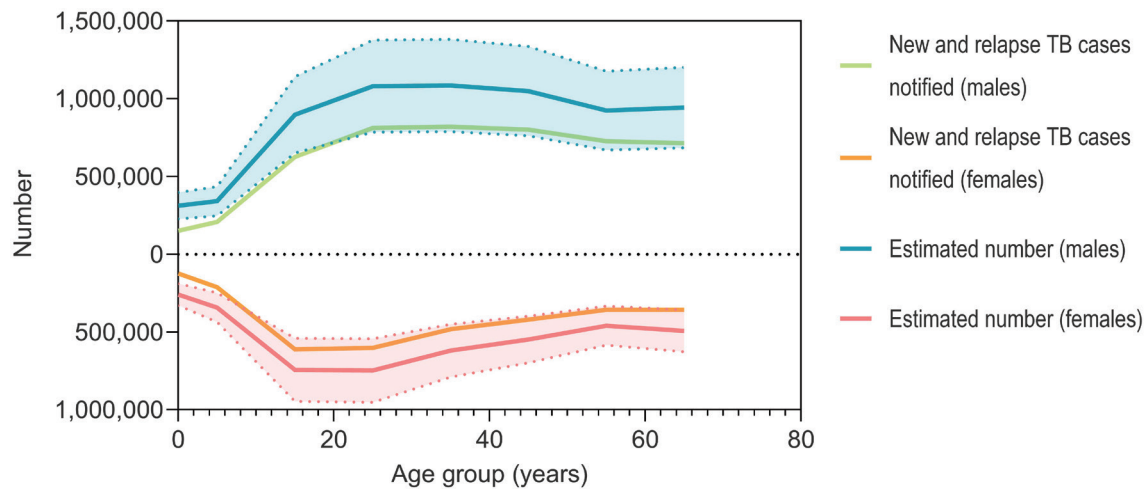


**FIGURE 2** | Estimated and reported number of TB cases by age group and gender in 2023. The original data obtained from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/data>).

**TABLE 2** | Estimates of TB burden in China.

| Items                                                                      | Number                    | Rate per 100,000 population* |
|----------------------------------------------------------------------------|---------------------------|------------------------------|
| Total TB incidence, 2023                                                   | 741,000 (626,000–864,000) | 52 (44–61)                   |
| TB incidence in people living with HIV, 2023                               | 9500 (8000–11,000)        | 0.67 (0.56–0.78)             |
| Multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) incidence, 2023 | 29,000 (24,000–35,000)    | 2.1 (1.7–2.5)                |
| TB deaths in HIV-negative people, 2023                                     | 25,000 (23,000–28,000)    | 1.8 (1.6–2)                  |
| TB deaths in people with HIV, 2023                                         | 2000 (1500–2500)          | 0.14 (0.1–0.18)              |

\*Estimates of TB burden are produced by the WHO in consultation with countries. Ranges represent uncertainty intervals. The original data obtained from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/data>).

MDR/RR-TB by the WHO for the period spanning 2021–2025. Amidst the 10.8 million individuals who contracted TB globally in 2023, China was estimated to have 741,000 new cases, marking China as the country with the third-highest TB incidence worldwide (Table 2). The TB incidence in China, calculated as new cases per 100,000 population, was 52 with 40 cases notified per 100,000 population for new and relapsed cases. The number of deaths attributed to TB was estimated at 27,469. The TB incidence in China has had a gradual decline since 2010, followed by a more significant decrease from 2018–2022, and then an uptick in 2023.

As a significant contributor to the high TB burden in the WHO Western Pacific region, China had a pivotal role in the resurgence of case notifications in 2023. Over the 5-year period from 2019–2023, China and the Philippines were responsible for 81% of all case notifications in the region. Despite these efforts, a notable gap remains between the estimated TB incidence and the number of new diagnoses in China. In 2023, ten countries accounted for most of this discrepancy globally. The top five countries were India, Indonesia, Pakistan, China, and Myanmar, which comprised approximately 50% of the global gap. The contribution of China to this gap was

6.5%, ranking among the top contributors. Regarding the global MDR-TB treatment gap, China is among the 10 countries responsible for approximately 75% of the discrepancy between the estimated number of individuals developing MDR-TB and those enrolled in treatment programs in 2023, placing China fourth in this regard.

China achieved a 20% reduction in the TB incidence and a 35% reduction in TB deaths from 2015–2023 when aligned with the 2025 milestones of the End TB Strategy, which target a 50% reduction in the TB incidence and a 75% reduction in TB-related deaths compared to 2015 (Fig 3). These data underscore the urgent need for China to continue and intensify its efforts to enhance the effectiveness of TB case detection and treatment strategies.

## ADVANCES IN TB DIAGNOSTICS, TREATMENT, AND PREVENTION

### Diagnostics for TB detection

#### *Increasing the utilization of rapid diagnostic tests*

The challenge of identifying individuals with TB remains significant. Of the 10.8 million people estimated to have fallen ill with TB (incident cases) in 2023, only 8.2 million were reported as newly diagnosed, indicating a gap

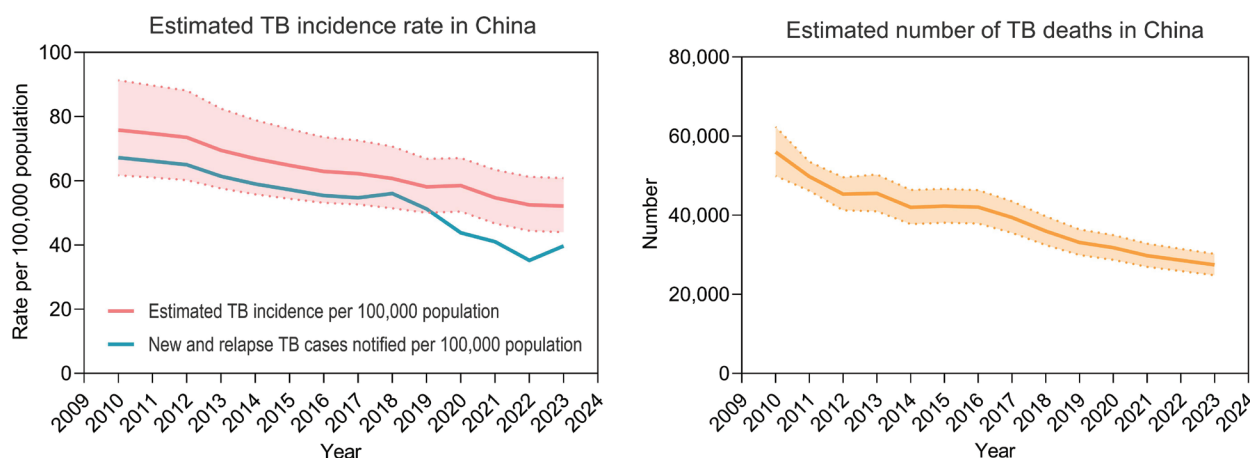


**FIGURE 3** | Estimated TB incidence and deaths in China from 2010–2023. The original data obtained from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/data>).

of 2.7 million individuals who either went undiagnosed or were not reported. This gap is even more pronounced in the case of DR-TB, for which only 175,923 of an estimated 400,000 people with MDR/RR-TB were diagnosed and treated in 2023.

There is a critical need to increase the proportion of bacteriologically confirmed TB cases. Only 62% of the 6.9 million people diagnosed with pulmonary TB had bacteriologically confirmed cases in 2023 despite the importance of early diagnosis for preventing TB transmission and reducing mortality [5]. High-income countries with widespread access to sensitive diagnostic tests had the highest confirmation rates (a median of 86%). A global effort to expand the use of rapid diagnostic tests is essential.

The utilization of rapid tests is growing but is still limited. Only 48% of the 8.2 million newly diagnosed TB cases were initially tested using a WHO-recommended rapid diagnostic test (WRD) in 2023, an increase from 47% in 2022 and 38% in 2021. While progress is being made, we are far from the 100% coverage target set for 2027 [6].

Access to TB diagnostics for drug resistance is too limited. Of 4.3 million bacteriologically confirmed pulmonary TB cases, 79% were tested for rifampicin resistance in 2023, which was higher than 73% in 2022, 69% in 2021, and 62% in pre-pandemic 2019. Access to drug resistance tests for second-line TB drugs was even more limited. There were 159,684 MDR/RR-TB and 28,982 pre-extensively drug-resistant (XDR)-TB or XDR-TB cases for a combined total of 188,666 cases (5.5% of those tested) in 2023. This finding was a smaller increase than 2022 (4.6%). However, the number of people diagnosed with MDR/RR-TB was lower in 2023 than 2019 (a total of 202,009 cases).

### **WHO-recommended rapid diagnostics for TB detection**

The WHO End TB Strategy emphasizes the importance of early TB diagnosis and universal drug susceptibility

testing (DST). The WHO updated the recommendations for rapid TB detection diagnostics in 2024 [7] (Table 3), which include the following (1) initial tests for TB diagnosis with drug-resistance detection (Xpert *Mycobacterium tuberculosis*/rifampicin (MTB/RIF) and Xpert MTB/RIF Ultra assays; Truenat MTB, MTB Plus, and MTB-RIF DX assays; and moderate complexity automated nucleic acid amplification tests [NAATs] for detection of TB and resistance to rifampicin and isoniazid); (2) initial tests for TB diagnosis without drug-resistance detection (loop-mediated isothermal amplification [TB-LAMP] and lateral flow urine lipoarabinomannan assay [LF-LAM]); and (3) follow-on tests for detection of additional drug-resistance after TB confirmation (low complexity automated NAATs for detection of resistance to isoniazid and second-line anti-TB agents; line probe assays [LPAs] for first- and second-line drug resistance; high complexity reverse hybridization-based NAATs for detection of pyrazinamide resistance and targeted next-generation sequencing for comprehensive resistance profiling).

### **Ongoing research on TB diagnostic tests**

TB research and innovation are central to the WHO End TB Strategy [8]. Priority is given to the development of rapid TB diagnostic tests that can diagnose TB infections and disease and detect drug resistance. The diagnostic pipeline has expanded to include 50 technologies under review by the WHO and 36 technologies undergoing policy review. These technologies encompass point-of-care tests for TB disease, automated NAATs for TB disease and drug resistance detection, next-generation sequencing and broth microdilution for comprehensive resistance profiling, interferon-gamma release assays (IGRAs), and TB antigen-based skin tests for TB infections, and computer-aided detection for digital chest radiography screening. Continued research and development are vital to transform these technologies into practical diagnostic tools for improved TB management.

**TABLE 3** | Classes of technologies and associated products recommended by the WHO in 2024.

| Technology class                                                                                           | Products included in the evaluation                             | Time to result (h) |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|--------------------|
| NA                                                                                                         | Xpert® MTB/RIF (Cepheid)                                        | 2 h                |
| NA                                                                                                         | Xpert® MTB/RIF Ultra (Cepheid)                                  | <2 h               |
| NA                                                                                                         | Truenat™ (Molbio)                                               | <1 h               |
| Moderate complexity automated NAATs for detection of TB and resistance to rifampicin and isoniazid         | Abbott RealTime® MTB (Abbott)                                   | 6 h                |
|                                                                                                            | Abbott RealTime MTB RIF/INH (Abbott)                            | Additional 4.5 h   |
|                                                                                                            | BD MAX™ MDR-TB (Becton Dickinson)                               | <4 h               |
|                                                                                                            | Cobas® MTB (Roche)                                              | 3.5 h              |
|                                                                                                            | Cobas MTB-RIF/INH (Roche)                                       | Additional 3.5 h   |
|                                                                                                            | FluoroType® MTBDR (Hain Lifescience/Bruker)                     | 3 h                |
|                                                                                                            | FluoroType® MTB (Hain Lifescience/Bruker)                       | 3 h                |
| NA                                                                                                         | TB-LAMP (Eiken)                                                 | <1 h               |
| Antigen detection in a lateral flow format (biomarker-based detection) (LF-LAM)                            | Alere Determine™ TB LAM Ag (Alere)                              | <1 h               |
| Low complexity automated NAATs for the detection of resistance to isoniazid and second-line anti-TB agents | Xpert® MTB/XDR (Cepheid)                                        | <1.5 h             |
| Line probe assays (LPAs)                                                                                   | GenoType® MTBDR <i>plus</i> v1 and v2 (Hain Lifescience/Bruker) | 5 h                |
|                                                                                                            | GenoType MTBDRsl (Hain Lifescience/Bruker)                      | 1 day              |
|                                                                                                            | Genoscholar™ NTM+MDRTB II                                       | 5 h                |
|                                                                                                            | Genoscholar PZA-TB II (Nipro)                                   | 5 h                |
| Targeted next-generation sequencing (NGS)                                                                  | Deeplex® Myc-TB test (Genoscreen)                               | NA                 |
|                                                                                                            | AmPORE-TB® test (Oxford Nanopore Diagnostics)                   | NA                 |
|                                                                                                            | TBseq® test (Hangzhou ShengTing Medical Technology Co)          | NA                 |

## WHO recommended TB treatment regimens and new drugs in 2024

### Treatment regimens

The Global TB Report for 2024 indicated that since 2022 the WHO has recommended a 4-month regimen of isoniazid, rifapentine, moxifloxacin, and pyrazinamide (HPMZ) for the treatment of rifampicin-susceptible TB [9]. A 4-month regimen of isoniazid, rifampicin, pyrazinamide, and ethambutol (2HRZ(E)/2HR) is recommended for children 3 months-to-16 years of age with non-severe TB. Five countries reported using the 4-month HPMZ regimen by the end of 2023, while 15 countries and regions reported using the 4-month 2HRZ(E)/2HR regimen [10].

The WHO latest recommendations primarily encompass three categories of regimens for DR-TB patients. The first category includes two 6-month all-oral regimens suitable for MDR/RR-TB patients regardless of resistance to fluoroquinolones. The second category comprises several 9-month short-course all-oral regimens for MDR/RR-TB patients who have not developed resistance to fluoroquinolones. The third category involves 18–20 month long-course regimens that may include injectable drugs, such as amikacin.

Several optimizations in short-course regimens for DR-TB have been developed in recent years. In 2020 a 6-month short-course treatment regimen (BPALM/BPaL) for DR-TB, including bedaquiline, linezolid, and pretomanid, was reported to have a 90% cure rate [11]. The WHO approved a 6-month short-course all-oral regimen (BPALM/BPaL) for MDR/RR-TB in 2022. The BDLLfxC regimen was mentioned in the 2024 Global Tuberculosis Report, expanding the eligible population to include children, adolescents, pregnant women, and nursing mothers.

The WHO released a rapid communication earlier this year entitled “Key updates to the treatment of drug-resistant tuberculosis” [12] that suggests a 9-month all-oral regimen (BLMZ, BLLfxCZ, and BDLLfxZ) can be used for MDR/RR-TB patients who have been excluded from fluoroquinolone resistance with BLMZ as the preferred option, followed by BLLfxZ and BDLLfxZ as the last recommendation. Additionally, BEtoLfx/MCZEHh and BLLfx/MCZEHh are recommended for MDR/RR-TB patients who have not previously received second-line treatment (including bedaquiline), who have no fluoroquinolone resistance, and who do not have extensive

pulmonary or severe extra-pulmonary TB. For patients with XDR-TB or patients who do not meet the criteria for short-course regimens or patients in whom short-course treatments have failed, the report recommends an individualized long-course regimen (18–20 months) based on the WHO guidelines.

The Global TB Report for 2024 concludes that among the three categories, the 6-month regimens are the preferred choice, while the 18–20 month long-course regimens are typically used as a last resort.

### **New anti-TB drugs**

The Global TB Report for 2024 highlighted that as of August 2024 the clinical trial tracking for anti-tuberculosis drugs has 29 ongoing trials: alpipectir (BVL-GSK098); BTZ-043; delpazolid; GSK-286; ganfeborole (GSK-3036656); macozinone; MK-7762 (TBD09); quabodepistat (OPC-167832); TBAJ-587; TBAJ-876; TBI-223; pyrifazimine (TBI-166); TBA-7371; telacebec (Q203); sanfetrinem; SQ109; sutezolid; sudapyridine (WX-081); bedaquiline; delamanid; pretomanid; clofazimine; levofloxacin; linezolid; moxifloxacin; high-dose rifampicin; rifapentine; sitafloxacin; and tedizolid. This drug development effort represents an increase from 28 drugs in 2023 and 8 drugs in 2015.

Other studies not included in the report have also shown that recent international efforts in anti-tuberculosis drug development remain focused on bedaquiline, pretomanid, and delamanid. An observational prospective study based on data collected and provided by the Global Tuberculosis Network Center reported that among 883 patients treated with bedaquiline and/or delamanid across 52 centers in 29 countries the proportion of patients achieving sputum smear and culture conversion was 93.4% and 92.8%, respectively, with a median time-to-conversion of 58 days (range, 30–90 days) [13]. In 2024 the TB-PRACTECAL trial reported that the 24-week BPaLM regimen, which includes bedaquiline and delamanid, demonstrated significantly superior efficacy and safety compared to the standard regimen [14]. These drugs have shown substantial maturity in research and hold promise for inclusion in recommended treatment regimens for DR-TB.

Currently, domestically developed anti-tuberculosis drugs include sudapyridine and pyrifazimine. Multiple clinical trials involving sudapyridine, such as the “Evaluation of WX-081 Tablets’ Efficacy and Safety in Drug-Resistant Pulmonary Tuberculosis Patients: A Multicenter, Randomized, Open, Controlled Phase III Clinical Trial (Registration No. CTR20221162),” “WX-081 Mass Balance Clinical Trial in Healthy Chinese Subjects (Registration No. CTR20242598),” and “Evaluation of the Drug Interaction and Food Effect of WX-081 in Chinese Adult Healthy Volunteers (Registration No. CTR20242670),” are ongoing. Four clinical trials involving pyrifazimine for treating DR-TB (Registration Nos. CTR20202476, CTR20202464,

CTR20181736, and CTR20171630) have also been successfully completed. Sudapyridine and pyrifazimine are derivatives derived from the structural optimization of bedaquiline and clofazimine, respectively. Sudapyridine and pyrifazimine aim to mitigate the adverse effects of the original drugs, while enhancing therapeutic efficacy and facilitating broader application prospects.

### **Status of TB vaccines**

The Global TB Report for 2024 indicates that there are 15 novel TB vaccines in various stages of clinical trials globally as of August 2024. Among these 15 novel TB vaccines, 4 are in phase I clinical trials, 5 are in phase II trials (including phase IIa and IIb trials), and 6 have entered phase III clinical trials. The total number of novel TB vaccines in clinical trials has not shown a significant change over the past 5 years according to the WHO Global TB Reports from 2020–2024. However, the number of vaccines in phase III trials has shown an overall increasing trend and for the first time has surpassed the number in phase II trials (Fig 4).

Given the inherent limitations in the time frame of the Global TB Report for 2024 search for novel TB vaccine trials, a query of the U.S. ClinicalTrials.gov database revealed that there are currently 3 novel TB vaccines in phase I clinical trials, excluding those trials that have completed phase I but the data for which have not been formally published: BNT 164a1 and BNT164b1 (NCT05537038, expected to end in January 2026; NCT05547464, expected to end in May 2027; both are RNA vaccines); and H107e/CAF®10b [nTB-01] (NCT06050356, expected to end in May 2026). There are 4 novel TB vaccines in phase II clinical trials: RUTI (NCT05455112, expected to end in December 2024; NCT04919239, expected to end in March 2025); AEC/BC02 (NCT05284812, expected to end in December 2024); ID93+GLA-SE (NCT06205589, expected to end in April 2029); and H56:IC31 (NCT03512249, expected to end in March 2024, but not yet completed). Additionally, 5 novel TB vaccines have entered phase III clinical trials: VPM1002 (NCT03152903, expected to end in July 2024 but not yet completed; NCT04351685, expected to end in December 2025), BCG re-vaccination (NCT05330884, paused due to changes in the protocol, expected to end in December 2027), MTBVAC (NCT04975178, expected to end in September 2029), GamTBvac (NCT04975737, expected to end in November 2025), and M72/AS01E (NCT06062238, expected to end in April 2028; Table 4 and Fig 5). Some vaccines, such as MTBVAC, are also undergoing earlier-stage clinical trials in different populations: phase I (NCT06438978, expected to end in August 2024, but not yet completed); and phase II (NCT05947890, expected to end in February 2026; NCT06272812, expected to end in March 2028; Table 4). Currently, these novel TB vaccines in clinical trials are primarily aimed at preventing MTB infections, onset, recurrences, and improving patient outcomes [15].

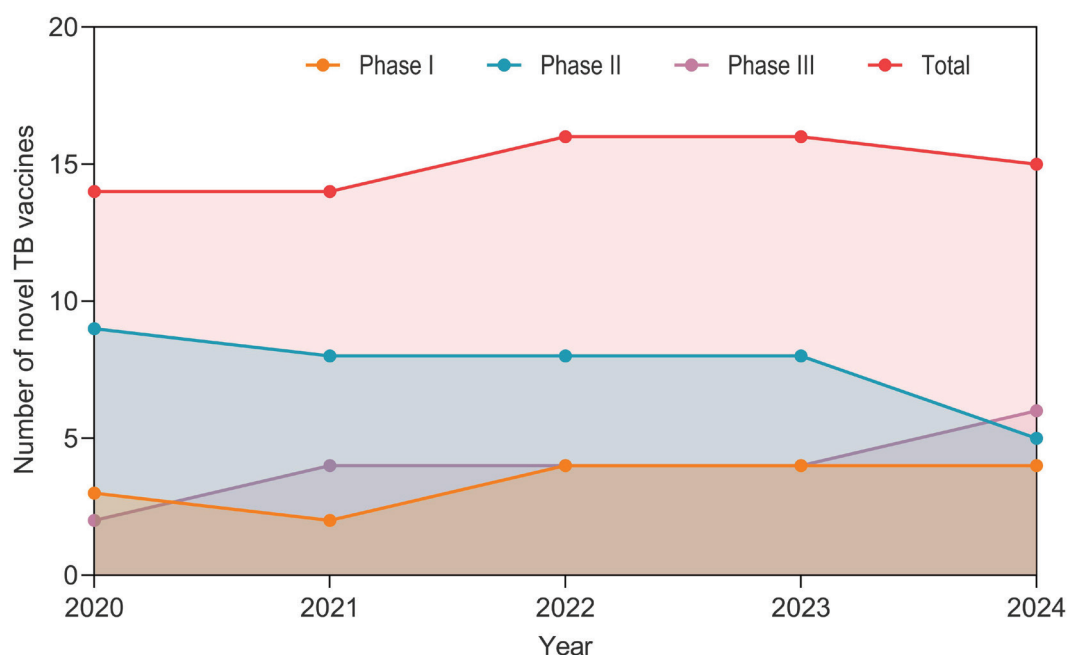


**FIGURE 4** | Trends in the number of novel TB vaccines in clinical trials from 2020–2024.

The WHO Director-General launched a new 5-year initiative (2023–2027) in March 2023 to accelerate progress towards ending TB, calling for at least one new vaccine to be approved by 2027. In September 2023 the second UNHLM on TB proposed leveraging global cooperation mechanisms and WHO initiatives, such as the New Tuberculosis Vaccine Facilitation Council, to expedite research and development with the goal of promoting safe, effective, affordable, and accessible vaccines within the next 5 years. M72/AS01E is currently the most promising novel TB vaccine for providing high efficacy in adults [16]. M72/AS01E is undergoing phase III clinical trials (Table 4 and Fig 5).

The WHO has recently (2023–2024) implemented a series of high-level actions to accelerate research and innovation in TB vaccines, as follows: participating in and supporting various research platforms and networks; serving as the secretariat for the BRICS Tuberculosis Research Network; convening annual consultation meetings to exchange views on emerging areas requiring global TB policy guidance; launching a TB sequencing portal to share the MTB sequencing and phenotypic knowledge base, which features >56,000 sequences and data visualization capabilities using the WHO mutation directory; releasing an investment case for TB screening and preventive therapy aligned with the global target for preventive therapy coverage agreed upon at the 2023 UNHLM on TB, which underscores relatively modest investments that can yield substantial health and economic benefits with a proposed social return of up to 39 dollars for every dollar invested; hosting the second meeting of the New Tuberculosis Vaccine Facilitation Council to gather further insights on accelerating the translation of scientific breakthroughs

into effective and accessible TB vaccines; agreeing on key objectives and related milestones for the Council's first term (2024–2025), and convening a consultation meeting to establish a “trial platform” to fast-track the testing and evaluation of effective TB treatment regimens, aiming to improve trial efficiency (compared to traditional methods) and enhance collaboration among countries, clinical trial sponsors, funders, and civil society.

## GLOBAL LANDSCAPE OF DR-TB

### Global analysis of drug resistance: insights into the 2023 global DR-TB scenario

DR-TB, with a particular focus on RR-TB, continues to pose a substantial threat to global public health. When TB is resistant to both rifampicin and isoniazid, TB is classified as MDR-TB.

There was a gradual decline in the number of new MDR/RR-TB cases worldwide from 2015–2020. However, from 2020–2023 this number has remained relatively stable (Fig 6). It has been estimated that the global MDR/RR-TB caseload was 400,000 (95% UI: 360,000–440,000) in 2023 [1]. Greater than 50% of the new MDR/RR-TB cases were concentrated in 5 countries in 2023, as follows: India (27%); Russia (7.4%); Indonesia (7.4%); China (7.3%); and the Philippines (7.2%). The proportion of MDR/RR-TB cases among new TB cases has been estimated to be 3.2% (95% UI: 2.5%–3.8%), while among previously treated patients, the proportion of MDR/RR-TB cases was 16% (95% UI: 9.0%–24%; Fig 6). This finding marks a decrease from 2020, when the proportion of new and previously treated cases was 3.4% and 20%, respectively. Despite an overall increase in new TB cases,

**TABLE 4** | List of TB vaccines currently in clinical trial (<https://clinicaltrials.gov>).

| Vaccine                | NCT number                                                                         | Phase  | Duration of test            | Population                                                                                                                  | Sample size |
|------------------------|------------------------------------------------------------------------------------|--------|-----------------------------|-----------------------------------------------------------------------------------------------------------------------------|-------------|
| BNT164a1               | NCT05537038                                                                        | I      | 2023.4~2026.1               | IGRA-negative, BCG naïve subjects/adults (18y~55 y)                                                                         | 120         |
|                        | NCT05547464                                                                        | I/II   | 2023.7~2027.5               | BCG vaccinated, HIV-negative subjects, and people living with HIV/adults (18–55 y)                                          | 732         |
| BNT164b1               | NCT05537038                                                                        | I      | 2023.4~2026.1               | IGRA-negative, BCG naïve subjects/adults (18–55 y)                                                                          | 120         |
|                        | NCT05547464                                                                        | I/II   | 2023.7~2027.5               | BCG vaccinated, HIV-negative subjects, and people living with HIV/adults (18–55 y)                                          | 732         |
| H107e/CAF®10b (nTB-01) | NCT06050356                                                                        | I      | 2024.3~2026.5               | Healthy adults (18–45 y)                                                                                                    | 140         |
| RUTI                   | NCT05455112                                                                        | II     | 2022.10~2024.12             | Patients with TB (>18 y)                                                                                                    | 44          |
|                        | NCT04919239                                                                        | II     | 2021.9~2025.3               | DS and MDR-TB patients favorably responding to standard MDR-TB treatment (>18 y)                                            | 140         |
| AEC/BC02               | NCT05284812                                                                        | II     | 2022.2~2024.12              | Healthy adults (>18 y)                                                                                                      | 200         |
| ID93+GLA-SE            | NCT06205589                                                                        | II     | 2024.10~2029.4              | Participants with rifampicin-susceptible pulmonary TB (18–65 y)                                                             | 1500        |
| H56:IC31               | NCT03512249                                                                        | II     | 2019.1~2024.3 (unfinished)  | HIV negative adults successfully treated for drug-susceptible pulmonary TB (18–60 y)                                        | 831         |
| VPM1002                | NCT03152903                                                                        | II/III | 2017.12~2024.7 (unfinished) | Pulmonary TB patients after successful TB treatment (18–65 y)                                                               | 2000        |
|                        | NCT04351685                                                                        | III    | 2020.11~2025.12             | Newborn infants compared to BCG (0–14 d)                                                                                    | 6940        |
| BCG Revaccination      | NCT04152161 (Directed by Gates MRI, Aeras Sanofi Pasteur)                          | II     | 2019.10~2025.9              | Healthy individuals (10–18 y)                                                                                               | 1836        |
|                        | NCT05330884 (Suspended/changes in protocol, directed by TB Research Centre, India) | III    | 2024.7~2027.12              | Household contacts (6–18 y) compared to oral chemoprophylaxis                                                               | 9200        |
| MTBVAC                 | NCT06438978                                                                        | I      | 2024.1~2024.8 (unfinished)  | Healthy Indian adults (18–65 y)                                                                                             | 30          |
|                        | NCT05947890                                                                        | II     | 2024.1~2026.2               | Adolescents and adults living with and without HIV in South Africa (12–55 y)                                                | 276         |
|                        | NCT06272812                                                                        | II     | 2024.9~2028.3               | IGRA-positive adolescents and adults living in a TB endemic region (14–45 y)                                                | 4300        |
|                        | NCT04975178                                                                        | III    | 2022.9~2029.9               | Healthy HIV unexposed (HU) and HIV exposed uninfected (HEU) newborns in TB-endemic regions of Sub-Saharan Africa (5 m–7 d ) | 7120        |
| GamTBvac               | NCT04975737                                                                        | III    | 2022.1~2025.11              | Healthy adults (1845 y)                                                                                                     | 7180        |
| M72/AS01E              | NCT06062238                                                                        | III    | 2024.3~2028.4               | IGRA-positive cohort, IGRA-negative cohort, and HIV cohort (15–44 y)                                                        | 20,000      |

Abbreviations: IGRA, interferon gamma release assay; HIV, human immunodeficiency virus; DS, drug-sensitive; MDR-TB, multidrug-resistant; Gates MRI, Bill & Melinda Gates Medical Research Institute.

the stability in MDR/RR-TB cases from 2020–2023 was attributed to a decreasing trend in the proportion of MDR/RR-TB cases among TB patients since 2015, particularly among those with a history of treatment. The situation is particularly dire in Russia and several countries in Eastern Europe and Central Asia, where >50% of previously treated cases were diagnosed with MDR/RR-TB in 2023, underscoring significant challenges in TB control in these regions.

In 2023, 79% (3.4 of 4.3 million) of bacteriologically confirmed pulmonary TB patients globally underwent rifampicin resistance testing, which was a significant improvement from 73% (2.9 of 4.0 million) in 2022, 69% (2.4 of 3.5 million) in 2021, and 62% (2.2 of 3.6 million) before the COVID-19 pandemic in 2019. The testing rate in the Southeast Asia, European, and Western Pacific regions all reached or exceeded 80%. Among those individuals tested, 159,684 MDR/RR-TB cases and 28,982

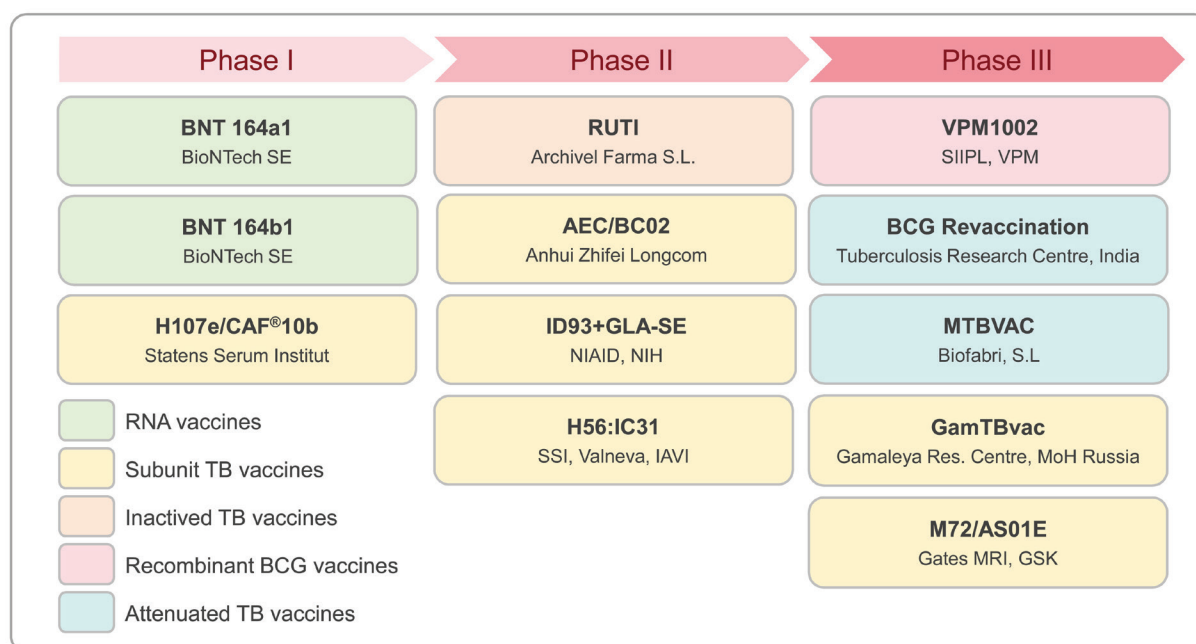


**FIGURE 5 |** Current TB vaccines in clinical trials. (NIAID: National Institute of Allergy and Infectious Diseases; NIH: National Institutes of Health; SSI: Statens Serum Institute; IAVI: International AIDS Vaccine Initiative; SIPL: Serum Institute of India Private Limited; VPM: Vakzine Projekt Management GmbH; Gates MRI: Bill & Melinda Gates Medical Research Institute; GSK: GlaxoSmithKline).

cases of pre-XDR-TB or XDR-TB were identified, totaling 188,666 cases (5.5% of the tested population). This number slightly increased from 180,426 cases (4.6%) in 2022. In 2023, 175,923 MDR/RR-TB patients were enrolled in treatment, a slight decrease from 177,912 in 2022 (1.1%) and below the pre-pandemic level of 181,533 in 2019. This treatment enrollment represents approximately 44% of the estimated new MDR/RR-TB cases in 2023. In recent years there has been significant progress in the treatment success rate for MDR/RR-TB patients. For patients who started treatment in 2021 (the most recent year with available outcome data), the treatment success rate was 68%, an improvement from 64% in 2020, 60% in 2019, and 50% in 2012. Treatment success rates in 2021 varied across WHO regions, ranging from 61% in the European region to 74% in the Eastern Mediterranean region. By the end of 2023, 58 countries had adopted the 6-month BPaLM regimen for treating MDR/RR-TB or pre-XDR-TB patients, an increase from 41 countries at the end of 2022. Additionally, 100 countries were using the 9-month all-oral regimen for MDR/RR-TB, up from 95 countries in 2022 and 93 countries in 2021.

### Analysis of drug resistance in China: insights into the state of 2023 DR-TB in China

China estimated 29,000 new DR-TB cases (95% UI: 24,000–35,000) in 2023, accounting for 7.3% of global DR-TB cases, ranking 4<sup>th</sup> globally. This number indicates that DR-TB control in China remains challenging. The proportion of MDR/RR-TB cases is 2.9% (95% UI: 2.9%–3.0%) among new patients and 19% (95% UI: 18%–19%) among previously treated patients. Of

the bacteriologically confirmed TB cases, 89% underwent rifampicin resistance testing and 91% of previously treated patients were tested; both percentages exceeded the global average. In 2023, 14,918 laboratory-confirmed MDR/RR-TB cases were identified and 13,140 patients began treatment with a drug-resistant regimen, resulting in a treatment coverage rate of 88% (13,140/14,918). The treatment success rate for MDR/RR-TB cases registered and treated with second-line anti-TB drugs in 2021 (evaluated in 2023) was 65.89%. This success rate was a substantial improvement from previous years for the following reasons: the introduction of new drugs; the scientific formulation of treatment regimens; and increased government investment (Fig 7). Despite the global increase in MDR/RR-TB treatment success rates, China has not yet implemented the 6-month all-oral short-course regimen recommended by the WHO due to limited access to treatment drugs. Therefore, China needs to enhance diagnostic capabilities, increase investment in primary healthcare institutions, and improve the ability to diagnose DR-TB. Drawing on international best practices and adapting to the specific circumstances in China, more scientifically sound and reasonable treatment regimens for DR-TB need to be formulated. Additionally, efforts should focus on patient health education to improve treatment adherence.

The status of DR-TB in China remained severe in 2023, facing multiple challenges such as high diagnostic difficulty, high treatment costs, and low drug accessibility. Effective control of the spread and proliferation of DR-TB requires collaborative efforts from the government, healthcare institutions, social organizations, and

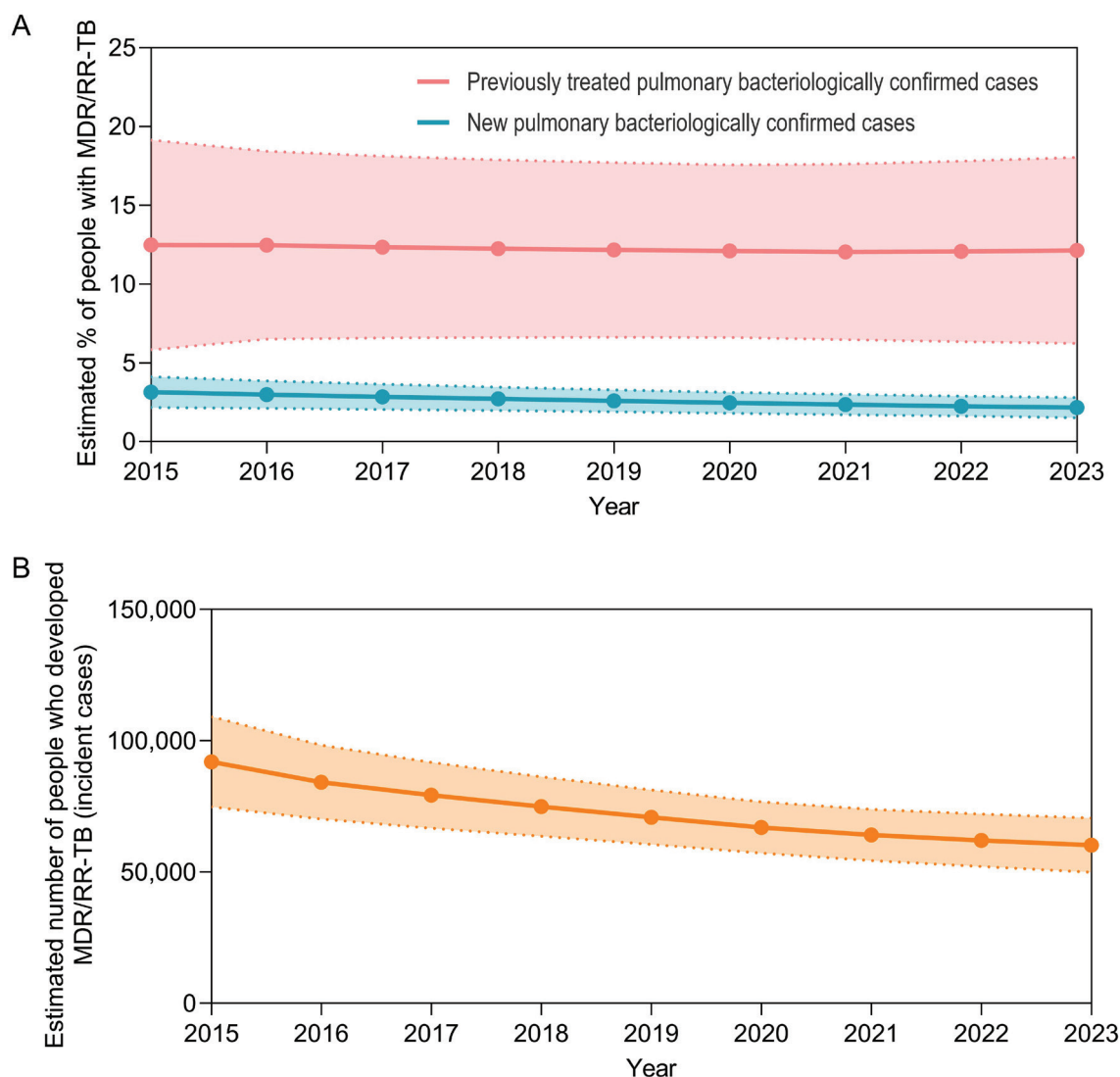


**FIGURE 6** | Estimated percentage of people with TB who had MDR/RR-TB (A) and estimated number of people who developed MDR/RR-TB (incident cases, B). The original data obtained from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/data>).

the public to strengthen diagnostic capabilities, optimize treatment regimens, improve drug accessibility, and intensify prevention and control awareness campaigns.

## THE INTERPLAY OF HIV INFECTION AND TB

### Global perspective on HIV and TB in 2023

An estimated 662,000 new cases of TB were co-infected with HIV in 2023, accounting for 6.1% of all new TB cases globally, a proportion that has been on a steady decline in recent years [17]. The highest prevalence of HIV-positive patients among new TB cases was notably in Africa, particularly in southern regions where the prevalence surpassed 50%. This trend is likely linked to the high HIV prevalence, insufficient TB control measures, and the vulnerability of health systems in these areas. The total number of TB-related deaths worldwide was approximately 1.25 million in 2023, including 161,000 among

HIV-positive individuals. This number, while lower than HIV-negative individuals, still underscores the elevated mortality rate among individuals with HIV co-infections. Among those who died from TB and were HIV-positive, 48% were adult males, 36% were adult females, and 16% were children and adolescents, highlighting the varied impact of TB across different demographics. The global coverage for HIV testing among confirmed TB patients remained at 80% in 2023, mirroring the previous year numbers, with particularly high rates in Africa (90%) and Europe (94%).

For individuals with TB co-infected with HIV, the global coverage rate for antiretroviral therapy (ART) was 88%. However, this rate falls short when compared to the total estimated number of HIV-positive individuals with TB, reaching only 58% in 2023 [18]. This discrepancy may be due to inadequate diagnosis, limited treatment accessibility, and suboptimal patient adherence. It was estimated

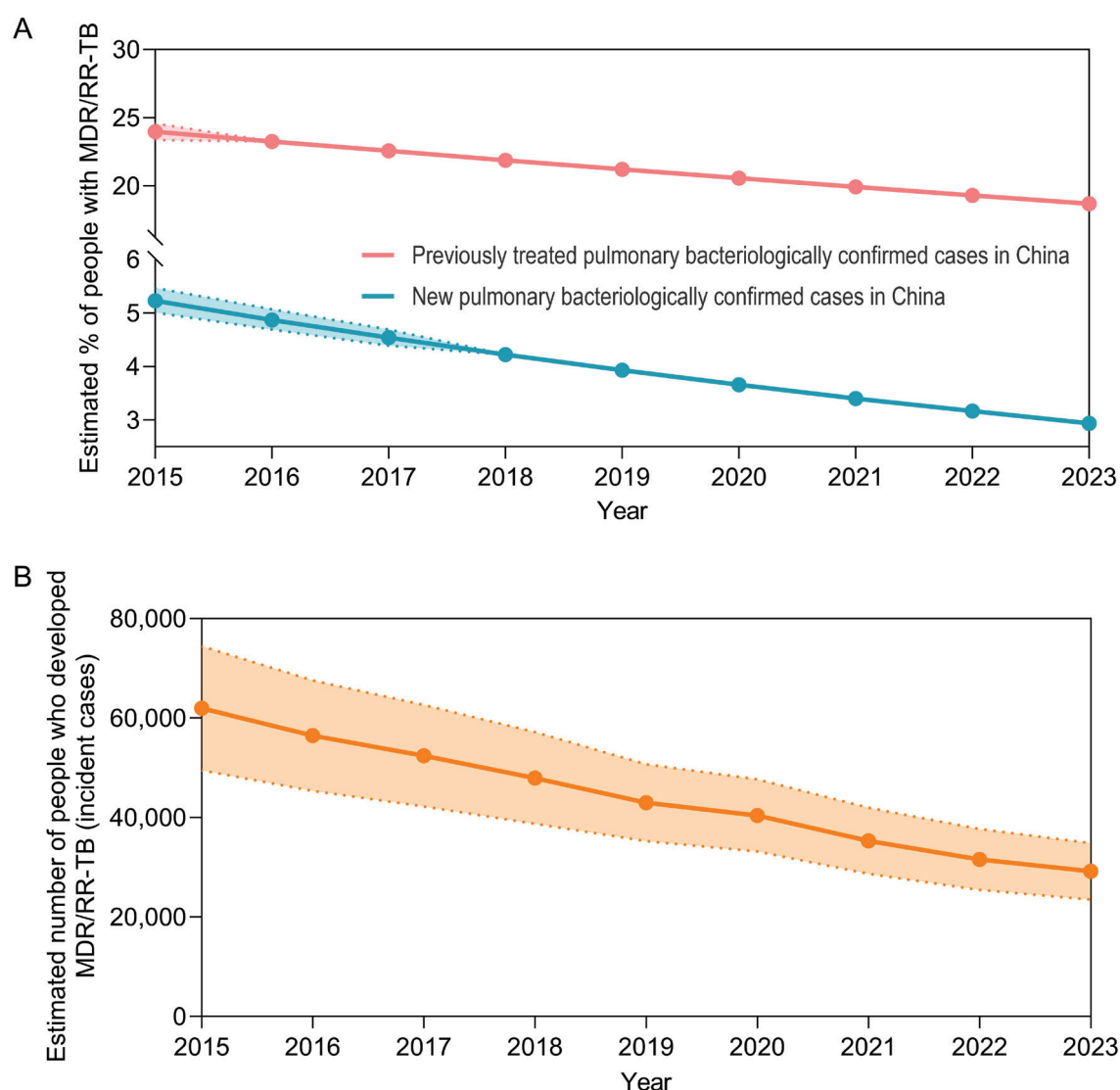


**FIGURE 7** | Estimated percentage of people with TB who had MDR/RR-TB (A) and estimated number of people who developed MDR/RR-TB (incident cases, B) in China. The original data obtained from the WHO website (<https://www.who.int/teams/global-tuberculosis-programme/> data).

that between 2010 and 2023, 6.8 million deaths occurred among HIV-positive individuals diagnosed with TB who received TB and antiretroviral therapy. This represents a significant reduction compared to the 79 million deaths between 2000 and 2023, underscoring the pivotal role of ART in reducing mortality rates among dual-infected individuals.

The objective of TB preventive therapy is to cover 90% of high-risk populations by 2027. In 2023, 21% of household contacts were diagnosed with TB, of which 56% were HIV-positive. The WHO advocates for preventive TB therapy for HIV-positive individuals and emphasizes the need for enhanced TB screening among close household contacts and HIV-positive individuals, increasing access to shorter (1–3 months) rifampentine-based preventive therapy [19]. This recommendation highlights the significance of preventive therapy in high-risk populations, which not only aids in reducing TB transmission but also

decreases the incidence and mortality rates of TB among HIV-positive individuals.

In summary, the global burden of TB-HIV co-infections in 2023 remained severe with nations actively seeking effective control strategies. These strategies include bolstering screening, diagnosis, and treatment efforts, and raising awareness of TB-HIV co-infections.

### HIV and TB in China: A 2023 overview

The WHO estimated that China had 741,000 new TB cases in 2023 with an incidence of 52 per 100,000 population, including 9500 HIV-positive individuals with an incidence of 0.67 per 100,000 population [1]. The number of TB-related deaths among HIV-negative individuals was 25,000, with a mortality rate of 1.8 per 100,000 population, while the number of TB-related deaths among HIV-positive individuals was 2000 with a mortality rate of 0.14 per 100,000 population. The HIV awareness rate

was 68% with 4925 TB-HIV co-infected individuals (1.3%). In 2022, 6085 TB-HIV co-infected individuals (56%) initiated anti-TB treatment. The TB incidence and mortality rate among HIV-positive individuals in China were lower than HIV-negative individuals, yet this issue warrants attention. The relatively low HIV awareness rate may impede the timely diagnosis and treatment of HIV-positive individuals. The TB treatment coverage among TB-HIV co-infected individuals was also relatively low, likely due to inadequate diagnosis and poor treatment accessibility. China needs to further strengthen TB and HIV control efforts, improve diagnosis rates, and increase treatment coverage to reduce the transmission and impact of both diseases.

In conclusion, despite various measures, TB and HIV infections remain significant public health challenges in China, necessitating sustained effort and resource allocation. By enhancing screening and preventive therapy, China has the potential to reduce TB/HIV co-infections and better control the spread of both diseases in the coming years.

## THE IMPACT OF THE COVID-19 PANDEMIC ON THE GLOBAL TB EPIDEMIC

TB is poised to regain its status as the leading cause of death from a single infectious disease globally by 2023 after being eclipsed by COVID-19 for 3 years [3]. The upward trend in global TB cases, which emerged during the COVID-19 pandemic, has begun to slow and stabilize with a total of 10.8 million cases reported in 2023 (95% CI: 10.1–11.7 million), a modest increase from 10.7 million in 2022 and significantly higher than the 10.4 million in 2021 and 10.1 million in 2020 [1].

The number of newly diagnosed TB cases worldwide reached 8.2 million in 2023, an increase from 7.5 million in 2022 and 7.1 million in 2019 [1]. The COVID-19 pandemic caused severe disruptions in TB healthcare services over a 2-year period with a significant drop in newly diagnosed TB cases below pre-pandemic levels, particularly in 2020 when there was an 18% global decline to 5.8 million cases. A partial recovery was observed in 2021 with cases rising to 6.4 million. The increase in newly diagnosed cases in 2022 and 2023 likely included a backlog of undetected cases from previous years. By 2023 the gap between estimated global TB incidence and reported newly diagnosed cases had narrowed to 2.7 million, an improvement from nearly 4 million in 2020 and 2021, and even lower than the pre-pandemic level of 3.2 million in 2019, indicating a strong recovery in TB diagnosis and treatment services during 2022 and 2023.

In 2023 TB was estimated to cause approximately 1.25 million deaths globally (95% UI: 1.13–1.37 million), down from 1.32 million in 2022, 1.42 million in 2021, and 1.40 million in 2020, and below the pre-pandemic level of 1.34 million in 2019 [1]. It was estimated that from 2020–2023 disruptions related to COVID-19 contributed to an excess

of approximately 700,000 TB-related deaths compared to a scenario in which pre-pandemic trends had remained unchanged.

The COVID-19 pandemic has had a profound impact on global TB control and has provided invaluable insights for the future. The pandemic has underscored the necessity for resilient health systems, increased investment in research and innovation, and a holistic approach to addressing the social determinants of health [20]. The interconnected futures of TB and COVID-19 demand a sustained commitment to global health security, focusing on preventing future pandemics and bolstering the capacity of health systems to respond effectively to emerging threats.

## GLOBAL TB COMMITMENTS, STRATEGIES, AND THE REALIZATION OF TARGETS

### Overview of the end TB strategy

The End TB Strategy, as outlined by the WHO, is a comprehensive and ambitious plan aimed at significantly reducing the global burden of TB by specific milestones [21]. The strategy envisions a world free of TB-related deaths, disease, and suffering with clear goals to end the global TB epidemic. The End TB Strategy sets forth indicators and milestones for 2020 and 2025, as well as targets for 2030 and 2035, focusing on substantial reductions in TB deaths, TB incidence, and the proportion of TB-affected households facing catastrophic costs [22]. The strategy is built on three pillars: integrated, patient-centered care, and prevention; bold policies and supportive systems; and intensified research and innovation. These components encompass early diagnosis, universal drug susceptibility testing, systematic screening, and the development and uptake of new tools and interventions to combat TB.

### Global TB milestones and targets

The global milestones and targets for TB are critical benchmarks for tracking progress towards the End TB Strategy. The 2025 milestones include a 50% reduction in TB incidence and a 75% reduction in TB deaths compared to the 2015 baseline. Additionally, the strategy aims to achieve zero TB-affected households facing catastrophic costs by 2025. However, the latest data indicates that while some progress has been made, the global community is still far from reaching these ambitious targets. The net reduction in the TB incidence rate from 2015–2023 was only 8.3% and the reduction in the number of TB deaths was 23%, falling short of the interim goals [1].

### Targets set by the UNHLM and the achievement status

The 2023 UNHLM on TB established a series of global targets for the period 2023–2027, which are crucial for accelerating progress towards ending the TB epidemic [23]. Key targets include achieving 100% coverage of rapid diagnostic testing for all newly diagnosed TB patients,

90% coverage for TB treatment, and 90% coverage for TB preventive treatment among high-risk populations, including household contacts and people living with HIV. Funding targets were also set at \$22 billion annually for universal access to TB prevention, diagnosis, treatment, and care, and \$5 billion annually for TB research by 2027. As of the latest report, while there has been some progress, significant gaps remain in achieving these targets. For example, only 48% of newly diagnosed TB patients were initially tested with a WHO-recommended rapid test, and the funding for TB prevention, diagnosis, treatment, and care was at \$5.7 billion, significantly below the target [1].

In conclusion, while the global community has made strides in setting ambitious targets to combat TB, the realization of these goals requires a concerted and accelerated effort. The achievements made so far are a testament to the commitment of nations and organizations but the road to ending the TB epidemic remains long and challenging. It is imperative that the global health community translates these commitments into action to achieve the targets set forth in the End TB Strategy and the UNHLM.

## GLOBAL CHALLENGES AND OPPORTUNITIES IN TB CONTROL

The WHO Global Tuberculosis Report 2024 offers a comprehensive review of the progress and challenges in global TB control. The report indicated that approximately 8.2 million new cases of TB were recorded globally in 2023, marking the highest number since the initiation of global TB surveillance by the WHO in 1995. This finding suggests that TB has once again become the leading infectious disease globally in terms of mortality, highlighting the persistent nature of the TB epidemic and the urgency for more effective control measures.

### Challenges

Despite significant advancements in TB research and control measures, several major obstacles hinder the global effort to effectively combat TB. These challenges span a range of issues, including the persistent high burden of the disease, the growing problem of DR-TB, insufficient funding, and the lack of effective diagnostic, preventive, and therapeutic tools. Addressing these issues is crucial for making substantial progress in TB control and ultimately achieving the goal of ending the TB epidemic.

#### *The global burden of TB remains severe*

The Global Tuberculosis Report 2024 revealed that there were 10.8 million new cases of TB worldwide in 2023 with an incidence of 134 per 100,000 population. Compared to 2015, there has been only an 8.3% decrease, which is far from the End TB Strategy second milestone target of a 50% reduction in incidence by 2025. The slow progress in reducing the incidence of TB underscores the need for innovative prevention strategies and a reevaluation of current TB control measures. The high number

of deaths indicates the severity of the disease impact and the importance of improving access to early diagnosis and effective treatment.

#### *Prominence of DR-TB*

Although the treatment success rate for DR-TB has improved with a 68% success rate for MDR/RR-TB, the number of cases continues to rise. The Global Tuberculosis Report 2024 indicated that there were 400,000 new cases of DR-TB globally in 2023, yet only 176,000 (44%) received treatment. The increase in DR-TB cases complicates treatment and control efforts, and the high cost and long duration of treatment for DR-TB pose significant barriers to patient access and adherence, necessitating the development of more affordable and effective treatment regimens.

#### *Significant funding shortfalls*

Funding shortages are a critical constraint in TB research. The Global Tuberculosis Report 2024 highlights that low- and middle-income countries, which bear 98% of the global TB burden, face severe funding shortages. The significant gap between the funding target and the actual amount raised in 2023 underscores the need for increased financial commitments from both domestic and international sources. This funding is crucial for advancing research, developing new diagnostics, drugs, and vaccines, and improving TB services.

#### *Lack of effective diagnostic, preventive, and treatment measures*

The BCG vaccine is effective in preventing severe forms of TB in children but the protection for adolescents and adults is suboptimal. While global efforts are underway to develop new TB vaccines, progress has been slow and no new vaccines are yet available for preventing TB. Additionally, although new diagnostic technologies, such as genomic sequencing, have greatly assisted in confirming TB, the accessibility and availability, especially in low- and middle-income countries, are limited. Lastly, traditional anti-TB drugs have issues with side effects and long treatment durations, leading to poor patient compliance. The increasing prevalence of DR-TB and the need for new drugs with improved accessibility and affordability underscore the need for increased efforts in vaccine, diagnostic, and drug development to effectively control the spread and prevalence of TB.

### Opportunities

While the challenges in TB control are substantial, there are also several important opportunities that can be leveraged to improve the situation. These opportunities include a slowing incidence growth rate, increased awareness and protective measures, technological innovation, and strengthened international cooperation. Each of these areas presents a potential pathway to enhance TB control and ultimately achieve the goal of ending the TB epidemic.

### ***Slowing incidence growth***

Although the global number of new TB cases reached 10.8 million, the annual growth rate of the incidence has significantly slowed to 0.2%, indicating a trend towards stabilization. This shift provides a valuable opportunity to intensify control efforts and reduce the incidence. The slowing growth rate suggests that certain regions or countries may be effectively implementing control measures, offering a blueprint for other areas to follow.

### ***Enhanced government and public health awareness***

The health behaviors promoted during the COVID-19 pandemic, such as social distancing, mask-wearing, and cough etiquette, have also contributed to TB control. The widespread use of masks and adherence to social distancing have presented unprecedented opportunities for TB control, particularly in public settings, including health-care facilities, and significantly reducing the transmission of TB.

### ***Technological innovations in TB diagnosis, vaccines, and drug development***

Advances in biotechnology and immunology offer new approaches and accelerate the development of TB diagnostics and novel vaccines. A deeper understanding of the pathophysiology of TB is leading to drug development strategies targeting specific TB pathways and immune modulation, providing new directions for drug research.

### ***Strengthened international collaboration***

Increasing global cooperation in TB control facilitates the sharing of resources, exchange of experiences and technologies, and a collective response to the challenges posed by TB. This collaboration also accelerates the development and dissemination of new diagnostic technologies, vaccines, and drugs, enhancing the effectiveness of TB control efforts.

In summary, while global TB control faces significant challenges, such as funding gaps, the rise of DR-TB, and low treatment success rates, there are also notable opportunities. The stabilization of the epidemic provides a much-needed respite, but it is imperative to enhance control strategies, improve detection technologies and treatment levels, and increase investment and innovation to work together towards the goal of “ending the TB epidemic.”

## **CONCLUSIONS**

The WHO Global Tuberculosis Report 2024 offers a nuanced and comprehensive assessment of the global fight against TB. While notable advances have been made in several areas, such as a slowdown in the annual increase of TB cases and a decline in TB-related deaths, the global community still faces significant challenges in achieving the ambitious milestones set by the End TB Strategy. This conclusion synthesizes the key takeaways from our

interpretation of the report and underscores the critical actions required to accelerate progress towards ending the TB epidemic.

First, the high global TB burden, with 10.8 million new cases reported in 2023, highlights the urgent need for enhanced case detection and treatment. The slow progress in reducing the TB incidence and the number of TB deaths underscores the necessity for more effective and accessible diagnostic tools, as well as improved treatment regimens that are both shorter and less toxic.

Second, the issue of DR-TB remains a significant threat. There is a considerable gap between the number of new DR-TB cases and those receiving appropriate treatment. Although the success rate for treating DR-TB has improved, the overall number of cases continues to rise. This indicates the need for more robust surveillance systems, better access to quality-assured diagnostics, and the development of new drugs and treatment regimens.

Third, the funding shortfall for TB prevention, diagnosis, treatment, and research is alarming. The current level of financing is far from the global targets, hindering the development of new diagnostic methods, drugs, and vaccines. Increased domestic and international investment is imperative to meet the growing demand for TB services and to support research and innovation in TB control.

Moreover, the Global Tuberculosis Report 2024 emphasizes the importance of universal health coverage (UHC) in achieving the End TB Strategy's targets. Progress towards UHC has stagnated in many regions and the financial burden of TB on affected households remains high. Strengthening health systems and ensuring that TB services are integrated into primary health care are essential steps towards achieving UHC and reducing the catastrophic costs associated with TB.

Additionally, the Global Tuberculosis Report 2024 discusses the significant impact of the COVID-19 pandemic on the global TB epidemic. After being overshadowed by COVID-19 for 3 years, TB is poised to regain its status as the leading cause of death from a single infectious disease globally by 2023. The pandemic has provided invaluable insights, emphasizing the need for resilient health systems, increased investment in research and innovation, and a holistic approach to addressing the social determinants of health.

Lastly, the report underscores the value of international cooperation and the role of the UNHLM on TB in setting new targets and mobilizing global action. The commitments made at these meetings must be translated into concrete actions, with a focus on preventing future pandemics and strengthening health systems' capacity to respond to emerging threats.

In summary, the global fight against TB is at a critical juncture. The challenges are formidable but the opportunities for progress are significant. The global community must seize the moment by increasing investment, intensifying research and innovation, and implementing

effective strategies to control and ultimately end the TB epidemic. The stakes are high, but with concerted effort and a renewed commitment to global health security, the goal of a world free from TB is within reach.

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## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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