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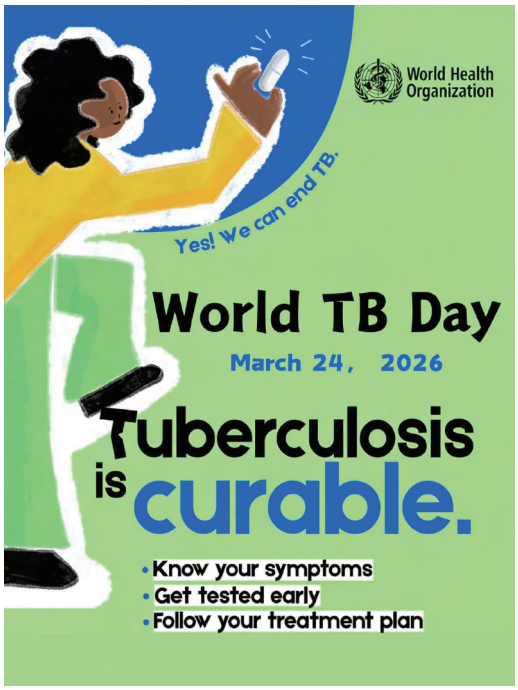

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This week's issue was organized by Guest Editor Yanlin Zhao.

Perspectives

China's TB Portfolio for Advancing the 2030 End TB Goals

Shaojun Pei[1,2,&]; Caihong Xu[3,4,&]; Dongmei Hu[3]; Yanlin Zhao[3,#]

ABSTRACT

The global trajectory for tuberculosis (TB) elimination remains precarious, characterized by a recent but fragile and insufficient decline in its incidence by 2024, the first since the coronavirus disease 2019 (COVID-19) pandemic. Progress is severely hampered by the failure to meet the ambitious 2025 End TB targets and is further threatened by anticipated funding cuts, necessitating a translation of widely accepted concepts of "high-level multi-sectoral cooperation" and "strict accountability" to concrete solutions. In contrast, China has achieved remarkable progress, meeting its goal of a 20% reduction in TB incidence from 2015 to 2024, suggesting a transition toward a lower-incidence setting. This success reflects a deliberate, science-driven, and strategic transformation. In this Personal View, we describe China's clearly defined national and provincial TB incidence-reduction targets for 2025 and 2030, as well as its comprehensive TB control program spanning the full continuum of care. China's integrated strategy, combining political commitment, rigorous strategy, sustainable financing, empowering research and innovation, the zoonotic and anthroponotic TB approach, and strong accountability mechanisms, offers a blueprint for low- and middle-income countries. It outlines a specific implementation pathway to revitalize global efforts to combat TB and restore confidence in the feasibility of ending TB.

Tuberculosis (TB) remains the leading cause of death due to infectious diseases worldwide. According to the Global Tuberculosis Report 2025 released by the World Health Organization (WHO), an estimated 10.7 million people developed TB and approximately 1.23 million died from the disease in 2024, underscoring the persistent gap between global targets and epidemiological reality (*1*). Although the WHO End TB Strategy defines a unified set of ambitious global targets to reduce incidence, mortality, and catastrophic expenditures by 2030 (*2*), progress has been uneven across regions and countries, reflecting differences in health system capacity, socioeconomic conditions, and epidemic trajectories. In some low- and intermediate-burden settings, progress that once appeared promising has slowed or even reversed. At the same time, concerns over reduced international donor funding threaten the sustainability of TB control gains in many countries (*3–4*). These trends underscore that achieving End TB targets will require not only effective technical interventions but also sustained financing, strong governance, and context-specific implementation strategies.

In stark contrast to the overall stagnation of global TB control efforts, China has achieved remarkable progress. According to the WHO Global Tuberculosis Report 2025, China is estimated to have reduced its TB incidence rate by approximately 20% from 65 per 100,000 people in 2015 to 49 per 100,000 people in 2024, suggesting a transition toward a lower incidence setting (*1*). Nevertheless, significant disparities persist across provincial-level administrative divisions (PLADs), largely driven by differences in economic development, health system capacity, population density, and internal migration patterns (*5*). Western and central PLADs generally exhibit a higher incidence and longer diagnostic delays, whereas the more economically developed eastern PLADs benefit from stronger surveillance and treatment infrastructure.

In response to the renewed global commitments emphasized in the 2023 United Nations High-Level Meeting Political Declaration on Ending TB, China has strengthened its comprehensive TB control strategy across a continuum of prevention, diagnosis, treatment, and care. National targets have been translated into specific provincial goals to support implementation and accountability, while innovative policy initiatives, particularly the nationwide expansion of zero-TB communities, demonstrate China's efforts to operationalize broad strategic frameworks into locally adapted interventions. This multilayered, goal-oriented framework reflects a country's efforts to

harmonize national priorities with local realities, reduce inter-provincial disparities, and provide a directly replicable blueprint for low- and middle-income countries.

National and Provincial TB Incidence Targets in China

In 2024, national planning targets were established to reduce the incidence of TB to below 50 per 100,000 people by 2025 and to below 43 per 100,000 people by 2030 (*6*). To support the achievement of the 2030 goal, the 2025 TB incidence was estimated using notification data adjusted for underreporting and underdiagnosis, and provincial-specific incidence reduction targets were formulated (Figure 1). By 2025, the PLADs with relatively high TB burdens are expected to remain concentrated in western China, including Guizhou (87.2 per 100,000), Tibet (80.0 per 100,000), Qinghai (79.4 per 100,000), Xinjiang (65.0 per 100,000), and Hainan (60.0 per 100,000), all exceeding the national target threshold of 50 per 100,000.

Each PLAD subsequently establishes its own 2030 incidence-reduction target based on local epidemiological trends and programmatic capacity. Notably, Chongqing (15.34%), Guizhou (14.73%), Tibet (8.97%), Qinghai (8.83%), and Xinjiang (7.93%) had annual decline rates exceeding 7%. If all PLADs achieve their respective targets, the population-weighted national TB incidence will decline to 34.9 per 100,000 people by 2030, thereby meeting the national goal of remaining below 43 per 100,000.

Comprehensive TB Control Strategy in China

China is implementing a comprehensive strategy that covers the entire process of TB prevention and control (Figure 2), ranging from reducing incidence through robust early detection and prevention using a community-based zero-TB approach, to ensuring

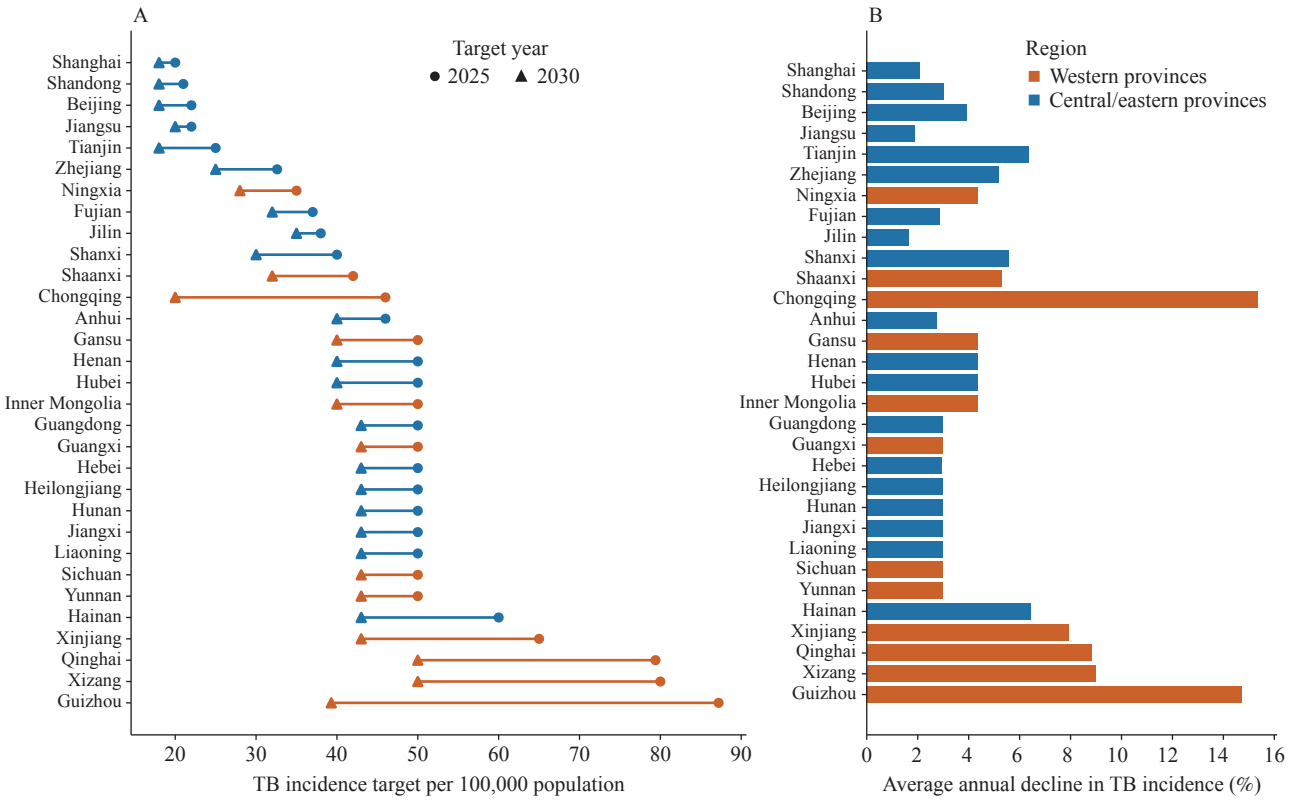

FIGURE 1. Provincial TB incidence targets and projected annual declines across provinces in China. (A) Provincial TB incidence targets for 2025 to 2030. (B) Provincial average annual decline in TB incidence from 2025 to 2030 across provinces, shown using the same regional classification.
Note: In panel A, the circles denote the 2025 target and triangles denote the 2030 target, with lines linking the two targets within each province. Provinces are grouped by region as western provinces and central/eastern provinces.
Abbreviation: TB=tuberculosis.

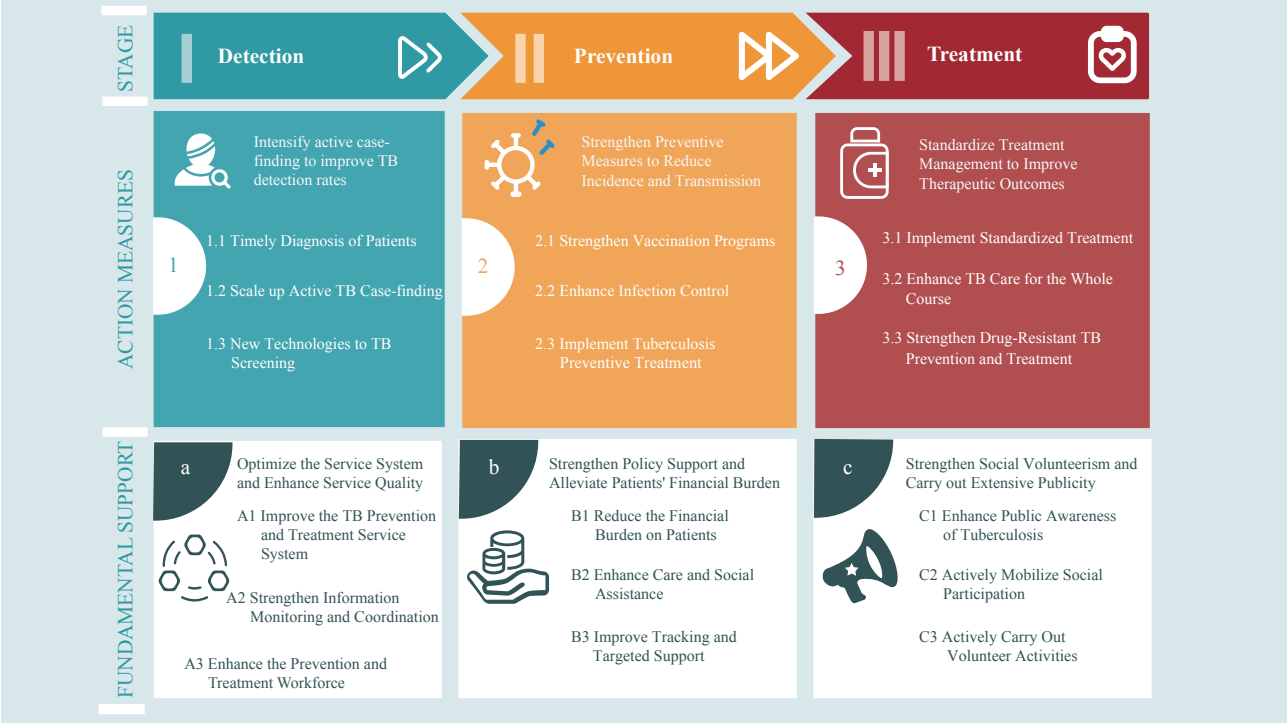

FIGURE 2. The comprehensive TB control strategy in China.
Abbreviation: TB=tuberculosis.

timely treatment and comprehensive patient management through a multi-sectoral collaboration mechanism to implement the One Health policy. This strategy relies on a strong health system, sound financial support mechanisms, and extensive public awareness campaigns to ensure the achievement of the national TB control goals.

Intensify Active Case-finding to Improve TB Detection Rates

As the entry point of the full continuum of TB care, early and effective case detection is essential to reduce diagnostic delays, interrupt transmission, and enable timely treatment. From 2022 to 2024, China expanded its "Zero-TB Community initiative" pilot program from 36 to 790 sites, gradually establishing a community-based comprehensive intervention network centered on active screening and preventive treatment (*7*). Screening efforts prioritize key high-risk populations, such as close contacts of TB patients, HIV-infected individuals, patients with prior TB treatment, the elderly, and diabetic patients, with evidence demonstrating improved case detection in these groups. In settings with a high risk of transmission, such as schools and workplaces, mandatory screening during pre-enrollment medical examinations and annual routine checks further enhance early detection and outbreak prevention. To enhance the diagnostic capacity, designated healthcare facilities are equipped with the necessary equipment to perform molecular testing on suspected TB cases and molecular drug susceptibility testing to rapidly identify drug-resistant strains. Since 2010, the Chinese Center for Disease Control and Prevention has conducted annual evaluations of *Mycobacterium tuberculosis* drug-susceptibility testing capacity in laboratories of designated healthcare facilities nationwide. AI-assisted digital radiography and remote consultation systems are increasingly used in primary healthcare institutions to improve diagnostic accuracy and support healthcare providers in resource-limited areas (*8*). Additionally, some innovative screening modalities, such as mobile radiography vans, pooled sputum testing strategies, and emerging non-sputum molecular assays (e.g., tongue swab qPCR), are being assessed to expand the reach and efficiency of active case finding.

Strengthen Preventive Measures to Reduce Incidence and Transmission

Building on enhanced case detection, China has implemented a multifaceted prevention framework to reduce TB transmission, prevent progression to active

disease, and lower the overall incidence. These strategies include vaccination, infection control, preventive treatment, and zoonotic and anthroponotic TB control. Maintaining high coverage and rigorous quality control of the Bacillus Calmette–Guérin (BCG) vaccination remains fundamental. At the same time, ongoing clinical and translational research into novel vaccines, including subunit, inactivated mycobacterial, and RNA-based platforms, offers new opportunities for long-term TB prevention in China (*9*). Efforts are being strengthened through standardized isolation and leave policies for infected individuals, heightened awareness of personal protective measures, and targeted risk assessment and guidance at the household level, particularly among those in close contact with TB patients and among healthcare workers in high-exposure settings. Simultaneously, expanding the coverage of TB-preventive treatments (TPT) has become a key priority. This includes improving accessibility to preventive treatment clinics, optimizing screening to accurately identify eligible individuals, and enhancing diagnostic and therapeutic capacities to ensure timely initiation and adherence. Recent clinical and follow-up studies demonstrated that well-managed TPT significantly lowers the risk of progression to active disease in high-risk populations. However, barriers to acceptance and adherence remain. One study selected 10 counties/districts across five PLADs (Hebei, Henan, Hunan, Guangdong, and Chongqing) as survey sites and screened medical workers, students, teachers, and other occupational groups aged 15–65 years for LTBI between May and December 2023. The study found that the overall acceptance rate of TPT among individuals with LTBI was 17.0% (*10*). Therefore, China has begun to strengthen its preventive efforts through shorter rifamycin-based regimens (*11*), expanded policy support and financing mechanisms (*12*), and enhanced education and adherence support for target populations (*13*). In the field of prevention and control of zoonotic tuberculosis, China is strengthening source control at the national strategic level, requiring nationwide cross-departmental coordinated prevention and control efforts, and strengthening regional cooperation to achieve effective prevention and control. Together, these coordinated approaches aim to reduce infections, prevent disease progression, and block the spread of TB at the population level.

Standardize Treatment Management to Improve Therapeutic Outcomes

Standardized and patient-centered treatment management is a core priority in the TB care continuum to translate gains in detection and prevention into improved patient outcomes. This includes ensuring strict adherence to recommended regimens, implementing isolation measures for infected patients, and prioritizing fixed-dose combination therapies for drug-susceptible TB, with support from expert consultations and robust quality control systems. Comprehensive patient management should cover the entire treatment process, from screening and diagnosis to treatment and follow-up, to improve service coherence and consistency, especially in primary and rural healthcare institutions. The incorporation of digital health tools, such as electronic medication monitors and mobile health applications, has proven to significantly enhance treatment adherence and clinical outcomes, offering scalable solutions to support real-world patient management. Social support interventions, including psychological counseling and nutritional assistance, play a key role in eliminating non-medical barriers to treatment adherence and improving overall patient health. For drug-resistant TB, strengthening drug-resistance testing capacity and expanding coverage of shorter, all-oral regimens are key priorities, with emerging clinical evidence demonstrating improved patient tolerability and treatment success (*14*). In December 2024, the novel antituberculosis drug pretomanid was officially approved for marketing in China. This signifies the formal implementation of the WHO's recommended 6-month all-oral short-term treatment regimen for drug-resistant TB (i.e., the BPaL/M regimen) in China. These strategies reflect a shift toward integrated patient-centered TB care aimed at achieving sustained treatment success and reducing disease transmission.

Optimize the Service System and Enhance Service Quality

To sustain an effective delivery across the full continuum of care, China has focused on strengthening its underlying TB service system and improving service quality. The TB control service system is being progressively strengthened through clearer role divisions and improved coordination within an integrated healthcare network. Collaboration among the Chinese Centers for Disease Control, designated TB hospitals, and primary healthcare

facilities has enhanced the effectiveness of tiered diagnosis and treatment, supporting more standardized and continuous patient management (*15*). Concurrently, the development and optimization of integrated information systems are improving the real-time data exchange between clinical and public health departments, enabling more efficient surveillance, earlier detection of outbreaks, and evidence-based policy adjustments. Measures to strengthen professional capacity have further solidified system performance, including high-level workforce training, structured competency development, and incentive mechanisms to improve staff motivation and retention (*16*). China has actively participated in the development of international technical standards and laboratory quality frameworks, thereby contributing to the advancement of global tuberculosis control practices. These measures will contribute to a more cohesive, responsive, and sustainable TB service system capable of supporting progress toward national TB goals.

Strengthen Policy Support and Alleviate Patients' Financial Burden

Since economic hardship can undermine access to diagnosis, prevention, and treatment, financial protection is an indispensable component of a comprehensive TB care framework. Financial protection mechanisms for patients with TB in China are being strengthened through a multi-source financing framework that integrates infectious disease control funds, basic medical insurance schemes, local government subsidies, social assistance programs, and charitable donations (*17*). This diversified financing approach aims to reduce out-of-pocket expenditures and improve equitable access to healthcare services. The prices of anti-TB drugs are regulated through centralized procurement and negotiated pricing. The national essential medicine list and insurance reimbursement catalog are continuously updated to ensure the inclusion of cost-effective and clinically necessary TB drugs. To further reduce the risk of catastrophic healthcare expenditures, targeted monitoring systems are used to identify vulnerable patients, and tailored household-level support programs are implemented to prevent poverty induced by long-term treatment and loss of income. Evidence suggests that these integrated financial support strategies can effectively reduce both medical and non-medical economic burdens while improving treatment affordability and adherence among economically disadvantaged TB patients. These measures contribute to a more equitable and sustainable TB system.

Strengthen Social Volunteerism and Carry out Extensive Publicity

Finally, effective implementation of the full continuum of TB care relies on strong public engagement, health communication, and broader social participation. Through multidimensional innovative health education strategies that combine traditional media and new digital communication platforms, public awareness and participation in tuberculosis prevention are constantly improving. These campaigns aim to improve TB-related health literacy among the general population, high-risk groups, and key institutions, thereby promoting timely care seeking and reducing delays in diagnosis and treatment. A nationwide cross-sectional study conducted across all PLADs during recent TB control initiatives showed gradual improvements in public knowledge, with an overall awareness rate of 82.51% for key TB information (*18*). However, substantial gaps remained among specific regions and population groups. Participants aged 60 and older, those with primary education or below, and students and individuals who had not received public TB education were less likely to be aware of all key TB information, underscoring the need for more targeted and practical communication strategies. Simultaneously, broad social participation is encouraged by expanding multi-sectoral collaboration and creating supportive community environments. Volunteer engagement and community health promotion activities should be encouraged to enhance individual health responsibilities, strengthen patient support networks, and maintain long-term behavioral changes. These initiatives collectively promote increased public awareness, reduce discrimination, and strengthen social participation in TB prevention and control.

CONCLUSION

China has made substantial progress in TB control over the past few decades through sustained political commitment, expansion of prevention and diagnostic coverage, strengthening treatment management, and continuous improvement in service delivery across the full continuum of care. These achievements demonstrate the value of combining national strategic

direction with increasingly localized implementation and accountability. At the same time, the path toward ending TB in China remains challenging. Persistent disparities in surveillance, diagnostic capacity, and service quality across PLADs and between urban and rural areas have left some cases undetected or untreated, particularly among rural and remote populations (*5*). The expansion of TBT remains constrained by low acceptance, implementation gaps, and geographic variations, while financial protection is not uniform across all settings and population groups (*10*). A balanced assessment of these gaps is essential to understand both the strengths and limitations of China's current TB control models.

To address these challenges, China has gradually developed a comprehensive TB control strategy that spans the full continuum of care, linking national strategic priorities to provincial accountability mechanisms, while continuously strengthening diagnostic and treatment capacities, improving financial protection for patients, and promoting broader public and community engagement (*6*). However, the effective implementation of this model depends largely on a strong governance capacity, a relatively well-developed public health network, a high degree of health system integration, and stable domestic public financing. These conditions may not be readily available in countries with fragmented healthcare systems or a long-term reliance on external aid. However, some interventions adopted in China may be more readily transferable because they are relatively low-cost and operationally feasible, including the use of AI-assisted chest radiography to support TB screening (*19*), scale-up of shorter all-oral regimens for drug-resistant TB (*14*), and the application of digital adherence support tools to improve treatment management and patient follow-up (*20*). These approaches are all broadly aligned with recent WHO policy updates and technical guidance and may help improve service efficiency and strengthen patient-centered care in resource-constrained settings. Overall, China's experience should not be viewed as a one-size-fits-all solution that can be directly replicated; rather, it is better understood as a policy framework whose components can be selectively adapted according to local institutional conditions, service capacity, and fiscal space, thereby offering a practical and valuable reference for other countries seeking to strengthen TB control across the full continuum of care.

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Vital Surveillances

Epidemiological Characteristics of Asymptomatic Tuberculosis — China, 2021–2024

Caihong Xu[1,2]; Yaxin Wen[2]; Yanlin Zhao[2,#]; Biao Kan[1,3,#]

ABSTRACT

Introduction: Tuberculosis (TB) remains a major public health challenge in China, which ranks fourth among the 30 high-burden countries worldwide. Individuals with asymptomatic Pulmonary TB (aPTB) may act as "silent transmitters", contributing to undetected community transmission and hindering progress toward the End-TB goals. This study examined the epidemiological characteristics of patients with aPTB in China from 2021 to 2024 to inform targeted control strategies.

Methods: Data were obtained from the China Information System for Disease Control and Prevention for the period 2021–2024 and included TB cases with complete symptom records. aPTB was defined as cases without recorded cough symptoms, whereas symptomatic TB was defined as cases with recorded cough symptoms. Descriptive statistical analyses compared the demographic, clinical, and healthcare-seeking characteristics of patients with aPTB and symptomatic TB.

Results: Among 973,299 PTB cases with complete symptom records, 16.66% were classified as aPTB. This proportion remained relatively stable throughout the study period, with a slight peak observed in 2022. Higher proportions of aPTB were observed among individuals aged 55–64 years (17.07%), 65–74 years (15.51%), and 15–24 years (14.03%), and among farmers and herders (50.87%). A mild seasonal trend was observed. Geographically, high-incidence areas were concentrated in western and southwestern China.

Conclusions: aPTB constitutes a substantial component of the total TB burden in China. Strengthening active case detection in high-risk populations, optimizing medical resources in western China, and integrating aPTB control programs into national prevention and control plans for TB to mitigate hidden transmissions and advance national End-TB objectives.

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains one of the leading causes of death worldwide. According to the World Health Organization (WHO) Global TB Report, an estimated 10.7 million new TB cases occur annually, and approximately one-fourth of the global population is infected with *M. tuberculosis* (*1*). China reports approximately 696,000 new TB cases each year, ranking fourth among the 30 high-burden countries. Consequently, TB control remains a central priority under the "Healthy China 2030" strategy.

TB has a multi-stage natural history that includes latent infection, asymptomatic infection, and symptomatic active disease (*2*). Asymptomatic pulmonary tuberculosis (aPTB) is defined as "individuals without, unaware of, or not reporting symptoms during screening or history-taking, and without clinical signs indicative of TB" (*3*). National prevalence surveys indicate that 36%–80% of bacteriologically confirmed TB cases are asymptomatic (*4*). Although these individuals do not present with typical symptoms, such as persistent cough or fever, they may remain infectious and contribute to unrecognized community transmission (*5*). Preventing such transmission is essential to achieving the WHO End-TB strategy.

Traditional TB surveillance systems and burden estimates have focused primarily on symptomatic and active cases of TB, resulting in a limited understanding of the prevalence and burden of aPTB in China. To address this gap, a systematic analysis of the epidemiological characteristics and temporal trends of aPTB was performed across China. This study aimed to provide evidence to inform TB surveillance, prevention, and control policies, thereby addressing existing gaps, supporting national efforts to reduce TB incidence and advance progress toward the elimination of TB.

METHODS

Data Source

Data were obtained from the China Information System for Disease Control and Prevention, a mandatory nationwide surveillance platform operated by the China CDC. The eligibility criteria included TB cases reported between January 1, 2021, and December 31, 2024, with complete symptom records. During this study period, 2,210,063 TB cases were registered in the system. Of these, 1,228,398 cases were excluded due to incomplete symptom data, leaving 981,665 eligible cases for further analysis. Subsequently, 8,366 records were excluded because they were ineligible, including extrapulmonary TB, non-tuberculous mycobacterial (NTM) infection, duplicate entries, and logical inconsistencies. The final analytical sample comprised 973,299 PTB cases.

Case Definition

aPTB was defined as PTB cases without documentation of "cough" in the symptom field (*6*). Cough is the most common and characteristic symptom of PTB and is typically the primary reason individuals seek TB-related medical care. This operational definition is consistent with clinical practice.

Statistical Analysis

Data were cleaned and organized using Microsoft Excel (version 2021, Microsoft, Redmond, USA, https://www.microsoft.com/) to remove duplicate records and resolve logical inconsistencies. Descriptive statistics were used to examine temporal (annual and monthly) and demographic (age, sex, and occupation) distributions. All statistical analyses were conducted using R software (version 4.3.0, Vienna, Austria, https://www.r-project.org/). Temporal trends were assessed using the Cochran-Armitage trend test.

RESULTS

Overall Burden

A total of 973,299 PTB cases with complete symptom records from 2021 to 2024 were included in the analysis. Of these, 162,151 (16.66%) were asymptomatic and classified as aPTB. Bacteriological confirmation was obtained in 48.60% of aPTB cases and 68.45% of symptomatic PTB cases. Statistical analysis revealed significant annual differences in the proportion of aPTB cases (χ^2=633.70, P<0.001), along with a significant downward temporal trend (Z=–9.35, P<0.001). The proportion of aPTB cases peaked in 2022 (18.07%; incidence: 3.69 per 100,000), followed by slight fluctuations in 2023 (16.04%; incidence: 3.82 per 100,000) and 2024 (16.31%; incidence: 3.30 per 100,000) (Table 1).

Epidemiological Characteristics

Population distribution The analysis examined the age, gender, and occupational distributions of nationally registered PTB cases from 2021 to 2024. Significant differences were observed between the aPTB and sPTB groups across all three characteristics (Figure 1; χ^2=603.99 for sex, χ^2=16,103.30 for age, and χ^2=19,288.66 for occupation; all P<0.001). Regarding age distribution, the highest incidence of aPTB was observed among individuals aged ≥75 years (20.47 per 100,000), 65–74 years (20.37 per 100,000), and 55–64 years (15.93 per 100,000). Similarly, sPTB cases were most concentrated in the same age groups: ≥ 75 years (150.65 per 100,000), 65–74 years (141.34 per 100,000), and 55–64 years (94.94 per 100,000). With respect to sex distribution, the male-to-female ratio was 1.96∶1 in the aPTB group and 2.26∶1 in the sPTB group, indicating a consistent male predominance across most age groups in both cohorts. Among individuals aged ≥75 years, males accounted for 68.38% of aPTB cases. In terms of occupation, the

TABLE 1. Number and proportions of aPTB cases in China, 2021–2024.

Year	Asymptomatic PTB			Symptomatic PTB			Total
	Number	Incidence (/100,000)	Proportion (%)	Number	Incidence (/100,000)	Proportion (%)	
2021	9,750	0.69	15.17	54,520	3.86	84.83	64,270
2022	52,050	3.69	18.07	236,031	16.72	81.93	288,081
2023	53,882	3.82	16.04	282,145	20.01	83.96	336,027
2024	46,469	3.30	16.31	238,452	16.93	83.69	284,921
Total	162,151	2.87	16.66	811,148	14.38	83.34	973,299

Abbreviation: PTB=pulmonary tuberculosis; aPTB=asymptomatic pulmonary tuberculosis.

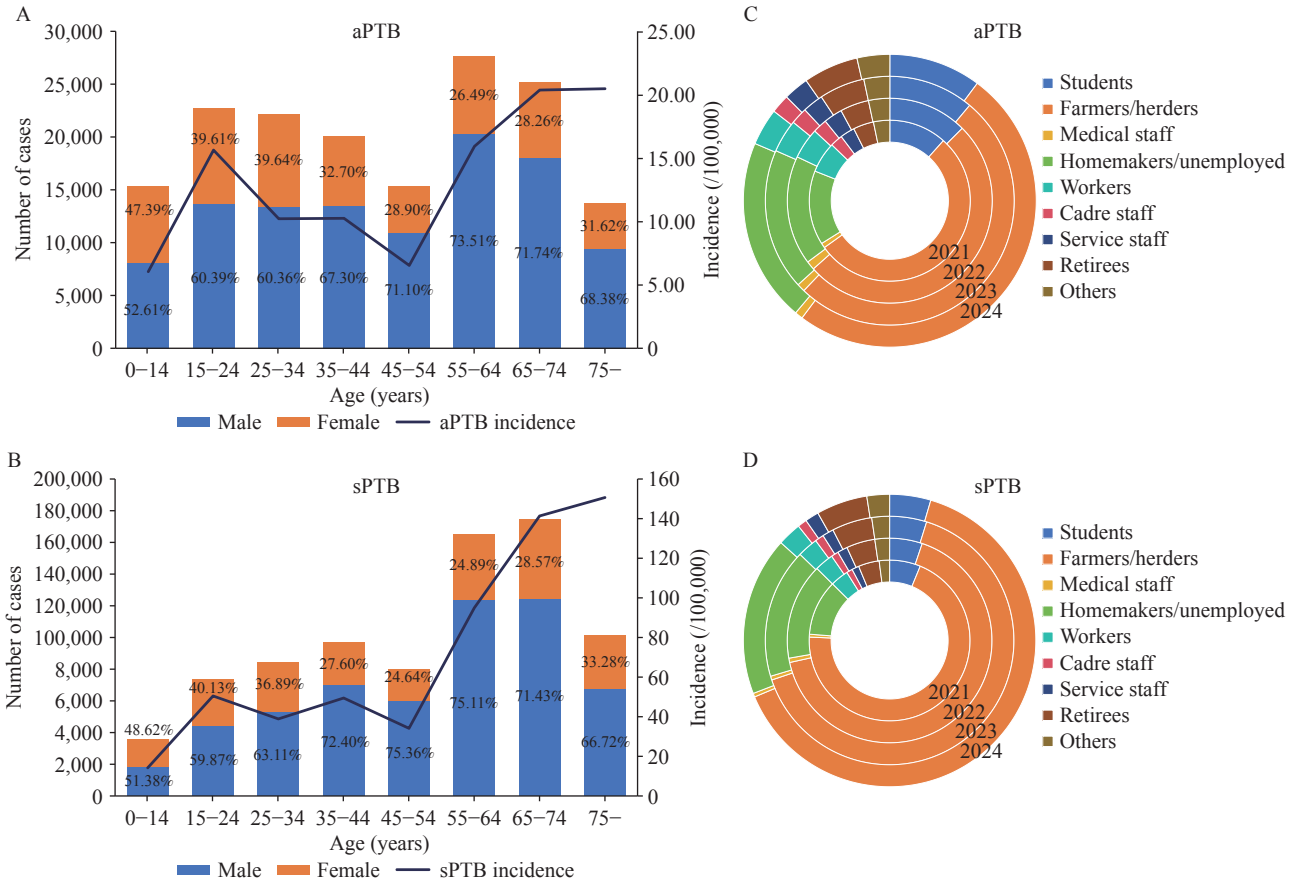

FIGURE 1. Population distribution of aPTB and sPTB cases in China between 2021 and 2024. (A) Age distribution of aPTB cases; (B) Age distribution of sPTB cases; (C) Occupational distribution of aPTB cases; (D) Occupational distribution of sPTB cases .
Abbreviation: aPTB=asymptomatic pulmonary tuberculosis; sPTB=symptomatic pulmonary tuberculosis.

three most common categories among aPTB were farmers and herders (50.87%), homemakers and unemployed (18.36%), and students (11.32%). Among sPTB cases, farmers and herders (65.47%), homemakers and unemployed (16.19%), and retirees (5.08%) were the predominant occupational groups (Figure 1).

Temporal distribution Over the four-year study period, the annual number of aPTB cases remained relatively stable (9,750 in 2021, 53,882 in 2023 (peak), and 46,469 in 2024), whereas the number of sPTB cases fluctuated more substantially (54,520 in 2021, 282,145 in 2023 (peak), and 238,452 in 2024). Statistical analysis confirmed significant monthly variation in the proportion of aPTB cases (χ^2=2,790.27, P<0.001). The number of aPTB cases increased from February (10,354 cases, accounting for 6.39% of the cumulative TB total) to a peak in August (15,722 cases, 9.70%), followed by a gradual decline through December (11,172 cases, 6.89%). For sPTB, the number of cases peaked in March (79,047 cases, 9.75% of the monthly TB total) and July (73,724 cases, 9.09%), with the lowest number of cases recorded in December (57,177 cases, 7.05%) (Figure 2).

Regional Distribution

From 2021 to 2024, the 5 provincial-level administrative divisions (PLADs) with the highest registration rates of aPTB were Xizang (9.50 per 100,000 population), Guizhou (7.56 per 100,000 population), Yunnan (5.30 per 100,000 population), Xinjiang (5.09 per 100,000 population), and Hubei (4.92 per 100,000 population). During the same period, the 5 PLADs with the highest registration rates of sPTB were Guizhou (42.12 per 100,000 population), Xizang (40.62 per 100,000 population), Xinjiang (35.19 per 100,000 population), Qinghai (34.39 per 100,000 population), and Guangxi (30.18 per 100,000 population) (Figure 3).

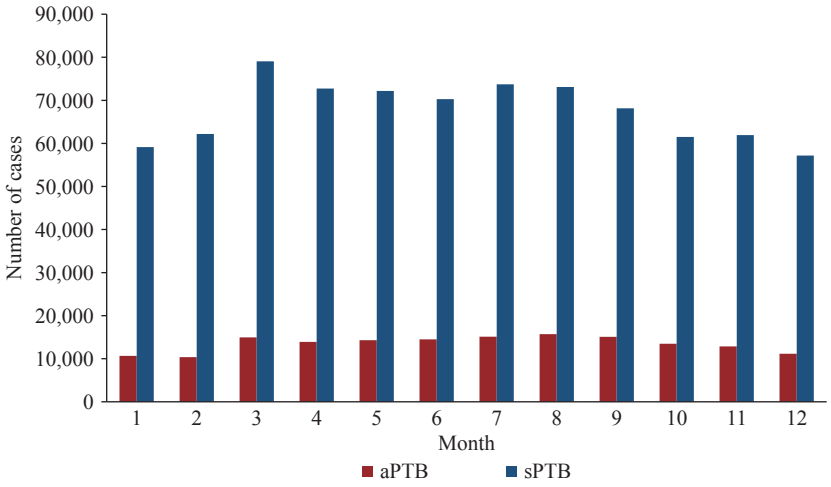

FIGURE 2. Temporal distribution of aPTB and sPTB cases in China between 2021 and 2024.
Abbreviation: aPTB=asymptomatic pulmonary tuberculosis; sPTB= symptomatic pulmonary tuberculosis.

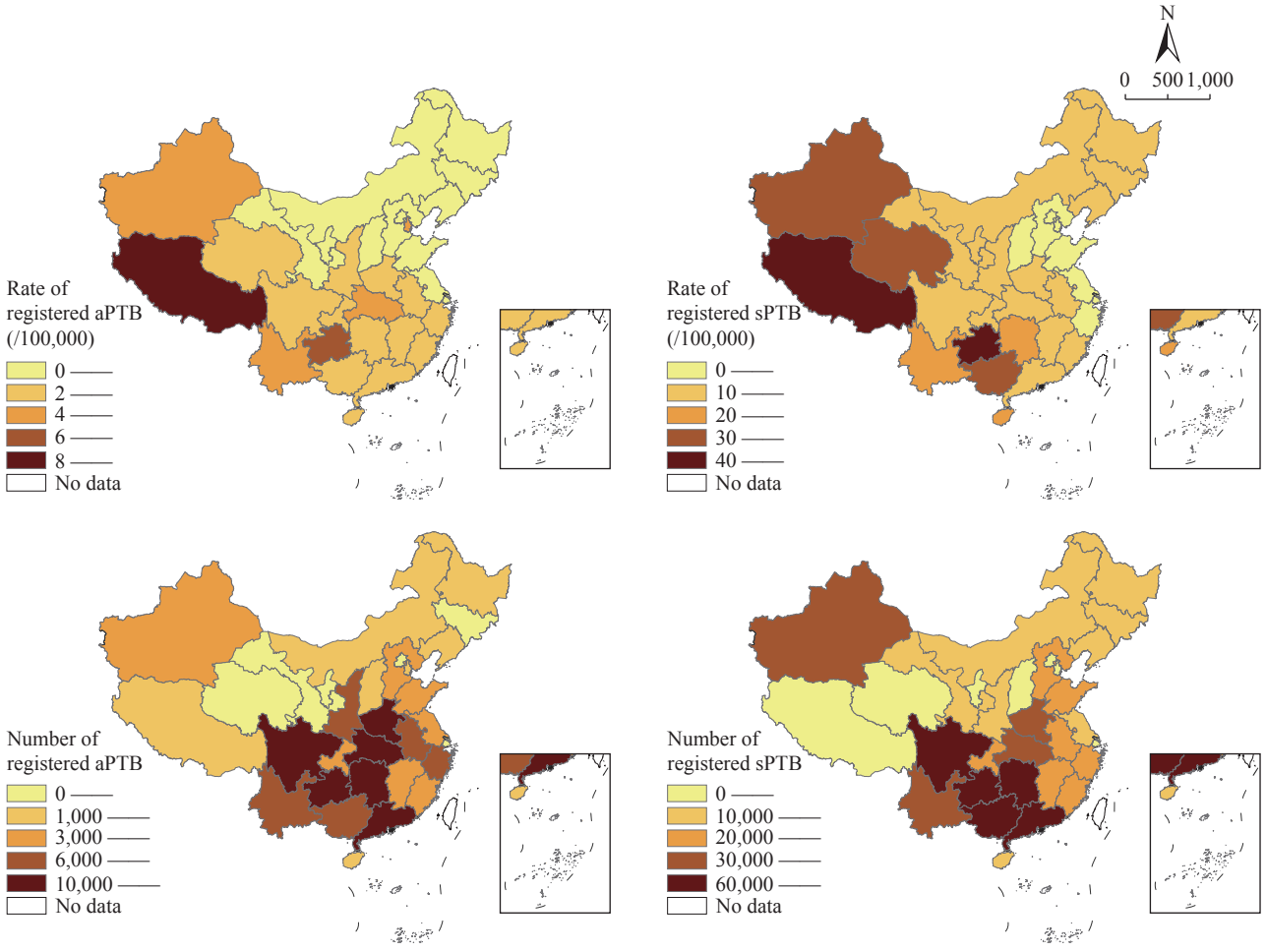

FIGURE 3. Regional distribution of aPTB and sPTB cases in China, 2021–2024.
Abbreviation: aPTB= asymptomatic pulmonary tuberculosis; sPTB=symptomatic pulmonary tuberculosis.
Map approval number: GS 京 (2026) 0610 号.

DISCUSSION

This analysis describes the epidemiological characteristics of aPTB in China from 2021 to 2024 and provides insight into its burden and distribution. aPTB accounted for 16.66% of all TB cases with complete symptom records during the study period, indicating a substantial hidden burden. Although the proportion of aPTB declined over the four-year period, this trend may reflect changes in diagnostic sensitivity and healthcare-seeking behavior rather than a true reduction in asymptomatic disease. In terms of population distribution, aPTB was most common among individuals aged ≥75 years (corresponding to the highest aPTB incidence of 20.47 per 100,000) and 65–74 years (20.37 per 100,000). The male-to-female ratio for aPTB was lower than that for sPTB, although a male predominance persisted. Farmers and herders, homemakers and unemployed, and students represented the primary occupational groups. Spatially, high-incidence areas of aPTB were concentrated in western and southwestern China, partially overlapping with sPTB hotspots.

The 16.66% proportion of aPTB in this study falls within the 14.2%–43.1% range reported by the national epidemiological surveys conducted in 2000 and 2010 (*7*–*8*), but is lower than the 47.7% reported in a high-risk population study by Zhang et al. (*9*). This discrepancy likely reflects differences in study populations. Zhang et al. focused on high-risk groups such as older adults and patients with diabetes who may be more likely to have asymptomatic disease, whereas the present study included all registered TB cases with complete symptom records. Internationally, a multicountry study across 12 Asian and African countries reported a 39.8% proportion of aPTB (adjusted to 62.5%) using a "no cough" definition (*6*), exceeding the current estimate. Differences in epidemic disparities, screening strategies, and case definitions may explain this variation (*10*). The use of a "no cough" definition in this study may have modestly overestimated the proportion of aPTB compared with stricter definitions requiring the absence of all TB-related symptoms. Nevertheless, cough is the principal symptom prompting TB-related healthcare-seeking; therefore, this operational definition aligns with public health priorities. The lower bacteriological confirmation rate observed for aPTB compared with sPTB likely reflects earlier disease stage and lower mycobacterial load, which reduce microbiological detectability. Despite this limitation, bacteriologically positive aPTB cases warrant close attention, as they may contribute to silent transmission and sustain hidden transmission chains.

Several factors may explain the epidemiological patterns observed (*11*). The higher incidence of aPTB among older adults may be related to the age-associated immune decline, which increases susceptibility to *Mycobacterium tuberculosis* while producing atypical or mild clinical manifestations. This interpretation is consistent with findings from a study conducted in Zhejiang Province (*8*), where aPTB was more common among older individuals. In terms of occupational distribution, the high proportion of farmers and herders with aPTB likely reflects limited access to healthcare services, lower awareness of TB prevention and control, and fewer routine health examinations in rural and pastoral areas, resulting in the delayed detection of asymptomatic infections. Similar conclusions were reported by Gao et al. (*12*).

In terms of temporal distribution, the relative stability of aPTB and its mild seasonal variation may reflect the chronic nature of asymptomatic infection. Unlike symptomatic TB, which may be influenced by climatic conditions and population gathering activities, aPTB often progresses slowly and may be less sensitive to short-term seasonal changes.

The regional concentration of aPTB in high-incidence areas appears to be closely linked to geographical environment and socioeconomic factors (*13*). The western and southwestern regions of China have complex geographical environments, relatively low socioeconomic levels, poor living conditions, and insufficient medical resources, which may facilitate the spread of *M. tuberculosis*. Furthermore, high levels of internal migration may further increase the risk of undetected aPTB transmission. The regional distribution detected by the current analyses was also affected by regional epidemic levels and screening strategies.

Regions with high incidence of both sPTB and aPTB, including Tibet, Guizhou, and Xinjiang, are nationally recognized high-burden areas. Among non-overlapping high-incidence regions, areas with high sPTB incidences (e.g., Qinghai and Guangxi) are also high-TB-incidence regions nationally, whereas elevated aPTB detection in Yunnan, Hubei, and other regions may reflect proactive case-finding initiatives. Yunnan piloted an active pulmonary TB case-finding strategy in 2016 and promoted expanded active screening efforts in 2019 (*14*). These interventions likely enhanced aPTB detection, thus enabling the timely

identification and reporting of more aPTB cases.

This study has several limitations. First, the analysis was restricted to registered TB cases with complete symptom records, which may have introduced selection bias. Unregistered aPTB cases, including individuals who were not screened or had incomplete records, were not captured. Therefore, the true burden of aPTB may be underestimated. Second, the analysis focused on epidemiological characteristics of aPTB from the perspectives of population, time, and region and did not examine biological factors (e.g., *M. tuberculosis* strain virulence) or individual behavioral factors (e.g., smoking, alcohol use, and living conditions) that may influence the occurrence of aPTB. The absence of these variables limits a more comprehensive understanding of the pathogenesis of aPTB.

These findings have important implications for optimizing TB prevention and control strategies in China and strengthening aPTB management. The relatively high proportion of aPTB cases indicates that reliance solely on symptom-based screening may be insufficient. Expanding imaging and etiological screening is crucial, particularly among high-risk populations. First, stratified active case finding (ACF) should be implemented for high-risk groups, including older adults, adolescents, farmers, and herders. Regular TB screening among elderly individuals and students, along with expanded outreach in rural and pastoral areas, could facilitate earlier detection and reduce the potential risk of transmission. Second, given the geographic concentration of high-incidence areas, increased investment in medical and healthcare resources in western and southwestern China is needed. Upgrade TB diagnosis and treatment capacity in these regions, and intensify health education initiatives to raise public awareness in the prevention and control of aPTB. Third, the substantial proportion of aPTB cases during the study period suggests that aPTB is an important component of the TB burden in China. It is necessary to incorporate aPTB prevention and control into the national TB prevention and control plan, formulate targeted prevention and control measures, and promote the early realization of the global goal of ending the TB epidemic. Finally, these analyses showed that aPTB has a mild seasonal pattern. This finding can provide a basis for the rational allocation of medical resources and the strengthening of screening, diagnosis, and treatment strategies in peak months (such as August) to improve the efficiency of case management.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Scaling Up Tuberculosis Preventive Treatment: Progress and Factors Influencing Optimization — China, 2022–2025

Caihong Xu[1,2]; Jinhao Li[2]; Yaxin Wen[2]; Dongmei Hu[2]; Rongbin Yu[1,#]; Yanlin Zhao[2,#]

Summary

What is already known about this topic?

Tuberculosis preventive treatment (TPT) is critical in preventing latent tuberculosis infection (LTBI) progression to active tuberculosis. China has integrated TPT into national Tuberculosis (TB) control; however, systematic national data on TPT implementation in China are scarce.

What is added by the report?

TPT recipient number in China increased 2.5-fold (2022–2025), with around 79% using short-course regimens. Among 2,676 individuals with LTBI, TPT acceptance and completion rates were 45.14% and 85.18%, respectively. Key acceptance factors included age, ethnicity, occupation, treatment institution, immunocompromised status, and purified protein derivative results.

What are the implications for public health practice?

To improve TPT effectiveness, public health strategies should integrate TPT into routine clinics, promote short-course regimens, and target high-risk groups (e.g., immunocompromised individuals and the elderly) to increase acceptance rates and reduce disparities to achieve TB elimination.

ABSTRACT

Introduction: Tuberculosis preventive treatment (TPT) is pivotal in preventing the progression of latent tuberculosis infection (LTBI) to active tuberculosis (ATB). However, systematic, national data on TPT implementation in China are scarce. We characterized the scale-up of the TPT between 2022 and 2025, and identified the factors associated with its acceptance and completion.

Methods: This preplanned cross-sectional study utilized two levels of national TPT surveillance [31 provincial-level administrative divisions (PLADs), 2022–2025] and 2,676 individuals with LTBI (five PLADs, 2023–2024). The analyses included descriptive statistics and Firth-penalized logistic regression (R 4.3.1).

Results: The number of TPT recipients increased 2.5-fold (37,514–92,331) with approximately 79% short-course regimen use. The acceptance and completion rates were 45.14% and 85.18%, respectively. Higher acceptance was observed in individuals aged 15–44 years [odds ratio (*OR*)=0.648, 95% confidence interval (*CI*): 0.469, 0.896], ethnic minorities (*OR*=5.045, 95% *CI*: 1.910, 16.914), healthcare workers (*OR*=82.029, 95% *CI*: 16.422, 822.390), and designated hospitals (*OR*=3.620, 95% *CI*: 2.507, 5.281). It was lower in immunocompromised individuals (*OR*=0.409, 95% *CI*: 0.219, 0.749) and those with moderate PPD positivity (*OR*=0.384, 95% *CI*: 0.275, 0.533).

Conclusions: China has progressed in scaling up the TPT; however, low acceptance and subgroup disparities persist. Integrating TPT into routine clinical practice, prioritizing short-course regimens, and targeting high-risk groups are critical for TB elimination.

Tuberculosis (TB) remains a major global public health challenge, with 10.7 million new cases reported worldwide in 2024. China accounts for 6.5% of global cases (ranking fourth globally) (*1*), bearing a substantial TB burden. Latent tuberculosis infection (LTBI) refers to a persistent immune response to *Mycobacterium tuberculosis* antigens without clinical, bacteriological, or radiological evidence of active TB. As a vast reservoir for future TB cases, 5%–10% of individuals with LTBI develop active TB during their lifetime, severely hindering the global aim of ending the TB epidemic (*2*). The LTBI rates in China are 18.1% in individuals aged ≥5 years and 20.3% in those aged ≥15 years, indicating a considerable potential risk of active TB transmission. In the absence of an effective adult TB vaccine, tuberculosis preventive treatment (TPT) has emerged as a cornerstone intervention to block the progression of LTBI to active

disease, making it indispensable for reducing TB incidence and advancing the elimination of the TB epidemic (*3*). Recognizing its critical significance, China has integrated TPT into its national TB control strategies and has successively issued key policies, including the TB Prevention and Control Management Guidelines (*4*) and the National TB Prevention and Control Plan (2024–2030) (*5*), which explicitly designate TPT as a core indicator of TB prevention efforts. However, despite these clear policy commitments, there remains a critical gap in national-level systematic data on TPT implementation, including coverage, adherence, and factors influencing its effectiveness. Moreover, both global and national TPT implementations face major challenges, such as low acceptance and completion rates, further limiting their effectiveness in TB control. This knowledge deficit not only restricts the ability to assess whether the TPT is meeting its intended public health goals but also hinders the optimization of strategies to achieve a broader impact. To address this gap, we analyzed the national TPT data from 2022 to 2025 to characterize the current implementation status, identify barriers in the care cascade, and explore the key influencing factors. The findings of this study provide evidence-based insights to refine China's TPT policies and accelerate progress toward ending the TB epidemic.

This preplanned cross-sectional study used two-level data. Nationally, the TPT progress was analyzed using the 2022–2025 data for 31 provincial-level administrative divisions (PLADs) obtained from the Chinese Disease Control and Prevention Information System. Provincially, to identify factors influencing TPT acceptance, the Centers for Disease Control and Prevention (CDC) designated hospitals and health centers in five PLADs (Jiangsu, Henan, Shaanxi, Yunnan, and Xinjiang Uygur Autonomous Region) were selected via convenience sampling based on the implementation feasibility. Anonymized data were extracted using structured forms from routinely registered individuals with LTBI documented between 2023 and 2024. All eligible individuals recorded during the study period were included. The investigators were trained by public health staff from the participating institutions to ensure standardized procedures and consistent variable definitions. Quality control measures included supervisory reviews and data verification to ensure completeness and logical consistency across PLADs. Statistical analyses were performed using R (Version 4.4.3, Vienna, Austria, https://www.r-project.org/). Descriptive statistics summarized the national TPT progress. Associations with TPT acceptance were evaluated using univariate and multivariate Firth-penalized logistic regressions. Bidirectional stepwise selection (α =0.05 for entry and removal) was used to determine the final model. As a sensitivity analysis, multilevel logistic regression, with PLAD specified as a random intercept, was conducted to account for potential regional clustering.

The number of national TPT recipients increased steadily from 37,514 in 2022 to 92,331 in 2025, with students who have been in close contact with TB patients being the largest group across all years (21,654 in 2022 to 34,616 in 2025). In addition, close contacts with patients having bacteriologically positive TB also reported a sharp increase (7,683 in 2022 to 28,854 in 2025). Short-course regimens were the main TPT strategies, with utilization rates of 79.2% (29,725/37,514) in 2022, 78.8% (41,639/52,836) in 2023, 76.5% (66,555/87,034) in 2024, and 79.6% (73,517/92,331) in 2025, which remained consistently high throughout the study period (Figure 1).

In total, 2,676 individuals with LTBI were included in the survey. The overall acceptance rate of the TPT was 45.14% (1,208/2,676). Among those who initiated TPT, 85.18% (1,029/1,208) completed the full course (Table 1).

Multivariate logistic regression analysis identified several factors that were significantly associated with TPT acceptance. Key factors included age [15–44 *vs.* 0–14: odds ratio (*OR*)=0.648, 95% confidence interval (*CI*): 0.469, 0.896, *P*=0.009]; ethnicity (other ethnic groups vs. Han: *OR*=5.045, 95% *CI*: 1.910, 16.914, *P*<0.001); PLAD (e.g., Jiangsu *vs.* Henan: *OR*=31.499, 95% *CI*: 15.320, 68.720, *P*<0.001; Xinjiang *vs.* Henan: *OR*=8.610, 95% *CI*: 2.353, 26.462, *P*=0.002); education level (senior high school *vs.* junior school and below: *OR*=0.721, 95% *CI*: 0.527, 0.986, *P*=0.041); population classification (HIV/AIDS/immunocompromised *vs.* densely populated place population: *OR*=0.409, 95% *CI*: 0.219, 0.749, *P*=0.004; healthcare workers vs. densely populated place population: *OR*=82.029, 95% *CI*: 16.422, 822.390, *P*<0.001); TPT-providing institution (designated hospital *vs.* CDC: *OR*=3.620, 95% *CI*: 2.507, 5.281, *P*<0.001); and infection test result (PPD moderate positive *vs.* PPD strong positive: *OR*=0.384, 95% *CI*: 0.275, 0.533, *P*<0.001) (Table 2). Completion rates varied considerably across subgroups, being notably low for healthcare workers (41.67%) and those on immunotherapy regimens (51.21%) but high for ethnic minorities (91.51%) and the elderly (90.64%). The random-intercept variance for the PLADs was 1.93, suggesting moderate between-provincial heterogeneity. However, the fixed-effect

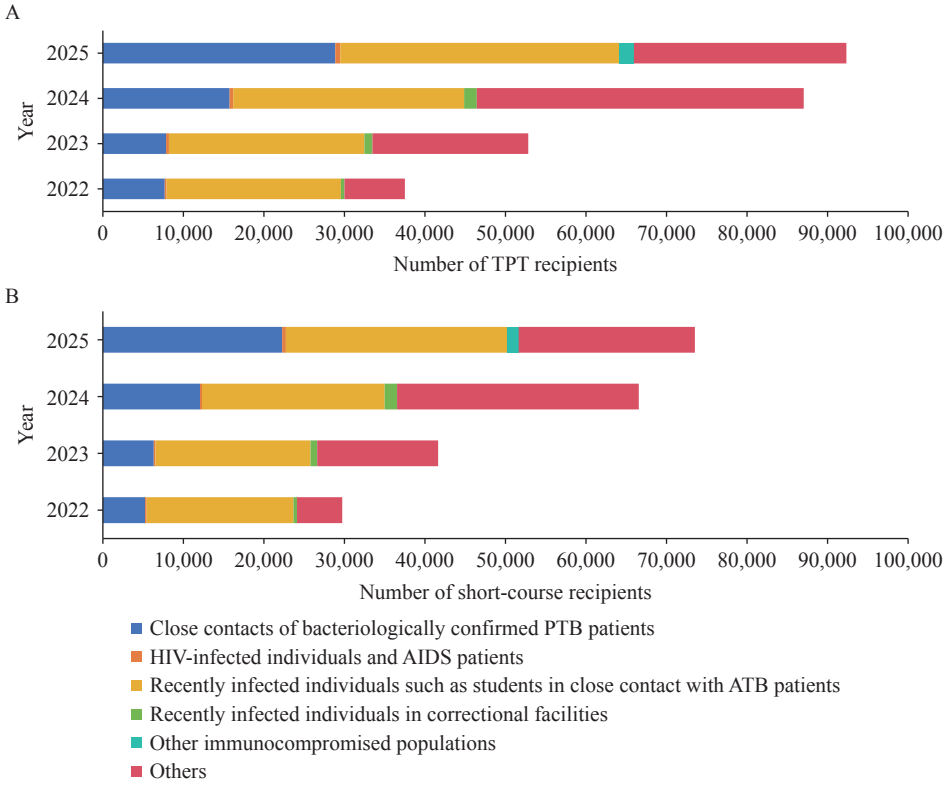

FIGURE 1. TPT implementation and scale-up in China from 2022 to 2025. (A) Individuals on TPT; (B) Individuals on shorter regimens.
Abbreviation: PTB=pulmonary tuberculosis; HIV=human immunodeficiency virus; AIDS=acquired immunodeficiency syndrome; ATB=active tuberculosis; TPT=tuberculosis preventive treatment.

estimates were not materially altered (Supplementary Table S1, available at https://weekly.chinacdc.cn).

DISCUSSION

LTBI affects nearly one-quarter of the global population, forming the largest reservoir of ATB and hindering its global elimination (*6*). TPT effectively halts LTBI progression to ATB (*7*); however, its global implementation is compromised by low acceptance and completion rates (*8*). We addressed the evidence gap by investigating TPT uptake, completion, and associated factors among individuals with LTBI in China to identify optimized national prevention strategies.

We demonstrated that China's TPT scale-up achieved remarkable progress during 2022–2025, with a 2.5-fold increase in recipients and consistently high utilization (around 79%) of WHO-recommended short-course regimens, validating the effectiveness of national TB control policies. Although the post-acceptance completion rate (85.18%) indicated good adherence, the overall acceptance rate (45.14%) was a critical bottleneck, with stark disparities across subgroups: acceptance was extremely low in adults ≥60 years, individuals living with HIV/AIDS (PLHIV), immunocompromised individuals and Shaanxi residents, but high in healthcare workers, ethnic minorities, and Jiangsu/Xinjiang residents. Grassroots institutions (designated TB hospitals and community health centers) outperformed CDCs in TPT delivery, underscoring the value of routine clinical settings for preventive care. Therefore, policies must shift the focus from merely promoting completion to actively facilitating acceptance. Our data strongly advocate for the integration of TPT services into designated hospitals and health centers, which are associated with four-fold and two-fold higher odds of acceptance, respectively, compared to CDC facilities. This suggests a policy shift toward not "mainstreaming" TPT into routine clinical care settings where patients already seek services, potentially improving the accessibility and perceived legitimacy of treatment (*9*). Secondly, the superior completion rate of the $3H_2P_2$ regimen (90.93%) supports the urgent need for national programs to prioritize the procurement and rollout of shorter, patient-friendly regimens to improve overall

TABLE 1. TPT acceptance and completion rates among individuals with LTBI by demographic and clinical characteristics, China, 2023–2024.

Variable	Total (*n*)	TPT acceptance [*n*/(%)]		TPT completion [*n*/(%)]	
Total	2,676	1,208	45.14	1,029	85.18
Age (years)					
0–14	453	215	47.46	193	89.77
15–44	1,416	599	42.30	491	81.97
45–59	273	191	69.96	161	84.29
≥60	534	203	38.01	184	90.64
Gender					
Male	1,343	587	43.71	512	87.22
Female	1,333	621	46.59	517	83.25
Ethnicity					
Han	2,179	784	35.98	641	81.76
Other ethnic groups	497	424	85.31	388	91.51
PLAD					
Henan	1,038	143	13.78	105	73.43
Jiangsu	387	304	78.55	253	83.22
Shanxi	207	14	6.76	2	14.29
Xinjiang Uygur Autonomous Region	460	387	84.13	354	91.47
Yunnan	584	360	61.64	315	87.50
Education level					
Junior school and below	1,292	692	53.56	617	89.16
Senior high school	1,066	294	27.58	247	84.01
College and above	318	222	69.81	165	74.32
Population classification					
HIV/AIDS and other immunocompromised	402	76	18.91	66	86.84
Household close contacts of TB patients	568	448	78.87	385	85.94
Densely populated place population	1,646	635	38.58	545	85.83
Healthcare workers	25	24	96.00	10	41.67
Other	35	25	71.43	23	92.00
TPT-providing institution					
CDC	297	63	21.21	41	65.08
Designated hospital	1,948	962	49.38	837	87.01
Health center	431	183	42.46	151	82.51
Infection test result					
PPD strong positive	1,479	811	54.83	713	87.92
PPD moderate positive	675	96	14.22	85	88.54
TBST positive	438	229	52.28	177	77.29
IGRA positive	84	72	85.71	54	75.00
TPT regimen					
6-9H	–	46	–	39	84.78
$3H_2P_2$	–	474	–	431	90.93
3HR	–	529	–	453	85.63
Immunotherapy	–	207	–	106	51.21

Note: "–" means data not available.
Abbreviation: TPT=tuberculosis preventive treatment; LTBI=latent tuberculosis infection; PLAD=provincial-level administrative division; HIV=human immunodeficiency virus; AIDS=acquired immunodeficiency syndrome; TB=tuberculosis; CDC=Centers for Disease Control and Prevention; PPD=purified protein derivative; TBST=tuberculosis skin test; IGRA=interferon-gamma release assay; H=isoniazid; P=rifapentine; R=rifampicin; Ref.=reference group; 6-9H=a 6-month or 9-month regimen of daily isoniazid monotherapy, H 5 mg/kg (max 300 mg) daily; $3H_2P_2$=a 3-month regimen of twice-weekly isoniazid plus rifapentine, ≥50 kg: H 600 mg and P 600 mg twice weekly, <50 kg: H 500 mg and P 450 mg twice weekly; 3HR=a 3-month regimen of weekly isoniazid plus rifampicin, ≥50 kg: H 300 mg and P 600 mg twice weekly, <50 kg: H 300 mg and P 450 mg daily; Immunotherapy=a 3-month immunotherapy regimen consisting of *Mycobacterium bovis* vaccine administered once every 2 weeks.

TABLE 2. Univariate and multivariable logistic regression analyses of factors associated with TPT acceptance among individuals with LTBI, China, 2023–2024.

Variable	Univariate analysis		Multivariate analysis	
	P	*OR* (95% *CI*)	*P*	*OR* (95% *CI*)
Age (years)				
0–14	Ref.		Ref.	
15–44	0.054	0.812 (0.656, 1.004)	0.009	0.648 (0.469, 0.896)
45–59	<0.001	2.569 (1.876, 3.539)	0.136	0.695 (0.432, 1.122)
≥60	0.003	0.679 (0.527, 0.875)	0.254	0.735 (0.435, 1.250)
Gender				
Male	Ref.		Ref.	
Female	0.135	1.123 (0.965, 1.308)	0.388	1.096 (0.890, 1.350)
Ethnicity				
Han	Ref.		Ref.	
Other ethnic groups	<0.001	10.274 (7.949, 13.450)	<0.001	5.045 (1.910, 16.914)
PLAD				
Henan	Ref.		Ref.	
Jiangsu	<0.001	22.757 (16.948, 30.861)	<0.001	31.499 (15.320, 68.720)
Shaanxi	0.004	0.468 (0.256, 0.794)	0.470	0.726 (0.301, 1.723)
Xinjiang Uygur Autonomous Region	<0.001	32.900 (24.382, 44.927)	0.002	8.610 (2.353, 26.462)
Yunnan	<0.001	10.021 (7.881, 12.804)	<0.001	6.198 (4.363, 8.869)
Education level				
Junior school and below	Ref.		Ref.	
Senior high school	<0.001	0.331 (0.278, 0.393)	0.041	0.721 (0.527, 0.986)
College and above	<0.001	1.999 (1.542, 2.609)	0.208	0.787 (0.542, 1.142)
Population classification				
HIV/AIDS and other immunocompromised	<0.001	0.373 (0.284, 0.485)	0.004	0.409 (0.219, 0.749)
Household close contacts of TB patients	<0.001	5.924 (4.749, 7.438)	0.002	0.454 (0.275, 0.744)
Densely populated place population	Ref.		Ref.	
Healthcare workers	<0.001	25.997 (6.752, 233.246)	<0.001	82.029 (16.422, 822.390)
Other	<0.001	3.865 (1.924, 8.342)	0.014	0.260 (0.097, 0.752)
TPT-providing institution				
CDC	Ref.		Ref.	
Designated hospital	<0.001	3.603 (2.710, 4.855)	<0.001	3.620 (2.507, 5.281)
Health center	<0.001	2.727 (1.956, 3.838)	0.064	1.892 (0.963, 3.664)
Infection test result				
PPD strong positive	Ref.		Ref.	
PPD moderate positive	<0.001	0.137 (0.108, 0.173)	<0.001	0.384 (0.275, 0.533)
TBST positive	0.347	0.902 (0.729, 1.117)	0.734	0.901 (0.485, 1.626)
IGRA positive	<0.001	4.778 (2.695, 9.205)	0.514	1.363 (0.539, 3.506)

Abbreviation: TPT=tuberculosis preventive treatment; LTBI=latent tuberculosis infection; PLAD=provincial-level administrative division; HIV=human immunodeficiency virus; AIDS=acquired immunodeficiency syndrome; TB=tuberculosis; PPD=purified protein derivative; TBST=tuberculosis skin test; IGRA=interferon-gamma release assay; *OR*=odds ratio; *CI*=confidence interval; Ref.=reference group.

program effectiveness (*10*). Third, identified risk groups, such as immunocompromised individuals and residents of low-performing PLADs, require tailored proactive outreach strategies. For example, seamlessly integrating TPT acceptance into HIV care clinics and implementing performance-based financing for TPT in

lagging regions could be effective measures derived from our evidence.

The findings in this report are subject to at least two limitations. First, the survey on TPT influencing factors used convenience sampling, selecting PLADs/counties with active screening and complete data, which may have led to selection bias and limited the generalizability of the results to the whole country. Second, the surveillance data did not include detailed information on TPT follow-up and adverse reactions, which may be crucial factors influencing TPT completion, and were not analyzed in this study.

To optimize China's TPT strategy and effectiveness, targeted recommendations based on study findings include prioritizing TPT for high-risk groups, such as student close contacts and bacteriologically positive TB patient contacts. In addition, personalized measures (simplified screening, free drugs, and regular follow-ups) should be used for the elderly (≥60 years), HIV-infected, and immunocompromised individuals to improve acceptance. Optimizing grassroots services involves shifting TPT from CDCs to designated hospitals and community/township health centers; training grassroots staff on TPT screening, regimen selection, and adverse reactions; and establishing standardized processes to improve accessibility and quality. Standardizing short-course regimens and expanding coverage require maintaining high utilization of 3HR/$3H_2P_2$ through regular safety and effectiveness evaluations, resuming standardized TPT for detainees, and expanding coverage for immunocompromised groups via standardized protocols. Establishing a comprehensive TPT cascade system involves integrating LTBI screening, TPT acceptance, adherence, and follow-up into the national TB surveillance to track cascade losses and promptly address implementation barriers. Finally, promoting regional balance includes increasing financial and technical support for low-acceptance central/western regions (e.g., Shaanxi), establishing cross-regional platforms for experience sharing, and narrowing implementation disparities.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIAL

To account for potential regional clustering, a multilevel logistic regression model with province specified as a random intercept was used for the sensitivity analysis. Fixed-effects estimates are presented as odds ratios (*OR*s) with 95% confidence intervals (*CI*s).

The random-intercept variance for the province was 1.93 (standard deviation=1.39), indicating moderate between-province heterogeneity. The model did not exhibit a singular fit (isSingular=FALSE), suggesting a stable estimation of the random effects.

Provincial-specific random intercept estimates are shown below: 1) PLAD 2: −1.38, 2) PLAD 3: 2.06, 3) PLAD 4: −1.66, 4) PLAD 6: 0.56, 5) PLAD 7: 0.44.

These findings indicate variability in the baseline TPT initiation probability across PLADs; however, the fixed-effects estimates remained directionally consistent with the primary Firth-penalized logistic regression analysis.

SUPPLEMENTARY TABLE S1. Multilevel logistic regression analysis of factors associated with TPT initiation.

Variable	Multilevel logistic regression analysis	
	P	***OR* (95% *CI*)**
Age (years)		
0–14	Ref.	
15–44	0.010	0.653 (0.472, 0.903)
45–59	0.145	0.700 (0.434, 1.131)
≥60	0.265	0.740 (0.435, 1.257)
Gender		
Male	Ref.	
Female	0.387	1.096 (0.890, 1.351)
Ethnicity		
Han	Ref.	
Other ethnic groups	0.001	6.205 (2.086, 18.457)
Education level		
Junior school and below	Ref.	
Senior high school	0.034	0.712 (0.520, 0.975)
College and above	0.220	0.791 (0.544, 1.150)
Population classification		
HIV/AIDS and other immunocompromised	0.003	0.398 (0.216, 0.737)
Household close contacts of patients with TB	0.002	0.464 (0.282, 0.763)
Densely populated place population	Ref.	
Healthcare workers	0.000	117.768 (13.496, 1,027.662)
Other	0.014	0.275 (0.098, 0.770)
TPT-providing institution		
CDC	Ref.	
Designated hospital	<0.001	3.711 (2.552, 5.397)
Health center	0.061	1.883 (0.971, 3.650)
Infection test result		
PPD strong positive	Ref.	
PPD moderate positive	<0.001	0.378 (0.271, 0.526)
TBST positive	0.764	0.913 (0.505, 1.652)
IGRA positive	0.427	1.460 (0.574, 3.710)

Abbreviation: TPT=tuberculosis preventive treatment; HIV=human immunodeficiency virus; AIDS=acquired immunodeficiency syndrome; TB=tuberculosis; CDC=Centers for Disease Control and Prevention; PPD=purified protein derivative; TBST=tuberculosis skin test; IGRA=interferon-gamma release assay; *OR*=odds ratio; 95% *CI*=95% confidence interval; Ref.=reference group.

Preplanned Studies

Drug Resistance and Risk Factors of Bacteriologically Confirmed Tuberculosis Cases in 10 Sites — Hunan Province, China, 2018–2025

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Summary

What is already known about this topic?

Tuberculosis (TB) is a deadly global infectious disease, and China has a high burden of rifampicin-resistant (RR) and multidrug-resistant (MDR) TB, according to the World Health Organization. Prior treatment, Regional disparities, demographics (age/sex), and comorbidities (e.g., diabetes) are associated with an elevated risk of drug-resistant TB.

What is added by this report?

We analyzed 25,978 bacteriologically confirmed pulmonary TB (PTB) cases in 10 sites in Hunan Province and found lower first-line drug resistance rates than national/provincial estimates (2018–2025). Retreatment, age 25–44 years, diabetes, and Lengshuitan residence were independent predictors of resistance. Resistance declined during the pandemic, rebounded slightly thereafter, and displayed a 4.0% annual decrease (statistically significant). There was notable inter-county heterogeneity (intraclass correlation coefficient=0.11). Hunan shifted to molecular testing (82.79% of susceptibility tests in 2021–2025).

What are the implications for public health practice?

Surveillance should be intensified for groups at high risk of drug-resistant TB, including retreatment patients, those aged 25–44 years, patients with diabetes and TB, and Lengshuitan residents. A scale-up of molecular diagnostic technologies and increased testing panels to cover isoniazid resistance for accurate resistance assessment should be included. Post-pandemic TB control interventions should continue to optimize the quality of routine surveillance data, and in-depth research on non-laboratory factors that lead to regional disparities in drug resistance rates should be performed.

ABSTRACT

Introduction: Drug-resistant tuberculosis (TB) poses a significant threat to public health. This study aimed to analyze the drug resistance patterns of *Mycobacterium tuberculosis* (MTB) and its risk factors in 10 districts of Hunan Province from 2018–2025. The study provides a reference for formulating strategies to prevent and control drug-resistant TB.

Methods: Isolates were collected from patients with pulmonary TB between January 2018 and December 2025 at 10 surveillance sites in Hunan Province. Drug resistance profiles were determined for two anti-TB drugs, rifampicin (RIF) and isoniazid (INH). Statistical analyses of epidemiological characteristics and risk factors for drug resistance were performed.

Results: Among the 25,978 MTB isolates tested, 1,320 (5.08%) strains were resistant to one or more anti-TB drugs. The prevalence of rifampicin-resistant (RR) and multidrug-resistant (MDR) TB was 553 (2.13%) and 310 (1.19%), respectively. Univariate analysis revealed that sex, age, occupation, patient source, prior treatment history, comorbidities, residential district, and time of diagnosis were significantly associated with overall TB drug resistance (all $P<0.05$). RR-TB was significantly associated with all variables except occupation (all $P<0.05$). Multivariate logistic regression revealed the following independent predictors of drug resistance: male sex, retreatment status, age 25–44 years, diabetes mellitus, and residence in Lengshuitan.

Conclusion: The results demonstrated the factors that indicated a significant risk of MDR-TB. Therefore, intensifying MDR-TB surveillance to develop treatment and monitoring guidelines is urgently needed.

Tuberculosis (TB), a chronic infectious disease caused by *Mycobacterium tuberculosis* (MTB), is primarily treated with anti-TB drugs. According to a 2025 report from the World Health Organization (*1*), TB remains one of the deadliest infectious diseases worldwide, causing over 1.2 million deaths and infecting 10.7 million people in 2024. China ranks fourth in estimated TB incidence among the top 30 high-burden TB countries, with approximately 28,000 new patients diagnosed with multidrug-resistant (MDR)- and rifampicin-resistant (RR)-TB annually. The MDR/RR rate was 3.2% in newly diagnosed patients and 16.0% in retreated patients. Rifampicin (RIF) is a first-line drug; once resistance occurs, treatment is adjusted to a complex second-line anti-TB drug regimen (*2*). The transmission of MDR-TB strains plays a significant role in the burden of MDR-TB in China (*3*). To understand the characteristics and risk factors of patients with MDR/RR-TB, we used partial research data from the National Science and Technology Major Project for the 13th Five-Year Plan to analyze the RR-TB status and risk factors of patients with bacteriologically positive pulmonary TB (PTB) in Hunan Province.

We adopted a multi-stage stratified cluster random sampling method to select ten counties across three cities in Hunan and included patients with bacteriologically confirmed PTB. The inclusion criteria were: 1) diagnosis between January 1, 2018, and December 31, 2025; 2) sputum smear-positive and/or mycobacterial culture-positive with the cultured strain identified as MTB complex and/or molecular biology-positive samples; and 3) signed informed consent forms and cooperation with the study.

Data of 30,505 patients with etiologically positive PTB between 2018−2025 were obtained from the China Disease Prevention and Control Information System. This included demographic (sex, age, ethnicity, occupation, and household registration), diagnosis, and treatment information (patient source, treatment category, comorbidities, area of residence, and time of diagnosis). A total of 4,527 cases tested positive using only sputum smear acid-fast staining but did not yield successful MTB isolation or nucleic acid amplification test confirmation. Hence, we enrolled 25,978 etiologically confirmed cases, defined as those with positive sputum smear acid-fast staining and MTB culture or nucleic acid amplification test results. The molecular biological method was an Xpert MTB/RIF assay for the detection of MTB and RR genes.

All analyses were performed using WPS Office software (WPS Software, Singapore) and SPSS (version 20.0, IBM Corp., Armonk, NY, USA). Count data were expressed as the composition ratio or rate (%) and measurement data as ($\bar{x}\pm s$). Inter-group differences were compared using χ^2 tests and multivariate analysis using binary logistic regression analyses. All the tests were two-sided. Statistical significance was set at $P<0.05$.

Of the 25,978 patients with pathogen-confirmed PTB included in the analysis, 1,320 (5.08%) exhibited resistance to at least one first-line anti-TB drug. Between 2018−2020, molecular assays accounted for most tests (69.05%), whereas phenotypic methods accounted for 30.95%. From 2021 onwards, molecular testing became the predominant modality, and it comprised 82.79% of all tests during 2021–2025, while phenotypic testing declined to 17.21%.

Univariate analysis identified sex, age, occupation, patient source, history of prior treatment, comorbidities, district of residence, and time of diagnosis as statistically significant correlates of drug resistance (all $P<0.05$). No significant association was observed between ethnicity and drug resistance ($P>0.05$). A total of 553 patients (2.13%) were resistant to RIF. Univariate analysis revealed that sex, age, patient source, prior treatment history, comorbidities, residential district, and time of diagnosis were significantly associated with RR-TB (all $P<0.05$) but not ethnicity or occupation ($P>0.05$).

Multivariate logistic regression analysis (Table 1) identified the following independent predictors of anti-TB drug resistance: male sex [adjusted odds ratio (a*OR*)=0.842; 95% confidence interval (*CI*), 0.732, 0.969] and retreatment status (a*OR*=4.416; 95% *CI*: 3.794, 5.141); age 25–44 years (versus ≥65 years; a*OR*=1.329, 1.491; 95% *CI*: 1.168, 1.785), diabetes mellitus (a*OR*=1.486; 95% *CI*: 1.200, 1.842), and Lengshuitan residence (versus Qiyang City; a*OR*=1.603; 95% *CI*: 1.315, 1.956). In contrast, residence in other counties and cities (versus Qiyang City) was associated with a significantly lower risk (a*OR*=0.123–0.686; 95% *CI*: 0.093, 0.884). Additionally, a later diagnosis was protective against drug resistance (a*OR*=0.969 per unit increase; 95% *CI*: 0.943, 0.996).

Overall drug resistance was defined as resistance to at least one first-line anti-tuberculosis drug (INH and/or RIF). Model was adjusted for the testing method (molecular *vs*. phenotypic).

Figure 1 illustrates the spatiotemporal distribution of

TABLE 1. Multivariable logistic regression analysis of factors associated with rifampicin resistance among pathogen-positive PTB patients in 10 districts and counties, Hunan Province, China, 2018–2025.

Influencing factor	*β*	Wald χ^2	*P*	a*OR* (95% *CI*)
Sex	−0.172	5.785	0.016	0.842 (0.732–0.969)
Age (years)		27.894	<0.001	
<25	0.081	0.359	0.549	1.085 (0.831–1.415)
25–44	0.400	19.024	<0.001	1.491 (1.246–1.785)
45–64	0.284	18.766	<0.001	1.329 (1.168–1.511)
≥65 (reference)	–	–	–	1
Treatment classification	1.485	367.194	<0.001	4.416 (3.794–5.141)
Comorbidity		19.215	0.001	
Pneumoconiosis	0.166	0.414	0.520	1.181 (0.712–1.957)
Diabetes mellitus	0.396	13.149	<0.001	1.486 (1.200–1.842)
HIV/AIDS	0.718	3.139	0.076	2.051 (0.927–4.541)
Other comorbidities	−0.311	2.082	0.149	0.733 (0.481–1.118)
No comorbidity (reference)	–	–	–	1
Residence		573.868	<0.001	
Changning City	−1.942	154.705	<0.001	0.143 (0.106–0.195)
Hengnan County	−2.099	215.732	<0.001	0.123 (0.093–0.162)
Hengshan County	−0.767	30.878	<0.001	0.464 (0.354–0.609)
Hengyang County	−1.155	98.615	<0.001	0.315 (0.251–0.396)
Leiyang City	−1.092	110.288	<0.001	0.336 (0.274–0.411)
Lengshuitan District	0.472	21.700	<0.001	1.603 (1.315–1.956)
Liling City	−0.520	19.885	<0.001	0.595 (0.473–0.747)
Lingling District	−0.377	8.518	0.004	0.686 (0.533–0.884)
Qidong County	−0.827	63.271	<0.001	0.438 (0.357–0.536)
Qiyang City	–	–	–	1
Diagnosis time (per year increase)	−0.031	4.927	0.026	0.969 (0.943–0.996)
Constant (Intercept)	−3.662	503.824	<0.001	0.026

Note: "–" means the reference category (*OR*=1.000) in the logistic regression model. Reference categories: ≥65 years of age; no comorbidity; Qiyang City for residence.
Abbreviations: SE=standard error; a*OR*=adjusted odds ratio; *CI*=confidence interval.

RR-TB and MDR-TB across the 10 districts and counties from 2018 to 2025. Drug resistance exhibited geographically concentrated hotspots during 2018–2021, which diminished by 2025. RR-TB remained moderate throughout the study period, whereas that of MDR-TB persisted at a low level. Figure 1 Annual county-level resistance rates are expressed as percentages. The color scale represents the district-level resistance rate (%). Color scales were classified using equal interval grouping and kept consistent across years within each panel to ensure comparability.

We used a multilevel mixed-effects negative binomial regression model with a log link to analyze temporal trends in rifampicin-resistant tuberculosis (RR-TB) between 2018 and 2025, considering overdispersion and clustering at the county level.

If Y_{ik} denotes the number of RR-TB cases in the county during the year and n_{ik} denotes the corresponding number of tested cases, we assumed:

$$Y_{ik} \sim \text{Negative Binomial}(\mu_{ik}, \theta) \quad (1)$$

Where μ_{ik} is the expected count and θ is the dispersion parameter.

The model was as follows:

$$\log(\mu_{ik}) = \beta_0 + \beta_1 Year_k + \beta_2 Period_k + b_i + \log(n_{ik}) \quad (2)$$

Where:

β_0 is the fixed intercept.

β_1 represents the annual temporal trend.

β_2 represents the diagnostic period effect (2018–

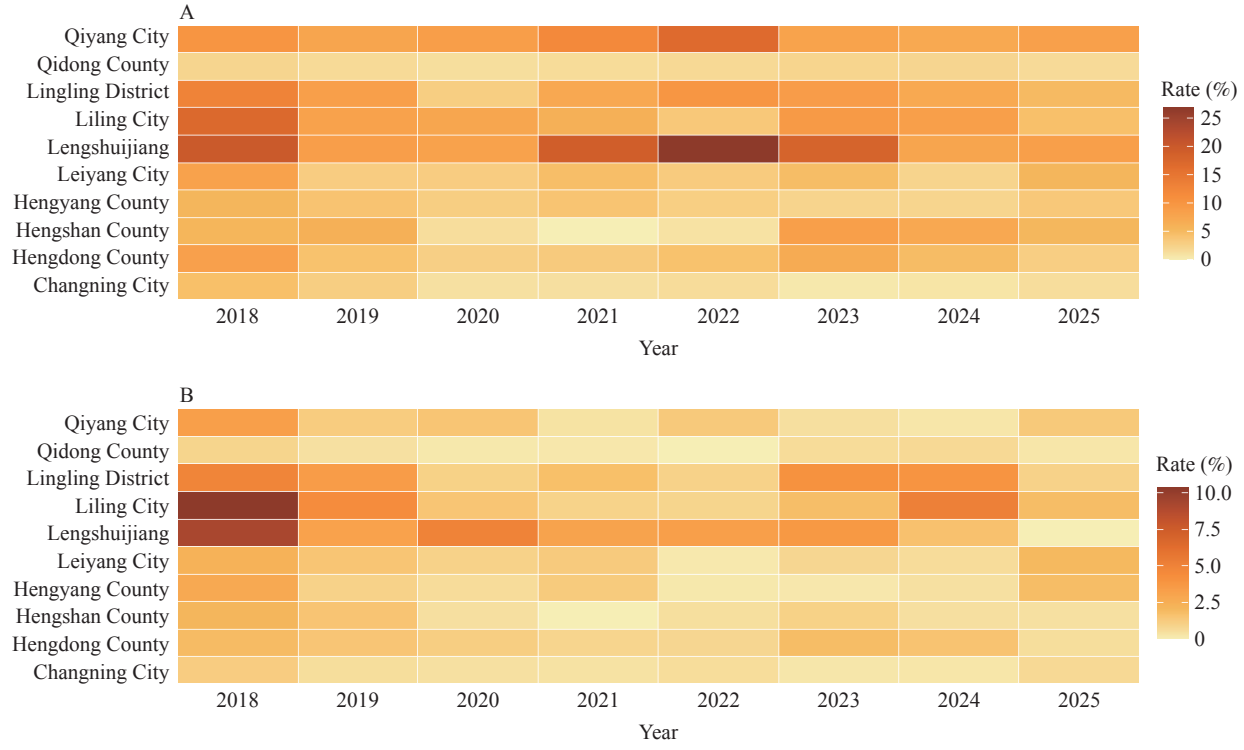

FIGURE 1. Spatial distribution of county-level (A) rifampicin-resistant tuberculosis and (B) multidrug-resistant tuberculosis rates in Hunan Province, China, 2018–2025.
Abbreviation: RR-TB=rifampicin-resistant tuberculosis; MDR-TB=multidrug-resistant tuberculosis.

2020 *vs*. 2021–2025).

$b_i \sim N(0,\sigma_b^2)$ denotes the county-level random intercept.

$\log(n_{ik})$ was included as an offset term.

County-specific deviations were estimated as best linear unbiased predictors (BLUPs).

After adjusting for testing volume and diagnostic period (2018–2020 *vs*. 2021–2025) to account for potential diagnostic shift bias, the multilevel negative binomial regression model showed a modest, though insignificant, annual decline in RR-TB rates (incidence rate ratio per year=0.97; 95% *CI*: 0.863–1.089). The values predicted by the model closely paralleled the observed annual rates (Figure 2A), capturing the initial fluctuation followed by a gradual downward trend over time. The shaded areas represent the 95% *CI* of the model-predicted estimates. Although a general downward trend was observed across most counties, country-specific projected trajectories — estimated using a multilevel model — revealed persistent and statistically significant heterogeneity throughout the study period (Figure 2B).

Sensitivity analyses (Figure 2C) comparing the negative binomial and Poisson regression models yielded highly consistent temporal patterns, supporting the robustness of the findings. The intraclass correlation coefficient (ICC) indicated a measurable proportion of total variability attributable to differences between counties, reflecting geographic heterogeneity in RR-TB risk. County-level random effects, expressed as BLUPs, further demonstrate significant spatial variation, with several counties exhibiting model-adjusted risks that were either significantly higher or lower than the overall mean (Figure 2D).

DISCUSSION

The results showed that the prevalence of resistance to first-line anti-TB drugs was 5.08% and the RR-TB rate was 2.13%, which was lower than previously reported studies (*4*–*5*). The drug resistance rate in Hunan declined from 7.78% in 2018 to 3.48% in 2020. This is attributable to the restricted scope of molecular drug susceptibility tests (DSTs), the epidemiological impact of COVID-19, and associated provincial containment measures (*6*).

A modest rebound in anti-TB drug resistance was observed during the immediate post-pandemic period. This rate stabilized at 4.42% in 2024 and 4.60% in

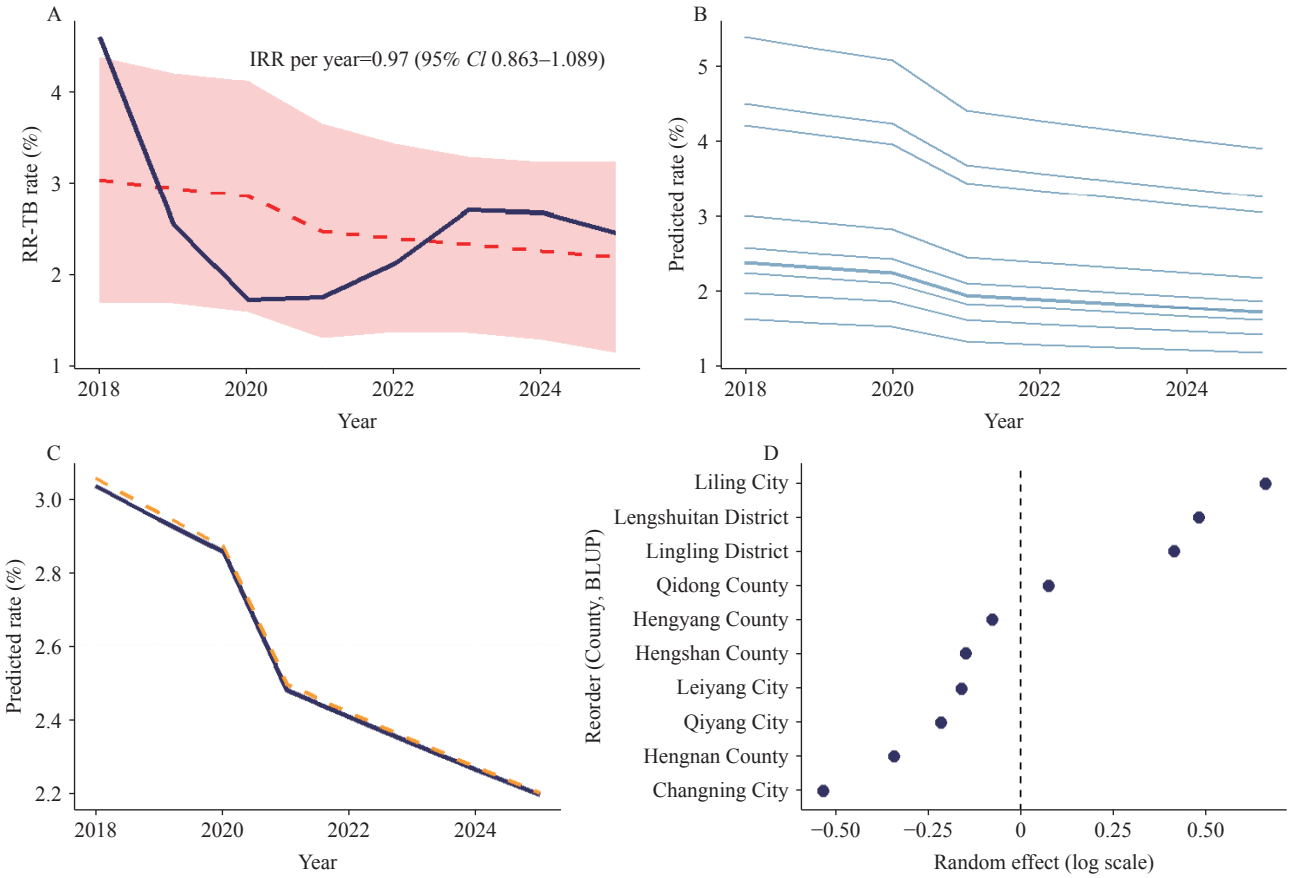

FIGURE 2. Multilevel negative binomial regression analysis of temporal trends in RR-TB rates, adjusted for diagnostic period, Hunan Province, China, 2018–2025.
Abbreviation: RR-TB=rifampicin-resistant tuberculosis.

2025. This trend coincided with the progressive implementation of intensified TB control interventions, including expanded comprehensive DSTs, standardized first- and second-line treatment regimens, enhanced surveillance among high-risk populations, and strengthened referral pathways, contributing to transmission reductions (*7*). Furthermore, molecular testing accounted for only 69.05% of DSTs during 2018–2020 but rose to 82.79% during 2021–2025 following a nationwide scale-up of rapid molecular assays, establishing it as the dominant DST modality. These findings indicate a deliberate, province-wide strategic transition toward rapid, molecular-based diagnostics to strengthen surveillance.

Univariate analysis identified that the independent risk factors significantly associated with drug resistance were retreatment status, middle age (25–64 years), diabetes mellitus, and geographic region, consistent with a previous study (*8*). Lengshuitan employed identical laboratory methodologies at all other study sites, including the same DST platform (proportional method combined with Xpert MTB/RIF), the same panel of first-line anti-TB drugs, and strictly standardized experimental procedures and interpretation criteria. These procedures were governed by a unified and centrally validated standard laboratory operating procedure. No methodological or procedural heterogeneity was found across the sites. The elevated resistance prevalence observed in Lengshuitan, despite methodological equivalence, suggests that non-laboratory factors may have caused this disparity, warranting detailed investigation. After adjusting for specimen testing volume, the annual incidence of drug resistance declined by 4.0%, with statistically consistent downward trends observed across all administrative regions. These results underscore the critical importance of adherence to standardized treatment regimens and implementing stratified, risk-informed clinical management, particularly for individuals with prior treatment histories, metabolic comorbidities, or residents in high-burden areas. Our results agree with recent provincial epidemiological studies linking intensified active surveillance, protocol-

driven clinical decision-making, and systematic quality assurance of diagnostic and therapeutic practices to reduce TB drug resistance in Hunan (*5*,*7*). The model-predicted trends aligned closely with the observed temporal patterns and demonstrated consistent downward trajectories across all districts.

Our findings demonstrate marked spatiotemporal heterogeneity in TB drug resistance across Hunan. The drug resistance rate declined during COVID-19, followed by a modest and temporary rebound during the immediate post-pandemic period and a sustained downward trajectory, consistent with reported global epidemiological patterns (*9*). RR-TB and MDR-TB levels remained consistently low and stable throughout the study period, reflecting the effectiveness of early case identification and prompt therapeutic initiation. Substantial inter-county variation was quantified using an intraclass correlation of 0.11, highlighting the need for geographically tailored and precise public health interventions in high-burden subregions. Interventions should prioritize comprehensive DSTs, integrated referral systems, and data-driven resource allocation. Policymakers should consider regional disparities, age, sex-related vulnerabilities, and dynamic sociodemographic changes (*10*).

Model diagnostics confirmed the suitability of the negative binomial regression framework in yielding statistically robust and policy-relevant estimates to guide evidence-based TB control strategies at the provincial level.

Strengthening patient adherence, intensifying drug resistance screening in vulnerable populations, and strengthening tuberculosis control interventions in high-burden areas are epidemiologically feasible and operationally critical. These measures can be effectively integrated into the existing national tuberculosis control framework by leveraging established infrastructure, cost-effectiveness, and scalability. Implementing these strategies requires coordinated collaboration across all levels of healthcare. From a public health perspective, such interventions facilitate the early detection and standardized management of drug-resistant TB, thereby reducing transmission among susceptible groups and in high-prevalence regions, and contributing to tangible progress in curbing drug-resistant TB.

Our study had several limitations. First, for some patients with etiologically confirmed TB, only smear results were available, which precluded further analysis of drug resistance. Second, the demographic and diagnostic data were derived from routine surveillance systems; hence, the analytical outcomes may have been affected by data entry quality and availability. Third, since 2021, with the widespread adoption of molecular biology testing methods, the proportion of facilities using these techniques increased significantly. However, owing to methodological constraints, these tests only assessed RIF resistance and did not include INH resistance, potentially leading to an underestimation of drug resistance rates.

Ethical statement: Approved by the Medical Ethics Committee of Hunan Institute for Tuberculosis Control (Hunan Chest Hospital). This study was approved in accordance with the 1975 Declaration of Helsinki and its later amendments, or comparable ethical standards. Written informed consent was obtained from all participants or their legal guardians.

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Outbreak Reports

An Imported Case of Dengue/Zika Coinfection — Sichuan Province, China, 2026

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Summary

What is already known about this topic?

Dengue virus (DENV) and Zika virus (ZIKV), primarily transmitted by *Aedes aegypti* and *Aedes albopictus*, belong to the Flaviviridae family. Their clinical presentations overlap considerably, including acute fever, nausea, rash, joint pain, and myalgia, making differential diagnosis challenging.

What is added by this report?

Because DENV and ZIKV share a common mosquito vector, their co-circulation increases the likelihood of dengue–Zika coinfection in both human and mosquito populations. This study documents the first laboratory-confirmed case of dengue/Zika coinfection in China. The patient presented with a fever on the day of entry.

What are the implications for public health practice?

This study provides a comprehensive epidemiological and phylogenetic analysis of a dengue/Zika coinfection case imported from Malaysia. Climate change and frequent cross-border travel are heightening the risk of imported mosquito-borne infectious diseases in China. International port cities must therefore strengthen surveillance and diagnostic testing for imported mosquito-borne diseases. For suspected febrile cases, clinicians should consider arbovirus coinfection based on travel history to prevent serious public health risks arising from missed diagnoses.

ABSTRACT

Introduction: On January 19, 2026, customs screening identified a foreign national arriving in Sichuan, China from Kuala Lumpur, Malaysia with an elevated body temperature. Subsequent testing yielded positive results for dengue virus (DENV) and Zika virus (ZIKV). Upon notification, local CDCs immediately launched a comprehensive epidemiological investigation, performed laboratory testing, and implemented preventive control measures.

Methods: Blood samples collected from the patient underwent quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR) for viral nucleic acid detection. Next-generation sequencing (NGS) was performed on serum samples to obtain complete viral genome sequences. Phylogenetic analysis was then conducted to determine the origin and genotype of the viruses in this imported case.

Results: The qRT-PCR analysis confirmed the simultaneous presence of DENV and ZIKV in the patient's serum. NGS successfully yielded the complete DENV and ZIKV genome sequences. Phylogenetic analysis revealed that the ZIKV belongs to the Asian lineage, sharing 99.48% nucleotide homology with a Thailand ZIKV strain (OR264645.1); the DENV was classified as clade 3I_A.1, sharing 99.10% nucleotide homology with a Singapore DENV strain (OP410996.1).

Conclusion: Based on the epidemiological history, clinical presentation, and laboratory results, the patient was confirmed as an imported dengue/Zika coinfection case. Phylogenetic analysis demonstrated that the ZIKV and DENV strains were most closely related to those from Thailand and Singapore, respectively.

On January 20, 2026, the Customs notified that a Malaysian national had tested positive for dengue virus (DENV) and Zika virus (ZIKV) during port quarantine. Municipal and District CDCs promptly initiated investigation, response, and laboratory testing. On January 20 and 21, Provincial and Municipal CDCs performed laboratory analyses on the collected blood samples, with both DENV and ZIKV nucleic acid tests returning positive results. On January 23, China CDC formally confirmed the patient's coinfection with DENV and ZIKV.

INVESTIGATION AND RESULTS

On January 19, 2026, a 35-year-old female Malaysian national arrived in Sichuan, China by flight from Kuala Lumpur, Malaysia. During Customs clearance, infrared temperature screening registered 37.0 ℃ (98.6 °F), and a subsequent axillary reading confirmed 37.2 °C (99.0 °F). Upon questioning by the Customs officer, she reported experiencing fever but denied rash, muscle pain, headache, conjunctival hyperemia, facial flushing, chest erythema, or neurological symptoms. The Customs collected a blood sample on-site and cleared her for passage. On January 24, she traveled by high-speed rail from Sichuan to Chongqing and flew back to Malaysia on the 25th.

The patient had been a long-term resident of Kuala Lumpur, Malaysia. Within the 14 days preceding fever onset, she denied any history of mosquito bites or blood transfusions and had not traveled to other countries or visited forested areas. Co-residing family members and colleagues reported no related symptoms. The patient traveled to China with 11 individuals from the same tour group, none of whom developed related symptoms.

On January 20, 2026, the Customs performed pathogen screening for vector-borne infectious diseases on the patient's blood samples. Results indicated positive findings for DENV and ZIKV, prompting immediate notification to the Municipal CDC. The same day, the Municipal CDC carried out parallel testing on the samples, detecting DENV-3 and ZIKV nucleic acids. On January 21, the Provincial CDC conducted confirmatory testing with consistent results. On January 23, China CDC confirmed the positive results, and on February 24, DENV and ZIKV particles were successfully isolated and serially passaged, confirming their infectivity.

On January 22, 2026, the Municipal CDC constructed sequencing libraries from serum samples using a commercial DENV whole-genome multiplex PCR kit (MicroFuture, Beijing, China), a ZIKV whole-genome multiplex PCR kit (Macro & Micro-test, Jiangsu, China), and the Nextera XT DNA Sample Preparation and Index kit (Illumina, San Diego, CA, USA). Sequencing was performed on the Illumina MiniSeq platform, and complete DENV and ZIKV genome sequences were assembled using CLC Workbench software (version 23.0, Qiagen, Düsseldorf, Germany). Phylogenetic analysis revealed that ZIKV belongs to the Asian lineage and is genetically linked to a ZIKV strain from Thailand (OR264645.1/Dec-2022) (Figure 1), sharing 99.48% nucleotide identity. The DENV was classified as clade 3I_A.1, closely related to a DENV strain from Singapore (OP410996.1/Nov-2019) (Figure 2) with 99.10% sequence similarity.

PUBLIC HEALTH RESPONSE

Upon receiving the screening results from the Customs, Municipal and District CDCs immediately initiated coordinated prevention and control measures. Given that the patient traveled through cities with temperatures ranging from 3 °C to 9 °C, and following an assessment of local mosquito vector density and transmission risk, timely health advisories were issued to the patient and her traveling companions. Additionally, clinical experts convened a consultation for the foreign patient, with health follow-up maintained until her departure.

DISCUSSION

DENV and ZIKV are closely related mosquito-borne flaviviruses that share similar transmission cycles, geographic distributions, and clinical manifestations (*1*). According to WHO statistics, approximately half of the world's population is now at risk of dengue (*2*), and while ZIKV cases declined globally from 2017 onward, transmission persists at low levels in several countries across the Americas, Asia, and Africa (*3*). Because they share a common vector, DENV and ZIKV endemicity may expand in concert, resulting in widespread co-circulation (*4*). To date, clinical studies have reported human dengue/Zika coinfections in countries such as Malaysia, Thailand, and Singapore (*5*–*7*).

In China, dengue fever cases were primarily imported during the early stages until the first local outbreak occurred in Foshan, Guangdong Province, in 1978. China's first imported ZIKV case was confirmed in Jiangxi Province in February 2016 (*8*). To date, all recorded ZIKV cases in China have been imported from endemic regions, including South America, Oceania, and Southeast Asia (*9*). However, no imported cases of DENV and ZIKV coinfection had been reported. On January 20, 2026, the Customs reported an individual testing positive for both DENV and ZIKV nucleic acids who had departed from Kuala Lumpur, Malaysia and arrived in Sichuan, China.

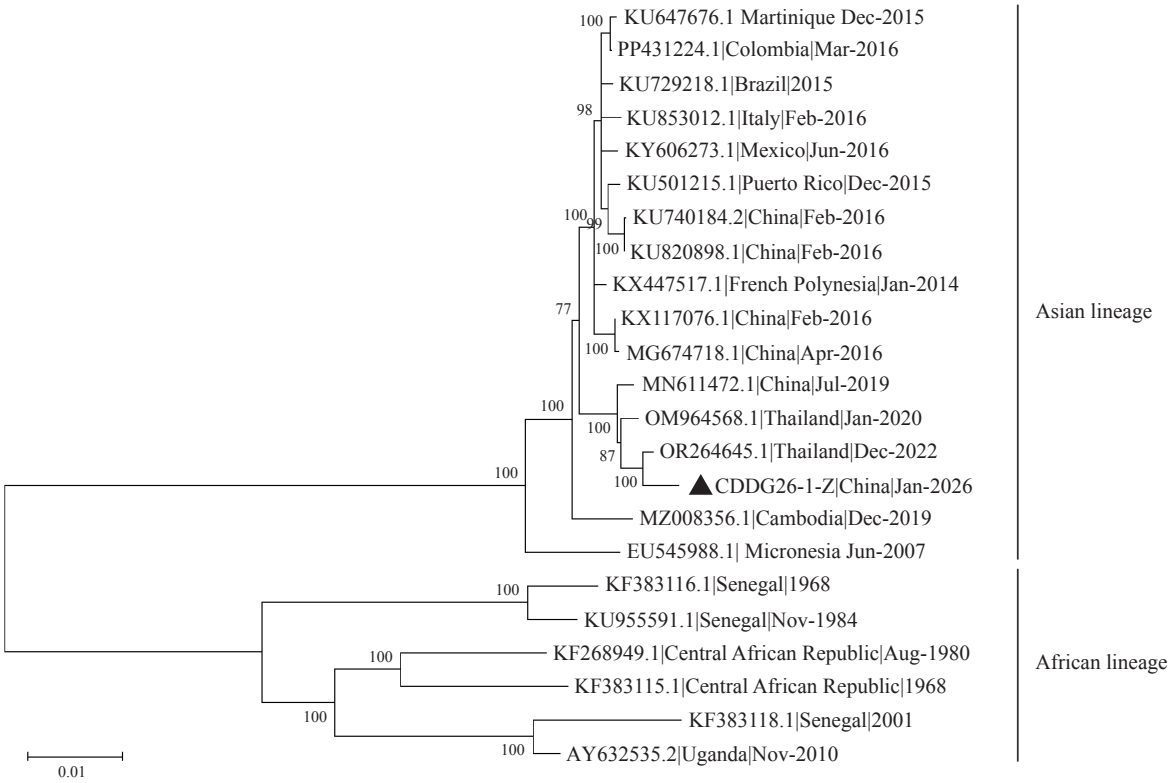

FIGURE 1. Phylogenetic analysis of CDDG26-1-Z|China|Jan-2026 ZIKV whole-genome sequences using the neighbor-joining method.
Note: ▲ CDDG26-1-Z|China|Jan-2026: ZIKV strain from the imported dengue/Zika coinfection case in China.
Abbreviation: ZIKV=Zika virus.

Following laboratory testing by Municipal and Provincial CDCs and subsequent verification by China CDC, the patient was confirmed as coinfected with both DENV and ZIKV, representing the first imported case of dengue/Zika coinfection in China. Given the patient's arrival during winter, with low ambient temperatures and minimal mosquito activity, the overall transmission risk was relatively low. However, the possibility of similar cases entering during high mosquito activity seasons or in warmer regions cannot be ruled out.

DENV and ZIKV are both single-stranded positive-sense RNA viruses with genomes of approximately 11,000 nucleotides, encoding three structural proteins and seven non-structural proteins. DENV is classified into four serotypes based on antigenic differences in the E protein. Among these, DENV serotype 3 comprises five genotypes (G-I, G-II, G-III, G-IV, and G-V). G-I predominates in Southeast Asian countries such as Malaysia, the Philippines, and Singapore (*10*). ZIKV is primarily divided into African and Asian genotypes; the Asian genotype has driven global epidemics and is closely associated with neurological complications, including neonatal microcephaly and Guillain-Barré syndrome (*11*). Phylogenetic analysis indicated that the DENV identified in this case belongs to the 3I_A.1 branch, exhibiting the highest homology with a Singapore strain (OP410996.1); ZIKV belongs to the Asian lineage and shares high homology with reference sequence OR264645.1, originating from Thailand. However, epidemiological investigation revealed no recent travel history to Thailand or Singapore, suggesting the potential existence of a hidden transmission chain.

Dengue/Zika coinfection cases predominantly present with mild symptoms similar to those of single infections, making differential diagnosis challenging (*12*). Currently, China's port-of-entry prevention and control measures for imported infectious diseases rely primarily on a "single-pathogen-targeted screening" model based on clinical symptoms and travel history, which carries a high risk of missed diagnoses and misclassification. This coinfection case underscores the need to shift port-of-entry prevention strategies toward "multi-disease co-detection and co-prevention." On the one hand, for suspected febrile cases, clinicians should consider arbovirus coinfection based on travel history, particularly for febrile individuals arriving

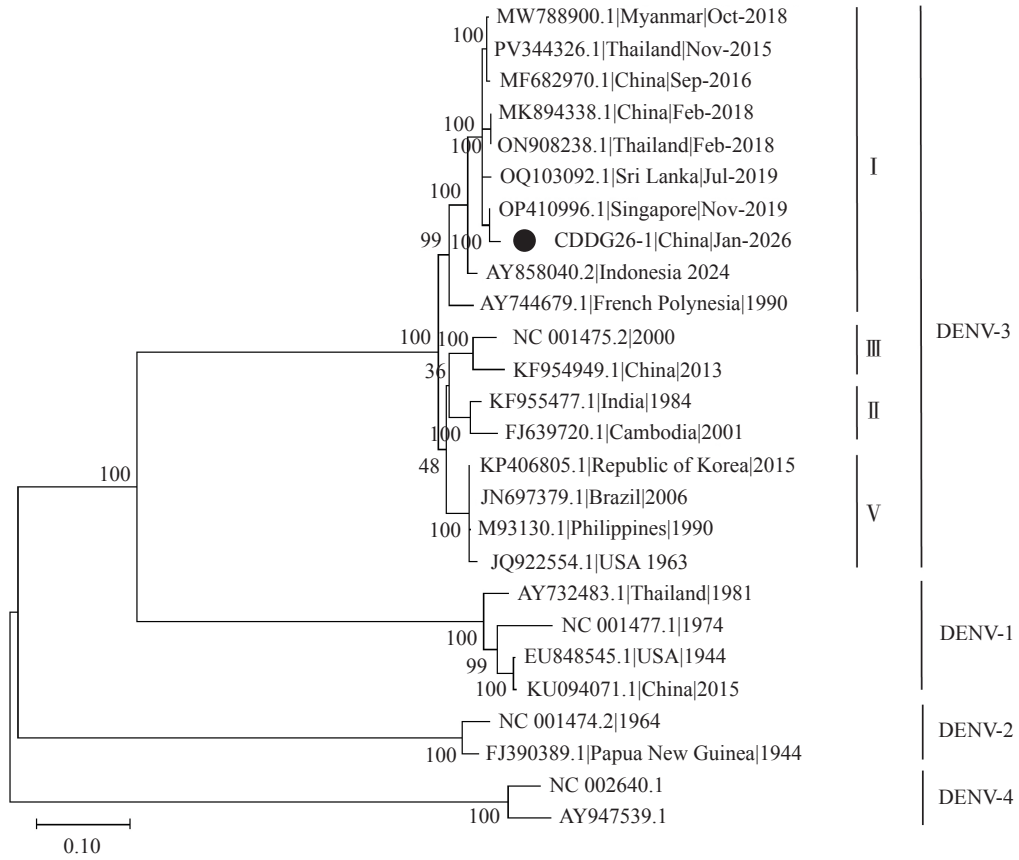

FIGURE 2. Phylogenetic analysis of CDDG26-1|China|Jan-2026 DENV whole-genome sequences using the neighbor-joining method.
Note: ● CDDG26-1|China|Jan-2026: DENV strain from the imported dengue/Zika coinfection case in China.
Abbreviation: DENV=dengue virus.

from regions endemic for multiple mosquito-borne diseases, to prevent serious public health risks from missed diagnoses. On the other hand, domestic efforts should prioritize developing commercial multiplex nucleic acid assay kits capable of simultaneously detecting key pathogens, including DENV, ZIKV, Chikungunya virus, yellow fever virus, Rift Valley fever virus, West Nile virus, Japanese encephalitis virus, and *Plasmodium*. Such a "single-sample, comprehensive screening" approach would enable source-level interruption of importation and transmission risks at points of entry. Furthermore, substantial evidence indicates that simultaneous arbovirus coinfection within mosquitoes may promote co-circulation and trigger disease outbreaks (*13*). Consequently, enhanced vector surveillance and control efforts are essential, alongside intensified health education campaigns to raise public awareness and ensure adherence to personal protective measures.

With global warming, accelerated urbanization, economic globalization, and increasingly frequent cross-regional travel, the prevention and control of imported vector-borne infectious diseases remains an urgent priority. The successful management of this case demonstrated highly effective collaboration among health authorities, disease control agencies, and customs departments, enabling timely detection of the imported dengue/Zika coinfection case and successful prevention of further spread. This experience highlights the need for a routine multi-departmental collaboration mechanism to facilitate real-time data sharing, establish early warning systems for infectious diseases, and strengthen overall public health security.

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