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Impact of population migration and seasonality on tuberculosis transmission: A multi-regional dynamic modeling and cost-effectiveness analysis in Jiangsu Province, China

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Abstract

Background Tuberculosis (TB) remains a significant public health challenge in Jiangsu, China, influenced by population migration and seasonality. This study integrates epidemiological modeling with cost-effectiveness analysis to evaluate the impact of these factors on TB transmission and proposes optimized intervention strategies.

Objective Based on the epidemic situation and epidemiological characteristics of tuberculosis in Jiangsu Province, this paper established a multi-regional ***SCLIT*** model incorporating seasonality, population migration (both within and outside Jiangsu), fast/slow disease progression, reinfection, imperfect treatment, and vaccination. This model aims to analyze the risk factors for tuberculosis epidemics and identify the most cost-effective control strategies.

Methods Using tuberculosis case data and migration records from 2009 to 2019, we fitted the dynamic model parameters and analyzed their sensitivity to the average basic reproduction number ($\bar{\boldsymbol{\mathcal{R}}}_{\mathbf{0}}$) and infected populations. Ignoring the impact of COVID-19, we also used the model to predict the number of tuberculosis outbreaks in Jiangsu Province as a whole from 2023 to 2025, and the predicted trends were largely consistent with the actual data. Combined with the actual epidemiological situation of tuberculosis in Jiangsu, we simulated population mobility and conducted a detailed study on tuberculosis prevention and control in the province through cost-effectiveness analysis.

Results The results showed that ($\bar{\boldsymbol{\mathcal{R}}}_{\mathbf{0}}$) for TB in Jiangsu was 3.5633 (95% CI: 3.4988–3.6278), with an epidemic cycle of approximately one year. Compared to baseline methods, the most cost-effective strategy could prevent 16,380 total infections (1.7%), reduce 62,880 deaths, and avoid 3,269,500 DALYs, while cutting total costs by 461.65 million (14.4% reduction). Incorporating climatic factors and population mobility dynamics enables the tuberculosis model to capture the long-term outbreak patterns in greater detail. During peak travel periods (e.g., holiday migration and Spring Festival travel), high-density population movement increases the risk of outbreaks. In contrast, mobility restrictions have no significant impact on tuberculosis control.

Keywords: Tuberculosis (TB), Multi-regional ***SCLIT*** model, Population migration, Partial rank correlation coefficients (PRCC), Cost-effectiveness analysis

1 Introduction

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium tuberculosis (M. tuberculosis), which can damage various organs but primarily invades the lungs [1]. The bacteria spread through airborne droplets when an infected person coughs, sneezes, or talks. Common symptoms include persistent cough (lasting three weeks or longer), hemoptysis, fever, fatigue, and weakness [2]. Individuals with HIV infection [3–5], diabetes [6], pneumoconiosis, or those taking immunosuppressants are at higher risk. Additional risk factors include drug abuse [7], smoking [8] , and excessive alcohol consumption [9].

Accurate classification of TB is critical for diagnosis, treatment, and prevention. According to China's Tuberculosis Classification (WS196-2017), TB cases are categorized into three types: latent M. tuberculosis infection, active tuberculosis, and inactive tuberculosis [2]. Latent and inactive pulmonary TB patients are typically non-infectious, whereas those with active pulmonary TB are highly contagious. Based on lesion location and disease progression, TB is further classified into primary pulmonary tuberculosis, hematogenous disseminated pulmonary tuberculosis, secondary pulmonary tuberculosis, tracheal (bronchial) tuberculosis, and tuberculous pleurisy. Drug resistance classification divides TB into drug-susceptible and drug-resistant types, with the latter posing a significant challenge [3]. Additional classification methods may also consider treatment history or etiological test results.

If individuals experience symptoms such as fever, unexplained weight loss, night sweats, or persistent cough lasting more than two weeks, they are advised to seek medical evaluation for tuberculosis (TB) [10]. TB diagnosis follows a principle that combines etiological examinations (including bacteriology and molecular biology) with comprehensive assessments of epidemiological history, clinical manifestations, and chest imaging. Unlike most bacterial infections, TB treatment is a prolonged process; China implements a national program providing free anti-tuberculosis drugs under a unified treatment plan [10]. For active TB, standard drug regimens typically require 6-9 months of treatment, while drug-resistant TB necessitates an extended course of 18-24 months [11]. Treatment approaches include chemotherapy, surgery, and traditional Chinese medicine [11]. Newborns should receive BCG (Bacillus Calmette-Guérin) vaccination immediately after birth, as infants are the primary target population for this immunization [10]. BCG vaccination effectively prevents severe TB forms in children, including tuberculous meningitis.

According to the World Health Organization (WHO), an estimated 10.8 million people developed TB in 2023, with approximately 1.25 million deaths worldwide. TB has emerged as a leading global cause of death, surpassing HIV/AIDS in mortality rates despite HIV/AIDS having a single infectious source. In 2020, China reported a TB incidence rate of 52 cases per 100,000 population. However, due to its large population, China's estimated TB case count ranked third globally in 2023, accounting for about 6.8% (741,000 cases) of the world's total [12]. Consequently, TB prevention and control remain significant challenges in China. In response, the Chinese Health Commission has implemented the Stop TB Action Plan (2019-2022) [13], aligning with WHO's goal to end the TB epidemic by 2030 [14].

Studies in many countries have shown that tuberculosis follows a cyclical pattern, with peak incidence varying by season. In South Africa, peaks occur at the turn of winter and spring [15], while in Spain, they are observed in summer and autumn [16]. Summer peaks are reported in England [17] and Hong Kong [18], whereas Japan sees peaks in spring and summer [19]. Similar seasonal characteristics are evident in Jiangsu Province's tuberculosis cases (seeing Figure 4 (a), (b) and (c)). The exact cause of this seasonal pattern remains unclear, but it may be linked to seasonal changes and human behavior (e.g., travel, returning home). Dynamic models have been widely used to study the periodic outbreaks of tuberculosis [20–22].

Evidence also suggests a spring peak in TB outbreaks among migrant workers from high-burden countries entering Kuwait [23]. Many studies highlight the impact of population migration on TB transmission [24–26]. Research by Crimi [27] and Miguel [28] demonstrates transmission between immigrants and local residents, indicating permeable transmission networks. Epidemiological strategies are recommended to investigate transmission patterns in such complex scenarios. Immigrants from high-incidence countries significantly influence TB epidemiology in low-incidence regions, underscoring the need for targeted eradication efforts [29–31]. Therefore, decision-makers must account for migration from high-incidence areas and support epidemiological analyses to inform control strategies.

From the perspective of tuberculosis control, analyzing the periodic outbreak characteristics of tuberculosis can help predict long-term epidemic trends and inform targeted prevention and control programs. While several dynamic studies have examined TB periodicity, to our knowledge, no existing model has simultaneously incorporated both seasonality and population migration effects on TB transmission. Therefore, this study focuses on these two aspects. Specifically, we have established an epidemiological model to investigate the combined impact of migration and seasonality on TB transmission dynamics, using Jiangsu Province, China as a case study. In addition to accounting for key factors commonly addressed in classical TB transmission models, such as fast and slow disease progression [3, 5, 32–41], reinfection [32, 36, 40, 42–49], imperfect treatment [35, 38, 50–55], and vaccination [3, 38, 40, 56], our model gives special emphasis to migration and seasonality. The paper is structured as follows: Section 2 presents the multi-regional $SCLIT$ (Susceptible-Immune-Latent-Infectious-Treated) model, parameter estimation, data fitting and parameter sensitivity to the average basic reproduction number ($\mathcal{R}_0$) and infection dynamics; Section 3 conducts a cost-effectiveness analysis using DALY (Disability-Adjusted Life Years) and ICER (Incremental Cost-Effectiveness Ratio) to evaluate the economic efficiency of integrated control measures; Section 4 presents some important results from the data fitting and cost-effectiveness analysis, and provides some discussion; and Section 5 concludes with key findings and policy implications.

2 Model and methods

This section introduces our tuberculosis model incorporating population migration, presenting the dynamic model, biological significance of parameters, clinical data, parameter ranges, and estimation methods.

2.1 Geographical division and data

Jiangsu Province is divided into three regions (see Figure 1): Northern Jiangsu (Xuzhou, Lianyungang, Suqian, Huai'an, and Yancheng), Central Jiangsu (Yangzhou, Taizhou, Nantong, Gaoyou, Yizheng, Jingjiang, Xinghua, Rugao, Haimen, Hai'an, Qidong, Taixing, Rudong, and Baoying), and Southern Jiangsu (Nanjing, Suzhou, Wuxi, Changzhou, and Zhenjiang). To account for population flows into and out of Jiangsu Province [57], we treat areas outside the province as a fourth region. To exclude the impact of COVID-19 on tuberculosis data collection, we use reported monthly

TB data from January 2009 through December 2019 and from January 2023 through December 2025 provided by the Jiangsu Provincial Center for Disease Control and Prevention [58].

2.2 Model and basic reproduction number

Based on economic development levels and migrant worker flows, we focus on seven key migration paths: from Northern Jiangsu to Central Jiangsu (ω_{12}), to Southern Jiangsu (ω_{13}), and to other provinces (ω_{14}); from Central Jiangsu to Southern Jiangsu (ω_{23}); from Southern Jiangsu to Central Jiangsu (ω_{32}); from other provinces to Central Jiangsu (ω_{42}); and from other provinces to Southern Jiangsu (ω_{43}). Other migration paths are not considered in this study. Regions 1, 2, 3, and 4 represent Northern Jiangsu, Central Jiangsu, Southern Jiangsu, and Outside Jiangsu Province, respectively.

In line with TB's epidemiological characteristics, the population in each region is stratified into five subgroups: susceptible individuals (S) individuals, immune individuals (vaccinated or recovered after treatment) (C), latently infected individuals (asymptomatic) (L), actively infected individuals (I), and treated individuals (T). The total population in each region is given by $N_i = S_i + C_i + L_i + I_i + T_i$ for $i = 1, 2, 3, 4$. The transmission dynamics among these subpopulations are illustrated in Figure 2.

Next, we explain the epidemiological characteristics of tuberculosis depicted in Figure 2. We assume that a proportion $q\Lambda$ of newborns are vaccinated with BCG and enter the immune class, while the remaining $(1-q)\Lambda$ newborns remain unvaccinated and enter the susceptible class. Immunity wanes over time at a rate of ϕ for all individuals, regardless of vaccination in other age groups. It is important to note that, due to exogenous reinfection, we introduce the parameter θ_r to represent this pathway. In addition to susceptible individuals who may become infected with Mycobacterium tuberculosis, a small fraction of immune individuals may also become infected through endogenous reactivation (including relapse, recurrence, or reactivation), with this proportion denoted by θ_v. For simplicity, we focus on the combined effect of $\theta = \theta_r + \theta_v$ in subsequent analysis. The progression of tuberculosis is generally slow, with a proportion η becoming latent and the rest developing symptoms and entering the infected class. Not all patients are cured: a proportion $1-\kappa$ (treatment success) move to the immune class, while the remaining (treatment failure) return to the latent class. Thus, the multi-regional tuberculosis model for Jiangsu Province, incorporating population migration, is formulated as follows:

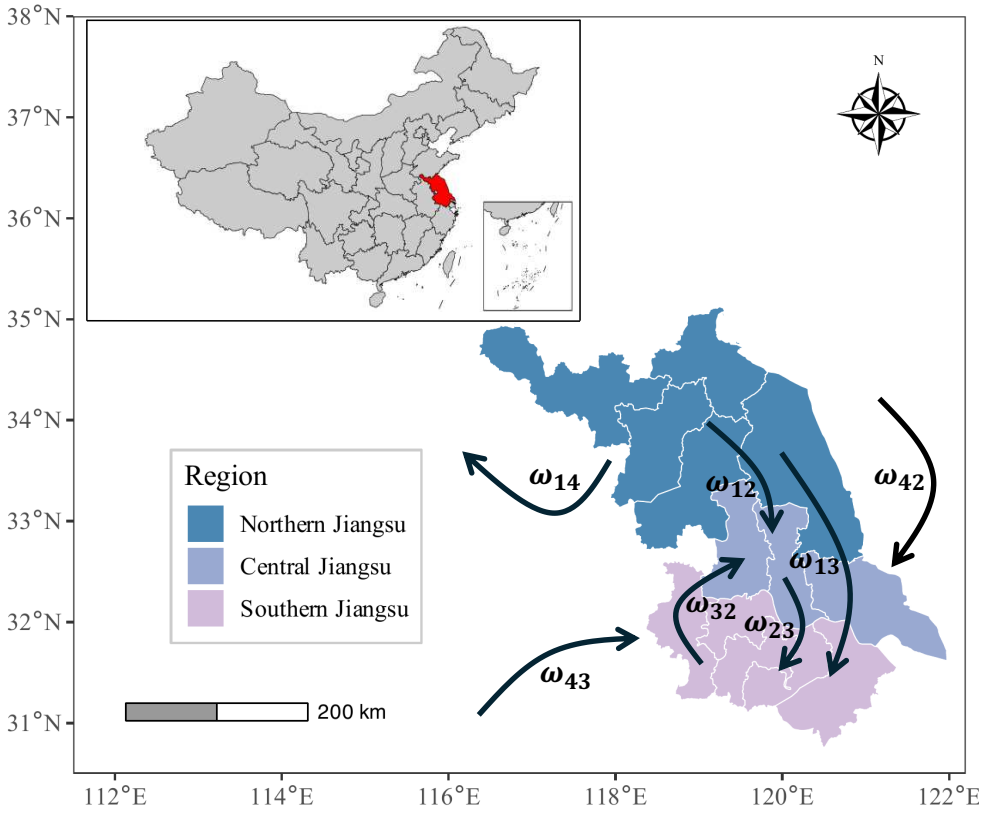


Fig. 1 Population flows within Jiangsu Province and from Jiangsu to other provinces.

$$
\begin{cases}
\dfrac{dS_i}{dt} = (1-q)\Lambda_i - \dfrac{\beta_i S_i(I_i+\rho T_i)}{N_i} - \mu S_i + \phi C_i - \sum\limits_{j=1,j\neq i}^{4}\omega_{ij}S_i + \sum\limits_{j=1,j\neq i}^{4}\omega_{ji}S_j, \\
\dfrac{dC_i}{dt} = \underbrace{q\Lambda_i}_{birth\ vaccination} + \underbrace{(1-\kappa)\gamma T_i}_{treatment\ success} - \underbrace{\dfrac{\theta_v\beta_i C_i(I_i+\rho T_i)}{N_i}}_{endogenous\ reactivated} - \underbrace{\dfrac{\theta_r\beta_i C_i(I_i+\rho T_i)}{N_i}}_{exogenous\ reinfection} \\
\qquad -(\phi+\mu)C_i - \sum\limits_{j=1,j\neq i}^{4}\omega_{ij}C_i + \sum\limits_{j=1,j\neq i}^{4}\omega_{ji}C_j, \\
\dfrac{dL_i}{dt} = \underbrace{\eta\dfrac{\beta_i S_i(I_i+\rho T_i)}{N_i}}_{slow\ process\ infection} + \dfrac{\theta_v\beta_i C_i(I_i+\rho T_i)}{N_i} + \dfrac{\theta_r\beta_i C_i(I_i+\rho T_i)}{N_i} \\
\qquad + \underbrace{(1-p)\delta I_i}_{not\ to\ treat} + \underbrace{\kappa\gamma T_i}_{treatment\ failure} -(\alpha+\mu)L_i - \sum\limits_{j=1,j\neq i}^{4}\omega_{ij}L_i + \sum\limits_{j=1,j\neq i}^{4}\omega_{ji}L_j, \\
\dfrac{dI_i}{dt} = \underbrace{(1-\eta)\dfrac{\beta_i S_i(I_i+\rho T_i)}{N_i}}_{fast\ process\ infection} + \alpha L_i - (\delta+\mu+d_a)I_i - \sum\limits_{j=1,j\neq i}^{4}\omega_{ij}I_i + \sum\limits_{j=1,j\neq i}^{4}\omega_{ji}I_j, \\
\dfrac{dT_i}{dt} = \underbrace{p\delta I_i}_{to\ treat} -(\gamma+\mu+d_b)T_i - \sum\limits_{j=1,j\neq i}^{4}\omega_{ij}T_i + \sum\limits_{j=1,j\neq i}^{4}\omega_{ji}T_j.
\end{cases}
\tag{2.1}
$$

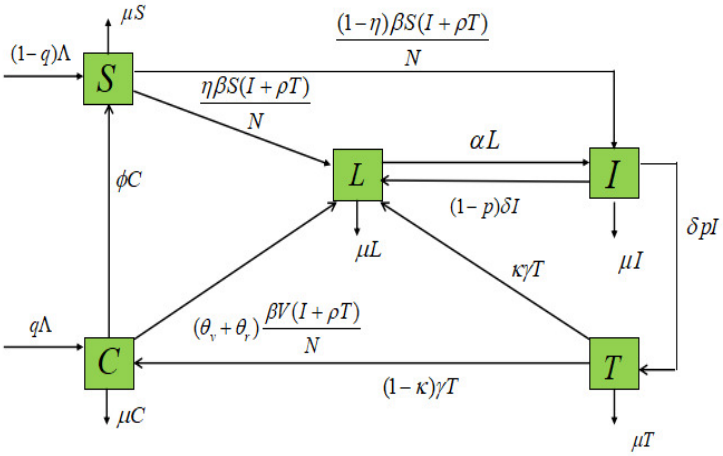


Fig. 2 Flow chart of compartments of tuberculosis model.

The parameters in model (2.1) are defined as follows:

- μ, d_a: Natural death rate and disease-related mortality rate;
- β_i (Λ_i), $i = 1, 2, 3, 4$: Transmission rate (recruitment rate) in region i;
- q, ϕ: Infant vaccination rate and rate of waning vaccine-induced immunity;
- ρ: Reduction factor of virus transmission from treated to susceptible/immune individuals;
- θ_r (θ_v): Reduction factor of infections due to exogenous reinfection (endogenous reactivation);
- η: Proportion of susceptible individuals becoming infectious via slow progression;
- p: Proportion of infectious individuals receiving treatment;
- δ: Progression rate from active infectious to treated/latent state;
- κ: Proportion of non-recovered patients after treatment;
- α: Progression rate from latent to active infectious state;
- γ: Treatment rate;
- $\omega_{ij}, i, j = 1, 2, 3, 4$: Migration rate from region i to region j.

Good cyclical characteristics are observed in many seasonal infectious disease models, including measles, hand-foot-and-mouth disease (HFMD) [59, 60], diphtheria, chickenpox, mumps [61, 62], influenza, malaria and scarlet fever [63]. Migrant workers' movement during festivals, environmental climate effects, and TB transmission dynamics also exhibit periodic patterns. Such periodicity is often modeled using trigonometric functions [20–22]. As population mobility increases, both the frequency of individual contacts and the probability of transmission rise. Thus, mobility and transmission rate are assumed to be positively correlated. We employ a monotonically increasing exponential function to describe this relationship. Since mobility is a relatively small parameter and its impact on TB spread is uncertain, we introduce strength coefficients to adjust the relationship. These coefficients, determined through data fitting, quantitatively capture the influence of mobility on transmission rates.

Here, $a_i, i = 1, 2, 3, 4$, represent the intensity of influence for each region. Accordingly, we define the transmission rates as follows: $\beta_0 = a_0 + (1 + b_0 \sin(\frac{\pi t}{Z} + c_0))$, $\beta_1 = \beta_0 \exp(a_1 \times (\omega_{12} + \omega_{13} + \omega_{14}))$, $\beta_2 = \beta_0 \exp(a_2 \times (\omega_{12} + \omega_{32} + \omega_{42} + \omega_{23}))$, $\beta_3 = \beta_0 \exp(a_3 \times (\omega_{13} + \omega_{23} + \omega_{32} + \omega_{43}))$ and $\beta_4 = \beta_0 \exp(a_4 \times (\omega_{14} + \omega_{42} + \omega_{43}))$, where $2Z$ is the outbreak period, a_0 is the baseline contact rate, b_0 is the magnitude of forcing, and c_0 the phase shift constant.

The basic reproduction number $\mathcal{R}_0$ represents the average number of secondary cases generated by one infectious individual during their infectious period [59]. A lower $\mathcal{R}_0$ indicates better disease control. Bacaër [64] defined $\mathcal{R}_0$ for periodic ODEs, and Wang [65] provided the theory and computational method for $\mathcal{R}_0$ in periodic environments. For clarity, we present only the method for computing the average basic reproduction number. Detailed calculations for $\bar{\mathcal{R}}_0$ are provided in Section 1 of the Supplementary Material.

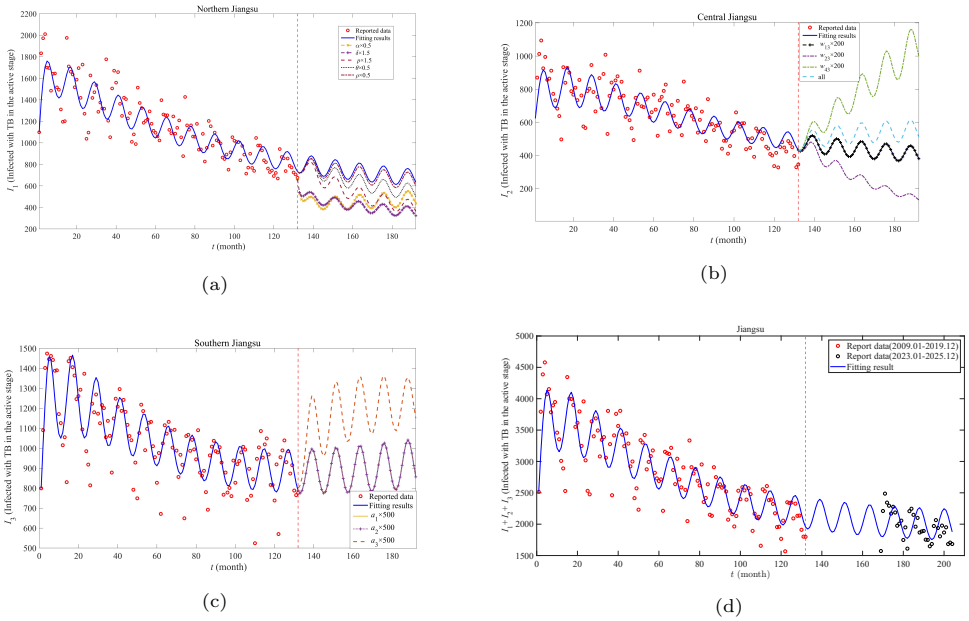
2.3 Parameter estimation and data fitting

We use system (2.1) to conduct parameter estimation and data fitting for the number of TB cases (active infectious individuals) in each region of Jiangsu from January 2009 through December 2019, with the fitting results presented in Figures 3 (a), (b), and (c). To exclude the interference of COVID-19 on data statistics, we also predicted TB outbreak cases in Jiangsu Province from January 2023 through December 2025. The results indicate an accurate basic trend, as shown in Figure 3 (d). A detailed description of the parameter estimation ranges and sources, data fitting methods, and objective function selection can be found in Section 2 of the Supplementary Material. The parameter values, standard errors, confidence intervals, and error analysis are presented in Supplementary material. A detailed discussion of the effects of different prevention and control intensities is provided in Section 3 of the Supplementary Material, and the specific results are also illustrated in Figure 3 (a), (b), and (c).

2.4 Sensitivity analysis of $\mathcal{R}_0$ and infected populations

Consistent with previous TB model sensitivity analyses [21, 38, 49, 66], the transmission rate β is typically the most sensitive parameter. In our model (2.1), the transmission rate $\beta_i, i = 1, 2, 3, 4$ is decomposed into trigonometric and exponential functions incorporating multiple factors: baseline contact rate (a_0), magnitude of forcing (b_0), level fluctuations constant (c_0), regional influence intensity ($a_i, i = 1, 2, 3, 4$) and migration rates ($\omega_{ij}, i, j = 1, 2, 3, 4$). Therefore, we do not analyze the sensitivity of β in detail.

To assess the sensitivity of different parameters to both the average basic reproduction number $\bar{\mathcal{R}}_0$ and infected populations, we employed Latin Hypercube Sampling (LHS) and partial rank correlation coefficients (PRCC) [67]. The parameters were assumed to follow normal distributions, with their expectations and standard deviations consistent with those presented in the Supplementary material.With $\bar{\mathcal{R}}_0$ as the output and a significance level of 0.01, Figure 4 (a) presents the PRCC values for $\bar{\mathcal{R}}_0$. A positive (negative) PRCC indicates a positive (negative) correlation, with larger absolute values indicating greater sensitivity. Using the same method, we obtained the



(a) (b) (c) (d)

Fig. 3 Comparison between reported data (January 2009-December 2019) and model (2.1) fitting results for I_1, I_2, I_3 in Northern (a), Central (b), and Southern Jiangsu (c), respectively. The figure also shows TB prevalence predictions from January 2023 through December 2025 (d) and simulation results of various intervention effects across four schematic diagrams (a–d).

sensitivity of parameters to the total number of patients in the three regions (Figures 4 (b), (c) and (d)). The results show that the parameters most significantly affecting $\bar{\mathcal{R}}_0$ are, in descending order: δ, p, ρ, ω_{32}, ω_{23}, a_0, and ω_{42}. For Northern Jiangsu, the key parameters are p, θ, α, δ, and ω_{13}; for Central Jiangsu, they are p , θ, α, ω_{42}, δ, ω_{23}, ρ, and ω_{32}; and for Southern Jiangsu, the main parameters are p, θ, α, δ, ρ, and ω_{43}.

3 Cost-effectiveness analysis

Based on the actual treatment and control costs of tuberculosis in Jiangsu Province, we provide a detailed breakdown of expenditures for tuberculosis prevention and control covering five aspects: preventive measures, screening, treatment, primary healthcare, and transmission control costs. Further details are available in Section 4 of the Supplementary Material.

3.1 Disability adjusted life years (DALYs)

We define DALYs (Disability-Adjusted Life Years) and ICER (Incremental Cost-Effectiveness Ratio) as key metrics for assessing the cost-effectiveness of tuberculosis (TB). DALYs measures the overall health burden caused by the disease and is

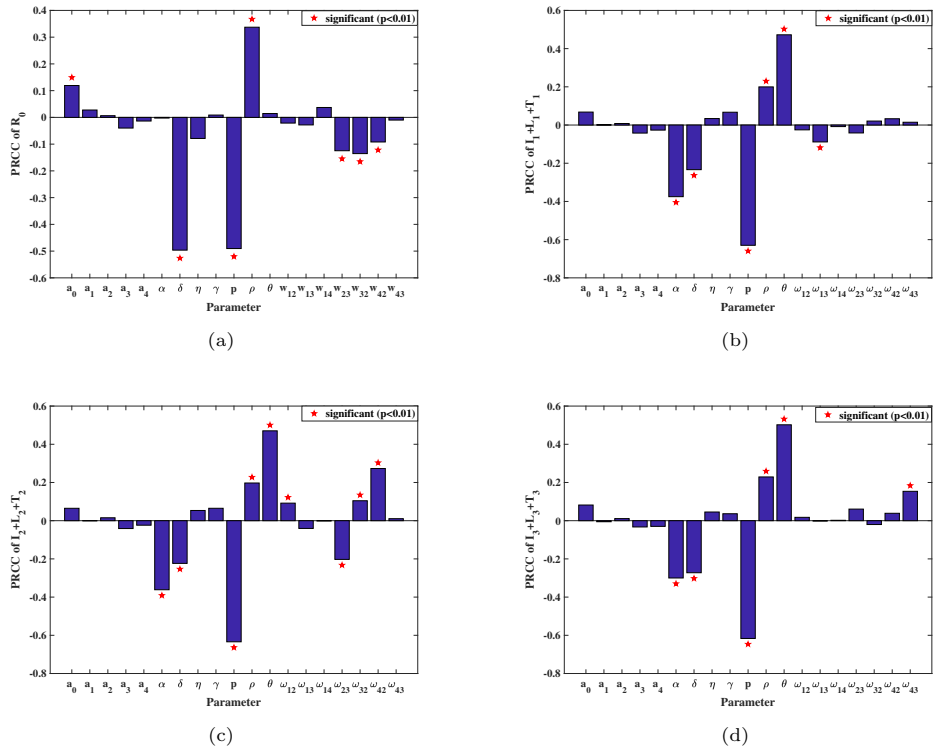


Fig. 4 Partial rank correlation coefficients (PRCC) for the average basic reproduction number $\bar{\mathcal{R}}_0$ and total infected individuals (sum of I, L, T) in Northern Jiangsu($I_1 + L_1 + T_1$), Central Jiangsu ($I_2 + L_2 + T_2$), and Southern Jiangsu ($I_3 + L_3 + T_3$) across all parameters. * indicates a PRCC significance level< 0.01.

calculated using the formula:

$$DALY = YLL + YLD,$$

where YLL (Years of Life Lost) = Ns×Le (Ns = number of deaths, Le = standardized life expectancy at age of death), and YLD (Years Lived with Disability) = I×DW×Ld (I = number of illness events, DW = disability weight, Ld = average duration of disability) [68, 69].

3.2 Incremental cost effectiveness ratio (ICER)

The Incremental Cost-Effectiveness Ratio (ICER) measures the change in cost and health benefits between two intervention strategies. It is crucial to specify both the cost and the corresponding change in DALYs for different intervention strategies. The ICER is calculated using the following formula:

$$ICER = \frac{Costs_{Intervention} - Costs_{Statusquo}}{DALYs_{Intervention} - DALYs_{Statusquo}},$$

where, $Costs = C_{pre} + C_{screen} + C_{test} + C_{HC} + C_{KZ}$ and $C_{KZ} = C_{YS} + C_{HS} + C_{QX} + C_{HF} + C_{TD} + C_{SH}$.

In tuberculosis (TB) prevention and control, different strategies are implemented from multiple dimensions to reduce the risk of disease transmission and enhance prevention effectiveness. These approaches comprehensively address TB transmission through increased government investment, strengthened health education, optimized treatment policies, improved screening coverage, and enhanced management of mobile populations, among other measures. The following section elaborates on six prevention and control strategies. Additionally, to ensure adjusted parameters remain within confidence intervals after applying multiplicity factors, the following scaling factors were selected: decreasing multiplicity: $\times 0.9$ (low degree), $\times 0.2$ (high degree); and the increasing multiplicity: $\times 1.1$ (low degree), $\times 1.3$ (high degree).

(1) Strategy **I** reduces baseline contact rates by improving medical infrastructure and promoting TB prevention education, lowering a_0 and adjusting other parameters accordingly:

$$a_0 \times 0.2, p \times 1.1, \delta \times 1.3, \rho \times 0.9.$$

(2) Strategy **II** builds on Strategy **I** by enhancing treatment policies, which improves patient access to care and reduces transmission through shorter infectious periods and lower infectiousness:

$$a_0 \times 0.2, p \times 1.3, \delta \times 1.3, \rho \times 0.2.$$

(3) Strategies **III** focuses on early detection and treatment, reducing infection risks from waning immunity and reinfection while accelerating diagnosis and intervention:

$$a_0 \times 0.2, p \times 1.1, \delta \times 1.1, \rho \times 0.9, \theta \times 0.9, \alpha \times 1.1.$$

(4) Strategy **IV** further optimizes Strategy **III** by intensifying treatment and control measures, significantly reducing transmission risks through enhanced parameter adjustments.

$$a_0 \times 0.2, p \times 1.3, \delta \times 1.3, \rho \times 0.2, \theta \times 0.2, \alpha \times 1.3.$$

(5) Strategy **V** manages mobile populations to reduce TB spread by regulating migration flows and adjusting related parameters:

$$a_0 \times 0.2, p \times 1.1, \delta \times 1.1, \rho \times 0.9, \theta \times 0.9, \alpha \times 1.1, \omega_{43} \times 0.9, \omega_{13} \times 1.1, \omega_{23} \times 1.1.$$

(6) Strategy **VI** combines all preventive and control measures at maximum levels for comprehensive TB control:

$$a_0 \times 0.2, p \times 1.3, \delta \times 1.3, \rho \times 0.2, \theta \times 0.2, \alpha \times 1.3, \omega_{43} \times 0.2, \omega_{13} \times 1.3, \omega_{23} \times 1.3.$$

Table 1 Cost-effectiveness analysis of six tuberculosis control strategies (2019–2039).

	Total Costs (mil. RMB)	Incremental Costs (mil. RMB)	Total DALYs	Total DALYs for TB Infections Avoided (mil.)	New TB Infections Patients (mil.)	Total Infections Prevented (%)	Total TB Related Deaths (mil.)	ICER Relative to the Status Quo
I	320.39	-	5.2733	-	0.9632	-	0.1072	-
II	284.81	-35.58	3.0487	2.2246	0.9604	0.29	0.0670	-11.67
III	329.76	9.37	5.2078	0.0655	0.9560	0.74	0.1059	1.80
IV	274.23	-46.17	2.0038	3.2695	0.9468	1.70	0.0443	-23.04
V	329.77	9.38	5.2080	0.0653	0.9561	0.74	0.1059	1.80
VI	274.25	-46.15	2.0043	3.2690	0.9469	1.69	0.0443	-23.02

4 Results and discussion

4.1 The results of data fitting

The results indicate that tuberculosis prevalence exhibits periodic behavior with a cycle of approximately 12.2068 months ($\approx$ 1 year). The average basic reproduction number $\bar{\mathcal{R}}_0$ of Jiangsu Province is estimated to be 3.5633 (95% CI: 3.4988-3.6278). Numerical calculations following the method in [65] yield a slightly higher basic reproduction number of 3.5934. Since both estimates exceed 1, the TB epidemic in Jiangsu Province remains in a state of continuous outbreak, consistent with previous studies [49, 66, 70–72]. For further discussion on $\bar{\mathcal{R}}_0$ of tuberculosis, see the review by Ma et al. [73].

4.2 The results of cost-effectiveness analysis

The total DALYs costs and losses for the six strategies are shown in the Supplementary material. Table 1 provides a cost-effectiveness analysis of the six tuberculosis control strategies implemented between 2019 and 2039. The total cost over 20 years for all strategies ranges from ¥200 million to ¥300 million, which is a relatively small difference. However, the cumulative DALYs are reduced from the original 5 million to about 2 million.

At the baseline level of Strategy **I**, we estimate that the cumulative number of infections in Jiangsu Province from 2019 to 2039 will be 963,200, with 107,200 deaths and a total cost of ¥320.39 million, resulting in 527,330,000 DALYs. Compared to the base case:

- Strategy **II** is expected to prevent 2,760 total infections (0.29%), reduce deaths by 40,180, achieve cost savings of ¥355.79 million, and avoid 2,224,600 DALYs.;
- Strategy **III** is expected to prevent 7,160 new TB infections (0.7433%), reduce deaths by 1,330, and avoid 65,500 DALYs, with an increased cost of ¥9.3679 million.;

- Strategy **IV** is expected to prevent 16,380 total infections (1.7%), reduce deaths by 62,880, avoid 3,269,500 DALYs, and reduce total costs by ¥461.65 million (14.4% lower than the base case);
- Strategy **V** is expected to prevent 7,150 total infections (0.7432%), reduce deaths by 1,320, avoid 65,300 DALYs, but increase costs by ¥9.3787 million.
- Strategy **VI** is expected to prevent 16,348 total infections (1.69%), reduce deaths by 62,864, avoid 3,269,000 DALYs, and reduce total costs by ¥461.47 million.

The ICERs for the remaining five strategies, compared to Strategy **I**, are -11.67, 1.80, -23.04, 1.80, and -23.02. It can be concluded that Strategy **IV** is the most cost-effective under our assumptions, reducing spending by ¥23.04 per DALYs avoided compared to Strategy **I**. Ensuring timely treatment for more patients can reduce infectious sources, shorten the infectious period, and lower transmission risk, leading to better TB control.

5 Conclusion

Based on real-time reported case data of tuberculosis (TB) in Jiangsu Province (January 2009-December 2019) and population flow data from the past decade, this study establishes a multi-regional $SCLIT$ model. By reviewing prior TB models, we incorporated key factors including birth vaccination, imperfect treatment, reinfection, immunity loss, fast/slow disease progression, and importantly, the effects of rapid population mobility and seasonality. Using a hybrid optimization approach combining global differential evolution and local sequential quadratic programming, we calibrated the model parameters. Error analysis confirmed the model's ability to simulate TB spread in Jiangsu Province, while sensitivity analysis identified parameters most influential on the average basic reproduction number ($\bar{\mathcal{R}}_0$) and infection prevalence. Data fitting yielded an average $\bar{\mathcal{R}}_0$ of 3.5633 (95% CI: 3.4988–3.6278) and an estimated one-year epidemic cycle for TB in the region.

The model demonstrates dual capabilities: simulating TB epidemic trajectories and projecting baseline transmission patterns over a 24-month period post-January 2023. This requires explicit integration of mobility-driven transmission dynamics and seasonal fluctuation mechanisms into the modeling framework. Empirical analyses show that abrupt mobility surges (e.g., holiday migrations, Spring Festival travel rush) significantly amplify TB outbreak risks by enhancing pathogen dispersion. In contrast, prolonged mobility suppression (e.g., lockdowns) has negligible impact due to TB's airborne transmission characteristics. These findings underscore the need for vigilance against disease outbreaks triggered by rapid population movements.

We further evaluated the current TB situation in Jiangsu Province using disability-adjusted life years (DALYs) and incremental cost-effectiveness ratios (ICER). From a public health perspective, the most cost-effective strategy (Strategy **4**) involves controlling transmission rates, increasing hospitalization rates, shortening diagnosis delays, reducing nosocomial infections, and lowering recurrence rates.

While our framework provides preliminary insights into mobility and seasonal patterns, it inherently simplifies the socio-spatial complexity of real-world population dynamics. Key limitations include the omission of micro-scale mobility networks (e.g.,

cross-district commuting) and meso-scale climatological variations (e.g., humidity-temperature interactions). Future research should prioritize multi-resolution analyses integrating mobile signaling data and meteorological covariates to advance TB transmission modeling.

Abbreviations

AIDS: Acquired immunodeficieney syndrome;
BCG: Bacillus Calmette-Guérin;
COVID-19: Coronavirus Disease 2019;
DALYs: Disability-adjusted life years;
HIV: Human immunodeficiency virus;
HFMD: hand-foot-and-mouth disease;
ICER: Incremental cost-effectiveness ratio;
LHS: Latin hypercube sampling;
PRCC: Partial rank correlation coefficients;
SCLIT: susceptible-immune-latently-actively infected-treated;
TB: Tuberculosis;
WHO: World health organization;
YLD: Years lived with disability;
YLL: Years of life lost;

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Author's contributions

Y. Jiao and S. Wang contributed equally to this work. They collected the data and reviewed the literature, prepared Figure 2, performed data analysis and all experiments, and drafted the initial manuscript. Y. Luo and X. Li assisted with data collection, preprocessing and visualization, and prepared Figure 1. C. Tan and Y. Wu conducted parameter estimation and data fitting, and prepared Figures 3 and 4.B. Jia assisted with partial data query and analysis. Y. Li and Z. Peng conceived and designed the study, developed the SCLIT model, supervised the overall project, provided critical revisions, and finalized the manuscript. All authors reviewed and approved the final version of the manuscript.

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Data availability

The data on the number of tuberculosis cases involved in this paper are all sourced from the Jiangsu Provincial Center for Disease Control and Prevention [58].

Declarations

Ethics approval and consent to participate

This paper does not contain any studies with human or animal subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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