

A Stochastic Projection for Tuberculosis Elimination in Indonesia by 2030

Novi Reandy Sasmita^{1*}, Maya Ramadani², Muhammad Ikhwan³, Munawwarah Munawwarah⁴, Latifah Rahayu⁵, Selvi Mardalena⁶, M. Ischaq Nabil Asshiddiqi⁷, Suyanto Suyanto⁸, Nanda Safira⁹

¹Department of Statistics, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia

²Department of Statistics, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia

³Department of Mathematics, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia

⁴Department of Statistics, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia

⁵Department of Statistics, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia

⁶Department of Statistics, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia

⁷School of Nursing, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong

⁸Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia

⁹Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hatyai, Thailand

*Corresponding Author: E-mail: novireandys@usk.ac.id

ARTICLE INFO	ABSTRACT
Manuscript Received: 07 Jun, 2025 Revised: 11 Oct, 2025 Accepted: 19 Oct, 2025 Date of Publication: 01 Nov, 2025 Volume: 8 Issue: 11 DOI: 10.56338/mppki.v8i11.8548	Introduction: Indonesia, with the world's second-highest tuberculosis (TB) burden, has targeted TB elimination (65 cases per 100,000) by 2030. This study aimed to evaluate the feasibility of achieving this goal by projecting TB incidence trends using a stochastic epidemic model that accounts for the uncertainties inherent in TB transmission dynamics in latent TB infections. Methods: The initial values for state variables and parameters were derived from a comprehensive literature review and calibrated against publicly available epidemiological data from the Indonesian Ministry of Health reports from 2018-2022. A Susceptible, Vaccinated, Three Exposed, Three Infectious, Recovered (SVE3I3R) model was developed, incorporating Gaussian noise into the exposed compartments to simulate real-world unpredictability in latent infection dynamics. The model was solved numerically using the fourth-order Runge-Kutta (RK4) method in R software. Key outcomes measured were the projected incidence of drug-susceptible TB (DS-TB), multidrug-resistant TB (MDR-TB), and extensively drug-resistant TB (XDR-TB). Results: Model projections suggest that the overall TB incidence rate will fall from 387 cases per 100,000 people in 2023 to a projected 320 cases per 100,000 by 2030. However, this remains far above the national target. While DS-TB cases decreased to 730,283, MDR-TB and XDR-TB cases were projected to surge dramatically to 120,939 cases and 104,651 individuals, respectively. The estimation signals a critical shift in the epidemic's profile. Conclusions: Indonesia is not on track to achieve its 2030 TB elimination target under current interventions. The alarming rise of drug-resistant TB necessitates an urgent, aggressive, and multifaceted policy response. This study underscores the critical value of incorporating stochasticity into epidemiological models for more realistic forecasting and public health planning in high-burden settings.
KEYWORDS	
Tuberculosis; Stochastic Epidemic Model; Gaussian Noise; Indonesia	
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INTRODUCTION

Tuberculosis (TB) remains a significant global health challenge, primarily caused by the bacterium *Mycobacterium tuberculosis* (Mtb). While TB predominantly affects the lungs, it can also impact other vital organs, including the kidneys, brain, and spine (1). The transmission of TB occurs through respiratory droplets expelled by an infected individual, making it highly contagious (2).

In 2023, TB emerged as the leading cause of death from a single infectious agent, surpassing COVID-19 and resulting in nearly double the fatalities of HIV/AIDS. Despite being preventable and curable, over 10 million individuals contracted TB annually, with an incidence rate of 134 new cases per 100,000 people globally. The burden of TB is disproportionately concentrated in 30 high-burden countries, which account for 87% of global cases, with India, Indonesia, China, the Philippines, and Pakistan representing 56% of these cases. Demographically, affected individuals comprised 55% men, 33% women, and 12% children, leading to approximately 1.25 million deaths in total. The rise in newly diagnosed TB cases to 8.2 million in 2023 can be attributed to delays caused by COVID-19 disruptions, alongside the alarming emergence of multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB), with approximately 175,923 individuals diagnosed out of an estimated total of 400,000 that year (3,4).

In Indonesia, the situation is particularly dire. According to the Global TB Report 2024, Indonesia accounts for 10% of total global TB cases as of 2023, making it the second-largest contributor to the TB epidemic worldwide. With a population of 281 million, Indonesia has an estimated TB incidence rate of 387 cases per 100,000 people, reporting 286 new and relapse TB cases per 100,000. The total estimated number of TB deaths is around 130,927, while the incidence of rifampicin-resistant TB (RR-TB) cases is approximately 29,535. Further, Indonesia is estimated to have about 1,090,000 TB cases annually, with a mortality rate of 125,000 deaths, equating to roughly 14 deaths per hour in 2023 (5). The urgent need for action to combat the TB epidemic is underscored by the United Nations Sustainable Development Goals (SDGs), which aim to eliminate TB by 2030. The WHO's End TB Strategy sets ambitious targets for reducing TB deaths and incidence rates by 2030 and 2035, respectively (6,7).

Indonesia Presidential Regulation No. 67 of 2021 outlines a strategic plan for TB elimination by 2030, aiming to reduce the incidence to 65 cases per 100,000 population and the mortality rate to 6 deaths per 100,000 population (8). This strategy emphasizes improving access to health services, early diagnosis, appropriate treatment, and prevention through vaccination and control of risk factors. However, significant challenges persist due to inadequate healthcare systems and limited funding. The complexity of TB transmission dynamics necessitates innovative approaches to address these challenges effectively.

Recent advancements in epidemic modeling, particularly deterministic and stochastic models, have proven instrumental in understanding TB transmission dynamics and evaluating the effectiveness of intervention strategies. These models utilize mathematical, statistical, and computational tools to analyze the spread of infectious diseases within populations, relying on data that encapsulates demographic processes, environmental factors, and health impacts (9). Deterministic models, such as the Susceptible, Infectious, Recovered (SIR) and Susceptible, Exposed, Infectious, Recovered (SEIR) frameworks, have been employed to predict TB spread. For instance, a study in Ghana utilizing the SEIR model recommended enhancing early detection mechanisms for TB (10). Similarly, studies in China and Pakistan employing the Susceptible, Vaccine, Exposed, Infectious, Recovered (SVEIR) and Susceptible, Latent, Infectious, Treated, Recovered (SLITR) models identified increasing treatment rates with low cost as a feasible strategy for TB elimination (11,12).

However, the inherent complexities of TB, including latent phases and drug resistance, render deterministic models insufficient for capturing the actual dynamics of TB transmission. These models often fail to account for the uncertainty and variability, leading to less accurate predictions (13). Consequently, there is a pressing need for more sophisticated modeling approaches that can realistically simulate TB spread.

A recent study has explored using the Susceptible, Three Exposed, Three Infectious, Recovered (SE3I3R) model to assess the impact of cure rates on latent TB infections in the elimination process from 2019 to 2030 (14). A modified SVEIR model has also been proposed to enhance prediction accuracy regarding TB spread (15). This study introduces the Susceptible, Vaccinated, Three Exposed, Three Infectious, Recovered (SVE3I3R) model, which integrates elements from both previous models while incorporating Gaussian noise parameters to create a stochastic framework. Gaussian Noise is a statistical term referring to random variations that follow a normal distribution, characterized by a symmetric bell-shaped curve around a mean value. In epidemiological modeling, it is used to

represent uncertainties, measurement errors, or unobserved variability in data, enhancing the realism of predictions by accounting for randomness that deterministic models often ignore. Gaussian noise enhances the model's ability to handle uncertainties often overlooked by deterministic approaches (16,17).

The evolution of the Gaussian noise as a component of stochastic effects highlights the significance of incorporating stochastic elements in modeling infectious diseases like TB (18). This approach allows for a more nuanced understanding of the fluctuating data that deterministic models cannot adequately address. The increasing severity of TB further underscored the necessity of flexible and adaptive modeling to comprehend TB transmission dynamics. Disruptions in TB health services during the pandemic have led to an increase in undiagnosed and untreated cases, exacerbating the TB burden (19). Incorporating Gaussian noise is expected to yield more accurate predictions.

The study aims to evaluate Indonesia's target of achieving its TB elimination target by 2030, as outlined in Presidential Regulation No. 67 of 2021, using an epidemiological model with Gaussian noise as a stochastic approach. The study employs the SVE3I3R model integrated with Gaussian noise to account for uncertainties and variability in TB transmission dynamics in latent infections. This innovative approach has not been widely applied in the Indonesian context, positioning this study as a critical contribution to understanding TB dynamics, developing effective control strategies, and informing public health policy in Indonesia to achieve the TB elimination target by 2030 in accordance with the Sustainable Development Goals (SDGs).

METHOD

Study Procedure

This study procedure will be conducted systematically through several key stages. The initial stage begins with developing a disease transmission flowchart to illustrate the dynamics of TB spread, establishing the foundational structure for a Susceptible-Vaccinated-Exposed-Infectious-Recovered (SVEIR) compartmental model. Based on this structure, the epidemiological model will be formed through a system of ordinary differential equations. Following model development, constant initial values for each compartment will be determined based on available epidemiological data, assigning relevant parameter values (e.g., infection rate, recovery rate, vaccination parameters, etc.) sourced from previous studies or adjusted for the Indonesian context. Some stochastic Gaussian Noise following a normal distribution will be incorporated into the model to simulate random variability, test model robustness, prevent overfitting, and improve long-term prediction accuracy to enhance realism and capture data uncertainty. The ODE system will then be estimated using the fourth-order Runge-Kutta (RK4) method to iteratively calculate changes in each compartment over time, generating a monthly estimated TB incidence rate dataset from 2024 to 2030 ($n=84$ months) with a stopping iteration criterion. This estimated dataset will be subjected to descriptive statistical analysis. It does so to elucidate trends and patterns, including tabulation and visualization (20–22). Finally, the estimated TB incidence, calculated as a proportion of the infectious population against the total population, will be evaluated against Indonesia's 2030 TB elimination targets to assess the country's progress and to inform data-driven recommendations, culminating in a conclusion that summarizes the principal findings from the application of the SVEIR model.

Assumptions and Model Formulation

In the pathogenesis of TB, droplet nuclei are airborne particles that carry *Mtb*. When inhaled, they contain tubercle bacilli that enter the lungs of susceptible individuals. Susceptible individuals are those who can incur the disease but are not yet infected by *Mtb*. We symbolize susceptible individuals as S . After receiving the infection, within weeks, the immune system in susceptible individuals can stop the multiplication and development of tubercle bacilli. At that moment, susceptible individuals are changed to LTBI (23,24).

We denote anyone who has LTBI as an exposed individual. Exposed individuals are those who *Mtb* infects, do not feel sick, and cannot spread TB bacteria to others. They are at risk for active TB disease in the future. We symbolize the exposed individuals group as E and the infection rate of susceptible individuals to exposed individuals as α . We divide E into three compartments according to the transmission of each infectious individual: exposed individuals for drug-susceptible TB (DS-TB), exposed individuals for multidrug-resistant TB (MDR-TB), and exposed individuals for the extensively drug-resistant TB (XDR-TB) are denoted as E_1 , E_2 , and E_3 , respectively.

In this model, vaccinated individuals (V) represent a population subset that has acquired temporary immunity against TB through vaccination. The model assumes vaccination reduces susceptibility to TB infection, but immunity wanes over time, reflecting real-world limitations in vaccine durability. This condition causes vaccinated individuals to return to susceptible status, denoted by the parameter ξ . Conversely, susceptible individuals who receive the vaccine move into compartment V , with this switch denoted by the parameter τ .

Any exposed individuals can progress to active TB as infectious individuals. In such cases, infectious individuals are characterized by symptomatic active TB. Unlike exposed individuals, who harbour *Mtb* without symptoms, active TB involves clinical manifestations such as cough, fever, or weight loss. Infectious individuals can transmit *Mtb* to susceptible persons through close interpersonal contact (25). They are the primary drivers of TB transmission. The compartments for Infectious individuals are categorized as I_1 (DS-TB), I_2 (MDR-TB), and I_3 (XDR-TB) with parameters β_1 , β_2 dan β_3 as the transition rate from exposed to infectious according to the route of transmission.

DS-TB, MDR-TB, and XDR-TB refer to different types of TB based on the resistance of the TB bacteria to anti-TB medications. DS-TB is TB that can be treated with standard first-line anti-TB drugs. MDR-TB is TB resistant to at least isoniazid and rifampin, two of the most effective first-line drugs. XDR-TB is a more severe form of MDR-TB where the bacteria are also resistant to certain fluoroquinolones and at least one of the second-line injectable drugs like bedaquiline or linezolid (26).

DS-TB is generally considered less dangerous than MDR-TB and XDR-TB in terms of treatment complexity, mortality risk, and public health impact. Treatment for XDR-TB involves therapies that are more harmful to patients, costlier to administer, and less successful in achieving recovery compared to MDR-TB treatments, even more so DS-TB Treatment. This study assumes that each susceptible individual must go through the exposed individual stage before becoming an infectious individual.

This model's recovery rate encompasses both spontaneous resolution and treatment-mediated recovery. Recovered individuals (R) are those who have fully healed from the infection. Transition to the R compartment occurs through two distinct pathways: first, spontaneous recovery, in which Exposed individuals clear the infection without medical intervention. This condition is denoted by ρ_1 , ρ_2 , and ρ_3 from E_1 , E_2 , and E_3 to the R compartment, respectively. The second is treatment success, in which infectious individuals adhere to therapy, achieving outcomes classified as cured or treatment completed. This condition is denoted by δ_1 , δ_2 , and δ_3 from I_1 , I_2 , and I_3 to the R compartment, respectively. The latter pathway reflects clinical success contingent on strict adherence to prescribed regimens, ensuring the elimination of the pathogen or completion of the treatment protocol. This dual mechanism highlights the roles of natural immunity and healthcare efficacy in reducing the infected population.

Infectious individuals with DS-TB can progress to MDR-TB and XDR-TB. Likewise, Infectious individuals with MDR-TB can progress to XDR-TB due to inadequate treatment, leading to the development of antibiotic resistance in the TB bacteria. Infectious individuals with MDR-TB can then further develop into XDR-TB if second-line drugs are misused or if the patient does not comply with the treatment regimen. Limited diagnostics, delayed treatment, and fragmented healthcare systems exacerbate this cycle (27). In this model, progression from DS-TB to MDR-TB and XDR-TB is represented by γ_1 and γ_3 , respectively, and from MDR-TB to XDR-TB by γ_2 .

Relapse, a critical feature of TB epidemiology, is explicitly integrated into the Epidemic model in this study to reflect the heightened risk of reinfection or reactivation among individuals who have previously recovered from TB. Unlike diseases that confer lifelong immunity, TB is characterized by the absence of permanent immune protection, meaning Recovered individuals (R) remain vulnerable to reinfection or recurrence of latent infection. This phenomenon is central to the model's realism, as relapse significantly sustains TB transmission in endemic regions.

There are two kinds of relapses as parameters, namely Loss of immunity (φ) and Direct Reactivation ($\theta_1, \theta_2, \theta_3$). Loss of Immunity (φ) is the rate at which recovered individuals gradually lose partial immunity over time, reverting to the susceptible individual (S). This transition acknowledges that immunity wanes, leaving individuals prone to new exposures and reinfection. Direct reactivation ($\theta_1, \theta_2, \theta_3$) is the rate at which recovered individuals may experience relapse without re-entering the susceptible stage, transitioning directly back into the infectious compartments (I_1, I_2, I_3) at strain-specific rates $\theta_1, \theta_2, \theta_3$. This pathway captures the reactivation of latent TB infection (LTBI) or treatment-incomplete recovery, where residual bacteria resurge, leading to active disease.

In this epidemic model, Λ is the natural birth rate. We divide the death rate into two components: μ is the natural death rate in susceptible, vaccinated, exposed, and recovered individuals. μ_t is the rate of death that occurs before or during treatment in infectious individuals. This study will develop a mathematical model in epidemiology based on the SVEIRS model. Based on all our assumptions, the study evolved and partitioned the model into nine compartments according to their epidemiological status, representing each population group. The nine compartments are susceptible, vaccinated, exposed for DS-TB, exposed for MDR-TB, exposed for XDR-TB, DS-TB, MDR-TB, XDR-TB, and the recovered compartment. Compartments (e.g., S, V, R) define the model's conceptual stages of disease progression, while state variables (e.g., $S(t), V(t), R(t)$) quantify the population size in each compartment over time, evolving via parameters and differential equations. Furthermore, $N(t)$ is the total population size at time t , and therefore, the study has:

$$N(t) = S(t) + V(t) + E_1(t) + E_2(t) + E_3(t) + I_1(t) + I_2(t) + I_3(t) + R(t) \quad (1)$$

Based on these assumptions, the study constructed a flowchart for TB transmission, as shown in Figure 1, to visualize the progression of individuals across epidemiological compartments.

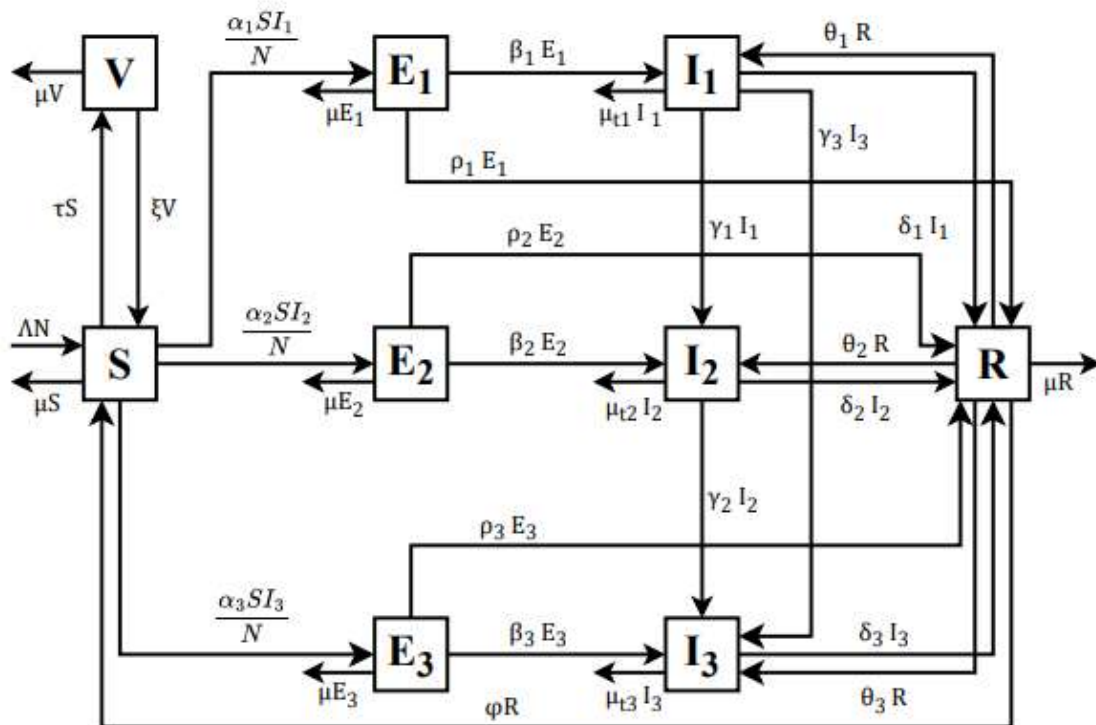


Figure 1. Flowchart of TB Transmission using SV3E3IR Compartment

Further, another assumption in the model is that the rate of increase of any state is equal to the number entering into the state minus the number leaving the state per unit time. Based on the assumption, we formulate the epidemic model as follows.

$$\frac{dS}{dt} = \lambda N + \xi V + \varphi R - \frac{S}{N} \sum_{i=1}^3 \alpha_i I_i - \mu S - \tau S \quad (2)$$

$$\frac{dV}{dt} = \tau S - V(\xi + \mu) \quad (3)$$

$$\frac{dE_1}{dt} = \frac{\alpha_1 S I_1}{N} - E_1(\beta_1 + \rho_1 + \mu) \quad (4)$$

$$\frac{dE_2}{dt} = \frac{\alpha_2 S I_2}{N} - E_2(\beta_2 + \rho_2 + \mu) \quad (5)$$

$$\frac{dE_3}{dt} = \frac{\alpha_3 S I_3}{N} - E_3(\beta_3 + \rho_3 + \mu) \quad (6)$$

$$\frac{dI_1}{dt} = \beta_1 E_1 + \theta_1 R - I_1(\delta_1 + \gamma_1 + \gamma_3 + \mu_{t1}) \quad (7)$$

$$\frac{dI_2}{dt} = \beta_2 E_2 + \theta_2 R + \gamma_1 I_1 - I_2(\delta_2 + \gamma_2 + \mu_{t2}) \quad (8)$$

$$\frac{dI_3}{dt} = \beta_3 E_3 + \theta_3 R + \gamma_3 I_1 + \gamma_2 I_2 - I_3(\delta_3 + \mu_{t3}) \quad (9)$$

$$\frac{dR}{dt} = \sum_{i=1}^3 (\delta_i I_i + \rho_i E_i) - R(\varphi + \sum_{i=1}^3 \theta_i + \mu) \quad (10)$$

In study work, all parameters in the epidemic model are positive constants except for the Gaussian noise. This epidemic model integrates Gaussian noise, a parameter that randomizes normally distributed fluctuations with zero mean, only into the exposed compartments (E_1, E_2, E_3) to account for real-world unpredictability in TB transmission. The value of gaussian noise were not chosen arbitrarily but were calibrated based on normal condition in real life where it references to using normal distribution (Gaussian distribution). It is defined by two parameters: the mean (average) and the standard deviation (spread or variability). Statistically, this noise introduces variability into differential equations, mimicking uncertainties like underreported latent infections, diagnostic inconsistencies, or environmental factors. Epidemiologically, it reflects challenges in detecting LTBI, where asymptomatic individuals often evade surveillance due to limited testing, healthcare access barriers, or silent disease progression.

In practice, Gaussian noise captures hidden dynamics: random spikes may represent undetected LTBI clusters, while dips could signal temporary improvements in screening. It also models biological heterogeneity (e.g., immune response variability) and behavioral factors (e.g., irregular contact patterns) that deterministic models oversimplify. In this epidemic model, Gaussian noise is symbolized by ε . Based on this concept, this epidemic model uses Stochastic principles. Stochastic principles refer to using probability and random processes in modeling and understanding phenomena where outcomes are not predetermined but depend on chance or randomness. It is a fundamental concept used in various fields to describe and predict the behavior of systems over time, even when unpredictable factors influence those systems. This stochastic term modifies their differential equations:

$$\frac{dE_i}{dt} = \frac{\alpha_i S I_i}{N} - E_i(\beta_i + \rho_i + \mu - \varepsilon); \quad (i = 1, 2, 3) \quad (11)$$

Initial Values of State Variables and Parameters

The initial value of state variables and parameters used in this study are obtained from a literature review, including research articles, books, reports, and other studies related to the study as close to Indonesia's condition as possible. The initial values of each compartment used in the study can be seen in Table 1. Some initial values of the state variable in the model are calculated through estimation. Using WHO's report, the number of DS-TB individuals (I_1) is obtained by calculating total infectious individuals less the number of MDR-TB individuals and the number of XDR-TB individuals ($I_1 = I - I_2 - I_3$). The number of each type of exposed individual is calculated by the proportion

of each infectious compartment multiplied by the number of the exposed individuals as follows: $E_1 = (E \times \text{proportion of DS-TB in infectious individuals})$, $E_2 = (E \times \text{proportion of MDR-TB in infectious individuals})$, $E_3 = (E \times \text{proportion of XDR-TB in infectious individuals})$. Additionally, the number of susceptible individuals (S) is estimated based on the calculation of total population less the number of vaccinated individuals, the number of exposed individuals, infectious individuals, and recovered individuals, as follows: $S = N - V - E - I - R$.

Table 1. Initial values of state variables for TB disease transmission in Indonesia

No.	Symbol	Value*	Reference
1	S	156,288,179	Data fitted
2	V	3,069,255	(28)
3	E	120,000,000	(3), (29)
4	E_1	116,633,945	Data fitted
5	E_2	3,302,752	Data fitted
6	E_3	63,303	Data fitted
7	I	1,090,000	(3)
8	I_1	1,059,425	Data fitted
9	I_2	30,000	(3)
10	I_3	575	(3)
11	R	552,566	(30)
12	N	281,000,000	(3)

*The unit of state variable is the number of individuals

Some parameters in the model were calculated through estimation because data were not available. Those parameters were derived from a combination of sources to accurately reflect the epidemiological context of Indonesia. Primary data were sourced from the World Health Organization (WHO) Global Tuberculosis Reports (3), BPS-Statistics Indonesia (31) and a literature (32). According to the pathogenesis of TB, infectious individuals can infect up to 10-15 other people in the course of a year (33). Based on this statement, the infection rate of susceptible individuals to each exposed individual was calculated by the number of each infectious individual multiplied by 15 and divided by the number of susceptible individuals as follows: $\alpha_1 = (I_1 \times 15) / S$, $\alpha_2 = (I_2 \times 15) / S$, and $\alpha_3 = (I_3 \times 15) / S$. Then, the loss-of immunity rate (φ) is estimated based on the calculation of 1 minus the death rate in R compartment, relapse rate for DS-TB, relapse rate for MDR-TB and relapse rate for XDR-TB as follows: $\varphi = 1 - \mu - \theta_1 - \theta_2 - \theta_3$.

Finally, the Gaussian noise in the system is described through the Gaussian noise parameters ($\varepsilon_1, \varepsilon_2, \varepsilon_3$), which are generated using the normal distribution $X \sim N(\mu = 0, \sigma^2 = 0.01^2)$. The Gaussian noise parameters use $\mu = 0$ and $\sigma = 0.01$ to introduce controlled, unbiased randomness (e.g., undetected TB cases or measurement errors) while minimizing disruption to core TB transmission dynamics. The zero mean avoids systematic bias, and the small variance reflects realistic data variability (e.g., inconsistent case detection, healthcare access, or other reasons) without obscuring deterministic trends. This balance preserves model interpretability for policy analysis while aligning with stochastic modelling standards that simulate background uncertainty in complex systems. The parameter values in Table 2 provide information on parameters to support the simulation and analysis of the epidemic model of TB spread in Indonesia in order to understand the epidemic dynamics and evaluate effective health intervention strategies.

Table 2. Initial values of parameters for TB disease transmission in Indonesia

No.	Symbol	Value	References
1	Λ	0.1659	(31)
2	μ	0.0592	(31)
3	τ	0.019268	(32)
4	ξ	0.066667	(32)
5	α_1	0.1017	Data fitted
6	α_2	0.0029	Data fitted
7	α_3	0.0001	Data fitted

8	$\beta_1, \beta_2, \beta_3$	0.003	(34)
9	γ_1	0.05	(35)
10	γ_2	0.1	(35)
11	γ_3	0.05	(35)
12	δ_1	0.87	(3)
13	δ_2	0.57	(3)
14	δ_3	0.49	(3)
15	$\theta_1, \theta_2, \theta_3$	0.008843	(32)
16	ρ_1, ρ_2, ρ_3	0.787718	(32)
17	φ	0.914271	Data fitted
18	μ_{t1}	0.2	(35); (36)
19	μ_{t2}	0.4	(35); (36)
20	μ_{t3}	0.6	(35); (36)
21	$\varepsilon_1, \varepsilon_2, \varepsilon_3$	$X \sim N(\mu = 0, \sigma^2 = 0.01^2)$	Data fitted.

Note: the unit of parameter is the number of individuals

The SVE3I3R model simulations were solved using the Fourth-order Runge-Kutta (RK4) method for numerical integration, chosen for its high accuracy and computational efficiency in handling differential equations. Analyses and visualizations were performed in R-4.5.1 software, utilizing *the deSolve* packages and modified R programming syntax to manage stochastic components, illustrate transmission trends, and generate uncertainty bands simulations. The iterative estimation of TB incidence for 2024 to 2030 employed convergence criteria ($\Delta \leq 1 \times 10^{-4}$), where simulations halted when compartmental differences between consecutive iterations fell below this threshold. The system of stochastic differential equations was solved numerically using the RK4 method with a fixed time step of $\Delta \leq 1 \times 10^{-4}$ months. Convergence of the numerical solution was evaluated by monitoring the stability of the cumulative incidence trajectories. We tested smaller time steps and observed that the resulting trajectories for all compartments deviated by convergence criteria, confirming that our chosen step size provided a stable and convergent solution. Parameters were calibrated against epidemiological data to ensure accuracy, while the 85-month study period, starting in December 2023, using initial values and January 2024 until December 2030, based on simulation values, provided a structured timeline for evaluating the trend of TB Transmission. This systematic workflow combines RK4 precision, R-based analytics, iterative validation, and parameter calibration to ensure reproducible, policy-aligned insights into TB dynamics, adhering to robust epidemiological and computational standards.

Ethical Approval

This study did not involve human participants or animal subjects. As such, ethical approval was not required for this study.

RESULTS

The ODE system developed in this study was solved using the fourth-order Runge-Kutta (RK4) method in R software to calculate compartmental changes over time. This method was selected for its ability to provide highly accurate numerical solutions. The process was conducted iteratively to estimate the TB incidence rate from December 2023 to December 2030. The iterative process continued until a convergence criterion was met, signifying that the simulation results showed no significant changes between consecutive iterations. Convergence was assessed by calculating the difference between the previous and current iteration for each compartment in the SVE3I3R model. The iteration was halted after a maximum of 10 runs or once the minimum value of all these compartment differences was greater than or equal to zero. This process achieved a high degree of accuracy, with a Δ value of 1.29×10^{-5} , well below the termination criterion of 1×10^{-4} .

Furthermore, Gaussian noise was incorporated into the model via the epsilon parameters ($\varepsilon_1, \varepsilon_2, \varepsilon_3$) for the exposed compartment (E). A preliminary statistical summary of this noise (Table 3) indicates stable and controlled fluctuations. All three parameters have means close to zero and low standard deviations, confirming a symmetrical distribution with minimal variation. The interquartile ranges (IQR) are narrow, further reflecting this stability, though ε_3 exhibits a slightly wider range. For instance, the graph for ε_1 (representing exposed individuals for DS-TB) shows

values fluctuating between $9,90 \times 10^{-8}$ and $1,93 \times 10^{-5}$ from 2023 to 2030. These controlled dynamics likely reflect random variations influenced by external factors like health policies, yet they remain within manageable limits, indicating overall model stability.

Table 3. Summary Statistics of Gaussian Noise in exposed compartments

Parameter	Min	Mean	Max	SD	IQR
Gaussian Noise 1 (ε_1)	$9,90 \times 10^{-8}$	$5,63 \times 10^{-6}$	$1,93 \times 10^{-5}$	$4,58 \times 10^{-6}$	$6,26 \times 10^{-6}$
Gaussian Noise 2 (ε_2)	$1,00 \times 10^{-8}$	$5,90 \times 10^{-6}$	$2,09 \times 10^{-5}$	$4,81 \times 10^{-6}$	$5,78 \times 10^{-6}$
Gaussian Noise 3 (ε_3)	$2,47 \times 10^{-7}$	$6,35 \times 10^{-6}$	$1,92 \times 10^{-5}$	$4,35 \times 10^{-6}$	$5,66 \times 10^{-6}$

Min is the minimum value; mean is the average value; max is the maximum value; SD is the standard deviation value; IQR is the interquartile range value.

Furthermore, the Gaussian noise 2 graph, which is related to exposed individuals for MDR-TB, shows greater fluctuations with a range of values from approximately $1,00 \times 10^{-8}$ to $2,09 \times 10^{-5}$. This more frequent and sharp fluctuation pattern indicates more significant differences in the number of exposed individuals for MDR-TB. This may be due to more complex challenges in controlling the spread of MDR TB, such as higher drug resistance, limited access to effective treatment, or lack of early detection. This instability emphasizes the need for more effective and responsive strategies in dealing with the spread of MDR-TB. The Gaussian noise 3 graph, which reflects exposed individuals for XDR-TB, shows a fluctuation range of approximately $2,47 \times 10^{-7}$ to $1,92 \times 10^{-5}$. Despite the variation, the fluctuations in Gaussian noise 3 indicate that the number of exposed individuals for XDR-TB experiences random dynamics that remain within more controlled limits than MDR-TB. This may reflect the success of stricter control efforts or more specific interventions against the spread of XDR TB. This relative stability may also be due to greater awareness of the dangers of XDR-TB and more effective prevention efforts. The visualization of the distribution of each Gaussian noise is illustrated in Figure 2.

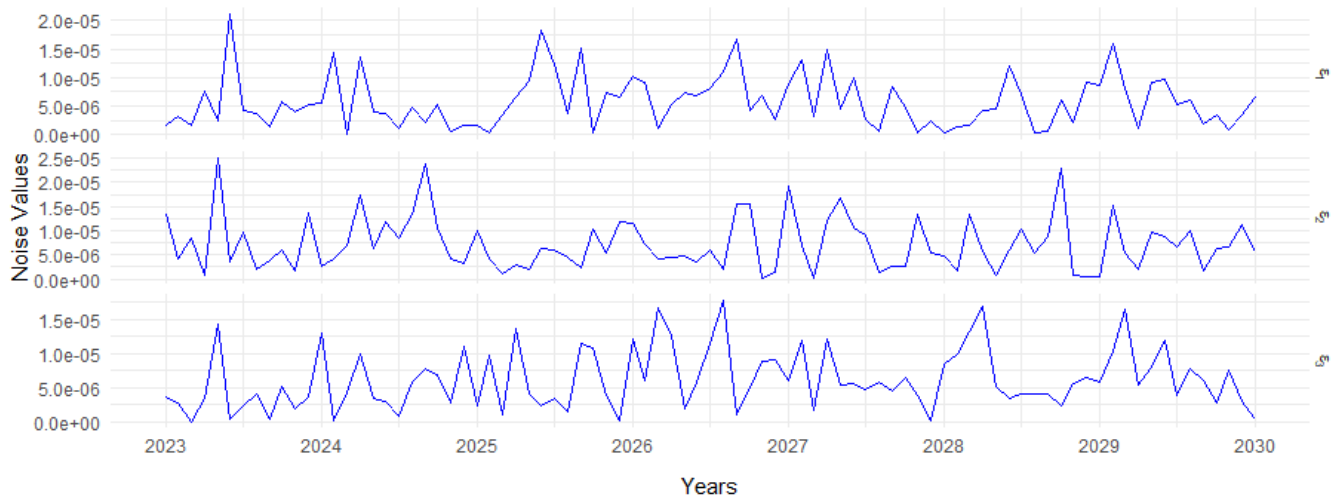


Figure 2. The visualization of the distribution of each Gaussian noise from December 2023 to 2030

The study estimated the population size for each compartment in Indonesia based on the SVE3I3R model. Table 4 and Figure 3 present descriptive statistics summarizing statistics and visualizations from December 2023 to December 2030 for each compartment. This information provides critical insights into the projected dynamics of Indonesia's TB epidemic.

Table 4. Summary statistics for each compartment (in individuals)

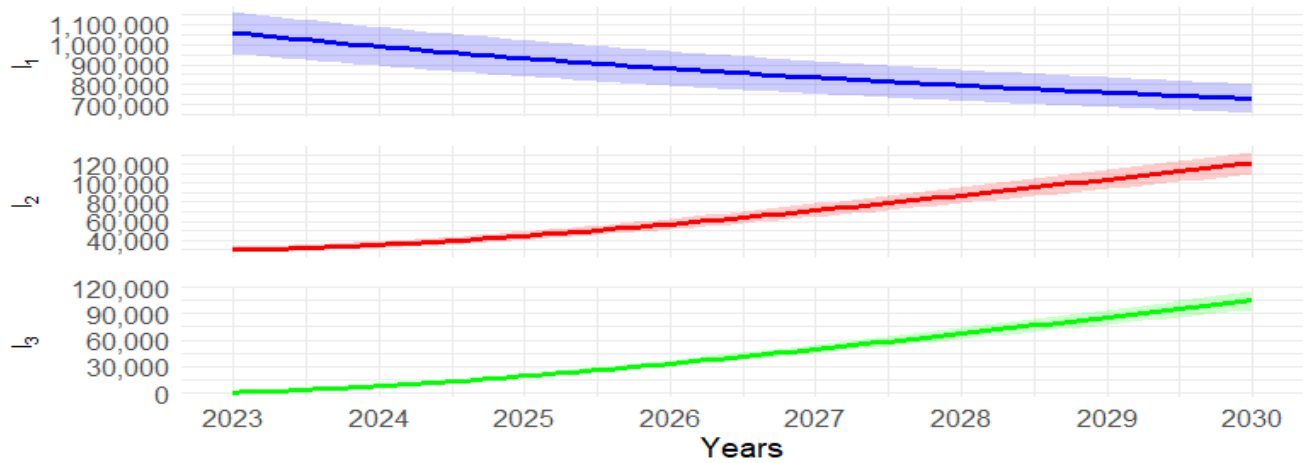
Symbol	Min	Mean	Max	SD	IQR
S	156,288,179	167,626,783	181,711,340	7,602,624	12,955,962
V	3,069,255	6,128,972	9,306,955	1,830,124	3,074,421
E_1	71,067,374	91,998,874	116,633,945	13,363,925	22,273,395
E_2	2,011,831	2,604,802	3,302,752	378,605	631,006
E_3	38,561	49,926	63,303	7,257	12,094
I_1	730,283	869,777	1,059,425	95,663	155,962
I_2	30,000	67,852	120,939	28,137	49,093
I_3	575	45,132	104,651	31,944	55,516
R	552,566	199,88,739	32,828,936	9,448,065	15,300,228

Min is the minimum value; mean is the average value; max is the maximum value; SD is the standard deviation value; IQR is the interquartile range value.

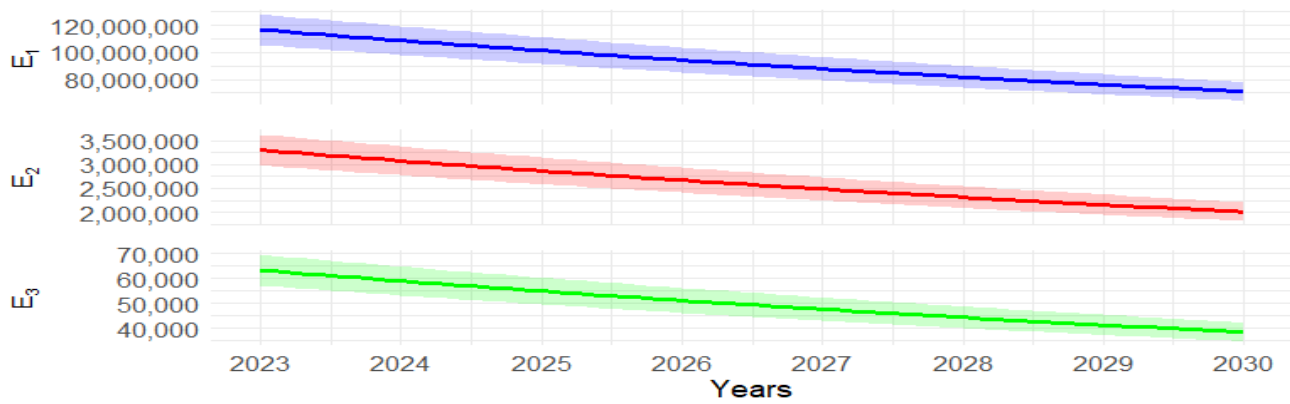
The population distribution across model compartments is visualized in Figure 3. Subfigure 3(a) illustrates the projected number of infectious individuals with TB, categorized as DS-TB (I_1), MDR-TB (I_2), and XDR-TB (I_3) from December 2023 to December 2030, revealing significant epidemiological shifts. DS-TB cases (I_1) show a promising decline from approximately 1,059,425 to 730,283 individuals, with a standard deviation of 95,663, indicating the success of current treatment and prevention protocols. In contrast, MDR-TB cases (I_2) are projected to rise sharply from 30,000 to 120,939 individuals (SD: 28,137), likely due to treatment non-adherence or limited therapy access. Most alarmingly, XDR-TB cases (I_3) are predicted to surge from 575 to 104,651 individuals (SD: 31,944), signaling an urgent public health crisis. While the reduction in DS-TB is encouraging, the dramatic increase in drug-resistant variants underscores the critical need for a more integrated approach, including improved diagnostics, enhanced treatment adherence strategies, and the development of new therapies.

Furthermore, the dynamics within the exposed compartments are detailed in Figure 3(b), which shows a decrease in individuals exposed to each TB category. The number of exposed individuals for DS-TB (E_1) is projected to fall from 116,633,945 to 71,067,374 (SD: 13,363,925), indicating the effectiveness of interventions like vaccination. Those exposed to MDR-TB (E_2) decreased from 3,302,752 to 2,011,831 (SD: 378,605), demonstrating successful though complex prevention efforts. Similarly, individuals exposed to XDR-TB (E_3) declined from 63,303 to 38,561 (SD: 7,257), a positive trend albeit at a slower rate. Overall, the decline across all exposed categories reflects successful prevention; however, the persistently high numbers, especially for DS-TB, coupled with the complexity of drug-resistant strains, demand more massive and sustainable interventions to ensure future TB control.

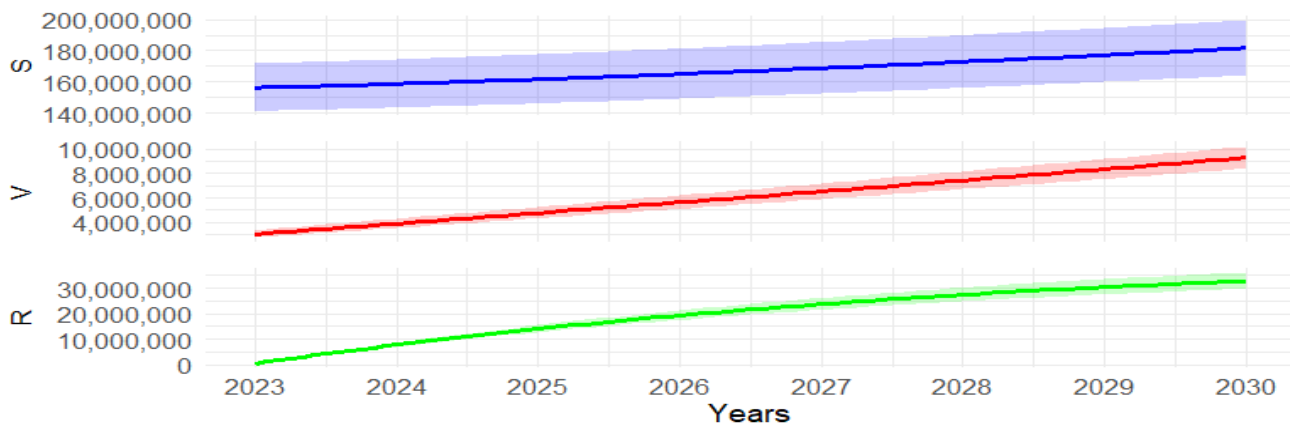
Finally, Figure 3(c) depicts the dynamics of susceptible (S), vaccinated (V), and recovered (R) populations. The susceptible individuals (S) are projected to grow from 156,288,179 to 181,711,340, indicating that despite successful interventions, a large at-risk pool remains, necessitating ongoing prevention measures. The vaccinated individuals (V) show substantial growth from 3,069,255 to 9,306,955, highlighting the success of vaccination programs in expanding protection. Meanwhile, the recovered compartment (R) is forecast to increase dramatically from 552,566 to 32,828,936, reflecting TB's effective treatment and case management. These trends collectively indicate positive progress in TB control, though continued efforts are essential to expand vaccination coverage and ensure effective treatment reaches all at-risk groups. In this model, uncertainty intervals for each compartment are represented by the shadows around the line at each time point. The purpose of uncertainty intervals is to show the range of likely values for a prediction or measurement at each point in time, indicating the degree of doubt or variability in the data.



(a)



(b)



(c)

Figure 3. (a) The number of individuals for all infectious individuals ($I_1 - I_3$), (b) the number of individuals for all exposed individuals ($E_1 - E_3$), (c) the number of individuals for susceptible, vaccinated individuals, and recovered individuals (S, V, R)

The SVE3I3R model is designed to capture the random fluctuations in epidemiological data that deterministic TB models cannot address. Simulation results from this model, detailed in Table 5, indicate a downward trend in the TB incidence rate. Specifically, the incidence rate is projected to decline from 387 cases per 100,000 population in 2023 to 320 cases per 100,000 by 2030. Despite this positive trend, the projected figures remain critically high. As illustrated in Figure 4, the 2030 prediction of 320 cases per 100,000 population falls drastically short of the national elimination target of 65 cases per 100,000, as mandated by Indonesia's Presidential Regulation No. 67 of 2021. This significant gap indicates that the current rate of decline is insufficient to meet the national objective.

Table 5. Estimation of TB incidence rate based on the SVE3I3R Model

Year	Total Population	Total Infected Individuals	Proportion in 100.000
2023	281,000,000	1,090,000	387
2024	283,357,928	1,034,191	364
2025	285,735,825	995,591	348
2026	288,133,508	970,718	336
2027	290,550,790	956,613	329
2028	292,987,817	950,778	324
2029	295,444,478	951,116	321
2030	297,920,867	955,872	320

Consequently, achieving the 2030 target will require additional strategies, an intensification of existing intervention programs, and a strengthened commitment to TB prevention and treatment efforts beyond the current trajectory.

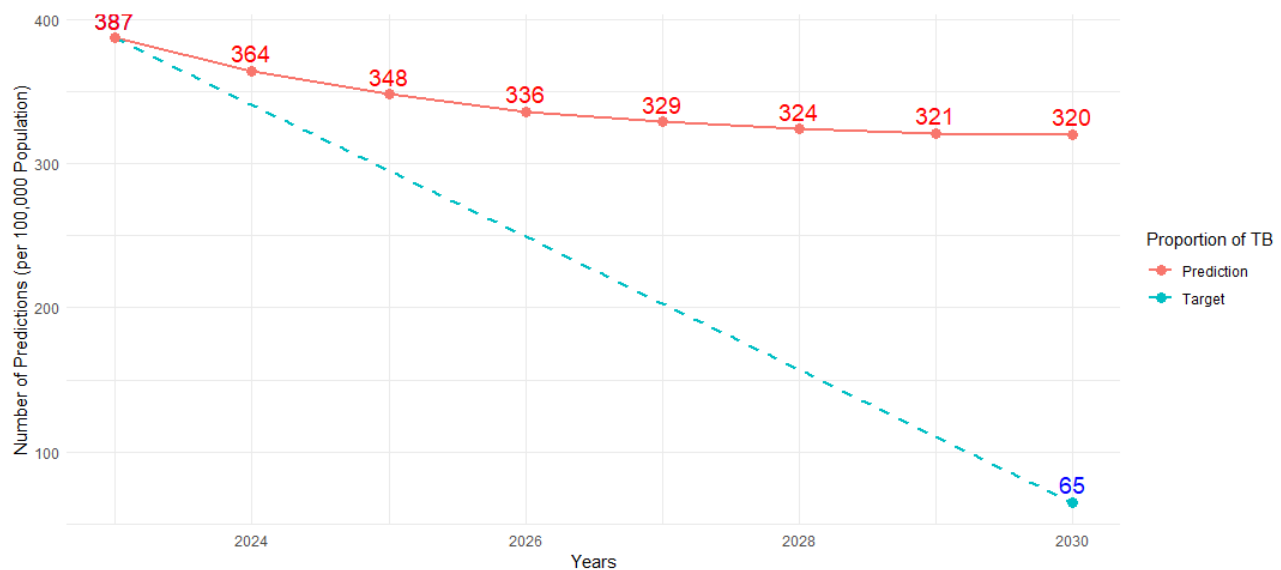


Figure 4. Evaluation of TB incidence rates in Indonesia based on the SVE3I3R Model

DISCUSSION

This study employed a stochastic SVE3I3R model integrated with Gaussian noise to project TB incidence in Indonesia from 2023 to 2030. The results indicate a gradual decline in TB incidence, from 387 cases per 100,000 population in 2023 to 320 per 100,000 by 2030. However, this projection falls significantly short of Indonesia's national elimination target of 65 cases per 100,000, as outlined in Presidential Regulation No. 67 of 2021. This situation generally means that Indonesia may also be unable to meet the WHO's End TB 2030 target to drastically reduce the global tuberculosis epidemic, aiming for an 80% reduction in TB incidence and a 90% reduction in TB

deaths compared to 2015 levels, given that Indonesia is one of the countries contributing to the global burden of TB cases (37). Notably, while DS-TB cases are projected to decrease, MDR-TB and XDR-TB cases show alarming increases, highlighting a critical shift in the epidemiological burden. The model also captured substantial variability in exposed compartments due to Gaussian noise, reflecting real-world uncertainties in LTBI detection and reporting.

The findings suggest that current TB control strategies, though effective in reducing DS-TB incidence, are insufficient to curb the rise of drug-resistant strains or achieve elimination by 2030. This aligns with previous studies emphasizing the growing threat of MDR/XDR-TB in high-burden settings like Indonesia. For instance, similar modelling efforts in Thailand, China, and India also stressed the need for enhanced detection and treatment adherence to reduce transmission (38–40). However, our stochastic approach offers a more realistic representation of TB dynamics by incorporating variability often overlooked in deterministic models. The significant underperformance relative to national targets may be attributed to systemic challenges such as fragmented healthcare services, diagnostic delays, and suboptimal treatment completion rates. (41).

The SVE3I3R model developed in this study, with its integrated stochastic elements, provides a flexible framework that is potentially applicable to other high-burden TB settings sharing similar epidemiological profiles, such as India or the Philippines. The incorporation of Gaussian noise specifically enhances its relevance for contexts characterized by data uncertainty, underreporting, or variable surveillance systems. However, the model's specific projections are contingent on Indonesian parameters and should not be directly extrapolated. Successful application to other countries requires rigorous recalibration using local data on contextual factors including vaccination policies, demographic structure, and healthcare access to ensure the generation of meaningful and context specific insights.

The study reinforces the value of stochastic modelling in infectious disease epidemiology, particularly for diseases with latent phases and complex transmission dynamics like TB. By integrating Gaussian noise into exposed compartments, the model better captures the unpredictability of LTBI progression and detection, challenging the deterministic assumption that all parameters are fixed and known. This contributes to theoretical advances in compartmental modelling, supporting probabilistic approaches for more robust public health forecasting.

From methodological side, future research should expand this model to include socio-economic, behavioural, and environmental determinants of TB transmission. Integrating agent-based modelling or network-based approaches could further refine understanding of spatial and social heterogeneity in TB spread (42,43). Additionally, longitudinal studies are needed to validate the noise parameters and improve parameter estimation, especially for drug-resistant TB strains in high-burden settings like Indonesia (44). Research should also explore the impact of emerging interventions, such as new vaccines or shorter treatment regimens, within this stochastic framework. In detail, firstly, the impact of novel vaccine candidates or increased BCG coverage could be modeled by adjusting the vaccination rate (τ) and efficacy parameters, assessing their potential to accelerate progress toward elimination. Secondly, the effect of expanding active case-finding (ACF) strategies could be simulated by increasing the transition rates from exposed to infectious compartments (β_i), reflecting earlier detection and removal from the latent pool. Thirdly, integrating treatment adherence dynamics is crucial; this could be achieved by making treatment success rates (δ_i) a function of adherence support programs, allowing for the evaluation of interventions like video-observed therapy (VOT) or enhanced patient counseling. Implementing these extensions within the current stochastic framework would provide a powerful tool for comparing the cost-effectiveness and potential impact of various combination interventions against TB and drug-resistant TB in Indonesia. Furthermore, while stochastic models offer a more realistic representation by incorporating the inherent randomness in disease transmission. The choice of a numerical solver is critical for the validity of such stochastic simulations. Euler-Maruyama or Milstein schemes can be alternative numerical analysis beside RK4 to solve stochastic models for future research. Next, sensitivity analysis will be conducted in future work to apportion the variation in the stochastic model's outputs to their different sources of uncertainty. Lastly, the future work, the next study's novelty is primarily contextual rather than methodological. Comparative assessment against deterministic baselines would clarify the incremental insight afforded by stochastic modelling and substantiate the claim of conceptual advancement.

From a practical standpoint, our findings underscore the urgent need to strengthen MDR-TB/XDR-TB management through a multi-pronged strategy encompassing improved diagnostics, robust treatment adherence support, and rigorous infection control measures. To operationalise these recommendations, three key public health interventions are recommended by the WHO. One critical area is intensifying preventive measures. It aligns with the

strategic priority of active case finding and ensuring timely therapy. Furthermore, addressing the rise of drug resistance requires a direct focus on diagnostics (45). The second scenario modelled an expansion of rapid Drug Susceptibility Testing (DST) to reduce treatment delays. Together, these simulations provide quantitative support for a strategy that combines broad public health actions such as awareness campaigns to reduce stigma and encourage early care-seeking with targeted, high-impact clinical interventions. The data strongly suggest that immediate investment in scaling up both diagnostic and preventive services is essential to alter Indonesia's TB trajectory and accelerate progress toward elimination goals (46). Last, public health campaigns must also address misconceptions about TB and reduce stigma to encourage early care-seeking behaviour (47,48).

The significant gap between projected incidence and national targets calls for intensified policy action. Policymakers should increase funding for TB programs, enhance integration of TB services with primary healthcare, and expand access to molecular diagnostics and second-line drugs (49–51). Regulatory support for faster approval of new treatments and vaccines is also critical (52,53). Furthermore, inter-sectoral collaboration involving education, social welfare, and urban planning departments may help address the social determinants of TB (54,55).

This study has several limitations. First, parameter estimates were derived from literature and fitted data, which may not fully capture local heterogeneity. Second, the model assumed homogeneous mixing, ignoring spatial and social network effects. Third, Gaussian noise was applied only to exposed compartments, potentially underestimating variability in other states. Lastly, the model did not incorporate socio-economic factors or health system constraints, which could influence TB transmission and control. These limitations may introduce bias towards overoptimistic projections, particularly regarding the decline in DS-TB.

CONCLUSION

In conclusion, this study demonstrates that Indonesia is unlikely to achieve its TB elimination target by 2030, based on current strategies. The stochastic SVE3I3R model provided a realistic projection of TB trends, highlighting the persistent challenge of drug-resistant TB and the need for more aggressive interventions. Integrating Gaussian noise enhanced the model's ability to reflect real-world uncertainties, offering a valuable tool for future epidemiological assessments. These findings underscore the importance of reinforcing TB control efforts through research, policy, and practice to move closer to the goal of TB elimination. More effective health interventions, such as increased vaccination coverage, early detection, and better treatment, are urgently needed to approach the desired target.

AUTHOR'S CONTRIBUTION STATEMENT

NRS: Concepts, Design, Definition of intellectual content, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review; MR, MI, MM: Concepts, Design Data analysis, Statistical analysis, Manuscript preparation; LR, SM: Manuscript preparation and editing, Manuscript review; MINA, SS, NS: Manuscript preparation, Manuscript editing, Manuscript review;

CONFLICTS OF INTEREST

The authors have no conflicts of interest

DECLARATION OF GENERATIVE AI AND AI- ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

This manuscript was developed without using Generative AI or AI-assisted technologies at any stage. The writing, idea generation, image production, graphical elements, data collection, and analysis were all conducted manually.

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