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A Mathematical Modeling of Two-Strain Tuberculosis Transmission: Deterministic and Stochastic Approaches to Screening, Treatment, and Quarantine Strategies*

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Abstract This research observes the transmission dynamics of drug-sensitive tuberculosis (DS-TB), drug-resistant tuberculosis (DR-TB) and undiagnosed tuberculosis infections using deterministic and stochastic models. The study focuses on the impacts of contact rates, screening of latent individuals or high-risk groups, treatment, and quarantine measures on the basic reproduction rate (R_0) and the estimated number of infected individuals (m). The results show that undiagnosed infected individuals are the greatest factor on the spread of tuberculosis within the system, which emphasizes the importance of screening on latent individuals. Analysis on the effects of screening on latent individuals also emphasizes the importance of treatment and quarantine for both DS-TB and DR-TB infections, respectively. However, analysis on the effects of both treatment and quarantine states that relying on either treatment or quarantine efforts is not enough to stop the spread of the two-strain TB within the system; thus a combined strategies is required to help eradicate the disease.

Keywords Deterministic model, stochastic model, screening, treatment, quarantine

MSC(2010) 60G05, 60G07, 60J27, 60J28, 60J80, 65C40.

1. Introduction

Tuberculosis (TB) is one of the long-standing health problems faced by the global community. Despite being a preventable and curable disease, TB remains a major global health threat, causing significant morbidity and mortality around the world [1]. World Health Organization (WHO) reported in the Global Tuberculosis Report in 2022 that there were an estimated 969,000 tuberculosis (TB) cases in Indonesia.

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This makes Indonesia the second largest contributor to TB cases in the world after India [2].

Tuberculosis (TB) spreads from person to person through airborne particles containing *Mycobacterium tuberculosis* (MTB). This means that TB can be transmitted through the air when an infected person coughs, sneezes, or talks, releasing droplets that contain the bacteria. The bacteria can then be inhaled by a healthy person, leading to infection [3,4]. Once infected, TB bacteria can reside in the body without causing noticeable clinical symptoms, known as latent TB infection. However, the latent MTB bacteria can become active, which may take weeks, months, or even the entire lifetime of the infected person [4].

Drug-resistant TB is a significant threat to TB control globally, requiring effective treatment strategies to improve treatment outcomes and reduce mortality [5]. Drug-resistant TB (DR-TB), which is resistant to at least rifampicin and isoniazid, the two most potent first-line anti-TB drugs, is a particularly concerning form of drug-resistant and difficult-to-treat TB [5,6]. New prevention and treatment guideline options are being developed to address this challenge [5].

Mathematical modeling of tuberculosis (TB) transmission plays a crucial role in understanding the dynamics of the disease, offering valuable insights into its epidemiology and informing the development of effective control strategies. Over the past few decades, a diverse group of mathematicians, statisticians, and biologists have contributed to the establishment of various transmission dynamic models for TB [7–16].

By analyzing the dynamics of TB transmission and the impact of different interventions, mathematical models can help identify the most effective ways to prevent and treat TB and the optimal strategies for controlling the disease [6, 7]. For instance, Jinhui Zhang et al. [8] developed a mathematical model of tuberculosis (TB) transmission in China. The model is based on the data of TB incidence and mortality rates in China from 1990 to 2015. The article concluded that the mathematical model of TB transmission in China is a useful tool for understanding the dynamics of TB transmission and for evaluating the effectiveness of different control strategies. The model suggested that the transmission dynamics of TB in China are influenced by a variety of factors, including demographic and economic factors. The model also suggested that the control of TB in China will require a combination of treatment and control measures, as well as changes in demographic and economic factors [8].

Ayinla et al. [9] developed a mathematical model for TB that employs a compartmental approach, incorporating seven distinct classes: susceptible (S), vaccinated (V), exposed (E), undiagnosed infectious (I_1), diagnosed infectious (I_2), treated (T), and recovered (R). The model was designed to analyze the dynamics of TB transmission and evaluate the impact of various control strategies, such as vaccination, diagnosis, and treatment. Their stability analysis revealed that due to the occurrence of backward bifurcation, merely reducing the basic reproduction number below one ($R_0 < 1$) is insufficient to eradicate TB. The study underscored the necessity of high vaccination rates, effective diagnostic methods, and timely treatment to manage and control the TB epidemic. Prioritizing diagnosis over treatment is particularly emphasized, as early detection is crucial for effective disease management [9].

Kasbawati et al. [10] developed a deterministic model for TB infections and compared it with a continuous Markov chain model. The study aimed to analyze

TB transmission dynamics and evaluate the effectiveness of various control strategies [10]. A 6-compartment TB model, constructed by Kuddus et al. [11], focused on the epidemiology of tuberculosis (TB) in Bangladesh, particularly the dynamics between drug-susceptible (DS) and drug-resistant (DR) strains of *Mycobacterium tuberculosis* (MTB). The authors developed a two-strain TB model to describe the transmission dynamics and interactions between these strains within the population. The study highlighted the alarming rise of DR TB strains, exacerbated by inadequate or inappropriate treatments [11].

Moreover, a theoretical framework for TB control strategies was developed by Okolo Noah et al. [12] to investigate TB transmission dynamics by incorporating various control strategies such as testing, therapy, isolation, and treatment. The goal was to analyze the impact of these strategies on the spread of TB and determine optimal approaches to control the disease. Results showed that increasing testing and early detection significantly reduce the spread of TB by identifying and isolating infectious individuals quickly. Effective treatment further decreases TB prevalence, while implementing isolation measures for infectious individuals substantially reduces transmission rates. Combining these strategies is crucial for optimal TB control, emphasizing the need for an integrated approach to managing the disease effectively [12].

The public health emergency caused by tuberculosis (TB), especially two-strain TB, has had a serious impact on the world, especially in Indonesia. Based on the data from Indonesia's Informatics System for Tuberculosis (SITB), as of 2 October 2023, there were 64% of the 90% target confirmed TB cases. Treatment success for drug-sensitive TB (DS-TB) was 83% of the 90% target, and 54% of the 90% target for drug-resistant TB (DR-TB). Meanwhile, based on SITB data as of 6 October 2023, the achievement of Indonesia's TB preventive therapy administration was 1.9% (target 58%) for household contact cases, and in other risk groups, it was 2.1% (target 30%) [38]. This means that there is still a gap in TB case finding, treatment success, and TB preventive therapy provision [13].

One of the efforts needed to accelerate TB case finding is Active Case Finding (ACF) activities through active screening in the household contact population and close contacts. Furthermore, the primary factor hindering optimal TB management is the inadequate implementation of active TB screening tests for early detection. This deficiency has resulted in significant gaps in TB case finding and treatment success, highlighting the urgent need for improved strategies and interventions to combat the TB epidemic in Indonesia [3, 6, 9, 19, 26, 28–31].

This study will be focused on the critical gaps in TB case finding and treatment success that previous researchers have not thoroughly investigated. It becomes essential for developing more effective public health strategies. Based on the description of prior research and the challenges in implementing TB treatment, this study also aims to provide an alternative approach to unravel the complexity of disease management through epidemiological modeling. The expected outcomes are to demonstrate the effects of active TB screening efforts on latent individuals or high-risk groups and incorporate compartments for undiagnosed TB infections, treatment, and quarantine in the control of two-strain TB cases.

Since deterministic models have limitations regarding capturing the variation and uncertainty that become key characteristics of epidemiological models in populations, a stochastic epidemic model is necessary to account for variations in epidemic calculations from a probabilistic perspective. Deterministic models often fail to adequately represent the inherent randomness and unpredictability inherent in disease transmission processes, particularly when dealing with small populations or rare events. In contrast, stochastic models incorporate probability distributions to simulate the random nature of disease progression, allowing for a more realistic representation of the system's dynamics [17–21].

By incorporating stochasticity, researchers can better understand the likelihood of different outcomes, such as the probability of disease extinction or the expected number of infected individuals over time. This probabilistic approach provides a more comprehensive understanding of the epidemiological landscape and helps inform public health decision-making by quantifying the risks associated with various intervention strategies [19, 20, 22–25, 29].

A continuous-time stochastic process can be used to model the change in the number of infected individuals with a probabilistic perspective due to the inherent randomness and time-dependent nature of disease transmission. The spread of diseases such as tuberculosis can be viewed as a random event influenced by temporal variables, making it a stochastic process [10, 19, 22–25]. Therefore, we apply a deterministic and continuous-time Markov chain stochastic (CTMC) approach to this study. The continuous-time Markov chain stochastic (CTMC) approach is a valuable analytical tool for understanding the dynamics of two-strain TB disease spread.

This paper is organized as follows: in Section 2, we present the mathematical preliminaries and model derivation, laying the foundation for our analysis. Section 3 focuses on model analysis, where we explore the dynamics and implications of the proposed models. In Section 4, we conduct numerical simulations to illustrate the behavior of the models under various scenarios. Finally, we conclude our paper with some concluding remarks, summarizing our findings and discussing their significance in the context of tuberculosis transmission dynamics.

2. Mathematical preliminaries and model derivation

2.1. Mathematical preliminaries

Definition 2.1. (Allen [32]; Maliyoni et al. [36]) A multitype Galton-Watson branching process (GWbp) $\{\mathbf{I}(t)\}_{t=0}^{\infty}$ is a collection of vector random variables $\mathbf{I}(t)$, where each vector consists of k different types, $\mathbf{I}(t) = (I_1(t), I_2(t), \dots, I_k(t))$, and each random variable $I_i(t)$ has k associated offspring random variables for the number of offspring of type $j = 1, 2, \dots, k$ from a parent of type i.

Theorem 2.1. (Allen [32]; Maliyoni et al. [36]) *Let the initial sizes for each type of infected individuals be $I_i(0) = i_i$, $i = 1, 2, \dots, k$. Suppose that the generating functions f_i for each of the types k are non-linear functions of u_j with $f_i(0, 0, \dots, 0) > 0$. Also, suppose that the expectation matrix $\boldsymbol{M} = [m_{ji}] = \left.\frac{\partial f_i}{\partial u_j}\right|_{u=1}$ is an $n \times n$ non-*

negative and irreducible matrix, and $\rho(\boldsymbol{M})$ is the spectral radius of the matrix $\boldsymbol{M}$

$$M = \begin{pmatrix} \frac{\partial f_1}{\partial u_1} & \frac{\partial f_2}{\partial u_1} & \frac{\partial f_3}{\partial u_1} & \frac{\partial f_4}{\partial u_1} \\ \frac{\partial f_1}{\partial u_2} & \frac{\partial f_2}{\partial u_2} & \frac{\partial f_3}{\partial u_2} & \frac{\partial f_4}{\partial u_2} \\ \frac{\partial f_1}{\partial u_3} & \frac{\partial f_2}{\partial u_3} & \frac{\partial f_3}{\partial u_3} & \frac{\partial f_4}{\partial u_3} \\ \frac{\partial f_1}{\partial u_4} & \frac{\partial f_2}{\partial u_4} & \frac{\partial f_3}{\partial u_4} & \frac{\partial f_4}{\partial u_4} \end{pmatrix}.$$

(i) If $\rho(\boldsymbol{M}) < 1$ or $\rho(\boldsymbol{M}) = 1$ (subcritical and critical cases, respectively), then the probability of ultimate extinction is one:

$$\lim_{t\to\infty} Prob\{\boldsymbol{I}(t) = 0\} = 1.$$

(ii) If $\rho(\boldsymbol{M}) > 1$ (supercritical case), then the probability of ultimate disease extinction is less than one:

$$\lim_{t\to\infty} Prob\{\boldsymbol{I}(t) = 0\} = q_1^{i_1} q_2^{i_2} \cdots q_k^{i_k} < 1,$$

where $(q_1, q_2, \ldots, q_k)$ is the unique fixed point of the k offspring probability generating functions (pgf), $f_i(q_1, q_2, \ldots, q_k) = q_i$ and $0 < q_i < 1$, $i = 1, 2, \ldots, k$. The value of q_i is the probability of disease extinction for infectives of type i and the probability of an outbreak is approximately

$$1 - q_1^{i_1} q_2^{i_2} \cdots q_k^{i_k}.$$

The role of the stochastic threshold $\rho(M)$ is analogous to that of the basic reproduction number (R_0) in deterministic models. According to Maity and Mandal [35], it has been established that the deterministic threshold for disease extinction, R_0, and the stochastic threshold $\rho(M)$ satisfy a specific relationship: $R_0 < 1$ iff $\rho(M) < 1$; $R_0 = 1$ iff $\rho(M) = 1$; and $R_0 > 1$ iff $\rho(M) > 1$.

2.2. Model derivation

We developed a deterministic mathematical model to simulate the transmission of DS-TB and DR-TB between mutually exclusive compartments. We incorporated a quarantine compartment for DR-TB infections and a treatment compartment for DS-TB infections. Homogenous mixing of the population is assumed. The total population, denoted by $N(t)$, is divided into eight mutually exclusive classes, namely susceptible denoted by $S(t)$, latently infected denoted by $L(t)$, infectious DR-TB denoted by $I_R(t)$, infectious DS-TB denoted by $I_T(t)$, undiagnosed infectious denoted by $I_U(t)$, quarantined individuals denoted by $Q(t)$, treated individuals denoted by $T(t)$, and recovered individuals denoted by $R(t)$. Therefore, the total population size is given by

$$N = S(t) + L(t) + I_R(t) + I_U(t) + I_S(t) + Q(t) + T(t) + R(t), \quad \text{for all } t \geq 0. \quad (2.1)$$

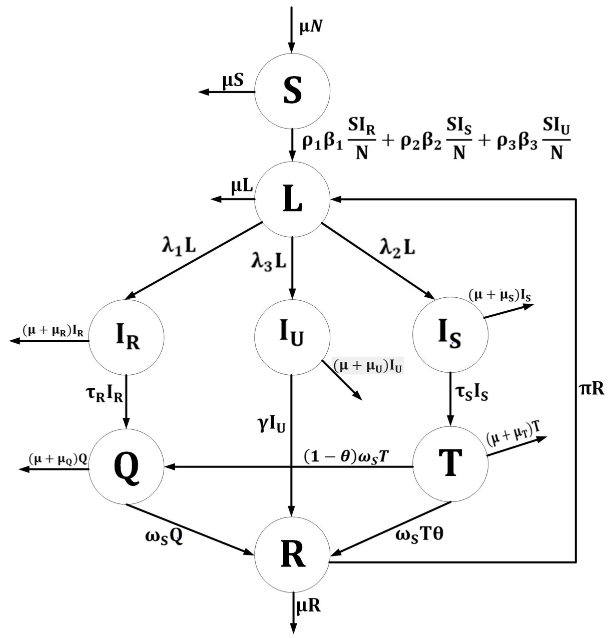


Figure 1. Transmission diagram of the TB compartmental mathematical model showing eight states. Here, N = Total population, S = Susceptible population, L = Latent population, I_R = Infected DR-TB, I_S = Infected DS-TB, I_U = Undiagnosed infectious TB, Q = Quarantined individuals, T = Treated individuals, R = Recovered population, μ = Birth rate / Death rate, ρ = Probability of infection, β_1 = Contact rate, λ = Screening rate, τ_R = Quarantine rate, μ_i = Disease-related death rate, τ_S = Treatment rate, ω = Recovery rate, θ = Proportion of amplification, γ = Rate of undiagnosed TB individuals cured, and π = Rate at which recovered individuals relapse or become latent individuals.

The dynamics of individual movement between classes in a disease transmission model are illustrated in a schematic diagram, as shown in Figure 1. Latent individuals are those who have not yet developed symptoms and whose infection status is unknown. They cannot transmit TB disease but are considered part of the high-risk group [4]. Individuals who are latently infected are often unaware of their condition and may only become aware after undergoing active TB screening. We assumed that DR-TB is initially generated by inadequate and poor treatment of DS-TB and could latently be transmitted to other individuals. Individuals may also return to the susceptible compartment following recovery at the constant per-capita rate (π) due to loss of immunity. The population grows at the recruitment rate μ, either through childbirth or immigration of uninfected individuals. Individuals in the different compartments suffer from natural death at the same constant rate μ, and active TB cases in $I_{i_{(i=R,S,U)}}$ experience disease-related death at a rate $\mu_{i_{(i=R,S,U)}}$ Additionally, deaths in the quarantine and treatment compartments can also be caused by disease at rates $\mu_{i_{(i=Q,T)}}$. After effective contact with an infectious individual, susceptible individuals $S(t)$ who contract TB are classified as latent $L(t)$. Latent individuals $L(t)$ undergo a screening to identify active TB patients and determine the type of TB variant that affects them. The screening rate is denoted by λ_i ($i = 1, 2, 3$). In practice, the TB screening process is imperfect due to various factors, leading to the formation of the undiagnosed TB infection compartment $I_U(t)$, which comprises latent TB patients who are not diagnosed at the rate of λ_3. Drug-sensitive TB ($I_S(t)$) and drug-resistant TB ($I_R(t)$) can eventually be detected and treated at rates τ_S and τ_R for DS-TB and DR-TB, respectively. Those with DR-TB should be quarantined to stop further spread and treated with second-line TB drugs for effective treatment. Meanwhile, patients with DS-TB should receive first-line TB drugs, which are typically more effective and have fewer side effects. A fraction (θ) of active treated DS-TB cases recover, transitioning to the recovered compartment $R(t)$. At the same time, the remaining portion develops drug resistance due to incomplete or non-compliant treatment and moves to the compartment $I_R(t)$. Thus, the TB model can be written as a system of differential equations with the form

$$
\begin{aligned}
\frac{dS(t)}{dt} &= \mu N - \mu S(t) - \left[\frac{\rho_1\beta_1 S(t) I_R(t)}{N} + \frac{\rho_2\beta_2 S(t) I_S(t)}{N} + \frac{\rho_3\beta_3 S(t) I_U(t)}{N}\right], \\
\frac{dL(t)}{dt} &= \left[\frac{\rho_1\beta_1 S(t) I_R(t)}{N} + \frac{\rho_2\beta_2 S(t) I_S(t)}{N} + \frac{\rho_3\beta_3 S(t) I_U(t)}{N}\right] \\
&\quad + \pi R(t) - [\mu + \lambda_1 + \lambda_2 + \lambda_3] L(t), \\
\frac{dI_R(t)}{dt} &= \lambda_1 L(t) - (\mu + \mu_R + \tau_R) I_R(t), \\
\frac{dI_U(t)}{dt} &= \lambda_3 L(t) - [\gamma + \mu + \mu_U] I_U(t), \\
\frac{dI_S(t)}{dt} &= \lambda_2 L(t) + I_U(t) - (\mu + \mu_S + \tau_S) I_S(t), \\
\frac{dQ(t)}{dt} &= \tau_R I_R(t) + (1-\theta) T(t) - (\mu + \mu_Q + \omega_R) Q(t), \\
\frac{dT(t)}{dt} &= \tau_S I_S(t) - [\mu + \mu_T + \omega_S \theta + (1-\theta)] T(t), \\
\frac{dR(t)}{dt} &= \omega_R Q(t) + \gamma I_U(t) + \omega_S \theta T(t) - (\mu + \pi) R(t).
\end{aligned} \tag{2.2}
$$

Additionally, the initial conditions are given by

$$S(0) > 0, L(0) > 0, I_R(0) > 0, I_U(0) > 0, I_S(0) > 0, Q(0) > 0, T(0) > 0, R(0) > 0.$$

The model parameters are positive, and their description is presented in Table 1.

3. Model analysis

3.1. Basic properties of the model

First, we give some basic properties of the solution to model (2.2).

3.1.1. Positivity of the solution

Lemma 3.1. *The solutions $S(t)$, $L(t)$, $I_R(t)$, $I_U(t)$, $I_S(t)$, $Q(t)$, $T(t)$, $R(t)$ of the system (2.2) are positive for all $t \geq 0$, with given initial values $S(t) \geq 0, L(t) \geq 0, I_R(t) \geq 0, I_U(t) \geq 0, I_S(t) \geq 0, Q(t) \geq 0, T(t) \geq 0, R(t) \geq 0$.*

Table 1. Description of parameters used in the TB two-strain compartmental model.

Parameter	Description
μ	Birth rate or death rate per year
ρ_1	Probability of infection from I_R (dimensionless)
ρ_2	Probability of infection from I_S (dimensionless)
ρ_3	Probability of infection from I_U (dimensionless)
β_1	Contact rate or transmission rate from I_R per year
β_2	Contact rate or transmission rate from I_S per year
β_3	Contact rate or transmission rate from I_U per year
λ_1	Screening rate from L to I_R per year
λ_2	Screening rate from L to I_S per year
λ_3	Screening rate from L to I_U per year
π	Rate at which recovered individuals relapse or become latent individuals per year
μ_R	Disease-related death rate for I_R per year
μ_S	Disease-related death rate for I_S per year
μ_Q	Disease-related death rate for Q per year
μ_T	Disease-related death rate for T per year
τ_R	Quarantine rate for I_R per year
τ_S	Treatment rate for I_S per year
ω_R	Recovery rate for Q per year
ω_S	Recovery rate for T per year
γ	Rate of undiagnosed TB individuals cured per year
θ	Proportion of amplification (dimensionless)

Proof. Following [37], we have,

$$
\begin{aligned}
\left.\frac{dS(t)}{dt}\right|_{S(t)=0} &= \mu N \geq 0, \\
\left.\frac{dL(t)}{dt}\right|_{L(t)=0} &= \rho_1\beta_1\frac{S(t)I_R(t)}{N} + \rho_2\beta_2\frac{S(t)I_S(t)}{N} + \rho_3\beta_3\frac{S(t)I_U(t)}{N} + \pi R(t) \geq 0, \\
\left.\frac{dI_R(t)}{dt}\right|_{I_R(t)=0} &= \lambda_1 L(t) \geq 0, \\
\left.\frac{dI_U(t)}{dt}\right|_{I_U(t)=0} &= \lambda_3 L(t) \geq 0, \\
\left.\frac{dI_S(t)}{dt}\right|_{I_S(t)=0} &= \lambda_2 L(t) \geq 0, \\
\left.\frac{dQ(t)}{dt}\right|_{Q(t)=0} &= \tau_R I_R(t) + (1-\theta)T(t) \geq 0, \\
\left.\frac{dT(t)}{dt}\right|_{T(t)=0} &= \tau_S I_S(t) \geq 0, \\
\left.\frac{dR(t)}{dt}\right|_{R(t)=0} &= \omega_R Q(t) + \gamma I_U(t) + \omega_S\theta T(t) \geq 0.
\end{aligned}
\tag{3.1}
$$

Since equation (3.1) is all positive with initial values $S(t) \geq 0$, $L(t) \geq 0$, $I_R(t) \geq 0$, $I_U(t) \geq 0$, $I_S(t) \geq 0$, $Q(t) \geq 0$, $T(t) \geq 0$, $R(t) \geq 0$, the solutions $S(t)$, $L(t)$, $I_R(t)$, $I_U(t)$, $I_S(t)$, $Q(t)$, $T(t)$, $R(t)$ are positive for all $t \geq 0$. □

3.1.2. Boundedness of the solution

Lemma 3.2. *The solution $S(t), L(t), I_R(t), I_U(t), I_S(t), Q(t), T(t), R(t)$ of the system* (2.2) *is bounded to the feasible region Ω defined as follows:*

$$\Omega = \left\{(S(t), L(t), I_R(t), I_U(t), I_S(t), Q(t), T(t), R(t)) \in \mathbb{R}_+^8 \mid 0 \leq N(t) \leq N(0)\right\}.$$

Proof. Given the total population at time t, represented as:

$$N(t) = S(t) + L(t) + I_R(t) + I_U(t) + I_S(t) + Q(t) + T(t) + R(t),$$

we can derive the rate of change of the total population over time:

$$
\begin{aligned}
\frac{dN(t)}{dt} =& \mu N - \mu S(t) - \mu L(t) - [\mu + \mu_R]I_R(t) - [\mu + \mu_U]I_U(t) \\
&- [\mu + \mu_S]I_S(t) - [\mu + \mu_Q]Q(t) - [\mu + \mu_T]T(t) - \mu R(t).
\end{aligned}
$$

This equation accounts for the birth and death rates across different compartments of the TB model. The terms represent the natural death rate (μ) affecting each compartment, with additional rates for the infected compartments (I_R, I_U, I_S) and other states (Q, T, R). By simplifying the equation, we can express it as:

$$\frac{dN(t)}{dt} = -(\mu_R I_R(t) + \mu_U I_U(t) + \mu_S I_S(t) + \mu_Q Q(t) + \mu_T T(t)) \leq 0.$$

This indicates that the total population is either constant or decreasing over time, as the rates of infection and quarantine contribute to the loss of individuals from the population. From this, we can derive the bounds for the population:

$$0 \leq N(t) \leq N(0),$$

where

$$N(0) = S(0) + L(0) + I_R(0) + I_U(0) + I_S(0) + Q(0) + T(0) + R(0)$$

represents the initial population at time zero. Since $N(0)$ is constant, we can define the feasible region Ω of the system as follows:

$$\Omega = \{S(t), L(t), I_R(t), I_U(t), I_S(t), Q(t), T(t), R(t) \in \mathbb{R}^8_+ \mid 0 \leq N(t) \leq N(0)\}.$$

Thus, $\lim_{t\to\infty} \sup N(t) = N(0)$, which implies that the region Ω is a positive invariant set for system (2.2). Therefore, the model (2.2) is mathematically well-posed and epidemiologically meaningful. □

3.2. Equilibrium points of the system

This subsection discusses about the two possible equilibria of the model (2.2); the disease-free equilibrium and the endemic equilibrium. First, at the equilibrium, assume that:

$$\frac{dS(t)}{dt} = \frac{dL(t)}{dt} = \frac{dI_R(t)}{dt} = \frac{dI_U(t)}{dt} = \frac{dI_S(t)}{dt} = \frac{dQ(t)}{dt} = \frac{dT(t)}{dt} = \frac{dR(t)}{dt} = 0.$$

For the disease-free equilibrium, assume that no two-strain TB is present within the human population, i.e., $I_R = 0$, $I_U = 0$, and $I_S = 0$. Thus, we are left with a susceptible and recovered population from the model in Equation (2.2) and we get

$$S_0 = N.$$

Since $L = 0$, $I_R = 0$, $I_U = 0$, and $I_S = 0$, the disease-free equilibrium lies at the point

$$E_0 = (S_0, L_0, I_{R_0}, I_{S_0}, I_{U_0}, Q_0, T_0, R_0) = (N, 0, 0, 0, 0, 0, 0, 0). \tag{3.2}$$

Next, let $E_1 = (S_1^*, L_1^*, I_{R1}^*, I_{U1}^*, I_{S1}^*, Q_1^*, T_1^*, R_1^*)$ be the endemic equilibrium where I_R, I_U, and I_S are non-zero. Considering the system of equations (2.2), we have

$$\begin{aligned}
S_1^* &= \frac{\mu N}{\mu + \rho_1\beta_1 I_{R1}^* + \rho_2\beta_2 I_{S1}^* + \rho_3\beta_3 I_{U1}^*}, \\
L_1^* &= \frac{(\mu + \rho_1\beta_1 I_{R1}^* + \rho_2\beta_2 I_{S1}^* + \rho_3\beta_3 I_{U1}^*)S_1^* + \pi R_1^*}{\mu + \lambda_1 + \lambda_2 + \lambda_3}, \\
I_{R1}^* &= \frac{\lambda_1 L_1^*}{\mu + \mu_R + \tau_R}, \\
I_{U1}^* &= \frac{\lambda_3 L_1^*}{1 + \gamma + \mu + \mu_U}, \\
I_{S1}^* &= \frac{\lambda_2 L_1^*}{\mu + \mu_S + \tau_S}, \\
Q_1^* &= \frac{\tau_R I_{R1}^* + (1-\theta)T_1^*}{\mu + \mu_Q + \omega_R}, \\
T_1^* &= \frac{\tau_S I_{S1}^*}{\mu + \mu_T + \omega_S\theta + (1-\theta)}, \\
R_1^* &= \frac{\omega_R Q_1^* + \gamma I_{U1}^* + \omega_S\theta T_1^*}{\mu + \pi}.
\end{aligned}$$

For positive values of all parameters, then the endemic equilibrium E_1 exists within the feasible region Ω.

3.3. Basic reproduction number

The reproduction number of model (2.2) can be found by considering the latent and infectious compartments as follows

$$\begin{aligned}
\frac{dL(t)}{dt} &= [\rho_1\beta_1 x_3 + \rho_2\beta_2 x_5 + \rho_3\beta_3 x_4]\, x_1 + \pi x_8 - [\mu + \lambda_1 + \lambda_2 + \lambda_3]\, x_2,\\
\frac{dI_R(t)}{dt} &= \lambda_1 x_2 - (\mu + \mu_R + \tau_R)\, x_3,\\
\frac{dI_U(t)}{dt} &= \lambda_3 x_2 - (1 + \gamma + \mu + \mu_U)\, x_4,\\
\frac{dI_S(t)}{dt} &= \lambda_2 x_2 - (\mu + \mu_S + \tau_S)\, x_5.
\end{aligned} \tag{3.3}$$

Let $X = (L, I_R, I_U, I_S)^T$. Then system (2.2) can be written as

$$\frac{dX}{dt} = F(x) - V(x) \tag{3.4}$$

where

$$F(x) = \begin{pmatrix} F_1 \\ F_2 \\ F_3 \\ F_4 \end{pmatrix} = \begin{pmatrix} [\rho_1\beta_1 x_3 + \rho_2\beta_2 x_5 + \rho_3\beta_3 x_4]x_1 + \pi x_8 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \tag{3.5}$$

$$V(x) = \begin{pmatrix} V_1 \\ V_2 \\ V_3 \\ V_4 \end{pmatrix} = \begin{pmatrix} [\mu + \lambda_1 + \lambda_2 + \lambda_3]x_2 \\ (\mu + \mu_R + \tau_R)x_3 - \lambda_1 x_2 \\ [1 + \gamma + \mu + \mu_U]x_4 - \lambda_3 x_2 \\ (\mu + \mu_S + \tau_S)x_5 - \lambda_2 x_2 \end{pmatrix}, \tag{3.6}$$

where F is the appearance rate of new infection, and let V be the transfer rate of new infection into and out of the compartment. The Jacobian of F and V at the disease-free equilibrium $E_0 = (N, 0, 0, 0, 0, 0, 0, 0)$ are respectively

$$\mathrm{D}(F(E_0)) = \begin{pmatrix} 0 & \rho_1\beta_1 & \rho_3\beta_3 & \rho_2\beta_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$\mathrm{D}(V(E_0)) = \begin{pmatrix} \mu + \lambda_1 + \lambda_2 + \lambda_3 & 0 & 0 & 0 \\ -\lambda_1 & \mu + \mu_R + \tau_R & 0 & 0 \\ -\lambda_3 & 0 & 1 + \gamma + \mu + \mu_U & 0 \\ -\lambda_2 & 0 & 0 & \mu + \mu_S + \tau_S \end{pmatrix}.$$

Therefore, the reproduction number of model (2.2) denoted by R_0, is given by [39]

$$R_0 = \rho(FV^{-1}) = \frac{(\lambda_1\rho_1\beta_1)CD + \rho_3\beta_3(\lambda_3\mu + \lambda_3\mu_R + \lambda_3\tau_R)D + (\lambda_2\rho_2\beta_2)BC}{ABCD}, \tag{3.7}$$

with

$$
\begin{aligned}
A &= \mu + \lambda_1 + \lambda_2 + \lambda_3,\\
B &= \mu + \mu_R + \tau_R,\\
C &= 1 + \gamma + \mu + \mu_U,\\
D &= \mu + \mu_S + \tau_S.
\end{aligned}
$$

According to [39], the local stability of the disease-free equilibrium E_0 are stated in the following theorem.

Theorem 3.1. *The disease-free equilibrium E_0 is locally asymptotically stable when the basic reproduction number R_0 is less than 1, and it becomes unstable when R_0 is greater than or equal to 1.*

Theorem 3.1 is particularly relevant in two-strain tuberculosis (TB) models, where R_0 serves as a critical threshold for determining the potential for disease persistence in a population. In two-strain TB models, variations in transmission dynamics and treatment effectiveness can lead to differing values of R_0, which directly influences the stability of the disease-free equilibrium. When R_0 exceeds 1, it indicates a likelihood of ongoing transmission, resulting in instability of E_0, while $R_0 < 1$ suggests that the disease can be effectively controlled and will eventually die out.

3.4. CTMC stochastic model

3.4.1. Transition probability

The transition probability is the probability of a stochastic process moving from state i to state j. Here, the stochastic two-strain TB disease model consists of seven random variables, that is, $L(t)$, $I_R(t)$, $I_U(t)$, $I_S(t)$, $Q(t)$, $T(t)$, and $R(t)$ with the constant of the total population size $N(t)$. Thus, the variable $S(t)$ is determined by $S(t) = N(t) - L(t) - I_R(t) - I_U(t) - I_S(t) - Q(t) - T(t) - R(t)$. The modified model (2.2) is assumed to have Markov properties as follows

$$
\begin{aligned}
&\mathrm{Prob}\{L(t+\Delta t), I_R(t+\Delta t), I_U(t+\Delta t), I_S(t+\Delta t),\\
&Q(t+\Delta t), T(t+\Delta t), R(t+\Delta t) \mid L(0), I_R(0), I_U(0),\\
&I_S(0), Q(0), T(0), R(0), \ldots, L(t), I_R(t), I_U(t), I_S(t),\\
&Q(t), T(t), R(t)\}\\
&= \mathrm{Prob}\{L(t+\Delta t), I_R(t+\Delta t), I_U(t+\Delta t), I_S(t+\Delta t),\\
&Q(t+\Delta t), T(t+\Delta t), R(t+\Delta t) \mid (L(t), I_R(t), I_U(t), I_S(t),\\
&Q(t), T(t), R(t))\}.
\end{aligned}
\tag{3.8}
$$

The transition probability at time $(t + \Delta t)$ depends only on the process one-time step earlier, i.e. at time (t). Suppose an ordered pair $(L(t), I_R(t), I_U(t), I_S(t), Q(t), T(t), R(t)) = (a, b, c, d, e, f, g)$ and $(L(t+\Delta t), I_R(t+\Delta t), I_U(t+\Delta t), I_S(t+\Delta t), Q(t+\Delta t), T(t+\Delta t), R(t+\Delta t)) = (i, j, k, l, m, n, o)$, with $a, b, c, d, e, f, g = 0, 1, 2, \ldots$, then the displacement from state (a, b, c, d, e, f, g) to state (i, j, k, l, m, n, o) can be expressed as follows:

$$
\begin{aligned}
&\mathrm{Prob}_{(a,b,c,d,e,f,g),(i,j,k,l,m,n,o)}(t, t+\Delta t) = \mathrm{Prob}\{L(t+\Delta t) = i,\\
&I_R(t+\Delta t) = j, I_U(t+\Delta t) = k, I_S(t+\Delta t) = l, Q(t+\Delta t) = m,\\
&T(t+\Delta t) = n, R(t+\Delta t) = o \mid (L(t) = a, I_R(t) = b, I_U(t) = c,\\
&I_S(t) = d, Q(t) = e, T(t) = f, R(t) = g)\}.
\end{aligned}
\tag{3.9}
$$

Suppose an ordered pair is shown in the equation below:

$$
\mathrm{Prob}_{(a,b,c,d,e,f,g),(i,j,k,l,m,n,o)}(t,t+\Delta t) =
\begin{cases}
(\rho_1\beta_1\frac{SI_R}{N}+\rho_2\beta_2\frac{SI_S}{N}+\rho_3\beta_3\frac{SI_U}{N})\Delta t & \\
+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a+1,b,c,d,e,f,g),\\
(\mu L)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a-1,b,c,d,e,f,g),\\
((\lambda_1)L)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a-1,b+1,c,d,e,f,g),\\
((\lambda_3)L)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a-1,b,c+1,d,e,f,g),\\
((\lambda_2)L)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a-1,b,c,d+1,e,f,g),\\
(\pi R)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a+1,b,c,d,e,f,g-1),\\
((\mu+\mu_R)I_R)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b-1,c,d,e,f,g),\\
((1-\theta)\omega_S T)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d,e+1,f-1,g),\\
((\mu+\mu_U)I_U)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c-1,d,e,f,g),\\
(\gamma I_U)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c-1,d,e,f,g+1),\\
((\mu+\mu_S)I_S)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d-1,e,f,g),\\
(\tau_R I_R)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b-1,c,d,e+1,f,g),\\
((\mu+\mu_Q)Q)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d,e-1,f,g),\\
(\omega_R Q)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d,e-1,f,g+1),\\
(\tau_S I_S)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d-1,e,f+1,g),\\
((\mu+\mu_T)T)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d,e,f-1,g),\\
(\omega_S T\theta)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d,e,f-1,g+1),\\
(\mu R)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d,e,f,g-1),\\
(1-E)\Delta t+o(\Delta t), & \text{if } (i,j,k,l,m,n,o)=(a,b,c,d,e,f,g),\\
o(\Delta t), & \text{otherwise}
\end{cases}
\tag{3.10}
$$

where

$$
\begin{aligned}
\varepsilon = {} & \Lambda N+\mu S+\rho_1\beta_1\frac{SI_R}{N}+\rho_2\beta_2\frac{SI_S}{N}+\rho_3\beta_3\frac{SI_U}{N}+(\mu+\lambda_1+\lambda_2+\lambda_3)L\\
& +(\mu+\mu_R+\tau_R)I_R+(\mu+\mu_U+\alpha+\gamma)I_U+(\mu+\mu_S+\tau_S)I_S\\
& +(\mu+\mu_Q+\omega_R)Q+(\mu+\mu_T+\omega_R\theta+(1-\theta))T+(\mu+\pi)R.
\end{aligned}
$$

The transition probabilities of susceptible, infected, and quarantined individuals in the time interval $t+\Delta t$ only depend on time t, where $t \geq 0$. The time step value Δt is assumed to be very small, so the change that occurs in susceptible, infected, and quarantined individuals is the maximum of one individual in such a short time interval Δt. The value of $o(\Delta t)$ represents a small probability value and satisfies $\lim_{t\to\infty}\frac{o(\Delta t)}{\Delta t}=0$ [32].

3.4.2. Determination of outbreak probability

Outbreak events occur when the number of infected individuals increases over time. The basic reproduction number (R_0) and the expected number of infected individuals (m) are used as criteria for the occurrence of disease outbreaks in the long term. In general, the basic reproduction number (R_0) has a similar meaning as the expected number of infected individuals (m) that estimates the number of susceptible individuals getting infected after an infected individual is introduced into the system. In deterministic models, disease outbreak events occur when $R_0 > 1$. However, when R_0 is greater than 1, it cannot be ascertained that m is also greater than 1, although it may be true in some cases [41]. The values of R_0 and m are obtained with different approaches. The value of R_0 is calculated using the Next Generation method while for m value, the probability of disease outbreak and the probability of disease-free is determined using a branching process [32, 35] with a probability generating function (PGF) given as follows. Suppose $(u_1, u_2, u_3, u_4) = (L, I_R, I_U, I_S)$. The PGF for the latent class $L(t)$ with initial values $L(0) = 1$, $I_R(0) = 0$, $I_U(0) = 0$, and $I_S(0) = 0$ is

$$f_1(u_1, u_2, u_3, u_4) = \frac{\mu + \rho_1\beta_1 u_1 u_2 + \rho_3\beta_3 u_1 u_3 + \rho_2\beta_2 u_1 u_4}{\mu + \rho_1\beta_1 + \rho_3\beta_3 + \rho_2\beta_2}.$$

For the resistant infectious class $I_R(t)$ with initial values $L(0) = 0$, $I_R(0) = 1$, $I_U(0) = 0$, and $I_S(0) = 0$, the PGF is

$$f_2(u_1, u_2, u_3, u_4) = \frac{\mu + \mu_R + \tau_R + \lambda_1 u_2^2}{\mu + \mu_R + \tau_R + \lambda_1}.$$

For the undiagnosed infectious class $I_U(t)$ with initial values $L(0) = 0$, $I_R(0) = 0$, $I_U(0) = 1$, and $I_S(0) = 0$ is

$$f_3(u_1, u_2, u_3, u_4) = \frac{\gamma + \mu + \mu_U + \lambda_3 u_3^2}{\gamma + \mu + \mu_U + \lambda_3}.$$

For the sensitive infectious class $I_S(t)$ with initial values $L(0) = 0$, $I_R(0) = 0$, $I_U(0) = 0$, and $I_S(0) = 1$ is

$$f_4(u_1, u_2, u_3, u_4) = \frac{\mu + \mu_S + \tau_S + \lambda_2 u_4^2}{\mu + \mu_S + \tau_S + \lambda_2}.$$

Next, we determine the non-negative matrix $M = [m_{ji}]$ that captures the expected contributions of each infected type to the overall infection dynamics, which is critical for understanding the spread of TB in populations with multiple strains. The elements of matrix $M = [m_{ji}]$ represent the expected values of the number of infected individuals of type j produced by individuals of type i, i.e.

$$m_{ji} = \left(\left. \frac{\partial f_i}{\partial u_j} \right|_{u=1} \right) < \infty.$$

Therefore we have

$$M = \begin{pmatrix} \frac{\rho_1\beta_1+\rho_3\beta_3+\rho_2\beta_2}{\mu+\rho_1\beta_1+\rho_3\beta_3+\rho_2\beta_2} & 0 & 0 & 0 \\ \frac{\rho_1\beta_1}{\mu+\rho_1\beta_1+\rho_3\beta_3+\rho_2\beta_2} & \frac{2\lambda_1}{\mu+\mu_R+\tau_R+\lambda_1} & 0 & 0 \\ \frac{\rho_3\beta_3}{\mu+\rho_1\beta_1+\rho_3\beta_3+\rho_2\beta_2} & 0 & \frac{2\lambda_3}{\gamma+\mu+\mu_U+\lambda_3} & 0 \\ \frac{\rho_2\beta_2}{\mu+\rho_1\beta_1+\rho_3\beta_3+\rho_2\beta_2} & 0 & 0 & \frac{2\lambda_2}{\mu+\mu_S+\tau_S+\lambda_2} \end{pmatrix}.$$

Furthermore, by determining the dominant eigenvalue of the matrix M, the expected number of infected individuals is given as follows:

$$m = \max(m_R, m_S, m_U, m_L), \tag{3.11}$$

with

$$m_R = \frac{2\lambda_1}{\mu + \mu_R + \tau_R + \lambda_1}, \qquad m_S = \frac{2\lambda_2}{\mu + \mu_S + \tau_S + \lambda_2}, \quad m_U = \frac{2\lambda_3}{\gamma + \mu + \mu_U + \lambda_3},$$

$$m_L = \frac{\rho_1\beta_1 + \rho_3\beta_3 + \rho_2\beta_2}{\mu + \rho_1\beta_1 + \rho_3\beta_3 + \rho_2\beta_2}.$$

Stochastically, an outbreak occurs when the value of $m > 1$ [17].

Based on the branching process, there is a certain point (q_1, q_2, q_3, q_4) for pgf $f_i(q_1, q_2, q_3, q_4) = q_i,\ 0 < q_i < 1$. This gives

$$\begin{aligned} f_1(q_1, q_2, q_3, q_4) &= \frac{\mu + \rho_1\beta_1 q_1 q_2 + \rho_3\beta_3 q_1 q_3 + \rho_2\beta_2 q_1 q_4}{\mu + \rho_1\beta_1 + \rho_3\beta_3 + \rho_2\beta_2} = q_1, \\ f_2(q_1, q_2, q_3, q_4) &= \frac{\mu + \mu_R + \tau_R + \lambda_1 q_2^2}{\mu + \mu_R + \tau_R + \lambda_1} = q_2, \\ f_3(q_1, q_2, q_3, q_4) &= \frac{\gamma + \mu + \mu_U + \lambda_3 q_3^2}{\gamma + \mu + \mu_U + \lambda_3} = q_3, \\ f_4(q_1, q_2, q_3, q_4) &= \frac{\mu + \mu_S + \tau_S + \lambda_2 q_4^2}{\mu + \mu_S + \tau_S + \lambda_2} = q_4. \end{aligned} \tag{3.12}$$

By solving equation 3.12 for q_1, q_2, q_3, and q_4, we get the following results:

$$q_1 = \frac{\lambda_1\lambda_2\lambda_3\mu}{\lambda_2\lambda_3 E - \rho_1\beta_1\lambda_2\lambda_3 F - \rho_3\beta_3\lambda_1\lambda_2 G - \rho_2\beta_2\lambda_3 H}, \quad q_2 = \frac{F}{\lambda_1}, \quad q_3 = \frac{G}{\lambda_3}, \quad q_4 = \frac{H}{\lambda_2},$$

with

$$\begin{aligned} E &= \mu + \rho_1\beta_1 + \rho_3\beta_3 + \rho_2\beta_2, \\ F &= \mu + \mu_R + \tau_R, \\ G &= \gamma + \mu + \mu_U, \\ H &= \mu + \mu_S + \tau_S. \end{aligned}$$

To ensure that $q_i, i = 1, \ldots, 4$ exists, we must have $\lambda_2\lambda_3 E - \rho_1\beta_1\lambda_2\lambda_3 F - \rho_3\beta_3\lambda_1\lambda_2 G - \rho_2\beta_2\lambda_3 H \neq 0$, $\lambda_1 \neq 0$, $\lambda_3 \neq 0$, and $\lambda_2 \neq 0$.

Suppose $I(t) = (L(t), I_R(t), I_U(t), I_S(t))$ with $I(0) = (\alpha, \sigma, \phi, \psi)$. Using the value of $q_i, i = 1, \ldots, 4$ and the approach method in [40], the two-strain TB model has the following disease-free probability,

$$\text{Prob}\{I(t) = 0\} = \begin{cases} 1, & \text{if } m \leq 1, \\ q_1^{\alpha} q_2^{\sigma} q_3^{\phi} q_4^{\psi}, & \text{if } m > 1. \end{cases} \tag{3.13}$$

Consequently, the probability of an outbreak occurring is

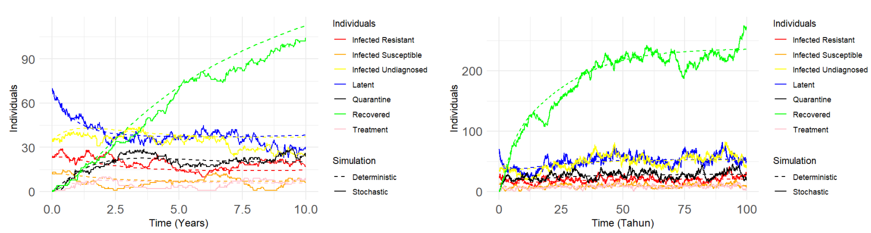
$$1 - \text{Prob}\{I(t) = 0\} = \begin{cases} 0, & \text{if } m \leq 1, \\ 1 - q_1^{\alpha} q_2^{\sigma} q_3^{\phi} q_4^{\psi}, & \text{if } m > 1. \end{cases} \tag{3.14}$$

4. Numerical simulation

Simulations were carried out to describe the spread of the two-strain TB model based on the resulting analysis. The initial conditions are chosen as $(L(0), I_R(0), I_U(0), I_S(0), Q(0), T(0), R(0)) = (70, 23, 35, 12, 0, 0, 0)$, with a total population $N = 1000$ individuals. The models were simulated using the R-version 4.3.2 with adaptivetau package. The value of all parameters are presented in Table 2.

Table 2. Parameter values.

Parameter	Parameter Values	Unit	Source
μ	0.01	1/year	[9]
β_1	0.00833	1/year	[Assumed]
β_2	0.01667	1/year	[Assumed]
β_3	0.975	1/year	[Assumed]
λ_1	0.33	1/year	[Assumed]
λ_2	0.17	1/year	[Assumed]
λ_3	0.5	1/year	[Assumed]
π	0.10	1/year	[11]
μ_R	0.2	1/year	[2]
μ_S	0.04	1/year	[2]
μ_U	0.3	1/year	[9]
μ_Q	0.2	1/year	[2]
μ_T	0.04	1/year	[2]
τ_R	0.65	1/year	[2]
τ_S	0.866	1/year	[2]
ω_R	0.51	1/year	[2]
ω_S	0.82	1/year	[2]
γ	0.2	1/year	[9]
θ	0.143		[2]



(a) time interval $0 \leq t \leq 10$.

(b) time interval $0 \leq t \leq 100$.

Figure 2. Deterministic solution and stochastic sample path fields when 50% of the total latent population is actively screened for TB.

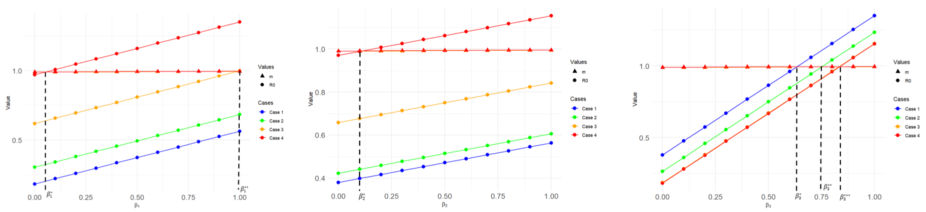
For the first simulation, it is assumed that only 50% of the total latent population is actively screened for TB. The simulation results are shown in Figures 2a and 2b. Furthermore, the deterministic model solution exhibits an exponential growth curve in Figures 2a and 2b. This reflects a smooth and predictable trajectory of the population dynamics over time. In contrast, the continuous time Markov chain model presents a fluctuating sample path. This variability is indicative of the stochastic nature of the model, where random events and transitions between compartments lead to unpredictable changes in the population dynamics. The fluctuations observed in the continuous time Markov chain model arise from the transition opportunities for each sample path from one compartment to another. Each individual's transition (e.g., from susceptible to infected, or from infected to recovered) is influenced by probabilistic events, leading to variations in the number of individuals in each compartment over time. Despite the fluctuations in the stochastic model, the overall dynamics often exhibit a trend that aligns closely with the deterministic solution for certain parameter values. This suggests that while the stochastic model captures the inherent randomness and variability of real-world scenarios, it can still reflect similar long-term trends as the deterministic model when averaged over many realizations.

In the early years, effective screening for latent TB infection can significantly reduce the number of individuals with latent TB before it progresses to active disease. However, as new individuals become infected and enter the latent phase, the number of latent individuals may begin to increase again, potentially leading to an eventual equilibrium. Subpopulations of drug-resistant TB (DR-TB) and drug-sensitive TB (DS-TB) infections may initially experience a sharp decline, reflecting successful containment efforts. Over time, as treatment programs become routine and the population reaches a new equilibrium, DS-TB and DR-TB infections may stabilize at lower levels. The treatment and quarantine subpopulations significantly increase in the early years as more people are diagnosed and treated. Conversely, during the initial years, undiagnosed TB infections rise significantly. Unlike diagnosed and treated populations, undiagnosed infections didn't experience a notable decline over time because if these individuals continue to interact with others, they can maintain the transmission cycle, preventing a decrease in undiagnosed cases. Therefore, it is crucial to enhance active case-finding efforts through comprehensive screening strategies to identify and treat latent TB effectively, ultimately reducing the risk of progression to active disease and breaking the transmission cycle.

The basic reproduction number (R_0) is a key parameter in deterministic models that indicates the average number of secondary infections produced by an infected individual in a fully susceptible population. In this case, we have $R_0 = 0.9526 < 1$ indicating a disease-free stability. This means that, under the given conditions, the disease is unlikely to persist in the population. In stochastic models, the type of stability is assessed using the expected value of the number of infected individuals (m). This value reflects the average number of infected individuals in the population over time. In this case, we have $m = 0.9901 < 1$. This also suggests that there will be no outbreak in the long run, with the probability of outbreak approaching zero. Although both R_0 and m are close to 1, indicating the potential for outbreaks, their values still suggest that the system can achieve disease-free equilibrium. This is significant because it implies that while disease dynamics are precarious, effective control measures can lead to disease elimination. The results of the simulation provide a valuable foundation for examining how various parameter values such as screening rate, undiagnosed TB infection rate, quarantine rate, and treatment rate affect the population dynamics of two-strain tuberculosis (TB). In particular, the next simulations were conducted to determine the effect of screening for latent individuals, quarantine, and treatment on the expected time until the disease became extinct. Four scenarios are considered i.e., (1) effects of the change of contact rate (β) on susceptible individuals; (2) effects of the increasing or decreasing latent individuals screening rate (λ); (3) effects of increasing the treatment rate; and (4) effects of increasing the quarantine rate.

4.1. Scenario 1: effects of the change of contact rate (β) on susceptible individuals.

In this scenario, we investigate the dynamics of tuberculosis (TB) outbreak by simulating how different contact rates among various subpopulations affect the basic reproduction rate (R_0) and the expected number of infected individuals (m). Figure 3 shows the impact of varying the contact rate of drug-resistant tuberculosis (DR-TB) on the spread of the two-strain model of TB disease. By adjusting the contact rate between susceptible individuals and the drug-resistant TB infections (β_1); the contact rate between susceptible individuals and the drug-sensitive TB infections (β_2); and the contact rate between susceptible individuals and the undiagnosed TB infections (β_3), we get the effect of changes with respect to the basic reproduction rate (R_0) and the expected number of infected individuals (m) as shown in Figure 3.



(a) β_1, along with decreasing β_2 and increasing β_3; (b) β_2, along with decreasing β_1 and increasing β_3; (c) β_3, along with decreasing β_1 and increasing β_2.

Figure 3. Graphs on the changes of the values of R_0 and m by varying the values of: β_1; β_2; and β_3. Case 1: control; Case 2: decreasing 40%, increasing 20%; Case 3: decreasing 80%, increasing 60%; Case 4: decreasing 100%, increasing 100%.

Figure 3 illustrates the relationship between TB infection contact rates (β_1, β_2, and β_3) and two important epidemiological parameters: the basic reproduction number (R_0) for the deterministic approach and the expected number of infected individuals (m) for the stochastic approach, across four different cases. All three graphs demonstrate that the value of R_0 increases linearly as the infection contact rate increases. This linear relationship indicates that higher infection contact rates lead to greater potential for disease transmission, thus increasing the risk of sustained outbreaks. Conversely, the value of m remains relatively constant despite increases in the contact rate. This indicates that, in the stochastic model, the average number of infected individuals does not change significantly with increased contact rates.

The rate of increase of R_0 varies for each contact level, with the sharpest increase observed at the undiagnosed TB contact level (β_3), followed by β_1 and β_2. This suggests that the undiagnosed TB contact rate has a more significant impact on the potential spread of the disease compared to diagnosed infections.

5. Conclusions

In this paper, we formulated and analyzed a novel two-strain TB model with amplification: one strain for DS-TB; and another for DR-TB. An Undiagnosed TB compartment was also considered in the model, along with screening efforts, treatment, and quarantine. The model was analyzed by considering both deterministic and stochastic approaches. From the analysis of the deterministic two-strain tuberculosis (TB) epidemic model, two equilibria of the system were obtained, which are the disease-free equilibrium and the endemic equilibrium. Then, the basic reproduction number (R_0) was derived from the disease-free equilibrium. The value of R_0 depends on several key parameters, including the disease contact rate, active TB screening rate, the treatment rate, and the level of quarantine. These four parameters were then analyzed within four different scenarios in the numerical simulation. With the stochastic approach, the transition opportunities in the model were assumed to be Markovian in nature, meaning that the state at time $(t+\Delta t)$ depends only on the state at time t. Each compartment within the model has multiple transition opportunities, resulting in a total of 20 transitions formed from eight compartments. This detailed structure allows for a nuanced representation of TB transmission dynamics. Then, to determine the outbreak probability, a multiple branching process with a probability generating function (pgf) was employed. The outbreak criterion is defined as: when the expected value of the number of infected individuals is less than one $(m < 1)$, there are no fixed points, and thus the outbreak probability is zero. Conversely, when $m > 1$, there are fixed points q_1, q_2, q_3, and q_4 such that the outbreak probability is given by $1 - q_1^{\sigma} q_2^{\phi} q_3^{\psi} q_4^{\Omega}$.

The results of the simulation provided a valuable foundation for examining how various parameter values such as screening rate, undiagnosed TB infection rate, quarantine rate, and treatment rate affect the population dynamics of tuberculosis (TB). Scenario 1, which analyzed the effects of contact rate among infected subpopulations with the susceptible individuals, stated that the spread of two-strain TB within the system is most affected by the contact between susceptible individuals and the undiagnosed TB infected subpopulation (β_3). This emphasizes the importance of active screening on latent subpopulation. Scenario 2, which talked about the effects of screening on latent individuals, showed that at least a 50% screening rate is sufficient to get the basic reproduction number (R_0) and the expected value of infected individuals (m) below 1, which indicates that no outbreaks will occur in a long run. However, a screening result that returns at least 90% of the latent individuals detected to have DR-TB infection $(\lambda_1 \geq 0.9)$ or 100% detected to have DS-TB infection $(\lambda_2 = 1)$ gives two different conclusions where the deterministic approach says that it would not cause an outbreak in the long run, but stochastic approach says that it would still cause an outbreak in the long run. This emphasized on the importance of treatment on DS-TB infection and quarantine on DR-TB infection to eradicate the disease in the long run. Scenario 3, which talked about the effects of treatment on DS-TB infections, suggested that increasing the rate of treatment to at least 20% is enough to suppress the probability of an outbreak, although increasing the rate of treatment above 20% does not give a significant decrease on the values of R_0 and m. Scenario 4, which talked about the effects of quarantine on DR-TB infections, also suggested that increasing the level of quarantine to at least 20% is enough to suppress the probability of an outbreak, even though increasing the level of quarantine does not affect the decrease of R_0 and m significantly. Overall, both Scenarios 3 and 4 suggested that even though treatment and quarantine efforts greatly help in fighting against DS-TB and DR-TB infected individuals, respectively, it is still not enough to eradicate the spread of two-strain TB within the system, and therefore, has to be combined with other strategies to help fight against the transmission of TB.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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