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Mathematical Analysis and Optimal Control of a Tuberculosis Model with Early Diagnosed Latent Infections

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Abstract. Tuberculosis (TB) remains one of the most dangerous infections disease and a major public health problem. This study develops an SEIR model for TB transmission, taking into account the early diagnosed latent infections. The model is used to derive the basic reproductive number $\mathcal{R}_0$, study equilibrium points, and identify the most influential parameters through sensitivity analysis on $\mathcal{R}_0$. An optimal control is formulated using four interventions: transmission reduction, early diagnosed latent TB, treatment, and vaccination. Different strategies are compared using infection averted, total cost, the average cost effectiveness ratio (ACER) and incremental cost effectiveness ratio (ICER). The results show that combined strategy which involve all interventions reduce the total cost, while transmission reduction only strategy gives the greatest reduction in infected individuals.

1. Introduction

Tuberculosis (TB) remains one of the most dangerous infectious diseases and is considered a major public health problem. It is caused by a type of bacteria called Mycobacterium tuberculosis. The disease mainly affects the lungs, but it can also affect other parts of the body. It spreads through the air when an infected person coughs, sneezes, or spits.

The infection often begins silently as latent TB. At this stage, the immune system of the body controls the entering bacteria, and the disease remains latent. Over time, if the immune system becomes weak, these bacteria may become active and develop into active TB. At this stage, the

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bacteria can leave the body during coughing, sneezing, or spitting, and may then infect another person.

In active TB, infected individuals show symptoms and can transmit the disease to others if they are not diagnosed or treated properly. Therefore, early diagnosis, effective treatment, vaccination, and prevention play an important role in reducing the transmission of TB.

Mathematical modeling is considered one of the useful tools that helps us study the spread of infectious diseases and identify the factors that increase or reduce transmission. Several authors have studied mathematical models of tuberculosis by dividing the population into different compartments, such as susceptible, latent, infectious, and recovered individuals. Ucakan et al. [1] analyzed tuberculosis in Turkey using SIR, SEIR, and BSEIR models, Side et al. [2] proposed a SEIR model for tuberculosis transmission, Ochieng [3] studied a SEIRS tuberculosis model with environmental transmission and optimal control. These models have been analyzed mathematically by investigating important properties such as existence, uniqueness, positivity, boundedness, equilibrium points, disease free equilibrium (DFE), endemic equilibrium (EE), and the basic reproduction number $\mathcal{R}_0$, which is used to describe whether the disease dies out or persists in the population. In this study, a new compartment is introduced to represent individuals who have been screened for tuberculosis and diagnosed at an early stage before progressing to active TB. First, we formulate the model and study the positivity and boundedness of solutions. Then, we determine the disease free equilibrium and endemic equilibrium, derive the basic reproduction number $\mathcal{R}_0$, and carry out sensitivity analysis to identify the most influential parameters affecting $\mathcal{R}_0$. Based on the results of the sensitivity analysis, we introduce an optimal control model by considering intervention strategies related to transmission reduction, diagnosis, treatment, and vaccination. Finally, a cost effectiveness analysis is performed using infections averted, the infection averted ratio (IAR), the average cost effectiveness ratio (ACER), and the incremental cost effectiveness ratio (ICER). These measures help us choose the best strategy that reduces TB infections while keeping the interventions cost low. The paper is organized as follows. Section 1 presents the formulation of the model. Section 2 provides the mathematical analysis. Section 3 discusses the sensitivity analysis. Section 4 introduces the optimal control model. Section 5 presents the cost effectiveness analysis. Finally, the conclusion summarizes the main findings of the study.

2. Mathematical Formulation

The model divide the total population $N(t)$ into five compartments, susceptible $S(t)$, exposed $E_1(t)$ and $E_2(t)$, infectious $I(t)$, and recovered $R(t)$.

$S(t)$: Susceptible individuals are those who are at risk of TB disease

$E(t)$: Exposed individuals are those who are infected with TB but the disease is in incubation period. They are not infectious yet, they are divided into two compartments E_1 and E_2.

$E_1(t)$: represent the exposed individuals who have been diagnosed.

$E_2(t)$: represent the exposed individuals who have not been diagnosed.

$I(t)$: Infectious individuals are those who are infected with active TB, at this stage, they can transmit the disease.

$R(t)$: Recovered individuals are those who have recovered from TB, whether recovered by treatment or by vaccination.

Susceptible individuals are recruited into the population at a constant rate Λ. All individuals are subject to natural death at rate μ. Susceptible individuals may infected with TB through the contact with infectious individuals with rate of transnission β. A proportion p of newly infected individuals enter the diagnosed latent class E_1, while the remaining proportion $1-p$ enter the undiagnosed latent class E_2. Individuals in the diagnosed latent class E_1 may receive treatment at rate η_1. A proportion q of these individuals successfully move to the recovered class, while the remaining proportion $1-q$ progress to active TB at rate σ. Individuals in the undiagnosed latent class E_2 progress to active infectious TB at rate σ. Infectious individuals in class I receive treatment at rate η_2, die due to TB induced mortality at rate δ, or die naturally at rate μ. Recovered individuals lose immunity at rate ω and return to the susceptible class. In addition, susceptible individuals may move to the recovered class due to vaccination at rate γ. Based on these assumptions, the TB transmission model is given by diagram 1.

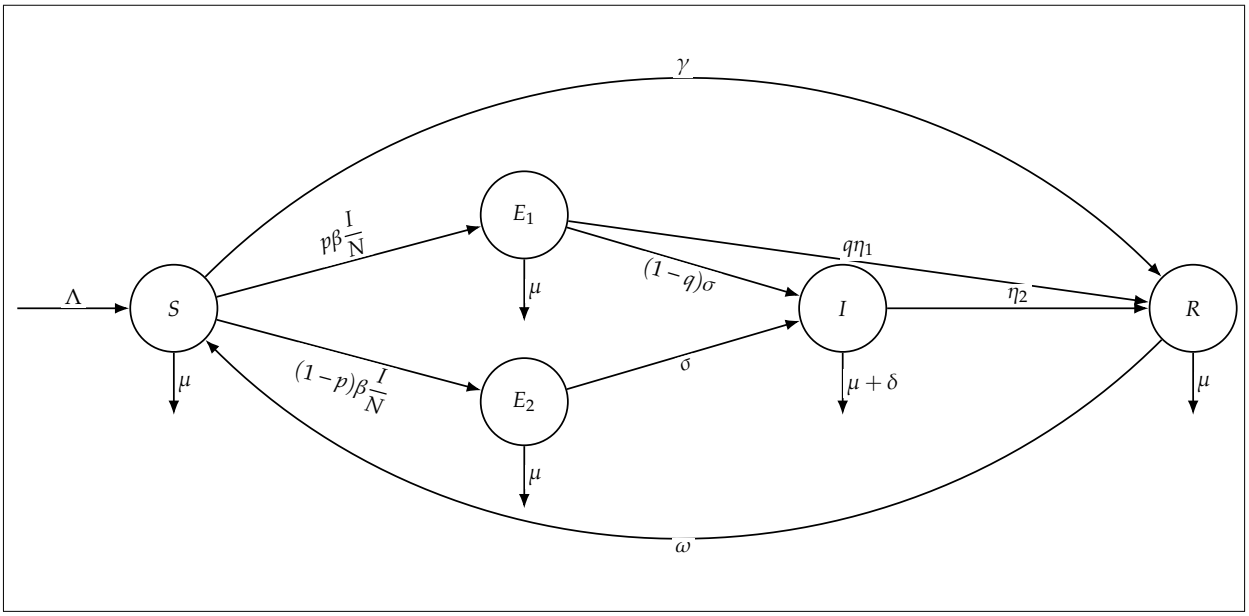

FIGURE 1. Compartmental flow diagram for the TB model

The following system of differential equations represents the flows of the population through the five compartments S, E_1, E_2, I, R.

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta\frac{IS}{N} - \mu S - \gamma S + \omega R, \\
\frac{dE_1}{dt} &= p\beta\frac{IS}{N} - (q\eta_1 + (1-q)\sigma + \mu)\, E_1, \\
\frac{dE_2}{dt} &= (1-p)\beta\frac{IS}{N} - (\sigma + \mu)E_2, \\
\frac{dI}{dt} &= (1-q)\sigma E_1 + \sigma E_2 - (\eta_2 + \delta + \mu)I, \\
\frac{dR}{dt} &= q\eta_1 E_1 + \eta_2 I - \mu R - \omega R + \gamma S, \\
N(t) &= S(t) + E1(t) + E2(t) + I(t) + R(t)
\end{aligned} \tag{2.1}$$

with initial conditions:

$$\{S(0), E_1(0), E_2(0), I(0), R(0)\} = \left\{S^0, E_1^0, E_2^0, I^0, R^0\right\} \tag{2.2}$$

where, $S^0, E_1^0, E_2^0, I^0, R^0$ all are positive.

3. Analysis of the Model

3.1. **Existence, Uniqueness, Positivity and Boundedness.**

Existence and Uniqueness of the solutions. Let

$$X(t) = (S(t), E_1(t), E_2(t), I(t), R(t))^T.$$

Then system (2.1) can be written in the vector form

$$\frac{dX}{dt} = F(t, X), \qquad X(0) = X_0,$$

where

$$X_0 = (S^0, E_1^0, E_2^0, I^0, R^0)^T.$$

Assume that all parameters and initial values $X(0)$ are nonnegative. Since the right-hand side $F(t, X)$ consists of polynomial terms and rational terms $\frac{IS}{N}$, it is continuous and locally Lipschitz with respect to X on the biologically feasible domain where $N(t) > 0$. Therefore, by the Picard Lindelöf existence and uniqueness theorem, the initial value problem (2.1)–(2.2) has a unique local solution. [4–6].

Positivity of the Solutions.

Theorem 3.1. *Assume that all parameters and initial values 2.2 are nonnegative, then the solution of the system* (2.1) *remains nonnegative for all* $t \geq 0$.

Proof. Let

$$\Omega = \{(S, E_1, E_2, I, R) \in \mathbb{R}^5 : S, E_1, E_2, I, R \geq 0\}.$$

To prove positivity, it is enough to verify that the nonnegative region Ω is positively invariant under the flow of the system. This means that any solution starting in Ω remains in Ω for all $t \geq 0$. A solution can leave Ω only by crossing one of its boundary,
$S = 0$, $E_1 = 0$, $E_2 = 0$, $I = 0$, or $R = 0$.
Therefore, it is sufficient to show that on each boundary, the corresponding derivative is nonnegative.
From the first equation, we can write

$$\frac{dS}{dt} + \left(\frac{\beta I(t)}{N(t)} + \mu + \gamma\right) S(t) = \Lambda + \omega R(t),$$

therefore,

$$S(t) = S(0)e^{-\int_0^t \left(\frac{\beta I(r)}{N(r)} + \mu + \gamma\right) dr} + \int_0^t e^{-\int_\tau^t \left(\frac{\beta I(r)}{N(r)} + \mu + \gamma\right) dr} \left(\Lambda + \omega R(\tau)\right) d\tau > 0$$

so $S(t)$ remain positive for all $t > 0$. Similarly, we can prove

$$E_1(t) = E_1(0)e^{-(q\eta_1 + (1-q)\sigma + \mu)t} + \int_0^t e^{-(q\eta_1 + (1-q)\sigma + \mu)(t-\tau)} p \frac{\beta I(\tau)}{N(\tau)} S(\tau)\, d\tau > 0,$$

$$E_2(t) = E_2(0)e^{-(\sigma+\mu)t} + \int_0^t e^{-(\sigma+\mu)(t-\tau)} (1-p) \frac{\beta I(\tau)}{N(\tau)} S(\tau)\, d\tau > 0,$$

$$I(t) = I(0)e^{-(\eta_2 + \delta + \mu)t} + \int_0^t e^{-(\eta_2+\delta+\mu)(t-\tau)} \left((1-q)\sigma E_1(\tau) + \sigma E_2(\tau)\right) d\tau > 0,$$

$$R(t) = R(0)e^{-(\mu+\omega)t} + \int_0^t e^{-(\mu+\omega)(t-\tau)} \left(q\eta_1 E_1(\tau) + \eta_2 I(\tau) + \gamma S(\tau)\right) d\tau > 0.$$

Therefore, for all $t \geq 0$,

$$S(t), E_1(t), E_2(t), I(t), R(t) \geq 0$$

□

Boundedness of the Solutions. To prove the boundedness of the solutions, consider the total population at any time t,

$$N(t) = S(t) + E_1(t) + E_2(t) + I(t) + R(t).$$

Differentiating both sides with respect to t, we obtain

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE_1}{dt} + \frac{dE_2}{dt} + \frac{dI}{dt} + \frac{dR}{dt}.$$

By substituting the rates of change of each compartment from the model, and simplify, we obtain

$$\frac{dN}{dt} = \Lambda - \mu N - \delta I.$$

Since $\delta I(t) \geq 0$, it follows that

$$\frac{dN}{dt} \leq \Lambda - \mu N.$$

Therefore,

$$\frac{dN}{dt} + \mu N \leq \Lambda.$$

Solving this differential equation, we get

$$N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}\left(1 - e^{-\mu t}\right).$$

Equivalently,

$$N(t) \leq \frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu}\right)e^{-\mu t}.$$

As $t \to \infty$, we have

$$N(t) \leq \frac{\Lambda}{\mu}.$$

Therefore,

$$\limsup_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}.$$

Hence, the total population $N(t)$ is bounded. Since each compartment is nonnegative and satisfies

$$0 \leq S(t), E_1(t), E_2(t), I(t), R(t) \leq N(t),$$

it follows that all compartments are bounded for all $t \geq 0$.

Thus, the feasible region of the model is given by

$$\Omega = \left\{(S, E_1, E_2, I, R) \in \mathbb{R}^5_+ : 0 < S + E_1 + E_2 + I + R \leq \frac{\Lambda}{\mu}\right\}. \tag{3.1}$$

Moreover, if the initial condition satisfies

$$N(0) \leq \frac{\Lambda}{\mu},$$

then $N(t) \leq \frac{\Lambda}{\mu}$ for all $t \geq 0$. Therefore, the region Ω is positively invariant. This means that every solution starting in Ω remains in Ω for all $t \geq 0$, which ensures that the model is biologically and mathematically realistic.

3.2. **Equilibrium Points.** To study the behavior of the model, we investigate its equilibrium points. An equilibrium point represents a steady state of the system at which the population in each compartment does not change with time. Therefore, the equilibrium points are obtained by setting all time derivatives equal to zero,

$$\frac{dS}{dt} = \frac{dE_1}{dt} = \frac{dE_2}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0. \tag{3.2}$$

Solving the resulting algebraic system gives the steady states of the model. There are two points: the disease-free equilibrium (DFE), and the endemic equilibrium (EE).

3.2.1. *Disease Free Equilibrium.* The disease free equilibrium (DFE), is the case that there is no infection in the population,

$$E_1 = E_2 = I = 0, \tag{3.3}$$

therefore, the disease free equilibrium has the form

$$\mathcal{E}_0 = (S^0, 0, 0, 0, R^0). \tag{3.4}$$

Substituting 3.3 into 3.2, and solving the resulting algebraic system, we obtain

$$\mathcal{E}_0 = \left(\frac{\mu + \omega}{\mu + \omega + \gamma} N^0, 0, 0, 0, \frac{\gamma_c}{\mu + \omega + \gamma} N^0 \right) \tag{3.5}$$

3.2.2. *Endemic Equilibrium.* The endemic equilibrium is denoted by

$$\mathcal{E}^* = (S^*, E_1^*, E_2^*, I^*, R^*), \qquad S^*, E_1^*, E_2^*, I^*, R^* > 0.$$

At equilibrium, let the force of infection be denoted by

$$\lambda^* = \frac{\beta I^*}{N^*} > 0. \tag{3.6}$$

For simplicity, define

$$A = q\eta_1 + (1-q)\sigma + \mu, \qquad B = \sigma + \mu, \qquad C = \eta_2 + \delta + \mu, \qquad D = \mu + \omega.$$

Setting the right hand sides of the system equal to zero gives

$$E_1^* = \frac{p\lambda^* S^*}{A}, \qquad E_2^* = \frac{(1-p)\lambda^* S^*}{B}.$$

Using the infectious equation, we obtain

$$I^* = \frac{(1-q)\sigma E_1^* + \sigma E_2^*}{C}.$$

Substituting E_1^* and E_2^* into this equation gives

$$I^* = M\lambda^* S^*,$$

where

$$M = \frac{1}{C}\left[\frac{p(1-q)\sigma}{A} + \frac{(1-p)\sigma}{B} \right].$$

From the recovered equation, we have

$$R^* = \frac{q\eta_1 E_1^* + \eta_2 I^* + \gamma S^*}{D}.$$

Hence,

$$R^* = \frac{S^*}{D}\left(\gamma + H\lambda^*\right),$$

where

$$H = \frac{pq\eta_1}{A} + \eta_2 M.$$

Using the susceptible equilibrium equation,

$$0 = \Lambda - (\lambda^* + \mu + \gamma)S^* + \omega R^*,$$

we obtain

$$S^* = \frac{\Lambda}{\mu + \gamma + \lambda^* - \dfrac{\omega}{D}\left(\gamma + H\lambda^*\right)}.$$

Therefore, the endemic equilibrium can be written in terms of λ^* as

$$\mathcal{E}^* = (S^*, E_1^*, E_2^*, I^*, R^*)$$

where

$$\begin{aligned} S^* &= \frac{\Lambda}{\mu + \gamma + \lambda^* - \dfrac{\omega}{\mu + \omega}\left(\gamma + H\lambda^*\right)}, \\ E_1^* &= \frac{p\lambda^* S^*}{A}, \\ E_2^* &= \frac{(1-p)\lambda^* S^*}{B}, \\ I^* &= M\lambda^* S^*, \\ R^* &= \frac{S^*}{\mu + \omega}\left(\gamma + H\lambda^*\right). \end{aligned} \tag{3.7}$$

3.3. **Basic Reproductive number.** The basic reproduction number, $\mathcal{R}_0$, is the expected number of secondary infections produced by one infectious individual. To derive $\mathcal{R}_0$, we use the next generation matrix method [7,8].

The infected compartments of the model are $E_1, \quad E_2, \quad I$.

Let

$$A = q\eta_1 + (1-q)\sigma + \mu, \qquad B = \sigma + \mu, \qquad C = \eta_2 + \delta + \mu. \tag{3.8}$$

So we define,

$$x = (E_1, E_2, I)^T.$$

We can write the infected subsystem in the form

$$\frac{dx}{dt} = \mathcal{F}(x) - \mathcal{V}(x),$$

where, $\mathcal{F} = \begin{pmatrix} \mathcal{F}_1 \\ \mathcal{F}_2 \\ \mathcal{F}_3 \end{pmatrix} = \begin{pmatrix} p\frac{\beta I}{N}S \\ (1-p)\frac{\beta I}{N}S \\ 0 \end{pmatrix}$ and $\mathcal{V} = \begin{pmatrix} \mathcal{V}_1 \\ \mathcal{V}_2 \\ \mathcal{V}_3 \end{pmatrix} = \begin{pmatrix} AE_1 \\ BE_2 \\ CI-(1-q)\sigma E_1 - \sigma E_2 \end{pmatrix}$.

Thus, the matrices F and V, evaluated at the disease free equilibrium 3.5, are given by

$$F = J\left(\frac{\mathcal{F}_1, \mathcal{F}_2, \mathcal{F}_3}{E_1, E_2, I}\right) = \begin{pmatrix} 0 & 0 & p\beta\frac{S^0}{N^0} \\ 0 & 0 & (1-p)\beta\frac{S^0}{N^0} \\ 0 & 0 & 0 \end{pmatrix},$$

and

$$V = J\left(\frac{\mathcal{V}_1, \mathcal{V}_2, \mathcal{V}_3}{E_1, E_2, I}\right) = \begin{pmatrix} A & 0 & 0 \\ 0 & B & 0 \\ -(1-q)\sigma & -\sigma & C \end{pmatrix}.$$

The next generation matrix is given FV^{-1},

$$FV^{-1} = \begin{pmatrix} \frac{p\beta S^0(1-q)\sigma}{ACN^0} & \frac{p\beta S^0\sigma}{BCN^0} & \frac{p\beta S^0}{CN^0} \\ \frac{(1-p)\beta S^0(1-q)\sigma}{ACN^0} & \frac{(1-p)\beta S^0\sigma}{BCN^0} & \frac{(1-p)\beta S^0}{CN^0} \\ 0 & 0 & 0 \end{pmatrix}.$$

$$\text{Eigen values of } (FV^{-1}) = \left\{0,\ 0,\ \frac{\beta S^0}{CN^0}\left[\frac{p(1-q)\sigma}{A} + \frac{(1-p)\sigma}{B}\right]\right\}.$$

The spectral radius $\rho(FV^{-1})$ (the largest absolute value of eigenvalues)

$$\mathcal{R}_0 = \rho(FV^{-1}) = \frac{\beta S^0}{CN^0}\left[\frac{p(1-q)\sigma}{A} + \frac{(1-p)\sigma}{B}\right].$$

From 3.5, $\frac{S^0}{N^0} = \frac{\mu+\omega}{\mu+\omega+\gamma}$, and substitute $A, B,$ and C, from 3.8, then

$$\mathcal{R}_0 = \frac{\beta}{\eta_2+\delta+\mu}\left(\frac{\mu+\omega}{\mu+\omega+\gamma}\right)\left[\frac{p(1-q)\sigma}{q\eta_1+(1-q)\sigma+\mu} + \frac{(1-p)\sigma}{\sigma+\mu}\right]. \tag{3.9}$$

The value of $\mathcal{R}_0$ determines whether the disease dies out or persists in the population. If $\mathcal{R}_0 < 1$, then each infectious individual produces, on average, less than one secondary infection, and the disease free equilibrium exists. On the other hand, if $\mathcal{R}_0 > 1$, then each infectious individual produces, on average, more than one secondary infection, and the endemic equilibrium exists.

3.4. **Estimation of the Parameter Values.** The parameter values used in this study were estimated using the biological meanings of the parameters. all the values were measured by a year.

(1) The natural birth and death rate is estimated based on demographic data [9]. as the average life expectancy,

$$\mu = \frac{1}{\text{average life expectancy}} = \frac{1}{49} \approx 0.02041 \quad \text{year}^{-1}.$$

(2) The progression rate from the latent to active TB disease is estimated from the fact that the risk of developing TB disease is highest during the first two years after infection [10]. Hence, the average of latent period is assumed to be approximately 2 years, therefore

$$\sigma = \frac{1}{\text{average latent period}} = \frac{1}{2} = 0.5.$$

(3) The treatment rate of diagnosed latent TB is estimated by

$$\eta_1 = \frac{1}{\text{average latent TB treatment duration}} = \frac{1}{4/12} = 3 \quad \text{year}^{-1}.$$

Based on short course latent TB treatment [11, 12].

(4) The treatment rate of active TB is estimated by

$$\eta_2 = \frac{1}{\text{average active TB treatment duration}} = \frac{1}{6/12} = 2 \quad \text{year}^{-1}.$$

Based on a standard treatment duration of about 6 months. [13, 14].

(5) The parameter p the proportion of newly susceptible infected who are diagnosed and enter the diagnosed latent class E_1. In this study, we assume

$$p = 0.5.$$

(6) The parameter q represents the proportion of diagnosed latent TB individuals who receive successful treatment. In this study, we assume that 70% of diagnosed latent TB individuals are successfully treated, hence,

$$q = 0.7.$$

(7) The loss of immunity rate is estimated by

$$\omega = \frac{1}{\text{average duration of immunity}} = \frac{1}{10} = 0.1 \quad \text{year}^{-1},$$

the average duration of immunity is assumed to be 10 years, [15].

(8) **The vaccination parameter γ:**
The parameter γ represents the rate or effectiveness of vaccination in moving susceptible individuals into the recovered class. In this study, we use a moderate to high vaccination [16]

$$\gamma = 0.7.$$

(9) **TB disease induced death rate δ:**
According to the World Health Organization (WHO), about 1.23 million people died from TB in 2024, and the global TB case fatality rate was approximately 11.5% [17]. Therefore, we take

$$\delta = 0.115 \text{ year}^{-1}.$$

(10) The parameter β can be estimated by fitting the model to reported data or by using the expression for the basic reproduction number $\mathcal{R}_0$. If $\mathcal{R}_0$ is known, then β can be obtained from the formula of $\mathcal{R}_0$, 3.9.

$$\beta = \mathcal{R}_0(\eta_2+\delta+\mu)\left(\frac{\mu+\omega+\gamma}{\mu+\omega}\right)\left[\frac{p(1-q)\sigma}{q\eta_1+(1-q)\sigma+\mu}+\frac{(1-p)\sigma}{\sigma+\mu}\right]^{-1}. \tag{3.10}$$

The study [18] shows that the reproductive number of TB estimates ranged from 0.24 in the Netherlands (during 1933–2007) to 4.3 in China in 2012. That is, from 3.10 β is ranged

$$\text{from } \beta \approx 6.8 \text{ to } \beta \approx 122$$

Thus, the parameter values used in the numerical simulation are summarized as follows

$$\begin{aligned} &\mu = 0.02041, \quad p = 0.5, \quad q = 0.7, \quad \eta_1 = 3, \\ &\sigma = 0.5, \quad \eta_2 = 2, \quad \delta = 0, \quad \omega = 0.1, \\ &\gamma = 0.7, \quad \beta = [6.8, 122]. \end{aligned} \tag{3.11}$$

3.5. **Dynamic Behavior of the population.** In this section, we present the dynamical behavior of the population compartments in two cases: when the disease dies out from the population ($\mathcal{R}_0 < 1$), and when the disease persists in the population ($\mathcal{R}_0 > 1$).

Dynamical Behavior in the Disease Free Case $\mathcal{R}_0 < 1$.

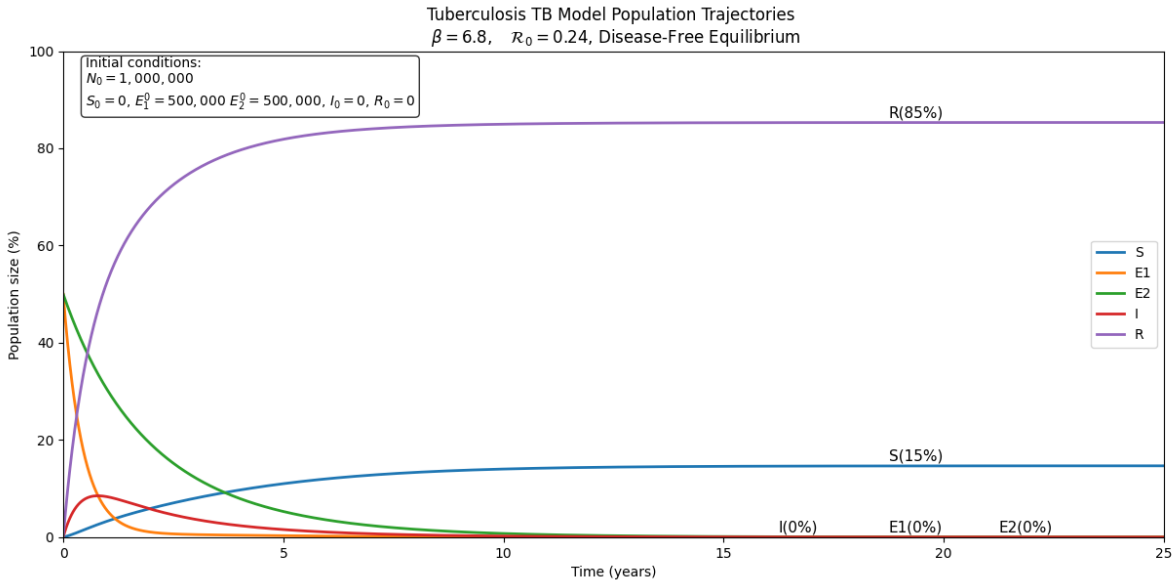

FIGURE 2. Dynamical behavior when $\mathcal{R}_0 = 0.24$ - Disease Free Equilibrium

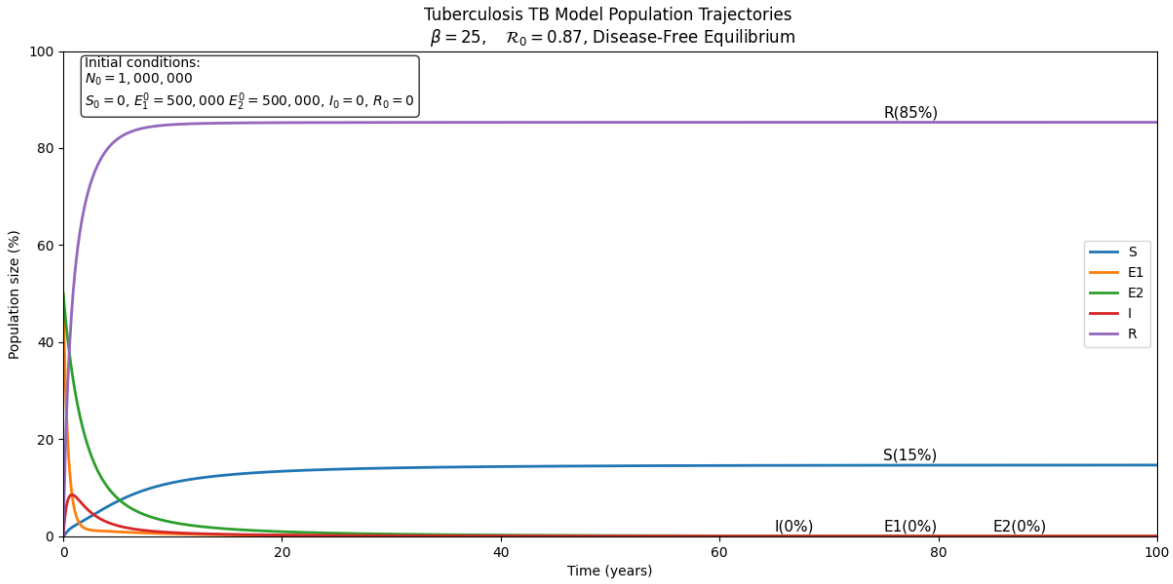

FIGURE 3. Dynamical behavior when $\mathcal{R}_0 = 0.87$ - Disease Free Equilibrium

Figures 2 and 3 show the dynamical behavior of the model in the disease free case, where $\mathcal{R}_0 < 1$. In both figures, the infected compartments $E_1(t)$, $E_2(t)$, and $I(t)$ decrease and approach zero, so the disease dies out and the solution tends to the disease free equilibrium. In Figure 2, where $\mathcal{R}_0 = 0.24$, the infected compartments vanish within approximately 25 years. However, in Figure 3, where $\mathcal{R}_0 = 0.87$, the disease still dies out, but the convergence to the disease free equilibrium is slower and requires a longer time, approximately 100 years.

In both cases, the susceptible and recovered populations approach their disease free equilibrium levels, with approximately 15% of the population in the susceptible class and 85% in the recovered class.

Dynamical Behavior of the Endemic Equilibrium ($\mathcal{R}_0 > 1$). Figure 4 shows the behavior of the model when $\mathcal{R}_0 = 4.23 > 1$. The disease persists in the population, and the solution approaches the endemic equilibrium

$$S = 3\%, \quad E_1 = 2\%, \quad E_2 = 8\%, \quad I = 2\%, \quad \text{and} \quad R = 85\%$$

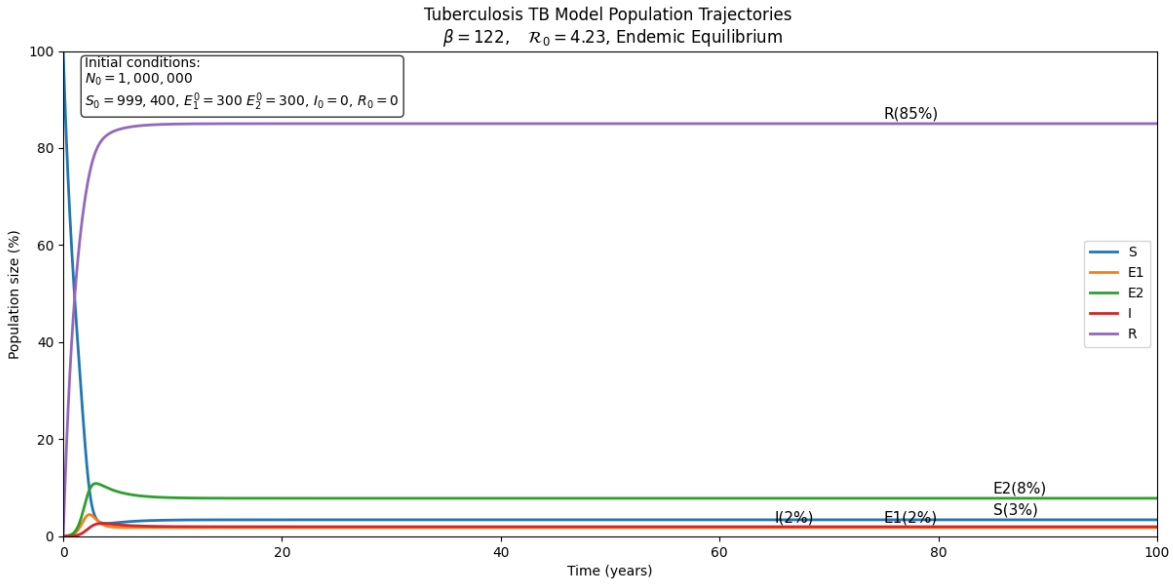

FIGURE 4. Dynamical behavior when $\mathcal{R}_0 = 4.23$ - Endemic Equilibrium

4. SENSITIVITY ANALYSIS

In this section, we will show the effect of each parameters on $\mathcal{R}_0$, whether its a positive effect or negative effect, that helps us to determine which parameters should be targeted to reduce the value of $\mathcal{R}_0$.

The sensitivity index of $\mathcal{R}_0$ with respect to a parameter P is defined by

$$\Upsilon_P^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial P} \cdot \frac{P}{\mathcal{R}_0}. \tag{4.1}$$

A positive value means that increasing the parameter increases $\mathcal{R}_0$. A negative value means that increasing the parameter decreases $\mathcal{R}_0$.

Parameter	**Sensitivity Index**	**Effect on $\mathcal{R}_0$**	**Rank**
β	1.0000	Positive	1
η_2	−0.9366	Negative	2
p	−0.9061	Negative	3
γ	−0.8532	Negative	4
ω	0.7086	Positive	5
q	−0.1043	Negative	6
μ	0.0974	Positive	7
σ	0.0821	Positive	8
δ	−0.0539	Negative	9
η_1	−0.0444	Negative	10

TABLE 1. Sensitivity indices of $\mathcal{R}_0$.

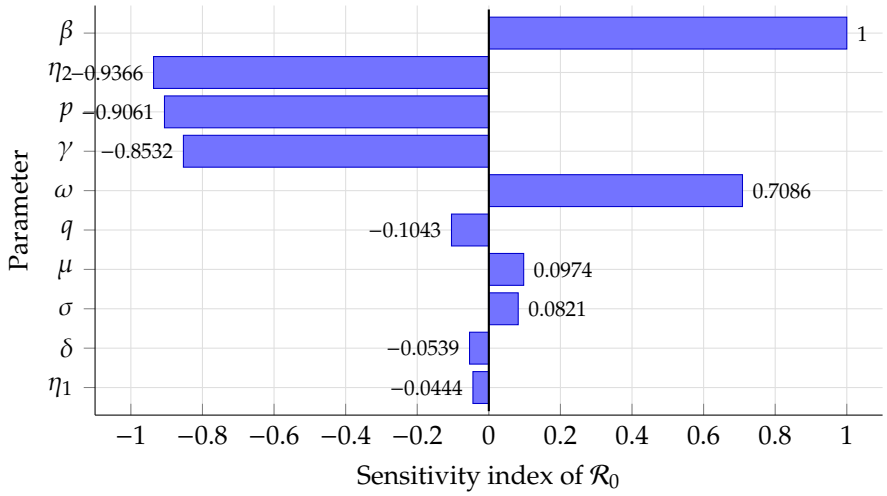

FIGURE 5. Sensitivity diagram of the effect of the parameters on $\mathcal{R}_0$.

From Table 1 and Figure 5, the parameter β and ω have strong positive effect on $\mathcal{R}_0$, the parameters η_2, p, and γ have a strong negative effect on $\mathcal{R}_0$, the remaining parameters have weak effect on $\mathcal{R}_0$.

5. Optimal Control Model

As shown in the sensitivity analysis, each parameter has a different effect on the basic reproduction number $\mathcal{R}_0$. Some parameters are controllable through interventions, while others are not controllable. For example, the transmission rate β, diagnosis proportion p, latent treatment rate η_1, active TB treatment rate η_2, and vaccination rate γ can be control by interventions. The parameters such as the natural death rate μ and the disease induced death rate δ are generally not suitable to control.

Since the main objective is to reduce the value of $\mathcal{R}_0$, we should decrease β, increase p, η_2, and γ. Based on this idea, the control parameters are defined as follows:

$$\begin{aligned} \beta_c &= (1-u_1(t))\beta, \\ p_c &= p + u_2(t)(1-p), \\ \eta_{1c} &= (1+u_3(t))\eta_1, \\ \eta_{2c} &= (1+u_3(t))\eta_2, \\ \gamma_c &= (1+u_4(t))\gamma. \end{aligned} \tag{5.1}$$

Where,

$u_1(t)$ represents the efforts that is done to reduce the transmission,

$u_2(t)$ represents the efforts that is done to enhance diagnosis,

$u_3(t)$ represents the additional treatment efforts,
$u_4(t)$ represents the additional vaccination efforts.
Therefore, the optimal control TB model is given by

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \lambda_c S - \mu S - \gamma_c S + \omega R, \\
\frac{dE_1}{dt} &= p_c \lambda_c S - (q\eta_{1c} + (1-q)\sigma + \mu)\, E_1, \\
\frac{dE_2}{dt} &= (1-p_c)\lambda_c S - (\sigma + \mu) E_2, \\
\frac{dI}{dt} &= (1-q)\sigma E_1 + \sigma E_2 - (\eta_{2c} + \delta + \mu)\, I, \\
\frac{dR}{dt} &= q\eta_{1c} E_1 + \eta_{2c} I - \mu R - \omega R + \gamma_c S,
\end{aligned} \tag{5.2}$$

where

$$\begin{aligned}
\lambda_c(t) &= \frac{\beta_c(t) I(t)}{N(t)}, \\
N(t) &= S(t) + E_1(t) + E_2(t) + I(t) + R(t).
\end{aligned} \tag{5.3}$$

The control variables

$$\mathcal{U} = \{(u_1, u_2, u_3, u_4) : 0 \le u_i(t) \le 1,\ i = 1,2,3,4,\ t \in [0,T]\}. \tag{5.4}$$

We aim to minimize the total cost associated with infected individuals $E_1, E_2,$ and I together with the cost of interventions u_1, u_2, u_3 and u_4 over the time interval $[0,T]$. Thus, the objective is to minimize the function:

$$\begin{aligned}
J(u_1,u_2,u_3,u_4) = \int_0^T \Bigg[& w_1 E_1(t) + w_2 E_2(t) + w_3 I(t) \\
& + \frac{A_1}{2} u_1^2(t) + \frac{A_2}{2} u_2^2(t) + \frac{A_3}{2} u_3^2(t) + \frac{A_4}{2} u_4^2(t) \Bigg] dt.
\end{aligned} \tag{5.5}$$

Where, w_1, w_2 and w_3 represent the weights of the cost per infected individual, A_1, A_2, A_3 and A_4 represent the weights of the costs of the interventions.
To find the optimal controls $u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)$, associated with the optimal state solutions, we apply the Pontryagin Maximum Principle (PMP) [19,20].

Pontryagin Maximum Principle. Pontryagin's Maximum Principle provides necessary conditions for optimality through the Hamiltonian function, adjoint system, transversality conditions, and optimality control variables [19,20]. Let $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ be the costate variables corresponding to

S, E_1, E_2, I, R, respectively. The Hamiltonian function is given by

$$\begin{aligned}\mathbf{H} &= w_1E_1 + w_2E_2 + w_3I + \frac{A_1}{2}u_1^2 + \frac{A_2}{2}u_2^2 + \frac{A_3}{2}u_3^2 + \frac{A_4}{2}u_4^2 \\ &+ \lambda_1\left(\Lambda - \lambda_c S - \mu S - \gamma_c S + \omega R\right) \\ &+ \lambda_2\left(p_c\lambda_c S - (q\eta_{1c} + (1-q)\sigma + \mu)\,E_1\right) \\ &+ \lambda_3\left((1-p_c)\lambda_c S - (\sigma+\mu)E_2\right) \\ &+ \lambda_4\left((1-q)\sigma E_1 + \sigma E_2 - (\eta_{2c} + \delta + \mu)\,I\right) \\ &+ \lambda_5\left(q\eta_{1c}E_1 + \eta_{2c}I - \mu R - \omega R + \gamma_c S\right).\end{aligned} \tag{5.6}$$

The costate system is given by

$$\frac{d\lambda_i}{dt} = -\frac{\partial \mathbf{H}}{\partial x_i}, \qquad x_i \in \{S, E_1, E_2, I, R\} \tag{5.7}$$

For simplicity, define

$$D_1 = q\eta_{1c} + (1-q)\sigma + \mu, \qquad D_2 = \sigma + \mu, \qquad D_3 = \eta_{2c} + \delta + \mu.$$

Also, since

$$\lambda_c = \frac{\beta_c I}{N},$$

we have

$$\frac{\partial \lambda_c}{\partial S} = \frac{\partial \lambda_c}{\partial E_1} = \frac{\partial \lambda_c}{\partial E_2} = \frac{\partial \lambda_c}{\partial R} = -\frac{\lambda_c}{N},$$

and

$$\frac{\partial \lambda_c}{\partial I} = \frac{\beta_c}{N} - \frac{\lambda_c}{N}.$$

Thus, the adjoint system 5.7 becomes

$$\begin{aligned}\frac{d\lambda_1}{dt} &= -\frac{\partial \mathbf{H}}{\partial S} = \lambda_1\left[\lambda_c\left(1 - \frac{S}{N}\right) + \mu + \gamma_c\right] - \lambda_2 p_c\lambda_c\left(1 - \frac{S}{N}\right) \\ &\quad - \lambda_3(1-p_c)\lambda_c\left(1 - \frac{S}{N}\right) - \lambda_5\gamma_c, \\ \frac{d\lambda_2}{dt} &= -\frac{\partial \mathbf{H}}{\partial E_1} = -w_1 - \lambda_1\frac{\lambda_c S}{N} + \lambda_2\left(D_1 + \frac{p_c\lambda_c S}{N}\right) \\ &\quad + \lambda_3\frac{(1-p_c)\lambda_c S}{N} - \lambda_4(1-q)\sigma - \lambda_5 q\eta_{1c}, \\ \frac{d\lambda_3}{dt} &= -\frac{\partial \mathbf{H}}{\partial E_2} = -w_2 - \lambda_1\frac{\lambda_c S}{N} + \lambda_2 p_c\frac{\lambda_c S}{N} \\ &\quad + \lambda_3\left(D_2 + (1-p_c)\frac{\lambda_c S}{N}\right) - \lambda_4\sigma,\end{aligned} \tag{5.8}$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial \mathbf{H}}{\partial I} = -w_3 + (\lambda_1 - p_c\lambda_2 - (1-p_c)\lambda_3)\, S\left(\frac{\beta_c - \lambda_c}{N}\right) + \lambda_4 D_3 - \lambda_5\eta_{2c},$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial \mathbf{H}}{\partial R} = -\lambda_1\left(\frac{\lambda_c S}{N} + \omega\right) + \lambda_2 p_c\frac{\lambda_c S}{N} + \lambda_3(1-p_c)\frac{\lambda_c S}{N} + \lambda_5(\mu+\omega).$$

The transversality conditions are

$$\lambda_i(T) = 0, \qquad i = 1,2,3,4,5. \tag{5.9}$$

The optimal controls satisfy

$$\frac{\partial \mathbf{H}}{\partial u_i} = 0, \qquad i = 1,2,3,4.$$

Therefore,

$$\frac{\partial \mathbf{H}}{\partial u_1} = A_1 u_1 + \frac{\beta S I}{N}\left[\lambda_1 - p_c\lambda_2 - (1-p_c)\lambda_3\right] = 0, \tag{5.10}$$

$$\frac{\partial \mathbf{H}}{\partial u_2} = A_2 u_2 + (1-p)\lambda_c S\left[\lambda_2 - \lambda_3\right] = 0, \tag{5.11}$$

$$\frac{\partial \mathbf{H}}{\partial u_3} = A_3 u_3 + q\eta_1 E_1(\lambda_5 - \lambda_2) + \eta_2 I(\lambda_5 - \lambda_4) = 0, \tag{5.12}$$

$$\frac{\partial \mathbf{H}}{\partial u_4} = A_4 u_4 + \gamma S(\lambda_5 - \lambda_1) = 0. \tag{5.13}$$

Hence, the optimal controls are characterized by

$$u_1^*(t) = \max\left\{0, \min\left(1, \frac{\beta S^*(t) I^*(t)}{A_1 N^*(t)}\left[p_c^*(t)\lambda_2(t) + (1-p_c^*(t))\lambda_3(t) - \lambda_1(t)\right]\right)\right\}, \tag{5.14}$$

$$u_2^*(t) = \max\left\{0, \min\left(1, \frac{(1-p)\lambda_c^*(t) S^*(t)}{A_2}\left[\lambda_3(t) - \lambda_2(t)\right]\right)\right\}, \tag{5.15}$$

$$u_3^*(t) = \max\left\{0, \min\left(1, \frac{q\eta_1 E_1^*(t)\left[\lambda_2(t) - \lambda_5(t)\right] + \eta_2 I^*(t)\left[\lambda_4(t) - \lambda_5(t)\right]}{A_3}\right)\right\}, \tag{5.16}$$

$$u_4^*(t) = \max\left\{0, \min\left(1, \frac{\gamma S^*(t)}{A_4}\left[\lambda_1(t) - \lambda_5(t)\right]\right)\right\}. \tag{5.17}$$

6. Numerical Solution

Solving the system 5.2 of state equations forward in time from 0 to T with initial conditions 2.2, coupled with the system 5.8 of costate equations backward in time from T to 0 with boundary conditions 5.9, this coupled problem is solved numerically by Forward Backward Sweep Method (FBSM), to find the optimal controls u_1, u_2, u_3, and u_4, with the corresponding state variables $S(t), E_1(t), E_2(t), I(t)$, and $R(t)$.

Steps of the Forward Backward Sweep Method (FBSM).

Step 1: Initialization:

- Choose an initial guess for the controls $u_j^{(0)}(t) = 0, \quad j = \{1, 2, 3, 4\}$

- State the maximum iterations (Max), set the iteration index $k = 0$ and the convergence tolerance Tol.

Step 2: Forward Sweep:

Using the current controls solve the sate equation forward in time from $t = 0$ to $t = T$ using Runge Kutta method (RK4).

Step 3: Backward Sweep:

Solve the costate equation with the computed state variables and the current controls backward in time from $t = T$ tp $t = 0$ using Runge Kutta method (RK4).

Step 4: Update Control:

Update the control using the optimality condition:

$$u_j^{(k+1)}(t) = u_j^*, \text{where} \left(\frac{\partial \mathbf{H}}{\partial u_j} = 0 \right).$$

Step 5: Check the Convergence: If

$$||u^{(k+1)} - u^{(k)}|| < Tol,$$

then stop, otherwise, increase k and repeat from Step 2.

Figure 6, shows the optimal control profiles

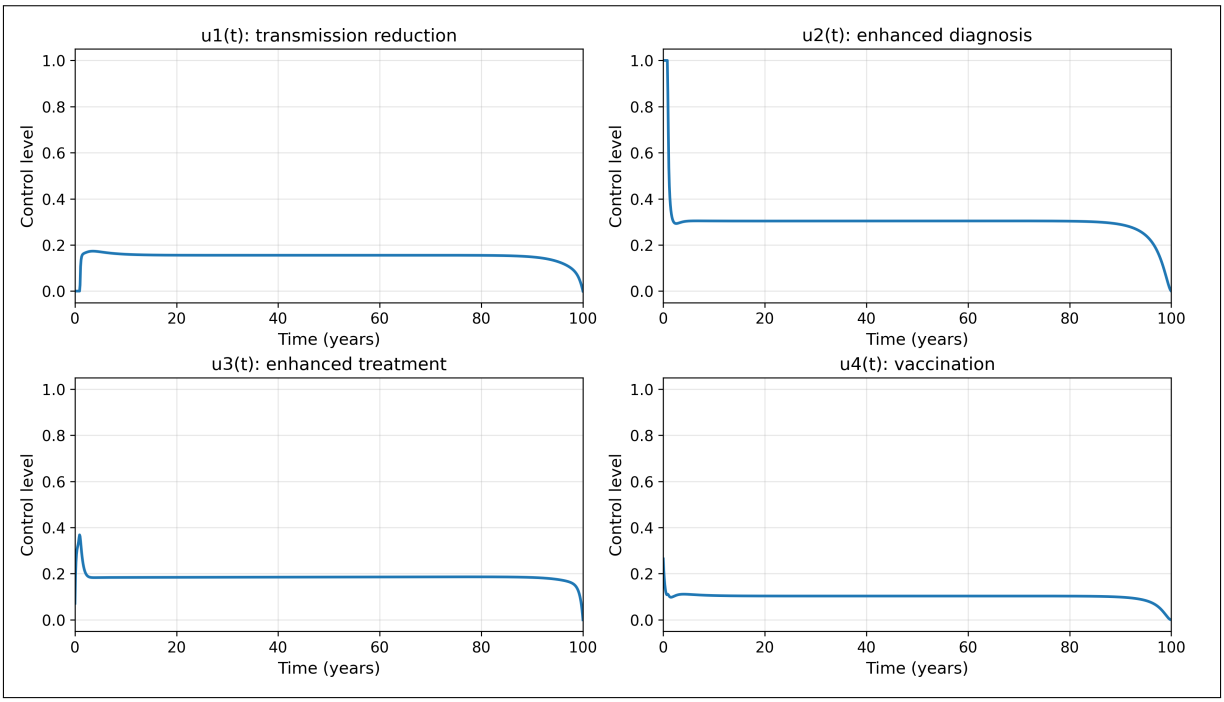

FIGURE 6. Optimal control profiles

7. Cost effectiveness Analysis

In this section, we evaluate several intervention strategies in order to identify the strategies that provide the best balance between reducing infection and minimizing intervention cost. Table 2 lists the active controls used in each strategy.

Strategy	Active controls
S_0	No control
S_1	u_1 only
S_2	u_2 only
S_3	u_3 only
S_4	u_4 only
S_5	u_1, u_2
S_6	u_1, u_3
S_7	u_1, u_4
S_8	u_2, u_3
S_9	u_2, u_4
S_{10}	u_3, u_4
S_{11}	u_1, u_2, u_3
S_{12}	u_1, u_2, u_4
S_{13}	u_1, u_3, u_4
S_{14}	u_2, u_3, u_4
S_{15}	u_1, u_2, u_3, u_4

Table 2. Control interventions used in the the strategies

For each strategy, we compute the infection averted ratio (IAR), the average cost effectiveness ratio (ACER), and the incremental cost effectiveness ratio (ICER). These measures are used to compare the infection reduction benefit benefit of each strategy with its corresponding intervention cost.

Strategy	Final S (%)	Final E_1 (%)	Final E_2 (%)	Final I (%)	Final R (%)	Final $E_1 + E_2 + I$ (%)
S_0	24.243	1.402	6.136	1.537	66.682	9.074
S_1	21.386	1.460	6.289	1.569	69.296	9.318
S_2	17.681	1.530	5.718	1.401	73.670	8.649
S_3	20.865	1.352	6.199	1.435	70.149	8.986
S_4	23.811	1.405	6.122	1.531	67.131	9.059
S_5	16.982	1.546	5.657	1.377	74.438	8.581
S_6	18.258	1.401	6.282	1.445	72.614	9.129
S_7	20.837	1.464	6.267	1.560	69.872	9.291
S_8	15.445	1.448	5.649	1.286	76.172	8.383
S_9	17.294	1.528	5.676	1.388	74.114	8.592
S_{10}	20.391	1.355	6.166	1.425	70.663	8.947
S_{11}	14.570	1.466	5.553	1.255	77.156	8.274
S_{12}	16.446	1.545	5.600	1.359	75.050	8.505
S_{13}	17.503	1.407	6.240	1.432	73.418	9.079
S_{14}	14.991	1.445	5.587	1.270	76.707	8.302
S_{15}	13.736	1.467	5.470	1.232	78.095	8.169

TABLE 3. Final compartment values at $T = 100$ year, expressed as percentages of the total population.

Table 3 presents the final compartment percentages at the end of the simulation period, $T = 100$ years, for all strategies. For the case $\beta = 122$ and $\mathcal{R}_0 = 4.23$, the total infected population,

$$E_1 + E_2 + I,$$

does not vanish after 100 years. Therefore, the disease persists in the population under all intervention strategies. However, the strategies still differ in their ability to reduce the cumulative infection burden.

Cumulative Infections. The total cumulative infection burden for strategy s is defined by

$$B_s = \int_0^T \left[E_1^s(t) + E_2^s(t) + I^s(t)\right] dt.$$

Strategy	$\int E_1(t)\,dt$	$\int E_2(t)\,dt$	$\int I(t)\,dt$	$B_s = \int (E_1 + E_2 + I)\,dt$
S_0	1.732	7.486	1.877	11.094
S_1	1.490	6.427	1.612	9.529
S_2	2.260	4.603	1.239	8.101
S_3	1.429	7.320	1.541	10.291
S_4	1.694	7.322	1.836	10.852
S_5	2.154	4.302	1.162	7.618
S_6	1.208	6.110	1.292	8.610
S_7	1.442	6.217	1.559	9.218
S_8	1.812	4.397	0.997	7.206
S_9	2.195	4.456	1.201	7.852
S_{10}	1.388	7.105	1.495	9.988
S_{11}	1.667	3.964	0.897	6.528
S_{12}	2.039	4.104	1.107	7.250
S_{13}	1.140	5.784	1.219	8.143
S_{14}	1.735	4.199	0.951	6.885
S_{15}	1.530	3.595	0.812	5.937

TABLE 4. Cumulative infection compartments $T : 0 \to 100$, expressed as percentages of the total cumulative population.

Table 4 shows the cumulative infection burden for the infected compartments over the simulation interval $[0, T]$. Lower values of B_s indicate a stronger reduction in the infection.

Infections Averted. The number of infections averted by strategy s is defined as

$$IA_s = B_0 - B_s,$$

where B_0 is the cumulative infection burden under the no-control strategy S_0, and B_s is the cumulative infection burden under strategy s.

Infection Averted Ratio (IAR). The infection averted ratio is defined by

$$IAR_s = \frac{B_0 - B_s}{B_0}$$

This ratio measures the proportion of infections averted relative to the no control case.

Burden Cost (BC). The infection burden cost for strategy s is defined by

$$BC_s = \int_0^T (w_1 E_1(t) + w_2 E_2(t) + w_3 I(t))\ dt.$$

Here, w_1, w_2, and w_3 are the weight parameters associated with the costs of the infected individuals in E_1, E_2 and I compartments respectively. In this study, we assume that

$$w_1 = 1, \qquad w_2 = 1.5, \qquad w_3 = 10,$$

Intervention Cost (IC). The total intervention cost for strategy s is defined by

$$IC_s = \int_0^T \frac{1}{2}\left[A_1 u_1^2(t) + A_2 u_2^2(t) + A_3 u_3^2(t) + A_4 u_4^2(t)\right] dt.$$

Here, A_1, A_2, A_3, and A_4 are the weight parameters associated with the costs of the control measures u_1, u_2, u_3, and u_4, respectively. In this study, we assume that

$$A_1 = 1, \qquad A_2 = 1, \qquad A_3 = 1, \qquad A_4 = 1.$$

The total objective value for strategy s is therefore given by

$$J_s = BC_s + IC_s.$$

Average Cost Effectiveness Ratio (ACER). The average cost effectiveness ratio for strategy s is defined by

$$ACER_s = \frac{IC_s}{IA_s}.$$

measures the average intervention cost needed to avert one infection.

Incremental Cost Effectiveness Ratio (ICER). The incremental cost effectiveness ratio between two strategies i and j is defined as

$$ICER = \frac{\text{The change in the Cost}}{\text{The change in the Infections Averted}} = \frac{IC_i - IC_j}{IA_i - IA_j}.$$

It shows how much extra cost is needed to avert one additional infection when changing from one strategy to another.

Strategy	BC_s	IC_s	IA_s	IAR	ACER	Objective J
S_0	31.729	0.000	0.000	0.000	–	31.729
S_1	27.247	2.447	1.566	0.141	1.563	29.694
S_2	21.557	4.761	2.993	0.270	1.591	26.318
S_3	27.821	1.739	0.804	0.072	2.164	29.560
S_4	31.037	0.326	0.242	0.022	1.347	31.363
S_5	20.223	5.596	3.477	0.313	1.609	25.819
S_6	23.296	4.266	2.484	0.224	1.717	27.562
S_7	26.359	2.945	1.876	0.169	1.570	29.304
S_8	18.380	6.042	3.888	0.350	1.554	24.422
S_9	20.886	5.134	3.242	0.292	1.583	26.020
S_{10}	26.997	2.158	1.106	0.100	1.950	29.155
S_{11}	16.584	7.210	4.566	0.412	1.579	23.794
S_{12}	19.268	6.269	3.844	0.346	1.631	25.537
S_{13}	22.007	5.069	2.951	0.266	1.718	27.076
S_{14}	17.541	6.524	4.210	0.379	1.550	24.065
S_{15}	15.040	8.255	5.157	0.465	1.601	23.295

TABLE 5. Total cost, infection averted and ACER for the control strategies.

Strategy	Cost	IA	Decision	Comparator	Δ cost	Δ*IA*	ICER
S_0	0.000	0.000	Reference	–	–	–	–
S_4	0.326	0.242	Non dominated	S_0	0.326	0.242	1.347
S_3	1.739	0.804	Non dominated	S_4	1.413	0.561	2.517
S_{10}	2.158	1.106	Non dominated	S_3	0.419	0.303	1.384
S_1	2.447	1.566	Non dominated	S_{10}	0.289	0.459	0.629
S_7	2.945	1.876	Non dominated	S_1	0.497	0.310	1.603
S_6	4.266	2.484	Non dominated	S_7	1.321	0.608	2.172
S_2	4.761	2.993	Non dominated	S_6	0.495	0.509	0.974
S_{13}	5.069	2.951	Strongly dominated	S_2	–	–	–
S_9	5.134	3.242	Non dominated	S_2	0.373	0.249	1.495
S_5	5.596	3.477	Non dominated	S_9	0.462	0.234	1.969
S_8	6.042	3.888	Non dominated	S_5	0.446	0.412	1.083
S_{12}	6.269	3.844	Strongly dominated	S_8	–	–	–
S_{14}	6.524	4.210	Non dominated	S_8	0.483	0.321	1.502
S_{11}	7.210	4.566	Non dominated	S_{14}	0.686	0.357	1.924
S_{15}	8.255	5.157	Non dominated	S_{11}	1.045	0.591	1.769

TABLE 6. ICER analysis.

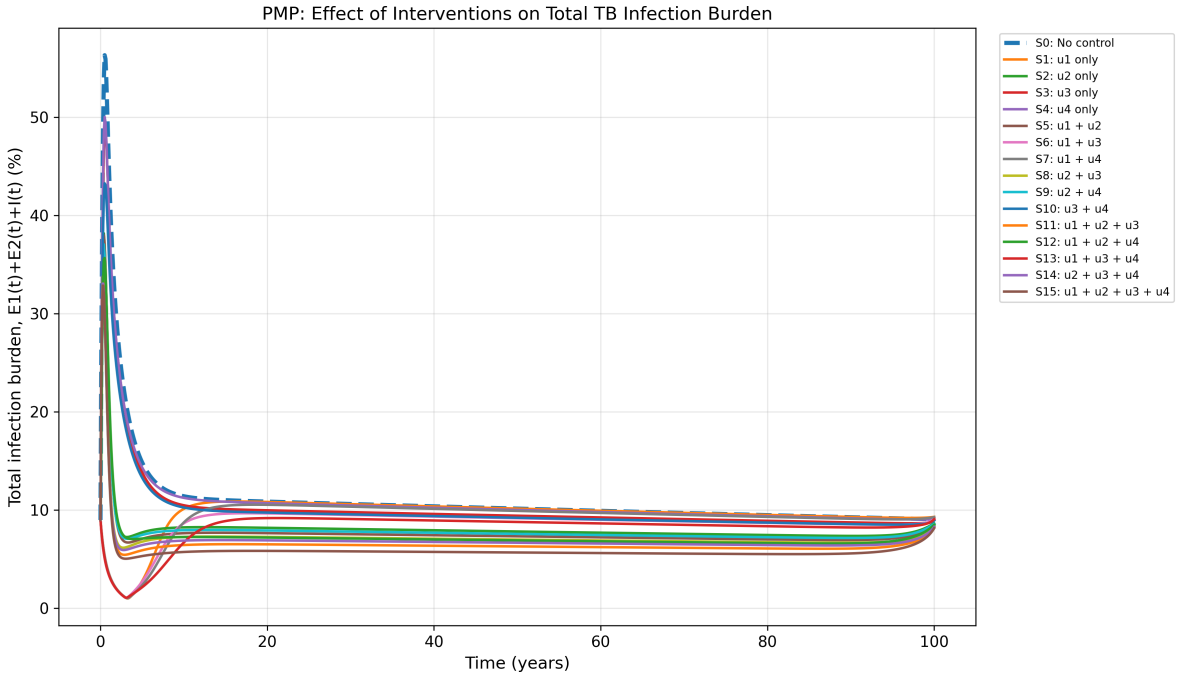

FIGURE 7. Effect of interventions on total TB infections

Figure 7 shows the total infected population, $E_1(t) + E_2(t) + I(t)$, for each strategy. It is clear that all intervention strategies reduce the total number of TB infections compared with the no

control strategy S_0. The dashed line represents S_0, where no control is applied. Since all controlled strategy curves lie below this dashed line, the results indicate that all strategies are effective in reducing the total TB infection burden.

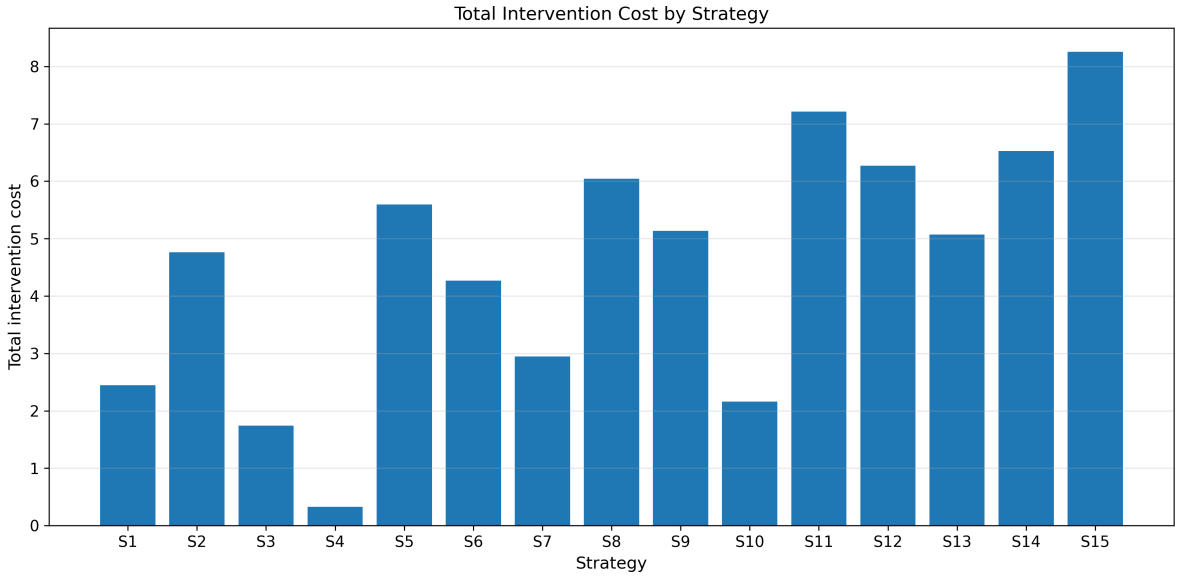

FIGURE 8. Total intervention cost by strategy.

This figure compares the total intervention cost of each strategy. Higher bars mean that the strategy is more expensive. The full combined strategy S_{15} has the highest cost because it uses all four controls.

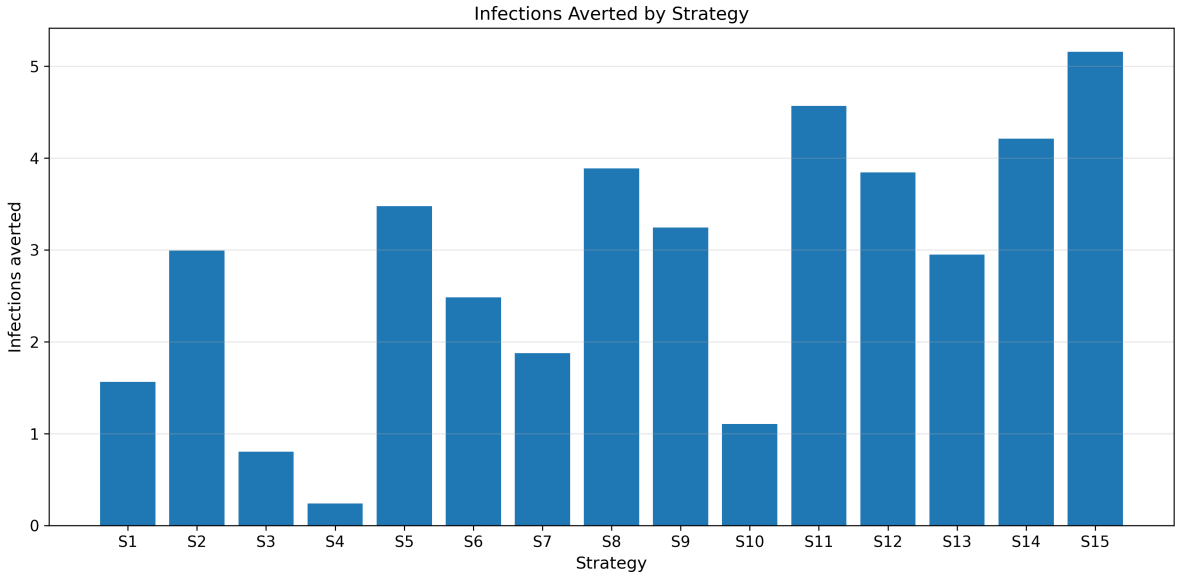

FIGURE 9. Infections averted by strategy.

This figure shows how much TB burden is prevented compared with no control. Higher bars are better because they mean more infections are averted. The full combined strategy S_{15} gives the largest infections averted.

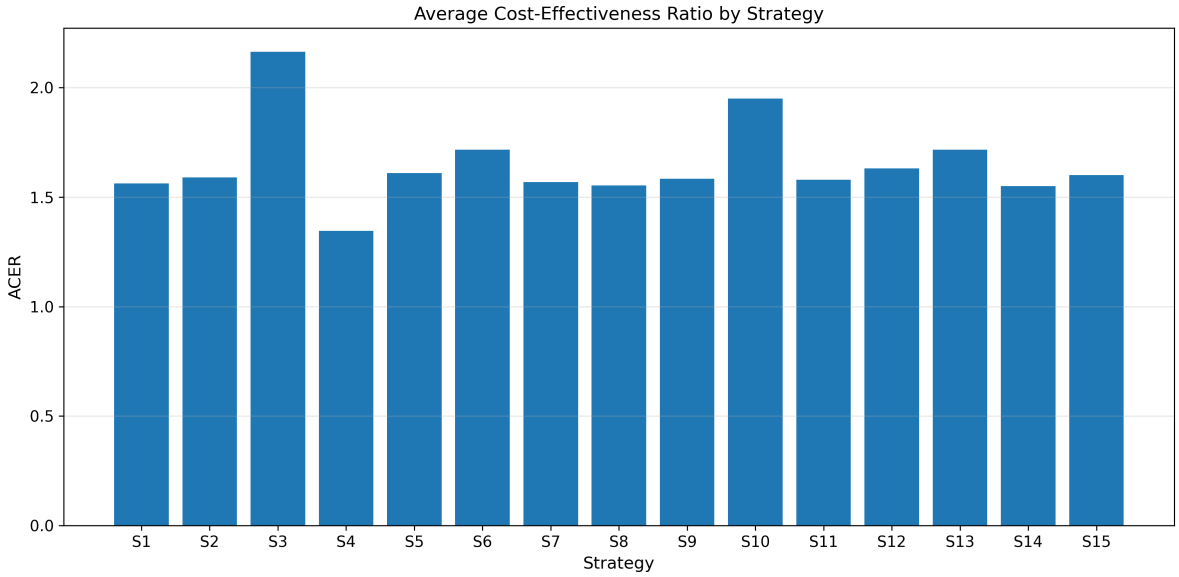

FIGURE 10. Average cost effectiveness ratio by strategy.

This figure shows the ACER for each strategy. Lower bars are better because they indicate a lower average cost per infection burden averted. The vaccination only strategy S_4 has the lowest ACER.

8. CONCLUSION

The main conclusions of this study can be summarized as follows:

- A mathematical model for tuberculosis transmission was formulated by dividing the population into susceptible, diagnosed latent TB, undiagnosed latent TB, infectious, and recovered/vaccinated individuals.
- The basic mathematical properties of the model were investigated, including positivity, boundedness, and the existence of the solutions.
- The disease free equilibrium was obtained, and the basic reproduction number $\mathcal{R}_0$ was derived using the next generation matrix method.
- The mathematical analysis showed that the behavior of the disease depends mainly on the value of $\mathcal{R}_0$. When $\mathcal{R}_0 < 1$, the disease tends to die out, while when $\mathcal{R}_0 > 1$, the disease may persist in the population.
- Sensitivity analysis was performed to identify the most influential parameters affecting $\mathcal{R}_0$. The results showed which parameters should be targeted to reduce tuberculosis transmission.

- An optimal control model was developed by introducing control strategies related to transmission reduction, diagnosis, treatment, and vaccination.
- Numerical simulations showed that all proposed intervention strategies reduce the total number of infections compared with the no control strategy.
- Cost effectiveness analysis was carried out using infections averted, IAR, ACER, and ICER. These measures were used to compare the health benefits of each strategy with its intervention cost.
- The results indicated that the most effective strategy is the one that achieves a high number of infections averted with a low intervention cost.
- The cost effectiveness analysis shows that the full combined strategy S_{15} gives the greatest reduction in TB burden and the largest number of infections averted. However, it is also the most expensive strategy. The vaccination only strategy S_4 has the lowest ACER, meaning it is the cheapest on average per unit of burden averted. However, its total disease reduction is smaller.

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