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THE DYNAMICS OF TUBERCULOSIS TRANSMISSION WITH OPTIMAL CONTROL ANALYSIS IN INDONESIA

FATMAWATI*, UTAMI D. PURWATI, MOH. I. UTOYO, CICIK ALFINIYAH, YUNI PRIHARTINI

Department of Mathematics, Faculty of Science and Technology, Universitas Airlangga,
Surabaya 60115, Indonesia

Abstract. This paper proposes the dynamics of tuberculosis (TB) transmission in Indonesia through a mathematical model. We determine the reproduction number and the equilibria. The parameters model is estimated based on TB data in Indonesia. We obtain the reproduction number of the TB model is $\mathcal{R}_0 = 10.9635$. This shows that eliminating TB in Indonesia requires more efforts. Thus, the optimal control strategy is performed to assess the effect of interventions in reducing TB transmission. We use three controls term in the form of prevention and two treatments. The simulation results indicate that the performance of three controls is the best strategy to reduce the spreading of TB disease among all strategies.

Keywords: tuberculosis; model; stability; parameter estimation; optimal control.

2010 AMS Subject Classification: 34A34, 37N25, 93D20.

1. Introduction

Tuberculosis (TB) caused by the bacillus *Mycobacterium tuberculosis* is an airborne infectious disease. These bacteria attack the lungs (pulmonary TB) but do not rule out the possibility for the bacteria to attack other parts of the body (extrapulmonary TB) such as the brain, kidney,

*Corresponding author
E-mail address: fatmawati@fst.unair.ac.id
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spine, and others [1]. In most TB cases, the bacteria attack and damage the lungs making it difficult for pulmonary TB patients to breathe [2]. TB bacteria is transmitted through the air when people with active TB are lung or coughing throat, sneezing, talking, or singing. There are two possibilities for people infected with TB bacteria, namely latent TB infection and active TB [3]. The latent TB cannot transmit the disease. About one-quarter of the world's population has latent TB [4].

TB is ranked second after HIV as one of the 10 deadliest diseases in the world. There are eight countries that have a high number of TB cases: India, China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh, and South Africa. In 2018, it is an estimated 10 million people were suffering from TB and 1.5 million people died from this disease. More than 95% of deaths caused by TB occur in developing countries [4]. The high rate of TB sufferers is influenced by socioeconomic conditions in various groups of society such as poverty in developing countries. At present, Indonesia is one of the countries with the third-largest number of TB sufferers in the world after India and China. Moreover, the rate of TB transmissions in Indonesia is also high. About 75% of people with TB are economically productive (15-50 years). In addition to being economically detrimental, TB sufferers also experience other negative social impacts, such as stigma and being ostracized by the community [4].

TB is a treatable and curable disease. Various efforts to cure TB continue to be carried out. One of them is the implementation of the Directly Observed Treatment Short-Course (DOTS) strategy. DOTS is a strategy by finding and healing patients whose prioritized in infectious TB patients [3]. TB can also be prevented early by administering the BCG vaccine (Bacillus Calmette-Guerin). The body's defense power of individuals who have been given the BCG vaccine will increase in such a way they can control and kill the bacteria that cause TB that enters the body [5].

Mathematical models have played an essential role in understanding the dynamics of TB transmission. Several mathematical models and strategies control for TB transmission have been established in a number of literature to capture the dynamics of the disease in a more effective method (see, for example, [6, 7, 8, 9, 10] and references therein). Liu and Zhang [6] developed the TB model in the presence of vaccinated populations and populations undergoing

treatment. Ullah, et al. [9] discussed the TB model that include a population of individuals who recover after undergoing treatment. Khan, et al. [10] have studied a model dynamic of TB transmission in Khyber Pakhtunkhwa, Pakistan. Several researchers have presented the optimal control strategies to explore the effectiveness of the intervention [11, 12, 13, 14, 15, 16, 17, 18]. For example, the authors in [17] have extended the TB model of [6] by incorporating the optimal control variable in the form of vaccination, treatment, and successful treatment efforts. Fatmawati et al [18] proposed the discrete age-structured model of TB transmission by taking into account the prevention, chemoprophylaxis, and treatment efforts as control variables.

In this present paper, we developed the dynamics of a TB transmission in [17] by using the standard incidence rate and ignoring the vaccinated compartment. We take into account a recovered compartment in the model and utilize the TB data in Indonesia from 2008 to 2017 to estimate the parameters of the model. We also investigate the effect of the optimal control strategy in reducing latent, active TB, and treated individuals populations. The controls are represented by TB prevention, treatment, and successful treatment efforts. The remaining of the paper is structured as follows: the formulation of the TB model is presented in Section 2. The basic properties and stability analysis are given in Sections 3 and 4. The parameter estimation is devoted in Section 5. The formulation of the optimal control and the numerical simulation are discussed in Sections 6 and 7. Some conclusions are summarized in Section 8.

2. Formulation of TB Model

We construct a TB spread model by taking into account a treated population. The population is assumed to be closed and is split into five classes, which are the susceptible class (S), the latent TB class (E), the active TB class (I), the treated class (T) and the recovered class (R). The latent TB class consists of individuals infected by TB bacteria, but without an infectious status. The active TB class consists of individuals with infectious status. The treated individuals are also infectious. The susceptible population can get TB disease after interacting with infectious TB or treated individual. We assume that newly infected individuals can move to directly to infectious class, while the remaining enters the latent class. The TB spread model is as follows.

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\beta S\,(I+qT)}{N} - \mu S,\\
\frac{dL}{dt} &= \frac{k\beta S\,(I+qT)}{N} - (\delta+\mu)\,L + \rho T,\\
\frac{dI}{dt} &= \frac{(1-k)\beta S\,(I+qT)}{N} + \delta L - (\gamma+\mu+\alpha)\,I,\\
\frac{dT}{dt} &= \gamma I - (\mu+\rho+\theta)\,T,\\
\frac{dR}{dt} &= \theta T - \mu R,
\end{aligned}
\tag{1}
$$

with $0 < \rho + \theta \leq 1$.

The parameters used in the model equation (1) are assumed constant and non-negative. Table 1 presents the interpretation of the parameters.

TABLE 1. Parameters interpretation of the model (1)

Parameter	Interpretation
Λ	recruitment rate
β	transmission rate
q	the reduction in the risk of transmission due to treatment
μ	natural death rate
k	proportion of slow progression
δ	progression rate from L to I
ρ	progression rate from T to L
γ	progression rate from I to T
α	death rate due to the disease
θ	progression rate from T to R

3. BASIC PROPERTIES

In this work, we establish the basic properties of the model (1). We will verify that all variables of the model for all time are non-negative. It can also be explained as, the solution of the TB model with non-negative initial conditions will remain non-negative for every time $t > 0$.

Lemma 1. *For the initial data $H(0) \geq 0$, where $H(t) = (S(t), L(t), I(t), T(t), R(t))$, the solutions of the model (1) will be non-negative whenever they exist and*

$$\lim_{t\longrightarrow\infty} N(t) \leq \frac{\Lambda}{\mu},$$

with $N(t) = S(t) + L(t) + I(t) + T(t) + R(t)$.

Proof. Let $t_1 = \sup\{t > 0 : H(t) > 0 \in [0, t]\}$, then the first equation of the TB model (1) leads to the following,

$$\frac{dS}{dt} = \Lambda - \vartheta(t)S - \mu S \tag{2}$$

with $\vartheta(t) = \frac{\beta(I+qT)}{N}$.

The equation (2) can be expressed as follows,

$$\begin{aligned} S(t_1) &= S(0)\exp\Big\{-\Big(\mu t_1 + \int_0^{t_1} \vartheta(z)dz\Big)\Big\} + \exp\Big\{-\Big(\mu t_1 + \int_0^{t_1} \vartheta(z)dz\Big)\Big\} \\ &\quad \times \int_0^{t_1} \Lambda \exp\Big(\mu y + \int_0^{y} \vartheta(z)dz\Big)dy > 0. \end{aligned}$$

Likewise, we can exhibit for the rest of the variables in H, that is, $H > 0$, $\forall t > 0$. Furthermore, summing all compartments in model (1) lead to the following:

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

Hence

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

□

The TB model (1) has a biologically feasible region given as $\Omega \subset \mathbb{R}^5_+$ with

$$\Omega = \Big\{(S(t), L(t), I(t), T(t), R(t)) \in \mathbb{R}^5_+ : N(t) \leq \frac{\Lambda}{\mu}\Big\}.$$

We have the following results for this feasible region.

Lemma 2. *The region given by $\Omega \subset \mathbb{R}^5_+$ is positively invariant for the TB model (1) with the non-negative initial conditions in $\mathbb{R}^5_+$.*

Proof. The summation of the compartment of the TB model (1), we have

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

Clearly, $\frac{dN(t)}{dt} \leq 0$, if $N(t) \geq \frac{\Lambda}{\mu}$. Thus, $N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}\left(1 - e^{-\mu t}\right)$. Hence, $N(t) \leq \frac{\Lambda}{\mu_h}$ if $N(0) \leq \frac{\Lambda}{\mu}$. Also, if $N(0) > \frac{\Lambda}{\mu}$, then $N(t) \to \frac{\Lambda}{\mu}$ as $t \to \infty$. Therefore, the region Ω is positively invariant and attracts all the solutions in $\mathbb{R}^5_+$. □

4. Model Analysis

The TB model (1) has a disease free equilibrium (DFE), E_0, given by

$$E_0 = \left(S^0, 0, 0, 0, 0\right) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right).$$

Next, we will determine the basic reproduction number ($\mathcal{R}_0$) which has the important role in the disease modeling [19, 20]. The basic reproduction number $\mathcal{R}_0$ can be computed using the next generation matrix on the TB model (1). Consider the infected compartments in TB model (1) are L, I, and T. Using the approach in [21], the matrices F and V at DFE are given as follows:

$$(3)\quad F = \begin{pmatrix} 0 & k\beta & k\beta q \\ 0 & (1-k)\beta & (1-k)\beta q \\ 0 & 0 & 0 \end{pmatrix}, \text{ and V} = \begin{pmatrix} \mu+\delta & 0 & -\rho \\ -\delta & \mu+\alpha+\gamma & 0 \\ 0 & -\gamma & \mu+\rho+\theta \end{pmatrix}.$$

The basic reproduction number of the model (1) is obtained through the spectral radius of the matrix $\mathcal{R}_0 = \rho(FV^{-1})$, which is given by

$$\mathcal{R}_0 = \frac{\beta[\mu+\rho+\theta+\gamma q][(1-k)\mu+\delta]}{(\mu+\rho+\theta)[(\mu+\delta)(\mu+\alpha)+\mu\gamma]+\gamma\delta(\mu+\theta)}.$$

In the following theorem, we present stability of the DFE E_0. We have the following result.

Theorem 1. *The DFE E_0 of the TB model (1) is locally asymptotically stable when $\mathcal{R}_0 < 1$.*

Proof. The Jacobian matrix by evaluated the model (1) at the DFE E_0 is given by

$$J(E_0) = \begin{pmatrix} -\mu & 0 & -\beta & -\beta q & 0 \\ 0 & -(\mu+\delta) & k\beta & k\beta q+\rho & 0 \\ 0 & \delta & (1-k)\beta-(\mu+\alpha+\gamma) & (1-k)\beta q & 0 \\ 0 & 0 & \gamma & -(\mu+\rho+\theta) & 0 \\ 0 & 0 & 0 & 0 & -\mu \end{pmatrix}.$$

It can be seen from the above matrix $J(E_0)$, the eigenvalues are $-\mu$ and $-\mu$ that obviously negative, while the remaining of the eigenvalues with negative reals parts can be determine

through the Theorem 2 of [21].

Let $J_M = F - V$, where F and V are matrices defined by (3).

Define $s(M) = \max(\mathrm{Re}(\lambda) : \lambda \text{is an eigenvalue of } M)$, where $s(M)$ is the simple eigenvalue of matrix M having a positive eigenvector. Thus from [21], we have if $\mathcal{R}_0 < 1$, then $s(M) < 0$. □

Next, we present the existence of the endemic equilibrium. We will carry out the special case of the TB model (1) with no disease-induced mortality ($\alpha = 0$). Consider $E_1 = (S^*, L^*, I^*, T^*, R^*)$ is the endemic equilibrium of the model where

$$S^* = \frac{\Lambda^2}{\mu I Q + \mu\Lambda}, \text{where } Q = \beta\frac{(m+\gamma q)}{m} \text{ and } m = \mu + \rho + \theta$$

$$L^* = \frac{IQk\mu m + \gamma\rho I(IQ+m)}{(\mu+\delta)(IQ+\mu)m},\ T^* = \frac{\gamma I}{m},\ R^* = \frac{\theta\gamma I}{m}.$$

Thus, substituting the above expression in the third equation of the model (1), we have

$$a_1 I_h^{*2} + a_2 I_h^* + a_3 = 0,$$

where

$$\begin{aligned}
a_1 &= -\frac{\theta^2\beta(m+\gamma q)[(1-k)\mu+\delta]}{\mathcal{R}_a},\\
a_2 &= Q(\Lambda+\mu)\Big(m[\mu(\mu+\delta)+\mu\gamma]+\gamma\delta(\mu+\theta)\Big)(K_a-1),\\
a_3 &= \mu\Lambda\Big(m[\mu(\mu+\delta)+\mu\gamma]+\gamma\delta(\mu+\theta)\Big)(\mathcal{R}_a-1),\\
\mathcal{R}_a &= \frac{\beta[m+\gamma q][(1-k)\mu+\delta]}{m[(\mu+\delta)\mu+\mu\gamma]+\gamma\delta(\mu+\theta)},\\
K_a &= \frac{Qm\Big((1-k)(\mu+\delta)\Lambda+k\delta\mu\Big)}{(\Lambda+\mu)\Big(m[(\mu+\delta)\mu+\mu\gamma]+\gamma\delta(\mu+\theta)\Big)}
\end{aligned}$$

Here, $a_1 < 0$ and a_3 is positive when $\mathcal{R}_a > 1$, and negative when $\mathcal{R}_a < 1$. We establish the following result:

Theorem 2. *The TB model (1) has:*

(1) if $a_3 > 0$ and $\mathcal{R}_a > 1$, then there exists a unique endemic equilibrium,

(2) if $a_2 > 0$ and either $a_3 = 0$ or $a_2^2 - 4a_1a_3 = 0$, then we have a unique endemic equilibrium,

(3) if $\mathcal{R}_a < 1$, *so* $a_3 < 0$, *and* $a_2 > 0$ *and their discriminant is positive then two endemic equilibria exists.*

(4) no endemic equilibria otherwise.

5. Parameter Estimation

The aim of this section is to estimate the unknown parameters of the TB model (1). We utilize the cumulative TB case data per 100,000 population in Indonesia from 2008 to 2017. The data refer to the Indonesia Ministry of Health Data and Information Center 2018 [22]. In this study, we employ the least squares method to estimate the model parameters (1) except the parameters μ and Λ are obtained from demographic conditions of Indonesian population. The natural human mortality rate, μ, is obtained from the inverse of the average life expectancy of the population in Indonesia in 2017. The average life expectancy of the Indonesian population in 2017 is 71.06 years [23], so $\mu = 1/71.06$ per year . For parameter Λ the level of human recruitment is calculated as follows. Total population of Indonesia in 2017 is 263,991,400 [24], so that the total population of Indonesia per 100,000 people is $2639,914 \approx 2640$ people. Therefore, $\frac{\Lambda}{\mu} = 2640$, which is the total human population without disease per 100,000 people, so $\Lambda = 2640/71.06$ per year. The rest of the model parameters (1) are estimated using the least squares method with the algorithm referring to [25]. Based on the least squares method, the estimation results of the parameters in model (1) are given in Table 2. The results of the comparison of model solutions (1) and the data of TB sufferers per 100,000 population are given in Figure 1. Using the parameter values from Table 2, we find $\mathcal{R}_0 \approx 10.9635$.

6. Formulation of the Optimal Control

We examine the application of optimal control in model (1) to reduce the spread of TB. There are three control variables applied to the model, namely prevention of TB (u_1) for susceptible population, treatment efforts (u_2) for active TB populations and successful TB treatment effort (u_3) in the populations that receive treatment. The TB model with three control variables is given as follows.

TABLE 2. Fitted and estimated values of the parameters

Parameter	value	References
Λ	2640/71.06	Estimated
β	0.6506	Fitted
q	0.0038	Fitted
μ	1/71.06	Estimated
k	0.1280	Fitted
δ	0.0102	Fitted
ρ	0.0831	Fitted
γ	0.0586	Fitted
α	0.0142	Fitted
θ	0.4405	Fitted

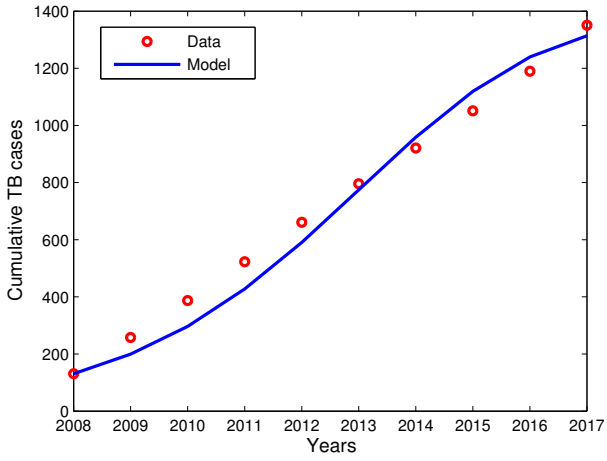

FIGURE 1. Model (1) fitting of the cumulative TB case data per 100,000 population.

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\beta(1-u_1)S\,(I+qT)}{N} - \mu S,\\
\frac{dL}{dt} &= \frac{k\beta(1-u_1)S\,(I+qT)}{N} - (\delta+\mu)\,L + \rho u_3 T,\\
\frac{dI}{dt} &= \frac{(1-k)\beta(1-u_1)S\,(I+qT)}{N} + \delta L - (\gamma u_2 + \mu + \alpha)\,I,\\
\frac{dT}{dt} &= \gamma u_2\, I - (\mu + (\rho+\theta)u_3)\,T,\\
\frac{dR}{dt} &= u_3\theta T - \mu R,
\end{aligned}
\tag{4}
$$

The aim of the optimal control strategies is to minimize the following cost function.

$$(5)\quad J(u_1,u_2,u_3)=\int_0^{t_f} A_1L+A_2I+A_3T+\frac{c_1}{2}u_1^2+\frac{c_2}{2}u_2^2+\frac{c_3}{2}u_3^2\,dt,$$

where A_1, A_2 and A_3 state the weighting constant for latent TB, active TB, and treatment populations respectively, whereas c_1, c_2, and c_3 are weighting constants for the TB prevention, treatment for active TB, and successful TB treatment effort respectively. The main aim is minimize the populations of latent TB, active TB and treatment class with a minimum cost for prevention, treatment, and successful treatment. We take a quadratic form to quantify the control costs [26, 27, 28, 29]. The terms $c_1u_1^2, c_2u_2^2$ and $c_3u_3^2$ represent the costs associated with the TB prevention, TB treatment, and successful TB treatment controls, respectively.

Hence, we investigate the optimal controls u_1^*, u_2^*, and u_3^* such that

$$(6)\quad J(u_1^*,u_2^*,u_3^*)=\underbrace{min}_{\Gamma} J(u_1,u_2,u_3),$$

where $\Gamma=\{(u_1,u_2,u_3)\,|\,0\le u_i\le 1, i=1,2,3\}$.

The conditions necessary for setting the optimal controls u_1^*, u_2^*, and u_3^* that satisfy condition (6) with constraint model (4) will be established via Pontryagin's Maximum Principle [30]. This principle changes equations (4), (5), and (6) into a problem of minimizing the Hamiltonian function H, pointwise with respect to (u_1,u_2,u_3), i.e.,

$$H=A_1L+A_2I+A_3T+\frac{c_1}{2}u_1^2+\frac{c_2}{2}u_2^2+\frac{c_3}{2}u_3^2+\sum_{i=1}^{5}\lambda_i f_i,$$

where f_i represents the right-hand side of the model (4). The adjoint variables λ_i for $i=1,2,\ldots,5$ meet the following co-state system.

$$\begin{aligned}
\dot{\lambda_1}&=-\frac{\partial H}{\partial S}=\lambda_1\mu+(1-u_1)\frac{\left(\beta I+qT\right)}{N}\Big(1-\frac{S}{N}\Big)(\lambda_1-\lambda_2k-\lambda_3(1-k)),\\
\dot{\lambda_2}&=-\frac{\partial H}{\partial L}=-A_1+\lambda_2(\mu+\delta)-\lambda_3\delta+\frac{\beta S(1-u_1)(I+qT)}{N^2}\Big(\lambda_3(1-k)+\lambda_2k-\lambda_1\Big),\\
\dot{\lambda_3}&=-\frac{\partial H}{\partial I}=-A_2+\Big(\lambda_1-\lambda_2k-\lambda_3(1-k)\Big)\frac{\beta S}{N}\Big((1-u_1)-(1-u_1)(\frac{I+qT}{N})\Big)+(\lambda_3-\lambda_4)\gamma u_2+\lambda_3(\alpha+\mu),\\
\dot{\lambda_4}&=-A_3+\Big(\lambda_1-\lambda_2k-\lambda_3(1-k)\Big)\frac{\beta S}{N}\Big(q+(1-u_1)\frac{(I+qT)}{N}\Big)-\lambda_2\rho u_3+\lambda_4(\rho u_3+\mu)+(\lambda_4-\lambda_5)\theta u_3,\\
\dot{\lambda_5}&=-\frac{\partial H}{\partial R}=\beta S(1-u_1)\frac{(I+qT)}{N^2}\Big(\lambda_3(1-k)+\lambda_2k-\lambda_1\Big)+\lambda_5\mu,
\end{aligned}$$

where the transversality conditions $\lambda_i(t_f)=0$, $i=1,2,\ldots,5$.

The algorithms required to get the optimal controls $u=\left(u_1^*,u_2^*,u_3^*\right)$ are as follows [31, 32].

(1) Minimize the function H to the variable u. We have

$$u_1^* = \begin{cases} 0, & \text{for } u_1 \le 0 \\ \frac{((1-k)\lambda_3 - k\lambda_2 - \lambda_1)\beta S I}{c_1 N}, & \text{for } 0 < u_1 < 1 \\ 1, & \text{for } u_1 \ge 1 \end{cases}$$

$$u_2^* = \begin{cases} 0, & \text{for } u_2 \le 0 \\ \frac{(\lambda_3 - \lambda_4)\gamma I}{c_2}, & \text{for } 0 < u_2 < 1 \\ 1, & \text{for } u_2 \ge 1 \end{cases}$$

$$u_3^* = \begin{cases} 0, & \text{for } u_3 \le 0 \\ \frac{(\lambda_4 - \lambda_2)\rho T + (\lambda_4 - \lambda_5)\theta T}{c_3}, & \text{for } 0 < u_3 < 1 \\ 1, & \text{for } u_3 \ge 1 \end{cases}$$

(2) Solve the state equations $\dot{x}(t) = \frac{\partial H}{\partial \lambda}$, where $x = (S, L, I, T, R)$, $\lambda = (\lambda_1, \lambda_2, \ldots, \lambda_5)$, using the initial condition x_0.

(3) Solve the co-state equations $\dot{\lambda}(t) = -\frac{\partial H}{\partial x}$ with terminal conditions $\lambda_i(t_f) = 0$, for $i = 1, 2, 3, \ldots, 5$.

By applying the algorithm, the theorem of the optimum control $\left(u_1^*, u_2^*, u_3^*\right)$ is stated as follows.

Theorem 3. *The optimal control* (u_1^*, u_2^*, u_3^*) *that minimize* $J(u_1, u_2, u_3)$ *over* Γ *is*

$$u_1^* = \max\left\{0, \min\left\{1, \frac{((1-k)\lambda_3 - k\lambda_2 - \lambda_1)\beta S I}{c_1 N}\right\}\right\}$$

$$u_2^* = \max\left\{0, \min\left\{1, \frac{(\lambda_3 - \lambda_4)\gamma I}{c_2}\right\}\right\}$$

$$u_3^* = \max\left\{0, \min\left\{1, \frac{(\lambda_4 - \lambda_2)\rho T + (\lambda_4 - \lambda_5)\theta T}{c_3}\right\}\right\}$$

where λ_i, $i = 1, 2, 3, \ldots, 5$, *are the solutions of co-state equations* $\dot{\lambda}(t) = -\frac{\partial H}{\partial x}$.

7. Numerical Results

We address the numerical solution of the control model (4) with and without control. We utilize the fourth-order Runge-Kutta (RK4) algorithm to obtain the numerical solution of the control model. The forward RK4 algorithm is employed to solve the state systems. Thus, the backward RK4 algorithm is used to solve the co-state system [33].

Parameters used for the simulations could be seen in Table 2, for which the basic reproduction ratio $\mathcal{R}_0 = 10.9635$. We assume that the values of the weighting constant are $A_1 = A_2 = A_3 = 1$, $c_1 = 1.3, c_2 = 1.8$, and $c_3 = 2.3$. Moreover, the initial condition is $S(0) = 2398.09, L(0) = 0, I(0) = 131, T(0) = 0, R(0) = 111$. We display a period of 10 years to simulate the optimal control.

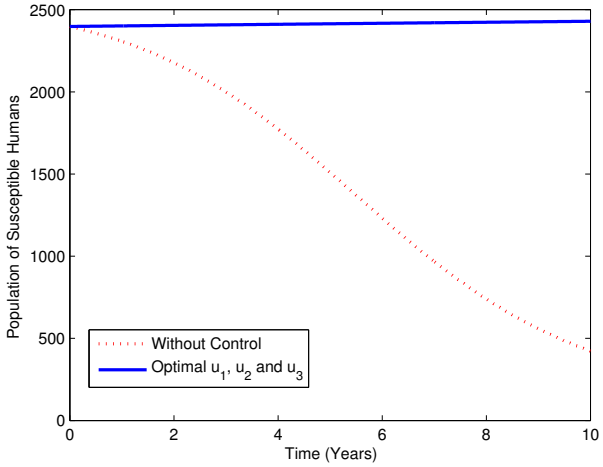

FIGURE 2. Susceptible population with and without control

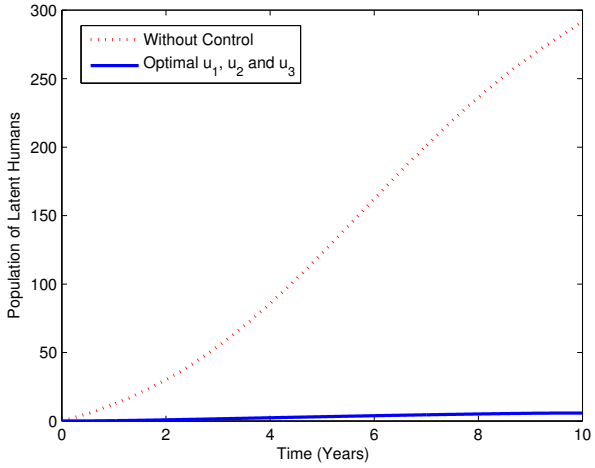

FIGURE 3. Latent population with and without control

To investigate the impact of the intervention strategy, we compare the results of the simulation for the case with and without control. In Figure 2, we observe that the susceptible population increases using the controls compared to the uncontrolled. As depict in Figure 3 and Figure 4, we

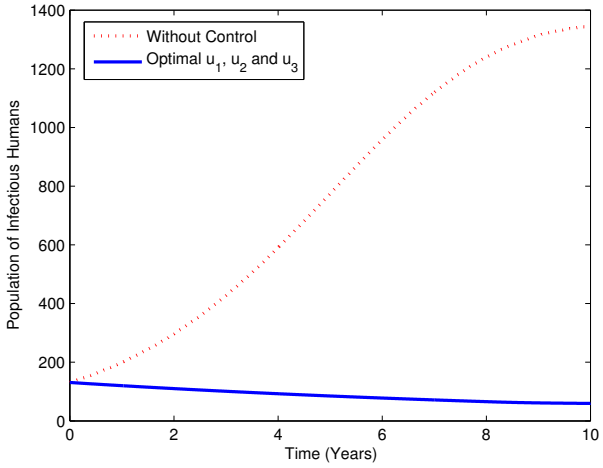

FIGURE 4. Infectious population with and without control

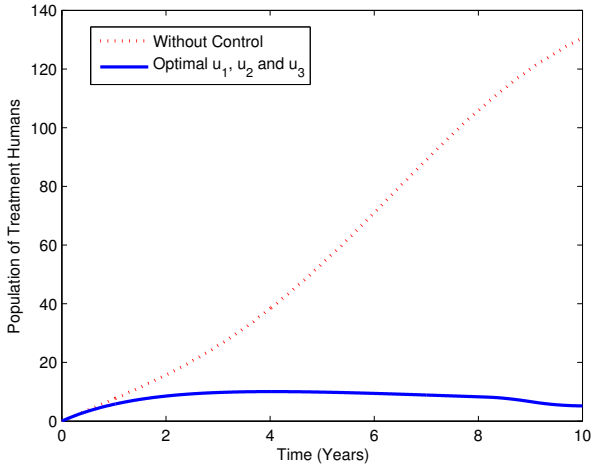

FIGURE 5. Treated population with and without control

can see that the individuals infected with TB in the latent phase and in the active phase decrease significantly using the optimal control. The yield in Figure 5 predicts that the implementation of the optimal control significantly reduces the number of the treated population.

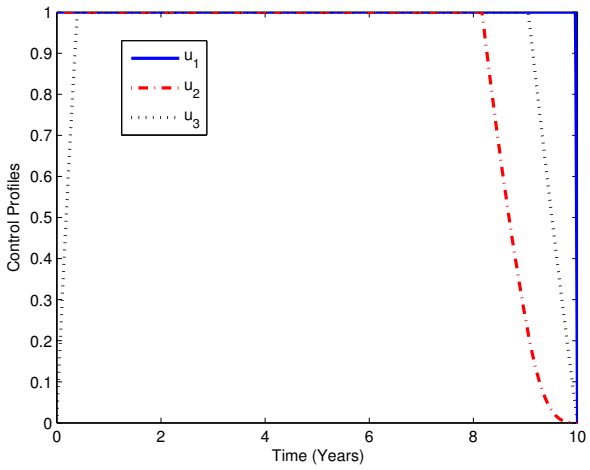

FIGURE 6. Profile of optimal controls u_1^*, u_2^* and u_3^*

The profile of the optimal controls is set out in Figure 6. The simulation results in Figure 6 recommend that the implementation of the prevention (u_1^*) should be at the maximum level for the period of intervention, while the treatment control u_2^* should be maintained at the maximum effort for 8 years before it decreases to zero. Meanwhile, the treatment u_3^* is given full effort starting in the half of the first year to the 9th year and decreases to zero at the end of the intervention.

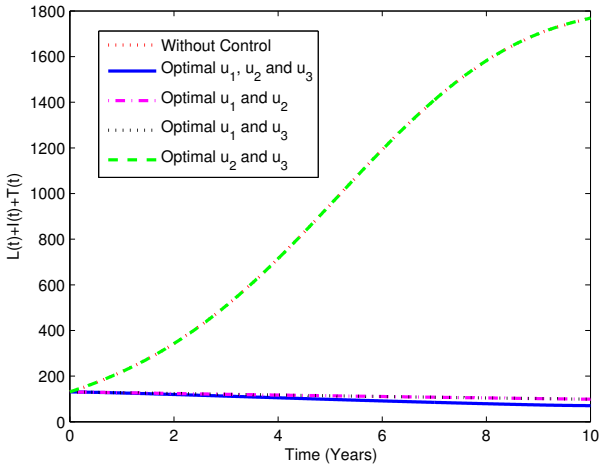

FIGURE 7. Infected individuals (latent, infectious, treated individuals) using various control strategies

The comparison of the latent, infectious, and treated individuals for different strategy controls is summarized in Figure 7. We display in Figure 7 that the number of the latent, infectious, and treated individuals is lowest when three controls are applied.

8. Conclusion

In this study, we have presented the mathematical model of TB transmission in Indonesia. The TB model was parameterized based on the cumulative TB case data per 100,000 population in Indonesia from 2008 to 2017. The basic properties, the reproduction number ($\mathcal{R}_0$) and the equilibria of the model are obtained. The DFE is locally asymptotically stable when reproduction number less than one. The endemic equilibrium of the model is carried out whenever disease-induced mortality is set to zero. Based on the result of the estimated parameters, the value of $\mathcal{R}_0$ is $\mathcal{R}_0 = 10.9635$. This yield indicates that TB disease is still persistent in Indonesia. Thus, we implemented the optimal control strategies to verify the effect of prevention and two treatments to reduce the TB transmission in Indonesia. The numerical simulation was set out for various control strategies. The results show that the simultaneous application of the three control variables has a very significant effect on controlling the spread of TB in the population, especially in Indonesia.

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Conflict of Interests

The author(s) declare that there is no conflict of interests.

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