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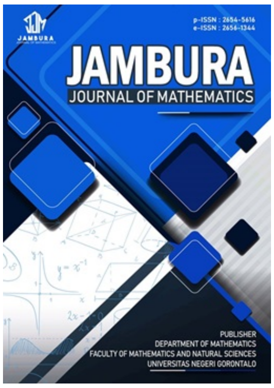

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Research Article

Control Analysis on Dynamic System Model of Tuberculosis Disease with Educational Campaign, Vaccination, and Treatment

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ABSTRACT. *Tuberculosis (TB) is caused by bacteria (Mycobacterium tuberculosis) that most commonly attacks the lungs. TB is spread from person to person through the air. When people with pulmonary TB cough, sneeze, or spit, they propel TB germs into the air. By inhaling only a small number of these germs, a person can become infected. Tuberculosis is curable and preventable. Prevention that can be done is by providing education about TB and vaccines. While treatment can be done by treating infected individuals. This study examines the TB epidemic model with the application of control, by finding optimal control solutions using the Pontryagin Minimum Principle method. In this study, three control variables were applied, namely education, vaccination and treatment. Numerical calculations were carried out using the Forward Backward Sweep 4th order Runge Kutta method and and then simulated. The results of the numerical simulation of the TB epidemic model show that by implementing control in the form of education, vaccination, and treatment, the population of infected individuals can be reduced.*

1. Introduction

Tuberculosis (TB), or Tb (short for "Tubercle bacillus") or kematus is a common infectious disease, and in many cases fatal. It is caused by various strains of mycobacteria, most commonly Mycobacterium tuberculosis (abbreviated "MTb" or "MTbc") [1]. Tuberculosis usually attacks the lungs, but can also affect other parts of the body. Tuberculosis is spread through the air when someone with active TB infection coughs, sneezes, or otherwise spreads their saliva droplets through the air [2]. Most TB infections are asymptomatic and latent (often called latent TB). However, one in ten cases of latent infection progress to active disease (active TB). If tuberculosis is not treated, more than 50% of people who are infected can die. Before the discovery of effective antibiotics to treat TB (around the early 1900s), an estimated 1 in 7 people in the world died from the disease.

According to the World Health Organization, TB is still a global health problem today. TB is the second leading cause of death in the world after COVID-19 in 2022. More than 10 million people are infected with TB each year. Without treatment, the death rate from TB is high (around 50%). Globally in 2022, TB caused around 1.30 million deaths. With WHO-recommended treatment, 85% of TB cases can be cured. The number of people newly diagnosed with TB globally was 7.5 million in 2022. Thirty countries with a high TB burden accounted for 87% of the world's TB cases in 2022 and two-thirds of the global total occurred in eight countries: India (27%), Indonesia (10%), China (7.1%), Philippines (7.0%), Pakistan (5.7%), Nigeria (4.5%), Bangladesh (3.6%) and the Democratic Republic of the Congo (3.0%). In 2022, 55% of TB patients were male, 33% female, and 12% were children (aged 0–14 years) [1].

Tuberculosis (TB) is a chronic infectious disease that is still a public health problem. Based on the 2023 Global TB Report, Indonesia is in second place with the largest number of TB cases in the world after India, followed by China. With an estimated number of TB cases of 1,060,000 TB cases and 134,000 deaths due to TB per year in Indonesia (there are 17 people who die from TB every hour). As an effort to control TB, the government issued Presidential Regulation No. 67 of 2021 concerning TB Control. There are six TB control strategies in Indonesia, namely: 1) Strengthening the commitment and leadership of the central, provincial, and district/city governments to support the acceleration of TB elimination by 2030; 2) Increasing access to quality and patient-centered TB services; 3) Optimization of promotion and prevention efforts, provision of preventive TB treatment, and infection control; 4) Utilization of research results and screening technology, diagnosis, and management of TB; 5) Increasing the role of communities, partners, and other multi-sectors in eliminating TB; and 6) Strengthening program management through strengthening the health system.

Mathematical researchers use dynamic system modeling in order to participate in predicting and preventing this outbreak from becoming an epidemic. Dynamic system modeling is an an-

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alytical approach used to understand and describe the behavior of a complex system. Dynamic system modeling not only predicts the dynamics of changes in the number of infected individuals but can also include the role of control to overcome the outbreak; the theory of using such control is called the Pontryagin Minimum Principle [3–10]. Mathematical models have an important role in understanding the dynamics of infectious diseases, including Tuberculosis [11, 12]. Most TB models are of the SEIR type, where the population is divided into susceptible, exposed, infectious, and excluded [13]. In previous studies, this type of tuberculosis model discussed disease control by considering the role of disease transmission parameters that can help reduce values below threshold values [14–16]. Many authors have used the concept of fractional calculus [17–26], and obtained several significant contributions that are useful in many disease dynamics [27–35]. Mahardika and Kartika [36] in his research explained the Tuberculosis epidemic model with control using the Pontryagin Minimum Principle. In the study, the dynamic modeling of Tuberculosis with control stated that vaccination and treatment successfully reduced the population of infected individuals. This study will examine the addition of optimal control in the form of an educational campaign to prevent TB and analyze how this control works in the model used.

In previous studies of Mahardika and Kartika [36], the SEIR type TB model was used using control measures in the form of vaccination and treatment. Furthermore, this study used the SEIR type TB model with control measures in the form of educational campaign, vaccination, and treatment with the aim of reducing the number of infected individuals.

2. Model

2.1. Dynamic System Model of Tuberculosis Disease

In this section, we discuss the mathematical model of tuberculosis spread. There are many mathematical theories about the concept of disease spread. The basic idea of this theory is that everyone becomes healthy and suppresses the spread of the disease. In this study, four population classes are used, Susceptible (S), Exposed (E), Infectious (I), and Cured (R), the dynamic model of tuberculosis is described in the following differential equation system [36]:

$$\dot{S} = \varrho - \varphi SI - \sigma S, \tag{1}$$
$$\dot{E} = (1-\omega)\varphi SI - \sigma E - \gamma E, \tag{2}$$
$$\dot{I} = \omega\varphi SI + \gamma E - \sigma I - \psi I - \tau I, \tag{3}$$
$$\dot{R} = \tau I - \sigma R, \tag{4}$$

with initial conditions $S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0$.

The birth rate is constant in the susceptible class and is given by ϱ, disease transmission occurs as a result of contact between susceptible and infected individuals. The parameter rate from exposed to infectious form given as γ, the transmission coefficient form given as φ and ω. The natural death rate in each compartment is assumed to be the same and is given as σ, and deaths due to disease occur only in the Infection compartment and are given as ψ.

2.2. Dynamic System Model of Tuberculosis Disease with Optimal Control

Then in this study, from the TB dynamic system model with the SEIR type, it was developed by applying control actions, so that the mathematical model of the TB dynamic system with the application of control actions is as follows:

$$\dot{S} = \varrho - \varphi SI - \sigma S - \zeta_1 S, \tag{5}$$
$$\dot{E} = (1-\omega)\varphi SI - \sigma E - \gamma E - \zeta_2 E, \tag{6}$$
$$\dot{I} = \omega\varphi SI + \gamma E - \sigma I - \psi I - \tau I - \zeta_3 I, \tag{7}$$
$$\dot{R} = \tau I - \sigma R + \zeta_1 S + \zeta_2 E + \zeta_3 I, \tag{8}$$

with initial conditions $S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0$.

Optimal control is a way to determine which control variables will cause the process to meet some physical constraints and minimize the objective function that has been determined in this study. The formulation requires a control process for mathematical description (or model), specification of performance indices, and statement of boundary conditions and physical and/or control constraints [10]. The control variables used in this model are $\zeta_1,\ \zeta_2,\ \zeta_3$ which represent the education campaign, vaccination, and treatment. First, assume that all susceptible populations have the opportunity to be aware of the dangers of TB disease (education campaign) $\zeta_1(t)$, vaccination $\zeta_2(t)$, so that the susceptible TB population $\zeta_1(t)$ transmits from population $S(t)$ to population $E(t)$ and $\zeta_2(t)$ transmits from population $E(t)$ to population $I(t)$. Active treatment $\zeta_3(t)$ can reduce the number of infected individuals transmitting from population $I(t)$ to population $R(t)$.

3. Results and Discussion

3.1. Control Analysis

The goal of optimal control is to reduce the number of infected population and carry out control actions. Then the objective function according to the control variables and dynamic model (5)-(8) is as follows:

$$J(\zeta_1,\ \zeta_2) = \int_0^{t_f} A_1 I + \frac{A_2}{2}\zeta_1^2(t) + \frac{A_3}{2}\zeta_2^2(t) + \frac{A_4}{2}\zeta_3^2(t)dt\ , \tag{9}$$

The implementation cost of the controls is represented by a quadratic term of objective functional $F(\zeta_1(t), \zeta_2(t), \zeta_3(t))$. $A_1,\ A_2,\ A_3,\ A_4$ represent the weights related to infected humans, educational campaign control, vaccination control, and treatment control, respectively. The objective of this study is to use the minimal possible control variables $\zeta_1,\ \zeta_2,\ \zeta_3$ and minimize the population of infected individuals.

The optimal control problem is to find the control $\zeta_1,\ \zeta_2,\ \zeta_3$ with the appropriate state variables on the time interval, which minimizes the objective function (9) with the system dynamics constraints (5)-(8):

$$J(\zeta_1^*, \zeta_2^*, \zeta_3^*) = \underbrace{\min}_{\Omega}\ J(\zeta_1, \zeta_2, \zeta_3)\,, \tag{10}$$

with $\Omega = (\zeta_1, \zeta_2, \zeta_3)\,|0 \leq \zeta_1 \leq \zeta_1^*,\ 0 \leq \zeta_2 \leq \zeta_2^*,\ 0 \leq \zeta_3 \leq \zeta_3^*$.

In this study, the Hamiltonian function is obtained as follows

$$H = (I, \zeta_1, \zeta_2, \zeta_3, \vartheta_1,\ \vartheta_2,\ \vartheta_3,\ \vartheta_4) \tag{11}$$

$$= A_1 I + \frac{A_2}{2}\zeta_1^2(t) + \frac{A_3}{2}\zeta_2^2(t) + \frac{A_4}{2}\zeta_3^2(t) + \xi_1 \dot{S}(t) + \xi_2 \dot{E}(t) + \xi_3 \dot{I}(t) + \xi_4 \dot{R}(t).$$

Theorem 1. *Given the solutions $S^*(t)$, $E^*(t)$, $I^*(t)$, $R^*(t)$ and the optimal controls $\zeta_1^*(t)$, $\zeta_2^*(t)$, $\zeta_3^*(t)$ of the corresponding state system in eq. (5)–(8) are the adjoint variables that satisfy the following equations:*

$$\begin{aligned}
\dot{\xi_1}(t) &= -(\xi_1(-\varphi I - \sigma - \zeta_1) + \xi_2((1-\omega)\varphi I) \\
&\quad + \xi_3(\omega\varphi I) + \xi_4(\zeta_1)), \\
\dot{\xi_2}(t) &= -(\xi_2(-\sigma - \gamma - \zeta_2) + \xi_3(\gamma) + \xi_4(\zeta_2)), \\
\dot{\xi_3}(t) &= -(A_1 + \xi_1(-\varphi S) + \xi_2((1-\omega)\varphi S) \\
&\quad + \xi_3(\omega\varphi S - \sigma - \psi - \tau - \zeta_3) + \xi_4(\tau + \zeta_3)), \\
\dot{\xi_4}(t) &= -(\xi_4(-\sigma)), \\
\zeta_1^* &= \max\left\{0,\ \min\left\{\frac{S(\xi_1 - \xi_4)}{A_2}\right\}, 1\right\}, \\
\zeta_2^* &= \max\left\{0,\ \min\left\{\frac{E(\xi_2 - \xi_4)}{A_3}\right\}, 1\right\}, \\
\zeta_3^* &= \max\left\{0,\ \min\left\{\frac{I(\xi_3 - \xi_4)}{A_4}\right\}, 1\right\}.
\end{aligned}$$

Proof. Differentiate the Hamiltonian equation H based on their respective conditions and use the PMP method to obtain the adjoint variable equation and with respect to transversality conditions, we have

$$\begin{aligned}
\frac{d\xi_1}{dt} &= -\frac{\partial H}{\partial S} \\
&= -(\xi_1(-\varphi I - \sigma - \zeta_1) + \xi_2((1-\omega)\varphi I) \\
&\quad + \xi_3(\omega\varphi I) + \xi_4(\zeta_1)), \\
\frac{d\xi_2}{dt} &= -\frac{\partial H}{\partial E} \\
&= -(\xi_2(-\sigma - \gamma - \zeta_2) + \xi_3(\gamma) + \xi_4(\zeta_2)), \\
\frac{d\xi_3}{dt} &= -\frac{\partial H}{\partial I} \\
&= -(A_1 + \xi_1(-\varphi S) + \xi_2((1-\omega)\varphi S) \\
&\quad + \xi_3(\omega\varphi S - \sigma - \psi - \tau - \zeta_3) + \xi_4(\tau + \zeta_3)), \\
\frac{d\xi_4}{dt} &= -\frac{\partial H}{\partial R} = -(\xi_4(-\sigma)), \\
\frac{\partial H}{\partial \zeta_1} &= 0 \Rightarrow A_2\zeta_1 - \xi_1 S + \xi_4 S = 0, \\
\zeta_1 &= \frac{S(\xi_1 - \xi_4)}{A_2}, \\
\frac{\partial H}{\partial \zeta_2} &= 0 \Rightarrow A_3\zeta_2 - \xi_2 E + \xi_4 E = 0, \\
\zeta_2 &= \frac{E(\xi_2 - \xi_4)}{A_3}, \\
\frac{\partial H}{\partial \zeta_3} &= 0 \Rightarrow A_4\zeta_3 - \xi_3 I + \xi_4 I = 0, \\
\zeta_3 &= \frac{I(\xi_3 - \xi_4)}{A_4},
\end{aligned}$$

$$\begin{aligned}
\zeta_1^* &= \max\left\{0, \min\left\{\frac{S(\xi_1 - \xi_4)}{A_2}\right\}, 1\right\}, \\
\zeta_2^* &= \max\left\{0, \min\left\{\frac{E(\xi_2 - \xi_4)}{A_3}\right\}, 1\right\}, \\
\zeta_3^* &= \max\left\{0, \min\left\{\frac{I(\xi_3 - \xi_4)}{A_4}\right\}, 1\right\}.
\end{aligned}$$

□

3.2. Numerical Simulation

The mathematical model of tuberculosis introduced in this study includes several important factors in the handling and prevention of the spread of TB disease. We use numerical methods to solve the optimal control problem [24–27]. In this study we use the PMP method using the Forward Backward Sweep 4th order Runge Kutta. The parameter values are presented in Table 1.

Table 1. Description and values of parameters

No	Descriptions	Parameter	Value
1	Initial value (point) of Recovered	$R(0)$	1000
2	Initial value (point) of Infectious	$I(0)$	2292
3	Initial value (point) of Exposed	$E(0)$	10000
4	Initial value (point) of Susceptible	$S(0)$	1.668×10^6
5	Natural Death rate	σ	0.0101
6	Death rate due to infection	ψ	0.2
7	Rate from infectious to recovery	τ	0.25
8	Rate from exposed to infectious	γ	0.05
9	Transmission coefficient	ω	0.128
10	Transmission coefficient	φ	0.00002
11	Birth rate	ϱ	0.0121

In this chapter, the graphs of the dynamic system without optimal control (1) and with optimal control (2) will be compared. The type of optimal control in this case is fixed time ($T = 10$ years) and free endpoint ($x(0)$ is determined, but $x(T)$ is free) [16], where x is a state variable ($x = S, E, I, R$).

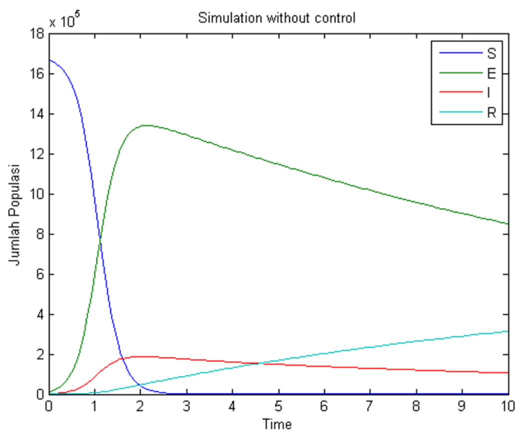

Figure 1. Simulation of SEIR without control

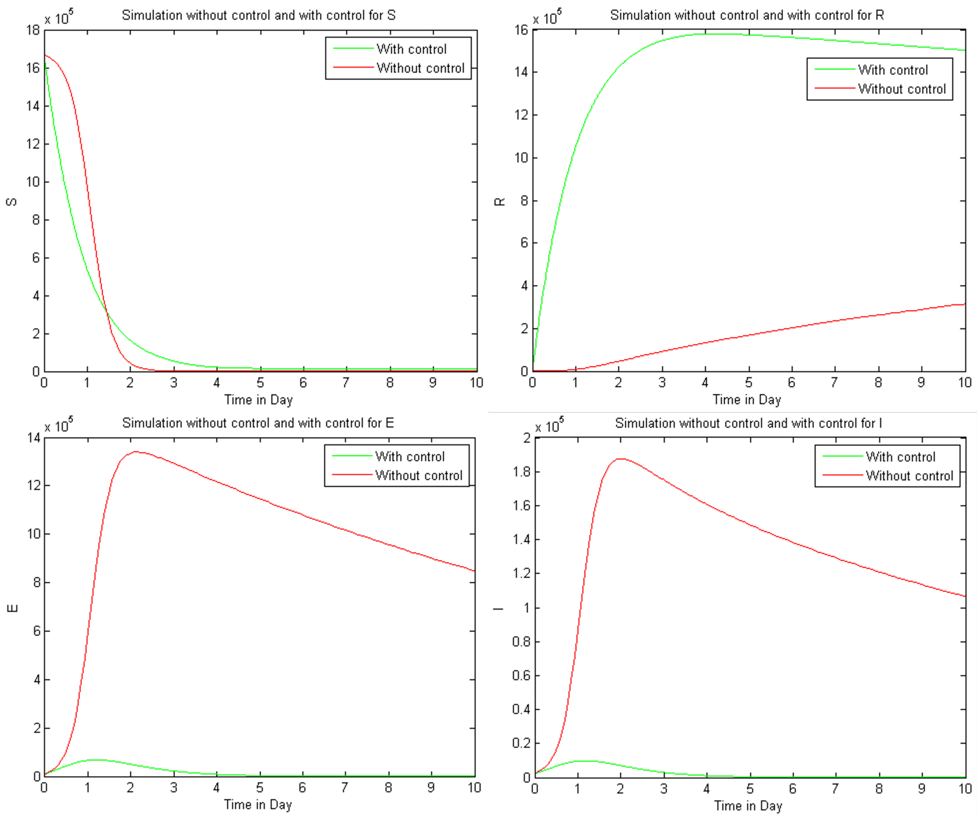

Figure 2. Simulations of SEIR without and with control for each subpopulation

Figure 1 and Figure 2 is the result of a numerical simulation using Matlab software in solving the optimal control problem in a mathematical model of the spread of Tuberculosis. The simulation results show that in the population of susceptible and infected individuals, before being given control measures, there was a decrease as well as when given control measures, but when given control measures at the beginning of the observation there was a faster decrease compared to without control. In the population of exposed individuals, it can be seen that before being given control, there was a very significant increase, and after being given control at the beginning of the observation there was a slight increase after that there was a decrease and towards 0. In the population of recovered individuals, it shows that before being given control measures there was an increase but not significant, but after being given control measures there was a significant increase.

We develop a mathematical model of the spread of SEIR type tuberculosis disease by implementing control measures. There are three control measures used in this study, namely with education campaigns, vaccinations and treatment. The existence of optimal control and its properties are calculated and evaluated. Based on the simulation results, the provision of optimal control in the form of education campaigns, vaccinations and treatment, which shows that the optimal control offered can meet the research objectives of reducing the population of infected individuals. This study will provide statistics to assist the government in making choices and implementing actions to combat tuberculosis disease.

4. Conclusion

In this study, the model for the spread of tuberculosis consists of four subpopulations: Susceptible (S), Exposed (E), Infectious (I), and Cured (R), known as the SEIR model. Furthermore, three control measures are applied based on the mathematical model: ζ_1, ζ_2, and ζ_3, representing education campaigns, vaccination, and treatment, respectively. The objective of optimal control is to reduce the number of infected individuals. The existence of optimal control within the SEIR mathematical model for tuberculosis spread has been demonstrated. In this study, the Pontryagin Maximum Principle (PMP) method was applied, combined with the fourth-order Runge-Kutta numerical method, and simulations were conducted using MATLAB software. Based on the simulation results, the control variables implemented in this study effectively achieved the research objective of reducing the infected population.

Author Contributions. **Nur Ilmayasinta:** Conceived of the presented idea, developed the theory and performed the computations, derived the models and performed the numerical simulations. **Prismahardi Aji Riyantoko:** Conceived the study and were in charge of overall direction and planning, analysis the semulation. **Annisa Rahmita Soemarsono:** Conceived the study and were in charge of overall direction and planning, analysis the semulation. **Ulifatur Rochmatin**: Resources, assist in compiling scientific articles and adapting them to journal templates. All authors have read and agreed to the published version of the manuscript.

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