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DYNAMIC SYSTEM OF TUBERCULOSIS MODEL USING OPTIMAL CONTROL IN SEMARANG CITY INDONESIA

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ABSTRACT

Tuberculosis is a disease that is very contagious among humans. To prevent this from happening, the Semarang city government has enacted vaccination for exposed individuals and treatment for the infected individuals. Vaccination and treatment are forms of control that will be applied to dynamic model systems of Tuberculosis. The present paper will describe an epidemic model of Tuberculosis with control using the Pontryagin Minimum Principle to find the optimal solution of the control with a fixed time and free endpoint. The optimal control will aim to reduce or minimize the number of infected populations. Numerical calculation is carried out with MATLAB software programming to illustrate and compare the graph of the dynamic model with and without optimal control. The results of dynamic modeling of Tuberculosis with control state that vaccination and treatment have succeeded in reducing the population of infected individuals.

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1. INTRODUCTION

Tuberculosis (TB) is a human disease caused by Mycobacterium tuberculosis, which mainly affects the human respiratory system, which is the lungs. This disease is contagious among humans and has the potential to cause an outbreak. To prevent this outbreak becoming an epidemic, mathematical scientists use dynamic systems modeling to predict changes in the number of healthy and infected individuals in a certain population in certain time [1].

Dynamic system modeling not only predicts the dynamics of changes in the number of infected individuals but can also include a control role to overcome the outbreak; the theory of the use of control is called the Pontryagin Minimum Principle [2] [3]. Tuberculosis is one of disease which is a very contagious disease that causes death globally and the leading cause of death from a single infectious pathogen [4], Tuberculosis is considered one of the 10 deadliest diseases in the world and ranked second after HIV [5]. More than 95% of deaths caused by Tuberculosis occur in developing countries; it is estimated 10 million people were suffering from Tuberculosis, and 1.5 million people died from this disease in 2018 [6].

Nowadays, Indonesia is one of the countries with the third-largest number of Tuberculosis sufferers in the world after India and China. The high rate of Tuberculosis sufferers is influenced by social and economic conditions in various groups of society. Moreover, the rate of Tuberculosis transmission in Indonesia is also high. Tuberculosis sufferers also experience other negative social impacts, such as stigma and being ostracized by the community [6]. Tuberculosis can be cured and treated. Various efforts to cure be carried out by giving the patient drugs such as isoniazid (INH), rifampin (RIF), ethambutol (EMB), pyrazinamide (PZA) [7] and another effort made to prevent Tuberculosis is by giving vaccines such as BCG which is first used on humans in 1921 [8]. In this paper, we developed the dynamic model of tuberculosis transmission using vaccine and treatment as optimal control to minimize the infected population in Semarang City, Indonesia. It is important to note that the mathematical model of Tuberculosis was first introduced by Waaler et al. in 1962 as a differential equation system [9].

2. RESEARCH METHODS

We construct a Tuberculosis spread model by taking four population classes; these populations are assumed to have a natural death rate in each class; their class is Susceptible class (S), Exposed class (E), Infectious class (I), and Recovered class (R). Then, the dynamic model of Tuberculosis without optimal control can be described as differential equation system:

$$\begin{aligned}
\dot{S} &= b - \beta SI - \mu S \\
\dot{E} &= (1-p)\beta SI - \mu E - \alpha E \\
\dot{I} &= p\beta SI + \alpha E - \mu I - \delta I - \varphi I \\
\dot{R} &= \varphi I - \mu R
\end{aligned} \tag{1}$$

With initial condition $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$, $R(0) \geq 0$.

System (1) can be describe using flow diagram as:

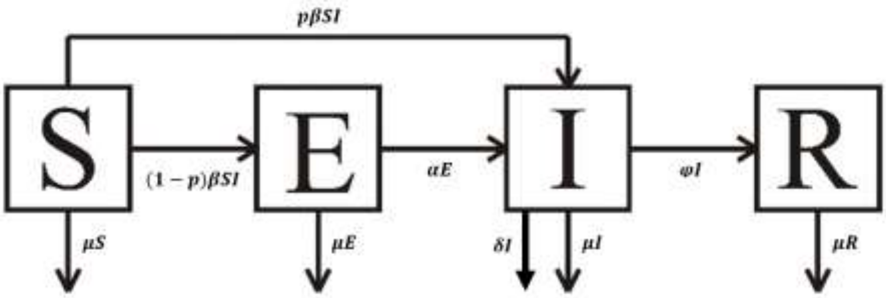

Figure 1. Flow Diagram of Dynamic System (1)

And then we define the dynamic model of Tuberculosis using optimal control as:

$$\begin{aligned} \dot{S} &= b - \beta SI - \mu S \\ \dot{E} &= (1-p)\beta SI - \mu E - \alpha E - u_1 E \\ \dot{I} &= p\beta SI + \alpha E - \mu I - \delta I - \phi I - u_2 I \\ \dot{R} &= \phi I - \mu R + u_1 E + u_2 I \end{aligned} \qquad (2)$$

With initial condition $S(0)\geq 0$, $E(0)\geq 0$, $I(0)\geq 0$, $R(0)\geq 0$.

In the system (1) and (2) b represent parameter of birth rate, β and p represent transmission coefficient, α represent parameter rate from exposed to infectious, ϕ represent parameter of natural recovery rate of infectious, δ represent parameter of death rate due to infection, and μ represent parameter of natural death rate.

System (2) can be describe using flow diagram as:

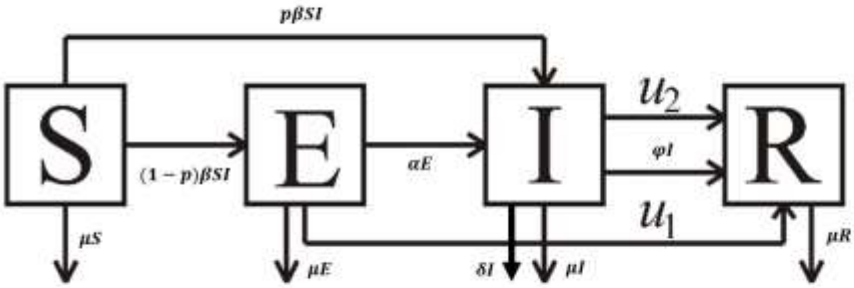

Figure 2. Flow diagram of dynamic system (2)

We present the optimal control mechanism to reduce the spread of the Tuberculosis disease using the following control variables:

i. $u_1(t)$ is control function representing vaccination effectiveness for exposed people.
ii. $u_2(t)$ is control function represent treatment effectiveness for infected people.

The purpose of the optimal control is to reduce the number of infected population and control measures. Then the objective functional correspond with control variables and dynamic model (2):

$$J(u_1,u_2) = \text{minimize} \int_0^T K_1 I + \frac{K_2}{2}u_1^2(t) + \frac{K_3}{2}u_2^2(t)dt \qquad (3)$$

subject to (2).

The weight of the infected and the costs function of u_1, u_2 represent as K_1, K_2, K_3 respectively. The goal of objective functional is to minimize the number of infected individuals and the cost of the control measures. Then define control functions $\left(u_1^*, u_2^*\right)$ such that:

$$J\left(u_1^*, u_2^*\right) = \text{minimize } \{(u_1,u_2); u_1,u_2 \in U\} \text{ subject to (1)} \qquad (4)$$

and control set by:

$$U = \{(u_1,u_2) | u_i \text{ are Lebesque measurable on } [0,T], 0 \leq u_i \leq 1, i = 1,2\} \qquad (5)$$

Theorem 1. There exists control $u^* = \left(u_1^*, u_2^*\right) \in U$ such that:

i. The variables of state and variables of control are positive.
ii. Control set (4) is closed and convex.
iii. The right-hand side of the state system (2) is continuous, is bounded above by a linear combination of the control and state, and can be written as a linear function of u with coefficients depending by the time and the state.
iv. The integrand of the objective functional (2) is convex on u.
v. There exists constant $C_1, C_2 > 0$ and $\phi > 1$ such that the integrand of the objective functional satisfies:

$$L(x,u) = -C_2 + C_1|u|^{\phi} \tag{6}$$

To find the optimal solution, we begin by defining the Lagrangian and the Hamiltonian associated with the optimal control problem [15].

The Lagrangian is given by:

$$L(I,u_1,u_2) = K_1 I + \frac{K_2}{2}u_1^2(t) + \frac{K_3}{2}u_2^2(t) \tag{7}$$

and the Hamiltonian:

$$H(I,u_1,u_2,\lambda_1,\lambda_2,\lambda_3,\lambda_4) = K_1 I + \frac{K_2}{2}u_1^2(t) + \frac{K_3}{2}u_2^2(t) + \lambda_1(\dot{S}) + \lambda_2(\dot{E}) + \lambda_3(\dot{I}) + \lambda_3(\dot{R}) \tag{8}$$

Here λ_1, λ_2, λ_3 and λ_4 are adjoin variables that satisfies:

$$\begin{aligned}
\frac{d\lambda_1}{\mathrm{dt}} &= -\frac{\partial H}{dS} = \lambda_1(\beta I + \mu) - \lambda_2\beta(1-p) - \lambda_3 p\beta I \\
\frac{d\lambda_2}{\mathrm{dt}} &= -\frac{\partial H}{\partial E} = \lambda_2(\mu + \alpha + u_1) - \lambda_3\alpha + \lambda_4 u_1 \\
\frac{d\lambda_3}{\mathrm{dt}} &= -\frac{\partial H}{\partial I} = \lambda_1\beta S + \lambda_3(u_2 + \delta + \mu + \phi - Sp\beta) - \lambda_4(u_2 + \phi) - K_1 \\
\frac{d\lambda_4}{\mathrm{dt}} &= -\frac{\partial H}{\partial R} = \lambda_4\mu
\end{aligned} \tag{9}$$

with terminal (transversality) condition $\lambda_1(T) = \lambda_2(T) = \lambda_3(T) = \lambda_4(T) = 0$. These adjoin variables will minimize the state variable with respect to the state function. Then the optimal variables of control:

$$\frac{\partial H}{\partial u_1} = E(\lambda_2 - \lambda_4) - K_2 u_1 = 0 \Rightarrow u_1^* = \frac{E(\lambda_2 - \lambda_4)}{K_2} \tag{10}$$

with $u_1 = u_1^*$

$$\frac{\partial H}{\partial u_2} = I(\lambda_3 - \lambda_4) - K_3 u_2 = 0 \Rightarrow u_2^* = \frac{I(\lambda_3 - \lambda_4)}{K_3} \tag{11}$$

with $u_2 = u_2^*$

Since $0 \le u_1 \le 1$ and $0 \le u_2 \le 1$, we can rewrite for u_1^*:

$$u_1^* = \max\left\{0, \min\left(\frac{E(\lambda_2 - \lambda_4)}{K_2}, 1\right)\right\} \tag{12}$$

and u_2^*

$$u_2^* = \max\left\{0, \min\left(\frac{I(\lambda_3 - \lambda_4)}{K_3}, 1\right)\right\} \tag{13}$$

3. RESULTS AND DISCUSSION

The numerical result of the optimal control problem in the system (2) will be in the form of a graph and calculated using MATLAB programming [15]. In this chapter, we will compare the graph of the dynamic system without optimal control (1) and with optimal control (2). The type of optimal control in this case is fixed time (T = 10 years) and free end point ($x(0)$ determined, but $x(T)$ are free) [16], where x is the variable of state $(x = S, E, I, R)$.

Table 1. Parameter Data of Dynamic System Model (1) and (2)

Parameter	Description	Values	Reference

b	Birth rate	0.0121	[11]
β	Transmission coefficient	0.00002	[10]
p	Transmission coefficient	0.128	[10]
α	Rate from exposed to infectious	0.05	[10]
ϕ	Rate from infectious to recovery	0.25	[10]
δ	Death rate due to infection	0.2	[13]
μ	Natural Death rate	0.0101	[11]
$S(0)$	Initial value (point) of Susceptible	1.668×10^{6}	[11]
$E(0)$	Initial value (point) of Exposed	10000	Fitted
$I(0)$	Initial value (point) of Infectious	2292	[12]
$R(0)$	Initial value (point) of Recovered	1000	Fitted

Table 1 shows parameter data of system (2); these data are needed to run the program using MATLAB software **[14]** to generate graph functions of susceptible, exposed, infectious, and recovered.

The simulation graph function of susceptible, exposed, infectious, and recovered is shown in the figure below:

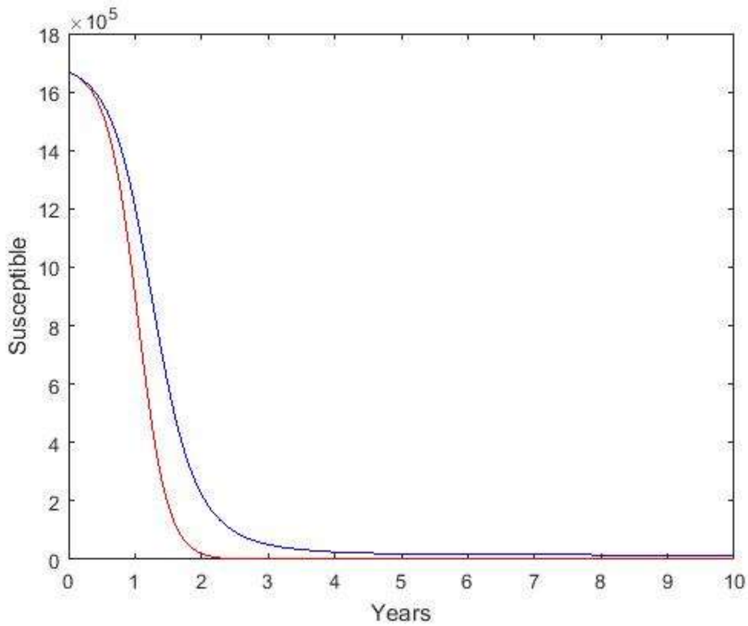

Figure 3. Dynamics of Susceptible Population vs Time

Figure 3 describes a comparison chart of the dynamics of a susceptible population with control (blue curve) and without control (red curve). We can see that by applying optimal control, the population of susceptible increased (blue curve). Susceptible population graphs with control converged to the value of 35070, while susceptible population graphs without control converged to the value of 0.005.

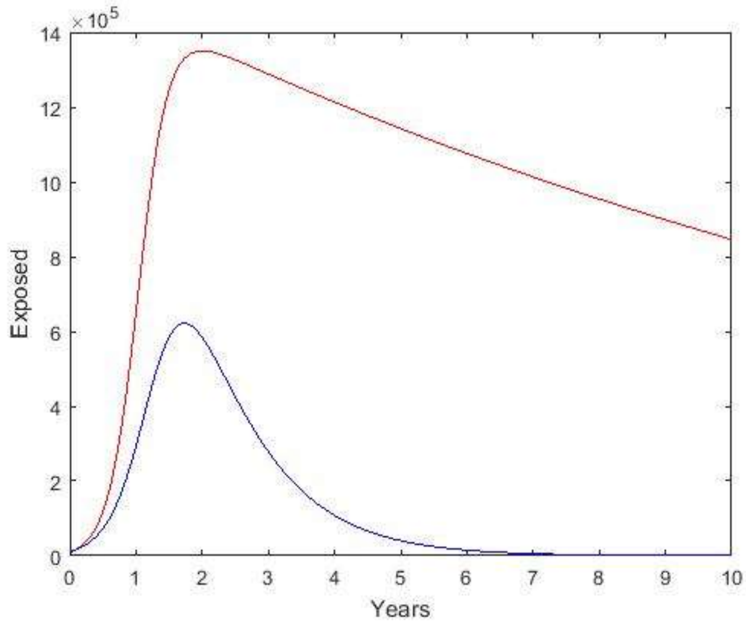

Figure 4. Dynamics of Exposed Population vs Time

In **Figure 4** describe comparison chart of dynamics of exposed population with control (blue curve) and without control (red curve). We can see that by applying optimal control, population of exposed decreased significantly (blue curve). For exposed population graphs with control converging to value of 430, while exposed population graphs without control converging to value of 848500.

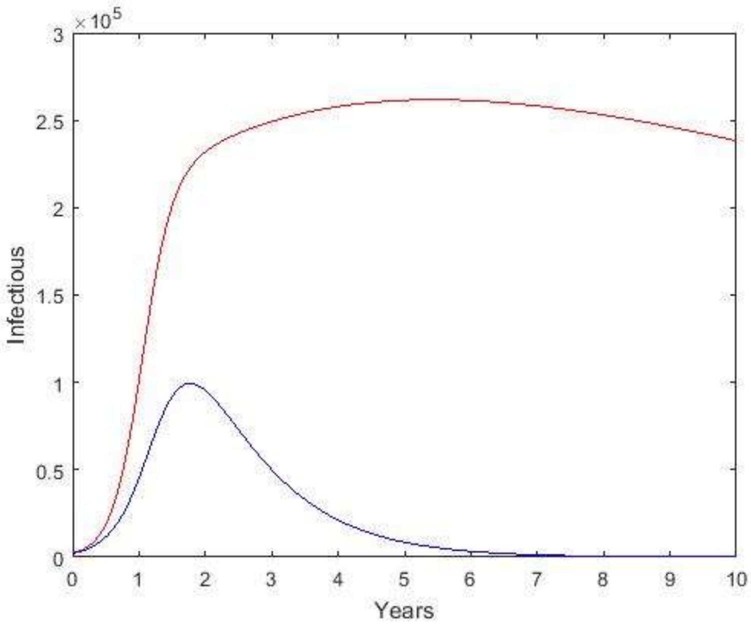

Figure 5. Dynamics of Recovered Population vs Time

In **Figure 5** describe comparison chart of dynamics of infected population with control (blue curve) and without control (red curve). We can see that by applying optimal control, population of infected decreased significantly (blue curve). For infected population graphs with control converging to value of 46, while infected population graphs without control converging to value of 242700.

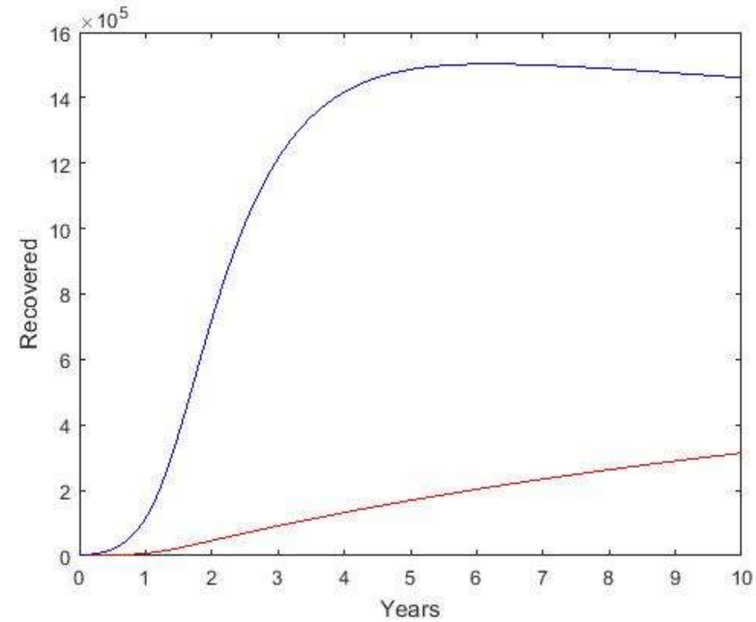

Figure 6. Dynamics of Susceptible Population vs Time

Figure 6 describes a comparison chart of the dynamics of the recovered population with control (blue curve) and without control (red curve). By applying optimal control, we can see that the recovered population increased significantly (blue curve). Recovered population graphs with control converged to the value of 1449000, while recovered population graphs without control converged to the value of 314100.

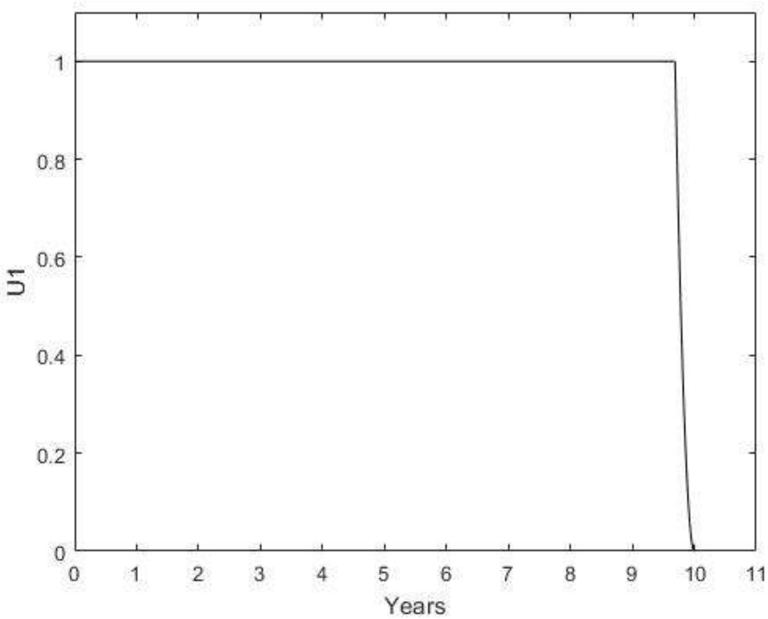

Figure 7. Control u_1 vs Time

Figure 7 depicts the control graph u_1. As we can see the x axis is time and y axis is the value of the control effectiveness. Control u_1 is the effectiveness of vaccination.

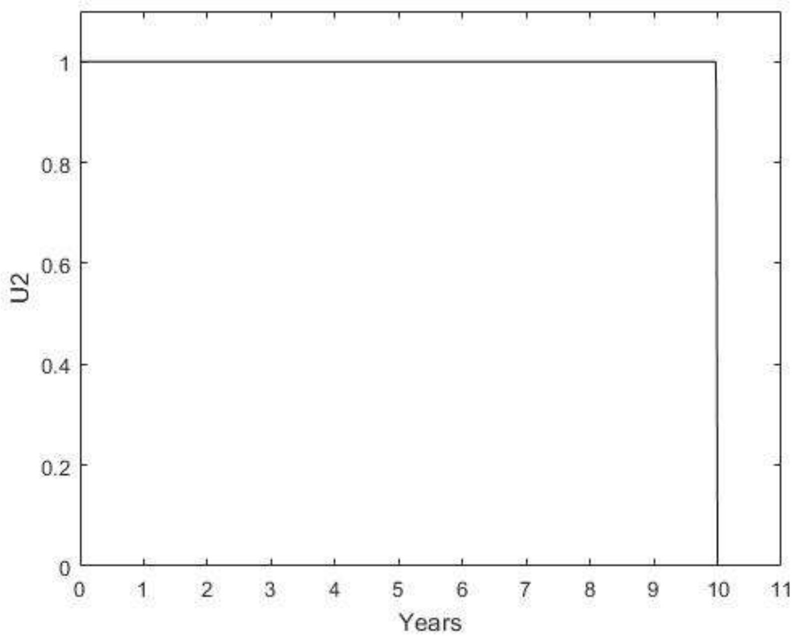

Figure 8. Control u_2 vs Time

Figure 8 depicts the control graph u_2. As we can see, the x axis is time and y axis is the value of the control effectiveness. Control u_2 is the effectiveness of treatment.

The terms $-u_1E(t)$ and $-u_2I(t)$, in the dynamic system (2) means that there is a reduction in the rate of change of the exposed and infected population by $u_1E(t)$ and $u_2I(t)$ respectively. A detail description will be given in the following example:

By numerical calculation (iteration) using MATLAB software it is known that $u_1(2)E(2) = 566{,}386$, $u_2(2)I(2) = 80{,}680$, with $t = 2$ years, means on the second year we should aim to vaccinate 566,386 exposed individuals and giving treatment to 80,680 infected individuals simultaneously, u_1 and u_2 play role as effectiveness of the vaccine and treatment since $0 \le u_1 \le 1$ and $0 \le u_2 \le 1$. When this is done, the infected population will decrease rather than not being vaccinated and treated, and then the number of recovered populations will increase because people who have been vaccinated and treated are cured (considered cured).

4. CONCLUSIONS

The main result of this paper is to find the value of optimal control (u_1 and u_2) using the Pontryagin Minimum Principle method, which is applied to the dynamic modeling of Tuberculosis spread. The value of optimal control here is 566,386 exposed individuals should be vaccinated $(u_1(t)E(t))$, and 80,680 infected individuals should be treated $(u_2(t)I(t))$ simultaneously correspond with time t. This control is intended to reduce the spread of the Tuberculosis disease in Semarang city. In the end, the use of the control function in the dynamic model is to provide advice to the health authorities on how to handle and control the tuberculosis outbreak.

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