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OPTIMAL CONTROL ANALYSIS OF TUBERCULOSIS DYNAMICS WITH DUAL QUARANTINE STRATEGIES USING REAL DATA IN INDONESIA

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Abstract: Tuberculosis is a serious health problem worldwide, with high transmission rates specifically in developing countries. Indonesia lies on the second rank with an estimated more than a million of new cases per years and about hundred thousand of death. This study aimed to explore an optimal control analysis of tuberculosis involved two kind of quarantines strategies in Indonesia. First, models were constructed by considering several subhuman populations, such as healthy, infected, and diagnosed individuals. Some parameters such as transmission rate, recovery rate, and medical interventions are involved. Dynamical analysis has been conducted through several algorithms in mathematical modelling analysis, which consists of 1) critical point analysis, 2) stability analysis, and 3) threshold value analysis. Optimal control has been applied in the constructed model for the final study to observe the long-term behavior of the disease and the impact of interventions on reducing infected individual. This research resulted in two critical points, which is a critical point of disease-free equilibrium and endemic equilibrium. Regarding the next generation matrix and the disease-free equilibrium, basic reproduction number was generated, and it had been used to explore local and global analysis stability. The first condition, basic reproduction number will be less than one means that disease-free equilibrium is stable which the infection will die out of the human population while in the second, basic reproduction number will be more than one and it means that disease-free equilibrium is unstable or endemic equilibrium will arise and the infection will persist in the human population. To enhance control, Pontryagin Maximum Principle is applied to characterize the necessary condition in reducing the prevalence of TB. This study highlights that the implementation of two quarantines strategies, combined with medication treatment, significantly lower the

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number of infected individuals and minimizes both infection burden and interventions cost.
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1. INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis and this bacterium belongs to the acid-fast bacteria group which has a complex cell wall. It mainly attacks the lungs in humans, but there are also many cases of TB infecting other organs in the human body. The disease is transmitted through the air when an active TB patient coughs or sneezes, releasing droplets containing the bacteria into the air then infecting people who are exposed to the droplets. People with weak immune systems will eventually become infected with TB (Arsyad et al., [1]; De Martino et al., [2]; Mohammadnabi et al., [3]).

Transmission can occur more easily in places with high density and poor ventilation, such as prisons or hospitals. After being inhaled, Mycobacterium tuberculosis reaches the pulmonary alveoli and is taken up by macrophages. These macrophages function to fight infection, but TB bacteria can survive inside macrophages and evade the body's immune response (Scordo et al., [4]). In most healthy individuals, the body will form granulomas to limit the spread of bacteria, which usually does not cause symptoms. However, individuals with weakened immune systems, such as those with HIV, diabetes, or those taking immunosuppressive drugs, the infection can develop into an active disease that causes damage to the lungs and other organs (Cribbs et al., [5]; Li et al., [6]).

The main symptoms of pulmonary TB are a cough lasting more than two weeks, accompanied by phlegm that sometimes contains blood. In addition, patients may experience fever, weight loss, night sweats, and fatigue that can interfere with daily activities (Luies & Du Preez, [7]; Radović et al., [8]). In cases of pulmonary tuberculosis, the most common symptoms are as follows:1) Chronic cough: A cough that lasts more than two weeks, often accompanied by blood; 2) Fever: A mild fever that occurs mainly in the afternoon or evening; 3) Weight loss: Unexplained weight loss, often accompanied by a loss of appetite; 4) Night Sweats: Excessive sweating at night; 5) Fatigue: Fatigue and weakness that often interfere with daily activities. Meanwhile, in cases of extrapulmonary TB or TB that attack other organs, the symptoms vary greatly, depending on the organ infected, including TB meningitis, kidney TB, bone TB, and lymphatic TB. Bone TB can cause bone pain, while TB meningitis can cause headaches, confusion, and seizures (Radović et

al., [8]; Usmonov & Kobilov, [9]; Verma et al., [10]).

Up to now, tuberculosis (TB) remains a significant global health problem, including its spread in Indonesia. As a country with a large and complex population, Indonesia faces challenges in controlling the spread of TB. Therefore, the constructed dynamical model and optimal control analysis for TB in Indonesia are crucial. Data shows that Indonesians still suffer from a high burden of TB. Based on a report provided by the World Health Organization (WHO) in 2022, Indonesia ranks fourth in the world in terms of the number of TB cases, with more than 800,000 new cases each year, while a report issued by the Indonesian Minister of Health in 2024 recorded 1,092,000 new TB cases with 125,000 deaths each year (Devita, [11]; Siahaan et al., [12]).

Based on several studies related to the TB in Indonesia, the disease spread is caused by several factors involving social and economic complexities. Poverty, limited access to health services, and high population mobility are factors that contribute to the spread of the disease (Siahaan et al., [12]; Susanti et al., [13]). Another equally important factor is the challenges in diagnosis and treatment techniques provided to TB patients. The long treatment period for patients causes some patients to not complete their therapy, which ultimately leads to recurrence or drug resistance (Odoom et al., [14]; Soumya et al., [15]).

One important approach in TB treatment is the quarantine or isolation of infected patients, especially those with active TB who have the potential to transmit the disease to others. Quarantine is an infection control measure that involves separating TB patients from the community to prevent the spread of bacteria. Patients newly diagnosed with active TB, for those who have not yet started treatment, should be isolated in a well-ventilated healthcare facility or in their homes with strict preventive measures (Bergman & Thomas, [16]; Soumya et al., [15]).

Patient isolation is also important in cases of drug-resistance, such as MDR-TB and XDR-TB, as treatment for these two types of TB is longer and more complex. Patients with active TB who are not properly isolated can continue to transmit the disease, exacerbating the spread of disease in the community. In some countries, hospitals or special health facilities are provided to treat TB patients with strict isolation and close monitoring of treatment compliance.

In addition, treatment with this quarantine approach also needs to be supported by efforts to raise public awareness about the dangers of TB transmission and the importance of maintaining physical distance and wearing masks. Overall, quarantine serves to minimize direct contact with infected people, reduce the risk of transmission, and ensure that patients receive appropriate

treatment before they can interact with the community again. If treatment is carried out correctly, the majority of people with TB can be completely cured and return to a normal life without symptoms. However, if patients do not follow the treatment correctly, patients can continue and cause serious complications, even death. Someone who has recovered from TB can still be infected again. Even though treatment has successfully cured a previous infection, the body is not be completely immune to the disease infection in the future.

2. PRELIMINARIES

Mathematical models play an important role in detailing and predicting patterns of TB spread. By understanding the dynamics between susceptible, infected, and recovered individuals, mathematical models can provide deeper insights into how the disease can develop within a population. The SIR (Susceptible-Infectious-Removed) model and agent-based models are some types of mathematical models that have been successfully used to model TB spread in various contexts. These models consider parameters such as contact rate, transmission probability, and infection duration to provide a more accurate picture of disease spread.

When applying mathematical models to the Indonesian context, it is important to adjust the parameters to local demographic, social, and economic characteristics. This requires accurate data and a deep understanding of the local community. The use of mathematical models can assist the Indonesian government in designing more effective interventions. By predicting the impact of various intervention scenarios, health policies can be more targeted and efficient.

The main challenges in using mathematical models to model TB in Indonesia are parameter uncertainty and data limitations. Therefore, efforts are needed to improve the quality and quantity of available data and develop more complex models to address this uncertainty. The implications of these model findings can assist the government and health organizations in developing policies that are more adaptive and responsive to the dynamics of tuberculosis in Indonesia.

By combining a multidisciplinary approach and collaboration between researchers, the government and health institutions, mathematical models can be a powerful tool in the fight against TB in Indonesia. Through a better understanding of the factors that influence the spread of this disease, it is hoped that TB control efforts can be more effective and targeted.

Based on the characteristics of TB disease transmission, which has specific symptoms, prevention, and treatment through quarantine and non-quarantine measures, all disease transmission scenarios must be considered when developing a mathematical model. The

mathematical model is constructed by dividing the human population into seven time-dependent sub-populations, namely: the vaccinated human population ($V(t)$), the susceptible human population ($S(t)$), the infected but not yet infectious human population ($L(t)$), infected human population ($I(t)$), quarantined human population ($T_1(t)$), non-quarantined human population ($T_2(t)$), and recovered human population ($R(t)$).

3. MAIN RESULTS

a. Model Formulation

The TB disease spread model was constructed using the following assumptions: a) This study only used cases of pulmonary TB with active TB and passive (latent) TB conditions, b) The vaccine used was the BCG vaccine, administered at birth until the age of 2 months, c) No vaccines were administered to adults, d) Treatment used the DOTS system during quarantine, e) Quarantine is carried out in hospitals or homes with strict rules for treatment (T_1), f) No quarantine is imposed on individuals who have been infected with TB, and only non-strict treatment is provided (T_2), and g) Individuals who have recovered cannot be exposed to TB bacteria again.

Based on the research assumptions that have been compiled, the following is a compartmental diagram that serves as a guide in constructing a mathematical model of TB disease spread.

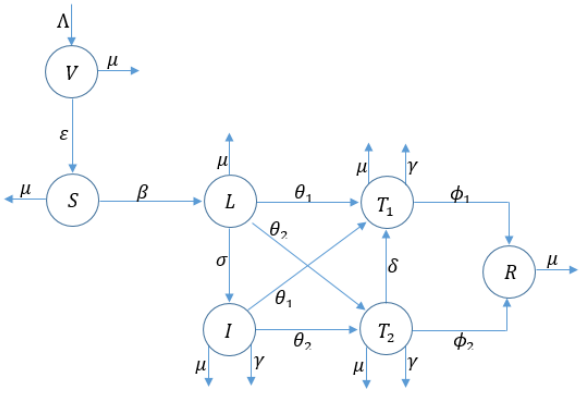

Figure 1 Compartmental diagram of TB

Furthermore, based on the compartmental diagram in Figure 1 and the model assumptions, we construct a system of differential equations about the spread of TB for each human subpopulation as follows.

$$\frac{dV}{dt} = \Lambda - \varepsilon V - \mu V \qquad (1)$$

$$\frac{dS}{dt} = \varepsilon V - \mu S - \beta SI \quad (2)$$

$$\frac{dL}{dt} = \beta SI - \mu L - \theta_1 L - \theta_2 L - \sigma L \quad (3)$$

$$\frac{dI}{dt} = \sigma L - \mu I - \gamma I - \theta_1 I - \theta_2 I \quad (4)$$

$$\frac{dT_1}{dt} = \theta_1 L + \theta_1 I + \delta T_2 - \mu T_1 - \gamma T_1 - \phi_1 T_1 \quad (5)$$

$$\frac{dT_2}{dt} = \theta_2 L + \theta_2 I - \delta T_2 - \mu T_2 - \gamma T_2 - \phi_2 T_2 \quad (6)$$

$$\frac{dR}{dt} = \phi_1 T_1 + \phi_2 T_2 - \mu R \quad (7)$$

For simplicity, define

$$A = \mu + \theta_1 + \theta_2 + \sigma \text{ and } B = \mu + \gamma + \theta_1 + \theta_2$$

Sub-population of vaccinated individual increases with the recruitment rate denoted by Λ and after loss of immunity, the individual move to the susceptible sub-population with rate ε. Susceptible sub-population decrease due to the individual in this population has contact with infected individuals denoted by β and it causes the increases of latent sub-population. In this latent sub-population, there are two transmision route for each individual, first route that individual can be treated into quarantine or non quarantined treatment and the second route they will go to the infected sub-population with progression rate to the TB active denoted by σ. Treatment which give to the infected individual also have two transmission. They move to the quarantine or non quarantined sub-population denoted by θ_1 and θ_2 respectively. Finally, individual from quarantine and non quarantined then move to recovered sup-population. This study consider natural death in each population with the rate μ and death cuased by the disease with rate γ for infected, quarantine, and non quarantined sub-population.

b. Model Validation

We estimate the parameter in our model using the real data of TB in Indonesia. The data have been collected from the ministry of Health of the Republic of Indonesia. The parameter have been obtained through nonlinear least squares method and the value of $MAPE = 0.0348$ and fit quality $R^2 = 0.85$. The average relative error of the prediction against actual data is only about 3.5%, meaning that the model closely mimics the annual case trend. Approximately 85% of the data variation can be explained by the model, indicating a strong match between the simulation

results and the observational data. The result of estimating parameters seems to match the infection data as shown in Figure 2 and the estimation of parameter values are obtained based on the condition in Indonesia as follows in Table 1.

Figure 2. Fitting Parameter based on the real data in Indonesia

Tabel 1. Parameter values based on the infected cases of TB in Indonesia

No	Parameter	Value	Source
1.	β	0.000000239	Estimated
2.	σ	0.267	Estimated
3.	Λ	2789350	Estimated
4.	ε	1.15576	Estimated
5.	μ	0.0143	Assumed
6.	θ_1	0.1095	Estimated
7.	θ_2	0.1932	Estimated
8.	γ	2	Estimated

c. Positivity and Boundedness of Solutions

Furthermore, it is necessary to show that the system has a bounded solution set. Suppose N is the total population then $N = V + S + L + I + T_1 + T_2 + R$. It can be obtained

$$\frac{dN}{dt} = \frac{dV}{dt} + \frac{dS}{dt} + \frac{dL}{dt} + \frac{dI}{dt} + \frac{dT_1}{dt} + \frac{dT_2}{dt} + \frac{dR}{dt}$$

$$\frac{dN}{dt} = \Lambda - \mu V - \mu S - \mu L - \mu I - \gamma I + \delta T_2 - \mu T_1 - \gamma T_1 - \delta T_2 - \mu T_2 - \gamma T_2 - \mu R$$

$$\frac{dN}{dt} = \Lambda - \mu(V + S + L + I + T_1 + T_2 + R) - \gamma(I + T_1 + T_2)$$

since $-\gamma(I + T_1 + T_2) \leq 0$ so that the inequality have been determined

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

Furthermore $\frac{dN}{dt}$ in the form of a first-order linear differential equation, then the solution is as follows

$$e^{\mu t} N \leq \frac{\Lambda e^{\mu t}}{\mu} + c$$

where c is a constant

$$N \leq \frac{\Lambda}{\mu} + ce^{-\mu t}$$

Suppose we have an initial condition $N(t) = N(0)$ at $t = 0$. The following solutions were obtained

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

Consequently, for $t \to \infty$ then $\lim_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}$. It can be concluded that N is bounded at $N(t) \leq \frac{\Lambda}{\mu}$ so that the model has a bounded solution the region of Ω.

$$\Omega = \left\{(V, S, L, I, T_1, T_2, R) | N(t) \leq \frac{\Lambda}{\mu}\right\}$$

Next, it can be shown that the constructed system always has a positive solution. For system $x' = f(x)$ where $x = (x_1, x_2, \ldots, x_n)$, for every i then $f_i(x) \geq 0$ holds at $x_i = 0$ and $x \in \mathbb{R}^n_{\geq 0}$ then $\mathbb{R}^n_{\geq 0}$. It means that if any compartment touches zero then its gradient should be non-negative. According to the equation $(1) - (7)$, positive parameter assumption and positive initial condition then this statement holds.

$$V = 0, \dot{V} = \Lambda \geq 0, S = 0, \dot{S} = \varepsilon V \geq 0, L = 0, \dot{L} = \beta SI \geq 0, I = 0, \dot{I} = \sigma L \geq 0,$$

$T_1 = 0, \dot{T_1} = \theta_1(L + I) + \delta T_2 \geq 0, T_2 = 0, \dot{T_2} = \theta_2(L + I) \geq 0, R = 0, \dot{R} = \phi_1 T_1 + \phi_2 T_2 \geq 0$.

It follows that all solutions are positive for $t \geq 0$.

d. Equilibrium Point and Basic Reproduction Number

The equilibrium points of those equation (1)-(7) is obtained by setting the right hand side to zeros

$$\frac{dV}{dt} = \frac{dS}{dt} = \frac{dL}{dt} = \frac{dI}{dt} = \frac{dT_1}{dt} = \frac{dT_2}{dt} = \frac{dR}{dt} = 0$$

Therefore, two equilibrium point is obtained. The first point is known as a disease-free equilibirum, this is the condition where there is no disease spread.

$$E^0 = \left(V = V(0), S = S(0), L = L(0), I = I(0), T_1 = T_1(0), T_2 = T_2(0), R = R(0)\right)$$

$$E^0 = \left(\frac{\Lambda}{\varepsilon + \mu}, \frac{\Lambda\varepsilon}{\mu(\varepsilon + \mu)}, 0,0,0,0,0\right)$$

The second point, endemic equilibrium point, is a condition in which disease transmission occurs.

$$E^1 = (V = V^*, S = S^*, L = L^*, I = I^*, T_1 = T_1^*, T_2 = T_2^*, R = R^*)$$

where

$$V^* = \frac{\Lambda}{\varepsilon + \mu}$$

$$S^* = \frac{AB}{\beta\sigma}$$

$$L^* = \frac{B}{\sigma} I^*$$

$$I^* = I^*$$

$$T_1^* = \frac{\theta_1(L^* + I^*) + \delta T_2^*}{\mu + \gamma + \phi_1}$$

$$T_2^* = \frac{\theta_1(L^* + I^*)}{\delta + \mu + \gamma + \phi_1}$$

$$R^* \frac{\phi_1 T_1^* + \phi_2 T_2^*}{\mu}$$

In the constructed system, only compartments L and I contain infected individuals who can spread the disease, so the next generation matrix for this system is

$$\frac{dL}{dt} = \beta SI - \mu L - \theta_1 L - \theta_2 L - \sigma L$$

$$\frac{dI}{dt} = \sigma L - \mu I - \gamma I - \theta_1 I - \theta_2 I$$

It can be written as follows

$$\dot{x} = \mathcal{F}(x) - \mathcal{V}(x)$$

$\mathcal{F}(x)$: rate of new infection

$\mathcal{V}(x)$: rate of transfer and loss from the infection compartment

In the disease-free equilibrium, matrix $\mathcal{F}$ and $\mathcal{V}$ as follows

$$\mathcal{F} = \begin{pmatrix} \frac{\partial(\beta SI)}{\partial L} & \frac{\partial(\beta SI)}{\partial L} \\ 0 & 0 \end{pmatrix} = \begin{pmatrix} 0 & \frac{\beta\varepsilon\Lambda}{\mu(\varepsilon + \mu)} \\ 0 & 0 \end{pmatrix}$$

$$\mathcal{V} = \begin{pmatrix} A & 0 \\ 0 & B \end{pmatrix}$$

$$\mathcal{V}^{-1} = \frac{1}{AB}\begin{pmatrix} B & 0 \\ 0 & A \end{pmatrix}$$

By using next generation matrix method, it can be obtained

$$\mathcal{K} = \mathcal{F}\mathcal{V}^{-1} = \frac{1}{AB}\begin{pmatrix} \beta\dfrac{\Lambda\varepsilon}{\mu(\varepsilon+\mu)}\sigma & \beta A\dfrac{\Lambda\varepsilon}{\mu(\varepsilon+\mu)} \\ 0 & 0 \end{pmatrix}$$

Thus, the spectral radius of the next generation matrix is obtained

$$R_0 = \frac{\beta}{AB}.\frac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)}.\sigma$$

e. Local Stability Analysis

Based on the constructed system, Jacobian matrix for linearization is determined as follows

$$\begin{bmatrix} -(\varepsilon+\mu) & 0 & 0 & 0 & 0 & 0 & 0 \\ \varepsilon & -(\mu+\beta I) & 0 & -\beta S & 0 & 0 & 0 \\ 0 & \beta I & -A & \beta S & 0 & 0 & 0 \\ 0 & 0 & \sigma & -B & 0 & 0 & 0 \\ 0 & 0 & \theta_1 & \theta_1 & -(\mu+\gamma+\phi_1) & \delta & 0 \\ 0 & 0 & \theta_2 & \theta_2 & 0 & -(\delta+\gamma+\mu+\phi_2) & 0 \\ 0 & 0 & 0 & 0 & \phi_1 & \phi_2 & -\mu \end{bmatrix}$$

For disease-free equilibrium

$$E^0 = \left(\frac{\Lambda}{\varepsilon+\mu}, \frac{\Lambda\varepsilon}{\mu(\varepsilon+\mu)}, 0,0,0,0,0\right)$$

In the system, it is only L and I compartments effectively spread the disease so that the Jacobian matrix for these, as follows

$$J_{(L,I)}(E^0) = \begin{pmatrix} -(\mu+\theta_1+\theta_2+\sigma) & \beta\dfrac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)} \\ \sigma & -(\mu+\gamma+\theta_1+\theta_2) \end{pmatrix}$$

The characteristic polynomial for the Jacobian matrix

$$\lambda^2 + \big((\mu+\theta_1+\theta_2+\sigma)+(\mu+\gamma+\theta_1+\theta_2)\big)\lambda + \left((\mu+\theta_1+\theta_2+\sigma)(\mu+\gamma+\theta_1+\theta_2) - \beta\sigma\frac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)}\right)$$

It will be stable when

$$(\mu+\theta_1+\theta_2+\sigma)(\mu+\gamma+\theta_1+\theta_2) - \beta\sigma\frac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)} > 0$$

$$\frac{\beta\sigma}{(\mu+\theta_1+\theta_2+\sigma)(\mu+\gamma+\theta_1+\theta_2)}\frac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)}<1$$

$$R_0<1$$

For V and S compartment, they have two negative eigenvalue that satisfy the stability condition $-(\varepsilon+\mu)$ and $-\mu$. Meanwhile, T_1, T_2 and R compartments are diagonal matrix in which have negative eigenvalue for each that satisfy stability condition $-(\mu+\gamma+\phi_1), -(\delta+\mu+\gamma+\phi_1), -\mu$. Based on the analysis of eigenvalues, it can be concluded that disease-free equilibrium point is locally asymptotically stable equilibrium point when $R_0<1$ and unstable when $R_0>1$.

For endemic equilibrium

$$E^1=(V=V^*, S=S^*, L=L^*, I=I^*, T_1=T_1^*, T_2=T_2^*, R=R^*)$$

One negative eigenvalue is obtained from V compartment that satisfied the stability condition $-(\varepsilon+\mu)$. In S, L and I compartment, for the endemic equilibrium point, the Jacobian matrix is obtained as follows.

$$J_{(S,L,I)}(E^1)=\begin{pmatrix} -\mu R_0 & 0 & -\frac{AB}{\sigma} \\ \mu(R_0-1) & -A & \frac{AB}{\sigma} \\ 0 & \sigma & -B \end{pmatrix}$$

The characteristic polynomial for the Jacobian matrix of an endemic point is

$$\lambda^3+a_1\lambda^2+a_2\lambda+a_3$$

where

$$a_1=A+B+\mu R_0$$

$$a_2=\mu R_0(A+B)$$

$$a_3=AB\mu(R_0-1)$$

The Routh–Hurwitz condition for all roots to have negative real parts are

$$a_1>0, a_2>0, a_3>0, a_1a_2>a_3$$

All parameters A, B, μ, σ are positive

$a_1=A+B+\mu R_0>0$ holds

$a_2=\mu R_0(A+B)$ holds

Condition for $a_3>0$ then $a_3=AB\mu(R_0-1)$ have to satisfy $R_0>1$

$a_1a_2-a_3=(A+B+\mu R_0)\mu R_0(A+B)-AB\mu(R_0-1)$

$$= \mu[A^2R_0 + B^2R_0 + ABR_0 + AB + A\mu R_0^2 + B\mu R_0^2] > 0$$

All Routh–Hurwitz conditions are satisfied, so the eigenvalues of the Jacobian matrix $J_{(S,L,I)}(E^1)$ at the endemic equilibrium has a negative real part. For T_1, T_2 and R compartment are a diagonal matrix so that the eigenvalues possessed by each component are negative and satisfy the stability condition, namely $-(\mu+\gamma+\phi_1), -(\delta+\mu+\gamma+\phi_1), -\mu$. Based on the analysis of eigenvalues, it was concluded that the endemic equilibrium point is a locally asymptotically stable equilibrium point when $R_0 > 1$ and unstable when $R_0 < 1$.

f. Global Stability Analysis

For disease-free equilibrium

By using the Castillo-Chavez Song framework, variable decomposition was performed. Suppose

$x = (V, S)$: uninfected compartment

$y = (L, I)$: infected compartment

Thus, the system can be written as

$$\dot{x} = F(x, y)$$

$$\dot{y} = \mathcal{F}(x, y) - \mathcal{V}(y)$$

where

$$\mathcal{F}(x,y) = \begin{pmatrix} \beta SI \\ 0 \end{pmatrix}, \mathcal{V}(y) = \begin{pmatrix} (\mu+\theta_1+\theta_2+\sigma)L \\ -(\sigma L) + (\mu+\gamma+\theta_1+\theta_2)I \end{pmatrix}$$

It is compulsory to satisfy H1-H2, so that the disease-free equilibrium point becomes Globally Asymtotically Stable ketika $R_0 \leq 1$

a. H1 (A subsystem without disease is Globally Asymtotically Stable): for $y = 0$

$$\dot{V} = \Lambda - (\varepsilon + \mu)V$$

$$\dot{S} = \varepsilon V - \mu S$$

have only one single equilibrium point

$$(V_0, S_0) = \left(\frac{\Lambda}{\varepsilon+\mu}, \frac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)}\right)$$

b. H2 (Infection structure)

$$\mathcal{F}(x,y) = \begin{pmatrix} \beta SI \\ 0 \end{pmatrix}, \mathcal{V}(y) = \begin{pmatrix} (\mu+\theta_1+\theta_2+\sigma)L \\ -(\sigma L) + (\mu+\gamma+\theta_1+\theta_2)I \end{pmatrix}$$

Using the Next Generation Matrix, the following $\mathcal{F}$ and $\mathcal{V}$ matrices are obtained

$$\mathcal{F} = \begin{pmatrix} \beta SI \\ 0 \end{pmatrix}$$

$$\mathcal{V} = \begin{pmatrix} A & 0 \\ -\sigma & B \end{pmatrix}, \mathcal{V}^{-1} = \frac{1}{AB}\begin{pmatrix} B & 0 \\ -\sigma & A \end{pmatrix}$$

So that it can be obtained

$$R_0 = \rho(\mathcal{K}) = \frac{\beta}{AB}\frac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)}\sigma$$

Under these conditions, the theorem states that when $R_0 \leq 1$, therefore, the disease-free equilibrium point is globally asymptotically stable.

Endemic Equilibrium Point

Using the Volterra-type Lyapunov function for compartments (S, L, I), we obtain

$$\mathcal{V} = \left(S - S^* - S^* \ln\frac{S}{S^*}\right) + \frac{B}{\sigma}\left(L - L^* - L^* \ln\frac{L}{L^*}\right) + \left(I - I^* - I^* \ln\frac{I}{I^*}\right)$$

For all $S, L, I > 0, \mathcal{V} > 0$ with equality only in E^1. By using equilibrium similarities ($\beta S^* I^* = AL^*, \sigma L^* = BI^*, \varepsilon V^* = \mu S^* + \beta S^* I^*$) and standard algebra (grouping into shaper $(x-1)\ln x$ and convexity identity), obtained

$$\frac{d\mathcal{V}}{dt} \leq 0$$

With similarities only when $(S, L, I) = (S^*, L^*, I^*)$. For (T_1, T_2, R) compartment linearly follow to (T_1^*, T_2^*, R^*). Therefore, according to LaSalle, E^1 is globally asymptotically stable when $R_0 > 1$.

g. Sensitivity Analysis

After conducting local and global stability analyses, the next step is to perform sensitivity analyses to identify the parameters that cause the spread of TB. The sensitivity index of the basic reproduction number depends on the derivative of the parameter (p) in the basic reproduction number obtained as follows.

$$E_p = \frac{\partial R_0}{\partial p}\frac{p}{R_0}$$

with the basic reproduction number obtained

$$R_0 = \frac{\beta\sigma}{(\mu+\theta_1+\theta_2+\sigma)(\mu+\gamma+\theta_1+\theta_2)} \cdot \frac{\varepsilon\Lambda}{\mu(\varepsilon+\mu)}$$

The sensitivity index formulation for each parameter is as follows

$E_\beta = 1$

$E_\sigma = \frac{\mu+\theta_1+\theta_2}{\mu+\theta_1+\theta_2+\sigma}$

$E_\Lambda = 1$

$$E_{\varepsilon} = \frac{\mu}{\varepsilon + \mu}$$

$$E_{\mu} = -1 - \frac{\mu}{\varepsilon + \mu} + \left(-\frac{\mu}{\mu + \theta_1 + \theta_2 + \sigma}\right) + \left(-\frac{\mu}{\mu + \gamma + \theta_1 + \theta_2}\right)$$

$$E_{\theta_1} = -\frac{\theta_1}{\mu + \theta_1 + \theta_2 + \sigma} - \frac{\theta_1}{\mu + \gamma + \theta_1 + \theta_2}$$

$$E_{\theta_2} = -\frac{\theta_2}{\mu + \theta_1 + \theta_2 + \sigma} - \frac{\theta_2}{\mu + \gamma + \theta_1 + \theta_2}$$

$$E_{\gamma} = -\frac{\gamma}{\mu + \gamma + \theta_1 + \theta_2}$$

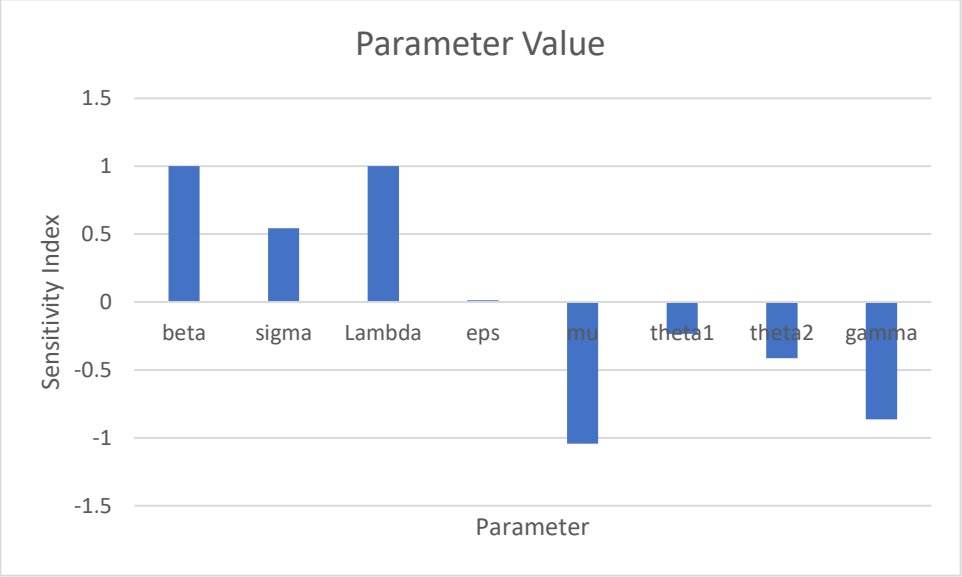

Figure 3. Sensitivity Index of Parameter

h. Optimal Control

The control provided in the constructed model is the acceleration of transferring latent cases to treatment through the screening process $u_1(t)$ and the acceleration of transferring infectious cases to treatment through case management $u_2(t)$. The system changes with the following control variables

$$\frac{dV}{dt} = \Lambda - \varepsilon V - \mu V$$

$$\frac{dS}{dt} = \varepsilon V - \mu S - \beta SI$$

$$\frac{dL}{dt} = \beta SI - \mu L - \theta_1 L - \theta_2 L - \sigma L - u_1 L$$

$$\frac{dI}{dt} = \sigma L - \mu I - \gamma I - \theta_1 I - \theta_2 I - u_2 I$$
$$\frac{dT_1}{dt} = \theta_1 L + \theta_1 I + \delta T_2 - \mu T_1 - \gamma T_1 - \phi_1 T_1 + u_1 L$$
$$\frac{dT_2}{dt} = \theta_2 L + \theta_2 I - \delta T_2 - \mu T_2 - \gamma T_2 - \phi_2 T_2 + u_2 I$$
$$\frac{dR}{dt} = \phi_1 T_1 + \phi_2 T_2 - \mu R$$

with the objective of minimising prevalence (latent and infectious sub population) and control cost as follows.

$$J(u_1, u_2) = \int_0^T \left(A_1 L + A_2 I + \frac{1}{2} B_1 u_1^2 + \frac{1}{2} B_2 u_2^2 \right) dt$$

The Hamiltonian function $H = A_1 L + A_2 I + \frac{1}{2} B_1 u_1^2 + \frac{1}{2} B_2 u_2^2 + \xi_1(\Lambda - \varepsilon V - \mu V) + \xi_2(\varepsilon V - \mu S - \beta S I) + \xi_3(\beta S I - \mu L - \theta_1 L - \theta_2 L - \sigma L - u_1 L) + \xi_4(\sigma L - \mu I - \gamma I - \theta_1 I - \theta_2 I - u_2 I) + \xi_5(\theta_1 L + \theta_1 I + \delta T_2 - \mu T_1 - \gamma T_1 - \phi_1 T_1 + u_1 L) + \xi_6(\theta_2 L + \theta_2 I - \delta T_2 - \mu T_2 - \gamma T_2 - \phi_2 T_2 + u_2 I) + \xi_7(\phi_1 T_1 + \phi_2 T_2 - \mu R)$. With transversal condition

$$\xi_1(T) = \xi_2(T) = \xi_3(T) = \xi_4(T) = \xi_5(T) = \xi_6(T) = \xi_7(T) = 0$$

The steady state conditions for optimal control are obtained by differentiating the Hamiltonian function with respect to the control variables $u_1(t)$ and $u_2(t)$

$$\frac{\partial H}{\partial u_1} = B_1 u_1 + L(\xi_5 - \xi_3) = 0, u_1 = \frac{L(\xi_3 - \xi_5)}{B_1}$$
$$\frac{\partial H}{\partial u_2} = B_2 u_2 + I(\xi_6 - \xi_4), u_2 = \frac{I(\xi_4 - \xi_6)}{B_2}$$

These two controls are defined at interval $0 \le u_1 \le 1$ and $0 \le u_2 \le 1$ so that a solution is obtained

$$u_1^* = \begin{cases} 0 & u_1 \le 0 \\ u_1 & 0 < u_1 < 1 \\ 1 & u_1 \ge 1 \end{cases}$$
$$u_2^* = \begin{cases} 0 & u_2 \le 0 \\ u_2 & 0 < u_2 < 1 \\ 1 & u_2 \ge 1 \end{cases}$$

Thus, optimal control u_1^* and u_2^* can be stated as

$$u_1^* = \max\left\{0, \min\left(\frac{L(\xi_3 - \xi_5)}{B_1}, 1\right)\right\}$$

$$u_2^* = \max\left\{0, \min\left(\frac{I(\xi_4 - \xi_6)}{B_2}, 1\right)\right\}$$

i. Numerical Simulation

After establishing a mathematical model of tuberculosis with two control strategies and determining the key parameters through an estimation process, the next step is to conduct numerical simulations to obtain a quantitative picture of the dynamics of disease spread. These simulations are performed using MATLAB software, where parameter values such as infection rate, quarantine rate, and recovery rate are used according to the real data of TB spread in Indonesia. Through this numerical approach, it is possible to observe how each compartment from the vaccinated, susceptible, latent to the recovered sub-population changes over time under the influence of optimal control. The following numerical simulation results not only validate the theoretical analysis that has been carried out, but also provide important insights into the effectiveness of intervention strategies in suppressing the spread of tuberculosis in the population.

To more clearly illustrate the dynamics of the system, the results of the numerical simulation are presented in the form of graphs showing the changes in each compartment over time. This simulation was conducted using previously estimated parameter values, namely $\Lambda = 2{,}789{,}353.03, \varepsilon = 1.1558, \mu = 0.0144, \beta = 2.39 \times 10^{-7}, \theta_1 = 0.1095, \theta_2 = 0.1932, \sigma = 0.2670, \gamma = 2, \delta = 0.05$. These values were obtained through a data-based estimation process using real-world cases, thereby reflecting realistic conditions for the spread of tuberculosis in the observed population.

With these parameters, the simulation results show dynamics consistent with the epidemiological behaviour of TB, where the number of individuals in the latent sub-population (L) and infected sub-population (I) compartments decreases significantly when controls are applied (Figure 5), while the recovered (R) and quarantined (T_1 and T_2) populations increase (Figure 6 and 7). This visualisation helps to explain how small changes in key parameters, particularly β, θ_1, and γ, can affect the long-term equilibrium of the system. Thus, these simulation results provide numerical evidence that the dual control strategy implemented is effective in reducing the prevalence of active infection while accelerating the recovery process of the population.

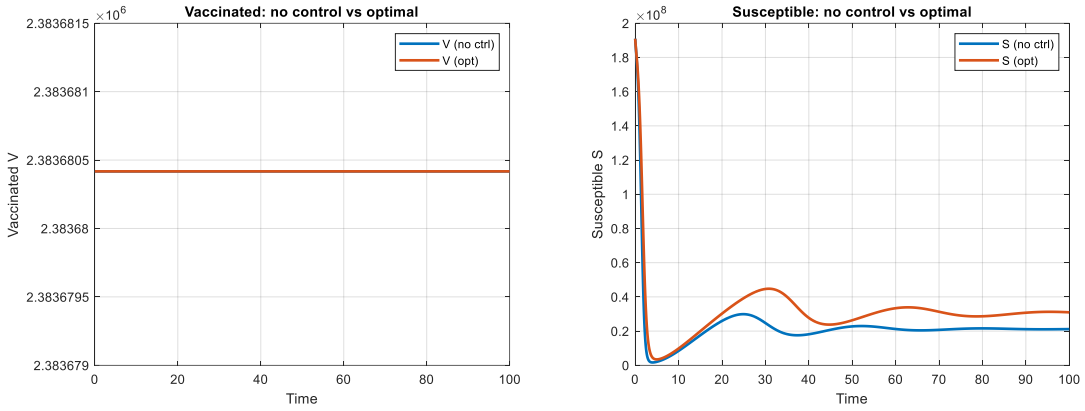

Figure 4. Vaccinated and Susceptible Sub-Population

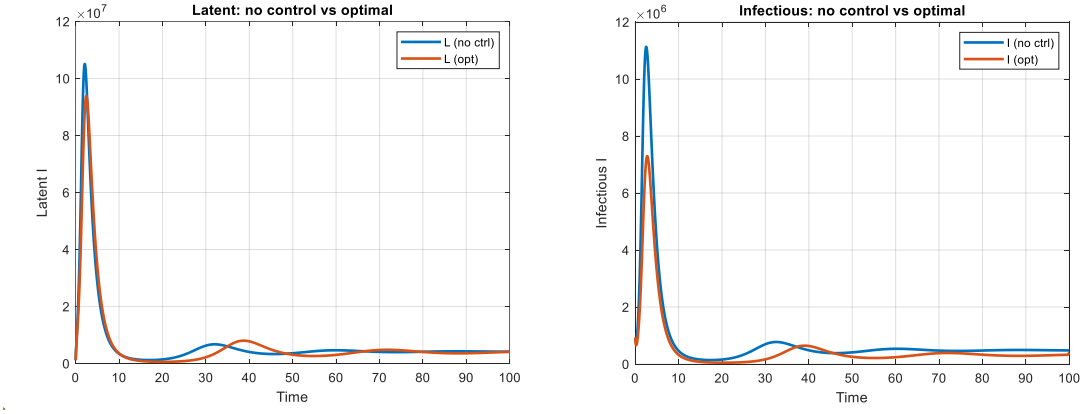

Figure 5. Latent and Infectious Sub-Population

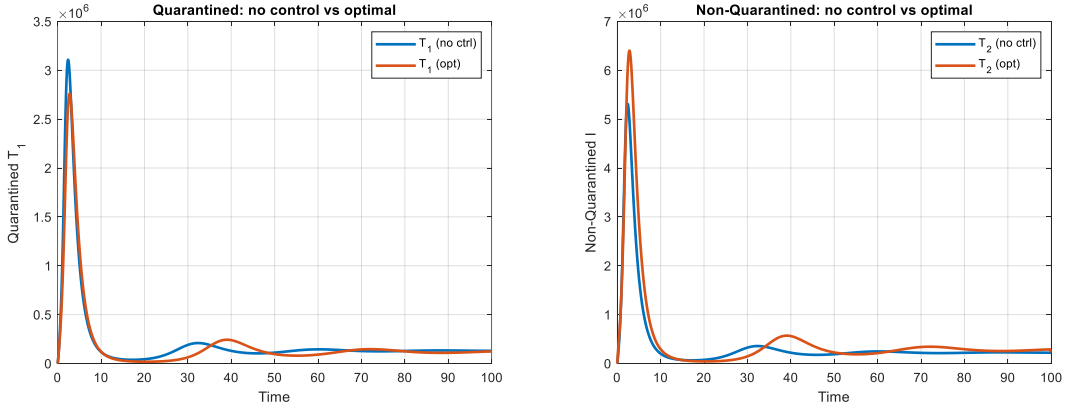

Figure 6. Quarantine and Non-Quarantined Sub-Population

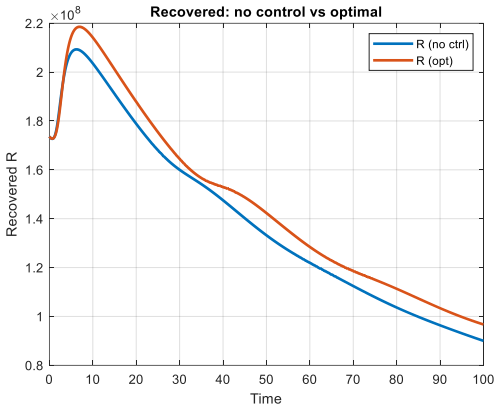

Figure 7. Recovered Sub-Population

4. CONCLUSION

The results of the analysis and numerical simulations show that the tuberculosis dynamics model with two optimal control strategies is able to accurately describe the spread of the disease within the population. The use of two forms of intervention, namely tiered quarantine (T_1 and T_2) and active treatment, has proven effective in reducing the rate of infection transmission and accelerating the recovery process. The simulation results show that the application of dual control results in a significant decrease in the number of individuals who are latently or actively infected, in line with an increase in the recovered population. The estimated parameter values, such as the high recovery rate (γ) and quarantine rate (θ_1 and θ_2), play an important role in stabilising the system and accelerating the achievement of disease-free conditions.

In particular, the optimal control approach applied provides quantitative insights into the efficiency of interventions in terms of cost and effectiveness. The cost function involving a combination of the number of infected individuals and the intensity of control shows that strategies with targeted and gradual control are able to balance prevention efforts and the allocation of health resources. Overall, this study confirms that the application of a dual control strategy in tuberculosis models not only provides a strong theoretical basis but also supports the formulation of more adaptive, efficient, and sustainable public health policies in combating infectious diseases such as tuberculosis.

APPENDIX

$$V = \frac{\Lambda}{\varepsilon + \mu}$$

$$S = \frac{\gamma\mu + \gamma\sigma + \gamma\theta_1 + \gamma\theta_2 + \mu^2 + \mu\sigma + 2\mu\theta_1 + 2\mu\theta_2 + \sigma\theta_1 + \sigma\theta_2 + \theta_1^2 + 2\theta_1\theta_2 + \theta_2^2}{\beta\sigma}$$

$$\begin{aligned} L = {} & \left(\Lambda\beta\varepsilon\sigma - \varepsilon\gamma\mu^2 - \varepsilon\gamma\mu\sigma - \varepsilon\gamma\mu\theta_1 - \varepsilon\gamma\mu\theta_2 - \varepsilon\mu^3 - \varepsilon\mu^2\sigma - 2\varepsilon\mu^2\theta_1 - 2\varepsilon\mu^2\theta_2 \right. \\ & - \varepsilon\mu\sigma\theta_1 - \varepsilon\mu\sigma\theta_2 - \varepsilon\mu\theta_1^2 - 2\varepsilon\mu\theta_1\theta_2 - \varepsilon\mu\theta_2^2 - \gamma\mu^3 - \gamma\mu^2\sigma - \gamma\mu^2\theta_1 - \gamma\mu^2\theta_2 \\ & \left. - \mu^4 - \mu^3\sigma - 2\mu^3\theta_1 - 2\mu^3\theta_2 - \mu^2\sigma\theta_1 - \mu^2\sigma\theta_2 - \mu^2\theta_1^2 - 2\mu^2\theta_1\theta_2 - \mu^2\theta_2^2\right) \Big/ \\ & \left(\left(\varepsilon\mu + \varepsilon\sigma + \varepsilon\theta_1 + \varepsilon\theta_2 + \mu^2 + \mu\sigma + \mu\theta_1 + \mu\theta_2\right)\beta\sigma\right), \end{aligned}$$

$$\begin{aligned} A = {} & \left(\Lambda\beta\varepsilon\sigma - \varepsilon\gamma\mu^2 - \varepsilon\gamma\mu\sigma - \varepsilon\gamma\mu\theta_1 - \varepsilon\gamma\mu\theta_2 - \varepsilon\mu^3 - \varepsilon\mu^2\sigma - 2\varepsilon\mu^2\theta_1 - 2\varepsilon\mu^2\theta_2 \right. \\ & - \varepsilon\mu\sigma\theta_1 - \varepsilon\mu\sigma\theta_2 - \varepsilon\mu\theta_1^2 - 2\varepsilon\mu\theta_1\theta_2 - \varepsilon\mu\theta_2^2 - \gamma\mu^3 - \gamma\mu^2\sigma - \gamma\mu^2\theta_1 - \gamma\mu^2\theta_2 \\ & \left. - \mu^4 - \mu^3\sigma - 2\mu^3\theta_1 - 2\mu^3\theta_2 - \mu^2\sigma\theta_1 - \mu^2\sigma\theta_2 - \mu^2\theta_1^2 - 2\mu^2\theta_1\theta_2 - \mu^2\theta_2^2\right) \Big/ \\ & \left(\beta\left(\varepsilon\gamma\mu + \varepsilon\gamma\sigma + \varepsilon\gamma\theta_1 + \varepsilon\gamma\theta_2 + \varepsilon\mu^2 + \varepsilon\mu\sigma + 2\varepsilon\mu\theta_1 + 2\varepsilon\mu\theta_2 + \varepsilon\sigma\theta_1 + \varepsilon\sigma\theta_2 \right.\right. \\ & \left.\left. + \varepsilon\theta_1^2 + 2\varepsilon\theta_1\theta_2 + \varepsilon\theta_2^2 + \gamma\mu^2 + \gamma\mu\sigma + \gamma\mu\theta_1 + \gamma\mu\theta_2 + \mu^3 + \mu^2\sigma + 2\mu^2\theta_1 + 2\mu^2\theta_2 \right. \right. \\ & \left.\left. + \mu\sigma\theta_1 + \mu\sigma\theta_2 + \mu\theta_1^2 + 2\mu\theta_1\theta_2 + \mu\theta_2^2\right)\right) \end{aligned}$$

$$\begin{aligned} T_1 = {} & \left(\left(\Lambda\beta\varepsilon\sigma - \varepsilon\gamma\mu^2 - \varepsilon\gamma\mu\sigma - \varepsilon\gamma\mu\theta_1 - \varepsilon\gamma\mu\theta_2 - \varepsilon\mu^3 - \varepsilon\mu^2\sigma - 2\varepsilon\mu^2\theta_1 - 2\varepsilon\mu^2\theta_2 \right.\right. \\ & - \varepsilon\mu\sigma\theta_1 - \varepsilon\mu\sigma\theta_2 - \varepsilon\mu\theta_1^2 - 2\varepsilon\mu\theta_1\theta_2 - \varepsilon\mu\theta_2^2 - \gamma\mu^3 - \gamma\mu^2\sigma - \gamma\mu^2\theta_1 - \gamma\mu^2\theta_2 \\ & \left.\left. - \mu^4 - \mu^3\sigma - 2\mu^3\theta_1 - 2\mu^3\theta_2 - \mu^2\sigma\theta_1 - \mu^2\sigma\theta_2 - \mu^2\theta_1^2 - 2\mu^2\theta_1\theta_2 - \mu^2\theta_2^2\right)\right. \\ & \left(\delta\gamma\theta_1 + \delta\gamma\theta_2 + \delta\mu\theta_1 + \delta\mu\theta_2 + \delta\sigma\theta_1 + \delta\sigma\theta_2 + \delta\theta_1^2 + 2\delta\theta_1\theta_2 + \delta\theta_2^2 + \gamma^2\theta_1 \right. \\ & + 2\gamma\mu\theta_1 + \gamma\sigma\theta_1 + \gamma\phi_2\theta_1 + \gamma\theta_1^2 + \gamma\theta_1\theta_2 + \mu^2\theta_1 + \mu\sigma\theta_1 + \mu\phi_2\theta_1 + \mu\theta_1^2 + \mu\theta_1\theta_2 \\ & \left.\left. + \sigma\phi_2\theta_1 + \phi_2\theta_1^2 + \phi_2\theta_1\theta_2\right)\right) \Big/ \left(\beta\left(\varepsilon\gamma\mu + \varepsilon\gamma\sigma + \varepsilon\gamma\theta_1 + \varepsilon\gamma\theta_2 + \varepsilon\mu^2 + \varepsilon\mu\sigma \right.\right. \\ & + 2\varepsilon\mu\theta_1 + 2\varepsilon\mu\theta_2 + \varepsilon\sigma\theta_1 + \varepsilon\sigma\theta_2 + \varepsilon\theta_1^2 + 2\varepsilon\theta_1\theta_2 + \varepsilon\theta_2^2 + \gamma\mu^2 + \gamma\mu\sigma + \gamma\mu\theta_1 \\ & \left.\left. + \gamma\mu\theta_2 + \mu^3 + \mu^2\sigma + 2\mu^2\theta_1 + 2\mu^2\theta_2 + \mu\sigma\theta_1 + \mu\sigma\theta_2 + \mu\theta_1^2 + 2\mu\theta_1\theta_2 + \mu\theta_2^2\right)\right. \\ & \left.\sigma\left(\delta\gamma + \delta\mu + \delta\phi_1 + \gamma^2 + 2\gamma\mu + \gamma\phi_1 + \gamma\phi_2 + \mu^2 + \mu\phi_1 + \mu\phi_2 + \phi_1\phi_2\right)\right) \end{aligned}$$

$$\begin{aligned} T_2 = {} & \left(\left(\Lambda\beta\varepsilon\sigma - \varepsilon\gamma\mu^2 - \varepsilon\gamma\mu\sigma - \varepsilon\gamma\mu\theta_1 - \varepsilon\gamma\mu\theta_2 - \varepsilon\mu^3 - \varepsilon\mu^2\sigma - 2\varepsilon\mu^2\theta_1 - 2\varepsilon\mu^2\theta_2 \right.\right. \\ & - \varepsilon\mu\sigma\theta_1 - \varepsilon\mu\sigma\theta_2 - \varepsilon\mu\theta_1^2 - 2\varepsilon\mu\theta_1\theta_2 - \varepsilon\mu\theta_2^2 - \gamma\mu^3 - \gamma\mu^2\sigma - \gamma\mu^2\theta_1 - \gamma\mu^2\theta_2 \\ & \left.\left. - \mu^4 - \mu^3\sigma - 2\mu^3\theta_1 - 2\mu^3\theta_2 - \mu^2\sigma\theta_1 - \mu^2\sigma\theta_2 - \mu^2\theta_1^2 - 2\mu^2\theta_1\theta_2 - \mu^2\theta_2^2\right)\theta_2\left(\gamma\right.\right. \\ & \left.\left. + \mu + \sigma + \theta_1 + \theta_2\right)\right) \Big/ \left(\beta\left(\varepsilon\gamma\mu + \varepsilon\gamma\sigma + \varepsilon\gamma\theta_1 + \varepsilon\gamma\theta_2 + \varepsilon\mu^2 + \varepsilon\mu\sigma + 2\varepsilon\mu\theta_1 \right.\right. \\ & + 2\varepsilon\mu\theta_2 + \varepsilon\sigma\theta_1 + \varepsilon\sigma\theta_2 + \varepsilon\theta_1^2 + 2\varepsilon\theta_1\theta_2 + \varepsilon\theta_2^2 + \gamma\mu^2 + \gamma\mu\sigma + \gamma\mu\theta_1 + \gamma\mu\theta_2 \\ & \left.\left. + \mu^3 + \mu^2\sigma + 2\mu^2\theta_1 + 2\mu^2\theta_2 + \mu\sigma\theta_1 + \mu\sigma\theta_2 + \mu\theta_1^2 + 2\mu\theta_1\theta_2 + \mu\theta_2^2\right)\sigma\left(\delta + \gamma\right.\right. \\ & \left.\left. + \mu + \phi_2\right)\right) \end{aligned}$$

$$R = \Big(\Big(\delta\gamma\phi_1\theta_1 + \delta\gamma\phi_1\theta_2 + \delta\mu\phi_1\theta_1 + \delta\mu\phi_1\theta_2 + \delta\sigma\phi_1\theta_1 + \delta\sigma\phi_1\theta_2 + \delta\phi_1\theta_1^2 + 2\delta\phi_1\theta_1\theta_2 + \delta\phi_1\theta_2^2 + \gamma^2\phi_1\theta_1 + \gamma^2\phi_2\theta_2 + 2\gamma\mu\phi_1\theta_1 + 2\gamma\mu\phi_2\theta_2 + \gamma\sigma\phi_1\theta_1 + \gamma\sigma\phi_2\theta_2 + \gamma\phi_1\phi_2\theta_1 + \gamma\phi_1\phi_2\theta_2 + \gamma\phi_1\theta_1^2 + \gamma\phi_1\theta_1\theta_2 + \gamma\phi_2\theta_1\theta_2 + \gamma\phi_2\theta_2^2 + \mu^2\phi_1\theta_1 + \mu^2\phi_2\theta_2 + \mu\sigma\phi_1\theta_1 + \mu\sigma\phi_2\theta_2 + \mu\phi_1\phi_2\theta_1 + \mu\phi_1\phi_2\theta_2 + \mu\phi_1\theta_1^2 + \mu\phi_1\theta_1\theta_2 + \mu\phi_2\theta_1\theta_2 + \mu\phi_2\theta_2^2 + \sigma\phi_1\phi_2\theta_1 + \sigma\phi_1\phi_2\theta_2 + \phi_1\phi_2\theta_1^2 + 2\phi_1\phi_2\theta_1\theta_2 + \phi_1\phi_2\theta_2^2 \Big) \Big(\Lambda\beta\varepsilon\sigma - \varepsilon\gamma\mu^2 - \varepsilon\gamma\mu\sigma - \varepsilon\gamma\mu\theta_1 - \varepsilon\gamma\mu\theta_2 - \varepsilon\mu^3 - \varepsilon\mu^2\sigma - 2\varepsilon\mu^2\theta_1 - 2\varepsilon\mu^2\theta_2 - \varepsilon\mu\sigma\theta_1 - \varepsilon\mu\sigma\theta_2 - \varepsilon\mu\theta_1^2 - 2\varepsilon\mu\theta_1\theta_2 - \varepsilon\mu\theta_2^2 - \gamma\mu^3 - \gamma\mu^2\sigma - \gamma\mu^2\theta_1 - \gamma\mu^2\theta_2 - \mu^4 - \mu^3\sigma - 2\mu^3\theta_1 - 2\mu^3\theta_2 - \mu^2\sigma\theta_1 - \mu^2\sigma\theta_2 - \mu^2\theta_1^2 - 2\mu^2\theta_1\theta_2 - \mu^2\theta_2^2 \Big) \Big) \Big/ \Big(\mu\left(\delta+\gamma+\mu+\phi_2\right)\left(\gamma+\mu+\phi_1\right)\sigma\beta \Big(\varepsilon\gamma\mu + \varepsilon\gamma\sigma + \varepsilon\gamma\theta_1 + \varepsilon\gamma\theta_2 + \varepsilon\mu^2 + \varepsilon\mu\sigma + 2\varepsilon\mu\theta_1 + 2\varepsilon\mu\theta_2 + \varepsilon\sigma\theta_1 + \varepsilon\sigma\theta_2 + \varepsilon\theta_1^2 + 2\varepsilon\theta_1\theta_2 + \varepsilon\theta_2^2 + \gamma\mu^2 + \gamma\mu\sigma + \gamma\mu\theta_1 + \gamma\mu\theta_2 + \mu^3 + \mu^2\sigma + 2\mu^2\theta_1 + 2\mu^2\theta_2 + \mu\sigma\theta_1 + \mu\sigma\theta_2 + \mu\theta_1^2 + 2\mu\theta_1\theta_2 + \mu\theta_2^2 \Big) \Big)$$

CONFLICT OF INTERESTS

The authors declared that there is no conflict of interests.

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