Mathematical Model of Pulmonary Tuberculosis Disease Spread

Yuni Yulida[1*], Eko Suhartono[2], Dewi Anggraini[3], Syamsul Arifin[4], Muhammad Ahsar Karim[5], Faisal[6]

{y_yulida@ulm.ac.id[1]}

[1]Student of Doctoral Program of Environment Science, Universitas Lambung Mangkurat, Banjarmasin, Indonesia
[2]Department of Medical Chemistry and Biochemistry, Faculty of Medicine and Health Science, Universitas Lambung Mangkurat, Banjarbaru, South Kalimantan, Indonesia
[3]Department of Statistics, Faculty of Mathematics and Natural Science, Universitas Lambung Mangkurat, Banjarbaru, Indonesia
[4]Department of Public Health, Faculty of Medicine and Health Science, Universitas Lambung Mangkurat, Banjarbaru, Indonesia
[1,5,6]Department of Mathematics, Faculty of Mathematics and Natural Science, Universitas Lambung Mangkurat, Banjarbaru, Indonesia

Abstract. This study presents the development of a mathematical framework to model the spread of pulmonary tuberculosis. The analysis includes determining equilibrium points, calculating the basic reproduction number, and examining the local stability of the formulated model. Additionally, a sensitivity assessment and numerical simulations are conducted using the fourth-order Runge–Kutta approach. The constructed SEIRI (Susceptible–Exposed–Infected–Recovered–Infected) epidemic model incorporates the recurrence rate into its formulation. Under this framework, equilibrium points for both disease-free and endemic scenarios are identified for each model variation. The basic reproduction number is computed through the Next Generation Matrix technique. Furthermore, based on the eigenvalues of the Jacobian matrix, the stability classification of each equilibrium point is established, with certain cases being locally asymptotically stable. Sensitivity analysis indicates that the transmission rate and recovery rate are the most influential parameters affecting changes in the basic reproduction number, exhibiting direct and inverse proportionality, respectively. Higher relapse rates tend to accelerate transitions in the susceptible and exposed compartments, while maintaining higher proportions in the infected group. These findings, supported by numerical simulations, strengthen the stability and sensitivity conclusions obtained in this research.

Keywords: SEIRI model, Basic reproduction number, Stability analysis, Pulmonary tuberculosis

ICWSDGs 2024, September 09-10, Banjarmasin, Indonesia

DOI 10.4108/eai.9-9-2024.2359107

1 Introduction

Tuberculosis (TB) is an airborne infectious disease caused by the slow-growing bacterium Mycobacterium tuberculosis (MT). Transmission occurs from person to person either through direct contact or via infectious particles dispersed in the air within enclosed spaces [1],[2]. The majority of MT bacteria infect the lungs, leading to pulmonary TB; however, they can also invade other organs, resulting in extrapulmonary TB. In Indonesia, more than 0.7 million new TB cases are expected annually, with approximately 92% being pulmonary and only 8% extrapulmonary [3]. The bacteria are primarily spread through airborne droplets released by TB patients.

Recognized as one of the top ten causes of mortality worldwide in 2015, TB continues to be a major global health threat, claiming millions of lives each year. It is regarded both as a re-emerging infectious disease and a condition closely associated with poverty. Drug resistance poses a persistent challenge for treatment, despite the World Health Organization's comprehensive initiatives to reduce mortality rates, including the End TB Strategy, which targets ending the TB epidemic by 2030 [4]. Whole genome sequencing has gained increasing attention as a powerful approach for diagnosing TB, identifying drug resistance patterns, tracing transmission pathways, and distinguishing between reinfection and relapse. The COVID-19 pandemic has further complicated TB control, exerting significant impacts on global healthcare systems and intensifying the risks to TB prevention and treatment programs [5],[6],[7].

TB infection is divided into two types, namely latent TB and active TB. Individuals with latent TB are not contagious, as the bacteria that infect them do not replicate and cannot transmit to other organisms, even though the MT bacteria are already present in the patient's body. Active TB, on the other hand, refers to people with TB who are showing symptoms of infection, which means they are actively transmitting the bacteria to others. Individuals infected with MT can develop into active TB disease depending on the individual's immune system [8].

Certain populations face a greater likelihood of developing tuberculosis (TB), including individuals in frequent contact with patients who have active TB, those living or working in poorly ventilated environments, and healthcare personnel [2]. TB transmission often occurs in enclosed spaces with inadequate airflow, allowing microscopic droplets to remain suspended for extended periods [9]. Extended close contact with an infected individual significantly elevates the risk of transmission [2]. Preventing the progression of TB through timely treatment is a central component of the WHO's End TB Strategy [9]. In the absence of appropriate treatment, TB mortality rates can rise sharply—by approximately 50%—whereas the standard anti-TB therapy administered for 4–6 months can result in recovery for about 85% of patients. The incidence of drug-resistant TB (DR-TB) has been projected to increase between 2020 and 2021, with an estimated 450,000 (95% UI: 399,000–501,000) new cases of rifampicin-resistant TB (RR-TB) reported in 2021. The COVID-19 pandemic has further worsened TB outcomes, contributing to a reduction in the number of patients receiving RR-TB treatment between 2019 and 2020 [10].

Research on TB disease continues to develop, including in the field of mathematics, especially mathematical modeling. TB disease transmission can be modeled in the form of an epidemic model [11] because human populations can be differentiated or grouped into several groups based on the characteristics studied, for example, healthy individuals and sick or infected individuals. Studies that have studied the transmission of TB disease using mathematical modeling include [12]

presenting the SIR model for the spread of TB disease, [13] paying attention to control in the form of detection and care of infected individuals, Fadilah and Zulakmal [14] studying the behavior of TB disease, [1] discussing the analysis of transmission and control of TB disease in China, [15] discussing the TB model taking into account bilinear incidence rate and treatment effects, [16] discussing the analysis of TB disease models, and [17] TB disease spread model with case detection and treatment effects.

Tuberculosis (TB) relapse may occur due to recurrence of the initial infection or exogenous reinfection with a different strain of Mycobacterium tuberculosis. Factors associated with high relapse rates include treatment non-adherence, sex differences, malnutrition, comorbidities such as diabetes and renal failure, immunosuppressive states such as HIV, substance abuse, and environmental exposures [18],[19]. In high-burden countries, exogenous reinfection is more common, especially in the presence of HIV infection [20]. In contrast, poor adherence to treatment, multidrug resistance, and persistence of cavities in the lung parenchyma are factors recognized as contributing to TB recurrence [21]. Relapsed TB cases have poorer outcomes, including lower treatment completion rates and higher mortality. Understanding the clinical, epidemiologic, and social determinants of TB relapse is critical for effective TB control.

This study addresses the development and examination of mathematical models describing the transmission dynamics of pulmonary TB. The proposed model builds upon previous works [16], [22] by incorporating latent TB cases, as well as accounting for treatment interventions and reinfection rates. Numerical simulations were conducted to evaluate the stability of both disease-free and endemic equilibrium states. In addition, simulation results illustrate how variations in transmission rate, reinfection rate, and treatment rate influence the population sizes of the susceptible, exposed, infected, and recovered compartments.

2 Methods

The methodology applied in this study involved several sequential stages, including model formulation, stability assessment, and numerical simulation. The SIR epidemiological framework was adopted to construct mathematical models of disease transmission, following approaches described in previous works [23], [24]. Initially, the model was formulated, the equilibrium points were identified [25], and the basic reproduction number was calculated using the next generation matrix technique [20],[21]. In the subsequent stage, the stability of the system was examined through linearization methods [27], [28], [29], [30], [31]. The third stage involved determining the sensitivity index based on the basic reproduction number. The fourth stage focused on obtaining the model solution using the fourth-order Runge–Kutta (RK4) scheme [32],[33],[34] and visualizing the results graphically. Finally, the analysis was completed by presenting the impact of variations in the basic reproduction number on the relevant parameters.

3 Results and Discussion

3.1 Mathematical Modeling Of Pulmonary TB

In the model for the spread of tuberculosis in this study, the population consists of four groups, namely:

a. The Susceptible group is denoted by $S(t)$, representing the number of individuals vulnerable to contracting TB at a given time t.
b. The Exposed group, denoted by $E(t)$, referring to individuals who have been exposed to pulmonary TB at time t but are not yet infectious, although latent TB bacteria are present in their bodies.
c. The Infected group is denoted by $I(t)$, indicating the number of individuals who have active pulmonary TB at time t and are capable of transmitting the disease due to the activation of TB bacteria in their systems.
d. The Recovered group is denoted by $R(t)$, corresponding to individuals who have recovered from pulmonary TB at time t.

The model incorporates several parameters: the recruitment rate of the population through births (π), the natural mortality rate (μ), the TB-induced mortality rate (μ_t), the infection rate of susceptible individuals (β), the endogenous reactivation rate (ε), he recovery rate from active TB (γ) and the relapse rate (ω). A schematic representation of the model structure is provided in Figure 1.

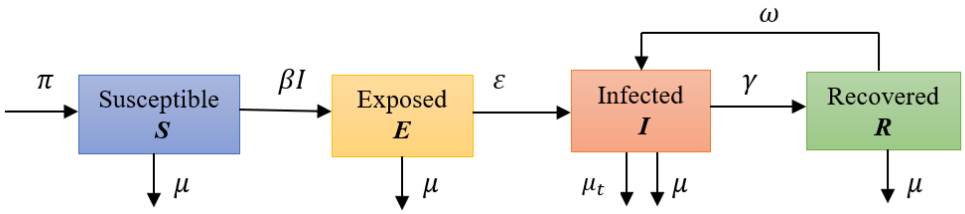

Fig. 1. The Flow Diagram for Pulmonary TB Disease Spread Model

Considering the established facts and underlying assumptions, the system of differential equations presented in Figure 1 was formulated.

$$\begin{aligned} \frac{dS}{dt} &= \pi - \beta SI - \mu S \\ \frac{dE}{dt} &= \beta SI - (\varepsilon + \mu)E \\ \frac{dI}{dt} &= \varepsilon E + \omega R - (\gamma + \mu_t + \mu)I \\ \frac{dR}{dt} &= \gamma I - (\mu + \omega)R \end{aligned} \tag{1}$$

Model (1) is called the SEIRI Model.

3.2 Equilibrium And Basic Reproduction Number

The equilibrium points of the model are identified by setting the system's rate of change to zero, namely $\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$ and solving these equations simultaneously [25]. This process yields the steady-state conditions for each compartment susceptible, exposed, infected, and recovered, which are represented in the system of equations (1). By applying this approach, the model can determine the population distribution at equilibrium, providing a foundation for further analysis of the basic reproduction number and the stability of each equilibrium state. We have the following system of equations (1) to be solved simultaneously for S, E, I, R,

$$\pi - \beta SI - \mu S = 0 \quad (2)$$
$$\beta SI - (\varepsilon + \mu)E = 0 \quad (3)$$
$$\varepsilon E + \omega R - (\gamma + \mu_t + \mu)I = 0 \quad (4)$$
$$\gamma I - (\mu + \omega)R = 0 \quad (5)$$

The Disease-Free Equilibrium (DFE) represents a steady state in which tuberculosis is absent from the population. For the model described in equation (1), the DFE is denoted as E_0 and using equations (2)–(5), is expressed as $E_0 = (\hat{S}_0, \hat{E}_0, \hat{I}_0, \hat{R}_0) = \left(\frac{\pi}{\mu}, 0,0,0\right)$. This equilibrium serves as the basis for calculating the threshold parameter R_0, known as the basic reproduction number. R_0 is defined as the expected number of secondary infections generated by a single infectious individual during the entire infectious period, within a fully susceptible population [35]. This parameter is widely used to assess both the potential for disease invasion and the stability of endemic states. In this study, the basic reproduction number is determined using the next generation matrix method, which provides an approximate approach for its computation [27],[35],[36], [37].

For this, $\underline{x} = (E, I)^T$. From Model (1), we can write

$\frac{d\underline{x}}{dt} = \mathcal{F} - \mathcal{H}$, with $\mathcal{F} = \begin{pmatrix} \beta SI \\ 0 \end{pmatrix}$ and $\mathcal{H} = \begin{pmatrix} (\varepsilon + \mu)E \\ -\varepsilon E + \left((\gamma + \mu_t + \mu) - \frac{\omega\gamma}{(\mu+\omega)}\right)I \end{pmatrix}$

By considering the Jacobian of $\mathcal{F}$ and $\mathcal{H}$ at DFE (E_0), we get

$$F = \begin{pmatrix} 0 & \beta\frac{\pi}{\mu} \\ 0 & 0 \end{pmatrix} \text{ dan } H = \begin{pmatrix} (\varepsilon + \mu) & 0 \\ \varepsilon & (\gamma + \mu_t + \mu) - \frac{\omega\gamma}{(\mu+\omega)} \end{pmatrix}$$

In this model, the threshold parameter R_0 is obtained as the dominant eigenvalue of the matrix $G = FH^{-1}$, where F and H are defined as shown above. Thus, $R_0 = \rho(G)$ which yields the expression:

$$R_0 = \frac{\varepsilon\beta\frac{\pi}{\mu}(\mu + \omega)}{(\mu + \mu_t + \gamma)(\mu + \omega)(\mu + \varepsilon) - \omega\gamma(\mu + \varepsilon)} \quad (6)$$

The *Endemic Equilibrium* (EE) of the model, denoted by E_1, exists uniquely when $R_0 > 1$. This equilibrium is expressed as:

$$E_1 = (\hat{S}_1, \hat{E}_1, \hat{I}_1, \hat{R}_1) = \left(\frac{\pi}{\mu R_0}, \frac{\pi}{(\varepsilon+\mu)R_0}(R_0 - 1), \frac{\mu}{\beta}(R_0 - 1), \frac{\gamma\mu}{\beta(\mu+\omega)}(R_0 - 1)\right).$$

3.3 Local Stability Of The Disease - Free Equilibrium (DFE)

We state Theorem 1, which applies R_0 in the analysis of the DFE's stability. We provide

Theorem 1. In model (1), the Disease-Free Equilibrium $E_0 = \left(\frac{\pi}{\mu}, 0,0,0\right)$ with R_0 given by (8) is locally asymptotically stable whenever $R_0 < 1$ but loses stability if $R_0 > 1$.

Proof. The Jacobian matrix is evaluated at the DFE $E_0 = \left(\frac{\pi}{\mu}, 0,0,0\right)$ as follows

$$J(E_0) = \begin{pmatrix} -\mu & 0 & -\beta\frac{\pi}{\mu} & 0 \\ 0 & -(\varepsilon+\mu) & \beta\frac{\pi}{\mu} & 0 \\ 0 & \varepsilon & -(\gamma+\mu_t+\mu) & \omega \\ 0 & 0 & \gamma & -(\mu+\omega) \end{pmatrix}$$

The characteristics equation corresponding to $J(E_0)$ is given as

$$(-\mu-\lambda)\Big(\lambda^3 + [(\mu+\omega)+(\varepsilon+\mu)+(\mu+\mu_t+\gamma)]\lambda^2 + \Big[(\mu+\omega)(\varepsilon+\mu)+(\mu+\omega)(\mu+\mu_t+\gamma)+(\varepsilon+\mu)(\mu+\mu_t+\gamma)-\gamma\omega-\left(\frac{\varepsilon\beta\pi}{\mu}\right)\Big]\lambda + \Big[(\mu+\omega)(\varepsilon+\mu)(\mu+\mu_t+\gamma)-\gamma\omega(\varepsilon+\mu)-\left(\frac{\varepsilon\beta\pi}{\mu}\right)(\mu+\omega)\Big]\Big) = 0$$

This implies that

$(-\mu-\lambda) = 0$ or

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \qquad (7)$$

Where:

$a_0 = 1$

$a_1 = (\mu+\omega)+(\varepsilon+\mu)+(\mu+\mu_t+\gamma) > 0$

$$a_2 = (\mu+\omega)(\varepsilon+\mu)+(\mu+\omega)(\mu+\mu_t+\gamma)+(\varepsilon+\mu)(\mu+\mu_t+\gamma)-\gamma\omega-\left(\frac{\varepsilon\beta\pi}{\mu}\right)$$

$$= (\mu+\omega)(\varepsilon+\mu)+(\mu)(\mu+\mu_t+\gamma)+(\omega)(\mu+\mu_t)+\frac{\omega\gamma(\mu+\varepsilon)R_0}{(\mu+\omega)} > 0$$

$$a_3 = (\mu+\omega)(\varepsilon+\mu)(\mu+\mu_t+\gamma)-\gamma\omega(\varepsilon+\mu)-\left(\frac{\varepsilon\beta\pi}{\mu}\right)(\mu+\omega)$$

$$= [(\omega)(\varepsilon+\mu)(\mu+\mu_t)+(\mu)(\varepsilon+\mu)(\mu+\mu_t+\gamma)][1-R_0] > 0, \text{ if } R_0 < 1$$

The Jacobian matrix $J(E_0)$ yields a set of eigenvalues, where one of them is $\lambda_1 = -\mu_1$, while the remaining eigenvalues $(\lambda_2, \lambda_3, \lambda_4)$ satisfy equation (7). According to the Routh–Hurwitz stability criterion [38], eigenvalues of equation (7) have negative real parts when $R_0 < 1$. Therefore, the DFE E_0 s locally asymptotically stable for $R_0 < 1$, and becomes unstable if $R_0 > 1$.

3.4 Local Stability Of The Endemic Equilibrium (EE)

We employ Theorem 2, which applies the basic reproduction number R_0 to examine the stability of the EE

Theorem 2. Considering model (1) with the endemic equilibrium E_2 and and the basic reproduction number R_0 as stated in (8), E_2 remains locally asymptotically stable If $R_0 > 1$ and unstable otherwise.

Proof. The Jacobian matrix is evaluated at the EE $E_2 = \left(\hat{S}, \hat{E}, \hat{I}, \hat{R}\right)$ as follows:

$$J(E_2) = \begin{pmatrix} -\beta\hat{I} - \mu & 0 & -\beta\hat{S} & 0 \\ \beta\hat{I} & -(\varepsilon + \mu) & \beta\hat{S} & 0 \\ 0 & \varepsilon & -(\gamma + \mu_t + \mu) & \omega \\ 0 & 0 & \gamma & -(\mu + \omega) \end{pmatrix}$$

The matrix $J\left(\hat{Y}\right)$ can be expressed as a lower triangular matrix by performing the following elementary row operations

$$\tilde{J}(E_2) = \begin{pmatrix} -\mu(R_0 - 1) & 0 & 0 & 0 \\ -\mu & -(\varepsilon + \mu) & 0 & 0 \\ 0 & \varepsilon & \frac{\gamma\omega}{(\mu + \omega)} - (\gamma + \mu_t + \mu) & 0 \\ 0 & 0 & \gamma & -(\mu + \omega) \end{pmatrix}$$

Since matrix $J(E_2)$ and $\tilde{J}(E_2)$ are similar matrices, then based on [39] and [40], $det\left(J(E_2)\right) = det\left(\tilde{J}(E_2)\right)$. Furthermore, if λ is the eigenvalue of matrix $J(E_2)$, then λ is also the eigenvalue of matrix $\tilde{J}(E_2)$.

The characteristic equation of the matrix $\tilde{J}(E_2)$ is given by $\left|\tilde{J}(E_2) - \lambda I\right| = 0$, from which the eigenvalues are obtained as: $\lambda_1 = -\mu(R_0 - 1)$, $\lambda_2 = -(\varepsilon + \mu) < 0$, $\lambda_3 = \frac{\gamma\omega}{(\mu+\omega)} - (\gamma + \mu_t + \mu) < 0$, $\lambda_4 = -(\mu + \omega) < 0$. If $R_0 > 1$, the equilibrium E_2 is locally asymptotically stable; otherwise, if $R_0 < 1$, it becomes unstable.

3.5 Numerical Simulation

The RK4 method is employed to perform numerical simulations using different sets of parameter values and initial conditions, as summarized in Table 1.

Table 1. Values of Parameters and Initial Conditions Used in the Model

Parameter values and initial values	Simulation 1	Simulation 2
β	0.035	0.0035

ε	0.025	0.025
γ	0.85	0.85
μ	0.019896	0.019896
ω	0.02	0.02
μ_t	0.01	0.01
π	3	3
$S(0)$	100	100
$E(0)$	25	25
$I(0)$	15	15
$R(0)$	15	15

Based on the parameter values in Table 1, the equilibrium point, eigenvalues, and basic reproduction number of the model are summarized in Table 2.

Table 2. The Values of Eigen Value, DFE and $\boldsymbol{R_0}$

Symbol	**Simulation 1** **DFE $\boldsymbol{E_0}$**	**Simulation 2** **EE $\boldsymbol{E_2}$**
λ_1	-0.019896 $<$ 0	-0.108949 $<$ 0
λ_2	-0.914504 $<$ 0	-0.044896 $<$ 0
λ_3	-0.042893 $<$ 0	-0.453788 $<$ 0
λ_4	-0.007291 $<$ 0	-0.039896 $<$ 0
S	150.784077	23.283740
E	0.000000	56.502730
I	0.000000	3.112837
R	0.000000	66.320213
R_0	0.647594 $<$ 1	6.475939 $>$ 1

The simulation uses the initial values and parameters in Table 1 with different R_0 values. Table 2 is a calculation of the eigenvalues, DFE and R_0. The results of the numerical simulation model for the spread of TB disease are presented in Figures 2 and 3.

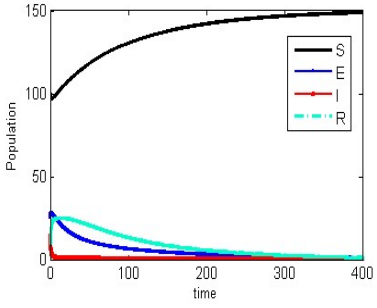

Fig. 2. Population dynamics over time under the condition $R_0 < 1$ (Simulation 1)

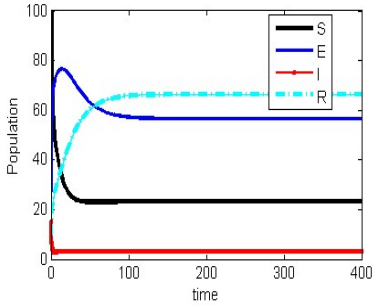

Fig. 3. Population dynamics over time under the condition $R_0 > 1$ (Simulation 2)

Figure 2: This shows the dynamic behavior of the population when $R_0 < 1$. In this scenario, the susceptible population *S* (black line) gradually increases, while the exposed *E* (blue), infected *I* (red), and recovered *R* (cyan) populations decline over time. This indicates that, with $R_0 < 1$, the disease will eventually die out, and the majority of the population will remain susceptible without significant infection spread. Figure 3: This illustrates the population dynamics when $R_0 > 1$. Here, the susceptible population *S* decreases rapidly, while the exposed *E* and recovered *R* populations initially increase. The infected population *I* stabilizes at a lower level. This suggests that when $R_0 > 1$, the disease will persist in the population, with infections continuing over time but stabilizing, rather than causing a widespread outbreak.

3.6 Sensitivity Index of the Basic Reproduction Number

In this section, a sensitivity analysis is performed to identify which parameters have an impact on the basic reproduction number R_0. The analysis is conducted under the condition $R_0 > 1$. ndicating that TB is actively spreading. Under this circumstance, it becomes essential to evaluate the parameters in order to determine the necessary measures for controlling disease transmission. The sensitivity analysis is carried out by calculating the sensitivity index of the relevant parameters. According to [41] and [37], the normalized sensitivity index of the basic reproduction number is given by:

$$C_l^{R_0} = \frac{\partial R_0}{\partial l} \times \frac{l}{R_0}$$

where lll represents the parameters included in the expression of the basic reproduction number (6). The model's dynamic behavior is governed by R_0, which is defined as the average number of secondary infections generated by a single infectious individual. Since R_0 is dependent on model parameters, the influence of parameters $\beta, \omega, \gamma, \mu_t, \varepsilon$ and π on disease transmission is examined through sensitivity analysis. A summary of the formula for the normalized sensitivity index of R_0 with respect to the parameters in Model (1) is presented below.

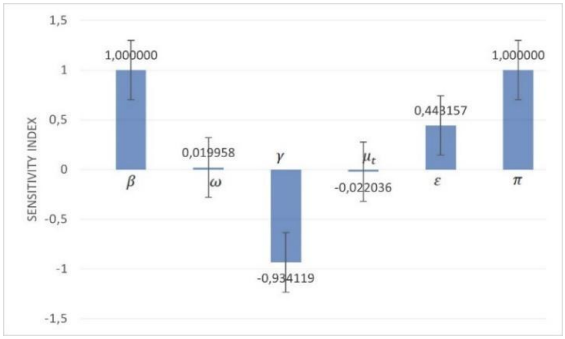

Fig. 4. Sensitivity index of the basic reproduction number (R_0) for the TB model.

Figure 4 presents the sensitivity index of the basic reproduction number in the TB disease spread model. The sensitivity index illustrates how changes in certain parameters of the TB model affect the basic reproduction number, which is a key measure in epidemiology to determine the potential spread of a disease. Parameters β and π have the largest positive influence on R_0. This means controlling the transmission rate of TB and managing the rate at which new susceptible individuals enter the population are crucial for reducing the spread of TB. Parameter γ has a strong negative impact, meaning that enhancing the recovery rate from TB will greatly reduce R_0 . Other parameters such as ω, μ_t, and ε have smaller effects on R_0 but still play a role in influencing the dynamics of the disease.

Figure 5 provides an illustration of how the parameters of the TB model affect the basic reproduction number.

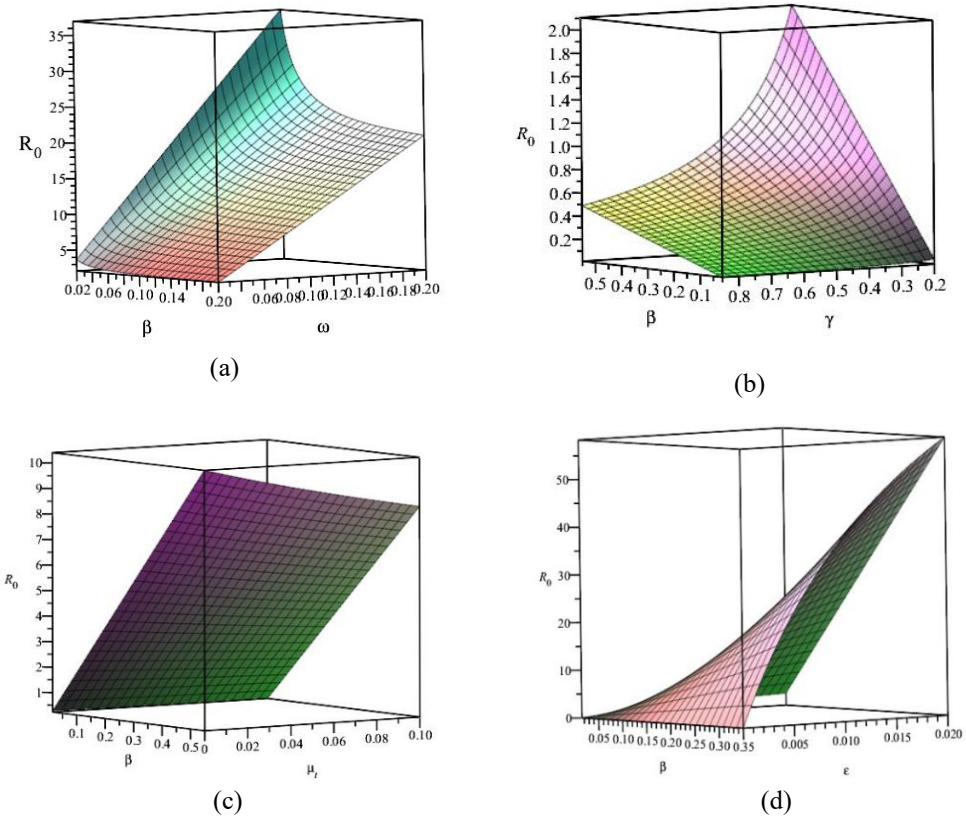

Fig. 5. Graphs of the Basic Reproduction Number (R_0) against four key parameters affecting TB transmission: (a) R_0 vs. β and ω, (b) R_0 vs. β and γ, (c) R_0 vs. β and μ_t, (d) R_0 vs. β and ε.

Based on Figure 5, it is clear that the transmission rate (β) has the most significant influence on increasing the basic reproduction number (R_0) across all parameter combinations, indicating that

controlling the spread of TB requires a primary focus on reducing transmission. While parameters such as reinfection rate (ω) and endogenous reactivation rate (ε) also contribute to increasing R_0, their impact is less pronounced compared to β. Conversely, the recovery rate (γ) and TB-related death rate (μ_t) have a decreasing or minimal effect on R_0, emphasizing the importance of improving recovery rates alongside managing transmission to effectively control TB spread.

3.7 Dynamic Behavior of Each Population with Varying Parameter Values

The dynamic behavior of each population with varying parameter values is presented in Figure 6-8 below.

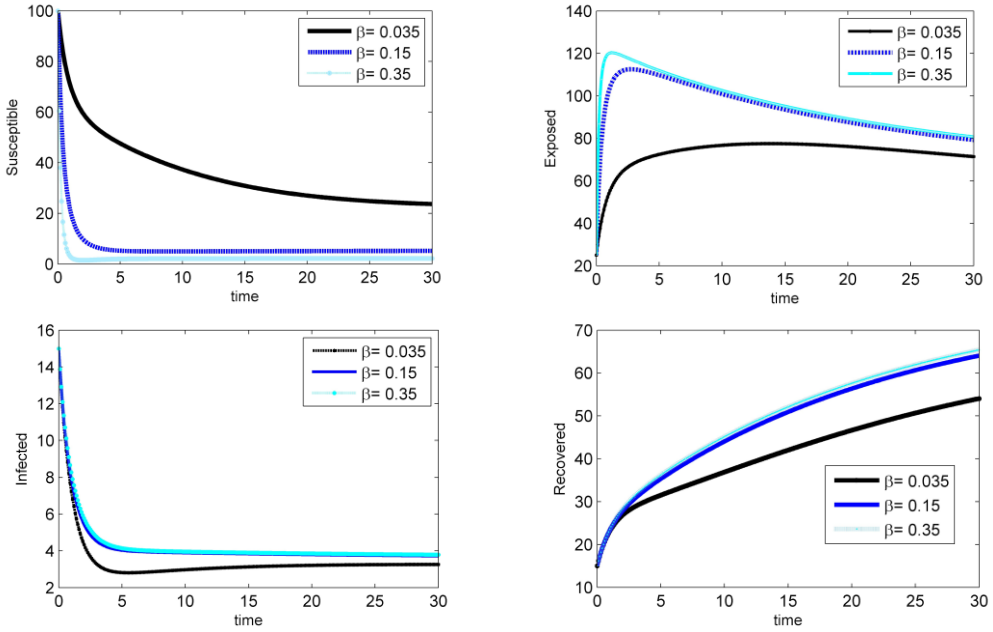

Fig. 6. Dynamic Behavior of Susceptible, Exposed, Infected, Recovered with Varying β

Figure 6 shows the population dynamics over time with three different values of β (0.035, 0.15, 0.35). As the β value increases, the susceptible population decreases more rapidly. This indicates that with a higher transmission rate, more individuals from the susceptible population become exposed more quickly. For higher β values, the exposed population increases more rapidly and reaches its peak before starting to decline. This suggests that

increasing β results in more individuals being exposed in a shorter period. At all β values, the infected population decreases, but with higher β, the decline is sharper initially, although the total number of infections is slightly higher when β is larger. With higher β, more people recover quickly from the infection. An increase in the transmission rate results in a more rapid growth of the recovered TB population.

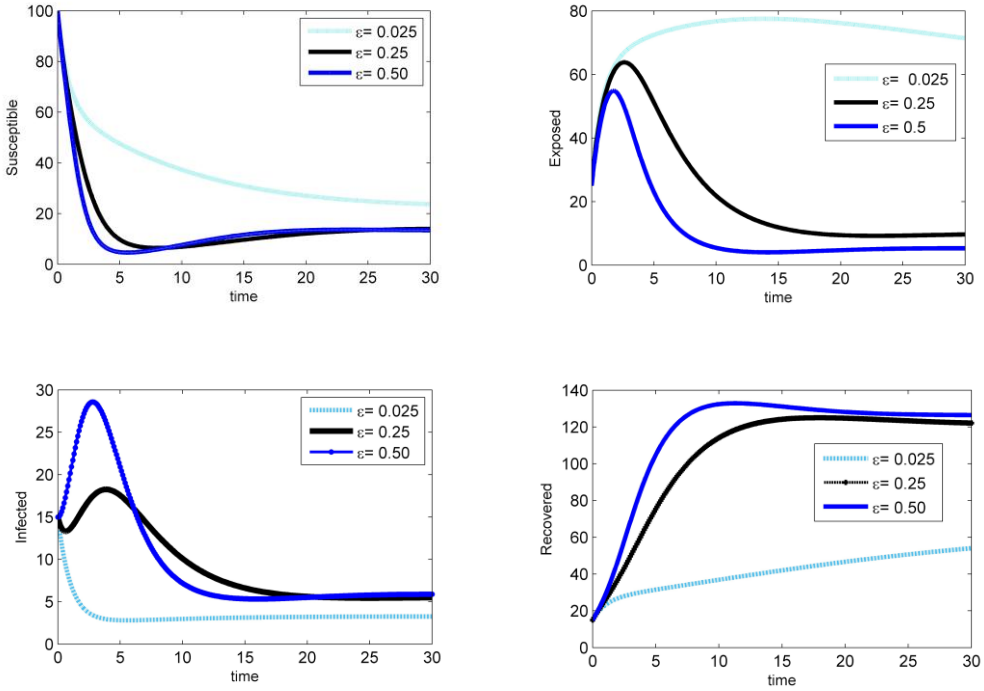

Fig. 7. Dynamic Behavior of Susceptible, Exposed, Infected, Recovered with Varying ε

Figure 7 shows the susceptible population over time with three different values of ε (0.025, 0.25, 0.50). As ε increases, the susceptible population declines more rapidly. A higher ε value indicates a faster transition from susceptible individuals to other groups, such as exposed or infected. In the exposed population, it peaks earlier and decreases faster compared to lower ε values. This indicates that an increase in the reactivation rate (ε) causes individuals exposed to pulmonary TB to become infected or recover more quickly. With a higher ε, there is an initial higher peak in the infected population, but the infection decreases more rapidly over time. This suggests that at higher reactivation rates, the infection spreads faster but is also resolved more quickly. Meanwhile, the recovered population increases faster and reaches a higher level in a shorter period of time.

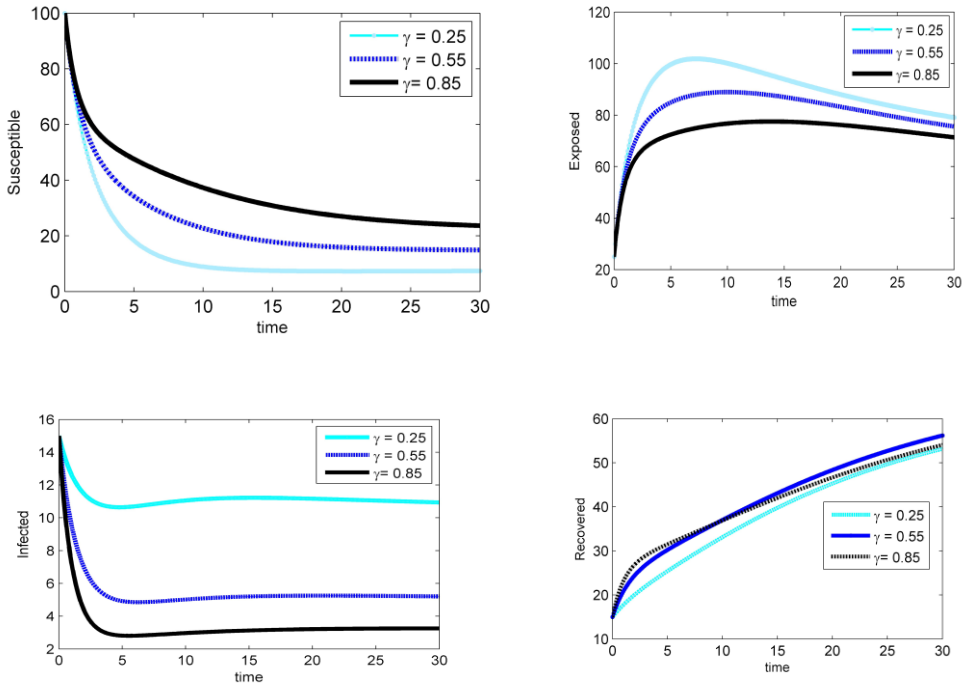

Fig. 8. Dynamic behavior of Susceptible, Exposed , Infected, Recovered with varying γ

Figure 8 shows the population dynamics with different γ values (0.25, 0.55, 0.85). The higher the γ value, the faster the decline in the susceptible population, while the exposed population increases more quickly and reaches its peak before declining more rapidly. At lower γ values (0.25), the infected population is initially higher but gradually decreases. In contrast, at higher γ values (0.85), the infection decreases faster, indicating that a higher recovery rate reduces the number of infected individuals more quickly. The recovered population increases faster with higher γ values, reaching a higher level earlier. This shows that with a higher recovery rate, more people recover from pulmonary TB in a shorter amount of time.

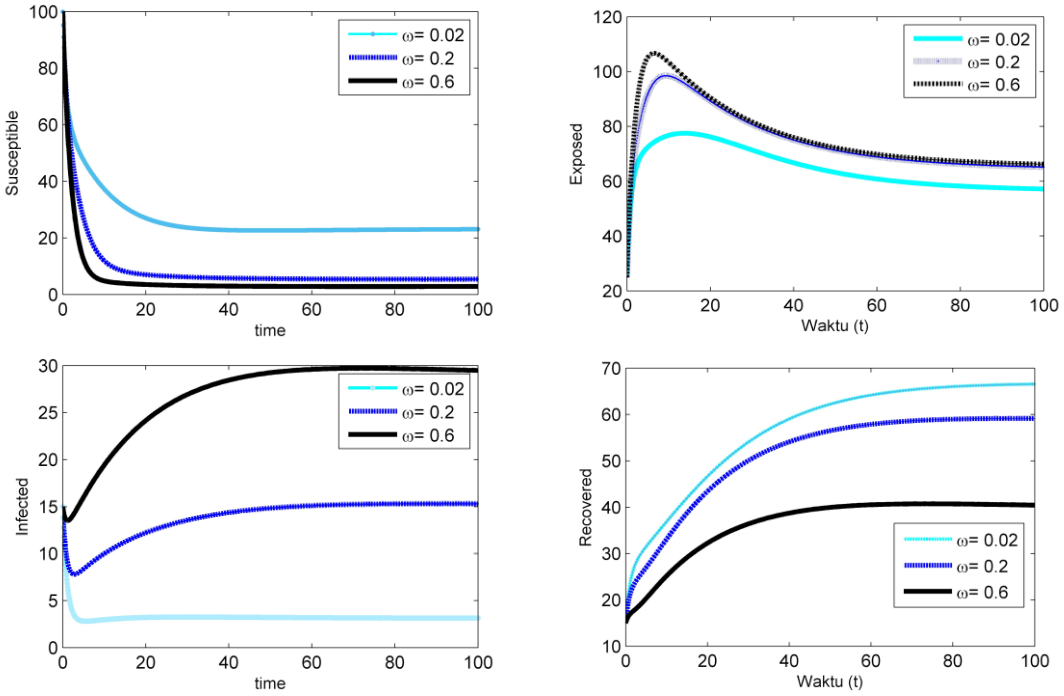

Fig. 9. Dynamic behavior of susceptible, Exposed, Infected, Recovered with varying ω

Figure 9 shows the dynamic behavior of the population with varying values of ω (0.02, 0.2, 0.6). The higher the ω value, the faster the decline in the susceptible population, while the exposed population reaches its peak earlier and declines more quickly. In contrast, with lower ω values, the exposed population increases more slowly and declines more gradually. With a larger ω, the infected population is higher and decreases more slowly, whereas the recovered population increases more slowly as well.

4 Conclusions

The mathematical model describing the spread of pulmonary TB consists of four subpopulations: susceptible, exposed, infected, and recovered. It adopts the SEIRI framework, considering that recovered individuals may relapse into the infected class. The model yields two equilibrium points: the disease-free equilibrium, which is locally asymptotically stable when $R_0 < 1$, and the endemic equilibrium, which is asymptotically stable when $R_0 > 1$. These stability results are supported by numerical simulations using the fourth-order Runge–Kutta method and illustrated through graphical visualization. To control the spread of pulmonary TB, strategies should focus on

reducing the contact rate between susceptible and infected individuals and increasing the treatment rate among the infected population. Sensitivity analysis indicates that the relapse rate contributes minimally to disease transmission compared to other parameters, suggesting that control measures should prioritize interventions targeting transmission and treatment rather than relapse prevention alone.

References

[1] Y. Zhao, M. Li, and S. Yuan, "Analysis of transmission and control of tuberculosis in Mainland China, 2005-2016, based on the age-structure mathematical model," *Int. J. Environ. Res. Public Health*, vol. 14, no. 10, pp. 2005–2016, 2017, doi: 10.3390/ijerph14101192.

[2] Keputusan Menteri Kesehatan Republik Indonesia, *Pedoman Nasional Pelayanan Kedokteran Tata Laksana Tuberkulosis*. 2019, pp. 5–10. [Online]. Available: https://yankes.kemkes.go.id/unduhan/fileunduhan_1610422577_801904.pdf

[3] H. Haryati, E. A. Mahfud, and M. A. Faisal, "Extra ocular TB coexisting pulmonary TB: An infrequent case," *Pneumon*, vol. 37, no. 3, pp. 1–5, 2024, doi: 10.18332/pne/191739.

[4] A. H. Rahim *et al.*, "Clinical epidemiology pattern of orthopedic trauma during the COVID-19 pandemic: A multicenter study (Dr. Hasan Sadikin General Hospital and Ulin General Hospital)," *Bali Med. J.*, vol. 12, no. 3, pp. 2703–2706, 2023, doi: 10.15562/bmj.v12i3.4634.

[5] M. Mozini, F. Bernardi, A. C. Mioto, V. Cassão, A. Kritski, and D. Alves, "A Computational Infrastructure for Analyzing Tuberculosis Research Data in Brazil," *Stud. Health Technol. Inform.*, vol. 305, pp. 558–561, 2023, doi: 10.3233/SHTI230557.

[6] I. Tatang, S. U. . Pratiwi, and I. F. Yasmin, "Antituberculosis Activity of Active Compound of Ethyl Acetate Extract for Patikan Kebo (Euphorbia hirta L.)," *Jordan J. Pharm. Sci.*, vol. 15, no. 4, pp. 461–473, 2022, [Online]. Available: https://typeset.io/papers/antituberculosis-activity-of-active-compound-of-ethyl-2s41aa8k

[7] U. Dasmahapatra and K. Chanda, "Synthetic approaches to potent heterocyclic inhibitors of tuberculosis: A decade review," *Front. Pharmacol.*, vol. 13, 2022, doi: 10.3389/fphar.2022.1021216.

[8] R. dr. S. T. K. Tim Promkes RSST, "TBC," Kementrian Kesehatan Direktorat Jenderal Pelayanan Kesehatan. [Online]. Available: https://yankes.kemkes.go.id/view_artikel/1375/tbc

[9] S. Soedarsono, "Tuberculosis: Development of New Drugs and Treatment Regimens," *J. Respirasi*, vol. 7, no. 1, pp. 36–45, 2021, doi: 10.20473/jr.v7-i.1.2021.36-45.

[10] WHO, *Global tuberculosis report*, no. August. 2022. [Online]. Available: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022

[11] Y. Yulida, E. Suhartono, D. Anggraini, and S. Arifin, "Mathematical Models of Tuberculosis Disease and Environmental Factors: A Systematic Review," *Pakistan J. Life Soc. Sci.*, vol. 22, no. 1, pp. 4116–4130, 2024, [Online]. Available: https://www.pjlss.edu.pk/pdf_files/2024_1/4116-4130.pdf

[12] K. Q. Fredlina, T. B. Oka, and I. M. E. Dwipayana, "Model SIR (Susceptible, Infectious, Recovered) Untuk Penyebaran Penyakit Tuberkulosis," *E-Jurnal Mat.*, vol. 1, no. 1, pp. 52–58, 2012.

[13] S. Athithan and M. Ghosh, "Optimal control of tuberculosis with case detection and treatment," *World J. Model. Simul.*, vol. 11, no. 2, pp. 111–122, 2015.

[14] F. H. Fadilah and . Z., "Kajian Perilaku Model Matematika Penularan Penyakit Tuberculosis," *J. Mat. UNAND*, vol. 5, no. 2, pp. 26–32, 2016, doi: 10.25077/jmu.5.2.26-32.2016.

[15] N. Qomariyah, Sutimin, R. Herdiana, R. H. S. Utomo, and A. H. Permatasari, "Stability analysis of a tuberculosis epidemic model with nonlinear incidence rate and treatment effects," *J. Phys. Conf. Ser.*,

vol. 1943, no. 1, 2021, doi: 10.1088/1742-6596/1943/1/012118.
[16] K. Das, B. S. N. Murthy, S. A. Samad, and M. H. A. Biswas, "Mathematical transmission analysis of SEIR tuberculosis disease model," *Sensors Int.*, vol. 2, no. August, pp. 1–11, 2013, doi: 10.1016/j.sintl.2021.100120.
[17] S. Athithan and M. Ghosh, "Mathematical modelling of TB with the effects of case detection and treatment," *Int. J. Dyn. Control*, vol. 1, no. 3, pp. 223–230, 2013, doi: 10.1007/s40435-013-0020-2.
[18] G. Abebe and W. K. , Zegeye Bonsa, "Treatment Outcomes and Associated Factors in Tuberculosis Patients at Jimma University Medical Center: A 5-Year Retrospective Study Gemeda," *Int. J. Mycobacteriology*, vol. 6, no. 3, pp. 239–245, 2017, doi: 10.4103/ijmy.ijmy.
[19] C. Schiroli and F. Franzetti, "Recurrent tuberculosis: Relapse or reinfection?," *Infez. Med.*, vol. 21, no. 4, pp. 251–260, 2013, [Online]. Available: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L372042439%5Cnhttp://www.infezmed.it/VisualizzaArticolo.aspx%5Cnhttp://bj7rx7bn7b.search.serialssolutions.com?sid=EMBASE&issn=11249390&id=doi:&atitle=Recurrent+tuberculosis%3A+Relaps
[20] J. D. Interrante, M. B. Haddad, L. Kim, and N. R. Gandhi, "Exogenous reinfection as a cause of late recurrent tuberculosis in the United States," *Ann. Am. Thorac. Soc.*, vol. 12, no. 11, pp. 1619–1626, 2015, doi: 10.1513/AnnalsATS.201507-429OC.
[21] L. Kim, P. K. Moonan, C. M. Heilig, R. S. Yelk Woodruff, J. S. Kammerer, and M. B. Haddad, "Factors associated with recurrent tuberculosis more than 12 months after treatment completion," *Int. J. Tuberc. Lung Dis.*, vol. 20, no. 1, pp. 49–56, 2016, doi: 10.5588/ijtld.15.0442.
[22] R. Embay, S. Wardatun, and A. Andriyati, "Stability Analysis Model of Spreading and Controlling of Tuberculosis," *Appl. Math. Sci.*, vol. 59, pp. 2559–2566, 2015.
[23] S. M. Lestari, Y. Yulida, A. S. Lestia, and M. A. Karim, "Stability analysis of a smoking behavior model," in *Journal of Physics: Conference Series*, 2021. doi: 10.1088/1742-6596/2106/1/012025.
[24] P. Affandi, M. Ahsar, E. Suhartono, I. Syauqiah, H. Santanapurba, and J. Dalle, "Mathematics Model: Dominant Factors of Dengue Hemorrhagic Fever Disease," *Oper. Res. Eng. Sci. Theory Appl.*, vol. 6, no. 3, pp. 287–303, 2023, doi: 10.31181/oresta/060314.
[25] L. Perko, *Differential Equation and Dynamics*. Verlag New York: Springer Verlag New York, 2001.
[26] P. Driessche and J. Watmough, "Reproduction Numbers and Sub-threshold Endemic Equilibria for Compartmental Models of Disease Transmission," *Math. Biosci.*, vol. 180, no. 2002, pp. 29–48, 2002.
[27] M. Martcheva, *An Introduction to Mathematical Epidemiology*. New York: Springer, 2015. doi: 10.1007/978-1-4899-7612-3.
[28] N. Bellomo and L. Preziosi, *Modelling mathematical Methods and Scientific Computation*. New York: Springer-Verlag New York Inc, 1995.
[29] F. Brauer and C. Chavez, *Mathematical Models in Population Biology and Epidemiology*. New York: Springer, 2010.
[30] D. Cheng and E. Al, *Linearization of Nonlinear Systems*. Beijing: Berlin Heidelberg: Science Press Beijing and Springer-Verlag, 2010.
[31] M. R. Taylor and P. H. Bhathawala, "Linearization of Nonlinear Differential Equation by Taylor's Series Expansion and Use of Jacobian Linearization Process," *Int. J. Theor. Appl. Sci.*, vol. 4, no. 1, pp. 36–38, 2012.
[32] Mulyono, "Kajian Sejumlah Metode untuk Mencari Solusi Numerik Persamaan Diferensial," in *Konferensi Nasional Penelitian Matematika dan Pembelajarannya*, Surakata: Universitas Muhammadiyah Surakarta, 2016.
[33] Y. Yulida and M. A. Karim, "Pemodelan Matematika Penyebaran COVID-19 di Provinsi Kalimantan Selatan," *J. Binawakya*, vol. 14, no. 10, pp. 3257–3264, 2020, [Online]. Available: http://ejurnal.binawakya.or.id/index.php/MBI/article/view/572
[34] M. A. Karim and A. Y. Gunawan, "Parameter Estimations of Fuzzy Forced Duffing Equation: Numerical Performances by the Extended Runge-Kutta Method," *Abstr. Appl. Anal.*, vol. 2020, 2020,

doi: 10.1155/2020/6179591.
[35] P. Van Den Driessche and J. Watmough, “Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission,” *Math. Biosci.*, vol. 180, no. 1–2, pp. 29–48, 2005, doi: 10.1016/S0025-5564(02)00108-6.
[36] P. Van Den Driessche and J. Watmough, “Further notes on the basic reproduction number,” *Lect. Notes Math.*, vol. 1945, pp. 159–178, 2008, doi: 10.1007/978-3-540-78911-6_6.
[37] M. A. Karim and Y. Yulida, “Analisis Kestabilan dan Sensitivitas pada Model Matematika SEIRD dari Penyebaran Covid-19: Studi Kasus di Kalimantan Selatan,” *Media Bina Ilm.*, vol. 16, no. 5, pp. 7003–7012, 2021.
[38] F. Gantmacher, *The Theory Of Matrices*. New York: Chelsea Publishing Company, 2000.
[39] B. P. Tomasouw, “Karakteristik Matriks Centro-Simetris,” *BAREKENG J. Ilmu Mat. dan Terap.*, vol. 10, no. 2, pp. 69–76, 2016, doi: 10.30598/barekengvol10iss2pp69-76.
[40] P. Singh, S. K. Srivastava, and U. Arora, “Stability of SEIR Model of Infectious Diseases with Human Immunity,” *Glob. J. Pure Appl. Math.*, vol. 13, no. 6, pp. 1811–1819, 2017, [Online]. Available: http://www.ripublication.com/gjpam.htm
[41] N. Chitnis, J. M. Hyman, and J. M. Cushing, “Determining Important Parameters in the Spread of Malaria,” vol. 70, pp. 1272–1296, 2008, doi: 10.1007/s11538-008-9299-0.