Jurnal Matematika UNAND
Vol. **15** No. **2** Hal. 224 – 236
Edisi April 2026
ISSN : 2303–291X
e-ISSN : 2721–9410

https://doi.org/10.25077/jmua.15.2.224-236.2026

AN EXPLORATION OF THE OPTIMAL SOLUTION FOR THE TUBERCULOSIS TRANSMISSION MODEL CONSIDERS THE POST-RECOVERY TREATMENT USING OPTIMAL CONTROL THEORY

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Received May 5, 2025, Received in revised form January 21, 2026
Accepted March 11, 2026 Available online April 30, 2026

Abstract. *Tuberculosis, also known as TB, is among the most communicable diseases. It is strenuous to detect TB infection early, so the number of cases increases over time. Consequently, the cost of treating the TB-infected sufferer is getting higher. However, since people recovered from TB can become reinfected, the post-treatment intervention needs to be conducted. Mathematical models are well-used to study TB transmission. Many researchers utilized an SEIR-type model to explain TB transmission, including incubation periods and reinfection. Nafisah and Adi [1] are among the researchers who proposed an SEIR-type model to explain TB transmission and to estimate parameter values based on data. However, optimal control and its cost-effectiveness analysis are not studied in it. Therefore, we continue to study the existing SEIR-type TB transmission model in [1] as an optimal control problem. The post-treatment intervention, such as maintaining the awareness level to remain in a healthy lifestyle, was selected to assess its impact on reducing the number of reinfected TB cases. Numerical simulations are performed to project its population dynamics under TB transmission. Next, we calculate the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER) to explore the most cost-effective strategy. The results show that the post-treatment intervention is more effective and efficient when delivered as an individual-based intervention rather than a community-based intervention or a mixed control. It means that each person who just recovered from TB must be monitored individually by the health workers to make sure that they will not be reinfected during the post-treatment period.*

Keywords: Cost-effectiveness analysis, optimal control model, Tuberculosis.

1. Introduction

Tuberculosis is one of the most dangerous communicable diseases. Globally, around 4,100 daily deaths cases of TB, and almost 28,000 people are infected by this

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intervention-able disease. Any efforts to fight against TB have saved around 66 million sufferers since 2000 [2]. Statistically, Indonesia is one of the countries with the top cases of TB [3]. In 2022, the number of new cases of TB was recorded as much as 159,000. It increased compared to recorded cases in 2021, as much as 92,000. Papua, Banten, and Jawa Barat provinces are among the top three in terms of prevalence rate [4].

TB is transmitted directly and indirectly from one infectious person to another [5]. People with tuberculosis who are not cured appropriately can transmit 10 people yearly. High-risk transmitted groups are people with close interaction with TB sufferers and people with malnutrition or immune system problems [6]. Many interventions have been conducted to suppress the incidence of TB infection. Efforts at prevention and curation of TB are studied and conducted. However, post-TB treatments are not well-studied, whereas TB can re-infect the recovered people [7].

Mathematical modeling is frequently used to represent many disease transmissions. Diseases such as TB [8], Hepatitis B [9], COVID-19 [10], and others have already been well-modeled to explore and project the long-term dynamics of behavior. This method interprets the dynamic situation under many conditions as a case to be projected and formulates the need for any policies to control it [11]. Mathematical models help us quantify the situation and assess whether the hypotheses achieve the aims of the research [12]. As in [1], the authors have modeled TB transmission and numerically explored the model using an estimated value based on real data. Nevertheless, optimal control and cost-effectiveness analysis are not revealed in the published study. Therefore, both studies need to be conducted to expand the exploration and gain further insights through modeling. This study allows us to consider the intervention's conduct while attending to the cost burden.

Based on the elucidation above, it is pivotal to utilize the advantage of a mathematical model to explore the population dynamics under TB transmission, considering any intervention with the cost burden. To realize the goal, we reconstruct the model in [1] into an optimal control model. Here, we consider one variable control, well-known as u, that represents the effort of post-TB treatment to reduce TB cases due to the possibility of reinfection. The value of the control parameter can be varied as it represents any strategies of post-TB treatment, such as medical, mixed, and full educational efforts. The optimal control model is simulated numerically to project its population dynamics. Next, the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER) are calculated to identify the most cost-effective strategy for reducing the reinfection case.

We write the remaining explanation of this article in the following section. In the second section, we present the theoretical basis, such as the constructed model, optimal control theory, and cost-effectiveness theory. Next, we discuss the reformulation of the prior model into an optimal control model, numerical simulation, and its cost-effectiveness analysis to justify the most cost-effective strategy. This article ends with the conclusion to give some highlightable information directly.

2. Some Concepts

2.1. *Mathematical Model of TB Transmission*

Nafisah and Adi [12] proposed a mathematical model representing TB transmission among people. The model was constructed with four compartments, namely susceptible (S), exposed (E), infectious (I), and recovered (R). The authors consider the fact that the recovered people can be re-infected or experience pseudo-recovery. In addition, the model was constructed by involving an inhibiting factor against the recovery rate due to the number of infectious people, which is true when we study limited medical factors. The proposed model in [12] can be rewritten as:

$$\frac{dS(t)}{dt} = \Lambda - (\mu + \alpha I(t))S(t), \tag{2.1}$$

$$\frac{dE(t)}{dt} = \alpha S(t)I(t) - (\mu + \beta)E(t), \tag{2.2}$$

$$\frac{dI(t)}{dt} = \beta E(t) - (\mu + \delta)I(t) - \frac{\gamma I(t)}{(1 + \theta I(t))} + \omega R(t), \tag{2.3}$$

$$\frac{dR(t)}{dt} = \frac{\gamma I(t)}{(1 + \theta I(t))} - (\mu + \omega)R(t), \tag{2.4}$$

with the described parameters and their value elaborated in Table 1.

Table 1. Definition and Value Parameters.

Parameters	Descriptions	Values
Λ	Growth rate	1,351,000
α	Transmission rate	1.0563×10^{-8}
β	Infection rate	0.0010921
γ	Recovery rate	0.0083693
θ	Inhibiting level	0.0012755
μ	Natural death rate	0.01515
δ	Disease death rate	0.0072373
ω	Re-infection rate	0.031165
ω	Re-infection rate	0.031165

The values of all listed parameters in Table 1 are taken from the fitting result in [12].

The system (2.1) – (2.4) describes the dynamics of the subpopulations S, E, I, and R, driven by the factors listed in Table 1. Eq. (2.1) represents that susceptible people may increase due to the birth rate and decrease due to the mass transmission and natural mortality rates. Next, Eq. (2.2) shows that the mass transmission rate increases the number of people exposed to TB bacteria, but the natural death rate and the infection rate decrease it. The infection rate determines how many exposed people become infectious. It increases the number of people with TB, but the natural death rate and death rate due to the disease decrease it. In addition, the reinfection rate is increasing the number of infectious people over time. However, Eq. (2.3) shows that the number of people with TB may decrease due to the recovery rate, but the higher the number of people with TB, the lower the recovery rate decreases, as it is formulated as a Holling-type II function. Note that the inhibiting level may represent the limited medical facilities. Finally, Eq. (2.4) describes the dynamics of recovered people increased by the recovery rate and decreased by the natural death rate and reinfection rate due to TB.

2.2. *Sensitivity Analysis*

Sensitivity analysis is conducted to quantify the uncertainty of the constructed model against each parameter. This analysis aims to identify the influence of a parameter on a model, as measured by a value indicating the degree of dependence of the model's output on the parameter. Partial Rank Correlation Coefficient (PRCC) [13] is widely used for sensitivity analysis, while the sample is generated via Latin Hypercube Sampling (LHS) [14].

2.3. *Optimal Control Theory*

Optimal control theory is a mathematical method for determining the controller variable that fulfills the objective function and certain conditions [15]. Generally, the optimal control problem formulation can be expressed as follows. First, define an objective function as:

$$J(u) = S\left(\mathbf{x}\left(t_f\right), t_f\right) + \int_0^{t_f} F\left(\mathbf{x}, \mathbf{u}, t\right) dt, \tag{2.5}$$

with the ordinary differential equation system (ODE), such as:

$$s.t.\ \dot{x} = f\left(\mathbf{x}, \mathbf{u}, t\right),\ \mathbf{x}\left(t_0\right) = \mathbf{x}_0,\ \mathbf{x}\left(t_f\right)\ \text{arbitrary}, \tag{2.6}$$

with $\mathbf{x} = \mathbf{x}(t) \in \mathbb{R}, \mathbf{u} = \mathbf{u}(t) \in \mathbb{R}, x\left(t_f\right) \in \mathbb{R}, t \geq 0$. In this term, the initial time, final time, state variable, and control variable are denoted by t_0, t_f, x, and u, respectively. This approach aims to find the optimal value of u so that the objective function J is maximized or minimized. Next, the Hamiltonian function can be formulated as:

$$H(x, \mathbf{u}, \lambda, t) = F(\mathbf{x}, \mathbf{u}, t) + \lambda f\left(\mathbf{x}, u, t\right), \tag{2.7}$$

with λ representing the Lagrange multiplier. There are two conditions in optimal control problems [13]. First, the necessary condition that can be expressed as:

(a) Optimal condition:

$$\frac{\partial H}{\partial u} = 0, t_0 \leq t \leq t_f,$$

(b) Adjoint function:

$$\frac{d\lambda}{dt} = -\frac{\partial H}{\partial x}, t_0 \leq t \leq t_f,$$

(c) Transversal condition:

$$\lambda\left(t_1\right) = 0.$$

Next, the sufficient condition for maximized and minimized problems can be written as $\frac{\partial^2 H}{\partial u^2} \leq 0$ and $\frac{\partial^2 H}{\partial u^2} \geq 0$, respectively.

2.4. *Cost-Effectiveness Theory*

In determining the most cost-effective strategy from several considered strategies, we performed a cost-effectiveness analysis. First, the Infectious Averted Ratio (IAR) estimates the ratio between the number of infectious averted people and the number of recovered people under control. The IAR can be expressed as:

$$IAR_i = \frac{\text{Total number of infected averted under strategy } i}{\text{Total recovered individuals under strategy } i}. \tag{2.8}$$

Based on the above equation, a higher IAR means a better strategy. Next, we calculate the Average Cost-Effectiveness Ratio (ACER) to know the average cost that must be spent for each infectious averted individual. The ACER can be formulated as:

$$ACER_i = \frac{\text{Total cost for intervention under strategy } i}{\text{Total number of infected averted under strategy} i}. \tag{2.9}$$

Note that a smaller ACER represents a better strategy. Finally, the Incremental Cost-Effectiveness Ratio (ICER) is calculated to compare the results between two controls by comparing the difference cost between strategy i and j against the difference in the number of infectious averted people between strategy i and j. The formula for ICER is given by:

$$ICER_{i,j} = \frac{\text{Difference cost between strategy } i \text{ and } j}{\text{Difference infected averted between strategy } i \text{ and } j}. \tag{2.10}$$

Consequently, a smaller ICER indicates a better strategy.

3. Result and Discussion

3.1. *Sensitivity Analysis*

The sensitivity analysis was conducted using 5000 samples for each parameter, generated by LHS. Next, the PRCC was used to quantify the model's uncertainty for each parameter change. The results were presented as a bar plot in Figure 1.

Figure 1 shows that all five controllable factors exert relatively different influences on the model. It shows that only δ shows a similar correlation on both infectious and recovered cases, which is a negative correlation. In addition, δ is the most influential parameter in the model, rather than the other three. This means that when the risk of death from TB increases, the number of infectious and recovered cases decreases. The remaining parameters exhibit different correlations with the infectious and recovered subpopulations. The recovery rate γ is the most influential in this term, followed by ω and θ. The sensitivity index of the recovery rate (γ) shows that increasing γ increases the number of recovered people while decreasing the number of infectious people. Meanwhile, the changes of ω and θ lead the system to a different impact. Increasing the rate of each parameter increases the number

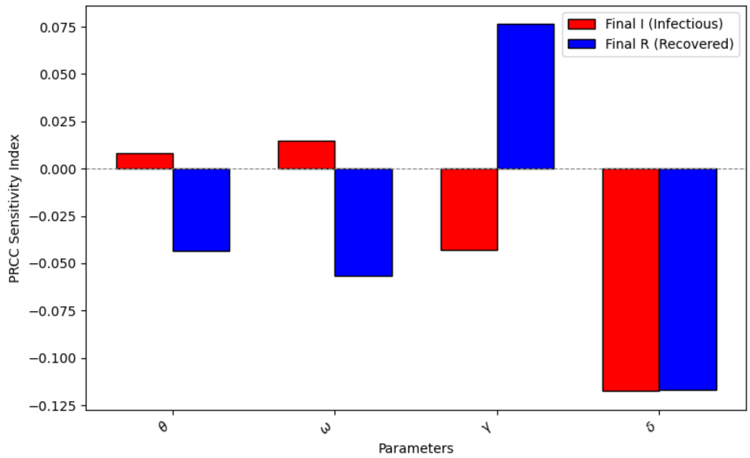

Figure. 1. Sensitivity Analysis on Final Infectious and Recovered in Systems (2.3) and (2.4)

of infectious people while decreasing the number of recovered people. However, the reinfection rate (ω) is chosen as the control parameter, as this study focuses on reducing the reinfection cases. The formulation of the control function is discussed in the following subsection.

3.2. *Optimal Control Model*

The previous model in Eq. (2.1) − Eq. (2.4) was enough to represent the phenomenon in a simple form. However, it was limited in considering interventions for TB prevention and curation. Consequently, it leaves much room for development of the model. We are curious to study the pseudo-recovery effect on the population dynamics under TB transmission as ωR. As a straightforward interpretation, it is true, but more parameters are needed to describe the other influential factors, such as awareness and control in staying healthy after TB recovery.

The optimal control model was formulated by accommodating the awareness level of people in maintaining health conditions after during post-TB treatment. Its level is denoted as a. In the controlling study, the value of a depends on the control mode, such as individual-based, mixed, and community-based interventions. Noted that mixed interventions are controls that use both modes of control. However, controls for each mode are not conducted as frequently as controls conducted solely with the individual-based or community-based mode. Consequently, the individual-based intervention gives the highest value of a, followed by mixed and individual-based interventions. It follows the fact that medical effort during post-TB treatment offers full influence in maintaining the health condition and preventing re-infection. Next, we add $u(t)$ as the variable control to represent the level of control implementation over time, considering the cost burden. Both a and $u(t)$ are formulated with ωR in Eq. (2.3) and Eq. (2.4), and can be rewritten as:

$$(1 - u(t))\,(1 - a)\omega R.$$

The formulas $(1-a)$ and $(1-u(t))$ indicate that a higher value of a and $u(t)$ reduces the re-infection case further. Finally, the model in Eq. (2.1) – Eq. (2.4) can be reformulated into an optimal control model and can be written as:

$$\frac{dS(t)}{dt} = \Lambda - (\mu + \alpha I(t))S(t), \tag{3.1}$$

$$\frac{dE(t)}{dt} = \alpha S(t)I(t) - (\mu + \beta)E(t), \tag{3.2}$$

$$\frac{dI(t)}{dt} = \beta E(t) - (\mu + \delta)I(t) - \frac{\gamma I(t)}{(1+\theta I(t))} + (1-u(t))(1-a)\omega R(t), \tag{3.3}$$

$$\frac{dR(t)}{dt} = \frac{\gamma I(t)}{(1+\theta I(t))} - (\mu + (1-u(t))(1-a)\omega)R(t). \tag{3.4}$$

Based on the explanations above, we formulate the objective function as:

$$J(u(t)) = \min \int_0^{t_f} \left(AR(t) - Cu^2(t)\right) dt \tag{3.5}$$

to maximize the recovered people by using the minimum control to suppress the cost. The parameter A defines the weight of recovered people, whereas C represents the cost of control implementation that satisfies $A, C \geq 0$. In addition, the system in (3.1)-(3.4) must fulfill the condition $0 < t < t_f, 0 \leq u(t) \leq U_p$, where U_p is the upper bound limit of control representation. Note that the control u represents the percentage of possible conducted control. This value describes the maximum effort in implementing the control and can be expressed as $U_p = 1$.

3.3. *Necessary and Sufficient Condition Fulfillment*

To fulfill the necessary conditions and follow the formula in Eq. (2.7), the Hamiltonian function for our constructed optimal control problem can be written as:

$$\begin{aligned} H =& AR(t) - Cu^2(t) + (\Lambda_1 - (\alpha I(t) + \mu)S(t))\lambda_1(t) \\ &+ (\alpha I(t)S(t) - (\beta+\mu)E(t))\lambda_2(t) \\ &+ \left(\beta E(t) - \frac{\gamma I(t)}{\theta I(t)+1} + \omega(1-a)(1-u(t))R(t) - (\delta+\mu)I(t)\right)\lambda_3(t) \\ &+ \left(\frac{\gamma I(t)}{\theta I(t)+1} - (\mu + \omega(1-a)(1-u(t)))R(t)\right)\lambda_4(t). \end{aligned} \tag{3.6}$$

Next, following the formulated Hamiltonian function, we obtain the adjoint function that can be expressed as:

$$\begin{aligned} \dot{\lambda_1}(t) = \frac{dH}{dS} =& -\alpha I(t)\lambda_2(t) - (-\alpha I(t) - \mu)\lambda_1(t), \\ \dot{\lambda_2}(t) = \frac{dH}{dE} =& -\beta\lambda_3(t) - (-\beta-\mu)\lambda_2(t), \\ \dot{\lambda_3}(t) = \frac{dH}{dI} =& \alpha S(t)\lambda_1(t) - \alpha S(t)\lambda_2(t) - \left(-\delta + \frac{\gamma\theta I(t)}{(\theta I(t)+1)^2} - \frac{\gamma}{\theta I(t)+1} - \mu\right)\lambda_3(t) \\ &- \left(-\frac{\gamma\theta I(t)}{(\theta I(t)+1)^2} + \frac{\gamma}{\theta I(t)+1}\right)\lambda_4(t), \\ \dot{\lambda_4}(t) = \frac{dH}{dR} =& -A - \omega(1-a)(1-u(t))\lambda_3(t) - (-\mu - \omega(1-a)(1-u(t)))\lambda_4(t). \end{aligned}$$

The optimal condition is obtained by calculating the first-order derivative of the Hamiltonian function against u, where equal to zero, resulting in:

$$u(t) = \frac{\omega(a\lambda_3(t) - a\lambda_4(t) - \lambda_3(t) + \lambda_4(t))R(t)}{2C}. \tag{3.7}$$

The sufficient condition is fulfilled as we find the second-order derivative of the Hamiltonian function against the control variable u, which can be written as:

$$\frac{\partial^2 H}{\partial u^2} = -2C \leq 0.$$

The result shows that the value of $\partial^2 H/\partial u^2$ is negative. Consequently, the value of u^* will be minimal over time but remain to maximize the recovered number. Finally, we can express the optimal condition in Eq. 3.7 as:

$$u^*(t) = \min\left\{\max\left\{0, \frac{\omega(a\lambda_3(t) - a\lambda_4(t) - \lambda_3(t) + \lambda_4(t))R(t)}{2C}\right\}, 1\right\}. \tag{3.8}$$

3.4. *Numerical Simulation*

In this subsection, a numerical simulation was performed to show the projected dynamical population under TB transmission with and without control implementation. The Runge-Kutta method is used to solve the system Eq. (2.1) – Eq. (2.4), while the Forward-Backward Sweep Method is used to solve the Hamiltonian and ajoint function in the optimal control problem. As mentioned, the control aimed to maximize the number of recovered individuals by reducing the re-infection rate using post-TB interventions, namely individual-based, mixed, and community-based. In the following scenarios, the value of a is defined accordingly. First, if the recovered individual is treated by individual-based intervention, then the value of a is 0.9. This means that the individual will need to maintain an awareness level of 90% to remain healthy and prevent re-infection with TB. Following its meaning, the values of a for the mixed and Community-based interventions are 0.5 and 0.1, respectively. Each value of a corresponds to a different control weight, denoted C, which is assigned the value 3, 2, or 1. Each value represents the average cost of implementing the intervention that impacted an individual. For instance, the Individual-based intervention is more costly than the Mixed-based or Community-based. The optimal control results in projecting the recovered population dynamics over time, as shown in Figure 2.

Figure 2 shows that the individual-based control resulted in the recovered individual remaining significantly more than the other intervention. This means that individual-based control is the most effective in maximizing the recovered people. Furthermore, it shows that the number of recovered people under mixed and community-based intervention decreases around the final time. Therefore, we have to confirm this result by looking at the control profile of each strategy. We serve the control profile dynamics of each strategy in Figure 3.

Figure 3 shows that the control profile or optimal condition of the individual-based intervention strategy is the lowest, followed by mixed and community-based control. This is interesting since the individual-based control is still more effective

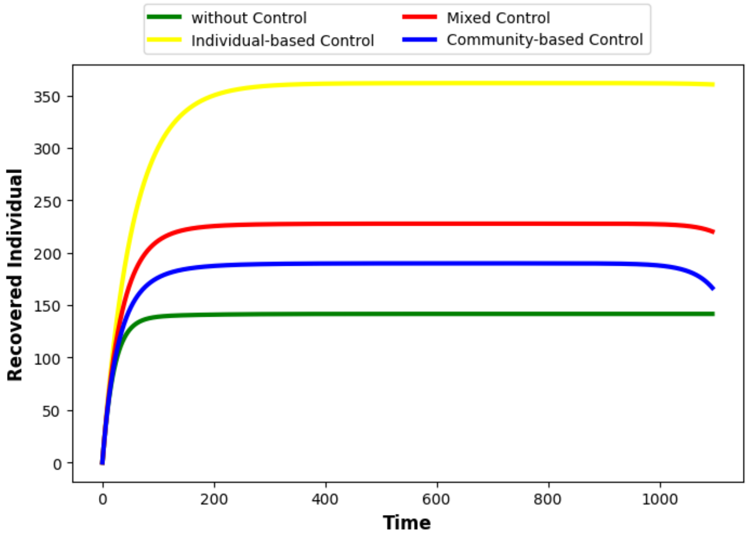

Figure. 2. Projection of Recovered Population Dynamics without and with Control.

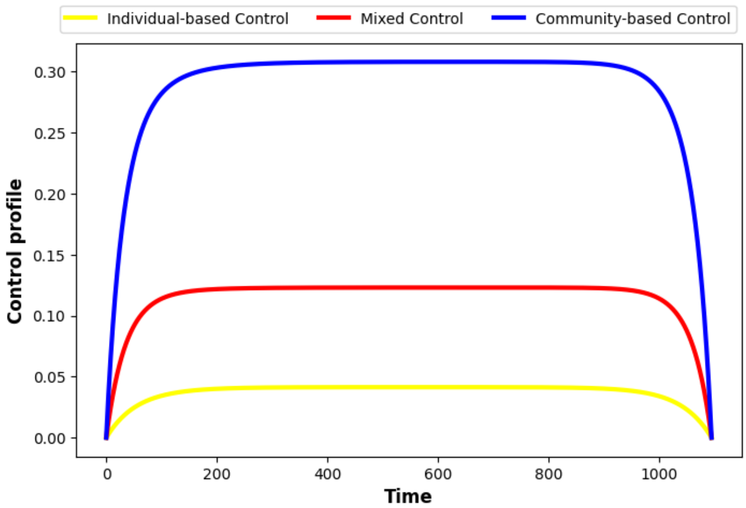

Figure. 3. Control Profile Dynamics.

in maintaining recovered people by preventing re-infection, as shown in Figure 2. We can see that the control profile of mixed and community-based interventions is declining quite significantly as it reaches the final time. This situation impacts the recovered people under its intervention decrease, which is shown in Figure 2. The control profile represents the percentage of control implementation that needs to be carried out based on the strategy planned, considering the cost control. For instance, the optimal condition of community-based intervention has a maximum value of around 0.3, representing that the intervention implementation can be done around 30% compared to the planned strategy. Nevertheless, the highest optimal condition does not guarantee the best result in reaching the aim of control. It depends on the other factors involved in reducing the re-infection risk, which in this study was denoted by a as the awareness level based on each control mode. As an early conclusion, individual-based control is chosen to be the best strategy for maintaining recovered people. Next, the cost-effectiveness analysis was performed to justify this glimpse conclusion.

3.5. *Cost-Effectiveness Analysis*

In this subsection, the cost-effectiveness analysis was performed using IAR, ACER, and ICER, which are formulated in Eq. (2.8), Eq. (2.9), and Eq. (2.10), respectively. The result of the numerical solution in the previous simulation was utilized to calculate each ratio. We rank all results in an increasing order based on the total infectious averted in Table 2.

Table 2. An Increasing Order based on the Number of Infectious Averted.

Strategy	Infectious Averted	IAR	ACER
Community-based	234004.0594	1.169843196	0.099308023
Mixed	445455.0603	1.853203229	0.016703086
Individual-based	1049032.012	2.795448782	0.001136228

Community-based intervention has the lowest number of infectious averted cases, while individual-based intervention has the highest number. Table 2 shows that the IAR of individual-based intervention is the highest, representing the best strategy for maintaining the recovered people. Furthermore, the ACER of its intervention has the lowest value of the other, which means that the cost that must be spent to reach the aim is less.

Next, we perform the first ICER calculation for each strategy and serve the result in Table 3.

Table 3. First Cost-effectiveness Determination.

Strategy	Infectious Averted	Total Cost	ICER
Community-based	234004.0594	23238.48059	0.099308023
Mixed	445455.0603	7440.474096	-0.074712375
Individual-based	1049032.012	1191.93993	-0.010352506

Tabel 3 shows that ICER for Community-based is greater than Mixed intervention. Consequently, we exclude the Community-based intervention from the next ICER calculation. We continue the ICER calculation using the same method as before, and the results are served in Table 4.

Table 4. Second Cost-effectiveness Determination.

Strategy	Infectious Averted	Total Cost	ICER
Mixed	445455.0603	7440.474096	0.016703086
Individual-based	1049032.012	1191.93993	-0.010352506

Table 4 indicates that the ICER for the Individual-based intervention is less than that of the Mixed intervention. This means the Mixed intervention implementation is more costly than the Individual-based intervention in maintaining the recovered people during post-TB treatment. Therefore, the initial conclusion in the previous subsection is confirmed, as the Individual-based intervention is calculated to be the cost-effective strategy for retaining recovered people over time. Nevertheless, implementing the Individual-based intervention is more challenging due to the limited healthcare resources. Thus, a policy must be formulated to cover the limitations of healthcare resources. For instance, due to the limited number of health workers to monitor each person after TB treatment, digitalization may be used to address this. Each recovered person during post-treatment for TB can be monitored digitally by their daily report of drug consumption, which can be submitted to an app.

4. Conclusion

In this article, the constructed model in [12] is developed into an optimal control model. The control aims to maximize the remaining recovered people while using the minimum cost of control over time. We defined a control variable as the multiplier on the re-infection rate in the form of $(1 - a)$, in which a represents the awareness level based on the control model, namely individual-based, mixed, and community-based interventions. This means that a higher a leads to better results in reducing the risk of re-infection. Next, following the control form, the control profile of u is formulated as $(1-u(t))$. The formulation represents the condition in which a higher percentage of control implementation may result in a greater reduction in reinfection cases. Nevertheless, the best strategy for achieving the aim at minimal cost control must be confirmed by calculating cost-effectiveness ratios, such as the Infectious Averted Ratio (IAR), Average Cost-Effectiveness Ratio (ACER), and Incremental Cost-Effectiveness Ratio (ICER). We found that the IAR of the individual-based intervention has the highest value, whereas its ACER value is the lowest. This means that Individual-based intervention is the best strategy for maintaining the recovered people and reducing the cost of reaching the aim. Furthermore, the ICER calculation indicates that the Individual-based intervention is the most cost-effective strategy for achieving the control aim. These findings confirm the glimpse conclusion as we see the projection of recovered people dynamics and its control profile dynamics. Hence, we conclude that the Individual-based intervention is most appropriate for reducing the number of TB cases from the re-infection risk under the observed condition. However, implementing Individual-based intervention is quite challenging due to the limited healthcare resources, such as workers or facilitates. To addess this issue, besides formulating any related policy, digitalization would be a breakthrough in reducing the reinfecion case by monitor the activity, such as drug consumption, recovered people during the post-treatment. All of these findings are not revealed in the previous study in [1] and indirectly address the gap against the study.

This study much some rooms for further study. In term of control scenario time, combination of ramp-ups or short-term versus long-term interventions may be studied for the next. Next, it would be more fruitful and easy to implement if the next study considering any actual data related, such as up-to-date number of TB cases both inside and ouside Wes Java, and cost of intervention. Moreover, it can be validate the model and exploring potential upcoming bias due to the varying data. These can be ease the policymaker in formulating related policy based on scientific reasoning. In addition, considering multi-intervention as WHO or national policy of TB as control parameters is one the improvement for further study as long as the data were available and accessible.

5. Acknowledgment

We thank Universitas Pamulang, which has funded this research via Penelitian Dosen Pemula, No. 0093/D5/SPKP/LPPM/UNPAM/X/2024.

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