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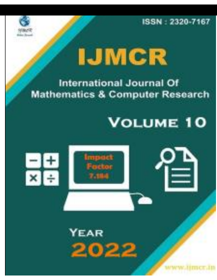

Mathematical Modeling and Optimal Control Strategies for Reducing the Spread of the Tuberculosis Infection

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ARTICLE INFO	ABSTRACT
Published Online: 30 March 2022 Corresponding Author: **Widowati**	Tuberculosis is an infectious disease with transmission through the air and droplets of infected people. The problem of spreading and treating tuberculosis needs some development. The model used in this study is a model of development, in which infected individuals are divided into two subpopulations, namely the active infection subpopulation stage one and second stage infection is MDR (multi drug resistant). Four optimal control strategies are implemented with the aim of reducing the rate of spread of tuberculosis TB infection, prevention by increasing a clean and healthy lifestyle, and using masks when interacting between infected and susceptible, vaccination for family and close friends of infected individuals, implementing the DOTS strategy (Directly Observed Treatment Shortcourse) for infected individuals, and Intensive care in hospital. Then the optimal control of the model was analyzed using Pontriagin's Maximum Principle while for global stability using Lyapunov. The numerical results are obtained that the optimal control strategy given can accelerate in reducing the rate of spread of tuberculosis in Indonesia. this is evidenced by the graph of the population infected with tuberculosis every year after the control has decreased the number of infected, and the graph is heading to the equilibrium point.

KEYWORDS: Stability analysis, Tuberculosis, Pontryagin's maximum principle, Lyapunov, Optimal control

I. INTRODUCTION

Based on the Global Tuberculosis (TB) Report in December 2020 [1] the number of tuberculosis cases found and treated in Indonesia was 271,750. Where in 2018 TB cases in Indonesia reached 570,289 and in 2019 there were 568,987. In addition, based on data from the Semarang City Health Service, the number of tuberculosis patients in 2020 in Semarang has decreased, where in 2018 there were 4253 cases, 2019 there were 4307 cases and 2296 cases in 2020. This is one form of achievement of the targets that have been declared by the United Nations on 26 September 2018 regarding Tuberculosis. One of its targets is to diagnose and treat 40 million people with tuberculosis in the 5-year period from 2018-2022. The decrease in the number of cases of tuberculosis in 2020 cannot make individuals ignore the seriousness of tuberculosis, because tuberculosis can attack anyone, when and wherever individuals are. Therefore, development in the field of medical science plays a very important role in overcoming tuberculosis. The problem of the spread and treatment of tuberculosis is very complicated, so it is necessary to make analyzes and estimates so that the global target for ending tuberculosis can achieve the expected results. Mathematical models were used to analyze and simulate the spread and impact of tuberculosis treatment.

The dynamics of the spread of tuberculosis has been studied by several previous researchers, including; research by Abdullah Idris, et al [2] analyzed the spread of tuberculosis with a case study model in Nigeria with the linearization method. N. Anggiani, et al[3] analyzed the optimal control of the epidemic SIR model with the effect of vaccination and immigration factors. Virendra Kumar Gupta, et al [4] also analyzed a mathematical model of the spread of tuberculosis with the effect of resistance levels on the first or second treatment for infected and resistant individuals, using the Ruth-Hurwitz and Lyapunov method. Fatmawati, et al [5] also discussed the optimal control strategy for tuberculosis control, but focused more on the pediatric and adult population. The model used was the method used in analyzing the model was the Pontryagin maximum principle. In addition to discussing TB control based on age, Fatmawati, et al [17] also analyzed the optimal control strategy with prevention using the model. Isa Abdillah baba, et al [6] analyzed the tuberculosis model using a model with optimal control of care and therapy given to infected people. Saif Ullah, et al [7] analyzed tuberculosis with 3 controls, namely vaccination and treatment of infected individuals, the methods used were Routh-Hurwitz, Center manifold and Hamiltonian. Siyu Liu, et al[8] discussed the tuberculosis model in the form of a model to study tuberculosis control in China with the Pontryagin maximum principle analysis method. Sutimin, et al [9] analyzed tuberculosis with an epidemic model used in saturated infection strength and only used one type of infection with two treatment scenarios. Dhiraj K, et al [10] in their research discusses the analysis of global dynamics of a tuberculosis model with sensitivity of the smear microscopy. From some of these researchers there are several differences with this study including the form of the model used and the method chosen, in this study using a model which is a development of the tuberculosis model [9].

In this study, the subpopulation was devided into five, namely susceptible, latent or exposed, infectious 1, MDR infected and recovery. Where the optimal control strategy is also applied to the model which aims to reduce the spread of tuberculosis. Optimal control with four control variables, namely prevention by promoting a healthy lifestyle and wearing masks when interacting with infected individuals, vaccination for family and closest friends, outpatient treatment with DOTS strategy, intensive care in hospital.

II. MATHEMATICAL MODEL FORMULATION

As a preliminary study, we have been publishing a local stability analysis of a tuberculosis epidemic model [11] and the model proposed in this paper was developed by considering four controls. Significant novelties have been considered in this new work, which are explained as follows. In this study, we proposed the global stability analisys and control involved in our proposed model so that it becomes the novelty in this work.

Let SEI_1I_2R epidemic mathematical model as follows,

$$\begin{aligned}
\frac{dS}{dt} &= \lambda - \beta_1 SI_1 - \beta_2 SI_2 - \mu S \\
\frac{dE}{dt} &= \beta_1 p_1 SI_1 + \beta_2 q_1 SI_2 - (\mu + \alpha)E \\
\frac{dI_1}{dt} &= p\beta_1 SI_1 + q\beta_2 SI_2 + \alpha E - (\phi + \mu + \delta_1)I_1 \\
\frac{dI_2}{dt} &= \phi(1 - r_1)I_1 - (\mu + \delta_2)I_2 - \varphi r_2 I_2 \\
\frac{dR}{dt} &= \phi r_1 I_1 + \varphi r_2 I_2 - \mu R
\end{aligned} \tag{1}$$

The notations and descriptions of the parameters for mathematical modelling are given in Table 1.

Table 1: Descriptions of parameters.

Symbol	Descriptions
λ	:Recruitment rate
μ	:Natural death rate
α	:The rate of change of the latent subpopulation to infected-1
δ_1	:Death rate due to tuberculosis in infecte individuals
δ_2	:Death rate due to tuberculosis in infected-2 individuals
ϕ	:The rate of change in the subpopulation infected-1 to infected-2
φ	:The rate of change in the infected 2 subpopulation to recovery
r_1	:Fraction number of the infected-1 treatment effectiveness
r_2	:Fraction number of the infected-2 (MDR) treatment effectiveness
p	:The rate of contact with tuberculosis infected-1 individuals
q	:The rate of contact with tuberculosis infected-2 (MDR) individuals
β_1	:Transmission rate of the susceptible individual become infected due to contact with a tuberculosis infected-1 individuals
β_2	:Transmission rate of the susceptible individuals become infected due to contact with tuberculosis infected-2 (MDR) individuals

Then model is developed by adding optimal control so the equation becomes:

$$\begin{aligned}
\frac{dS}{dt} &= \lambda - (\beta_1 I_1 + \beta_2 I_2)(1 - u_1)S - \mu S \\
\frac{dE}{dt} &= (\beta_1(1-p)I_1 + \beta_2(1-q)I_2)S(1-u_1) - (\mu + \alpha)E - u_2 E \\
\frac{dI_1}{dt} &= (p\beta_1 I_1 + q\beta_2 I_2)S + \alpha E - (\phi + \mu + \delta_1)I_1 - u_3 I_1 \\
\frac{dI_2}{dt} &= \phi(1 - r_1)I_1 - (\mu + \delta_2 + \varphi r_2)I_2 - u_4 I_2 \\
\frac{dR}{dt} &= \phi r_1 I_1 + \varphi r_2 I_2 - \mu R + u_2 E + u_3 I_1 + u_4 I_2
\end{aligned} \tag{2}$$

TB model in equation 1 is built by five variables, that is SEI_1I_2R where S (Susceptible), E (laten), I_1 (infected 1) , I_2 (infected 2 or TB-MDR), and R (Recovery)). in this model have two possibilities are; the first possibility is the susceptible individual passes through the exposed phase then becomes infected by tuberculosis and the second possibility is susceptible individuals can be directly infected with active tuberculosis without going through the exposed phase who have weak body immunity. Tuberculosis infection is devided into two categories are infectious 1 and Infectious 2 (MDR). first and second treatment are intered into the parameters r_1 and r_2. The difference between the first and second treatment is the duration of the treatment and addition of injection drug in the second infection. Then the optimal control strategy is added to model (2) where the strategy has the aim of minimizing the cost function which includes first and second infection as well as prevention costs by improving a clean and healthy lifestyle, and always using mask when interacting with infected(u_1), Vaccination(u_2), and maximizing the DOTS strategy in the treatment of infected individuals(u_3), and intensive care in the hospital(u_4).

III. MODEL ANALYSIS

Model (1) has two equilibrium points, namely the disease-free equilibrium (DFE) and the endemic equilibrium point. The value of DFE and endemic equilibrium point can be seen in [11] then the eigen values are obtained from the matrix $NGM = FV^{-1}$ and $\Re_0 = \rho(FV^{-1})$ obtained as follows;

$$\Re_0 = \frac{(p\mu+\alpha)\lambda\beta_1}{(\mu+\alpha)(\phi+\mu+\delta_1)\mu} - \frac{\lambda\beta_2\phi(-1+r_1)(\alpha+q\mu)}{\mu(\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\phi+\mu+\delta_1)}, \quad (3)$$

with $r_1 > 0$.

Case 1: $0 < r_1 < 1$, so equation (3) becomes;

$$\Re_0 = \frac{(p\mu+\alpha)\lambda\beta_1}{\mu(\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\phi+\mu+\delta_1)} - \frac{\lambda\beta_2\phi(-1+r_1)(\alpha+q\mu)}{\mu(\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\phi+\mu+\delta_1)} \quad (4)$$

$$\Re_0 = \frac{(p\mu+\alpha)\lambda\beta_1 - (\lambda\beta_2\phi(-1+r_1)(\alpha+q\mu))}{\mu(\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\phi+\mu+\delta_1)}$$

It is proven that $\Re_0 > 0$.

Case 2: $r_1 > 1$, we have

$$(p\mu+\alpha)\lambda\beta_1(\mu+\delta_2+\varphi r_2) > \left(\lambda\beta_2\phi(-1+r_1)(\alpha+q\mu)\right)$$

so that $\Re_0 > 0$.

Theorem 1. If $\Re_0 < 1$, the non-endemic equilibrium point ε_0 is locally asymptotically stable, if $\Re_0 = 1, \varepsilon_0$ it is stable, and if $\Re_0 > 1, \varepsilon_0$ it is unstable.

Proof

Theorem 1 has been proven on paper [11]

Theorem 2. If $\Re_0 > 1$ then the endemic equilibrium point (ε_1) will be global asymptotically stable.

Proof.

Based on the equation in the model at an endemic equilibrium state, it is obtained that:

$$0 = \lambda - \beta_1 S^* I_1^* - \beta_2 S^* I_2^* - \mu S^*$$
$$0 = \beta_1(1-p)S^* I_1^* + \beta_2(1-q)S^* I_2^* - (\mu+\alpha)E^*$$
$$0 = p\beta_1 S^* I_1^* + q\beta_2 S^* I_2^* + \alpha E^* - (\phi+\mu+\delta_1)I_1^*$$
$$0 = \phi(1-r_1)I_1^* - (\mu+\delta_2)I_2^* - \varphi r_2 I_2^*$$

In case,

$$A_1 = \mu + \alpha$$
$$A_2 = \phi + \mu + \delta_1$$
$$A_3 = (\mu+\delta_2) + \varphi r_2$$

Therefore, the system of equations can be written as;

$$\begin{aligned} &\lambda = \beta_1 S^* I_1^* + \beta_2 S^* I_2^* + \mu S^* \\ &A_1 E^* = \beta_1(1-p)S^* I_1^* + \beta_2(1-q)S^* I_2^* \\ &A_2 I_1^* = p\beta_1 S^* I_1^* + q\beta_2 S^* I_2^* + \alpha E^* \\ &A_3 I_2^* = \phi(1-r_1)I_1^* \end{aligned} \quad (5)$$

Than, defined function $V : D \in \mathbb{R}^5 \to \mathbb{R}$ and $x_e \in D$ the equilibrium point of the non-linear differensial system,with $D = \{(S, E, I_1, I_2, R) \mid S, E, I_1, I_2, R\}$,

$$V = S - S^* \ln S + b_0(E - E^* \ln E) + b_1(I_1 - I_1^* \ln I_1) + b_2(I_2 - I_2^* \ln I_2)$$

With b_0, b_1, b_2 positive constant. The function V is a Lyapunov function because it ful fill:

1. The function is continuous in D because the function V contains a logarithmic function. The first partial derivative V is also a continue function on D.
2. Function $V(x) > 0$ for $x \in D$ with $x \neq x_e$ and $V(x_e) = 0$ with $x = x_e$, the Hassian Matrix of ε_1^* is;

$$H(\varepsilon_1^*) = \begin{bmatrix} \frac{1}{S^*} & 0 & 0 & 0 \\ 0 & \frac{b_0}{E^*} & 0 & 0 \\ 0 & 0 & \frac{b_1}{I_1^*} & 0 \\ 0 & 0 & 0 & \frac{b_2}{I_2^*} \end{bmatrix}$$

The matrix $H(\varepsilon_1^*)$ is positive definite because the determinant $H(\varepsilon_1^*) = \frac{b_0 b_1 b_2}{S^* E^* I_1^* I_2^*} > 0$, so, the point $H(\varepsilon_1^*)$ is a global minimum.

The derivative of the function V is;

$$\frac{dV}{dt} = \frac{\partial V}{\partial S}\frac{dS}{dt} + \frac{\partial V}{\partial E}\frac{dE}{dt} + \frac{\partial V}{\partial I_1}\frac{dI_1}{dt} + \frac{\partial V}{\partial I_2}\frac{dI_2}{dt}$$

$$= \left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + b_0\left(1 - \frac{E^*}{E}\right)\frac{dE}{dt} + b_1\left(1 - \frac{I_1^*}{I_1}\right)\frac{dI_1}{dt} + b_2\left(1 - \frac{I_2^*}{I_2}\right)\frac{dI_2}{dt}$$

$$= \left(1 - \frac{S^*}{S}\right)\left(\lambda - \beta_1 SI_1 - \beta_2 SI_2 - \mu S\right) + b_0\left(1 - \frac{E^*}{E}\right)\left(\beta_1(1-p)SI_1 + \beta_2(1-q)SI_2 - (\mu+\alpha)E\right)$$
$$+ b_1\left(1 - \frac{I_1^*}{I_1}\right)\left(p\beta_1 SI_1 + q\beta_2 SI_2 + \alpha E - (\phi+\mu+\delta_1)I_1\right) + b_2\left(1 - \frac{I_2^*}{I_2}\right)\left(\phi(1-r_1)I_1 - (\mu+\delta_2)I_2 - \varphi r_2 I_2\right)$$

$$= \left(1 - \frac{S^*}{S}\right)\left(\beta_1 S^* I_1^* + \beta_2 S^* I_2^* + \mu S - \beta_1 SI_1 - \beta_2 SI_2 - \mu S\right) + b_0\left(1 - \frac{E^*}{E}\right)\left(\beta_1(1-p)SI_1 + \beta_2(1-q)SI_2 - (\mu+\alpha)E\right)$$
$$+ b_1\left(1 - \frac{I_1^*}{I_1}\right)\left(p\beta_1 SI_1 + q\beta_2 SI_2 + \alpha E - (\phi+\mu+\delta_1)I_1\right) + b_2\left(1 - \frac{I_2^*}{I_2}\right)\left(\phi(1-r_1)I_1 - (\mu+\delta_2)I_2 - \varphi r_2 I_2\right)$$

$$= -\left(\frac{S-S^*}{S}\right)^2(\mu) + \left(1 - \frac{S^*}{S}\right)\left(\beta_1 S^* I_1^* + \beta_2 S^* I_2^* - \beta_1 SI_1 - \beta_2 SI_2\right) + b_0\left(1 - \frac{E^*}{E}\right)\left(\beta_1(1-p)SI_1 + \beta_2(1-q)SI_2 - (A_1)E\right)$$
$$+ b_1\left(1 - \frac{I_1^*}{I_1}\right)\left(p\beta_1 SI_1 + q\beta_2 SI_2 + \alpha E - (A_2)I_1\right) + b_2\left(1 - \frac{I_2^*}{I_2}\right)\left(\phi(1-r_1)I_1 - A_3 I_2\right)$$

$$= -\left(\frac{S-S^*}{S}\right)^2(\mu) + \left(1 - \frac{S^*}{S}\right)\left(\beta_1 S^* I_1^* + \beta_2 S^* I_2^*\right) - \beta_1 SI_1 - \beta_2 SI_2 + \beta_1 S^* I_1^* + \beta_2 S^* I_2^* +$$
$$b_0\left(1 - \frac{E^*}{E}\right)\beta_1(1-p)SI_1 + \beta_2(1-q)SI_2 - b_0 A_1 E + b_0 A_1 E^*$$
$$+ b_1\left(1 - \frac{I_1^*}{I_1}\right)\left(p\beta_1 SI_1 + q\beta_2 SI_2 + \alpha E\right) - b_1 A_2 I_1 + b_1 A_2 I_1^* + b_2\left(1 - \frac{I_2^*}{I_2}\right)\left(\phi(1-r_1)I_1\right) - b_2 A_3 I_2 + b_2 A_3 I_2^*$$

$$= -\left(\frac{S-S^*}{S}\right)^2(\mu) + \left(1 - \frac{S^*}{S}\right)\left(\beta_1 S^* I_1^* + \beta_2 S^* I_2^*\right) - \beta_1 SI_1 - \beta_2 SI_2 + \beta_1 S^* I_1^* + \beta_2 S^* I_2^* +$$
$$b_0\left(1 - \frac{E^*}{E}\right)(\beta_1(1-p)SI_1 + \beta_2(1-q)SI_2) - b_0 A_1 E + b_0\left(\beta_1(1-p)S^* I_1^* + \beta_2(1-q)S^* I_2^*\right)$$
$$+ b_1\left(1 - \frac{I_1^*}{I_1}\right)\left(p\beta_1 SI_1 + q\beta_2 SI_2 + \alpha E\right) - b_1 A_2 I_1 + b_1\left(p\beta_1 S^* I_1^* + q\beta_2 S^* I_2^* + \alpha E^*\right) + b_2\left(1 - \frac{I_2^*}{I_2}\right)\left(\phi(1-r_1)I_1\right) - b_2 A_3 I_2 + b_2\left(\phi(1-r_1)\right)I_1^*$$

$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+\left(1-\frac{S^*}{S}\right)\left(\beta_1 S^* I_1^*+\beta_2 S^* I_2^*\right)-\beta_1 SI_1-\beta_2 SI_2+\beta_1 S^* I_1^*+\beta_2 S^* I_2^*+$$
$$b_0(\beta_1(1-p)SI_1+\beta_2(1-q)SI_2)-b_0\frac{E^*}{E}(\beta_1(1-p)SI_1+\beta_2(1-q)SI_2)-b_0A_1E+b_0\left(\beta_1(1-p)S^*I_1^*+\beta_2(1-q)S^*I_2^*\right)$$
$$+b_1\left(p\beta_1 SI_1+q\beta_2 SI_2+\alpha E\right)-b_1\frac{I_1^*}{I_1}\left(p\beta_1 SI_1+q\beta_2 SI_2+\alpha E\right)-b_1A_2I_1+b_1\left(p\beta_1 S^*I_1^*+q\beta_2 S^*I_2^*+\alpha E^*\right)$$
$$+b_2\left(\phi(1-r_1)I_1\right)-b_2\frac{I_2^*}{I_2}\left(\phi(1-r_1)I_1\right)-b_2A_3I_2+b_2\left(\phi(1-r_1)\right)I_1^*$$
$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+\left(1-\frac{S^*}{S}\right)\left(\beta_1 S^* I_1^*\right)+\left(1-\frac{S^*}{S}\right)\beta_2 S^* I_2^*-\beta_1 SI_1-\beta_2 SI_2+\beta_1 S^* I_1^*+\beta_2 S^* I_2^*+$$
$$b_0(\beta_1(1-p)SI_1+\beta_2(1-q)SI_2)-b_0A_1E+b_0\left(\beta_1(1-p)S^*I_1^*\right)\left(1-\frac{S}{S^*}\frac{I_1}{I_1^*}\frac{E^*}{E}\right)+b_0\left(\beta_2(1-q)S^*I_2^*\right)\left(1-\frac{S}{S^*}\frac{I_2}{I_2^*}\frac{E^*}{E}\right)$$
$$+b_1\left(p\beta_1 SI_1+q\beta_2 SI_2+\alpha E\right)-b_1A_2I_1+b_1\left(p\beta_1 S^*I_1^*\right)\left(1-\frac{S}{S^*}\frac{I_1}{I_1^*}\frac{E^*}{E}\right)+b_1\left(q\beta_2 S^*I_2^*\right)\left(1-\frac{S}{S^*}\frac{I_2}{I_2^*}\frac{E^*}{E}\right)+b_1\alpha E^*\left(1-\frac{I_1^*}{I_1}\frac{E}{E^*}\right)$$
$$+b_2\left(\phi(1-r_1)I_1\right)-b_2A_3I_2+b_2\left(\phi(1-r_1)\right)I_1^*\left(1-\frac{I_2^*}{I_2}\frac{I_1}{I_1^*}\right) \qquad (6)$$

Suppose $\left(\frac{S^*}{S},\frac{E^*}{E},\frac{I_1^*}{I_1},\frac{I_2^*}{I_2}\right)=(x,y,z,w)$, then (6) be;

$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+(1-x)\left(\beta_1 S^* I_1^*\right)+(1-x)\beta_2 S^* I_2^*-\beta_1 SI_1-\beta_2 SI_2+\beta_1 S^* I_1^*+\beta_2 S^* I_2^*+$$
$$b_0(\beta_1(1-p)SI_1+\beta_2(1-q)SI_2)-b_0A_1E+b_0\left(\beta_1(1-p)S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+b_0\left(\beta_2(1-q)S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{w}y\right)$$
$$+b_1\left(p\beta_1 SI_1+q\beta_2 SI_2+\alpha E\right)-b_1A_2I_1+b_1\left(p\beta_1 S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+b_1\left(q\beta_2 S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{Iw}y\right)+b_1\alpha E^*\left(1-z\frac{1}{y}\right)$$
$$+b_2\left(\phi(1-r_1)I_1\right)-b_2A_3I_2+b_2\left(\phi(1-r_1)\right)I_1^*\left(1-w\frac{1}{z}\right) \qquad (7)$$

The value b_0, b_1, b_2 is taken such that the coefficient SI_1, SI_2, I_1, I_2, E is 0 so that;

$$\begin{aligned}
&-\beta_1+b_0\beta_1 p_1=0\\
&-\beta_2+b_o\beta_2 q_1=0\\
&\beta_1 S^*-b_1A_2+b_2\phi(1-r_1)=0\\
&\beta_2 S^*-b_2A_3=0\\
&-b_0A_1+b_1\alpha=0
\end{aligned} \qquad (8)$$

Then calculate the value b_0, b_1, b_2 as follows;

$$b_0\beta_1 p_1=\beta_1$$
$$b_0=\frac{\beta_1}{\beta_1 p_1}=\frac{1}{p_1}$$

With $p_1=(1-p)$

$$b_o\beta_2 q_1=\beta_2$$
$$b_o=\frac{\beta_2}{\beta_2 q_1}=\frac{1}{q_1}$$

Where $q_1=(1-q)$

Next, look for the value of b_1;

$$b_1\alpha=\left(\frac{1}{1-p}\right)A_1 \qquad\qquad b_1\alpha=\left(\frac{1}{1-q}\right)A_1$$
$$b_1=\left(\frac{A_1}{1-p}\right)\left(\frac{1}{\alpha}\right) \quad \text{and} \quad b_1=\left(\frac{A_1}{1-q}\right)\left(\frac{1}{\alpha}\right)$$
$$b_1=\frac{A_1}{\alpha(1-p)} \qquad\qquad b_1=\frac{A_1}{\alpha(1-q)}$$

And value of b_2 obtained;

$$\beta_2 S^*-b_2A_3=0$$
$$b_2A_3=\beta_2 S^*$$
$$b_2=\frac{\beta_2 S^*}{A_3}$$

Based on the equation (11) we get the value $b_0=\frac{1}{(1-p)}$ or $b_0=\frac{1}{(1-q)}$, $b_1=\frac{A_1}{\alpha(1-p)}$ or $b_1=\frac{A_1}{\alpha(1-q)}$, and $b_2=\frac{\beta_2 S^*}{A_3}$

So that it is obtained;

$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+(1-x)\left(\beta_1 S^* I_1^*\right)+(1-x)\beta_2 S^* I_2^*+b_0\left(\beta_1(1-p)S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+$$
$$b_0\left(\beta_2(1-q)S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{w}y\right)+b_1\left(p\beta_1 S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+b_1\left(q\beta_2 S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{w}y\right)+$$
$$b_1\alpha E^*\left(1-z\frac{1}{y}\right)+b_2\left(\phi(1-r_1)\right)I_1^*\left(1-w\frac{1}{z}\right) \qquad (9)$$

Because value $b_0=\frac{1}{(1-p)}$ and $b_0=\frac{1}{(1-q)}$ so, the equation becomes;

$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+b_0(1-x)\left(\beta_1 S^* I_1^*\right)+b_0(1-x)\beta_2 S^* I_2^*+\left(\frac{1}{(1-p)}\right)\left(\beta_1(1-p)S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+$$
$$\left(\frac{1}{(1-q)}\right)\left(\beta_2(1-q)S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{w}y\right)+b_1\left(p\beta_1 S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+b_1\left(q\beta_2 S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{w}y\right)+$$
$$b_1\alpha E^*\left(1-z\frac{1}{y}\right)+b_2\left(\phi(1-r_1)\right)I_1^*\left(1-w\frac{1}{z}\right)$$

$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+b_0(1-x)\left(\beta_1 S^* I_1^*\right)+b_0(1-x)\beta_2 S^* I_2^*+\left(\beta_1 S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+$$
$$\left(\beta_2 S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{w}y\right)+b_1\left(p\beta_1 S^*I_1^*\right)\left(1-\frac{1}{x}\frac{1}{z}y\right)+b_1\left(q\beta_2 S^*I_2^*\right)\left(1-\frac{1}{x}\frac{1}{w}y\right)+$$
$$b_1\alpha E^*\left(1-z\frac{1}{y}\right)+b_2\left(\phi(1-r_1)\right)I_1^*\left(1-w\frac{1}{z}\right)$$
$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+b_0(1-x)\left(\beta_1 S^* I_1^*\right)+b_0(1-x)\beta_2 S^* I_2^*+\left(\beta_1 S^*I_1^*\right)\left(1-\frac{y}{xz}\right)+$$
$$\left(\beta_2 S^*I_2^*\right)\left(1-\frac{y}{xw}\right)+b_1\left(p\beta_1 S^*I_1^*\right)\left(1-\frac{y}{xz}\right)+b_1\left(q\beta_2 S^*I_2^*\right)\left(1-\frac{y}{xw}\right)+$$
$$b_1\alpha E^*\left(1-\frac{z}{y}\right)+b_2\left(\phi(1-r_1)\right)I_1^*\left(1-\frac{w}{z}\right)$$

$$=-\frac{\left(S-S^*\right)^2}{S}(\mu)+b_0\left(2-x-\frac{y}{xz}\right)\left(\beta_1 S^* I_1^*\right)+b_0\left(\beta_2 S^*I_2^*\right)\left(2-x-\frac{y}{xw}\right)+b_1\left(p\beta_1 S^*I_1^*\right)\left(1-\frac{y}{xz}\right)+$$
$$b_1\left(q\beta_2 S^*I_2^*\right)\left(1-\frac{y}{xw}\right)+b_1\alpha E^*\left(1-\frac{z}{y}\right)+b_2\left(\phi(1-r_1)\right)I_1^*\left(1-\frac{w}{z}\right) \qquad (10)$$

Multiplying the fifth equation of (8) by E^* and the second equation of (6) by b_0 to get

$$\begin{aligned}
&b_0A_1E^*=b_1\alpha E^*\\
&b_0A_1E^*=b_0\beta_1(1-p)S^*I_1^*+\beta_2(1-q)S^*I_2^*
\end{aligned} \qquad (11)$$

Then using elimination, obtain;

$$\begin{aligned}
&b_1\alpha E^*=b_0\beta_1(1-p)S^*I_1^*+\beta_2(1-q)S^*I_2^*\\
&b_1\alpha E^*-b_0\beta_1(1-p)S^*I_1^*-\beta_2(1-q)S^*I_2^*=0
\end{aligned} \qquad (12)$$

Multiplying the equation (17) by $F_1(u)$ where $u=(x,y,z,w)^T$ and $F_1(u)$ is a function that will be determined later, so we get;

$$b_1\alpha E^* F_1(u) - b_0\beta_1(1-p)S^* I_1^* F_1(u) - \beta_2(1-q)S^* I_2^* F_1(u) = 0 \quad (13)$$

Next, multiply the third equation of (8) by I_1^* and the third equation of (6) by b_1 as follows;

$$\begin{aligned}&\beta_1 S^* I_1^* + b_2\phi(1-r_1)I_1^* = b_1 A_2 I_1^* \\ &b_1 p\beta_1 S^* I_1^* + b_1 q\beta_2 S^* I_2^* + b_1\alpha E^* = b_1 A_2 I_1^*\end{aligned} \quad (14)$$

Use elimination so that it is obtained;

$$\begin{aligned}&b_1 p\beta_1 S^* I_1^* + b_1 q\beta_2 S^* I_2^* + b_1\alpha E^* = \beta_1 S^* I_1^* + b_2\phi(1-r_1)I_1^* \\ &\beta_1 S^* I_1^* + b_2\phi(1-r_1)I_1^* - b_1 p\beta_1 S^* I_1^* - b_1 q\beta_2 S^* I_2^* - b_1\alpha E^* = 0\end{aligned} \quad (15)$$

Multiply the equation (15) with $F_2(u)$ where $u = (x, y, z, w)^T$ and $F_2(u)$ is a function that will be determined later, so that it was obtained;

$$\begin{aligned}&\beta_1 S^* I_1^* F_2(u) + b_2\phi(1-r_1)I_1^* F_2(u) - b_1 p\beta_1 S^* I_1^* F_2(u) \\ &-b_1 q\beta_2 S^* I_2^* F_2(u) - b_1\alpha E^* F_2(u) = 0\end{aligned} \quad (16)$$

Substitution (14) and (15) to (10) so, that it produces;

$$= -\frac{(S-S^*)^2}{S}(\mu) + b_0\left(2 - x - \frac{y}{xz} - F_1(u) + F_2(u)\right)(\beta_1 S^* I_1^*) + b_0(\beta_2 S^* I_2^*)\left(2 - x - \frac{y}{xw} - F_1(u)\right) +$$
$$b_1(p\beta_1 S^* I_1^*)\left(1 - \frac{y}{xz} - F_2(u)\right) + b_1(q\beta_2 S^* I_2^*)\left(1 - \frac{y}{xw} - F_2(u)\right) + b_1\alpha E^*\left(1 - \frac{z}{y} + F_1(u) - F_2(u)\right) +$$
$$b_2(\phi(1-r_1))I_1^*\left(1 - \frac{w}{z} + F_2(u)\right)$$

Function $F_1(u)$ and $F_2(u)$ are determined in such a way until the coefficient E^* and I_1^* are 0, will produce;

$$1 - \frac{z}{y} + F_1(u) - F_2(u) = 0 \text{ and } 1 - \frac{w}{z} + F_2(u) = 0$$

So

$$1 - \frac{w}{z} + F_2(u) = 0$$

$$F_2(u) = -1 + \frac{w}{z}$$

And substitution of value $F_2(u)$ to

$1 - \frac{z}{y} + F_1(u) - F_2(u) = 0$, obtained;

$$1 - \frac{z}{y} + F_1(u) - F_2(u) = 0$$

$$F_1(u) = F_2(u) - 1 + \frac{z}{y}$$

$$F_1(u) = -1 + \frac{w}{z} - 1 + \frac{z}{y}$$

$$F_1(u) = -2 + \frac{w}{z} + \frac{z}{y}$$

So, the value of $\dot{V}(t)$ is

$$\dot{V}(t) = -\frac{(S-S^*)^2}{S}(\mu) + b_0\left(2 - x - \frac{y}{xz} - \left(-2 + \frac{w}{z} + \frac{z}{y}\right) + \left(-1 + \frac{w}{z}\right)\right)(\beta_1 S^* I_1^*) +$$
$$b_0(\beta_2 S^* I_2^*)\left(2 - x - \frac{y}{xw} - \left(-2 + \frac{w}{z} + \frac{z}{y}\right)\right) + b_1(p\beta_1 S^* I_1^*)\left(1 - \frac{y}{xz} + \left(-2 + \frac{w}{z} + \frac{z}{y}\right)\right) +$$
$$b_1(q\beta_2 S^* I_2^*)\left(1 - \frac{y}{xw} - \left(-1 + \frac{w}{z}\right)\right) + b_1\alpha E^*\left(1 - \frac{z}{y} + \left(-2 + \frac{w}{z} + \frac{z}{y}\right) - \left(-1 + \frac{w}{z}\right)\right) +$$
$$b_2(\phi(1-r_1))I_1^*\left(1 - \frac{w}{z} + \left(-1 + \frac{w}{z}\right)\right)$$

$$\dot{V}(t) = -\frac{(S-S^*)^2}{S}(\mu) + b_0\left(3 - x - \frac{y}{xz} - \frac{z}{y}\right)(\beta_1 S^* I_1^*)$$
$$+ b_0(\beta_2 S^* I_2^*)\left(4 - x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y}\right) + b_1(p\beta_1 S^* I_1^*)\left(-1 - \frac{y}{xz} + \frac{w}{z} + \frac{z}{y}\right)$$
$$+ b_1(q\beta_2 S^* I_2^*)\left(2 - \frac{y}{xw} - \frac{w}{z}\right)$$

By applying the principle of arithmetical progression and geometric means obtained;

1) For $3 - x - \frac{y}{xz} - \frac{z}{y} = 1$,

Known value $AM \geq GM$ where AM is *Arithmetic means* and GM is *Geometric means*, so;

$$\frac{3 - x - \frac{y}{xz} - \frac{z}{y}}{2} \geq \sqrt{(3) \times \left(-x - \frac{y}{xz} - \frac{z}{y}\right)}$$

$$\left(\frac{3 - x - \frac{y}{xz} - \frac{z}{y}}{2}\right)^2 \geq \left(\sqrt{(3) \times \left(-x - \frac{y}{xz} - \frac{z}{y}\right)}\right)^2$$

$$\frac{1}{4} \geq (3) \times \left(-x - \frac{y}{xz} - \frac{z}{y}\right)$$

$$\frac{1}{4} \times \frac{1}{3} \geq \left(-x - \frac{y}{xz} - \frac{z}{y}\right)$$

$$\frac{1}{12} \geq \left(-x - \frac{y}{xz} - \frac{z}{y}\right)$$

So, the maximum value is $\left(-x - \frac{y}{xz} - \frac{z}{y}\right) \leq \frac{1}{12}$.

2) For $4 - x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y} = 1$,

$AM \geq GM$,so

$$\frac{4 - x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y}}{2} \geq \sqrt{4 \times \left(-x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y}\right)}$$

$$\left(\frac{4 - x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y}}{2}\right)^2 \geq \left(\sqrt{4 \times \left(-x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y}\right)}\right)^2$$

$$\frac{1}{4} \ge 4 \times \left(-x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y} \right)$$

$$\frac{1}{4} \times \frac{1}{4} \ge \left(-x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y} \right)$$

$$\frac{1}{16} \ge \left(-x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y} \right)$$

So, maximum value is $\left(-x - \frac{y}{xw} - \frac{w}{z} - \frac{z}{y} \right) \le \frac{1}{16}$.

3) For $\left(-1 - \frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right) = 1$

$AM \ge GM$,so

$$\frac{\left(-1 - \frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right)}{2} \ge \sqrt{-1 \times \left(-\frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right)}$$

$$\left(\frac{\left(-1 - \frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right)}{2} \right)^2 \ge \left(\sqrt{-1 \times \left(-\frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right)} \right)^2$$

$$\frac{1}{4} \ge -1 \times \left(-\frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right)$$

$$\frac{1}{4} \times \frac{1}{-1} \ge \left(-\frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right)$$

$$-\frac{1}{4} \ge \left(-\frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right)$$

So, maximum value is $\left(-\frac{y}{xz} + \frac{w}{z} + \frac{z}{y} \right) \le -\frac{1}{4}$.

4) For $\left(2 - \frac{y}{xw} - \frac{w}{z} \right) = 1$, $AM \ge GM$, so

$$\frac{\left(2 - \frac{y}{xw} - \frac{w}{z} \right)}{2} \ge \sqrt{2 \times \left(-\frac{y}{xw} - \frac{w}{z} \right)}$$

$$\left(\frac{\left(2 - \frac{y}{xw} - \frac{w}{z} \right)}{2} \right)^2 \ge \left(\sqrt{2 \times \left(-\frac{y}{xw} - \frac{w}{z} \right)} \right)^2$$

$$\frac{1}{4} \ge 2 \times \left(-\frac{y}{xw} - \frac{w}{z} \right)$$

$$\frac{1}{4} \times \frac{1}{2} \ge \left(-\frac{y}{xw} - \frac{w}{z} \right)$$

$$\frac{1}{8} \ge \left(-\frac{y}{xw} - \frac{w}{z} \right)$$

So, maximum value is $\left(-\frac{y}{xw} - \frac{w}{z} \right) \le \frac{1}{8}$.

From Arithmetic and geometry means are seen that $\dot{V}(t) \le 0$ at $\Re_0 > 1$, so the endemic equilibrium point is globally asymptotically stable. This means that the disease is out of control.

IV. OPTIMAL CONTROL STRATEGIES

a) Optimal control existence

The endemic equilibrium point is the state where there are infected individuals in a population. Therefore, then the value of $I_1 \ne 0$ and $I_2 \ne 0$. From (1) the obtained endemic equilibrium point $\varepsilon_1^* = (S^*, E^*, I_1^*, I_2^*)$, the point R^* is omitted because it does not enter into the previous variables. From the system of equations (1), the endemic points are obtained as follows;

$$S^* = \frac{\lambda(\mu + \delta_2 + \varphi r_2)}{I_1^*(\mu + \delta_2 + \varphi r_2)\beta_1 + \mu^2 + \mu\delta_2 + \mu\varphi r_2 + \beta_2\phi(1 - r_1)I_1^*}$$

$$E^* = \frac{\lambda I_1^*(\beta_2(1-q)\phi r + \beta_1(1-p)(\mu + \delta_2 + \varphi r_2))}{I_1^*\phi(1-r_1)(\mu+\alpha)\beta_2 + (\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\mu+\beta_1 I_1^*)}$$

$$I_2^* = \frac{\phi(1-r_1)I_1^*}{\mu + \delta_2 + \varphi r_2} \qquad (17)$$

where

$$I_1^* = -\frac{-\lambda(r_2\varphi + \mu + \delta_2)(\mu p + \alpha)\beta_1 - \lambda\phi r(\mu q + \alpha)\beta_2 + \mu(r_2\varphi + \mu + \delta_2)(\mu + \phi + \delta_1)(\alpha + \mu)}{(r_2\varphi + \mu + \delta_2)(\mu + \phi + \delta_1)(\alpha + \mu)\beta_1 + \beta_2\phi r(\mu + \phi + \delta_1)(\alpha + \mu)}$$

the endemic equilibrium fulfill the following polynomial [13];

$$P(X) = AX^2 + BX + C \qquad (18)$$

where

$$A = -(\mu + \delta_2 + \varphi r_2)\lambda(\mu p + \alpha)\beta_1 - \lambda\phi(1-r)\big(\alpha(1-q) + q(\mu+\alpha)\big)\beta_2 + \mu(\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\phi+\mu+\delta_1)$$

$$B = -\lambda\big(\alpha(1-p) + p(\delta_2 + \varphi r_2 + \alpha + 2\mu)\big)\beta_1 + \alpha\mu(\delta_2+\delta_1) + 2\phi\mu^2 + 2\mu^2(\delta_2+\delta_1) + 2\alpha\mu^2 + \delta_1\mu(\delta_2 + \varphi r_2) + 2\mu^2\varphi r_2 + \alpha\phi\mu + \phi\mu\delta_2 + 3\mu^3$$

$$C = \mu\varphi r_2 + \phi\mu + (\delta_2 + \delta_1)\mu + \alpha\mu - p\beta_1\lambda + 3\mu^2$$

For the case $p = q = 0$ a quadratic (17) having one root, $X = 0$. This corresponds to a Disease-Free Equilibrium. Another root is

$$X_2 = \frac{p\lambda\phi r(\alpha + q\mu)\beta_2}{(\alpha + p\mu)(\mu + \delta_2 + \varphi r_2)} + \frac{\mu\Big(\alpha^2 + \big(\delta_1(1-p) + (1-p)\phi + \varphi r_2 + \delta_2 + 3\mu\big)\alpha + \mu p(\delta_2 + \varphi r_2 + 2\mu)\Big)}{\alpha + p\mu}$$

will be positive if and only if;

$$K = p\lambda\phi r(\alpha + q\mu)\beta_2(\alpha + p\mu) + \mu\Big(\alpha^2 + \big(\delta_1(1-p) + (1-p)\phi + \varphi r_2 + \delta_2 + 3\mu\big)\alpha + \mu p(\delta_2 + \varphi r_2 + 2\mu)\Big) > 0$$

with $p > 0, q > 0$. If the quadratic equation $P(X) = 0$ can be written as follows;

$$AX^2 + BX + C = 0$$

It has one positive root and one negative root. Positive roots are as follows;

$$X = \frac{B + \sqrt{B^2 - 4AC}}{2\lambda(\mu + \delta_2 + \varphi r_2)(\mu p + \alpha)\beta_1 - \lambda\phi(1-r)\big(\alpha(1-q) + q(\mu+\alpha)\big)\beta_2 + \mu(\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\phi+\mu+\delta_1)}$$

Therefore, the endemic equilibrium point is given as in (17) with

$$\lim_{\delta 1,\delta 2\to 0} X = \frac{K+|K|}{2A} = \begin{cases} 0 & (K<0) \\ \frac{K}{A} & (K>0) \end{cases}$$

So, $K=0$ is the threshold, which indicates that there is a basic reproduction number $(\Re_0)$. It means that the number of secondary infections produced by one infected individual who has just entered the population during the average period [13]. Values $(\Re_0)$ are given as follows;

$$\Re_0 = \frac{(p\mu+\alpha)\lambda\beta_1}{(\mu+\alpha)(\phi+\mu+\delta_1)\mu} - \frac{\lambda\beta_2\phi(-1+r_1)(\alpha+q\mu)}{\mu(\mu+\alpha)(\mu+\delta_2+\varphi r_2)(\phi+\mu+\delta_1)}$$

With $\lim_{\delta_1,\delta_2\to 0} X = 0$, if $\Re_0 < 1$

$\lim_{\delta_1,\delta_2\to 0} X > 0$, if $\Re_0 > 1$

For p,q approach zero, using the binomial approximation $(1+x)^{\frac{1}{2}} = 1+\frac{x}{2}$, so that from the equation (17) we get;

$$2AX = K+|K|\left[1+\frac{2CA}{K^2}\right]$$

If $\Re_0 > 1$, so $K>0$;

$$X \approx \frac{K}{A}+\frac{C}{K}$$

And if $\Re_0 < 1$, so $K<0$;

$$X \approx \frac{C}{|K|}$$

This indicates that it is at least p,q close to zero. So the model (17) has a threshold of $\Re_0 = 1$. For $p>0$, and/or $q>0$, disease remains endemic, so the system (1) has an endemic equilibrium point for the parameter value at which the disease will persist in the population. If $\Re_0 < 1$ as p,q is toward zero, then the endemic equilibrium tends to be disease free equilibrium. Conversely, if $\Re_0 > 1$ it is p,q towards zero, then the dynamics model of the spread of tuberculosis has a unique endemic equilibrium.

b) Optimal Control Analysis

The model (1) is modified by reducing the transmission rate $(1-u_1)$ where u_1 is prevention by increasing a clean and healthy lifestyle and always using a mask when interacting with infected individuals for susceptible populations. Vaccination (u_2) for family and close friends for infected (latently infected). Maximizing the DOTS strategy (u_3) in the treatment of infected individuals. Intensive treatment and care (u_4)in the hospital. Due to the addition of these actions, the system of equations becomes a system of model equation (2).

$$\frac{dS}{dt} = \lambda - (\beta_1 I_1 + \beta_2 I_2)(1-u_1)S - \mu S$$

$$\frac{dE}{dt} = (\beta_1(1-p)I_1 + \beta_2(1-q)I_2)S(1-u_1) - (\mu+\alpha)E - u_2 E$$

$$\frac{dI_1}{dt} = (p\beta_1 I_1 + q\beta_2 I_2)S + \alpha E - (\phi+\mu+\delta_1)I_1 - u_3 I_1$$

$$\frac{dI_2}{dt} = \phi(1-r_1)I_1 - (\mu+\delta_2+\varphi r_2)I_2 - u_4 I_2$$

$$\frac{dR}{dt} = \phi r_1 I_1 + \varphi r_2 I_2 - \mu R + u_2 E + u_3 I_1 + u_4 I_2 \quad (19)$$

Functional objective J formulate optimization problems to identify effective strategies. The optimal control strategy has the aim of minimizing the following cost functions which include infected 1 and infected 2 as well as prevention costs by improving a clean and healthy lifestyle and always using masks when interacting with infected individuals for susceptible populations $T_1 u_1^2$. Vaccination $T_2 u_2^2$. Maximizing the DOTS strategy in the treatment of infected individuals $T_3 u_3^2$. Treatments and intensive care in the hospital $T_4 u_4^2$. Functional objective of (2) defined as;

$$J = \min_{u_1,u_2,u_3,u_4} \int_0^{tf} N_1 I_1 + N_2 I_2 + \frac{T_1}{2}u_1^2 + \frac{T_2}{2}u_2^2 + \frac{T_3}{2}u_3^2 + \frac{T_4}{2}u_4^2 dt \qquad (20)$$

Where t_f is the final deadline and the coefficient of $N_1, N_2, T_1, T_2, T_3, T_4$ balancing the cost factor caused by the scale and importance of the six parts of the objective function. To find optimal control on $u_1^*, u_2^*, u_3^*, u_4^*$ using;

$$J\left(u_1^*,u_2^*,u_3^*,u_4^*\right) = \min\left\{J\left(u_1,u_2,u_3,u_4\right) \mid u_1,u_2,u_3,u_4 \in U\right\}, (21)$$

where

$$U = \left\{\left(u_1,u_2,u_3,u_4\right)\right. \qquad (22)$$

Theorem 3. [14] Given an objective function J on the equation (20), where the control set given by (20) is a subject that can be measured in the equation (19) with the initial conditions given at $t=0$, then there is an optimal control

$$u^* = \left(u_1^*(t),u_2^*(t),u_3^*(t),u_4^*(t)\right)$$

such that

$$J\left(u_1^*(t),u_2^*(t),u_3^*(t),u_4^*(t)\right) := \min\left\{J\left(u_1,u_2,u_3,u_4\right),\left(u_1,u_2,u_3,u_4\right)\in U\right\}$$

proof: the existence of optimal control due to the convexity of the integrand J to the control measure $u_j, j=1,2,3,4$ which is a priori solution boundedness between the equations of state and the adjoining equations and the Lipchitz property of the state system with respect to the state variables from [15]. Langrangian (L) and Hamiltonian (H) are used to find the optimal solution of the optimal control problem (19) and (20). the Lagrangian on the control problem is given by

$$L := N_1 I_1 + N_2 I_2 + \frac{1}{2}\sum_{i=1}^{4} T_j u_j^2(t)$$

To get the minimum value of the Lagrangian, we define the Hamiltonian function for the following system [16];

$$H\left(S,E,I_1,I_2,R,u_j,\lambda\right)=N\left(t\right)+\frac{T}{2}u_j^2+\sum_{i=1}^{4}\lambda_i f_i ,$$

thus obtained;

$$H=N_1I_1+N_2I_2+\frac{1}{2}\left(T_1u_1^2+T_2u_2^2+T_3u_3^2+T_4u_4^2\right)+\lambda_1\left(b-S\left(\beta_1I_1+\beta_2I_2\right)(1-u)-\mu S\right)$$
$$+\lambda_2\left(S\left(\beta_1(1-p)I_1+\beta_2(1-q)I_2\right)(1-u)-\mu E-\alpha E-u_2E\right)$$
$$+\lambda_3\left(S\left(p\beta_1I_1+q\beta_2I_2\right)(1-u)+\alpha E-\phi I_1-\mu I_1-\delta_1I_1-u_3I_1\right)$$
$$+\lambda_4\left(\phi(1-r)I_1-\mu I_2-\delta_2I_2-\varphi r_2I_2-u_4I_2\right)$$
$$+\lambda_5\left(\phi r_1I_1+\varphi r_2I_2-\mu R+u_2E+u_3I_1+u_4I_2\right) \qquad (23)$$

Where $\lambda_i, i\in\{1,2,3,4,5\}$ is an adjoin variable or a co-state variable. The system is found by taking partial derivatives that correspond to the Hamiltonian (23) associated with the related state variables.

Theorem 4. given an optimal control u_1^*,u_2^*,u_3^*,u_4^* and solution of S,E,I_1,I_2,R a suitable state system (19) and (20) that minimizes $J\left(u_1,u_2,u_3,u_4\right)$ against U. Then there is an adjoin variable $\lambda_1,\lambda_2,\lambda_3,\lambda_4$ that fulfil

$$\frac{-d\lambda_i}{dt}=\frac{\partial H}{\partial_j}.$$

Where $i=1,2,3,4,5$, $j=S,E,I_1,I_2,R$,

and with the condition of transversality

$$\lambda_1\left(t_f\right)=\lambda_2\left(t_f\right)=\lambda_3\left(t_f\right)=\lambda_4\left(t_f\right)=0$$

$$u_1^*=\min\left\{1,\max\left\{0,\frac{-\lambda_1S(I_1\beta_1+I_2\beta_2)+\lambda_2S(\beta_1(1-p)I_1-\beta_2(1-q)I_2)+\lambda_3S(\beta_1I_1p+I_2\beta_2q)}{T_1}\right\}\right\}$$

$$u_2^*=\min\left\{1,\max\left\{0,\frac{E(\lambda_2-\lambda_5)}{T_2}\right\}\right\}$$

$$u_3^*=\min\left\{1,\max\left\{0,\frac{I_1(\lambda_3-\lambda_5)}{T_3}\right\}\right\}$$

$$u_4^*=\min\left\{1,\max\left\{0,\frac{I_2(\lambda_4-\lambda_5)}{T_4}\right\}\right\} \qquad (24)$$

Proof:

Because (19) it provides optimal control existence due to the convexity of the integral J with respect to u_1,u_2,u_3,u_4. A priority constraint of the state solution, and the Lipschitz property of the system with respect to state variables. The Hamiltonian function is used to determine the adjoin variable, so that the adjoining equation can be written;

$$-\frac{d\lambda_1}{dt}=-(u_1-1)\left(I_1(p-1)\beta_1+I_2\beta_2(q-1)\right)\lambda_2+I_1(u_1-1)(\lambda_3p-\lambda_1)\beta_1$$
$$+I_2(u_1-1)(\lambda_3q-\lambda_1)\beta_2+\lambda_1\mu$$

$$-\frac{d\lambda_2}{dt}=(u_2+\mu+\alpha)\lambda_2-\lambda_5u_2-\lambda_3\alpha$$

$$-\frac{d\lambda_3}{dt}=-(u_1-1)\left(-\lambda_3p+(p-1)\lambda_2+\lambda_1\right)S\beta_1$$
$$+(u_3+\delta_1+\mu+\phi)\lambda_3+\left((r_1-1)\lambda_4-\lambda_5r_1\right)\phi-u_3\lambda_5-N_1$$

$$-\frac{d\lambda_4}{dt}=-(u_1-1)\left(-\lambda_3q+(q-1)\lambda_2+\lambda_1\right)S\beta_2+\left(r_2\varphi+u_4+\delta_2+\mu\right)\lambda_4$$
$$+\left(-r_2\varphi-u_4\right)\lambda_5-N_2$$

$$-\frac{\lambda_5}{dt}=\lambda_5\mu$$

The solution for u_1^*,u_2^*,u_3^*,u_4^* depending on the constraints, the characteristics on (24) can be derived, so that it is owned;

$$0=\frac{\partial H}{\partial u_1}=T_1u_1+\lambda_1S\left(I_1\beta_1+I_2\beta_2\right)-\lambda_2S\left(\beta_1(1-p)I_1+\beta_2(1-q)I_2\right)$$
$$-\lambda_3S\left(I_1\beta_1p+I_2\beta_2q\right)$$

$$0=\frac{\partial H}{\partial u_2}=u_2T_2-E\lambda_2+E\lambda_5$$

$$0=\frac{\partial H}{\partial u_3}=u_3T_3-I_1\lambda_3+I_1\lambda_5$$

$$0=\frac{\partial H}{\partial u_4}=-I_2\lambda_4+I_2\lambda_5+u_4T_4$$

Therefore, it is obtained

$$u_1^*=\frac{-\lambda_1S(I_1\beta_1+I_2\beta_2)+\lambda_2S(\beta_1(1-p)I_1-\beta_2(1-q)I_2)+\lambda_3S(\beta_1I_1p+I_2\beta_2q)}{T_1}$$

$$u_2^*=\frac{E(\lambda_2-\lambda_5)}{T_2},$$

$$u_3^*=\frac{I_1(\lambda_3-\lambda_5)}{T_3},$$

$$u_4^*=\frac{I_2(\lambda_4-\lambda_5)}{T_4}$$

with the explanation of control standards involving control limits, it can be concluded that;

$$u_1^*=\begin{cases}0, & \psi_1^*\le 0\\ \psi_1^*, & 0<\psi_1^*<1\\ 1, & \psi_1^*\ge 1\end{cases}$$

$$u_2^*=\begin{cases}0, & \psi_2^*\le 0\\ \psi_2^*, & 0<\psi_2^*<1\\ 1, & \psi_2^*\ge 1\end{cases}$$

$$u_3^*=\begin{cases}0, & \psi_3^*\le 0\\ \psi_3^*, & 0<\psi_3^*<1\\ 1, & \psi_3^*\ge 1\end{cases}$$

$$u_4^*=\begin{cases}0 & jika \quad \psi_4^*\le 0\\ \psi_4^* & jika \quad 0<\psi_4^*<1\\ 1 & jika \quad \psi_4^*\ge 1\end{cases}$$

Where,

$$\psi_1^* = \frac{-\lambda_1 S(I_1\beta_1 + I_2\beta_2) + \lambda_2 S(\beta_1(1-p)I_1 - \beta_2(1-q)I_2) + \lambda_3 S(\beta_1 I_1 p + I_2\beta_2 q)}{T_1}$$

$$\psi_2^* = \frac{E(\lambda_2 - \lambda_5)}{T_2},$$

$$\psi_3^* = \frac{I_1(\lambda_3 - \lambda_5)}{T_3},$$

$$\psi_4^* = \frac{I_2(\lambda_4 - \lambda_5)}{T_4}$$

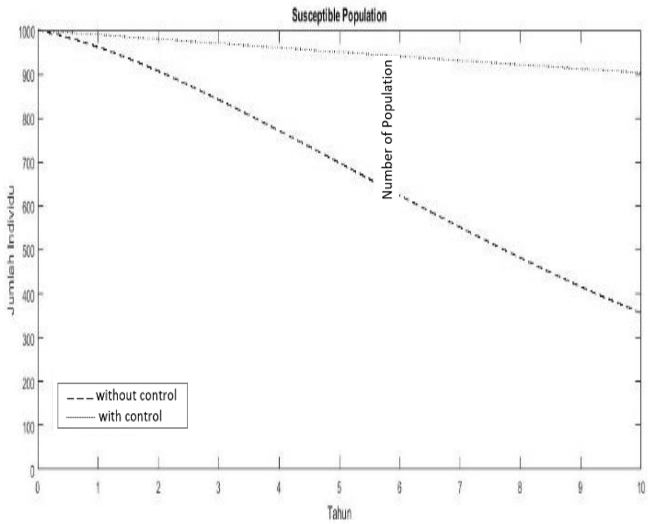
V. NUMERICAL RESULTS

The data that has been obtained from http://.stoptb.org/resources/cd/IDN_Dashboard.html taken from the data from 2010 to 2021. Numerical results are given for the model with control and model without control.

Parameters obtained by using the non-linear least square method, as follows

$\lambda = 4.008; \mu = 0.10835; \beta_1 = 0.040468; \beta_2 = 0.030981; p = 0.0064145;$
$q = 0.71578; \alpha = 0.10425; \delta_1 = 0.048470; \delta_2 = 0.0091056; \phi = 0.086943;$
$\varphi = 0.01541; r_1 = 0.5; r_2 = 0.016223.$

Based on the value of these parameters and the initial values are $S = 1000, E = 500, I_1 = 8, I_2 = 1, R = 2$. We used Runge-Kutta 4th order method to solve control model, where to solve the state system using forward Runge-kutta, while the backward Runge-kutta is used to solve the co-state system.



Time (Year)

Figure 1. Susceptible population when given control and without control

The model simulation in figure 1 Shows the effect after administration of control. It can be seen that after giving control the susceptible graph is higher than without control, this is because giving control makes individuals more free without any restrictions on interacting with infected individuals, so that the level of population susceptibility becomes higher. So that the application of control is not appropriate if it is applied without other controls.

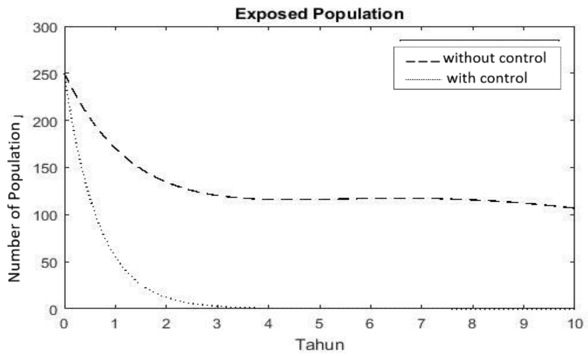


Figure 2. Exposed population when given and without control

Time (Year)

Then for exposed individuals besides doing control are also given control (Vaccination), so the number of individuals who are exposedly controlled as shown in Fgure 2.

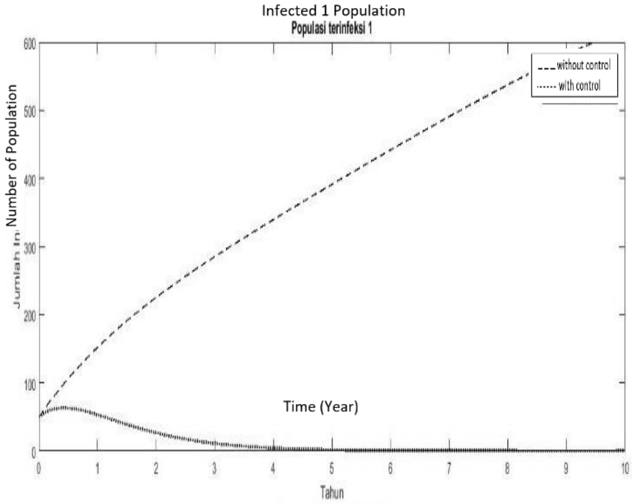


Figure 3. Population infected 1 ehen given and without control

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It is seen in Figure 3 the graph of the tuberculosis infected population stage 1 without control increase every year, but after administration of graph control has decreased towards the equilibrium point, so that tuberculosis can be controlled

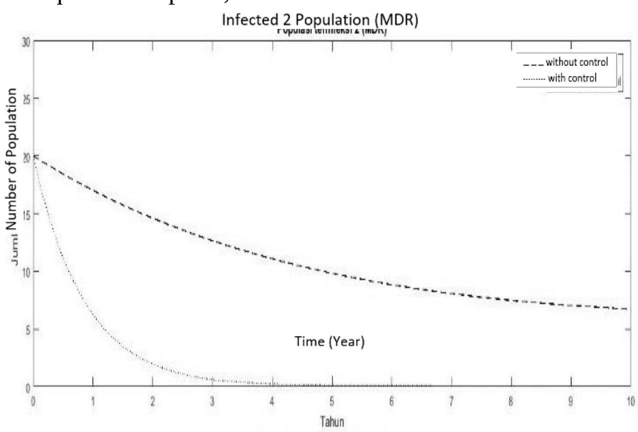

Figure 4. Population Infected 2 when given and without control

In the infected population stage 2(MDR) after administration of the control of the number of individuals is infected, it is less, this is seen in the graphics that are illustrated in Figure 4 which increasingly decreases close to the equilibrium point.

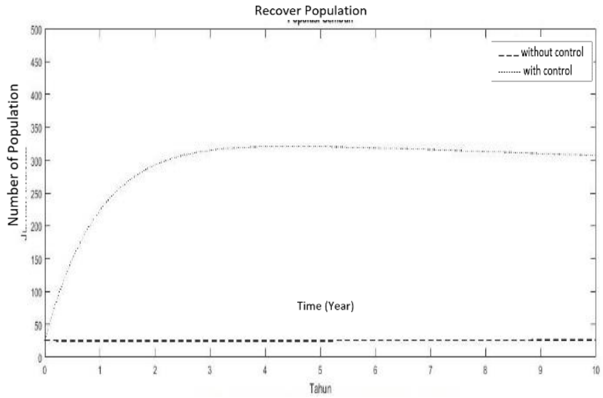

Figure 5. Population recovered when given and without control

Maximum control has an impact on the decrease in the number of infected populations and increasing the population heals significantly, as shown in Figure 5 of the five images above can be seen that the reduction in the spread of tuberculosis requires a long time, but with optimal control it can accelerate the control tuberculosis.

VI. CONCLUSION

Based on the results of the analysis obtained two equilibrium points, namely endemic and non-endemic. From the equilibrium, the stability at that equilibrium point is sought. Stability analysis is determined by the basic reproduction number, then searched using Routh Hurwitz criteria and Center manifold and Lyapunov. Next is to determine the optimal control conditions. Optimal control was determined using the Pontyagin Maximum principle method. Finally, a numerical simulation was sought to describe the differences in the dynamics of the spread of tuberculosis using optimal controls. Prevention and treatment are carried out as an effort to control the spread of TB infection. Optimal control analysis shows that preventing the spread of TB by susceptible and latent individuals can help reduce the rate of spread of TB, but if what is done is only prevention without intensive treatment and appropriate strategies for infected individuals, the spread of TB cannot be said to be controlled and still potentially endemic. Prevention and treatment must be done simultaneously, so as to get maximum results. Treatment with the DOTS strategy is carried out as one of the important things to reduce the rate of spread of TB. With the implementation of optimal control simultaneously, the spread of TB will be controlled within a period of 10 years.

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