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# Analysis of the Stability of the Tuberculosis Disease Spread Model

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**Abstract.** This paper discusses the stability analysis of the model for the spread of tuberculosis and the effects of treatment. It is shown the analyze the dynamic behavior of the model to investigate the local stability properties of the model equilibrium point. The Routh-Hurwitz criterion is used to analyze local stability at the disease-free equilibrium point, while the Transcritical Bifurcation theorem is used to investigate the local stability properties of the endemic equilibrium point. The discussion results show that the equilibrium point's stability properties depend on the value of the basic reproduction number, which is calculated based on the Next Generation Matrix (NGM). When the basic reproduction number value is less than one, then the disease-free equilibrium point is locally asymptotically stable, whereas if it is more than one, then the endemic equilibrium point is locally asymptotically stable. Numerical simulations are included to explain the dynamic behavior of disease spread and to understand the effectiveness of tuberculosis treatment in a given population. The simulation results show that treatment in the infected individual phase is known to be more effective than treatment in latent individuals.

**Keywords:** *stability analysis, transcritical bifurcation, Routh-Hurwitz criteria tuberculosis*

## 1 Introduction

Mycobacterium tuberculosis (Mtb) is the bacteria that typically causes tuberculosis (TB), a lung infection. This illness can affect the kidneys, lymphatic system, central nervous system, and brain in addition to the lungs. It can also attack the spine, kidneys, and brain. The immune system of a person will fight off these bacteria, but when that system is compromised, the bacteria will become active again [1]. Indonesia is among the Top Five Countries, along with China, India, Pakistan, and the Philippines, accounting for 56% of the estimated cases. To provide the most recent information on the evolution of the TB epidemic, its prevention, diagnosis, and treatment globally at both regional and national levels, the World Health Organization (WHO) has been publishing its annual TB case report since 1997. This report is intended to become a Strategy for 2016–2035 and Sustainable Development Goals (SDGs) to end TB cases [2]. As a result, more targeted TB disease prevention is required.

While advances in medical science are critical in the fight against tuberculosis, several other fields that rely on operational research and evidence-based research are also involved. One such field is applied technology and epidemiology, whose analysis is inextricably linked to mathematics. Through the mathematical modeling branch of the field, mathematics plays a significant role in mitigating the spread of tuberculosis [3]. Zhang [4] applied the treatment function to the infected phase with the susceptible (suspected) subpopulation moving to the exposed phase in the SEIR model (with no susceptible individuals immediately entering the active infected phase). Next, in the infected phase, Elkhaiar and Kaddar [5] also conducted a non-linear treatment function analysis. Additionally, in [6], a nonlinear incidence function that was created based on a linear incidence function is used in a SEIR model. Even though the non-linear incidence function isn't used in this article, it's a fascinating subject for future research.

Many theoretical investigations have been carried out to understand Mtb infection data, from an epidemiological point of view. Different mathematical models, such as [7][8][9], have been proposed to evaluate the influence of factors such as Mtb population dynamics, immune system, vaccination, treatment, bacterial resistance on infection development and optimal control.

In this article, the model for the spread of tuberculosis is divided into susceptible (S), exposed (E), Actively-Infected (I) and Recovery (R) subpopulations with the rate towards susceptibility after recovery and the equilibrium point analyzed locally. The author developed a model based on the model introduced by Bowong and Tewa [10], namely the model for the spread of tuberculosis with subpopulations susceptible (S), latently infected (E), Infectious (I) and Loss of Sight (L).

## 2 Mathematical Formulation

The flow of TB disease spread proposed by the author in this paper is illustrated in Figure 1. Based on the scheme proposed in [7][11]. The characteristics of Bowong and Tewa [10] the internal disease spread scheme are explained as follows: (1) the model does not contain transmission from the latently infected (E) directly to the recovered subpopulation (R), (2) the model does not contain the recovered subpopulation (R) and instead contains the subpopulation of individuals missing from surveillance (L), (3) treatment in the latently infected phase (E) allows individuals to worsen to become Infectious and does not address the recovered subpopulation, while treatment in the Infectious subpopulation (I) allows infected individuals to progress to the latently infected period (E) or the subpopulation of individuals lost from surveillance (L).

While the scheme proposed in Figure 1, the model does not contain transmission from the susceptible phase (S) directly to the infected subpopulation (I) but rather to the latent (E), treatment $p$ in the latent phase allows latent individuals (E) with a rate of change $k$ to can progress to the recovery (R) subpopulation or get worse and become actively

infected. Treatment $r$ in the infected phase can also allow infected individuals with a rate of change $\alpha$ to recover (R) or simply improve towards a latent subpopulation (E) with a rate of change $\gamma$. In the recovery phase, individuals can become susceptible again at a rate of $\delta$, and some have immunity due to previous infections. The variables and parameters involved in the model can be seen in Table 1. The author formulated a model based on the scheme in Figure 1 where the applicable system of differential equations is modeled as follows:

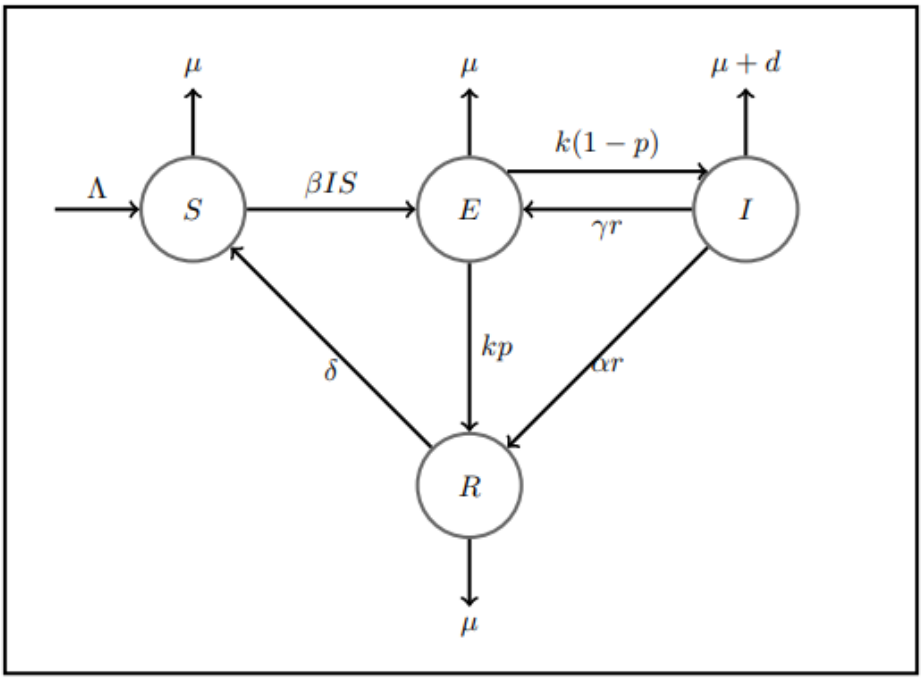



**Figure 1** The flow chart for the tuberculosis disease spread model

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta IS + \delta R - \mu S \\
\frac{dE}{dt} &= \beta IS + \gamma rI - kE - \mu E \\
\frac{dI}{dt} &= k(1-p)E - (\gamma + \alpha)rI - (\mu + d)I \\
\frac{dR}{dt} &= kpE + \alpha rI - (\mu + \delta)R
\end{aligned} \tag{1}$$

**Table 1** Description of parameters

| Parameter | Definition |
|---|---|
| $\Lambda$ | Recruitment rate of susceptible |
| $\beta$ | TB contact and transmission rates |
| $k$ | Rate of movement from latent to infected subpopulation |
| $p$ | Rate of effective treatment in the latent phase |
| $(1-p)$ | Rate of ineffective treatment in the latent phase |
| $r$ | Treatment rates in infected subpopulations |
| $\gamma$ | Rate of progression from infected subpopulation to latent |
| $\alpha$ | Rate of infected subpopulation to recovered |
| $\mu$ | Natural death rate |
| $d$ | Infectious death rate |
| $\delta$ | Rate of movement from recovered to susceptible |

In analyzing the stability properties of the model's equilibrium point, the following lemmas are needed.

**Lemma 1.1** The feasible region Ω is defined by:

$$\Omega = \left\{(S(t), E(t), I(t), R(t)) \in \mathbb{R}_+ \middle| 0 \leq S(t), E(t), I(t), R(t) \leq \frac{\Lambda}{\mu}\right\}$$

is positively invariant for model (1) with initial conditions in $\mathbb{R}_+$

**Proof.** By adding all the equations in the model (1), it is obtained $\frac{dN}{dt} = \Lambda - \mu N - dI \leq \Lambda - \mu N$. So it is also found that $0 \leq N(t) \leq \frac{\Lambda}{\mu} + N(0)e^{-\mu t}$ where $N(0)$ represents the initial value of the population. Therefore $\lim_{t\to\infty} \sup N(t) \leq \frac{\Lambda}{\mu}$ which means that area Ω is positively invariant. Consequently, model (1) is finite.

## 3 Stability of Equilibrium Solutions

By looking for the equilibrium points, it is found that (1) has a disease-free equilibrium point $E_0(S^0, E^0, I^0, R^0) = \left(\frac{\Lambda}{\mu}, 0,0,0\right)$ and the endemic equilibrium point $E_1(S^*, E^*, I^*, R^*)$

$$S^* = \frac{\Lambda}{\mu R_0}$$

$$E^* = \frac{\mu h(\delta+\mu)(R_0-1)(\alpha r+\gamma r+d+\mu)}{\beta g(1-p)k}$$
$$I^* = \frac{\mu h(\delta+\mu)(R_0-1)}{\beta g}$$
$$R^* = \frac{\mu h(R_0-1)(\alpha r+\gamma rp+dp+\mu p)}{\beta g(1-p)} \quad (2)$$

With

$$g = \mu h + \delta(\mu^2 + (\alpha r + \gamma r + (1-p)k + d)\mu + d(1-p)k)$$
$$h = \gamma kpr + \alpha kr + \alpha\mu r + \gamma\mu r + dk + d\mu + k\mu + \mu^2$$

By using the NGM Method [12], [13] the basic reproduction number of (1) is obtained

$$R_0 = \frac{\Lambda\beta k(1-p)}{\mu h} \quad (3)$$

The following theorems explain the stability properties of the equilibrium points that have been obtained.

**Theorem 1.2** If $R_0 < 1$ then the disease-free equilibrium point $E_0(S^0, E^0, I^0, R^0)$ is locally asymptotically stable. Conversely, if $R_0 > 1$, then $E_0(S^0, E^0, I^0, R^0)$ is unstable.

**Proof** Linearization of model (1) around the disease-free equilibrium point produces a Jacobian matrix

$$J(E_0) = \begin{bmatrix} -\mu & 0 & -\frac{\Lambda\beta}{\mu} & \delta \\ 0 & -(k+\mu) & \frac{\gamma\mu r + \Lambda\beta}{\mu} & 0 \\ 0 & k(1-p) & -(\alpha r+\gamma r+d+\mu) & 0 \\ 0 & kp & \alpha r & -(\delta+\mu) \end{bmatrix} \quad (4)$$

Suppose $\lambda$ represents the eigenvalue of (4), the characteristic equation of the Jacobian matrix is in the form of a polynomial $(\lambda+\mu)(\lambda+\delta+\mu)\big(\lambda^2 + (\alpha r+\gamma r+d+k+2\mu)\lambda + h(1-R_0)\big) = 0$. It is obtained that the eigen $\lambda = -\mu < 0$, $\lambda = -(\mu+\delta) < 0$ and the other eigen values will be negative if $R_0 < 1$. Based on the Routh-Hurwitz criterion, these results conclude that the equilibrium $E_0(S^0, E^0, I^0, R^0)$ is locally asymptotically stable.

**Theorem 1.3** If $R_0 > 1$ then the endemic equilibrium point $E_1$ is locally asymptotically stable.

**Proof.** Bifurcation analysis in [10] and Manifold Center Theory in [11] are used in this proof. Assume $R_0 = 1$ and choose $\beta = \beta^*$ to be the bifurcation parameter in the equation $R_0$ to obtain

$$\beta^* = \frac{\mu h}{\Lambda k(1-p)}$$

The value of the Jacobian matrix of system (4) when $\beta = \beta^*$ is

$$J(E_0, \beta^*) = \begin{bmatrix} -\mu & 0 & -\frac{h}{k(1-p)} & \delta \\ 0 & -(k+\mu) & \frac{h+(1-p)\gamma k r}{k(1-p)} & 0 \\ 0 & k(1-p) & -(\alpha r + \gamma r + d + \mu) & 0 \\ 0 & kp & \alpha r & -(\delta+\mu) \end{bmatrix}$$

The eigenvalues of the Jacobian matrix are $\lambda = -\mu$, $\lambda = 0$, $\lambda = -(\mu + \delta)$ and $\lambda = -(\alpha r + \gamma r + d + k + 2\mu)$. The Jacobian matrix $J(E_0, \beta^*)$ has a simple eigenvalue $\lambda = 0$ for that the right eigenvector corresponding to the eigenvalue $\lambda = 0$ can be denoted by $w = [w_1 \quad w_2 \quad w_3 \quad w_4]^T$ which the right eigenvector must satisfy

$$J(E_0, \beta^*) \cdot w = 0$$

and the value of the right eigenvector is obtained

$$w = \left[ -\frac{g w_3}{k\mu(1-p)(\delta+\mu)} \quad \frac{(\alpha r + \gamma r + d + \mu) w_3}{k(1-p)} \quad w_3 \quad \frac{(\alpha r + \gamma r p + d p + \mu p) w_3}{(1-p)(\delta+\mu)} \right]^T$$

Then look for the left eigenvector corresponding to the eigenvalue $\lambda = 0$ which is denoted by $v = [v_1 \quad v_2 \quad v_3 \quad v_4]$. The left eigenvector v satisfies

$$v \cdot J(E_0, \beta^*) = 0,$$

that is $v = [v_1 \quad v_2 \quad v_3 \quad v_4] = \left[ 0 \quad \frac{v_3 k(1-p)}{k+\mu} \quad v_3 \quad 0 \right]$. Then look for the values of $w_3$ and $v_3$ satisfies $w \cdot v = 1$, and obtains

$$w_3 = 1 > 0$$

$$v_3 = \frac{k+\mu}{\alpha r + \gamma r + d + k + 2\mu} > 0$$

Suppose $S(t) = f_1, E(t) = f_2, I(t) = f_3$ and $R(t) = f_4$ then the model (1) can be written as

$$\frac{df_1}{dt} = \Lambda - \beta f_3 f_1 + \delta f_4 - \mu f_1 = y_1$$
$$\frac{df_2}{dt} = \beta I f_1 + \gamma r f_3 - k f_2 - \mu f_2 = y_2$$
$$\frac{df_3}{dt} = k(1-p) f_2 - (\gamma + \alpha) r f_3 - (\mu + d) f_3 = y_3$$
$$\frac{df_4}{dt} = kp f_2 + \alpha r f_3 - (\mu + \delta) f_4 = y_4$$

Second-order partial derivative of the above system of equations at the disease-free equilibrium point $E_0(S^0, E^0, I^0, R^0) = \left({f_1}^0, {f_2}^0, {f_3}^0, {f_4}^0\right) = \left(\frac{\Lambda}{\mu}, 0,0,0\right)$ is

$$a = \sum_{n,i,j}^{4} v_n w_i w_j \frac{\partial^2 y_k}{\partial f_i \partial f_j}(E_0, 0).$$

Because $v_1 = v_4 = 0$ is obtained

$$a = -\frac{2\mu\left(\delta\left(\alpha r + \gamma r + d + k + 2(1-p)\right) + \mu(\alpha r + \gamma r + d + \mu + 2)\right)h}{(\alpha r + \gamma r + d + 2\mu + 2)(\delta + \mu)\Lambda k(1-p)}$$
$$-\frac{2\mu\left(2(\alpha r + \gamma p r + d) + 2d\delta(1-p)\right)h}{(\alpha r + \gamma r + d + 2\mu + 2)(\delta + \mu)\Lambda k(1-p)} < 0$$

and

$$b = \sum_{n,i}^{4} v_n w_i \frac{\partial^2 y_k}{\partial f_i \partial \beta^*}(E_0, 0) = \frac{2(1-p)\Lambda}{(\alpha r + \gamma r + d + 2\mu + 2)\mu} > 0.$$

Based on Central Manifold Theory, because $a < 0$ and $b > 0$, this shows that model (1) experiences a transcritical bifurcation when $R_0 = 1$, and there is an exchange of stability from a stable disease-free equilibrium point to an endemic equilibrium point, when $R_0 > 1$. This means that the endemic equilibrium point $E_1(S^*, E^*, I^*, R^*)$ is locally asymptotically stable when $R_0 > 1$.

## 4 Simulation

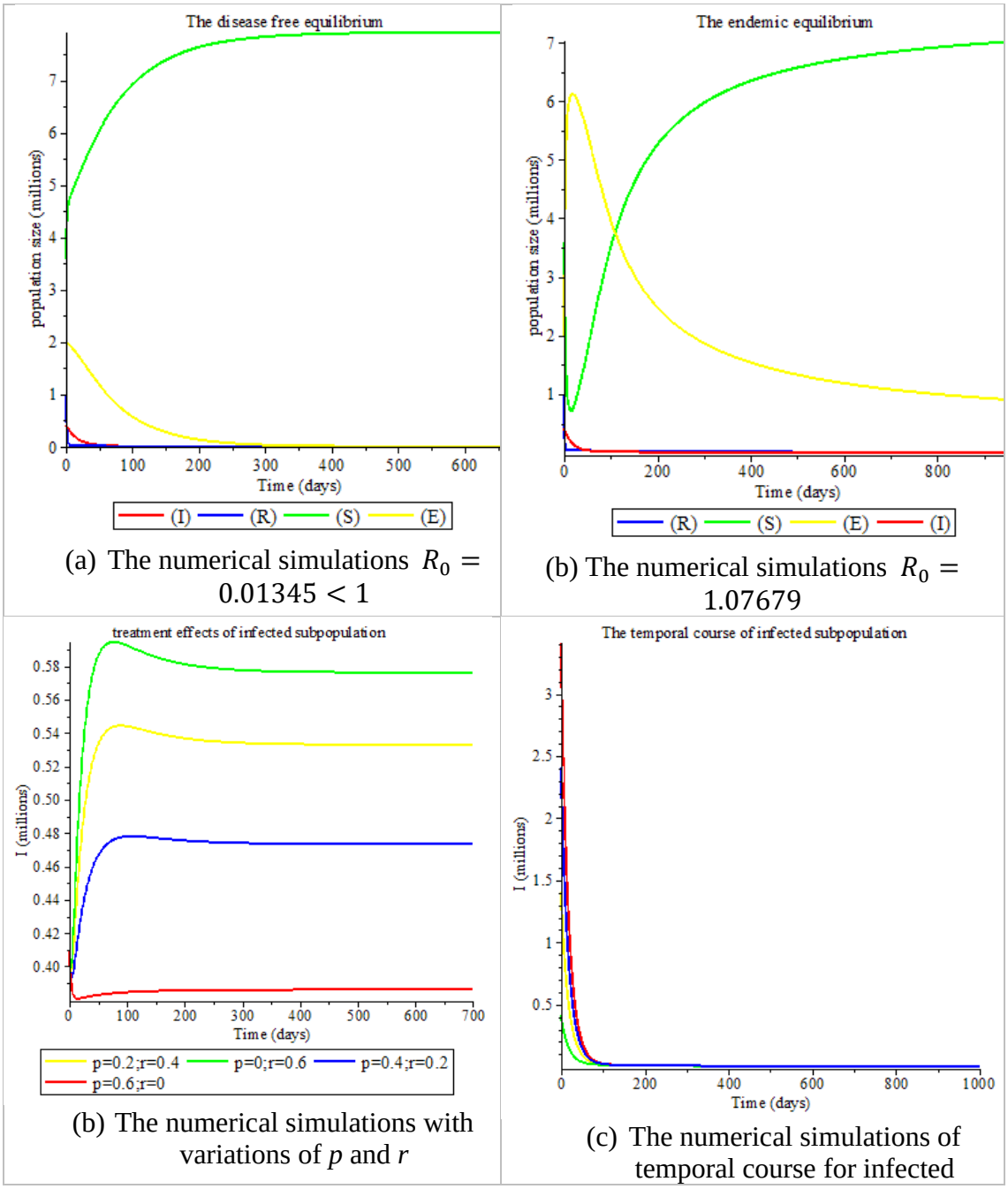
In this section, numerical simulation results are given using the parameter values in Table 2.

**Table 2** Values of the parameters. Data are deduced from the literature (references).

| **Parameter** | $\boldsymbol{\Lambda}$ | $\boldsymbol{\beta}$ | $\boldsymbol{k}$ | $\boldsymbol{p}$ | $(\boldsymbol{1-p})$ | $\boldsymbol{r}$ |
|---|---|---|---|---|---|---|
| Value | 0.08 | 0.8 | 0.005 | 0.9706 | 0.0294 | 0.8182 |
| Reference | [14] | Generated | [10] | [15] | [15] | [10] |

| **Parameter** | $\boldsymbol{\gamma}$ | $\boldsymbol{\alpha}$ | $\boldsymbol{\mu}$ | $\boldsymbol{d}$ | $\boldsymbol{\delta}$ |
|---|---|---|---|---|---|
| Value | 0.01 | 0.02 | 0.0101 | 0.022722 | 0.8 |
| Reference | [11] | [10] | [10] | [10] | Generated |

The numerical simulation in Figure 2(a) shows that conditions with $\beta = 0.01$ produce $R_0 < 1$, according to Theorem 1.2, a locally asymptotically stable disease-free equilibrium point. Meanwhile, the numerical simulation of Figure 2(b) with $\beta = 0.8$ produces a value of $R_0 > 1$, and according to Theorem 1.3, the endemic equilibrium point is locally asymptotically stable.




(a) The numerical simulations $R_0 = 0.01345 < 1$

(b) The numerical simulations $R_0 = 1.07679$

(b) The numerical simulations with variations of $p$ and $r$

(c) The numerical simulations of temporal course for infected

**Figure 2** The numerical simulations result (a) when $R_0 = 0.01345 < 1$, (b) when $R_0 1.07679 => 1$, (c) with variations of $p$ and $r$, and (d) temporal course for infected.

Third, by using variations in the value of the portion of treatment in the latent phase $p$ and treatment in the infected phase $r$, various effects occur on the infected subpopulation which corresponds to the results in Figure 2(c). This can be taken into consideration if the

problem is faced with the situation of having to choose to treat latent or infected individuals. Both processes of treating latent and infected subpopulations can certainly reduce the number of latent and infected populations. From Figure 2(c) it can be seen that the large portion of treatment (which is proportional to the level of effectiveness) in the latent and infected subpopulations shows that treatment in the latent phase produces a smaller infected population and vice versa. This means that detection and treatment in the latent phase must be prioritized to anticipate developments in the infection stage. in Figure 2(d) which depicts the temporal course of infected subpopulations for several initial conditions.

## 5 Conclusion

From the results of existence and stability it can be concluded that for $R_0 < 1$ where the balance is stable, and free from disease, $E_0$ and branching become endemic, stable at a value of $R_0 > 1$. The process of handling and treating latent and infected subpopulations can certainly reduce the number of latent and infected populations. However, detection and treatment in the latent phase should be prioritized to anticipate the development of the infection stage.

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