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# Dynamical System of Tuberculosis Considering Lost Sight Compartment

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**ABSTRACT**

**In this study, a model for the tuberculosis infection considering vaccination and lost-sight compartement is formulated. there are six populations in this model, Susceptibled, vaccinated, exposed, lost sight, infected, and recovered. The lost sight populations are infected but do not get any treatment and still can spread the tuberculosis, the infected population are infected but already got a treatment and no longer spread the tuberculosis. The local stability are obtained by analyzing the epidemic threshold $\mathcal{R}_0$. The result shows that the disease-free equilibrium is locally asymptotically stable when the condition $\mathcal{R}_0$<1 is satisfied, and the unique endemic equilibrium exist and it is locally asymptotically stable if $\mathcal{R}_0$>1 is satisfied. The numerical simulation are also performed to support the analytical result.**

***Keywords*—** Tuberculosis, HIV, Equilibrium

## I. INTRODUCTION

Tuberculosis (TB) is one of the most infectious diseases caused by mycobacterium tuberculosis. It can attack various organs, mainly the lungs. This disease can lead to complications and death if the sufferer does not take any treatment or involved in incomplete treatment. Tuberculosis had allegedly appeared since 5000 years BC but the cure was just discovered in the last two century [7].

TB bacteria are spread through the air when infected person coughs or speaks. When a person nearby breaths the air, the bacteria will settle in the lungs and they can move to other organs. Individuals with TB will experience several symptoms such as bad coughs, weight loss and night sweating. The symptoms usually appear slowly within a few months and it impacts on the delay of the treatment. Without intensive treatment, two out of three cases of TB disease will lead to death [11].

Worldwide, TB is one of the major public health issues. It is among one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). In 2017 TB caused an estimated 1,3 million deaths among HIV negative people and also 300.000 deaths from TB among HIV-positive people. Globally, there are 10 million people developed TB disease in 2017: 5,8 million men, 3,2 million women, and 1 million children [11]. From the latest data, Indonesia ranks the third place after India and China in terms of the infected number of TB in the world. There are estimated more than 1 million cases of TB in Indonesia but only 420.000 cases were reported to Ministry of Health [12].

The controlling of the TB cases in Indonesia were done by several strategies. Started with Directly Observed Treatment Short-Course (DOTS) at 1995-2005, followed by stop TB strategy at 2006-2015. Then according to the results of the prevalence survey, the strategy was revised to the TB elimination strategy. According to this strategy, the notification of tuberculosis cases increase drastically and the success of national tuberculosis treatment remains high at 87% [12].

One of the challenge of the TB prevention program is Multi Drug Resistance (MDR) TB. This is the state when the body is resistant to at least izonaid and rifampin, the two most potent TB drugs [3]. It worsens the patient's condition and increases the infectious rate. It is caused by misuse or mismanagement of TB drugs treatment such as the wrong dose of drugs or incomplete treatment. It is more common in people who do not take their drugs regularly and continuously by reason of the cost of the drugs, the access to public health facilities, and side effect of the drugs. Reported cases of MDR-TB in Indonesia keep increasing since 2011 and not all of them were confirmed to retake the treatment [12].

In eradicating the infectious diseases including tuberculosis, one essential thing that should be considered is controlling the number of infection. Mathematics had been an important tool in analyzing the transmission behavior of the disease [5]. Many studies about mathematical models and its analysis of TB infection had been conducted. Temgoua*et al*. [8] developed the model for tuberculosis with lost sight and multi-latent compartment. Another study conducted by Aprilian*et al*. [1] analyzed the SEIR model along with the vaccination compartment. This study combines the existing models mentioned before to analyze the effect of treatment, treatment adherence, and vaccination in suppressing the spread of TB infectious.

## II. MATHEMATICAL MODEL

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The total population denoted by $N(t)$ is divided into seven compartments, $S(t)$ represents the susceptible population, $V(t)$ represents the number of infected vaccinated population, $E(t)$ represents the number of exposed population, $L(t)$ represents the number of lost sight population, $I(t)$ represents the number of infected population, and $R(t)$ represents the number of recovered population.

In this model, the susceptible individual will go to the exposed population first before becoming infectious. The exposed individual will progress either to infected population or lost sight population. Individuals at Infected population are given a treatment and progress to recovered population after they complete the treatment. Lost sight population are the individuals from exposed population who does not take any treatment and individuals from infected population who does not complete the treatment. It can also go back to the infected population whenever they retake the treatment. We consider that the infected individuals in treatment cannot spread the disease because they are under surveillance, therefore the disease can only be spread by lost sight population. Vaccinated populations can also be infected but in lower rate depending on the vaccination effectiveness rate. The flow diagram is shown in Figure 1.

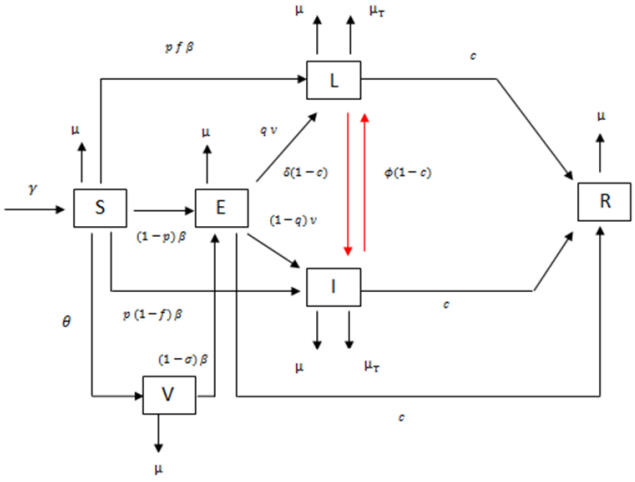


Fig 1. Diagram flow of tuberculosis infectious

Based on the diagram flow above, we formulate the following system of ordinary differential equation:

$$\frac{dS}{dt} = \Gamma - \beta SL - (\mu + \theta)S,$$
$$\frac{dV}{dt} = \theta S - \mu V - (1-\sigma)\beta VL, \quad (1)$$
$$\frac{dE}{dt} = (1-p)\beta SL + (1-\sigma)\beta VL - (\mu + v + c)E,$$
$$\frac{dL}{dt} = pf\beta SL + qvE + \phi(1-c)I - (\mu + \mu_t + c)L - \delta(1-c)L,$$
$$\frac{dI}{dt} = p(1-f)\beta SL + (1-q)vE + \delta(1-c)L - (\mu + \mu_t + c) - \phi(1-c)I,$$
$$\frac{dR}{dt} = c(E + L + I) - \mu R,$$

## III. RESULT AND DISCUSSION

System (1) has a disease-free equilibrium given by:

$$T_0(S,V,E,L,I,R) = \left(\frac{\gamma}{\theta+\mu}, \frac{\gamma\theta}{\mu(\theta+\mu)}, 0,0,0,0\right),$$

And an endemic equilibrium given by:

$$T^*(S,V,E,L,I,R) = (S^*, V^*, E^*, L^*, I^*, R^*),$$

Where

$$S^* = \frac{\gamma}{L\beta + \theta + \mu} \qquad L^* = \frac{eqv + I\phi - cI\phi}{c - pS\beta + \delta - c\delta + \mu + \mu t}$$

$$V^* = \frac{S\theta}{L\beta + \mu - L\beta\sigma} \qquad I^* = \frac{L(S\beta + \delta - c\delta) - e(q-1)v}{c + \mu + \mu t + \phi - c\phi}$$

$$E^* = \frac{L\beta(S(1-p) + V - V\sigma)}{c + \mu + v} \qquad R^* = \frac{c(e + L + I)}{\mu}$$

Basic reproduction number, denoted by $\mathcal{R}_0$, is an expected number of secondary cases produced by a typical infective individual in a completely susceptible population. It is obtained by the next generation matrix formulated in [4]. We obtain the basic reproduction number as follows:

$$\mathcal{R}_0 = \mathcal{R}_0^1 + \mathcal{R}_0^2 + \mathcal{R}_0^3 + \mathcal{R}_0^4 \quad (2)$$

where

$$\mathcal{R}_0^1 = \frac{\beta\gamma fp}{(\theta+\mu)(\mu + \mu t + c + \delta - \delta c + \phi - \phi c)}$$

$$\mathcal{R}_0^2 = \frac{\beta\gamma qv[\theta(1-\sigma) + \mu(1-p)]}{\mu(\theta+\mu)(\mu+\mu t + c)(\mu + c + v)(\mu + \mu t + c + \delta - \delta c + \phi - \phi c)}$$

$$\mathcal{R}_0^3 = \frac{\beta\gamma v\theta(1-\sigma)(\phi - \phi c)}{\mu(\theta+\mu)(\mu+\mu t + c)(\mu + c + v)(\mu + \mu t + c + \delta - \delta c + \phi - \phi c)}$$

$$\mathcal{R}_0^4 = \frac{\mu\beta\gamma p(c+\mu)(\phi - \phi c)}{\mu(\theta+\mu)(\mu+\mu t + c)(\mu + c + v)(\mu + \mu t + c + \delta - \delta c + \phi - \phi c)}$$

*Theorem 1: The disease-free equilibrium is locally asymptotically stable if* $\mathcal{R}_0 < 1$.

Proof: After linearization for system (1) at $T_0$ we have a Jacobian matrix as follows:

$$J_{T_0} = \begin{pmatrix} J_{11} & 0 & 0 & J_{14} & 0 & 0 \\ J_{21} & J_{22} & 0 & J_{24} & 0 & 0 \\ 0 & 0 & J_{33} & J_{34} & 0 & 0 \\ 0 & 0 & J_{43} & J_{44} & J_{45} & 0 \\ 0 & 0 & J_{53} & J_{54} & J_{55} & 0 \\ 0 & 0 & J_{63} & J_{64} & J_{65} & J_{66} \end{pmatrix}$$

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where:

$J_{11} = -\theta - \mu$ $J_{53} = (1-q)\nu$

$J_{14} = -\frac{\beta\gamma}{\theta+\mu}$ $J_{54} = (1-c)\delta + \frac{(1-f)p\beta\gamma}{\theta+\mu}$

$J_{22} = -\mu$ $J_{55} = -c - \mu - \mu t - (1-c)\phi$

$J_{24} = -\frac{\beta\gamma\theta\,(1-\sigma)}{\mu(\theta+\mu)}$ $J_{63} = c$

$J_{33} = -c - \mu - \nu$ $J_{64} = c$

$J_{34} = \frac{\beta\gamma\,[\mu(1-p)+\theta(1-\sigma)]}{\mu(\theta+\mu)}$ $J_{65} = c$

$J_{43} = q\nu$ $J_{66} = -\mu$

$J_{44} = \frac{fp\beta\gamma}{\theta+\mu} - (1-c)\delta - \mu - \mu t$ $J_{45} = (1-c)\phi$

The eigen values are obtained by $|J_{T_0} - \lambda I| = 0$ therefore we have the characteristic equation as follows:

$$(\lambda - J_{11})(\lambda - J_{22})(\lambda - J_{66})(\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3) = 0 \quad (3)$$

where

$$a_1 = (\mu + \mu t + c) + (\mu + \mu t + c + \delta - \delta c + \phi - \phi c) - \frac{\beta\gamma fp}{(\theta+\mu)}$$

$$a_2 = ((\mu + \mu t + c) + (\mu + c + \nu))\left((\mu + \mu t + c + \delta - \delta c + \phi - \phi c) - \frac{\beta\gamma fp}{(\theta+\mu)}\right) + (\mu + c + \nu)(\mu + \mu t + c)\left(1 - \left(\frac{q\nu[\theta(1-\sigma)+\mu(1-p)]}{\mu(\theta+\mu)(\mu+\mu t+c)(\mu+c+\nu)} + \frac{\beta\gamma p(\phi-\phi c)}{\mu(\theta+\mu)(\mu+\mu t+c)(\mu+c+\nu)}\right)\right)$$

$$a_3 = (\mu + \mu t + c)(\mu + c + \nu)(\mu + \mu t + c + \delta - \delta c + \phi - \phi c)((1 - (\mathcal{R}_0 + \mathcal{R}_0^4(\frac{1}{\theta(1-\sigma)})$$

From equation (3) we obtain the eigenvalues as follows:

$\lambda_1 = -\theta - \mu,$ $\lambda_3 = -\mu$ $\lambda_2 = -\mu$

All the eigenvalues above are negative, the others will be obtained by solving the following equation:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 \quad (4)$$

There are three conditions that must be satisfied for the cubic equation above:

$$\lambda_4 + \lambda_5 + \lambda_6 = -a_1$$
$$\lambda_4\lambda_5 + \lambda_4\lambda_6 + \lambda_5\lambda_6 = a_2 \quad (5)$$
$$\lambda_4\lambda_5\lambda_6 = -a_3$$

Let $\mathcal{R}_0 < 1$, such that according to equation (2) we have:

$$\mathcal{R}_0^1 + \mathcal{R}_0^2 + \mathcal{R}_0^3 + \mathcal{R}_0^4 < 1 \quad (6)$$

Since $\mathcal{R}_0^1 > 0,\ \mathcal{R}_0^2 > 0,\ \mathcal{R}_0^3 > 0,\ \mathcal{R}_0^4 > 0$,therefore $\mathcal{R}_0^1 < 1,\ \mathcal{R}_0^2 < 1,\ \mathcal{R}_0^3 < 1,\ \mathcal{R}_0^4 < 1.\ \mathcal{R}_0^1 < 1$gives:

$$(\mu + \mu t + c + \delta - \delta c + \phi - \phi c) > \frac{\beta\gamma fp}{(\theta+\mu)} \quad (7)$$

Inequality (7) gives $a_1 > 0$

$\mathcal{R}_0^2 < 1$gives

$\frac{\beta\gamma q\nu\,[\theta(1-\sigma)+\mu(1-p)]}{\mu(\theta+\mu)(\mu+\mu t+c)(\mu+c+\nu)(\mu+\mu t+c+\delta-\delta c+\phi-\phi c)} < 1,$ and $\mathcal{R}_0^4 < 1$ gives

$\frac{\mu\beta\gamma p\ (c+\mu)(\phi-\phi c)}{\mu(\theta+\mu)(\mu+\mu t+c)(\mu+c+\nu)(\mu+\mu t+c+\delta-\delta c+\phi-\phi c)} < 1.$ Then we assume that

$$\frac{\beta\gamma q\nu[\theta(1-\sigma)+\mu(1-p)]}{\mu(\theta+\mu)(\mu+\mu t+c)(\mu+c+\nu)} < 1 \quad (8)$$

$$\frac{\beta\gamma p(\phi-\phi c)}{\mu(\theta+\mu)(\mu+\mu t+c)(\mu+c+\nu)} < 1 \quad (9)$$

Inequalities (8) and (9) gives $a_2 > 0$ and we also assume that $\mathcal{R}_0^4\left(\frac{1}{\theta(1-\sigma)}\right) < 1$which gives $a_3 > 0$. Therefore, the conditions (7) will be satisfied when $\lambda_5 < 0$and $\lambda_6 < 0$.

Since all the eigenvalues are negative when $\mathcal{R}_0 < 1$, according to [9], it is proved that the disease-free equilibrium is locally asymptotically stable if $\mathcal{R}_0 < 1$.

*Theorem 3: the endemic equilibrium is locally asymptotically stable if* $\mathcal{R}_0 > 1$

Proof: According to Castillo-Chaves and Song [2], let $\varphi = \beta_3$ be a bifurcation parameter. When $\mathcal{R}_0 = 1$, we have

$$\varphi = \varphi^* = \frac{\mu(\theta+\mu)(c+\mu+\mu t)(c+\mu+\nu)(\delta+\mu+\mu t+\phi-c(-1+\delta+\phi))}{\gamma p\mu f(c+\mu+\mu t)(c+\mu+\nu)+\beta\gamma q\nu(\theta(1-\sigma)+\mu(1-p))+\beta\gamma(\phi-\phi c)(\theta\nu(1-\sigma)+\mu(p(c+\mu)))}$$

The disease-free equilibrium has five negative eigenvalue and one zero eigenvalue. The zero eigenvalue has a right-side eigenvector $(u_1, u_2, u_3, u_4, u_5, u_6)$ and a left-side eigenvector $(v_1, v_2, v_3, v_4, v_5, v_6)$ where
$u_1 < 0, u_2 < 0, u_3 > 0, u_4 > 0, u_5 > 0, u_6 > 0, v_1 = 0,$
$v_2 = 0, v_3 > 0, v_4 > 0, v_5 > 0,$ and$v_6 = 0$

Now we define

$$a = \sum_{k,i,j=1}^{6} v_k u_i u_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(\boldsymbol{T_0}, 0).$$
$$b = \sum_{k,i=1}^{6} v_k u_i \frac{\partial^2 f_k}{\partial x_i \partial \varphi}(\boldsymbol{T_0}, 0). \quad (12)$$

where

$x_1 = S,\ f_1 = \gamma - \beta x_1 x_4 - (\mu+\theta)x_1,$
$x_2 = V,\ f_2 = \theta x_1 - \mu x_2 - (1-\sigma)\beta x_2 x_4,$
$x_3 = E,\ f_3 = (1-p)\beta x_1 x_4 + (1-\sigma)\beta x_2 x_4 - (\mu+\nu+c)x_3,$
$x_4 = L,\ f_4 = p\beta x_1 x_4 + q\nu x_3 + \phi(1-c)x_5 - (\mu + \mu t + cx4 - \delta(1-c)x4$
$x_5 = I,\ f_5 = \beta x_1 x_4 + (1-q)x_2 x_3 + \delta(1-c)x_4 - (\mu + \mu t + c)x_5 - \phi(1-c)x_5,$
$x_6 = R,\ f_6 = c(x_4 + x_5 + x_3) - \mu x_6,$

And we obtain partial derivatives for $a$:

$$\frac{\partial^2 f_3}{\partial x_2 \partial x_4}(\boldsymbol{T_0}, \varphi^*) = (1-\sigma)\varphi^*$$
$$\frac{\partial^2 f_4}{\partial x_1 \partial x_4}(\boldsymbol{T_0}, \varphi^*) = pf\varphi^*$$

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$$\frac{\partial^2 f_2}{\partial x_1 \partial x_4}(\boldsymbol{T_0}, \varphi^*) = (1-p)\varphi^*$$
$$\frac{\partial^2 f_5}{\partial x_1 \partial x_4}(T_0, \varphi^*) = p(1-f)\varphi^*$$

also partial derivatives for $b$:

$$\frac{\partial^2 f_3}{\partial x_1 \partial \varphi}(\boldsymbol{T_0}, \varphi^*) = (1-p)x_4$$
$$\frac{\partial^2 f_4}{\partial x_4 \partial \varphi}(\boldsymbol{T_0}, \varphi^*) = pfx_1$$
$$\frac{\partial^2 f_3}{\partial x_2 \partial \varphi}(\boldsymbol{T_0}, \varphi^*) = (1-\sigma)x_4$$
$$\frac{\partial^2 f_5}{\partial x_1 \partial \varphi}(\boldsymbol{T_0}, \varphi^*) = p(1-f)x_4$$
$$\frac{\partial^2 f_3}{\partial x_4 \partial \varphi}(\boldsymbol{T_0}, \varphi^*) = (1-p)x_1$$
$$\frac{\partial^2 f_5}{\partial x_4 \partial \varphi}(\boldsymbol{T_0}, \varphi^*) = p(1-f)x_1$$
$$\frac{\partial^2 f_4}{\partial x_1 \partial \varphi}(\boldsymbol{T_0}, \varphi^*) = pfx_4$$

According to equation (12) we obtain $a < 0$and $b > 0$.

Consequently, when $\varphi$ changes from $\varphi < \varphi^*$to $\varphi > \varphi^*$, the free-disease equilibrium changes from stable to unstable and the endemic equilibrium changes from negative to
positive and it is locally asymptotically stable. It proves that the endemic equilibrium is locally asymptotically stable if $\mathcal{R}_0 > 1$.

## IV. NUMERICAL RESULT

We perform the numerical simulation to support the analytical result. The simulation visualizes the dynamical population in both condition, $\mathcal{R}_0 < 1$ and $\mathcal{R}_0 > 1$ according to theorem 1 and theorem 2. The initial conditions we use for this simulation are: $S(0) = 10.000, V(0) = 50.000, E(0) = 10.000, L(0) = 5000$dan $R(0) = 0$. And the parameter values are presented as follows:

**Table 1** Parameter Values

| Parameter | Value | | Source |
|---|---|---|---|
| | $\mathcal{R}_0 < 1$ | $\mathcal{R}_0 > 1$ | |
| $\gamma$ | 1 | 1 | [1] |
| $\mu$ | -0.996691 | -1.06243 | [1] |
| $\mu_T$ | -0.302297 | -0.148983 | [1] |
| $\beta$ | 0.236319 | 0.578424 | [1] |
| $\theta$ | 1 | 1 | [1] |
| $\sigma$ | 0.10979 | 0.127638 | [1] |
| $c$ | 0.139156 | 0.129349 | [1] |
| $v$ | -0.89669 | -0.052261 | [1] |
| $\delta$ | 0.375597 | 0.0997238 | [8] |
| $\phi$ | 0.73202 | 0.389793 | [8] |
| $p$ | -0.603326 | -0.648159 | [1] |
| $f$ | -0.778148 | -0.553713 | [1] |
| $q$ | -0.187724 | -0.107216 | [1] |

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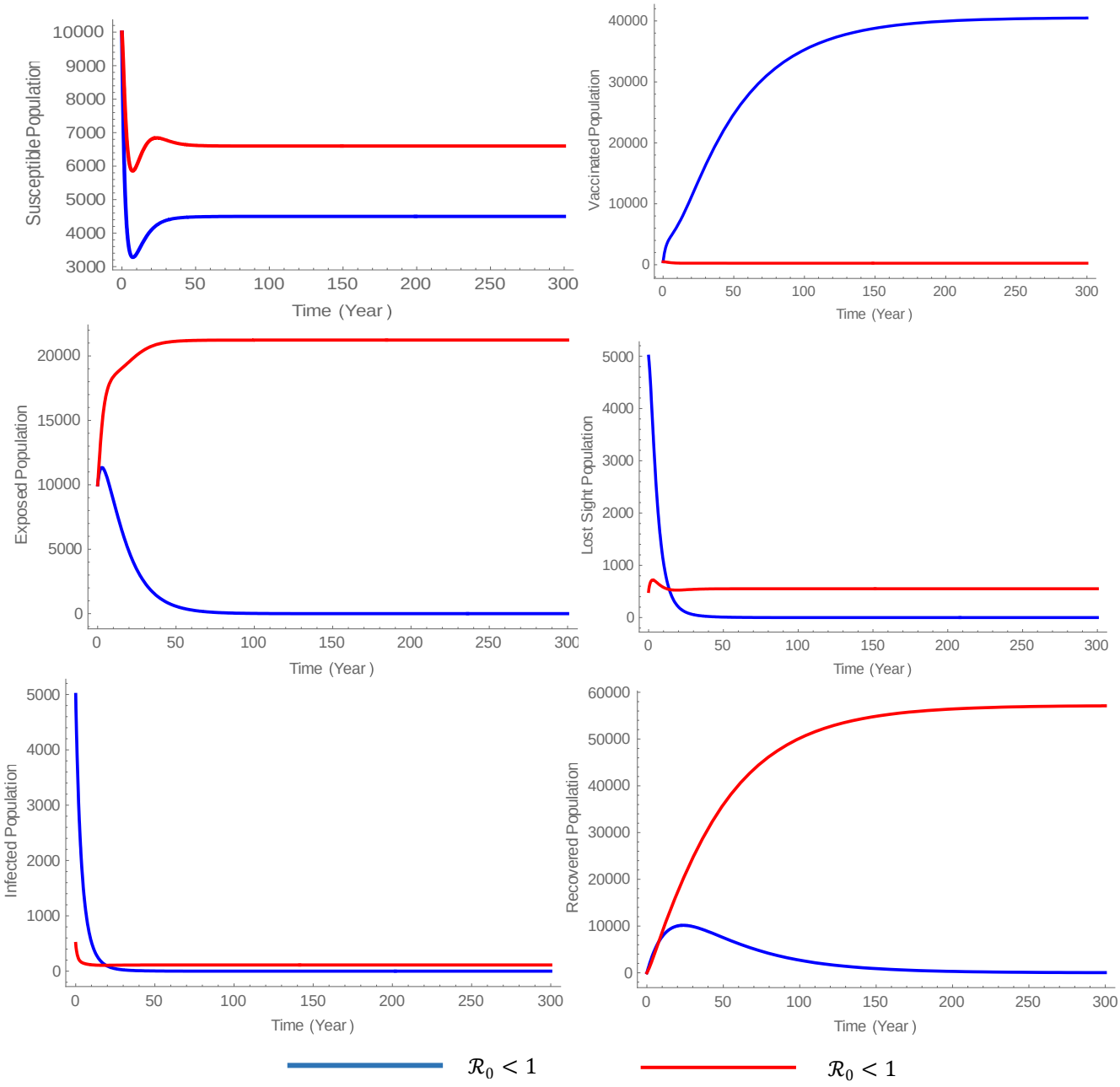


Figure 2: the population dynamic at $\mathcal{R}_0 < 1$ and $\mathcal{R}_0 > 1$

## V. CONCLUSION

We've formulated a model for TB transmission by combining the existing model with vaccinated and lost sight in a form of ordinary differential equation system. The system gives two equilibrium, a free-disease equilibrium and an endemic equilibrium. A free-disease equilibrium is a state when there is no outbreak in population, and endemic equilibrium is a state when the disease is endemic in population.

The stability analysis shows that the disease-free equilibrium is locally asymptotically stable if $\mathcal{R}_0 < 1$ is satisfied and the endemic equilibrium is locally asymptotically stable if $\mathcal{R}_0 > 1$ is satisfied. The numerical simulation shows the suitable result with the stability analysis.

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