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Analysis of SVEIL Model of Tuberculosis Disease Spread with Imperfect Vaccination

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ABSTRACT

This study proposes a SVEIL model of tuberculosis disease spread with imperfect vaccination. Susceptible individuals can receive imperfect vaccination, but over the time the vaccine efficacy will decrease. Vaccinated individuals are in vulnerable class since they still have probability to get reinfected. The proposed model includes treatment for both high-risk latent and active TB patients. In fact, after getting appropriate treatment (get recovered) the individuals still have bacteria in their body and it is classified to low-risk laten class. Dynamical behaviour of the model is analyzed to understand the local stability equilibrium. The *Routh-Hurwitz criterion* is used to analyze the local stability equilibrium in disease free equilibrium (DFE) point and *Center Manifold theorem* is used to prove the local stability of the endemic equilibrium (EE) point. The local stability equilibrium state totally depends on the effective reproduction number $\Re_v$. If $\Re_v < 1$ then the DFE point is locally asymtotically stable, while if $\Re_v > 1$ the EE point is locally asymptotically stable The parameter used in this paper is based on the previous researches related to TB and the initial subpopulations are assumed. Numerical simulations show that the disease transmission rate affect the effective reproduction number, therefore it influences the stability of equilibrium points.

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A. INTRODUCTION

Tuberculosis is a lung infection disease caused by bacteria called *Mycobacterium Tuberculosis*. This disease is not just infecting the lungs, but also can attack another part of the body such as spine, kidneys, brain, so that it can also affect the part of central nervous system, lymphatic system, and kidneys. These bacteria will be contained by an individual's body immunity, later on will be active when the patient's immunity is weak (Whang et al., 2011).

Tuberculosis is a global problem. This deadly disease has already been becoming a serious problem since the case number of TB is greater than the case number of HIV/ AIDS. Meanwhile, according to 2019 data, WHO mentioned that geographically TB cases are recorded 44% in Southeast Asia, 25% in Africa, 18% in Western Pacific Region, 8.2% in Eastern Mediterranean Region, 2.5% in Europe, and 2.9% in the US. As many as two-third of the total estimated global cases that occurred, Indonesia is included in the Top Eight Countries with a percentage of India 26%, Indonesia 8.5%, China 8.4%, Philippines 6%, Pakistan 5.7%, Nigeria 4.4%, Bangladesh 3.6% dan South Africa 3.6% (World Health Organization, 2021).

Although the incidence rate of tuberculosis spread is globally decreasing during the Covid-19, but not fast enough to reach the 2020 milestone of a 20% reduction between 2015 and 2020. The cumulative reduction from 2015 to 2019 was 9% (from 142 to 130 new cases per 100,000 population), including a reduction of 2.3% between 2018 and 2019 (World Health Organization, 2021). In Indonesia, based on the Ministry of Health data, 568,987 tuberculosis cases were found. However, in 2020, it was only recorded 271,750 cases, while the estimation the number of the case in that year should be around 840,000 cases (Ika, 2021). Based on the tuberculosis information online system (SITB), in Indonesia the case finding in 2019 was 67%, while in 2020, the case finding was only 41.7%. It means that there was a decrease in the case finding/detection by 25.3% (Dinas Kesehatan Daerah Istimewa Yogyakarta, 2021). According to data in 2017, it is only 24% of the tuberculosis symptomatic individuals who came to the health service. Nowadays, World Health Organization (WHO) has targeted to end the tuberculosis disease in 2030 (Ika, 2021). In general, there are three alternative solutions for TB treatments: treating the latent individual so that they do not become actively infected, treating the actively TB infected individuals, and giving vaccination to reduce the spread of tuberculosis (Sulayman et al., 2021). The elimination strategy will be dependent on preventing disease reactivation through vaccination or preventive treatment of those who are latently infected (Harris et al., 2016).

Vaccination can be done to overcome this tuberculosis problem, even the WHO has declared currently that developing a new vaccine for tuberculosis has become a top priority for health workers (Brennan et al., 2012). Depending on the TB epidemiology of a nation, the BCG vaccination is advised as a component of the national children immunization programs. 153 nations reported receiving BCG vaccines in 2018, and 113 of those had at least 90% BCG coverage (Martin et al., 2020). WHO advises giving children in leprosy and tuberculosis (TB) endemic nations a single dose of BCG, and almost 130 million infants worldwide receive the vaccine each year (Aspatwar et al., 2022). BCG was first introduced in 1921 as a licensed tuberculosis vaccine and still used today for the prevention of tuberculosis infection (Bhargava et al., 2016). BCG can provide decades of protection against tuberculosis disease, and it has been a proof that vaccines are a possible medium to protect the body from tuberculosis (Fletcher et al., 2018). Despite the facts that BCG lowers the incidence of disseminated tuberculosis in children, research on how well it works to prevent pulmonary tuberculosis in adults has been inconsistent (Mangtani et al., 2014). Because of the limitation of BCG, various potential TB vaccine candidates have been created and divided into three following groups: priming vaccines as preventive pre-exposure vaccines, boosting vaccines as preventive post-exposure vaccines targeted at adolescents and adults with LTBI and prior BCG immunization, and therapeutic vaccines to persons at higher risk of developing recurrent disease (Kaufmann et al., 2017).

In dealing with tuberculosis, medical science has an important role. Several fields of applied science and epidemiology also contributed (Sari & Rachmawati, 2019), including mathematics which plays an important role in the prevention and decision-making against the spread of tuberculosis disease, precisely through the branch of mathematics: mathematical modelling. Through differential equations, mathematical modelling can be applied to present phenomenon of change, such as epidemiology field. Therefore, the addition of vaccination variable into a

mathematical model is a right decision. Vaccination in mathematical model is often represented as a linear exchange between the compartment of susceptible individuals and cured individuals (Buonomo & Lacitignola, 2011). Some vaccinations are known to prevent possible infection but not to guarantee vaccinated individuals to always be safe from getting infected and also transmitting the infection to others (Buonomo & Marca, 2019).

Mathematical models in the field of epidemiology, especially models of the spread of tuberculosis that applies vaccination have been widely used. Egonmwan and Okuonghae (2019) constructed a model of *SVEIT* (susceptible, vaccinated, exposed, infected, treated). In the same year, Mengistu and Witbooi (2019) also constructed the *SVEIL* (susceptible, vaccinated, exposed, infected, low-risk latent) model included vaccinations for newborns. Instead of being cured, individuals who have been treated are assumed to be in the low-risk latent class (L) because tuberculosis bacterium cannot be completely eliminated from the patient's body. In this model vaccination is assumed to be perfect vaccination, therefore there is no disease transmission from vaccinated class to exposed class. In addition, treatment is also applied in the exposed class (E) and infected class (I). Then, Sulayman et al. (2021) were inspired by Kar & Mondal (2012) and constructed the *SVEIRE* (susceptible, vaccinated, exposed, infected, recovered, exposed) model that contains imperfect vaccination. Sulayman et al. (2021) considered that the vaccinated class is like the susceptible class since it allows a decrease in vaccine efficacy over the time between these two classes. Moreover, it is a fact that treated individuals can relapse again when the patient's immunity is down (Kar & Mondal, 2012).

Nowadays, susceptible individuals are likely to be able to receive imperfect vaccination to reduce their susceptibility to tuberculosis. But over the time, the efficacy of the vaccine will also decrease. As a result, vaccinated individuals can be classified into vulnerable classes since they still have probability to get reinfected. Thus, according to Sulayman et al. (2021), it is important to understand the effects of the use of imperfect vaccination on the modeling of tuberculosis which is currently not widely studied by many scientists. Motivated by these previous studies, we proposed an *SVEIL* tuberculosis model. In this research, we assume that vaccinated individuals can still be infected and go to exposed class as an impact of imperfect vaccination. As mentioned above, since the TB bacteria can't be totally eliminated we proposed *SVEIL,* instead of *SVEIRE* and *SVEIT* model. We also consider the fast and slow progression of infection rate from susceptible class. This study also applies treatments to both latent class (E) and infected class (I), so that latent and actively infected individuals could later become low-risk latent (L) after getting appropriate treatment.

Our paper is divided in some sections. In section B, the model is formulated and the nonnegativity and the boundedness of the solution are analysed. Section C describes the equilibrium points and its conditions, and the effective reproduction numbers. The local stability is analysed and numerical simulation are also presented in this section. At the end, our conclusions and suggestions are presented in Section D. The steps of this research are depicted by Figure 1.

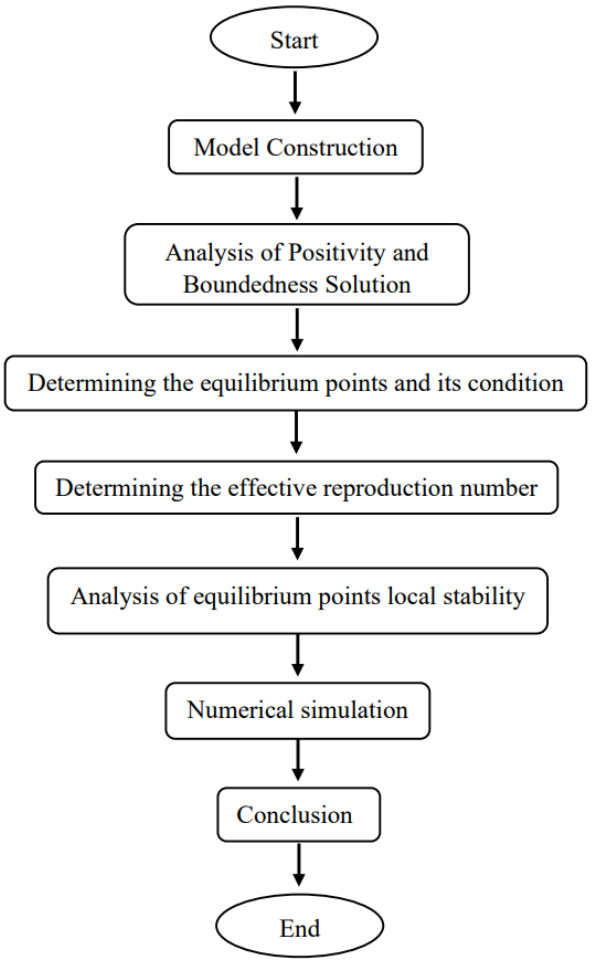

Figure 1. The flowchart of this research

B. METHOD

To study the spread of tuberculosis disease with imperfect vaccination, we construct a mathematical model which is a modification of some existing models (Egonmwan & Okuonghae, 2019; Mengistu & Witbooi, 2019; Sulayman et al., 2021). We divide the total population $N(t)$ at time t into five subpopulations, namely susceptible $(S(t))$, vaccinated $(V(t))$, exposed $(E(t))$, actively-infected $(I(t))$, and low-risk latent $(L(t))$ subpopulations. Hence, we have $N(t) = S(t) + V(t) + E(t) + I(t) + L(t)$. In this case, the recruitment rate into the population is assumed to be Λ. All subpopulations have the same rate of natural death μ, while the death caused by tuberculosis disease only happens in actively-infected subpopulation and it is denoted by δ. This *SVEIL* model describes the flow of disease spread from susceptible individuals who get vaccinated so they go to vaccinated class, and by the time the efficacy of the vaccine decreases so they might go to susceptible class again. Since the given vaccine is an imperfect vaccine, so the vaccinated individuals can still be infected and go to the exposed class with a rate of β_1. Since β_1 is a transmission of tuberculosis due to imperfect vaccination, it is assumed that $\beta_1 < \beta$ and thus we can write $\beta_1 = \alpha\beta$, where α is a rate of of risk reduction due to vaccination $(0 < \alpha < 1)$ and β is the rate of tuberculosis transmission in general. Meanwhile, due to interaction with infected individuals in the susceptible class, the vulnerable individual will become latent (exposed) at a rate $(1 - p)\beta$, or directly can go to infected class at a rate of $p\beta$.

The exposed class individuals can develop and become actively infected due to certain factors. In this work, we assumed that there are two treatments carried out: treatment in the exposed class as an initial treatment and consultation of new symptomatically exposed patients, and the treatment in the actively-infected class in the form of treatment for patient with active tuberculosis. Exposed individuals who have undergone the treatment process properly, will be cured and moved to low-risk latent class with a rate of γ. On the other hand, those who do not obey the recommendation on handling, they will become worse and go to actively-infected class with a rate of k. Meanwhile, the treatment in the actively-infected class at a rate of r allows a successful treatment with a rate $(1-q)$ so that they become cured (low-risk latent) and the rests with a rate of q will just get better and go back to latent class. Based on assumptions above, we have the following compartment diagram that describes the interactions between classes, as shown in Figure 2.

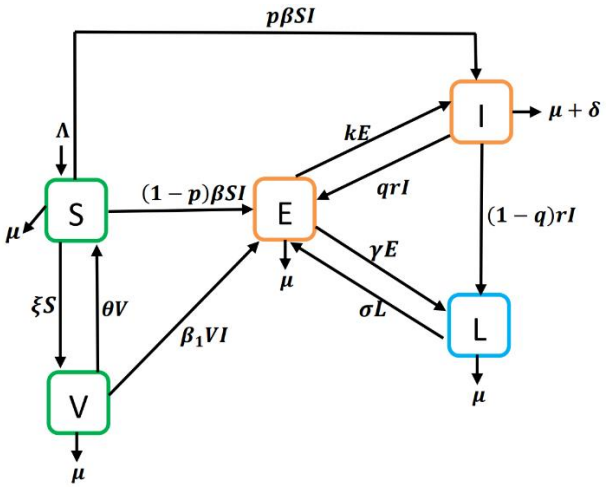

Figure 2. The compartment diagram of the *SVEIL* tuberculosis transmission model

The system of ODE that describes the dynamics of tuberculosis is formulated as follows:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda + \theta V - p\beta SI - (1-p)\beta SI - \xi S - \mu S,\\
\frac{dV}{dt} &= \xi S - \theta V - \beta_1 VI - \mu V,\\
\frac{dE}{dt} &= (1-p)\beta SI + \beta_1 VI + qrI + \sigma L - kE - \mu E - \gamma E,\\
\frac{dI}{dt} &= p\beta SI + kE - qrI - (1-q)rI - \mu I - \delta I,\\
\frac{dL}{dt} &= \gamma E + (1-q)rI - \sigma L - \mu I.
\end{aligned} \tag{1}$$

with non-negative initial conditions given by $S(0) = S_0 \geq 0$, $V(0) = V_0 \geq 0$, $E(0) = E_0 \geq 0$, $I(0) = I_0 \geq 0$ and $L(0) = L_0 \geq 0$. All parameters of system (1) are assumed to be positive for all time $t > 0$. In order to have epidemiological significance, all solutions of model (1) must be non-negative and bounded. The non-negativity and boundedness solution are described by the following two Lemmas.

Lemma 1. Let the initial condition $S_0 \geq 0, V_0 \geq 0, E_0 \geq 0, I_0 \geq 0$ and $L_0 \geq 0$. Then the solution set $(S(t), V(t), E(t), I(t), L(t))$ is non-negative for all t.

Proof.

We first assume the initial condition is non-negative and show that $S(t) \geq 0, \forall t > 0$. Suppose that this is incorrect, then there exists $T > 0$ such that $S(t) > 0$ for $t \in [0, T), S(T) = 0$ and $S(t) < 0$ for $t > T$. Then, the first equation of system (1) gives

$$\left.\frac{dS(t)}{dt}\right|_{t=T} = \Lambda + \theta V \geq 0,$$

which shows that the function $S(t)$ does not cross to negative part or $S(T^+) \geq 0$. This contradicts the fact that $S(T^+) < 0$. Hence, $S(t) \geq 0, \forall t \geq 0$. Analogously, we can prove that $V(t) \geq 0, E(t) \geq 0, I(t) \geq 0$, and $L(t) \geq 0, \forall t \geq 0$.

Lemma 2. With the non-negative initial conditions, the feasible region Ω of the model (1) is defined by $\Omega = \left\{(S(t), V(t), E(t), I(t), L(t)) \in R_+^5 | 0 \leq S(t) + V(t) + E(t) + I(t) + L(t) \leq \frac{\Lambda}{\mu}\right\}$.

Proof.

By adding all the class equations of the model (1), then we get

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dV}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dL}{dt} = \Lambda - \mu N - \delta I \leq \Lambda - \mu N. \tag{2}$$

The inequality (2) implies $0 \leq N(t) \leq \frac{\Lambda}{\mu} + N(0)e^{-\mu t}$ which $N(0)$ is the initial conditions of the total population. Hence, it holds $\lim_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}$ which means the region Ω is positive invariant, so the solution of the model (1) is bounded.

C. RESULT AND DISCUSSION

1. Equilibrium Points and Effective Reproduction Number

By setting the right-hand side (RHS) of the model (1) to be equal to zero, we get the solutions as equilibrium points, that are the disease-free equilibrium point $P^0 = (S^0, V^0, E^0, I^0, L^0)$ and the endemic equilibrium point $P^* = (S^*, V^*, E^*, I^*, L^*)$, where

$$S^0 = \frac{\Lambda(\mu+\theta)}{\mu(\xi+\mu+\theta)}, V^0 = \frac{\Lambda\xi}{\mu(\xi+\mu+\theta)}, E^0 = 0, I^0 = 0, L^0 = 0, \text{and}$$

$$\begin{aligned}
S^* &= \frac{\Lambda(\beta_1 I^* + \theta + \mu)}{(\beta I^* + \mu)(\beta_1 I^* + \theta + \mu) + \xi(\beta_1 I^* + \mu)}, \\
V^* &= \frac{\Lambda\xi}{(\beta I^* + \mu)(\beta_1 I^* + \theta + \mu) + \xi(\beta_1 I^* + \mu)}, \\
E^* &= \frac{(1-p)\beta\Lambda I^*(\beta_1 I^* + \theta + \mu)(\sigma+\mu) + \beta_1 I^* \Lambda\xi(\sigma+\mu)}{[(\beta I^* + \mu)(\beta_1 I^* + \theta + \mu) + \xi(\beta_1 I^* + \mu)][(k+\mu)(\sigma+\mu) + \gamma\mu]} \\
&\quad + \frac{qr\mu I^*}{[(k+\mu)(\sigma+\mu) + \gamma\mu]} + \frac{\sigma r I^*}{[(k+\mu)(\sigma+\mu) + \gamma\mu]}, \\
L^* &= \frac{\gamma(1-p)\beta\Lambda I^*(\beta_1 I^* + \theta + \mu) + \gamma\beta_1 I^* \Lambda\xi}{[(\beta I^* + \mu)(\beta_1 I^* + \theta + \mu) + \xi(\beta_1 I^* + \mu)][(k+\mu)(\sigma+\mu) + \gamma\mu]} \\
&\quad + \frac{\gamma qr\mu I^*}{[(k+\mu)(\sigma+\mu) + \gamma\mu](\sigma+\mu)} + \frac{\gamma\sigma r I^*}{[(k+\mu)(\sigma+\mu) + \gamma\mu](\sigma+\mu)} + \frac{(1-q)r I^*}{(\sigma+\mu)},
\end{aligned} \tag{3}$$

where I^* will be described in the last part of this subsection.

We now determine the effective reproduction number R_v of the model (1). First, we notice that system (1) can be written as

$$\frac{dX}{dt} = \mathcal{F}(X) - \mathcal{V}(X) \tag{4}$$

where $X = (S, V, E, I, L)^T$ and

$$\mathcal{F}(X) = \begin{pmatrix} 0 \\ 0 \\ (1-p)\beta SI + \beta_1 VI \\ p\beta SI \\ 0 \end{pmatrix}, \qquad \mathcal{V}(X) = \begin{pmatrix} -\Lambda - \theta V + p\beta SI + (1-p)\beta SI + \xi S + \mu S \\ \theta V + \beta_1 VI - \xi S + \mu V \\ -qrI - \sigma L + (k+\mu+\gamma)E \\ -kE + qrI + (1-q)rI + \mu I + \delta I \\ -\gamma I - (1-q)rI + \sigma L + \mu L \end{pmatrix}.$$

By applying the next generation matrix method to the system (4), we get an effective reproduction number

$$R_v = \frac{\Lambda\big((\mu+\sigma)(\beta\mu + \beta\theta + \xi\beta_1)k + \beta\mu p(\theta+\mu)(\gamma+\mu+\sigma)\big)}{\mu(\xi+\mu+\theta)C_1}. \tag{5}$$

Notice that I^*in equation (3) is the positive solution of the following quadratic equation

$$m_0 I^{*2} + m_1 I^* + m_2 = 0 \tag{6}$$

where

$$\begin{aligned} m_0 &= \beta\beta_1 C_1 > 0, \\ m_1 &= -[\beta\beta_1(\mu+\sigma)k + \beta\beta_1\mu p(\gamma+\mu+\sigma)]\Lambda + [\beta(\theta+\mu) + \beta_1(\xi+\mu)]C_1, \\ m_1 &= \frac{1}{\mu+\theta}\Big[(1-R_v)\mu(\xi+\mu+\theta)\beta_1 C_1 + \Lambda k\xi{\beta_1}^2(\mu+\sigma)^2 + C_1[(\mu+\theta)^2\beta + \beta_1\theta\xi]\Big], \\ m_2 &= [-(\mu+\sigma)(\beta\mu + \beta\theta + \xi\beta_1)k + \beta\mu p(\theta+\mu)(\gamma+\mu+\sigma)]\Lambda + \mu(\xi+\mu+\theta)C_1, \\ m_2 &= (1-R_v)\mu(\xi+\mu+\theta)C_1, \end{aligned}$$

and

$$C_1 = [(\mu+\delta)(\mu+\sigma) + (1-q)\mu r]k + \mu(r+\delta+\mu)(\gamma+\mu+\sigma).$$

2. Since $m_0 > 0$, we obtain $I^* = \frac{-m_1 \pm \sqrt{{m_1}^2 - 4m_0m_2}}{2m_0}$, and I^* will be a real number if ${m_1}^2 - 4m_0m_2 \geq 0$. If $R_v = 1$ then $m_2 = 0$ and $m_1 > 0$, and consequently we have $I^* = 0$ or $I^* = \frac{-m_1}{m_0} < 0$. If $R_v < 1$ then $m_2 > 0$ and $m_1 > 0$. Furthermore, if $R_v < 1$ then the endemic equilibrium point does not exist because $I^* < 0$ or $I^* \in \mathbb{C}$. If $R_v > 1$ then $m_2 < 0$ and $m_1 \in \mathbb{R}$ and therefore the endemic equilibrium point exists uniquely where $I^* = \frac{-m_1 \pm \sqrt{{m_1}^2 - 4m_0m_2}}{2m_0} > 0$. **Local Stability Analysis of Equilibrium Points**

This subsection discusses the local stability of equilibrium points, i.e. by studying the Jacobian matrix of the system (1) at each equilibrium point.

Lemma 3. *For model (1), the disease-free equilibrium point is locally asymptotically stable if* $\Re_v < 1$.

Proof.

The Jacobian matrix evaluated at the disease-free equilibrium point is given by

$$J(P^0) = \begin{bmatrix} -\xi-\mu & \theta & 0 & -C_2 & 0 \\ \xi & -\mu-\theta & 0 & -C_3 & 0 \\ 0 & 0 & -(k+\mu+\gamma) & (1-p)C_2 + C_3 + qr & \sigma \\ 0 & 0 & k & -(r+\mu+\delta) + pC_2 & 0 \\ 0 & 0 & \gamma & (1-q)r & -\mu-\sigma \end{bmatrix},$$

where $C_2 = \frac{\beta\Lambda(\mu+\theta)}{\mu(\mu+\theta+\xi)}$ and $C_3 = \frac{\beta_1\Lambda\xi}{\mu(\mu+\theta+\xi)}$. The characteristics equation of the Jacobian matrix $J(P^0)$ is

$$L(\lambda) = (\lambda+\mu)(\lambda+\xi+\mu+\theta)L_1(\lambda) = 0, \tag{7}$$

where

$$L_1(\lambda) = \lambda^3 + l_1\lambda^2 + l_2\lambda + l_3$$

with

$$\begin{aligned} l_1 &= \frac{(1-\Re_v)pC_2C_1+G_1}{(C_2+C_3)(\mu+\sigma)k+\mu p(\gamma+\mu+\sigma)C_2}, \\ l_2 &= (\delta+\mu+r-pC_2)(k+2\mu+\gamma+\sigma)+\gamma\mu+(k+\mu)(\mu+\sigma) \\ &\quad -k[(1-p)C_2+C_3+qr], \\ l_3 &= (1-\Re_v)C_1, \end{aligned} \tag{8}$$

and

$$\begin{aligned} G_1 &= (C_2+C_3)(\mu+\sigma)k^2 \\ &\quad +\big[(\mu+\sigma)(3\mu+r+\gamma+\delta+\sigma)C_3 \\ &\quad +C_2[\mu pqr+\gamma\mu p+\gamma\mu+\gamma\sigma+\delta\mu(1-p)+\delta\sigma(1-p)+3\mu^2+\mu r(1-p)+4\mu\sigma \\ &\quad +r\sigma+\sigma^2]\big]k+\mu pC_2(\gamma+\mu+\sigma)(\gamma+2\mu+\sigma), \\ G_2 &= k\big[(\mu+\sigma)(\mu+\delta)\big((1-p)C_2+C_3\big)+(\mu pq+\mu(1-p)+\sigma)rC_2+(\mu+\sigma)rC_3\big]. \end{aligned}$$

From equation (7), it is clear that two eigenvalues of $J(P^0)$ are $\lambda_1 = -\mu < 0$ and $\lambda_2 = -(\xi+\mu+\theta) < 0$, while the other eigenvalues are determined by

$$L_1(\lambda) = \lambda^3 + l_1\lambda^2 + l_2\lambda + l_3 = 0.$$

According to the expressions in (8), it is clear that if $\Re_v < 1$ then $l_1 > 0$ and $l_3 > 0$. We find that

$$\begin{aligned} \Delta_2 &= l_1l_2 - l_3 \\ &= k^2[2\mu+\delta+\sigma+r(1-q)-(C_2+C_3)] \\ &\quad +k\big[\zeta(2\mu+\gamma+\sigma)+\gamma\mu+\sigma(2\mu+\sigma+r(1-q))+\mu(2\mu+\sigma) \\ &\quad +(\mu+\gamma+\zeta)[2\mu+\delta+\sigma+r(1-q)-(C_2+C_3)]\big] \\ &\quad +(2\mu+\gamma+\sigma)(\zeta+\mu)(\zeta+\mu+\gamma+\sigma), \end{aligned}$$

where $\zeta = r+\mu+\delta-C_2p$ and $\zeta = \frac{(1-\Re_v)C_2pC_1+G_2}{(C_1+C_2)(\mu+\sigma)k+\mu p(\gamma+\mu+\sigma)C_1}$. It is also clear that if $\Re_v < 1$ and $2\mu+\delta+\sigma+r(1-q) > (C_2+C_3)$, then $\Delta_2 > 0$. Based on the Routh-Hurwitz criterion (Murray, 2007), all roots of $L_1(\lambda) = 0$ have negative real parts if $l_1 > 0$, $l_3 > 0$, and $\Delta_2 = l_1l_2 - l_3 > 0$. Therefore, the disease-free equilibrium point is locally asymptotically stable if $\Re_v < 1$ and $2\mu+\delta+\sigma+r(1-q) > (C_2+C_3)$.

Lemma 4. System (1) undergoes a forward bifurcation at $\Re_v = 1$.

Proof.

It was proven in Lemma 3 that if $\Re_v < 1$ then the disease-free equilibrium point is locally asymptotically stable. We now investigate the behavior of the system (1) around $\Re_v = 1$. By remembering that $\beta_1 = \alpha\beta$ with $0 < \alpha < 1$, $\Re_v = 1$ is achieved when $\beta = \beta^*$, where

$$\beta^* = \frac{\mu(\mu+\theta+\xi)\big((\delta\mu+\delta\sigma+\mu^2+\mu r(1-q)+\mu\sigma)k+\mu(\delta+\mu+r)(\gamma+\mu+\sigma)\big)}{\Lambda\big((\mu+\sigma)(\mu+\theta+\xi\alpha)k+\mu p(\mu+\theta)(\gamma+\mu+\sigma)\big)}.$$

If $\beta = \beta^*$, then the characteristic equation (6) is given by

$$L(\lambda) = \lambda(\lambda+\mu)(\lambda+\xi+\mu+\theta)L_2(\lambda) = 0, \tag{9}$$

where $L_2(\lambda) = \lambda^2 + k_1\lambda + k_2$,

$$\begin{aligned} k_1 = \frac{1}{G_3}\Big[&(\mu+\sigma)(\mu+\theta+\xi\alpha)k^2 \\ &+ \Big((\mu+\theta)(\mu rq+\mu\gamma)p \ + \alpha\xi(\mu+\sigma)(3\mu+\delta+r+\gamma+\sigma) \\ &+ (\mu+\theta)\big(\sigma r + (\mu+\sigma)(3\mu+\gamma+\sigma)\big) + (1-p)(\mu+\theta)\big((\mu+\sigma)\delta+\mu r\big)\Big)k \\ &+ \mu p(\gamma+\sigma+2\mu)(\mu+\theta)(\gamma+\mu+\sigma)\Big], \end{aligned}$$

$$\begin{aligned} k_2 = \frac{1}{G_3}\big[&\big(\sigma(1-q)(\mu+\theta+\xi\alpha)r + (\mu+\sigma)^2(\mu+\theta+\xi\alpha)\big)k^2 \\ &+ \big(((\delta+2\mu+r)(\sigma^2+(2\mu+\gamma)\sigma+\mu^2) + \ \mu^2\gamma)\alpha\xi \\ &+ (\mu+\theta)(\delta p+\delta+2\mu+r)(\sigma^2+(2\mu+\gamma)\sigma) + \mu^2(\mu+\theta)(pqr+\delta p+\delta+2\mu) \\ &+ \mu^2(r+\gamma)(1-p)(\mu+\theta)\big)k + \mu^2 p(\gamma+\sigma+\mu)^2(\mu+\theta)\big], \end{aligned}$$

and

$G_3 = (\mu+\sigma)(\mu+\theta+\xi\alpha)k + \mu p(\mu+\theta)(\gamma+\mu+\sigma)$.

Clearly that the characteristic equation (9) has a simple zero eigenvalue ($\lambda_1 = 0$), two negative eigenvalues: $\lambda_2 = -\mu$ and $\lambda_3 = -(\xi+\mu+\theta)$. Since $k_1 > 0$ and $k_2 > 0$, the two other eigenvalues are negative real, i.e., $\lambda_4, \lambda_5 \in \mathbb{R}^-$. The right eigen vector of $J(E_0, \beta^*)$ which corresponds to the zero eigenvalue $\lambda_1 = 0$ is

$$\vec{w} = \left[-\frac{w_5 C_1(\alpha\theta\xi+\mu^2+2\mu\theta+\theta^2)}{G_4\mu(\xi+\mu+\theta)} \quad -\frac{\xi w_5 C_1(\alpha\theta+\alpha\xi+\mu+\theta)}{G_4\mu(\xi+\mu+\theta)} \quad \frac{w_5 G_5}{G_4} \quad \frac{w_5 G_3}{G_4} \quad w_5\right]^T,$$

where

$$\begin{aligned} G_4 = {}&(\mu+\theta)\mu pr(1-q) + (kr(1-q)+r\gamma)(\alpha\xi+\mu+\theta) + (1-p)(\mu+\theta)(\delta\gamma+\mu\gamma) \\ &+ \alpha\xi(\delta\gamma+\mu\gamma), \end{aligned}$$

$G_5 = \xi(\mu+\sigma)(\mu+r+\delta)\alpha + (\mu+\theta)(\mu pq+\mu(1-p)+\sigma)r + (\mu+\theta)(1-p)(\mu+\sigma)(\mu+\delta)$,

and w_5 is any positive constant. The left eigen vector of $J(E_0, \beta^*)$ which corresponds to $\lambda_1 = 0$ is

$$\vec{v} = \left[0 \quad 0 \quad \frac{(\mu+\sigma)v_5}{\sigma} \quad \frac{(k\mu+k\sigma+\mu^2+\mu\gamma+\mu\sigma)v_5}{k\sigma} \quad v_5\right]^T$$

where v_5 is chosen such that $\vec{w}\cdot\vec{v} = 1$. Here, we get $w_5 = \frac{1}{((\mu+\sigma)(G_3+G_5)+\sigma G_4)k+\mu G_3(\gamma+\sigma+\mu)} > 0$ and $v_5 = k\sigma G_4 > 0$. Let us denote,

$$x_1 = S, x_2 = V, x_3 = E, x_4 = I, x_5 = L,$$
$$f_1 = \frac{\partial S}{\partial t}, f_2 = \frac{\partial V}{\partial t}, f_3 = \frac{\partial E}{\partial t}, f_4 = \frac{\partial I}{\partial t}, f_5 = \frac{\partial L}{\partial t}.$$

It is straighforward to show that

$$\begin{aligned} a = \sum_{k,i,j=1}^{5} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_k \partial x_j}(0,0) = &-\frac{2(\mu+\sigma)v_5 {w_5}^2 C_1(\alpha\theta\xi+\mu^2+2\mu\theta+\theta^2)G_3\beta}{\sigma {G_4}^2(\alpha\xi+\mu+\theta)\mu(\xi+\mu+\theta)} \\ &-\frac{2\alpha\beta(\mu+\sigma)v_5 {w_5}^2 C_1(\alpha\mu+\alpha\xi+\mu+\theta)G_3}{\sigma {G_4}^2\mu(\xi+\mu+\theta)} \\ &-\frac{2\beta p(\mu+\gamma+\sigma)v_5 {w_5}^2 G_2(\alpha\theta\xi+\mu^2+2\mu\theta+\theta^2)}{\sigma {G_4}^2(\alpha\xi+\mu+\theta)k(\xi+\mu+\theta)} < 0 \end{aligned}$$

and

$$b = \sum_{k,i=1}^{5} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta^*}(0,0) = \frac{(1-p)\Lambda(\mu+\theta)(\mu+\sigma)v_5 w_5 G_3}{\sigma G_4 \mu(\xi+\mu+\theta)}$$

$$+\frac{p\Lambda(\mu+\theta)(k\mu+k\sigma+\mu^2+\mu\gamma+\mu\sigma)v_5w_5G_3}{\sigma kG_4\mu(\xi+\mu+\theta)}>0.$$

Since $a<0$ and $b>0$, the well-known *Center Manifold theorem,* see Theorem 4.1 in (Castillo-Chavez & Song, 2004), says that a forward bifurcation occurs at $\Re_v=1$. This implies that if $\Re_v>1$ then the disease-free equilibrium point is unstable, while the endemic equilibrium point is locally asymptotically stable.

3. Numerical Simulation

In this subsection, we present several numerical simulations to illustrate and understand the spread of tuberculosis disease. We generate numerical simulations using the fourth-order Runge-Kutta method with step size $h=0.001$. The parameters for these simulations are shown in Table 1.

Based on the parameter values in Table 1 and $\beta=0.3, \alpha=0.2, \beta_1=0.06$, and $\xi=0.98$, we obtain $\Re_v=0.4470984426<1$. The Jacobian matrix evaluated at the disease-free equilibrium has eigenvalues $\lambda_1=-0.15, \lambda_2=-1.197$, and the other three eigenvalues are negative real number, since $l_1=1.986013450>0, l_2=0.3062159124, l_3=0.02314429664>0$, and $\Delta_2=l_1l_2-l_3=0.5850046240>0$. According to the *Routh-Hurwitz criterion*, the disease-free equilibrium P^0 is locally asymptotically stable. Figure 3 shows that the solution of the system converges to the disease-free equilibrium point $E_0=(6.0429, 27.2904, 0, 0, 0)$. This confirms the presence of TB stable steady-state when $\Re_v<1$ and the disease will die out by the time.

If we take $\beta=1.05, \xi=0.98$, and $\alpha=0.2$ then we have $\beta_1=\alpha\beta=0.2\times1.05=0.21$ and $\Re_v=1.5648445481>1$. We obtain the disease-free equilibrium point $E_0=(6.0429, 27.2904, 0, 0, 0)$ and the endemic equilibrium point $E_1=(4.1096, 14.3297, 6.6265, 0.3050, 7.6167)$. The Jacobian matrix evaluated at the disease-free equilibrium has eigenvalues $\lambda_1=-0.15, \lambda_2=-1.197$, and we get $l_1=1.532797076>0$, $l_2=-0.07219490620$, $l_3=-0.02364422675<0$, and $\Delta_2=-0.08701591435<0$. Since the *Routh-Hurwitz criterion* is not completely fulfilled, the other three eigenvalues are not all negative real number. Therefore, the disease-free equilibrium point is not stable. Next, the Jacobian matrix evaluated at the endemic equilibrium has eigenvalues $\lambda_1=0, \lambda_2=-0.15, \lambda_3=-1.197$, while the two other eigenvalues must both be negative since the quadratic equation $\lambda^2+k_1\lambda+k_2=0$ has $k_1=0.9348265461>0$ and $k_2=0.1192192459>0$. This $\lambda=0$ leads the system (1) to have a bifurcation phenomenon. We obtain $a=-2.414331455{v_5}{w_5}^2<0$ and $b=65.92824386v_5w_5>0$ with $v_5>0$ and $w_5>0$. Therefore, based on the well-known *Center Manifold theorem*, if $a<0$ and $b>0$ then system (1) undergoes a forward bifurcation which means when $\Re_v>1$ the endemic equilibrium point is locally asymptotically stable as seen in Figure 4(a). It confirms that the tuberculosis disease can be an endemic disease in the system, as shown in Table 1.

Table 1. Parameter values of the model (1)

Parameters	Descriptions	Value	Source
S^0	The initial number of susceptible individuals	21 millions	Assumed
V^0	The initial number of vaccinated individuals	1 million	Assumed
E^0	The initial number of exposed individuals	0.2 millions	Assumed
I^0	The initial number of actively-infected individuals	0.1 millions	Assumed
L^0	The initial number of low-risk latent individuals	8 millions	Assumed
Λ	Recruitment rate	5	(Sulayman et al., 2021)
θ	Rate at vaccine wanes	0.067	(Sulayman et al., 2021)
p	Fraction of fast disease progression	0.1	(Egonmwan and Okuonghae, 2019)
ξ	Rate of vaccinated individuals	0.3,0.98	(Sulayman et al., 2021)
β	Transmission rate	0.3,1.05	(Sulayman et al., 2021)
$\beta_1 = \alpha\beta$	Transmission rate from vaccinated individuals	0.06,0.21	(Sulayman et al., 2021)
α	Reduction in risk of infection due to vaccination	0.2	(Sulayman et al., 2021)
$1 - q$	Successful treatment rate	0.832	(Mengistu and Witbooi, 2019)
r	Treatment rate in infected class (I)	0.546	Fitted, (Mengistu and Witbooi, 2019)
γ	Treatment rate in latent class (E)	0.153	Fitted, (Mengistu and Witbooi, 2019)
k	Progression rate from latent class (E) to infected class (I)	0.02	(Sulayman et al., 2021)
σ	Progression rate from low-risk latent class (L) to latent class (E)	0.0013	Fitted, (Mengistu and Witbooi, 2019)
μ	Natural death rate	0.15	(Sulayman et al., 2021)
δ	Tuberculosis induced death rate	0.17	(Mengistu and Witbooi, 2019)

If we decrease the vaccine efficacy into $\xi = 0.3$, then we have $\Re_v = 2.957491030 > 1$. We obtain the disease-free equilibrium point $E_0 = (13.99097356, 19.34235977, 0, 0, 0)$ and the endemic equilibrium point $E_1 = (4.9092, 4.3008, 10.4690, 0.5973, 12.3800)$. The Jacobian matrix evaluated at the disease-free equilibrium has eigenvalues $\lambda_1 = -0.15, \lambda_2 = -0.517$, and we get $l_1 = 0.018247776 > 0$, $l_2 = -0.5848585413$, $l_3 = -0.081939999 < 0$, and $\Delta_2 = 0.07126763135 > 0$. We understand that the *Routh-Hurwitz criterion* is not completely satisfied, and as a result the other three eigenvalues are not all negative real number. Therefore, the disease-free equilibrium point is not stable. Now, the Jacobian matrix evaluated at the endemic equilibrium has eigenvalues $\lambda_1 = 0, \lambda_2 = -0.15, \lambda_3 = -0.517$, while the two other eigenvalues must both be negative since the quadratic equation $\lambda^2 + k_1\lambda + k_2 = 0$ has $k_1 = 0.8435775383 > 0$ and $k_2 = 0.1053354211 > 0$. This $\lambda = 0$ causes the system (1) to undergo a bifurcation phenomenon. Finally, we have $a = -21.62806725 v_5 {w_5}^2 < 0$ and $b = 184.6966099 v_5 w_5 > 0$ with $v_5 > 0$ and $w_5 > 0$. Therefore, based on the *Center Manifold theorem*, again if $a < 0$ and $b > 0$ then system (1) undergoes a forward bifurcation. The system (1) undergoes the change from the unstable disease-free equilibrium point into the locally

asymptotically stable endemic equilibrium point, see also Figure 4(b), as shown in Figure 3 and Figure 4.

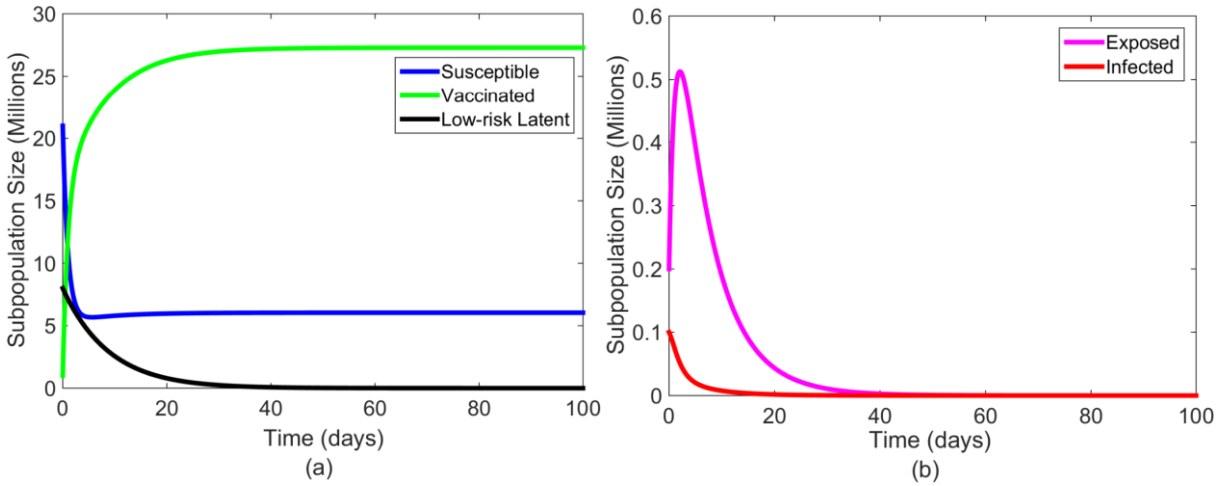

Figure 3. The solution of model (1) converges to the disease-free equilibrium point with parameters in Table 1 at time interval [0,100] for: (a) *SVL* subpopulation in [0, 30] and (b) *EI* subpopulation individuals in [0, 0.6] millions

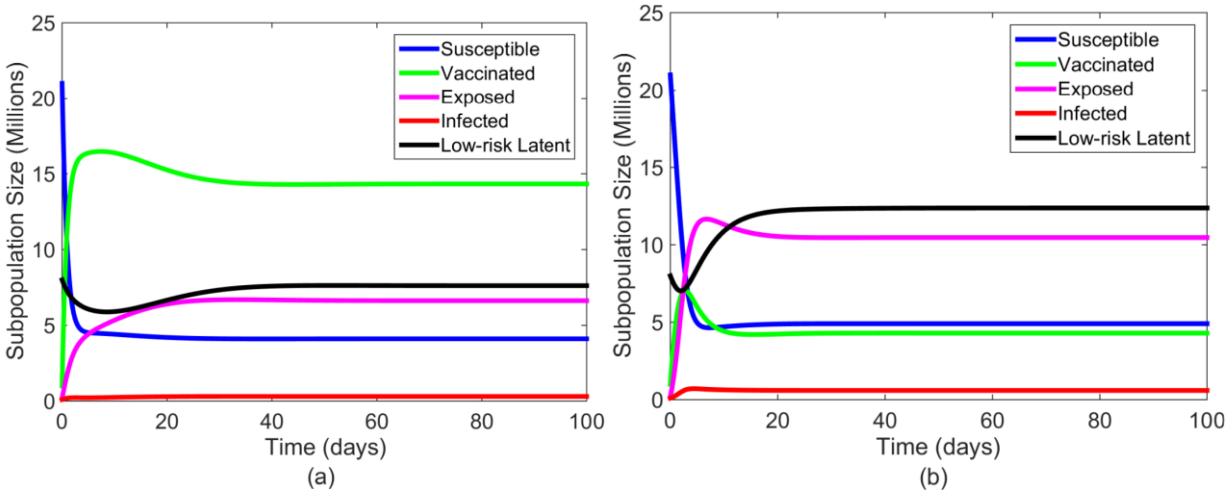

Figure 4. Simulation of endemic equilibrium point stability with different value of vaccination rate: (a) $\xi = 0.98$ and gives $\Re_v = 1.5648445481$, (b) $\xi = 0.3$ and gives $\Re_v = 2.957491030$.

All these results verify that in this research a forward bifurcation occurred, which is different from what Sulayman et al. (2021) has found. Figure 3 illustrates that the bigger rate of vaccination ξ, the bigger $\Re_v$ is. Moreover, from Figure 3 and Figure 4 we understand that the bigger parameter of disease transmission rate, β, the bigger $\Re_v$ is.

D. CONCLUSION AND SUGGESTIONS

This work presents a proposed basic tuberculosis SVEIL model with imperfect vaccination. As an impact of imperfect vaccination, we assume that vaccinated individuals can still be infected and go to exposed class. We also consider the fast and slow progression of infection rate from susceptible class. Our proposed model includes the treatment in both latent and actively-infected subpopulation.

The positivity and the bounded of each solution in this model has been proven. This model has two equilibrium points: a disease-free equilibrium point and an endemic equilibrium point.

The disease-free equilibrium point always exist whenever the effective reproduction number ($\Re_v$) is less than unity. Otherwise, a unique endemic equilibrium point exists whenever the effective reproduction number is greater than unity. Using linearization, Jacobian matrix, and the *Routh-Hurwitz criterion*, we showed that the disease-free equilibrium point is locally asymptotically stable when $\Re_v < 1$ and $2\mu + \delta + \sigma + r(1-q) > (C_2 + C_3)$. Using the *Center Manifold theorem,* we found that this model undergoes a forward bifurcation when $\Re_v = 1$ and the endemic equilibrium point is locally asymptotically stable when $\Re_v > 1$. The numerical simulations illustrate that the effective reproduction number is directly proportional to the rate of disease transmission and reversely proportional to the rate of vaccination. It confirms the result that the effectiveness of the imperfect vaccine implemented in the model can effectively reduce the tuberculosis disease.

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