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RESEARCH ARTICLE

# The Dynamics of Tuberculosis through BSEIR Model with Immigration in Malaysia

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Abstract Tuberculosis or known as TB is an airborne disease that exists in Malaysia caused by *Mycobacterium Tuberculosis*. Despite that, TB infection is curable with early diagnosis and treatment. The disease can be prevented through Bacillus Calmette-Guérin (BCG) vaccine, which is given among infants at birth. Numerous mathematical models on infectious diseases have been formulated in earlier studies since it is crucial to comprehend infectious disease transmission patterns and predict future outcomes. However, there is minimal study on the dynamics of TB transmission, particularly in Malaysia concerning immigration. Hence, this study aims to formulate a mathematical BCG-vaccinated, susceptible, exposed, infected, and recovered (BSEIR) model for TB infection in Malaysia by considering the immigration parameter. The model parameters are obtained from the literature and some with reported data in 2013 as initial value for the simulation using MAPLE software. The obtained results revealed that the basic reproduction number, $R_0$ for the model is more than one. The graphical plot shows that the BSEIR model with immigration demonstrates a rise in TB-infected cases. The best strategy to lessen the number of infected individuals in Malaysia is by increasing the transmission rate and recovery rate. Additionally, the local stability analysis on the diseases-free equilibrium point and sensitivity analysis of its parameter is also provided and discussed. To conclude, a proper screening test should be mandated by the authorities before permitting new immigrants and refugees into Malaysia.

**Keywords**: Tuberculosis (TB) Model, Infectious Disease, Basic Reproduction, Disease-free equilibrium.

## Introduction

Tuberculosis (TB) is one of the global leading causes of death where a total of 1.5 million people dying from the illness in 2020. The disease exists throughout the world including Malaysia where the South-East region had the highest number of new TB cases with 43% of all new cases, followed by the African region which had 25% of new cases, and the Western Pacific with 18% of cases in 2020. The reported cases of TB in Malaysia between 1990 and 2020 are depicted in Figure 1. According to the data, the trend of new TB incidence cases was rising and slightly decrease in 2020. Meanwhile, World Health Organization stated that the annual number of TB mortality dropped by 45% nationwide between 2000 and 2019 [1]. However, the 2030 Sustainable Development Goals (SDGs) target of 90% mortality reduction from the 2015 baseline and extinction of the TB endemic has yet to be met.

The disease can be categorized into two types, namely active TB, and latent TB, which is not contagious to others but possibly active among people with weakened immune systems. Approximately 10% of patients with latent TB would be responsive during half of the first year and the balance over their lifetime, primarily by reactivation of the dormant tubercle bacilli obtained from original infection or less commonly reinfection [2]. The germs can be transmitted through the lungs or other parts of the body among people with active TB where its complications might develop over weeks or months if the immune system fails to suppress the infection. TB usually affects the lungs, but any part of the body like the abdomen, glands, bones, and nervous system. Coughing up mucus or blood at times, chest pains, weakness, loss of appetite or unintentional weight loss, fever, and night sweats are all common signs of active lung TB [3].

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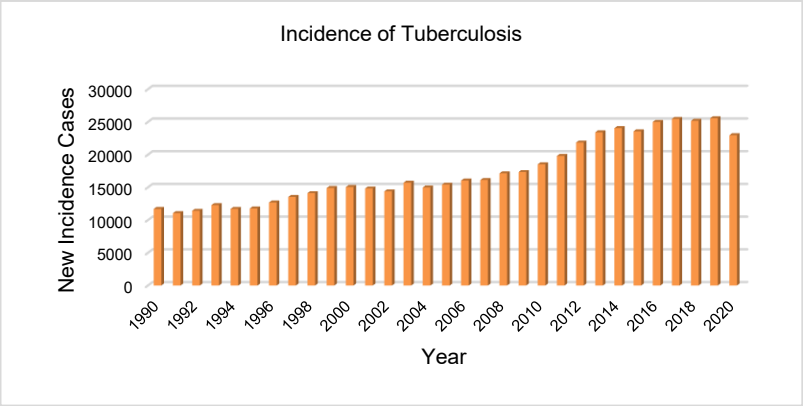


**Figure 1.** New Incidence Cases of Tuberculosis in Malaysia over years [21]

*Bacillus Calmette-Guérin* vaccine or known as BCG is utilized in countries with a high prevalence of TB including Malaysia. The national BCG immunization program in Malaysia was implemented around 1962 where it is administered to infants at birth. Initially in 2016 up until now, BCG revaccination is offered to children without BCG scar or a history of BCG vaccination. About 98.48% of infants received the BCG vaccine in Malaysia by 2019 [4]. However, BCG does not provide complete protection against TB infection, but TB illness is curable if early diagnosis and treatment are practiced. Thus, mathematical modelling of TB vaccination has gained more importance to make accurate predictions. There are numerous extended vaccination mathematical models on infectious disease have been published in the literature. Nasution *et al*. [5] suggested SIR model with a vaccination compartment to investigate the effectiveness of vaccines in lessening TB transmission. Next, Liu *et al*. [6] proposed a new vaccination strategy that is the combination of constant vaccination and pulse vaccination through BSEIR model. Ucakan *et al*. [7] then investigated the TB dynamics in Turkey by comparing three models: SIR, SEIR and BSEIR models. Nkamba *et al*. [8] extended TB transmission through SV-ELI model which consists susceptible, vaccinated, early latent, late latent and infectious classes, concerning both effective contact and vaccination rate. The study proved that immunization coverage did not fully prevent TB since the effective contact rate has a major impact on the spread of the disease.

Immigration activities have a major effect on the evolution of healthcare systems, economic and social problems globally including in Malaysia. Malaysia as one of the leading economies in Southeast Asia had attracted laborers from neighbouring countries like Bangladesh, Nepal, Myanmar, and Cambodia to work with around 1.24 million Indonesians were the main contributor of immigrants [9]. The immigrants mostly work in manufacturing, plantation, agriculture, services, and domestic helpers' industries. Hence, the economic growth in this country was undeniably rising due to their contributions but the possibility that immigrant laborers may carry the disease is more alarming. Furthermore, Malaysia has accepted about 130 thousand refugees alongside the immigrants in 2020 and the refugee population was steadily rising over the years compared to about 90 thousand back then in 2011 [10]. Wong and Lee [1] studied the occurrence and health risk of TB and latent TB infection (LTBI) among Malaysian refugee children in three learning centres. The finding discovered that the occurrence of latent TB infection within Malaysia refugee children is significantly greater, with nearly one (12.8%) in every eight refugee children having LTBI compared to Germany and the United States where the prevalence is just 6%. Meanwhile, Eiset and Wejse [11] found that the most common infectious diseases among refugee and asylum seeker populations in Europe are latent TB (9%-45%), active TB up to 11% and hepatitis B with 12%.

A mathematical model is applied in the medical field to assist authorities in taking the best precautionary measures and preventing the spread of infection diseases. Furthermore, the mathematical model offers essential information in investigating the intensity of disease intervention and estimating the likelihood and severity of the disease [12]. Kermack and McKendrick [13] were among the first who introduced the compartment dynamic model in 1927. They employ differential equations to study the infectious disease spread rule, in which the entire population comprises three compartments: Susceptible (S), infected (I) and recovered (R) called as the SIR-type model. However, the classic SIR was considered impractical since the model overlooks other control strategies like vaccination, treatment, quarantine and the influence of age or gender in explaining the disease dynamics [7]. The classic SIR model has been widely implemented and modified for several infectious diseases such as measles [14], dengue [15] and tuberculosis [7].

Hence, we would like to extend an infectious disease BSEIR model by [6] which considers the BCG vaccination compartment and the immigrant rate as a parameter. Since Malaysia has relied on the BCG vaccine for a relatively long time to prevent TB infection, it became one of the essential factors to consider, which is why the BSEIR model by was chosen as opposed to other models. According to [16], immigrants could be the epidemiological creator of an epidemic crisis since they are possible to transmit the infection from their home countries. Furthermore, the refugees are categorised as a high-risk TB population since they were not subjected to a thorough medical screening upon their arrival in Malaysia [1]. Thus, this study aims to propose a BSEIR model with an immigration model, analyses the influence of immigration activities on TB transmission and determine the disease-free equilibrium state for the model. Moreover, based on our review of literature, such a comprehensive study has still not been initiated for TB in Malaysia thus far.

The structure of this study is organized as follows: the modified BSEIR model for describing the TB dynamics and the estimation of model parameters is introduced. Then, the stability analysis of disease-free equilibrium and the sensitivity analysis of the parameters of the model is discussed. Next, the numerical simulation for the model is presented. Finally, the conclusion is summarized in the last section.

# Materials and Methods

## Model Formulation

In this section, we present the proposed mathematical model of TB infection. To formulate the BSEIR model with immigration, firstly, we refer the modified mathematical model by Liu *et al*. [9]. The population is assumed to be closed which divided into five compartments, BCG vaccinated ($B$), susceptible ($S$), exposed ($E$), infected ($I$) and recovered ($R$). However, there is no migrant population involved in the proposed model. Thus, the model is represented as,

$$\begin{aligned}
\frac{dB(t)}{dt} &= \alpha p - kB(t) \\
\frac{dS(t)}{dt} &= kB(t) + \alpha(1-p) - \frac{\beta S(t) I(t)}{N} - \mu S(t) \\
\frac{dE(t)}{dt} &= \frac{\beta S(t) I(t)}{N} - (\epsilon + \mu) E(t) \\
\frac{dI(t)}{dt} &= \epsilon E(t) - (\gamma + \mu + d) I(t) \\
\frac{dR(t)}{dt} &= \gamma I(t) - \mu R(t)
\end{aligned} \tag{1}$$

with subject to $B(0) \geq 0,\ S(0) \geq 0,\ E(0) \geq 0,\ I(0) \geq 0,\ R(0) \geq 0,$ and all the parameters have positive values. The total population, $N = B(t) + S(t) + E(t) + I(t) + R(t)$ where the natural death rate and birth rate are not regarded as being equal.

In comparison to the standard SIR model, the BSEIR model incorporates the BCG vaccination class which denoted as *B*, signifies the number of new-borns who received BCG vaccine. They will not get infected even if they come into contact with infected individual since they are immune to the disease during this BCG protection period. Hence, the percentage of successfully immunised new-borns is indicated by the parameter $p$ ($0 < p < 1$). Next, those who are susceptible and at risk of contracting TB infection are depicted as $S$ class. While exposed class denoted as $E$, refers to those who are infected but show not outward signs of illness.

Furthermore, the natural death rate in class $B$ is disregarded since children in Malaysia die of natural causes at a rate of about 3.3 [17] and the BCG vaccine is only expected to prevent TB transmission for 10 to 15 years. Since the BCG vaccine has a minimal effect, so the immunised individuals revert to the susceptible class at a rate of $k$. These variables are functions of time where each parameter will be treated as a nonnegative constant.

Further we look at modified SEIR model without vaccination compartment proposed by Widyaningsih *et al*. [18] which the study includes an immigration parameter where the equation is expressed as,

$$\frac{dS}{dt} = \mu N - \frac{\beta S I}{N} - (\mu + \alpha) S$$

$$\begin{aligned}\frac{dE}{dt} &= \frac{\beta SI}{N} - (\epsilon + \mu + \alpha)E \\ \frac{dI}{dt} &= \epsilon E + \alpha N - (\gamma + \mu + \alpha)I \\ \frac{dR}{dt} &= \gamma I - (\mu + \alpha)R\end{aligned} \tag{2}$$

with subject to $S(0) \geq 0,\ E(0) \geq 0,\ I = (0) \geq 0,\ R(0) \geq 0$, and these parameters have nonnegative values.

Thus, we develop a TB transmission model using the BSEIR model by considering the immigration impact. The proposed model is a modified model from equation (1) and equation (2). We assume that there are no immunizations for new immigrants and that they are all infected in this model. Hence, the number of infected individual rises by as much as $N$ if $\alpha$ is the immigrant rate. Since we assume that the population is constant, the rate of natural death at each class is assumed to be $\mu$ change to be $\mu + \alpha$. The modified BSEIR model employed in this study can be seen in the following expression,

$$\begin{aligned}\frac{dB}{dt} &= \Lambda p - kB \\ \frac{dS}{dt} &= kB + \Lambda(1-p) - \frac{\beta SI}{N} - (\mu + \alpha)S \\ \frac{dE}{dt} &= \frac{\beta SI}{N} - (\epsilon + \mu + \alpha)E \\ \frac{dI}{dt} &= \epsilon E + \alpha N - (\gamma + \mu + d + \alpha)I \\ \frac{dR}{dt} &= \gamma I - (\mu + \alpha)R\end{aligned} \tag{3}$$

with subject to

$$B(0) \geq 0,\ S(0) \geq 0,\ E(0) \geq 0,\ I = (0) \geq 0,\ R(0) \geq 0,$$

where all the parameters have nonnegative values. The number of new TB infections per unit time, the disease mortality rate and the rate of natural death are denoted by parameter $\beta$, $d$ and $\mu$ respectively. The parameter $\alpha$ represents immigrant rate. The progression rate from exposed to infected class is indicated as $\epsilon$ while the infected individuals are recovered at the rate $\gamma$. The schematic diagram of model (3) is depicted in Figure 2, and the description of the variables and parameters are given in Table 1 and Table 2, respectively.

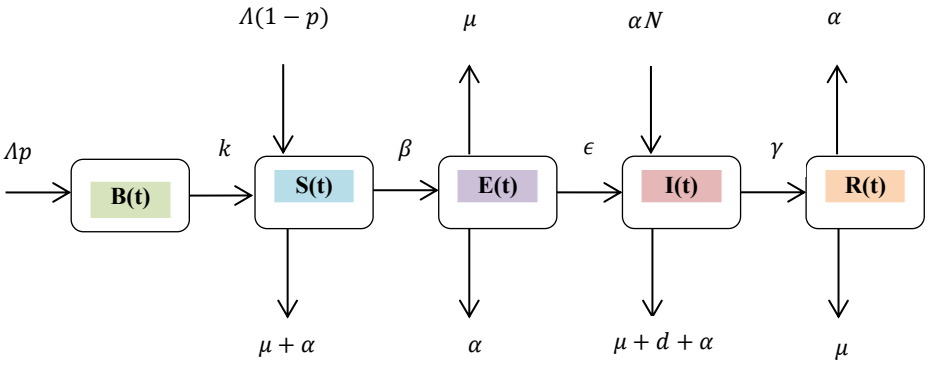


**Figure 2.** Schematic flow diagram of BSEIR model

## Estimation of Model Parameters

In this subsection, we estimate the initial model parameters based on the actual TB incidence data in Malaysia obtained from World Health Organization (WHO) in 2013. Some of the parameters obtained from the literature [7], as presented in Table 2 while others were estimated. The natural death rate $\mu$ is approximately estimated as $\mu = \frac{166{,}507}{32{,}657{,}300} = 0.0051$ , where 166,507 is the number of death individuals and 32,657,300 is the population of Malaysia as reported by Department of Statistics Malaysia in 2020.

Using the same total population, we assumed that the recruitment rate $\Lambda = b \times N$ [7], where $b = \frac{472,608}{32,657,300} = 0.0145$ is the natural birth rate [17], so that $\Lambda$ = 473,531 per year. Besides, the estimated immigrant rate for 2020 is roughly calculated as follows $\alpha = \frac{3,476,560}{32,657,300} = 0.1065$. The basic reproduction number is calculated using equation (6) with the parameter values given in Table 2.

**Table 1.** Description of variables of model (3) and Initial Values

| Variable | Description | Value | Source |
|---|---|---|---|
| N | Total population | 32657300 | [17] |
| $B(0)$ | Initial number of BCG vaccinated | 463156 | [17] |
| $S(0)$ | Initial number of susceptible | 30387923 | [17] |
| $E(0)$ | Initial number of exposed | 11709 | Estimated |
| $I(0)$ | Initial number of infected | 23417 | [17] |
| $R(0)$ | Initial number of recovered | 18747 | [17] |

**Table 2.** Description of parameters of model (3) and its value

| Parameter | Description | Value | Source |
|---|---|---|---|
| $b$ | Natural birth rate | 0.0145 | Estimated |
| $\Lambda$ | Recruitment rate | 473531 $year^{-1}$ | Estimated |
| $p$ | Fraction of the successfully vaccinated | 0.948 | [7] |
| $k$ | Rate of waning immunity | 0.054 | [7] |
| $\beta$ | Transmission rate | 0.955 | [7] |
| $\mu$ | Natural death rate | 0.0051 | [7] |
| $\epsilon$ | Latent period | 1.435 | [7] |
| $d$ | Disease-induced death rate | 0.03 | [7] |
| $\gamma$ | Recovery rate | 0.935 | [7] |
| α | Immigrant rate | 0.1065 | [17] |
| $R_0$ | Reproduction number | 1.955 | Calculated |

## Basic Reproduction Number, $R_0$

A mathematical expression, $R_0$ or the basic reproduction number explains the dynamic of disease transmission. It describes the average number of individuals who are most likely to catch contagious illness from a single infected person. Thus, by examining $R_0$, one can verify how widely a disease is spread in the population. If $R_0$ less than 1, each existing infection results in fewer than one new infection, where the illness will progressively deteriorate and eventually die out. But if $R_0$ is greater than 1, each existing infection spreads to at least one additional individual resulting in an epidemic. Hence, we consider the generation matrix method to evaluate $R_0$. The method was first proposed by [20] and modified by [21].

To evaluate the basic reproduction number $R_0$ using a next generation matrix method [21], suppose there are $n$ disease compartments in the system (3). Let $X = (x_1, x_2, \dots, x_n)$ where $i = 1,2, \dots, n$ represent individuals in $ith$ infected class. Next, the rate of occurrence of new infections in $ith$ class is denoted by $F_i(x)$ and the transfer rate of individuals into $ith$ class is denoted by $V_i(x)$. The next step is to linearize the $ith$ infected class with respect to the disease-free equilibrium to determine the rate of disease spread within the population. Hence, using the partial derivative of $F_i(x)$ and $V_i(x)$, the generation matrix is calculated as follows:

$$F_i(x) = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right] \quad \text{and} \quad V_i(x) = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right], i = 1,2,\dots,n \tag{4}$$

where $x_0$ is the disease-free equilibrium point. The basic reproduction number $R_0$ will be found through the dominant eigenvalue of matrix $FV^{-1}$. Note that for system (3) we have two classes that spread the infection which are $E$ and $I$ given as:

$$\frac{dE}{dt} = \frac{\beta SI}{N} - (\epsilon + \mu + \alpha)E \tag{5}$$
$$\frac{dI}{dt} = \epsilon E + \alpha N - (\gamma + \mu + d + \alpha)I$$

From $(6)$, we obtained

$F_1 = \frac{\beta SI}{N}$, $F_2 = 0$, $V_1 = -(\epsilon + \mu + \alpha)E$, $V_2 = \epsilon E + \alpha N - (\gamma + \mu + d + \alpha)I$, where

$$F = \begin{bmatrix} \frac{\partial(F_1)}{\partial E} & \frac{\partial(F_1)}{\partial I} \\ \frac{\partial(F_2)}{\partial E} & \frac{\partial(F_2)}{\partial I} \end{bmatrix} = \begin{bmatrix} 0 & \frac{\beta S}{N} \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & \beta S \frac{k(\mu+\alpha)}{\Lambda(p(\mu+\alpha)+k)} \\ 0 & 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} \frac{\partial(V_1)}{\partial E} & \frac{\partial(V_1)}{\partial I} \\ \frac{\partial(V_2)}{\partial E} & \frac{\partial(V_2)}{\partial I} \end{bmatrix} = \begin{bmatrix} \epsilon + \mu + \alpha & 0 \\ -\epsilon & \gamma + \mu + d + \alpha \end{bmatrix}$$

Then, the matrices F and V are evaluated at the equilibrium point $x_0$, are given respectively, as follows:

$$F = \begin{bmatrix} 0 & \beta(\frac{\Lambda}{\mu+\alpha})\frac{k(\mu+\alpha)}{\Lambda(p(\mu+\alpha)+k)} \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & \frac{\beta k}{p(\mu+\alpha)+k} \\ 0 & 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} \epsilon + \mu + \alpha & 0 \\ -\epsilon & \gamma + \mu + d + \alpha \end{bmatrix}$$

The inverse of matrix $V$ is given by:

$$V^{-1} = \begin{bmatrix} \frac{1}{\epsilon+\mu+\alpha} & 0 \\ \frac{\epsilon}{(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)} & \frac{1}{\gamma+\mu+d+\alpha} \end{bmatrix}$$

So, the product of $FV^{-1}$ is obtained as:

$$FV^{-1} = \begin{bmatrix} \frac{\beta k\epsilon}{(\mu+\alpha)(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)} & \frac{\beta k}{(\mu+\alpha)(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)} \\ 0 & 0 \end{bmatrix}$$

The $R_0$ is defined by the spectral radius $\rho$, which is the dominant eigenvalue in magnitude of the matrix $FV^{-1}$

$$\rho(FV^{-1}) = \begin{bmatrix} \frac{\beta k\epsilon}{(\mu+\alpha)(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)} - \lambda & \frac{\beta k}{(\mu+\alpha)(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)} \\ 0 & -\lambda \end{bmatrix}$$

This implies that either $\lambda = 0$ or $\lambda = \frac{\beta k\epsilon}{(p\,(\mu+\alpha)+k)(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)}$. Therefore, $R_0$ of system (3) can be written as

$$R_0 = \frac{\beta k\epsilon}{(p\,(\mu+\alpha)+k)(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)} \tag{6}$$

## Stability Analysis of Disease-free Equilibrium

In this subsection, the local stability of the disease-free equilibrium is examined through Jacobian matrix. A state of no infection in the population is known as disease-free equilibrium. Hence, all the infected class will be zero and only susceptible individuals exist in the population [19]. The disease-free equilibrium point of the system (3) are determined by equated the derivatives to zero,

$$\frac{dB}{dt} = \frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$$

This leads to

$$\Lambda p - kB = 0 \tag{7}$$
$$kB + \Lambda(1-p) - \beta SI - (\mu+\alpha)S = 0 \tag{8}$$
$$\beta SI - (\epsilon+\mu+\alpha)E = 0 \tag{9}$$
$$\epsilon E + \alpha - (\gamma+\mu+d+\alpha)I = 0 \tag{10}$$
$$\gamma I - (\mu+\alpha)R = 0 \tag{11}$$

from (4), we get

$$B = \frac{\Lambda p}{k} \tag{12}$$

while adding (5) and (6) by putting (9), we get

$$S = \frac{\Lambda}{\mu+\alpha} \tag{13}$$

from (6) we obtain

$$E = \frac{\beta SI}{\epsilon+\mu+\alpha} \tag{14}$$

from (8) we get that

$$R = \frac{\gamma I}{\mu+\alpha} \tag{15}$$

Consequently, for $I = 0$, a disease-free equilibrium of the model exists at:

$$x_0 = (B^*, S^*, E^*, I^*, R^*) = \left(\frac{\Lambda p}{k}, \frac{\Lambda}{\mu+\alpha}, 0, 0, 0\right) \tag{16}$$

**Theorem 2.1**. *The disease-free equilibrium, $x_0$ of the system (3) is locally asymptotically stable when $R_0 < 1$, otherwise unstable.*

*Proof.* It is sufficient to show that all eigenvalues of the Jacobian matrix of the system (3), evaluated at $x_0$, have negative real parts, in order to examine the local stability of $x_0$. The Jacobian matrix of the system (3) is calculated as follows:

$$\begin{bmatrix} \frac{dB}{dt} \\ \frac{dS}{dt} \\ \frac{dE}{dt} \\ \frac{dI}{dt} \\ \frac{dR}{dt} \end{bmatrix} = \begin{bmatrix} \Lambda p - kB \\ kB + \Lambda(1-p) - \beta SI - (\mu+\alpha)S \\ \beta SI - (\epsilon+\mu+\alpha)E \\ \epsilon E + \alpha - (\gamma+\mu+d+\alpha)I \\ \gamma I - (\mu+\alpha)R \end{bmatrix},$$

The partial derivatives of each component (B, S, E, I, R) with respect to each other component in represents as follows:

$$J(x_0) = \begin{bmatrix} \frac{\partial B}{\partial B} & \frac{\partial B}{\partial S} & \frac{\partial B}{\partial E} & \frac{\partial B}{\partial I} & \frac{\partial B}{\partial R} \\ \frac{\partial S}{\partial B} & \frac{\partial S}{\partial S} & \frac{\partial S}{\partial E} & \frac{\partial S}{\partial I} & \frac{\partial S}{\partial R} \\ \frac{\partial E}{\partial B} & \frac{\partial E}{\partial S} & \frac{\partial E}{\partial E} & \frac{\partial E}{\partial I} & \frac{\partial E}{\partial R} \\ \frac{\partial I}{\partial B} & \frac{\partial I}{\partial S} & \frac{\partial I}{\partial E} & \frac{\partial I}{\partial I} & \frac{\partial I}{\partial R} \\ \frac{\partial R}{\partial B} & \frac{\partial R}{\partial S} & \frac{\partial R}{\partial E} & \frac{\partial R}{\partial I} & \frac{\partial R}{\partial R} \end{bmatrix} \tag{17}$$

and evaluated equilibrium points to decide on the local stability which is directly determined by the eigenvalues λ as follows:

$$|J(x_0) - \lambda I| = 0 \tag{18}$$

$$J(x_0)=\begin{bmatrix} -k & 0 & 0 & 0 & 0 \\ k & -\frac{\beta I}{N}-(\mu+\alpha) & 0 & -\frac{\beta S}{N} & 0 \\ 0 & \frac{\beta I}{N} & -(\epsilon+\mu+\alpha) & \frac{\beta S}{N} & 0 \\ 0 & 0 & \epsilon & -(\gamma+\mu+d+\alpha) & 0 \\ 0 & 0 & 0 & \gamma & -(\mu+\alpha) \end{bmatrix}$$

By substituting the DFE point, $(B^*,S^*,E^*,I^*,R^*)=\left(\frac{\Lambda p}{k},\frac{\Lambda}{\mu+\alpha},0,0,0\right)$ into $J(x_0)$, the Jacobian matrix $J(x_0)$ for system (3) is obtained as:

$$J(x_0)=\begin{bmatrix} -k & 0 & 0 & 0 & 0 \\ k & -(\mu+\alpha) & 0 & -\frac{\beta\Lambda}{p(\mu+\alpha)+k} & 0 \\ 0 & 0 & -(\epsilon+\mu+\alpha) & \frac{\beta\Lambda}{p(\mu+\alpha)+k} & 0 \\ 0 & 0 & \epsilon & -(\gamma+\mu+d+\alpha) & 0 \\ 0 & 0 & 0 & \gamma & -(\mu+\alpha) \end{bmatrix}$$

with eigenvalues $\lambda$

$$|J(x_0)-\lambda I|=0$$

$$J(x_0-\lambda)=\begin{bmatrix} -k-\lambda & 0 & 0 & 0 & 0 \\ k & -(\mu+\alpha)-\lambda & 0 & -\frac{\beta\Lambda}{p(\mu+\alpha)+k} & 0 \\ 0 & 0 & -(\epsilon+\mu+\alpha)-\lambda & \frac{\beta\Lambda}{p(\mu+\alpha)+k} & 0 \\ 0 & 0 & \epsilon & -(\gamma+\mu+d+\alpha)-\lambda & 0 \\ 0 & 0 & 0 & \gamma & -(\mu+\alpha)-\lambda \end{bmatrix}$$

The calculated eigenvalues of the matrix are $\lambda_1=-k$, $\lambda_2=-\mu-\alpha$, the remaining roots are determined by roots of the quadratic equation

$$a_0\lambda^2+a_1\lambda+a_2=0, \tag{19}$$

where

$$\begin{aligned} a_0&=1>0, \\ a_1&=(\epsilon+2\mu+\gamma+d+2\alpha)>0, \\ a_2&=(\epsilon+\mu+\alpha)(\gamma+\mu+d+\alpha)(1-R_0). \end{aligned} \tag{20}$$

The local stability of the equilibrium $x_0$ is determined by following the Routh-Hurwitz criterion on the quadratic equation (19). For a quadratic equation, the required condition of the stability is given by

$$a_0>0, a_1>0, a_2>0,$$

that is saying all coefficients of the quadratic equation must be greater than zero. It is obvious that from (20), $a_0$ and $a_1$ are always positive. Meanwhile, for $a_2$ to be positive, $R_0<1$. Thus, the following results can be drawn:

- If $R_0<1$, then the coefficient $a_2>0$. Hence, all roots of characteristic equation (19) are negative. Therefore, $E_0$ is locally asymptotically stable.
- If $R_0>1$, $a_2<0$, then there exists at least one positive root for the characteristic equation (19). Therefore, $E_0$ is unstable.

Thus, $x_0$ is locally asymptotically stable when $R_0<1$ and it is unstable when $R_0>1$.

## Sensitivity Analysis of $R_0$

The impact of the model parameters is determined through the local sensitivity analysis using the normalized forward sensitivity index method described in [22] as shown in the Definition 2.1. Sensitivity analysis enables to measure any significant difference in the state variable when a parameter changes. Hence, we use it in this study to determine parameters that have a significant impact on the basic reproduction number $R_0$. With this analysis, we can identify parameters that significantly affect the disease transmission and indirectly help the health authorities to develop effective intervention strategies in preventing the epidemic in a population.

**Definition 2.1** The normalized forward sensitivity index of a variable, $u$, that depends differentiably on a parameter, $q$, is defined by

$$\Upsilon_q^u = \frac{\partial u}{\partial q} \times \frac{q}{u} \tag{21}$$

As we have an explicit formula of $R_0$ in (20), we derive an analytical expression of the sensitivity index of the basic reproduction number $R_0$ by following the Definition 2.1, to all model parameters of system (3). Thus, the general expression of the sensitivity index of the $R_0$ is given by:

$$\Upsilon_q^{R_0} = \frac{\partial R_0}{\partial q} \times \frac{q}{R_0} \tag{22}$$

The sensitivity indices of the basic reproduction number with respect to all model parameters are calculated using the formula (22) and are tabulated in Table 3. However, we are concerned about four parameters: p, k, β, and γ, as these parameters are expected to have a significant impact on the transmission of the disease. Parameter $p$ is the fraction of vaccinated newborns and $\frac{\partial R_0}{\partial p} < 0$, while parameter $\gamma$ is the rate of recovered individuals and $\frac{\partial R_0}{\partial \gamma} < 0$. Thus, by rising both of parameter $\gamma$ and $p$, the TB transmission can be controlled since the number of infected individuals are falling off. Besides, $\frac{\partial R_0}{\partial k} > 0$, therefore, the parameter $k$ (waning immunity rate) has a positive effect on $R_0$. It can be said that a higher $k$ rate cause a rising of infected population. Also, $\frac{\partial R_0}{\partial \beta} > 0$ which depicts that a smaller number of transmission rate $\beta$ lead to a lesser number of infected individuals.

**Table 3.** Sensitivity Indices of $R_0$ with respect to model parameters

| Parameter | Description | With Immigration | Without Immigration |
|---|---|---|---|
| $p$ | successful vaccinated newborns | $-0.6984$ | $-0.0867$ |
| $k$ | progression rate from B to S class | $+0.6621$ | $+0.0822$ |
| $\beta$ | transmission rate | $+1$ | $+1$ |
| $\mu$ | natural death rate | $-0.03721$ | $-0.09098$ |
| $\epsilon$ | latent period | $+0.0722$ | $+0.00354$ |
| $d$ | disease-induced death rate | $-0.02787$ | $-0.03092$ |
| $\gamma$ | recovery rate | $-0.8685$ | $-0.9638$ |
| α | immigrant rate | $-0.8209$ | - |

# Results and Discussion

To illustrate the numerical results, the following values were taken for the initial conditions to mimic TB infection in Malaysia. According to Department of Statistic Malaysia, the population in the 2013 census is estimated as 30,904,952 [17]. Since the 2013 epidemic data has been taken into consideration, the total initial population has been accepted as $N(0)$ = 30,904,952 and the initial infected population as $I(0)$ = 23,417 as the same reported data. While $B(0)$ has been estimated considering the number of newborns in recent years. The rate of exposed individuals, $E(0)$ has been assumed by comparing it to the data from Malaysia and the literature [7]. Then, $R(0)$ is the number of successful treated TB patients in Malaysia in 2013. The formula for initial susceptible populations for the BSEIR is considered by,

$$S(0) = N - B(0) - E(0) - I(0) - R(0)$$

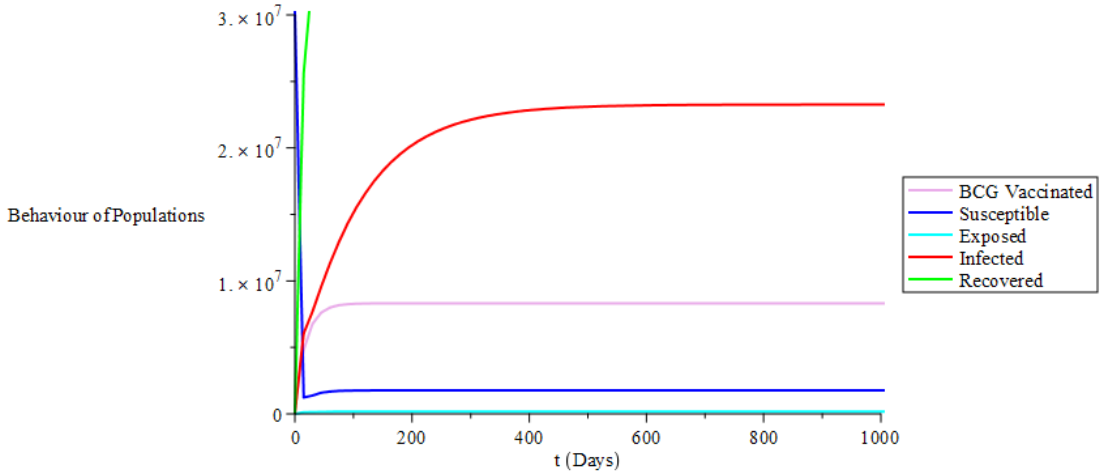


**Figure 3.** BSEIR Model with Immigration

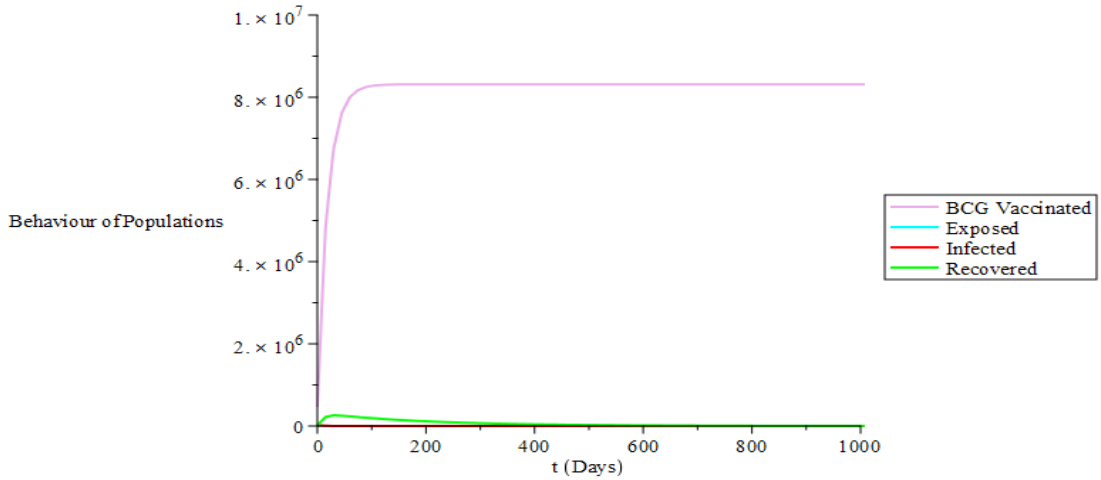


**Figure 4.** BSEIR Model without Immigration Parameter

Figures 3 and 4 depict the behaviour of the compartment for all populations, while Figure 5 displays the behaviour of infected population for both BSEIR model with and without immigration parameter. As seen in the figures, there is a difference on the trend of infected TB incidence for both models.

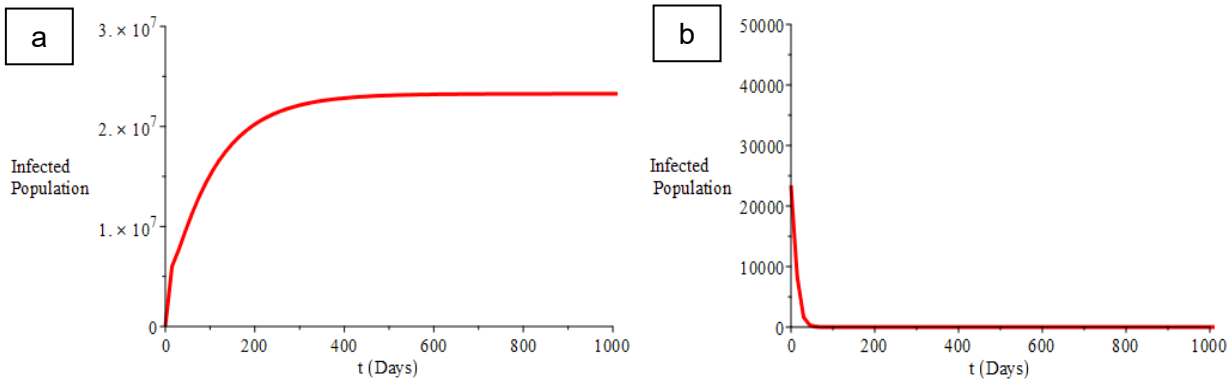


**Figure 5.** Behaviour of Infected Class for (a) BSEIR Model with Immigration, (b) BSEIR Model without Immigration

The calculated basic reproduction number, $R_0$ in Figure 3 is 1.955 which means that the disease in the population may resulting in epidemic. Thus, an epidemic occurs when the disease infects a large number of people within a population. It is clear shown on the graph, when $R_0 > 1$, the infected cases will keep increasing over time and reach a steady state. Thus, we can say that the immigrant rate has a direct relationship with basic reproduction number; when the immigrant rate increase, the number on infected TB cases will increase. Meanwhile, the BSEIR model on Figure 4 has $R_0 = 0.9 < 1$ which refer that the disease may diminish in the population. In other words, the disease will die out if there is no infected immigration.

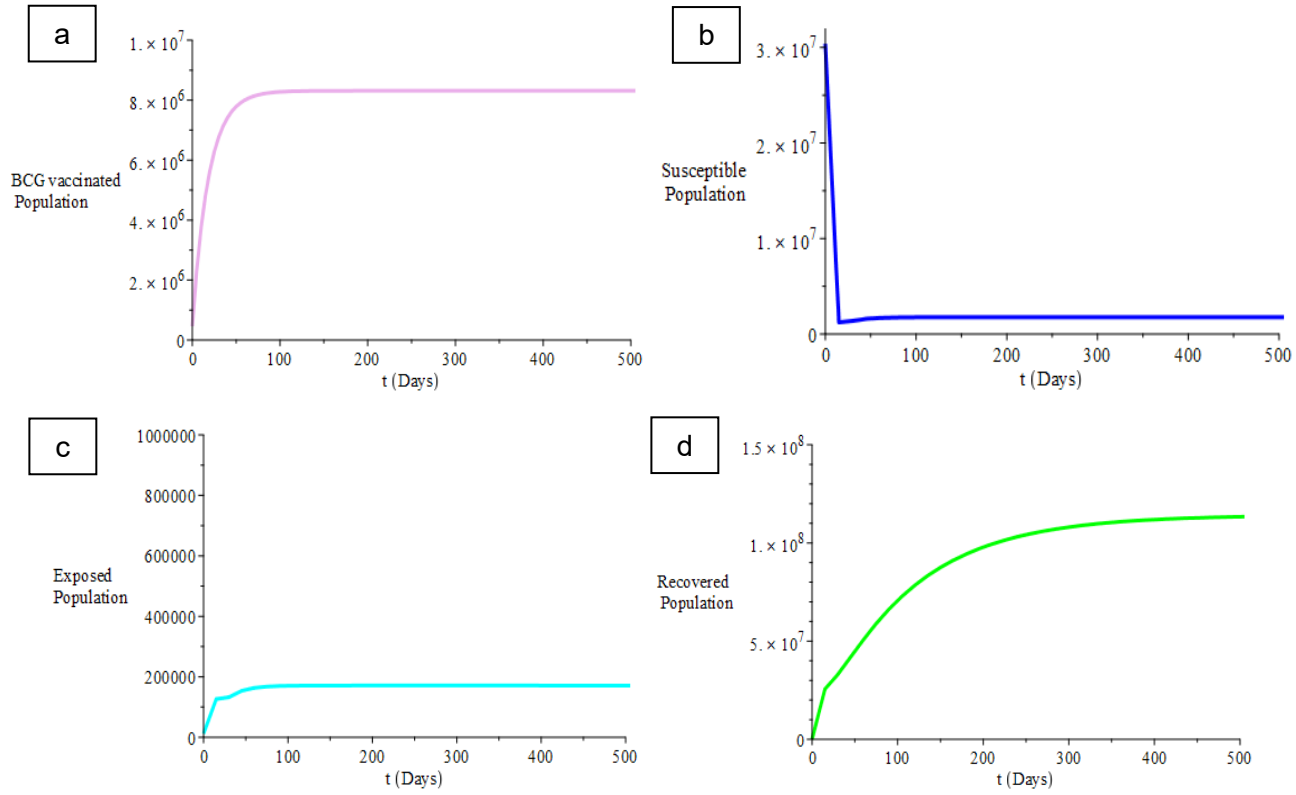


**Figure 6.** The Behaviour of each compartment for BSEIR Model with Immigration Parameter. (a) BCG vaccinated population, (b) Susceptible population, (c) Exposed Population, (d) Recovered population.

The behaviour of BCG vaccinated, susceptible, exposed, infected, and recovered populations for the BSEIR model with immigration is plotted in Figure 6. Based on Figure 5 and Figure 6, the BCG vaccinated class has increases define that the number of immunized infants is rising over the years. It can be said, the majority of parents in Malaysia are aware of and follow the regulations made by the authorities to take BCG vaccine in attempt to stop the TB transmission. Next, a decline movement appears in the number of susceptible populations since the number of infected individuals increases and thus, the recovered population also increases. Also, the behaviour of the exposed population increases and achieve a steady state.

Figure 7 presents the behaviour of BCG vaccinated, exposed and recovered classes population over time for the BSEIR model with no immigration parameter. The BCG vaccinated show an increase pattern. Additionally, the number of exposed populations fall since the infected individuals have been decreasing. So, it can be argued that the TB infection can be reduced if the population have a smaller values of immigrant rate. Furthermore, the recovered class has increases and gradually drop due to no infected cases in the population. Initially, the recovered class experiences an increase as individuals successfully recover from the illness. However, as no new infections occur, the rate of recovery gradually fall, eventually leading to a decline in the number of newly recovered cases.

The dynamic of disease transmission is explained by $R_0$ which it describes the average number of individuals who are most likely to catch contagious illness from a single infected person. Since $R_0$

depends on the model parameters, sensitivity analysis was performed to determine the effect of the parameter on TB disease transmission. Thus, we calculate the sensitivity indices of the basic reproduction number $R_0$ with respect to model parameters by using the formula given in (22), where we evaluate the partial derivative of $R_0$ with respect to the parameter then multiply by the parameter divide by the $R_0$. Based on Table 3 and Figure 8, it clearly shows that the parameters $k$, $\beta$, and $\epsilon$ have a positive sign, meaning that $R_0$ rises with the parameter. This indicates that adjusting these parameters by either increasing or decreasing by $10\%$, will affect the basic reproduction number $R_0$ in the manners of $6.621\%$, $10\%$, and $0.722\%$ respectively.

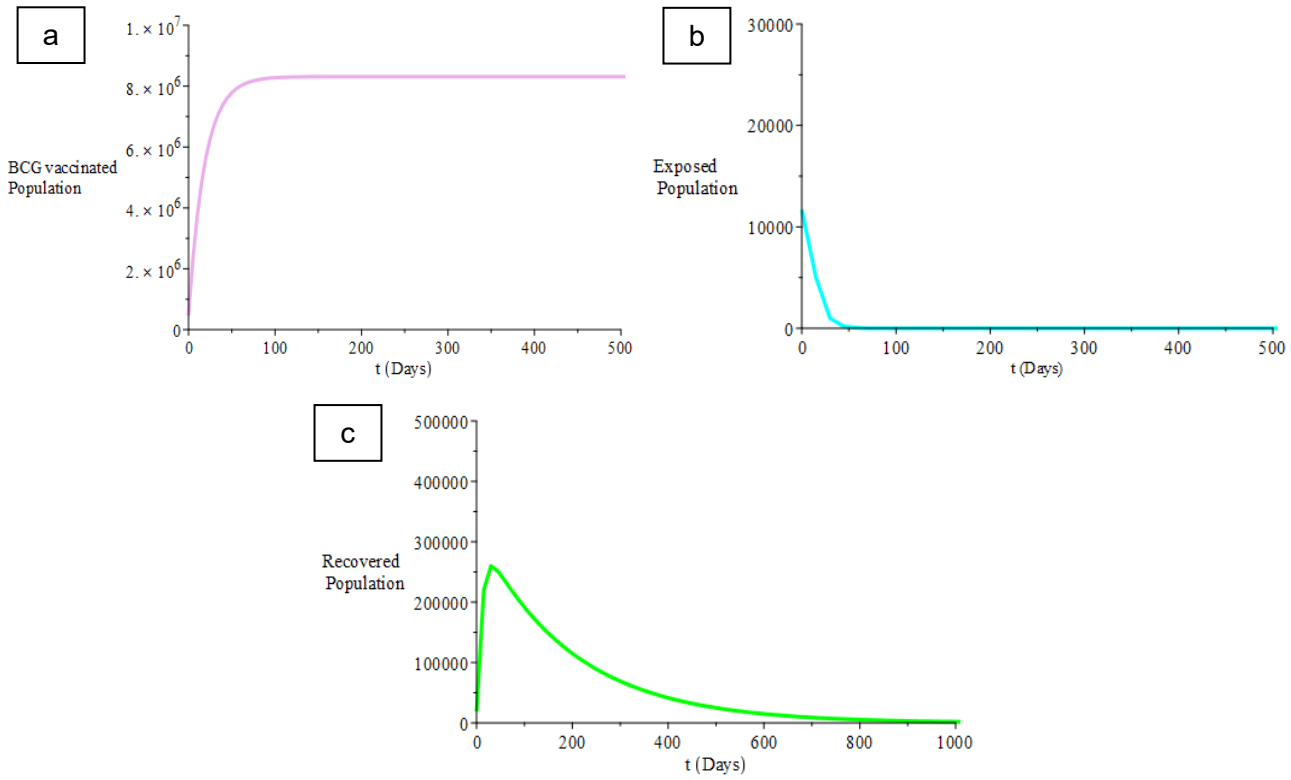


**Figure 7.** The Behaviour of each compartment for BSEIR Model without Immigration Parameter. (a) BCG vaccinated population, (b) Exposed Population, (c) Recovered population

In contrast, other parameters have a negative sign which indicates that $R_0$ declines as the parameter values increase. Further, this implies that a $10\%$ change in the parameter $p$ will result in a $6.984\%$ change in the basic reproduction number $R_0$. Correspondingly, the basic reproduction number will drop by $8.685\%$ if parameter $\gamma$ increased by $10\%$. In addition, we ignore the parameters $\epsilon$, $d$ and $\mu$ since they have a minimum impact on the transmission. However, the immigrant rate α, based on the calculation has a negative sign which contradict the initial theory. Supposedly, when immigrant rate increase, the basic reproduction number is greater than one and the number of infected individuals increases. Thus, we can conclude that the other factors have a greater impact than immigration.

Based on these results, it shed significant understanding on the dynamics of TB transmission. The infection probability $\beta$ ranked first for the most sensitive parameter, thus, it can be controlled by isolating an infectious individual from others during a period in order to reduce the likelihood of transmitting germs. Besides, TB patients should be obliged to complete the prescribed course of treatment and be prohibited from travelling until the attending doctor is confident that the patient is not contagious and poses no risk to other person. Also, an individual should take an initiative to prevent TB spreading by following to proper sneeze etiquette, maintaining good hygiene, and wearing a mask if a family member or acquaintance is known to be infected.

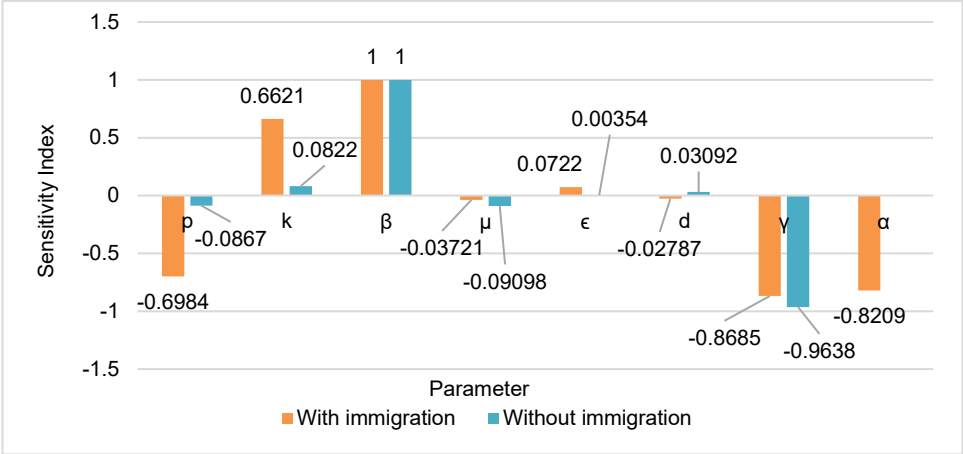


**Figure 8.** Sensitivity Indices of $R_0$

The analysis of sensitivity indices also reveals that the probability of recovered individuals greatly contributes to the spread of TB. Therefore, the treatment failure cases should be reduced. Despite the fact that TB detection and various treatment programmes have been improved by the health authorities, the TB-related deaths in Malaysia were caused by patients delayed seeking medical help. In addition, each individual and parents should understand the importance of vaccination in preventing the spreading of the virus in a population, so there will no contradiction of opinion regarding the regulations. Thus, everyone should play their own role to increase the amount of recovery rate to decrease TB infection. Also, the parameter $p$ can be controlled by using these strategies in a similar way since it contributes to the spread of the disease.

## Conclusions

In this study, the behaviours of TB transmission in Malaysia are analysed through the existing mathematical BSEIR model by considering an immigrant rate. Due to lack of data, some of the parameter used for the model is determined through estimation, and some were taken from the literature. The mathematical analysis and the significance of the basic reproduction number $R_0$ have been discussed as it is crucial form in categorizing the dynamic of the model. Hence, from the calculation, we notice that the basic reproduction number for the BSEIR model with immigration is greater than one $(R_0 > 1)$. It could be said that TB situation in Malaysia contributed to an epidemic, so it is essential to ensure that $R_0 < 1$ as to stop the disease spread. Besides, a numerical and sensitivity analysis on the basic reproduction number $R_0$ with respect to the parameter is performed and explained. As a result, one of a strategy to minimize or reduce the number on infected individuals is by increasing the value of disease transmission rate, $\beta$ and recovery rate, $\gamma$. Based on the comparison between the behaviours of the two model, we can conclude that TB infection without immigration effect is falling off. Meanwhile, the result including immigrant rate shows an increase on TB-infected cases. Therefore, we suggest that a proper screening test should be mandated by the authorities when allowing new immigrants or refugees to enter Malaysia. Also, they must be promptly tested for TB infection and kept isolated for a period to guarantee that they are free from TB bacteria, so that they can receive preventive therapy. Last but not least, public awareness and the necessary precautions should be taken seriously as the disease in Malaysia has not yet been eradicated.

In a nutshell, we can conclude that immigration has a significant impact on the dynamics of TB transmission because it significantly affects the prevalence of the disease in the population, based on Figure 5. Nevertheless, the rate of TB treatment must be increased, while the contact with infected person should be minimize in attempt to eliminate the disease infection. For instance, a population with low TB-incidence cases can be controlled with an efficient treatment and the immigration has a little impact on the population. The limitation in this study is that the parameter used were not precise enough to accurately represent the disease dynamics in Malaysia. Thus, a better estimation of immigration and other factors might be used in the future research. Furthermore, the model can be modified by taking other control strategies into account like the influence of age and sex, isolation, and treatment to improve its accuracy.

## Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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