Preventing Superinfection in Malaria Spreads with Repellent and Medical Treatment Policy

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Abstract. Malaria is a kind of a vector-borne disease. That means this disease needs a vector (in this case, the *anopheles* mosquito) to spread. In this article, a mathematical model for malaria disease spread will be discussed. The model is constructed as a seven-dimensional of a non-linear ordinary differential equation. The interventions of treatment for infected humans and use of repellent are included in the model to see how these interventions could be considered as alternative ways to control the spread of malaria. Analysis will be made of the disease-free equilibrium point along with its local stability criteria, construction of the next generation matrix which followed with the sensitivity analysis of basic reproduction number. We found that both medical treatment and repellent intervention succeeded in reducing the basic reproduction number as the endemic indicator of the model. Finally, some numerical simulations are given to give a better interpretation of the analytical results.

1. Introduction
Malaria is a disease caused by a type of *Plasmodium* parasite. This parasite enters the human body through the bite of the female *anopheles* mosquito and the parasite breeds asexually in the human body [1]. Generally, the incubation period of malaria or the time between a mosquito bite and the appearance of clinical symptoms depends on the number of parasites that enter the human body, but is in the range of about 7-30 days. The clinical symptoms are fever, chills, general malaise, sweats, headaches, body aches, nausea and vomiting. There are specific symptoms such as repetitive fever that appear in three stages: a cold stage (sensation of cold, shivering), a hot stage (fever, headaches, vomiting; seizures in young children), and finally a sweating stage (sweating, return to normal temperature, tiredness) [2]. Severe malaria occurs when infections are complicated by serious organ failures or abnormalities in the patient’s blood or metabolism. Based on the epidemiological side, this disease is one of the three major infectious diseases in the world, along with acquired immunodeficiency syndrome (AIDS) and *tuberculosis* (TB) [3].The disease is life-threatening to the people who live in tropics and subtropics countries [4] such as Asia Pacific [5], Africa [6], and Latin America [7].

In 2003, malaria was spread over 30 provinces, 226 districts, and 6,053 villages in Indonesia [8]. The condition is exacerbated in developing areas which have resistance to drugs that have been used for malaria. The spread of malaria can be combatted by educating the public about the dangers of malaria, and by using mosquito nets or repellents while sleeping [9, 10, 11]. However, the ministry of health imported anti-malaria medicine from China. The medicine is made from vegetable matter containing an artemisinin derivatives combination [12]. Malaria parasites have a complex life cycle. Therefore, the malaria vaccine is given in different ways at each stage.
For the asexual exoerythrocytic stage, the vaccine is the circumsporozoite protein (CSP), for the asexual erythrocytes stage the vaccine is the merozoite surface protein (MSP), and for the sexual stage, the vaccine is Pfs 28 and Pfs 25 [13].

Some researchers have developed a mathematical model of the spread of malaria i.e. an age-structured mathematical model of malaria transmission in which acquired immunity can act in three ways (immunity functions): reducing the probability of clinical disease, speeding the clearance of parasites, and increasing tolerance to sub-patent infections [14]. The other authors that also discuss about the spread of malaria model is the transmission and maintenance of malaria, paying attention both to the overall dynamics and to the population biology of the infection in human hosts and mosquito vectors [15]. Spreading drug resistance makes malaria control even more difficult. Therefore, JC Koella and R Antia developed epidemiological models for the spread of anti-malarial resistance based on the Macdonald-Ross model of malaria transmission. In our simplest model, resistance does not spread if the proportion of infected individuals treated is less than a threshold value; if drug treatment exceeds this threshold, resistance will eventually become fixed in the population. In more complex models, where hosts can be infected by multiple parasite strains or where treatment varies spatially, resistance is generally not fixed, but rather some level of sensitivity is often maintained in the population [16]. Some authors have explained about malaria transmission model for different levels of acquired immunity and temperature-dependent parameters (vector). A mathematical model was developed based on the following parameters: human host immunity, assuming the existence of acquired immunity and immunological memory, which boosts the protective response upon reinfection; mosquito vector, taking into account that the average period of development from egg to adult mosquito and the extrinsic incubation period of parasites (transformation of infected but non-infectious mosquitoes into infectious mosquitoes) are dependent on the ambient temperature [17]. Other authors also discuss how large-scale climate simulations and infectious disease systems may be modeled and analyzed and how these methods may be applied to predicting changes in the basic reproduction number of malaria across Tanzania. This research has concluded that disease emergence, extinction, and transmission all depend strongly on climate. Mathematical models offer powerful tools for understanding geographic shifts in incidence as climate changes [18].

Different from the models above, the superinfection process in malaria spread discuss about two types of symptom, namely symptomatic and asymptomatic. It also considers humans that use repellents. Medical treatment is only given to symptomatic infected humans. This article is constructed as follows. Sections 1 and 2 describe the introduction and the mathematical model construction, respectively. Mathematical model analysis concerning the equilibrium point and the basic reproduction number is given in section 3. Finally, a numerical simulation for various conditions, and some conclusions are given in sections 4 and 5.

2. Mathematical model
Let the human and mosquito population be divided into five and two compartments, respectively. Let us assume that the human population can be differentiated explicitly into susceptible ($S_h$), exposed ($E_h$), infected with symptomatic malaria ($D_h$), infected with asymptomatic malaria ($A_h$), and asymptomatic with undetectable parasite ($U_h$). In the other hand, the mosquito population can only divided into susceptible and infected mosquitoes, denoted by $S_m$ and $I_m$, respectively. We assume that total of human population is given by

$$N_h(t) = S_h(t) + E_h(t) + D_h(t) + A_h(t) + U_h(t),$$

while total of mosquitoes population is given by

$$N_m(t) = S_m(t) + I_m(t).$$
The compartment of susceptible human (S_h) is increased by the recruitment rate from newborns (B_h) (please note that we assume that malaria is not transmit vertically). This compartment also increased due to the recovery rate of infected compartments D_h, A_h, U_h with rates of \( \gamma_D, \gamma_A \) and \( \gamma_U \), respectively. To construct the recovery process, we assume that not all those infected with symptomatic and asymptomatic malaria could recovered from this disease. We assume only \( f \) proportion of infected with symptomatic malaria compartment will get medical treatment that will increase their natural recovery rate from \( \gamma_D \) into \( \gamma_T \). Therefore, total of individual in \( D_h(t) \) who recovered from malaria is \( f \gamma_T D_h \) for they who got medical treatment and \( (1 - f) \gamma_D D_h \) for those who do not get medical treatment. If the recovery rate is succeeded, then they will enter the susceptible population with the rate of \( \xi_T f \gamma_T D_h \) and \( \xi_D(1 - f) \gamma_D D_h \) for \( D_h \) who get and do not get medical treatment, respectively. The rest of it, \( 1 - \xi_D \) and \( 1 - \xi_T \), will transmit into infected with asymptomatic compartment. The susceptible human compartment will decrease caused by infection from infected mosquitoes at the rate of \( \beta_h S_h I_m \) where \( \beta_h \) is the probability of successful transmission rate. Since we assume that portion \( p \) of total human population are using repellent to prevent them from direct contact with infected mosquitoes, then the total of susceptible human who gets infected by infected mosquito is given by \( \beta_h (1 - p) S_h I_m \) and \( r \beta_h p S_h I_m \) for human who do not and use repellent, respectively. Please note that \( r \) is the reduction of \( \beta_h \) as an effect of repellent use. Therefore, we have that

\[
\frac{dS_h}{dt} = B_h(N_h) - \beta_h (1-p) S_h I_m - r \beta_h p S_h I_m + \xi_T f \gamma_T D_h + \xi_D(1-f) \gamma_D D_h + \gamma_U U_h - \mu_h S_h.
\]

Exposed human compartment (E_h) is generated by infection rate from susceptible human compartment (S_h). The individual will remain in this compartment for mean duration of \( \frac{1}{\mu_h} \) and will transfer into symptomatic and asymptomatic compartments with fraction of \( \phi \) and \( 1 - \phi \), respectively. This compartment also decreased caused by natural death rate of \( \mu_h \). Thus, we have

\[
\frac{dE_h}{dt} = \beta_h(1-p)S_h I_m + r \beta_h p S_h I_m - \delta h E_h - \mu_h E_h.
\]

There are two types of infected compartment, symptomatic (D_h) and asymptomatic (A_h). Both compartments are generated by transition from exposed compartments, i.e \( \phi \delta h E_h \) and \( (1 - \phi) \delta h E_h \), respectively for D_h and A_h. Some proportion \( f \) of D_h will receive get medical treatment which increase the recovery rate from \( \gamma_D \) into \( \gamma_T \), where \( \gamma_T > \gamma_D \). On the other hand, D_h also generated from superinfection from asymptomatic compartment with a rate of \( \beta_h A_h I_m \). Thus, we have :

\[
\frac{dD_h}{dt} = \phi \delta h E_h - (1-f) \gamma_D D_h - f \gamma_T D_h + \phi r \beta_h p A_h I_m + \phi \beta_h (1-p) A_h I_m - \mu_h D_h.
\]

The asymptomatic compartments increased by transition from exposed compartment, failure of natural recovery rate with rate of \( (1 - \xi_D)(1-f) \gamma_D D_h \) and \( (1 - \xi_T) f \gamma_T D_h \), for symptomatic human who get and do not get medical treatment, respectively. This compartment also will be decreased by superinfection process, natural recovery rate into asymptomatic with undetectable parasites (\( \gamma_A \)) and also natural death rate. Therefore,

\[
\frac{dA_h}{dt} = (1 - \phi) \delta h E_h + (1 - \xi_D)(1-f) \gamma_D D_h + (1 - \xi_T) f \gamma_T D_h - \phi r \beta_h p A_h I_m - \phi \beta_h (1-p) A_h I_m - \gamma_A A_h - \mu_h A_h.
\]

The last, asymptomatic undetectable parasite (U_h) is generated by natural recovery rate from A_h at a rate of \( \gamma_A \) and decreased by natural recovery rate \( \gamma_U \) and natural death rate. Thus,

\[
\frac{dU_h}{dt} = \gamma_A A_h - \gamma_U U_h \mu_h U_h.
\]
Susceptible mosquito \((S_m)\) is generated by a recruitment rate \((B_m)\) and decreased by infection with symptomatic and asymptomatic human compartments \((D_h, A_h, U_h)\) at the rate of \(\beta_m\) and natural death rate \((\mu_m)\). On the other hand, an infected compartment \((I_m)\) is generated by infected individuals from susceptible compartment and decreased by natural death rate. Since life expectancy of mosquitoes is relatively short, about one month, recovered population is not included in to the model. Thus,

\[
\frac{dS_m}{dt} = B_m(N_m) - r\beta_m S_m p(A_h + D_h + U_h) - \beta_m S_m (1 - p)(A_h + D_h + U_h) - \mu_m S_m
\]

\[
\frac{dI_m}{dt} = r\beta_m S_m p(A_h + D_h + U_h) + \beta_m S_m (1 - p)(A_h + D_h + U_h) - \mu_m I_m.
\]

Description of transmission process of the model that will be constructed can be seen in Figure 1, where yellow arrows for the transmission process and blue arrows for the transition process.

Thus, the model for the malaria transmission with superinfection process is given by the following deterministic system of non-linear differential equations:

\[
\frac{dS_h}{dt} = B_h(N_h) - \beta_h(1 - p)S_h I_m - r\beta_h p S_h I_m + \xi_T f \gamma_T D_h + \xi_D(1 - f) \gamma_D D_h + \gamma_U U_h - \mu_h S_h,
\]

\[
\frac{dE_h}{dt} = \beta_h(1 - p)S_h I_m + r\beta_h p S_h I_m - \delta h E_h - \mu_h E_h,
\]

\[
\frac{dD_h}{dt} = \phi \delta h E_h - (1 - f) \gamma_D D_h - f \gamma_T D_h + \phi r \beta_h p A_h I_m + \phi \beta_h(1 - p) A_h I_m - \mu_h D_h,
\]

\[
\frac{dA_h}{dt} = (1 - \phi) \delta h E_h + (1 - \xi_D)(1 - f) \gamma_D D_h + (1 - \xi_T) f \gamma_T D_h - \phi r \beta_h p A_h I_m
\]

\[
\frac{dU_h}{dt} = \gamma_A A_h - \gamma_U U_h - \mu_h U_h,
\]

\[
\frac{dS_m}{dt} = B_m(N_m) - r\beta_m S_m p(A_h + D_h + U_h) - \beta_m S_m (1 - p)(A_h + D_h + U_h) - \mu_m S_m
\]

\[
\frac{dI_m}{dt} = r\beta_m S_m p(A_h + D_h + U_h) + \beta_m S_m (1 - p)(A_h + D_h + U_h) - \mu_m I_m.
\]
with \( S_{h0}, E_{h0}, D_{h0}, A_{h0}, U_{h0}, S_{m0}, \) and \( I_{m0} \) are the initial condition for above system are given for \( t = 0 \). Please note that the change rate of total of human population respect to time is given by:

\[
\frac{dN_h}{dt} = \frac{d(S_h + E_h + D_h + A_h + U_h)}{dt} = B_h(N_h) - \mu_h (S_h + E_h + D_h + A_h + U_h) = B_h(N_h) - \mu_h N_h.
\]

If we choose that total of human population is constant for all time \( t > 0 \), then we have that recruitment rate of human population is given by \( B_h(N_h) = \mu_h N_h \), which also constant for all time \( t > 0 \).

Similar with human population, in mosquitoes population we have that

\[
\frac{dN_m}{dt} = \frac{d(S_m + I_m)}{dt} = B_m(N_m) - \mu_m(S_m + I_m) = B_m(N_m) - \mu_m N_m.
\]

Again, if total of mosquitoes population is constant for all time \( t > 0 \), we have that \( B_m(N_m) = \mu_m N_m \), which also mean that recruitment rate of mosquitoes population are constant for all time \( t > 0 \).

3. Model analysis

In this section, mathematical model analysis about the existence of equilibrium points and the local stability criteria will be discussed analytically and numerically. Basic reproduction number as the endemic criteria of the model in system 1 will be constructed along with the parameter sensitivity.

3.1. Disease free equilibrium point and it local stability criteria

The disease-free equilibrium point is a condition when there is no disease present in a population or when all individuals are susceptible. Disease-free equilibrium point in the system 1 is obtained when \( E_h = D_h = A_h = U_h = I_m = 0 \). Setting the right-hand side of system 1 equal to 0, we find that the disease-free equilibrium point is obtained as follows.

\[
DFE = \left\{ A_h = 0, D_h = 0, E_h = 0, I_{nm} = 0, S_h = \frac{B_h}{\mu_h}, S_m = \frac{B_m}{\mu_m}, U_h = 0 \right\}. 
\]

Using the Jacobian matrix approach, the local stability of DFE will be analyzed.

The Jacobian matrix of system 1 when it is evaluated in DFE is given by:

\[
J = \begin{bmatrix}
-\mu_h & 0 & C4 & 0 & \gamma_U & 0 & -C1 \\
0 & -\delta_h - \mu_h & 0 & 0 & 0 & 0 & C1 \\
0 & \phi \delta_h & C5 & 0 & 0 & 0 & 0 \\
0 & (1 - \phi) \delta_h & C3 & -\gamma_A - \mu_h & 0 & 0 & 0 \\
0 & 0 & 0 & \gamma_A & -\gamma_U - \mu_h & 0 & 0 \\
0 & 0 & -C2 & -C2 & -C2 & -\mu_m & 0 \\
0 & 0 & C2 & C2 & C2 & 0 & -\mu_m \\
\end{bmatrix},
\]
The eigenvalues of above matrix is taken from the root of characteristic polynomial

\[-(\lambda + \mu_m)(\lambda + \mu_h) \left( \sum_{i=0}^{4} a_i \lambda^i \right) = 0, \]  

(4)

where

\[
x_1 = -B_m \beta_m (1 + (r - 1)p)^2 \beta_h \\
x_2 = -\left[ (\phi \xi_D - 1) (\gamma_A + \gamma_U + \mu_h) (f - 1) \gamma_D + \gamma_T (\gamma_A + \gamma_U + \mu_h) (\phi \xi_T - 1) f - \mu_h^2 + (\gamma_A - \gamma_U) \mu_h - \gamma_A \gamma_U \phi \right] \\
x_3 = (\gamma_A + \mu_h) ((f - 1) \gamma_D - f \gamma_T - \mu_h) \mu_h^2 \gamma_U + \mu_h) \\
x_4 = (\gamma_A + \mu_h) ((f - 1) \gamma_D - f \gamma_T - \mu_h) \mu_h^2 \gamma_U + \mu_h) \\
x_5 = (-3 \mu_m + (f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_6 = ((1 - f) (f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_7 = 2 B_m \beta_m (1 + (r - 1)p)^2 \beta_h \\
x_8 = (\gamma_A + \mu_h) ((f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_9 = (-4 \mu_m + (f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{10} = (1 - f) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{11} = (2 \gamma_A + \gamma_U) (f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{12} = -4 \mu_h \mu_m + 3 \mu_h (2 \mu_m + 2 f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{13} = 3 + (3/2 f - 3/2) \gamma_D - 3 f \gamma_T - 3/2 \gamma_A - 3/2 \gamma_U) \mu_m \\
x_{14} = ((f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{15} = (1 - f) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{16} = (2 \gamma_A + \gamma_U) (f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{17} = B_m \beta_m (1 + (r - 1)p)^2 \beta_h \\
x_{18} = (1 - f) \mu_h + 3 f \mu_m + 1/3 \mu_m + 1/3 \gamma_A + 1/3 \gamma_U) \gamma_D - f \gamma_T (\mu_h + 1/3 \mu_m + 1/3 \gamma_A + 1/3 \gamma_U) f \\
x_{19} = -2 \mu_h \mu_m + (4 - 3 \mu_m + 2 f - 1) \gamma_D - f \gamma_T - \gamma_A - \gamma_U) \mu_h \mu_m \\
x_{20} = (-1/3 \gamma_A - 1/3 \gamma_U) \mu_h - 1/3 \gamma_A - 1/3 \gamma_U) \mu_m \\

Using the Routh-Hurwitz criterion [19] for the 4 degree polynomial, all the roots of above polynomial will be negative if and only if \( a_i > 0 \) for \( i = 1, 2, 3, 4 \) and also \( a_1 a_2 a_3 > a_5^2 + a_4^2 \).
number, denoted by $R_0$ [23, 24, 25, 26, 27]. The basic reproduction number is defined as the expected number of secondary cases caused by one primary case in a virgin population during one infection period [20, 21, 22]. The term of “virgin” population here is defined as a population in which, in initial condition, there is no single infection at all in a whole population. If $R_0 = 2$, then one primary infected individual will produce two new infected individuals. On the other hand, if $R_0 = 0.5$, it needs two infected individuals in the initial condition to produce one secondarily infected individual in the next generation. If $R_0 = 1$, then a number of infected individuals will always be the same from generation to generation. Therefore, the endemicity of the disease in the case of $R_0 = 1$ is determined by the initial condition.

Using the next-generation matrix approach, the basic reproduction number of system 1 Mathematical modelequation. 2.1 is given by

$$R_0 = \sqrt{da + db + dc}$$

with:

$$a = \frac{\phi B_h \delta_h \beta_h (1 + (r - 1) p)}{\mu_h (\mu_h + (1 - f) \gamma_D + f \gamma_T) (\delta_h + \mu_h)}$$

$$b = -B_h \delta_h \beta_h ((1 - \phi) \mu_h + (\phi \xi_D - 1) (f - 1) \gamma_D - f \gamma_T (\phi \xi_T - 1)) (1 + (r - 1) p)$$

$$c = -\frac{\delta_h \gamma_A \beta_h B_h ((1 - \phi) \mu_h + (\phi \xi_D - 1) (f - 1) \gamma_D - f \gamma_T (\phi \xi_T - 1)) (1 + (r - 1) p)}{\mu_h (\gamma_A + \mu_h) (\delta_h + \mu_h) (-\mu_h + (f - 1) \gamma_D - f \gamma_T)}$$

$$d = -\frac{1}{\mu_m} \left( r \beta_m m p B_m + \frac{\beta_m B_m (1 - p)}{\mu_m} \right).$$

The disease-free equilibrium will locally asymptotic stable if and only if $R_0 < 1$, and unstable otherwise. To see the dependency of each parameter, respect to the magnitude of basic reproduction number, one alternative method is using the level set of basic reproduction number respect to some free parameters, with setting the other parameters to remain constant. Except it is stated, the parameter’s value that is using in this section are given in Table 2.

First, analysis is given in Figure 2 to perform the dependency of the proportion of treatment $(f)$ respect to recovery rate caused by the treatment intervention $(\gamma_T)$. It can be seen that as it was expected, more massive the treatment given to infected human (larger value of $f$), the basic reproduction number will become smaller. Similar behavior also is shown in the recovery rate caused by treatment intervention. More effective the treatment implemented to infected human (larger $\gamma_T$, which means that the duration of infection become shorter) will reduce basic reproduction number. It can be seen also that $\gamma_T$ is more sensitive rather than $f$. Therefore, it is more effective to accelerate the effect of treatment to reduce basic reproduction number, rather than implementation of treatment into infected human. 

Next sensitivity analysis is given in Figure 3 to show how basic reproduction number will reduced depend on natural recruitment rate of human and mosquitoes. It can be seen that larger the magnitude of recruitment rate of human or mosquitoes, then the magnitude of basic reproduction number will increase.
Figure 2. Sensitivity analysis of basic reproduction number ($R_0$) respect to treatment proportion ($f$) and the recovery rate caused by treatment intervention ($\gamma_T$). Please note that black, green, blue and red curve is the curve for $R_0$ equals to 0.89, 0.87, 0.85 and 0.8, respectively.

Figure 3. Sensitivity analysis of basic reproduction number ($R_0$) respect to recruitment rate of human $B_h$ and mosquitoes $B_m$. Please note that blue, black, red and green curve is the curve for $R_0$ equals to 0.6, 1, 1.4 and 1.8, respectively.

4. Numerical simulations
In this section, some numerical simulation will be conducted to describe the effect of how the variation of magnitude of parameters might affect the change of the dynamics of system 1Mathematical modelequation.2.1. To perform the following simulations, the initial condition is given in Table 1 and value of each parameter (except it stated differently) is given in Table 1Initial Condition of system 1Mathematical modelequation.2.1table.1.

| initial condition | $S_h$ | $E_h$ | $D_h$ | $A_h$ | $U_h$ | $S_m$ | $I_m$ |
|------------------|-------|-------|-------|-------|-------|-------|-------|
| value            | 990   | 2     | 3     | 5     | 0     | 990   | 10    |
Table 2. Parameters Value for simulation in section 3 and 4.

| Parameters | Value |
|------------|-------|
| $f$  | 0     |
| $p$  | 0.9   |
| $r$  | 0.4   |
| $B_h$  | 1000 |
| $B_m$  | 0.1   |
| $\beta_h$  | 0.2   |
| $\beta_m$  | 0.45  |
| $\xi_D$  |       |

| Parameters | Value |
|------------|-------|
| $\delta_h$  | $\frac{1}{15}$   |
| $\gamma_A$  | $\frac{1}{180}$   |
| $\gamma_D$  | $\frac{1}{180}$   |
| $\gamma_U$  | $\frac{1}{21}$   |
| $\mu_h$  | $\frac{1}{180}$   |
| $\mu_m$  | $\frac{1}{65 \times 365}$   |
| $\xi_T$  | 0.9   |

4.1. Numerical simulation for effect of $p$

In this section, variation of $p$ which present the presentation of human who is using repellent is given to see how these parameters give an impact to the dynamic of system 1 Mathematical model equation. The value of $p$ is given for $p = 0.1n$, with $n = 0, 1, \ldots, 10$, and the decreasing of $R_0$ as an impact of these various value of $p$ are given in Table 3. It can be seen that with $p > 0.5$, which present that more than 50% human are using repellent to avoid direct contact to infected mosquito could not reduce $R_0$ which is smaller than 1. This is mean that the disease-free equilibrium point will locally stable, as shown in Figure 4.

From Figure 4 Dynamic of infected individuals respect to the change of $p$ figure.4, it can be seen that increasing number of human who is using repellent in fact not make the system tends to the disease-free equilibrium as $t \to \infty$. Also, it can be seen that increasing value of $p$ will delay the rapid increase of infected individuals in both human and mosquito population, and also reduce the level of endemicity (number of infected individuals when $t \to \infty$).

Table 3. Change of $R_0$ respect to different values of $p$.

| $p$ | 0 | 0.1 | 0.2 | 0.3 | 0.4 | 0.5 | 0.6 | 0.7 | 0.8 | 0.9 | 1     |
|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|
| $R_0$ | 1.49 | 1.40 | 1.31 | 1.22 | 1.13 | 1.04 | 0.95 | 0.86 | 0.77 | 0.69 | 0.69  |

Figure 4. Dynamic of infected individuals respect to the change of $p$. 

![Table 2](image1)

![Table 3](image2)
4.2. Numerical simulation for effect of $f$

In this section, variation of $f$ which present the symptomatic infected human who gets medical treatment is given to see how these parameters give an impact to the dynamic of system 1Mathematical modeequation.2.1. Similar with the previous scenario, the value of $f$ is given for $f = 0.1n$, with $n = 0, 1, \ldots, 10$, and the decreasing of $R_0$ caused by these various values of $f$ are given in Table 4. It can be seen that with more than 20% of infected human following medical treatment, can reduce $R_0$ which is smaller than 1. This is mean that the disease-free equilibrium point will locally stable, as shown in Figure 5.

From Figure 5, it can be seen that increase in the number of symptomatic infected human who gets medical treatment, in fact, make the system tends to the disease-free equilibrium as $t \to \infty$. Also, it can be seen that the intervention of medical treatment is more sensitive to suppress the dynamic of infected human and mosquito when $f < 0.4$, since when $f > 0.4$, it is true that the dynamic is tend to the disease-free equilibrium point, but the difference is not significant anymore. This result confirms our result in the previous section (Figure 2) that $f$ only significantly change the magnitude of $R_0$ in the beginning of intervention value.

| $f$ | 0  | 0.1 | 0.2 | 0.3 | 0.4 | 0.5 | 0.6 | 0.7 | 0.8 | 0.9 | 1  |
|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| $R_0$ | 1.49 | 1.18 | 1.03 | 0.94 | 0.88 | 0.83 | 0.80 | 0.77 | 0.75 | 0.73 | 0.72 |

5. Conclusions

Malaria is a vector-borne disease which is caused by *Plasmodium* and spread by female *anopheles* mosquitoes. In this article, a mathematical model has been constructed to understand how Malaria might spreads. The intervention of repellent to avoid or to minimize contact between mosquitoes and humans included in the model along with medical treatment to cure people from Malaria.

From the analysis about the equilibrium point and the basic reproduction number, the latter denoted by $R_0$, we find that repellent and medical treatment is succeeding to reducing the occurrence of disease. This is can be seen from the sensitivity analysis and numerical simulation of the dynamics of infected humans and mosquitoes, which tend to disease-free equilibrium when repellent and medical treatment is given in some specific values. We also find that an intervention using repellent and medical treatment is very sensitive to the reduction of the basic reproduction
number in the early values of them, please see section 3 and tables 3 and 4. Therefore, if the government wants to control the spread of malaria, intervention in a not very massive policy could be an option if there is a limited budget.

This study could be continued by making the control parameters of repellent and medical treatment control variables which will depend on time. This approach is used to minimize the size of the infected population while using the minimum budget. One option to handle this problem is to reconstruct it as a control optimum problem. Please see [28, 29] for some references to the application of optimal control in some different forms of disease spread.

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