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An optimal control of malaria transmission model with mosquito seasonal factor

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ABSTRACT

Malaria is an infectious disease which causes a global health problem. This paper aims to construct and analyze a malaria model with a seasonal factor and also apply optimal control variables in the form of insecticide, prevention, and treatment. The malaria model without seasonal factor has two equilibria, namely, the disease-free equilibrium (DFE) and the endemic equilibrium (EE). The existence and local stability of the equilibria depend on the basic reproduction number. We further analyze the sensitivity of the parameters to determine which parameters are the most influential in the model. Then, the malaria model by considering a seasonal factor is presented. The simulation results indicate that the seasonal factor tends to be more influential on the dynamics of the infected mosquitoes and humans population in region with hot climate. Furthermore, the existence of the optimal control variable in the malaria model with seasonal factor is determined through the Pontryagin Maximum Principle. Numerical simulation of the model with the optimal control shows that providing controls in the form of insecticide, prevention, and treatment simultaneously are effective in reducing the number of the exposed and infectious of the human population and also the infectious mosquito population.

Introduction

Malaria is an infectious disease caused by the presence of *Plasmodium* parasites in the red blood cells. The four types of *Plasmodium* that can infect humans are namely; *Plasmodium vivax*, *Plasmodium falciparum*, *Plasmodium malariae*, and *Plasmodium ovale*. Among the four types of *Plasmodium*, *Plasmodium falciparum* and *Plasmodium vivax* are dominant in Indonesia [1]. Malaria is transmitted to humans through the bite of malaria infected female *Anopheles* mosquitoes. On the other hand, other forms of transmissions of malaria can be from pregnant women infected with malaria to their fetuses through the placenta, and as well as through blood transfusion of a person contaminated by the *Plasmodium* parasite [2]. According to World Health Organization, there are 228 million cases of malaria with a total of 405 thousand deaths worldwide in 2018 [3].

Indonesia is located in the tropics and has two kinds of seasons, which are the rainy season and the dry season. In each of these seasons, climatic conditions will change according to the influence of the environmental factors. This is very influential in the spread of malaria, with the reason being that mosquitoes are cold-blooded, so climate change drastically affects its population distribution, bite rate, survival, and the time of development of pathogens in mosquitoes. An increase in temperature of only half a degree Celsius can increase 30% to 100% of the mosquito population [4]. With higher temperature, mosquitoes and malaria parasites can mature more quickly so that the spread of malaria increases at a very fast rate. However, if the temperature becomes too high, the mosquitoes or malaria parasite cannot survive. Notwithstanding, stationary water such as dams which is a breeding ground for mosquitoes also affects the spread of malaria. The higher rainfall causes an increase in the breeding of larvae which in turn produces more mosquitoes to spread malaria [5].

Mathematical models are tools to understand the dynamics of the transmission of infectious diseases (see [6–12] and the references therein). Another form of mathematical models that can be used to control the spread of diseases is by incorporating optimal control strategies that are effective in preventing and treating the infectious diseases [13–19]. Some of the researchers have used optimal control theory to study the transmission dynamics of malaria, for instance, the authors in [20] have reviewed an optimal control which reduces the spread of malaria by using durable mosquitoes nets, residual spraying indoors,

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Table 1
The parameters and description.

Parameter	Description	Unit
β_h	Infection rate from mosquito to human	day^{-1}
β_v	Infection rate from human to mosquito	day^{-1}
μ_h	Natural death/birth rate of human	day^{-1}
μ_v	Natural death/birth rate of mosquito	day^{-1}
ρ	Probability of exposed humans going through short-term incubation periods	–
$1/\alpha_s$	Short-term latent period for human	day
$1/\alpha_l$	Long-term latent period for human	day
ω	Spontaneous recovery rate	day^{-1}
q	Wanning immunity rate	day^{-1}

screening for the treatment of symptomatic and asymptomatic individuals. Fatmawati and Tasman [21] have discussed an optimal control model which aims to reduce the spread of malaria with treatment and insecticides as optimal control. Authors in [22] reviewed a mathematical model of the relationship of climate factors in the form of changes in temperature and rainfall in malaria which plays an important role in the rate of malaria spread. Authors in [23] analyzed a mathematical model considering the relationship of climate factors in malaria and the breakdown of exposed individuals into exposed individuals with short-term and long-term incubation periods. The influence of seasonal factors has also been discussed by [24,25], who researched on the spread of dengue fever by administering the effects of seasons on mosquitoes births.

Based on the description above, the authors are interested in modifying the mathematical model of malaria transmission by subdividing the exposed individuals into two categories, which are individuals based on the incubation periods, that is, exposed individuals with short-term and long-term incubation periods with addition of seasonal factors to the model. The difference in incubation period for malaria infection usually occurs in cases of *P. vivax* malaria [26]. In addition, we will formulate an optimal control problem which takes into account the permissible controls in the form of using insecticides, prevention, and treatment effort on the control of malaria.

This paper is organized as follows. First, we give the formulation of a malaria model without seasonal factor. The stability analysis of the equilibria is done in Section "Stability Analysis of Equilibrium" and parameter sensitivity analysis presented in Section "Global Sensitivity Analysis". The mathematical model of malaria with seasonal factor is given in Section "Malaria Model with Seasonal Factor". The optimal control model and the completion of optimal control are given in Sections "Model Formulation with Control Variables" and "Completion of Optimal Control" respectively. Further, in Section "Numerical Simulation" we present the results from numerical simulations of the optimal control model. Finally, Section "Conclusion" concludes the paper.

A malaria model without seasonal factor

In this section we formulate a mathematical model of malaria transmission without seasonal factor. The mosquito population consists of the susceptible mosquito subpopulation S_v and the infectious mosquito subpopulation I_v. While the human population consists of the susceptible human subpopulation S_h, the exposed human with short-term incubation period subpopulation E_{sh}, the exposed human with long-term incubation period subpopulation E_{lh}, the infectious human subpopulation I_h, and the recovered human subpopulation R_h.

The assumptions used for the construction for the model are as follows. All newborn humans and mosquitoes are susceptible. The birth rate is equal to the death rate in both of mosquito and human populations. No malaria transmission in blood transmission. The human and mosquito populations are constant. Malaria immunity in human recovering from malaria is temporary.

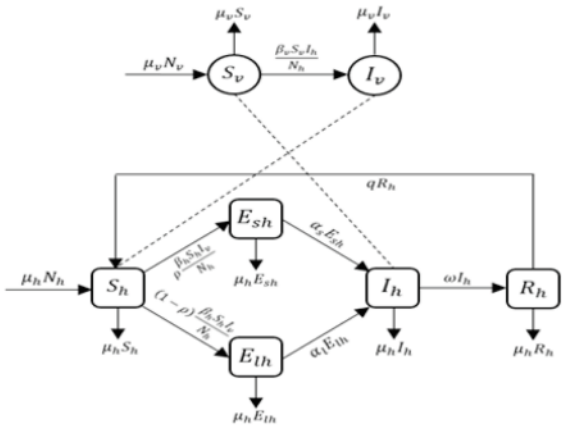


Fig. 1. The transmission diagram.

The parameters that are used for the model are presented in Table 1. All of the parameters are assumed positive and constant. In this case, the infection rates β_h and β_v are computed as $\beta_h = \theta\beta_{vh}$ and $\beta_v = \theta\beta_{hv}$, where parameter θ is the biting rate. Moreover, β_{vh} denotes the transmission probability from the infected mosquitoes to humans, and β_{hv} denotes the transmission probability from infected humans to susceptible mosquitoes.

Based on the assumptions and descriptions of the variables that have been explained previously, the transmission diagram of the model is presented in Fig. 1. The mathematical model of the malaria transmission without seasonal factor can be written as follows.

$$\begin{aligned}
\frac{dS_v}{dt} &= \mu_v N_v - \frac{\beta_v S_v I_h}{N_h} - \mu_v S_v,\\
\frac{dI_v}{dt} &= \frac{\beta_v S_v I_h}{N_h} - \mu_v I_v,\\
\frac{dS_h}{dt} &= \mu_h N_h + q R_h - \frac{\beta_h S_h I_v}{N_h} - \mu_h S_h,\\
\frac{dE_{sh}}{dt} &= \rho\frac{\beta_h S_h I_v}{N_h} - \left(\alpha_s + \mu_h\right) E_{sh},\\
\frac{dE_{lh}}{dt} &= \left(1-\rho\right)\frac{\beta_h S_h I_v}{N_h} - \left(\alpha_l + \mu_h\right) E_{lh},\\
\frac{dI_h}{dt} &= \alpha_s E_{sh} + \alpha_l E_{lh} - \left(\mu_h + \omega\right) I_h,\\
\frac{dR_h}{dt} &= \omega I_h - \mu_h R_h - q R_h,
\end{aligned} \tag{1}$$

where $N_v = S_v + I_v$ is the total population of mosquitoes and $N_h = S_h + E_{sh} + E_{lh} + I_h + R_h$ is the total population of humans. Both of the total populations are constant due to $\frac{dN_v}{dt} = 0$ and $\frac{dN_h}{dt} = 0$.

The biologically feasible region of model (1) is given by $\Omega = \Omega_v \times \Omega_h$, where

$$\Omega_v = \left\{(S_v, I_v) \in \mathbb{R}_+^2 : S_v + I_v = N_v\right\},$$

and

$$\Omega_h = \left\{(S_h, E_{sh}, E_{lh}, I_h, R_h) \in \mathbb{R}_+^5 : S_h + E_{sh} + E_{lh} + I_h + R_h = N_h\right\}.$$

Stability analysis of equilibrium

In this section, we analyze the local stability of equilibria of model (1). First, we determine the equilibrium with its conditions of existence and the basic reproduction number. From model (1), we obtain two

equilibria, namely the disease-free equilibrium and the endemic equilibrium. The disease-free equilibrium is given by

$$E_0 = (N_v, 0, N_h, 0, 0, 0, 0).$$

Next, we determine the basic reproduction number R_0 that can be used to measure the potential of infection distribution in a population. By using the Next Generation Matrix method [27], we obtain the basic reproduction number R_0 as

$$R_0 = \sqrt{\frac{\beta_h \beta_v N_v \left[\alpha_s \mu_h \rho + \alpha_l (\mu_h (1-\rho) + \alpha_s)\right]}{\mu_v N_h (\omega + \mu_h)(\alpha_l + \mu_h)(\alpha_s + \mu_h)}}.$$

The term $\frac{\beta_h}{\mu_v}$ represents the number of new infected hosts produced from one infectious mosquito. Moreover, the term $\frac{\beta_v N_v \left[\alpha_s \mu_h \rho + \alpha_l (\mu_h (1-\rho) + \alpha_s)\right]}{N_h (\omega + \mu_h)(\alpha_l + \mu_h)(\alpha_s + \mu_h)}$ represents the number of new infected mosquitoes produced from one infectious host during infectious period.

Furthermore, model (1) has the endemic equilibrium $E_1 = (S_v^*, I_v^*, S_h^*, E_{sh}^*, E_{lh}^*, I_h^*, R_h^*)$ where

$$S_v^* = \frac{\mu_v N_v N_h}{\beta_v I_h^* + \mu_v N_h},$$

$$I_v^* = \frac{\beta_v N_v I_h^*}{\beta_v I_h^* + \mu_v N_h},$$

$$S_h^* = \frac{N_h \left[\mu_h N_h (\mu_h + q) + q \omega I_h^*\right]}{(\beta I v + \mu_h N_h)(\mu_h + q)},$$

$$E_{sh}^* = \frac{\rho \beta_h \beta_v N_v S_h^* I_h^*}{N_h (\alpha_s + \mu_h)(\beta_v I_h^* + \mu_v N_h)},$$

$$E_{lh}^* = \frac{(1-\rho) \beta_h \beta_v N_v S_h^* I_h^*}{N_h (\alpha_l + \mu_h)(\beta_v I_h^* + \mu_v N_h)},$$

$$R_h^* = \frac{\omega I_h^*}{q + \mu_h},$$

$$I_h^* = \frac{\mu_v N_h \triangle_1 (R_0^2 - 1)}{\beta_v \triangle_1 + \mu_v R_0^2 \triangle_2},$$

and $\triangle_1 = (\mu_h + q)\left[\alpha_s \mu_h \rho + \alpha_l (\mu_h (1-\rho) + \alpha_s)\right]$ and $\triangle_2 = \mu_h (\mu_h + \omega)(\mu_h + q) + \alpha_s \left[\mu_h (\omega + \mu_h + q) + q\omega(1-\rho)\right] + \alpha_l \left[(\mu_h + \alpha_s)(\omega + \mu_h + q) + \omega \rho q\right]$. The endemic equilibrium E_1 exists if $R_0 > 1$.

The stability of disease-free equilibrium is given in the following theorem.

Theorem 1. The disease-free equilibrium E_0 is locally asymptotically stable if $R_0 < 1$.

Proof. First, we linearized model (1) near the disease-free equilibrium. The Jacobian matrix of model (1) at E_0 is as following.

$$J_{E_0} = \begin{pmatrix} -\mu_v & 0 & 0 & 0 & 0 & \frac{-\beta_v N_v}{N_h} & 0 \\ 0 & -\mu_v & 0 & 0 & 0 & \frac{\beta_v N_v}{N_h} & 0 \\ 0 & -\beta_h & -\mu_h & 0 & 0 & 0 & q \\ 0 & \rho\beta_h & 0 & -(\alpha_s+\mu_h) & 0 & 0 & 0 \\ 0 & (1-\rho)\beta_h & 0 & 0 & -(\alpha_l+\mu_h) & 0 & 0 \\ 0 & 0 & 0 & \alpha_s & \alpha_l & -(\mu_h+\omega) & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega & -(\mu_h+q) \end{pmatrix}.$$

Table 2
The parameter value.

Parameter	Unit	Value	Source
β_h	day^{-1}	0.0044	[24,25,29]
β_v	day^{-1}	0.0044	[24,25,29]
μ_h	day^{-1}	$\frac{1}{70 \times 365}$	[7]
μ_v	day^{-1}	$\frac{1}{15}$	[29]
ρ	-	0.25	[23]
α_s	day^{-1}	$\frac{1}{25.9}$	[23]
α_l	day^{-1}	$\frac{1}{360.3}$	[23]
ω	day^{-1}	0.00014	[22]
q	day^{-1}	0.005	[22]

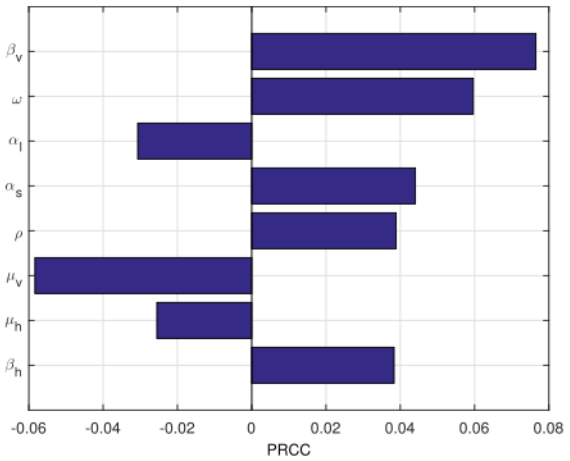


Fig. 2. PRCC results for the parameters of R_0.

The Jacobian matrix gives seven eigenvalues, these are $-\mu_v$, $-\mu_h$, and $-(q + \mu_h)$. The other eigenvalues are the roots of quartic equation

$$\lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4 = 0, \tag{2}$$

where

$$a_1 = 3\mu_h + \mu_v + \alpha_s + \alpha_l + \omega,$$

$$a_2 = (\mu_h + \omega)(\mu_h + \mu_v + \alpha_l) + \mu_v (\mu_h + \alpha_l) + (\mu_h + \alpha_s)(2\mu_h + \mu_v + \alpha_l + \omega),$$

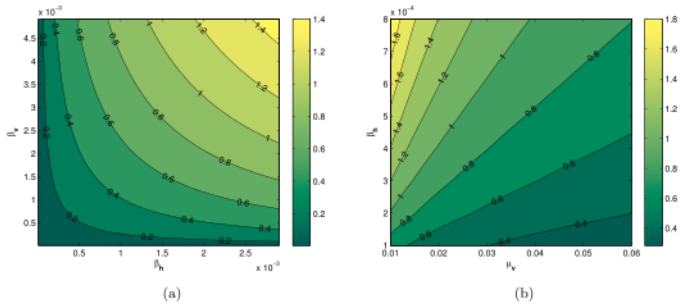
$$a_3 = \mu_v \left(\alpha_s + \mu_h\right)\left(\alpha_l + \mu_h\right) + \left(\alpha_s + \mu_h\right)\left(\alpha_l + \mu_h\right)\left(\omega + \mu_h\right) + \mu_v \left(\alpha_s + \mu_h\right)\left(\omega + \mu_h\right)\left(1 - \frac{\beta_h \beta_v N_v \alpha_s \rho}{\mu_v N_h (\alpha_s + \mu_h)(\omega + \mu_h)}\right) + \mu_v \left(\alpha_l + \mu_h\right)\left(\omega + \mu_h\right)\left(1 - \frac{\beta_h \beta_v N_v \alpha_l (1-\rho)}{\mu_v N_h (\alpha_l + \mu_h)(\omega + \mu_h)}\right),$$

$$a_4 = \mu_v (\mu_h + \alpha_s)(\mu_h + \alpha_l)(\mu_h + \omega)\left(1 - R_0^2\right),$$

Based on the Routh-Hurwitz criteria, the quartic Eq. (2) has roots whose real parts are negative if and only if $a_1, a_2, a_3, a_4 > 0$, and $a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$. It is clear that the coefficients $a_1, a_2 > 0$. It is also clear that the coefficient a_4 is positive if $R_0 < 1$. If $R_0 < 1$, then $\beta_h \beta_v N_v$

$$\frac{\alpha_s \rho}{\mu_v N_h (\alpha_s + \mu_h)(\omega + \mu_h) + \frac{\beta_h \beta_v N_v \alpha_l (1-\rho)}{\mu_v N_h (\alpha_l + \mu_h)(\omega + \mu_h)}} < 1$$

. Hence, the coefficient a_3 is positive if $R_0 < 1$. It also can be verified that the condition $a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$ is satisfied. Therefore, the disease-free



(a) (b)

Fig. 3. Contour plots of R_0 in (a) plane $\beta_h\beta_v$ and (b) plane $\mu_v\beta_h$.

equilibrium E_0 is locally asymptotically stable if $R_0 < 1$. Theorem 1 shows that malaria will disappear from the population whenever $R_0 < 1$.

Global sensitivity analysis

In this section, we perform the global sensitivity analysis using Partial Rank Correlation Coefficient (PRRC) to determine the parameters that have a large influence on the basic reproduction number. We use the approach described in [28]. The parameter values to plot the PRCC of the malaria model are placed in the Table 2. The parameters θ, β_{vh}, β_{hv} are given as $\theta = 0.022$ and $\beta_{vh} = \beta_{hv} = 0.2$. The PRCC plot of the model (1) can be seen in Fig. 2.

Based on the Fig. 2, the parameters that have great influence are parameters $\beta_v, \omega, \mu_v, \alpha_s, \rho$, and β_h. The sensitivity of parameters β_v, β_h, and μ_v to the $R_0$are shown in Fig. 3. From Fig. 3a, it can be seen that the increasing value of β_h (using positive slope line) would increase the value of R_0. On the contrary, based on the Fig. 3b, the decreasing value of μ_v (using negative slope line) will reach the endemic condition.

Malaria model with seasonal factor

In this section, the model of malaria transmission (1) is modified with addition of a seasonal factor. It is assumed that the birth rate of mosquito varies seasonally following the cosine function with a period of 1 year as follows:

$$\mu_v\left(1 + \alpha\cos\left(\frac{2\pi t}{365} + \varphi\right)\right)$$

where μ_v is the natural birth rate of mosquito which is constant, α is the amplitude of the seasonal variation, and $0 \leqslant \alpha \leq 1$, and φ is the season phase with the value is constant. Hence, the model of malaria transmission with a seasonal factor can be written as follows.

$$\begin{aligned}
\frac{dS_v}{dt} &= \mu_v\left(1 + \alpha\cos\left(\frac{2\pi t}{365} + \varphi\right)\right)N_v - \frac{\beta_v S_v I_h}{N_h} - \mu_v S_v,\\
\frac{dI_v}{dt} &= \frac{\beta_v S_v I_h}{N_h} - \mu_v I_v,\\
\frac{dS_h}{dt} &= \mu_h N_h + qR_h - \frac{\beta_h S_h I_v}{N_h} - \mu_h S_h,\\
\frac{dE_{sh}}{dt} &= \rho\frac{\beta_h S_h I_v}{N_h} - \left(\alpha_s + \mu_h\right)E_{sh},\\
\frac{dE_{lh}}{dt} &= \left(1-\rho\right)\frac{\beta_h S_h I_v}{N_h} - \left(\alpha_l + \mu_h\right)E_{lh},\\
\frac{dI_h}{dt} &= \alpha_s E_{sh} + \alpha_l E_{lh} - \left(\mu_h + \omega\right)I_h,\\
\frac{dR_h}{dt} &= \omega I_h - \mu_h R_h - qR_h.
\end{aligned} \tag{3}$$

Table 3
The parameter values for three scenarios.

Parameter	Scenario 1	Scenario 2	Scenario 3
β_{vh}	0.12	0.99	0.2
β_{hv}	0.11	0.95	0.2
μ_v	0.04	0.03	$\frac{1}{15}$

In carrying out numerical simulations of model (3), we use 400 days for the time horizon. The initial values used in the simulation are $S_v(0) = 10{,}000$, $I_v(0) = 2{,}000$, $S_h(0) = 5{,}000$, $E_{sh}(0) = 500$, $E_{lh}(0) = 350$, $I_h(0) = 100$, and $R_h(0) = 50$. There are three amplitudes of the seasonal variations to be simulated which are $\alpha = 0.3, \alpha = 0.5$ and $\alpha = 0.8$, with $\varphi = 0$, as stated in [25].

Temperature conditions greatly affect the transmission both from mosquitoes to humans and vice versa as well mosquito lifespan. Hence, we consider 3 scenarios for the effect of temperature on the spread of malaria in the population. The first scenario concerns with cold climate where the temperature is 14 °C. The second one is correlated with hot climate where the temperature is 26 °C. The third scenario is used to simulate mild climate which has temperature between 18 °C and 24 °C. Furthermore, we assume that the three scenarios provide different values for the three parameters as indicated in the Table 3 [24,25].

Using the parameter values in Table 2 and Table 3, the results of the numerical simulation are shown in Figs. 4–6. Figs. 4–6 give the dynamics of the infectious mosquito subpopulation I_h and the infected human subpopulations E_{sh}, E_{lh}, I_h with and without the seasonal variation in the three scenarios.

Fig. 4 gives simulation of Scenario 1 (cold climate). We see that there is a small different in the dynamics of the subpopulations with and without seasonal factor.

Fig. 5 gives simulation of Scenario 2 (hot climate). As shown in Fig. 5a and Fig. 5b, the seasonal variation has the most effect on the malaria exposed with short-term incubation period subpopulation E_{sh} and the malaria exposed with long-term incubation period subpopulation E_{lh}. As Fig. 5d shows, the seasonality has little effect on the infectious human population I_h.

For dengue cases, the authors in [24,25] found that the simulations with the seasonal variations provide more infected people. The model used by [24,25] does not pay attention to the exposed human population. This differs from the malaria model presented here. We also consider the exposed human with two incubation periods, namely the short term and the long term, which are estimated at 25.9 days and 360.3 days, respectively [23,26]. Thus, in this study, seasonal variation has a more significant effect on the exposed human subpopulations E_{sh} and E_{lh} compared to the infectious human subpopulation I_h.

Fig. 6 gives simulation of Scenario 3 (mild climate). From the result, We see that there is a small different in the dynamics of the subpopulations with and without seasonal factor.

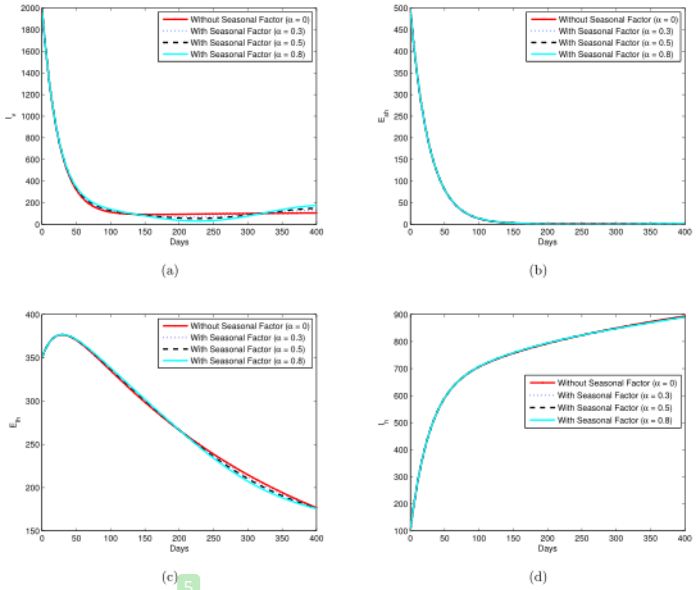


Fig. 4. Dynamics of malaria model with and without seasonal factor for Scenario 1.

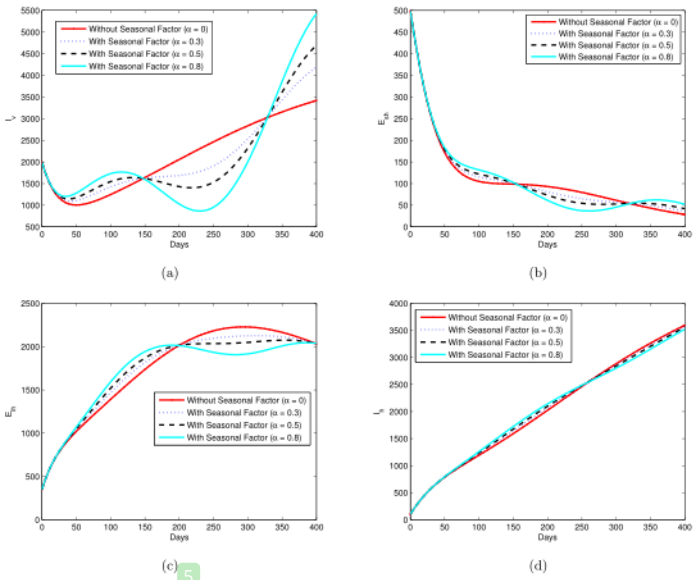


Fig. 5. Dynamics of malaria model with and without seasonal factor for Scenario 2.

From the simulation of three scenarios, we obtain that seasonal factor greatly affect the dynamics of infected malaria populations for region with hot climate (Scenario 2).

Model formulation with control variables

In this section, the mathematical model of malaria transmission with seasonal factors is formulated by incorporating the control variables. Based on the sensitivity analysis, a control strategy of the transmission rate will sufficiently reduce the spread of malaria in the community. Moreover, a strategy that increases the natural death rate of mosquitoes will be effective in diminishing the spread of malaria in the community. Therefore, the control variables are used in the form of insecticide effort u_1, prevention effort u_2 and treatment effort u_3 in order to mitigate the malaria transmission in the population. Insecticide includes spraying and fogging against mosquitoes, while prevention refers to the use of

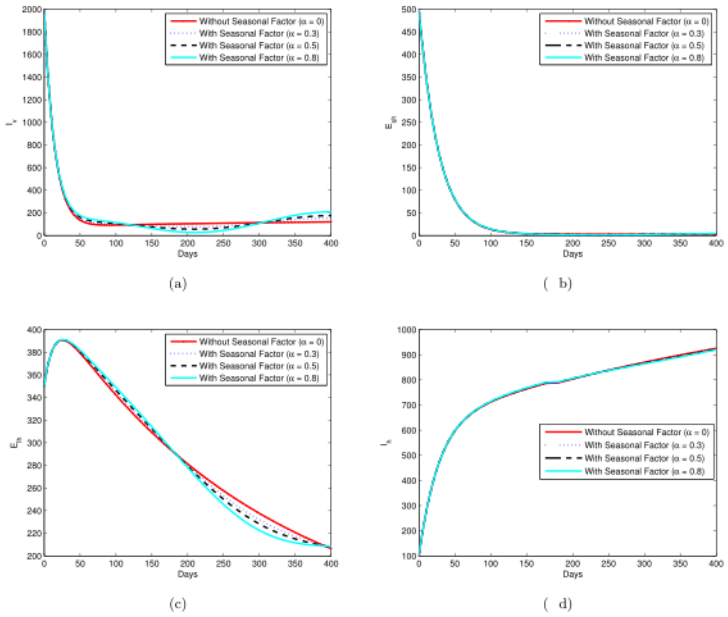


Fig. 6. Dynamics of malaria model with and without seasonal factor for Scenario 3.

mosquito nets and mosquito repellent lotion. Furthermore, treatment control represents a giving antimalarial drug to the infectious humans.

The malaria model with seasonal factors and the presence of controls is as follows.

$$\begin{aligned}
\frac{dS_v}{dt} &= \mu_v\left(1+\alpha\cos\left(\frac{2\pi t}{365}+\varphi\right)\right)N_v - \frac{\beta_v S_v I_h}{N_h} - \mu_v S_v - a u_1 S_v,\\
\frac{dI_v}{dt} &= \frac{\beta_v S_v I_h}{N_h} - \mu_v I_v - a u_1 I_v,\\
\frac{dS_h}{dt} &= \mu_h N_h + qR_h - \left(1-u_2\right)\frac{\beta_h S_h I_v}{N_h} - \mu_h S_h,\\
\frac{dE_{sh}}{dt} &= \left(1-u_2\right)\rho\frac{\beta_h S_h I_v}{N_h} - \left(\alpha_s+\mu_h\right)E_{sh},\\
\frac{dE_{lh}}{dt} &= \left(1-u_2\right)\left(1-\rho\right)\frac{\beta_h S_h I_v}{N_h} - \left(\alpha_l+\mu_h\right)E_{lh},\\
\frac{dI_h}{dt} &= \alpha_s E_{sh} + \alpha_l E_{lh} - \left(\mu_h+\omega\right)I_h - b u_3 I_h,\\
\frac{dR_h}{dt} &= \omega I_h - \mu_h R_h - qR_h + b u_3 I_h,
\end{aligned} \tag{4}$$

where a and b are the rate of insecticide use in mosquito population and the rate of treatment in infectious human population respectively. The aim of the objective function is to minimize the infectious mosquito population, the exposed human with short and long-term incubation period, the infectious human population and the implementing controls with smallest cost. Thus, the objective function is given by

$$\min \mathcal{J}\left(u_1,u_2,u_3\right) = \int_0^{t_f}\left(A_1 I_v + A_2 E_{sh} + A_3 E_{lh} + A_4 I_h + \frac{1}{2}\left(C_1 u_1^2 + C_2 u_2^2 + C_3 u_3^2\right)\right)dt, \tag{5}$$

where t_f is the final time and $u_1(t), u_2(t), u_3(t) \in [0,1]$. The coefficients A_1, A_2, A_3, and A_4, respectively declare weighting constants of I_v, E_{sh}, E_{lh}, and I_h subpopulations, while C_1, C_2, and C_3 are the weighting constants in the form of costs for insecticides, prevention, and treatment, respectively.

In this study, we consider a quadratic objective functional in order to quantify the control cost due to the cost of the interventions is non-linear. This is confirmed by the fact that there is no linear relationship between the impact of the intervention and the cost of intervention of the infective populations. The quadratic form of the control cost is consistent with some previous works, such as in literature [30–33].

The purpose of this problem is to find an optimal control u_1^*, u_2^* and u_3^* such that

$$J\left(u_1^*, u_2^*, u_3^*\right) = \min_{\Omega} J\left(u_1, u_2, u_3\right), \tag{6}$$

where $\Omega = \{(u_1,u_2,u_3) \mid u_i \text{ is Lebesguemeasurablefunctionon } [0,1],\ 0 \leqslant u_i(t) \leqslant 1, i = 1,2,3\}$

.

Completion of optimal control

The problem of optimal control in the malaria transmission model with season factor is solved by applying the Pontryagin Maximum Principle [34]. Suppose the state variable in the model is accompanied by optimal control as follows:

$$x = [S_v, I_v, S_h, E_{sh}, E_{lh}, I_h, R_h]^T.$$

Based on the Pontryagin Maximum principle, the first step is to form the Hamiltonian function as follows:

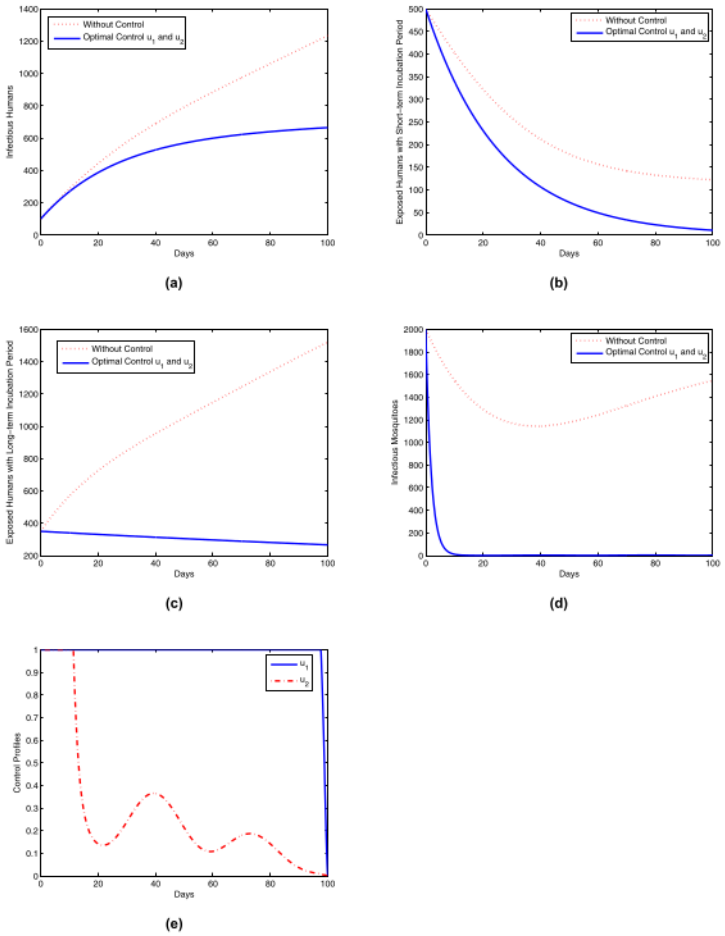


Fig. 7. Simulations of the malaria model using controls u_1 and u_2.

$$\mathscr{H} = A_1 I_v + A_2 E_{sh} + A_3 E_{lh} + A_4 I_h + \frac{1}{2}\left(C_1 u_1^2 + C_2 u_2^2 + C_3 u_3^2\right) + \gamma^T\left(t\right) f\left(x\left(t\right), u\left(t\right)\right), \tag{7}$$

where $f(x(t), u(t))$ is the right hand side of model (4). The variable $\gamma(t)$ is the Lagrange multiplier or co-state variable, where $\gamma^T(t)$ is transpose of $\gamma(t)$.

The existence of the optimal control $u_i \in \Omega, i = 1, 2, 3$ is ensured by the result in [35] from the convexity of the objective function (6) with respect to the controls and the boundedness and Lipschitz property of the state system (4).

In order to obtain optimal conditions, the $\mathscr{H}$-function must fulfill stationary conditions

$$\frac{\partial \mathscr{H}}{\partial u} = 0 \text{ where } u = \left(u_1, u_2, u_3\right). \tag{8}$$

Based on Eq. (8), it is obtained the values for u_1, u_2, and u_3, where $0 \leqslant u_i(t) \leq 1, i = 1, 2, 3$ as follows:

$$u_1^* = \begin{cases} 0 & \text{if } u_1 \leq 0, \\ \dfrac{\alpha(\gamma_1 S_v + \gamma_2 I_v)}{C_1} & \text{if } 0 < u_1 < 1, \\ 1 & \text{if } u_1 \geqslant 1, \end{cases}$$

$$u_2^* = \begin{cases} 0 & \text{if } u_2 \leq 0, \\ \dfrac{\beta_h S_h I_v(\gamma_5 - \gamma_3) + \rho\beta_h S_h I_v(\gamma_4 - \gamma_5)}{N_h C_2} & \text{if } 0 < u_2 < 1, \\ 1 & \text{if } u_2 \geqslant 1, \end{cases}$$

$$u_3^* = \begin{cases} 0 & \text{if } u_3 \leq 0, \\ \dfrac{bI_h(\gamma_6 - \gamma_7)}{C_3} & \text{if } 0 < u_3 < 1, \\ 1 & \text{if } u_3 \geqslant 1. \end{cases}$$

Hence, we have the following theorem.

Theorem 2. *Given the optimal controls (u_1^*, u_2^*, u_3^*) and the solutions $S_v^*, I_v^*, S_h^*, E_{sh}^*, E_{lh}^*, I_h^*, R_h^*$ of the state system (4) that minimize J, then there exists adjoint variables γ_i for $i = 1, 2, \ldots 7$ that satisfying*

with transversality conditions $\gamma_i(t_f) = 0$ for $i = 1, 2, \cdots, 7$, and the control

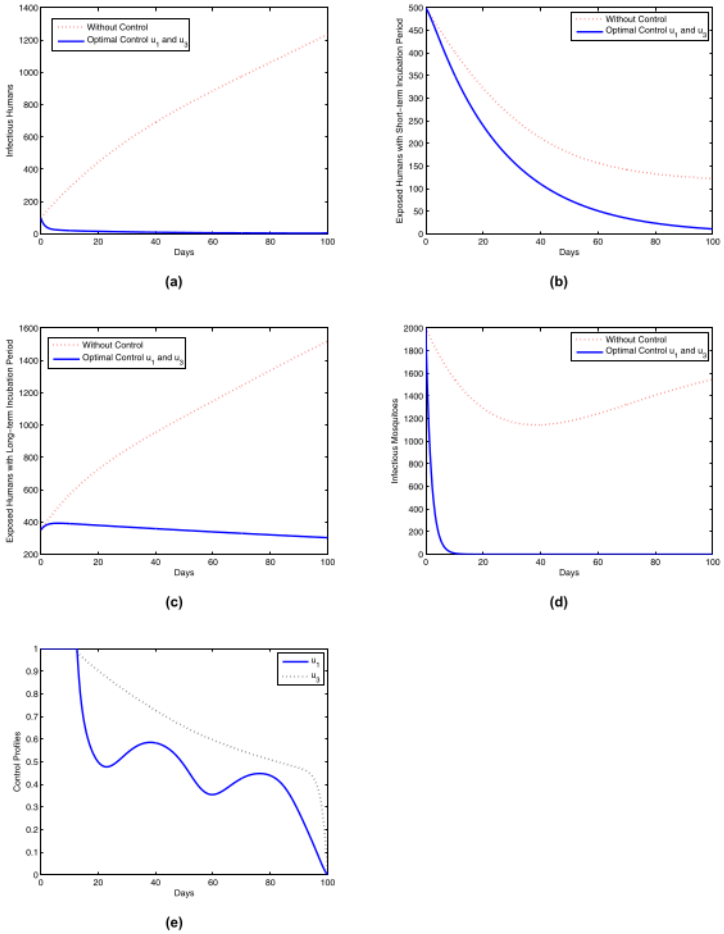


Fig. 8. Simulations of the malaria model using controls u_1 and u_3.

$$\dot{\gamma}_1 = -\left[\gamma_1\left[\frac{\beta_v I_h}{N_h} - \mu_v - au_1\right] + \gamma_2\frac{\beta_v I_h}{N_h}\right]$$

$$\dot{\gamma}_2 = -\left[A_1 + \gamma_2[-\mu_v - au_1] + \gamma_3\left[-\left(1-u_1\right)\frac{\beta_h S_h}{N_h}\right] + \gamma_4\left[\left(1-u_2\right)\frac{\rho\beta_h S_h}{N_h}\right] + \gamma_5\left[\left(1-u_2\right)\left(1-\rho\right)\frac{\rho\beta_h S_h}{N_h}\right]\right]$$

$$\dot{\gamma}_3 = -\left[\gamma_3\left[-\left(1-u_1\right)\frac{\beta_h I_v}{N_h} - \mu_h\right] + \gamma_4\left[\left(1-u_2\right)\frac{\rho\beta_h I_v}{N_h}\right] + \gamma_5\left[\left(1-u_2\right)\left(1-\rho\right)\frac{\rho\beta_h I_v}{N_h}\right]\right]$$

$$\dot{\gamma}_4 = -[A_2 + \gamma_4[-\alpha_s - \mu_h] + \gamma_6\alpha_s]$$

$$\dot{\gamma}_5 = -[A_3 + \gamma_5[-\alpha_l - \mu_h] + \gamma_6\alpha_l]$$

$$\dot{\gamma}_6 = -\left[A_4 + \gamma_1\left[\frac{-\beta_v S_v}{N_h}\right] + \gamma_2\frac{\beta_v S_v}{N_h} + \gamma_6[-\mu_h - \omega - bu_3] + \gamma_7[\omega + bu_3]\right]$$

$$\dot{\gamma}_7 = -[\gamma_3 q + \gamma_7(-\mu_h - q)].$$

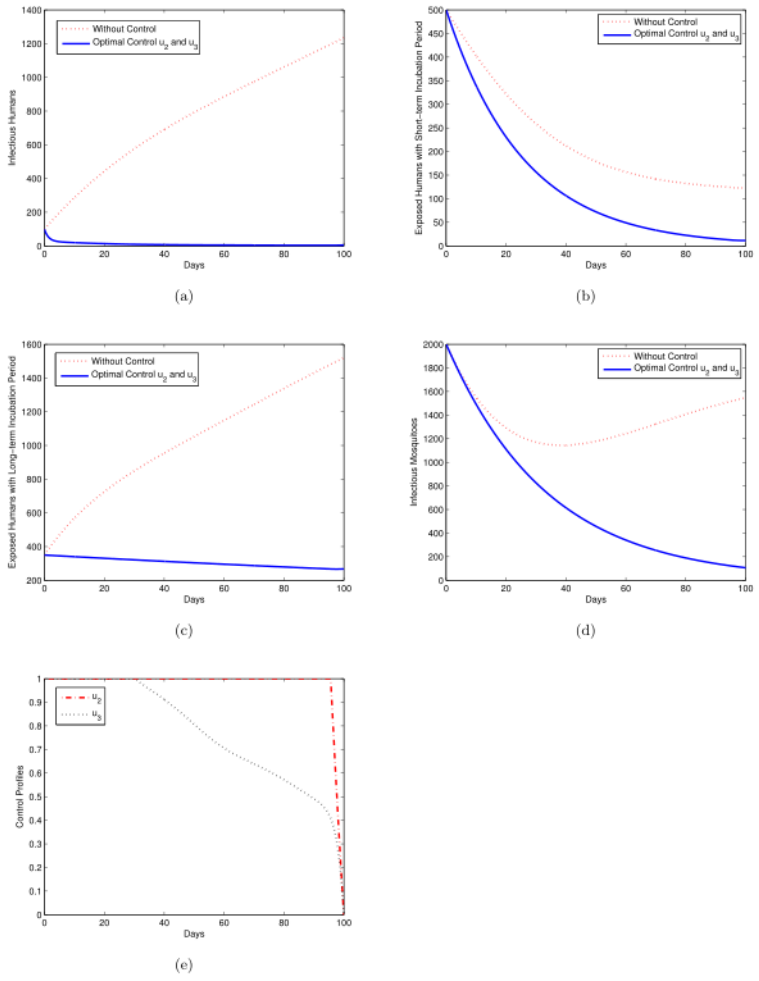


Fig. 9. Simulations of the malaria model using controls u_2 and u_3.

variables

$$
\begin{aligned}
u_1^* &= \min\left\{\max\left(0, \frac{\alpha(\gamma_1 S_v + \gamma_2 I_v)}{C_1}\right), 1\right\},\\
u_2^* &= \min\left\{\max\left(0, \frac{\beta_h S_h I_v(\gamma_5 - \gamma_3) + \rho\beta_h S_h I_v(\gamma_4 - \gamma_5)}{N_h C_2}\right), 1\right\},\\
u_3^* &= \min\left\{\max\left(0, \frac{bI_h(\gamma_6 - \gamma_7)}{C_3}\right), 1\right\}.
\end{aligned}
\tag{9}
$$

Proof. The adjoint system is determined by taking the derivative of the Hamiltonian $\mathscr{H}$ with respect to each state variables: $\dot{\gamma_1}\left(t\right) = -\frac{\partial \mathscr{H}}{\partial S_v}$, $\dot{\gamma_2}\left(t\right) = -\frac{\partial \mathscr{H}}{\partial I_v}, \dot{\gamma_3}\left(t\right) = -\frac{\partial \mathscr{H}}{\partial S_h}, \dot{\gamma_4}\left(t\right) = -\frac{\partial \mathscr{H}}{\partial E_{sh}}, \dot{\gamma_5}\left(t\right) = -\frac{\partial \mathscr{H}}{\partial E_{lh}}, \dot{\gamma_6}\left(t\right) = -\frac{\partial \mathscr{H}}{\partial I_h}$, and $\dot{\gamma_7}\left(t\right) = -\frac{\partial \mathscr{H}}{\partial R_h}$, with $\gamma_i(t_f) = 0$ for $i = 1, 2, \cdots, 7$. To find the optimal controls (9), we employ $\frac{\partial \mathscr{H}}{\partial u_i} = 0$, for $i = 1, 2, 3$..

Numerical simulation

The purpose of this section is to examine the numerical simulation of the control problem for the malaria model with seasonal factor (4) and without control (3). To demonstrate the simulation, we use the forward–backward iterative method [36].

The initial values used in this simulation are $S_v(t_0) = 10,000, I_v(t_0) = 2,000, S_h(t_0) = 5,000, E_{sh}(t_0) = 500, E_{lh}(t_0) = 350, I_h(t_0) = 100, R_h(t_0) = 50$. The amplitude of the season variations that will be simulated is $\alpha = 0.5$. The start and end times of observations in this simulation are $t_0 = 0$ and $t_f = 100$ in units of days. The weighting constants of population are $A_1 = A_2 = A_3 = A_4 = 1$ and weighting constants for the controls are $C_1 = 10, C_2 = 10$ and $C_3 = 20$ The rate of use of insecticides in mosquitoes and the rate of treatment in humans are respectively $a = 0.5$ and $b = 0.75$.

We used the parameter values from Scenario 2 (hot climate region) due to in this case the infected mosquito population was more volatile. This can lead to an increased spread of malaria in the community. Hence, the parameter values refer to Table 2 and the value of Scenario 2 in Table 3.

The simulation experiment is deployed to investigate the effectiveness of insecticide, prevention, and treatment efforts carried out through

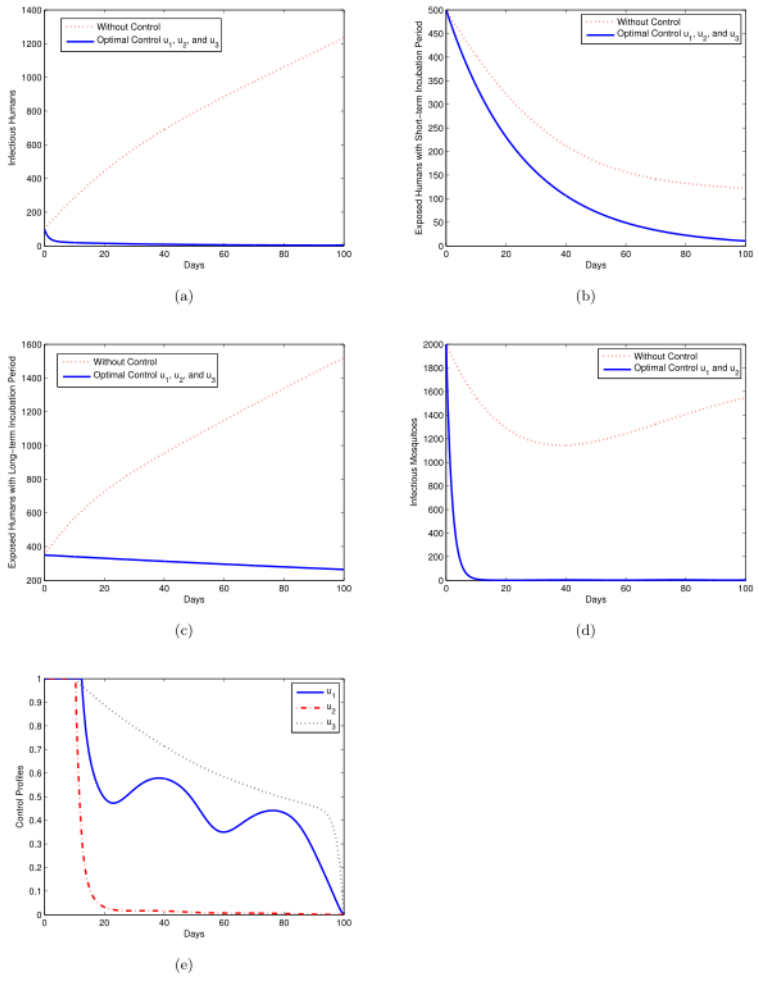


Fig. 10. Simulations of the malaria model using controls u_1, u_2 and u_3.

four cases in providing control strategies as follows.

Case 1: Optimal use of insecticide control u_1 and prevention control u_2.

In this case, we utilize the control variables u_1 and u_2 only and set $u_3 = 0$. The simulation results are depicted in Fig. 7. As shown in Fig. 7 (a)-(d) that the number of the exposed and infectious humans and also infectious mosquitoes are lower when the controls u_1 and u_2 are applied than the Case without controls. The optimal control profiles in the present Case are given in Fig. 7(e). In Fig. 7(e), we can see that the insecticide is maintained at 100% for 97 days before reduces to zero in the final time intervention, while prevention is kept at 100% for around 11 days before decreasing to 14 % on day 20 and then fluctuating until the end of the observation to zero.

Case 2: Optimal use of insecticide control u_1 and treatment control u_3.

In this case, we employ the control variables u_1 and u_3 only and set $u_2 = 0$. The numerical simulations of this strategy are displayed in Fig. 8 (a)-(d). Looking at Fig. 8 that the number of the infectious humans more decrease compared to the result in Case 1, while the exposed human with the long-term period (E_{lh}) increased ia a small number. The exposed human with short-term period (E_{sh}) and also the infectious mosquitoes show the same behaviour with Case 1. The optimal control profiles in this Case are summarized in Fig. 8(e). In this strategy, it is recognized that insecticide effort has adhered at the maximum level of 100% for 12 days before decreasing to 48 % on day 23 and then given fluctuating until the rest of the intervention to zero, while the treatment is attempted at the maximum level of 100% for 12 days before declining to zero in the final time of the intervention.

Case 3: Optimal use of prevention control u_2 and treatment control u_3.

In this case, we explore the control variables u_2 and u_3 only and set $u_1 = 0$. The graphical results of this Case can be seen in Fig. 9 (a)-(d). Fig. 9 shows that the size of the infectious mosquitoes increases less compared to the result in Case 1 and Case 2, while the exposed and infectious humans show the same behaviour with Case 1 and Case 2. The optimal control profiles in this Case are set out in Fig. 9(e). As shown in Fig. 9(e), the prevention effort should be sustained at the maximum coverage 100% until 95 days before it reduces to zero in the final time, whereas the treatment effort is retained at the maximum level 100% for about 31 days before gradually declining to zero in the final time of the intervention.

Case 4: Optimal use of insecticide control u_1, prevention control u_2 and treatment control u_3.

In this case, we implement all the control variables u_1, u_2 and u_3. The

graphical simulations of this Case are presented in Fig. 10. Looking at Fig. 10(a)-(d), one can observe that the number of the infectious humans (I_h), the exposed human with the long-term period (E_{lh}), and the infectious mosquitoes (I_v) decrease more sharply compared to Case 1, Case 2 and Case 3 respectively. While the number of the exposed human with the short-term period (E_{sh}) gives the same result with other strategies. The optimal control profiles of the last Case are displayed in Fig. 10(e). As can be seen from Fig. 10(e), the insecticide is given at a maximum level for around 13 days before decreasing to 47 % on day 23 and then given fluctuating until the end of the intervention to zero. Furthermore, the prevention is kept at maximum coverage for just 11 days before it reduces to 2% on day 23 and reaching to zero in the final time, while the treatment is sustained at full effort for about 11 days and then gradually decreases to zero at the end of the intervention.

Based on Case 1 to Case 4, it can be seen that combination of the three optimal control variables simultaneously is the most prominent strategy to minimize the malaria disease in the community as well. In particular, insecticides can be applied in a fluctuating manner when combined with treatment measures alone or in combination with all controls. Meanwhile, prevention can be given fluctuating when combined with insecticides alone.

Conclusion

In this paper, we have studied some mathematical models of malaria transmission with and without seasonal factor. The model without seasonal factor has two equilibria, namely the disease-free equilibrium and the endemic equilibrium. The disease-free equilibrium is locally asymptotically stable if $R_0 < 1$. The malaria model has a unique endemic equilibrium when $R_0 > 1$. The global sensitivity analysis is then investigated using Partial rank correlation coefficient (PRCC) to reveal the parameters that give the most influence on malaria transmission. The analysis result exhibits that the transmission rate and mosquitoes lifespan show the most strong sensitive parameters.

The simulation results of the malaria model with seasonal factor have been implemented in three scenarios. From the three scenarios, the seasonal factors have the most influence on infectious mosquitoes and also human populations exposed in region with hot climate.

Thereafter, we have integrated the optimal control strategy in the form of insecticide, prevention, and treatment efforts to minimize the spread of malaria in the population. We have demonstrated four different strategies for malaria mitigation. From the simulation experiments, it can be seen that the number of infected (exposed and infectious) humans and infectious mosquitoes can be reduced by various combinations of the control variables. However, activating the three controls simultaneously is the best intervention strategy to minimize malaria transmission in the community. These results are in line with previous studies which show that temperature and rainfall are important factors in modeling seasonal vector-borne diseases that can affect the biting rate, survival, and abundance of mosquitoes.

CRediT authorship contribution statement

Fatmawati: Conceptualization, Formal analysis, Funding acquisition, Methodology, Software, Writing - review & editing. **Faishal Farrel Herdicho:** Conceptualization, Writing - original draft, Software, Visualization. **Windarto:** Writing - original draft, Formal analysis. **Williams Chukwu:** Writing - original draft, Visualization, Writing - review & editing. **Hengki Tasman:** Formal analysis, Visualization, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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