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Understanding the effects of individual awareness and vector controls on malaria transmission dynamics using multiple optimal control

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ABSTRACT

Malaria is a vector-borne diseases caused by parasite of genus *Plasmodium* and is transmitted via a bite of mosquitoes. Although the number of malaria cases has been reduced, an outbreak still happens, which causes deaths particularly in children. In this paper, mathematical models in the absence and presence of awareness programs and vector controls have been formulated and studied. The qualitative analysis of the model has been conducted. A global sensitivity analysis of the model has been performed to determine the most influential parameters on the increasing number of infected individuals and the reproduction number. An optimal control approach has been used to analyse the effects of control strategies and the model is fitted to data of malaria cases from Weeluri Health Center, Central Sumba, Indonesia. Qualitative analysis of the model showed that the disease-free and endemic equilibrium are globally stable. Furthermore, the reproduction number for malaria is found to be $\mathcal{R}_0 = 1.1199$. Results from global sensitivity analyses showed that the biting rate, the transmission probability from mosquitoes to human, and human to mosquitoes, and the number of mosquitoes per human are the most influential parameters, which indicate the importance of reducing the contact between human and mosquitoes. This suggests the awareness of individuals to take the prevention actions hold an important role for reducing the contact with mosquitoes. Furthermore, using the Pontryagin maximum principle, we found that the awareness programs and vector control should be implemented at a higher level and the vector controls need to be applied for the entire period to obtain the reduction in the number of infected individuals at the minimum costs. Interestingly, in the absence of vector control programs, it is still possible to reduce the number of malaria cases when the awareness programs have been implemented and aware individuals are willing to take the prevention actions.

1. Introduction

Malaria is the vector-borne disease caused by parasite of genus *plasmodium* and is transmitted via a bite of *Anopheles* mosquitoes. There are four species of parasites which cause malaria: *P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale*. An estimated 229 million cases happens in 2019 with 409,000 deaths and 67% of deaths are children under five years old [1]. Furthermore, the malaria poses social and economic burden [2–4] and hence its elimination is of importance.

Strategies for eliminating malaria such as insecticides treated nets (ITNs), indoor residual spraying, have been implemented, some of them are found effective in reducing the number of malaria cases [5–7]. The efficacy of current control strategies has stagnated and temporarily effective [8,9], and malaria incidence tends to increase recent years [10–12]. For example, the use of mass drug administration can reduce the number of malaria cases temporary and it is suggested that this should be combined with other intervention such as vector controls [8]. The combination of several intervention strategies may not be effective for long-term [13] and hence individual's awareness to take the prevention actions may play important role in reducing the number of malaria cases. Studies on the effects of individual's awareness on malaria transmission dynamics are important. This would provide scientific information regarding the role of individual's awareness in the effort for malaria elimination.

Understanding the complex phenomena using mathematical models is common [14–18]. Many mathematical model have been formulated and studied to investigate the disease transmission dynamics such as malaria [16,17,19–22], dengue [23–26], and others [27–29], and the effectiveness of their interventions. Studies on effects of controls have frequently used optimal control approach

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which aims to minimise the number of infected individuals with minimal cost [23,30,31]. Various mathematical models of malaria have been formulated and studied [16,17,19,31,32]. Aldila and Angelina [19] formulated a malaria mathematical model and studied the effects of vector bias and its effects of malaria controls. An optimal control approach has been used to analyse the effects of controls. They perform a theoretical approach and have not validated their model against data. They found that the time-dependent fumigation and medical treatment could slow the transmission of malaria efficiently at minimum cost. The same approach has also been used by Fatmawati and Tasman [16] to theoretically analyse the malaria transmission dynamics by considering the resistance of malaria parasites to the anti-malarial drug, and found that the implementation of the mass treatment and insecticide provide better and efficient results for reducing malaria incidence. Furthermore, the effects of partial immunity and protected travellers on malaria transmission dynamics have been studied in [17] and showed that the presence of protected travellers in a population does not constitute threat to the control of malaria. Most malaria mathematical models have been formulated and analysed to investigate the effects of control strategies: pharmaceutical and non-pharmaceutical controls [13,21,22,31,33–39]. The questions that have been answered centered around the the transmission dynamics of malaria and effectiveness of the malaria control strategies.

An important aspect for the implementation of malaria control strategies is the individual awareness about malaria and their willing to take effective prevention actions to reduce disease transmission. A number of mathematical models for studying the effects of awareness of individuals on disease transmission dynamics have been formulated and studied [40–44] including the effects of individuals awareness on malaria transmission dynamics [45,46]. Kar et al. [40] studied the effects of awareness through media on disease transmission dynamics. They found that the awareness program through media campaign can be effective on reducing disease incidence. Their model considered the effects of awareness through media control by assuming that the aware individuals move to recovered class. Khatua and Kar [41] explored the effects of media awareness on disease transmission dynamics using stage-structured epidemic model. They found that the media campaign can reduce the disease incidence and disease extinction time. Most mathematical models to study the effects of awareness have been formulated by assuming the awareness individuals moves to recovered class or reduction in the transmission rate. To the best of our knowledge, not many mathematical models has been formulated to study the effects of awareness on malaria transmission dynamics [45–47]. Ibrahim et al. [45] formulated mathematical models for malaria and studied the effects of awareness on malaria transmission dynamics. In their model, they divided infected population into aware and unaware infected individuals. They found that the awareness is an important factor which contributes to the reduction in malaria incidence. However, they do not consider the awareness of susceptible individuals who may take the prevention actions which can potentially minimize the transmission rate. The effects of mass campaigns on malaria transmission dynamics have also been studied [46]. They used an individual-based simulation model of malaria transmission by considering seasonal transmission setting. Basir et al. formulated a mathematical model for malaria where the level of awareness is in a separate compartment and the reduction in the transmission rate is modeled as a function of the level of awareness [47]. In this work, we investigated the effects of awareness programs and vector controls on malaria transmission dynamics using mathematical models and optimal control approach. Different to aforementioned studies, we divided the susceptible population into unaware and aware population. An increase in the population of aware individuals comes from natural awareness and awareness due to intervention. The aware population still has chance to get infected with reduced transmission rate when they take the prevention actions. Furthermore, the model is validated against data of Malaria incidence from Weeluri Health Center, Central Sumba, Indonesia, and the basic reproduction number is calculated.

The organization of the paper is the following. Section 2 presents a mathematical model and followed by analysis of the model. Optimal control approach is presented in the following section and it is followed by parameter estimation of the model. Numerical simulations as well as discussion and conclusions are presented in the last two section.

2. Formulation of mathematical model

In this section, we present the formulation of mathematical model in the presence of natural awareness. We assume that there are individuals who are aware of the presence of malaria and are willing to take prevention actions to reduce the contact with mosquitoes, which can reduce the transmission rate.

The population is divided into susceptible individuals who are not aware and aware of malaria (S_{hu} and S_{ha}, respectively), infected individuals (I_h), recovered individuals (R_h). The mosquito population is divided into susceptible (S_v and infected mosquitoes (I_v). In the model, the population is divided into

$$\begin{aligned}
\frac{dS_{hu}}{dt} &= (1-\tau)\Lambda_h - \frac{bp_h I_v}{N_h} S_{hu} - \mu_h S_{hu},\\
\frac{dS_{ha}}{dt} &= \tau\Lambda_h - (1-u_2)\frac{bp_h I_v}{N_h} S_{ha} - \mu_h S_{ha},\\
\frac{dI_h}{dt} &= \frac{bp_h I_v}{N_h} S_{hu} + (1-u_2)\frac{bp_h I_v}{N_h} S_{ha} - \gamma I_h - \mu_h I_h,\\
\frac{dR_h}{dt} &= \gamma I_h - \mu_h R_h,\\
\frac{dS_v}{dt} &= \Lambda_v - \frac{bp_v I_h}{N_h} S_v - \mu_v S_v,\\
\frac{dI_v}{dt} &= \frac{bp_v I_h}{N_h} S_v - \mu_v I_v.
\end{aligned} \tag{1}$$

A proportion τ of newborn is naturally aware of malaria due to the awareness of their parents, and the aware individuals are likely to take prevention actions which can reduce the transmission rate. When an infected mosquito bites susceptible individuals, they are likely to attract malaria at a rate $bp_v I_v/N_h$ where the transmission from infected mosquitoes to aware individuals has been reduced by u_2 and hence the chance to be infected is $(1-u_2)bp_v I_v/N_h$. We assume constant population of humans and mosquitoes and hence $\Lambda_h = \mu_h N_h$ and $\Lambda_v = \mu_v N_v$.

3. Analysis of the model

3.1. Positivity and boundedness

Theorem 1. *Solution of system (1) with non-negative initial conditions $S_{hu}(0)$, $S_{hw}(0)$, $I_h(0)$, $R_h(0)$, $S_v(0)$, $I_v(0)$,a remain nonnegative for all $t > 0$.*

Proof. The first equation of the system (1) gives

$$\frac{dS_{hu}}{dt} + \frac{bp_h I_v}{N_h} S_{hu} + \mu_h S_{hu} \geq 0$$

which on integration gives

$$\frac{d}{dt}\left[S_{hu}(t) \exp\left\{ \int_0^t \frac{bp_h I_v(s)}{N_h} ds + \mu_h t \right\} \right] \geq 0$$

This implies that

$$S_{hu}(t) \geq S_{hu}(0) \exp\left\{ -\left(\int_0^t \frac{bp_h I_v(s)}{N_h} ds + \mu_h t \right) \right\} > 0\,, \forall t > 0$$

Using the similar approach, we can show that the other state variables are non-negative for all time $t > 0$. □

Theorem 2. *Let* $\Omega_h = \left\{S_{hu}(t), S_{hw}(t), I_h(t), R_h(t) \text{ in} \mathcal{R}^4 : N_h(t) \leq \frac{\Lambda_h}{\mu_h}\right\}$ *and* $\Omega_v = \left\{S_v(t), I_v(t) \text{ in} \mathcal{R}^2 : N_v \leq \frac{\Lambda_v}{\mu_v}\right\}$, *so that* $\Omega = \Omega_h \times \Omega_v \subset R_+^4 \times R_+^2$. *The biologically feasible region of the system (1) is positively invariant.*

Proof. It is clear that the sum of the first four equations gives

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h$$

Solving the equations to obtain

$$N_h(t) = N_h(0)e^{-\mu_h t} + (\Lambda_h/\mu_h)(1 - e^{-\mu_h t}).$$

Adding the last two equations gives

$$\frac{dN_v}{dt} = \Lambda_v - \mu_v N_v$$

Solving the equation to obtain

$$N_v(t) = N_v(0)e^{-\mu_v t} + (\Lambda_v/\mu_v)(1 - e^{-\mu_v t}).$$

We can see clearly that $N_h(t) \to \Lambda_h/\mu_h$ and $N_v(t) \to \Lambda_v/\mu_v$ as $t \to \infty$. Particulary, $N_h(t) \leq \Lambda_h/\mu_h$ if $N_h(0) \leq \Lambda_h/\mu_h$ and $N_v(0) \leq \Lambda_v/\mu_v$ if $N_v(0) \leq \Lambda_v/\mu_v$. Hence Ω is positively invariant. □

3.2. Existence of equilibrium points and bifurcation Analysis

By setting the right hand side of Model (1), we obtain two equilibrium points: the disease free equilibrium point, denoted by $\mathcal{E}_0$, and endemic equilibrium point, denoted by $\mathcal{E}_1$. The disease free equilibrium is

$$\mathcal{E}_0 = \left(S_{hu}^*, S_{ha}^*, I_h^*, R_h^*, S_v^*, I_v^*\right) = \left(\frac{(1-\tau)\Lambda_h}{\mu_h}, \frac{\tau\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0\right)$$

The reproduction number is obtained by constructing the next generation matrix and found the spectral radius of the matrix [48,49]. The transmission vector is

$$\mathcal{T} = \begin{pmatrix} \frac{bp_h I_v}{N_h} S_{hu} + (1-u_1)\frac{bp_h I_v}{N_h} S_{ha} \\ \frac{bp_v I_h}{N_h} S_v \end{pmatrix}, \tag{2}$$

and the transition vector is

$$\Sigma = \begin{pmatrix} -(\gamma + \mu_h) I_h \\ -\mu_v I_v \end{pmatrix}. \tag{3}$$

The transmission and transition matrix has then been determined, the inverse of the transition matrix has been found. The multiplication of the transmission matrix and the inverse of the transition matrix is the next generation matrix. The largest eigenvalue of the next generation matrix is the reproduction number. The reproduction number for Model (1) is given by

$$\mathcal{R}_0^2 = \frac{b^2 p_h p_v (1 - \tau u_2)}{\mu_v(\gamma + \mu_h)} \frac{N_v}{N_h} \tag{4}$$

The following theorem states the stability of the disease-free equilibrium point.

Theorem 3. *If* $\mathcal{R}_0 < 1$ *then the disease-free equilibrium is locally asymptotically stable.*

Proof. The Jacobian matrix of (1) at E_0 is

$$J(\mathcal{E}_0) = \begin{bmatrix} -\mu_h & 0 & 0 & 0 & 0 & -\frac{\beta_h(1-\tau)\Lambda_h}{\mu_h} \\ 0 & -\mu_h & 0 & 0 & 0 & -\frac{\beta_h(1-u_2)\tau\Lambda_h}{\mu_h} \\ 0 & 0 & -(\gamma+\mu_h) & 0 & 0 & \frac{\beta_h\Lambda_h(1-\tau u_2)}{\mu_h} \\ 0 & 0 & \gamma & -\mu_h & 0 & 0 \\ 0 & 0 & -\frac{bp_v N_v}{N_h} & 0 & -\mu & 0 \\ 0 & 0 & \frac{bp_v N_v}{N_h} & 0 & 0 & -\mu \end{bmatrix}.$$

The Jacobian matrix $J(\mathcal{E}_0)$ have four negative eigenvalues, $\lambda_1 = -\mu_h$ with a multiplicity of three and $\lambda_2 = -\mu_v$. The two others eigenvalues are the solution of equation

$$\lambda^2 + (\gamma + \mu_h + \mu_v)\lambda + (\gamma + \mu_h)\mu_v(1 - \mathcal{R}_0^2) = 0 \tag{5}$$

The Eq. (5) has a real negative part if $\mathcal{R}_0 < 1$. Hence, the disease-free equilibrium $\mathcal{E}_0$ of Model 1 is locally asymptotically stable if $\mathcal{R}_0 < 1$. This completes the proof. □

In fact, we can prove the global stability of $\mathcal{E}_0$ when $\mathcal{R}_0 \leq 1$.

Theorem 4. *If* $\mathcal{R}_0 \leq 1$, *then the disease-free equilibrium is globally asymptotically stable.*

Proof. Consider the following Lyapunov Function:

$$L = bp_v \frac{N_v}{N_h} I_h + (\gamma + \mu_h) I_v. \tag{6}$$

The Lyapunov derivative is

$$\begin{aligned} \frac{dL}{dt} &= bp_v \frac{N_v}{N_h}\frac{dI_h}{dt} + (\gamma+\mu_h)\frac{dI_v}{dt} \\ &= bp_v \frac{N_v}{N_h}\left(\frac{bp_h I_v}{N_h} S_{hu} + (1-u_2)\frac{N_v}{N_h}\frac{bp_h I_v}{N_h} S_{ha} - (\gamma+\mu_h) I_h\right) \\ &\quad + (\gamma+\mu_h)\left(\frac{bp_h I_h}{N_h} S_v - \mu_v I_v\right) \\ &\leq bp_v \frac{N_v}{N_h}\left(\frac{bp_h I_v}{N_h}\frac{(1-\tau)\Lambda_h}{\mu_h} + (1-u_2)\frac{N_v}{N_h}\frac{bp_h I_v}{N_h}\frac{\tau\Lambda_h}{\mu_h} - (\gamma+\mu_h) I_h\right) \\ &\quad + (\gamma+\mu_h)\left(\frac{bp_h I_h}{N_h} N_v - \mu_v I_v\right) \\ &\leq (\mathcal{R}_0^2 - 1) I_v. \end{aligned}$$

It follows that $\frac{dL}{dt} \leq 0$ whenever $\mathcal{R}_0 \leq 1$, with $\frac{dL}{dt} = 0$ if and only if $I_v = 0$. Hence, L is a Lyapunov function on Ω. By LaSalle's Invariance Principle, we get $I_v(t) \to 0$ as $t \to \infty$. Since $lim_{t\to\infty} I_v(t) = 0$, there exist a constant M such that for sufficiently small $\varepsilon > 0$, $lim_{t\to\infty} I_v(t) \leq \varepsilon$ for all $t > M$. More over, for $t > M$ we have

$$\frac{dI_h}{dt} \leq \left(\frac{bp_h S_{hu}}{N_h} + (1-u_2)\frac{N_v}{N_h}\frac{bp_h S_{ha}}{N_h}\right)\varepsilon - (\gamma+\mu_h) I_h$$

Thus, by comparison theorem, we get

$$lim_{t\to\infty} \text{sup} I_h \leq \left(\frac{bp_h S_{hu}}{N_h} + (1-u_2)\frac{N_v}{N_h}\frac{bp_h S_{ha}}{N_h}\right)\frac{\varepsilon}{\gamma+\mu_h}.$$

By letting $\varepsilon \to \infty$, we get $lim_{t\to\infty} \text{sup} I_h \leq 0$. Similarly, by using $lim_{t\to\infty} \text{inf} I_v \leq 0$, we get $lim_{t\to\infty} \text{inf} I_h \geq 0$. Hence $lim_{t\to\infty} I_h = 0$.

Similarly, it can be shown that

$$lim_{t\to\infty} R_h = 0, lim_{t\to\infty} S_{hu} = \frac{(1-\tau)\Lambda_h}{\mu_h}, lim_{t\to\infty}$$

$$S_{ha} = \frac{\tau\Lambda_h}{\mu_h}, lim_{t\to\infty} S_v = \frac{\Lambda_v}{\mu_v}.$$

Therefore, every solution of Model 1 with initial condition in Ω tend to the disease-free equilibrium point $\mathcal{E}_0$ as t goes to infinity. This completes the proof. □

The endemic equation is

$$\mathcal{E}_1^* = \left(\frac{(1-\tau)\Lambda_h}{\beta_h I_v^* + \mu_h}, \frac{\tau\Lambda_h}{(1-u_2)\beta_h I_v^* + \mu_h}, \frac{\mu_v(\beta_h I_v^* + \mu_v) I_v^*}{\beta_v \Lambda_v}, \frac{\gamma I_v^*}{\mu_h}, \frac{\Lambda_v}{\beta_h I_v^* + \mu_v}, I_v^*\right)$$

where

$$\beta_h = \frac{bp_h}{N_h}, \beta_v = \frac{bp_v}{N_h}.$$

and I_v^* is positive solution of cubic equation

$$c_3 I_v^3 + c_2 I_v^2 + c_1 I_v + c_0 = 0, \tag{7}$$

with

$$\begin{aligned}
c_3 &= (1-u_2)\frac{(\gamma+\mu_h)\mu_v\beta_h^3}{\beta_v},\\
c_2 &= \frac{(\gamma+\mu_h)\mu_v}{\beta_v}(1-u_2)(\mu_v+\mu_h)\beta_h^2,\\
c_1 &= \frac{\beta_h(\gamma+\mu_h)\mu_v}{\beta_v}(\mu_v\mu_h(1-u_2)\\
&\quad+\mu_h\beta_h+(\mu_v+\mu_h)\mu_h)+\beta_h^2\Lambda_v\Lambda_h(1-\tau)u_2\\
&\quad+\frac{\mu_v\mu_h(\gamma+\mu_h)\mu_v p_h}{p_v N_h}(1-\mathcal{R}_0^2),\\
c_0 &= \frac{\mu_v^2\mu_h^2(\gamma+\mu_h)N_h}{bp_v}(1-\mathcal{R}_0^2).
\end{aligned}$$

The coefficients c_3 and c_2 are always positive, while the coefficient c_1 and c_0 can be positive or negative. We found that if $\mathcal{R}_0 < 1$, then both of c_1 and c_0 are positive, so that the Eq. (7) has no positive real solution. Meanwhile, if $\mathcal{R}_0 > 1$, then c_1 can be positive or negative and c_0 is always negative. Even so, there is only one change of sign in the coefficient of Eq. (7) in both cases. Hence, Eq. (7) has only one positive real root. We state the results in the following theorem.

Theorem 5. *The following results holds:*

1. *The system (1) has no endemic equilibrium point if* $\mathcal{R}_0 \le 1$,
2. *The system (1) has a unique endemic equilibrium point if* $\mathcal{R}_0 > 1$

Thus, it is clear from Theorem 5 that the system 1 has no endemic equilibrium whenever $\mathcal{R}_0 \le 1$ and has a unique endemic equilibrium point if $\mathcal{R}_0 > 1$ and $c_1 > 0$. For the stability of endemic equilibrium point, in the following theorem we prove that endemic equilibrium $\mathcal{E}_1^*$ is globally asymptotically stable.

Theorem 6. *If* $\mathcal{R}_0 > 1$, *then the endemic equilibrium* $\mathcal{E}_1^*$ *is globally asymptotically stable.*

Proof. Consider the Lyapunov function

$$L^* = S_v - S_v^* \ln S_v + I_v - I_v^* \ln I_v - (S_v^* - S_v^* \ln S_v^* + I_v^* - I_v^* \ln I_v^*). \tag{8}$$

The derivative of L^* along the solution of system (1) is

$$\begin{aligned}
\frac{dL^*}{dt} &= \left(1-\frac{S_v^*}{S_v}\right)\frac{dS_v}{dt}+\left(1-\frac{I_v^*}{I_v}\right)\frac{dI_v}{dt}\\
&= \left(1-\frac{S_v^*}{S_v}\right)\left(\Lambda_v-\frac{bp_v I_h}{N_h}S_v-\mu_v S_v\right)+\left(1-\frac{I_v^*}{I_v}\right)\left(\frac{bp_v I_h}{N_h}S_v-\mu_v I_v\right)\\
&= \Lambda_v-\frac{bp_v I_h}{N_h}S_v-\mu_v S_v-\Lambda_v\frac{S_v^*}{S_v}+\frac{bp_v I_h}{N_h}S_v^*+\mu_v S_v^*+\frac{bp_v I_h}{N_h}S_v-\mu_v I_v\\
&\quad-\frac{bp_v I_h}{N_h}\frac{S_v I_h}{I_v^*}+\mu_v I_v^*.
\end{aligned}$$

Taking $\Lambda_v = \frac{bp_v}{N_h}I_h S_v^* + \mu_v S_v^*$, we obtain

$$\begin{aligned}
\frac{dL^*}{dt} &= \frac{bp_v}{N_h}I_h S_v^*+\mu_v S_v^*-\frac{bp_v I_h}{N_h}S_v-\mu_v S_v-\frac{bp_v}{N_h}I_h S_v^*\frac{S_v^*}{S_v}-\mu_v S_v^*\frac{S_v^*}{S_v}\\
&\quad+\frac{bp_v}{N_h}I_h S_v^*+\mu_v S_v^*+\frac{bp_v}{N_h}I_h S_v-\mu_v I_v-\frac{bp_v}{N_h}I_h S_v\frac{I_v^*}{I_v}+\mu_v I_v^*.
\end{aligned}$$

Substitute $\frac{bp_v}{N_h}I_h S_v = \mu_v I_v^*$ to get

$$\begin{aligned}
\frac{dL^*}{dt} &= \frac{bp_v}{N_h}I_h S_v^*\left(2-\frac{S_v}{S_v^*}-\frac{S_v^*}{S_v}\right)+\mu_v S_v^*\left(2-\frac{S_v}{S_v^*}-\frac{S_v^*}{S_v}\right)\\
&\quad+\mu_v I_v^*\left(2-\frac{I_v}{I_v^*}-\frac{I_v^*}{I_v}\right).
\end{aligned}$$

Since $\left(2-\frac{I_v}{I_v^*}-\frac{I_v^*}{I_v}\right)\le 0$ and $\left(2-\frac{S_v}{S_v^*}-\frac{S_v^*}{S_v}\right)\le 0$, we get $\frac{dL^*}{dt}\le 0$. Hence, the endemic equilibrium point $\mathcal{E}_1^*$ is globally asymptotically stable whenever $R_0 > 1$. This completes the proof. □

3.3. Sensitivity analysis

In this section, we perform a global sensitivity analysis of the model by using the combination of Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficient (PRCC) multivariate analysis. We measure against the reproduction number and an increasing number of infected individuals. The increasing number of infected individuals is given by the following equations

$$C_{ih} = \int_0^t \left(\frac{bp_h I_v}{N_h}S_{hu}+(1-u_2)\frac{bp_h I_v}{N_h}S_{ha}\right)d\omega. \tag{9}$$

and the reproduction numbers are given in Eqs. (4) and (12).

4. Optimal control approach

4.1. Formulation of mathematical model in the presence of awareness programs and vector controls

In this section, we implement an optimal control approach to understand the effects of control on malaria transmission dynamics. We extend Model (1) to include the awareness program and the vector control in the model. The rate of awareness program and vector controls are u_1 and u_3, respectively. The model is governed by the following system of differential equations.

$$\begin{aligned}
\frac{dS_{hu}}{dt} &= (1-\tau)\Lambda_h-\frac{bp_h I_v}{N_h}S_{hu}-\epsilon u_1 S_{hu}-\mu_h S_{hu},\\
\frac{dS_{ha}}{dt} &= \tau\Lambda_h+\epsilon u_1 S_{hu}-(1-u_2)\frac{bp_h I_v}{N_h}S_{ha}-\mu_h S_{ha},\\
\frac{dI_h}{dt} &= \frac{bp_h I_v}{N_h}S_{hu}+(1-u_2)\frac{bp_h I_v}{N_h}S_{ha}-\gamma I_h-\mu_h I_h,\\
\frac{dR_h}{dt} &= \gamma I_h-\mu_h R_h,\\
\frac{dS_v}{dt} &= \Lambda_v-\frac{bp_v I_h}{N_h}S_v-(u_3+\mu_v)S_v,\\
\frac{dI_v}{dt} &= \frac{bp_v I_h}{N_h}S_v-(u_3+\mu_v)I_v.
\end{aligned} \tag{10}$$

with initial conditions

$$\begin{aligned}
&S_{hu}(0) = S_{hu0}\ge 0, S_{ha}(0) = S_{ha0}\ge 0, I_h(0) = I_{h0}\ge 0,\\
&R_h(0) = R_{h0}\ge 0, S_v(0) = S_{v0}\ge 0, I_v(0) = I_{v0}\ge 0.
\end{aligned} \tag{11}$$

The description of the parameters is given in Table 1.

The reproduction number of Model (10) is found by construction the next generation matrix, and is given by

$$\mathcal{R}_E^2 = \frac{b^2 p_h p_v \mu_v(\epsilon u_1(1-u_2)+\mu_h(1-\tau u_2))N_v}{(\gamma+\mu_h)(\epsilon u_1+\mu_h)(\mu_v+u_3)^2 N_h}. \tag{12}$$

A global sensitivity analysis on the reproduction number (Eq. (12)) would be performed in the next section.

4.2. Existence and characterisation of optimal controls

The existence and characterisation of optimal control are presented in this section. The problem is to minimise the following objective function,

$$\mathcal{J} = \int_0^{t_f}\left(A_1 I_h + A_2(S_v+I_v)+\frac{1}{2}A_3 u_1^2+\frac{1}{2}A_4 u_2^2++\frac{1}{2}A_5 u_3^2\right)dt \tag{13}$$

Table 1
Parameter descriptions, values and units and references of the parameter values.

Symbol	Description	Value	Unit	Source
b	biting rate	1.26	$Month^{-1}$	Fitting
p_h	the transmission probability from mosquito to human	0.95	N/A	Fitting
p_v	the transmission probability from human to mosquitoes	0.75	N/A	Fitting
τ	proportion of individuals who are naturally aware of malaria	0.1	N/A	Assumed
μ_v	death rate of mosquitoes	30/20	$Month^{-1}$	[24,25]
μ_h	death rate of human	$1/(65\times 12)$	$Month^{-1}$	[57]
ϵ	efficacy of awareness program	0.1	N/A	Assumed
u_1	the rate of awareness program	[0 , 1]	$Month^{-1}$	Simulated
u_2	efficacy of prevention action taken by awareness individuals	[0 , 1]	N/A	Simulated
u_3	the rate of vector controls	[0 , 1]	$Month^{-1}$	Simulated

subject to System (10). We aim to minimise the number of infected individuals and the mosquito population and the costs of implementing the awareness programs and vector controls. The control function u_1, u_2 and u_3 are bounded and Lebesque measurable function. The coefficient A_1, A_2, A_3, A_4, and A_5 are balancing coefficient for the controls. We use the quadratic objective functional because the intervention is generally nonlinear [16,50–52].

We aim to find the pair of controls such that

$$\mathcal{J}(u_1^*, u_2^*, u_3^*) = \min\{J(u_1, u_2, u_3)\} \tag{14}$$

The Hamiltonian is written as

$$\begin{aligned}\mathcal{H} = {} & \left(A_1 I_h + A_2(S_v + I_v) + \tfrac{1}{2}A_3u_1^2 + \tfrac{1}{2}A_4u_2^2 + +\tfrac{1}{2}A_5u_3^2\right)\\ & + \lambda_{S_{hu}}\left((1-\tau)\Lambda_h - \tfrac{bp_hI_v}{N_h}S_{hu} - \epsilon u_1 S_{hu} - \mu_h S_{hu}\right)\\ & + \lambda_{S_{ha}}\left(\tau\Lambda_h + \epsilon u_1 S_{hu} - (1-u_1)\tfrac{bp_hI_v}{N_h}S_{ha} - \mu_h S_{ha}\right)\\ & + \lambda_{I_h}\left(\tfrac{bp_hI_v}{N_h}S_{hu} + (1-u_1)\tfrac{bp_hI_v}{N_h}S_{ha} - \gamma I_h - \mu_h I_h\right)\\ & + \lambda_{R_h}(\gamma I_h - \mu_h R_h)\\ & + \lambda_{S_v}\left(\Lambda_v - \tfrac{bp_vI_h}{N_h}S_v - (u_3+\mu_v)S_v\right)\\ & + \lambda_{I_v}\left(\tfrac{bp_vI_h}{N_h}S_v - (u_3+\mu_v)I_v\right).\end{aligned} \tag{15}$$

Theorem 7. *There exists an optimal control pair u_1^*, u_2^*, and u_3^* such that*

$$\mathcal{J}(u_1^*, u_2^*, u_3^*) = \underbrace{\min}_{\Gamma}\{J(u_1, u_2, u_3)\} \tag{16}$$

where $\Gamma = \{(u_1, u_2, u_3) | 0 \le u_1 \le u_1^{\max}, 0 \le u_2 \le u_2^{\max}, 0 \le u_3 \le u_3^{\max}\}$ *subject to the system (10) and initial conditions (11).*

Proof. We use the results from Flemming and Risher [53] and Lukes [54] to prove the existence of optimal control. In order to show the existence of optimal controls, we need to verify the following

1. the set of state and control variables is non empty.
2. Convexity and Closure of the set Γ.
3. Boundedness of the state system by a linear function in the state and control variables.
4. There exists constant $n_1 > 0$, $n_2 > 0$ and $p > 1$ such that the integrand in (13) is convex and satisfy

$$H(I_h, S_v, I_v, u_1, u_2, u_3) \ge n_2 + n_1\left(\sum_{i=1}^{2}|u_i|^2\right)^{\frac{p}{2}}.$$

It can be seen that condition 1 and 2 are satisfied since the state variables and the control variables are non-empty and bounded. Condition 2 is satisfied with the definition of control set Γ. The condition 3 holds due to the linear dependence of the state system on controls u_1 and u_2. Condition 4 can be easily verified by writing

$$\left(A_1 I_h + A_2(S_v + I_v) + A_3u_1^2 + A_4u_2^2 + +A_5u_3^2\right) \ge \omega_2 + \omega_1\left(\sum_{i=1}^{2}|u_i|^2\right)^{\frac{p}{2}}$$

□

Theorem 8. *There exists optimal controls u_1^*, u_2^*, and u_3^* such that the cost function is minimised to over Ω. There exists costate variables*

$$\begin{aligned}\frac{d\lambda_1}{dt} &= -\lambda_1\left(-\frac{bp_hI_v}{N_h} - \mu_h - \epsilon u_1\right) - \lambda_2\epsilon u_1 - \frac{\lambda_3 bp_hI_v}{N_h},\\ \frac{d\lambda_2}{dt} &= -\lambda_2\left(-\frac{(1-u_2)bp_hI_v}{N_h} - \mu_h\right) - \lambda_3\left(\frac{(1-u_2)bp_hI_v}{N_h}\right),\\ \frac{d\lambda_3}{dt} &= -A_1 - \lambda_3(-\gamma - \mu_h) - A_4\gamma + \frac{bp_vS_v}{N_h}(\lambda_5 - \lambda_6)\\ \frac{d\lambda_4}{dt} &= \lambda_4\mu_h,\\ \frac{d\lambda_5}{dt} &= -A_2 - \lambda_5\left(-\frac{bp_vI_h}{N_h} - u_3 - \mu_v\right) - \lambda_6\left(\frac{bp_vI_h}{N_h}\right),\\ \frac{d\lambda_6}{dt} &= -A_2 + \frac{\lambda_1 bp_hS_{hu}}{N_h} + \frac{\lambda_2 bp_h(1-u_2)S_{ha}}{N_h}\\ &\quad -\lambda_3\left(\frac{bp_hS_{hu}}{N_h} + \frac{bp_h(1-u_2)S_{ha}}{N_h}\right) - \lambda_6(-u_3 - \mu_v),\end{aligned} \tag{17}$$

with transversality condition $\lambda_i(t_f) = 0$, $i = 1, 2, 3, 4, 5, 6$ and the optimal control variables are

$$\begin{aligned}u_1^* &= \max\left\{0, \min\left(u_1^{\max}, \frac{\epsilon S_{hu}(\lambda_1 - \lambda_2)}{A_3}\right)\right\},\\ u_2^* &= \max\left\{0, \min\left(u_2^{\max}, \frac{bp_hS_{ha}I_v(\lambda_3 - \lambda_2)}{A_4N_h}\right)\right\},\\ u_3^* &= \max\left\{0, \min\left(u_3^{\max}, \frac{\lambda_5S_v + \lambda_6I_v}{A_5}\right)\right\},\end{aligned} \tag{18}$$

Proof. The system differential equations for the adjoint variables is determined by differentiating the Hamiltonian with respect to the state variables, which are

$$\frac{d\lambda_i}{dt} = -\frac{\partial\mathcal{H}}{\partial x_i}$$

where $i = 1, 2, 3, 4, 5, 6$ denote $\{S_{hu}, S_{ha}, I_h, R_h, S_v, I_v\}$, respectively and we obtain the system of differential equations as given in Eq. (17).Taking the derivative of Hamilton with respect to control variables u_1, u_2, and u_3, we obtain

$$\begin{aligned}\frac{\partial\mathcal{H}}{\partial u_1} &= -\epsilon S_{hu}\lambda_1 + \epsilon S_{hu}\lambda_2 + A_3u_1,\\ \frac{\partial\mathcal{H}}{\partial u_2} &= A_4u_2 + \frac{\lambda_2 bp_hI_vS_{ha}}{N_h} - \frac{\lambda_3 bp_hI_vS_{ha}}{N_h},\\ \frac{\partial\mathcal{H}}{\partial u_3} &= A_5u_3 - S_v\lambda_5 - \lambda_6I_v.\end{aligned}$$

Solving for u_1, u_2, and u_3 to obtain

$$\begin{aligned}u_1 &= \frac{\epsilon S_{hu}(\lambda_1 - \lambda_2)}{A_3},\\ u_2 &= \frac{bp_hS_{ha}I_v(\lambda_3 - \lambda_2)}{A_4N_h},\\ u_3 &= \frac{\lambda_5S_v + \lambda_6I_v}{A_5}.\end{aligned}$$

Using the bounds, we obtain the characterisation as given in Eq. (18). □

5. Parameter estimation

In this section, we estimate the parameter values using the method in [55]. We fit the model to the time series data and obtain the best parameter values using the nonlinear square fitting. We then generate N-times replicated simulated data sets by assuming the Poisson error structure and re-estimate the parameter values for each of the N-simulated data sets. Finally, using the re-estimated parameter values is to construct the confidence interval of the parameters [55]. We fit against monthly data from Weeluri Health Center, Central Sumba Regency, Indonesia. The data is from December 2017 to April 2019. We use the initial condition $S_{hu}(0) = 14400$, $S_{hu}(a) = 1600$, $I_h(0) = 7$, $R_h(0) = 0$, $S_v(0) = 48000$, $I_v(0) = 21$. The total number of susceptible human is the approximate number of population in Mamboroo District which is the area of serive for Weeluri Health Center [56]. The parameters to be estimated are the biting rate (b), the transmission probability from mosquitoes to human (p_h), the transmission probability from human to mosquitoes (p_v), and the reduction in the transmission rate of aware individuals (u_2). The other parameters are obtained from the literature and given in Table 1.

The fitted parameters are $b = 1.26$ (CI=1.1–1.4), $p_h = 0.95$ (CI=0.76–0.98), $p_v = 0.75$ (CI=0.44–0.97), $u_2 = 0.093$ (CI=0.029–0.75). Using these parameter values we obtain the basic reproduction number as $\mathcal{R}_0 = 1.1199$. This means that an outbreak is likely to happen in Mamboroo district, service areas of Weeluri Health Center. These parameter values are used in numerical simulations.

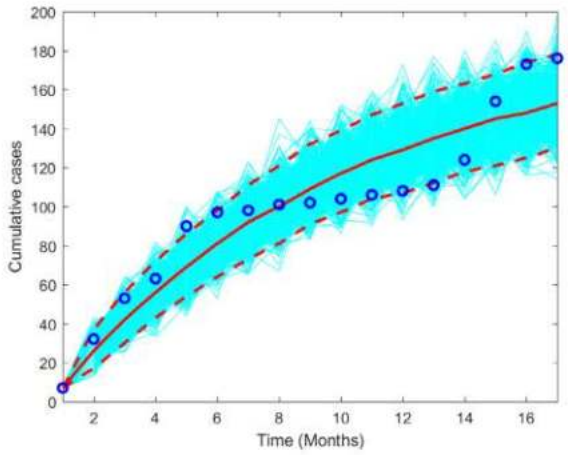

Fig. 1. Fitting parameter the data and the model simulation.

6. Numerical simulations

6.1. Sensitivity analysis

We perform a global sensitivity analysis to investigate the influential parameters on the model outcome. We measure against the increasing number of infected individuals and the reproduction number. We denote the number of mosquitoes per human N_v/N_h

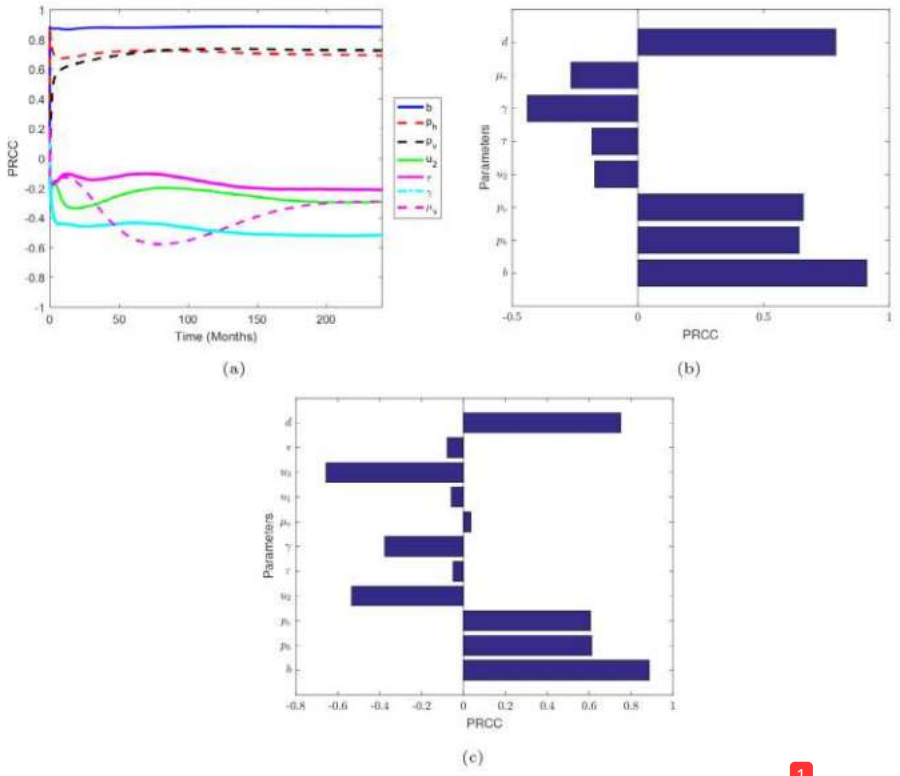

Fig. 2. Sensitivity analysis of the model in the absence and presence of awareness programs and vector control strategies. (a) Plot of PRCC indices when measured against the increasing number of infected individuals in the absence of awareness programs and vector control strategies. (b) Plot of PRCC indices of basic reproduction number in the absence of awareness programs and vector control strategies. (c) PRCC indices of the reproduction number in the presence of control strategies.

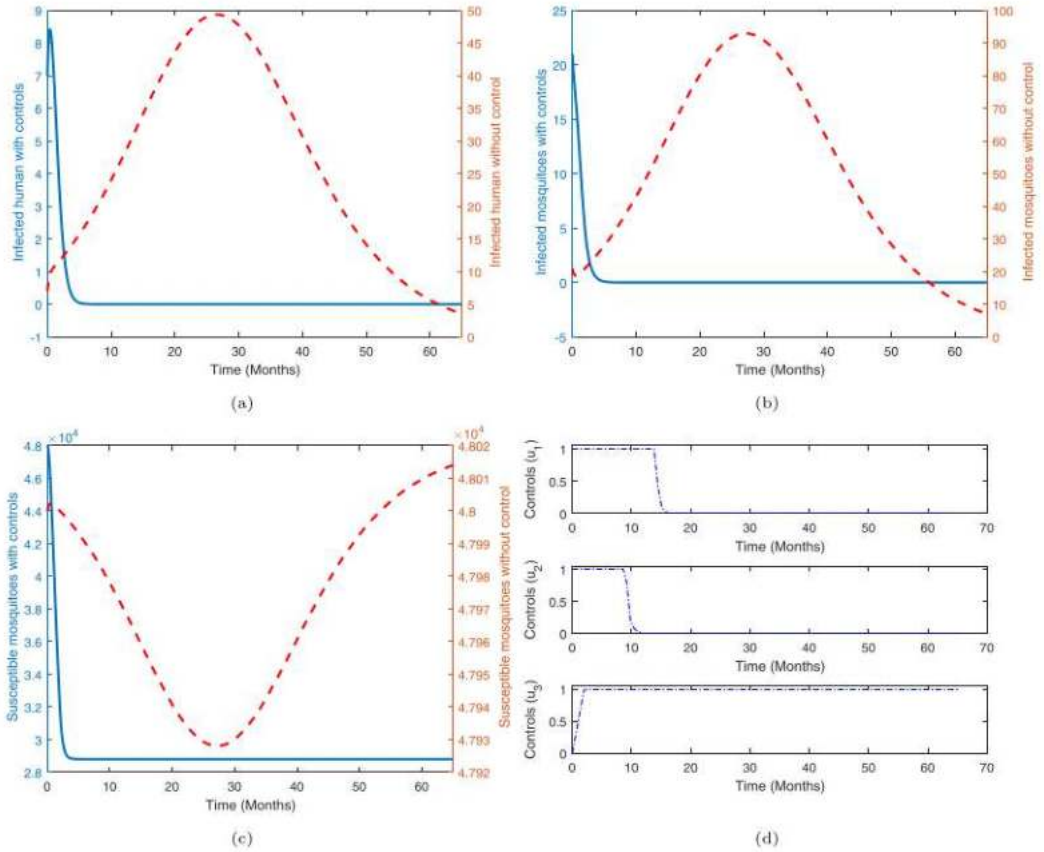

Fig. 3. plot of human and mosquito populations in the with and without controls: (a) infected individuals (b) infected mosquitoes, (c) susceptible mosquitoes (d) Control profiles for u_1, u_2, and u_3.

by d. The increasing number of infected individuals is the solution of the equation

$$\frac{dC}{dt} = \frac{bp_h I_v}{N_h} S_{hu} + (1-u_2)\frac{bp_h I_v}{N_h} S_{ha} \tag{19}$$

where C is the cumulative number of infected individuals (Fig. 1).

Fig. 2 showed the results of global sensitivity analysis when measured against an increasing number of infected individuals in the absence of awareness programs and vector control strategies (plot a) and the reproduction number in the absence and presence of awareness programs and vector control strategies (plot b and c, respectively).

Results showed that in the absence of awareness programs and vector controls, the biting rate (b), the transmission probability from mosquito to human (p_h) and human to mosquitoes (p_v), and the recovery rate (γ) determine an increase in the number of infected individuals (plot a). The first three has positive relationship and the latter has negative relationship. This indicates that an increase in the values of the first three parameters results in an increase in the number of infected individuals. Interestingly, the influence of the death rate of mosquitoes fluctuates over the period. The results of sensitivity analysis on the reproduction number in the absence of awareness also showed the similar results (plot b). The biting rate (b), the transmission probability from mosquito to human (p_h) and human to mosquitoes (p_v), and the number of mosquito per human (d) determines the reproduction number. In the presence of awareness programs and vector controls, the same parameter values as in the absence of control strategies, and the control parameters u_2, u_3 are influential parameters on the reproduction number (plot c). The control parameters have negative relationship, which means that an increase the the values of control variables leads to the decrease in the reproduction number. Interestingly, the awareness program (u_2) do not significantly affect the reproduction number. However, the reduction in the transmission rate of the awareness individuals has significant effects on the reproduction number (plot c).

6.2. Optimal control

In this section, we simulate the model for optimal control problem using the backward-forward sweep method [58] but the rungge-kutta orde4 is replaced by ode45 in Matlab [59]. Generally, the algorithm works as follows. An initial guess of control variables u_1, u_2, u_3 has been made for $t \in [0, t_f]$ where t_f is the final time. This initial guess is used to solve the Model (1) forward in time. Furthermore, the costate variables (Eq. (17)) have been calculated backward in time using the transversality condition and the resulting values for the states and control variables. Then, the control variables have been updated using the optimality condition (18). The iterative process continue until it meets the specified covergence criteria, which is the relative error between the state variables.

Fig. 3 showed that in the presence of awareness programs and vector controls, an outbreak does not happen. Furthermore, al-

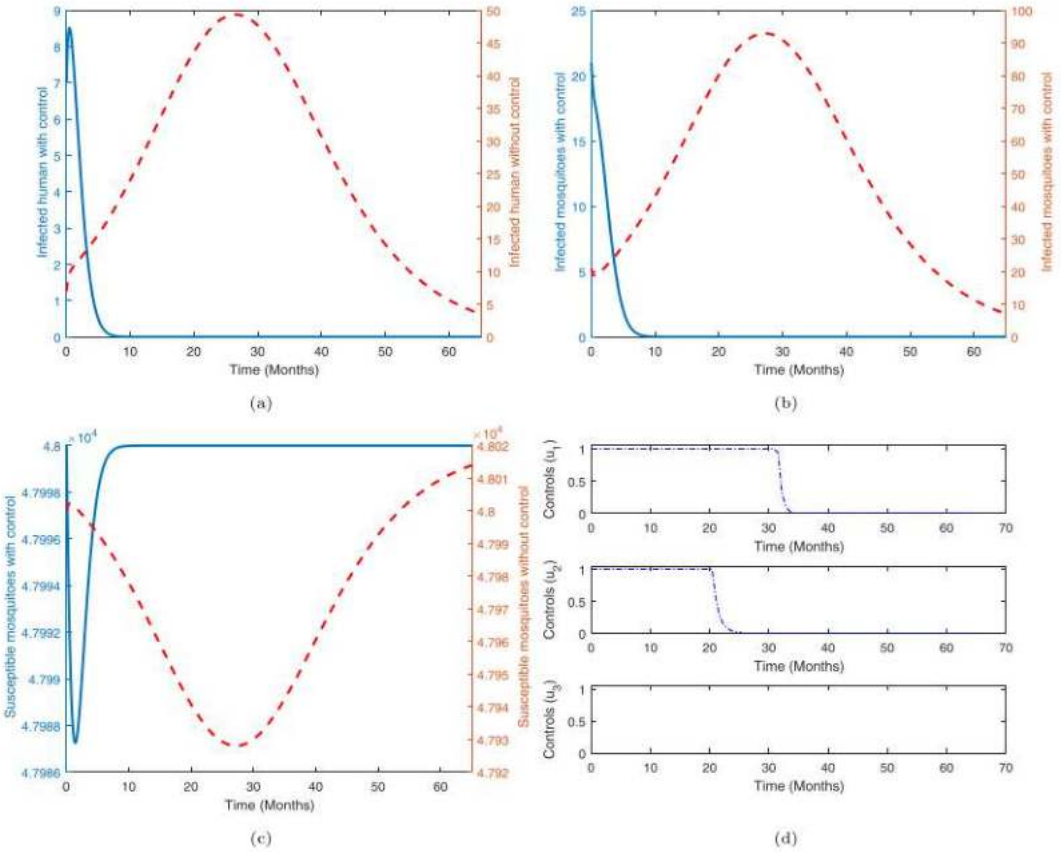

Fig. 4. plot of human and mosquito populations in the absence and presence of controls but the vector controls have not been implemented ($u_3 = 0$): (a) infected individuals (b) infected mosquitoes, (c) susceptible mosquitoes, (d) Control profiles for u_1 and u_2.

though individuals are naturally aware of malaria, it does not guarantee that the number of malaria infections can be reduced if they do not seriously take the prevention action which can reduce greatly the transmission probability (red line of the plot a). The control profiles also showed that the vector controls and awareness programs should be implemented in higher level, where vector controls should be implemented for the entire period. Furthermore, the level of reduction in the transmission rate due to prevention actions taken by aware individuals should be higher (u_2).

Fig. 4 showed the optimal control simulation when the vector controls have not been implemented. It is interesting that in the absence of vector controls, an outbreak does not take off. This is due to the awareness programs and the willingness of awareness individuals to take prevention actions to reduce the transmission rate. In other words, the results indicate the importance of awareness programs and willingness of aware individuals to take prevention actions which can lead to the reduction in malaria incidence although the mosquitoes population still exist. Control profiles suggest that higher level of implementation of awareness programs and reduction in the transmission rate should be implemented.

7. Discussion and conclusions

This paper presents mathematical models in the absence and presence of awareness programs and vector controls. In the absence of awareness programs, we take into account the natural awareness where individuals who are aware of malaria transmission in the absence of awareness programs. Qualitative analysis of the model is performed. An optimal control approach has been implemented in analysing the effects of control on malaria transmission dynamics. A global sensitivity analysis has been performed to determine the most influential parameters on the increasing number of infected individuals and the reproduction number in the absence and presence of awareness programs and vector controls.

Qualitative analyses of the model showed that the disease-free is globally stable when the reproduction number is less than unity and the endemic equilibrium is globally stable when the reproduction number is greater than unity. Furthermore, the results show that the solutions are always non-negative for all time $t > 0$ with non-negative initial conditions. This means that the solutions converge to the non-negative values for non-negative the initial conditions. Therefore, the model is mathematically and epidemiologically well-posed [60]. A global sensitivity analysis showed that the biting rate, the transmission probability from human to mosquitoes and mosquitoes to human, and the number of mosquitoes per human are the influential parameters on the basic reproduction number in the absence of awareness and vector control programs. The results suggest that reducing the contact between mosquitoes aid in minimising the chance for an outbreak to take off. An analysis implies that when individuals take the prevention actions, it has possibility to reduce the number of malaria incidence. The results have been corroborated by results from optimal control approach. It showed that although vector controls have not been implemented, the rate of awareness and willingness of aware in-

dividuals to take prevention actions are likely to reduce malaria incidence. Results suggest that an implementation of awareness program such as media campaign using radio, television or social media should be encouraged in order to increase the population of aware individuals. Furthermore, the aware individuals should be motivated to take effective prevention actions such as using the bednets or mosquito repellent to reduce disease transmission. This would reduce the transmission rate and hence minimize the malaria incidence.

The intervention strategies have long been implemented and an outbreak still happen. Several research showed that the efficacy of control strategies has stagnated [8,9] and therefore human awareness and willingness to take prevention actions hold an important role in reducing malaria incidence [32]. This has been confirmed by our results, that is the importance of awareness individuals in reducing malaria incidence. Further exploration needs to include the other factors such as relapse and reinfection which possibly affect the disease transmission dynamics. As the aim of this research is to obtain general understanding of malaria transmission dynamics under the influence of individual awareness and vector control, this work does not investigate a particular intervention either for vector control, prevention actions to reduce the transmission rates, or programs to increase the population of aware individuals. Therefore, further research needs to investigate specific malaria elimination strategies to obtain comprehensive understanding of the malaria transmission dynamics under specific strategy. These are the subject of future work.

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.

CRediT authorship contribution statement

Meksianis Z. Ndii: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Writing – original draft. **Yudi Ari Adi:** Validation, Formal analysis, Writing – review & editing.

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