A SEIR-SEI Malaria Transmission Model with Optimal Control

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Abstract

In this paper, we propose a SEIR-SEI epidemic model for malaria transmission which describes the interaction between human and mosquito population, with the effects of antibodies produced by the incidence rates for humans and mosquitoes respectively and two optimal controls. We introduce an optimal problem with an objective function, where two control functions, use of treated bed-nets and control effort on malaria treatment , have been used as control measures for infected individuals. The existence of feasible region where the model is well-known is established. Stability analysis of the disease -free equilibrium is investigated. The basic reproduction number $\mathcal{R}_0$, is obtained using the next generation matrix approach. The existence of the endemic equilibrium is also specified under certain conditions. Numerical simulations are carried out to confirm our analytic results and

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our simulation also suggests that, two control strategies are more effective than only one control in controlling the increase of number of infected individuals in the Democratic Republic of the Congo (DRC).

1 Introduction

Malaria is a life threatening vector borne disease caused by parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes. It is a preventable and curable disease [1]. In 2016, an estimated 216 million cases of malaria occurred world wide compared with 237 million cases in 2010 and 214 million new cases of malaria and deaths in 2015. Approximately 80% of malaria death are concentrated in 15 countries most of them in Africa [2, 3]. The Democratic Republic of the Congo(DRC)is one of the two major contributors to the global burden of sickness due to malaria [4]. Mathematical models could mimic the process of malaria and provide very useful tool to analyze the spread and control of malaria behavior. Several different mathematical models for malaria had been formulated and studied since the first model was introduced by Ronald Ross [5]. In 2013, [6], proposed a seven dimensional ordinary differential equation modelling the malaria transmission between humans and mosquitoes with non-linear forces of infection in form of saturated incidence rates which produced antibodies in both human and mosquito populations in response to the presence of parasite-causing malaria. According to their results,increasing the proportions of antibodies has significant effect in reducing the transmission of the malaria infection. Altaf Khan et al. [7] formulated a SEIR model with non-linear saturated rate and temporary immunity, they assumed that the total population is constant, and the new born children are susceptible with no migration. According to their results when $\mathcal{R}_0 < 1$ the disease-free equilibrium is stable locally as well as globally and endemic equilibrium is stable locally as well as globally when $\mathcal{R}_0 > 1$. Their theoretical results was verified by the numerical simulations. Ngwa and Shu [8] analyzed a model which incorporate compartments for the mosquito population. They also introduce into their model a class of persons who are partially immune to the malaria disease but may be infectious. They assumed density dependent death rates in both vector and human populations so that the total population varied with time through a modification of the logistic equation that included disease related deaths. Chitnis et al, [9] evaluated the sensitivity of the reproduction number and the endemic equilibrium. They also generalized the mosquito biting rate and included immigration in a logistic model for the human population with disease-induced mortality. Jia Li [10] developed a SEIR malaria model with stage-structured mosquitoes in which he included metamorphic stages in the mosquito as well as a simple stage mosquito population where the mosquito population is divided into two classes namely, the aquatic stage in one class and all adults in the other class. He concluded that the possible occurrence of backward bifurcation makes the control of malaria more difficult. Many works have been done on modeling the malaria transmission and control using SEIR-SEI model see [11–13]. In this paper, we formulate a SEIR-SEI model with optimal control strategies which is different from the above models by introducing a saturated incidence function with antibodies v_h, v_v for humans and mosquitoes respectively, with two optimal control strategies $u_1(t), u_2(t)$ which differs from most of the mentioned models. Our main objective of this study is to investigate the stability and the sensitivity analysis for the reproduction number, also to show the effect of the antibodies on malaria transmission and how to control the disease with the optimal control strategies. The rest of this paper is organized as follow: Section 2 presents the SEIR-SEI model description and proved the positivity and boundedness of the solutions. In section 3, we analyze the model equilibria including the derivation of the basic reproduction number and stability analysis. In section 4, we perform numerical simulations of the model. In section 5 a sensitivity analysis of the basic reproduction number is presented. Section 6 is devoted to optimal control analysis of the model with the numerical simulations and the conclusion is presented in Section 7.

2 Model Framework

The model is formulated for both humans population and mosquitoes population at time t. The human population is divided into four compartments: Susceptible humans (S_h), Exposed humans (E_h), Infectious humans (I_h), and Recovery humans (R_h) and that of the mosquitoes into three compartments: susceptible mosquitoes (S_v), Exposed mosquitoes (E_v), and Infectious mosquitoes (I_v), respectively. We denote $N_h = S_h + E_h + I_h + R_h$, $N_v = S_v + E_v + I_v$ as the total size of humans and mosquitoes, respectively. The mosquitoes have no recovered compartment and humans enter the susceptible compartment either through birth or immigration. Infected individuals are assumed to recover at a rate $(m\rho_1 + cu_2)$, m is the rate of spontaneous recovery u_2 control on treatment of infected individual $c \in [0, 1]$ is the efficacy of treatment. Among those who recovered naturally, ρ_1 part of them progress to a temporarily immune state and the reaming part immediately become susceptible to re-infected. Similarly, among the recovered due the treatment control, ρ_2 part of them progress to a temporarily immune state and the remaining part immediately become susceptible to re-infection. Thus, the model parameters and their description are listed in Table 1.

Table 1. Description of parameters for model (2.1)

Parameter	Description
Λ_h	Recruitment of the susceptible humans
Λ_v	Recruitment of the susceptible mosquitoes
b	Mosquito Biting rate
β_h	probability of biting by an infectious mosquito
β_v	probability of biting that results in transmission of parasite to S_v
μ	Natural death rate of human
η	Natural death rate of mosquito
δ	disease induced death rate
δ_1	Progression rate from E_h to I_h class
δ_2	Progression rate from E_v to I_v class
w	Loss of the immunity rate in human
m	Infection human recovery rate
v_h	proportion of an antibody produced by human
v_v	proportion of an antibody produced by mosquito

By applying above assumptions, the SEIR-SEI model with optimal control for the dynamics of malaria transmission is given by :

$$
\begin{cases}
\dfrac{dS_h}{dt} = \Lambda_h - (1 - u_1)\dfrac{b\beta_h I_v S_h}{1 + v_h I_v} + m(1 - \rho_1)I_h + cu_2(1 - \rho_2)I_h + wR_h - \mu S_h, \\[2mm]
\dfrac{dE_h}{dt} = (1 - u_1)\dfrac{b\beta_h I_v S_h}{1 + v_h I_v} - (\alpha_1 + \mu)E_h, \\[2mm]
\dfrac{dI_h}{dt} = \alpha_1 E_h - m(1 - \rho_1)I_h - cu_2(1 - \rho_2)I_h - (m\rho_1 + cu_2)I_h - (\delta + \mu)I_h, \\[2mm]
\dfrac{dR_h}{dt} = (m\rho_1 + cu_2)I_h - (\mu + w)R_h, \\[2mm]
\dfrac{dS_v}{dt} = \Lambda_V - (1 - u_1)\dfrac{b\beta_v I_h S_v}{1 + v_v I_h} - \eta S_v, \\[2mm]
\dfrac{dE_v}{dt} = (1 - u_1)\dfrac{b\beta_v I_h S_v}{1 + v_v I_h} - (\alpha_2 + \eta)E_v, \\[2mm]
\dfrac{dI_v}{dt} = \alpha_2 E_v - \eta I_v,
\end{cases}
\qquad (2.1)
$$

With the initial conditions: $S_h(0) > 0, E_h(0) \geq 0, I_h(0) \geq 0$, $R_h(0) \geq 0$, $S_v(0) > 0$, $E_v(0) \geq 0$, $I_v(0) \geq 0$.

The term $b\beta_h S_h(t) I_v(t)$ is a bilinear incidence see [14], indicates the ratio at which the $S_h(t)$ gets infected by infectious mosquitoes $I_v(t)$. In this paper, we use a saturated incidence function of the form $\frac{b\beta_h S_h(t) I_v(t)}{1+v_h I_v(t)}$, it produces the antibodies at $v_h \in [0,1]$ in response to the existence of antigens produced by infectious anopheles mosquitoes. Also mosquitoes develop antibodies against the malaria parasites. Thus, we have a saturated force of infection of the form $\frac{b\beta_v I_h(t)}{1+v_v I_h(t)}$, such that $v_v \in [0,1]$ is the rate at which antibodies are produced against the antigens contacted from infectious humans. The model (2.1) without control strategies, that is $u_1 = 0$, and $u_2 = 0$ becomes

$$\begin{cases} \dfrac{dS_h}{dt} = \Lambda_h - \dfrac{b\beta_h I_v S_h}{1+v_h I_v} + m(1-\rho_1)I_h + wR_h - \mu S_h, \\[2mm] \dfrac{dE_h}{dt} = \dfrac{b\beta_h I_v S_h}{1+v_h I_v} - (\alpha_1 + \mu)E_h, \\[2mm] \dfrac{dI_h}{dt} = \alpha_1 E_h - (m+\delta+\mu)I_h, \\[2mm] \dfrac{dR_h}{dt} = \rho_1 m I_h - (\mu+w)R_h, \\[2mm] \dfrac{dS_v}{dt} = \Lambda_V - \dfrac{b\beta_v I_h S_v}{1+v_v I_h} - \eta S_v, \\[2mm] \dfrac{dE_v}{dt} = \dfrac{b\beta_v I_h S_v}{1+v_v I_h} - (\alpha_2 + \eta)E_v, \\[2mm] \dfrac{dI_v}{dt} = \alpha_2 E_v - \eta I_v, \end{cases} \qquad (2.2)$$

2.1 Positivity and boundedness of the solutions

We assume that all the variables of the model (2.2), that represent different human and mosquito classes are nonnegative for all $t \geq 0$. Then the system (2.2) is well-posed epidemiologically and mathematically in a feasible region Γ introduced by

$$\Gamma := \{(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \in \mathbb{R}_+^7 : 0 \leq N_h \leq \tfrac{\Lambda_h}{\mu}, 0 \leq N_v \leq \tfrac{\Lambda_v}{\eta}\}.$$

Firstly, we introduce the following theorem.

Theorem 2.1. *The solutions of the system* (2.2) *with non-negative initial conditions in the feasible region $\Gamma \subset \mathbb{R}_+^7$ is positively invariant in Γ for all $t > 0$.*

Proof. Assume there exist $t_1 > 0$, such that $S_h(t_1) = 0$, $S_h'(t_1) \leq 0$ and S_h, E_h, I_h, R_h, S_v, E_v, I_v > 0.
for $0 < t < t_1$, we have

$$\begin{aligned} \tfrac{dS_h}{dt} &= \Lambda_h - \tfrac{b\beta_h I_v(t_1)S_h(t_1)}{1+v_h I_v(t_1)} + m(1-\rho_1)I_h(t_1) + wR_h(t_1) - \mu S_h(t_1) \\ &= \Lambda_h + wR_h(t_1) > 0 \end{aligned} \qquad (2.3)$$

which is a contradiction to our assumption. Hence $S_h(t) > 0$

Also let

$$t_1 = Sup\{t > 0 : S_h, E_h, I_h, R_h, S_v, E_v, I_v > 0\}.$$

then we have

$$\begin{aligned} \tfrac{dE_h}{dt} &= \tfrac{b\beta_h I_v S_h}{1+v_h I_v} - (\alpha_1 + \mu)E_h, \\ \tfrac{dE_h}{dt} + (\alpha_1 + \mu)E_h &= \tfrac{b\beta_h I_v S_h}{1+v_h I_v}, \\ \int_0^{t_1}(e^{(\alpha_1+\mu)t}E_h)' &= \int_0^{t_1}(\tfrac{b\beta_h I_v(r)S_h(r)}{1+v_h I_v(r)})e^{(\alpha_1+\mu)r}dr, \\ E_h(t_1) &= E_h(0)e^{-(\alpha_1+\mu)t_1} + e^{-(\alpha_1+\mu)t_1}[\int_0^{t_1} \tfrac{b\beta_h I_v(r)S_h(r)}{1+v_h I_v(r)}e^{(\alpha_1+\mu)r}dr] > 0 \end{aligned} \qquad (2.4)$$

Hence $E_h(t) > 0$.

Next for $I_h(t)$

$$\frac{dI_h}{dt} = \alpha_1 E_h - (m + \delta + \mu)I_h,$$
$$\int_0^{t_1}(e^{(m+\delta+\mu)}I_h(t))' = \int_0^{t_1}\alpha_1 E_h(r)e^{(m+\delta+\mu)r}dr, \qquad (2.5)$$
$$I_h(t_1) = I_h(0)e^{-(m+\delta+\mu)t_1} + e^{-(m+\delta+\mu)t_1}[\int_0^{t_1}\alpha_1 E_h(r)e^{(m+\delta+\mu)r}dr] > 0,$$

which contradicts $I_h(t_1) = 0$, similarly for $R_h(t)$. We assume that there exist $t_1 > 0$, such that $I_h(t_1) = 0$, and $I_h(t) > 0$, then

$$\frac{dR_h}{dt} = m\rho_1 I_h - (w + \mu)R_h,$$
$$\int_0^{t_1}(e^{(w+\mu)}R_h(t))' = \int_0^{t_1}m\rho_1 I_h(r)e^{(w+\mu)r}dr, \qquad (2.6)$$
$$R_h(t_1) = R_h(0)e^{-(w+\mu)t_1} + e^{-(w+\mu)t_1}[\int_0^{t_1}m\rho_1 I_h(r)e^{(w+\mu)r}dr] > 0,$$

which contradicts $R_h(t_1) = 0$

Also assuming that $S_v > 0, t \in [0, t_1]$, it follows that

$$\frac{dS_v(t_1)}{dt} = \Lambda_V - \frac{b\beta_v I_h(t_1)S_v(t_1)}{1 + v_v I_h(t_1)} - \eta S_v(t_1),$$

which is a contradiction. Hence there is no such time t_1 for which $S_v(t_1) = 0$,
Next for E_v we have

$$\frac{dE_v(t_1)}{dt} = \frac{b\beta_v I_h S_v}{1 + v_v I_h} - (\alpha_2 + \eta)E_v,$$
$$\int_0^{t_1}(e^{(\alpha_2+\eta)t}E_v)' = \int_0^{t_1}e^{(\alpha_2+\eta)t}\frac{b\beta_v I_h(t_1)S_v(t_1)}{1 + v_v I_h(t_1)}dt, \qquad (2.7)$$
$$E_v(t_1) = e^{-(\alpha_2+\eta)t_1}E_v(0) + e^{-(\alpha_2+\eta)t_1}[\int_0^{t_1}e^{(\alpha_2+\eta)r}]\frac{b\beta_v I_h(r)S_v(r)}{1 + v_v I_h(r)}dr > 0,$$

which showing that $E_v(t) > $. Similarly, $I_v(t) > 0$. $\qquad\square$

3 Basic Reproduction Number and the Existence of Equilibria

The most important epidemiologically threshold value which is used to determine the ability of an infectious disease in pervading a population is the basic reproduction number $\mathcal{R}_0$ of the model(2.2). The model(2.2) has a disease-free equilibrium given by $E_0(\frac{\Lambda_h}{\mu}, 0, 0, 0, \frac{\Lambda_v}{\eta}, 0, 0)$. We apply the next generation matrix approach [15, 16] to find the basic reproduction number. Let $\mathcal{F}$, $\mathcal{V}$ be the non-negative matrix of the infection terms and the non-singular matrix of transition terms calculated at E_0 respectively.

$$\mathcal{F} = \begin{bmatrix} \frac{b\beta_h I_v S_h}{1+v_h I_v} \\ 0 \\ \frac{b\beta_v I_h S_v}{1+v_v I_h} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad \mathcal{V} = \begin{bmatrix} (\alpha_1 + \mu)E_h \\ -\alpha_1 E_h + (m + \delta + \mu)I_h \\ (\alpha_2 + \eta)E_v \\ -\alpha_2 E_v + \eta I_v \\ -\Lambda_h - m(1 - \rho_1)I_h + \mu S_h - wR_h \\ (\mu + w)R_h - \rho_1 m I_h \\ -\Lambda_h + \eta S_v \end{bmatrix}.$$

Consequently, the next generation matrix $\mathcal{F}\mathcal{V}^{-1}$

$$\mathcal{F}\mathcal{V}^{-1} = \begin{bmatrix} 0 & 0 & \frac{\alpha_2 b \beta_h \Lambda_h}{\eta \mu (\alpha_2 + \eta)} & \frac{b \beta_h \Lambda_h}{\eta \mu} \\ 0 & 0 & 0 & 0 \\ \frac{b \beta_v \Lambda_v}{\eta (\alpha_1 + \mu)(m + \delta + \mu)} & \frac{b \beta_v \Lambda_v}{\eta (m + \delta + \mu)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{\beta_v \phi_{vh} m}{\eta (\beta_v + \eta)} & \frac{\phi_{vh} m}{\eta} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_h \phi_{hv} m b \mu}{\eta a (\beta_h + \mu)(\mu + \delta + \gamma)} & \frac{\beta_h \phi_{hv} m b \mu}{\eta a (\mu + \delta + \gamma)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Then $\mathcal{R}_0$ is given by spectral radius of $\mathcal{F}\mathcal{V}^{-1}$ which is denoted by $\rho(\mathcal{F}\mathcal{V}^{-1})$ and defined as:

$$\mathcal{R}_0 = \rho(\mathcal{F}\mathcal{V}^{-1}) = \sqrt{\frac{b^2 \alpha_1 \alpha_2 \beta_h \beta_v \Lambda_h \Lambda_v}{\eta^2 \mu (\alpha_1 + \mu)(m + \delta + \mu)(\alpha_2 + \eta)}}, \tag{3.1}$$

3.1 Disease-free equilibrium

In this subsection, we investigate the local geometrical properties of the disease-free equilibrium of the model (2.2) at $E_0 = (\frac{\Lambda_h}{\mu}, 0, 0, 0, \frac{\Lambda_v}{\eta}, 0, 0)$ by taking the Jacobian matrix and obtained

$$J(E_0) = \begin{bmatrix} -\mu & 0 & k_1 & w & 0 & 0 & -k_2 \\ 0 & -k_3 & 0 & 0 & 0 & 0 & k_2 \\ 0 & \alpha_1 & -k_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & \rho_1 m & -k_5 & 0 & 0 & 0 \\ 0 & 0 & -k_6 & 0 & -\eta & 0 & 0 \\ 0 & 0 & k_6 & 0 & 0 & -k_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_2 & -\eta \end{bmatrix}$$

It is clear that $\lambda_1 = -\mu$, $\lambda_2 = -k_5$, $\lambda_3 = -\eta$ are negative eginvalues and the sign of the rest of the eginvalues can be determined by the characteristic equation

$$f(\lambda) = \lambda^4 + b_1 \lambda^3 + b_2 \lambda^2 + b_3 \lambda + b_4 = 0 \tag{3.2}$$

where:

$$b_1 = \eta + k_3 + k_4 + k_7,$$
$$b_2 = k_3 k_4 + k_3 k_7 + \eta k_3 + k_4 k_7 + \eta k_4 + \eta k_7,$$
$$b_3 = k_3 k_4 k_7 + \eta k_3 k_4 + \eta k_3 k_7 + \eta K_4,$$
$$b_4 = \eta k_3 k_4 k_7 (1 - \frac{\alpha_1 \alpha_2 k_2 k_6}{\eta k_3 k_4 k_7}) = \eta k_3 k_4 k_7 (1 - \mathcal{R}_0^2),$$

where $k_1 = m(1 - \rho_1), k_2 = \frac{b \beta_h \Lambda_h}{\mu}$, $k_3 = (\alpha_1 + \mu)$, $k_4 = (m + \delta + \mu), k_5 = (w + \mu)$, $k_6 = \frac{b \beta_v \Lambda_v}{\eta}$ and $k_7 = (\alpha_2 + \eta)$. Since all the parameters are positive then b_1, b_2, b_3 and b_4 are also positive when $\mathcal{R}_0 < 1$.

By Using Routh-Hurwitz criterion [17], it can be seen that all the eigenvalues of the characteristic equation (3.2) have negative real part if and only if:

$$D_1 = b_1 > 0, D_2 = \begin{vmatrix} b_1 & 1 \\ b_3 & b_2 \end{vmatrix} > 0, D_3 = \begin{vmatrix} b_1 & 1 & 0 \\ b_3 & b_2 & b_1 \\ 0 & b_1 & b_3 \end{vmatrix} > 0, D_4 = \begin{vmatrix} b_1 & 1 & 0 & 0 \\ b_3 & b_2 & b_1 & 0 \\ 0 & b_4 & b_3 & b_2 \\ 0 & 0 & 0 & b_4 \end{vmatrix} > 0, \tag{3.3}$$

Obviously, all the eigenvalues of $J(E_0)$ have negative real parts when $\mathcal{R}_0 < 1$. This implies that model (2.2) has a unique disease-free equilibrium E_0 when $\mathcal{R}_0 < 1$ if and only if condition (3.3) is satisfied, Thus, we have the following theorem.

Theorem 3.1. *The system* (2.2) *has the disease-free equilibrium* E_0 *if* $\mathcal{R}_0 < 1$,*which is locally asymptotically stable if and onl.y if the condition* (3.3) *is satisfied and unstable if* $\mathcal{R}_0 > 1$.

3.1.1 Endemic equilibrium

We assume that there exist an endemic equilibrium $E^* = (S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^*)$ for the model (2.2) as

$$
\begin{aligned}
&S_h^* = \frac{\eta\Lambda_h k_5 + [\Lambda_h k_5(b\beta_v + \eta v_v + v_h\alpha_2\beta_v\Lambda_v) + k_1 k_2(\eta + (b\beta_v + v_v)I_h^*)]I_h^*}{\eta\mu k_5 + [\alpha_2\beta_v\Lambda_v k_5(b^2\beta_h + \mu v_h) + k_5\mu(b\beta_v + v_v)]I_h^*}, \ E_h^* = \frac{k_4 I_h^*}{\alpha_1}, \ R_h^* = \frac{\rho_1 m I_h^*}{k_5}, \\
&S_v^* = \frac{\Lambda_v(1 + v_v I_h^*)}{b\beta_v I_h^* + \eta(1 + v_v I_h^*)}, \ E_v^* = \frac{b\beta_v\Lambda_v I_h^*}{(\alpha_2 + \eta)[b\beta_v I_h^* + \eta(1 + v_v I_h^*)]}, \ I_v^* = \frac{\alpha_2 b\beta_v\Lambda_v I_h^*}{b\beta_v I_h^* + \eta(1 + v_v I_h^*)},
\end{aligned}
\tag{3.4}
$$

and I_h^* is a positive solution of the given equation

$$
d_1 I_h^{*2} + d_2 I_h^* + d_3 = 0,
\tag{3.5}
$$

where

$$
\begin{aligned}
d_1 &= k_3 k_4 k_5\beta_h[\alpha_2 b^3\beta_h\beta_v\Lambda_v(1 + \alpha_2\beta_v\Lambda_v) + \mu(b\alpha_2\beta_v\Lambda_v v_h + b^2\beta_v + bv_v + \Lambda_v\alpha_2 v_v v_h\eta + \eta v_v + \\
&\quad \alpha_2^2\Lambda_v^2\beta_v bv_h + b^2\beta_v\alpha_2\Lambda_v)] + k_3 k_4 k_5\mu v_v(v_v\eta + \underline{a}lpha_2\beta_v) - k_1 k_2\beta_v\beta_h\alpha_1\alpha_2\Lambda_v b^2(b\beta_v + v_v) \\
d_2 &= k_3 k_4 k_5\beta_v[\eta(b\mu + \alpha_2 b^2\beta_h\Lambda_v + \alpha_2\mu\Lambda_v v_h + b\mu + b\mu\alpha_2 v_v\Lambda_v)] + k_3 k_4 k_5\eta\mu v_v(1 + \eta) - \\
&\quad \alpha_1\alpha_2 b^2\beta_v\beta_h\Lambda_v[k_5\Lambda_h(b\beta_v + \eta v_v) + \alpha_2\beta_v^2\Lambda_v v_h + \eta k_1 k_2] \\
d_3 &= \eta^2 k_3 k_4 k_5\mu(1 - \frac{\alpha_1\alpha_2 b^2\beta_h\beta_v\Lambda_v\Lambda_h}{\eta\mu k_3 k_4})
\end{aligned}
$$

For $d_1 > 0$, $d_2 > 0$, and $d_3 < 0$, an endemic equilibrium point exists and when $d_3 > 0$, the model has no positive solution. Numerical simulations in section 4, also confirm the existence of an equilibrium and it's stability when $R_0 > 1$.

4 Numerical Simulations

In this section, we use our model (2.2) to simulate the reported annual malaria human infected cases from WHO [18, 19]. We present numerically the behavior of the system (2.2), using the parameter values in Table 2 and by considering the initial conditions. The numerical simulations are conducted using Matlab software and the simulation results given in Figures(1-5) to clarify the models behavior for the values of model parameters. Fig 1 (a) shows the simulation of the reported malaria cases in DRC from 2007 to 2013 and Fig 1(b) shows the prediction of human malaria for DRC 2007 to 2030. Fig 2(a-e) presents the model (2.2) solution with parameter values from Table 2, for the human and mosquito compartments respectively. Figures 3(a-d) and Figures 4(a-c) illustrates the varying effects of ratios of antibodies v_h, v_v on human and mosquito populations, while the remaining parameters maintain the same as in Table 2, where $\mathcal{R}_0 < 1$ and b=0.161. In particular, Fig 3(a) shows the behavior of the susceptible human $S_h(t)$, when the antibody v_h, increases in ratio. An increase in the ratio of the antibody reduces the acute decrease in the susceptible human population. The volumes of the exposed human $E_h(t)$, and infectious human $I_h(t)$, population in Fig 3(a) and Fig 3(c), decrease with increase presence of the antibody v_h. Consequently, the decreased number of infectious human contributes to increase in the number of recovered human $R_h(t)$ as seen in Fig 3(d).

Similarly, in Fig 4(a), the number of susceptible mosquitoes $S_v(t)$, decreases with time. But, increasing the ratio of antibody, v_v prevent the reduction in susceptible mosquitoes $S_v(t)$. In Figures

4 (b) and (c), the number of exposed and infectious mosquitoes population decreases due to increase in resistance to the malaria parasite.

Generally, Figures 5(a-d) and Figures 6(a-c) show the varying effects of ratios of antibodies v_h, v_v on humans and mosquitoes population, where the other parameter are maintained as in Table 2, where $\mathcal{R}_0$ is greater than one and b=0.39. So far,when we increase the ratio of the antibody with $b = 0.39$ and $\mathcal{R}_0 > 1$, it has lower effect in reducing the burden of the endemic malaria infection when compared with Figures 3(a-c). Figures 6(a,b,c) present the effect of the mosquitoes resistance to the malaria on susceptible, exposed and infectious mosquito populations, where the human- mosquito contact rate is increased. Clearly, the number of infectious mosquito decreases with increased in the ratio of antibody, v_v.

Table 2. Parameter values for model (2.2)

Parameter	Value	Source
Λ_h	0.0043	Assumed
Λ_v	0.0071	Assumed
b	0.39	[20]
μ	0.0000472	[21]
w	0.00274	[21]
η	0.1	[21]
β_h	0.048	[22]
β_v	0.48	[22]
α_1	0.08333	[22]
α_2	0.48	[22]
m	0.0035	[22]
δ	0.083	[23]
ρ_1	0.23	Fitting
ρ_2	0.331	Fitting
v_h	0.29	Fitting
v_V	0.3	Fitting

5 Sensitivity Analysis of $\mathcal{R}_0$

In this section, we investigate the nature of the system by conducting sensitivity analysis of the reproduction number $\mathcal{R}_0$.
(a) If the value of b is reduced from 0.39 to 0.24 and the values of other parameters are
maintained then $\mathcal{R}_0$ is reduced from 1.4946 to 0.9198.
(b) If the value of β_1 is reduced from 0.0833 to 0.0000233 and the other parameters
remain the same then $\mathcal{R}_0$ is reduced from 1.4946 to 0.8595.
(c) If we reduced the value of α_2 from 0.48 to 0.048 and the other parameters are the same then $\mathcal{R}_0$ will reduced from 1.4946 to 0.9357.
(d) If the value of m is increased to 0.4435 then $\mathcal{R}_0$ will reduced to 0.6060.
(e) If we reduced the value of β_h to 0.0195 then $\mathcal{R}_0$ will reduced to 0.9381.
(f) If the value of β_v is reduced to 0.18 then $\mathcal{R}_0$ will reduced to 0.9153.
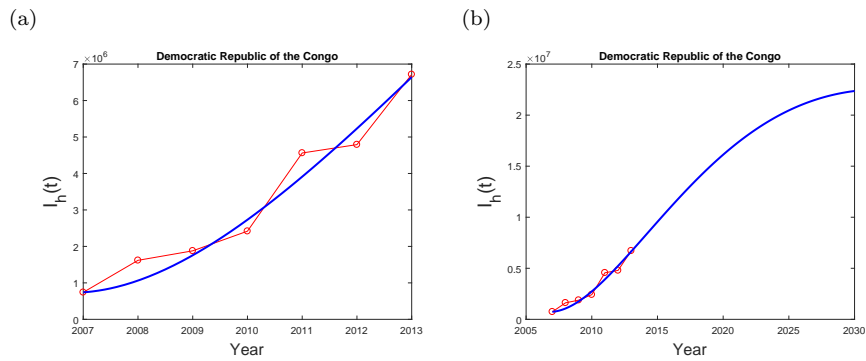
(a)

(b)

Figure 1: **Comparisons of the reported malaria cases from WHO (red curve) and the solution of infectious human I_h for model** (2.2). (a)**: Simulation of the reported malaria cases in DRC from 2007 to 2013.** (b)**: Prediction of human malaria for DRC 2007 to 2030.**
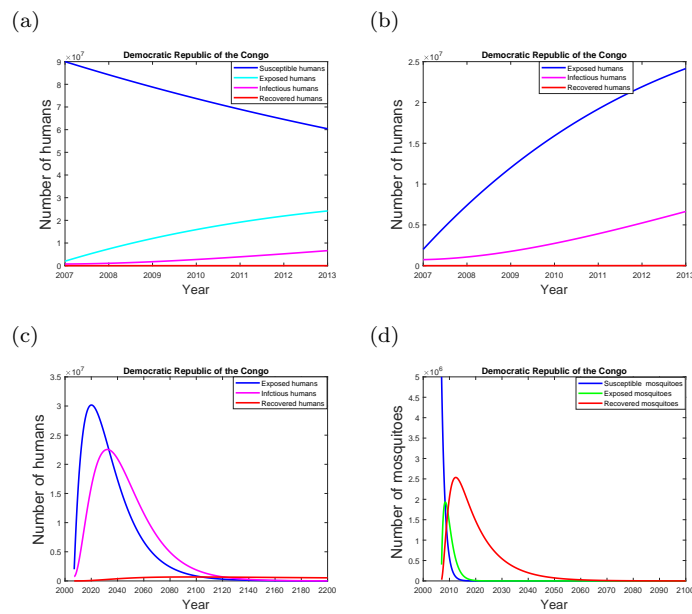
(a)

(b)

(c)

(d)

Figure 2: **Solution of model** (2.2) **with parameters from Table 2.**

6 Analysis of Optimal Control

In this section, we make use of Pontryagin's Principle in order to find the necessary conditions that establishes the presence of optimal control of the malaria transmission model. We include time dependent controls into the SEIR-SEI malaria model and attempt to explore the suitable optimal control strategy for setting the malaria under control. We use two control variables, the control
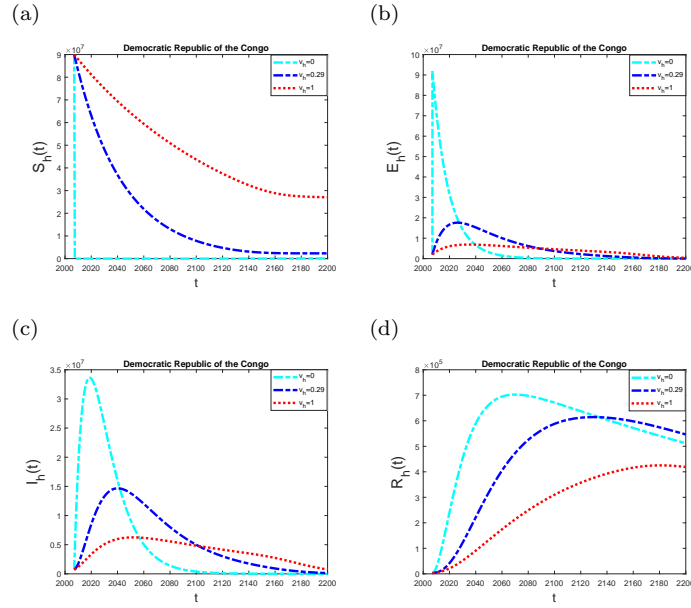
(a)   (b)

(c)   (d)

Figure 3: **The behaviors of susceptible, Exposed, Infectious and Recovered humans for different values of v_h when $\mathcal{R}_0 < 1$ and b=0.161.**

$u_1(t)$ represents the effort on preventing malaria infections through the use of treated bed-nets and the control effort on malaria treatment of infected individuals $u_2(t)$. The objective function used for the model is similar to [24–26], and is given by

$$J(u_1, u_2) = \int_0^{t_f} (A_1 E_h + A_2 I_h + \frac{B_1}{2}u_1^2 + \frac{B_2}{2}u_2^2)dt, . \tag{6.1}$$

where A_1 and A_2 are the balancing cost factors due to scale while B_1 and B_2, denote the weighting constants for making use of prevention strategy using treated net-bed and the control effort on malaria treatment of infectious individuals. Consequently, we attempt to expect an optimal control u_1^*, u_2^* such that,

$$J(u_1^*, u_2^*) = minJ(u_1, u_2), \Delta = \{(u_1, u_2)|0 \le u_i \le 1, i = 1, 2\}. \tag{6.2}$$

$$
\begin{cases}
\dfrac{dS_h}{dt} = \Lambda_h - (1 - u_1)\dfrac{b\beta_h I_v S_h}{1 + v_h I_v} + m(1 - \rho_1)I_h + cu_2(1 - \rho_2)I_h + wR_h - \mu S_h, \\[2mm]
\dfrac{dE_h}{dt} = (1 - u_1)\dfrac{b\beta_h I_v S_h}{1 + v_h I_v} - (\alpha_1 + \mu)E_h, \\[2mm]
\dfrac{dI_h}{dt} = \alpha_1 E_h - m(1 - \rho_1)I_h - cu_2(1 - \rho_2)I_h - (m\rho_1 + cu_2)I_h - (\delta + \mu)I_h, \\[2mm]
\dfrac{dR_h}{dt} = (m\rho_1 + cu_2)I_h - (\mu + w)R_h, \\[2mm]
\dfrac{dS_v}{dt} = \Lambda_V - (1 - u_1)\dfrac{b\beta_v I_h S_v}{1 + v_v I_h} - \eta S_v, \\[2mm]
\dfrac{dE_v}{dt} = (1 - u_1)\dfrac{b\beta_v I_h S_v}{1 + v_v I_h} - (\alpha_2 + \eta)E_v, \\[2mm]
\dfrac{dI_v}{dt} = \alpha_2 E_v - \eta I_v,
\end{cases}
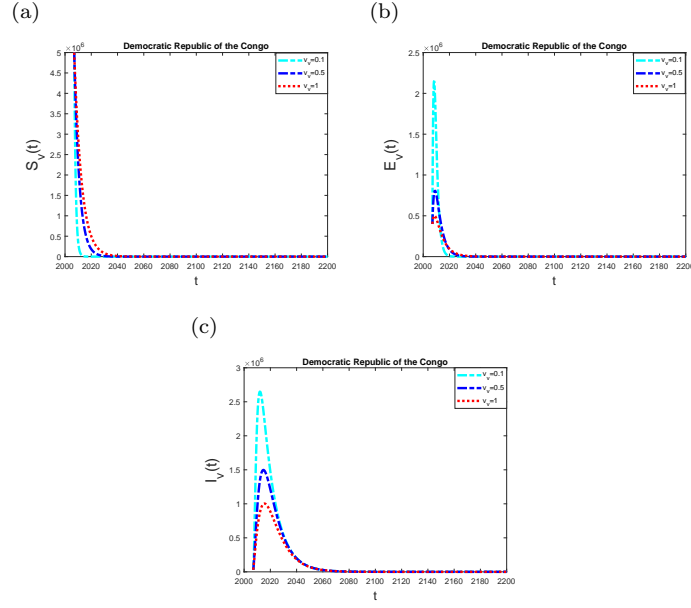\tag{6.3}
$$

(a) (b)

(c)

Figure 4: **The behaviors of Susceptible, Exposed and Infectious mosquitoes for different values of v_v when $\mathcal{R}_0 < 1$ and b=0.161.**

The optimal control must conform the necessary conditions that is emanated from the Pontryagin Maximum Principle [27].This concept transpose the equations (6.2) and (6.3) into a type of problem characterised with minimizing pointwise a Hamililtonian H, with respect to u_1 and u_2

$$
\begin{aligned}
H &= A_1 E_h + A_2 I_h + \frac{B_1}{2} u_1^2 + \frac{B_2}{2} u_2^2 \\
&+ \lambda_1 \left\{ \Lambda_h - (1 - u_1) \frac{b\beta_h I_v S_h}{1 + v_h I_v} + m(1 - \rho_1) I_h + cu_2(1 - \rho_2) I_h + wR_h - \mu S_h \right\} \\
&+ \lambda_2 \left\{ (1 - u_1) \frac{b\beta_h I_v S_h}{1 + v_h I_v} - (\alpha_1 + \mu) E_h \right\} \\
&+ \lambda_3 \left\{ \alpha_1 E_h - m(1 - \rho_1) I_h - cu_2(1 - \rho_2) I_h - (m\rho_1 + cu_2) I_h - (\delta + \mu) I_h \right\} \\
&+ \lambda_4 \left\{ (m\rho_1 + cu_2) I_h - (\mu + w) R_h \right\} \\
&+ \lambda_5 \left\{ \Lambda_V - (1 - u_1) \frac{b\beta_v I_h S_v}{1 + v_v I_h} - \eta S_v \right\} \\
&+ \lambda_6 \left\{ (1 - u_1) \frac{b\beta_v I_h S_v}{1 + v_v I_h} - (\alpha_2 + \eta) E_v \right\} \\
&+ \lambda_7 \left\{ \alpha_2 E_v - \eta I_v \right\}
\end{aligned}
\tag{6.4}
$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6$ and λ_7, represent the adjoint variables.

The system solution is attained by suitably taking partial derivatives of the Hamiltonian (6.4) with respect to the associated state variable.

Theorem 6.1. *Given an optimal control u_1^*, u_2^* and the solutions $S_h, E_h, I_h, R_h, S_v, E_v, I_v$ of the corresponding state systems (2.1) and (6.3) that minimize $J(u_1, u_2)$ over Γ. Then there exist adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7$, satisfying*

$$
\frac{-d\lambda_i}{dt} = \frac{\partial H}{\partial i}
\tag{6.5}
$$

Where $i = 1, 2, 3, 4, 5, 6, 7$ and with transversality conditions

$$
\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = \lambda_6(t_f) = \lambda_7(t_f) = 0
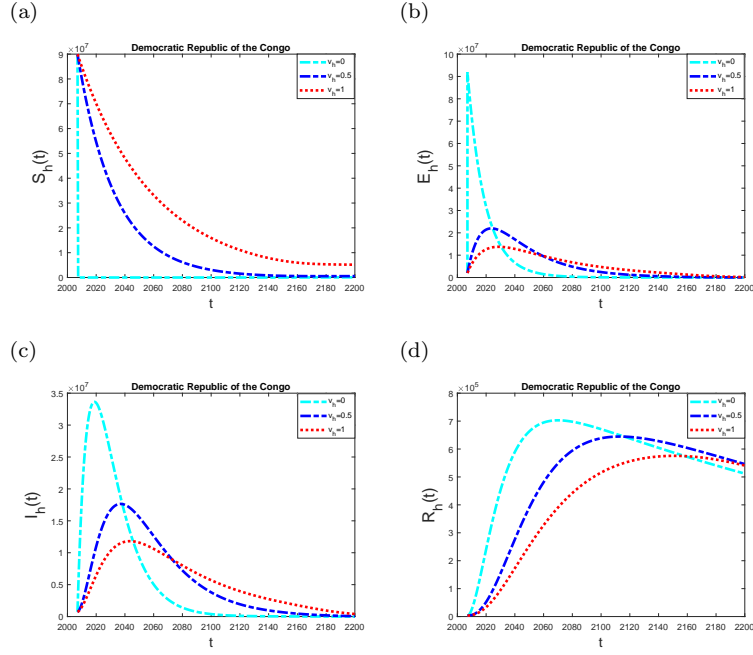\tag{6.6}
$$

(a)   (b)

(c)   (d)

Figure 5: **The behaviors of Susceptible, Exposed, Infectious and Recovered humans for different values of v_h when $\mathcal{R}_0 > 1$ and b=0.39.**

and

$$u_1^* = min\left\{1, max(0, \frac{1}{2B_1}\left(\frac{b\beta_h I_v S_h}{1+v_v I_v}(\lambda_2 - \lambda_1) + \frac{b\beta_v I_h S_v}{1+v_v I_h}(\lambda_6 - \lambda_5)\right)\right\} \qquad (6.7)$$

$$u_2^* = min\left\{1, max(0, \frac{I_h}{2B_2}\left(c(1-\rho_2)\lambda_3 - c\rho_2\lambda_4 - c(1-\rho_2)\lambda_1\right)\right\} \qquad (6.8)$$

Proof. Theorem 4.1 and Corollary 4.1 of [27] gives the conditions of possible existence of an optimal control based on the convexity of the integrand of $J(u_1, u_2)$ with respect to u_1 and u_2 a priori boundedness of the state solutions, and the resulting Lipschitz characteristics of the state system of the ODE's with the state variables. The Hamiltonian function determined at the optimal control level leads to the adjoint variables. Thus, the adjoint equations can be rearranged as

$$\frac{d\lambda_1}{dt} = \frac{(1-u_1)b\beta_h I_v}{1+v_v I_v}(\lambda_1 - \lambda_2) + \mu\lambda_1$$

$$\frac{d\lambda_2}{dt} = -A_2 + (\alpha_1 + \mu)\lambda_2 - \alpha_1\lambda_3$$

$$\frac{d\lambda_3}{dt} = -A_2 - (m(1-\rho_1) + cu_2(1-\rho_2))\lambda_1 + (m + cu_3 + \delta + \mu)\lambda_3 - (m\rho_1 + cu_2\rho_2)\lambda_4 +$$

$$\qquad \frac{(1-u_1)b\beta_v S_v}{1+v_v I_h}(\lambda_5 - \lambda_6) + \frac{(1-u_1)b\beta_v v_v I_h S_v}{(1+v_v I_h)^2}$$

$$\frac{d\lambda_4}{dt} = (\mu + w)\lambda_4 - w\lambda_1$$

$$\frac{d\lambda_5}{dt} = \frac{(1-u_1)b\beta_v I_h S_v}{1+v_V I_h}(\lambda_5 - \lambda_6) + \eta\lambda_5$$

$$\frac{d\lambda_6}{dt} = (\alpha_2 + \eta)\lambda_6 - \alpha_2\lambda_7$$

$$\frac{d\lambda_7}{dt} = \frac{(1-u_1)b\beta_h S_h}{1+v_h I_v}(\lambda_1 - \lambda_2) + \frac{(1-u_1)b\beta_h v_h S_h}{1+v_h I_v}(\lambda_2 - \lambda_1) + \eta\lambda_7$$
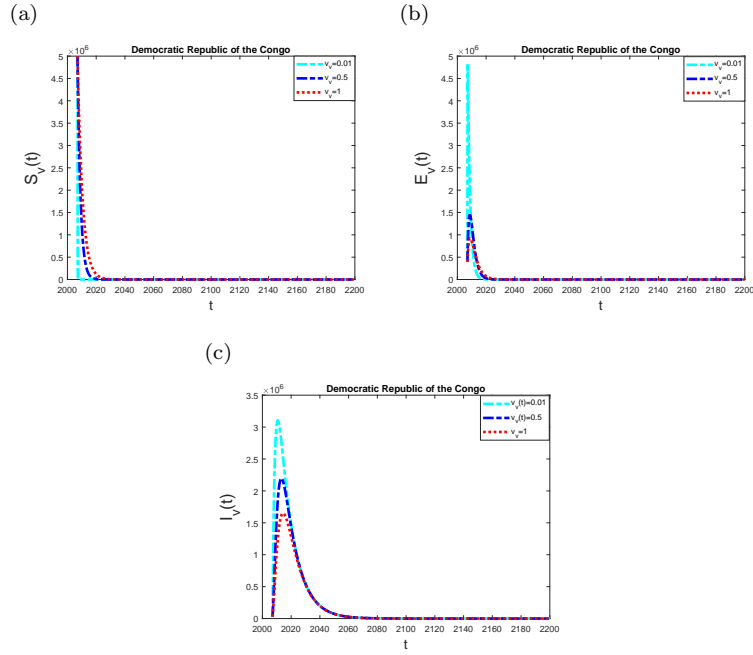
Figure 6: **The behaviors of Susceptible, Exposed and Infectious mosquitoes for different values of v_v when $\mathcal{R}_0 > 1$ and b=0.39.**

$\square$

6.1 Numerical simulations of optimal control

In this section, we discuss the numerical outcomes of our various optimal control strategies on the spread of malaria in DRC.

6.1.1 Malaria Prevention $u_1(t)$ Control only

In this strategy, prevention effort targeting the use of treated bed-net $u_1(t)$ was employed while the control $u_2(t) = 0$ is employed to optimize the objective function $J(u_1, u_2)$. In Fig 7(a) , there is a significant different between the cases with control $u_1 \neq 0, u_2 = 0$ and the cases without control $u_1 = u_2 = 0$, the number of exposed mosquitoes decreases till the day 3 but starts increasing after that. The strategy is not effective in reducing the number of exposed mosquitoes E_v. Similarly it is not effective in reducing the number of exposed humans in Fig 7(c). In Fig 7(b) and (d), there are no significant difference between the cases with control and those that without control. It is clear that the strategy employed is not effective in reducing the number of infective mosquitoes I_v and malaria infective humans I_v respectively.

6.1.2 Malaria Prevention treatment $u_2(t)$ Control only

In this strategy, treatment effort is employed to optimize the objective function $J(u_1, u_2)$ when u_1 is set to be zero. In Fig 8(a),(b),(c),(d), there are no significant difference between the cases with
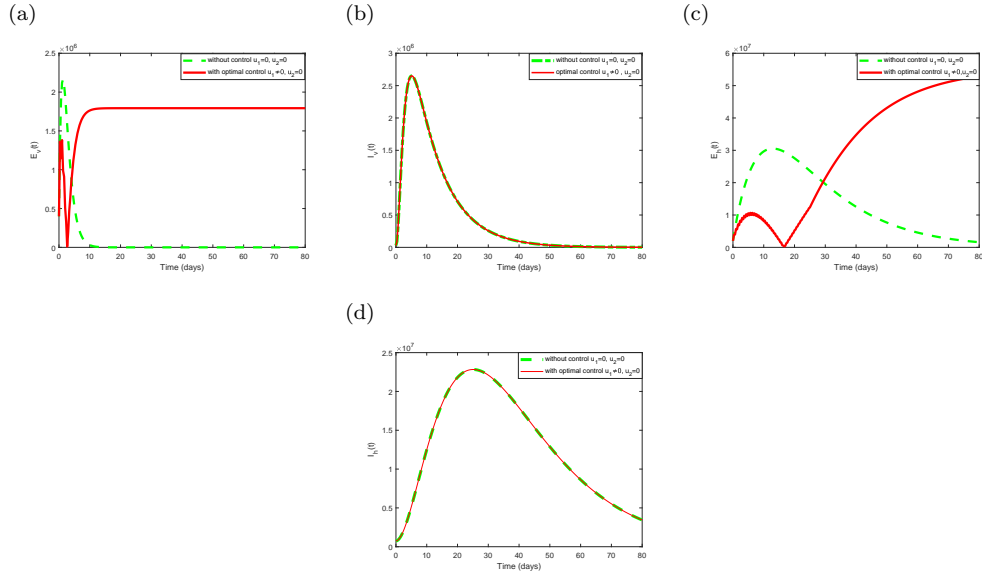
(a)

(b)

(c)

(d)

Figure 7: **Simulations of the model showing the effect of malaria prevention only on transmission. Fig 6 (a) and (b) represents the behavior infected humans and infected mosquitoes respectively. Dashed line represents system without control ($u_1 = 0, u_2 = 0$) and solid line shows the system with control ($u_1 \neq 0, u_2 = 0.$)**

control and that without control. Therefore the strategy is not effective to reduce the number of Exposed mosquitoes, Infectious mosquitoes, Exposed humans and Infectious humans respectively.

6.1.3 Malaria Prevention $u_1(t)$ and $u_2(t)$ Control only

In this strategy malaria prevention treated bed-net control $u_1(t)$ and malaria treatment effort control $u_2(t)$ are used to optimize the objective function $J(u_1, u_2)$. It is obvious in Fig 9(a) that there is a significant difference between the number of exposed mosquitoes E_v under control, compared to those without control the number of exposed mosquitoes were initially controlled but it starts rising after day 4. The strategy is not effective in controlling E_v. In Fig 9(b), there is no significant difference between the number of infectious mosquitoes I_v under the control and without control. The strategy is not effective in controlling the Infectious mosquitoes I_v. In Fig 9(c), there is a significant difference between the number of Exposed humans E_h with control and without control, the number of E_h was initially controlled but starts rising before day 18. This strategy is not effective in controlling Exposed humans. In Fig 9(d), there is a significant difference between the presence of control and without control cases. It was observed that the number of malaria Infections in humans I_h which was increasing initially has been reduced. This indicates that the control strategy employed is effective in reducing the number of malaria Infected humans.
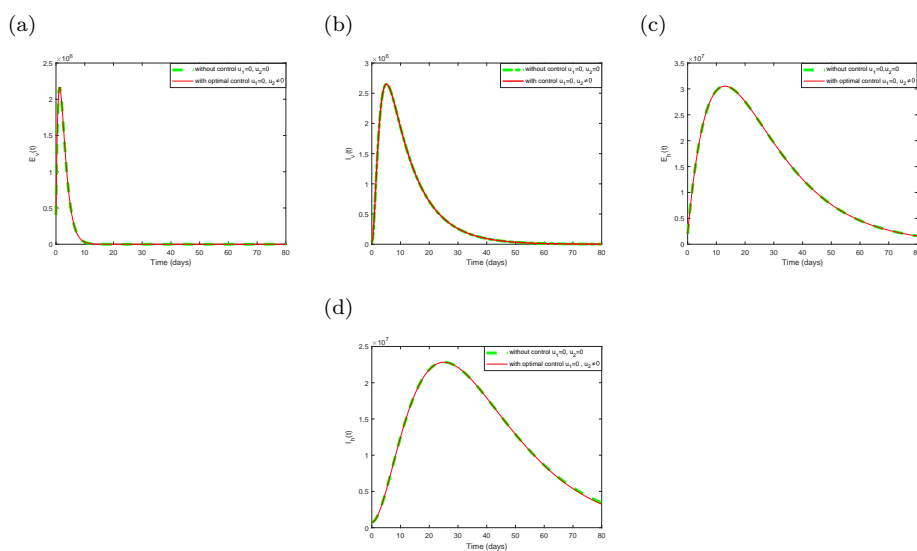
14

Figure 8: **Simulations of the model showing the effect of malaria prevention only on transmission. Fig 6 (a) and (b) represents the behavior infected humans and infected mosquitoes respectively. Dashed line represents system without control ($u_1 = 0, u_2 = 0$) and solid line shows the system with control ($u_1 = 0, u_2 \neq 0$.)**
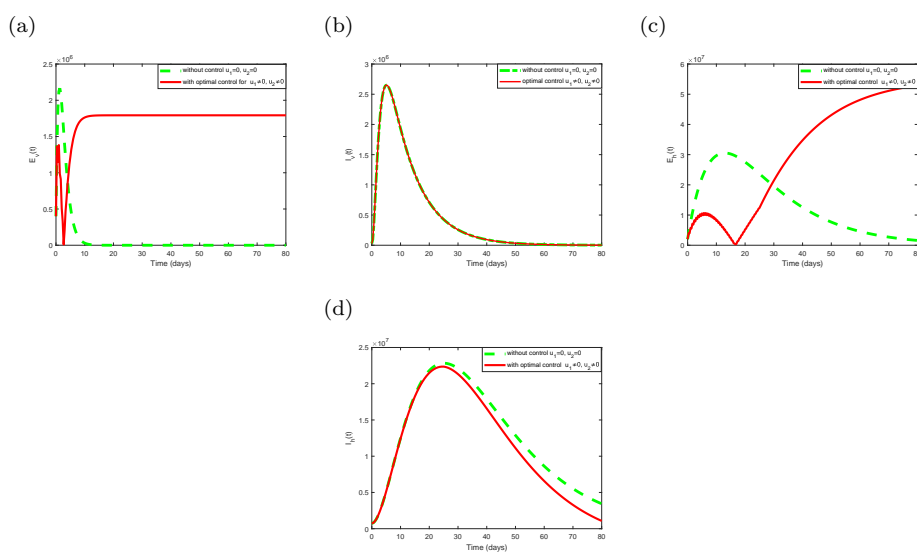

Figure 9: **Simulations of the model showing the effect of malaria prevention only on transmission. Fig 6 (a) and (b) represents the behavior infected humans and infected mosquitoes respectively. Dashed line represents system without control ($u_1 = 0, u_2 = 0$) and solid line shows the system with control ($u_1 \neq 0, u_2 \neq 0$.)**

7 Conclusion

In this paper, we formulated and analysed a seven-dimensional differential equation model for malaria transmission in human and mosquito populations with non-linear incidence forces of infections for human and mosquito with two optimal control strategies, use of treated bed-nets $u_1(t)$ and control effort on malaria treatment of infected individual $u_2(t)$. We established the feasible region where the model is mathematically and epidemiologically well-posed. The existence and stability of a disease-free equilibrium was shown when $u_1(t) = u_2(t) = 0$. Furthermore, we obtained the basic reproduction number ,$\mathcal{R}_0$, by applying the next generation matrix method. Further we showed that there exists a unique endemic equilibrium point for the model when $\mathcal{R}_0 > 1$. Our numerical simulation results showed that increasing the ratios of antibodies has significant effect in reducing the transmission of the malaria infection. In addition to that, we used two optimal control strategies $u_1(t)$ and $u_2(t)$ to minimize the infected human individual (to control the infectious human $I_h(t)$). Numerical simulation for the optimal control suggests that the two controls $u_1(t)$ and $u_2(t)$ together are more effective in reducing the number of infected human than one control strategy. In future we will study the spatial pattern of malaria transmission. This will deal with the consideration of environmental, genetic and infections risk factors. We will also add more control strategies.

Competing Interests

Authors have declared that no competing interests exist.

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