Electronic Journal of Differential Equations, Vol. 2012 (2012), No. 81, pp. 1–22.
ISSN: 1072-6691. URL: http://ejde.math.txstate.edu or http://ejde.math.unt.edu
ftp ejde.math.txstate.edu

APPLICATION OF OPTIMAL CONTROL TO THE EPIDEMIOLOGY OF MALARIA

FOLASHADE B. AGUSTO, NIZAR MARCUS, KAZEEM O. OKOSUN

Abstract. Malaria is a deadly disease transmitted to humans through the bite of infected female mosquitoes. In this paper a deterministic system of differential equations is presented and studied for the transmission of malaria. Then optimal control theory is applied to investigate optimal strategies for controlling the spread of malaria disease using treatment, insecticide treated bed nets and spray of mosquito insecticide as the system control variables. The possible impact of using combinations of the three controls either one at a time or two at a time on the spread of the disease is also examined.

1. Introduction

Malaria is a common and serious disease. It is reported that the incidence of malaria in the world may be in the order of 300 million clinical cases each year. Malaria mortality is estimated at almost 2 million deaths worldwide per year. The vast numbers of malaria deaths occur among young children in Africa, especially in remote rural areas. In addition, an estimated over 2 billion people are at risk of infection, no vaccines are available for the disease [25, 43].

Malaria is transmitted to humans through the bite of an infected female Anopheles mosquito, following the successful sporozoite inoculation, *plasmodium falciparum* is usually first detected 7-11 days. This is followed after few days of the bites, by clinical symptoms such as sweats, shills, pains, and fever. Mosquitoes on the other hand acquire infection from infected human after a blood meal. Although malaria is life-threatening it is still preventable and curable if the infected individual seek treatment early. Prevention is usually by the use of insecticide treated bed nets and spraying of insecticide but according to the World Health Organization position statement on insecticide treated mosquito nets [44], the insecticide treated bed nets(ITNs), long-lasting insecticide nets (LLINs), indoor residual spraying (IRS), and the other main method of malaria vector control, may not be sufficiently effective alone to achieve and maintain interruption of transmission of malaria, particularly in holo-endemic areas of Africa.

2000 *Mathematics Subject Classification.* 92B05, 93A30, 93C15.
Key words and phrases. Malaria; optimal control; insecticide treated bed nets; mosquito insecticide.

Submitted July 2, 2010. Published May 22, 2012.

Many studies have been carried out to quantify the impact of malaria infection in humans [6, 14, 19, 24, 33, 36]. Many of these studies focuses only on the transmission of the disease in human and the vector populations but recently, Chiyaka et.al [10] formulated a deterministic system of differential equations with two latent periods in the non-constant host and vector populations in order to theoretically assess the potential impact of personal protection, treatment and possible vaccination strategies on the transmission dynamics of malaria. Blayneh et al [5], used a time dependent model to study the effects of prevention and treatment on malaria, similarly Okosun [29] used a time dependent model to study the impact of a possible vaccination with treatment strategies in controlling the spread of malaria in a model that includes treatment and vaccination with waning immunity. Thus, following the WHO position statement [44] it is instructive to carry out modeling studies to determine the impact of various combinations of control strategies on the transmission dynamics of malaria. In this paper, we use treatment of symptomatic individuals, personal protection and the straying of insecticide as control measures and then consider this time dependent control measures using optimal control theory. Time dependent control strategies have been applied for the studies of HIV/AIDS disease, Tuberculosis, Influenza and SARS [1, 2, 7, 17, 20, 39, 42, 46]. Optimal control theory has been applied to models with vector-borne diseases [5, 31, 40, 45].

Our goal is to develop mathematical model for human-vector interactions with control strategies, with the aim of investigating the role of personal protection, treatment and spraying of insecticides in malaria transmission, in line with concerns raised WHO [44]; in order to determine optimal control strategies with various combinations of the control measures for controlling the spread of malaria transmission. The paper is organized as follows: in Section 2, we give the description of the human-vector model, stating the assumptions and definitions of the various parameters of the model. The analysis of the equilibrium points are discussed in Sections 2.2 and 3. In Section 4, we state the control problem as well as the objective functional to be minimized, we then apply the Pontryagin's Maximum Principle to find the necessary conditions for the optimal control. In Sections 5, we show the simulation results to illustrate the population dynamics with preventative measures and treatment as controls.

2. Model formulation

The model sub-divides the total human population at time t, denoted by $N_h(t)$, into the following sub-populations of susceptible individuals ($S_h(t)$), those exposed to malaria parasite ($E_h(t)$), individuals with malaria symptoms ($I_h(t)$), partially immune human ($R_h(t)$). So that

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t).$$

The total vector (mosquito) population at time t, denoted by $N_v(t)$, is subdivided into susceptible mosquitoes ($S_v(t)$), mosquitoes exposed to the malaria parasite ($E_v(t)$) and infectious mosquitoes($I_v(t)$). Thus,

$$N_v(t) = S_v(t) + E_v(t) + I_v(t).$$

It is assumed that susceptible humans are recruited into the population at a constant rate Λ_h. Susceptible individuals acquire malaria infection following contact with infectious mosquitoes (at a rate $\beta\varepsilon_h\phi$), where β is the transmission probability per bite and ε_h is the biting rate of mosquitoes, ϕ is contact rate of vector per

human per unit time. Susceptible individuals infected with malaria are moved to the exposed class (E_h) at the rate $\beta\varepsilon_h\phi$ and then progress to the infectious class, following the development of clinical symptoms (at a rate α_h). Individuals with malaria symptoms are effectively treated (at a rate τ) where ($0 \leq \tau \leq 1$). Human spontaneous recovery rate is given by b, where $0 \leq b < \tau$. And individuals infected with malaria suffer a disease-induced death (at a rate ψ). Infected individual then progress to the partially immuned group. Upon recovery, the partially immuned individual losses immunity (at the rate κ) and becomes susceptible again.

Susceptible mosquitoes (S_v) are generated at the rate Λ_v and acquire malaria infection (following effective contacts with humans infected with malaria) at a rate $\lambda\phi\varepsilon_v(I_h + \eta R_h)$, where λ is the probability of a vector getting infected through the infectious human and ε_v is the biting rate of mosquitoes. We assume that humans in the $R_h(t)$ class can still transmit the disease, thus, the modification parameter $\eta \in [0, 1)$ gives the reduced infectivity of the recovered individuals [11, 32]. Mosquitoes are assumed to suffer natural death at a rate μ_v, regardless of their infection status. Newly-infected mosquitoes are moved into the exposed class (E_v), and progress to the class of symptomatic mosquitoes (I_v) following the development of symptoms (at a rate α_v).

Thus, putting the above formulations and assumptions together gives the following human-vector model, given by system of ordinary differential equations below as

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \kappa R_h - \beta\varepsilon_h\phi I_v S_h - \mu_h S_h,\\
\frac{dE_h}{dt} &= \beta\varepsilon_h\phi I_v S_h - (\alpha_h + \mu_h)E_h,\\
\frac{dI_h}{dt} &= \alpha_h E_h - (b + \tau)I_h - (\psi + \mu_h)I_h,\\
\frac{dR_h}{dt} &= (b + \tau)I_h - (\kappa + \mu_h)R_h,\\
\frac{dS_v}{dt} &= \Lambda_v - \lambda\phi\varepsilon_v(I_h + \eta R_h)S_v - \mu_v S_v,\\
\frac{dE_v}{dt} &= \lambda\phi\varepsilon_v(I_h + \eta R_h)S_v - (\alpha_v + \mu_v)E_v,\\
\frac{dI_v}{dt} &= \alpha_v E_v - \mu_v I_v,
\end{aligned} \tag{2.1}$$

The associated model variables and parameters are described in Table 1.

2.1. **Basic properties of the malaria model.**

2.1.1. *Positivity and boundedness of solutions.* For the malaria transmission model (2.1) to be epidemiologically meaningful, it is important to prove that all its state variables are non-negative for all time. In other words, solutions of the model system (2.1) with non-negative initial data will remain non-negative for all time $t > 0$.

Theorem 2.1. *Let the initial data $S_h(0) \geq 0$, $E_h(0) \geq 0$, $I_h(0) \geq 0$, $R_h(0) \geq 0$, $S_v(0) \geq 0$, $E_v(0) \geq 0$, $I_v(0) \geq 0$. Then the solutions $(S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ of the malaria model (2.1) are non-negative for all $t > 0$. Furthermore*

$$\limsup_{t\to\infty} N_h(t) \leq \frac{\Lambda_h}{\mu_h}, \quad \limsup_{t\to\infty} N_v(t) \leq \frac{\Lambda_v}{\mu_v},$$

with $N_h = S_h + E_h + I_h + R_h$ *and* $N_v = S_v + E_v + I_v$.

Proof. Let $t_1 = \sup\{t > 0 : S_h(t) > 0, E_h(t) > 0, I_h(t) > 0, R_h(t) > 0, S_v(t) > 0, I_v(t) > 0, E_v(t) > 0\}$. Since $S_h(0) > 0, E_h(0) > 0, I_h(0) > 0, R_h(0) > 0, S_v(0) > 0, E_v(0) > 0, I_v(0) > 0$, then, $t_1 > 0$. If $t_1 < \infty$, then S_h, E_h, I_h, R_h, S_v, E_v or I_v is equal to zero at t_1. It follows from the first equation of the system (2.1), that

$$\frac{dS_h}{dt} = \Lambda_h - \beta\varepsilon_h\phi I_v S_h - \mu_h S_h + \kappa R_h$$

Thus,

$$\frac{d}{dt}\big\{S_h(t)\exp[(\beta\varepsilon_h\phi I_v + \mu_h)t]\big\} = (\Lambda_h + \kappa R_h)\exp[(\beta\varepsilon_h\phi I_v + \mu_h)t]$$

Hence,

$$S_h(t_1)\exp[(\beta\varepsilon_h\phi I_v + \mu_h)t] - S_h(0) = \int_0^{t_1}(\Lambda_h + \kappa R_h)\exp[(\beta\varepsilon_h\phi I_v + \mu_h)p]dp$$

so that

$$\begin{aligned} S_h(t_1) = S_h(0)\ exp[-(\beta\varepsilon_h\phi I_v + \mu_h)t_1] + \exp[-(\beta\varepsilon_h\phi I_v + \mu_h)t_1] \\ \times \int_0^{t_1}(\Lambda_h + \kappa R_h)\exp[(\beta\varepsilon_h\phi I_v + \mu_h)p]dp > 0. \end{aligned}$$

and

$$\begin{aligned} R_h(t_1) &= R_h(0)\exp[-(\mu_h + \kappa)t_1] + \exp[(\mu_h + \kappa)t_1]\int_0^{t_1}(b+\tau)I_h\exp[(\mu_h + \kappa)p]dp \\ &> 0. \end{aligned}$$

It can similarly be shown that $E_h > 0$, $I_h > 0$, $S_v > 0$, $E_v > 0$ and $I_v > 0$ for all $t > 0$. For the second part of the proof, it should be noted that $0 < I_h(t) \le N_h(t)$ and $0 < I_v(t) \le N_v(t)$.

Adding the first four equations and the last three equations of the model (2.1) gives

$$\begin{aligned} \frac{dN_h(t)}{dt} &= \Lambda_h - \mu_h N_h(t) - \psi I_h(t), \\ \frac{dN_v(t)}{dt} &= \Lambda_v - \mu_v N_v(t). \end{aligned} \tag{2.2}$$

Thus,

$$\begin{aligned} \Lambda_h - (\mu_h + \psi)N_h(t) \le \frac{dN_h(t)}{dt} \le \Lambda_h - \mu_h N_h(t), \\ \Lambda_v - \mu_v N_v(t) \le \frac{dN_v(t)}{dt} \le \Lambda_v - \mu_v N_v(t). \end{aligned}$$

Hence, respectively,

$$\frac{\Lambda_h}{\mu_h + \psi} \le \liminf_{t\to\infty} N_h(t) \le \limsup_{t\to\infty} N_h(t) \le \frac{\Lambda_h}{\mu_h},$$

and

$$\frac{\Lambda_v}{\mu_v} \le \liminf_{t\to\infty} N_v(t) \le \limsup_{t\to\infty} N_v(t) \le \frac{\Lambda_v}{\mu_v},$$

as required. □

2.1.2. *Invariant regions.* The malaria model (2.1) will be analyzed in a biologically-feasible region as follows. The system (2.1) is split into two parts, namely the human population (N_h; with $N_h = S_h + E_h + I_h + R_h$) and the vector population (N_v; with $N_v = S_v + E_v + I_v$). Consider the feasible region

$$\mathcal{D} = \mathcal{D}_h \cup \mathcal{D}_v \subset \mathbb{R}^4_+ \times \mathbb{R}^3_+,$$

with

$$\mathcal{D}_h = \{(S_h, E_h, I_h, R_h) \in \mathbb{R}^4_+ : S_h + E_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h}\},$$
$$\mathcal{D}_v = \{(S_v, E_v, I_v) \in \mathbb{R}^3_+ : S_v + E_v + I_v \leq \frac{\Lambda_v}{\mu_v}\}$$

The following steps are done to establish the positive invariance of $\mathcal{D}$ (i.e., solutions in $\mathcal{D}$ remain in $\mathcal{D}$ for all $t > 0$). The rate of change of the humans and mosquitoes populations is given in equation (2.2), it follows that

$$\begin{aligned} \frac{dN_h(t)}{dt} &\leq \Lambda_h - \mu_h N_h(t), \\ \frac{dN_v(t)}{dt} &\leq \Lambda_v - \mu_v N_v(t). \end{aligned} \tag{2.3}$$

A standard comparison theorem [21] can then be used to show that $N_h(t) \leq N_h(0)e^{-\mu_h t} + \frac{\Lambda_h}{\mu_h}(1 - e^{-\mu_h t})$ and $N_v(t) \leq N_v(0)e^{-\mu_v t} + \frac{\Lambda_v}{\mu_v}(1 - e^{-\mu_v t})$. In particular, $N_h(t) \leq \frac{\Lambda_h}{\mu_h}$ and $N_v(t) \leq \frac{\Lambda_v}{\mu_v}$ if $N_h(0) \leq \frac{\Lambda_h}{\mu_h}$ and $N_v(0) \leq \frac{\Lambda_v}{\mu_v}$ respectively. Thus, the region $\mathcal{D}$ is positively-invariant. Hence, it is sufficient to consider the dynamics of the flow generated by (2.1) in $\mathcal{D}$. In this region, the model can be considered as been epidemiologically and mathematically well-posed [15]. Thus, every solution of the basic model (2.1) with initial conditions in $\mathcal{D}$ remains in $\mathcal{D}$ for all $t > 0$. Therefore, the ω-limit sets of the system (2.1) are contained in $\mathcal{D}$. This result is summarized below.

Lemma 2.2. *The region $\mathcal{D} = \mathcal{D}_h \cup \mathcal{D}_v \subset \mathbb{R}^4_+ \times \mathbb{R}^3_+$ is positively-invariant for the basic model* (2.1) *with non-negative initial conditions in $\mathbb{R}^7_+$*

2.2. **Stability of the disease-free equilibrium (DFE).** The malaria model (2.1) has a DFE, obtained by setting the right-hand sides of the equations in the model to zero, given by

$$\mathcal{E}_0 = (S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^*) = \Big(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0\Big).$$

The linear stability of $\mathcal{E}_0$ can be established using the next generation operator method [42] on the system (2.1), the matrices F and V, for the new infection terms and the remaining transfer terms, are, respectively, given by

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & \beta\varepsilon_h\phi S_h^* \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \lambda\varepsilon_v\phi S_v^* & \lambda\varepsilon_v\phi\eta S_v^* & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} k_1 & 0 & 0 & 0 & 0 \\ -\alpha_1 & k_2 & 0 & 0 & 0 \\ 0 & -(b+\tau) & k_3 & 0 & 0 \\ 0 & 0 & 0 & k_4 & 0 \\ 0 & 0 & 0 & -\alpha_2 & \mu_v \end{pmatrix},$$

where $k_1 = \alpha_h + \mu_h$, $k_2 = b + \tau + \psi + \mu_h$, $k_3 = \kappa + \mu_h$, $k_4 = \alpha_v + \mu_v$.

It follows that the reproduction number of the malaria system (2.1), denoted by $\mathcal{R}_0$, is

$$\mathcal{R}_0 = \sqrt{\frac{\alpha_1\alpha_2\lambda\beta[k_3 + \eta(b+\tau)]\phi^2\epsilon_h\varepsilon_v S_h^* S_v^*}{k_3k_4k_2k_1\mu_v}}, \tag{2.4}$$

Further, using [42, Theorem 2], the following result is established.

Theorem 2.3. *The DFE of the model* (2.1)*, given by* $\mathcal{R}_0$*, is locally asymptotically stable (LAS) if* $\mathcal{R}_0 < 1$*, and unstable if* $\mathcal{R}_0 > 1$*.*

3. Existence of endemic equilibrium point (EEP)

Next conditions for the existence of endemic equilibria for the model (2.1) is explored. Let

$$\mathcal{E}_1 = \big(S_h^{**}, E_h^{**}, I_h^{**}, R_h^{**}, S_v^{**}, E_v^{**}, I_v^{**}\big),$$

be the arbitrary endemic equilibrium of model (2.1), in which at least one of the infected components of the model is non-zero. Let

$$\lambda_h^{**} = \beta\phi\varepsilon_h I_v, \tag{3.1}$$

$$\lambda_v^{**} = \lambda\phi\varepsilon_v(I_h + \eta R_h) \tag{3.2}$$

be the force of infection in humans and in the vector. Setting the right-hand sides of the equations in (2.1) to zero gives the following expressions (in terms of λ_h^{**} and λ_v^{**})

$$\begin{aligned} S_h^{**} &= \frac{\Lambda_h^{**}k_1k_2k_3}{(\lambda_h+\mu_h)k_1k_2k_3 - \kappa\lambda_h^{**}\alpha_h(b+\tau)}, \\ E_h^{**} &= \frac{k_2\lambda_h^{**}\Lambda_hk_3}{(\lambda_h+\mu_h)k_1k_2k_3 - \kappa\lambda_h^{**}\alpha_h(b+\tau)}, \\ I_h^{**} &= \frac{\lambda_h^{**}\Lambda_hk_3\alpha_1}{(\lambda_h+\mu_h)k_1k_2k_3 - \kappa\lambda_h^{**}\alpha_h(b+\tau)}, \\ R_h^{**} &= \frac{(b+\tau)\lambda_h^{**}\Lambda_h\alpha_1}{(\lambda_h+\mu_h)k_1k_2k_3 - \kappa\lambda_h^{**}\alpha_h(b+\tau)}, \\ S_v^{**} = \frac{\Lambda_v}{(\lambda_v^{**}+\mu_v)}, \quad E_v^{**} &= \frac{\lambda_v^{**}\Lambda_v}{k_4(\lambda_v^{**}+\mu_v)}, \quad I_v^{**} = \frac{\alpha_v\lambda_v^{**}\Lambda_v}{k_4\mu_v(\lambda_v^{**}+\mu_v)} \end{aligned} \tag{3.3}$$

Substituting (3.3) and (3.2) into (3.1), gives $a_0\lambda_h^{**} + b_0 = 0$, where

$$a_0 = k_4\mu_v\{\lambda\phi\varepsilon_v\Lambda_h\alpha_h[k_3 + \eta(b+\tau)] + \mu_v[k_3k_1k_2 - \kappa\alpha_h(b+\tau)]\}$$

$$b_0 = \mu_h\mu_v^2k_4k_3k_1k_2(1 - \mathcal{R}_0^2).$$

The coefficient a_0 is always positive, the coefficient b_0 is positive (negative) if $\mathcal{R}_0$ is less than (greater than) unity. Furthermore, there is no positive endemic equilibrium if $b_0 \geq 0$. If $b_0 < 0$, then there is a unique endemic equilibrium (given by $\lambda_h = b_0/a_0$). This result is summarized below.

Lemma 3.1. *The model* (2.1) *has a unique positive endemic equilibrium whenever* $\mathcal{R}_0 > 1$, *and no positive endemic equilibrium otherwise.*

3.1. **Global stability of endemic equilibrium for a special case.** In this section, we investigate the global stability of the endemic equilibrium of model (2.1), for the special case when $\kappa = 0$, that there is no lost of immunity. Using the approach in the proof of Lemma 2.2, it can be shown that the region

$$\tilde{\mathcal{D}} = \tilde{\mathcal{D}}_h \cup \tilde{\mathcal{D}}_v \subset \mathbb{R}^4_+ \times \mathbb{R}^3_+,$$

where

$$\tilde{\mathcal{D}}_h = \big\{(S_h, E_h, I_h, R_h) \subset \mathcal{D}_h \ : S_h \le S_h^*\big\},$$
$$\tilde{\mathcal{D}}_v = \big\{(S_v, E_v, I_v) \subset \mathcal{D}_v : S_v \le S_v^*\big\}.$$

is positively-invariant for the special case of the model (2.1) described above. It is convenient to define

$$\tilde{\mathcal{D}} = \big\{(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \in \mathcal{D} : E_h = I_h = R_h = E_v = I_v = 0\big\}.$$

Theorem 3.2. *The unique endemic equilibrium,* $\tilde{\mathcal{E}}_1$, *of the model* (2.1) *is GAS in* $\tilde{\mathcal{D}} \backslash \tilde{\mathcal{D}}_0$ *whenever* $\tilde{\mathcal{R}}_{0|_{\kappa=0}} > 1$.

Proof. Let $\tilde{\mathcal{R}}_0 > 1$, so that the unique endemic equilibrium ($\tilde{\mathcal{E}}_1$) exists. Consider the non-linear Lyapunov function

$$\begin{aligned}\mathcal{F} &= S_h^{**}\Big(\frac{S_h}{S_h^{**}} - \ln\frac{S_h}{S_h^{**}}\Big) + E_h^{**}\Big(\frac{E_h}{E_h^{**}} - \ln\frac{E_h}{E_h^{**}}\Big) + \frac{k_1}{\alpha_h} I_h^{**}\Big(\frac{I_h}{I_h^{**}} - \ln\frac{I_h}{I_h^{**}}\Big)\\ &\quad + \frac{k_2 k_1}{\alpha_h \gamma} R_h^{**}\Big(\frac{R_h}{R_h^{**}} - \ln\frac{R_h}{R_h^{**}}\Big) + S_v^{**}\Big(\frac{S_v}{S_v^{**}} - \ln\frac{S_v}{S_v^{**}}\Big) + E_v^{**}\Big(\frac{E_v}{E_v^{**}} - \ln\frac{E_v}{E_v^{**}}\Big)\\ &\quad + \frac{k_4}{\alpha_v} I_v^{**}\Big(\frac{I_v}{I_v^{**}} - \ln\frac{I_v}{I_v^{**}}\Big),\end{aligned}$$

where $\gamma = b + \tau$ and the Lyapunov derivative is

$$\begin{aligned}\dot{\mathcal{F}} &= \Big(1 - \frac{S_h^{**}}{S_h}\Big)\dot{S}_h + \Big(1 - \frac{E_h^{**}}{E_h}\Big)\dot{E}_h + \frac{k_1}{\alpha_h}\Big(1 - \frac{I_h^{**}}{I_h}\Big)\dot{I}_h + \frac{k_2 k_1}{\alpha_h \gamma}\Big(1 - \frac{R_h^{**}}{R_h}\Big)\dot{R}_h\\ &\quad + \Big(1 - \frac{S_v^{**}}{S_v}\Big)\dot{S}_v + \Big(1 - \frac{E_v^{**}}{E_v}\Big)\dot{E}_v + \frac{k_4}{\alpha_v}\Big(1 - \frac{I_v^{**}}{I_v}\Big)\dot{I}_v.\end{aligned}$$

Substituting the expressions for the derivatives in $\dot{\mathcal{F}}$ (from (2.1) with $\kappa = 0$) gives

$$\begin{aligned}\dot{\mathcal{F}} &= \Lambda_h - \lambda_h S_h - \mu_h S_h - \frac{S_h^{**}}{S_h}\Big(\Lambda_h - \lambda_h S_h - \mu_h S_h\Big)\\ &\quad + \lambda_h S_h - k_1 E_h - \frac{E_h^{**}}{E_h}\Big(\lambda_h S_h - k_1 E_h\Big)\\ &\quad + \frac{k_1}{\alpha_h}\Big(\alpha_h E_h - k_2 I_h\Big) - \frac{k_1}{\alpha_h}\frac{I_h^{**}}{I_h}\Big(\alpha_h E_h - k_2 I_h\Big)\\ &\quad + \frac{k_2 k_1}{\alpha_h \gamma}\Big(\gamma I_h - k_3 R_h\Big) - \frac{k_2 k_1}{\alpha_h \gamma}\frac{R_h^{**}}{R_h}\Big(\gamma I_h - k_3 R_h\Big)\\ &\quad + \Lambda_v - \lambda_v S_v - \mu_v S_v - \frac{S_v^{**}}{S_v}\Big(\Lambda_v - \lambda_v S_v - \mu_v S_v\Big)\\ &\quad + \lambda_v S_v - k_4 E_v + \frac{E_v^{**}}{E_v}\Big(\lambda_v S_v - k_4 E_v\Big)\end{aligned}$$

$$+\frac{k_4}{\alpha_v}\Big(\alpha_v E_v-\mu_v I_v\Big)+\frac{k_4}{\alpha_v}\frac{I_v^{**}}{I_v}\Big(\alpha_v E_v-\mu_v I_v\Big).$$

so that

$$\begin{aligned}\dot{\mathcal{F}}&=\lambda_h S_h^{**}\Big(1-\frac{S_h^{**}}{S_h}\Big)+\mu_h S_h^{**}\Big(2-\frac{S_h}{S_h^{**}}-\frac{S_h^{**}}{S_h}\Big)+\lambda_h S_h^{**}-\frac{E_h^{**}}{E_h}\lambda_h S_h\\&\quad+k_1E_h^{**}-k_1\frac{I_h^{**}}{I_h}E_h+\frac{k_2k_1}{\alpha_h}I_h^{**}-\frac{k_2k_1}{\alpha_h}\frac{R_h^{**}}{R_h}I_h+\frac{k_3k_2k_1}{\alpha_h\gamma}R_h-\frac{k_3k_2k_1}{\alpha_h\gamma}R_h\\&\quad+\lambda_v S_v^{**}\Big(1-\frac{S_v^{**}}{S_v}\Big)+\mu_v S_v^{**}\Big(2-\frac{S_v}{S_v^{**}}-\frac{S_v^{**}}{S_v}\Big)+\lambda_v S_v^{**}\\&\quad-\frac{E_v^{**}}{E_v}\lambda_v S_v+k_4E_v^{**}-k_4\frac{I_v^{**}}{I_v}E_v+\frac{k_4\mu_v}{\alpha_v}I_v^{**}-\frac{k_4\mu_v}{\alpha_v}I_v\end{aligned}\tag{3.4}$$

Finally, equation (3.4) can be further simplified to give

$$\begin{aligned}\dot{\mathcal{F}}&=\mu_h S_h^{**}\Big(2-\frac{S_h^{**}}{S_h}-\frac{S_h}{S_h^{**}}\Big)+k_1E_h^{**}\Big(5-\frac{S_h^{**}}{S_h}-\frac{E_h^{**}}{E_h}-\frac{E_h}{E_h^{**}}\frac{I_h^{**}}{I_h}\\&\quad-\frac{I_h}{I_h^{**}}\frac{R_h^{**}}{R_h}-\frac{R_h}{R_h^{**}}\Big)+\ \mu_v S_v^{**}\Big(2-\frac{S_v^{**}}{S_v}-\frac{S_v}{S_v^{**}}\Big)\\&\quad+k_4E_v^{**}\Big(4-\frac{S_v^{**}}{S_v}-\frac{E_v^{**}}{E_v}-\frac{E_v}{E_v^{**}}\frac{I_v^{**}}{I_v}-\frac{I_v}{I_v^{**}}\Big).\end{aligned}\tag{3.5}$$

Since the arithmetic mean exceeds the geometric mean, it follows that

$$\begin{gathered}2-\frac{S_h^{**}}{S_h}-\frac{S_h}{S_h^{**}}\le 0,\quad 2-\frac{S_v^{**}}{S_v}-\frac{S_v}{S_v^{**}}\le 0,\\4-\frac{S_v^{**}}{S_v}-\frac{E_v^{**}}{E_v}-\frac{E_v}{E_v^{**}}\frac{I_v^{**}}{I_v}-\frac{I_v}{I_v^{**}}\le 0,\\5-\frac{S_h^{**}}{S_h}-\frac{E_h^{**}}{E_h}-\frac{E_h}{E_h^{**}}\frac{I_h^{**}}{I_h}-\frac{I_h}{I_h^{**}}\frac{R_h^{**}}{R_h}-\frac{R_h}{R_h^{**}}\le 0\end{gathered}$$

Since all the model parameters are non-negative, it follows that $\dot{\mathcal{F}}\le 0$ for $\tilde{\mathcal{R}}_{0|_{\kappa=0}}>1$. Thus, it follows from the LaSalle's Invariance Principle, that every solution to the equations in the model (2.1) (with initial conditions in $\tilde{\mathcal{D}}\backslash\tilde{\mathcal{D}}_0$) approaches the EEP $(\tilde{\mathcal{E}}_1)$ as $t\to\infty$ whenever $\tilde{\mathcal{R}}_{0|_{\kappa=0}}>1$. □

4. Analysis of optimal control

We introduce into the model (2.1), time dependent preventive (u_1,u_3) and treatment (u_2) efforts as controls to curtail the spread of malaria. The malaria model (2.1) becomes

$$\begin{aligned}\frac{dS_h}{dt}&=\Lambda_h+\kappa R_h-(1-u_1)\beta\varepsilon_h\phi I_vS_h-\mu_hS_h,\\\frac{dE_h}{dt}&=(1-u_1)\beta\varepsilon_h\phi I_vS_h-(\alpha_h+\mu_h)E_h,\\\frac{dI_h}{dt}&=\alpha_hE_h-(b+u_2)I_h-(\psi+\mu_h)I_h,\\\frac{dR_h}{dt}&=(b+u_2)I_h-(\kappa+\mu_h)R_h,\end{aligned}$$

$$\frac{dS_v}{dt} = \Lambda_v - (1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h)S_v - u_3(1-p)S_v - \mu_v S_v, \tag{4.1}$$
$$\frac{dE_v}{dt} = (1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h)S_v - u_3(1-p)E_v - (\alpha_v+\mu_v)E_v,$$
$$\frac{dI_v}{dt} = \alpha_v E_v - u_3(1-p)I_v - \mu_v I_v.$$

The function $0 \le u_1 \le 1$ represent the control on the use of mosquitoes treated bed nets for personal protection, and $0 \le u_2 \le a_2$, the control on treatment, where a_2 is the drug efficacy use for treatment. The insecticides used for treating bed nets is lethal to the mosquitoes and other insects and also repels the mosquitoes, thus, reducing the number that attempt to feed on people in the sleeping areas with the nets [8, 44]. However, the mosquitoes can still feed on humans outside this protective areas, and so we have included the spraying of insecticide. Thus, each mosquitoes group is reduced (at the rate $u_3\ (1-p)$), where $(1-p)$ is the fraction of vector population reduced and $0 \le u_3 \le a_3$, is the control function representing spray of insecticide aimed at reducing the mosquitoes sub-populations and a_3 represent the insecticide efficacy at reducing the mosquitoes population. This is different from what was implemented in [5], where only two control measures of personal protection and treatment were used.

With the given objective function

$$J(u_1,u_2,u_3) = \int_0^{t_f} [mI_h + nu_1^2 + cu_2^2 + du_3^2]dt \tag{4.2}$$

where t_f is the final time and the coefficients m, n, c, d are positive weights to balance the factors. Our goal is to minimize the number of infected humans $I_h(t)$, while minimizing the cost of control $u_1(t),\ u_2(t),\ u_3(t)$. Thus, we seek an optimal control u_1^*, u_2^*, u_3^* such that

$$J(u_1^*,u_2^*,u_3^*) = \min_{u_1,u_2,u_3}\{J(u_1,u_2,u_3)|u_1,u_2,u_3 \in \mathcal{U}\} \tag{4.3}$$

where the control set

$$\mathcal{U} = \{(u_1,u_2,u_3) \mid u_i : [0,t_f] \to [0,1],\ \text{Lebesgue measurable } i = 1,2,3\}.$$

The term mI_h is the cost of infection while nu_1^2, cu_2^2 and du_3^2 are the costs of use of bed nets, treatment efforts and use of insecticides respectively. The necessary conditions that an optimal control must satisfy come from the Pontryagin's Maximum Principle [30]. This principle converts (4.1)-(4.2) into a problem of minimizing pointwise a Hamiltonian H, with respect to (u_1,u_2,u_3)

$$\begin{aligned} H = {} & mI_h + nu_1^2 + cu_2^2 + du_3^2 + \lambda_{S_h}\{\Lambda_h + \kappa R_h - (1-u_1)\beta\varepsilon_h\phi I_v S_h - \mu_h S_h\} \\ & + \lambda_{E_h}\{(1-u_1)\beta\varepsilon_h\phi I_v S_h - (\alpha_h+\mu_h)E_h\} \\ & + \lambda_{I_h}\{\alpha_h E_h - (b+u_2)I_h - (\psi+\mu_h)I_h\} \\ & + \lambda_{R_h}\{(b+u_2)I_h - (\kappa+\mu_h)R_h\} \\ & + \lambda_{S_v}\{\Lambda_v - (1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h)S_v - u_3(1-p)S_v - \mu_v S_v\} \\ & + \lambda_{E_v}\{(1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h)S_v - u_3(1-p)E_v - (\alpha_v+\mu_v)E_v\} \\ & + \lambda_{I_v}\{\alpha_v 2E_v - u_3(1-p)I_v - \mu_v I_v\} \end{aligned} \tag{4.4}$$

where the λ_{S_h}, λ_{E_h}, λ_{I_h}, λ_{R_h}, λ_{S_v}, λ_{E_v}, λ_{I_v} are the adjoint variables or co-state variables. [13, Corollary 4.1] gives the existence of optimal control due to the

convexity of the integrand of J with respect to u_1, u_2 and u_3, a *priori* boundedness of the state solutions, and the *Lipschitz* property of the state system with respect to the state variables. Applying Pontryagin's Maximum Principle [30] and the existence result for the optimal control from [13], we obtain the following theorem.

Theorem 4.1. *Given an optimal control u_1^*, u_2^*, u_3^* and solutions S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^* of the corresponding state system (4.1) that minimizes $J(u_1, u_2, u_3)$ over $\mathcal{U}$. Then there exists adjoint variables λ_{S_h}, λ_{E_h}, λ_{I_h}, λ_{R_h}, λ_{S_v}, λ_{E_v}, λ_{I_v} satisfying*

$$\begin{aligned}
-\frac{d\lambda_{S_h}}{dt} &= -[(1-u_1)\beta\varepsilon_h\phi I_v + \mu_h]\lambda_{S_h} + (1-u_1)\beta\varepsilon_h\phi I_v\lambda_{E_h}\\
-\frac{d\lambda_{E_h}}{dt} &= -(\mu_h+\alpha_h)\lambda_{E_h} + \alpha_h\lambda_{I_h}\\
-\frac{d\lambda_{I_h}}{dt} &= m - [(b+u_2)+(\mu_h+\psi)]\lambda_{I_h} + (b+u_2)\lambda_{R_h}\\
&\quad + (1-u_1)\lambda\varepsilon_v\phi S_v(\lambda_{E_v}-\lambda_{S_v})\\
-\frac{d\lambda_{R_h}}{dt} &= \kappa\lambda_{S_h} - (\mu_h+\kappa)\lambda_{R_h} + (1-u_1)\lambda\varepsilon_v\phi\eta S_v(\lambda_{S_v}-\lambda_{E_v})\\
-\frac{d\lambda_{S_v}}{dt} &= -[(1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h) + u_3(1-p) + \mu_v]\lambda_{S_v}\\
&\quad + (1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h)\lambda_{E_v}\\
-\frac{d\lambda_{E_v}}{dt} &= -[u_3(1-p)+\alpha_v+\mu_v]\lambda_{E_v} + \alpha_v\lambda_{I_v}\\
-\frac{d\lambda_{I_v}}{dt} &= -(1-u_1)\beta\varepsilon_h\phi S_h\lambda_{S_h} + (1-u_1)\beta\varepsilon_h\phi S_h\lambda_{E_h} - [u_3(1-p)+\mu_v]\lambda_{I_v}
\end{aligned} \tag{4.5}$$

and with transversality conditions

$$\lambda_{S_h}(t_f) = \lambda_{E_h}(t_f) = \lambda_{I_h}(t_f) = \lambda_{R_h}(t_f) = \lambda_{S_v}(t_f) = \lambda_{E_v}(t_f) = \lambda_{I_v}(t_f) = 0 \tag{4.6}$$

and the controls u_1^*, u_2^* and u_3^* satisfy the optimality condition

$$\begin{aligned}
u_1^* &= \max\Big\{0, \min\Big(1, \frac{\beta\varepsilon_h\phi I_v^*(\lambda_{E_h}-\lambda_{S_h})S_h^* + \lambda\varepsilon_v\phi(I_h^*+\eta R_h^*)(\lambda_{E_v}-\lambda_{S_v})S_v^*}{2n}\Big)\Big\},\\
u_2^* &= \max\Big\{0, \min\Big(1, \frac{(\lambda_{I_h}-\lambda_{R_h})I_h^*}{2c}\Big)\Big\}\\
u_3^* &= \max\Big\{0, \min\Big(1, \frac{(1-p)(S_v^*\lambda_{S_v} + E_v^*\lambda_{E_v} + I_v^*\lambda_{I_v})}{2d}\Big)\Big\}
\end{aligned} \tag{4.7}$$

Proof. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control. Then the adjoint system can be written as

$$\begin{aligned}
-\frac{d\lambda_{S_h}}{dt} &= \frac{\partial H}{\partial S_h} = -[(1-u_1)\beta\varepsilon_h\phi I_v + \mu_h]\lambda_{S_h} + (1-u_1)\beta\varepsilon_h\phi I_v\lambda_{E_h}\\
-\frac{d\lambda_{E_h}}{dt} &= \frac{\partial H}{\partial E_h} = -(\mu_h+\alpha_h)\lambda_{E_h} + \alpha_h\lambda_{I_h}\\
-\frac{d\lambda_{I_h}}{dt} &= \frac{\partial H}{\partial I_h} = m - [(b+u_2)+(\mu_h+\psi)]\lambda_{I_h} + (b+u_2)\lambda_{R_h}\\
&\quad + (1-u_1)\lambda\varepsilon_v\phi S_v(\lambda_{E_v}-\lambda_{S_v})
\end{aligned}$$

$$
\begin{aligned}
-\frac{d\lambda_{R_h}}{dt} &= \frac{\partial H}{\partial R_h} = \kappa\lambda_{S_h} - (\mu_h+\kappa)\lambda_{R_h} + (1-u_1)\lambda\varepsilon_v\phi\eta S_v(\lambda_{S_v}-\lambda_{E_v})\\
-\frac{d\lambda_{S_v}}{dt} &= \frac{\partial H}{\partial S_v} = -[(1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h) + u_3(1-p) + \mu_v]\lambda_{S_v}\\
&\quad + (1-u_1)\lambda\varepsilon_v\phi(I_h+\eta R_h)\lambda_{E_v}\\
-\frac{d\lambda_{E_v}}{dt} &= \frac{\partial H}{\partial E_v} = -[u_3(1-p)+\alpha_v+\mu_v]\lambda_{E_v} + \alpha_v\lambda_{I_v}\\
-\frac{d\lambda_{I_v}}{dt} &= \frac{\partial H}{\partial I_v} = -(1-u_1)\beta\varepsilon_h\phi S_h\lambda_{S_h} + (1-u_1)\beta\varepsilon_h\phi S_h\lambda_{E_h}\\
&\quad - [u_3(1-p)+\mu_v]\lambda_{I_v}
\end{aligned}
$$

with transversality conditions

$$
\lambda_{S_h}(t_f) = \lambda_{E_h}(t_f) = \ \lambda_{I_h}(t_f) = \lambda_{R_h}(t_f) = \lambda_{S_v}(t_f) = \lambda_{E_v}(t_f) = \lambda_{I_v}(t_f) = 0 \quad (4.8)
$$

On the interior of the control set, where $0 < u_i < 1$, for $i = 1, 2, 3$, we have

$$
\begin{aligned}
0 = \frac{\partial H}{\partial u_1} &= 2nu_1^* + \beta\varepsilon_h\phi I_v^*(\lambda_{S_h}-\lambda_{E_h})S_h^* + \lambda\varepsilon_v\phi(I_h^*+\eta R_h^*)(\lambda_{S_v}-\lambda_{E_v})S_v^*,\\
0 = \frac{\partial H}{\partial u_2} &= 2cu_2^* - (\lambda_{I_h}-\lambda_{R_h})I_h^*, \qquad (4.9)\\
0 = \frac{\partial H}{\partial u_3} &= 2du_3^* - (1-p)(S_v^*\lambda_{S_v} + E_v^*\lambda_{E_v} + I_v^*\lambda_{I_v}).
\end{aligned}
$$

Hence, we obtain (see [23])

$$
\begin{aligned}
u_1^* &= \frac{\beta\varepsilon_h\phi I_v^*(\lambda_{E_h}-\lambda_{S_h})S_h^* + \lambda\varepsilon_v\phi(I_h^*+\eta R_h^*)(\lambda_{E_v}-\lambda_{S_v})S_v^*}{2n},\\
u_2^* &= \frac{(\lambda_{I_h}-\lambda_{R_h})I_h^*}{2c},\\
u_3^* &= \frac{(1-p)(S_v^*\lambda_{S_v} + E_v^*\lambda_{E_v} + I_v^*\lambda_{I_v})}{2d}.
\end{aligned}
$$

and

$$
\begin{aligned}
u_1^* &= \max\Big\{0, \min\Big(1, \frac{\beta\varepsilon_h\phi I_v^*(\lambda_{E_h}-\lambda_{S_h})S_h^* + \lambda\varepsilon_v\phi(I_h^*+\eta R_h^*)(\lambda_{E_v}-\lambda_{S_v})S_v^*}{2n}\Big)\Big\},\\
u_2^* &= \max\Big\{0, \min\Big(1, \frac{(\lambda_{I_h}-\lambda_{R_h})I_h^*}{2c}\Big)\Big\}\\
u_3^* &= \max\Big\{0, \min\Big(1, \ \frac{(1-p)(S_v^*\lambda_{S_v} + E_v^*\lambda_{E_v} + I_v^*\lambda_{I_v})}{2d}\Big)\Big\}.
\end{aligned}
$$

□

Due to the a priori boundedness of the state and adjoint functions and the resulting Lipschitz structure of the ODE's, we can obtain the uniqueness of the optimal control for small t_f, following techniques from [30]. The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of (4.1) and (4.5), (4.6) with characterization (4.7). There is a restriction on the length of time interval in order to guarantee the uniqueness of the optimality system. This smallness restriction of the length on the time is due to the opposite time orientations of the optimality system; the state problem has initial values and the adjoint problem has final values. This restriction is very common in control problems (see [16, 20, 22]).

Next we discuss the numerical solutions of the optimality system and the corresponding optimal control pairs, the parameter choices, and the interpretations from various cases.

5. Numerical results

In this section, we study numerically an optimal transmission parameter control for the malaria model. The optimal control is obtained by solving the optimality system, consisting of 7 ODE's from the state and adjoint equations. An iterative scheme is used for solving the optimality system. We start to solve the state equations with a guess for the controls over the simulated time using fourth order Runge-Kutta scheme. Because of the transversality conditions (4.6), the adjoint equations are solved by a backward fourth order Runge-Kutta scheme using the current iterations solutions of the state equation. Then the controls are updated by using a convex combination of the previous controls and the value from the characterizations (4.7). This process is repeated and iterations are stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iterations [23].

We explore a simple model with preventive and treatment as control measures to study the effects of control practices and the transmission of malaria. Using various combinations of the three controls, one control at a time and two controls at a time, we investigate and compare numerical results from simulations with the following scenarios

i. using personal protection (u_1) without insecticide spraying ($u_3 = 0$) and no treatment of the symptomatic humans ($u_2 = 0$)
ii. treating the symptomatic humans (u_2) without using insecticide spraying ($u_3 = 0$) and no personal protection ($u_1 = 0$),
iii. using insecticide spraying (u_3) without personal protection ($u_1 = 0$) and no treatment of the symptomatic humans ($u_2 = 0$),
iv. treating the symptomatic humans (u_2) and using insecticide spraying (u_3) with no personal protection ($u_1 = 0$),
v. using personal protection (u_1) and insecticide spraying (u_3) with no treatment of the symptomatic humans ($u_2 = 0$),
vi using treatment (u_2) and personal protection (u_1) with no insecticide spraying ($u_3 = 0$), finally
vii. using all three control measures (u_1, u_2 and u_3).

For the figures presented here, we assume that the weight factor c associated with control u_2 is greater than n and d which are associated with controls u_1 and u_3. This assumption is based on the facts that the cost associated with u_1 and u_3 will include the cost of insecticide and insecticide treated bed nets, and the cost associated with u_2 will include the cost of antimalarial drugs, medical examinations and hospitalization. For the numerical simulation we have used the following weight factors, $m = 92$, $n = 20$, $c = 65$, and $d = 10$, initial state variables $S_h(0) = 700$, $E_h(0) = 100$, $I_h(0) = 0$, $R_h(0) = 0$, $S_v(0) = 5000$, $E_v(0) = 500$, $I_v(0) = 30$ and parameter values $\Lambda_v = 0.071$, $\Lambda_h = 0.00011$, $\beta = 0.030$, $\varepsilon_h = 0.01$, $\varepsilon_h = 0.01$, $\lambda = 0.05$, $\mu_h = 0.0000457$, $\mu_v = 0.0667$, $\kappa = 0.0014$, $\alpha_1 = 0.058$, $\alpha_2 = 0.0556$, $\sigma = 0.025$, $b = 0.5$, $\phi = 0.502$, $\psi = 0.02$, $\tau = 0.5$, $p = 0.85$, for which the reproduction number $R_0 = 4.3845$, to illustrate the effect of different

TABLE 1. Description of Variables and Parameters of the Malaria Model (4.1)

Var.	Description		
S_h	Susceptible human		
E_h	Exposed human		
I_h	Infected human		
R_h	Recovered human		
S_v	Susceptible vector		
E_v	Exposed vector		
I_v	Infected vector		
Par.	**Description**	**Est. val.**	**References**
ε_h	biting rate of humans	0.2-0.5	[4, 18]
ε_v	biting rate of mosquitoes	0.3	[18, 26, 38]
β	probability of human getting infected	0.03	[12, 36]
λ	probability of a mosquito getting infected	0.09	[12, 36]
μ_h	Natural death rate in humans	0.0004	[47]
μ_v	Natural death rate in mosquitoes	0.04	[10]
κ	rate of loss of immunity	$1/(2\times365)$	[3, 12, 34]
α_1	rate of progression from exposed to infected human	1/17	[3, 28]
α_2	rate of progression from exposed to infected mosquito	1/18	[35, 38, 27]
Λ_h	human birth rate	0.00011	[41]
Λ_v	mosquitoes birth rate	0.071	[3, 12]
ψ	disease induced death	0.05	[37]
ϕ	contact rate of vector per human per unit time	0.6	[9]
b	spontaneous recovery	0.005	[10]
η	modification parameter	0.01	assumed

optimal control strategies on the spread of malaria in a population. Thus, we have considered the spread of malaria in an endemic population.

Optimal personal protection. Only the control (u_1) on personal protection is used to optimize the objective function J, while the control on treatment (u_2) and the control on insecticide spray (u_3) are set to zero. In Figure 1, the results show a significant difference in the I_h and I_v with optimal strategy compared to I_h and I_v without control. Specifically, we observed in Figure 1(a) that the control strategies lead to a decrease in the number of symptomatic human (I_h) as against an increases in the uncontrolled case. Similarly, in Figure 1(b), the uncontrolled case resulted in increased number of infected mosquitoes (I_v), while the control strategy lead to a decrease in the number infected. The control profile is shown in Figure 1(c), here we see that the optimal personal protection control u_1 is at the upper bound till the time $t_f = 100$ days, before dropping to the lower bound.

Optimal treatment. With this strategy, only the control (u_2) on treatment is used to optimize the objective function J, while the control on personal protection (u_1) and the control on insecticide spray (u_3) are set to zero. In Figure 2, the results show a significant difference in the I_h and I_v with optimal strategy compared to I_h and I_v without control. But this strategy shows that effective treatment only has a significant impact in reducing the disease incidence among human population. The control profile is shown in Figure 2(c), we see that the optimal treatment control u_2 rises to and stabilizes at the upper bound for $t_f = 70$ days, before dropping to the lower bound.

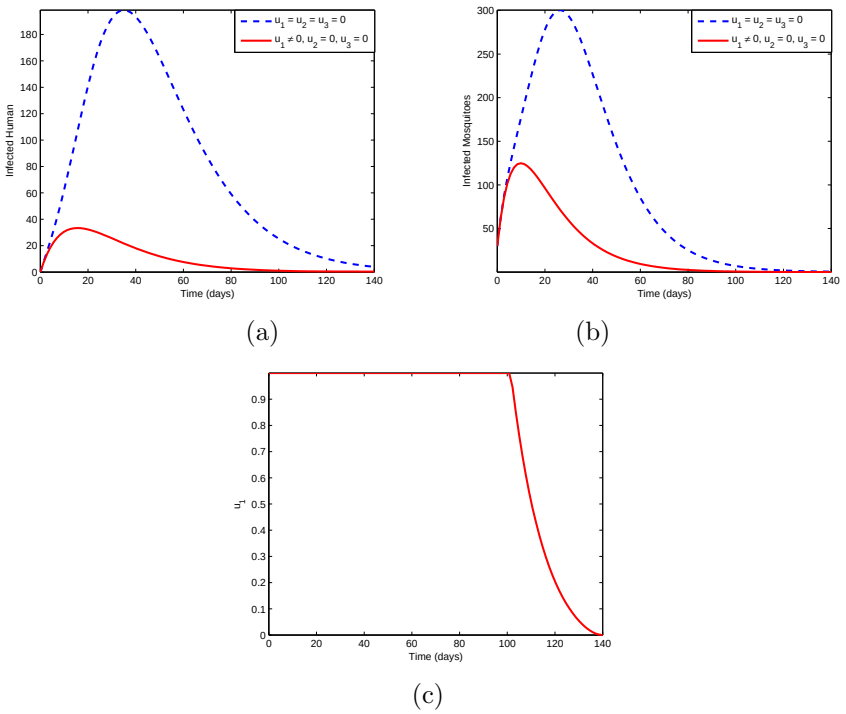

FIGURE 1. Simulations showing the effect of personal protection only on infected human and mosquitoes populations

Optimal insecticide spraying. With this strategy, only the control on insecticide spraying (u_3) is used to optimize the objective function J, while the control on treatment (u_2) and the control on personal protection (u_1) are set to zero. The results in Figure 3 show a significant difference in the I_h and I_v with optimal strategy compared to I_h and I_v without control. We see in Figure 3(a) that the control strategies resulted in a decrease in the number of symptomatic human (I_h) as against an increase in the uncontrolled case. Also in Figure 3(b), the uncontrolled case resulted in increased number of infected mosquitoes (I_v), while the control strategy lead to a drastic decrease in the number of infected mosquitoes. The control profile is shown in Figure 3(c), here we see that the optimal insecticide spray control u_3 is at the upper bound till the time $t_f = 90$ days, it then reduces gradually to the lower bound.

Optimal treatment and insecticide spray. With this strategy, the control (u_2) on treatment and the control on (u_3) insecticide spraying are both used to optimize the objective function J, while the control on personal protection (u_1) is set to zero. In Figure 4, the result shows a significant difference in the I_h and I_v with optimal control strategy compared to I_h and I_v without control. We observed in Figure 4(a) that the control strategies resulted in a decrease in the number of symptomatic humans (I_h) as against increases in the uncontrolled case. Similarly in Figure 4(b), the uncontrolled case resulted in increased number of infected mosquitoes (I_v), while the control strategy lead to a decrease in the number of infected mosquitoes.

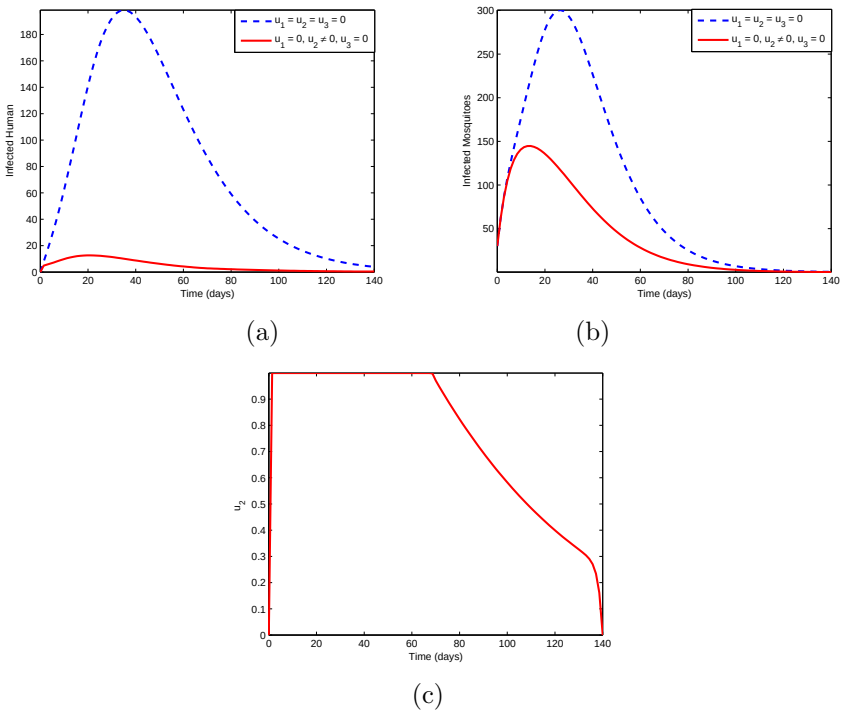

FIGURE 2. Simulations showing the effect of treatment only on infected human and mosquitoes populations

The control profile is shown in Figure 4(c), here we see that the optimal treatment control u_2 is at the upper bound till time $t_f = 50$, while the optimal insecticide spray u_3 is at the upper bound for 90 days before reducing gradually to the lower bound.

Optimal personal protection and insecticide spray. Here, the control on personal protection (u_1) and the spray of insecticide (u_3) are used to optimize the objective function J while setting the control on treatment $u_2 = 0$. For this strategy, shown in Figure 5, we observed that the number of symptomatic human (I_h) and mosquitoes (I_v) differs considerably from the uncontrolled case. Figure 5(a), reveals that symptomatic humans (I_h) is lower in comparison with the case without control. While Figure 5(b), reveals a similar result of decreased number of infected mosquitoes (I_v) for the controlled strategy as compared with the strategy without control. The control profile in Figure 5(c) shows that the control on personal protection (u_1) is at upper bound for 60 days, while insecticide spray (u_3) is at upper bound for $t = 100$ days before reducing to the lower bound.

Optimal personal protection and treatment. With this strategy, the control on personal protection (u_1) and the treatment (u_2) are used to optimize the objective function J while setting the control on spray of insecticide u_3 to zero. For this strategy, shown in Figure 6, there is a significant difference in the I_h and I_v with optimal strategy compared to I_h and I_v without control. We observed in Figure

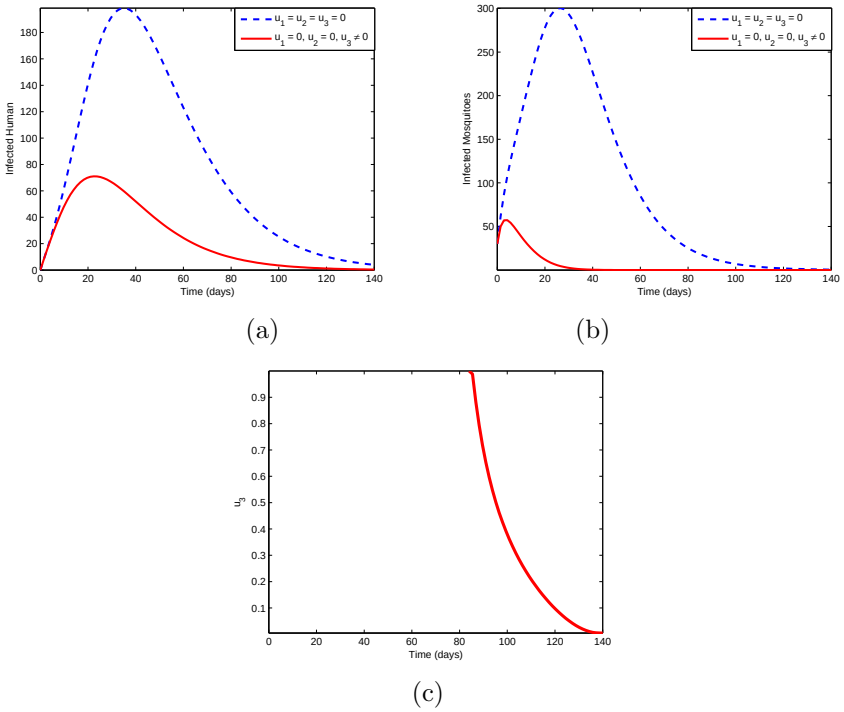

FIGURE 3. Simulations showing the effect of insecticide spraying only on infected human and mosquitoes populations

6(a) that due to the control strategies, the number of symptomatic humans (I_h) decreases as against the increase in the uncontrolled case. A similar decrease is observed in Figure 6(b) for infected mosquitoes (I_v) in the control strategy, while an increased number is observed for the uncontrolled case resulted. In Figure 6(c), the control profile, the control u_1 is at the upper bound for 118 (days) and drops gradually until reaching the lower bound, while control on treatment u_2 starts and remain at upper bound for 12 days before dropping gradually to the lower bound. The result here shows that with a personal protection coverage of 100% for 118 days and treatment coverage of 100% for 12 (days), the disease incidence will be greatly reduced.

Optimal personal protection, treatment and insecticide spray. Here, all three controls (u_1, u_2 and u_3) are used to optimize the objective function J, with weight factors $m = 92$, $n = 20$, $c = 65$, $d = 10$. For this strategy in Figure 7, we observed in Figure 7(a) and 7(b) that the control strategies resulted in a decrease in the number of symptomatic humans (I_h) and infected mosquitoes (I_v) as against the increased number of symptomatic humans (I_h) and infected mosquitoes in the uncontrolled case. The control profile shown in Figure 7(c), shows that the control u_1 is at upper bound for $t_f = 60$ days, while control u_2, starts high at about 77% and reduces to the lower bound gradually over time. The control u_3 on the other hand is at upper bound for about 100 days before reducing to the lower bound.

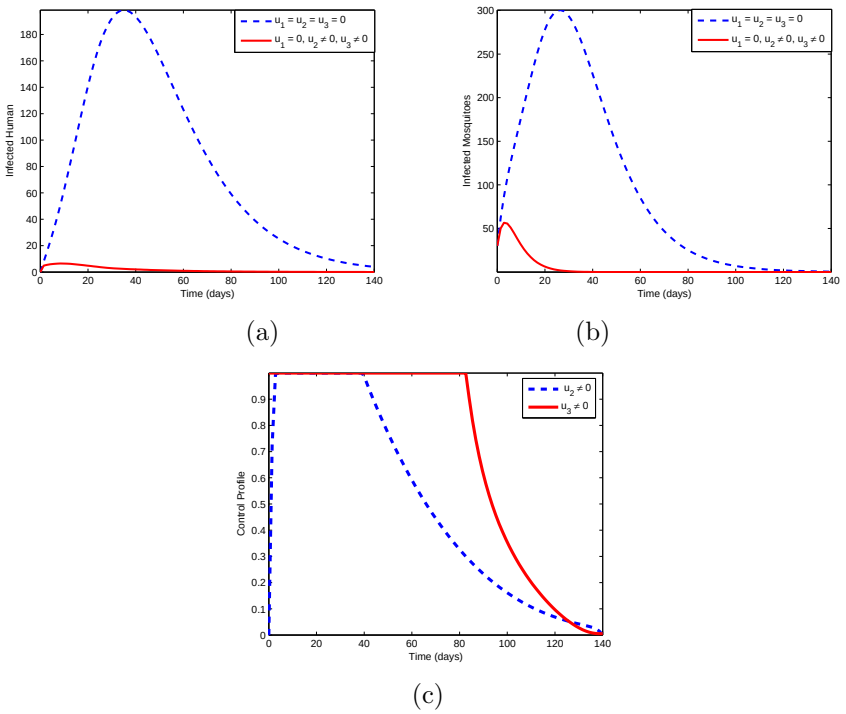

FIGURE 4. Simulations showing the effect of treatment and spray of insecticide on infected human and mosquitoes populations

A comparison of all four control strategies in Figures 8(a) and 8(b) shows that while all four strategies lead to a decrease in the number of infected, both in human and in mosquitoes. The control strategy without treatment resulted in a higher number of infected humans, followed by the strategy without personal protection. The strategy without the spray of insecticide even though, it gave a better result in reducing the infection in human, gave a poorer result in reducing the mosquitoes population. This result shows that with individuals total adherence to effective use of personal protection and spray of insecticide in the population, little treatment efforts will then be required by the community in the control of the spread of the disease.

Spray of insecticide. A scenario with reducing different fraction of vector population is simulated, the result shows that the value of $p = 0.2$ gave the lowest number of susceptible (S_v) vectors while $p = 0.85$ gave the least value of infected (I_v) vectors, this is followed by $p = 0.6$, $p = 0.85$ and lastly by $p = 1$ (a case corresponding to no use or ineffective insecticide) as expected. This has the resultant effect (not depicted here) on total number of vectors susceptible to malaria S_v. When $p = 0.85$, the total number of vectors susceptible to malaria, S_v is 4900, when $p = 0.6$, $S_v = 2000$, and lastly when $p = 0.2$, the total number of susceptible vectors to malaria, $S_v = 1000$.

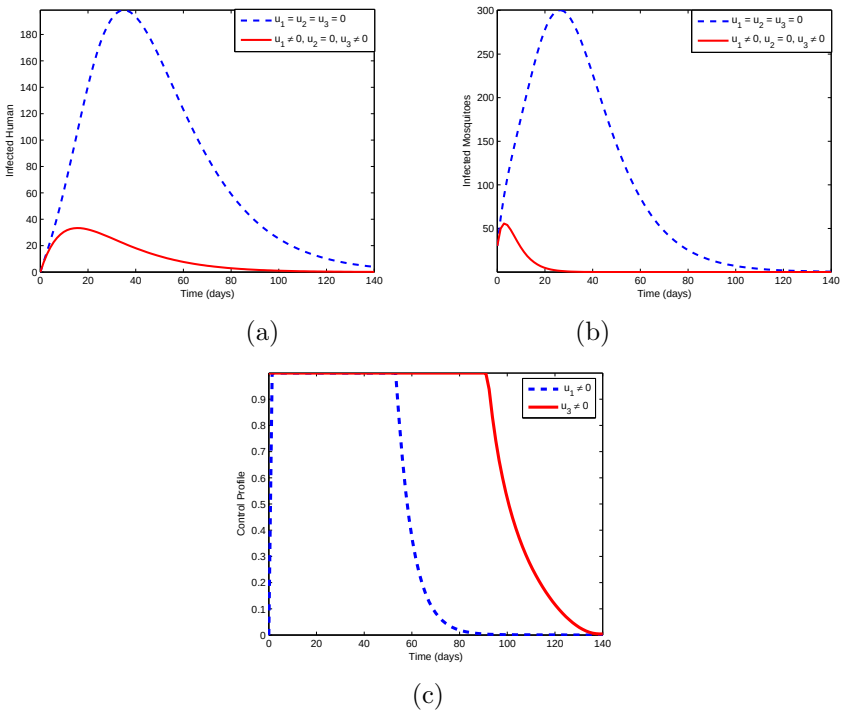

FIGURE 5. Simulations showing the effect of optimal personal protection and spray of insecticide on infected human and mosquitoes populations

5.1. **Concluding remarks.** In this paper, we presented a malaria model using a deterministic system of differential equations and established that the model is locally asymptotically stable when the associated reproduction number is less than unity. In the optimal control problem considered, we use one control at a time and the combination of two controls at a time, while setting the other(s) to zero to investigate and compare the effects of the control strategies on malaria eradication. This is different from what was investigated in [5] where only two control measures of personal protection and treatment were used while varying the vector-host contact rate. Our numerical results shows that the combination of the three (3) controls, personal protection, treatment and insecticides spray, has the highest impact on the control of the disease. This is followed by the combination of treatment and personal protection among the human population; and lastly by the combination involving the use of personal protection and insecticide use. In communities where resources are scarce, we suggest that the combination of treatment and personal protection should be adopted, having observed from the comparison of all four control strategies in Figure 8, that there is no significant difference between this strategy and the combination of the three (3) controls. Although, our recommendation agrees with the result obtained by Blayneh et al[5], our result however shows two possible control strategies, each with two combinations of control measures that are sufficient to effectively achieve and maintain interruption of transmission

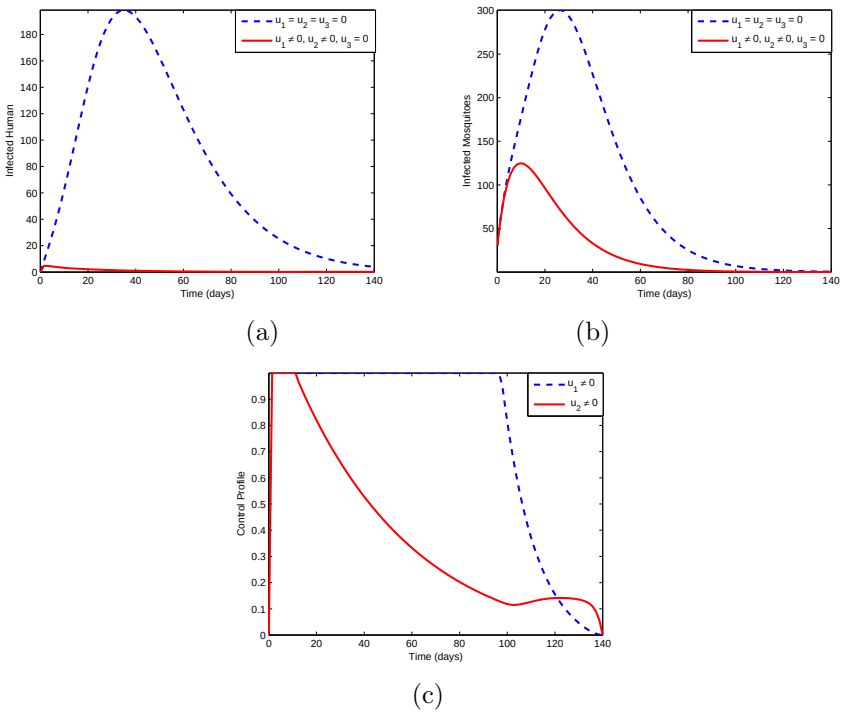

FIGURE 6. Simulations showing the effect of optimal personal protection and treatment on infected human and mosquitoes populations

of malaria. A result which addresses the WHO [44] concern about the insufficiency of only one control measure to achieve and maintain interruption of transmission of malaria.

Acknowledgments. K. O. Okosun acknowledges, with thanks, the support from the South African Center for Epidemiological Modeling and Analysis South Africa (SACEMA). F.B. Agusto conducted part of this work as a Postdoctoral Fellow at NIMBioS, National Institute for Mathematical and Biological Synthesis (NIMBioS) is an Institute sponsored by the National Science Foundation, the U.S. Department of Homeland Security, and the U.S. Department of Agriculture through NSF Award #EF-0832858, with additional support from The University of Tennessee, Knoxville.

REFERENCES

[1] Adams, B. M.; Banks, H. T.; Kwon, H.; Tran Hien, T.; Dynamic multidrug therapies for HIV: Optimal and STI control approaches, *Math. Bio. and Eng.*, **1** (2) (2004), 223–241.

[2] Agusto, F. B.; Gumel, A. B.; Theoretical assessment of avian influenza vaccine. *DCDS Series B.* **13** (1) (2010), 1–25.

[3] Anderson, R. M.; May, R. M.; *Infectious Diseases of Humans: Dynamics and Control*, Oxford University Press, Oxford, 1991.

[4] Ariey, F.; Robert, V.; The puzzling links between malaria transmission and drug resistance, *Trends in Parasitology*, **19** (2003), 158–160.

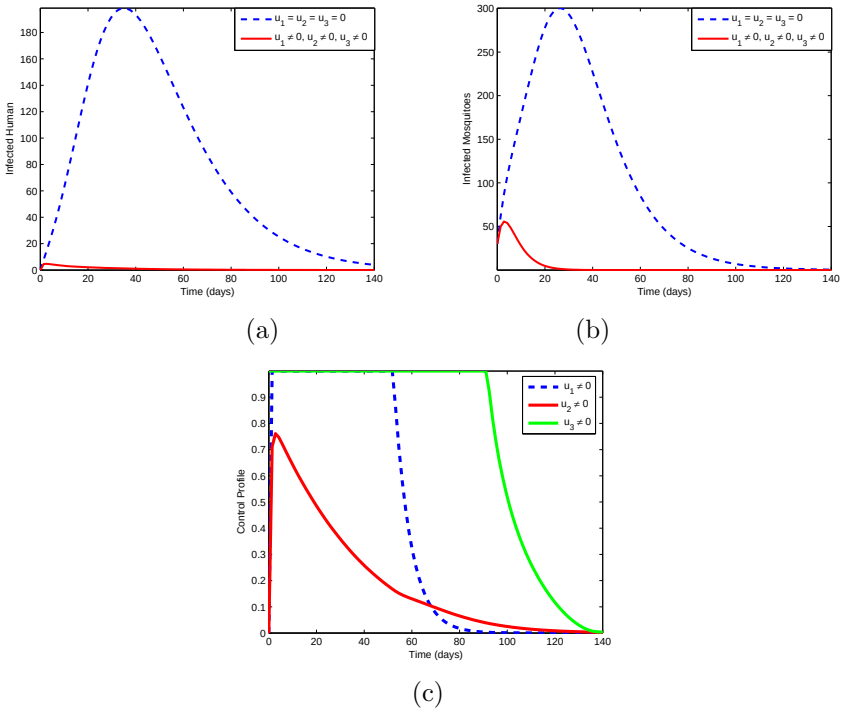

FIGURE 7. Simulations showing the effect of optimal personal protection, treatment and spray of insecticide on infected human and mosquitoes populations

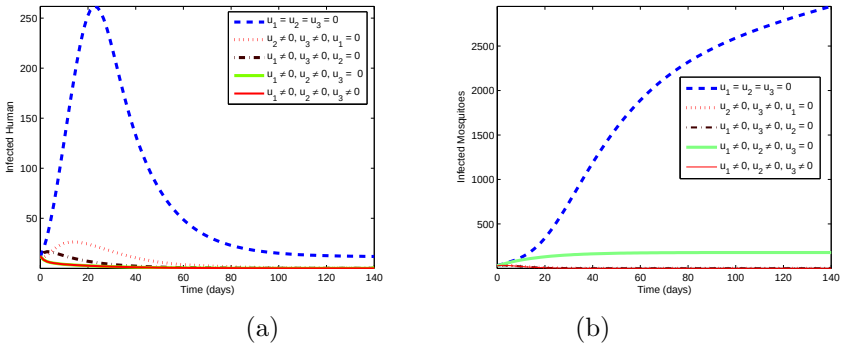

FIGURE 8. Simulations showing the Comparison of the effect of the different control strategies

[5] Blayneh, K.; Cao, Y.; Kwon, H.; Optimal control of vector-borne diseases: Treatment and Prevention. *Discrete and continuous dynamical systems series B*, **11** (3) (2009)., 587–611.
[6] Brown, C. W.; Kahoui, M. E. l.; Novotni, D.; Weber, A.; Algorithmic methods for investigating equilibria in epidemic modeling, *Journal of Symbolic Computation*, **41** (2006), 1157–1173.
[7] Castillo, C.; Optimal control of an epidemic through educational campaigns, *Electronic Journal of Differential Equations*, **2006**, no. 125, 1–11.

[8] Centers for Disease Control and Prevention (CDC) Malaria, http://www.cdc.gov/malaria/malaria_worldwide/reduction/itn.html. Accessed August 17, 2011.

[9] Chitnis, N.; Cushing, J. M.; Hyman, J. M.; Bifurcation Analysis of a Mathematical model for malaria transmission. *SIAM J. Appl. Math.* **67** (1) (2006), 24–45.

[10] Chiyaka, C.; Tchuenche, J. M.; Garira, W.; Dube, S.; A Mathematical analysis of the effects of control strategies on the transmission dynamics of Malaria. *Applied Mathematics and Computation*, **195** (2008), 641–662.

[11] Covell, G.; Relationship between malaria paresitaemia and symptoms of the disease: a review of the literature. *Bulletin of the World Health Organization*. **22** (1960), 605–619.

[12] Flahault, A.; Le Menach, A.; McKenzie, E. F.; Smith, D. L.; The unexpected importance of mosquito oviposition behaviour for malaria: non-productive larval habitats can be sources for malaria transmissionn. *Malaria Journal*, 4. (2005).

[13] Fleming, W. H.; Rishel, R. W.; Deterministic and Stochastic Optimal Control. Springer Verlag, New York, 1975.

[14] Greenhalgh, D.; Some results for an SEIR epidemic model with density dependent in the death rate. *IMA, Journal Math Appl. Med. Bio.* **9** (1992), 67–106.

[15] Hethcote, H. W.; The mathematics of infectious diseases. *SIAM Review*, **42**(4), (2000), 599–653.

[16] Joshi, H. R.; Optimal Control of an HIV Immunology Model, *Optim. Control Appl. Math*, **23** (2002), 199–213.

[17] Karrakchou, R. M.; Gourari, S.; Optimal control and infectiology: Application to an HIV/AIDS model. *Applied Mathematics and Computation*, **177** (2006), 807–818.

[18] Kawaguchi, I.; Sasaki, A.; Mogi, M.; Combining zooprophylaxis and insecticide spraying: a malaria-control strategy limiting the development of insecticide resistance in vector mosquitoes *Proc. R. Soc. Lond.* **271** (2004), 301–309. DOI 10.1098/rspb.2003.2575

[19] Kermack, W. O.; McKendrick, A. G.; Contributions to the Mathematical theory of epidemics - II. The Problem of endemicity. Bulletin of Mathematical Biolooy **53** (1/2) (1991), 57–87.

[20] Kirschner, D.; Lenhart, S.; Serbin, S.; Optimal Control of the Chemotherapy of HIV. *J. Math. Biol.* **35** (1997), 775–792.

[21] Lakshmikantham. V.; Leela, S.; Martynyuk, A. A.; Stability Analysis of Nonlinear Systems. Marcel Dekker, Inc., New York and Basel, 1989.

[22] Lenhart, S.; Bhat, M. G.; Application of Distributed Parameter Control Model in Wildlife Damage Management, *Math. Models & Methods in Appl. Sci.*, **2** (4) (1992), 423–439.

[23] Lenhart, S.; Workman, J. T.; Optimal Control Applied to Biological Models. Chapman and Hall, 2007.

[24] Macdonald, G.; The Epidemiology and Control of Malaria Oxford: Oxford University Press, 1957.

[25] Malaria Foundation International; Malaria: background information, http://www.malaria.org/backgroundinfo.html (1998).

[26] Mbogob, C. M.; Gu, W.; Killeena, G. F.; An individual-based model of plasmodium falciparum malaria transmission on the coast of kenya, *Transactions of the Royal Society of Tropical Medicine and Hygiene*. **97** (2003), 43–50.

[27] Mitchell, V. S.; Oaks, Jr. S. C.; Pearson, G. W.; Malaria: Obstacles and Opportunities, National Academy Press, Washington, DC (1991).

[28] Molineaux, L.; Gramiccia, G.; The Garki Project, World Health Organization, (1980).

[29] Okosun, K.; *Mathematical epidemiology of Malaria disease transmission and its optimal control analyses*. PhD thesis, University of the Western Cape, South Africa, 2010.

[30] Pontryagin, L. S.; Boltyanskii, V. G.; Gamkrelidze, R. V.; Mishchenko, E. F.; The mathematical theory of optimal processes, Wiley, New York, 1962.

[31] Rafikov, M.; Bevilacqua, L.; Wyse, A. P. P.; Optimal control strategy of malaria vector using genetically modified mosquitoes. *J. Theoretical Biology*, **258** (2009), 418–425.

[32] Rosenberg, R.; Andre, R. G.; Ketrangse, S.; Seasonal fluctuation of Plasmodium falciparum gametocytaemia. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, **84** (1990), 29–33.

[33] Ross R,; *The prevention of malaria*, 2nd edition. London: Murray. 1911.

[34] Ruiz, D.; Poveda, G.; Vlez, I. D. etal; Modelling entomological-climatic interactions of *plasmodium falciparum* malaria transmission in two colombian endemic-regions: contributions to a national malaria early warning system. *Malaria Journal*, **5** (66) (2006).
[35] Sherman, I. W.; Malaria: Parasite Biology, Pathogenesis, and Protection, AMS Press, Washington, DC (1998).
[36] Smith, D. L.; McKenzie, F. E.; Statics and dynamics of malaria infection in Anopheles mosquitoes. *Malaria Journal*, **3** (2004), 13 doi: 10.1186/1475-2875-3-13.
[37] Smith, R. J.; Hove-Musekwa, S. D.; Determining effective spraying periods to control malaria via indoor residual spraying in sub-saharan Africa. *J. Applied Mathematics and Decision Sciences*. Article ID 745463, (2008).
[38] Snow, R. W.; Omumbo, J.; Malaria, in Diseases and Mortality in Sub-Saharan Africa, D. T. et al Jamison, ed., The World Bank. (2006), 195–213.
[39] Suresh, P. S.; Optimal Quarantine programmes for controlling an epidemic spread, *Journal Opl. Res. Soc.* **29** (3) (1978), 265–268.
[40] Thomé, R. C. A.; Yang, H. M.; Esteva, L.; Optimal control of Aedes aegypti mosquitoes by the sterile insect technique and insecticide. *Mathematical Biosciences*, **223** (2010), 12–23.
[41] U.S. Census Bureau, International database, 2007.
[42] Van den Driessche P.; Watmough J.; Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, **180** (2002), 29-48.
[43] WHO; Malaria, fact sheets, http://www.who.int/inf-fs/en/fact094.html (1998).
[44] WHO; Global Malaria Programme: Position Statement on ITNs, (2009).
[45] Wickwire, K.; A note on the optimal control of carrier - borne epidemic. *J. Applied probability*, **12** (1975), 565–568.
[46] Yan, X.; Zou, Y.; Li, J.; Optimal quarantine and isolation strategies in epidemics control. *World Journal of Modelling and Simulation*, **3** (3) (2007), 202–211.
[47] Yang, H. M.; A mathematical model for malaria transmission relating global warming and local socioeconomic conditions. *Rev. Saude Publica*, **35** (3) (2001), 224–231.

Folashade B. Agusto
Department of Mathematics and Statistics, Austin Peay State University, Clarksville, Tennessee 37044, USA
E-mail address: fbagusto@gmail.com

Nizar Marcus
Department of Mathematics and Applied Mathematics, University of the Western Cape, South Africa
E-mail address: nmarcus@uwc.ac.za

Kazeem O. Okosun
Department of Mathematics, Vaal University of Technology, Private Bag X021, Vanderbijlpark, 1900, South Africa
E-mail address: kazeemoare@gmail.com