On the Optimal Control of Malaria Epidemic Model with Chemoprophylaxis

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Abstract

We present an optimal control of Malaria epidemic model with Chemoprophylaxis to describe the interaction between human and Malaria disease Mosquito population. We applied an optimal control strategy (single intervention) to the Malaria model.We derived the basic properties of the model, including the basic reproduction number. We applied an optimal control method in order to find the best strategy to combat the disease. Numerical simulations are further carried out to establish and extend our analytical results.

Keywords: *Optimal control*, Computational simulations, Disease Free Equilibrium, Infected Immigrants, Pontryagin's Maximum Principle, single intervention strategy, stability theory.

1 Introduction

The incidence of malaria has been growing recently due to increasing parasite drug-resistance and mosquito insecticide-resistance[4]. Therefore, we find it useful and important to study and understand the important parameters in the dynamics of transmission of the disease in order to help in the effective control strategies. Malaria is an infectious disease caused by a parasite that is transmitted by the bite of a female Anopheles mosquito.Malaria is one of the world's most prevalent vector-borne disease. Despite decades of global eradication and control efforts, the disease is re-emerging in areas where control efforts were once effective and emerging in areas thought free of the disease[32,17,25,15,26].As reported in World Health Organisation(WHO) fact sheet(2009),malaria a life threatening disease caused by parasites that are transmitted to people through the bites of infected mosquitoes, which resulted in the death of a child from malaria every $30secs$[16]. An estimated 40percent of the world's population live in malaria endemic

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areas. The disease kills about 1 to 3million people a year, 75percent of whom are African children.

Mathematical models for transmission dynamics of malaria are useful in providing a better knowledge of the disease, to plan for the future and consider appropriate control measures. Models have played great roles in the development of the epidemiology of the disease. The study on malaria using mathematical modeling originated from the works of Ross [21]. According to Ross, if the mosquito population can be reduced to below a certain threshold then malaria can be eradicated. MacDonald did some modification to the model and included superinfection [15,13]. He showed that reducing the number of mosquitoes have little effect on epidemiology of malaria in areas of intense transmission. Dietz et al [1,13] added two classes of humans in their mathematical model, namely those with low recovery rate (more infections, greater susceptibility) and high recovery rate (less infections, less susceptibility). Compartmental models of malaria and differential equations are constructed to model the disease [31,8,5,9,13,20].[1] compare two mathematical models of transmission for P.vivax and P.falciparum parasites their work suggested that artemisinin-based combination therapy combined with a hypnozoite killing drug, would eliminate both species. Nevertheless, P.vivax 's ability to relapse accelerated the acquisition of presenile clinical immunity. This parasite transmission persisted in areas of low mosquito abundance and was robust to drug administration initiatives due to relapse.Nevertheless, P.vivax was less lethal than P.falciparum.

Optimal control theory is a powerful mathematical tool that can be used to make decisions involving complex biological situations[26].It is another area of mathematics that is used extensively in controlling the spread of infectious diseases. It is often used in the control of the spread of most diseases for which either vaccine or treatment is available[42].[16] applied optimal control theory to a set of epidemiological model in their attempt to find the most effective control strategy to minimize the number of individuals who become infected in the course of an epidemic using both treatment and vaccination as control measures.[20] used optimal control theory to determine the optimal treatment strategy for the administration of antiretroviral drug(Reverse Transcriptase Inhibitors) in HIV positive individuals. Blayneh et al [4], used a time dependent model to study the effects of prevention and treatment on malaria, similarly [33] 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.[27] applied an optimal strategies for disease control using Pontryagin's Maximum Principle(PMP). They derived and analyzed a mathematical model that describes the dynamics of malaria infection with the recruitment of infected immigrants, treatment of infectives and spray of insecticides against mosquitoes in the population.[34] applied optimal control theory to a simple SI malaria model with non-linear incidence rate. They derived basic properties of the model, including the epidemic threshold. Their model is found to show transcritical bifurcation and they conclude from their study that an optimal controlled treatment strategy would ensure significant reduction in malaria incidence if fully adhered to.

Our goal is to develop mathematical model for human-mosquito interactions with single control strategy, with the aim of investigating the role of chemoprophylaxis in order to determine optimal control strategies with the control measure for controlling the spread of malaria transmission.In this paper, we present a malaria transmission model

formulation in section 2, where the general mathematical framework, notations and model equations including the $S_hI_hR_hS_h + S_vI_v$ model were analyzed and the basic reproduction number were derived. In Section 3, we state the control problem as well as the objective functional to be minimized, we then apply the Pontryagins Maximum Principle to find the necessary conditions for the optimal control. In Sections 4, we show the simulation results to illustrate the population dynamics with chemoprophylaxis measures as control while in section 5 we conclude.

2 Model formulation

We consider a standard $S_hI_hR_hS_h + S_vI_v$ with bilinear incidence and variable total human population. Suppose S_h represents the number of susceptible humans, I_h represents the number of individual who are infected and infectious, and R_h represents the number of individuals who recovered from the malaria disease for a while. The model subdivides the total vector population at time t denoted by $N_v(t)$, into susceptible vector $(S_v(t))$, Infected vectors $(I_v(t))$, so that

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

Similarly, the total human population at time t, denoted by $N_h(t)$ is subdivided into Susceptible humans $(S_h(t))$, Exposed humans E_h, Infected humans $(I_h(t))$, Recovered humans $(R_h(t))$. Therefore,

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

. The population of susceptible humans is generated by intrinsic growth rate of humans (at a per capita rate b_hN_h) and the recovered human losses their immunity due to wanning effect of the chemo-prophylaxis. It is reduced by infection, following contacts with infected vectors (at a rate $\frac{\alpha_1 S_h I_v}{N_v}$) where α_1 is the product of the transmission probability per bite and the biting rate of mosquitoes and the contact rate of vector per human per unit time, while M is the carrying capacity for human.It is further reduced by the effort of the control(chemo-prophylaxis). Thus,

$$\frac{dS_h}{dt} = b_hN_h - \frac{\alpha_1 S_h I_v}{N_v} + qu_1R_h - u_1S_h - \frac{b_hS_hN_h}{M}$$

The population of Infected humans is given by

$$\frac{dI_h}{dt} = \frac{\alpha_1 S_h I_v}{N_v} - \gamma I_h - \rho I_h - \frac{b_hI_hN_h}{M}$$

where γ is the per capita rate of recovery of the hosts.
The population of recovered human is generated following a human spontaneous recovery(at a rate γ) and decreased by loss of immunity(at a rate γ). The population of recovered humans is given by

$$\frac{dR_h}{dt} = u_1S_h - qu_1R_h + \gamma I_h - \frac{b_hR_hN_h}{M}$$

The population of susceptible vector is generated by birth (recruitment) of humans (at a per capita rate b_v,). It is reduced by Infection, following number of bites of a Susceptible vector on Infected human per unit time($\frac{\alpha_2 S_v I_h}{N_h}$) and also reduced by natural death at (a rate d_v).

$$\frac{dS_v}{dt} = b_v - \frac{\alpha_2 S_v I_h}{N_h} - d_v S_v$$

Hence, the population of Infected vector is given by

$$\frac{dI_v}{dt} = \frac{\alpha_2 S_v I_h}{N_h} - d_v I_v$$

The model equation is given below;

$$\begin{array}{rcl} \frac{dS_h}{dt} & = & b_h N_h - \frac{\alpha_1 S_h I_v}{N_v} + q u_1 R_h - u_1 S_h - \frac{b_h S_h N_h}{M} \\ \frac{dI_h}{dt} & = & \frac{\alpha_1 S_h I_v}{N_v} - \gamma I_h - \rho I_h - \frac{b_h I_h N_h}{M} \\ \frac{dR_h}{dt} & = & u_1 S_h - q u_1 R_h + \gamma I_h - \frac{b_h R_h N_h}{M} \\ \frac{dS_v}{dt} & = & b_v - \frac{\alpha_2 S_v I_h}{N_h} - d_v S_v \\ \frac{dI_v}{dt} & = & \frac{\alpha_2 S_v I_h}{N_h} - d_v I_v. \end{array} \quad (1)$$

subject to the initial conditions

$$S_h(0) = S_{h,0},\ I_h(0) = I_{h,0},\ R_h(0) = R_{h,0},\ S_v(0) = S_{v,0},\ I_v(0) = I_{v,0}.$$

which together with $N_h = S_h + I_h + R_h$ and $N_v = S_v + I_v$ imply
$\frac{dN_h}{dt} = b_h N_h(1 - \frac{N_h}{M}) - \rho I_h$
$\frac{dN_v}{dt} = b_v - d_v N_v$

Table 2.1 State Variables of the Malaria Model

Symbol	Descriptions
$S_h(t)$	Number of Susceptible humans at time t
$I_h(t)$	Number of Infected humans at time t
$R_h(t)$	Number of Recovered humans at time t
$S_v(t)$	Number of Susceptible vector at time t
$I_v(t)$	Number of Infected vector at time t.

2.1 Basic Properties of the Malaria Model with Single Intervention

Positivity and Boundedness of the Solutions
We realized that for our malaria transmission model with control variable to be epidemiologically meaningful. It is very important to prove that all its state variable are non-negative at time t. That is, the solution of the model system (1) with non-negative initial data will remain non-negative at all time $t > 0$. The system of equation $S_h I_h R_h + S_v I_v$ malaria model will be analyzed in a biologically feasible region. This region should be feasible for both humans and mosquito population. Hence, we have

Theorem 1. If the initial data $S_h \geq 0$, $I_h \geq 0$, $R_h \geq 0$, $S_v \geq 0$ and $I_v \geq 0$, then the

solution $(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t))$ of the malaria control model (1) are non-negative for all $t > 0$. Therefore,

$$\lim_{t\to \inf} \sup N_h(t) \leq M, \quad \lim_{t\to\infty} \sup N_v(t) \leq \frac{b_v}{dv}$$

and $N_v = S_v + I_v, \;\; N_h = S_h + I_h + R_h$.

Proof. We let $\theta_1 = \sup\{t > 0 : S_h(t) > 0, I_h(t) > 0, R_h(t) > 0, S_v(t) > 0, I_v(t) > 0\}$. The variables $S_h(0) > 0, I_h(0) > 0, R_h(0) > 0, S_v(0) > 0$ and $I_v(0) > 0$ then, $\theta_1 > 0$. If $\theta_1 < \infty$, then S_h, I_h, R_h, S_v, I_v is equal to zero at θ_1 following from the first equation of the model equation (1) that

$$\frac{dS_h}{dt} = b_h N_h - \frac{\alpha_1 S_h I_v}{N_v} + q u_1 R_h - u_1 S_h - \frac{b_h S_h N_h}{M}.$$

Therefore,

$$\frac{d}{dt}\{S_h(t) \exp\,[(\frac{\alpha_1 I_v}{N_v} + u_1 + \frac{b_h N_h}{M})t]\} = (b_h N_h + q u_1 R_h) \exp\,[(\frac{\alpha_1 I_v}{N_v} + u_1 + \frac{b_h N_h}{M})t].$$

Hence

$$S_h(t) \exp\,[(\frac{\alpha_1 I_v}{N_v} + u_1 + \frac{b_h N_h}{M})t] - S_h(0) = \int_0^{\theta_1} (b_h N_h + q u_1 R_h) \exp\,[(\frac{\alpha_1 I_v}{N_v} + u_1 + \frac{b_h N_h}{M})]dP$$

then

$$\begin{aligned} S_h(\theta_1) \;\; = \;\; & S_h(0) \exp\,[-(\frac{\alpha_1 I_v}{N_v} + u_1 + \frac{b_h N_h}{M})\theta_1] + \exp\,[-(\frac{\alpha_1 I_v}{N_v} + u_1 + \frac{b_h N_h}{M})\theta_1] \\ & \times \int_0^{\theta_1} (b_h N_h + q u_1 R_h) \exp\,[(\frac{\alpha_1 I_v}{N_v} + u_1 + \frac{b_h N_h}{M})P]dp > 0 \end{aligned}$$

and

$$I_v(\theta_1) = I_v(0) \exp[-d_v t] + \exp[-d_v t] \times \int_0^{\theta_1} \frac{\alpha_2 I_h S_v}{N_h} \exp[d_v] P dP > 0.$$

We can as well show this similarly for $I_h > 0$, $R_h > 0$ and $S_V > 0$ for all $t > 0$. For the other part of the proof, it should be noted that $0 \leq I_h(t) \leq N_h(t)$ and $0 \leq I_v(t) \leq N_v(t)$. Adding the first three equations of the model and we have

$$\frac{dN_h}{dt} = b_h N_h (1 - \frac{N_h}{M}) - \rho I_h.$$

Adding the last two equation of the model equation (1) we have

$$\frac{dN_v}{dt} = b_v - d_v N_v.$$

Therefore

$$b_h N_h (1 - \frac{N_h}{M}) - \rho N_h \leq \frac{dN_h}{dt} \leq b_h N_h (1 - \frac{N_h}{M})$$

$$b_v - d_v N_v \leq \frac{dN_v}{dt} \leq b_v - d_v N_v.$$

Hence

$$M - \frac{\rho}{b_h} \leq \lim_{t\to\infty} \inf N_h(t) \leq \lim_{t\to\infty} \sup N_h(t) \leq M$$

and

$$\frac{b_v}{d_v} \leq \lim t \to \infty \inf N_v(t) \leq \lim_{t\to\infty} \sup N_h(t) \leq \frac{b_v}{d_v}$$

Just as we need.

2.2 The Invariant Region

We analyzed the model equation (1) in a biological feasible region. We divided the system equation (1) into two parts such that: the human population; $N_h = S_h + I_h + R_h$ and the mosquito population $N_v = S_v + I_v$. We therefore consider the feasible region.
$\Omega = \Omega_h \cup \Omega_v \subset \mathbb{R}^3_+ \times \mathbb{R}^2_+$
$\Omega_h = \{(S_h, I_h, R_h) \in \mathbb{R}^2_+ : S_h + I_h + R_h \leq M\}$
$\Omega_v = \{(S_v, I_v) \in \mathbb{R}^2_+ : S_v + I_v \leq \frac{b_v}{d_v}\}$.
We established the positive invariance of Ω following the steps below:
The rate of change of humans and mosquitos population is given in equation (2) above. It follows that

$$\frac{dN_h}{dt} \leq b_h N_h(1 - \frac{N_h}{M})$$

$$\frac{dN_v}{dt} \leq b_v - d_v N_v.$$

We follow the standard comparison theorem to show that

$$N_h(t) \leq \frac{MN_h(0)}{N_h(0) + (M - N_h(0))e^{-tb_h}} \text{ and } N_v(t) \leq N_v(0)e^{-d_v t} + \frac{b_v}{d_v}(1 - e^{-d_v t}).$$

In particular

$$N_h(t) \leq \frac{M}{1 + (u-1)e^{-tb_h}} \text{ and } N_v(t) \leq \frac{b_v}{d_v}$$

whenever $N_h(0) \leq 1$ and $N_v(0) \leq 1$ respectively.
Therefore, the region Ω is positively invariant wherefore it is sufficient to consider the dynamics of the flow generated by (1) in Ω. In this region, the model can be taken to be epidemiologically and mathematically well posed. Therefore, every solution of the model equation (1) with initial condition in Ω remains in Ω for all $t > 0$.
Theorem 2. The region $\Omega = \Omega_h \cup \Omega_v \subset \mathbb{R}^3_+ \times \mathbb{R}^2_+$ is positively invariant for the model with single intervention (vaccination) (1) with non-negative initial condition in $\mathbb{R}^5_+$.

2.3 The Reproductive number

In this section, we determine the threshold parameter that govern the spread of the disease which is the effective reproduction number. We try to explore the local stability of E_0 first by using the next generation matrix. The next generation method is used to find the effective reproduction number. Mathematically, it is the spectral radius of the next generation matrix. Using the notation F as the non-negative matrix of new Infection

terms and the M-matrix, V of the transition associated with our model (1) are given respectively by

$$F = \begin{pmatrix} 0 & \frac{\alpha_2 S_v^*}{N_h} \\ \frac{\alpha_1 S_h^*}{N_v} & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \gamma + \rho + \frac{b_h N_h}{M} & 0 \\ 0 & d_v \end{pmatrix}$$

It follows that the effective equilibrium Reproduction number of the model (1) with single intervention (vaccination) denoted by R_{eff} is given by

$$R_{eff} = \rho(FV^{-1})$$

where ρ denotes the spectral radius or the dominant eigenvalues.
Hence, the positive dominant eigenvalues of the matrix FV^{-1} is given by
$R_0^2 = \frac{\alpha_1\alpha_2 b_v b_h N_h M^3\gamma - \alpha_1\alpha_2 b_v b_h N_h q u_1 M^3 - \alpha_1\alpha_2 b_v b_h^2 N_h M^2}{(N_v^3 N_h d_v M\gamma + N_v^3 N_h M\rho d_v + N_v^3 N_h^2 d_v b_h)(b_h N_h\gamma M - b_h N_h q u_1 M - N_h^2 b_h^2 + u_1 M^2\gamma - u_1 M b_h N_h)}$
The Reproduction number R_0 is solved by using system equation (1)

2.4 Non-dimensionalization of the system

For convenience we rewrite these equation in terms of proportion of the individual class by defining $s_h = \frac{S_h}{N_h}$, $i_h = \frac{I_h}{N_h}$, $r_h = \frac{R_h}{N_h}$, $s_v = \frac{S_v}{N_v}$, $i_v = \frac{I_v}{N_v}$ as the proportion for the classes S_h, I_h, R_h, S_v, and I_v and let $m = \frac{N_v}{N_h}$ be the female mosquito-human population ration defined as the number of female mosquito per human host.Note that the ratio m is taken as a constant because a mosquito vector takes a fixed number of blood meals per unit time independent of the population density of the host[25]. By differentiating with respect to time t,it is easy to verify that s_h, i_h, r_h, s_v, i_v and N_h satisfy the system of differential equations.
The model equation is now;

$$\begin{array}{rcl} \frac{ds_h}{dt} & = & b_h s_h - \rho i_h - b_h + \alpha_1 s_h i_v - q u_1 r_h + u_1 s_h \\ \frac{di_h}{dt} & = & b_h i_h - \rho i_h^2 - \alpha_1 s_h i_v + \gamma i_h + \rho i_h \\ \frac{dr_h}{dt} & = & b_h r_h - \rho r_h i_h - u_1 s_h + q u_1 r_h - \gamma i_h \\ \frac{ds_v}{dt} & = & \frac{b_v s_v}{N_v} - \frac{b_v}{N_v} + \alpha_2 s_v i_h \\ \frac{di_v}{dt} & = & \frac{b_v s_v}{N_v} - \alpha_2 s_v i_h. \end{array} \tag{2}$$

$s_h + i_h + r_h = 1$, $s_v + i_v = 1$ $\frac{dN_v}{dt} = b_v - d_v N_v$
We observe that the system(2) involves the total human population size N_h in the proportion for the human population. We now reduce system (2) to a four dimensional system by eliminating s_h and s_v. Since $r_h = 1 - s_h - i_h$ and $s_v = 1 - i_v$ respectively.

$$\begin{array}{rcl} \frac{ds_h}{dt} & = & (b_h + \alpha_1 i_v + q u_1 + u_1) s_h + (q u_1 - \rho) i_h - b_h - q u_1 \\ \frac{di_h}{dt} & = & (b_h - \rho i_h + \gamma + \rho) i_h - \alpha_1 s_h i_v \\ \frac{di_v}{dt} & = & \frac{b_v s_v}{N_v} - \alpha_2 i_v i_h \\ \frac{dN_v}{dt} & = & (\frac{b_v}{N_v} - d_v) N_v. \end{array} \tag{3}$$

where $\Omega = \{(s_h, i_h, i_v, N_v) \in \mathbb{R}_+^4 : 0 \le s_h, 0 \le i_h, s_h + i_h \le 1, 0 \le i_v \le 1, N_v \le \frac{b_v}{d_v}\}$ From system (3), we notice that the third equation depend on the total mosquito population,N_v.

So substituting for $\frac{b_v}{N_v} = d_v$ into the third equation of the system gives the following system :

$$\begin{aligned} \frac{ds_h}{dt} &= (b_h + \alpha_1 i_v + qu_1 + u_1)s_h + (qu_1 - \rho)i_h - b_h - qu_1 \\ \frac{di_h}{dt} &= b_h i_h - \rho i_h^2 - \alpha_1 s_h i_v + \gamma i_h + \rho i_h \\ \frac{di_v}{dt} &= i_v d_v - \alpha_2 i_h + \alpha_2 i_v i_h. \end{aligned} \tag{4}$$

It can be verified that the region
$V = \{(s_h, i_h, i_v) \in \mathbb{R}^3_+ : 0 \leq s_h, 0 \leq i_h, s_h + i_h \leq 1, 0 \leq i_v \leq 1\}$ is positively invariant with respect to system(4), where $\mathbb{R}^3_+$ denotes the non-negative cone of $\mathbb{R}^3_+$ including its lower dimensional face. We represent the boundary and the interior of V by ∂V and $\dot{V}$ respectively. Hence, the system (4) is bounded.
To compute the steady states of the system (4) we set the derivatives with respect to time in system (4) equal to zero and then on simplification, the following algebraic expressions are obtained
$s_h = \frac{(b_h+qu_1-qu_1i_h+\rho i_h)(d_v+\alpha_2 i_h)}{b_h(d_v+\alpha_2 i_h)+\alpha_1\alpha_2 i_h+qu_1(d_v+\alpha_2 i_h)+u_1(d_v+\alpha_2 i_h)}$
$i_h = \frac{\alpha_1\alpha_2 i_h s_h - b_h(d_v+\alpha_2 i_h)}{(d_v+\alpha_2 i_h)(b_h-\rho i_h+\gamma+\rho)}$
$i_v = \frac{\alpha_2 i_h}{d_v+\alpha_2 i_h}$
We now obtain the disease-free equilibrium point given by $P_0 = (1, 0, 0)$ and the endemic equilibrium point P_1, with the co-ordinates
$s_h = \frac{(b_h+qu_1-qu_1i_h+\rho i_h)(d_v+\alpha_2 i_h)}{b_h(d_v+\alpha_2 i_h)+\alpha_1\alpha_2 i_h+qu_1(d_v+\alpha_2 i_h)+u_1(d_v+\alpha_2 i_h)}$
$i_h = \frac{\alpha_1\alpha_2 i_h s_h - b_h(d_v+\alpha_2 i_h)}{(d_v+\alpha_2 i_h)(b_h-\rho i_h+\gamma+\rho)}$
$i_v = \frac{\alpha_2 i_h}{d_v+\alpha_2 i_h}$

3 Analysis of Optimal Control Techniques applied to the model under consideration

The control $0 \leq u_1 \leq 1$ is the use of chemo-prophylaxis. This control is bounded and our model equation is given below

$$\begin{aligned} \frac{ds_h}{dt} &= (b_h + \alpha_1 i_v + qu_1 + u_1)s_h + (qu_1 - \rho)i_h - b_h - qu_1 \\ \frac{di_h}{dt} &= b_h i_h - \rho i_h^2 - \alpha_1 s_h i_v + \gamma i_h + \rho i_h \\ \frac{di_v}{dt} &= i_v d_v - \alpha_2 i_h + \alpha_2 i_v i_h. \end{aligned} \tag{5}$$

Our goal is to minimize the total number of infective individuals and the cost associated with the use of chemoprophylaxis on $[0, T]$.Now we define the objective functional as

$$J(u_1) = \int_0^T (Ai_h + \frac{u_1^2}{2})\, dt$$

subject to the system of equation (4) with appropriate state initial condition while the Lebesgue measurable control set $\mathcal{U}$ is defined as

$$\mathcal{U} = \{(u_1(t)|0 \leq u_1 \leq 1, t \in [0, T])\} \tag{6}$$

where $u_1(t)$ is a measurable function such that: $0 \leq u_1 \leq 1, t \in [0, T]$. A is a weight parameter which describes the comparative importance of the two terms in the functional.

We consider a quadratic cost on the control, which is the simplest and widest used nonlinear representation of vaccination cost (Asano et.al;Math Biosci Engr 5 (2008), Jung et. al; Disc. Cont. Dyn. Syst. B, 2(2002), Jung et. al; J.Theor. Biol;260(2009)).The quadratic term is particularly chosen to describe the nonlinear behaviour of the cost of implementing the chemoprophylaxis.

3.1 The Optimal Control Problem

We are seeking $0 \leq u_1 \leq 1$, for $t \in [0, T]$, to minimize

$$J(u_1) = \int_0^T (Ai_h + \frac{u_1^2}{2})\, dt$$

subject to the system of equation (4)

$$\begin{array}{rcl} \frac{ds_h}{dt} & = & (b_h + \alpha_1 i_v + qu_1 + u_1)s_h + (qu_1 - \rho)i_h - b_h - qu_1 \\ \frac{di_h}{dt} & = & b_h i_h - \rho i_h^2 - \alpha_1 s_h i_v + \gamma i_h + \rho i_h \\ \frac{di_v}{dt} & = & i_v d_v - \alpha_2 i_h + \alpha_2 i_v i_h. \end{array} \tag{7}$$

and $s_h(0) \geq 0$, $i_h(0) \geq 0$, $i_v(0) \geq 0$, $N_h(0) = 0$, $s_h + i_h(0) \geq 1$, $0 \leq i_v(0) \geq 1$

3.2 Existence and Uniqueness of the control

Theorem 6.: Suppose the objective functional $J(u_1) = \min\{J(u_1) = \int_0^T (Ai_h + \frac{u_1^2}{2})\, dt$ where $u = \{u_1 : u_i \; measurable \;\; 0 \leq u_1(t) \leq 1, t \in [t_0, T] \in \mathbb{R}^+ \;\; for \;\; i = 1, 2...\}$ subject to the dynamic constraints of system equations (2) and (3) with $s_h(0) = S_{h0}$, $i_h(0) = i_{h0}$ and $i_v(0) = i_{v0}$, then there exists an optimal control $u^* = (u_1^*)$ such that $\min_{u_1 \in u} J(u_1) = J(u_1^*)$ Subject to the control system (4) with the initial conditions

Proof.:

To prove the existence of an optimal control pair we use the result in [16] and [Fleming and Rishel (1975)].The control and the state variables are non-negative values and are non-empty. In the minimization problem, the necessary convexity of the objective functional in u_1 is satisfied. The control variable $u_1 \in U$ is also convex and closed by definition. The optimal system is bounded which determines compactness needed for the existence of the optimal control. Furthermore, the integrand in the objective functional which is $(A\frac{u_1^2}{2})$ is convex on the control set U. There exists constants $b_1, \; b_2 \; > 0$ and $\beta > 1$ such that the integrand of the objective functional J is convex and satisfies $J(u_1, u_2) \geq b_1(|\frac{u_1^2}{2}|^2)^{\frac{\beta}{2}} - b_2$. By standard control arguments involving the bounds on the control, we conclude

$$u_1^* = \begin{cases} 0 \; if \; \eta_1^* \leq 0, \\ \\ \eta_1^* \; if \; 0 < \eta_1^* < 1, \\ \\ 1 \; if \; \eta_1^* \geq 1 \end{cases} \tag{8}$$

where

$$\eta_1^* = \lambda_1(q+1)s_h - q$$

By the apriori boundedness of the state system, adjoint system and the resulting Lipschitz structure of the ODEs, we obtain the uniqueness of the optimal control for small T.The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consist of (6), (7) and (8) with characterization (9) and (10). We impose a bound on the length of time interval in order to guarantee the uniqueness of the optimality system. The smallness restriction of the length on the state problem has initial values and the adjoint problem has final values. This restriction is very common in control problems(See Josh,2002;Lenhart and Workman, 2007; Lenhart and Yong, 1997).

3.3 Necessary conditions of the control

Theorem 7.: Given an optimal control u_1^* and a solution $X^*(t) = (s_h^*(t), i_h^*(t), i_v^*(t))$ of the corresponding state system (4) there exist adjoint variables $\lambda_1(t), \lambda_2(t)$ *and* $\lambda_3(t)$ which satisfies the following:
We first derive the Hamiltonian which is given by
$H = Ai_h + \frac{u_1^2}{2} + \lambda_1((b_h + \alpha_1 i_v + qu_1 + u_1)s_h + (qu_1 - \rho)i_h - b_h - qu_1) + \lambda_2(b_h i_h - \rho i_h^2 - \alpha_1 s_h i_v + \gamma i_h + \rho i_h) + \lambda_3(i_v d_v - \alpha_2 i_h + \alpha_2 i_v i_h)$

$$\lambda_1^{'} = -\frac{\partial H}{\partial S} = -[\lambda_1(b_h + \alpha_1 i_v + qu_1 + u_1) + \lambda_2(-\alpha_1 i_v)]$$

$$\lambda_2^{'} = -\frac{\partial H}{\partial I} = -[A + \lambda_1(qu_1 - \rho) + \lambda_2(b_h - \rho i_h + \gamma + \rho) + \lambda_3(-\alpha_2 - \alpha_2 i_v)]$$

$$\lambda_3^{'} = -\frac{\partial H}{\partial N} = -[\lambda_1(\alpha_1 s_h) + \lambda_2(-\alpha_1 s_h) + \lambda_3(d_v + \alpha_2 i_h)]$$

with the final conditions

$$\lambda_1(T) = \lambda_2(T) = \lambda_3(T) = 0$$

We differentiate the Hamiltonian with respect to u_1 in the interior of $\mathcal{U}$ to obtain the optimality condition as follows:we find the optimal control u_1^* such that

$$u_1^* = \min\{\max(0, q - \lambda_1(q+1)s_h, 1\}$$

Proof.
We form the Hamiltonian H given by
$H = Ai_h + \frac{u_1^2}{2} + \lambda_1((b_h + \alpha_1 i_v + qu_1 + u_1)s_h + (qu_1 - \rho)i_h - b_h - qu_1) + \lambda_2(b_h i_h - \rho i_h^2 - \alpha_1 s_h i_v + \gamma i_h + \rho i_h) + \lambda_3(i_v d_v - \alpha_2 i_h + \alpha_2 i_v i_h)$
By Pontryagin's Maximum Principle we derive

$$\lambda_1^{'} = -\frac{\partial H}{\partial S} = -[\lambda_1(b_h + \alpha_1 i_v + qu_1 + u_1) + \lambda_2(-\alpha_1 i_v)]$$

$$\lambda_2^{'} = -\frac{\partial H}{\partial I} = -[A + \lambda_1(qu_1 - \rho) + \lambda_2(b_h - \rho i_h + \gamma + \rho) + \lambda_3(-\alpha_2 - \alpha_2 i_v)]$$

$$\lambda_3^{'} = -\frac{\partial H}{\partial N} = -[\lambda_1(\alpha_1 s_h) + \lambda_2(-\alpha_1 s_h) + \lambda_3(d_v + \alpha_2 i_h)]$$

and the transversality conditions

$$\lambda_1(T) = \lambda_2(T) = \lambda_3(T) = 0$$

We differentiate the Hamiltonian with respect to u_1 in the interior of $\mathcal{U}$ we obtain the optimality condition that follows

$$\frac{\partial H}{\partial u_1} = u_1 + \lambda_1(q+1)s_h - q = 0$$

From this equation, we get the optimal control (u_1^* as stated below

$$u_1^* = \min\{\max(0, q - \lambda_1(q+1)s_h, 1\} \tag{9}$$

We impose some bounds on the control: $0 \leq u_1 \leq 1$ to yield (5) as needed.

3.4 Optimality System

Therefore, our resulting optimality system is given by:
State equations:

$$\begin{array}{rcl} \frac{ds_h}{dt} & = & (b_h + \alpha_1 i_v + qu_1 + u_1)s_h + (qu_1 - \rho)i_h - b_h - qu_1 \\ \frac{di_h}{dt} & = & b_h i_h - \rho i_h^2 - \alpha_1 s_h i_v + \gamma i_h + \rho i_h \\ \frac{di_v}{dt} & = & i_v d_v - \alpha_2 i_h + \alpha_2 i_v i_h. \end{array} \tag{10}$$

and $s_h(0) \geq 0$, $i_h(0) \geq 0$, $i_v(0) \geq 0$, $N_h(0) = 0$, $s_h + i_h(0) \geq 1$, $0 \leq i_v(0) \geq 1$
Adjoint equations:

$$\acute{\lambda_1} = -[\lambda_1(b_h + \alpha_1 i_v + qu_1 + u_1) + \lambda_2(-\alpha_1 i_v)]$$

$$\acute{\lambda_2} = -[A + \lambda_1(qu_1 - \rho) + \lambda_2(b_h - \rho i_h + \gamma + \rho) + \lambda_3(-\alpha_2 - \alpha_2 i_v)]$$

$$\acute{\lambda_3} = -[\lambda_1(\alpha_1 s_h) + \lambda_2(-\alpha_1 s_h) + \lambda_3(d_v + \alpha_2 i_h)]$$

Transversality equations:

$$\lambda_1(T) = \lambda_2(T) = \lambda_3(T) = 0. \tag{11}$$

Characterization of the optimal control u_1^*:
$\frac{\partial H}{\partial u_1} = 0$ at $u_1 = u_1^*$, on the set $\{t \in [0,T] : 0 \leq u_1 \leq 1\}$. That is:

$$u_1^* = \begin{cases} 0 \ if \ \eta_1^* \leq 0, \\ \eta_1^* \ if \ 0 < \eta_1^* < 1, \\ 1 \ if \ \eta_1^* \geq 1 \end{cases} \tag{12}$$

4 Numerical Simulations Results and Discussions

Here, we study the numerical approximation of optimal transmission parameter control for the malaria control model. We obtained the optimal control by calculating the optimality system which consist of the state system, the adjoint, transversality equations and characterization of optimal control.We use the iterative scheme to calculate the optimality system. We investigate a deterministic model with logistic function and study the impact of chemoprophylaxis on the Malaria transmission.The numerical algorithm presented below is a forward-backward sweep method. We want to solve the problem numerically, that is devise an algorithm that generates an approximation to an optimal piecewise continuous control u^*. We break the time interval by discretizing the interval $[t_0, t_1]$ into pieces with specific points of interest $t_0 = b_1, b_2, ..., b_N, b_{N+1} = t_1$, those points are usually equally spaced.The approximation will be a vector $\overrightarrow{u} = (u_1, u_2, ..., u_{N+1})$, where $u_i \approx u(b_i)$. There are many numerical methods which can be used to solve initial value problems, we have Runge-Kutta or adaptive schemes, and boundary value problems such as shooting method. We could use any of these methods to solve the optimality system and the optimal control problem (if we establish the right existence and uniqueness result). We gave a step by step outline of the algorithm below: where $\overrightarrow{x} = \{s_h, i_h, i_v\}$ and $\overrightarrow{\lambda} = \{\lambda_1, \lambda_2, \lambda_3\}$ are the vector approximations for the state and adjoint functions.

1. We make an initial guess for $\overrightarrow{u}$ over the interval.

2. We use the initial value e.g $s_h = s_h(0) = a$ and the values for $\overrightarrow{u_1}$, solve $\overrightarrow{x} = \{s_h, i_h, i_v\}$, forward in time according to their differential equation in the optimization.

3. We use the transversality condition $\lambda_{M+1} = \lambda(t_1) = 0$ and we have the values for $\overrightarrow{u} = \{u_1\}$ and $\overrightarrow{x} = \{s_h, i_h, i_v\}$, solving $\overrightarrow{\lambda} = \{\lambda_1, \lambda_2, \lambda_3\}$ backward in time according to their differential equation in the optimality system.

4. We update u_1 by entering the new $\overrightarrow{x} = \{s_h, i_h, i_v\}$ and $\overrightarrow{\lambda} = \{\lambda_1, \lambda_2, \lambda_3\}$ values into the characterization of the optimal control.

5. We check convergence. If values of the variables in the iteration and the last iteration are close negligibly, we output the recent values as solutions but if values are not close, return to step 2.

The simulation which we carried out were carried out by using the following values: $q = 0.2$, $\rho = 0.05$, $\alpha_1 = 0.006$, $\alpha_2 = 0.027$, $b_h = 0.00011$,$d_2 = 0.04$, $\gamma = 0.00137$, $s_h(0) = 0.3$, $i_h(0) = 0.2$, $s_v(0) = 0.4$, $A = 0.9$. $u_1^* = q - \lambda_1(q+1)s_h$ Considering $0 \leq u_1 \leq 1$, u_1^* is given by

$$u_1^* = \min\{\max(0, q - \lambda_1(q+1)s_h), 1\}$$

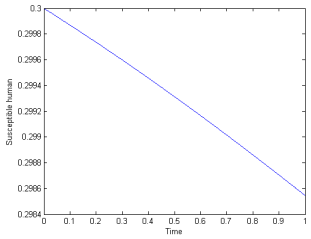
.

Parameter	Symbol	Value	Source
disease induced death rate	ρ	0.05	[34]
transmission rate of human	α_1	0.006	[15,16,35]
transmission rate of human	α_2	0.027	[13,33]
per capita birth rate of mosquitoes	b_v	0.071	[2,13]
Natural death rate of mosquitoes	d_2	0.04	[9]
efficacy of chemoprophylaxis	q	0.2	[assumed]
the carrying capacity of human	M	500000	[assumed]
rate of loss of immunity from humans	γ	0.00137	[2,13,32]
intrinsic growth rate of humans	b_h	0.00011	[41]

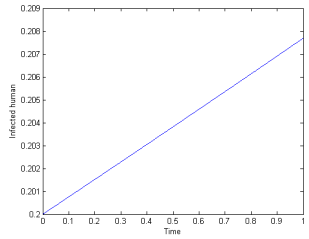
Table 1: Table showing numerical values of parameters used in the simulations.

4.1 Control with Chemoprophylaxis

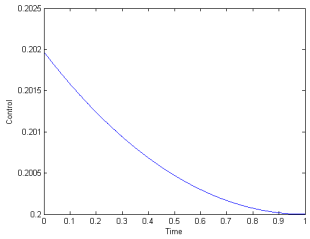
With this strategy, only the control(u_1) on chemoprophylaxis is used to optimize the objective function J. In fig. 1,fig. 2, and fig. 3 the result shows that applying chemoprophylaxis control does not appreciably bring down the number of infected individuals.We observe that applying the chemoprophylaxis as a control strategy reduce the susceptible to below certain threshold.Hence, the control u_1 reduces to a lower bound after 90days.In fig.8, fig.9 and fig.10,we observe that applying the chemoprophylaxis appreciably brings down the number of susceptible and does not appreciably bring down the number of infected individuals.



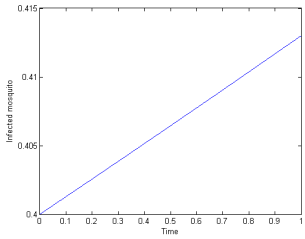
(a) fig. 1



(b) fig. 2

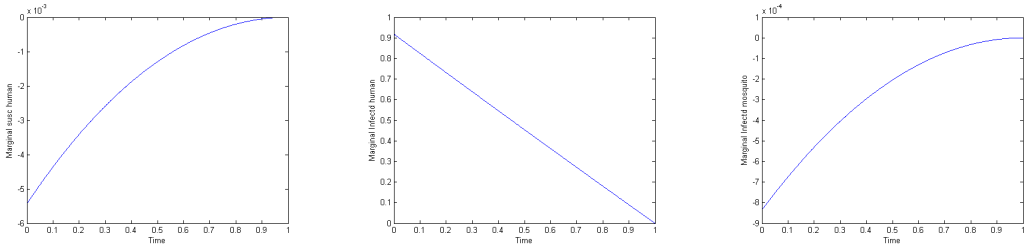


(c) fig. 3



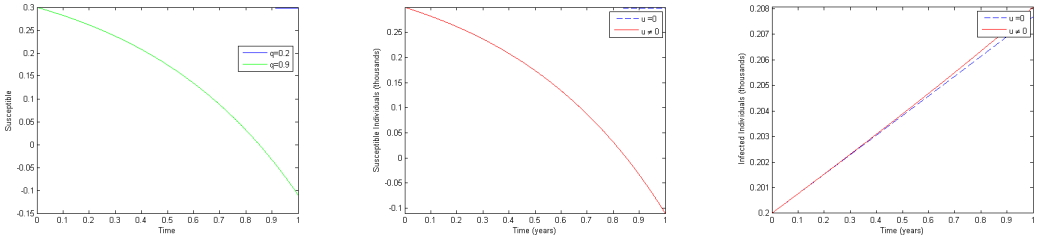
(d) fig. 4

Figure 1: Simulation showing the Optimal states and control



(a) fig. 5 (b) fig. 6 (c) fig. 7

Figure 2: Simulation showing the Marginal susceptible and infected human and Marginal infected Mosquitoes



(a) fig. 8 (b) fig. 9 (c) fig. 10

Figure 3: Simulations showing the efficacy of chemoprophylaxis only on susceptible and infected human

5 Conclusion

In this paper, we formulate and analyze a compartmental deterministic model for the transmission of malaria disease that with logistic function and chemoprophylaxis measures. We calculated the basic reproduction number and performed optimal control analysis of the model.In the course of applying the optimal control, we derived and analyzed the conditions for optimal control of the disease with preventive measures(chemoprophylaxis). From our numerical results, we found that prevention has a strong impact on the disease control. We therefore conclude that sufficient control measures which adhered to this control strategy (preventive) would be a very effective way for fighting the disease.

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