Analysis of Control Interventions against Malaria in communities with Limited Resources

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Abstract

The aim of this paper is to analyse the potential impact of multiple current interventions in communities with limited resources in order to obtain optimal control strategies and provide a basis for future predictions of the most effective control measures against the spread of malaria. We developed a population-based model of malaria transmission dynamics to investigate the effectiveness of five different interventions. The model captured both the human and the mosquito compartments. The control interventions considered were: educational campaigns to mobilise people for diagnostic test and treatment and to sleep under bed nets; treatment through mass drug administration; indoor residual spraying (IRS) with insecticide to reduce malaria transmission; insecticide treated net (ITN) to reduce morbidity; and regular destruction of mosquito breeding sites to reduce the number of new mosquito and bites/contact at dusks and dawn. Analysis of the potential impact of the multiple control interventions were carried out and the optimal control strategies that minimized the number of infected human and mosquito and the cost of applying the various control interventions were determined.

Key Words: Optimal control, Computational simulations, Disease Free Equilibrium, Pontryagin’s Maximum Principle, stability theory.

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1 Introduction

Mathematical modelling has been a very useful tool in the study and analysis of many infectious diseases because it is cheaper and effective in understanding the transmission dynamics of infectious diseases. It is also a useful tool in making the best decision on the type of control strategies to put in place in a particular defined geographical location [28, 30]. The optimal control theory has also been to optimise the coverage of many chosen control interventions in different infectious disease model. Pontryagin et al. [31] developed the theoretical foundation of optimal control models with underlying dynamics given by ordinary differential equations and this theory, its application areas, and corresponding numerical algorithm have steadily progressed. Applying Pontryagin’s Maximum Principle [31], its extension and appropriate numerical methods, can adjust the control in a model to achieve a goal Kang, Lenhart and Protopopescu [22].

There are several studies that have been carried out to quantify the impact of malaria infection in humans [3, 12, 15, 16, 20]. Several of these studies focuses only on the transmission of the disease in human and the vector populations. Aguas et al. [1] derived a malaria model with the assumption that acquired immunity in malaria is independent of exposure duration, different control measures and role of transmission rate on the disease prevalence were further examined. Brown [13] and Bryson et al. in [14] used mass action incidence to study malaria transmission model for different levels of acquired immunity and temperature dependent parameters, relating also to global warming and local socioeconomic conditions. Ariey et al. [6] proposed a model that account for acquired immunity in a mass action model. A deterministic model with two latent periods in the hosts and vector populations was formulated to assess the impact of personal protection, treatment and possible vaccination strategies on the transmission dynamics of malaria [4], and [5] considered treatment and spread of drug resistance in an endemic population. Li-Ming [15] developed a compartmental mathematical model for malaria transmission that includes incubation periods for both infected human hosts and mosquitoes was formulated and examined. Pontryagin et al. [31] applied optimal control theory to a continuous malaria model that includes treatment and vaccination with waning immunity to study the impact of a possible vaccination with treatment strategies in controlling the spread of malaria. Other areas of applications of optimal control theory can be found in [17, 27]. Agusto et al. [2] proposed and analyzed simple models for disease transmission that include immigration of infective individuals and variable population size. Yang [20] studied a mathematical model based on human host immunity, existence of acquired immunity and immunological memory, which boosts the protective
response upon reinfection; mosquito vector, and they incorporated an ambient temperature dependent extrinsic incubation period of parasites and average period of development from eg to adult mosquito. The equilibrium solutions were obtained and the reproduction number was calculated in terms of the model parameters. Makinde et al. in [26] derived and analyzed a malaria disease transmission mathematical model with inflow of infected immigrants parameter. They used this parameter also as control parameter, they studied and determine the possible impact of infected immigrants on the spread of malaria. Theoretically, they analyzed its stability properties and determine conditions on the parameters for the existence of equilibrium solutions. They also carried out detailed qualitative optimal control analysis of the resulting model and find the necessary conditions for optimal control of the disease using Pontryagin’s Maximum Principle in order to determine optimal strategies for controlling the spread of the disease [19]. There are also some recent studies that applied the theory of optimal control which includes [29, 33] or decision problems, e.g. [9, 23, 34, 35]. Potucek studied the life thread cycle and its various models in [32].

In this work, we developed a deterministic mathematical model that captures the dynamics of malaria epidemic in human-mosquito populations using a system of ordinary differential equations (ODEs) under some control interventions: educational campaign, insecticide-Treated Bed nets (ITNs), indoor residual spraying (IRS) with insecticides, regular destruction of mosquito breeding sites, and treatment with ACT drugs). The Pontryagin’s Maximum Principle is applied to establish the optimal strategies for malaria control. The aim here is to analyse the impact of current control interventions in community with limited resources in order to determine the best control strategies that will reduce the number of infected human and mosquito and the cost attached to the controls over time.

This paper is organized as follows; we present a malaria transmission model formulation in Section 2, the general mathematical framework, notations and model equations is developed. In Section 3, the basic properties of the model and its analysis were discussed. In Section 4, the control problem is presented 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 of the disease. In Section 5 we discuss the main conclusion and recommendations.
2 The Malaria Mathematical Model and its Biological Description

Here we describe a standard model of the type SEIRS (Susceptible-Exposed-Infected-Recovered-Susceptible) as earlier discussed in [7, 8] for the human compartment and SEI (Susceptible-Exposed-Infected) for the mosquito compartment in the presence of five different time dependent control intervention concurrently that is

1. the use of Insecticide treated bed nets (ITN) - \( u_1 \);
2. educational campaigns - \( u_2 \);
3. Indoor Residual spray (IRS) - \( u_3 \);
4. regular destruction of mosquito breeding sites to reduce the number of new mosquito and bites/contact at dusk and dawn - \( u_4 \) and;
5. treatment with ACT through mass drug administration- \( u_5 \).

The malaria model subdivides the total population of human, denoted by \( N_h \), into the following sub-classes of humans who are susceptible to infection with malaria (\( S_h \)), those exposed/latent to malaria parasite (\( E_h \)), humans with malaria symptoms (i.e. who are already infected and infective with malaria parasite) (\( I_h \)) and recovered humans (\( R_h \)), so that \( N_h = S_h + E_h + I_h + R_h \).

The total population of the female Anopheles mosquitoes, denoted \( N_v \), is given as a non-intersecting population of susceptible female Anopheles mosquitoes (\( S_v \)), female Anopheles mosquitoes exposed to the malaria parasite (\( E_v \)) and infectious female Anopheles mosquitoes (\( I_v \)). That is \( N_v = S_v + E_v + I_v \).

The dynamics of Susceptible humans population is developed through birth (at a constant per capita rate \( b_h \)), through the loss of immunity to the disease (at a constant per capita rate \( \gamma \)). It is reduced by natural death (at a rate \( d_h \)) and also by the rate of acquiring malaria through contact with infectious mosquitoes at a rate \((2 - u_1 - u_2)\beta_1 \varepsilon_h \phi\), where \( \beta_1 \) is the transmission probability per bite, \( \varepsilon_h \) is the per capita biting rate of mosquitoes, \( \phi \) is the contact rate of vector per human per unit time and \( u_1, u_2 \in [0, 1] \) are the control on the use of insecticide treated bed nets (ITN) and educational campaign.

The rate of change of the population of exposed humans is generated by \( \alpha \) which is the per capita rate of progression of humans from the exposed class to the infectious class. The infected human population is increased by the progression of human from the exposed state to the infectious state(at a per capita rate \( \alpha_h \)) and decreased by human spontaneous recovery(at a rate \( \theta \)). It is reduced by the disease induced death rate (at per capita rate \( \psi \)), by the natural death rate (at per capita rate \( d_h \)) and use of treatment with ACT through mass
drug administration\((u_5)\). The recovered human population is obtained following a human spontaneous recovery (at a rate \(\theta\)) and by treatment with ACT through mass drug administration (\(u_5\)) but decreased by loss of immunity (at a rate \(\gamma\)) and by natural death (at a rate \(d_h\)).

The dynamics of Susceptible mosquitoes are generated by the birth of mosquitoes (at a per capita rate of \(b_v\)). It is reduced by rate of acquiring malaria through contacts with infected humans at a rate \((2 - u_1 - u_2)\beta_2 \varepsilon_v \phi\), where \(\beta_2\) is probability for a vector to get infected by an infectious human. It is also reduced by natural death (at a rate \(d_v\)). It is decreased by the use of insecticides spray at a rate \(pu_3\), where \(u_3\) is the control on the use of indoor residual spray (IRS) and \(p\) is the efficacy of the indoor residual spray (IRS). It is also decreased by the use of regular destruction of mosquito breeding sites to reduce the number of new mosquito and bites/contact at dusks and dawn, at a rate \(qu_4\), where \(u_4\) is the control on the use of regular destruction of mosquito breeding sites to reduce the number of new mosquito and bites/contact at dusks and dawn. The rate of change of the exposed mosquitoes population is produced by the per capita rate \(\alpha_v\), which is the progression of mosquitoes from the exposed state to the infectious state. The population of infected mosquitoes is increased by the progression of mosquitoes from the exposed state to the infectious (at a per capita rate \(\alpha_v\)) and decreased by the natural death rate (at a rate \(d_v\)) and also reduced by the use of insecticides residual spray (IRS) and regular destruction of mosquito breeding sites to reduce the number of new mosquito and bites/contact at dusks and dawn (at a rate \(pu_3\) and \(qu_4\)) where \(p\) is the efficacy of the insecticides residual spray (IRS) and \(q\) is the efficacy of the regular destruction of mosquito breeding sites to reduce the number of new mosquito and bites/contact at dusks and dawn, \(u_3\) and \(u_4\) are the control on the use of insecticides residual spray (IRS) and regular destruction of mosquito breeding sites to reduce the number of new mosquito and bites/contact at dusks and dawn.

We obtained the malaria with control intervention model by bringing the above descriptions and assumptions together:

\[
\begin{align*}
\frac{dS_h}{dt} &= b_h + \gamma R_h - (2 - u_1 - u_2)\frac{\beta_1 \varepsilon_h \phi S_h I_v}{N_h} - d_h S_h \\
\frac{dE_h}{dt} &= (2 - u_1 - u_2)\frac{\beta_1 \varepsilon_h \phi S_h I_v}{N_h} - (\alpha_h + d_h)E_h \\
\frac{dI_h}{dt} &= \alpha_h E_h - (u_5 + \theta + \psi + d_h)I_h \\
\frac{dR_h}{dt} &= (u_5 + \theta)I_h - (\gamma + d_h)R_h \\
\frac{dS_v}{dt} &= b_v - (2 - u_1 - u_2)\frac{\beta_2 \varepsilon_v \phi S_v I_h}{N_h} - d_v S_v - (pu_3 + qu_4)S_v
\end{align*}
\]
\[
\frac{dE_v}{dt} = (2 - u_1 - u_2) \frac{\beta v \phi S_v I_h}{N_h} - (\alpha_v + d_v) E_v - (pu_3 + qu_4) E_v \\
\frac{dI_v}{dt} = \alpha_v E_v - d_v I_v - (pu_3 + qu_4) I_v, 
\]

subject to the initial conditions \(S_h(0) = S_{h,0}, \ E_h(0) = E_{h,0}, \ I_h(0) = I_{h,0}, \ R_h(0) = R_{h,0}, \ S_v(0) = S_{v,0}, \ E_v(0) = E_{v,0}, \ I_v(0) = I_{v,0}\). In addition, we rewrite the model equation (1) in the form below:

\[
\begin{align*}
\frac{dS_h}{dt} &= g_1(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\
\frac{dE_h}{dt} &= g_2(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\
\frac{dI_h}{dt} &= g_3(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\
\frac{dS_v}{dt} &= g_4(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\
\frac{dE_v}{dt} &= g_5(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\
\frac{dI_v}{dt} &= g_6(S_h, E_h, I_h, R_h, S_v, E_v, I_v), 
\end{align*}
\]

with \(N_h = N_{h,0} > 0\) and \(N_v(0) = N_{v,0} > 0\) for \(N_h = S_h, E_h, I_h, R_h\) and \(N_v = S_v, E_v, I_v\). The associated model parameters and variables are described in Tables 1. and 2. respectively.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S_h(t))</td>
<td>Susceptible Human Population</td>
</tr>
<tr>
<td>(E_h(t))</td>
<td>Exposed Human Population</td>
</tr>
<tr>
<td>(I_h(t))</td>
<td>Infected Human Population</td>
</tr>
<tr>
<td>(R_h(t))</td>
<td>Recovered Human Population</td>
</tr>
<tr>
<td>(S_v(t))</td>
<td>Susceptible Mosquito Population</td>
</tr>
<tr>
<td>(E_v(t))</td>
<td>Exposed Mosquito Population</td>
</tr>
<tr>
<td>(I_v(t))</td>
<td>Infected Mosquito Population</td>
</tr>
</tbody>
</table>

2.1 Description of the current malaria control interventions used in the model

According to WHO recommendation for all people at risk of malaria and those infected with malaria, the control interventions for control and elimination of malaria must be multiple interventions [37]. In this work, we present five different interventions to treat, prevent and reduce malaria transmission. The five different interventions introduced into our malaria model are vector control interventions which involve \(u_1-u_5\).
Table 2: Descriptions of malaria control model parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>disease induced death rate</td>
<td>$\psi$</td>
</tr>
<tr>
<td>probability of human getting infected</td>
<td>$\beta_1$</td>
</tr>
<tr>
<td>probability of mosquito getting infected</td>
<td>$\beta_2$</td>
</tr>
<tr>
<td>per capita birth rate of mosquitoes</td>
<td>$b_v$</td>
</tr>
<tr>
<td>Natural death rate of humans</td>
<td>$d_h$</td>
</tr>
<tr>
<td>progression of human from the exposed to the infectious state</td>
<td>$\alpha_h$</td>
</tr>
<tr>
<td>progression of mosquitoes from the exposed to the infectious state</td>
<td>$\alpha_v$</td>
</tr>
<tr>
<td>per capita biting rate of mosquitoes</td>
<td>$\varepsilon_v$</td>
</tr>
<tr>
<td>contact rate of vector per human per unit time</td>
<td>$\phi$</td>
</tr>
<tr>
<td>per capita biting rate of humans</td>
<td>$\varepsilon_h$</td>
</tr>
<tr>
<td>human spontaneous recovery</td>
<td>$\theta$</td>
</tr>
<tr>
<td>Natural death rate of mosquitoes</td>
<td>$d_v$</td>
</tr>
<tr>
<td>rate of loss of immunity from humans</td>
<td>$\gamma$</td>
</tr>
<tr>
<td>per capita birth rate of humans</td>
<td>$b_h$</td>
</tr>
</tbody>
</table>

Figure 1: Flow chart of Malaria model (1) from [8].

All these control interventions used are variable in time hence we applied the principle of optimal control theory to derive optimal control strategies that vary in time.
3 Basic mathematical properties of the Malaria Model with constant Control Interventions

The Malaria control intervention model (1) will be analyzed in a biologically feasible region for both human and mosquito populations. Hence, for it to be epidemiologically well posed, it is significant to prove that all its state variables are non-negative for all time $t > 0$. In this section, we obtained the existence and uniqueness of the solution to the model (1).

Proposition 3.1. Let the domain $\Delta = \{(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \in \mathbb{R}_+^7 : S_h \geq 0, E_h \geq 0, I_h \geq 0, R_h \geq 0, S_v \leq 0, E_v \geq 0, I_v \geq 0\}$ be positively invariant by the positive semi-wave produced by the system equation (1) with non-negative initial condition in $\mathbb{R}_+^7$.

Proof. We rewrite the model equation (1) in the following pattern:

$$\frac{d}{dt} \begin{pmatrix} S_h \\ E_h \\ I_h \\ R_h \\ S_v \\ E_v \\ I_v \end{pmatrix} = \begin{pmatrix} g_1(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ g_2(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ g_3(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ g_4(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ g_5(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ g_6(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ g_7(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \end{pmatrix} = G(S_h, E_h, I_h, R_h, S_v, E_v, I_v)$$

and from the model, we have:

\begin{align*}
&g_1(S_h = 0, E_h, I_h, R_h, S_v, E_v, I_v) = b_h + \gamma R_h \geq 0 \text{ for } E_h, I_h, R_h, S_v, E_v, I_v \geq 0, \\
g_2(S_h, E_h = 0, I_h, R_h, S_v, E_v, I_v) = (2-u_1-u_2) \frac{\beta h S_v E_v}{N_h} \geq 0 \text{ for } E_h, I_h, R_h, S_v, E_v, I_v \geq 0, \\
g_3(S_h, E_h, I_h = 0, R_h, S_v, E_v, I_v) = \alpha_h E_h \geq 0 \text{ for } E_h, I_h, R_h, S_v, E_v, I_v \geq 0, \\
g_4(S_h, E_h, I_h, R_h = 0, S_v, E_v, I_v) = u_5 + \theta I_h \geq 0 \text{ for } E_h, I_h, R_h, S_v, E_v, I_v \geq 0, \\
g_5(S_h, E_h, I_h, R_h, S_v = 0, E_v, I_v) = b_v \geq 0 \text{ for } E_h, I_h, R_h, S_v, E_v, I_v \geq 0, \\
g_6(S_h, E_h, I_h, R_h, S_v, E_v = 0, I_v) = (2-u_1-u_2) \frac{\beta h S_v E_v}{N_h} \geq 0 \text{ for } E_h, I_h, R_h, S_v, E_v, I_v \geq 0, \\
g_7(S_h, E_h, I_h, R_h, S_v, E_v, I_v = 0) = \alpha_v E_v \geq 0 \text{ for } E_h, I_h, R_h, S_v, E_v, I_v \geq 0.
\end{align*}

Therefore, the field remains on the interior of $\Delta$.

\[\square\]

Remark 3.1. It is observed that $\Delta$ is positively invariant. So that it is sufficient to consider solutions in $\Delta$ and every solution with initial conditions in the domain $\Delta = \Delta_h \cup \Delta_v \subset \mathbb{R}_+^4 \times \mathbb{R}_+^3$ remains in the region $\Delta$ as $t \to \infty$. The region is a positively invariant region with respect to the model (1). Hence, the malaria control model (1) is mathematically and epidemiologically well posed.

Corollary 3.1. The compact domain $\Delta_N := \{(N_h, N_v) \in \Delta : N_h \leq \frac{b_h}{d_v+u_2+u_3}, N_v \leq \frac{u_1}{(d_v+u_2+u_3)}\}$ is positively invariant and attracts all trajectory from $\Delta$. 

Proposition 3.2. Suppose the existence and uniqueness of the solution of the model equation (1) is obtained on an horizon of infinite time.

Proof. The model equation (1) is considered to be well posed and epidemiologically meaningful in the region \( \Delta = \Delta_h \cup \Delta_v \subset \mathbb{R}_+^4 \times \mathbb{R}_3^+ \). The region \( \Delta \) is defined by the boundaries of the solution of the model equations

\[
\Delta_h = \{(S_h, E_h, I_h, R_h) \}
\]
\[
\Delta_v = \{(S_v, E_v, I_v) \}
\]
\[
\Delta = \Delta_h \cup \Delta_v \subset \mathbb{R}_+^4 \times \mathbb{R}_3^+
\]

We consider the right hand side of the model equation (1) to be continuous with continuous partial derivative in \( \Delta \). It is assumed that an initial condition exists in the region \( \Delta \). Hence, we show that a solution of the model equation remain in the strip \( \Delta \) in the following way:

(a) If \( S_h = 0 \), then,

\[
\frac{dS_h}{dt} = b_h + \gamma R_h - (2 - u_1 - u_2) \frac{\beta_{1 \epsilon_{hv}} \phi I_v \cdot 0}{N_h} - d_h \cdot 0 \geq 0
\]

and if \( S_h = \frac{b_h}{d_h} \), then, \( \frac{dS_h}{dt} = b_h + \gamma R_h - (2 - u_1 - u_2) \frac{\beta_{1 \epsilon_{hv}} \phi S_h I_v \cdot \frac{b_h}{N_h}}{N_h} - b_h \leq 0 \).

(b) If \( E_h = 0 \), then,

\[
\frac{dE_h}{dt} = (2 - u_1 - u_2) \frac{\beta_{1 \epsilon_{hv}} \phi S_h I_v}{N_h} - (\alpha_h + d_h) \cdot 0 \geq 0
\]

and if \( E_h = 1 \), then, \( \frac{dE_h}{dt} = (2 - u_1 - u_2) \frac{\beta_{1 \epsilon_{hv}} \phi S_h I_v}{N_h} - (\alpha_h + d_h) \cdot 1 \leq 0 \).

(c) If \( I_h = 0 \), then,

\[
\frac{dI_h}{dt} = \alpha_h E_h - (u_5 + \theta + \psi + d_h) \cdot 0 \geq 0
\]

and if \( I_h = 1 \), then, \( \frac{dI_h}{dt} = \alpha_h E_h - (u_5 + \theta + \psi + d_h) \cdot 1 \leq 0 \).

(d) If \( R_h = 0 \), then,

\[
\frac{dR_h}{dt} = (u_5 + \theta) I_h - (\gamma + d_h) \cdot 0 \geq 0
\]

and if \( R_h = 1 \), then, \( \frac{dR_h}{dt} = (u_5 + \theta) I_h - (\gamma + d_h) \cdot 1 \leq 0 \).

(e) If \( S_v = 0 \), then,

\[
\frac{dS_v}{dt} = b_v - (2 - u_1 - u_2) \frac{\beta_{2 \epsilon_{sv}} \phi I_h \cdot 0}{N_h} - d_v \cdot 0 - (pu_3 + qu_4) \cdot 0 \geq 0
\]
and if $R_h = 1$, then, $\frac{dS_h}{dt} = b_v - (2 - u_1 - u_2) \frac{\beta_s \varepsilon_v \phi h_N h}{N_h} - d_v \cdot 0 - (pu_3 + qu_4) \cdot 1 \leq 0$.

(f) If $E_v = 0$, then,
$$\frac{dE_v}{dt} = (2 - u_1 - u_2) \frac{\beta_s \varepsilon_v \phi s_v I_h}{N_h} - (\alpha_v + d_v) \cdot 0 - (pu_3 + qu_4) \cdot 0 \geq 0$$

and if $E_v = 1$, then, $\frac{dE_v}{dt} = (2 - u_1 - u_2) \frac{\beta_s \varepsilon_v \phi s_v I_h}{N_h} - (\alpha_v + d_v) \cdot 1 - (pu_3 + qu_4) \cdot 1 \leq 0$.

(g) If $I_v = 0$, then, $\frac{dI_v}{dt} = \alpha_v E_v - d_v \cdot 0 - (pu_3 + qu_4) \cdot 0 \geq 0$ and if $I_v = 1$, then, $\frac{dI_v}{dt} = \alpha_v E_v - d_v \cdot 1 - (pu_3 + qu_4) \cdot 1 \leq 0$.

Therefore, these all follows in line with Picard-Lindelöf theorem that a unique solution exists for the model equation (1) in the region $\Delta$.

4 Optimal control Analysis of the controlled Malaria transmission Model

In this section, we considered the use of multiple control variables in order to obtain the optimal control strategy out of various sets of combined control strategies. The sets of combine control strategies can be the use of at least one control at a time. The control $u_1$ is the use insecticide treated nets (ITN), $u_2$ is the educational campaign, $u_3$ is the control by the use of insecticides spray, $u_4$ is the use of regular destruction of mosquito breeding sites and $u_5$ is the control by the use of treatment with ACT through mass drug administration' $u_i \in [0, 1]$. All these controls are bounded. The model equation is given below as:

$$\begin{align*}
\frac{dS_h}{dt} & = b_v + \gamma R_h - (2 - u_1(t) - u_2(t)) \frac{\beta_s \varepsilon_v \phi s_v I_h}{N_h} - d_v S_h \\
\frac{dE_v}{dt} & = (2 - u_1(t) - u_2(t)) \frac{\beta_s \varepsilon_v \phi s_v I_h}{N_h} - (\alpha_v + d_v) E_h \\
\frac{dI_h}{dt} & = \alpha_h E_h - (u_3(t) + \theta + \psi + d_h) I_h \\
\frac{dR_h}{dt} & = (u_3(t) + \theta) I_h - (\gamma + d_h) R_h \\
\frac{dS_v}{dt} & = b_v - (2 - u_1(t) - u_2(t)) \frac{\beta_s \varepsilon_v \phi s_v I_h}{N_h} - d_v S_v - (pu_3(t) + qu_4(t)) S_v \\
\frac{dE_v}{dt} & = (2 - u_1(t) - u_2(t)) \frac{\beta_s \varepsilon_v \phi s_v I_h}{N_h} - (\alpha_v + d_v) E_v - (pu_3(t) + qu_4(t)) E_v \\
\frac{dI_v}{dt} & = \alpha_v E_v - d_v I_v - (pu_3(t) + qu_4(t)) I_v.
\end{align*}$$

(4)

The costs associated with each control intervention appear as quadratic terms in the objective functional. We chose the quadratic term to describe the nonlinear behaviour of the cost of implementing any of the control programme. The form of the objective functional follows previous applications of optimal control to the management of infectious diseases [24, 34]. Combining the factors described above we obtain the objective functional. We now define the
objective functional as

$$J(u_1, u_2, u_3, u_4, u_5) = \min_{\{u_1, u_2, u_3, u_4, u_5\}} \int_0^{t_f} (A_1 I_h + A_2 I_v + A_3 u_1^2 + A_4 u_2^2 + A_5 u_3^2 + A_6 u_4^2 + A_7 u_5^2) \, dt$$

subject to malaria control model (3) with typical states initial conditions while the Lebesgue measurable control set $U$ is defined as $U = \{(u_1, u_2, u_3, u_4, u_5)| 0 \leq u_1 \leq 1, 0 \leq u_2 \leq 1, 0 \leq u_3 \leq 1, 0 \leq u_4 \leq 1, 0 \leq u_5 \leq 1, t \in [0, t_f]\}$ where the parameter $A_1 \geq 0, A_2 \geq 0, A_3 \geq 0, A_4 \geq 0, A_5 \geq 0, A_6 \geq 0, A_7 \geq 0$ such that $A_1 - A_7$ are positive constants which represents the weights of the costs of using treated bedNets, using educational campaign [35, 36], using insecticides spray, use of regular destruction of mosquito breeding sites and treatment with drug. Therefore our $u_1, u_2, u_3, u_4$ and $u_5$ lies between 0 and 1. The weights $A_1 - A_7$ measure the weights of the infected human and mosquito, costs of mosquito treated bed Nets, costs of educational campaigns, costs of insecticides spray, costs on the use of regular destruction of mosquito breeding sites and costs of treatment with drug in waging war against the spread of malaria disease and also the cost of implementing each of the control strategies per unit time. In our objective functional, we use the quadratic terms $u_1^2, u_2^2, u_3^2, u_4^2$ and $u_5^2$ on the assumption that the cost are non-linear. Hence, we are seeking an optimal control $u_1^*, u_2^*, u_3^*, u_4^*$ and $u_5^*$ such that

$$J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*) = \min_{u_1, u_2, u_3, u_4, u_5} \{J(u_1, u_2, u_3, u_4, u_5) \mid u_1, u_2, u_3, u_4, u_5 \in U\}$$

where $u_1, u_2, u_3, u_4, u_5 \in U$ such that the control $u_1^*, u_2^*, u_3^*, u_4^*$ and $u_5^*$ are called optimal control. We present the following assumptions in the case of our model under consideration:

(i) The control state variables are non-empty.

(ii) The admissible control set $U$ is closed and convex.

(iii) The right hand side of our model equation are continuous, bounded above a sum of the variable and state variable and can be written as a linear function of $\mu$ with coefficient depending on time and space.

(iv) There exist constant $m_1, m_2, m_3, m_4$ and $\beta > 1$ such that the integrand $f(t, x, u)$ of the objective functional $J$ is convex in $u$, and satisfies $f(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_1, u_2, u_3, u_4, u_5) \geq m_1(|u_1(t)|^2 + |u_2(t)|^2 + |u_3(t)|^2 + |u_4(t)|^2 + |u_5(t)|^2))^{\frac{\beta}{2}} - (m_2 + m_3 + m_4)$ and $\beta > 1$. 

4.1 Existence of optimal control

Proposition 4.1. The optimal control problem given by the objective functional $J(u_1, u_2, u_3, u_4, u_5) = \min_{u_1, u_2, u_3, u_4, u_5} \int_{t_0}^{T} \left( A_1 U_1 + A_2 U_2 + A_3 U_3^2 + A_4 U_4^2 + A_5 U_5^2 + A_6 U_6^2 + A_7 U_7^2 \right) dt$ where $U = \{u_1, u_2, u_3, u_4, u_5: u_i \text{ measurable } 0 \leq u_1(t) \leq 1, 0 \leq u_2(t) \leq 1, 0 \leq u_3(t) \leq 1, 0 \leq u_4(t) \leq 1, 0 \leq u_5(t) \leq 1 \forall t \in [t_0, T] \in \mathbb{R}^+$ for $i = 1, 2, 3, 4, 5$} and subject to the dynamic constraints of system equations (3) with $S_0(0) = S_{0,0}$, $E_{h}(0) = E_{h,0}$, $I_{h}(0) = I_{h,0}$, $R_{h}(0) = R_{h,0}$, $S_{v}(0) = S_{v,0}$, $E_{v}(0) = E_{v,0}$, $I_{v}(0) = I_{v,0}$, exist, and the optimal control are $u^* = (u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ such that

$$\min_{u_1, u_2, u_3, u_4, u_5 \in U} J(u_1, u_2, u_3, u_4, u_5) = J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$$

subject to the malaria control system (3) with the initial conditions, has a solution.

Proof. We define a set according to Filippov-Cesari Existence Theorem [25], for every $(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v) \in \mathbb{R}^{n+1}$ such that

$$\Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v) = \{ (A_1 U_1 + A_2 U_2 + A_3 U_3^2 + A_4 U_4^2 + A_5 U_5^2 + A_6 U_6^2 + A_7 U_7^2 + \xi_t) : g(x, u, t) \},$$

where $g(x, u, t) = (b_h + \gamma R_h - (2 - u_1(t) - u_2(t)) \frac{\beta_h S_h I_h}{N_h} - d_h S_h, (2 - u_1(t) - u_2(t)) \frac{\beta_h S_h I_h}{N_h} - (\alpha_h + d_h) E_h, \alpha_h E_h - (u_3(t) + \theta + \psi + d_h) I_h, (u_3(t) + \psi) I_h - (\gamma + d_h) R_h, b_v - (2 - u_1(t) - u_2(t)) \frac{\beta_v S_v I_h}{N_h} - d_v S_v, (p u_3(t) + q u_4(t)) S_v, (2 - u_1(t) - u_2(t)) \frac{\beta_v S_v I_h}{N_h} - (\alpha_v + d_v) E_v - (p u_3(t) + q u_4(t)) E_v, \alpha_v E_v - d_v I_v - (p u_3(t) + q u_4(t)) I_v \}$

Next, we need to show that $\Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ is convex for every $(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$.

(i) For every $\Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ is convex for all $(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$

Suppose $f_1, f_2 \in \Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ we prove that the line connecting $f_1$ and $f_2$ remain entirely in $\Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ in order to establish that $\Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ is convex for each $(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$.

Therefore, we establish that

$$\theta f_1 + (1 - \theta) f_2 \in \Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v) \quad \forall \theta \in [0, 1].$$

Let $f_i \in \Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ means that there exist $\xi_i \leq 0$ and the control vectors are $(u_1, U_2, u_3, u_4, u_5) \in U$ such that

$$f_i = \{ f(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_1, u_2, u_3, u_4, u_5) + \xi_i, g(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_1, u_2, u_3, u_4, u_5) \}$$

for $i = 1, 2$.

Hence, we obtain: $\theta(f(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_1, u_2, u_3, u_4, u_5) + \xi_1) + (1 -
(iii) Every solution of the optimal control problem (5) is bounded.

Next, we work on the second part of the function \( \Omega(t, S_h, I_h, R_h, S_v, E_v, I_v) \) such that: 

\[
g(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_{11}, u_{21}, u_{31}, u_{41}, u_{51}) = (b_h + \gamma R_h - (2 - u_1(t) - u_2(t))\frac{\beta_1 v_{10} S_h I_h}{N_h} - d_h S_h, (2 - u_1(t) - u_2(t))\frac{\beta_2 v_{10} S_h I_h}{N_h} - (\alpha_h + d_h) E_h, \alpha_h E_h - (u_2(t) + \theta + \psi + d_h) I_h, (u_3(t) + \theta) I_h - (\gamma + d_h) R_h, b_v - (2 - u_1(t) - u_2(t))\frac{\beta_3 v_{10} S_h I_h}{N_h} - d_v S_v - (pu_3(t) + qu_4(t))S_v, (2 - u_1(t) - u_2(t))\frac{\beta_4 v_{10} S_h I_h}{N_h} - (\alpha_v + d_v) E_v - (pu_3(t) + qu_4(t))E_v, \alpha_v E_v - d_v I_v - (pu_3(t) + qu_4(t))I_v)^T.
\]

(ii) Suppose \( U \) is compact.

It is clear that \( U \) is compact.

(iii) Every solution of the optimal control problem (5) is bounded.

We consider the total human and mosquito population of the model equation (3) at time \( t \), which are given by: 

\[
N_h = S_h + E_h + I_h + R_h \quad \text{and} \quad N_v = S_v + E_v + I_v.
\]

The derivatives of \( N_h \) and \( N_v \) with respect to time are given by:

\[
\frac{dN_h}{dt} = b_h - d_h N_h - \psi I_h, \quad \frac{dN_v}{dt} = b_v - (d_v + qu_4 + pu_3) N_v.
\]

For the proof of boundedness, it is of note that \( 0 < I_h(t) \leq N_h(t) \) and \( 0 < I_v(t) \leq N_v(t) \). All solutions of model (3) are bounded. The feasible region for the human population is:

\[
\Delta_h = \{ S_h, E_h, I_h, R_h | S_h + E_h + I_h + R_h \leq \frac{b_h}{d_h}, 0 \leq S_h \leq S_h(t) \leq \frac{b_h}{d_h}, E_h \geq 0, I_h \geq 0, R_h \geq 0 \} \text{ And the feasible region for the mosquito population is:}
\]

\[
\Delta_v = \{ S_v, E_v, I_v, R_v | S_v + E_v + I_v + R_v \leq \frac{b_v}{d_v}, 0 \leq S_v \leq S_v(t) \leq \frac{b_v}{d_v}, E_v \geq 0, I_v \geq 0, R_v \geq 0 \}.
\]

\[
(1 - \theta) \xi_2.
\]

Suppose \( u_0 = \sqrt{\theta A_3 u_1 + (1 - \theta) A_3 u_1^2} \), we observed that \( u_0 \in U \). Moreover, setting \( \xi_3 = \theta \xi_1 + (1 - \theta) \xi_2 \), it is observed that \( \xi_3 \leq 0 \). Hence, we also observed that the first part of the convex combination belongs to \( \Omega(t, S_h, I_h, R_h, S_v, E_v, I_v) \).

\[
\theta(f(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_{11}, u_{21}, u_{31}, u_{41}, u_{51}) + \xi_2) \theta(A_1 I_h + A_2 I_v + A_3 u_1^2 + A_4 u_1^2 + A_5 u_1^2 + A_7 u_1^2 + \xi_1) + (1 - \theta)(A_1 I_h + A_2 I_v + A_3 u_1^2 + A_5 u_1^2 + A_7 u_1^2) + (1 - \theta)(A_1 I_h + A_2 I_v + A_4 u_1^2 + A_5 u_1^2 + A_7 u_1^2) + \theta \xi_1 + (1 - \theta) \xi_2.
\]

\[
\theta(A_1 I_h + A_2 I_v + A_3 u_1^2 + A_4 u_1^2 + A_5 u_1^2 + A_7 u_1^2) + (1 - \theta)(A_1 I_h + A_2 I_v + A_3 u_1^2 + A_5 u_1^2 + A_7 u_1^2) + \theta \xi_1 + (1 - \theta) \xi_2.
\]
\[ \Delta_v = (S_v, E_v, I_v, S_v + E_v + I_v \leq \frac{b_v}{(d_v + qu_4 + pu_3)}; 0 \leq S_v \leq S_v(t) \leq \frac{b_v}{(d_v + qu_4 + pu_3)}; E_v \geq 0, I_v \geq 0). \]

Therefore,

\[ b_h - (d_h + \psi)N_h(t) \leq \frac{dN_h(t)}{dt} \leq b_h - d_h N_h(t) \]

\[ b_v - (d_v + qu_4 + pu_3)N_v(t) \leq \frac{dN_v(t)}{dt} \leq b_v - (d_v + qu_4 + pu_3)N_v(t) \]

Hence,

\[ \frac{b_h}{d_h + \psi} \leq \lim \inf_{t \to \infty} N_h(t) \leq \lim \sup_{t \to \infty} N_h(t) \leq \frac{b_h}{d_h} \]

and

\[ \frac{b_v}{(d_v + qu_4 + pu_3)} \leq \lim \inf_{t \to \infty} N_v(t) \leq \lim \sup_{t \to \infty} N_v(t) \leq \frac{b_v}{(d_v + qu_4 + pu_3)} \]

Therefore, we have that \( N_h(t) \leq \sup_t N_h \) where \( N_h \) remains the solution of the equation \( \frac{dN_h(t)}{dt} \leq b_h - (d_h + \psi)N_h(t) \). Hence, \( \sup_t N_h \leq \max\{N_h(0), N_h\} \).

Suppose \( N_h(0) \leq N_h \), then \( \max\{N_h(t)\} \leq N_h \).

To prove the existence of an optimal control pair we use the result in [18, 25, 31]. 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 \( u_1, u_2, u_3, u_4 \) and \( u_5 \) is satisfied. The set of all the control variables \((u_1, u_2, u_3, u_4, u_5 \in U)\) 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 \((A_1 I_h + A_2 I_v + A_3 u_1^2 + A_4 u_2^2 + A_5 u_3^2 + A_6 u_4^2 + A_7 u_5^2)\) 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 \(J(u_1, u_2, u_3, u_4, u_5) \geq b((|u_1(t)|^2 + |u_2(t)|^2 + |u_3(t)|^2 + |u_4(t)|^2 + |u_5(t)|^2) \frac{\beta}{\beta - 1} - b_2\). By standard control arguments involving the bounds on the controls, we conclude for \(i = 1, 2, ..., 5:\)

\[
\begin{align*}
\ u_i^* &= \begin{cases} 
0 & \text{if } r_i^* \leq 0, \\
\ r_i^* & \text{if } 0 < r_i^* < 1, \\
1 & \text{if } r_i^* \geq 1,
\end{cases} \\
\text{where } u_i^* &= \frac{\beta \sigma_i \phi I_v S_v (\lambda \gamma_1 - \lambda \gamma_2)}{2A_6 A_h}, \quad \text{for } i = 1, 2; \\
\text{and } u_5^* &= \frac{\beta \sigma_i \phi I_v S_v (\lambda \gamma_1 - \lambda \gamma_2)}{2A_6}, \quad \text{for } i = 1, 2; \\
\end{align*}
\]

where \( u_5^* = \frac{\beta \sigma_i \phi I_v S_v (\lambda \gamma_1 - \lambda \gamma_2)}{2A_6 A_h}, \) for \( i = 1, 2); \)

\[
\begin{align*}
\ u_3^* &= \frac{\beta \sigma_i \phi I_v S_v (\lambda \gamma_1 - \lambda \gamma_2)}{2A_6}, \\
\ u_4^* &= \frac{\beta \sigma_i \phi I_v S_v (\lambda \gamma_1 - \lambda \gamma_2)}{2A_6}, \\
\ u_5^* &= \frac{(I_h \lambda \gamma_1 + I_h \lambda \gamma_2)}{2A_7}.
\end{align*}
\]
4.1.1 Existence conditions for optimising the Hamiltonian

Since the solution exists we used the Pontryagin’s maximum principle to determine the optimal solution.

**Proposition 4.2.** Suppose the optimal control \((u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t), u_5^*(t))\) and the solution

\[ x^*(t) = (S_h^*(t), E_h^*(t), I_h^*(t), R_h^*(t), S_v^*(t), E_v^*(t), I_v^*(t)) \]

of the associated state system (3) is given then there exists adjoint variables \(\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t), \lambda_6(t)\), and \(\lambda_7(t)\) satisfying

The co-state equation given by

\[
\begin{align*}
\frac{d\lambda_{S_h}}{dt} &= \left(\frac{\lambda_{S_h} - \lambda_{E_h}}{N_h}\right) + d_h \lambda_{S_h} S_h \\
\frac{d\lambda_{E_h}}{dt} &= (\alpha_h + d_h) \lambda_{E_h} - \alpha_h \lambda_{I_h} \\
\frac{d\lambda_{I_h}}{dt} &= (u_5 + \theta + \psi + d_h) \lambda_{I_h} - \theta \lambda_{R_h} + \left(\frac{\lambda_{E_v} - \lambda_{E_h}}{2(1-u_1-u_2)}\right) \lambda_{E_v} S_e \\
\frac{d\lambda_{R_h}}{dt} &= \gamma \lambda_{S_h} + (\gamma + d_h) \lambda_{R_h} \\
\frac{d\lambda_{E_v}}{dt} &= \left(\frac{\lambda_{S_h} - \lambda_{E_v}}{N_h}\right) + (p u_3 + q u_4 + d_v) \lambda_{E_v} \\
\frac{d\lambda_{I_v}}{dt} &= \frac{\lambda_{S_h} (2-u_1-u_2) \beta_1 e_s \phi_{S_h} + (p u_3 + q u_4 + d_v) \lambda_{I_v} - \frac{\lambda_{E_h} (2-u_1-u_2) \beta_1 e_s \phi_{S_h}}{N_h}}{N_h} \\
\end{align*}
\]

with terminal conditions

\[
\begin{align*}
\lambda_{S_h}(t_f) &= \lambda_{E_h}(t_f) = \lambda_{I_h}(t_f) = \lambda_{R_h}(t_f) = \lambda_{S_v}(t_f) = \lambda_{E_v}(t_f) = \lambda_{I_v}(t_f) = 0 \\
\end{align*}
\]

Moreover,

\[
\begin{align*}
\lambda_{S_h}(t_f) &= \lambda_{E_h}(t_f) = \lambda_{I_h}(t_f) = \lambda_{R_h}(t_f) = \lambda_{S_v}(t_f) = \lambda_{E_v}(t_f) = \lambda_{I_v}(t_f) = 0 \\
\end{align*}
\]

\[
\begin{align*}
u_1(t) &= \left\{ \begin{array}{c}
1, \text{max} \left(0, \min \left(\frac{\beta_1 e_s \phi_{I_h} S_h (\lambda_{E_h} - \lambda_{S_h}) + \beta_2 e_s \phi_{I_h} S_h (\lambda_{E_v} - \lambda_{S_v})}{\lambda_{A_1} N_h} \right) \right)
\end{array} \right. \\
u_2(t) &= \left\{ \begin{array}{c}
1, \text{max} \left(0, \min \left(\frac{\beta_1 e_s \phi_{I_h} S_h (\lambda_{E_h} - \lambda_{S_h}) + \beta_2 e_s \phi_{I_h} S_h (\lambda_{E_v} - \lambda_{S_v})}{\lambda_{A_2} N_h} \right) \right)
\end{array} \right. \\
u_3(t) &= \left\{ \begin{array}{c}
1, \text{max} \left(0, \min \left(\frac{p S_v \lambda_{S_v} + E_v \lambda_{E_v} + I_v \lambda_{I_v}}{\lambda_A} \right) \right)
\end{array} \right. \\
u_4(t) &= \left\{ \begin{array}{c}
1, \text{max} \left(0, \min \left(\frac{q S_v \lambda_{S_v} + E_v \lambda_{E_v} + I_v \lambda_{I_v}}{\lambda_A} \right) \right)
\end{array} \right. \\
u_5(t) &= \left\{ \begin{array}{c}
\text{max} \left(0, \min \left(1, \frac{(\lambda_{I_h} + \lambda_{R_h})}{\lambda_{A_2} N_h} \right) \right)
\end{array} \right. \\
\end{align*}
\]

**Proof.** From Pontryagin’s Maximum Principle, there exists a vector \(\lambda(t) = (\lambda_{S_h}(t), \lambda_{E_h}(t), \lambda_{I_h}(t), \lambda_{R_h}(t), \lambda_{S_v}(t), \lambda_{E_v}(t), \lambda_{I_v}(t))\) satisfying model equation (3)

\[
\frac{d\lambda(t)}{dt} = -\frac{\partial H}{\partial x} = -f_x - W_x \lambda(t).
\]
Then the adjoint system can be written as

\[
\begin{align*}
\frac{d\lambda_{S_h}}{dt} &= (\lambda_{S_h} - \lambda_{E_h}) (1 - u_2) \frac{\beta_{I_h} \phi I_v}{N_h} + d_h \lambda_{S_h} S_h \\
\frac{d\lambda_{E_h}}{dt} &= (\alpha_h + d_h) \lambda_{E_h} - \alpha_h \lambda_{I_h} \\
\frac{d\lambda_{I_h}}{dt} &= (u_5 + \theta + \psi + d_h) \lambda_{I_h} - \theta \lambda_{R_h} + \frac{(\lambda_{S_v} - \lambda_{E_v}) (1 - u_2) \beta_{I_h} \phi S_v}{N_h} \\
\frac{d\lambda_{R_h}}{dt} &= \gamma \lambda_{S_h} + \frac{(\gamma + d_h) \lambda_{R_h}}{N_h} \\
\frac{d\lambda_{S_v}}{dt} &= \frac{(\lambda_{S_v} - \lambda_{E_v}) (1 - u_2) \beta_{I_h} \phi S_v}{N_h} + (pu_3 + qu_4 + d_v) \lambda_{S_v} \\
\frac{d\lambda_{I_v}}{dt} &= \frac{(pu_4 + qu_5 + d_v + \alpha_v) \lambda_{E_v} - \alpha_v I_v}{N_h} \\
\lambda_{S_h} (t_f) &= \lambda_{E_h} (t_f) = \lambda_{I_h} (t_f) = \lambda_{R_h} (t_f) = \lambda_{S_v} (t_f) = \lambda_{I_v} (t_f) = \lambda_{S_v} (t_f) = 0.
\end{align*}
\]

with transversality conditions

\[
\lambda_{S_h} (t_f) = \lambda_{E_h} (t_f) = \lambda_{I_h} (t_f) = \lambda_{R_h} (t_f) = \lambda_{S_v} (t_f) = \lambda_{I_v} (t_f) = \lambda_{S_v} (t_f) = 0.
\]

We have on the interior of the control set \( U \), where \( 0 \leq u_i \leq 1 \), for \( i = 1, 2, \ldots, 5 \):

\[
\begin{align*}
0 &= \frac{\partial H}{\partial u_1} = \frac{\beta_{I_h} \phi I_v}{N_h} \lambda_{S_h} + \frac{\beta_{I_h} \phi I_v}{N_h} \lambda_{E_h} + \frac{\beta_{I_h} \phi I_v}{N_h} \lambda_{I_h} - \frac{\beta_{I_h} \phi I_v}{N_h} \lambda_{R_h} + 2A_1 u_1^* \\
0 &= \frac{\partial H}{\partial u_2} = -p(S_v \lambda_{S_v} + I_v \lambda_{I_v}) + 2A_2 u_2^* \\
0 &= \frac{\partial H}{\partial u_3} = -q(S_v \lambda_{S_v} + E_v \lambda_{E_v} + I_v \lambda_{I_v}) + 2A_4 u_4^* \\
0 &= \frac{\partial H}{\partial u_5} = -(I_h \lambda_{I_h} + I_h \lambda_{R_h}) + 2A_3 u_5^*.
\end{align*}
\]

Hence we obtain the following

\[
\begin{align*}
r_{I_v}^* (t) &= \frac{p(S_v \lambda_{S_v} + I_v \lambda_{I_v})}{2A_2} \\
r_{I_h}^* (t) &= \frac{q(S_v \lambda_{S_v} + E_v \lambda_{E_v} + I_v \lambda_{I_v})}{2A_4} \\
r_{I_v}^* (t) &= \frac{(I_h \lambda_{I_h} + I_h \lambda_{R_h})}{2A_3}.
\end{align*}
\]

and receive the (10).

Now the Pontryagin’s Maximum Principle (PMP) gives the following necessary conditions to obtain the optimality pair \((x^*, u^*)\):

\[
\frac{\partial H(x,u^*,\lambda,t)}{\partial u_i} = 0,
\]

\(H(x, u^*, \lambda, t) = f(x, u, t) + \lambda^T g(x, u, t)\). Now the Optimality system is given by incorporating control pair in the state system coupled with the adjoint system. Thus, we have our resulting optimality system as follows: State Equations:
Subject to Initial conditions: $S_h(0) = S_{h,0}$, $E_h(0) = E_{h,0}$, $I_h(0) = I_{h,0}$, $R_h(0) = R_{h,0}$, $S_v(0) = S_{v,0}$, $E_v(0) = E_{v,0}$, $I_v(0) = I_{v,0}$.

Adjoint Equation:

\[
\begin{align*}
\frac{d\lambda_{Sh}}{dt} &= \frac{(\lambda_{Sh} - \lambda_{E_h})(2-u_1-u_2)}{N_h} + d_h \lambda_{Sh} S_h \\
\frac{d\lambda_{E_h}}{dt} &= (\alpha_h + d_h) \lambda_{E_h} - \alpha_h \lambda_{I_h} \\
\frac{d\lambda_{I_h}}{dt} &= (u_5 + \beta + d_h) \lambda_{I_h} - \beta \lambda_{R_h} + \frac{(\lambda_{Sh} - \lambda_{E_h})(2-u_1-u_2)\beta \phi S_v}{N_h} \\
\frac{d\lambda_{R_h}}{dt} &= \gamma \lambda_{Sh} + (\gamma + d_h) \lambda_{R_h} \\
\frac{d\lambda_{Sh}}{dt} &= pu_3 + qu_4 + d_v \lambda_{E_v} \\
\frac{d\lambda_{E_v}}{dt} &= \frac{\lambda_{Sh}(2-u_1-u_2)\beta \phi S_h}{N_h} + (pu_3 + qu_4 + d_v) \lambda_{E_v} - \frac{\lambda_{E_h}(2-u_1-u_2)\beta \phi S_h}{N_h} \\
\end{align*}
\]

Transversality conditions:

\[
\lambda_{Sh}(t_f) = \lambda_{E_h}(t_f) = \lambda_{I_h}(t_f) = \lambda_{Sh_v}(t_f) = \lambda_{E_v}(t_f) = \lambda_{I_v}(t_f) = 0.
\]

Characterization of the optimal control $u_1^*, u_2^*, u_3^*, u_4^*, u_5^*$:

\[
\frac{\partial H}{\partial u_1} = \frac{\partial H}{\partial u_2} = \frac{\partial H}{\partial u_3} = \frac{\partial H}{\partial u_4} = \frac{\partial H}{\partial u_5} = 0 \text{ at } u_1 = u_1^*, u_2 = u_2^*, u_3 = u_3^*, u_4 = u_4^*, u_5 = u_5^* \text{ on the set } \{t \in [0, t_f]: 0 \leq u_1 \leq 1, 0 \leq u_2 \leq 1, 0 \leq u_3 \leq 1, 0 \leq u_4 \leq 1, 0 \leq u_5 \leq 1\). \quad \Box
\]

By the a priori 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 $t_f$. The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consist of (11), (12), (13) with characterization (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 [10, 11, 21, 25].

**Remark 4.1.** An optimal control pair $(S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^*, u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ exists for minimizing the objective functional subject to model equation (3).

The numerical experiments of created models were done and the results were presented in [8].

**5 Conclusion**

In this work, we analyzed a non-linear model to study the effect of multiple control interventions on malaria transmission with its optimal control analysis. Both qualitative analysis and numerical simulation of the model have
been carried out. Optimal control analysis was applied to make decisions on the model where we minimize the total number of infected individuals and mosquitoes and the cost associated with the various control interventions on $[0, t_f]$. The Pontryagin’s maximum principle (PMP) was used to derive the necessary conditions for the optimal control of the disease and to minimize pointwise the Hamiltonian. Results on the existence of the control intervention in the model was shown and the optimality system was also presented. Hence, in the model we obtained the best control interventions that will minimize the number of infected human and mosquito and the cost of applying the multiple control interventions over time, which form a basis for future predictions of possible impact of using combinations of the five controls, either one at a time, two at a time, three at a time, or four at a time against the spread of malaria in areas with limited resources.

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