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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 amass 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 dusks 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 γ). 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 β_1 is the transmission probability per bite, ε_h is the per capita biting rate of mosquitoes, ϕ 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 α 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 α_h) and decreased by human spontaneous recovery(at a rate θ). It is reduced by the disease induced death rate (at per capita rate ψ), 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 θ) and by treatment with ACT through mass drug administration (u_5) but decreased by loss of immunity(at a rate γ) 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 β_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 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. The rate of change of the exposed mosquitoes population is produced by the per capita rate α_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 α_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:

$$\begin{aligned}
\frac{dS_h}{dt} &= b_h + \gamma R_h - (2-u_1-u_2)\frac{\beta_1\varepsilon_h\phi S_h I_v}{N_h} - d_h S_h \\
\frac{dE_h}{dt} &= (2-u_1-u_2)\frac{\beta_1\varepsilon_h\phi S_h I_v}{N_h} - (\alpha_h + d_h)E_h \\
\frac{dI_h}{dt} &= \alpha_h E_h - (u_5 + \theta + \psi + d_h)I_h \\
\frac{dR_h}{dt} &= (u_5+\theta)I_h - (\gamma + d_h)R_h \\
\frac{dS_v}{dt} &= b_v - (2-u_1-u_2)\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - d_v S_v - (pu_3 + qu_4)S_v
\end{aligned} \tag{1}$$

$$\begin{aligned} \frac{dE_v}{dt} &= (2-u_1-u_2)\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - (\alpha_v+d_v)E_v - (pu_3+qu_4)E_v \\ \frac{dI_v}{dt} &= \alpha_v E_v - d_v I_v - (pu_3+qu_4)I_v, \end{aligned} \tag{2}$$

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:

$$\begin{aligned} \frac{dS_h}{dt} &= g_1(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ \frac{dE_h}{dt} &= g_2(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ \frac{dI_h}{dt} &= g_3(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ \frac{dR_h}{dt} &= g_4(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ \frac{dS_v}{dt} &= g_5(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ \frac{dE_v}{dt} &= g_6(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \\ \frac{dI_v}{dt} &= g_7(S_h, E_h, I_h, R_h, S_v, E_v, I_v), \end{aligned} \tag{3}$$

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 1: Variables in the malaria control model

Variables	Description
$S_h(t)$	Susceptible Human Population
$E_h(t)$	Exposed Human Population
$I_h(t)$	Infected Human Population
$R_h(t)$	Recovered Human Population
$S_v(t)$	Susceptible Mosquito Population
$E_v(t)$	Exposed Mosquito Population
$I_v(t)$	Infected Mosquito Population

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

Parameter	Symbol
disease induced death rate	ψ
probability of human getting infected	β_1
probability of mosquito getting infected	β_2
per capita birth rate of mosquitoes	b_v
Natural death rate of humans	d_h
progression of human from the exposed to the infectious state	α_h
progression of mosquitoes from the exposed to the infectious state	α_v
per capita biting rate of mosquitoes	ε_v
contact rate of vector per human per unit time	ϕ
per capita biting rate of humans	ε_h
human spontaneous recovery	θ
Natural death rate of mosquitoes	d_v
rate of loss of immunity from humans	γ
per capita birth rate of humans	b_h

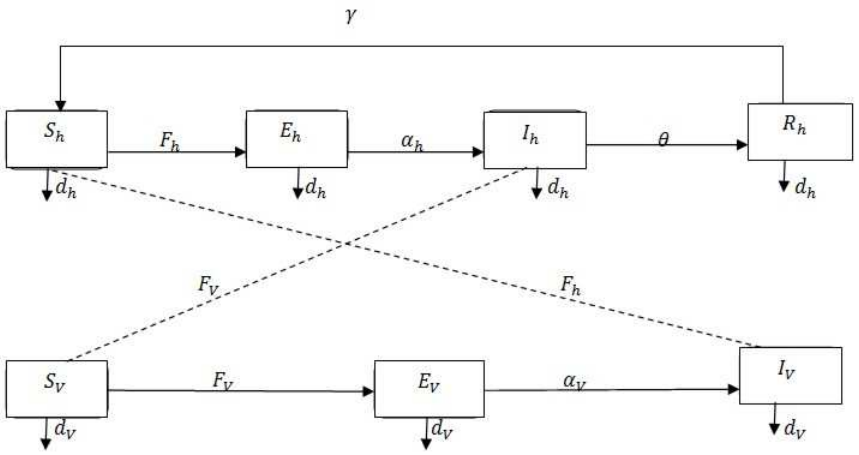

Figure 1: Flow chart of Malaria model (1) from [8].

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:
$g_1(S_h = 0, E_h, I_h, R_h, S_v, E_v, I_v) = b_h + \gamma R_h \geq 0$ for $E_h, I_h, R_h, S_v, E_v, I_v \geq 0$,
$g_2(S_h, E_h = 0, I_h, R_h, S_v, E_v, I_v) = (2 - u_1 - u_2)\frac{\beta_1 \varepsilon_h \phi S_h I_v}{N_h} \geq 0$ for $E_h, I_h, R_h, S_v, E_v, I_v \geq 0$,
$g_3(S_h, E_h, I_h = 0, R_h, S_v, E_v, I_v) = \alpha_h E_h \geq 0$ for $E_h, I_h, R_h, S_v, E_v, I_v \geq 0$,
$g_4(S_h, E_h, I_h, R_h = 0, S_v, E_v, I_v) = u_5 + \theta) I_h \geq 0$ for $E_h, I_h, R_h, S_v, E_v, I_v \geq 0$,
$g_5(S_h, E_h, I_h, R_h, S_v = 0, E_v, I_v) = b_v \geq 0$ for $E_h, I_h, R_h, S_v, E_v, I_v \geq 0$,
$g_6(S_h, E_h, I_h, R_h, S_v, E_v = 0, I_v) = (2 - u_1 - u_2)\frac{\beta_2 \varepsilon_v \phi S_v I_h}{N_h} \geq 0$ for $E_h, I_h, R_h, S_v, E_v, I_v \geq 0$,
$g_7(S_h, E_h, I_h, R_h, S_v, E_v, I_v = 0) = \alpha_v E_v \geq 0$ for $E_h, I_h, R_h, S_v, E_v, I_v \geq 0$.
Therefore, the field remains on the interior of Δ. □

Remark 3.1. *It is observed that* Δ *is positively invariant. So that it is sufficient to consider solutions in* Δ *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* Δ *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* $\Delta_N := \{(N_h, N_v) \in \Delta : N_h \leq \frac{b_h}{d_h}, N_v \leq \frac{b_v}{(d_v + qu_4 + pu_3)}\}$ *is positively invariant and attracts all trajectory from* Δ.

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 Δ 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 Δ. It is assumed that an initial condition exists in the region Δ. Hence, we show that a solution of the model equation remain in the strip Δ in the following way:
(a) If $S_h = 0$, then,

$$\frac{dS_h}{dt} = b_h + \gamma R_h - (2 - u_1 - u_2)\frac{\beta_1 \varepsilon_h \phi I_v \cdot 0}{N_h} - d_h \cdot 0 \geq 0$$

and if $S_h = \frac{b_h}{d_h}$, then, $\frac{dS_h}{dt} = b_h + \gamma R_h - (2 - u_1 - u_2)\frac{\beta_1 \varepsilon_h \phi I_v \cdot \frac{b_h}{d_h}}{N_h} - b_h \leq 0$.
(b) If $E_h = 0$, then,

$$\frac{dE_h}{dt} = (2 - u_1 - u_2)\frac{\beta_1 \varepsilon_h \phi S_h I_v}{N_h} - (\alpha_h + d_h) \cdot 0 \geq 0$$

and if $E_h = 1$, then, $\frac{dE_h}{dt} = (2 - u_1 - u_2)\frac{\beta_1 \varepsilon_h \phi S_h I_v}{N_h} - (\alpha_h + d_h) \cdot 1 \leq 0$.
(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,

$$\frac{dS_v}{dt} = b_v - (2 - u_1 - u_2)\frac{\beta_2 \varepsilon_v \phi I_h \cdot 0}{N_h} - d_v \cdot 0 - (pu_3 + qu_4) \cdot 0 \geq 0$$

and if $R_h = 1$, then, $\frac{dS_v}{dt} = b_v - (2-u_1-u_2)\frac{\beta_2\varepsilon_v\phi I_h \cdot 0}{N_h} - d_v \cdot 0 - (pu_3+qu_4)\cdot 1 \leq 0$.
(f) If $E_v = 0$, then,

$$\frac{dE_v}{dt} = (2-u_1-u_2)\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - (\alpha_v + d_v)\cdot 0 - (pu_3+qu_4)\cdot 0 \geq 0$$

and if $E_v = 1$, then, $\frac{dE_v}{dt} = (2-u_1-u_2)\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - (\alpha_v+d_v)\cdot 1 - (pu_3+qu_4)\cdot 1 \leq 0$.
(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 Δ □

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:

$$\begin{aligned}
\frac{dS_h}{dt} &= b_h + \gamma R_h - (2-u_1(t)-u_2(t))\frac{\beta_1\varepsilon_h\phi S_h I_v}{N_h} - d_h S_h \\
\frac{dE_h}{dt} &= (2-u_1(t)-u_2(t))\frac{\beta_1\varepsilon_h\phi S_h I_v}{N_h} - (\alpha_h + d_h)E_h \\
\frac{dI_h}{dt} &= \alpha_h E_h - (u_5(t)+\theta+\psi+d_h)I_h \\
\frac{dR_h}{dt} &= (u_5(t)+\theta)I_h - (\gamma+d_h)R_h \\
\frac{dS_v}{dt} &= b_v - (2-u_1(t)-u_2(t))\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - d_v S_v - (pu_3(t)+qu_4(t))S_v \\
\frac{dE_v}{dt} &= (2-u_1(t)-u_2(t))\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - (\alpha_v+d_v)E_v - (pu_3(t)+qu_4(t))E_v \\
\frac{dI_v}{dt} &= \alpha_v E_v - d_v I_v - (pu_3(t)+qu_4(t))I_v.
\end{aligned} \tag{4}$$

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

$$J(u_1, u_2, u_3, u_4, u_5) = \min_{\{u_1,u_2,u_3,u_4,u_5\}} \int_0^{t_f} (A_1 I_h + A_2 I_v + A_3 u_1^2 + A_4 u_2^2 + A_5 u_3^2 + A_6 u_4^2 + A_7 u_5^2)\, dt \tag{5}$$

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 μ 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* $J(u_1,u_2,u_3,u_4,u_5) = \min_{\{u_1,u_2,u_3,u_4,u_5\}} \frac{1}{2}\int_0^{t_f}(A_1I_h + A_2I_v + A_3u_1^2 + A_4u_2^2+A_5u_3^2+A_6u_4^2+A_7u_5^2)\,dt$ *where* $U = \{u_1,u_2,u_3,u_4,u_5 : u_i$ *measurable* $0 \le u_1(t) \le 1, 0 \le u_2(t) \le 1, 0 \le u_3(t) \le 1, 0 \le u_4(t) \le 1, 0 \le u_5(t) \le 1t \in [t_0,T] \in \mathbb{R}^+$ *for* $i = 1,2,3,4,5.\}$ *and subject to the dynamic constraints of system equations* (3) *with* $S_h(0) = S_{h,0},\ E_h(0) = E_{h,0},\ I_h(0) = I_{h,0},\ R_h(0) = R_{h,0},\ S_v(0) = S_{v,0},\ E_v(0) = E_{v,0},\ I_v(0) = I_{v,0}.$, *exist, and the optimal control are* $u^* = (u_1^*,u_2^*,u_3^*,u_4^*,u_5^*)$ *such that*

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

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
$\Omega(t,S_h,E_h,I_h,R_h,S_v,E_v,I_v) = \{(A_1I_h+A_2I_v+A_3u_1^2+A_4u_2^2+A_5u_3^2+A_6u_4^2+A_7u_5^2)+\xi_i, g(x,u,t)\}$,
where $g(x,u,t) = (b_h+\gamma R_h-(2-u_1(t)-u_2(t))\frac{\beta_1\varepsilon_h\phi S_hI_v}{N_h}-d_hS_h, (2-u_1(t)-u_2(t))\frac{\beta_1\varepsilon_h\phi S_hI_v}{N_h}-(\alpha_h+d_h)E_h, \alpha_hE_h-(u_5(t)+\theta+\psi+d_h)I_h, (u_5(t)+\theta)I_h-(\gamma+d_h)R_h, b_v-(2-u_1(t)-u_2(t))\frac{\beta_2\varepsilon_v\phi S_vI_h}{N_h}-d_vS_v-(pu_3(t)+qu_4(t))S_v, (2-u_1(t)-u_2(t))\frac{\beta_2\varepsilon_v\phi S_vI_h}{N_h}-(\alpha_v+d_v)E_v-(pu_3(t)+qu_4(t))E_v, \alpha_vE_v-d_vI_v-(pu_3(t)+qu_4(t))I_v)^T$.
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
$\theta f_1 + (1-\theta)f_2 \in \Omega(t,S_h,E_h,I_h,R_h,S_v,E_v,I_v)\ \forall\ \theta \in [0,1]$.
Let $f_i \in \Omega(t,S_h,E_h,I_h,R_h,S_v,E_v,I_v)$ means that there exist $\xi_i \le 0$ 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: $\theta(f(S_h,E_h,I_h,R_h,S_v,E_v,I_v,u_1,u_2,u_3,u_4,u_5)+\xi_1)+(1-$

$\theta)(f(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_{11}, u_{21}, u_{31}, u_{41}, u_{51})+\xi_2)\theta(A_1I_h+A_2I_v+A_3u_1^2$
$+A_4u_2^2+A_5u_3^2+A_6u_4^2+A_7u_5^2+\xi_1)+(1-\theta)(A_1I_h+A_2I_v+A_3u_{11}^2+A_4u_{21}^2+$
$A_5u_{31}^2+A_6u_{41}^2+A_7u_{51}^2+\xi_2)$.
$\theta(A_1I_h+A_2I_v+A_3u_1^2+A_4u_2^2+A_5u_3^2+A_6u_4^2+A_7u_5^2)+(1-\theta)(A_1I_h+A_2I_v+$
$A_3u_{11}^2+A_4u_{21}^2+A_5u_{31}^2+A_6u_{41}^2+A_7u_{51}^2)+\theta\xi_1+(1-\theta)\xi_2$.

Suppose $u_6=\sqrt{\theta A_3u_1^2+(1-\theta)A_3u_{11}^2}$, we observed that $u_6\in U$. 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 $\Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$.

Next, we work on the second part of the function $\Omega(t, S_h, E_h, I_h, R_h, S_v, E_v, I_v)$ such that: $g(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_1, u_2, u_3, u_4, u_5)=(b_h+\gamma R_h-(2-u_1(t)-u_2(t))\frac{\beta_1\varepsilon_h\phi S_hI_v}{N_h}-d_hS_h, (2-u_1(t)-u_2(t))\frac{\beta_1\varepsilon_h\phi S_hI_v}{N_h}-(\alpha_h+d_h)E_h, \alpha_hE_h-(u_5(t)+\theta+\psi+d_h)I_h, (u_5(t)+\theta)I_h-(\gamma+d_h)R_h, b_v-(2-u_1(t)-u_2(t))\frac{\beta_2\varepsilon_v\phi S_vI_h}{N_h}-d_vS_v-(pu_3(t)+qu_4(t))S_v, (2-u_1(t)-u_2(t))\frac{\beta_2\varepsilon_v\phi S_vI_h}{N_h}-(\alpha_v+d_v)E_v-(pu_3(t)+qu_4(t))E_v, \alpha_vE_v-d_vI_v-(pu_3(t)+qu_4(t))I_v)^T$
$g(S_h, E_h, I_h, R_h, S_v, E_v, I_v, u_{11}, u_{21}, u_{31}, u_{41}, u_{51})=\Big(b_h+\gamma R_h-\big(2-u_{11}(t)-u_{21}(t)\big)\frac{\beta_1\varepsilon_h\phi S_hI_v}{N_h}-d_hS_h, \big(2-u_{11}(t)-u_{21}(t)\big)\frac{\beta_1\varepsilon_h\phi S_hI_v}{N_h}-\big(\alpha_h+d_h\big)E_h, \alpha_hE_h-\big(u_{51}(t)+\theta+\psi+d_h\big)I_h, \big(u_{51}(t)+\theta\big)I_h-\big(\gamma+d_h\big)R_h, b_v-\big(2-u_{11}(t)-u_{21}(t)\big)\frac{\beta_2\varepsilon_v\phi S_vI_h}{N_h}-d_vS_v-\big(pu_{31}(t)+qu_{41}(t)\big)S_v, \big(2-u_{11}(t)-u_{21}(t)\big)\frac{\beta_2\varepsilon_v\phi S_vI_h}{N_h}-(\alpha_v+d_v)E_v-\big(pu_{31}(t)+qu_{41}(t)\big)E_v, \alpha_vE_v-d_vI_v-\big(pu_{31}(t)+qu_{41}(t)\big)I_v\Big)^T$.

(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: $N_h=S_h+E_h+I_h+R_h$ and $N_v=S_v+E_v+I_v$. The derivatives of N_h and N_v with respect to time are given by:

$$\frac{dN_h}{dt} = b_h-d_hN_h-\psi I_h, \tag{6}$$

$$\frac{dN_v}{dt} = b_v-(d_v+qu_4+pu_3)N_v. \tag{7}$$

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

$\Delta_v = (S_v, E_v, I_v | S_v + E_v + I_v \leq \frac{b_v}{(d_v+qu_4+pu_3)}, 0 \leq S_v \leq S_v(t) \leq \frac{b_v}{(d_v+qu_4+pu_3)}, E_v \geq 0, I_v \geq 0)$. 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,

$$\frac{b_h}{d_h + \psi} \leq \liminf_{t\to\infty} N_h(t) \leq \limsup_{t\to\infty} N_h(t) \leq \frac{b_h}{d_h}$$

and

$$\frac{b_v}{(d_v + qu_4 + pu_3)} \leq \liminf_{t\to\infty} N_v(t) \leq \limsup_{t\to\infty} N_v(t) \leq \frac{b_v}{(d_v + qu_4 + pu_3)}$$

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 are 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 $J(u_1, u_2, u_3, u_4, u_5) \geq b(|u_1(t)|^2 + |u_2(t)|^2 + |u_3(t)|^2 + |u_4(t)|^2 + |u_5(t)|^2)^{\frac{\beta}{2}} - b_2$. By standard control arguments involving the bounds on the controls, we conclude for $i = 1, 2, ..., 5$:

$$u_i^* = \begin{cases} 0 \text{ if } r_i^* \leq 0, \\ r_i^* \text{ if } 0 < r_i^* < 1, \\ 1 \text{ if } r_i^* \geq 1, \end{cases} \tag{8}$$

where $u_i^* = \frac{\beta_1 \varepsilon_h \phi I_v S_h (\lambda_{E_h} - \lambda_{S_h}) + \beta_2 \varepsilon_v \phi I_h S_v (\lambda_{E_v} - \lambda_{S_v})}{2A_i N_h}$, for $i = 1, 2$;
$u_3^* = \frac{p(S_v \lambda_{S_v} + I_v \lambda_{I_v})}{2A_5}$; $u_4^* = \frac{q(S_v \lambda_{S_v} + E_v \lambda_{E_v} + I_v \lambda_{I_v})}{2A_6}$; $u_5^* = \frac{(I_h \lambda_{I_h} + I_h \lambda_{R_h})}{2A_7}$.

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

$$\begin{aligned}
\frac{d\lambda_{S_h}}{dt} &= \frac{(\lambda_{S_h}-\lambda_{E_h})(2-u_1-u_2)\beta_1\varepsilon_h\phi I_v}{N_h} + d_h\lambda_{S_h}S_h \\
\frac{d\lambda_{E_h}}{dt} &= (\alpha_h + d_h)\lambda_{E_h} - \alpha_h\lambda_{I_h} \\
\frac{d\lambda_{I_h}}{dt} &= (u_5 + \theta + \psi + d_h)\lambda_{I_h} - \theta\lambda_{R_h} + \frac{(\lambda_{S_v}-\lambda_{E_v})(2-u_1-u_2)\beta_2\varepsilon_v\phi S_v}{N_h} \\
\frac{d\lambda_{R_h}}{dt} &= \gamma\lambda_{S_h} + (\gamma + d_h)\lambda_{R_h} \\
\frac{d\lambda_{S_v}}{dt} &= \frac{(\lambda_{S_v}-\lambda_{E_v})(2-u_1-u_2)\beta_2\varepsilon_v\phi S_v}{N_h} + (pu_3 + qu_4 + d_v)\lambda_{S_v} \\
\frac{d\lambda_{E_v}}{dt} &= (pu_4 + qu_5 + d_v + \alpha_v)\lambda_{E_v} - \alpha_v I_v \\
\frac{d\lambda_{I_v}}{dt} &= \frac{\lambda_{S_h}(2-u_1-u_2)\beta_1\varepsilon_h\phi S_h}{N_h} + (pu_3 + qu_4 + d_v)\lambda_{I_v} - \frac{\lambda_{E_h}(2-u_1-u_2)\beta_1\varepsilon_h\phi S_h}{N_h}.
\end{aligned} \tag{9}$$

with terminal conditions

$$\lambda_{S_h}(t_f) = \lambda_{E_h}(t_f) = \lambda_{I_h}(t_f) = \lambda_{R_h}(t_f) = \lambda_{S_v}(t_f) = \lambda_{E_v}(t_f) = \lambda_{I_v}(t_f) = 0 \tag{10}$$

Moreover,

$$\begin{aligned}
u_1^*(t) &= \left(1, \max\left(0, \min\frac{\beta_1\varepsilon_h\phi I_v S_h(\lambda_{E_h}-\lambda_{S_h}) + \beta_2\varepsilon_v\phi I_h S_v(\lambda_{E_v}-\lambda_{S_v})}{A_1 N_h}\right)\right) \\
u_2^*(t) &= \left(1, \max\left(0, \min\frac{\beta_1\varepsilon_h\phi I_v S_h(\lambda_{E_h}-\lambda_{S_h}) + \beta_2\varepsilon_v\phi I_h S_v(\lambda_{E_v}-\lambda_{S_v})}{A_2 N_h}\right)\right) \\
u_3^*(t) &= \left(1, \max\left(0, \min\frac{p(S_v\lambda_{S_v} + E_v\lambda_{E_v} + I_v\lambda_{I_v})}{A_3},\right)\right) \\
u_4^*(t) &= \left(1, \max\left(0, \min\frac{q(S_v\lambda_{S_v} + E_v\lambda_{E_v} + I_v\lambda_{I_v})}{A_4},\right)\right) \\
u_5^*(t) &= \max\left\{0, \min\left(1, \frac{(I_h\lambda_{I_h} + I_h\lambda_{R_h})}{2A_7}\right)\right\}.
\end{aligned} \tag{11}$$

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)

$$\frac{d\lambda(t)}{dt} = -\frac{\partial H}{\partial x} = -f_x - W_x\lambda(t). \tag{12}$$

Then the adjoint system can be written as

$$\begin{aligned}
\frac{d\lambda_{S_h}}{dt} &= \frac{(\lambda_{S_h}-\lambda_{E_h})(1-u_2)\beta_1\varepsilon_h\phi I_v}{N_h} + d_h\lambda_{S_h}S_h \\
\frac{d\lambda_{E_h}}{dt} &= (\alpha_h+d_h)\lambda_{E_h} - \alpha_h\lambda_{I_h} \\
\frac{d\lambda_{I_h}}{dt} &= (u_5+\theta+\psi+d_h)\lambda_{I_h} - \theta\lambda_{R_h} + \frac{(\lambda_{S_v}-\lambda_{E_v})(1-u_2)\beta_2\varepsilon_v\phi S_v}{N_h} \\
\frac{d\lambda_{R_h}}{dt} &= \gamma\lambda_{S_h} + (\gamma+d_h)\lambda_{R_h} \\
\frac{d\lambda_{S_v}}{dt} &= \frac{(\lambda_{S_v}-\lambda_{E_v})(2-u_1-u_2)\beta_2\varepsilon_v\phi S_v}{N_h} + (pu_3+qu_4+d_v)\lambda_{S_v} \\
\frac{d\lambda_{E_v}}{dt} &= (pu_4+qu_5+d_v+\alpha_v)\lambda_{E_v} - \alpha_v I_v \\
\frac{d\lambda_{I_v}}{dt} &= \frac{\lambda_{S_h}(2-u_1-u_2)\beta_1\varepsilon_h\phi S_h}{N_h} + (pu_3+qu_4+d_v)\lambda_{I_v} - \frac{\lambda_{E_h}(2-u_1-u_2)\beta_1\varepsilon_h\phi S_h}{N_h}.
\end{aligned} \tag{13}$$

with transversality conditions

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

We have on the interior of the control set U, where $0 \le u_i \le 1$, for $i = 1, 2, \ldots 5$;

$0 = \frac{\partial H}{\partial u_1} = \frac{\beta_1\varepsilon_h\phi I_v^* S_h^* \lambda_{S_h}}{N_h} - \frac{\beta_1\varepsilon_h\phi I_v^* S_h^* \lambda_{E_h}}{N_h} + \frac{\beta_2\varepsilon_v\phi I_h^* S_v^* \lambda_{S_v}}{N_h} - \frac{\beta_2\varepsilon_v\phi I_h^* E_v^* \lambda_{S_h}}{N_h} + 2A_1u_1^*$

$0 = \frac{\partial H}{\partial u_2} = \frac{\beta_1\varepsilon_h\phi I_v^* S_h^* \lambda_{S_h}}{N_h} - \frac{\beta_1\varepsilon_h\phi I_v^* S_h^* \lambda_{E_h}}{N_h} + \frac{\beta_2\varepsilon_v\phi I_h^* S_v^* \lambda_{S_v}}{N_h} - \frac{\beta_2\varepsilon_v\phi I_h^* E_v^* \lambda_{S_h}}{N_h} + 2A_2u_2^*$

$0 = \frac{\partial H}{\partial u_3} = -p(S_v\lambda_{S_v} + I_v\lambda_{I_v}) + 2A_5u_3^*$

$0 = \frac{\partial H}{\partial u_4} = -q(S_v\lambda_{S_v} + E_v\lambda_{E_v} + I_v\lambda_{I_v}) + 2A_6u_4^*$

$0 = \frac{\partial H}{\partial u_5} = -(I_h\lambda_{I_h} + I_h\lambda_{R_h}) + 2A_7u_5^*.$

Hence we obtain the following

$r_i^*(t) = \frac{\beta_1\varepsilon_h\phi I_v S_h(\lambda_{E_h}-\lambda_{S_h}) + \beta_2\varepsilon_v\phi I_h S_v(\lambda_{E_v}-\lambda_{S_v})}{2A_1N_h}$, for $i = 1, 2$,

$r_3^*(t) = \frac{p(S_v\lambda_{S_v}+I_v\lambda_{I_v})}{2A_5}$, $r_4^*(t) = \frac{q(S_v\lambda_{S_v}+E_v\lambda_{E_v}+I_v\lambda_{I_v})}{2A_6}$, $r_5^*(t) = \frac{(I_h\lambda_{I_h}+I_h\lambda_{R_h})}{2A_7}$

and receive the (10).

Now the Pontryagin's Maximum Principle (PMP) gives the following necessary conditions to obtain the optimality pair(x^*, u^*) $\frac{\partial H(x,u^*,\lambda,t)}{\partial u} = 0$, $H(x, u^*, \lambda, t) = f(x, u, t) + \lambda^{t_f} g(x, u, t)$. 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:

$$\begin{aligned}
\frac{dS_h}{dt} &= b_h + \gamma R_h - (2-u_1-u_2)\frac{\beta_1\varepsilon_h\phi S_h I_v}{N_h} - d_hS_h \\
\frac{dE_h}{dt} &= (2-u_1-u_2)\frac{\beta_1\varepsilon_h\phi S_h I_v}{N_h} - (\alpha_h+d_h)E_h \\
\frac{dI_h}{dt} &= \alpha_hE_h - (u_3+\theta+\psi+d_h)I_h \\
\frac{dR_h}{dt} &= (u_5+\theta)I_h - (\gamma+d_h)R_h \\
\frac{dS_v}{dt} &= b_v - (2-u_1-u_2)\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - d_vS_v - (pu_3+qu_4)S_v \\
\frac{dE_v}{dt} &= (2-u_1-u_2)\frac{\beta_2\varepsilon_v\phi S_v I_h}{N_h} - (\alpha_v+d_v)E_v - (pu_3+qu_4)E_v \\
\frac{dI_v}{dt} &= \alpha_vE_v - d_vI_v - (pu_3+qu_4)I_v.
\end{aligned} \tag{14}$$

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:

$$\begin{aligned}
\frac{d\lambda_{S_h}}{dt} &= \frac{(\lambda_{S_h}-\lambda_{E_h})(2-u_1-u_2)\beta_1\varepsilon_h\phi I_v}{N_h} + d_h\lambda_{S_h}S_h \\
\frac{d\lambda_{E_h}}{dt} &= (\alpha_h + d_h)\lambda_{E_h} - \alpha_h\lambda_{I_h} \\
\frac{d\lambda_{I_h}}{dt} &= (u_5 + \theta + \psi + d_h)\lambda_{I_h} - \theta\lambda_{R_h} + \frac{(\lambda_{S_v}-\lambda_{E_v})(2-u_1-u_2)\beta_2\varepsilon_v\phi S_v}{N_h} \\
\frac{d\lambda_{R_h}}{dt} &= \gamma\lambda_{S_h} + (\gamma + d_h)\lambda_{R_h} \\
\frac{d\lambda_{S_v}}{dt} &= \frac{(\lambda_{S_v}-\lambda_{E_v})(2-u_1-u_2)\beta_2\varepsilon_v\phi S_v}{N_h} + (pu_3 + qu_4 + d_v)\lambda_{S_v} \\
\frac{d\lambda_{E_v}}{dt} &= (pu_3 + qu_4 + d_v + \alpha_v)\lambda_{E_v} - \alpha_v I_v \\
\frac{d\lambda_{I_v}}{dt} &= \frac{\lambda_{S_h}(2-u_1-u_2)\beta_1\varepsilon_h\phi S_h}{N_h} + (pu_3 + qu_4 + d_v)\lambda_{I_v} - \frac{\lambda_{E_h}(2-u_1-u_2)\beta_1\varepsilon_h\phi S_h}{N_h}.
\end{aligned} \tag{15}$$

Transversality conditions:

$$\lambda_{S_h}(t_f) = \lambda_{E_h}(t_f) = \lambda_{I_h}(t_f) = \lambda_{R_h}(t_f) = \lambda_{S_v}(t_f) = \lambda_{E_v}(t_f) = \lambda_{I_v}(t_f) = 0. \tag{16}$$

Characterization of the optimal control u_1^*,u_2^*,u_3^*,u_4^*,u_5^*:
$\frac{\partial H}{\partial u_1} = \frac{\partial H}{\partial u_2} = \frac{\partial H}{\partial u_3} = \frac{\partial H}{\partial u_4} = \frac{\partial H}{\partial u_5} = 0$ at $u_1 = u_1^*$, $u_2 = u_2^*$,$u_3 = u_3^*$, $u_4 = u_4^*$,$u_5 = u_5^*$ on the set $\{t \in [0, t_f] : 0 \leq u_1 \leq 1, 0 \leq u_2 \leq 1, 0 \leq u_3 \leq 1, 0 \leq u_4 \leq 1, 0 \leq u_5 \leq 1\}$. That is we have (7). □

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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