Original Research Article

Mathematical Modelling of Malaria Transmission Dynamics with Optimal Control Strategies in Kebri Dehar District, Somali Regional State, Ethiopia

Abstract

Malaria is an infectious disease caused by the Plasmodium parasite and transmitted between humans through bites of female anopheles mosquito. In this study, we present a mathematical model of malaria transmission dynamics with optimal control. We estimated the basic reproduction number for the infected cases in Kebri Dehar district from September 2011 - June 2015 E.C is $R_0 \approx 24.494779$. *The parameters of the model are estimated by using the confirmed malaria cases of Kebri Dehar district, Ethiopia. We formulated the model for malaria and present its dynamics in details. Initially, we present the basic mathematical results and then show briefly the stability results for the model. Further, we formulate an optimal control problem with control functions and obtain the optimal control characterization. The optimal control problem is solved numerically and the results comprised of controls system for different strategies. The controls such as prevention, treatment and insecticide could use the best role in the disease eradication from the community. Our results suggest that the prevention of humans from the mosquitoes, treatment of infected humans and the insecticide spray on mosquitoes can significantly reduce the infection of malaria and may reduce further spread of infection in the community.*

Keywords: Malaria model, Basic reproduction number, sensitivity, Equilibrium, Numerical Analysis

1. Introduction

Malaria is an acute febrile illness caused by the plasmodium parasite and transmitted between humans through the bite of female Anopheles mosquito. The male mosquitoes survive by feeding on flower nectar and sweet juices. Female mosquitoes not only feed on various sugars for energy, but also require the nutrition of blood for the development of their eggs. Without regular intakes of blood, their ability to reproduce quickly diminishes (CDC, 2022., Shewakena and Temesgen, 2021).There is more than 100 species of Plasmodium, which can infect many animal species such as reptiles, birds, and various mammals (CDC, 2022). Until recently, there were four plasmodium species that were considered responsible for malaria disease in humans: *Plasmodium vivax, Plasmodium falciparum, Plasmodium ovale and Plasmodium malariae. Plasmodium falciparum* which is responsible for nearly 80% of all recorded malaria cases all over the world and 90% of deaths is very common in the tropical areas of Africa and South East Asia (Bakary *et al.*,2018).Malaria causes symptoms that typically include fever, tiredness, vomiting, and headaches.

Malaria is caused by the multiplication of parasitic protozoa of the family Plasmodia within the blood cells or other tissues of the vertebrate host; the clinical symptoms in man arise from multiplication of the blood stages. Although there are several genera of malarial parasites related to many varieties of hosts, the human malaria is caused by five different species of Plasmodium: *Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale, plasmodium vivax and*

Plasmodium knowlesi. Of these, Plasmodium *falciparum* is that the common in tropical regions, and Plasmodium *vivax* in temperate zones(Bakary *et al.*,2018).The biology of the five species of Plasmodium is mostly similar and consists of two distinct phases: a sexual stage at the mosquito host and an asexual stage at the human host (CDC, 2022., Olumese,2005).Malaria transmission occurs in five WHO (World Health Organization) regions, which are Africa, South-East Asia, Eastern Mediterranean, Western Pacific, and America. Approximately half of the world's population is at risk of malaria (WHO, 2020.,WHO, 2021., WHO, 2022). Most malaria cases and deaths occur in Sub-Saharan Africa (GHO, 2021). However, since 2000, substantial progress has been made in fighting malaria. According to the World Malaria Report 2020, between 2000 and 2020, malaria case incidence was reduced by 41% and malaria mortality rates by 62% (WHO, 2021., Shewakena and Temesgen,2021).

In, 2020, an estimated 241 million cases of malaria occurred worldwide most of which were in the WHO African Region (228 million or 95%), followed by the WHO South East Asia Region with 2% of the cases and the WHO Eastern Mediterranean Region with 2.1%.Twenty-nine countries in sub-Saharan Africa and India carried almost 83% of the global malaria burden. The incidence rate of malaria declined globally between 2000 and 2020, from 81 in 2000 to 59 in 2015 and 56 in 2019, before increasing again to 59 in 2020. The increase in 2020 was associated with disruption to services during the COVID-19 pandemic (WHO, 2021., Shewakena and Temesgen,2021).In 2020, there were an estimated 627 000, deaths from malaria globally, compared with 558 000 estimated deaths in 2019, and 558 000 in 2000. Children aged under five years are the most vulnerable group suffering from malaria. In 2020, they accounted for 80% (497 000) of all malaria deaths worldwide. The WHO African Region accounted for 95% of all malaria deaths in 2020. Although this region was home to the highest number of malaria deaths in 2020, Malaria is a severe disease in Ethiopia, more than 60 percent of the population lives in malarious areas, and 68 percent of the countries landmass is favorable for malaria transmission, with malaria primarily associated with altitude and rainfall (Deribew *et al.*,2017., Ethiopia Malaria Operational Plan, 2022). Peak malaria transmission occurs between September and December in most parts of Ethiopia, after the most seasons from June to August. Additionally, some areas experience a second minor malaria transmission period from April to June, following a brief season from February to March (Aschalew and Tadesse, 2016). *Plasmodium falciparum* and *plasmodium vivax* are commonly known species in Ethiopia to cause malaria accounting for 60% and 40%, respectively (Girum *et al*.,2019., Ethiopia Malaria Operational Plan,2022). The most recent, publicly available malaria case data was published in the FMOH Annual Review Meeting report from PHEM data spanning the twelvemonth interval between mid-2019 until mid-2020. It reported a total of 2,320,135 malaria illnesses including 1,325,409 laboratory confirmed *plasmodium falciparum* malaria illnesses, 707,901 laboratory confirmed *plasmodium vivax* malaria illnesses, and 286,825 clinical malaria cases. Mixed infections were counted as *P. falciparum* and there was no report of *plasmodium ovale* or *plasmodium malariae* from the routine health information system. Five hundred ten deaths were reported due to malaria (Ethiopia

Malaria Operational Plan, 2022). The burdens of malaria in Ethiopia are lost productive personnel due to illness, school absenteeism; medical costs and other indirect costs including adult laborers are infected by malaria (Aschalew and Tadesse, 2016).

The distribution and transmission of malaria in Ethiopia varies from place to place. For instance, the distribution of malaria in Ethiopia is essentially determined by altitude. Altitude affects the pattern of malaria distribution in Ethiopia through its effect on temperature (Chitnis *et al.*,2008).

Risk of malaria is highest within the western lowlands of Oromia, Amhara, Tigray and almost the whole regions of Gambella and Benishangul Gumuz regions. The midlands of Ethiopia between 1,000-meters and 2000-meters altitude experience seasonal transmission of malaria with sporadic (irregular) epidemics every few years. In the eastern lowlands of Ethiopia (primarily Afar and Somali), malaria is endemic only along the rivers, as this a part of the country is basically dry faraway from rivers. Transmission is limited by the shortage of water collections for mosquito breeding and low humidity because of low rainfall and sparse vegetation. The central highlands of Ethiopia are freed from malaria mainly because of the low temperatures, which slows the event of the vector and also the parasite (Ketema *et al.*,2009., Ethiopia EpidemiologicalMalaria,2022)

Ethiopia has registered remarkable progress in decreasing the burden of malaria and other major infectious diseases over the last two years (UNDP,2014., FMOH,2016). Over the last decade, the burden of malaria has decreasing significantly, which might be the results of improved coverage of high impact interventions, like prompt treatment of cases using artemisinin-based combination therapy (ACT), prevention and control of malaria among pregnant women using intermittent preventive therapy (IPT), use vector control methods including insecticide-treated bed nets (ITNs), and indoor residual spray (IRS) (Aregawi *et al.*,2014., Abeku, *et al.*,2015). Malaria deaths and admissions in children age under-5 fell by 81 and 73%, respectively, after the scale-up of ITNs, IRS and ACT interventions between 2006 and 2011 (Aregawi *et al.*,2014). However, malaria remains a serious health problem for Ethiopia where only 25% of the population board areas that are free from malaria (Adhanom *et al.,* 2006). It's still among the ten top leading causes of morbidity and mortality in children under-5 years (Deribew *et al.*,2017., Ethiopia Epidemiological Malaria,2022).In Somali Regional State, malaria ranks the second top disease and *Plasmodium Falciparum* is the dominant species (WHO, 2003).A total of 8,689 cases of malaria cases was reported during the reporting period of June – Oct 2012 of these, 3,779 cases from Shebelle; 198 cases with 6 deaths in Fafan zone; 1,368 cases with one death was reported from Korahey; 1,342 cases with one death was also reported from Erer Woreda of Siti zone. In addition Afder zone has reported 2,002 clinical and confirmed malaria cases with 17 deaths (WFP, UNICEF and INGO,2012). High population movements, Internally Displaced Persons (IDPs) and refugees characterize the Region. Frequent floods and man-made water reservoir contribute to periodic epidemics of malaria (WHO,2003).

Mathematical models are tools to understand the dynamics of the transmission of infectious diseases (Chitins *et al*.,2006., Olaniyi and Obabiyi ,2013., Ngwa and Shu,2000). Another form of mathematical models that can be used to control the spread of diseases is by incorporating optimal control strategies that are effective in preventing and treating the infectious diseases (Gabriel and Joseph, 2016., Fekade and Koya ,2015., Bundit and Unyong ,2018).Some of the researchers have used optimal control theory to study the transmission dynamics of malaria, for example, the authors in(Gabriel and Joseph,2016), have reviewed an optimal control which reduces the spread of malaria by using insecticide treated bed nets *(ITNs),* treatment, indoor residual spray *(IRS),* and intermittent preventive treatment of malaria in pregnancy *(IPTP).* Fekade and Koya (2015) have discussed an optimal control model which aims to reduce the spread of malaria with treatment and protective measurements like *IRS* and *ITN* as optimal control. Authors in (Abiodun and Okosun, 2018) reviewed a mathematical model of the relationship of climate factors in the form of changes in temperature and rainfall in malaria which plays an important role in the rate of malaria. Authors in(Fatmawati *et al.*,2021) analyzed

a mathematical model considering the relationship of climate factors in malaria model with seasonal factors and the breakdown of exposed individuals into exposed individuals with short-term and long-term incubation periods. Still know to the best knowledge of the researchers, there is no mathematical model has been done before this study in relating to malaria in Kebri Dehar district. Since, mathematical models are key tools to identify the dynamic of disease, influencing parameters and to provide better control polices. So those, dynamic of malaria and influencing parameters are not determined in this area of study. Based on the description above, the researcher will motivated in modifying *SEIR* model of malaria transmission, which will determine the extinction or persistence of the disease in Kebri Dehar district using real data by subdividing the exposed individuals into two categories, which are individuals based on the incubation periods, that is, exposed individuals with short-term and long-term incubation periods with addition of seasonal factors to the model. In addition, we will propose an optimal control problem which takes into account the permissible controls in the form of using insecticides, prevention, and treatment effort on the control of malaria

2. Study area

The study will be conducted in Kebri Dehar district of korahe zone, Somali region. The topography of the study area is predominantly lowland plain with an average altitude of 493 m above sea level with a few foothills of higher altitude. The study area has a latitude and longitude of $6^0 44' - 7^0 68'$N, $44^0 16' - 45^0 0'$E, respectively. It is located at 980 km away from Addis Ababa, the capital of Ethiopia and 380 km away from Jigjiga, the capital of

Somali region. The climate of the study area is found within the tropics and experiences high incoming solar insulation due to high angle of the solar rays. The region's temperature ranges from $23^0 C$ to $30^0 C$. This district has bimodal rainfall pattern. The first and main rainy season 'Gu' occurs from mid-April to the end of June. A secondary rainy season known as 'Deyr' occurs from early October to late December. Overall the annual precipitation averages 200mm.

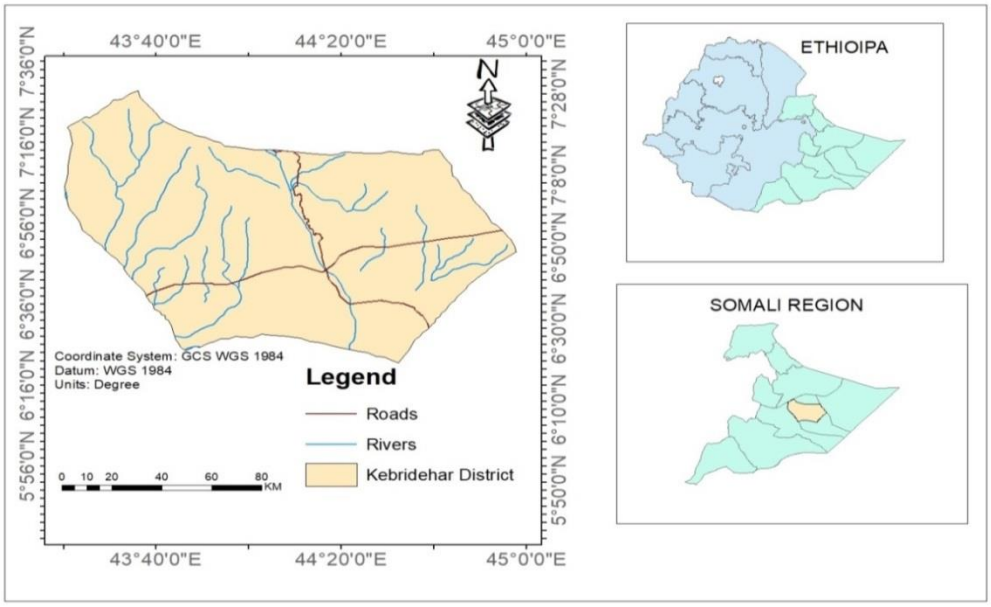

Figure 1: Map of the study area.

According to the 2007 Census conducted by the Central Statistical Agency of Ethiopia (CSA 2007), this district has a total population of 136,142, of whom 77,685 are men and 58,457 women. While 29,241 or 21.48% are urban inhabitants, a further 50,361 or 36.99% are pastoralists. Based on the result of housing and population census of May, 2007, in 2017 the projected population of Kebri Dehar district is 176,494 people, out of this 97,694 are males and 78,800 are females.

3. Model Formulation and Analysis

In this study transmission and spread of malaria disease between two interacting populations of humans (the host) and mosquitoes (the vector) has been considered. In the model the total human population, denoted by N_h is divided into five epidemiological categories representing the state variables: The susceptible class(S_h), which contains humans those do not have malaria disease but are likely to be bitten by infected female anopheles mosquitoes causing malaria. The exposed class(E_h)which contains humans those is already infected but not yet infectious. The infectious class(I_h), which contains humans those is already infected and got malaria disease so can transmit the disease and the recovered class(R_h), which contains the people who recover from the malaria disease and return to normal status of health.

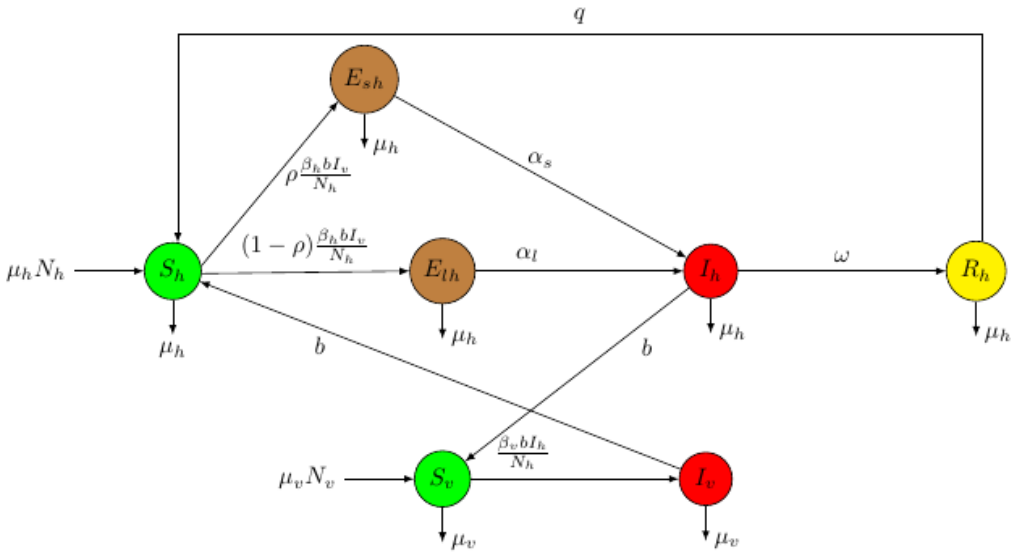

Figure 2: Schematic diagrams for the dynamic of the malaria.

3.1. Model assumption

To describe the transmission of malaria, we assume $SEIRS$ disease dynamics for the human and SI for the mosquito population. Exposed humans are divided into two classes by having short term or long term incubation periods. If a susceptible human S_h is successfully infected by a mosquito I_v, then this individual goes through short incubation period E_{sh} with probability ρ, or long incubation period E_{lh} with probability $(1-\rho)$; then becomes infectious I_h after this incubation time and be able to infect susceptible mosquitoes S_v. Recovered humans are in the class R_h, and return to S_h after their immunity decreases. Every class of humans population is decreased by natural death with the rates μ_h.

The cross-infection between mosquitoes and humans is described by the terms, $\frac{\beta_h S_h I_v}{N_h}$ and $\frac{\beta_v S_v I_h}{N_h}$,where the infection rates β_h and β_v are computed as $\beta_h = b\beta_h$ and $\beta_v = b\beta_v$, b, is the biting

rate. Moreover, $b\beta_h$ denotes the transmission probability from the infected mosquitoes to humans, and $b\beta_v$ denotes the transmission probability from infected humans to susceptible mosquitoes. All newborn humans and mosquitoes are susceptible. The birth rate is equal to the death rate in both of mosquito and human populations. No malaria transmission in blood transmission. The human and mosquito populations are constant.

Table 1: State variables of the model.

State variable	Description
S_h	Susceptible human population
S_v	Susceptible mosquito population
I_v	Infectious mosquito population
I_h	Infectious human population
E_{sh}	Exposed human population having a short-term incubation period
E_{lh}	Exposed human population having a long-term incubation period
R_h	Recovered human population

Table2: Parameters of the model.

Parameters	Description
β_h	Infection rate from mosquito to human
β_v	Infection rate from human to mosquito
μ_h	Natural death/birth rate of human
μ_v	Natural death/birth rate of mosquito
ρ	Probability of exposed humans going through short-term incubation periods
$\frac{1}{\alpha_s}$	Short-term latent period for human
$\frac{1}{\alpha_l}$	Long-term latent period for human
ω	Spontaneous recovery rate
q	Waning immunity rate

The above flow diagram can be written in the seven systems of non-linear differential equations such as:

$$\begin{cases} \frac{dS_h}{dt} = \mu_h N_h + qR_h - \frac{\beta_h S_h I_v}{N_h} - \mu_h S_h \\ \frac{dE_{sh}}{dt} = \frac{\rho\beta_h S_h I_v}{N_h} - (\alpha_s + \mu_h)E_{sh} \\ \frac{dE_{lh}}{dt} = \frac{(1-\rho)\beta_h S_h I_v}{N_h} - (\alpha_l + \mu_h)E_{lh} \\ \frac{dI_h}{dt} = \alpha_s E_{sh} + \alpha_l E_{lh} - (\mu_h + \omega)I_h \\ \frac{dR_h}{dt} = \omega I_h - \mu_h R_h - qR_h \\ \frac{dS_v}{dt} = \mu_v N_v - \frac{\beta_v S_v I_h}{N_h} - \mu_v S_v \\ \frac{dI_v}{dt} = \frac{\beta_v S_v I_h}{N_h} - \mu_v I_v \end{cases} \quad (3.1)$$

where, $N_v = S_v + I_v$ is the total population of mosquitoes and $N_h = S_h + E_{sh} + E_{lh} + I_h + R_h$ is the total population of humans. The biologically feasible domain region of model (3.1) is given by $\Omega = \Omega_v \times \Omega_h$ where, $\Omega_v = \{(S_v, I_v) \in R^{2+}: S_v + I_v = N_v\}$ and $\Omega_h = \{(S_h, E_{sh}, E_{lh}, I_h, R_h) \in R^{5+}: S_h + E_{sh} + E_{lh} + I_h + R_h = N_h\}$

3.2.1 . Model analysis

In this section, we analyze the local stability of equilibria of model(3.1). First, we determine the equilibrium with its conditions of existence and the basic reproduction number. From model(3.1), we obtain two equilibria, namely the disease-free equilibrium and the endemic equilibrium.

3.2. Equilibrium points

The equilibrium point of the system is the solution of the system of equations

$$\begin{cases} \mu_v N_v - \frac{\beta_v S_v I_h}{N_h} - \mu_v S_v = 0 \\ \frac{\beta_v S_v I_h}{N_h} - \mu_v I_v = 0 \\ \mu_h N_h + qR_h - \frac{\beta_h S_h I_v}{N_h} - \mu_h S_h = 0 \\ \frac{\rho\beta_h S_h I_v}{N_h} - (\alpha_s + \mu_h)E_{sh} = 0 \\ \frac{(1-\rho)\beta_h S_h I_v}{N_h} - (\alpha_l + \mu_h)E_{lh} = 0 \\ \alpha_s E_{sh} + \alpha_l E_{lh} - (\mu_h + \omega)I_h = 0 \\ \omega I_h - \mu_h R_h - qR_h = 0 \end{cases} \quad (3.2)$$

Disease-free equilibrium

The disease-free equilibrium point $\mathcal{E}_0$ is obtained by setting $I_v = 0, E_{sh} = 0, E_{lh} = 0, I_h = 0$ in the system of equation(3.2). Therefore the disease-free equilibrium of malaria model is

$\mathcal{E}_0 = (N_v, 0, N_h, 0,0,0,0)$.

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The basic reproduction number

We determine the basic reproduction number R_0 that can be used to measure the potential of infection distribution in a population. By using the Next Generation Matrix method (Van and Watmough, 2002), we obtain the basic reproduction number R_0 from the equations (3.1), we have the following:

$$\mathcal{F} = \begin{pmatrix} \frac{\beta_v S_v I_h}{N_h} \\ \frac{\rho\beta_h S_h I_v}{N_h} \\ \frac{(1-\rho)\beta_h S_h I_v}{N_h} \\ 0 \end{pmatrix} \text{ and } \mathcal{V} = \mathcal{V}^- - \mathcal{V}^+ = \begin{pmatrix} \mu_v I_v \\ (\alpha_s + \mu_h)E_{sh} \\ (\alpha_l + \mu_h)E_{lh} \\ (\mu_h + \omega)I_h - \alpha_s E_{sh} - \alpha_l E_{lh} \end{pmatrix}$$

The Jacobian matrix of $\mathcal{F}$ evaluated at the disease free equilibrium point, $\mathcal{E}_0 = (N_v, 0, N_h, 0,0,0,0)$.

$$F = \frac{\partial \mathcal{F}(\mathcal{E}_0)}{\partial x_j} = \begin{pmatrix} 0 & 0 & 0 & \beta_v \\ \rho\beta_h & 0 & 0 & 0 \\ (1-\rho)\beta_h & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad j = I_v, E_{sh}, E_{lh}, I_h, \text{ for } j = 1,2,3,4.$$

The Jacobian matrix of $\mathcal{V}$ evaluated at the disease free equilibrium point, $\mathcal{E}_0 = (N_v, 0, N_h, 0,0,0,0)$

$$V = \frac{\partial \mathcal{V}(\mathcal{E}_0)}{\partial x_j} = \begin{pmatrix} \mu_v & 0 & 0 & 0 \\ 0 & (\alpha_s + \mu_h) & 0 & 0 \\ 0 & 0 & (\alpha_l + \mu_h) & 0 \\ 0 & -\alpha_s & -\alpha_l & (\mu_h + \omega) \end{pmatrix}$$

and

$$V^{-1} = \begin{pmatrix} \frac{1}{\mu_v} & 0 & 0 & 0 \\ 0 & \frac{1}{(\alpha_s + \mu_h)} & 0 & 0 \\ 0 & 0 & \frac{1}{(\alpha_l + \mu_h)} & 0 \\ 0 & \frac{\alpha_s}{(\mu_h + w)(\alpha_s + \mu_h)} & \frac{\alpha_l}{(\mu_h + \omega)(\alpha_l + \mu_h)} & \frac{1}{(\alpha_l + \mu_h)} \end{pmatrix}$$

The next generation matrix FV^{-1} is given by

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\alpha_s\beta_v}{(\mu_h+\omega)(\alpha_s+\mu_h)} & \frac{\alpha_l\beta_v}{(\mu_h+\omega)(\alpha_l+\mu_h)} & \frac{\beta_v}{(\alpha_l+\mu_h)} \\ \frac{\rho\beta_h}{\mu_v} & 0 & 0 & 0 \\ \frac{(1-\rho)\beta_h}{\mu_v} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

The dominant eigenvalue of the matrix FV^{-1} is $R_0 = \sqrt{\frac{\beta_v\beta_h\,[\rho\alpha_s\mu_h+\alpha_l(1-\rho)+\alpha_s]}{\mu_v(\alpha_l+\mu_h)(\mu_h+\omega)(\alpha_s+\mu_h)}}$

The term $\frac{\beta_h}{\mu_v}$,represents the number of new infected hosts produced from one infectious mosquito. Moreover, the term $\frac{\beta_v\,[\rho\alpha_s\mu_h+\alpha_l(1-\rho)+\alpha_s]}{(\alpha_l+\mu_h)(\mu_h+\omega)(\alpha_s+\mu_h)}$ represents the number of new infected mosquitoes produced from one infectious host during infectious period.

3.2.2. Stability analysis

Theorem: The disease-free equilibrium $\mathcal{E}_0$ is locally asymptotically stable if $R_0 < 1$.

Proof: First, we linearized model (3.1) near the disease-free equilibrium. The Jacobian matrix of model(3.1) at $\mathcal{E}_0$ is as following.

$$J_{\mathcal{E}_0} = \begin{pmatrix} -\mu_v & 0 & 0 & 0 & 0 & \frac{\beta_v N_v}{N_h} & 0 \\ 0 & -\mu_v & 0 & 0 & 0 & \frac{\beta_v N_v}{N_h} & 0 \\ 0 & -\beta_h & -\mu_h & 0 & 0 & 0 & q \\ 0 & \rho\beta_h & 0 & -(\alpha_s+\mu_h) & 0 & 0 & 0 \\ 0 & (1-\rho)\beta_h & 0 & 0 & -(\alpha_l+\mu_h) & 0 & 0 \\ 0 & 0 & 0 & \alpha_s & \alpha_l & -(\mu_h+\omega) & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega & -(\mu_h+q) \end{pmatrix}$$

To determine the stability of disease-free equilibrium point, we use the characteristics equation of the Jacobin matrix $J_{\mathcal{E}_0}$. The characteristics equation is given by

$$(\lambda+\mu_v)(\lambda+\mu_h)\big(\lambda+(\mu_h+q)\big)[\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_3] = 0$$

The Jacobian matrix gives seven eigenvalues, these are $-\mu_v, -\mu_v,$ or $-(\mu_h+q)$. The other eigenvalues are the roots of quartic equation

$$\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_3 = 0 \qquad (3.3)$$

where,

$a_1 = 3\mu_h+\alpha_l+\alpha_s+\mu_v+\omega$

$a_2 = (\mu_h+\omega)(\mu_h+\mu_v+\alpha_l)+\mu_v(\alpha_l+\mu_h)+(\alpha_s+\mu_h)+(2\mu_h+\alpha_l+\mu_v+\omega)$

$a_3 = \mu_v(\alpha_l+\mu_h)(\alpha_s+\mu_h)+(\alpha_s+\mu_h)(\alpha_l+\mu_h)(\omega+\mu_h)$
$+\mu_v(\omega+\mu_h)(\alpha_s+\mu_h)\left(1-\frac{\beta_h\beta_v N_v\alpha_s\rho}{\mu_v(\mu_h+\omega)(\alpha_s+\mu_h)}\right)$
$+\mu_v(\omega+\mu_h)(\alpha_l+\mu_h)\left(1-\frac{\beta_h\beta_v N_v\alpha_l(1-\rho)}{\mu_v(\mu_h+\omega)(\alpha_l+\mu_h)}\right)$

$a_4 = \mu_v(\omega + \mu_h)(\alpha_s + \mu_h)\mu_v(\omega + \mu_h)(\alpha_l + \mu_h)\left(1 - {R_0}^2\right)$

Based on the Routh-Hurwitz criteria, the quartic Equation(3.3) has roots whose real parts are negative if and only if $a_1, a_2, a_3, a_4 > 0$, and $a_1 a_2 a_3 > {a_3}^2 + {a_1}^2 a_4$. It is clear that the coefficients $a_1 . a_2 > 0$. It is also clear that the coefficient a_4 is positive if $R_0 < 1$. If $R_0 < 1$, then

$$\frac{\beta_h \beta_v N_v \alpha_s \rho}{\mu_v(\mu_h + \omega)(\alpha_s + \mu_h) + \frac{\beta_h \beta_v N_v \alpha_l (1-\rho)}{\mu_v(\mu_h + \omega)(\alpha_l + \mu_h)}} < 1$$

Hence, the coefficient a_3 is positive if $R_0 < 1$. It also can be verified that the condition $a_1 a_2 a_3 > {a_3}^2 + {a_1}^2 a_4$ is satisfied. Therefore, the disease-free equilibrium $\mathcal{E}_0$ is locally asymptotically stable if$R_0 < 1$. Theorem 1 shows that malaria will disappear from the population whenever $R_0 < 1$.

Global stability of disease-free equilibrium point

Theorem: If the basic reproduction number $R_0 < 1$ then the disease-free equilibrium point $\mathcal{E}_0$ of the model (3.1) is globally asymptotically stable.

Proof. To prove the global asymptotic stability of the disease-free equilibrium E0 we use the method of Lyapunov functions. We defined a Lyapunov function V such that;

$$\frac{dV}{dt} = a_1 \frac{dI_v}{dt} + a_2 \frac{dE_{sh}}{dt} + a_3 \frac{dE_{lh}}{dt} + a_4 \frac{dI_h}{dt} \qquad (3.2)$$

Where, a_i ,$i = 1,2,3,4$ are positive constants to be determined.

By substituting expressions for $\frac{dI_v}{dt}$, $\frac{dE_{sh}}{dt}$, $\frac{dE_{lh}}{dt}$, and $\frac{dI_h}{dt}$ from the system (3.1) to equation (3.2) we obtain the following:

$$\frac{dV}{dt} = a_1\left(\frac{\beta_v S_v I_h}{N_h} - \mu_v I_v\right) + a_2\left(\frac{\rho \beta_h S_h I_v}{N_h} - (\alpha_s + \mu_h)E_{sh}\right)$$
$$+ a_3\left(\frac{(1-\rho)\beta_h S_h I_v}{N_h} - (\alpha_l + \mu_h)E_{lh}\right) + a_4(\alpha_s E_{sh} + \alpha_l E_{lh} - (\mu_h + \omega)I_h)$$

Simplifying it, by collecting like terms of the equation we obtain the following:

$$\frac{dV}{dt} = \left[a_2 \frac{\rho \beta_h S_h}{N_h} + a_3 \frac{(1-\rho)\beta_h S_h}{N_h} - a_1 \mu_v\right] I_v + [\alpha_s a_4 - a_2(\alpha_s + \mu_h)]E_{sh}$$
$$+ [\alpha_l a_4 - a_3(\alpha_l + \mu_h)]E_{lh} + \left[a_1 \frac{\beta_v S_v}{N_h} - a_4(\mu_h + \omega)\right] I_h$$

Take the coefficients of I_v, E_{sh}, E_{lh} are equal to zero. That is,

$$i) \quad a_2 \frac{\rho \beta_h S_h}{N_h} + a_3 \frac{(1-\rho)\beta_h S_h}{N_h} - a_1 \mu_v = 0$$
$$ii) \quad \alpha_s a_4 - a_2(\alpha_s + \mu_h) = 0$$
$$iii) \quad \alpha_l a_4 - a_3(\alpha_l + \mu_h) = 0$$

Then we get

$$\frac{dV}{dt} = a_1 \frac{\beta_v S_v}{N_h} I_h - a_4(\mu_h + \omega)I_h.$$

Now from (ii) and (iii) we get

$$a_2 = \frac{\alpha_s}{(\alpha_s + \mu_h)} a_4 \qquad , a_3 = \frac{\alpha_l}{(\alpha_l + \mu_h)} a_4$$

Substitute $a_2 \ and \ a_3$ in (i) we get

$$\frac{\alpha_s}{(\alpha_s+\mu_h)}\frac{\rho\beta_h S_h}{N_h}a_4+\frac{\alpha_l}{(\alpha_l+\mu_h)}\frac{(1-\rho)\beta_h S_h}{N_h}a_4=a_1\mu_v$$

$$\frac{dV}{dt}=\left(\frac{\beta_v\beta_h S_v S_h}{N_h}\left[\frac{\alpha_s\mu_h\rho+\alpha_l\alpha_s+\alpha_l\mu_h-\alpha_l\mu_h\rho}{\mu_v N_h(\alpha_s+\mu_h)(\alpha_l+\mu_h)}\right]\right)I_h a_4-(\mu_h+\omega)I_h a_4$$

$$\frac{dV}{dt}=a_4\left(\frac{\beta_v\beta_h S_v S_h}{N_h}\left[\frac{\alpha_s\mu_h\rho+\alpha_l\alpha_s+\alpha_l\mu_h-\alpha_l\mu_h\rho}{\mu_v N_h(\alpha_s+\mu_h)(\alpha_l+\mu_h)}\right]\right)I_h-(\mu_h+\omega)I_h$$

$$\frac{dV}{dt}=a_4(\mu_h+\omega)\left[\left(\frac{\beta_v\beta_h S_v S_h}{N_h}\left[\frac{\alpha_s\mu_h\rho+\alpha_l\alpha_s+\alpha_l\mu_h-\alpha_l\mu_h\rho}{\mu_v N_h(\alpha_s+\mu_h)(\alpha_l+\mu_h)(\mu_h+\omega)}\right]\right)-1\right]I_h$$

Since $S_h \le N_h$ and $S_v \le N_v$

$$\frac{dV}{dt}\le a_4(\mu_h+\omega)\left[\left(\frac{\beta_v\beta_h S_v S_h}{N_h}\left[\frac{\alpha_s\mu_h\rho+\alpha_l\alpha_s+\alpha_l\mu_h-\alpha_l\mu_h\rho}{\mu_v N_h(\alpha_s+\mu_h)(\alpha_l+\mu_h)(\mu_h+\omega)}\right]\right)-1\right]I_h$$

$\frac{dV}{dt}=\left[{R_0}^2-1\right]\le 0$. For $R_0\le 1$, where $a_4=\frac{1}{(\mu_h+\omega)}$

Therefore, if $R_0\le 1$, then$\left[{R_0}^2-1\right]\le 0$, so we obtain $\frac{dV}{dt}\le 0$.Furthermore, $\frac{dV}{dt}=0$ only if $I_h=0$ which leads to $S_h=N_h, E_{sh}=0, E_{lh}=0, R_h=0, S_v=N_v$ .Hence,V is a Lyapunov function on Ω and the largest compact invariant set in the set $\left\{(S_h,E_{sh},E_{lh},I_h,R_h,S_v,I_v)\in\Omega,:\frac{dV}{dt}=0\right\}$ is the singleton$(N_h,0,0,0,0,N_v,0)$. Therefore by LaSalle's invariance principle (LaSalle, 1976), solution to equations of the model (3.1) with initial conditions in Ω approaches the disease free-equilibrium point as time(t) tends to infinity $(t\longrightarrow\infty)$ whenever $R_0<1$. Hence the disease-free equilibrium is globally asymptotically stable in Ω if $R_0<1$

Endemic equilibrium

Endemic equilibrium points are steady-state solutions where the disease persists in the population (that is, equilibria where at least one of the infected components in the model is non-zero). For our model we can find an explicit representation of the endemic equilibrium point for $R_0>1$.

$${S_v}^*=\frac{\mu_v N_v N_h}{\beta_v {I_h}^*+\mu_v N_h}$$

$${I_v}^*=\frac{\beta_v\mu_v {I_h}^*}{\beta_v {I_h}^*+\mu_v I_h}$$

$${S_h}^*=\frac{N_h\left[\mu_h N_h\left((\mu_h+q)+q\omega {I_h}^*\right)\right]}{(\beta I_v+\mu_h N_h)(\mu_h+\omega)}$$

$${E_{Sh}}^*=\frac{\rho\beta_v\beta_h N_v {S_h}^* {I_h}^*}{N_h(\alpha_s+\mu_h)(\beta_v {I_h}^*+\mu_v I_h)}$$

$${E_{lh}}^*=\frac{(1-\rho)\beta_v\beta_h N_v {S_h}^* {I_h}^*}{N_h(\alpha_l+\mu_h)(\beta_v {I_h}^*+\mu_v I_h)}$$

$${I_h}^*=\frac{\nabla_1 N_h\mu_v\left({R_0}^2-1\right)}{\beta_v\nabla_1+\mu_v {R_0}^2\nabla_2}$$

$${R_h}^*=\frac{w {I_h}^*}{(\mu_h+q)}$$

where,

$\nabla_1=(\mu_h+\omega)[\alpha_s\mu_h\rho+\alpha_l(\mu_h(1-\rho)+\alpha_s)]$

and

$$\nabla_2 = \mu_h(\mu_h+\omega)(\mu_h+q)+\alpha_s[\mu_h(\omega+q+\mu_h)+q\omega(1-\rho)] + \alpha_l[(\alpha_s+\mu_h)(\omega+q+\mu_h)+\omega pq]$$

Local stability of the endemic equilibrium point

Theorem: The endemic equilibrium point $\mathcal{E}_0{}^* = (S_v{}^*, I_v{}^*, S_h{}^*, E_{Sh}{}^*, E_{lh}{}^*, I_h{}^*, R_h{}^*)$ of the malaria model(3.1), is locally asymptotically stable (LAS) if $R_0 > 1$.

Proof: We conduct linear stability on the endemic equilibrium. The Jacobian matrix at the endemic equilibrium point $\mathcal{E}_0{}^* = (S_v{}^*, I_v{}^*, S_h{}^*, E_{Sh}{}^*, E_{lh}{}^*, I_h{}^*, R_h{}^*)$of the malaria model (3.1) is become

$J(S_v{}^*, I_v{}^*, S_h{}^*, E_{Sh}{}^*, E_{lh}{}^*, I_h{}^*, R_h{}^*)$

$$= \begin{pmatrix} -\frac{\beta_v I_h}{N_h}-\mu_v & 0 & 0 & 0 & 0 & \frac{\beta_v S_v}{N_h} & 0 \\ \frac{\beta_v I_h}{N_h} & -\mu_v & 0 & 0 & 0 & \frac{\beta_v S_v}{N_h} & 0 \\ 0 & \frac{\beta_h S_h}{N_h} & \frac{\beta_h I_v}{N_h}-\mu_h & 0 & 0 & 0 & q \\ 0 & \frac{\rho\beta_h S_h}{N_h} & \frac{\rho\beta_h I_v}{N_h} & -(\alpha_s+\mu_h) & 0 & 0 & 0 \\ 0 & \frac{(1-\rho)\beta_h S_h}{N_h} & \frac{(1-\rho)\beta_h I_v}{N_h} & 0 & -(\alpha_l+\mu_h) & 0 & 0 \\ 0 & 0 & 0 & \alpha_s & \alpha_l & -(\mu_h+\omega) & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega & -\mu_h-q \end{pmatrix}$$

The corresponding characteristic equation of the Jacobian matrix with eigenvalue λ is given by $|J(\mathcal{E}_0{}^*) - \lambda I| = 0$; that is,

The global stability of the endemic equilibrium point

Theorem: The endemic equilibrium point $\mathcal{E}_0{}^* = (S_v{}^*, I_v{}^*, S_h{}^*, E_{Sh}{}^*, E_{lh}{}^*, I_h{}^*, R_h{}^*)$ of the system(3.1) , is globally asymptotically stable $R_0 > 1$.

Proof: First, we define an appropriate Lyapunov function V by applying the approach in (Martcheva, 2015) Such that;

$$V(x) = \sum_{i=1}^{7}\left(x_i - x_i{}^* - x_i{}^* \ln\left(\frac{x_i}{x_i{}^*}\right)\right)$$

Where $x_i{}^s$ are the population of compartment i and $x_i{}^{*s}$ are the endemic equilibrium points in R^{7+}. Thus,

$$V(x) = \left(S_v - S_v{}^* - S_v{}^* \ln\left(\frac{S_v}{S_v{}^*}\right)\right) + \left(I_v - I_v{}^* - I_v{}^* \ln\left(\frac{I_v}{I_v{}^*}\right)\right) + \left(S_h - S_h{}^* - S_h{}^* \ln\left(\frac{S_h}{S_h{}^*}\right)\right) + \left(E_{sh} - E_{sh}{}^* - E_{sh}{}^* \ln\left(\frac{E_{sh}}{E_{sh}{}^*}\right)\right) + \left(E_{lh} - E_{lh}{}^* - E_{lh}{}^* \ln\left(\frac{E_{lh}}{E_{lh}{}^*}\right)\right) + \left(I_h - I_h{}^* - I_h{}^* \ln\left(\frac{I_h}{I_h{}^*}\right)\right) + \left(R_h - R_h{}^* - R_h{}^* \ln\left(\frac{R_h}{R_h{}^*}\right)\right)$$

Then differentiating with respect to t gives,

$$\frac{dV}{dt}=\left(1-\frac{S_v^{\,*}}{S_v}\right)\frac{dS_v}{dt}+\left(1-\frac{I_v^{\,*}}{I_v}\right)\frac{dI_v}{dt}+\left(1-\frac{S_h^{\,*}}{S_h}\right)\frac{dS_h}{dt}+\left(1-\frac{E_{sh}^{\,*}}{E_{sh}}\right)\frac{dE_{sh}}{dt}+\left(1-\frac{E_{lh}^{\,*}}{E_{lh}}\right)\frac{dE_{lh}}{dt}+\left(1-\frac{I_h^{\,*}}{I_h}\right)\frac{dI_h}{dt}+\left(1-\frac{R_h^{\,*}}{R_h}\right)\frac{dR_h}{dt}$$

By replacing the derivatives in this equation, from the system of equation(3.1), it follows:

$$\begin{aligned}\frac{dV}{dt}=\;&\mu_vN_v-\frac{\beta_vS_vI_h}{N_h}-\mu_vS_v-\mu_vN_v\frac{S_v^{\,*}}{S_v}+\frac{\beta_vS_vI_h}{N_h}\frac{S_v^{\,*}}{S_v}+\mu_vS_v^{\,*}+\frac{\beta_vS_vI_h}{N_h}-\mu_vI_v-\frac{\beta_vS_vI_h}{N_h}\frac{I_v^{\,*}}{I_v}\\&+\mu_vI_v^{\,*}+\mu_hN_h+qR_h-\frac{\beta_hS_hI_v}{N_h}-\mu_hS_h-\mu_hN_h\frac{S_h^{\,*}}{S_h}-qR_h\frac{S_h^{\,*}}{S_h}+\frac{\beta_hS_h^{\,*}I_v}{N_h}\\&+\mu_hS_h^{\,*}+\frac{\rho\beta_hS_hI_v}{N_h}-(\alpha_s+\mu_h)E_{sh}-\frac{\rho\beta_hS_hI_v}{N_h}\frac{E_{sh}^{\,*}}{E_{sh}}+(\alpha_s+\mu_h)E_{sh}^{\,*}\\&+\frac{(1-\rho)\beta_hS_hI_v}{N_h}-(\alpha_l+\mu_h)E_{lh}-\frac{(1-\rho)\beta_hS_hI_v}{N_h}\frac{E_{lh}^{\,*}}{E_{lh}}+(\alpha_l+\mu_h)E_{lh}^{\,*}+\alpha_sE_{sh}\\&+\alpha_lE_{lh}-(\mu_h+\omega)I_h-\alpha_sE_{sh}\frac{I_h^{\,*}}{I_h}-\alpha_lE_{lh}\frac{I_h^{\,*}}{I_h}+(\mu_h+\omega)I_h^{\,*}+\omega I_h-\mu_hR_h\\&-qR_h-\omega I_h\frac{R_h^{\,*}}{R_h}+\mu_hR_h\frac{R_h^{\,*}}{R_h}+qR_h^{\,*}\end{aligned}$$

and then collecting positive terms together and negative terms also together leads to,

$$\begin{aligned}\frac{dV}{dt}=\;&\mu_vN_v+\frac{\beta_vS_vI_h}{N_h}\frac{S_v^{\,*}}{S_v}+\mu_vS_v^{\,*}+\frac{\beta_vS_vI_h}{N_h}+\mu_vI_v^{\,*}+\mu_hN_h+qR_h+\frac{\beta_hS_h^{\,*}I_v}{N_h}+\mu_hS_h^{\,*}\\&+\frac{\rho\beta_hS_hI_v}{N_h}+(\alpha_s+\mu_h)E_{sh}^{\,*}+\frac{(1-\rho)\beta_hS_hI_v}{N_h}+(\alpha_l+\mu_h)E_{lh}^{\,*}+\alpha_sE_{sh}+\alpha_lE_{lh}\\&+(\mu_h+\omega)I_h^{\,*}+\omega I_h+\mu_hR_h\frac{R_h^{\,*}}{R_h}+qR_h^{\,*}-\frac{\beta_vS_vI_h}{N_h}-\mu_vS_v-\mu_vN_v\frac{S_v^{\,*}}{S_v}-\mu_vI_v\\&-\frac{\beta_vS_vI_h}{N_h}\frac{I_v^{\,*}}{I_v}-\frac{\beta_hS_hI_v}{N_h}-\mu_hS_h-\mu_hN_h\frac{S_h^{\,*}}{S_h}-qR_h\frac{S_h^{\,*}}{S_h}-(\alpha_s+\mu_h)E_{sh}\\&-\frac{\rho\beta_hS_hI_v}{N_h}\frac{E_{sh}^{\,*}}{E_{sh}}-(\alpha_l+\mu_h)E_{lh}-\frac{(1-\rho)\beta_hS_hI_v}{N_h}\frac{E_{lh}^{\,*}}{E_{lh}}-(\mu_h+\omega)I_h-\alpha_sE_{sh}\frac{I_h^{\,*}}{I_h}\\&-\alpha_lE_{lh}\frac{I_h^{\,*}}{I_h}-\mu_hR_h-qR_h-\omega I_h\frac{R_h^{\,*}}{R_h}\end{aligned}$$

$\frac{dV}{dt}=H-K$, where

$$\begin{aligned}H=\;&\mu_vN_v+\frac{\beta_vS_vI_h}{N_h}\frac{S_v^{\,*}}{S_v}+\mu_vS_v^{\,*}+\frac{\beta_vS_vI_h}{N_h}+\mu_vI_v^{\,*}+\mu_hN_h+qR_h+\frac{\beta_hS_h^{\,*}I_v}{N_h}+\mu_hS_h^{\,*}\\&+\frac{\rho\beta_hS_hI_v}{N_h}+(\alpha_s+\mu_h)E_{sh}^{\,*}+\frac{(1-\rho)\beta_hS_hI_v}{N_h}+(\alpha_l+\mu_h)E_{lh}^{\,*}+\alpha_sE_{sh}+\alpha_lE_{lh}\\&+(\mu_h+\omega)I_h^{\,*}+\omega I_h+\mu_hR_h\frac{R_h^{\,*}}{R_h}+qR_h^{\,*}\end{aligned}$$

and

$$K = \frac{\beta_v S_v I_h}{N_h} + \mu_v S_v + \mu_v N_v \frac{S_v^*}{S_v} + \mu_v I_v + \frac{\beta_v S_v I_h}{N_h}\frac{I_v^*}{I_v} + \frac{\beta_h S_h I_v}{N_h} + \mu_h S_h + \mu_h N_h \frac{S_h^*}{S_h} + qR_h \frac{S_h^*}{S_h}$$
$$+ (\alpha_s + \mu_h)E_{sh} + \frac{\rho\beta_h S_h I_v}{N_h}\frac{E_{sh}^*}{E_{sh}} + (\alpha_l + \mu_h)E_{lh} + \frac{(1-\rho)\beta_h S_h I_v}{N_h}\frac{E_{lh}^*}{E_{lh}}$$
$$+ (\mu_h + \omega)I_h + \alpha_s E_{sh}\frac{I_h^*}{I_h} + \alpha_l E_{lh}\frac{I_h^*}{I_h} + \mu_h R_h + qR_h + \omega I_h \frac{R_h^*}{R_h}$$

Thus, if $H < K$, then $\frac{d\ V}{dt} \leq 0$ and $\frac{d\ V}{dt} = 0$ if and only if

$$S_v = S_v^*, I_v = I_v^*, S_h = S_h^*, E_{sh} = E_{sh}^*, E_{lh} = E_{lh}^*, I_h = I_h^*, R_h = R_h^*$$

From this, we see that $\mathcal{E}_0^* = (S_v^*, I_v^*, S_h^*, E_{Sh}^*, E_{lh}^*, I_h^*, R_h^*)$ is the largest compact invariant singleton set in $\left\{(S_v^*, I_v^*, S_h^*, E_{Sh}^*, E_{lh}^*, I_h^*, R_h^*) \in \Omega: \frac{d\ V}{dt} = 0\right\}$. Therefore, If $R_0 > 1$ by the principle of Lasalle (LaSalle, 1976), the endemic equilibrium $\mathcal{E}_0^*$ is globally asymptotically stable in the invariant region Ω if $H - K$.

3.3. Sensitivity indices of basic reproduction number (R_0) to the parameters

Since the exact values of parameters of epidemic models are not often known, it is proper to examine the robustness of the model to changes in parameter values. This will help to determine parameters that most influence the dynamics of the model. Sensitivity analysis is helpful for experimental design, data assimilation and reduction of complex non-linear models. Values for sensitivity indexes indicate which parameters should be targeted most for interventions purposes. A very high sensitivity index indicates that more care should be taken in the estimation of the associated parameter. The normalized forward sensitivity index is often used to determine the parameters that have higher influence on the basic reproduction number,R_0. The normalized forward sensitivity index of a variable to a parameter is the ratio of the relative change in the variable to the relative change in the parameter. When the variable is a differentiable function of the parameter, the sensitivity index may be alternatively defined using partial derivatives. These sensitivity indices allow us to determine the relative importance of different parameters in malaria transmission and prevalence. The most sensitive parameter has the magnitude of the sensitivity index larger than that of all other parameters [17].

Definition: The normalized forward sensitivity index of a variable, u that depends differentially on a parameter$P$, is defined as:

$$SI_P^{R_0} = \frac{\partial R_0}{\partial P} \times \frac{P}{R_0}$$

If the magnitude of sensitivity index is high for the parameter P out of other parameters then we say that P is more sensitive parameter to the basic reproduction number.

$$SI_{\beta_h}^{R_0} = \frac{\partial R_0}{\partial \beta_h} \times \frac{\beta_h}{R_0} = \frac{1}{2}$$

$$SI_{\beta_v}^{R_0} = \frac{\partial R_0}{\partial \beta_v} \times \frac{\beta_v}{R_0} = \frac{1}{2}$$

$$SI_{\mu_v}^{R_0} = \frac{\partial R_0}{\partial \mu_v} \times \frac{\mu_v}{R_0} = \frac{-\mu_v(\alpha_l + \mu_h)(\mu_h + \omega)(\alpha_s + \mu_h)}{\mu_v(\alpha_l + \mu_h)(\mu_h + \omega)(\alpha_s + \mu_h)}$$

$$SI_{\rho}^{R_0} = \frac{\partial R_0}{\partial \rho} \times \frac{\rho}{R_0} = \frac{1}{2} \times \frac{\rho\beta_h\beta_v[\alpha_s\mu_h - \alpha_l]}{\beta_h\beta_v[\rho\alpha_s\mu_h + \alpha_l(1-\rho) + \alpha_s]}$$

$$SI_{\alpha_s}^{R_0} = \frac{\partial R_0}{\partial \alpha_s} \times \frac{\alpha_s}{R_0} = \frac{1}{2} \times \frac{\alpha_s[(\rho\mu_h + 1) - (1 + \mu_h)(\rho\alpha_s\mu_h + \alpha_l(1 - \rho) + \alpha_s)]}{(\alpha_s + \mu_h)[\rho\alpha_s\mu_h + \alpha_l(1 - \rho) + \alpha_s]}$$

$$SI_{\alpha_l}^{R_0} = \frac{\partial R_0}{\partial \alpha_l} \times \frac{\alpha_l}{R_0} = \frac{1}{2} \times \frac{\alpha_l(1 - \rho)[(\alpha_l + \mu_h) - (1 + \mu_h)\rho\alpha_s\mu_h + \alpha_l + \alpha_s]}{(\alpha_l + \mu_h)[\rho\alpha_s\mu_h + \alpha_l(1 - \rho) + \alpha_s]}$$

$$SI_{w}^{R_0} = \frac{\partial R_0}{\partial w} \times \frac{\omega}{R_0} = \frac{1}{2} \times \frac{(\mu_h + 1)}{(\mu_h + \omega)}$$

These sensitivity indices along with signs are provide information that how crucial each parameter is to disease transmission and prevalence. A positive $(+)$ sign indicates that those parameters have great impact on expanding the disease in the community if their values are increasing. Due to the reason that the basic reproduction number increases as their values increase. On the other hand, an index with negative $(-)$ indicates that those parameters have an influence of minimizing the burden of the disease in the community as their values increase and also as their values increase, the basic reproduction number decreases, which leads to minimizing the endemic nature of the disease in the community.

4. Optimal Control

In chapter-4 we presented a mathematical model for malaria transmission dynamics and studied both mathematically and epidemiological well posedeness without giving intention mechanism. Detail intervention strategies are done in this chapter where, we introduced controls that minimize transmission dynamics. After we present the optimal control formulation, we study the transmission dynamics through numerical.

4.1. Extension of the model into an optimal control

We extend malaria model (3.1) by incorporating three control interventions. This helped us to identify the best intervention strategies that help to eradicate the disease in the specified time. The control interventions are defined as:

i) The control u_1 represents prevention effort of malaria disease, which protects susceptible from contacting the disease (treated bed net).
ii) The control u_2 represents treatment effort of malaria infected individuals.
iii) The control u_3 represents the use of insecticide.

After incorporating, $u_1, u_2,$ and u_3 in the model (3.1), we obtain the following optimal control model:

$$g(x,u,t) = \begin{cases} \frac{dS_h}{dt} = \mu_h N_h + qR_h - (1-u_1)\frac{\beta_h S_h I_v}{N_h} - \mu_h S_h \\ \frac{dE_{sh}}{dt} = (1-u_1)\frac{\rho\beta_h S_h I_v}{N_h} - (\alpha_s + \mu_h)E_{sh} \\ \frac{dE_{lh}}{dt} = (1-u_1)\frac{(1-\rho)\beta_h S_h I_v}{N_h} - (\alpha_l + \mu_h)E_{lh} \\ \frac{dI_h}{dt} = \alpha_s E_{sh} + \alpha_l E_{lh} - (\mu_h + \omega + u_2)I_h \\ \frac{dR_h}{dt} = (\omega + u_2)I_h - \mu_h R_h - qR_h \\ \frac{dS_v}{dt} = \mu_v N_v - (1-u_1)\frac{\beta_v S_v I_h}{N_h} - (\mu_v + u_3)S_v \\ \frac{dI_v}{dt} = (1-u_1)\frac{\beta_v S_v I_h}{N_h} - (\mu_v + u_3)I_v \end{cases} \quad (4.1)$$

The optimal control problem is to minimize the objective functional *J* considering the costs of malaria disease prevention, anti-malaria treatment and insecticide. The goal of the adopted strategy is to reduce exposed human population, infected human population, and infected mosquito population with optimal cost. Mathematically, the optimal control problem consists of minimizing the objective functional

$$J(u_1,u_2,u_3) = \min_{u_1,u_2,u_3} \int_0^T \left(A_1 E_{sh} + A_2 E_{lh} + A_3 I_h + A_4 I_v + \frac{1}{2}\sum_{i=1}^{3} B_i u_i^2 \right) dt \quad (4.2)$$

Subjected to $g(x,u,t)$.

Where T represents the final time of control implementation, and quantities $A_1, A_2,$ and $A_3$are weights constants or balance factors of the exposed human population, infected human population, and infected mosquito population, respectively, while $B_1, B_2,$ and B_3 are weight constants used for treated bed net, treatment control using anti-malaria drugs, and indoor residual

insecticide spraying (u_i for $i = 1,2,3$). We further assume that, due to technical reasons, the cost of controls u_i for $i = 1,2,3$ is non linear and quadratic as seen in the cost function (4.2) and $B_i u_i^2$ for $i = 1,2,3$ represents the cost of controls u_i for $i = 1,2,3$.
The main goal is to achieve the best control $u_1^*,\ u_2^*,$ and u_3^* so that

$$J(u_1, u_2, u_3) = \min_U J(u_1^*, u_2^*, u_3^*), \qquad (5.3)$$

where,

$$U = \{(u_1, u_2, u_3) | u_i \text{ is measureable on } [0, T], 0 \leq u_i \leq 1, i = 1,2,3\}.$$

4.1.1. Existence and characterization of the optimal control solutions

In this subsection, we examine conditions that can assure the existence of a solution to the optimal control problem (4.1).

4.1.2. Existence of optimal control solution

Theorem: There exists an optimal control $u^* = (u_1^*, u_2^*, u_3^*)$ and a corresponding solution $(S^*, E_{sh}^*, E_{lh}^*, I_h^*, R_h^*, S_v^*, I_v^*)$ to the state initial value problem (4.1) that minimizes the cost functional $J(u_1, u_2, u_3)$ of (4.2) over U.

Proof. The nontrivial requirement on the set of admissible controls and the set of end conditions are followed by Fleming and Rishel's theorem (Fleming *et al.*, 2012).

i) The set of all solution to system (4.1) with corresponding control functions in U is non empty.
ii) The control set is convex and closed.
iii) The right hand side of the state system is bounded by a linearized function in the state and control variables.
iv) The integrand of the objective functional is convex on U and is bounded below by $\gamma_1 \|(u_1, u_2, u_3)\|^r - \gamma_2$, where $\gamma_i > 0\ \forall i, i = 1,2,$ and $r > 1$.

In order to established condition (i), we refer to Picard-Lindel¨of existence theorem (Earl and Levinson, 1955). If $g(x, u, t)$ is bounded, continuous, and Lipschitz in the state variables, then there exists a unique solution corresponding to every admissible control U. Hence, for any $u \in U$ and the state variables, we have

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} \qquad (4.4)$$

where $N(t) \coloneqq N_h(t) + N_v(t)$, $\frac{\Lambda}{\mu} \coloneqq \frac{\Lambda_h}{\mu_h} + \frac{\Lambda_v}{\mu_v}$ and $\Lambda_h \coloneqq \mu_h N_h(t), \Lambda_v \coloneqq \mu_v N_v(t)$
and non empty by model assumption. Furthermore, with the bounded established (4.4) it implies that the state system is continuous and bounded. It is possible to show the Boundednes of the partial derivative w.r.t the state variable,

i. e. $\frac{\partial g}{\partial x_j}$ where $x_j = S_h, E_{sh}, E_{lh}, I_h, R_h, S_v, I_v$ for $j = 1, 2, 3, \ldots, 7$

exist and finite, which established the system is Lipschitz w.r.t the state variables (Sharomi *et al.*, 2007). This established the proof of condition (i).
By definition, U is closed. Take any controls $u_1,\ u_2 \in U,$ and $\theta \in [0, 1]$. Then

$$0 \leq \theta u_1 + (1 - \theta) u_2.$$

Additionally, observe that $\theta u_1 \leq \theta$ and $(1 - \theta) u_2 \leq (1 - \theta)$. Then $\theta u_1 + (1 - \theta) u_2 \leq \theta(1 - \theta) = 1$.

Hence, $\theta u_1 + (1-\theta)u_2 \leq 1$ for all $u_1,\ u_2 \in U$, and $\theta \in [0,1]$. Therefore, U is convex, and condition (ii) is satisfied.

The optimal system is bounded which determines the compactness needed for the existence of optimal control. In order to verify this argument we use the approach adopted by (Sadiq *et al.*, 2014) and (Laarabi *et al.*, 2012), whereby system (4.1) is put in the following form:

$$X = BX + F(X) \tag{4.5}$$

where $X = [S_h(t), E_{sh}(t), E_{lh}(t), I_h(t), R_h(t), S_v(t), I_v(t)]^T$,

$$B = \begin{pmatrix} -\mu_h & 0 & 0 & 0 & q & 0 & 0 \\ 0 & -(\alpha_s+\mu_h) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\alpha_l+\mu_h) & 0 & 0 & 0 & 0 \\ 0 & \alpha_s & \alpha_l & -(\mu_h+\omega+u_2) & 0 & 0 & 0 \\ 0 & 0 & 0 & (\omega+u_2) & -(q+\mu_h) & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\mu_v+u_3) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -(\mu_v+u_3) \end{pmatrix},$$

$$F(X) = \begin{pmatrix} \mu_h N_h - (1-u_1)\dfrac{\beta_h S_h I_v}{N_h} \\ (1-u_1)\dfrac{\rho\beta_h S_h I_v}{N_h} \\ (1-u_1)\dfrac{(1-\rho)\beta_h S_h I_v}{N_h} \\ 0 \\ 0 \\ \mu_v N_v - (1-u_1)\dfrac{\beta_v S_v I_h}{N_h} \\ (1-u_1)\dfrac{\beta_v S_v I_h}{N_h} \end{pmatrix}$$

and X' denotes the derivative of X with respect to time t. The system (4.5) is a non-linear system with a bounded coefficient. We set,

$$D(X) = X' = BX + F(X) \tag{4.6}$$

The second term on the right hand side of (5.6) satisfies

$$\begin{aligned} |F(X_2) - F(X_1)| \leq\ & M_1|S_{h2}(t) - S_{h1}(t)| + M_2|E_{sh2}(t) - E_{sh1}(t)| + M_3|E_{lh2}(t) - E_{lh1}(t)| \\ & + M_4|I_{h2}(t) - I_{h1}(t)| + M_5|R_{h2}(t) - R_{h1}(t)| + M_6|S_{v2}(t) - S_{v1}(t)| \\ & + M_7|I_{v2}(t) - I_{v1}(t)| \\ \leq\ & M\begin{pmatrix} |S_{h2}(t) - S_{h1}(t)| + |E_{sh2}(t) - E_{sh1}(t)| + |E_{lh2}(t) - E_{lh1}(t)| \\ + |R_{h2}(t) - R_{h1}(t)| + |S_{v2}(t) - S_{v1}(t)| + |I_{v2}(t) - I_{v1}(t)| \end{pmatrix}, \end{aligned}$$

where, the positive constant $M = \max\{M_1,\ M_2,\ M_3,\ M_4,\ M_5,\ M_6, M_7\}$ is independent of the state variables. Also we have

$$|D(X_1) - D(X_2)| \leq L|X_1 - X_2|,$$

where $L = \max\{M, \|B\|\} < \infty$. So, it follows that the function D is uniformly Lipchitz continuous. From the definition of control variables and non-negative initial conditions we can see that a solution of the system (4.6) exists.

To establish condition (iv), we observe that the integrand $f(x,u,t)$ in our objective functional is convex since it is quadratic in the controls (Choi and Jung, 2014). Then, we only need to prove the bound on $f(x,u,t)$. This is shown as follows:

$$f(x,u,t) = A_1E_{sh} + A_2E_{lh} + A_3I_h + A_4I_v + \frac{1}{2}\sum_{i=1}^{3} B_iu_i^2 \geq \frac{1}{2}\sum_{i=1}^{3} B_iu_i^2 \geq \left(\frac{1}{2}\sum_{i=1}^{3} B_iu_i^2\right) - \frac{1}{2}u_1$$

$$\geq \left(B\sum_{i=1}^{3} u_i^2\right) - \frac{1}{2}u_1 = B\|(u_1,u_2,u_3)\| - \frac{1}{2}u_1, \text{where, } B$$

$$= \min\left\{\frac{1}{2}B_1, \frac{1}{2}B_2, \frac{1}{2}B_3\right\}.$$

The above then establishes a bound on $f(x,u,t)$.

4.1.3. Characterization of the optimal control solutions

According to the Pontrygin's maximum principle, if $u^*(\cdot) \in U$ is optimal for problem (4.3) with fixed final time T, then there exists a non-trivial absolutely continuous mapping $\lambda: [0,\ T] \to \mathbb{R}^7$, $\lambda = \left(\lambda_1(t)\ ,\lambda_2(t)\ ,\lambda_3(t)\ ,\lambda_4(t),\ \lambda_5(t),\lambda_6(t),\ \lambda_7(t)\right)$ called the adjoint vector, such that:

1. the Hamiltonian function is defined as

$$\mathcal{H} = A_1E_{sh} + A_2E_{lh} + A_3I_h + A_4I_v + \frac{1}{2}\sum_{i=1}^{3} B_iu_i^2 + \sum_{i=1}^{7} \lambda_i(t)g_i(x(t),u(t),t), \tag{4.7}$$

2. the control system

$$S_h' = \frac{\partial\mathcal{H}}{\partial\lambda_1}, E_{sh}' = \frac{\partial\mathcal{H}}{\partial\lambda_2}, E_{lh}' = \frac{\partial\mathcal{H}}{\partial\lambda_3}\ \ I_h' = \frac{\partial\mathcal{H}}{\partial\lambda_4}, R_h' = \frac{\partial\mathcal{H}}{\partial\lambda_5}, S_v' = \frac{\partial\mathcal{H}}{\partial\lambda_6}, I_v' = \frac{\partial\mathcal{H}}{\partial\lambda_7}$$

3. The adjoint system

$$\lambda_1' = \frac{-\partial\mathcal{H}}{\partial S_h}, \lambda_2' = \frac{-\partial\mathcal{H}}{\partial E_{sh}}, \lambda_3' = \frac{-\partial\mathcal{H}}{\partial E_{lh}}, \lambda_4' = \frac{-\partial\mathcal{H}}{\partial I_h}, \lambda_5' = \frac{-\partial\mathcal{H}}{\partial R_h}, \lambda_6' = \frac{-\partial\mathcal{H}}{\partial S_v}, \lambda_7' = \frac{-\partial\mathcal{H}}{\partial I_v}$$

4. and the optimality condition

$$\mathcal{H}(x^*,u^*,\lambda^*) = \min_{u\in U}\mathcal{H}(x,u,\lambda) \quad \text{holds for almost all } t \in [0,T].$$

5. Moreover, the transversality condition

$$\lambda_i(T) = 0, \quad i = 1,\dots,7 \quad \text{also holds true}$$

Theorem: The optimal control problem (4.3) with fixed final time T admits a unique optimal solution $x^* = (S_h^*, E_{sh}^*, E_{lh}^*, I_h^*, R_h^*, S_v^*, I_v^*)$ associated with an optimal control $u^* = (u_1^*, u_2^*, u_3^*)$ for all $t \in [0,T]$. Moreover, there exist adjoint function $\lambda_i^*,\ i = 1,2,\dots,7$ such that

$$\begin{cases} \lambda_1' = (1-u_1)\frac{\beta_h I_v}{N_h}(\lambda_1-\lambda_3) + (1-u_1)\rho\frac{\beta_h I_v}{N_h}(\lambda_3-\lambda_2) + \mu_h\lambda_1 \\ \lambda_2' = -A_1 + \alpha_s(\lambda_2-\lambda_4) + \mu_h\lambda_2 \\ \lambda_3' = -A_2 + \alpha_l(\lambda_3-\lambda_4) + \mu_h\lambda_3 \\ \lambda_4' = -A_3 + (\omega+u_2)(\lambda_4-\lambda_5) + (1-u_1)\frac{\beta_v S_v}{N_h}(\lambda_6-\lambda_7) + \mu_h\lambda_4 \\ \lambda_5' = q(\lambda_5-\lambda_1) + \mu_h\lambda_5 \\ \lambda_6' = (1-u_1)\frac{\beta_v I_h}{N_h}(\lambda_6-\lambda_7) + (u_3+\mu_v)\lambda_6 \\ \lambda_7' = -A_4 + (1-u_1)\frac{\beta_h S_h}{N_h}(\lambda_1-\lambda_3) + (1-u_1)\rho\frac{\beta_h S_h}{N_h}(\lambda_3-\lambda_2) + (u_3+\mu_v)\lambda_7 \end{cases} \tag{4.8}$$

with transiversality conditions

$$\lambda_i^*(T) = 0, \quad i = 1, \dots, 7. \tag{4.9}$$

Moreover, the optimal control $u^* = (u_1^*, u_2^*, u_3^*)$is given by

$$u_1^*(t) = \max\left\{0, \min\left(1, \frac{\beta_h S_h I_v(\lambda_3 - \lambda_1) + \rho\beta_h S_h I_v(\lambda_2 - \lambda_3) + \beta_v S_v I_h(\lambda_7 - \lambda_6)}{B_1 N_h}\right)\right\},$$

$$u_2^*(t) = \max\left\{0, \min\left(1, \frac{I_h(\lambda_4 - \lambda_5)}{B_2}\right)\right\},$$

$$u_3^*(t) = \max\left\{0, \min\left(1, \frac{S_v\lambda_6 + I_v\lambda_7}{B_3}\right)\right\} \tag{4.10}$$

Proof: By using Pontryagin,s maximum principle (Pontryagin *et al.*, 1992) we obtain the following system of adjoint variables:

$$\lambda_1' = -\frac{\partial \mathcal{H}}{\partial S_h} = (1-u_1)\frac{\beta_h I_v}{N_h}(\lambda_1 - \lambda_3) + (1-u_1)\rho\frac{\beta_h I_v}{N_h}(\lambda_3 - \lambda_2) + \mu_h\lambda_1$$

$$\lambda_2' = -\frac{\partial \mathcal{H}}{\partial E_{sh}} = -A_1 + \alpha_s(\lambda_2 - \lambda_4) + \mu_h\lambda_2$$

$$\lambda_3' = -\frac{\partial \mathcal{H}}{\partial E_{lh}} = -A_2 + \alpha_l(\lambda_3 - \lambda_4) + \mu_h\lambda_3$$

$$\lambda_4' = -\frac{\partial \mathcal{H}}{\partial I_h} = -A_3 + (\omega + u_2)(\lambda_4 - \lambda_5) + (1-u_1)\frac{\beta_v S_v}{N_h}(\lambda_6 - \lambda_7) + \mu_h\lambda_4$$

$$\lambda_5' = -\frac{\partial \mathcal{H}}{\partial R_h} = q(\lambda_5 - \lambda_1) + \mu_h\lambda_5$$

$$\lambda_6' = -\frac{\partial \mathcal{H}}{\partial S_v} = (1-u_1)\frac{\beta_v I_h}{N_h}(\lambda_6 - \lambda_7) + (u_3 + \mu_v)\lambda_6$$

$$\lambda_7' = -\frac{\partial \mathcal{H}}{\partial I_v} = -A_4 + (1-u_1)\frac{\beta_h S_h}{N_h}(\lambda_1 - \lambda_3) + (1-u_1)\rho\frac{\beta_h S_h}{N_h}(\lambda_3 - \lambda_2) + (u_3 + \mu_v)\lambda_7$$

Similarly by following the approach of (Pontryagin *et al.*, 1992), to get the controls, we solved the equation,

$\frac{\partial \mathcal{H}}{\partial u_i} = 0$ at u_i^*, for $i = 1, 2, 3$ and obtained:

$$u_1^*(t) = \frac{\beta_h S_h I_v(\lambda_3 - \lambda_1) + \rho\beta_h S_h I_v(\lambda_2 - \lambda_3) + \beta_v S_v I_h(\lambda_7 - \lambda_6)}{B_1 N_h},$$

$$u_2^*(t) = \frac{I_h(\lambda_4 - \lambda_5)}{B_2},$$

$$u_3^*(t) = \frac{S_v\lambda_6 + I_v\lambda_7}{B_3}$$

In compact notation with boundary condition

$$u_1^*(t) = \max\left\{0, \min\left(1, \frac{\beta_h S_h I_v(\lambda_3 - \lambda_1) + \rho\beta_h S_h I_v(\lambda_2 - \lambda_3) + \beta_v S_v I_h(\lambda_7 - \lambda_6)}{B_1 N_h}\right)\right\},$$

$$u_2^*(t) = \max\left\{0, \min\left(1, \frac{I_h(\lambda_4 - \lambda_5)}{B_2}\right)\right\},$$

$$u_3^*(t) = \max\left\{0, \min\left(1, \frac{S_v\lambda_6 + I_v\lambda_7}{B_3}\right)\right\}.$$

5. Numerical simulation

This section present and discusses numerical results for the system (3.1) and (4.1) for different

Values of parameters given in the model. The simulation process is carried out using *MATLAB* software. We start by defining and estimating the values of parameter used in the model. Then we illustrate the simulation results graphically.

5.1. Parameter Estimation

In this section, we fit the proposed model to cumulative cases of malaria infection data and estimate the unknown model parameters. Table 3 depicts the cumulative cases of malaria infection from September 2011 E.C to June 2015 E.C extracted from Kebri Dehar health office, Ethiopia. The squared sum of errors (SSE) between model solution and the data can be computed as

$$SSE(\vartheta) = argmin \sum_{i=1}^{n} \|I_h(t) - \bar{I}_h(t)\|^2 \tag{5.1}$$

where $\|\cdot\|$denotes the Euclidean norm in $\mathbb{R}^n$ and n is the number of available real data points. The expression $\bar{I}_{hi}(t)$ represents the actual cumulative malaria infected cases
and $I_{hi}(t)$ is the corresponding model solutions at time t_i. In the process of least-squares fitting, we are looking for a value $\bar{\vartheta}$of model parameter ϑ such that the squared sum of errors is the minimum. Clearly, such a problem is nonlinear least squares problem, since the dependence of a solution$I(t, \vartheta)$onthe parameter ϑ is through a highly nonlinear system of differential equations.

Table 3: Cumulative malaria cases from 2011 – 2015 E.C (In Kebri Dehar district, Ethiopia).

Year	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.
2011	59	84	65	97	38	47	43	54	35	80	69	54
2012	37	84	87	75	44	48	28	45	27	50	57	44
2013	29	44	59	72	44	47	28	54	31	50	52	53
2014	28	55	23	15	63	34	9	28	96	34	98	50
2015	22	87	109	66	83	21	2	20	87	5		

In the next section, we study the dynamics of malaria through numerical simulations by estimating the values of parameters in the proposed model with appropriate initial conditions with the help of least square technique in order to get a good fit to the real dat.

5.2. Simulation results and discussion

The initial infected population based on collected data $I_h(0) = 59$ as given Table 3. Initially, we assumed $E_{sh}(0) = 1000, E_{lh}(0) = 750, and\ R_h(0) = 100$ while the initial susceptible population is given by $S_h(0) = N_h(0) - E_{sh}(0) - E_{lh}(0) - I_h(0) - R_h(0) = 174{,}585$. Since the real data for mosquito population is unavailable and due to the involvement of enormous number of mosquito individuals, we have assumed the initial mosquito population as $N_v(0) = 100{,}000$, initial infected mosquito population as $I_v(0) = 25{,}000$ and initial susceptible mosquito population as $S_v(0) = N_v(0) - I_v(0) = 75{,}000$.

We fitted the parameters except for the recruitment rate of human $\mu_h N_h = \Lambda_h$, the recruitment rate of mosquito $\mu_v N_v = \Lambda_v$, the natural death rate of human μ_h, natural death rate of mosquito μ_v, recovery rate of human ω and rate of loss of immunity of human q. The parameters μ_h and μ_v are calculated as the inverse of the average lifespan of the population in Ethiopia and

life span of Anopheles mosquito respectively, so that $\mu_h = \frac{1}{66.71}$ per year $= \frac{1}{66.71\times12}$ per month, where 66.71 years is the average lifespan of population in Ethiopia (Kereyu & Demie, 2021) and $\mu_v = \frac{1}{15}$ per day $= \frac{1\times30}{15}$ per month, where 15 days is the average lifespan of mosquito (Malaria, 2020). The parameters Λ_h and $\Lambda_v$are calculated as follows. Since the total population of Kebri Dehar district is 176,494 in 2017, we have $\frac{\Lambda_h}{\mu_h} = 176{,}494$ is the maximum human population without the disease, therefore $\Lambda_h = 220.4742$ per month, similarly $\Lambda_v = 200{,}000$ per month. Recovery rate ω and immunity loss rate q parameters are obtained or estimated from literature. $\frac{1}{\omega} = 9.5$ months is the average duration of the infectious period and $\frac{1}{q} = 5$ years is the average duration of the immune period, so that $\omega = \frac{1}{9.5} = 0.10526$ per month and $q = \frac{1}{5\times12} = 0.017$ per month (Chitnis *et al.*, 2008, Mohammed-Awel *et al.*, 2018). The remaining unknown parameters $\beta_h, \beta_v, \alpha_{sh}, \alpha_{lh}$ and ρ are obtained using least-square curve fitting method. The fitted and estimated parameter values of the model (4.1) are set out in Table 4. The result of fitting model (4.1) to the actual data of malaria incidence is displayed in Figure 3. The red-circle shows the monthly malaria cases reported in Kebri Dehar district while the solid line denotes the model fit. Residuals plots for the model and the real data in Table 4 are given in Figure 4. The residuals seem to be random and the standard errors are generally small for the model. In this manner the estimates acquired here are reasonable.

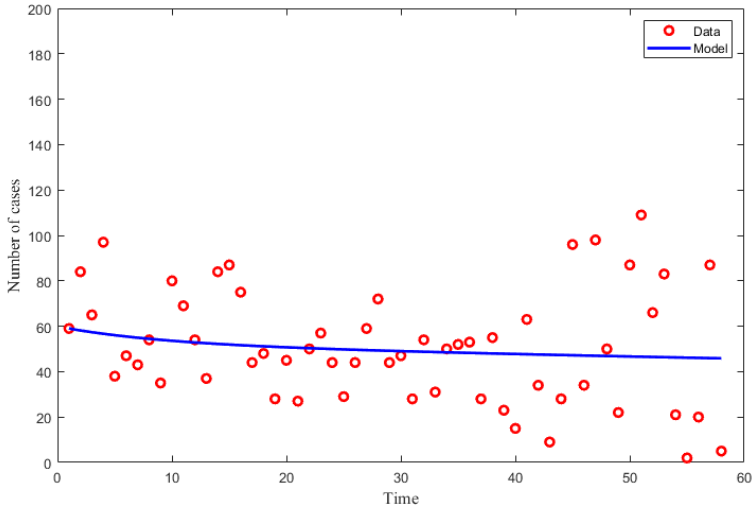

Figure 3: Malaria cases data fitting of cumulative infected humans using the model.

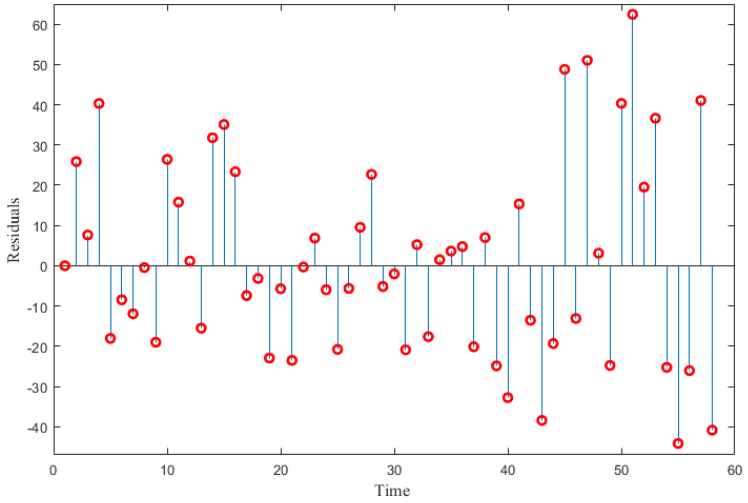

Figure 4: Residual of estimated parameters.

Table 4: Parameters value of the model.

Parameters	Description	Value	Units	References
β_h	Infection rate from mosquito to human	0.0203	$Month^{-1}$	Fitted
β_v	Infection rate from human to mosquito	10.4482	$Month^{-1}$	Fitted
μ_h	Natural death/birth rate of human	$\frac{1}{66.71 \times 12}$	$Month^{-1}$	(Kereyu & Demie, 2021)
μ_v	Natural death/birth rate of mosquito	$\frac{30}{15}$	$Month^{-1}$	(Malaria, 2020)
ρ	Probability of exposed humans going through short-term incubation periods	0.0527	$Month^{-1}$	Fitted
α_s	Progression rate of E_{sh} to I_h	0.00524	$Month^{-1}$	Fitted
α_l	Progression rate of E_{lh} to I_h	0.00012	$Month^{-1}$	Fitted
ω	Spontaneous recovery rate	0.10526	$Month^{-1}$	(Chitnis et al., 2008, Mohammed-Awel et al., 2018)
q	Waning immunity rate	0.017	$Month^{-1}$	

The associated parameters values of the model (4.1) are tabulated in Table 4 above. Consequently, using these parameter values we obtained in this study, the value of reproduction number R_0 for the September 2011 E.C - June 2015 E.C malaria cases in Kebri Dehar district is

$$R_0 = \sqrt{\frac{\beta_v \beta_h \left(\rho \alpha_s \mu_h + \alpha_l (1-\rho) + \alpha_s\right)}{\mu_v (\alpha_l + \mu_h)(\mu_h + \omega)(\alpha_s + \mu_h)}} \approx 24.494779 > 1.$$

The result shows that disease will be epidemic in the district.

The numerical solutions are illustrated using MATLAB program. The optimality system, which consists of the state system and the adjoint system, is solved to obtain the optimal control solution. An iterative scheme, fourth order Runge-Kutta, is used to solve the optimality system. The adjoint equations are solved by the backward fourth order RungeKutta scheme using the current iterations solutions of the state equations because of the transversality conditions of (4.9). Then the controls are updated by using a convex combination of the previous controls and the value from the characterizations (4.10). This process is repeated and the iterations are stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iteration (for more detail see (Rodrigues, 2012)).
The optimal control problem is simulated with the parameter values given in Table 4. The initial conditions that we used for simulation of the optimal control are $\left(S_h(0),\ E_{sh}(0), E_{lh}(0), I_h(0), R_h(0), S_v(0), I_v(0)\right) =$ $(174585{,}1000, 750, 59{,}100, 7500, 2500)$. The weight value constants of the state and controls that we used are given as $A_1 = 80, A_2 = 60, A_3 = 60, A_4 = 100, B_1 = 60, B_2 = 100\ and\ B_3 = 80$. To determine the impact of each controls on the reduction of malaria, we used the following three strategies with different combination of two controls at a time and three controls at a time.

Strategy 1: Applying the treatment of infected human u_2 and insecticide u_3.
In this strategy, we used a combination of two controls treatment for infected humans with antimalarial drugs u_2 and an insecticide u_3 to minimize the objective functional $J(u)$, while the protective using treated bed net u_1 is set to zero. The numerical results are given in Figure 5. Figures 5 (b) and 5(c) shows that in the absence of controls, the significant number of infected humans and infected mosquito is higher than in the presence of controls. At the end of the intervention, the total population of infected humans I_h and infected mosquito I_v are decreasing fast to reached its lowest point. Figure 5 (a) shows that exposed humans in the presence of controls are smaller than those in the absence of controls and $(E_{sh} + E_{lh})$ is increasing at the end of the intervention

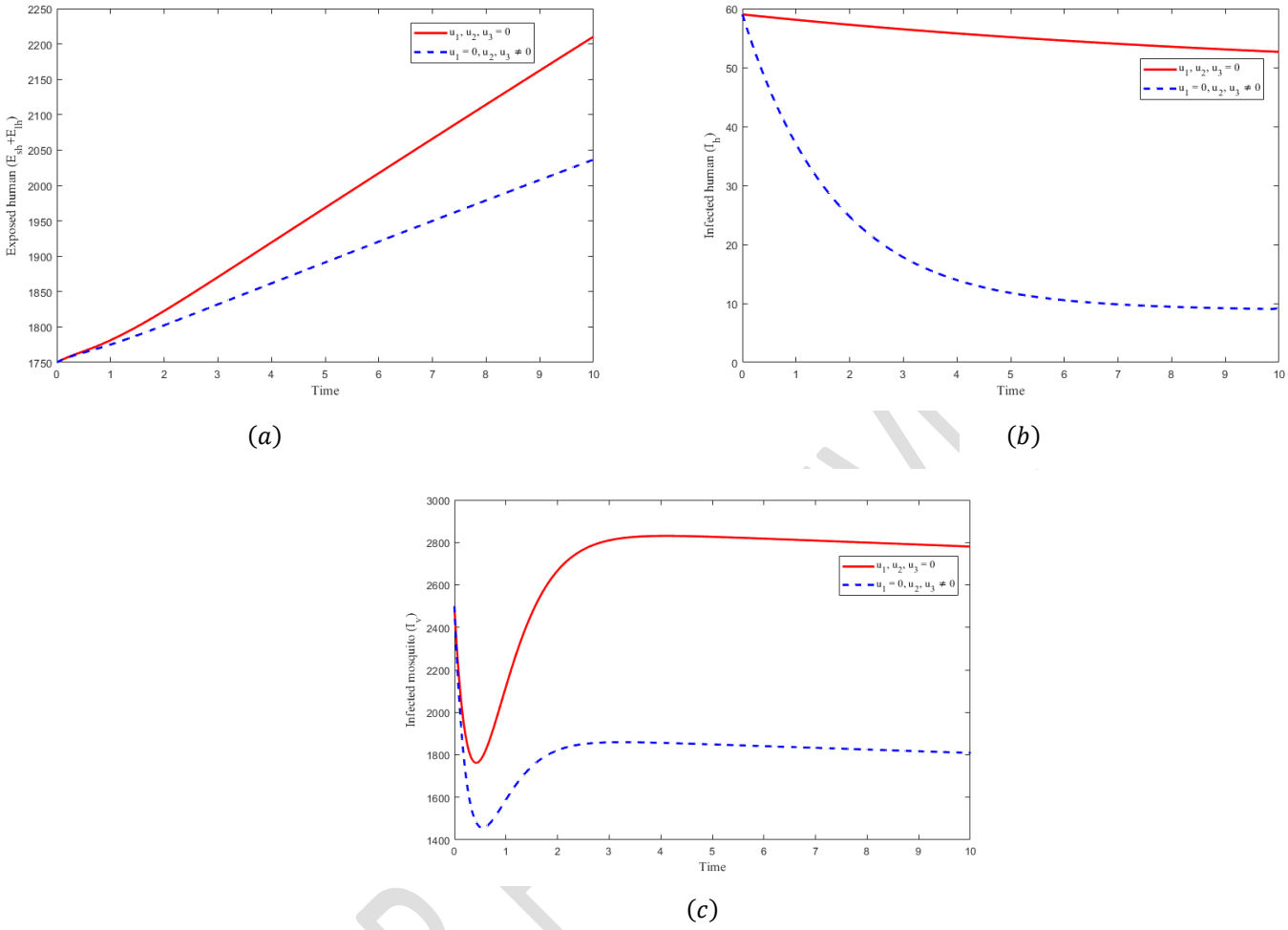

Figure 5: Numerical results of the model using treatment and insecticide only.

Strategy 2: Applying the treated bed net u_1 and insecticide u_3.

To reduce the objective functional $J(u)$, a combination of two controls protective using treated bed net u_1 and an insecticide u_3 is implemented, while the control treatment for the infected with antimalarial drugs u_2 is set to zero. The numerical results are depicted in Figure 6. Figures 6 (a) – 5.4 (c) show that using controls reduces the total population of exposed humans, infected humans, and infected mosquitos faster than not using controls. At the end of the intervention, the total number of exposed humans $(E_{sh} + E_{lh})$ and infected mosquitoes I_v are decreasing and at its lowest respectively. The infected human I_h is decreasing in both cases.

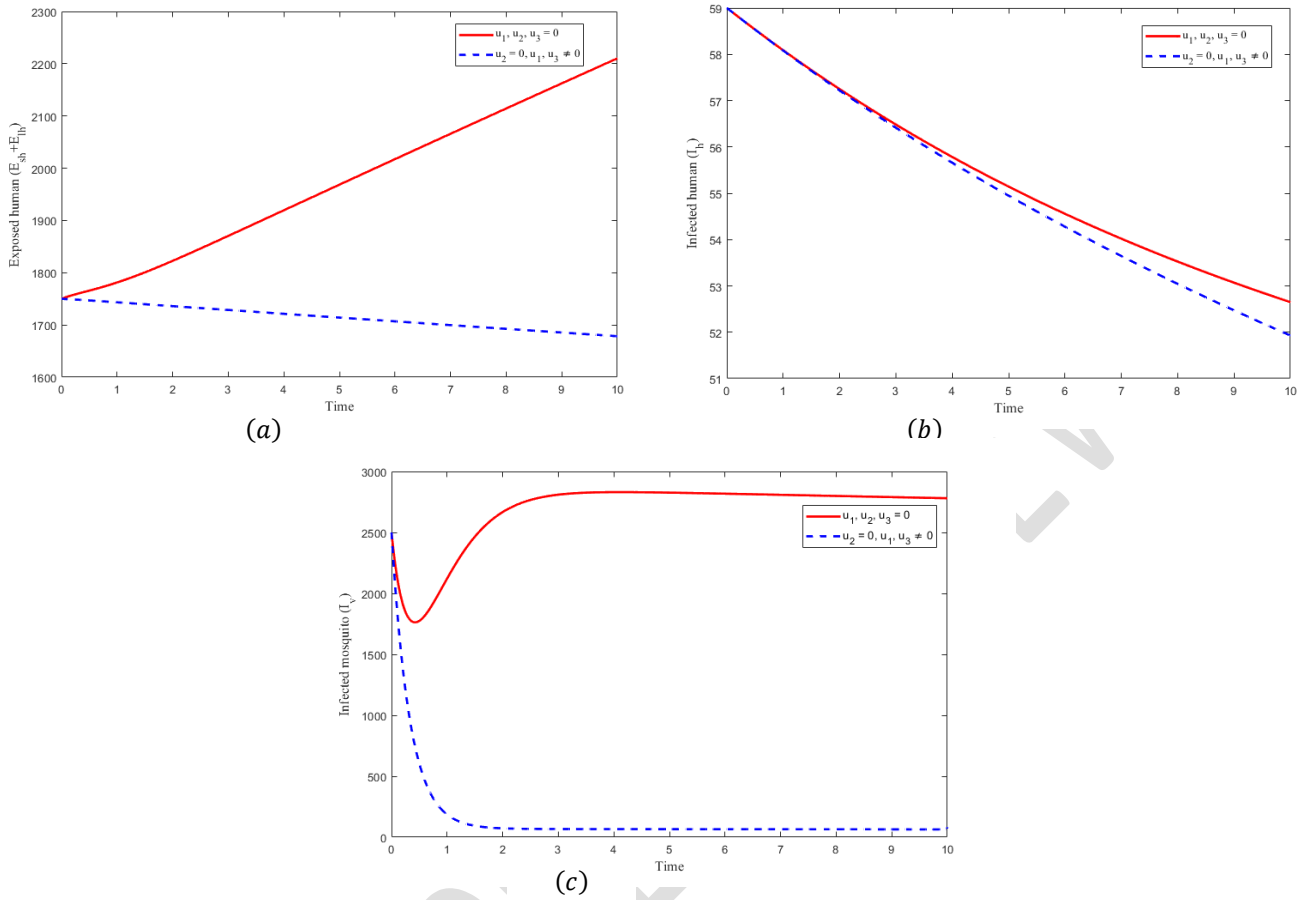

Figure 6: Numerical results of the model using preventive treated bed net and insecticide only.

Strategy 3: Using the treated bed net u_1, treatment of infected human u_2 and insecticide u_3.
To minimize the objective functional $J(u)$, we used all controls protective using treated bed net u_1, treatment for the infected human with antimalarial drugs u_2 and insecticide u_3. The numerical results are displayed in Figure 7. As depicted in Figures 7 (a) – 5.5 (c) that the controls indicate that the total population of exposed human, infected human and infected mosquito populations are increasing in the absence of controls while decreasing in the presence of controls. It can be observed that the implementation of all controls at the same time results in fast decreasing number of exposed human, infected human and infected mosquito when compared to the strategy 1 and 2.

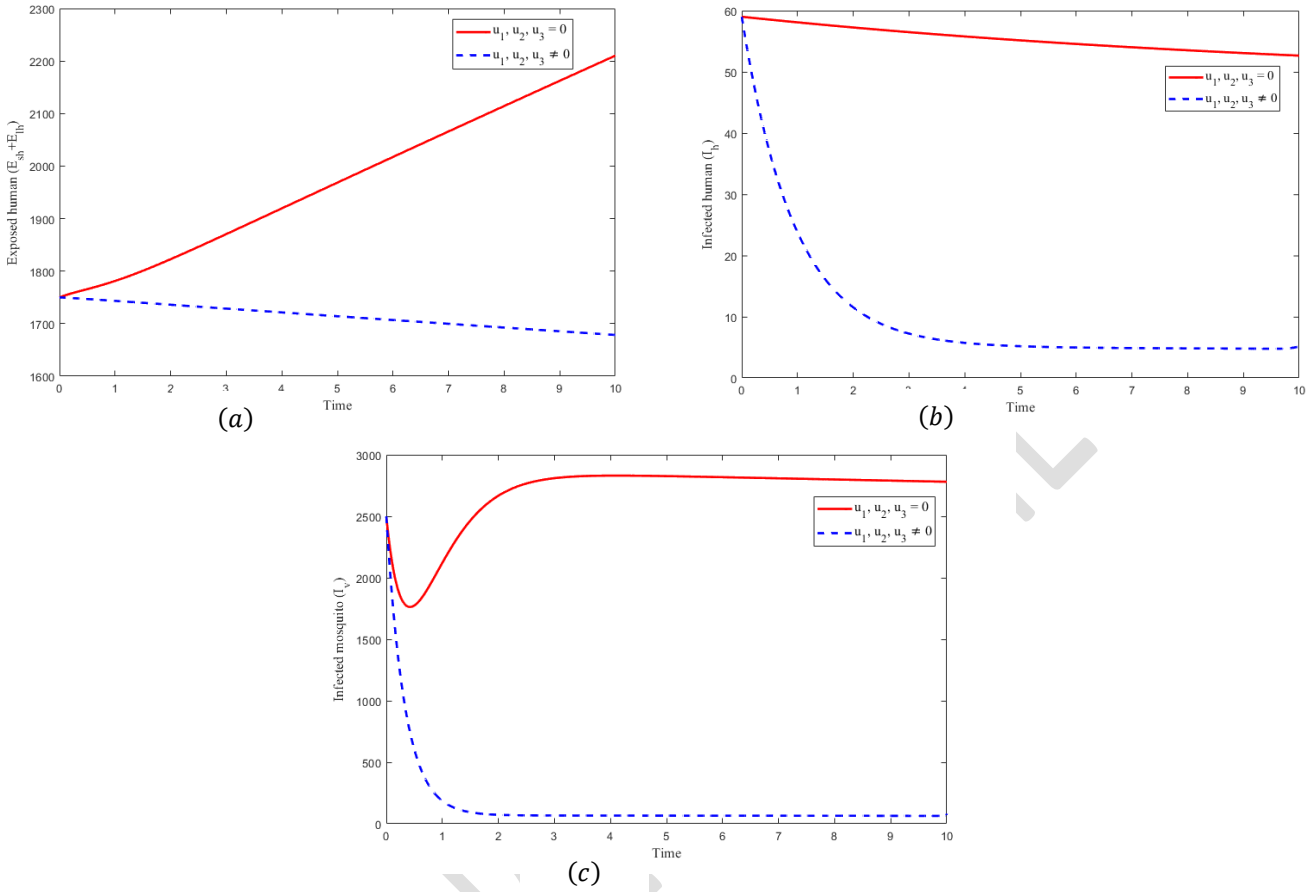

Figure 7: Numerical results of the model using all controls (treated bed net, treatment and insecticide).

From the strategies 1 to 3, we conclude that the strategy 3 is the best strategy to minimize the number of exposed human, infected human and mosquito in the community.

6. Conclusion

We proposed and developed a deterministic malaria transmission dynamic model with optimal controls this paper. The model analysis reveals that it is bounded, epidemiologically meaningful, and mathematically well-posed in a specific domain. Using the next-generation matrix method, we determined the basic reproduction number in relation to the disease-free equilibrium. The Routh-Hurwitz criterion is used to determine local stability of equilibria points, while the Lyapunov function is used to determine global stability. According to the model analysis, if the basic reproduction number is less than one, the disease-free equilibrium is locally and globally asymptotically stable, whereas if the basic reproduction number is greater than one, the unique endemic equilibrium exists. The model parameters are estimated using the monthly real data of Kebri Dehar district, Ethiopia from

September 2011 E.C to June 2015 E.C. Using the value of the estimated parameters, the basic reproduction number in Kebri Dehar district is $R_0 \approx 24.494779$. This finding confirms that the malaria is endemic in the district. In addition, the sensitivity analysis of the basic reproduction number with respect to all parameters was obtained. Furthermore, the malaria transmission model is extended to an optimal control problem by incorporating three continuous controls, namely, personal protection with treated bed nets, treatment of infected human with antimalarial drugs, and insecticide for vector killing strategy. The maximum principle of Pontryagin's is used to obtain the necessary condition of the optimal control problem. The numerical simulation was performed with different control strategies. The numerical results indicate that the integration of the all controls is the best strategy to minimize the number of exposed human, infected human and mosquito in the population.

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