
# Mathematical Modelling of Malaria Transmission Dynamics with Optimal Control Strategies

**Dejen Agachew**
Department of Mathematics
Collage of Natural and Computational Sciences

Advisor: **Manalebish Debalke (Phd)**

**A Thesis submitted to the Department of Mathematics, Addis Ababa University in partial fulfillment for the requirements of the degree of Master of Science in Mathematics.**

Addis Ababa, Ethiopia
August, 2024

# Contents

**Acknowledgment**

I want to start by expressing my gratitude to Almight God , who has given me the opportunity to live and experience a degree of learning that I never would have imagined. Second, I would like to express my sincere gratitude to my adviser, Dr. Manalebish Debalike, for her helpful advice and kind demeanor during the thesis. Lastly, I want to sincerely thank each and every one of my teachers for their unwavering support throughout my coursework.

Abbreviations and Acronyms

| | |
|---|---|
| ACT | Artemisinin-based Combination Therapy |
| API | Annual Parasite Incidence |
| CDC | Centers of Disease Control and Prevention |
| CSA | Central Statistical Agency |
| FMOH | Ethiopian Federal Ministry of Health |
| FY | Fiscal Year |
| IPT | Intermittent Preventive Therapy |
| IRS | Indoor Residual Spray |
| SEIR | Susceptible- Exposed -Infected -Recovered |
| ITNs | Insecticide-Treated bed Nets |
| PHEM | Public Health Emergency Management |
| UNDP | United Nations Development Programme |
| WHO | World Health Organization |

**Abstract**

Malaria is a tropical disease caused primarily by Plasmodium falciparum, which has been humanity's major adversary to this day. This research proposes a malaria model that incorporates the use of treated mosquito nets as a disease control approach, which is then turned into proportions to estimate the worldwide impact of ITNs on malaria prevalence. Using a matrix-theoretic approach to construct a Lyapunov function results in a malaria-free equilibrium state that is globally asymptotically stable if the control reproduction number,$R_m < 1$. This suggests that malaria can be controlled or eradicated beneath a certain threshold amount,$R_m$. A malaria-persistence equilibrium state occurs and is globally stable for $R_m > 1$, utilizing the geometric theoretic technique with the Lozoskii measure. Numerical experiments show that the prevalence of infection can be reduced to zero if the fraction of vulnerable persons using treated mosquito nets exceeds a particular threshold number.

# Chapter 1

# Introduction

## 1.1 Background of the study

Malaria is one of the oldest and most prevalent infectious diseases in humans. It is a parasitic vector-borne disease that is prevalent in many places of the globe. It is caused by eukaryotic parasites of the genus Plasmodium and affects at least 300 million people worldwide, resulting in $1 - 1.5$ million malaria-related deaths per year. This disease in humans is caused by an infection with one of the five Plasmodium species: Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, or Plasmodium knowlesi. Malaria is spread to vertebrates by female genus Anopheles mosquitoes that feed on blood meal. (Balbir et al., 2004; Lawi et al; Rose, 1911)

Malaria is an acute fever illness caused by the plasmodium parasite and transmitted to humans via the bite of a female Anopheles mosquito. Male mosquitoes thrive by consuming floral nectar and delicious fluids. Female mosquitoes not only feed on carbohydrates for energy, but they also require blood nourishment to build their eggs. Without regular blood intakes, their ability to reproduce swiftly declines (CDC, 2022; Shewakena and Temesgen, 2021).Plasmodium has about 100 species and can infect a wide range of animals, including reptiles, birds, and mammals. Until recently, four plasmodium species were thought to cause malaria in humans: Plasmodium vivax, Plasmodium falciparum, Plasmodium ovale, and Plasmodium malariae. Plasmodium falciparum, responsible for roughly 80% of all recorded malaria cases worldwide and 90% of deaths, is particularly common in the tropical areas of Africa and South East Asia (Bakary et al., 2018).Malaria symptoms usually include fever, fatigue, vomiting, and headaches.

Malaria is caused by the multiplication of parasitic protozoa from the Plasmodia family within the blood cells or other tissues of the vertebrate host; clinical symptoms in humans result from the multiplication of blood stages. Although there are multiple families of malarial parasites that infect a wide range of hosts, human malaria is caused by five distinct Plasmodium

species: Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale, Plasmodium vivax, and Plasmodium knowlesi. Plasmodium falciparum is most abundant in tropical regions, while Plasmodium vivax is found in temperate zones (Bakary et al., 2018). The life of the five species of Plasmodium is essentially identical and comprises of two different stages: a sexual stage at the mosquito host and an asexual stage at the human host (CDC, 2022., Olumese,2005).

Malaria spreads in five WHO (World Health Organization) regions: Africa, South-east Asia, Eastern Mediterranean, Western Pacific, and America. Malaria affects around half of the world's population (WHO, 2020; WHO, 2021; WHO, 2022). The majority of malaria cases and deaths occur in sub-Saharan Africa (GHO, 2021). However, since 2000, significant progress has been achieved in malaria control. The World Malaria Report 2020 shows that malaria case incidence and fatality rates decreased by 41% and 62%, respectively, between 2000 and 2020 (WHO, 2021; Shewakena and Temesgen,2021).

In 2020, an estimated 241 million cases of malaria occurred worldwide, the majority of which were in the WHO African Region (228 million or 95%), followed by the WHO South East Asia Region with 2% and the WHO Eastern Mediterranean Region with 2.1%.Sub-Saharan Africa and India accounted for about 83 percent of the worldwide malaria load. Malaria incidence rates fell internationally between 2000 and 2020, from 81 in 2000 to 59 in 2015 and 56 in 2019, before rising to 59 in 2020. The 2020 rise was linked to service disruptions caused by the COVID-19 pandemic (WHO, 2021; Shewakena and Temesgen, 2021). Malaria killed an estimated 627 000 people worldwide in 2020, up from 558000 in 2019 and 558000 in 2000. Malaria affects the most vulnerable group: children under the age of five. In 2020, they were responsible for 80% (497 000) of all malaria deaths globally. In 2020, the WHO African Region accounted for 95% of all malaria deaths. Despite having the largest number of malaria deaths in 2020, this area contributed for 85% of the 180000 fewer global malaria deaths reported in 2020 compared to 2000 (WHO,2021., WHO,2022).

In Ethiopia, malaria is a serious illness that affects over 60% of the population, 68% of the country's landmass is conducive to malaria transmission, and the disease is mainly linked to rainfall and altitude (Deribew et al., 2017; Ethiopia Malaria Operational Plan, 2022). In most of Ethiopia, the months of September through December are when malaria transmission peaks, with the majority of seasons falling between June and August. Furthermore, after a brief season from February to March, certain localities have a second mild malaria transmission phase from April to June (Aschalew and Tadesse, 2016). Plasmodium falciparum and Plasmodium vivax, which account for 60% and 40% of cases, respectively, are the two most well-known malaria-

causing species in Ethiopia (Girum et al.,2019., Ethiopia Malaria Operational Plan,2022). The FMOH Annual Review Meeting report included the most latest publicly accessible malaria case data, which was derived from PHEM data covering the twelve-month period from mid-2019 to mid-2020.
A total of 2,320,135 malaria illnesses were recorded, comprising 286,825 clinical cases, 1,325,409 laboratory-confirmed plasmodium falciparum malaria illnesses, and 707,901 laboratory-confirmed plasmodium vivax malaria illnesses. The routine health information system did not report any cases of Plasmodium ovale or Plasmodium malariae, and mixed infections were counted as *P.* falciparum. Malaria has been linked to 510 recorded deaths.

(Malaria Operational Plan, Ethiopia, 2022). The consequences of malaria in Ethiopia include adult laborers who contract the disease, missed work owing to illness, medical expenses, and other indirect expenditures (Aschalew and Tadesse, 2016).

In Ethiopia, there are regional variations in the prevalence and spread of malaria. For example, altitude largely determines the distribution of malaria in Ethiopia. Through its impact on temperature, altitude influences the distribution pattern of malaria in Ethiopia (Chitnis et al., 2008). The western lowlands of Oromia, Amhara, Tigray, and nearly the whole Gambella and Benishangul Gumuz regions are the areas with the highest risk of malaria. Seasonal transmission of malaria occurs in Ethiopia's midlands between 1,000 and 2000 meters above sea level, with occasional (irregular) epidemics occurring every few years. Malaria is only endemic along riverbanks in Ethiopia's eastern lowlands, which are mainly Afar and Somali. This is because the region is essentially arid and remote from rivers. The lack of water sources for mosquito breeding grounds and low humidity brought on by little precipitation and sparse vegetation serve as barriers to transmission. The cold temperatures in Ethiopia's central highlands have mostly prevented malaria from spreading there by delaying the parasite's and the vector's activities (Ketema et al., 2009; Ethiopia Epidemiological Malaria, 2022). Over the past two years, Ethiopia has made notable strides toward reducing the prevalence of malaria and other serious infectious diseases (UNDP,2014; FMOH, 2016). The last ten years have seen a significant decline in the prevalence of malaria. This decline may be attributed to increased uptake of high-impact interventions such as indoor residual spray (IRS), insecticide-treated bed nets (ITNs), intermittent preventive therapy (IPT), prompt treatment of cases with artemisinin-based combination therapy (ACT), and prevention and control of malaria among pregnant women (Aregawi et al., 2014, Abeku, et al., 2015). Following the scaling-up of ITNs, IRS, and ACT interventions between 2006 and 2011, malaria admissions and mortality in children under the age of five decreased by 81 and 73%, respectively (Aregawi et

al.,2014).Even so, only 25% of Ethiopians live in malaria-free areas, making malaria a severe health concern there (Adhanom et al., 2006). In children under five years old, it continues to rank among the top 10 causes of morbidity and mortality (Deribew et al.,2017; Ethiopia Epidemiological Malaria, 2022).

## 1.2 Statement of the problem

For many years, malaria has been regarded as a major problem on a global scale. As a result, numerous epidemiologists and other experts work hard to understand the disease's dynamics and stop its spread. In Ethiopia, where more than 60% of the population lives in malaria-prone areas and 68% of the country's landmass is conducive to malaria transmission, malaria is still a serious health concern. The disease is mostly linked to altitude and rainfall (Deribew et al., 2017). According to Dietz and Thomas (1974), it remains one of the top ten causes of illness and mortality for children under the age of five. The consequences of malaria in Ethiopia include adult laborers who contract the disease, missed work owing to illness, medical expenses, and other indirect expenditures (Aschalew and Tadesse, 2016).

Malaria is the second most common disease in Somali Regional State, where Plasmodium falciparum is the predominant species (WHO, 2003).Between June and October of 2012, a total of 8,689 cases of malaria were reported. Of these, 3,779 cases were from Shebelle; 198 cases in the Fafan zone resulted in six deaths; 1,368 cases from Korahey resulted in one death; and 1,342 cases from Erer Woreda in the Siti zone also resulted in one death. Furthermore, according to WFP, UNICEF, and INGO (2012), the Afder Zone has recorded 2,002 clinical and confirmed cases of malaria, with 17 fatalities. The region is characterized by high population movements, internally displaced people (IDPs), and refugees. Periodic malaria epidemics are exacerbated by artificial water reservoirs and frequent floods (WHO, 2003).

To comprehend the dynamics of infectious disease transmission, mathematical models are useful tools (Chitins et al., 2006; Olaniyi and Obabiyi, 2013; Ngwa and Shu, 2000). By including optimal control mechanisms that are successful in both treating and preventing infectious diseases, mathematical models can also be used to control the transmission of disease (Gabriel and Joseph, 2016., Fekade and Koya,2015., Bundit and Unyong,2018).The authors of Gabriel and Joseph (2016) reviewed an optimal control that lowers 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). This is just one example of how some researchers have applied optimal control theory to study the transmission dy-

namics of malaria.Fekade and Koya (2015) have examined an optimal control model that uses treatment and preventative measures like ITN and IRS as optimal control to try and stop the spread of malaria. Authors in (Abiodun and Okosun, 2018) examined a mathematical model of the association between climate factors—temperature variations and rainfall variations—and malaria, which is a major contributor in malaria incidence. The authors of (Fatmawati et al.,2021) examined a mathematical model that took into account the seasonal elements, the link between climate factors in the malaria model, and the division of exposed persons into those with short- and long-term incubation periods.

To the best of the researchers' knowledge, no mathematical model related to malaria has been created prior to this work. Considering that mathematical models are essential instruments for determining the dynamics of illness, affecting variables, and offering improved control policies. Therefore, those malaria dynamics and affecting factors are not identified in this field of research. Based on the above description, the researcher will be motivated to modify the SEIR model of malaria transmission in order to ascertain whether the disease will eventually disappear or persist using actual data. To do this, the exposed individuals will be divided into two categories: those with short- and long-term incubation periods; seasonal factors will also be added to the model. Furthermore, we will present an optimal control problem that considers the use of insecticides, preventative, and treatment efforts as acceptable means of controlling malaria. The goal of the researchers is to close this gap and provide answers to the following queries.

What fundamental presumptions underlie the modification of a mathematical model that depicts the dynamics of malaria transmission?

- What is the most influential parameter that helps the spread of malaria in the community?
- What is the most influential parameter that helps us to control the spread of Malaria infection based on the real data ?
- What are the biological interpretations of the solution of the mathematical model?

## 1.3 Significance of the study

In many nations around the world, the process of creating epidemiological policy now includes mathematical modeling of the transmission and management of infectious diseases. In other words, public health policies in different nations have been influenced by epidemiological modeling studies of diseases. As a result, modeling techniques are now crucial when deciding on infectious

disease intervention initiatives. In order to better understand how infectious diseases propagate and are managed, mathematical models are becoming indispensable resources. The goal of the control strategies for malaria's transmission dynamics is to reduce the disease's mortality and morbidity while also halting its spread across the community. Controlling epidemics requires an understanding of the dynamics of malaria transmission and the application of effective control measures. The study will shed light on the dynamics of the malaria virus, which is important for managing and controlling the illness. The community and the field of public health will also greatly benefit from the study's conclusions. It will also be useful in the planning, budgeting, resource allocation, and policy building process. It will enable the prescription of suitable actions and help in the control and prevention of diseases. Additionally, the study will broaden our understanding of the use of mathematics in epidemiology.

### Objective of the study

#### General objective

The general objective of this study is to investigate the transmission dynamics of malaria using mathematical modeling with optimal control.

#### Specific objectives

The specific objectives of the study are to: Make changes to a mathematical model that explains the dynamics of malaria transmission.

- Conduct the model analysis, which entails examining the general patterns of malaria epidemic activity.
- Examine the model's sensitivity analysis to identify the parameters that are most vulnerable.
- Provide the best possible control measures to reduce the dynamics of malaria transmission.
- Interpret the solution of mathematical model.

# Chapter 2

# Literature Review

Ross's model marked the beginning of the use of mathematical modeling to research malaria in 1911 (Ross, 1911). By splitting the human population into susceptible and infected compartments and then having the infected class return to the susceptible class once more, he developed the first deterministic differential equation model of malaria, which gave rise to the SIS (Susceptible-Infected-Susceptible) structure. The $SI$ (Susceptible-Infected) structure is followed by the mosquito population, which likewise consists of only two susceptible and infected compartments. However, because of their short lifespan, the mosquito population does not recover from infection. The model clearly illustrates the importance of the parasite's basic reproductive rate, $R_0$.In essence, the basic reproductive rate is the number of new infections caused by one infected person in a susceptible population; if this number is, on average, less than unity, the disease cannot persist; if the number is greater than unity, the disease can persist. Generally speaking, an illness is more resistant to being eradicated the higher its base reproduction rate. Thus, Ross's model demonstrated that eliminating malaria only required bringing the mosquito population below a particular threshold. By introducing the recovered class in humans in the Anderson-May model, Ngwa and Shu (2000) proposed an ordinary differential equation compartmental model for the spread of malaria with a susceptible-exposed-infectious-recovered susceptible (SEIRS) pattern for humans and a susceptible-exposed-infectious (SEI) pattern for mosquitoes. They believed that there is a high death rate from disease, that there is variation in the overall human population, and that there is a high degree of variability in mosquito populations as a result of interactions between human and mosquito populations, making the assumption of a constant population invalid. According to Mandal et al. (2011), the inclusion of shifting population sizes in the model makes mortality and migrations—two main elements that affect an area's population size—more realistic. Additionally, their approach permits humans to harbor a transient immunity to the illness, all the while continuing to transmit malaria to mosquitoes.

The bifurcation analysis of a mathematical model for malaria transmission was covered by Chitins et al. (2006). The Ngwa and Shu model (Ngwa and Shu, 2000) is expanded upon by the Chitins model, which takes into account immigration, eliminates the possibility of direct human recovery from the infected to the susceptible class, and generalizes the mosquito biting rate to a larger range of populations.

In the Chitin model, the total number of bites depends on both the human and mosquito population sizes, whereas in Ngwa and Shu (2000), the total number of bites on humans depends only on the number of mosquitoes. They added a steady immigration rate to the vulnerable group. They exclude infectious human immigration because they believe that most unwell people will not travel. Additionally, since there aren't many exposed people due to the brief duration of the exposed stage, they don't include the movement of exposed persons. They simplify things by assuming that there isn't any immigration of people who have recovered. Additionally, they do not include the direct infectious-to-susceptible recovery that Ngwa and Shu's model (Ngwa and Shu, 2000) includes. Due to the fact that most persons exhibit a brief period of immunity before reverting to susceptibility, this is a plausible simplifying assumption. This model will incorporate the rapid return of certain individuals to susceptibility; it will also include an exponential distribution of migration from the recovered to the susceptible class.

It was discovered that the disease-free equilibrium is unstable when $R_0 > 1$ and locally asymptotically stable when $R_0 < 1$. Additionally, they demonstrated that for every $R_0 > 1$, there is at least one endemic equilibrium point. They demonstrated by numerical simulations that the transcritical bifurcation at $R_0 = 1$ is supercritical (forward) in the absence of disease-induced death, and that a subcritical (backward) bifurcation is possible at $R_0 = 1$ at larger values of the disease-induced death rate. Accordingly, there are two endemic equilibrium points for various values of $R_0 < 1$; the bigger is locally asymptotically stable, while the smaller is unstable. Therefore, it's not always enough to just lower $R_0$ to a number below one in order to completely remove the illness.Because malaria can reemerge in populations with significantly higher disease prevalence in areas where it has been eradicated with only minor disruptions, such as changes in environmental or control variables or an influx of infectious humans or mosquitoes. In order to be sure that there are no endemic equilibria, $R_0$ must now be reduced to a value less than $R_0{}^*$ (a saddle node bifurcation) for some $R_0{}^* < 1$.

Chitins et al. (2008) also used a mathematical model's sensitivity analysis to identify the relatively significant parameters that influence the transmission of malaria. The model from Chitnis et al. (2006) was expanded upon here, and the endemic equilibrium point and $R_0$ sensitivity indices were as-

sessed. Two sets of baseline parameter values were developed by them: one for high transmission areas and another for low transmission areas. They calculated the sensitivity indices to the parameters at the baseline values for the reproductive number, $R_0$ (which measures starting illness transmission), and the endemic equilibrium point (which measures disease prevalence). They then discovered that the equilibrium proportion and the reproductive quantity of infectious individuals are particularly susceptible to mosquito bite rates in low-transmission locations.The reproductive number is once more most sensitive to the rate of mosquito bites in high transmission locations, but the equilibrium fraction of infectious humans is most sensitive to the pace of human recovery. This shows that effective malaria control techniques can target both the mosquito bite rate (e.g., insecticide-treated bed nets, indoor residual spraying) and the human recovery rate (e.g., early detection and treatment of infectious persons).

A seven-dimensional ordinary differential equation representing the nonlinear forces of infection in the form of saturated incidence rates that accompany the transmission of Plasmodium falciparum malaria between humans and mosquitoes is presented by Olaniyi and Obabiyi (2013). In response to the presence of parasite-causing malaria in both human and mosquito populations, these incidence rates generate antibodies. Since mosquitoes are lifelong infectious and lack a recovered class, their model comprises four compartments for humans: susceptible, exposed, infectious, and recovered; for mosquitoes, it consists of three compartments: susceptible, infectious, and exposed. Nonlinear forces of infection are included in the form of saturated incidence rates in both the host and vector populations. The model also takes into account the rates of disease-induced mortality in mosquitoes and people. They investigated how these additions affected the way the developed model behaved. Their findings demonstrated that raising the quantities of antibodies had a major impact on lowering the spread of the malaria virus. Nevertheless, raising the quantities of antibodies has less of an impact on lowering the malaria burden as mosquito bite rates rise. Additionally, they demonstrated that a rise in mosquito-borne diseases lowers the population of infectious humans. Therefore, they suggested that in order for humans to be able to control the invasion of parasites in the bloodstream, they would need to increase the production of antibodies.

Abadi and Harald (2015) add total population dependent births for human and mosquito populations, as well as a rise in death due to disease, to the model in Yang and Wei (2010). The model can be applied to diseases with vital dynamics that linger in a population for an extended period of time. They take into account susceptible-infected for the vector population and susceptible-infected-recovered compartment patterns for humans. They

analyzed their model using singular perturbation techniques, arguing that mosquito dynamics happen on a far faster time scale than human dynamics. As a result, they took into account the rapid and slow time scales.According to the analysis, intervention methods should be centered on treating and reducing the contact between mosquito vectors and human hosts in order to lower the basic reproduction number below one.

A SPITR (Susceptible-Protected-Infected Treatment-Recovered) model was created by Fekade and Koya (2015) to examine the role of intervention techniques in halting the spread of malaria. They took into consideration the SIR model and added two extra compartments for treatment and protection. As a result, they introduced the SPITR model, which explains the dynamics and moderating mechanism of malaria. According to their model, there are five classes or compartments for humans: Susceptible, Protected, Infected, Treatment, and Recovered. Similarly, there are two classes or compartments for female Anopheles mosquitoes: Susceptible and Infected. They made the assumption that members of the protected class, who are drawn from the susceptible and recovered classes, adopt protective measures like $IRS$ and $ITN$ in order to have complete protection against malaria disease. The two controlling strategies taken into consideration had a significant impact on halting the spread of malaria, as demonstrated by their model's analysis. They proposed that combining prevention and treatment strategies would result in effective malaria control or elimination. By reducing the rate of contact between mosquito populations and human populations—for example, by using ITNs—prevention techniques contributed more to the reduction of the number of affected individuals. Conversely, the implementation of both preventive techniques resulted in a decrease in the overall mosquito population, hence lowering the population of infected mosquitoes.

Insecticide-treated bed nets (ITNS), treatment, indoor residual spray (IRS), and intermittent preventive treatment of malaria in pregnancy (IPTP) are the four time-dependent control measures for malaria that Gabriel and Joseph (2016) proposed and analyzed in a mathematical model for the transmission dynamics of malaria in Kenya. First, they looked at constant control parameters, computed the fundamental reproduction number ($R_0$), and looked into stability analysis, equilibrium existence, and stability. They demonstrated that the disease-free equilibrium is globally asymptotically stable in the feasible region if $R_0 \leq 1$. The unique endemic equilibrium is globally asymptotically stable if $R_0 > 1$. In the interior of the feasible region, the model admits a single endemic equilibrium that is globally asymptotically stable. Additionally, their model displays backward bifurcation at $R_0 = 1$. The mosquito death and bite rates are the most sensitive measures, according to their sensitivity result. In order to determine the prerequisites for the

best possible control of the illness with the suggested model, they took into account the time-dependent control scenario and applied Pontryagin's Maximum Principle. They pose the question of whether optimal control exists. The numerical solution of the optimal control problem makes use of a range of sensible parameter values. According to their findings, the best course of action for controlling malaria in endemic areas is to combine treatment and indoor residual spraying (IRS). In epidemic-prone areas, treatment and IRS should also be used. Treatment should also be used in seasonal areas, and insecticide-treated bed nets (ITNs) and treatment should be used in low-risk areas. These tactics are used in their control efforts, which effectively limit the spread of malaria in various malaria transmission settings.

Bundit and Unyong (2018) made modifications to the SEIR model, which explained the dynamics of malaria transmission. The suggested model's behaviors are examined using the conventional approach. Their findings indicate that there were two equilibrium points: one that was devoid of sickness and the other that was endemic. The next generation matrix method approach was used to obtain the basic reproductive number, and the basic reproductive number $R_0$ is what determines the qualitative findings. Additionally, they employed the Routh-Hurwitz criteria to ascertain the model's stabilities. If $R_0 < 1$, the endemic equilibrium is local asymptotically stable; otherwise, the disease's free equilibrium point is local asymptotically stable, meaning the disease will eventually die out. Lastly, the optimal control functions were added to the initial model's SEIR by the authors. These functions included two dependent control functions, one of which minimized the contract between the vulnerable human and the infected vector and the other of which minimized the population of infected humans.

Abiodun and Okosun (2018) created and examined a mathematical model based on climate to look at how rainfall and temperature affect the spread of malaria. By analyzing the effect of climatic variability on malaria outbreaks throughout the province of Limpopo, South Africa, this study seeks to expand on the work of Makinde and Okosun (Okosun and Makinde, 2011). A model for the transmission of malaria disease that takes into account treatment measures and the class of individuals who are resistant to drugs was developed and examined in the earlier work by Okosun and Makinde; however, the effect of climate on malaria transmission was overlooked. They started by creating the SEIR malaria model using recovery classes and adding climate variables (temperature and rainfall) to the model. Their model subdivides the total human population, denoted by $N_h$ into sub-populations of susceptible individuals ($S_h$), those exposed to malaria parasite ($E_h$), individuals with malaria symptoms ($I_h$) and recovered humans ($R_h$) such that $N_h = S_h + E_h + I_h + R_h$. The total vector (mosquito)

population is denoted by $N_v$ and is sub-divided into susceptible mosquitoes ($S_v$), mosquitoes exposed to malaria parasite ($E_v$) and infectious mosquitoes ($I_v$). Hence, $N_v = S_v + E_v + I_v$.

Lastly, they looked at how temperature affected the number of parasites that reproduced, the rate at which they developed, and the rate at which mosquitoes died. It has been established that the pace of parasite development rises with temperature, yet the number and rate of mosquito bites are thermally limited at both low and high temperatures. The model is verified against the 2002–2004 malaria transmission in the South African province of Limpopo. The findings show that malaria transmission in the area is seasonal, peaking between December and February during periods of relatively high rainfall and temperature. They also look into the impact of the larval mortality rate on the total number of reproduction in South Africa in 2003. Their results demonstrate that when larval mortality is high, the number of reproductions decreases, and when it is low, it increases. This implies that eliminating mosquito breeding grounds and using larvicides on a regular basis have a significant chance of lowering the spread of malaria. The best months to promote further mosquito-killing practices, such as spraying and the usage of treated bed nets, are September through May, when South Africa's mosquito population thrives due to good weather.

In their analysis of a mathematical model, Fatmawati et al. (2021) took into account the interaction between climate factors and seasonal factors in the context of malaria, as well as the division of exposed persons into those with short- and long-term incubation periods. There are two equilibria in the author's malaria model without a seasonal factor: the endemic equilibrium (EE) and the disease-free equilibrium (DFE). First, they deduced that the basic reproduction number determines the existence and local stability of the equilibria. Subsequently, the sensitivity analysis of the parameters was conducted to ascertain the parameters with the greatest influence within the model. Then, their malaria model without a seasonal factor was presented. According to their simulation results, in regions with hot climates, the dynamics of the population of infected mosquitoes and humans are typically more influenced by the malaria model that does not account for seasonal variations. Additionally, the Pontryagin Maximum Principle was utilized to determine the presence of the ideal control variable in the malaria model in the absence of a seasonal element. Ultimately, a numerical simulation of their model without the best control indicates that concurrent application of treatment, prevention, and insecticide controls can effectively lower the number of infectious mosquitoes and exposed and infectious members of the human population.

# Chapter 3

# Methodology

## 3.1 Source of information

The applicable sources of information for this study are:

- Data comprised annual data of malaria infected people in governmental Hospital, Nongovernmental health station
- Other source of information are taken from WHO malaria report, Centres for Disease Control and Prevention (CDC) malaria report, books, published Journals and related studies from the internet.

## 3.2 Mathematical procedure

Our research used both analytical and numerical methods to achieve its goal. Therefore, we used a system of nonlinear ordinary differential equations to modify a mathematical model that uses optimal control to represent the dynamics of malaria transmission. Additionally, we calculated a basic reproduction number and used the Jacobin matrix and Lyapunov functions, respectively, to analyze the equilibrium points of the model equations for both local and global stability. The sensitivity index is used to study the system's sensitivity analysis and identify the parameter that has the greatest influence on the dynamics of malaria sickness. By applying the Pontryagin's minimal principle (PMP), the ideal control was determined. We used appropriate software (MATLAB software) to do a numerical simulation of the model using the Runge-Kutta fourth order method in order to complement the analytical solution of the model.

## Ethical consideration

The proposed study involves people infected by malaria. It contains only general research work that does not involve any kind of risk for its development. Moreover, the researcher is committed to follow all ethical issues during this study as per the rules and regulation of the university.

# Chapter 4

# Model Formulation and Analysis

## 4.1 Mathematical model formulation

The transmission and spread of malaria between two interacting populations of mosquitoes, the vector, and humans, the host, have been taken into consideration in this study. The entire human population, represented by $N_h$ in the model, is split into five epidemiological groups that correspond to the state variables: The susceptible class ($S_h$) includes those who do not currently have malaria but who are at risk of contracting the disease via bites from female anopheles mosquitoes carrying the infection. Humans in the exposed class ($E_h$) are already infected but not yet contagious. The class that is infectious ($I_h$), which consists of persons who have already contracted malaria and are therefore able to spread the disease, and the class that is recovered class ($R_h$), which consists of individuals who recover from malaria and resume their regular status of health.

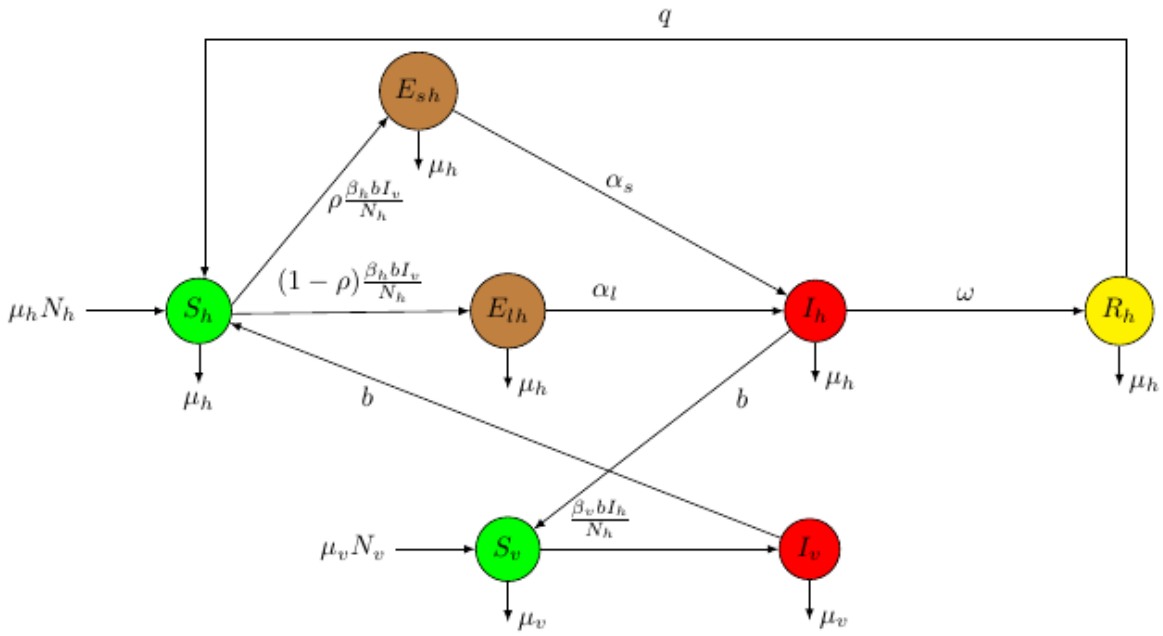



Figure 4. 1: Schematic diagrams for the dynamic of the malaria.

## 4.2 Model assumption

We use the assumptions of SI for the mosquito population and SEIRS disease dynamics for humans to explain the spread of malaria. Humans who have been exposed are classified into two groups based on how lengthy their incubation periods are. When a mosquito $I_v$ successfully infects a susceptible human $S_h$, the human undergoes either a short incubation period $E_{sh}$ with probability $\rho$ or a long incubation period $E_{lh}$ with probability $(1-\rho)$. After this incubation time, the human becomes infectious $I_h$ and can infect more susceptible mosquitoes $S_v$. After their immunity declines, recovered persons, who are in the class $R_h$, return to $S_h$. Natural death reduces the population of every type of individuals at rates $\mu_h$.

The terms $\frac{\beta_h S_h I_v}{N_h}$ and $\frac{\beta_v s_v I_h}{N_h}$ characterize the cross-infection between mosquitoes and humans. The biting rate is denoted by $\beta_v$, while the infection rates $\beta_h$ and $\beta_h$ are calculated using the following formulas: $\beta_h = b\beta_h$ and $\beta_v = b\beta_v, b$. Additionally, the transmission probability from infected mosquitoes to humans is shown by $b\beta_h$, and the transfer probability from infected humans to susceptible mosquitoes is indicated by $b\beta_v$. Both insects and newborn humans are vulnerable. In both mosquito and human populations, the birth rate is the same as the death rate. There is no blood transmission of malaria. The numbers of mosquitoes and humans never change.

Table 4. 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 |

Table 4. 2: Parameters of the model.

| Parameters | Description |
|---|---|
| $\beta_h$ | Infection rate from mosquito to human |
| $\beta_v$ | Infection rate from human to mosquito |
| $\mu_h$ | Natural death/birth rate of human |
| $\mu_v$ | Natural death/birth rate of mosquito |
| $\rho$ | 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 |
| $\omega$ | 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:

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

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 (4.1) is given by $\Omega = \Omega_v \times \Omega_h$ where, $\Omega_v = \left\{(S_v, I_v) \in R^{2+} : S_v + I_v = N_v\right\}$ and $\Omega_h = \left\{(S_h, E_{sh}, E_{lh}, I_h, R_h) \in R^{5+} : S_h + E_{sh} + E_{lh} + I_h + R_h = N_h\right\}$

## 4.3 Model analysis

This section examines the model (4.1)'s local stability of equilibria. First, we ascertain the equilibrium together with its existence requirements and the fundamental reproduction number. The disease-free equilibrium and the endemic equilibrium are the two equilibria that we get from model (4.1).

#### Equilibrium points

The system's equilibrium point is reached when the set of equations is solved.

$$\begin{cases} \mu_v N_v - \frac{\beta_v S_v I_h}{N_h} - \mu_v S_v = 0 \\ \frac{\beta_v S_v I_h}{N_h} - \mu_v I_v = 0 \\ \mu_h N_h + qR_h - \frac{\beta_h S_h I_v}{N_h} - \mu_h S_h = 0 \\ \frac{\rho\beta_h S_h I_v}{N_h} - (\alpha_s + \mu_h) E_{sh} = 0 \\ \frac{(1-\rho)\beta_h S_h I_v}{N_h} - (\alpha_l + \mu_h) E_{lh} = 0 \\ \alpha_s E_{sh} + \alpha_l E_{lh} - (\mu_h + \omega) I_h = 0 \\ \omega I_h - \mu_h R_h - qR_h = 0 \end{cases} \tag{4.2}$$

## 4.4 Disease-free equilibrium

To get the disease-free equilibrium point $\varepsilon_0$, solve equation 4.2 and set $I_v = 0$, $E_{sh} = 0$, $E_{lh} = 0$, and $I_h = 0$. Thus, $\varepsilon_0 = (N_v, 0, N_h, 0, 0, 0, 0)$ represents the malaria model's disease-free equilibrium.

## 4.5 The basic reproduction number

We compute the fundamental reproduction number $R_0$, which may be applied to quantify the possible distribution of infection in a population. The basic reproduction number $R_0$ is obtained from the equations (4.1) using the Next Generation Matrix approach (Van and Watmough, 2002). From there, 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, $\varepsilon_0 = (N_v, 0, N_h, 0, 0, 0, 0)$.

$$F = \frac{\partial \mathcal{F}(\varepsilon_0)}{\partial x_j} = \begin{pmatrix} 0 & 0 & 0 & \beta_v \\ \rho\beta_h & 0 & 0 & 0 \\ (1-\rho)\beta_h & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, j = I_v, E_{sh}, E_{lh}, I_h, \text{ for } j = 1, 2, 3, 4.$$

The $\mathcal{V}$ Jacobian matrix assessed at the disease-free equilibrium point, $\varepsilon_0 = (N_v, 0, N_h, 0, 0, 0, 0)$

$$V = \frac{\partial \mathcal{V}(\varepsilon_0)}{\partial x_j} = \begin{pmatrix} \mu_v & 0 & 0 & 0 \\ 0 & (\alpha_s + \mu_h) & 0 & 0 \\ 0 & 0 & (\alpha_l + \mu_h) & 0 \\ 0 & -\alpha_s & -\alpha_l & (\mu_h + \omega) \end{pmatrix}$$

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 $R_0 = \sqrt{\frac{\beta_v\beta_h[\rho\alpha_s\mu_h+\alpha_l(1-\rho)+\alpha_s]}{\mu_v(\alpha_l+\mu_h)(\mu_h+\omega)(\alpha_s+\mu_h)}}$

$\frac{\beta_h}{\mu_v}$ denotes the quantity of newly infected hosts that can be generated from a single infecting mosquito.

Additionally, the expression $\frac{\beta_v[\rho\ alpha_s\mu_h+\alpha_l(1-\rho)+\alpha_s]}{(\alpha_l+\mu_h)(\mu_h+\omega)(\alpha_s+\mu_h)}$ is the quantity of newly infected mosquitoes that are generated during the infectious period from a single infectious host.

#### Stability analysis

**Theorem 4.5.1.** *Provided that $R_0 < 1$, the disease-free equilibrium $\varepsilon_0$ is locally asymptotically stable.*

Proof: First, we linearized model (4.1) near the disease-free equilibrium. The Jacobian matrix of model(4.1) at $\varepsilon_0$ is as following.

$$J_{\varepsilon_0} = \begin{pmatrix} -\mu_v & 0 & 0 & 0 & 0 & \frac{\beta_v N_v}{N_h} & 0 \\ 0 & -\mu_v & 0 & 0 & 0 & \frac{\beta_v N_v}{N_h} & 0 \\ 0 & -\beta_h & -\mu_h & 0 & 0 & 0 & q \\ 0 & \rho\beta_h & 0 & -(\alpha_s+\mu_h) & 0 & 0 & 0 \\ 0 & (1-\rho)\beta_h & 0 & 0 & -(\alpha_l+\mu_h) & 0 & 0 \\ 0 & 0 & 0 & \alpha_s & \alpha_l & -(\mu_h+\omega) & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega & -(\mu_h+q) \end{pmatrix}$$

To determine the stability of disease-free equilibrium point, we use the characteristics equation of the Jacobin matrix $J_{\varepsilon_0}$. The characteristics equation is given by

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

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

$$\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_3 = 0 \tag{4.3}$$

where,

$$a_1 = 3\mu_h + \alpha_l + \alpha_s + \mu_v + \omega$$
$$a_2 = (\mu_h + \omega)(\mu_h + \mu_v + \alpha_l) + \mu_v(\alpha_l + \mu_h) + (\alpha_s + \mu_h) + (2\mu_h + \alpha_l + \mu_v + \omega)$$
$$a_3 = \mu_v(\alpha_l + \mu_h)(\alpha_s + \mu_h) + (\alpha_s + \mu_h)(\alpha_l + \mu_h)(\omega + \mu_h)$$
$$+ \mu_v(\omega + \mu_h)(\alpha_s + \mu_h)\left(1 - \frac{\beta_h\beta_v N_v\alpha_s\rho}{\mu_v(\mu_h + \omega)(\alpha_s + \mu_h)}\right)$$
$$+ \mu_v(\omega + \mu_h)(\alpha_l + \mu_h)\left(1 - \frac{\beta_h\beta_v N_v\alpha_l(1-\rho)}{\mu_v(\mu_h + \omega)(\alpha_l + \mu_h)}\right)$$
$$a_4 = \mu_v(\omega + \mu_h)(\alpha_s + \mu_h)\,\mu_v(\omega + \mu_h)(\alpha_l + \mu_h)\left(1 - {R_0}^2\right)$$

The quartic equation (4.3) has roots whose real portions are negative if and only if $a_1, a_2, a_3, a_4 > 0$ and $a_1a_2a_3 > {a_3}^2 + {a_1}^2a_4$, according to the Routh-Hurwitz criteria. The coefficients $a_1$ and $a_2 > 0$ are evidently clear. Furthermore, if $R_0 < 1$, it is evident that the coefficient $a_4$ is positive. If $R_0 < 1$, then

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

As a result, if $R_0 < 1$, the coefficient $a_3$ is positive. The condition $a_1a_2a_3 > {a_3}^2 + {a_1}^2a_4$ can also be confirmed to be satisfied. Consequently, if $R_0 < 1$, the disease-free equilibrium $\varepsilon_0$ is locally asymptotically stable. According to Theorem 1, malaria will vanish from the population as soon as $R_0 < 1$.

## 4.6 Global stability of disease-free equilibrium point

**Theorem 4.6.1.** *The disease-free equilibrium point $\varepsilon_0$ of model (4.1) is globally asymptotically stable if the fundamental reproduction number $R_0 < 1$.*

Proof.Using the Lyapunov function approach, we are able to demonstrate the global asymptotic stability of the disease-free equilibrium E0. A Lyapunov function $V$ was defined by us, such that;

$$\frac{dV}{dt} = a_1\frac{dI_v}{dt} + a_2\frac{dE_{sh}}{dt} + a_3\frac{dE_{lh}}{dt} + a_4\frac{dI_h}{dt} \tag{4.2}$$

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 (4.1) to equation (4.2) we obtain the following:

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

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

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

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

$$\begin{array}{ll} \text{i)} & a_2\frac{\rho\beta_h S_h}{N_h} + a_3\frac{(1-\rho)\beta_h S_h}{N_h} - a_1\mu_v = 0 \\ \text{ii)} & \alpha_s a_4 - a_2\left(\alpha_s + \mu_h\right) = 0 \\ \text{iii)} & \alpha_l a_4 - a_3\left(\alpha_l + \mu_h\right) = 0 \end{array}$$

Then we get

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

Now from (ii) and (iii) we get

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

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

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

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

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

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

Therefore, if $R_0 \leq 1$, then $\left[{R_0}^2 - 1\right] \leq 0$, so we obtain $\frac{dV}{dt} \leq 0$.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 $\Omega$ 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 (4.1) with initial conditions in $\Omega$ approaches the disease free-equilibrium point as time $(t)$ tends to infinity $(t \to \infty)$ whenever $R_0 < 1$.Accordingly, if $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable in $\Omega$.

## 4.7 Endemic equilibrium

Endemic equilibrium points are steady-state solutions (i.e., equilibria where at least one of the model's infected components is non-zero) where the disease continues to spread across the population. An explicit depiction of the endemic equilibrium point for $R_0 > 1$ may be found for our model.

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

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

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

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

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

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

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

where,

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

and

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

## 4.8 Local stability of the endemic equilibrium point

**Theorem 4.8.1.** *${\varepsilon_0}^* = ({S_v}^*, {I_v}^*, {S_h}^*, {E_{Sh}}^*, {E_{lh}}^*, {I_h}^*, {R_h}^*$, is the endemic equilibrium point.If $R_0 > 1$, then of the malaria model (4.1) is locally asymptotically stable (LAS).*

Proof: Our analysis of the endemic equilibrium involves linear stability. At the point of endemic equilibrium, the Jacobian matrix $**_0^E = (E_{Sh}{}^*, E_{lh}{}^*, I_h{}^*, R_h{}^*, S_v{}^*, I_v{}^*$ value (4.1) becomes

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

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

The corresponding characteristic equation of the Jacobian matrix with eigenvalue $\lambda$ is given by $|J(\varepsilon_0{}^*) - \lambda I| = 0$; that is,

$$\begin{cases} \mu_v N_v - \frac{\beta_v S_v I_h}{N_h} - \mu_v S_v = 0 \\ \frac{\beta_v S_v I_h}{N_h} - \mu_v I_v = 0 \\ \mu_h N_h + qR_h - \frac{\beta_h S_h I_v}{N_h} - \mu_h S_h = 0 \\ \frac{\rho\beta_h S_h I_v}{N_h} - (\alpha_s + \mu_h) E_{sh} = 0 \\ \frac{(1-\rho)\beta_h S_h I_v}{N_h} - (\alpha_l + \mu_h) E_{lh} = 0 \\ \alpha_s E_{sh} + \alpha_2 E_{lh} - (\mu_h + \omega) I_h = 0 \\ \omega I_h - \mu_h R_h - qR_h = 0 \end{cases}$$

## 4.9 The global stability of the endemic equilibrium point

**Theorem 4.9.1.** *$\varepsilon_0{}^* = (S_v{}^*, I_v{}^*, S_h{}^*, E_{Sh}{}^*, E_{lh}{}^*, I_h{}^*, R_h{}^*$, is the endemic equilibrium point. $R_0 > 1$, indicating global asymptotic stability of the system (4.1).*

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,

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

Then differentiating with respect to $t$ gives,

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

By replacing the derivatives in this equation, from the system of equation(4.1), it follows:

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

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

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

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

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

and

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

Thus, if $H < K$, then $\frac{dV}{dt} \leq 0$ and $\frac{dV}{dt} = 0$ 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 $\varepsilon_0{}^* = ({S_v}^*, {I_v}^*, {S_h}^*, {E_{Sh}}^*, {E_{lh}}^*, {I_h}^*, {R_h}^*)$ is the largest compact invariant singleton set in $\left\{(S_v{}^*, I_v{}^*, S_h{}^*, E_{Sh}{}^*, E_{lh}{}^*, I_h{}^*, R_h{}^*) \in \Omega : \frac{dV}{dt} =\right.$ Therefore, If $R_0 > 1$ by the principle of Lasalle (LaSalle, 1976), the endemic equilibrium $\varepsilon_0{}^*$ is globally asymptotically stable in the invariant region $\Omega$ if $H - K$.

### 4.9.1 Sensitivity indices of basic reproduction number

($\boldsymbol{R_0}$) to the parameters It is appropriate to assess the model's resilience to variations in parameter values because the precise values of epidemic models' parameters are frequently unknown. This will assist in identifying the parameters that have the most effects on the model's dynamics. Sensitivity analysis is useful for reducing complex non-linear models, assimilation of data, and experimental design. The parameters that should be targeted most for interventions are indicated by the values of the sensitivity indexes. A very high sensitivity index suggests that the linked parameter should be estimated with greater caution. It is common practice to use the normalized forward sensitivity index to identify the parameters that exert the greatest influence on the fundamental reproduction number, $R_0$. The ratio of the relative change in the variable to the relative change in the parameter is the normalized forward sensitivity index of a variable to a parameter. Partial derivatives can be used as an alternate definition of the sensitivity index when the variable is a differentiable function of the parameter. We can ascertain the relative significance of several parameters in the transmission and prevalence of malaria by using these sensitivity indices. The sensitivity index magnitude of the most sensitive parameter is greater than that of any other parameter [17].

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

We say that $P$ is a more sensitive parameter to the fundamental reproduction number if, when compared to other parameters, its magnitude of sensitivity index is high.

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

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

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

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

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

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

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

These sensitivity indices and indications provide insight into the relative importance of each element for the prevalence and transmission of disease. If the values of those parameters are rising, a positive (+) sign shows that those parameters have a significant impact on the spread of the disease in the population. because, when their values rise, so does the fundamental reproduction number. Conversely, an index that has a negative sign (-) means that the parameters have the potential to reduce the overall disease burden in the community as their values rise. Additionally, as their values rise, the basic reproduction number falls, which also contributes to reducing the endemic nature of the disease in the community.

## 4.10 Optimal Control

Without providing an intention mechanism, we examined both mathematical and epidemiological well-posedness in chapter 4, where we also introduced a mathematical model for the dynamics of malaria transmission. In this chapter, we address specific intervention tactics and establish controls designed to limit transmission dynamics. We first provide the optimal control formulation and then use numerical analysis to examine the transmission dynamics.

### 4.10.1 Extension of the model into an optimal control

The malaria model (4.1) is expanded by adding three control measures. This assisted us in determining the most effective intervention tactics that support the disease's eradication within the allotted time frame. Here is a definition of the control interventions:

i) The control $u_1$ denotes an attempt to avoid malaria by shielding susceptible individuals from infection (treated bed net).

ii) The control $u_2$ indicates the malaria-infected people's treatment attempt.

iii) The application of pesticide is represented by the control $u_3$.

Upon integrating $u_1, u_2$, and $u_3$ into model (4.1), we get the optimal control model that follows:

$$g(x,u,t)=\begin{cases}\frac{dS_h}{dt}=\mu_h N_h+qR_h-(1-u_1)\frac{\beta_h S_h I_v}{N_h}-\mu_h S_h\\ \frac{dE_{sh}}{dt}=(1-u_1)\frac{\rho\beta_h S_h I_v}{N_h}-(\alpha_s+\mu_h)E_{sh}\\ \frac{dE_{lh}}{dt}=(1-u_1)\frac{(1-\rho)\beta_h S_h I_v}{N_h}-(\alpha_l+\mu_h)E_{lh}\\ \frac{dI_h}{dt}=\alpha_s E_{sh}+\alpha_l E_{lh}-(\mu_h+\omega+u_2)I_h\\ \frac{dR_h}{dt}=(\omega+u_2)I_h-\mu_h R_h-qR_h\\ \frac{dS_v}{dt}=\mu_v N_v-(1-u_1)\frac{\beta_v S_v I_h}{N_h}-(\mu_v+u_3)S_v\\ \frac{dI_v}{dt}=(1-u_1)\frac{\beta_v S_v I_h}{N_h}-(\mu_v+u_3)I_v\end{cases}\tag{5.1}$$

The task of optimum control is to reduce the objective functional $J$ taking into account the price of insecticide, anti-malarial medication, and malaria prevention. Reducing the number of exposed people, sick people, and infected mosquitoes at the lowest possible cost is the aim of the adopted strategy. The optimal control problem is mathematically defined as minimizing the objective functional

$$J(u_1,u_2,u_3)=\min_{u_1,u_2,u_3}\int_0^T\left(A_1E_{sh}+A_2E_{lh}+A_3I_h+A_4I_v+\frac{1}{2}\sum_{i=1}^{3}B_iu_i^2\right)dt\tag{5.2}$$

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

whereas $B_1, B_2$, 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 $i=1,2,3$ ), and where $T$ represents the final time of control implementation, 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. We also assume that $B_iu_i^2$ for $i=1,2,3$ represents the cost of controls $u_i$ for $i=1,2,3$. This implies that, for technical reasons, the cost of controls $u_i$ for $i=1,2,3$ is non linear and quadratic as seen in the cost function (5.2).

Finding the optimal control for $u_1^*, u_2^*$, and $u_3^*$ is the primary objective in order to

$$J(u_1,u_2,u_3)=\min_U J(u_1^*,u_2^*,u_3^*)\tag{5.3}$$

where,

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

### 4.10.2 Existence and characterization of the optimal solutions

We look at circumstances that can guarantee the existence of a solution to the optimum control problem (5.1) in this paragraph.

#### Existence of optimal control solution

**Theorem 4.10.1.** *There exists an optimal control , the formula* $u^* = (u_1^*, u_2^*, u_3^*)$ *and an appropriate fix for it* $(S^*, I_h^*, R_h^*, S_v^*, I_v^*, E_{lh}^*, S_v^*)$ *solution the state initial value problem (5.1), which reduces the functional cost Of* (5.2) *over* $U$, $J(u_1, u_2, u_3)$.

Proof. Fleming and Rishel's theorem (Fleming et al., 2012) follows the nontrivial restriction on the set of admissible controls and the set of end conditions.

i) There is no empty set in the set of all solutions to system (5.1) with matching control functions in $U$.

ii) There is a convex and closed control set.

iii) A linearized function in the state and control variables bounds the state system's right side.

iv) For any i, i=1,2, *and*r>1, *theintegrandoftheobjectivefunctionalisconvexon*U*and*
$\gamma_2$.

We use the Picard-Lindel" of existence theorem (Earl and Levinson, 1955) to establish condition (i). For every admissible control $U$, there is a unique solution if $g(x, u, t)$ is bounded, continuous, and Lipschitz in the state variables. Therefore, given the state variables and any $u \in U$, we obtain

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} \tag{5.4}$$

where $N(t) := N_h(t) + N_v(t), \frac{\Lambda}{\mu} := \frac{\Lambda_h}{\mu_h} + \frac{\Lambda_v}{\mu_v}$ and $\Lambda_h := \mu_h N_h(t), \Lambda_v := \mu_v N_v(t)$

and, by model assumption, non-empty. Moreover, the bounded established in (5.4) suggests that the state system is both bounded and continuous. The boundedness of the partial derivative with respect to the state variable can be demonstrated,

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

The system is determined to be Lipschitz with respect to the state variables by its existence and finiteness (Sharomi et al., 2007). This proved that the criterion was met (i).

The set $U$ is closed by definition. Select any controls $\theta \in [0,1]$, $u_1, and u_2 \in U$. Next, $0 \leq (1-\theta)u_2 + \theta u_1$.

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

Therefore, for any $u_1, u_2 \in U$ and $\theta \in [0,1]$, $\theta u_1 + (1-\theta)u_2 \leq 1$. As a result, condition (ii) is met and $U$ is convex.

The boundedness of the optimal system establishes the required compactness for the existence of optimal control. We employ the methodology used by Sadiq et al., 2014 and Laarabi et al., 2012 to verify this argument, whereby system (5.1) is expressed as follows:

$$X = BX + F(X) \tag{5.5}$$

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

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

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

The derivative of $X$ with respect to time $t$ is indicated by the symbol $X'$. A non-linear system with a bounded coefficient is system (5.5). We decided,

$$D(X) = X' = BX + F(X) \tag{5.6}$$

In (5.6), the second term on the right side satisfies

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

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

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

$L = \max\{M, \|B\|\} < \infty$ is the case. It implies that $D$ is a uniformly Lipchitz continuous function. It is evident from the formulation of control variables and non-negative beginning conditions that the system (5.6) has a solution.

In order to prove condition (iv), we note that since $f(x, u, t)$ is quadratic in the controls, the integrand in our objective functional is convex (Choi and Jung, 2014). The bound on $f(x, u, t)$ is then all that has to be proven. This is displayed as follows:

$$
\begin{aligned}
f(x,u,t) = A_1E_{sh} + A_2E_{lh} + A_3I_h + A_4I_v + \tfrac{1}{2}\textstyle\sum_{i=1}^{3} B_i u_i^2 \geq \tfrac{1}{2}\textstyle\sum_{i=1}^{3} B_i u_i^2 \geq \left(\tfrac{1}{2}\textstyle\sum_{i=1}^{3} B_i \right. \\
\geq \left(B\textstyle\sum_{i=1}^{3} u_i^2\right) - \tfrac{1}{2}u_1 = B\,\|(u_1,u_2,u_3)\| - \tfrac{1}{2}u_1, \text{ where, } B = \min\left\{\tfrac{1}{2}B_1, \tfrac{1}{2}\right.
\end{aligned}
$$

Then, $f(x, u, t)$ has a bound established by the above.

**Characterization of the optimal control solutions**

If $u^*(\cdot) \in U$ is optimal for issue (5.3) with fixed final time $T$, then there exists a non-trivial absolutely continuous mapping, as per the Pontrygin's maximum principle. $\lambda : [0, T] \to \mathbb{R}^7, lambda =$The following are the values of lambda$_1(t), lambda_2(t), lambda_3(t), lambda_4(t), lambda_5(t), lambda_6(t), lambda_7(t)$ is referred to as the adjoint vector, so that

definition of the Hamiltonian function is

$$\mathcal{H} = A_1E_{sh} + A_2E_{lh} + A_3I_h + A_4I_v + \frac{1}{2}\sum_{i=1}^{3} B_i u_i^2 + \sum_{i=1}^{7} \lambda_i(t) g_i(x(t), u(t), t) \tag{5.7}$$

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

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

5. Moreover, the transversality condition

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

**Theorem 4.10.2.** *The optimal control problem (5.3) with a fixed final time $T$ permits a single best solution. $S_h^*, E_{sh}^*, E_{lh}^*, I_h^*, R_h^*, S_v^*, I_v^* = (x^*)$ related to the best possible control The formula $u^* = (u_1^*, u_2^*, u_3^*)$ for every $t \in [0, T]$. Furthermore, for any $i = 1$ to 7 there exists an adjoint function $\lambda_i^*$ such that*

$$\begin{cases} \lambda'_1 = (1-u_1)\frac{\beta_h I_v}{N_h}(\lambda_1 - \lambda_3) + (1-u_1)\rho\frac{\beta_h I_v}{N_h}(\lambda_3 - \lambda_2) + \mu_h \lambda_1 \\ \lambda'_2 = -A_1 + \alpha_s(\lambda_2 - \lambda_4) + \mu_h \lambda_2 \\ \lambda'_3 = -A_2 + \alpha_l(\lambda_3 - \lambda_4) + \mu_h \lambda_3 \\ \lambda'_4 = -A_3 + (\omega + u_2)(\lambda_4 - \lambda_5) + (1-u_1)\frac{\beta_v s_v}{N_h}(\lambda_6 - \lambda_7) + \mu_h \lambda_4 \\ \lambda'_5 = q(\lambda_5 - \lambda_1) + \mu_h \lambda_5 \\ \lambda'_6 = (1-u_1)\frac{\beta_v I_h}{N_h}(\lambda_6 - \lambda_7) + (u_3 + \mu_v)\lambda_6 \\ \lambda'_7 = -A_4 + (1-u_1)\frac{\beta_h S_h}{N_h}(\lambda_1 - \lambda_3) + (1-u_1)\rho\frac{\beta_h S_h}{N_h}(\lambda_3 - \lambda_2) + (u_3 + \mu_v)\lambda_7 \end{cases} \tag{5.8}$$

with transiversality conditions

$$\lambda_i^*(T) = 0, \quad i = 1, \ldots, 7 \tag{5.9}$$

Furthermore, $u^* = (u_1^*, u_2^*, u_3^*)$ is the best control.$isprovidedby$

$$u_1^*(t) = \max\left\{0, \min\left(1, \frac{\beta_h S_h I_v\left(\lambda_3 - \lambda_1\right) + \rho\beta_h S_h I_v\left(\lambda_2 - \lambda_3\right) + \beta_v S_v I_h\left(\lambda_7 - \lambda_6\right)}{B_1 N_h}\right)\right\}$$
$$u_2^*(t) = \max\left\{0, \min\left(1, \frac{I_h\left(\lambda_4 - \lambda_5\right)}{B_2}\right)\right\}$$
$$u_3^*(t) = \max\left\{0, \min\left(1, \frac{S_v\lambda_6 + I_v\lambda_7}{B_3}\right)\right\} \tag{5.10}$$

Proof: Through the application of Pontryagin's maximal principle (Pontryagin et al., n.d.), the subsequent system of adjoint variables is obtained:

$$\lambda_1' = -\frac{\partial\mathcal{H}}{\partial s_h} = \left(1 - u_1\right)\frac{\beta_h I_v}{N_h}\left(\lambda_1 - \lambda_3\right) + \left(1 - u_1\right)\rho\frac{\beta_h I_v}{N_h}\left(\lambda_3 - \lambda_2\right) + \mu_h\lambda_1$$
$$\lambda_2' = -\frac{\partial\mathcal{H}}{\partial E_{sh}} = -A_1 + \alpha_s\left(\lambda_2 - \lambda_4\right) + \mu_h\lambda_2$$
$$\lambda_3' = -\frac{\partial\mathcal{H}}{\partial E_{lh}} = -A_2 + \alpha_l\left(\lambda_3 - \lambda_4\right) + \mu_h\lambda_3$$
$$\lambda_4' = -\frac{\partial\mathcal{H}}{\partial I_h} = -A_3 + \left(\omega + u_2\right)\left(\lambda_4 - \lambda_5\right) + \left(1 - u_1\right)\frac{\beta_v s_v}{N_h}\left(\lambda_6 - \lambda_7\right) + \mu_h\lambda_4$$
$$\lambda_5' = -\frac{\partial\mathcal{H}}{\partial R_h} = q\left(\lambda_5 - \lambda_1\right) + \mu_h\lambda_5$$
$$\lambda_6' = -\frac{\partial\mathcal{H}}{\partial s_v} = \left(1 - u_1\right)\frac{\beta_v I_h}{N_h}\left(\lambda_6 - \lambda_7\right) + \left(u_3 + \mu_v\right)\lambda_6$$
$$\lambda_7' = -\frac{\partial\mathcal{H}}{\partial I_v} = -A_4 + \left(1 - u_1\right)\frac{\beta_h S_h}{N_h}\left(\lambda_1 - \lambda_3\right) + \left(1 - u_1\right)\rho\frac{\beta_h S_h}{N_h}\left(\lambda_3 - \lambda_2\right) + \left(u_3 + \mu_v\right)\lambda_7$$

In a similar manner, we solved the equation, using the methodology of (Pontryagin et al., n.d.), to obtain the controls.
$\frac{\partial\mathcal{H}}{\partial u_i} = 0$ 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

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

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

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

## 4.11 Numerical simulation

The numerical results for the systems (4.1) and (5.1) for various model parameter values are shown and discussed in this section. MATLAB software is used to carry out the simulation process. The first step is to define and estimate the model's parameter values. We then present a graphic representation of the simulation results.

### 4.11.1 Parameter Estimation

In this section, we estimate the unknown model parameters by fitting the proposed model to cumulative cases of malaria infection data. The cumulative cases of malaria infection from September 2011 E.C. to June 2015 E.C. are shown in Table 6.1, which was taken from the health office of Ethiopia. One way to calculate the squared sum of errors (SSE) between the model solution and the data is to

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

where $n$ is the total number of real data points that are available, and $\|\cdot\|$ represents the Euclidean norm in $\mathbb{R}^n$. The real cumulative malaria-infected cases are expressed as $\bar{I}_{hi}(t)$, while the corresponding model solutions at time $t_i$ are expressed as $I_{hi}(t)$. We search for a value $\bar{\vartheta}$ of the model parameter $\vartheta$ such that the squared sum of errors is the minimal during the least-squares fitting process. Since the reliance of a solution $I(t, \vartheta)$ on the parameter $\vartheta$ is through a highly nonlinear system of differential equations, it is evident that such a problem is a nonlinear least squares problem.

Table 6. 1: Cumulative malaria cases from 2011 - 2015 E.C .

| 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 following part, we employ numerical simulations to investigate the dynamics of malaria. To get a good match to the real data, we use the least squares technique to estimate the parameters in the proposed model with suitable initial conditions.

#### 4.11.2 Simulation results and discussion

According to statistics acquired, the initial population infected was $I_h(0) = 59$, as Table 6.1 indicates. The initial susceptible population is provided by $S_h(0) = N_h(0) - E_{sh}(0) - E_{lh}(0) - I_h(0) - R_h(0) = 174,585$. Initially, we assumed $E_{sh}(0) = 1000, E_{lh}(0) = 750$, and $R_h(0) = 100$. We have assumed the initial mosquito population as $N_v(0) = 100,000$, the initial infected mosquito population as $I_v(0) = 25,000$, and the initial susceptible mosquito population as $S_v(0) = N_v(0) - I_v(0) = 75,000$ because the real data for the mosquito population is unavailable and because a large number of mosquito individuals are involved.

The human recruitment rate $\mu_h N_h = \Lambda_h$, the mosquito recruitment rate $\mu_v N_v = \Lambda_v$, the natural death rate of both humans and mosquitoes $\mu_v$, the human recovery rate $\omega$, and the rate at which human immunity is lost $q$ were not fitted. The parameters $\mu_h$ and $\mu_v$ are determined by taking the inverse of the average lifespan of the Anopheles mosquito and the population in Ethiopia, respectively. This results in $\mu_h = \frac{1}{66.71}$ per year $= \frac{1}{66.71\times12}$ per month, where the average population lifespan in Ethiopia is 66.71 years (Kereyu & Demie, 2021) and $\mu_v = \frac{1}{15}$ per day $= \frac{1\times30}{15}$ per month, where the average lifespan of mosquitoes is 15 days (Malaria, 2020). Here is the calculation of $\Lambda_h$ and $\Lambda_v$. Given that the Kabridahar district has 176,494 total residents as of 2017, the greatest human population that can exist without disease is $\frac{\Lambda_h}{\mu_h} = 176,494$. Consequently, $\Lambda_h = 220.4742$per month, and $\Lambda_v = 200,000$ per month. The parameters for the immunity loss rate $q$ and the recovery rate $\omega$ are taken from, or calculated from, the literature. The average length of the infectious and immune periods, respectively, is $\frac{1}{\omega} = 9.5$ months and $\frac{1}{q} = 5$ years. This means 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). Using the least-square curve fitting method, the remaining unknown parameters $\beta_h, \beta_v, \alpha_{sh}, \alpha_{lh}$, and $\rho$ are found. Table 6.2 lists the model (4.1)'s fitted and estimated parameter values. Figure 6.1 shows the outcome of fitting model (4.1) to the real malaria incidence data. The solid line indicates the model fit, while the red circle displays the monthly number of malaria cases recorded in the Kabridahar district. Figure 6.2 displays the residuals plots for both the model and the actual data in Table 6.1. For the model, the standard errors are typically modest and the residuals appear to be random. The estimates obtained here are therefore reasonable.

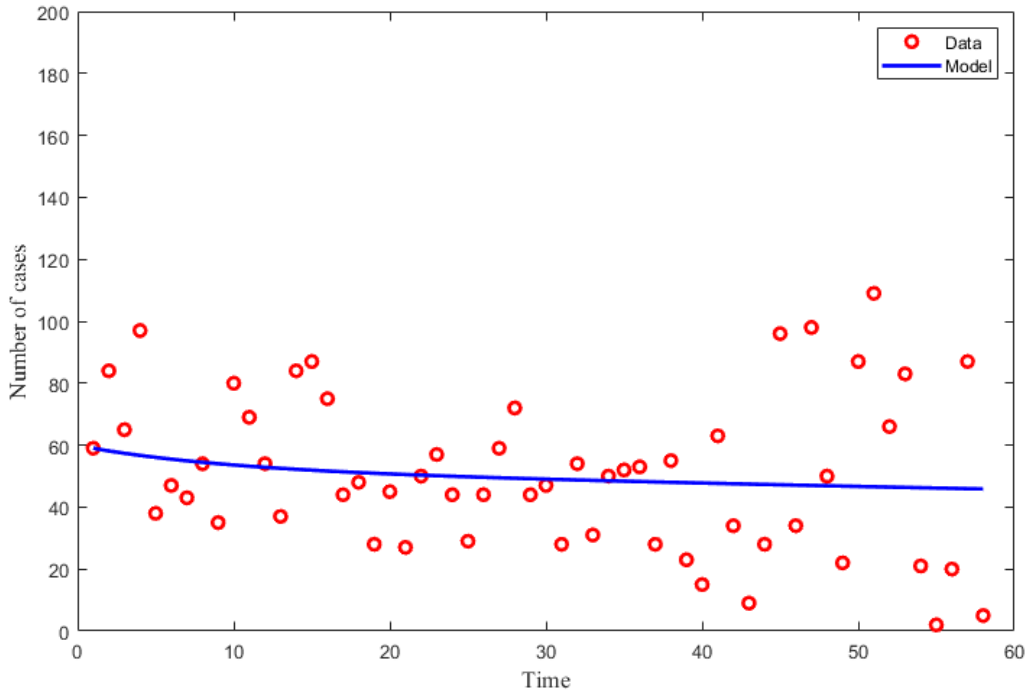



Figure 6. 1: Malaria cases data fitting of cumulative infected humans using the model.

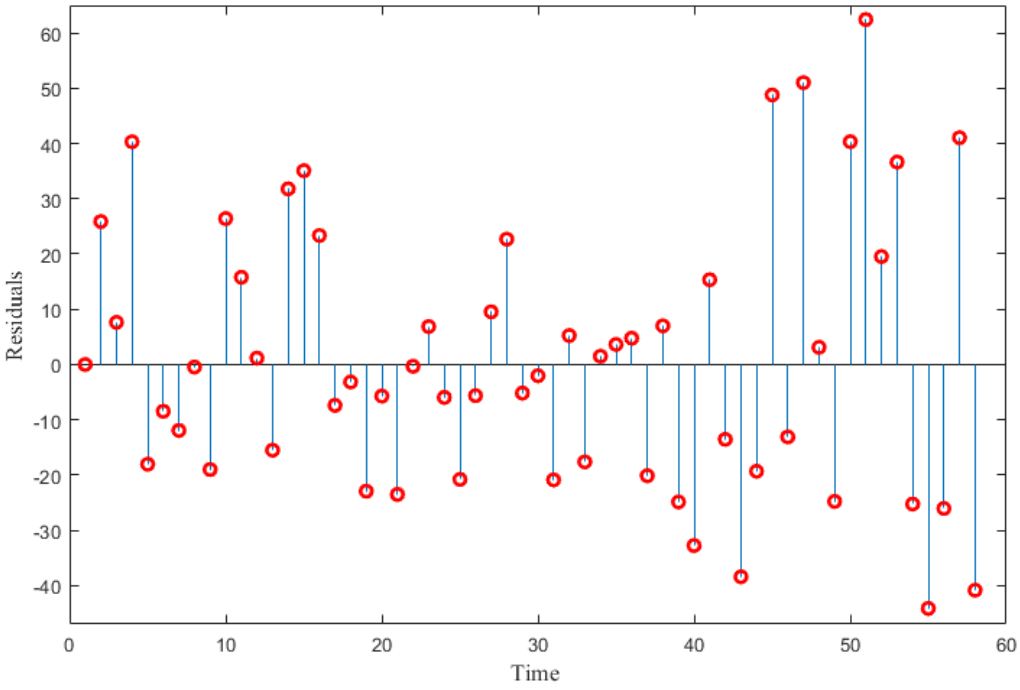



Figure 6. 2: Residual of estimated parameters.

Table 6. 2: Parameters value of the model.

| Parameters | Description | Value | Units | References |
|---|---|---|---|---|
| $\beta_h$ | Infection rate from mosquito to human | 0.0203 | Month $^{-1}$ | Fitted |
| $\beta_v$ | Infection rate from human to mosquito | 10.4482 | Month $^{-1}$ | Fitted |
| $\mu_h$ | Natural death/birth rate of human | $\frac{1}{66.71\times12}$ | Month $^{-1}$ | Demie, 20 |
| $\mu_v$ | Natural death/birth rate of mosquito | $\frac{30}{15}$ | Month $^{-1}$ | (Malaria, 2 |
| $\rho$ | Probability of exposed humans going through short-term incubation periods | 0.0527 | Month $^{-1}$ | Fitted |
| $\alpha_s$ | Progression rate of $E_{sh}$ to $I_h$ | 0.00524 | Month $^{-1}$ | Fitted |
| $\alpha_l$ | Progression rate of $E_{lh}$ to $I_h$ | 0.00012 | Month $^{-1}$ | Fitted |
| $\omega$ | 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 6.2 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 is

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

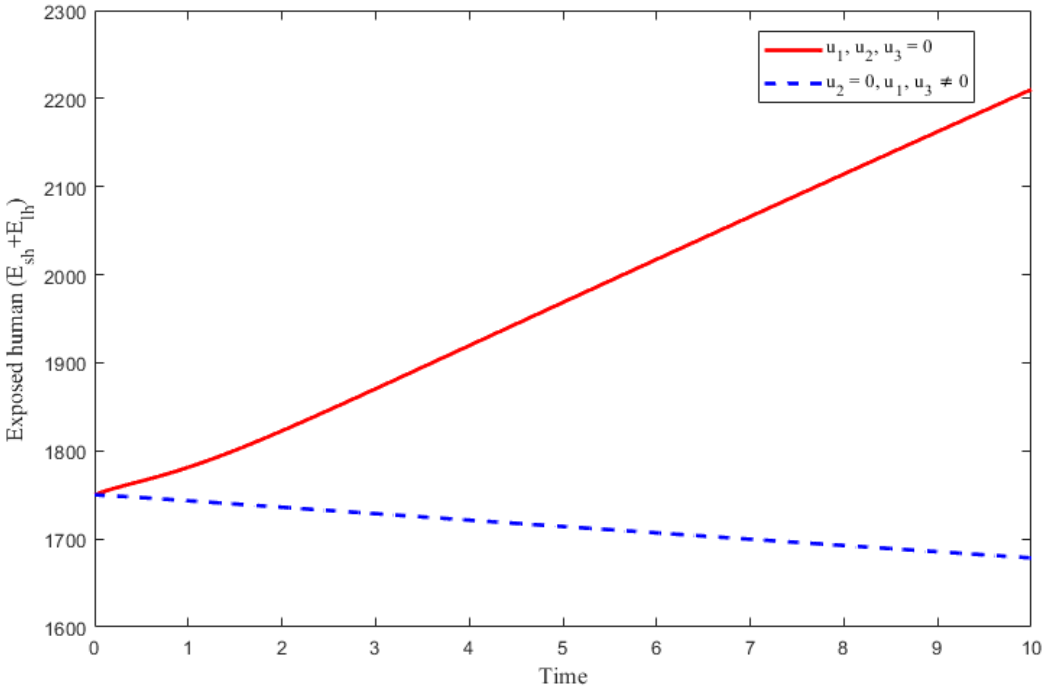
The result shows that disease will be epidemic in the district.

A MATLAB application is used to illustrate the numerical solutions. The optimal control solution is found by solving the optimality system, which is made up of the state system and the adjoint system. The optimality system is solved using a fourth order Runge-Kutta iterative approach. Because of the transversality constraints of (5.9), the adjoint equations are solved by the backward fourth order RungeKutta method utilizing the current iterations solutions of the state equations. Next, a convex combination of the prior controls and the value from the characterizations (5.10) is used to update the controls. If the values of the unknowns at the prior iterations are very near to the ones at the current iteration, this process is repeated and the iterations are ended (for more detail see (Rodrigues, 2012)).

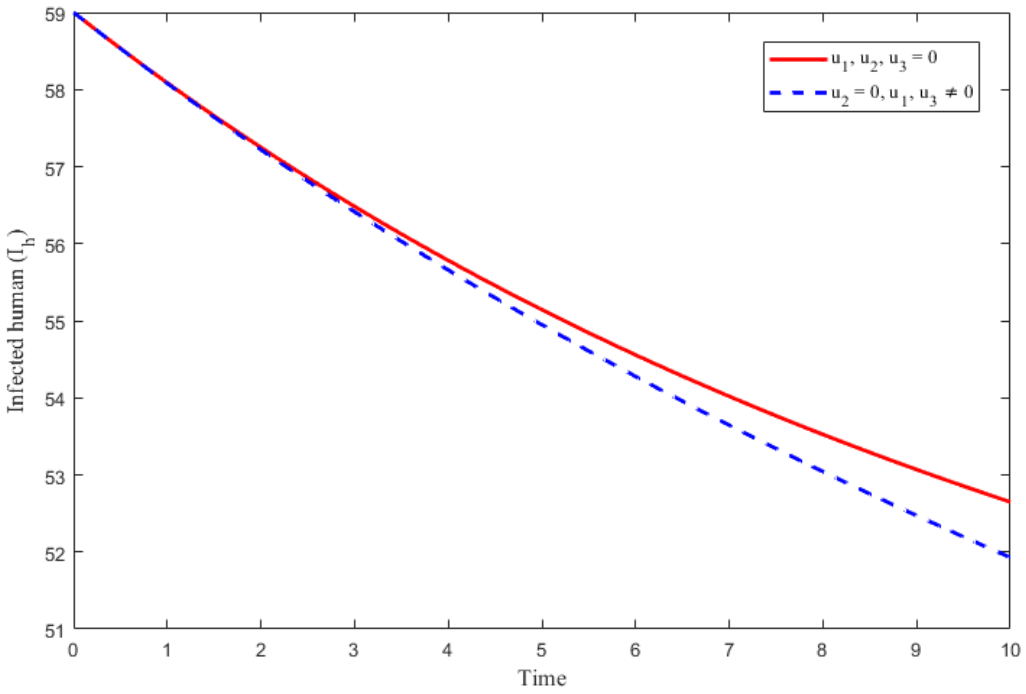
The values of the parameters provided in Table 6.2 are used to simulate the optimal control issue. $(S_h(0), E_{sh}(0), E_{lh}(0), I_h(0), R_h(0), S_v(0), I_v(0)) = (174585, 1000, 750, 59, 100, 7500, 2500)$ are the initial conditions that we utilized for the simulation of the optimal control. The state and control weight value constants that we employed are as follows: $A_1 = 80, A_2 = 60, A_3 = 60, A_4 = 100, B_1 = 60, B_2 = 100$, and $B_3 = 80$. We employed the following three tactics, each with a different combination of two controls at a time and three controls at a time, to ascertain the effect of each control on the reduction of malaria.

Strategy 1:Applying pesticide $u_3$ and treating infected human $u_2$.

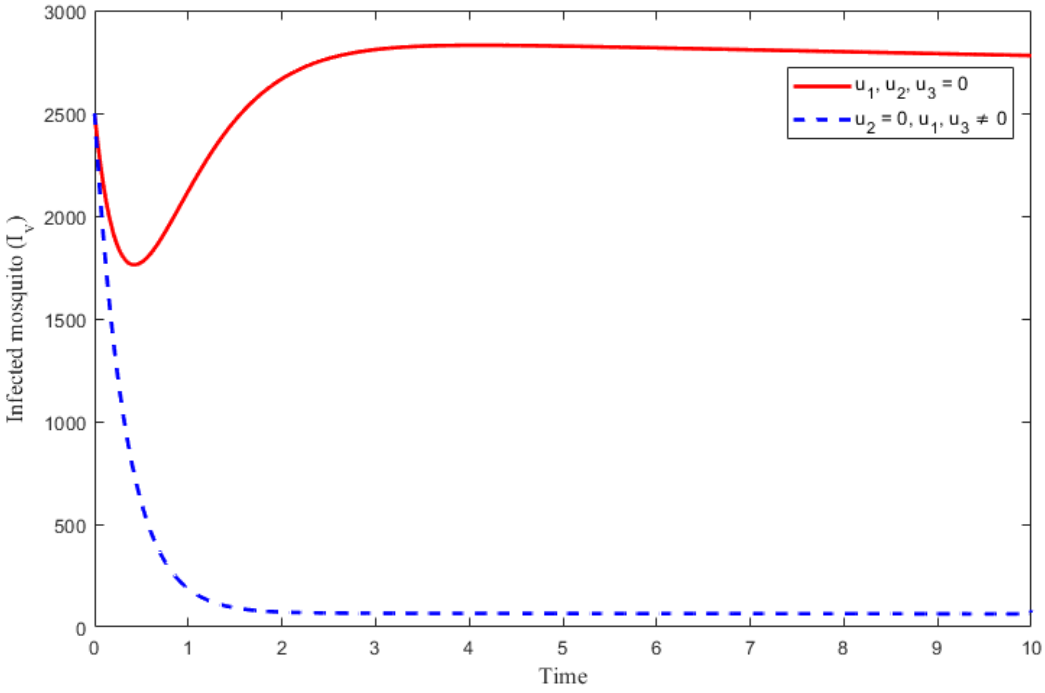
In order to minimize the objective functional $J(u)$, we employed a combination of two controls treatments for infected humans: antimalarial medications $u_2$ and an insecticide $u_3$. The protective treatment, which involved utilizing a treated bed net $u_1$, was set to zero. Figure 6.3 presents the numerical results. Figures 6.3(b) and 6.3(c) demonstrate that there are much more infected individuals and mosquitoes when there are no controls than when there are. The total number of infected humans $I_h$ and infected mosquitoes $I_v$ at the conclusion of the intervention are rapidly declining to reach their lowest point. As illustrated in Figure 6.3(a), exposed people with controls present are smaller than those without, and by the conclusion of the intervention, $(E_{sh} + E_{lh})$ is growing.


$u_1, u_2, u_3 = 0$
$u_2 = 0, u_1, u_3 \neq 0$
Exposed human ($E_{sh}$+$E_{lh}$)
Time

a


$u_1, u_2, u_3 = 0$
$u_2 = 0, u_1, u_3 \neq 0$
Infected human ($I_h$)
Time

b

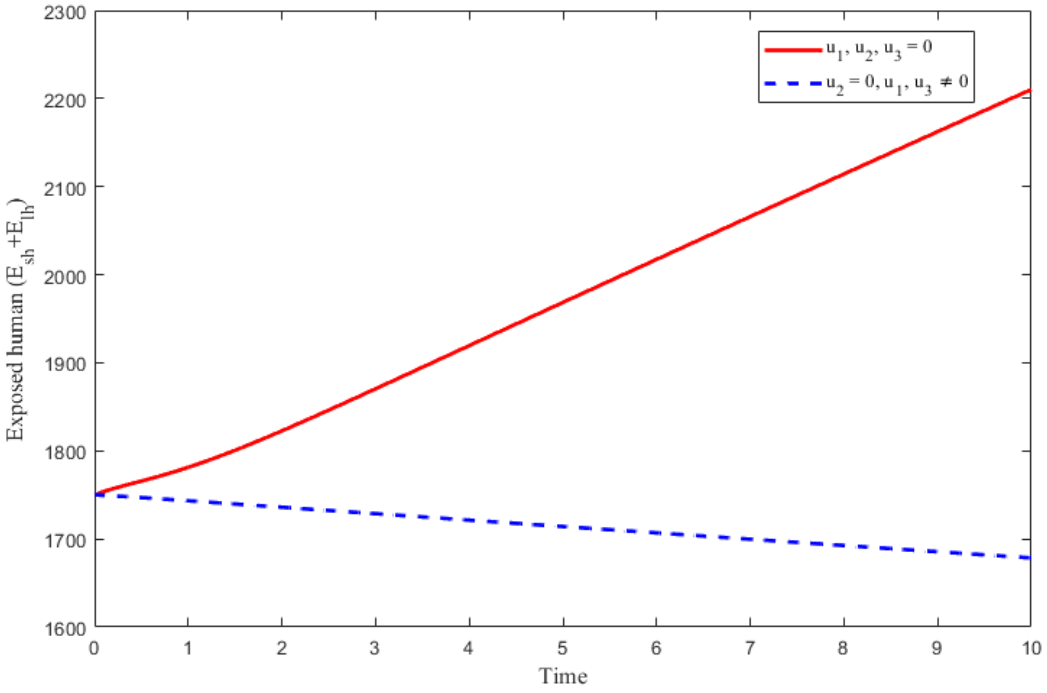



c

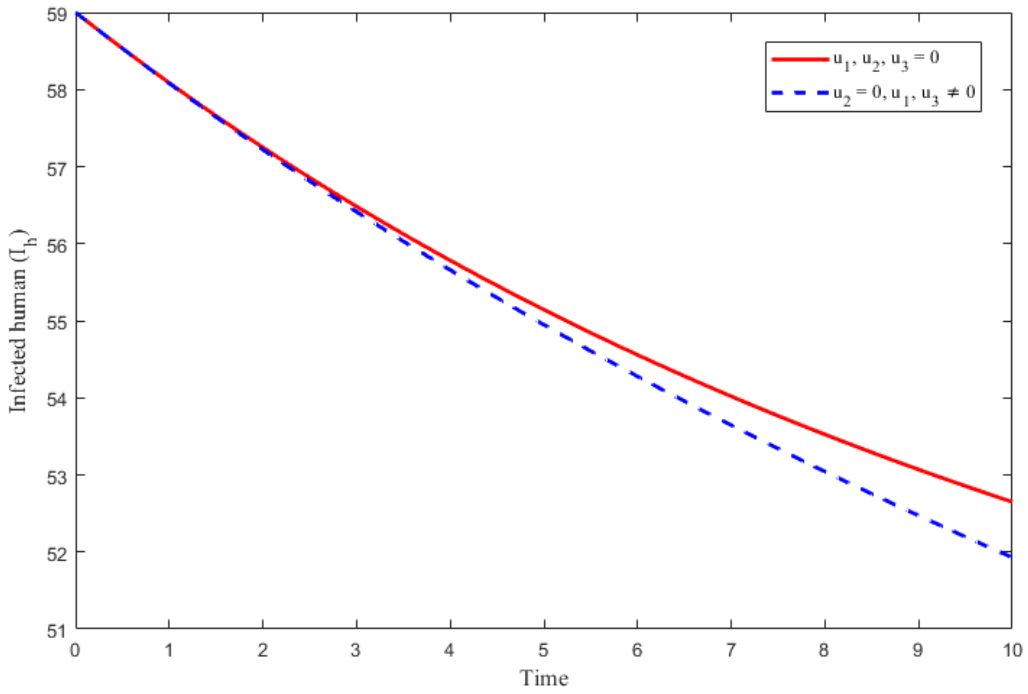
Figure 6. 3: Numerical results of the model using treatment and insecticide only.

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

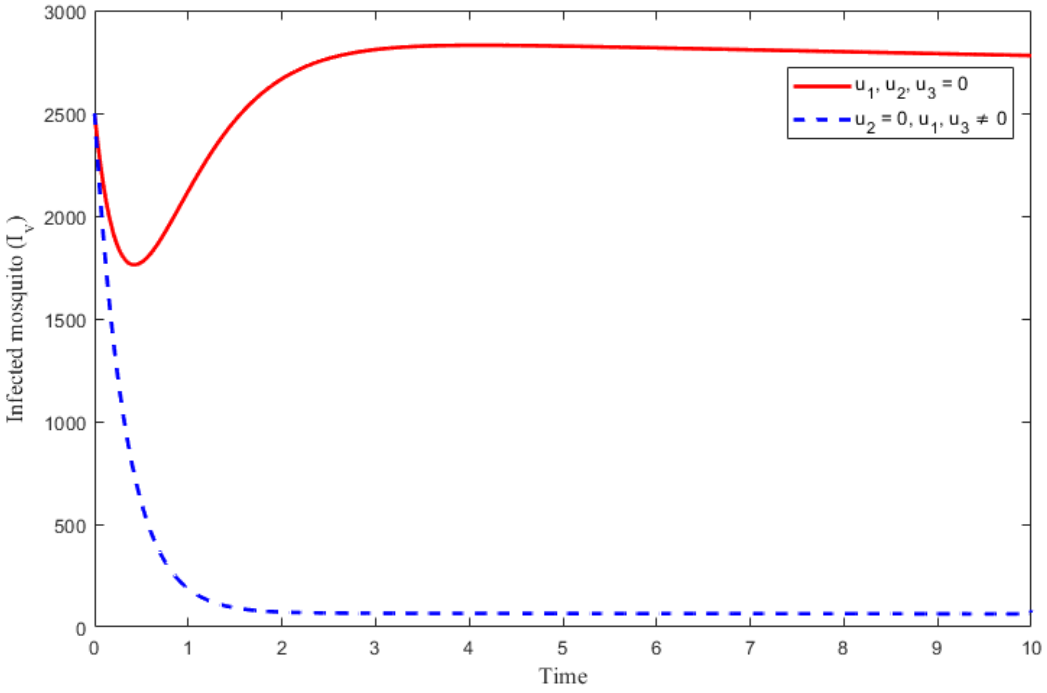
The combination of two controls, a treated bed net $u_1$ and an insecticide $u_3$, is used to reduce the objective functional $J(u)$. The control treatment for the infected with antimalarial medications $u_2$ is set to zero. Figure 6.4 presents the numerical results. Using controls reduces the overall population of exposed humans, infected humans, and infected mosquitos more quickly than without using controls, as seen in Figures 6.4(a)–6.4(c). The total number of exposed humans $(E_{sh} + E_{lh})$ and infected mosquitoes $I_v$ are at a minimum and declining, respectively, by the end of the intervention. In all scenarios, the infected human $I_h$ is declining.


$u_1, u_2, u_3 = 0$
$u_2 = 0, u_1, u_3 \neq 0$
Exposed human ($E_{sh}$+$E_{lh}$)
Time

a


$u_1, u_2, u_3 = 0$
$u_2 = 0, u_1, u_3 \neq 0$
Infected human ($I_h$)
Time

b

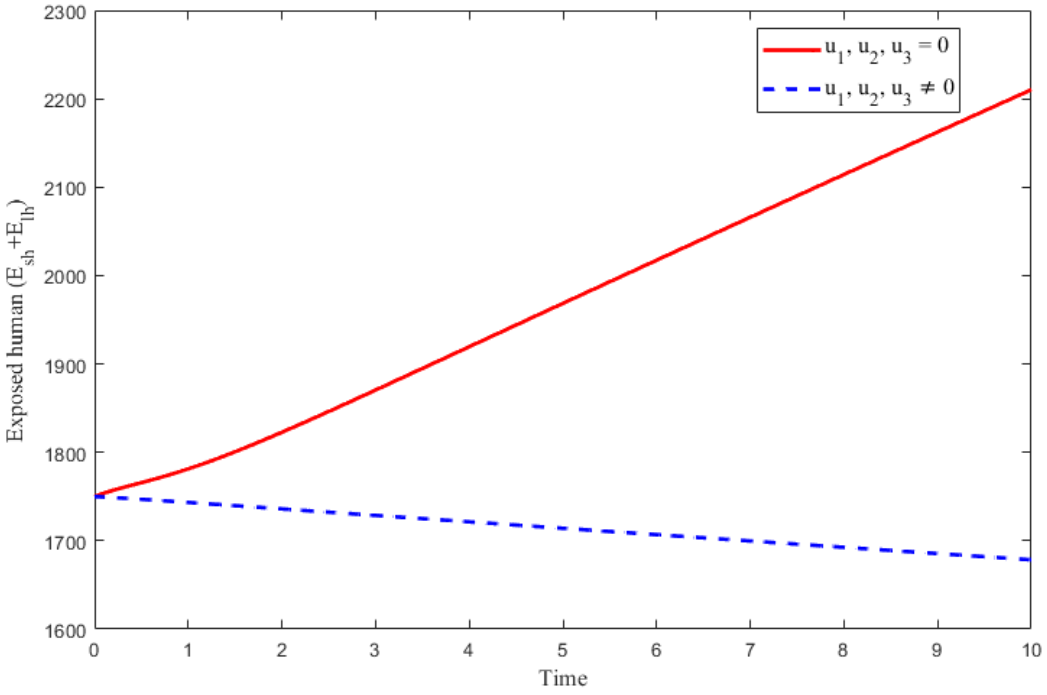



c

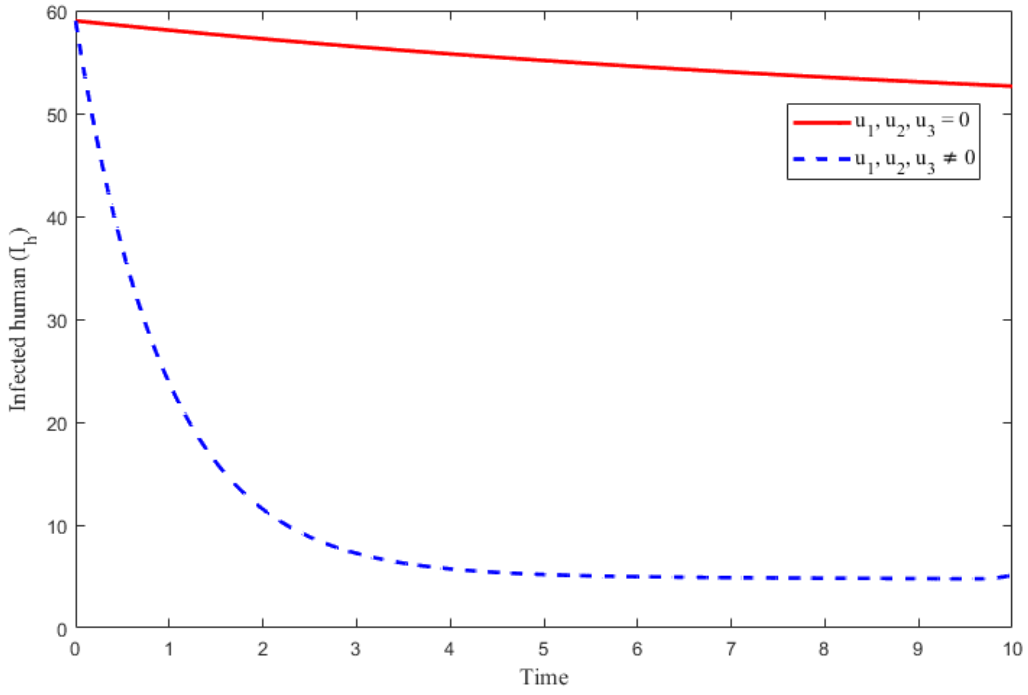
Figure 6. 4: Numerical results of the model using preventive treated bed net and insecticide only.

Strategy 3: Insecticide $u_3$, treatment of infected human $u_2$, and treated bed net $u_1$ are used.

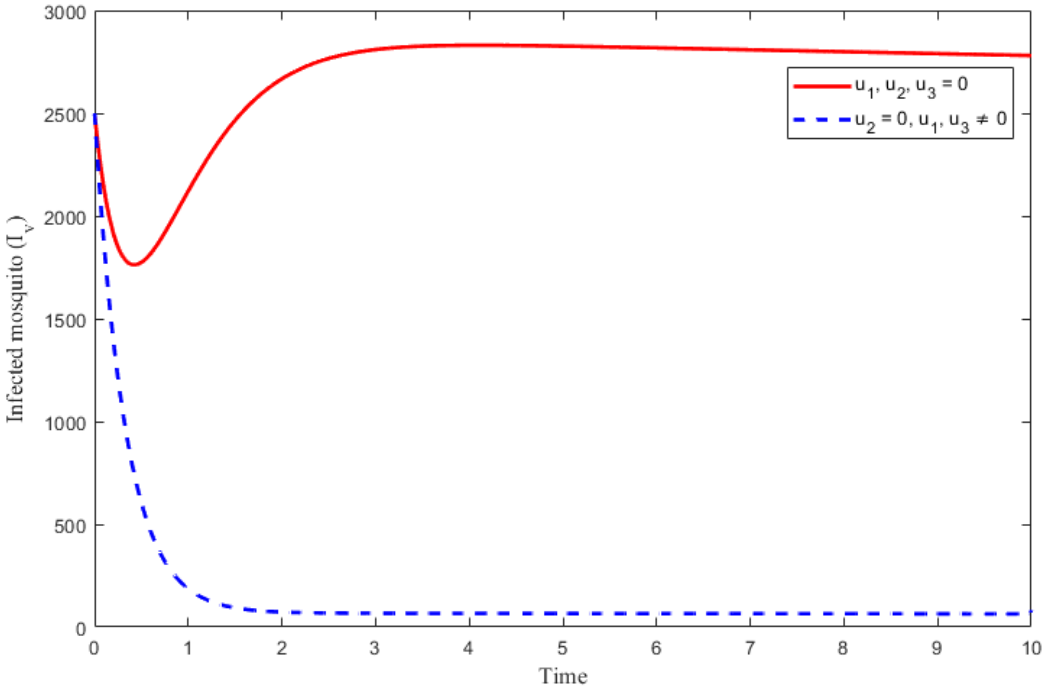
We employed all controls protective employing treated bed net $u_1$, treatment for the infected patient with antimalarial medications $u_2$, and insecticide $u_3$ in order to minimize the objective functional $J(u)$. Figure 6.5 presents the numerical results. The controls show that, as shown in Figures 6.5 (a)–6.5 (c), the overall number of exposed humans, infected humans, and infected mosquito populations is rising when controls are not present and falling when they are. When compared to strategies 1 and 2, it is evident that the simultaneous application of all controls rapidly reduces the number of exposed people, infected people, and infected mosquitoes.


Exposed human ($E_{sh}$+$E_{lh}$)
Time
$u_1, u_2, u_3 = 0$
$u_1, u_2, u_3 \neq 0$
2300
2200
2100
2000
1900
1800
1700
1600
0
1
2
3
4
5
6
7
8
9
10

a


Infected human ($I_h$)
Time
$u_1, u_2, u_3 = 0$
$u_1, u_2, u_3 \neq 0$
60
50
40
30
20
10
0
0
1
2
3
4
5
6
7
8
9
10

b




c

Figure 6. 5: Numerical results of the model using all controls (treated bed net, treatment and insecticide).

After comparing strategies 1 through 3, we can say that strategy 3 is the most effective in reducing the amount of exposed, infected, and mosquito-affected people in the community.

# Chapter 5

# Conclusion

In this study, we suggested and developed a deterministic dynamic model of malaria transmission with optimal controls. The model study shows that it is mathematically well-posed in a certain domain, limited, and epidemiologically meaningful. We calculated the basic reproduction number with respect to the disease-free equilibrium using the next-generation matrix method. The Lyapunov function is used to determine global stability, and the Routh-Hurwitz criterion is used to establish local stability of equilibrium sites. The model study indicates that the unique endemic equilibrium exists if the basic reproduction number is more than one, whereas the disease-free equilibrium is locally and globally asymptotically stable if it is less than one. From September 2011 E.C. to June 2015 E.C., the model parameters are estimated using monthly real data from the Kabridahar district in Ethiopia. The basic reproduction number in East Java Province, based on the estimated parameter values, is $R_0 \approx 24.494779$. This result demonstrates that the district has an endemic case of malaria. Furthermore, the fundamental reproduction number's sensitivity analysis across all parameters was acquired. Additionally, by adding three continuous controls—personal protection with treated bed nets, treatment of infected individuals with antimalarial medications, and insecticide as a vector killing strategy—the malaria transmission model is expanded to an optimum control issue. The optimal control problem's necessary condition is obtained by applying Pontryagin's maximal principle. The numerical results show that the most effective way to reduce the number of exposed, infected, and mosquitoes in the population is to integrate all controls.

## Reference


Abeku.T., Helinski.M.,Kirby.M., Kefyalew. T., Awano.T., Batisso.,2015. Monitoring changes in malaria epidemiology and effectiveness of interventions in Ethiopia and Uganda: beyond Garki project baseline survey. Malar J.

Abadi. A, and Harald. E., 2015. Mathematical Modelling of Endemic Malaria

Transmission. American Journal of Applied Mathematics

Abiodun. G and Okosun.K.,2018. Modelling the impact of climatic variables on malaria Transmission. Hacettepe Journal Of Mathematics And Statistics.

Adhanom. T.,Witten.H., Getachew.A., Seboxa.T.,2006. The epidemiology and ecology of health and disease in Ethiopia. Addis Ababa:

Aschalew. A and Tadesse.D.,2016. Current Status of Malaria in Ethiopia: Evaluation of the Analysis"; International Journal of Sciences: Basic and Applied Research Applied Mathematic

Aregawi.M., Lynch.M., Bekele. W., Kebede. H.,Jima. D., Taffese. H.,2014. Time series

Analysis of trends in malaria cases and deaths at hospitals and the effect of Antimalarial interventions.

Athithan. S and Minighosh. A., 2013. Mathematical Modelling of Malaria with Bednets

Available:

Boureima.S, and Sado.T.,2018. Mathematical model of malaria transmission

in a Periodic Environment. Journal of biological dynamics Bulletin of mathematical biology.

Bundit. A and Unyong, K.,2018. Optimal control for the transmission dynamics of Malaria disease model. Journal of Physics.

CDC.,2022. Malaria Parasites.

Chitnis. N., Hyman. J., and Cushing .M.,2008. Determining important parameters in the Spread of malaria through the sensitivity analysis of a mathematical model. Bulletin of mathematical biology.

Choi, S. and Jung, E., 2014. Optimal tuberculosis prevention and control strategy from a mathematical

model based on real data. Bulletin of mathematical biology, 76, pp.1566-1589.

Deribew. A., Dejene. T., Kebede.B., Tessema, G., Melaku, Y., Misganaw.A.,2017.

Incidence, prevalence and mortality rates of malaria in Ethiopia from 1990

To 2020: analysis of the global burden of diseases.

Diekmann .O., Heesterbeek. J and Metz .J.,1990. On the definition and computation of $R_0$ in the model for infectious disease in heterogeneous population.

Journal of mathematical Biology.

Dietz.K and Thomas. A.,1974. A malaria model tested in the African savannah. Bulletin

Disease. Journal of Systems Science and Complexity.

Earl, A. and Levinson, N., 1955. Theory of ordinary differential equations. McGraw-Hill

Ethiopia Malaria Operational Plan., 2022. Ethiopia-Malaria-Operational-Plan Ethiopia.

Federal Democratic Republic of Ethiopia, Ministry of Health. Health

Sector transformation plan. Addis Ababa.

9bc7-46a2-8c1f-8b32c2603208?version = 1.0

Fatmawati.B.,Faishal.F.,

Fikade.K and Koya.P.,2015.Controlling the Spread of Malaria Disease Using Findings from the

Global Health Estimates. Tropical Diseases

Fleming.W., Wendell. H., and Raymond. W.,2012. Deterministic and stochastic optimal control.

Springer Science and Business Media.

Gabriel. O and Joseph. K.,2016. Transmission Dynamics and Optimal control of Malaria in Kenya. Discrete Dynamics Nature and Society

GHO., 2021.Global Health Observatory Data.

Girum.T., Shumbej .T and Shewangizaw, M.,2019. Burden of malaria in Ethiopia:

Findings from the Global Health Estimates 2018. Tropical Disease Travel Medicine and Vaccines.

Kereyu, D., & Demie, S., 2021. Transmission dynamics model of Tuberculosis with optimal control strategies in Haramaya district, Ethiopia. Advances in Difference Equations, 2021(1).

Ketema. T.,Bacha .K., Birhanu. T., Petros ., B.,2009. Chloroquine-resistant Plasmodium Library/malaria operational-plans/fy19/fy.

Malaria journal.

Laarabi, H., Rachik, M. and Kaddar, A., 2012. Optimal control of an epidemic model with a saturated incidence rate. Nonlinear analysis: modelling and control, 17(4), pp.448-459.

LaSalle, J.P., 1976. The stability of dynamical systems, Regional Conf. Ser. Appl. Math. SIAM, Philadephia.

L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze, and E. F. Mischenko, "The Mathematical

Theory of Optimal Processes, " Wiley Interscience, New York, 1962. - References - Scientific Research Publishing (no date)

Malaria, T., 2020. Anopheles gambiae sl: morphology, life-cycle, ecology. Target Malaria. Available online at

Anopheles-gambiae-sl-morphology_August20. pdf, checked on, 4(26), p.2022.

Mandal. S., Sarkar. R., Sinha. S.,2011. Mathematical models of malaria-a review.

Model for malaria transmission. SIAM Journal on Applied Mathematics.

Mohammed-Awel, J., Agusto, F. B., Mickens, R. E., & Gumel, A. B., 2018. Mathematical assessment of the role of vector insecticide resistance and feeding/resting behavior on malaria transmission dynamics: Optimal control analysis. Infectious Disease Modelling, 3, 301-321.

Martcheva, M., 2015. An introduction to mathematical epidemiology (Vol. 61, pp. 9-31). New York: Springer.

Ngwa.G and Shu. W.,2000. A mathematical model for endemic malaria with variable

Human and mosquito populations. Mathematical and Computer Modelling.

Okosun. K and Makinde. O.,2011. Modeling the impact of drug resistance in malaria Transmission and its optimal control analysis. International Journal of Physical Sciences.

Olaniyi. S, and Obabiyi.B.,2013. Mathematical model for malaria transmission dynamics in human and mosquito populations with nonlinear forces of Infection. International Journal of Pure and Applied Mathematics.

Olumese.P., 2005.Epidemiology and surveillance: Changing the global picture of Malaria. Parasitological Global Physical Sciences.

Rodrigues, H.S.F., 2012. Optimal control and numerical optimization applied to epidemiological models (Doctoral dissertation, Universidade de Aveiro (Portugal)).

Ross. R.,(1911). The prevention of malaria. John Murray; London; 1911.

Sadiq, S.F., Khan, M.A., Islam, S., Zaman, G., Jung, I.H. and Khan, S.A., 2014. Optimal control of an epidemic model of leptospirosis with nonlinear saturated incidences. Annual Research & Review in Biology, pp.560-576.

Sharomi, O., Podder, C.N., Gumel, A.B. and Song, B., 2007. Mathematical analysis of the transmission dynamics of HIV/TB coinfection in the presence of treatment. Mathematical Biosciences & Engineering, 5(1), pp.145-174.

Shewakena.M and Temesgen. T.,2021.Impact of Climatic Factors and Intervention Spread of malaria through the sensitivity analysis of a mathe-

matical model.

WHO.,2003. Cross Border Review And Planning Meeting On Malaria Control Between Djibouti, Ethiopia and Somalia. Horn of Africa Initiative.

WHO., 2020. World malaria report 2019. Geneva: World Health Organization.

WHO.,2021. World malaria report 2020. Geneva: World Health Organization.

WHO.,2022. World malaria report 2021. Geneva: World Health Organization.

WFP., UNICEF., INGO.,2012.Somali Region: Multi - Agency Deyr/Karan Seasonal Assessment Report.

Yang. H, and Wei.H.,2010. Global stability of an epidemic model for vector-borne Disease. Journal of Systems Science and Complexity.

Van den Driessche, P. and Watmough, J., 2002. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical biosciences, 180(1-2), pp.29-48.