**KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI**




# AN EPIDEMIOLOGICAL MODEL OF MALARIA TRANSMISSION IN GHANA

By

PRINCE HARVIM

(BSc. Mathematics)

A THESIS SUBMITTED TO THE DEPARTMENT OF MATHEMATICS, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF

M.PHIL APPLIED MATHEMATICS

May 27, 2014

# DECLARATION

I hereby declare that this submission is my own work towards the award of the M. Phil degree and that, to the best of my knowledge, it contains no material previously published by another person nor material which had been accepted for the award of any other degree of the university, except where due acknowledgement had been made in the text.



| | | |
|---|---|---|
| PRINCE HARVIM | ..... | ..... |
| Student | Signature | Date |

Certified by:

| | | |
|---|---|---|
| Dr. FRANCIS T. ODURO | ..... | ..... |
| Supervisor | Signature | Date |

Certified by:

| | | |
|---|---|---|
| Prof. S.K AMPONSAH | ..... | ..... |
| Head of Department | Signature | Date |

# DEDICATION

I dedicate this work to God Almighty for His protection and guidance. He is my source of strength and inspiration and His grace is always sufficient for me.

To my dearest mother Lydia Atitsogbui and my brother Michael Harvim for their love, understanding and support.

# ABSTRACT

The study of the transmission dynamics and control of malaria
(an epidemiological model) in Ghana is done using differential equations. Using tools and conditions under which an epidemiological model is stable, this study determines the control measures that best decides how malaria can be eradicated from Ghana. Sensitivity analysis is also employed to find which model parameters are highly responsive to the basic reproduction number ($R_0$). From the results of the sensitivity analysis, the model is modified to assess the impact of four control measures; the use of treated bednets to minimize mosquito human contacts, the use of insecticide spray to control the mosquito population, the treatment control to the infected human and the intermittent treatment control to pregnant women. Numerical simulations using MATLAB is done to determine the effectiveness of all possible combinations of malaria control measures. The results contribute to effective ways of controlling the spread of malaria in Ghana.

# ACKNOWLEDGEMENTS

I am eternally indebted to Yahweh God, Jesus Christ and The Holy Spirit who will never leave nor forsake me no matter what happens. My most sincere thanks also go to my supervisor Dr. Francis T. Oduro for his patience in me while I was trying to learn so many things within a short time. Thank you for reading the thesis and your useful corrections. I would never have finished the thesis without you. Thank you for everything!

My deepest appreciation goes to all the lecturers (both classical and contemporary) at the Department of Mathematics in Kwame Nkrumah University of Science and Technology, Kumasi. If today I can teach mathematics, then it is because of the good tuition I have received from the Department of Mathematics.

My deepest gratitude goes to Zeenatu Adams, David Yaro, Akuamoah Walanyo Saviour and Gabriel Nyamalor for their love and support.

I am forever thankful to my parents and my brother Michael Harvim for their love and support.

I am grateful to Mawi Batimah and Eric Darko and all those who assisted me in diverse ways during the completion of this thesis. I would also like to thank the postgraduate students at the Department of Mathematics, for their contribution and encouragement during the whole period of my study.

Finally, I am indebted to Firtz Akumey, Collins Nii L. Lawson and Anna Adams for their love, prayer and support throughout my study.

# Contents

# List of Tables

# List of Figures

# Chapter 1

# INTRODUCTION

## 1.1 Overview

The World Health Organization (WHO) estimates that malaria caused approximately 627,000 deaths in 2012 mostly those of children under five years of age in Africa. This means 1300 young lives are lost to malaria every day - a strong reminder that victory over this ancient foe is still a long way off. The fact that so many people are dying from mosquito bites is one of the greatest tragedies of the 21st century. WHO (2013) In Africa alone, costs of illness, treatment, and premature death from malaria are at least 12 billion per year. Malaria's toll would be much higher without the efforts of Centre for Disease Control CDC (2013), World Health Organization (WHO) and other global partners. In the last decade, with large increases in funding to support scale-up of malaria prevention and treatment interventions, approximately 1.1 million lives have been saved, and malaria cases and deaths have sharply decreased-by 25% globally and by 33% in sub-Saharan Africa. However, malaria remains a major public health problem that is preventable and treatable. (CDC, 2013)

## 1.2 Background of the Study

### 1.2.1 Nature of malaria

Malaria is a life-threatening disease caused by plasmodium parasites that are transmitted to people through bites of infected female anopheles mosquitoes WHO(2012) Though in the 21st century the bites from mosquitoes are killing

many innocent people, it has become the greatest tragedies (WHO, 2013). Malaria causes symptoms that typically include fever, chills, headache and flu-like disease, which in severe cases can progress to coma or death. The disease is widespread in tropical and subtropical regions in a broad band around the equator, including much of Sub-Saharan Africa, Asia, and the Americas. Malaria still kills children every minute and is the greatest and the first leading killer of children below five years among African children. The presence of Malaria is a real threat and will likely destroy so many more lives unless support gaps are bridged: In Africa alone for instance, the expenditure on malaria that is: costs of illness, treatment, and premature death annually are at least $12 billion.



### 1.2.2 Causes of malaria

Malaria is caused by the plasmodium parasite which is transmitted from the female anopheles mosquito. About five species of Plasmodium can infect and be transmitted by human beings. The vast majority of deaths are caused by P. *falciparum* and P. *vivax*, while P. *ovale*, and P. *malariae* cause a generally milder form of malaria that is rarely fatal. The prevalence of Malaria in tropical and subtropical regions is because rainfall, warm temperatures, and stagnant waters provide habitats ideal for mosquito larvae.

### 1.2.3 Mode of transmission of malaria

Commonly, malaria is transmitted through a bite from an infected female Anopheles mosquito, which introduces the organisms from its saliva into a person's circulatory system. In the blood, the protists travel to the liver to mature and reproduce. The female Anopheles mosquito (the definitive host) in the life cycle of Plasmodium, transmits a motile infective form (called the sporozoite) to a vertebrate host such as a human (the secondary host), thus acting as a transmission vector. A sporozoite travels through the blood vessels to liver cells (hepatocytes), where it reproduces asexually (tissue schizogony), producing thousands of merozoites.

These contaminate new red blood cells and initiate a series of asexual multiplication cycles (blood schizogony) that generate 8 to 24 new infective merozoites, at which point the cells burst and the infective cycle begins anew. Other merozoites develop into immature gametocytes, which are the precursors of male and female gametes. Gametocytes are taken up with the blood and mature in the mosquito gut when a fertilised mosquito bites an infected person. The male and female gametocytes fuse and form an Ookinetes fertilized, motile zygote. Ookinetes develop into new sporozoites that migrate to the insect's salivary glands, prepared to infect a new vertebrate host. The sporozoites are injected into the skin, in the saliva, when the mosquito takes a consequent blood meal. It is only female mosquitoes that feed on blood but the male mosquitoes feed on plant nectar, and thus do not transmit the disease. The females of the Anopheles genus of mosquito desire to feed at night. They usually start searching for a meal at dusk, and will continue throughout the night until taking a meal. Through blood transfusions, Malaria parasites can also be transmitted although this is rare. Malaria infection develops through two phases: one that involves the liver (exoerythrocytic phase), and one that involves red blood cells or erythrocytes (erythrocytic phase). When an infected mosquito pierces a person's skin to take a blood meal, sporozoites in the mosquito's saliva enter the bloodstream and journey to the liver where they infect hepatocytes, multiplying asexually and asymptomatically for a period of 8-30 days. These organisms differentiate to yield thousands of merozoites, which, following rupture of their host cells, escape into the blood and infect red blood cells to begin the erythrocytic stage of the life cycle after a potential dormant period in the liver. The parasite escapes from the liver unnoticed by wrapping itself in the cell membrane of the infected host liver cell. Within the red blood cells, the parasites reproduce further, again asexually, periodically breaking out of their host cells to invade fresh red blood cells. Several such amplification cycles occur. Thus, classical descriptions of waves of fever arise from simultaneous waves of merozoites escaping and infecting red blood cells. Some P. *vivax* sporozoites do

not immediately develop into exoerythrocytic-phase merozoites, but instead produce hypnozoites that remain dormant for periods ranging from several months (7-10 months is typical) to several years. After a period of dormancy, they reactivate and produce merozoites. Hypnozoites are responsible for long incubation and late relapses in P. *vivax* infections, although their existence in P. *ovale* is uncertain. The parasite is relatively protected from attack by the body's immune system because for most of its human life cycle it resides within the liver and blood cells and is relatively invisible to immune surveillance. However, circulating infected blood cells are destroyed in the spleen. To avoid this outcome, the P. falciparum parasite displays adhesive proteins on the surface of the infected blood cells, causing the blood cells to stick to the walls of small blood vessels, thereby sequestering the parasite from passage through the general circulation and the spleen. The impasse of the microvasculature causes symptoms such as in placental malaria. Sequestered red blood cells can breach the blood-brain barrier and cause cerebral malaria.

### 1.2.4 Types of malaria

There are mainly five types of Malaria due to the five species of the plasmodium parasites. These are the plasmodium *flaciparum*, plasmodium *vivax*, plasmodium *ovale*, plasmodium *malariae* and plasmodium *knowlesi*. All five species of Plasmodium can infect and be transmitted by human beings. The vast majority of deaths are caused by P. *flaciparum* and P. *vivax*, while P. *ovale*, and P. *malariae* cause a generally milder form of malaria that is rarely fatal. The zoonotic species P. *knowlesi*, widespread in South-east Asia, cases malaria in macaques but can also cause severe infections in human beings.

### 1.2.5 Treatment of malaria

Despite a need, no effective vaccine exists, even though efforts to develop one are ongoing. Several medications are accessible to prevent malaria in travellers to malaria-endemic countries. A variety of antimalarial medications are available. Since the mid-2000s, severe malaria is treated with intravenous or intramuscular quinine or, the artemisinin derivative artesunate, which is superior to quinine in both children and adults and is given in permutation with a second anti-malarial such as mefloquine. Resistance has developed to several antimalarial drugs; for example, chloroquine-resistant P. *falciparum* has spread to most malarial areas, and emerging resistance to artemisinin has become a problem in some parts of Southeast Asia.



### 1.2.6 Preventive measures of malaria

To prevent malaria the following methods can be used: medications, mosquito elimination and the prevention of bites. A combination of high human population density, high anopheles mosquito population density and high rates of transmission from humans to mosquitoes and from mosquitoes to humans in an area makes the presence of malaria felt. If any of these is lowered satisfactorily, the parasite will in due course disappear from that area, as happened in North America, Europe and parts of the Middle East. However, unless the parasite is eliminated from the whole world, it could become re-established if conditions revert to a combination that favours the parasite's reproduction. Furthermore, the cost per person of eliminating anopheles mosquitoes rises with declining population density, making it economically impracticable in some areas. Prevention of malaria may be more cost-effective than treatment of the disease in the long run, but the capital costs requisite are out of reach of many of the world's poorest people as argued by many researchers. There is a wide distinction in the costs of control (i.e. maintenance of low endemicity) and elimination programs between coun-

tries. For instance, in China, whose government announced a strategy to pursue malaria elimination in the Chinese provinces in 2010, the required investment is a small proportion of public disbursement on health. In contrast, a similar program would cost an estimated one-fifth of the public health budget in Ghana. WHO recommended that four key control interventions are used by programs worldwide to fight malaria. These include

- Insecticide-treated bed nets (ITNs) to protect people from mosquitoes
- Rapid diagnostic tests and treatment with effective high-quality drugs: artemisinin-containing combination therapies (ACTs)
- Treatment to protect pregnant women and their new born children: intermittent preventive treatment (IPTp) for pregnant women
- Indoor spraying of homes to protect people from mosquitoes (IRS) (CDC, 2013).

### 1.2.7 Economical effects of malaria

Beyond the human toll, malaria wreaks significant economic havoc in the high-rate areas, decreasing Gross Domestic Product (GDP) by as much as 1.3% in countries with high levels of transmission. These aggregated yearly losses have resulted in substantial differences in GDP between countries with and without malaria (particularly in Africa) over the long-term. Malaria's health costs comprise both personal and public expenditures on prevention and treatment. In some heavy-burden countries for instance Ghana, according to the WHO in 2009, the disease accounts for: up to 40% of public health expenditures, 30% to 50% of inpatient hospital admissions, up to 60% of outpatient health clinic visits Malaria inexplicably affects poor people who cannot meet the expense of treatment or have restricted access to health care, and traps families and communities in a down spiral of poverty. Over half (US$2.8 billion) of the estimated per year global resource requirements of $5.1 billion is still unfunded which threatens to slow

down progress as high-burden African countries are incapable to replace expiring long-lasting insecticide treated nets (LLINs) nor provide diagnosis and treatment to all who need it . Malaria prevention through vector control, the two most powerful and most largely applied interventions for malaria vector control prevention are insecticide-treated mosquito nets (ITNs) and indoor residual spraying (IRS). However, malaria vector control is only effective with sustained high coverage. Except there is a substantial increase in funding for malaria control in 2013 major resurgences of malaria are highly likely. UNICEF's contributions to malaria control, averagely $ 1.8 billion are spent every year on child survival programming, including funding for malaria control.



## 1.3 Statement of the Problem

Malaria kills one child every 30 seconds, about 3,000 children every day. Over a quarter of all young child deaths in Africa occur due to malaria. Over one million people die from malaria each year, mostly children under five, with nine out of ten malaria cases occurring in sub-Saharan Africa. Pregnant women and their unborn children are particularly vulnerable to malaria, as a result of low birth weight and maternal anaemia. Infants born to mothers with malaria are likely to have low birth weight - the single greatest risk factor for death during the first months of life. Malaria contributes substantially to the poor health situation in Africa. Indeed, sub-Saharan Africa alone each year accounts for 90% of the world's 300 - 500 million cases of malaria and 1.5 - 2.7 million malaria - related deaths. About 90% of these deaths in Africa are of young children, suggesting some serious demographic consequences for the continent. Malaria is a great burden on the health system in Africa, as it is responsible for 20-40% of outpatient visits and 10-15% of hospital admissions, according to the World Health Organisation (WHO, 1999). The annual economic burden of malaria is estimated $1-2$ per cent of the Gross Domestic Product (GDP) in Ghana. The entire population of Ghana is at risk of malaria. Of the 3.7 million malaria cases reported in 2009,

26% were confirmed. Despite increasing use of rapid diagnostic tests (RDTs), the testing rate was not reported. At 77% reporting completeness, there was no evidence of a reduction in suspected malaria cases between 2000 and 2009, while inpatient cases in all ages increased. It is not known whether the data reflect a true rise in the incidence of malaria, or better reporting of cases. The national malaria control program (NMCP) delivered 3.7 million long-lasting insecticidal nets (LLINs) during 2007-2009, sufficient to cover 40% of the population at risk. Implementation of IRS protected about 665000 (3%) of the population at risk in selected areas in 2009. In the demographic health survey (DHS) 2008, 33% of households owned an ITN but only 19% of children under 5 had slept under an ITN the previous night (World Malaria Report, 2010). The programme delivered 4 million courses of ACT in 2009, sufficient to treat all suspected malaria cases. Funding for malaria control increased from almost none in 2005 to about US$ 27 million in 2008 and US$ 38 million in 2009, mainly provided by the Global Fund, PMI and the World Bank, with small contributions from UN agencies (World Malaria Report, 2010).

There are many malaria control measures that are applied at different malaria endemic areas but Ghana has no proven and tested malaria control measure that will effectively eradicate malaria. The disease is endemic in Ghana and claims so many lives. According to the (WHO, 2010) using only one control measure is insufficient to achieve and maintain interruption of malaria transmission. Mathematical models of the dynamics of this disease with effective control and cost-effectiveness analysis with special emphasis on Ghana are uncommon. Therefore, these motivated the need to study and to investigate the most effective control intervention measures on the transmission dynamics of malaria model in Ghana.

## 1.4 Objectives

The main objective of this study is to investigate the most effective control intervention measures on the transmission dynamics of malaria model in Ghana.

1. To formulate an (SEIR-SEI) epidemiological model of malaria transmission as a system of differential equations.

2. To investigate the stability of the equilibria and compute the basic reproduction number.

3. To apply sensitivity analysis to determine which parameters impacts the basic reproduction number the most.

4. To simulate using MATLAB to determine the effectiveness of all possible combinations of the four malaria control measures.



## 1.5 Methodology

An (SEIR-SEI) epidemiological model of malaria transmission with four control measures is formulated as a system of ordinary differential equations where the human population is made up of four compartments (Susceptible, Exposed, Infectious and Recovered) and the vector mosquito population is made up of three compartments (Susceptible, Exposed and Infectious). Sensitivity analysis is intended to determine which parameters impacts the basic reproduction number the most. Clinical malaria data for the thesis is obtain from the National malaria control programme (NMCP) in Ghana and other parameter values are obtain from the World Malaria Report 2013 by the World Health Organisation through the internet. Simulation using MATLAB and the fourth order Range-Kutta numerical method will be conducted to establish the most effective control measures and the most effective control combinations.

## 1.6 Significance of the Study

Malaria have been and are among the leading causes of death that remain challenges for many people in Ghana, claiming lives of thousands of people every year. The health as well as the socio-economic impacts of emerging and re-emerging

malaria diseases are significant. Thus, they are among the major concerns for several health organizations including, the World Health Organization, Centre for Disease Control and National Health Malaria Control Programme in Ghana. Vectors are found in areas ranging from tropical to temperate zones and at different landscapes, thus, the geographic distribution of malaria diseases is vast and diverse in Asia, South America and sub-Sahara Africa including Ghana. The disease is endemic and claims so many lives in Ghana and consequently makes its study valuable in Ghana. As a result of this the malaria model has special emphasis on Ghana. Since no previous mathematical study has been done in Ghana on the most effective control measure of the disease, the results on the control measures will provide relevant guidance for decision makers on which intervention to focus on and the most effective control measure to use in Ghana.

## 1.7 Study Area

The Study Area Ghana is situated in West Africa and its capital city is Accra. It is bordered by Togo to the east, Burkina Faso to the north, Cote d'voire to the west and the Atlantic Ocean to the south. Ghana achieved independence from British rule in 1957. After the 1966 ouster of its independence leader, Kwame Nkrumah, the country was rocked for 15 years by a series of military coups and experienced successive military and civilian governments. The central intelligence,'Word Fact Book', last updated January 2012, listed the area of the country at 238; 533$sqkm$. The provisional results of the 2010 population and Housing Census shows that the total population of Ghana is 24,233,431 (11,801,661 males and 12,233,770 females). The males form 48.7 percent of the population and the females constitute 51.7 percent. Additionally, it has growth rate 1.8 percent; birth rate of $28 : 0 = 1000$; infant mortality rate of $49 : 9 = 1000$; life expectancy of 64.5; and density per sq km: 101 (CIA Ghana at a glance, 2012).

## 1.8 Organization of the thesis

Chapter 1 is the introduction which comprises the background of the study, statement of the problem, objectives of the study, justification, methodology of the study and the study area. Chapter 2 contains the review of literature on malaria model and some malaria intervention programmes are reviewed. Some literature on SIR, SEIR and SEIRS models are also looked at in this chapter with some literature on optimal control theory and its applications. Chapter 3 consists of the basic malaria model with the underlying assumptions. We analyse the model with constant control parameters and perform a sensitivity analysis of the basic reproduction number. Chapter 4 consists of numerical simulations of the model with time dependent control measures using MATLAB. Chapter 5 consists of the discussion of the results which consists of summary of results, conclusion and recommendations.

# Chapter 2

# LITERATURE REVIEW

## 2.1 Introduction

This chapter deals with review of literature on malaria and some malaria intervention programmes. Some literature on SIR and SEIR malaria models and reproduction number ($R_0$) are also looked at in this chapter.



## 2.2 Overview

Malaria is a common and serious disease. It is reported that the incidence of malaria in the world may be in the order of 300 million clinical cases each year. Malaria mortality is estimated at almost 2 million deaths worldwide per year. The vast numbers of malaria deaths occur among young children in Africa, especially in remote rural areas. In addition, an estimated over 2 billion people are at risk of infection, no vaccines are available for the disease WHO(2012).

## 2.3 Mode of transmission of malaria

Malaria is transmitted to humans through the bite of an infected female Anopheles mosquito, following the successful sporozoite inoculation, plasmodium *falciparum* is usually first detected 7-11 days. This is followed after few days of the bites, by clinical symptoms such as sweats, shills, pains, and fever. Mosquitoes on the other hand acquire infection from infected human after a blood meal.

## 2.4 Intervention measures of malaria

Although malaria is life-threatening it is still preventable and curable if the infected individual seek treatment early. Prevention is usually by the use of insecticide treated bed nets and spraying of insecticide but according to the World Health Organization position statement on insecticide treated mosquito nets WHO(2012), the insecticide treated bed nets(ITNs), long-lasting insecticide nets (LLINs), indoor residual spraying (IRS), and the other main method of malaria vector control, may not be sufficiently effective alone to achieve and maintain interruption of transmission of malaria, particularly in holo-endemic areas of Africa.

The main rationale for taking protective and control measures against malaria is to reduce the occurrence of the disease and, if possible, eradicate it completely. That is, reducing the level of vulnerability of healthy individuals against the infection and the number of infectious individuals. Fact sheet (2009) report by World Health Organisation (WHO) said that, malaria was a life-threatening disease caused by parasites that are transmitted to people through the bites of infected mosquitoes, which resulted in the death of a child from malaria every 30's. In 2006, there were 247 million cases of malaria, causing nearly 1 million deaths; this is mostly among African children. It was approximated that well over 3000 young lives are lost daily across the globe. These estimates render malaria the pre-eminent tropical parasitic disease and one of the top three killers among contagious disease. (Sachs (2002)).

## 2.5 Effects of malaria

Malaria impedes development in so many ways; it affects fertility, population growth, saving and investment, worker productivity, absenteeism, premature mortality and medical cost (Sachs (2002)). In areas where malaria is extremely endemic, young children bear the larger burden in terms of the disease morbidity

and mortality. Malaria also affects foetal development during early stage of pregnancy in women due to loss of immunity. However, malaria is avertible and curable when treatment and prevention measures are sought early. The challenges posed by the resistance of parasites against drugs and resistance of mosquitoes against insecticides call for a better understanding of the disease transmission and development of efficient strategies for the control of the spread of malaria disease.

## 2.6 Mathematical models of malaria



Mathematical modelling has become an important instrument in understanding the dynamics of disease transmission and in decision making processes regarding intervention programs for disease control. Concerning malaria disease, (Ross (1911)) developed the models of malaria transmission. He focused his study on mosquito control and showed that for the disease to be eliminated the mosquito population should be brought below a certain threshold. His work was later extended by Macdonald (1957) to account for super-infection. These two works were further extended by Ngwa and Shu (2000) with the popular generalized SEIR malaria model, which includes both the human and mosquito interactions. Other further studies include Koella and Anita (2003) who included a latent class for mosquitoes. They well thought-out different strategies to decrease the spread of resistance and studied the sensitivity of their results to the parameters. Anderson and May (1991) derived a malaria model with the assumption that acquired immunity in malaria is independent of exposure duration. Different control measures and role of transmission rate on the disease frequency were further examined. Hyun (2001) studied a malaria transmission model for different levels of acquired immunity and temperature dependent parameters, relating also to global warming and local socioeconomic conditions. In Isao et al. (2004), Kawaguchi et al. examined the combined use of insecticide spray and zooprophylaxis as a strategy for malaria control. Dietz et al. (1974) proposed a model that

accounts for acquired immunity. Chiyaka et al. (2008) formulated a deterministic model with two latent periods in the host and vector populations to assess the impact of personal protection, treatment and possible vaccination strategies on the transmission dynamics of malaria. They also considered treatment and spread of drug resistance in an endemic population Chiyaka et al. (2008). Jia (2008) formulated and examined a compartmental mathematical model for malaria transmission that includes incubation periods for both infected humans and mosquitoes. Mukandavire et al. (2009) proposed and investigated a deterministic model for the co-infection of HIV and malaria in a community. Mwasa and Tchuenche (2011) examined a mathematical model that covers the dynamics of Cholera transmission to study the influence of public health educational campaigns, vaccination and treatment in controlling the disease. Although some of these studies considered different interventions for malaria control, they did not take into consideration the costs and cost-effectiveness of these interventions which may sometimes be restricted by availability of resources. Specifically, carrying out a comparative analysis, knowing costs and outcomes of alternative control strategies is important to decision makers who are often faced with the challenge of resource allocation. In view of this, application of control measures can be an important tool to estimate the efficacy of various policies and control measures in comparison with the cost of implementing them. Since the development of the Pontryagin maximum principle by Pontryagin et al. (1962), the theory of optimal control has been productively used in decision making in various applications. In epidemiology, applications of this theory include the optimization of the costs of using active and passive immunization in controlling infectious diseases Gupta and Rink (1973). Wickwire (1977) applied optimal control to mathematical models of pests and infectious diseases control. Wiemer (1987) studied Schistosomiasis using optimal control methods. Suresh (1978) formulated and analyzed an optimal control problem with a simple epidemic model to examine effect of a quarantine program. He also considered an optimal control problem

to study the effect of the level of medical program effort in minimizing the social and medical costs (Suresh, 1978). Marco and Takashi (2001) used optimal control to study dengue disease transmission. Adams et al. (2004) derived HIV therapeutic strategies by formulating and analyzing an optimal control problem using two types of dynamic treatments. Karrakchou et al. (2006) used optimal control to examine the role of chemotherapy in controlling the virus reproduction in HIV patients. Xiefei et al. (2007) applied optimal control methods to study the outbreak of SARS using Pontryagin's Maximum Principle and a genetic algorithm. Optimal control was used Zaman et al. (2008) to conclude the optimal vaccination strategy to reduce the susceptible and infective individuals for a general SIR epidemic model. More studies on the applications of optimal control to infectious diseases, mainly HIV/AIDS and Tuberculosis can be found in Felippe de Souza and Takashi (2000), Joshi (2002), Joshi et al. (2006),Jung et al. (2002),Kar and Batabyal (2011), Kirschner et al. (1997), Lenhart and Yong (1997) and Rachik et al. (2009), these studies focused more on cost minimization analysis of the examined control strategies. However, very few studies have been carried out on applying optimal control theory to malaria transmission models. Only recently,Kbenesh et al. (2009) used optimal control to study a model for vector-borne diseases with treatment and prevention as control measures. Rafikov et al. (2009) formulated a continuous model for malaria vector control with the aim of studying how genetically modified mosquitoes should be introduced in the environment using optimal control problem strategies. Okosun et al. (2011) derived and analyzed a malaria disease transmission mathematical model that includes treatment and vaccination with waning immunity and applied optimal control to study the impact of a possible vaccination with treatment strategies in controlling the spread of malaria.

Okosun et al. (2013) also applied Optimal control strategies and cost-effectiveness analysis of a malaria model.

## 2.7 Concluding Remarks

From the public health point of view, decision makers will be more interested in knowing if the infection will die out, or persist in a population through the important parameter . In this literature review, efforts have been taken to group the epidemiological models of malaria in terms of the complexity of infection processes included in its description, which makes them more realistic. The age-specific distribution of infection due to differential immunity across age is one such case. The assumption is that more realistic models would enhance the understanding of the infection transmission process at the population level, which, in turn, may help in better prediction of intervention strategies. Pure mathematical analysis of the models, although not so popular among the biologists, is important. They provide clear understanding of the logic of the system behaviour in terms of the relationship among the parameters and variables, which are representative to real biological processes. This literature review of different mathematical models of malaria would contribute to consolidate our understanding about the evolution of these models, and may also help in developing new models by incorporating features discussed above to improve predictions and deciding realistic control measures.

In this thesis, we use an epidemiological model with four control measures to study the effectiveness of all possible combinations of four malaria control measures, namely (i) treated bednets, (ii) treatment of infective humans and (iii) spray of insecticides and (iv) treatment to protect pregnant women and their new born children: intermittent preventive treatment (IPTp) for pregnant women. For this, we consider a standard model for malaria transmission similar to those considered in Ngwa (2000), Ngwa (2006), Oduro et al. (2012) in which we integrated four time dependent controls representing the interventions. Firstly, the model with constant control parameters and investigating the stability properties

will be analyzed. Secondly, in controlling the disease, we consider the control parameters to be time dependent controls and examine the impact of different combination measures.

# Chapter 3

# METHODOLOGY

## 3.1 Model formulation

The model that we consider here is a slight modification of models for malaria transmission considered in Oduro et al.(2013), Okosun et al. (2013), Ngwa and Shu (2000), Ngwa (2006) and Rafikov et al. (2009) it is not a generalization of these ones; nor is it a special case of them. It is a standard model of SEIRS type for humans and SEI for mosquitoes in which we incorporated four time dependent control measures simultaneously: (i) the use of treated bednets, (ii) treatment of infective humans, (iii) treatment to protect pregnant women and their new born children: intermittent preventive treatment (IPTp) for pregnant women and (iv) spray of insecticides. It is common knowledge that malaria treatment reduces the risk of disease but has only a low or negligible transmission blocking effect. Here we consider a possible treatment that blocks transmission from infective humans to mosquitoes. The model sub-divides the total human population, denoted by $N_h$, into the following sub-classes of: individuals who are susceptible to infection with malaria ($S_h$), those exposed to malaria parasite ($E_h$), individuals with malaria symptoms ($I_h$) and recovered individuals ($R_h$). So that, $N_h = S_h + E_h + I_h + R_h$. The total vector (mosquito) population, denoted by $N_v$, is sub-divided into susceptible mosquitoes ($S_v$), mosquitoes exposed to the malaria parasite ($E_v$) and infectious mosquitoes ($I_v$). That is, $N_v = S_v + E_v + I_v$. Susceptible individuals are recruited at a rate $\Lambda_h$. They either die from natural causes (at a rate $\mu_h$) or move to the exposed class by acquiring malaria through contact with infectious mosquitoes at a rate (1-$\mu_1$)$\beta\epsilon\phi$, where $\beta$ is the transmission probability per bite, $\epsilon$ is the per capita biting rate of mosquitoes,

$\phi$ is the contact rate of vector per human per unit time and 1-$u_1 \in [0,1]$ is the control on the use of treated bednets. Exposed individuals move to the infectious class at a rate $\alpha_1$. Infectious individuals are assumed to recover at a rate $b + \tau u_2 + \tau u_4$, where b is the rate of spontaneous recovery, $u_2$ is the control on treatment of infected individuals, $u_4$ is treatment to protect pregnant women and their new born children: intermittent preventive treatment (IPTp) for pregnant women and $\tau \in [0,1]$ is the efficacy of treatment. Infectious individuals who do not recover die at a rate $\psi + \mu_h$. Susceptible mosquitoes are generated at a rate $\Lambda_v$. They either die from natural causes (at a rate $\mu_v$) or move to the exposed class by acquiring malaria through contacts with infected humans at a rate $(1 - u_1)\ \lambda\epsilon\phi$, where $\lambda$ is the probability for a vector to get infected by an infectious human. Exposed mosquitoes are assumed to die at a rate $\mu_v$ or move to the infected class at a rate $\alpha_2$. Infected mosquitoes die at a rate $\mu_v$. The mosquito population is reduced, due to the use of insecticides spray, at a rate $pu_3$, where $u_3$ and p represent, respectively, the control and the efficacy of insecticides spray.

Table 3.1: State variables of the basic malaria model

| **Symbol** | **Description** |
|---|---|
| $S_h(t)$ | Number of susceptible humans at time t |
| $E_h$(t) | Number of exposed humans at time t |
| $I_h$(t) | Number of infectious humans at time t |
| $R_h$(t) | Number of recovered humans at time t |
| $S_v$(t) | Number of susceptible mosquitoes at time t |
| $E_v$(t) | Number of exposed mosquitoes at time t |
| $I_v$(t) | Number of infectious mosquitoes at time t |
| $N_h(t)$ | Total human population at time t |
| $N_v(t)$ | Total mosquito population at time t |

Table 3.2: Description of variables and parameters of the malaria model

| Parameter | Description |
|---|---|
| $\phi$ | Mosquito contact rate with human |
| $\epsilon$ | Mosquito biting rate |
| $\beta$ | Probability of human getting infected |
| $\lambda$ | Probability of a mosquito getting infected |
| $\mu_h$ | Natural death rate in humans |
| $\mu_v$ | Natural death rate in mosquitoes |
| $\kappa$ | Recovered individuals loss of immunity |
| $\alpha_1$ | Humans progression rate from exposed to infected |
| $\alpha_2$ | Mosquitoes progression rate from exposed to infected |
| $\Lambda_h$ | Human birth rate |
| $\Lambda_v$ | Mosquitoes birth rate |
| $\tau$ | Proportion of effectively treated individuals |
| $\psi$ | Disease induced death |
| b | Spontaneous recovery |
| p | Insecticides efficacy |



Putting the above formulations and assumptions together gives the following vector-host model

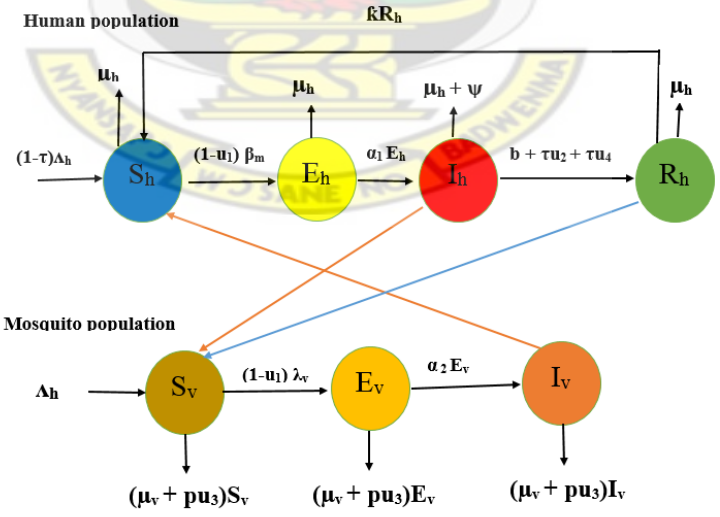



Figure 3.1: The malaria flowchart

$$
\begin{cases}
\dfrac{dS_h}{dt} = (1-\tau)\Lambda_h + \kappa R_h - \mu_h S_h - \dfrac{(1-u_1)\beta\epsilon\phi I_v S_h}{N_h} \\
\dfrac{dE_h}{dt} = \dfrac{(1-u_1)\beta\epsilon\phi I_v S_h}{N_h} - \mu_h E_h - \alpha_1 E_h \\
\dfrac{dI_h}{dt} = \alpha_1 E_h - (\psi + \mu_h) I_h - (b + \tau u_2 + \tau u_4) I_h \\
\dfrac{dR_h}{dt} = (b + \tau u_2 + \tau u_4) I_h - \mu_h R_h - \kappa R_h \\
\dfrac{dS_v}{dt} = \Lambda_v - \dfrac{(1-u_1)\lambda\epsilon\phi I_h S_v}{N_h} - (\mu_v + p u_3) S_v \\
\dfrac{dE_v}{dt} = \dfrac{(1-u_1)\lambda\epsilon\phi I_h S_v}{N_h} - \alpha_2 E_v - (\mu_v + p u_3) E_v \\
\dfrac{dI_v}{dt} = \alpha_2 E_v - (\mu_v + p u_3) I_v
\end{cases} \tag{1}
$$



Where $\lambda_v = \frac{\lambda\epsilon\phi I_h}{N_h}$ and $\beta_m = \frac{\beta\epsilon\phi I_v}{N_h}$. Here, $\beta_m$ and $\lambda_v$ represent the force of infection of humans and mosquitoes, respectively.

In the model $\beta_m$ denote the rate the susceptible humans $S_h$, become infected by infectious female anopheles mosquitoes $I_m$ and $\lambda_v$ refers to the rate at which the susceptible mosquitoes $S_h$ are infected by infectious humans $I_h$.

By Mwamtobe, 2010. It is important to note that the rate of infection of susceptible human $S_h$ by infected mosquito $I_v$ is dependent on the total number of Humans $N_h$ available per vector

## 3.2 Analysis of the model

The model is analyse to check if the control measures have any impact on the malaria disease, that is, whether the malaria disease can be control (eliminated) or not. The model parameters which determine persistence or elimination of malaria will be determined and studied. Therefore, we start by determining the invariant region to check whether the SEIR-SEI malaria model is in a biologically feasible region for both human and mosquito populations and showing that all solutions of equation (1) are positive at all t $\geq$ 0 and are attracted in that region.

that is to show that the model equations are mathematically well posed.

## 3.3 The positive invariant region

The total population sizes are $N_h = S_h + E_h + I_h + R_h$ and $N_v = S_v + E_v + I_v$ with their differential equations

$$\frac{N_h}{dt} = \frac{S_h}{dt} + \frac{E_h}{dt} + \frac{I_h}{dt} + \frac{R_h}{dt}$$

$$= (1-\tau)\Lambda_h - \psi I_h - \mu_h N_h \qquad (2)$$



and

$$\frac{N_v}{dt} = \frac{S_v}{dt} + \frac{E_v}{dt} + \frac{I_v}{dt}$$

$$= \Lambda_v - \mu_v N_v - pu_3 N_v \qquad (3)$$

The positive invariant region can be obtained by the following theorem.

**Theorem 3.1** The solutions of the system (1) are feasible for all $t < 0$ if they enter the invariant region $\mathcal{D} = \mathcal{D}_h \times \mathcal{D}_v$.

**Proof:**

Let $\mathcal{D}_h = (S_h, E_h, I_h, R_h, S_v, E_v, I_v) \in R_+^7$ be any solution of the system (1) with non-negative initial conditions.

Assuming the disease does not kill ($\psi = 0$) or in the absence of the disease (malaria), that is, $I_h = 0$, equation (2) becomes

$\frac{dN_h}{dt} \leq (1-\tau)\Lambda_h - \mu_h,$

$\frac{dN_h}{dt} + \mu N_h \leq (1-\tau)\Lambda_h \qquad (4)$

Using the differential equation of the form $y^1 + p(t)y = q(t)$ we have

$p(t) = \mu_h$ and $q(t) = (1-\tau)\Lambda_h$

therefore the integrating factor (IF) for (4) is $(IF) = e^{\int p(t)\,dt} = e^{\int \mu\,dt} = e^{\mu_h t}$

Multiplying both sides of equation (4) by $e^{\mu t}$ gives

$e^{\mu t}\frac{dN_h}{dt} + \mu_h N_h e^{\mu t} \leq e^{\mu t}(1-\tau)\Lambda_h,$

$\frac{d}{dt}(N_t e^{\mu t}) \leq e^{\mu t}(1-\tau)\Lambda_h$ (5)

Integrating on both sides of equation (5) we have

$N_h e^{\mu_h t} = \frac{(1-\tau)\Lambda_h}{\mu_h t} e^{\mu_h t} + c$ where c is the constant of integration

$N_h = \frac{\Lambda_h}{\mu_h t} e^{\mu_h t} \times \frac{1}{e^{\mu_h t}} + ce^{\mu_h t}$

$N_h = \frac{\Lambda_h}{\mu_h t} + ce^{-\mu_h t}$

Using the initial conditions at t = 0, $N_h(0) = N_h o$:

$N_h o \leq \frac{\Lambda_h}{\mu_h t} + c \rightarrow N_h o - \frac{\Lambda_h}{\mu t} \leq c,$

$N_h \leq \frac{\Lambda_h}{\mu_h} + (N_h o - \frac{\Lambda_h}{\mu_h})e^{-\mu t}$ (6)

Using the theorem of differential inequality by (Birkhoff and Rota, 1982), we obtain



$0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}$ as $t \rightarrow \infty,$ (7)

Therefore, as t $\rightarrow \infty$ in (6), the human population $N_h$ approaches $K = \frac{\Lambda_h}{\mu_h}$ (that is, $N_h \rightarrow K = \frac{\Lambda_h}{\mu_h}$), the parameter $K = \frac{\Lambda_h}{\mu_h}$ is usually called the carrying capacity, (Namawejje, 2011).

Hence all feasible solutions set of the human population of the model (1) enters the region

$\mathcal{D}_h = \{(S_h, E_h, I_h, R_h) \in R_+^4 : S_h > 0, E_h \geq 0, I_h \geq 0, R_h \geq 0, N_h \leq \frac{\Lambda_h}{\mu_h}\}$ .

Similarly, the feasible solutions set of the mosquito enters the region

$\mathcal{D}_v = \{(S_v, E_v, I_v) \in R_+^3 : S_v > 0, E_v \geq 0, I_v \geq 0, N_v \leq \frac{\Lambda_v}{\mu_v}\}$

Therefore, the feasible solutions set for the model (1 )is given by

$\mathcal{D} = \{(S_h, E_h, I_h, R_h, S_v, E_v, I_v) \in R_+^7 : (S_h, S_v) > 0, (E_h, I_h, R_h, E_v, I_v) \geq 0; N_h \leq \frac{\Lambda_h}{\mu_h}; N_v \leq \frac{\Lambda_v}{\mu_v}\}$.

Therefore, the region $\mathcal{D}$ is positively-invariant ( i.e. solution remain positive for all times, (t) and the model (1) is biologically, epidemiologically meaningful and mathematically well-posed in the domain $\mathcal{D}$. Therefore in this model it is sufficient to consider the dynamics of the flow generated by the model (1). In addition, the usual existence, uniqueness and continuation of results hold for the system.

## 3.4 Positivity of solutions

**Lemma 3.1** Let the initial data be

$\{(S_h(0), S_v(0)) > 0, (E_h(0), I_h(0), R_h(0), E_v(0), I_v(0)) \geq 0\} \in \mathcal{D}$.

Then the solution set $\{S_h, E_h, I_h, R_h, S_v, E_v, I_v\}(t)$ of the system (1) is positive for all $t > 0$.

**Proof**

From the first equation in the model (1), we have

$\frac{dS_h}{dt} = (1-\tau)\Lambda_h + \kappa R_h - \mu_h S_h - (1-u_1)\beta_m S_h \geq -\mu_h S_h - (1-u_1)\beta_m S_h$

$\frac{dS_h}{dt} \geq -(\mu_h + (1-u_1)\beta_m) S_h$



Using separation of variables and integrating both sides gives

$$\frac{1}{S_h} dS_h \geq -\int (\mu_h + (1-u_1)\beta_m)\, dt$$

$$lnS_h \; ge - (\mu_h + (1-u_1)\beta_m)t + c$$

$$\Rightarrow S_h(t) = e^{[-(\mu_h + (1-u_1)\beta_m)t + c]}$$

$$S_h(t) = e^{-(\mu_h + (1-u_1)\beta_m)t} \times e^c$$

$$S_h(t) = e^{-(\mu_h + (1-u_1)\beta_m)t} \times K$$

$$S_h(t) = K e^{-(\mu_h + (1-u_1)\beta_m)t}$$

$$S_h(t) \geq K e^{-(\mu_h + (1-u_1)\beta_m)t}$$

using the initial conditions: $t = 0$, $S_h(0) \geq K$

$$\Rightarrow S_h(t) \geq S_h(0) e^{-(\mu_h + (1-u_1)\beta_m)t} \geq 0$$

Therefore

$$S_h(t) \geq S_h(0) e^{-(\mu_h + (1-u_1)\beta_m)t} \geq 0.$$

From the second equation,

$$\frac{dE_h}{dt} = (1-u_1)\beta_m S_h - \mu_h E_h - \alpha_1 E_h$$

$$\frac{dE_h}{dt} = (1-u_1)\beta_m S_h - \mu_h E_h - \alpha_1 E_h \geq -(\mu_h + \alpha_1) E_h$$

$$\int \frac{1}{E_h}\, dE_h \geq \int -(\mu_h + \alpha_1)\, dt$$

$$ln(E_h) \geq -(\mu_h + \alpha_1)t + c$$

$$\Rightarrow E_h(t) = e^{-(\mu_h+\alpha_1)t+c}$$

$$E_h(t) = Ke^{(\mu_h+\alpha_1)t} \text{ where } K = e^c$$

Therefore

$$E_h \geq E_h(0)e^{-(\mu_h+\alpha_1)t} \geq 0$$

From the third equation we have



$$\frac{dI_h}{dt} = \alpha_1 E_h - (\psi + \mu_h)I_h - (b + \tau u_2 + \tau u_4)I_h$$

$$\frac{dI_h}{dt} = \alpha_1 E_h - (\psi + \mu_h)I_h - (b + \tau u_2 + \tau u_4)I_h \geq -[(\psi + \mu_h) + (b + \tau u_2 + \tau u_4)]I_h$$

$$\frac{dI_h}{dt} \geq -[(\psi + \mu_h) + (b + \tau u_2 + \tau u_4)]I_h$$

Using separation of variables and integrating both sides gives

$$\int \frac{1}{I+h}\, dI_h \geq \int -((\psi + \mu_h) + (b + \tau u_2 + \tau u_4))\, dt$$

$$ln(I_h) \geq -((\psi + \mu_h) + (b + \tau u_2 + \tau u_4))t + c$$

$$\Rightarrow I_h = e^{-[((\psi+\mu_h)+(b+\tau u_2+\tau u_4))t+c]}$$

$$I_h \geq Ke^{-[((\psi+\mu_h)+(b+\tau u_2+\tau u_4))t]}$$

$$I_h \geq I_h(0)e^{-[((\psi+\mu_h)+(b+\tau u_2+\tau u_4))t]}$$

where $K = I_h(0)$

$$I_h \geq I_h(0)e^{-[((\psi+\mu_h)+(b+\tau u_2+\tau u_4))t]} \geq 0$$

similarly, it can be shown that the remaining equations of the system (1) are positive for all $t > 0$, because $e^\eta > 0$ for all $\eta \in \mathbb{R}$.

Now it has been established that our model has both the invariant and positivity of solutions, we can move on to determine the existence of the disease free

equilibrium point which will assist in calculating the basic reproduction number using the next generation operator approach.

## 3.5 Stability of steady-state solutions



In this section, we assume that the control parameters are constant and determine the basic reproductive number, the steady state solutions or equilibrium points and their stabilities as well as the bifurcation behaviour of the system.

The $E = (S_h^*, E_h^*, I_h^*, R_h^* S_h^*, E_h^*, I_h^*)$ is the steady-state of the the system (1) which can be calculated by setting the right hand side of the model (1) to zero, giving us the following ;

$$\begin{cases} (1-\tau)\Lambda_h + \kappa R_h - \mu_h S_h - (1-u_1)\beta_m S_h = 0 \\ (1-u_1)\beta_m S_h - \mu_h E_h - \alpha_1 E_h = 0 \\ \alpha_1 E_h - (\psi + \mu_h) I_h - (b + \tau u_2 + \tau u_4) I_h = 0 \\ (b + \tau u_2 + \tau u_4) I_h - \mu_h R_h - \kappa R_h = 0 \\ \Lambda_v - (1-u_1)\lambda_v S_v - (\mu_v + p u_3) S_v = 0 \\ (1-u_1)\lambda_v S_v - \alpha_2 E_v - (\mu_v + p u_3) E_v = 0 \\ \alpha_2 E_v - (\mu_v + p u_3) I_v = 0 \end{cases} \tag{8}$$

## 3.6 The existence of the trivial equilibrium point

For as long as the human recruitment term $(1-\tau)\Lambda_h$ and the mosquito recruitment term $\Lambda_v$ are not zero, the population will not be extinct. This implies that there is no trivial equilibrium point, thus $(S_h^*, E_h^*, I_h^*, R_h^* S_h^*, E_h^*, I_h^*) \neq (0, 0, 0, 0, 0, 0, 0, )$.

## 3.7 Equilibrium points without disease

Disease-free equilibrium points (DFE) are steady state solutions where there is no malaria in the human population or Plasmodium parasite in the mosquito population. Let define the "diseased" classes as the human or mosquito populations that are either exposed or infectious; that is, $E_h, I_h, E_v$ and $I_v$.

In absence of the disease, this implies that ( $E_h, I_h, E_v, I_v$) also $R_h = 0$ since there is no disease to recover from, therefore reduces to

$$\left.\begin{aligned}(1-\tau)\Lambda_h - (\mu_h + (1-u_1)\beta_m)S_h^* = 0\\ \Lambda_v - ((1u_1)\lambda_v + (\mu_v + pu_3))S_v^* = 0\end{aligned}\right\} \quad (9)$$

which implies that

$$\left.\begin{aligned}S_h^* = \tfrac{(1-\tau)\Lambda_h}{\mu_h}\\ S_v^* = \tfrac{\Lambda_v}{(\mu_v + pu_3)}\end{aligned}\right\} \quad (10)$$

Therefore, the disease-free equilibrium point of the malaria model (1) is given by,

$$E_0 = (S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^*) = (\tfrac{(1-\tau)\Lambda_h}{\mu_h}, 0, 0, 0, \tfrac{\Lambda_v}{(\mu_v + pu_3)}, 0, 0) \quad (11)$$

which represents the state in which there is no infection (in the absence of malaria) in the society.

## 3.8 Basic reproduction number $R_0$

We use the next generation operator approach as described by Diekmann et al. (1990) to define the basic reproduction number, $R_0$, as the number of secondary infections that one infectious individual would create over the duration of the infectious period, provided that everyone else is susceptible.Reproduction number $R_0$ is the threshold for many epidemiology models, it determines whether a disease can invade a population or not. When $R_0 > 1$, each infected individual produces on average less than one new infected individual, so we would expect the disease to die out. On the other hand, if $R_0 > 1$ each individual produces more than one new

infected individual, so we would expect the disease to spread in the population. This means that the threshold quantity for eradicating the disease is to reduce the value of $R_0$ to value less than one. The basic reproduction number cannot be determined from the structure of the mathematical model alone, but depends on the definition of infected and uninfected compartments. Let us assume that there are $\eta$ compartments of which the first $m$ compartments correspond to infected individuals.

Let

$\mathcal{F}_i(\mathcal{X})$ be the rate of appearance of new infections in compartment ,

$\mathcal{V}_i(\mathcal{X}) = \mathcal{V}_i^-(\mathcal{X}) - \mathcal{V}_i^+(\mathcal{X})$ , where $\mathcal{V}_i^+(X)$ is the rate of transfer of individuals into compartment $i$ by all other means and $\mathcal{V}_i^-(\mathcal{X})$ is the rate of transfer of individual out of the $i$th compartment. It is assumed that each function is continuously differentiable at least twice in each variable. The disease transmission model consists of nonnegative initial conditions together with the following system of equations:

$$\dot{X} = h_i(X) = \mathcal{F}_i(X) - \mathcal{V}_i(\mathcal{X}),\ i = 1, ...n.$$

Where $\dot{X}$ is the rate of change of X.

The next step is the computation of the square matrices F and V of order $(m \times m)$, where $m$ is the number of infected classes, defined by

$F = [\frac{\partial \mathcal{F}_i}{\partial x_j}(X_0)]$ and $V = [\frac{\partial \mathcal{V}_i}{\partial x_j}(X_0)]$ with $1 \leq i,j \leq m$, such that F is nonnegative, V is a nonsingular M-matrix and $x_0$ is the disease-free equilibrium point (DFE). Since F is nonegative and V is nonsingular, then of $V^{-1}$ is nonnegative and also of $FV^{-1}$ is nonnegative. Hence the matrix of $FV^{-1}$ is called as the next generation matrix for the model. Finally, the basic reproduction number (reproduction ratio) $R_0$ is given by

$$R_0 = \vartheta FV^{-1},$$

where $\vartheta(A)$ denotes the spectral radius of a matrix A and the spectral radius, $\vartheta FV^{-1}$ , is the biggest nonnegative eigenvalue of the next generation matrix.

Rewriting the system (1) starting with the infected compartments for both populations;

$E_h, I_h, E_v, I_v$ also from the two populations, then the model system becomes:

$$\left.\begin{aligned}
\frac{dE_h}{dt} &= \frac{(1-U_1)\beta \in \phi S_h I_v}{N_h} - U_n E_n - \alpha_1 E_n \\
\frac{dI_h}{dt} &= \alpha_1 E_h - (\psi + U_h) I_h - (b + \tau U_2 + \tau U_4) I_h \\
\frac{dE_v}{dt} &= \frac{(1-U_1)\lambda\epsilon\phi I_h S_v}{N_h} - \alpha_2 E_v - (U_v + pU_3) E_v \\
\frac{dI_v}{dt} &= \alpha_2 E_v - (U_v + pU_3) I_v \\
\frac{dS_h}{dt} &= (1-\tau)\Lambda_h + \kappa R_h - U_h S_h - \frac{(1-U_1)\beta \in \phi S_h I_v}{N_h} \\
\frac{dR_h}{dt} &= (b + \tau U_2 + \tau U_4) I_h - U_h R_h - \kappa R_h \\
\frac{dS_v}{dt} &= \Lambda_v - \frac{(1-U_1)\lambda\epsilon\phi I_h S_v}{N_h} - (U_v + pU_3) S_v
\end{aligned}\right\} \tag{12}$$

From the system (12), $\mathcal{F}_i$ and $\mathcal{V}_i$ are defined as:

$$\mathcal{F}_i = \begin{bmatrix} \frac{(1-\mu_1)\beta\epsilon\phi I_v S_h}{N_h} \\ 0 \\ \frac{(1-\mu_1)\beta\epsilon\phi I_h S_v}{N_h} \\ 0 \end{bmatrix} \tag{13}$$

and

$$\mathcal{V}_i = \begin{bmatrix} (\mu_h + \alpha_1)\epsilon_h \\ (\psi + \mu_h + b\tau u_2 + \tau u_4) I_h - \alpha_1 E_h \\ (\alpha_2 + \mu_v + p u_3) E_v \\ (\mu_v + p u_3) I_v - \alpha_2 E_v \end{bmatrix} \tag{14}$$

The partial derivatives of (13) with respect to ($I_h$, $I_v$) and the Jacobian matrix

of $\mathcal{F}_i$ is:

$$F = \begin{bmatrix} 0 & 0 & 0 & \dfrac{(1-u_1)\beta\epsilon\phi S_h}{N_h} \\ 0 & 0 & 0 & 0 \\ 0 & \dfrac{(1-u_1)\lambda\epsilon\phi S_v}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

substituting the equilibrium points :

$$S_h^* = \frac{(1-\tau)\Lambda_h}{\mu_h}$$

$$S_v^* = \frac{\Lambda_v}{(\mu_v + pu_3)}$$

$$\text{and } N_h = \frac{(1-\tau)\Lambda_h}{\mu_h}$$

into the Jacobian of F we have

$$F = \begin{bmatrix} 0 & 0 & 0 & (1-u_1)\beta\epsilon\phi \\ 0 & 0 & 0 & 0 \\ 0 & \dfrac{(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v + pu_3)\Lambda_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{15}$$

Similarly, the partial derivatives of (14) with respect to ($E_h$, $I_h$ $E_v$ $I_v$) and the Jacobian matrix of $\mathcal{V}_i$ is :

$$V = \begin{bmatrix} (\mu_h + \alpha_1) & 0 & 0 & \\ -\alpha_1 & (\psi + \mu_h + b + \tau u_2 + \tau u_4) & 0 & 0 \\ 0 & 0 & \alpha_2 + \mu_v + pu_3 & 0 \\ 0 & 0 & -\alpha_2 & \mu_v + pu_3 \end{bmatrix} \tag{16}$$

The inverse of V is given as

$$V^{-1} = \begin{bmatrix} \frac{1}{(\mu_h+\alpha_1)} & 0 & 0 & 0 \\ \frac{\alpha_1}{(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)} & \frac{1}{\psi+\mu_h+b+\tau u_2+\tau u_4} & 0 & 0 \\ 0 & 0 & \frac{1}{\alpha_2+\mu_v+pu_3} & 0 \\ 0 & 0 & \frac{\alpha_2}{(\alpha_2+\mu_v+pu_3)(\mu_v+pu_3)} & \frac{1}{(\mu_v+pu_3)} \end{bmatrix}$$

We compute the matrix $FV^{-1}$

$$\begin{bmatrix} 0 & 0 & 0 & (1-u_1)\beta\epsilon\phi \\ 0 & 0 & 0 & 0 \\ 0 & \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)\Lambda_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{(\mu_h+\alpha_1)} & 0 & 0 & 0 \\ \frac{\alpha_1}{(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)} & \frac{1}{\psi+\mu_h+b+\tau u_2+\tau u_4} & 0 & 0 \\ 0 & 0 & \frac{1}{\alpha_2+\mu_v+pu_3} & 0 \\ 0 & 0 & \frac{\alpha_2}{(\alpha_2+\mu_v+pu_3)(\mu_v+pu_3)} & \frac{1}{(\mu_v+pu_3)} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{(1-u_1)\beta\epsilon\phi\alpha_2}{(\alpha_2+\mu_v+pu_3)(\mu_v+pu_3)} & \frac{(1-u_1)\beta\epsilon\phi}{(\mu_v+pu_3)} \\ 0 & 0 & 0 & 0 \\ \frac{\alpha_1(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)(1-\tau)(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)\Lambda_h} & \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)(\psi+\mu_h+b+\tau u_2+\tau u_4)\Lambda_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & 0 & a & b \\ 0 & 0 & 0 & 0 \\ c & d & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{17}$$

.

Where $a = \frac{(1-u_1)\beta\epsilon\phi\alpha_2}{(\alpha_2+\mu_v+pu_3)(\mu_v+pu_3)}$ $b = \frac{(1-u_1)\beta\epsilon\phi}{(\mu_v+pu_3)}$ $c = \frac{\alpha_1(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)\Lambda_h}$

$d = \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)(\psi+\mu_h+b+\tau u_2+\tau u_4)\Lambda_h}$.

From (17), we can now calculate the eigenvalues to determine the basic reproduction number $R_0$ by taking the spectral radius (dominant eigenvalue) of the matrix $FV^{-1}$.

The eigenvalues of $FV^{-1}$ are calculated as $J = [FV^{-1} - \lambda I]$, we have

$$J = \begin{bmatrix} 0-\lambda & 0 & a & b \\ 0 & 0-\lambda & 0 & 0 \\ c & d & 0-\lambda & 0 \\ 0 & 0 & 0 & 0-\lambda \end{bmatrix}$$

.

Thus $|J| = |FV^{-1} - \lambda I| = 0$ , we have

$$|J| = \begin{vmatrix} 0-\lambda & 0 & a & b \\ 0 & 0-\lambda & 0 & 0 \\ c & d & 0-\lambda & 0 \\ 0 & 0 & 0 & 0-\lambda \end{vmatrix} = \begin{vmatrix} -\lambda & 0 & a & b \\ 0 & -\lambda & 0 & 0 \\ c & d & -\lambda & 0 \\ 0 & 0 & 0 & -\lambda \end{vmatrix} = 0$$

.

$$= -b \begin{vmatrix} 0 & -\lambda & 0 \\ c & d & -\lambda \\ 0 & 0 & 0 \end{vmatrix} - \lambda \begin{vmatrix} -\lambda & 0 & a \\ 0 & -\lambda & 0 \\ c & d & -\lambda \end{vmatrix} = -b(0) - \lambda(-\lambda^3 + \lambda ac) = 0$$

$$= \lambda^2(\lambda^2 - ac) = 0 \Rightarrow \lambda^2 = 0 or \lambda^2 - ac = 0$$

$$\Rightarrow \lambda^2 = ac$$

$$\lambda = \pm\sqrt{ac}$$

.

Therefore $\lambda_1 = 0$, $\lambda_2 = 0$, $\lambda_3 = \sqrt{ac}$ and $\lambda_4 = -\sqrt{ac}$.

From the four eigenvalues, the dominant eigenvalue of the matrix

$FV^{-1}$ is $\lambda = \sqrt{ac}$

Therefore the basic reproduction number $R_0 = \sqrt{ac}$

Hence

$$R_o = \sqrt{\frac{\alpha_1(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v + pu_3)(\mu_h + \alpha_1)(\psi + \mu_h + b + \tau u_2 + \tau u_4)\Lambda_h} \times \frac{(1-u_1)\beta\epsilon\phi\alpha_2}{(\alpha_2 + \mu_v + pu_3)(\mu_v + pu_3)}}$$

$$R_0 = \sqrt{\frac{\alpha_1(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h(1-u_1)\beta\epsilon\phi\alpha_2}{(\mu_v+pu_3)(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)\Lambda_h(\alpha_2+\mu_v+pu_3)(\mu_v+pu_3)}} \tag{18}$$

Where

$\frac{\alpha_1}{\alpha_1+\mu_h}$ means the probability that a human will survive the exposed state to become infectious.

$\frac{\alpha_2}{\alpha_2+\mu_v+pu_3}$ is the probability that a mosquito will survive the exposed state to become infectious.

$\frac{\alpha_2\lambda\epsilon\phi(1-u_1)}{(\alpha_2+\mu_v+pu_3)(\mu_v+pu_3)}$ is the number of humans that one mosquito infects during its infectious lifetime, provided all humans are susceptible.

$\frac{\beta\epsilon\phi(1-u_1)}{(\alpha+\mu_h)(\epsilon+\mu_h+b+\tau u_2+\tau u_4)}$ is the number of mosquitoes that one human infects during the duration of the infectious period, provided all mosquitoes are susceptible.

$$R_0 = \sqrt{\frac{(1-u_1)\beta\epsilon\phi\alpha_1\mu_h}{\Lambda_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)} \times \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\alpha_2}{(pu_3+\mu_v)^2(pu_3+\mu_v+\lambda_2)}}$$

$$R_0 = \sqrt{R_{0h} \times R_{ov}}$$

where

$$R_{oh} = \frac{(1-u_1)\beta\epsilon\phi\alpha_1\mu_h}{\Lambda_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)}$$

and

$$R_{ov} = \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\alpha_2}{(pu_3+\mu_v)^2(pu_3+\mu_v+\lambda_2)}$$

The threshold parameter $R_0$ can be defined as square roots of the product of number of humans one mosquito infects during its infectious lifetime ($R_{oh}$) and number of mosquitoes one human infects during the duration of the infectious period ($R_{ov}$) provided all humans and mosquitoes are susceptible.

Where

$\frac{(1-u_1)\beta\epsilon\phi\alpha_1\mu_h}{\Lambda_h(\psi+\mu_h+b+\tau u_2+\tau u_4)}$ is the number of latent infections produced by a typical infectious individual during the mean infectious period.

$\frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\alpha_2}{(pu_3+\mu_v)^2}$ is the number of latent infections produced by a typical infectious mosquitoes during the mean infectious period.

The parameter $\epsilon$ and $\phi$ appear in both expressions because the mosquito biting rate ($\epsilon$) and mosquito contact rate with human ($\phi$) controls the transmission from humans to mosquitoes and from mosquitoes to humans.

The basic reproduction number can be used to determine the local stability of the disease free equilibrium point.



## 3.9 Local stability of disease free equilibrium

The local stability of the disease-free equilibrium can be analyzed using the Jacobian matrix of the malaria model (1) at the disease free equilibrium point. Using Van den Driessche P. and Watmough J., (2002), the following theorem holds.

**Theorem 3.2**

The disease free equilibrium point for system is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

**Proof:**

The Jacobian matrix (J) of the malaria model (1) with $S_h = N_h - (E_h + I_h + R_h)$ and $S_v = N_v - (E_v + I_v)$ at the disease-free equilibrium point is given by

$$\begin{bmatrix} -(\alpha_1+\mu_h) & 0 & 0 & 0 & (1-u_1)\beta\epsilon\phi \\ \alpha_1 & -(\psi+\mu_h+b+\tau u_2+\tau u_4) & 0 & 0 & 0 \\ 0 & (b+\tau u_2+\tau u_4) & -(\kappa+\mu_h) & 0 & 0 \\ 0 & \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)(1-\tau)\Lambda_h} & 0 & -(\alpha_2+\mu_v+pu_3) & 0 \\ 0 & 0 & 0 & \alpha_2 & -(\mu_v+pu_3) \end{bmatrix} \tag{19a}$$

The eigenvalues of the Jacobian matrix are the solutions of the characteristic equation

$$|J - \lambda I| = 0.$$

That is

$$\begin{bmatrix} -(\alpha_1+\mu_h+\lambda) & 0 & 0 & 0 & (1-u_1)\beta\epsilon\phi \\ \alpha_1 & -(\psi+\mu_h+b+\tau u_2+\tau u_4+\lambda) & 0 & 0 & 0 \\ 0 & (b+\tau u_2+\tau u_4) & -(\kappa+\mu_h+\lambda) & 0 & 0 \\ 0 & \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)(1-\tau)\Lambda_h} & 0 & -(\alpha_2+\mu_v+pu_3+\lambda) & 0 \\ 0 & 0 & 0 & \alpha_2 & -(\mu_v+pu_3+\lambda) \end{bmatrix} = 0$$

The third column has diagonal entry, therefore one of the eigenvalues of the Jacobian matrix is $-(\kappa+\mu_h)$.

The remaining eigenvalues can be obtained as follows:

$$\begin{vmatrix} -(\alpha_1+\mu_h+\lambda) & 0 & 0 & (1-u_1)\beta\epsilon\phi \\ \alpha_1 & -(\psi+\mu_h+b+\tau u_2+\tau u_4+\lambda) & 0 & 0 \\ 0 & \frac{(1-u_1)\lambda\epsilon\phi\Lambda_v\mu_h}{(\mu_v+pu_3)(1-\tau)\Lambda_h} & -(\alpha_2+\mu_v+pu_3+\lambda) & 0 \\ 0 & 0 & \alpha_2 & -(\mu_v+pu_3+\lambda) \end{vmatrix} = 0$$

$(\alpha_1+\mu_h+\lambda)(\psi+\mu_h+b+\tau u_2+\tau u_4+\lambda)(\alpha_2+\mu_v+pu_3+\lambda)(\mu_v+pu_3+\lambda) - \frac{(1-u_1)^2\lambda\epsilon^2\phi^2\Lambda_v\mu_h\alpha_2\beta\alpha_1}{(\mu_h+pu_3)(1-\tau)\Lambda_h} = 0$

To simplify the equation, let $A_1 = (\mu_v+pu_3), A_2 = (\alpha_2+\mu_v+pu_3), A_3 = (\psi+\mu_h+b+\tau u_2+\tau u_4), A_4 = (\alpha_1+\mu_h)$ and $Q = \frac{(1-u_1)^2\lambda\epsilon^2\phi^2\Lambda_v\mu_h\alpha_2\beta\alpha_1}{(\mu_h+pu_3)(1-\tau)\Lambda_h}$

This implies

$(\lambda+A_1)(\lambda+A_2)(\lambda+A_3)(\lambda+A_4) - Q = 0$

$$\lambda^4 + B_1\lambda^3 + B_2\lambda^2 + B_3\lambda + B_4 = 0 \qquad (19b)$$

where

$$\left.\begin{aligned} B_1 &= A_4 + A_3 + A_2 + A_1 \\ B_2 &= A_4(A_3+A_2+A_1) + A_3(A_2+A_1) + A_2A_1 \\ B_3 &= A_4A_3A_2 + A_4A_3A_1 + A_4A_2A_1 + A_3A_2A_1 \\ B_4 &= A_4A_3A_2A_1 - Q \end{aligned}\right\} \qquad (19c)$$

The expression for $R_0$ (19) can be written, in terms of $A_i$ as

$$R_0^2 = \frac{\alpha_1\alpha_2\Lambda_v\mu_h(1-u_1)^2\phi^2\epsilon^2\beta\lambda}{\Lambda_h A_4A_3A_2A_1^2} \qquad (19d)$$

Using the Routh-Hurwitz Criteria on (19b) , we can prove that all roots of the polynomial(19b) have negative real parts. The Routh-Hurwitz Criteria is stated

as follows: Important criteria that give necessary and sufficient conditions for all of the roots of the characteristic polynomial (with real coefficients) to lie in the left half of the complex plane are known as Routh-Hurwitz criteria (Flores, 2013).

**Theorem 3.3: Routh-Hurwitz Criteria**

Given the polynomial

$P(\lambda) = \lambda^n + B_1\lambda^{n-1} + .... + B_{n-1}\lambda + B_n.$

Where the coefficient $B_i$ are real constants, $i = 1, ..., n$ define the n Hurwitz matrices using the coefficients $B_i$ of the characteristic polynomial:

$$H_1 = (B_1),\ H_2 = \begin{pmatrix} B_1 & 1 \\ B_3 & B_2 \end{pmatrix},\ H_3 = \begin{pmatrix} B_1 & 1 & 0 \\ B_3 & B_2 & B_1 \\ B_5 & B_4 & B_3 \end{pmatrix}$$

and

$$H_n = \begin{pmatrix} B_1 & 1 & 0 & 0 & \dots & 0 \\ B_3 & B_2 & B_1 & 1 & \dots & 0 \\ B_5 & B_4 & B_3 & B_2 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \dots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & B_n \end{pmatrix}$$

where $B_J = 0$ if $j > n$. All of the roots of the polynomial $P(\lambda)$ are negatives or have negative real parts if and only if and only if the determinants of all Hurwitz matrices are positive:

$$det(H_j) > 0, j = 1, 2, ..., n.$$

For the characteristic polynomial in (19b), when $n = 4$, the Routh-Hurwitz criteria are

$B_1 > 0, B_2 > 0, B_3 > 0, B_4 > 0$ and $det(H_1) = B_1 > 0,$

$$det(H_2) = \begin{pmatrix} B_1 & 1 \\ 0 & B_2 \end{pmatrix} = B_1B_2 > 0,$$

$$det(H_3) = \begin{pmatrix} B_1 & 1 & 0 \\ B_3 & B_2 & B_1 \\ 0 & 0 & B_3 \end{pmatrix} = B_1B_2B_3 - B_3^2 > 0 \Rightarrow B_1B_2 - B_3 > 0, \text{ and}$$

$$det(H_4) = \begin{pmatrix} B_1 & 1 & 0 & 0 \\ B_3 & B_2 & B_1 & 1 \\ 0 & B_4 & B_3 & B_2 \\ 0 & 0 & 0 & B_4 \end{pmatrix} = B_3(B_2B_1 - B_3) - B_4B_1^2 > 0.$$



Now we show that all determinants of the Hurwitz matrices are positive, which means all the eigenvalues of the Jacobian (19a) have negative real part. Therefore, disease-free equilibrium point is stable.

$det(H_2) = B_1 = A_4 + A_3 + A_2 + A_1 > 0$

$$\left.\begin{aligned} &det(H_2) = B_1B_2 \\ &= 3A_4A_3(A_1 + A_2) + 3A_2A_1(A_4 + A_3) + A_4^2(A_3 + A_2 + \\ &A_1) + A_3^2(A_4 + A_2 + A_1) + A_2^2(A_4 + A_3 + A_1) + A_1^2(A_4 + A_3 + A_2) > 0 \end{aligned}\right\}$$

$$\left.\begin{aligned} &det(H_3) = B_1B_2 \\ &= 2A_4A_3(A_1 + A_2) + 2A_2A_1(A_4 + A_3) + A_4^2(A_3 + A_2 + \\ &A_1) + A_3^2(A_4 + A_2 + A_1) + A_2^2(A_4 + A_3 + A_1) + A_1^2(A_4 + A_3 + A_2) > 0 \end{aligned}\right\}$$

$$\left.\begin{aligned} &det(H_4) = B_3(B_2B_1 - B_3) - B_4B_1^2 \\ &= B_3C + QB_1^2 - A_4A_3A_2A_1B_1^2 > 0 \end{aligned}\right\}$$

where $C = B_2B_1 - B_3$

Since all the determinants of the Hurwitz matrices are positive, then it means all the eigenvalues of the Jacobian (19a) have negative real part and $R_0 < 1$. Therefore, disease-free equilibrium point is stable.

Conversely, if $R_0 > 1$ it implies that $B_4 < 0$, and since the remaining coefficients ($B_1, B_2$ and $B_3$) of the polynomial (19b) are positive then all the roots of this polynomial cannot have negative real parts. Therefore, the disease-free equilibrium point is unstable.

## 3.10 The endemic equilibrium points

Endemic equilibrium points are steady state solutions where the disease persists in the population (all the state variables are positive). That is, malaria infection will persists in the population and the endemic equilibrium (EEP) of the model is given by

$EEP = (S_h^{**}, E_h^{**}, I_h^{**}, R_h^{**}, S_v^{**}, E_v^{**}, I_v^{**})$,

Where $(S_h^{**}, E_h^{**}, I_h^{**}, R_h^{**}, S_v^{**}, E_v^{**}, I_v^{**}) > 0$.

To derive the EEP, we have to solve model (1) by equating it to zero .

$$\left.\begin{aligned}
(1-\tau)\Lambda_h + \kappa R_h - \mu_h S_h - \tfrac{(1-u_1)\beta\epsilon\phi S_h}{N_h} = 0 \quad (1)\\
\tfrac{(1-u_1)\beta\epsilon\phi S_h}{N_h} - \mu_h E_h - \alpha_1 E_h = 0 \quad (2)\\
\alpha_1 E_h - (\psi + \mu_h) I_h - (b + \tau u_2 + \tau u_4) I_h = 0 \quad (3)\\
(b + \tau u_2 + \tau u_4) I_h - \mu_h R_h - \kappa R_h = 0 \quad (4)\\
\Lambda_v - \tfrac{(1-u_1)\lambda\epsilon\phi I_h S_v}{N_h} - (\mu_v + p u_3) S_v = 0 \quad (5)\\
\tfrac{(1-u_1)\lambda\epsilon\phi I_h S_v}{N_h} - \alpha_2 E_v - (\mu_v + p u_3) E_v = 0 \quad (6)\\
\alpha_2 E_v - (\mu_v + p u_3) I_v = 0 \quad (7)
\end{aligned}\right\} \quad (1)$$

Solving the second equation of (1) for $E^{**}$ we have

$\frac{(1-u_1)\beta\epsilon\phi S_h}{N_h} - \mu_h E_h - \alpha_1 E_h = 0$

$E^{**} = \frac{(1-u_1)\beta\epsilon\phi I_v^{**}}{N_h(\mu_h+\alpha_1)} S_h^{**}$ (20)

From the sixth equation of model (1) we have

$\frac{(1-u_1)\lambda\epsilon\phi I_h S_v}{N_h} - \alpha_2 E_v - (\mu_v + p u_3) E_v = 0$

$E_v^{**} = \frac{(1-u_1)\alpha\epsilon\phi I_h^{**}}{N_h(\alpha_2+\mu_v+p u_3)} S_v^{**}$ (21)

From the seventh equation, we have

$$\alpha_2 E_v - (\mu_v + pu_3)I_v = 0$$

$$I_v^{**} = \frac{\alpha_2}{(\mu_v+pu_3)} E_v^{**} \qquad (22)$$

Substituting equation (21) into equation (22) for $I_h^{**}$ gives

$$I_v^{**} = \frac{\alpha_2(1-u_1)\lambda\epsilon\phi I_h^{**} S_v^{**}}{N_h(\mu_v+pu_3)(\alpha_2+\mu_v+pu_3)} \qquad (23)$$

But from the equation (5) we have

$$\Lambda_v - \frac{(1-u_1)\lambda\epsilon\phi I_h S_v}{N_h} - (\mu_v + pu_3)S_v = 0$$

$$S_v^{**} = \frac{\Lambda_v N_h}{(1-u_1)\lambda\epsilon\phi I_h^{**}+(\mu_v+pu_3)N_h} \qquad (24)$$

Substituting equation (24) into equation (23) we have

$$I_v^{**} = \frac{\alpha_2\Lambda_v(1-u_1)\lambda\epsilon\phi I_h^{**}}{(\mu_v+pu_3)(\alpha_2+\mu_v+pu_3)(1-u_1)\lambda\epsilon\phi I_h^{**}+N_h(\mu_v+pu_3)(\mu_v+pu_3)(\alpha_2+\mu_v+pu_3)} \qquad (25)$$

$$I_v^{**} = \frac{(1-u_1)(\mu_v+pu_3)R_{ov}I_h^{**}}{(1-u_1)\lambda\epsilon\phi I_h^{**}+N_h(\mu_v+pu_3)} \qquad (26)$$

From the second equation we have

$$\frac{(1-u_1)\beta\epsilon\phi S_h}{N_h} - (\mu_h + \alpha_1)E_h = 0$$

Substituting equation (26) into the second equation above, we have

$$\frac{(1-u_1)^2(\mu_v+pu_3)\beta\epsilon\phi R_{ov}I_h^{**}S_h^{**}}{N_h((1-u_1)\lambda\epsilon\phi I_h^{**}+N_h(\mu_v+pu_3))} - (\mu_h + \alpha_1)E_h = 0 \qquad (27)$$

From the third equation we have

$$\alpha_1 E_h - [(\psi + \mu_h) + (b + \tau u_2 + \tau u_4)]I_h = 0$$

$$E_h = \frac{(\psi+\mu_h+b+\tau u_2+\tau u_4)I_h^{**}}{\alpha_1} \qquad (28)$$

Substituting equation (28) into equation (27) we have

$$\frac{(1-u_1)^2(\mu_v+pu_3)\beta\epsilon\phi R_{ov}I_h^{**}S_h^{**}}{N_h((1-u_1)\lambda\epsilon\phi I_h^{**}+N_h(\mu_v+pu_3))} - \frac{(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)I_h^{**}}{\alpha_1} = 0 \qquad (29)$$

$$\frac{\alpha_1(1-u_1)^2(\mu_v+pu_3)\beta\epsilon\phi R_{ov}I_h^{**}S_h^{**} - N_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)I_h^{**}(N_h((1-u_1)\lambda\epsilon\phi I_h^{**}+N_h(\mu_v+pu_3))}{N_h\alpha_1((1-u_1)\lambda\epsilon\phi I_h^{**}+N_h(\mu_v+pu_3))} = 0$$

$$\alpha_1(1-u_1)^2(\mu_v+pu_3)\beta\epsilon\phi R_{ov}I_h^{**}S_h^{**} - N_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)I_h^{**}((1-u_1)\lambda\epsilon\phi I_h^{**} +$$

$$N_h(\mu_v+pu_3)) = 0$$

$$I_h^{**}[\alpha_1(1-u_1)^2(\mu_v+pu_3)\beta\epsilon\phi R_{ov}S_h^{**} - N_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)((1-u_1)\lambda\epsilon\phi I_h^{**} +$$

$$N_h(\mu_v+pu_3))] = 0$$

Hence $I_h^{**} = 0$ or

$$\alpha_1(1-u_1)^2(\mu_v+pu_3)\beta\epsilon\phi R_{ov}S_h^{**} - N_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)((1-u_1)\lambda\epsilon\phi I_h^{**} +$$

$N_h(\mu_v + pu_3)) = 0$

$\alpha_1(1-u_1)^2(\mu_v + pu_3)\beta\epsilon\phi R_{ov}S_h^{**} - N_h(\mu_h + \alpha_1)(\psi + \mu_h + b + \tau u_2 + \tau u_4)((1-u_1)\lambda\epsilon\phi I_h^{**} +$

$N_h(\mu_v + pu_3)) = 0$ (30)

Dividing through equation (30) through by $N_h(\mu_h + \alpha_1)(\psi + \mu_h + b + \tau u_2 + \tau u_4)$ we have

$\frac{\alpha_1(1-u_1)^2(\mu_v+pu_3)\beta\epsilon\phi R_{ov}S_h^{**}}{N_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)} - ((1-u_1)\lambda\epsilon\phi I_h^{**} + N_h(\mu_v + pu_3)) = 0, N_h = \frac{\Lambda_h}{\mu_h}$

$[\frac{\beta\epsilon\phi\alpha_1\mu_h}{\Lambda_h(\mu_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)}](1-u_1)^2(\mu_v + pu_3)R_{ov}S_h^{**} - (1-u_1)\lambda\epsilon\phi I_h^{**} + N_h(\mu_v + pu_3)) = 0$

$R_{oh} \times R_{ov}(1-u_1)^2(\mu_v + pu_3)S_h^{**} - (1-u_1)\lambda\epsilon\phi I_h^{**} + \frac{\Lambda_h}{\mu_h}(\mu_v + pu_3)) = 0$

$R_{oh} \times R_{ov}(1-u_1)^2(\mu_v + pu_3)S_h^{**} = \frac{\mu_h(1-u_1)\lambda\epsilon\phi I_h^{**}+\Lambda_h(\mu_v+pu_3)}{\mu_h}$

Let $R_{oh} \times R_{ov} = R_o^2$ hence we have

$R_o^2(1-u_1)^2(\mu_v + pu_3)S_h^{**} = \frac{\mu_h(1-u_1)\lambda\epsilon\phi I_h^{**}+\Lambda_h(\mu_v+pu_3)}{\mu_h}$

Therefore

$S_h^{**} = \frac{\mu_h(1-u_1)\lambda\epsilon\phi I_h^{**}+\Lambda_h(\mu_v+pu_3)}{\mu_h R_o^2(1-u_1)^2(\mu_v+pu_3)}$ (31)

From the fourth equation of model (1) we have

$(b + \tau u_2 + \tau u_4)I_h - (\mu_h + \kappa)R_h = 0$

$R_h = \frac{(b+\tau u_2+\tau u_4)I_h^{**}}{\mu_h+\kappa}$ (32)

Using the first equation of model (1) we can solve for $I_h^{**}$,

$(1-\tau)\Lambda_h + \kappa R_h - \mu_h S_h - \frac{(1-u_1)\beta\epsilon\phi S_h}{N_h} = 0$ (33)

substituting equation (26), (31) and (32) into equation (33) we have

$(1-\tau)\Lambda_h + \kappa\frac{(b+\tau u_2+\tau u_4)I_h^{**}}{\mu_h+\kappa} + [\frac{(1-u_1)\beta\epsilon\phi}{N_h}][\frac{(1-u_1)(\mu_v+pu_3)R_{ov}I_h^{**}}{(1-u_1)\lambda\epsilon\phi I_h^{**}+N_h(\mu_v+pu_3)}][\frac{\mu_h(1-u_1)\lambda\epsilon\phi I_h^{**}+\Lambda_h(\mu_v+pu_3)}{\mu_h R_o^2(1-u_1)^2(\mu_v+pu_3)}] -$

$\mu_h[\frac{\mu_h(1-u_1)\lambda\epsilon\phi I_h^{**}+\Lambda_h(\mu_v+pu_3)}{\mu_h R_o^2(1-u_1)^2(\mu_v+pu_3)}] = 0$

Finally we get

$A(I_h^{**})^2 + BI_h^{**} + C$ (34)

where

$A = \kappa(b + \tau u_2 + \tau u_4)(N_h\lambda\epsilon\phi\mu_h(1-u_1)(\mu_v + pu_3)R_0^2\mu_h)(1-u_1)(\mu_v + pu_3)R_0^2 - (\mu_h + \kappa)(1 -$

$u_1)^2(\mu_v+pu_3)R_0^2(1-u_1)\beta\epsilon\phi R_0^2\lambda\epsilon\phi(\mu_v+pu_3) - (\mu_h+\kappa)(N_h\lambda\epsilon\phi\mu_h(\mu_v+pu_3)R_0^2\mu_h)(\mu_h(1-u_1)\lambda\epsilon\phi)$

$B = (1-\tau)\Lambda_h(\mu_h + \kappa)(1-u_1)^2(\mu_v + pu_3)R_0^2(N_h(1-u_1)\lambda\epsilon\phi\mu_h(\mu_v + pu_3)R_0^2\mu_h) + \kappa(b + \tau u_2 +$

$\tau u_4)(1-u_1)^2(\mu_v + pu_3)R_0^2(N_h^2(\mu_v + pu_3)^2\mu_h R_0^2\mu_h) - (\mu_h + \kappa)(1-u_1)^2(\mu_v + pu_3)R_0^2(\Lambda_h(\mu_v +$

$pu_3)^2\beta\epsilon\phi R_{ov}) - (\mu_h + \kappa)(N_h(1-u_1)\lambda\epsilon\phi\mu_h(\mu_v + pu_3)R_0^2\mu_h)\Lambda_h(\mu_v + pu_3) + (\mu_h + \kappa)(N_h^2(\mu_v +$

$pu_3)^2\mu_h R_0^2\mu_h)(\mu_h(1-u_1)\lambda\epsilon\phi)$

$C = (1-\tau)\Lambda_h(\mu_h + \kappa)(1-u_1)^2(\mu_v + pu_3)R_0^2(N_h^2(\mu_v + pu_3)^2\mu_h R_0^2\mu_h) + (\mu_h + \kappa)(N_h^2(\mu_v +$

$pu_3)^2\mu_h R_0^2\mu_h)\Lambda_h(\mu_v + pu_3)$

Using the quadratic formula

$$x = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

we have

$$I_h^* = \frac{-B \pm \sqrt{B^2 - 4AC}}{2A}$$

$$= \frac{-B + \sqrt{B^2 - 4AC}}{2A} \text{ or } = \frac{-B - \sqrt{B^2 - 4AC}}{2A}$$

$$= \frac{-B \pm \sqrt{B^2 - 4AC}}{2A} = \frac{\sqrt{B^2 - 4AC} - B}{2A} = \Phi \tag{39}$$

Hence

$$I_h^{**} \geq 0$$

$$S_h^{**} = \frac{\mu_h(1-u_1)\lambda\epsilon\phi\Phi + \Lambda_h(\mu_v + pu_3)}{\mu_h R_o^2(1-u_1)^2(\mu_v + pu_3)} \tag{40}$$

$$E_h^{**} = \frac{(\psi + \mu_h + b + \tau u_2 + \tau u_4)\Phi}{\alpha_1} \tag{41}$$

$$R_h^{**} = \frac{(b + \tau u_2 + \tau u_4)\Phi}{\mu_h + \kappa} \tag{42}$$

$$S_v^{**} = \frac{\Lambda_v N_h}{(1-u_1)\lambda\epsilon\phi\Phi + (\mu_v + pu_3)N_h} \tag{43}$$

$$E_v^{**} = \frac{(1-u_1)\alpha\epsilon\phi\Lambda_v N_h I_h^{**}}{(N_h(\alpha_2 + \mu_v + pu_3))((1-u_1)\lambda\epsilon\phi\Phi + (\mu_v + pu_3)N_h)} \tag{44}$$

$$I_v^{**} = \frac{(1-u_1)(\mu_v + pu_3)R_{ov}\Phi}{(1-u_1)\lambda\epsilon\phi\Phi + N_h(\mu_v + pu_3)} \tag{45}$$

From the quadratic equation (38) we analyze the possibility of multiple equilibria. It is important to note that the coefficient A is always positive with B and C having different signs. We realize that C is positive if $R_0$ is less than unity, and negative if $R_0$ is greater than unity. Hence, we have established the following

results:

**Proposition 1.**

(i) Precisely one unique endemic equilibrium if $B < 0$ and $C = 0$ or $B^2 - 4AC = 0$,

(2) Precisely one unique endemic equilibrium if $C > 0 \Leftrightarrow R_0 > 1$,

(3) Precisely two endemic equilibrium if $C > 0$, $B < 0$ and $B^2 - 4AC > 0$,

(4) No endemic otherwise.

## 3.11 Local stability of the endemic stability



The stability of the endemic equilibrium of the model (1) can be analysed using the Centre Manifold Theory described by Castilo-Chavez. and Song (2004).

**Theorem 3.4 Castilo-Chavez. and Song (2004) Gumel et al. (2008)** consider the following general system of ordinary differential equation with a parameter $\Psi$.

$$\frac{dx}{dt} = h(x, \Psi), h : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R} \text{ and } h \in \mathbb{C}^2(\mathbb{R}^n \times \mathbb{R}) \tag{46}$$

where 0 is an equilibrium point of the system, that is $h(o, \Psi) \equiv 0$ for all $\Psi$ and

1. $A = D_x h(0,0) = (\frac{\partial h_i}{\partial x_i}(0,0))$ is the linearization matrix of the system around the equilibrium 0 with $\Psi$ evaluated at 0.

2. Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts.

3. Matrix A has a nonnegative right eigenvector w and a left eigenvector v corresponding to the zero eigenvalue.

Let $h_k$ be the kth component of h and

$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 h_k}{\partial x_i \partial x_j}(0,0)$

and

$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 h_k}{\partial x_i \partial \Psi}(0,0)$

then, the local dynamics of the system (1) around 0 is totally determined by the sign of a and b.

1. $a > 0$ , $b > 0$. When $\Psi < 0$ with $|\Psi| << 1$, 0 is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 < \Psi << 1$, 0 is unstable and there exists a negative, locally asymptotically stable equilibrium.

2. $a < 0, b < 0$. When $\Psi < 0$ with $|\Psi| << 1$, 0 is unstable; when $0 < \Psi << 1$, 0 is locally asymptotically stable, and there exist a positive unstable equilibrium.

3. $a > 0, b < 0$. When $\Psi < 0$ with $|\Psi| << 1$, 0 is unstable, and there exist a locally asymptotically stable negative equilibrium; when $0 < \Psi << 1$, 0 is stable, and a positive unstable equilibrium appears.

4. $a < 0, b > 0$. When $\Psi$ changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.

To apply this theorem we make the following change of variables in the system (1).

Let $x_1 = S_h$, $x_2 = E_h$, $x_3 = I_h$, $x_4 = R_h$, $x_5 = S_v$, $x_6 = E_v$, $x_7 = I_v$

The system (1) is written in vector form as

$$\frac{dX_i}{dt} = H(X_i)$$

Where $X_i = (x_1, x_2, ..., x_7)^T$ and $H = (h_1, h_2, ...h_7)^T$ are transposed matrices.

The system of equations (1) becomes

$$\frac{dS_h}{dt} = (1-\tau)\Lambda_h + \kappa R_h - \mu_h S_h - \frac{(1-u_1)\beta \in \phi S_h I_v}{N_h}$$

$$\frac{dE_h}{dt} = \frac{(1-u_1)\beta \in \phi S_h I_v}{N_h} - \mu_h E_h - \alpha_1 E_h$$

$$\frac{dI_h}{dt} = \alpha_1 E_h - (\psi + \mu_h) I_h - (b + \tau u_2 + \tau u_4) I_h$$

$$\frac{dR_h}{dt} = (b + \tau u_2 + \tau u_4) I_h - \mu_h R_h - \kappa R_h$$

$$\frac{dS_v}{dt} = \Lambda_v - (1-u_1)\lambda_v S_v - (\mu_v + p u_3) S_v$$

$$\frac{dE_v}{dt} = (1-u_1)\lambda_v S_v - \alpha_2 E_v - (\mu_v + p u_3) E_v$$

$$\frac{dI_v}{dt} = \alpha_2 E_v - (\mu_v + p u_3) I_v$$

where $\beta_m = \beta \in \phi I_v / N_h$ and $\lambda v = \lambda \in \phi I_n / N_h$

let $x_1 = S_h, x_2 = E_h, x_3 = I_h, x_4 = R_h, x_5 = S_v, x_6 = E_v$ and $x_7 = I_v$

therefore $\frac{dX_i}{dt} = H(X_i)$

where $X_i = (x_1, x_2, ..., x_7)^T$ and $H = (h_1, h_2, ...h_7)^7$ are transposed matrices

and $N_h = \frac{\Lambda_h}{\mu_h}$

$$\left.\begin{aligned}
\frac{dx_1}{dt} = (1-\tau)\Lambda_h + \kappa x_4 - \mu_h S_1 - \frac{(1-u_1)\psi^*\phi x_7 x_1 \mu_h}{\Lambda_h} &= h_1 \\
\frac{dx_2}{dt} = \frac{(1-u_1)\psi^* phi x_7 x_1 \mu_h}{\Lambda_h} - (\mu_h + \alpha_1)x_2 &= h_2 \\
\frac{dx_3}{dt} = \alpha_1 x_2 - (\psi + \mu_h + b + \tau U_2 + \tau U_4)x_3 &= h_3 \\
\frac{dx_4}{dt} = (b + \tau u_2 + \tau u_4)x_3 - (\mu_h + \kappa)x_4 &= h_4 \\
\frac{dx_5}{dt} = \Lambda_v - \frac{(1-u_1)\lambda \in \phi x_3 x_5 \mu_h}{\Lambda_h} - (\mu_v + pu_3)x_5 &= h_5 \\
\frac{dx_6}{dt} = \frac{(1-u_1)\lambda \in \phi x_3 x_5 \mu_h}{\Lambda h} - (\alpha_2 + \mu_v + pu_3)x_6 &= h_6 \\
\frac{dx_7}{dt} = \alpha_2 x_6 - (\mu_v + pu_3)x_7 &= h_7
\end{aligned}\right\} \quad (47)$$

where $N_h = x_1 + x_2 + x_3 + x_4$ and $N_v = x_5 + x_6 + x_7$ with $\psi^* = \beta \in$

Let $\Psi^*$ be the bifurcation parameter, the system (47) is linearised at disease free equilibrium point when $\psi = \Psi^*$with $R_0 = 1$

Thus $\psi$ can be solved from (19) when$\psi = \Psi^*$ with $R_0 = 1$. Thus $\Psi^*$ can be solved from (19) when

$$R_0 = \sqrt{\frac{\alpha_1\alpha_2\Lambda_v\mu_h(1-u_1)^2\phi^2 \in\in \beta\lambda}{\Lambda_h(pu_3+\mu_v)^2(U_h+\alpha_1)(pu_3+\mu_v+\alpha_2)(\mu_h+\psi+b+\tau u_2+\tau_4)}}$$

$$1^2 = \frac{\alpha_1\alpha_2\Lambda_v\mu_h(1-u_1)^2\phi^2 \in\in \beta\lambda}{\Lambda_h(pu_3+\mu_v)^2(\mu_h+\alpha_1)(pu_3+\mu_v+\alpha_2)(\mu_h+\psi+b+\tau U_2+\tau_4)}$$

$$\psi^* = \frac{\Lambda_h(pu_3+\mu_v)^2(\mu_h+\alpha_1)(pu_3+\mu_v+\alpha_2)(\mu_h+\psi+b+\tau u_2+\tau_4)}{\alpha_1\alpha_2\Lambda_v\phi^2\lambda \in (1-u_1)^2\mu_h}$$

The Jacobian matrix of (1) calculated at $\Psi^*$ is given by

$$\begin{pmatrix} -U_h & 0 & 0 & \kappa & 0 & 0 & -\Psi^*\phi \\ 0 & -\alpha_1-\mu_h & 0 & 0 & 0 & 0 & \Psi^*\phi \\ 0 & \alpha_1 & -\psi-\mu_h-b-\tau\mu_2+\tau U_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & b+\tau u_2+\tau u_4 & -U_h-\kappa & 0 & 0 & 0 \\ 0 & 0 & \frac{1-u_1\lambda\in\phi\Lambda_v\mu_h}{\Lambda_h\mu_v} & 0 & 0 & -\alpha_2-\mu_v & 0 \\ 0 & 0 & 0 & 0 & 0 & -\alpha_2 & -\mu_v \end{pmatrix} \tag{49}$$

A right eigenvector associated with the eigenvalue zero is $w = (w_1, w_2, ..., w_7)$. We get

$$\mu_h w_1 + \kappa w_4 - \psi\phi w_7 = 0$$

$$-(\alpha_1+\mu_h)w_2 + \psi\phi w_7) = 0$$

$$\alpha_1 w_2 - (\psi+\mu_h+b+w_2+\tau u_4)w_3 = 0$$

$$(b+\tau u_2+\tau u_4)w_3 - (\mu_h+\kappa)w_4 = 0$$

$$\frac{-(1-\mu_1)\lambda\in\phi\Lambda_v\mu_h w_3}{\Lambda_h\mu_v} - \mu_v w_v = 0$$

$$\frac{(1-u_1)\lambda\in\phi\Lambda_v\mu_h w_3}{\Lambda_h\mu_v} - (\alpha_2+\mu_v)w_6 = 0$$

$$\alpha_2 w_6 - \mu_v w_7 = 0$$

Solving the system (49) we have the following right eigenvector

$$w_1 = \frac{\kappa w_4 - \psi\phi w_7}{\mu_h}$$

$$w_2 = \frac{\psi\phi w_7}{\alpha_1+\mu_h}$$

$$w_3 = \frac{\alpha_1 w_2}{\psi\mu_h + b + \tau u_2 \tau u_4}$$

$$w_4 = \frac{(b+\tau u_2+\tau u_4)w_3}{\mu_h+\kappa}$$

$$w_5 = \frac{-(1-u_1)\lambda\in\phi\Lambda_v\mu_h}{\lambda_h\mu_v^2}$$

$$w_6 = \frac{(1-u_1)\lambda\in\phi\Lambda_v\mu_h w_5}{\mu_v\Lambda_h(\alpha_2+mu_v}$$

$$w_7 = \frac{\alpha_2 w_6}{\mu_v}$$

therefore $w_7 > 0$ and the left eigenvectors satisfying $v.w = 1$ is $v = (v_1, v_2, ..., v_7)$. To find these left eigenvector associated with the eigenvalue 0, the matrix (49) should be transposed to give $J_{left}$.

$$\begin{pmatrix} -U_h & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\alpha_1 - \mu_h & \alpha_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\psi - \mu_h - b - \tau u_2 - \tau u_4 & b + \tau u_2 + \tau u_4 & \frac{-(1-u_1)\lambda \in \phi \Lambda_v \mu_h}{\Lambda_h \mu_v} & \frac{(1-u_1)\lambda \in \phi \Lambda_v \mu_h}{\Lambda_h \mu_v} & 0 \\ \kappa & 0 & 0 & -\mu_h - \kappa & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_v & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\alpha_2 - \mu_v & \alpha_2 \\ -\psi\phi & \psi\phi & 0 & 0 & 0 & 0 & -\mu_v \end{pmatrix}$$



we have the following system

$-\mu_h v_1 = 0$

$-(\alpha_1+\mu_h)v_2+\alpha_1 v_3 = 0$ $-(\psi+\mu_h+b+\tau u_4)v_3+(b+\tau u_2+\tau u_4)v_4-\frac{-(1-u_1)\lambda \in \phi \Lambda_v \mu_h v_5}{\Lambda_h \mu_v}+$ $\frac{(1-u_1)\lambda \in \phi \Lambda_v \mu_h v_6}{\Lambda_h \mu_v} = 0$

$\kappa v_1 - (\mu_h + \kappa)v_4 = 0$

$-\mu_v V_5 = 0$

$-(\alpha_2 + \mu_v)v_6 + \alpha_2 v_7 = 0$

$-\psi\phi v_1 + \psi\phi v_2 - \mu_v v_7 = 0$

From the left eigenvector we have the following results.

$$v_1 = 0$$

$$v_2 = \frac{\alpha_1 \alpha_3}{\alpha_1 + \mu_h} \text{ therefore } v_2 > 0 \text{ free}$$

$$v_3 = \frac{\alpha_1 \mu_h}{\alpha_1}$$

$$v_4 = 0$$

$$v_5 = 0$$

$$v_6 = \frac{\alpha_2 v_7}{\alpha_2 + \mu_v}$$

$$v_7 = \frac{\psi\phi v_2}{\mu_v}$$

we now compute the sign of a and b as indicated in the theorem

$$w_1 = \frac{\kappa w_4 - w_2(\alpha_1 + \mu_h)}{\mu_h}$$

$$w_2 = \frac{\psi\phi}{\alpha_1 + \mu_h}$$

$$w_3 = \frac{\alpha_1 w_2}{\tau u_2 + \psi + \mu_h + \tau u_4 + b}$$

$$w_4 = \frac{(b + \tau u_2 + \tau u_4)w_3}{\kappa + \mu_h}$$

$$w_5 = \frac{(1-u_1)\lambda \in \phi\Lambda_v\mu_h(\kappa + \mu_h)w_4}{(b + w_2 + \tau w_4)\Lambda_h\mu_v^2}$$

$$w_6 = \frac{\mu_v}{\alpha_2}\ w_7 = 1$$

$$\text{and } v_1 = 0$$

$$v_2 = \frac{v_3\alpha_1}{\alpha_1 + \mu_h}$$

$$v_3 = \frac{\mu_v(\alpha_1 + \mu_h)}{\psi\phi\alpha_1}$$

$$v_4 = 0$$

$$v_5 = 0$$

$$v_6 = \frac{\alpha_2}{\alpha_2 + \mu_v}$$

$$v_7 = 1$$

$$a = \sum_{k,i,j=2}^{3} v_k w_i w_j \frac{\partial^2 h_k}{\partial x_i \partial x_j}(0,0) + \sum_{k,i,j=6}^{7} v_k w_i w_j \frac{\partial^2 h_k}{\partial x_i \partial x_j}(0,0)$$

$b = \sum_{k,i=2}^{3} v_k w_i \frac{\partial^2 h_k}{\partial x_i \partial \psi}(0,0) + \sum_{k,i=6}^{7} v_k w_i \frac{\partial^2 h_k}{\partial x_i \partial \psi}(0,0)$ since $v_1 = v_4 = v_5 = 0$ for

$K = 1, 4, 5$; then $K = 2, 3, 6, 7$ should be considered. That is, the following functions will be used to compute a and b from the system (51) $h_2 = \frac{(1-u_1)\psi^*\phi x_7}{\Lambda_h}\mu_h(N_h - x_2 - x_3) - (\mu_h + \alpha_1)x_2 = \frac{(1-u_1)\Psi^*\phi\mu_h x_7 N_h}{\Lambda_h} - \frac{(1-u_1)\Psi^*\phi\mu_h x_7 x_2}{\Lambda_h} - \frac{(1-u_1)\Psi^*\phi\mu_h x_7 x_3}{\Lambda_h} - (\mu_h + \alpha_1)x_2$

$h_6 = \frac{(1-u_1)\lambda\in\phi x_3\mu_h(N_v - x_6 - x_7)}{\Lambda_h} - ((\mu_v + p\mu_3) + \alpha_2)x_6 = \frac{(1-u_1)\lambda\in\phi x_3\mu_h N_v}{\Lambda_h} - \frac{(1-u_1)\lambda\in\phi x_3\mu_h x_6}{\Lambda_h} -$

$\frac{(1-u_1)\lambda\in\phi x_3\mu_h x_7}{\Lambda_h} - (\alpha_2+\mu_v+pu_3)x_6$

Partial derivatives that are not zero at the disease free equilibrium are

$$\frac{\partial^2 h_2}{\partial x_2\partial x_7} = \frac{-\psi\phi\mu_h(1-u_1)}{\Lambda_h}$$
$$\frac{\partial^2 h_2}{\partial x_3\partial x_7} = \frac{-(1-u_1)\Psi^*\phi\mu_h}{\Lambda_h}$$
$$\frac{\partial^2 h_6}{\partial x_6\partial x_3} = \frac{-(1-\mu_1)\lambda\in\phi\mu_h}{\Lambda_h}$$
$$\frac{\partial^2 h_6}{\partial x_7\partial x_3} = \frac{(1-u_1)\lambda\in\phi\mu_h}{\Lambda_h}$$

$a = v_2w_2w_7\frac{\partial^2 h_2}{\partial x_2\partial x_7}+v_2w_3w_7\frac{\partial^2 h_2}{\partial x_3\partial x_7}+v_6w_6w_3\frac{\partial^2 h_6}{\partial x_6\partial x_3}+v_6w_7w_3\frac{\partial^2 h_6}{\partial x_7\partial x_3} = v_2w_2w_7(\frac{\Psi^*u_2(1-u_1)}{\Lambda_h})+$
$v_2w_3w_7(\frac{-(1-\mu_1)\Psi^*\phi\mu_h}{\Lambda_h})+v_6w_6w_3(\frac{-(1-u_1)\lambda\in\phi\mu_h}{\Lambda_h})+v_6w_7w_3(\frac{-(1-u_1)\lambda\in\phi\mu_h}{\Lambda_h}) = \frac{-(1-u_1)\phi\mu_h}{\Lambda h}[v_2w_7(w_2+$
$w_3)\Psi^*+v_6w_3\lambda\in(w_6+w_7)]$



$a = \frac{-(1-u_1\phi\mu_h)}{\Lambda h}[\Psi^*v_2w_7(\frac{\psi\phi(\tau u_2+\psi+\mu_h+\tau u_4+b+\alpha_1w_2)(\alpha_1+\mu_h)}{(\alpha_1+\mu_h)(\tau u_2+\tau u_4+b+\mu_h+\phi)})+v_6w_3\lambda\in(\frac{2\alpha_2+\mu_v}{\alpha_2+\mu_v})]$

$a = \frac{-(1-u_1\phi\mu_h)}{\Lambda h}[\Psi^*v_2w_7(\frac{\Psi^*\phi(\tau u_2+\psi+\mu_h+\tau u_4+b)+\alpha_1w_2(\alpha_1+\mu_h)}{(\alpha_1+\mu_h)(\tau u_2+\tau u_4+b+\mu_h+\phi)})+v_6w_3\lambda\in(\frac{2\alpha_2+\mu_v}{\alpha_2+\mu_v})]$

similarly partial derivatives that are not zero when calculating b are

$$\frac{\partial h_2}{\partial\psi} = \frac{(1-u_1)\phi\mu_h x_1x_7}{\Lambda_h}$$
$$\frac{\partial^2 h_2}{\partial x_7\partial\psi} = \frac{(1-u_1)\phi\mu_h x_2}{\Lambda_h} = \phi$$

therefore

$$b = v_2w_7\epsilon\phi > 0.$$

Hence $a<0$ and $b>0$ . Therefore the following theorem holds.

**Theorem 3.6**

The model (1) has a unique endemic equilibrium which is locally asymptotically stable when $R_0<1$ and unstable when $R_0>1$.

## 3.12 Sensitivity Analysis

We would like to know different factors that are responsible for the disease transmission and prevalence. In this way we can try to reduce human mortality and

morbidity due to disease. Initial disease transmission depends upon the reproductive number whereas disease prevalence is directly related to the endemic equilibrium point. The class of infectious humans is the most important class because it represents the persons who may be clinically ill and is directly related to the disease induced deaths. We will calculate the sensitivity indices of the reproductive number, $R_0$, and the endemic equilibrium point with respect to the parameters given in Table 1 for the model. By the analysis of these indices we could determine which parameter is more crucial for disease transmission and prevalence.

**Definition**



The normalized forward sensitivity index of a variable, h , that depends on a parameter, l , is defined as : $\xi_l = \frac{l}{h} \times \frac{\partial h}{\partial l}$

Therefore the sensitivity index of $R_0$ that depends on $\alpha_1$ is given as

$$\xi_{\alpha_1}^{R_0} = \frac{\alpha_1}{R_0} \times \frac{\partial R_0}{\partial \alpha_1}$$

$$\frac{\alpha_1}{R_0} = \frac{\alpha_1(\mu_h + \alpha_1)^{\frac{1}{2}}}{\alpha_1^{\frac{1}{2}}}$$

and

$$\frac{\partial R_0}{\partial \alpha_1} = \frac{\alpha_1^{-\frac{1}{2}}(\mu_h + \alpha_1)^{\frac{1}{2}} \times \frac{1}{2} - \alpha_1^{\frac{1}{2}}(\mu_h + \alpha_1)^{\frac{1}{2}} \times \frac{1}{2}}{(\mu_h + \alpha_1)}$$

$$\xi_{\alpha_1}^{R_0} = \left(\frac{\alpha_1(\mu_h + \alpha_1)^{\frac{1}{2}}}{\alpha_1^{\frac{1}{2}}}\right) \times \left(\frac{\alpha_1^{-\frac{1}{2}}(\mu_h + \alpha_1)^{\frac{1}{2}} \times \frac{1}{2} - \alpha_1^{\frac{1}{2}}(\mu_h + \alpha_1)^{\frac{1}{2}} \times \frac{1}{2}}{(\mu_h + \alpha_1)}\right)$$

therefore

$$\xi_{\alpha_1}^{R_0} = \frac{\mu_h}{2(\alpha_1 + \mu_h)}$$

similarly the sensitivity index of other parameters are as follows

$$\xi_{\alpha_1}^{R_0} = \frac{pu_3 + \mu_v}{2(\alpha_2 + pu_3 + \mu_v)}, \qquad \xi_{\mu_v}^{R_0} = \frac{-\mu_v(2\alpha_2 + 3(\mu_v + pu_3))}{2(\alpha_2 + \mu_v + pu_3)(\mu_v + pu_3)},$$

$$\xi_{\alpha_2}^{R_0} = \frac{pu_3 + \mu_v}{2(\alpha_2 + pu_3 + \mu_v)}, \qquad \xi_{\psi}^{R_0} = \frac{-\psi}{2(b + \tau u_2 + \tau u_4 + \psi + \mu_h)},$$

$$\xi_{b}^{R_0} = \frac{-b}{2(b + \tau u_2 + \tau u_4 + \psi + \mu_h)},$$

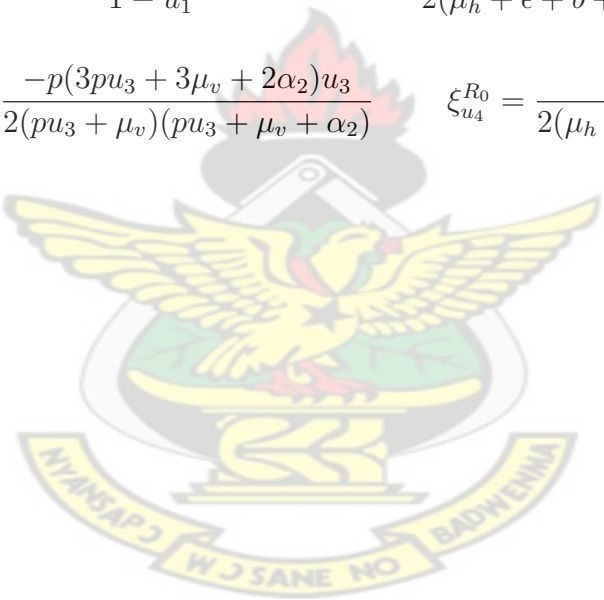
$$\xi_{\mu_h}^{R_0} = \frac{-\mu_h^2 + \alpha_1\psi + \alpha_1 b + \alpha_1\tau u_2 + \alpha_1\tau u_4}{2(\mu_h + \psi + b + \tau u_2 + \tau u_4)(\mu_h + \alpha_1)}$$

**Sensitivity indices for the control parameters**

$$\xi_{u_1}^{R_0} = \frac{-u_1}{1 - u_1} \qquad \xi_{u_2}^{R_0} = \frac{-\tau u_2}{2(\mu_h + \epsilon + b + \tau u_2)}$$

$$\xi_{u_3}^{R_0} = \frac{-p(3pu_3 + 3\mu_v + 2\alpha_2)u_3}{2(pu_3 + \mu_v)(pu_3 + \mu_v + \alpha_2)} \qquad \xi_{u_4}^{R_0} = \frac{-\tau u_4}{2(\mu_h + \epsilon + b + \tau u_4)}$$





# Chapter 4

# ANALYSIS AND RESULTS

## 4.1 Introduction

In this chapter, we study numerically an epidemiological model of malaria transmission with four control parameters. We carry out numerical simulations using a fourth order Rung-Kutta scheme in Matlab. The main aim is to verify some of the analytical results on the stability of the system (1). The parameter values were obtained from literature. We simulate the basic malaria model with different combinations of the control measures to find out the effects of varying each control parameter. The figures are plotted using the parameter values in table (4.1) and the initial conditions. Using various combinations of the four controls, one control at a time and two controls at a time, we investigate and compare numerical results from simulations with the following scenarios :

- Strategy A. using personal protection ($u_1$) without insecticide spraying ($u_3 = 0$) and no treatment of the symptomatic humans ($u_2 = 0$)
- Strategy B. treating the symptomatic humans ($u_2$) without using insecticide spraying ($u_3 = 0$) and no personal protection ($u_1 = 0$),
- Strategy C. using insecticide spraying ($u_3$) without personal protection ($u_1 = 0$) and no treatment of the symptomatic humans ($u_2 = 0$),
- Strategy D. treating the symptomatic humans ($u_2$) and using insecticide spraying ($u_3$) with no personal protection ($u_1 = 0$),
- Strategy E. using personal protection ($u_1$) and insecticide spraying ($u_3$) with no treatment of the symptomatic humans ($u_2 = 0$),

- Strategy F using treatment ($u_2$) and personal protection ($u_1$) with no insecticide spraying ($u_3 = 0$), finally

- Strategy G. using all four control measures ($u_1$, $u_2$, $u_3$, and $u_4$).

Table 4.1: Description of variables and parameters of the malaria model

| Parameter | Estimated values | References |
|---|---|---|
| $\phi$ | $0.502day^{-}1$ | Kbenesh et al.(2009) |
| $\epsilon$ | 0.2 | Kbenesh et al.(2009) |
| $\beta$ | 0.8333 | Nakul et al.(2006) |
| $\lambda$ | 0.09 | Kbenesh et al.(2009) |
| $\mu_h$ | $0.00004day^{-1}$ | Hyun(2001) |
| $\mu_v$ | $0.1429day^{-1}$ | Nakul et al.(2006) |
| $\kappa$ | $0.0014day^{-1}$ | NMC Ghana (2013) |
| $\alpha_1$ | $0.0588day^{-1}$ | Kbenesh et al.(2009) |
| $\alpha_2$ | $0.0556day^{-1}$ | Kbenesh et al.(2009) |
| $\Lambda_h$ | $0.0000034587day^{-1}$ | NMC Ghana.(2013) |
| $\Lambda_v$ | $0.071day^{-1}$ | Oduro et al.(2012) |
| $\tau$ | $0.01 - 0.7$ | Assumed |
| $\psi$ | $0.05day^{-1}$ | Robert and Hove-Musekwa (2008) |
| b | $0.005day^{-1}$ | Chiyaka et al. (2008) |
| p | 0.25 | Assumed |

## 4.2 Estimation of the model

After substituting the estimated parameter values in table (4.1) into model(1), we have the following system of non - linear differential equations

$\frac{dS_h}{dt} = 3.424113 \times 10^{-6} + 0.0014R_h - 0.0004S_h - \frac{(1-u_1)0.08366332S_hI_v}{N_h}$

$\frac{dE_h}{dt} = \frac{0.08366332S_hI_v}{N_h} - 0.05884E_h$

$\frac{dI_n}{dt} = 0.0588E_h - 0.05004I_h - (0.005 + 0.01u_2 + 0.01u_4)I_h$

$\frac{dR_h}{dt} = (0.005 + 0.01u_2 + 0.01u_4)I_h - 0.00144R_h$

$\frac{dS_v}{dt} = 10000 - \frac{(1-u_1)0.009036I_hS_v}{N_h} - (0.1429 + 0.25u_3)S_v$

$\frac{dE_v}{dt} = \frac{(1-u_1)0.009036I_hS_h}{N_h} - 0.0556E_v - (0.1429 + 0.25u_3)E_v$

$\frac{dI_v}{dt} = 0.0556E_v - (0.1429 + 0.25u_3)I_v$

From equation (2) and (3) we have the total population equations as follows:

$$\frac{dN_h}{dt} = 0.000003424 - 0.05I_h - 0.00004N_h$$

$$\frac{dN_v}{dt} = 10000 - 0.1429N_v - 0.25u_3N_v$$

### 4.2.1 Disease-free equilibrium points

The disease - free equilibrium point of the malaria model is given by

$E_0 = (0.085602825, 0, 0, 0, 0.4968509447, 0, 0)$



### 4.2.2 Basic reproduction number $R_0$

The basic reproduction number is given by

$$R_0 = \sqrt{\frac{\alpha_1(1-u_1)\lambda\epsilon\phi\mu_h(1-u_1)\beta\epsilon\phi\alpha_2}{(u_v+\rho_3)(u_h+\alpha_1)(\psi+\mu_h+b+\tau u_2+\tau u_4)\lambda_h(\alpha_2+\lambda_v+\rho u_3)(u_v+\rho u_3)}}$$

$$= \sqrt{\frac{0.0588 \times 0.09 \times 0.2 \times 0.502 \times 0.071 \times 0.00004 \times 0.8333 \times 0.2 \times 0.0556}{0.1429 \times 0.2017 \times 0.1979 \times 0.0000034587 \times 0.1985 \times 0.1429}}$$

$R_0 = 0.155768$

Therefore the basic reproduction number is $R_0 = 0.155768$

since $R_0 = 0.155768 < 1$, hence malaria disease can be eliminated or eradicated in the susceptible population in Ghana.

## 4.3 Sensitivity Indicies of $R_0$

$$\xi_{\alpha_1}^{R_0} = \frac{pu_3 + \mu_v}{2(\alpha_2 + pu_3 + \mu_v)}$$

$$= \frac{0.00004}{2(0.0588 + 0.00004)}$$

$$= \frac{0.00004}{0.11768}$$

$$= 0.00034$$

therefore $\xi_{\alpha_1}^{R_0} = +0.00034$

$$\xi_{\alpha_2}^{R_0} = \frac{pu_3 + \mu_v}{2(\alpha_2 + pu_3 + \mu_v)}$$

$$= \frac{0.25 + 0.1429}{2(0.0556 + 0.25 + 0.1429)}$$

$$= \frac{0.3929}{0.897}$$

$$= 0.43802$$

therefore $\xi_{\alpha_2}^{R_0} = +0.43802$

$$\xi_{\psi}^{R_0} = \frac{-\psi}{2(b + \tau u_2 + \tau u_4 + \psi + \mu_h)}$$

$$= \frac{-0.05}{2(0.005 + 0.01 + 0.05 + 0.00004)}$$

$$= \frac{-0.05}{0.13008}$$

$$= -0.4$$

therefore $\xi_{\alpha_2}^{R_0} = -0.4$

$$\xi_{b}^{R_0} = \frac{-b}{2(b + \tau u_2 + \tau u_4 + \psi + \mu_h)}$$

$$= \frac{-0.005}{2(0.005 + 0.01 + 0.05 + 0.00004)}$$

$$= \frac{-0.005}{0.13008}$$

$$= -0.04$$

therefore $\xi_b^{R_0} = -0.04$

The sensitivity indicies of the other parameters are given in the table below

Table 4.2: Sensitivity Indicies of $R_0$

| Parameter | Description | Estimated values |
|---|---|---|
| $\phi$ | Mosquito contact rate with human | $+1$ |
| $\epsilon$ | Mosquito biting rate | $+1$ |
| $\mu_v$ | Death rate of mosquitoes | $-1$ |
| $\beta$ | Probability of human getting infected | $+0.5$ |
| $\lambda$ | Probability of a mosquito getting infected | $+0.5$ |
| $\Lambda_h$ | Human birth rate | $-0.5$ |
| $\Lambda_v$ | Mosquitoes birth rate | $+0.5$ |
| b | Spontaneous recovery | $-0.04$ |
| $\Lambda_h$ | Human natural death rate | $+0.499$ |
| $\alpha_1$ | Humans progression rate from exposed to infected | $+0.0034$ |



By analysing the sensitivity indices we observe that the most sensitive parameters are mosquitoes biting rate ($\epsilon$) and mosquitoes death rate ($\mu_v$). The reproductive number $R_0$ is directly related to the mosquitoes biting rate and inversely related to the mosquitoes death rate.It can realized that an increase (or decrease) in biting rate $\epsilon$ by 10% increases (or decreases) $R_0$ by 10%. Similarly increase (or decrease) in death rate $\mu_v$ of mosquitoes by 10% decreases (or increases) $R_0$ by 10%.Therefore it suggest that strategies that can be applied in controlling and eradicating the disease are to target the mosquito biting rate and the mosquito death rate. These are; $u_1$ The use of insecticide-treated bed nets and $u_3$ Indoor residual spray.

## 4.4 Numerical simulations

Numerical simulation using the fourth order Range-Kutta method in matlab is use to solve the malaria model(1).

$y_{i+1} = y_i + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)$

$k_1 = hf(x_i, y_i)$

$k_2 = hf(x_i + \frac{h}{2}, y_i + \frac{1}{2}k_1)$

$k_3 = hf(x_i + \frac{h}{2}, y_i + \frac{1}{2}k_2)$

$k_4 = hf(x_i + h, y_i + \frac{1}{2}k_3)$

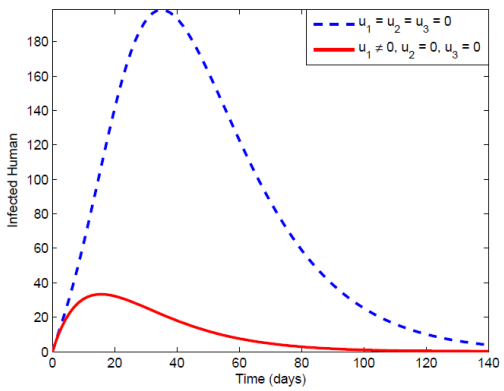
The function $f(x_i, y_i)$ is the malaria model(1) with h as the step size.

For the numerical simulation we used the following initial state variables and the parameter values from table (4.1) $S_h(0) = 700$, $E_h(0) = 100$, $I_h(0) = 0$, $R_h(0) = 0$, $S_v(0) = 5000$, $E_v(0) = 500$, $I_v(0) = 30$ and parameter values $\Lambda_h = 0.00011$, $\Lambda_v = 0.071$, $\beta = 0.030$, $\epsilon = 0.01$, $\lambda = 0.05$, $\mu_h = 0.0000457$, $\mu_v = 0.0667$, $\kappa = 0.0014$, $\alpha_1 = 0.058$, $\alpha_2 = 0.0556$, $b = 0.5$, $\phi = 0.502$, $\psi = 0.02$, $\tau = 0.5$, $p = 0.85$ to illustrate the effect of different control strategies on the spread of malaria in the Ghana population. Thus, we have considered the spread of malaria in an endemic population.

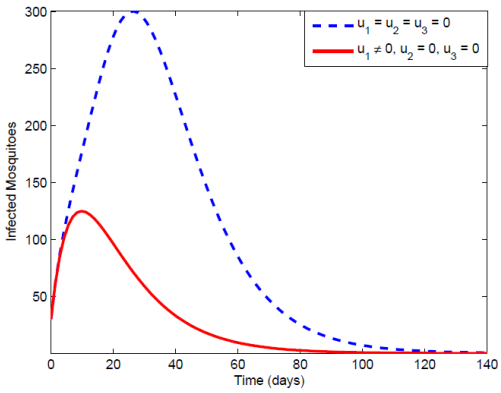


### 4.4.1 Simulation of treated bednets

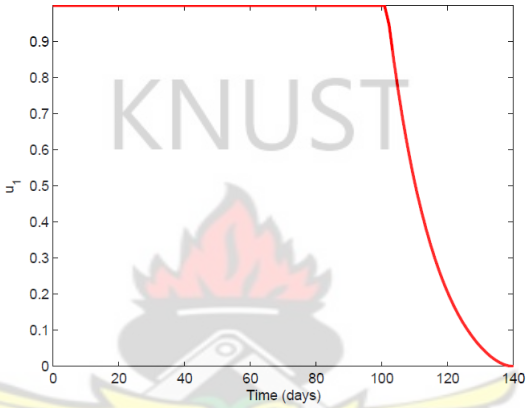
Only the control ($u_1$) on treated bednets is used while the control on treatment ($u_2$) and the control on insecticide spray ($u_3$) are set to zero. In Figure 4.1, the results show a significant difference in the $I_h$ and $I_v$ with control strategy compared to $I_h$ and $I_v$ without control. Specifically, we observed in Figure 4.1(a) that the control strategies lead to a decrease in the number of symptomatic human ($I_h$) as against an increases in the uncontrolled case. Similarly, in Figure 4.1(b), the uncontrolled case resulted in increased number of infected mosquitoes ($I_v$), while the control strategy lead to a decrease in the number infected. The control profile is shown in Figure 4.1(c), here we see that the personal protection control $u_1$ is at the upper bound till the time $t = 100$ days, before dropping to the lower bound.




(a)




(b)




(c)

Figure 4.1: Simulations showing the effect of treated bednets only on infected human and mosquitoes populations

### 4.4.2 Simulation of treatment

With this strategy, only the control ($u_2$) on treatment is used while the control on treated bednets ($u_1$) and the control on insecticide spray ($u_3$) are set to zero. In Figure 2, the results show a significant difference in the $I_h$ and $I_v$ with control strategy compared to $I_h$ and $I_v$ without control. But this strategy shows that effective treatment only has a significant impact in reducing the disease incidence among human population. The control profile is shown in Figure 2(c), we see that the treatment control $u_2$ rises to and stabilizes at the upper bound for $t = 70$ days, before dropping to the lower bound.

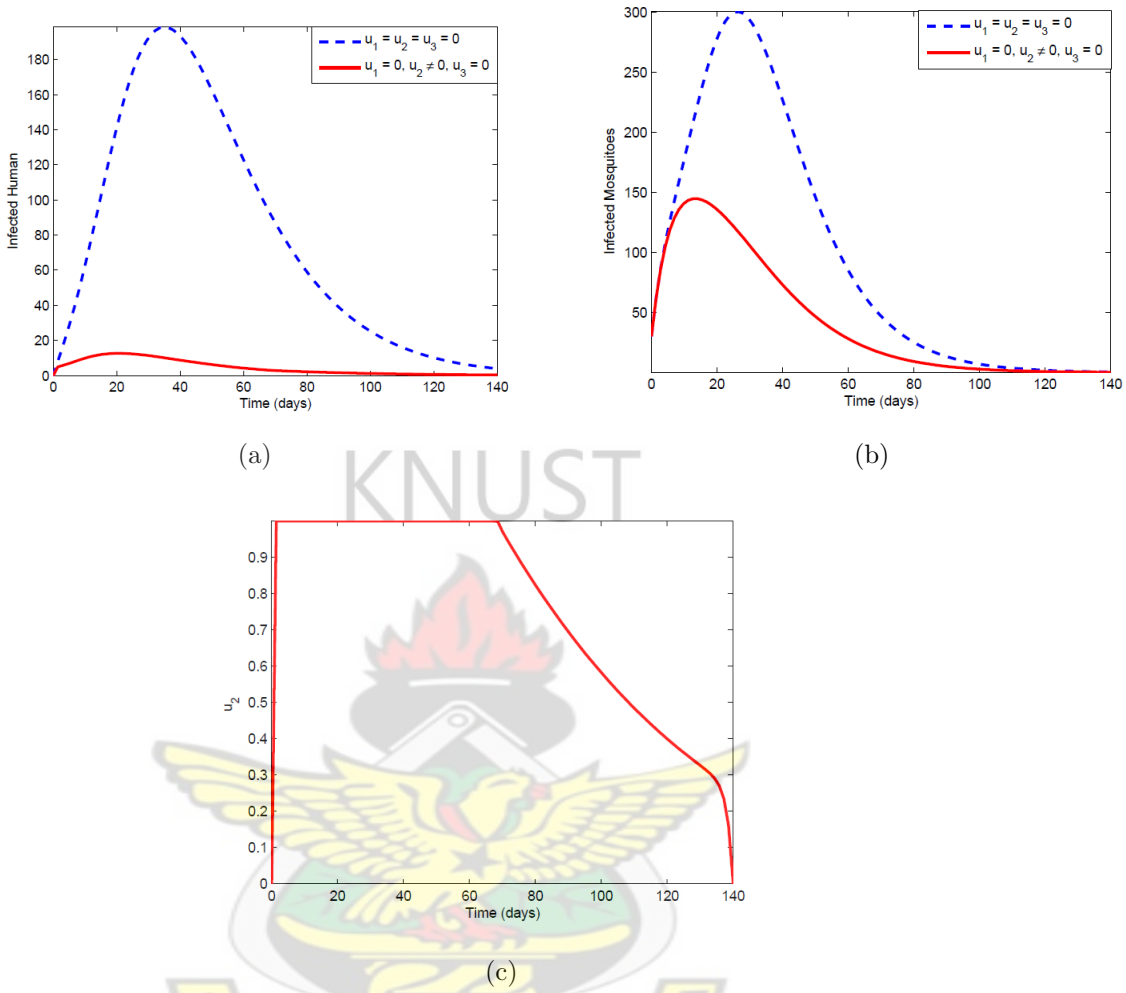
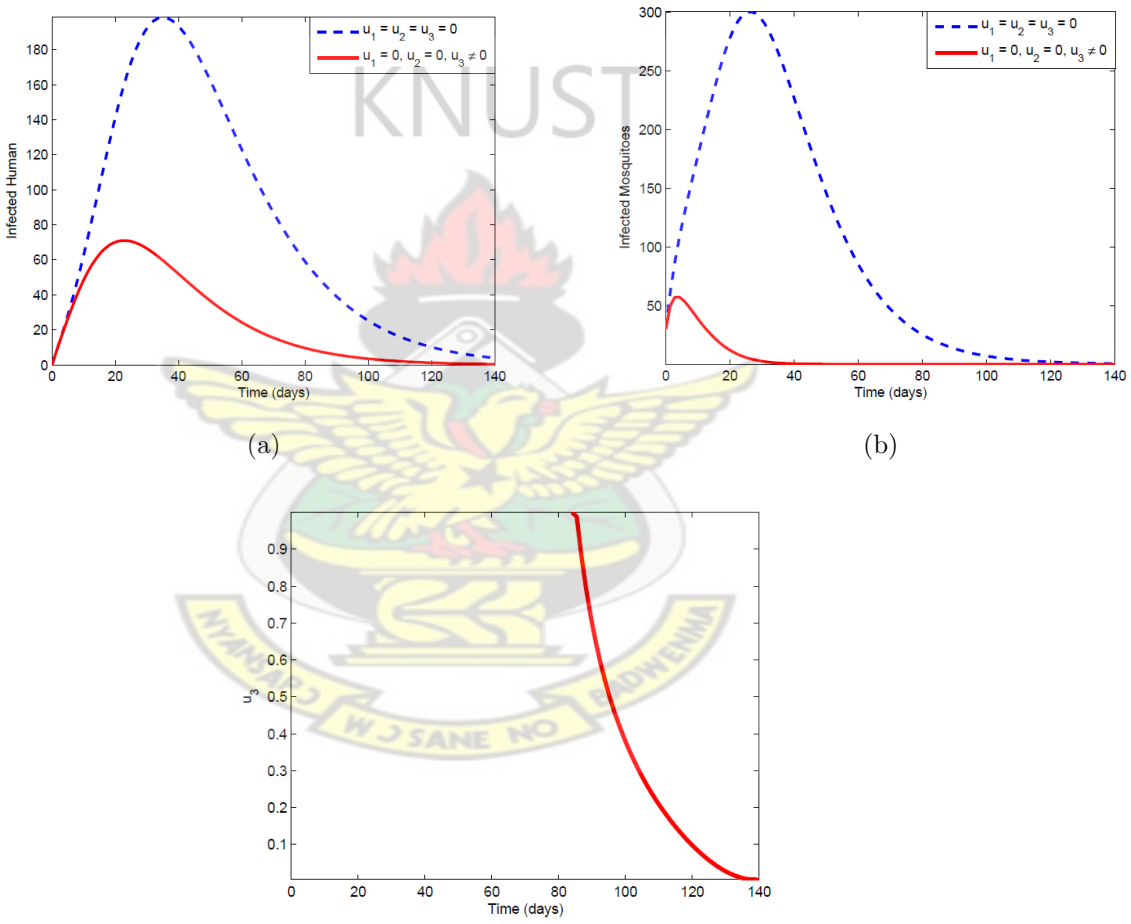



Figure 4.2: Simulations showing the effect treatment only on infected human and mosquitoes populations

### 4.4.3 Simulation of insecticide spraying

With this strategy, only the control on insecticide spraying ($u_3$) is used while the control on treatment ($u_2$) and the control on treated bednets ($u_1$) are set to zero. The results in Figure 3 show a significant difference in the $I_h$ and $I_v$ with control strategy compared to $I_h$ and $I_v$ without control. We see in Figure 4.3(a) that the control strategies resulted in a decrease in the number of symptomatic

human ($I_h$) as against an increase in the uncontrolled case. Also in Figure 4.3(b), the uncontrolled case resulted in increased number of infected mosquitoes ($I_v$), while the control strategy lead to a drastic decrease in the number of infected mosquitoes. The control profile is shown in Figure 4.3(c), here we see that the insecticide spray control $u_3$ is at the upper bound till the time $t = 90$ days, it then reduces gradually to the lower bound.



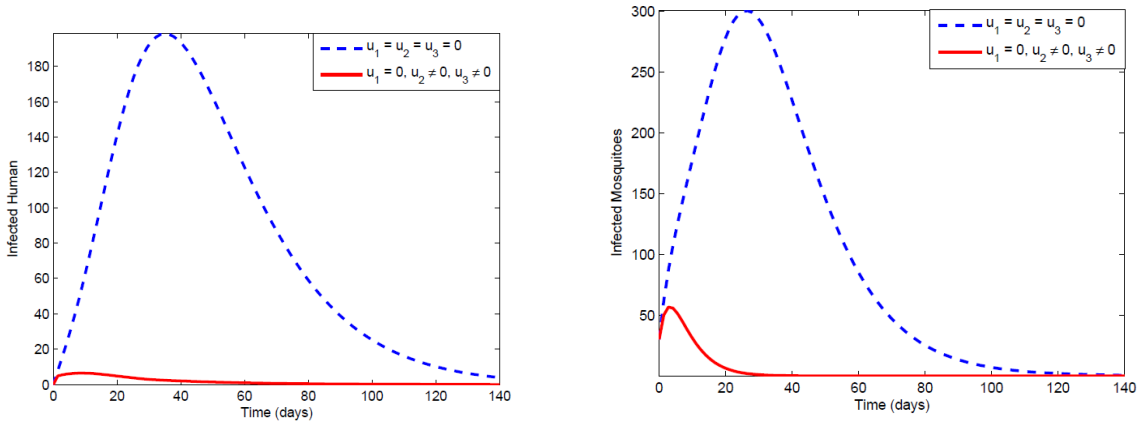

(a) (b)

(c)

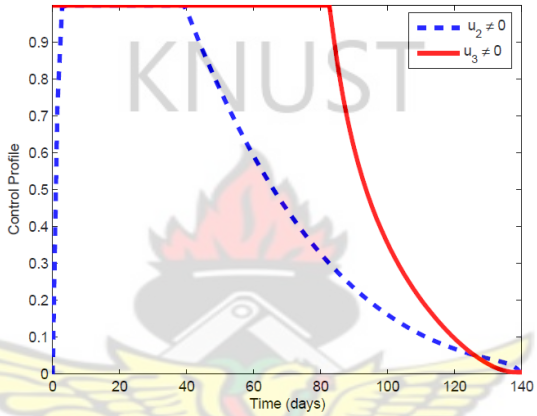
Figure 4.3: Simulations showing the effect of insecticide spraying only on infected human and mosquitoes populations

### 4.4.4 Simulation of treatment and insecticide spray

With this strategy, the control ($u_2$) on treatment and the control on ($u_3$) insecticide spraying are both used while the control on treated bednets ($u_1$) is set to zero. In Figure 4.4, the result shows a significant difference in the $I_h$ and $I_v$ with control strategy compared to $I_h$ and $I_v$ without control. We observed in Figure 4.4(a) that the control strategies resulted in a decrease in the number of symptomatic humans ($I_h$) as against increases in the uncontrolled case. Similarly in Figure 4.4(b), the uncontrolled case resulted in increased number of infected mosquitoes ($I_v$), while the control strategy lead to a decrease in the number of infected mosquitoes. The control profile is shown in Figure 4.4(c), here we see that the treatment control $u_2$ is at the upper bound till time $t = 50$, while the insecticide spray $u_3$ is at the upper bound for 90 days before reducing gradually to the lower bound.




(a) (b)



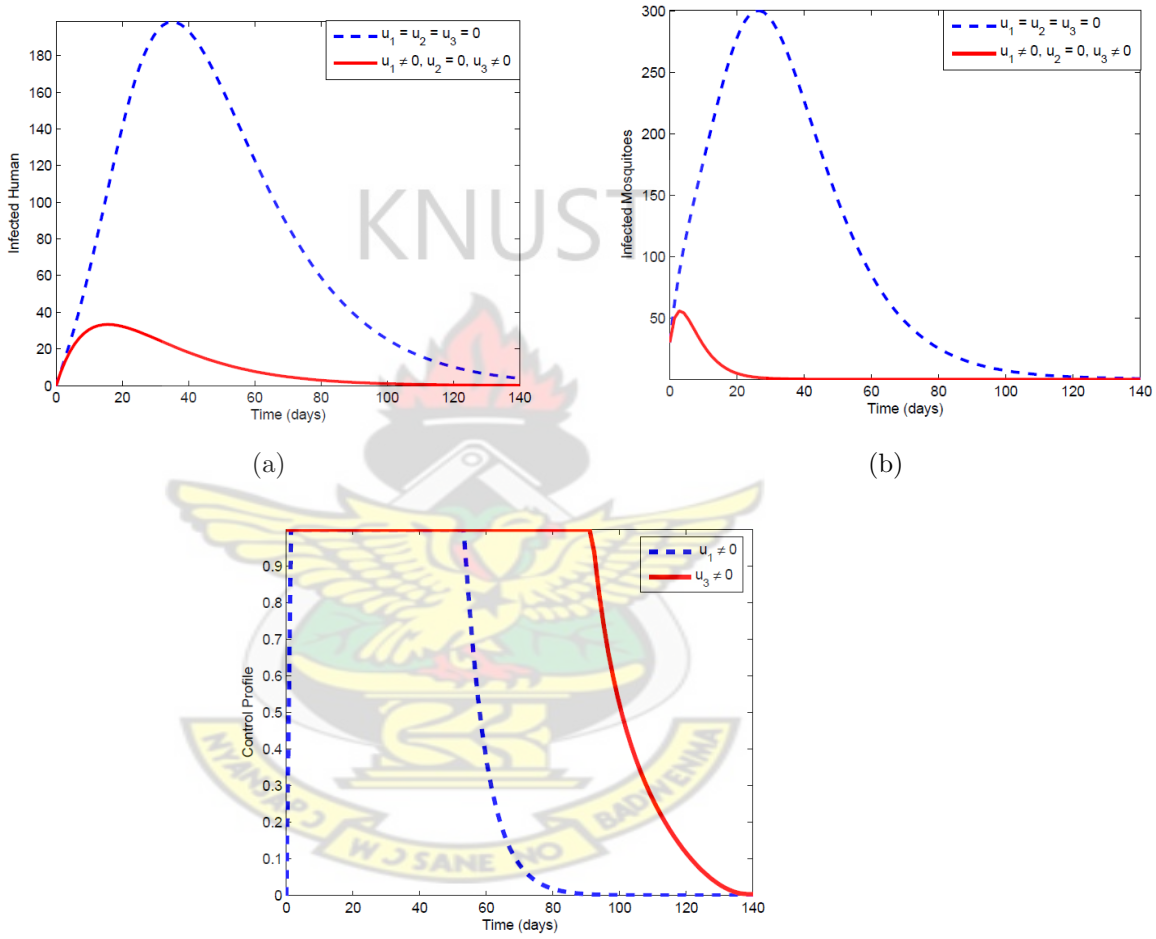

(c)

Figure 4.4: Simulations showing the effect of treatment and insecticide spray only on infected human and mosquitoes populations

### 4.4.5 Simulation of treated bednets and insecticide spray

Here, the control on treated bednets ($u_1$) and the spray of insecticide ($u_3$) are used while setting the control on treatment $u_2 = 0$. For this strategy, shown in Figure 5, we observed that the number of symptomatic human ($I_h$) and mosquitoes ($I_v$) differs considerably from the uncontrolled case. Figure 4.5(a), reveals that symptomatic humans ($I_h$) is lower in comparison with the case without control. While Figure 4.5(b), reveals a similar result of decreased number of infected mosquitoes

($I_v$) for the controlled strategy as compared with the strategy without control. The control profile in Figure 4.5(c) shows that the control on treated bednets ($u_1$) is at upper bound for 60 days, while insecticide spray ($u_3$) is at upper bound for $t = 100$ days before reducing to the lower bound.




(a) (b)

(c)

Figure 4.5: Simulations showing the effect of treated bednets and insecticide spray only on infected human and mosquitoes populations

### 4.4.6 Simulation of treated bednets and treatment

With this strategy, the control on treated bednets ($u_1$) and the treatment ($u_2$) are used while setting the control on spray of insecticide $u_3$ to zero. For this strategy, shown in Figure 4.6, there is a significant difference in the $I_h$ and $I_v$ with control strategy compared to $I_h$ and $I_v$ without control. We observed in Figure 4.6(a) that due to the control strategies, the number of symptomatic humans ($I_h$) decreases as against the increase in the uncontrolled case. A similar decrease is observed in Figure 4.6(b) for infected mosquitoes ($I_v$) in the control strategy, while an increased number is observed for the uncontrolled case resulted. In Figure 4.6(c), the control profile, the control $u_1$ is at the upper bound for 118 (days) and drops gradually until reaching the lower bound, while control on treatment $u_2$ starts and remain at upper bound for 12 days before dropping gradually to the lower bound. The result here shows that with a treated bednets coverage of 100% for 118 days and treatment coverage of 100% for 12 (days), the disease incidence will be greatly reduced.

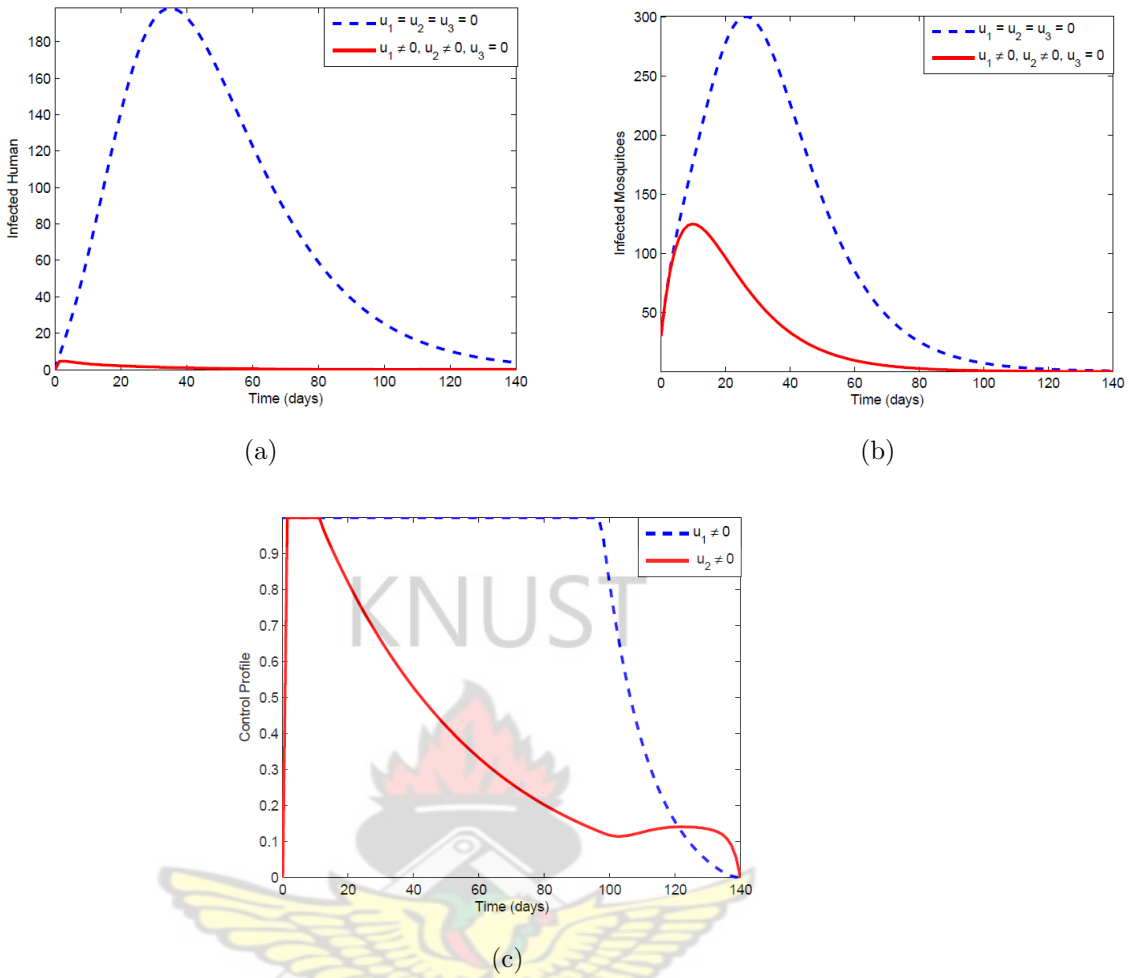
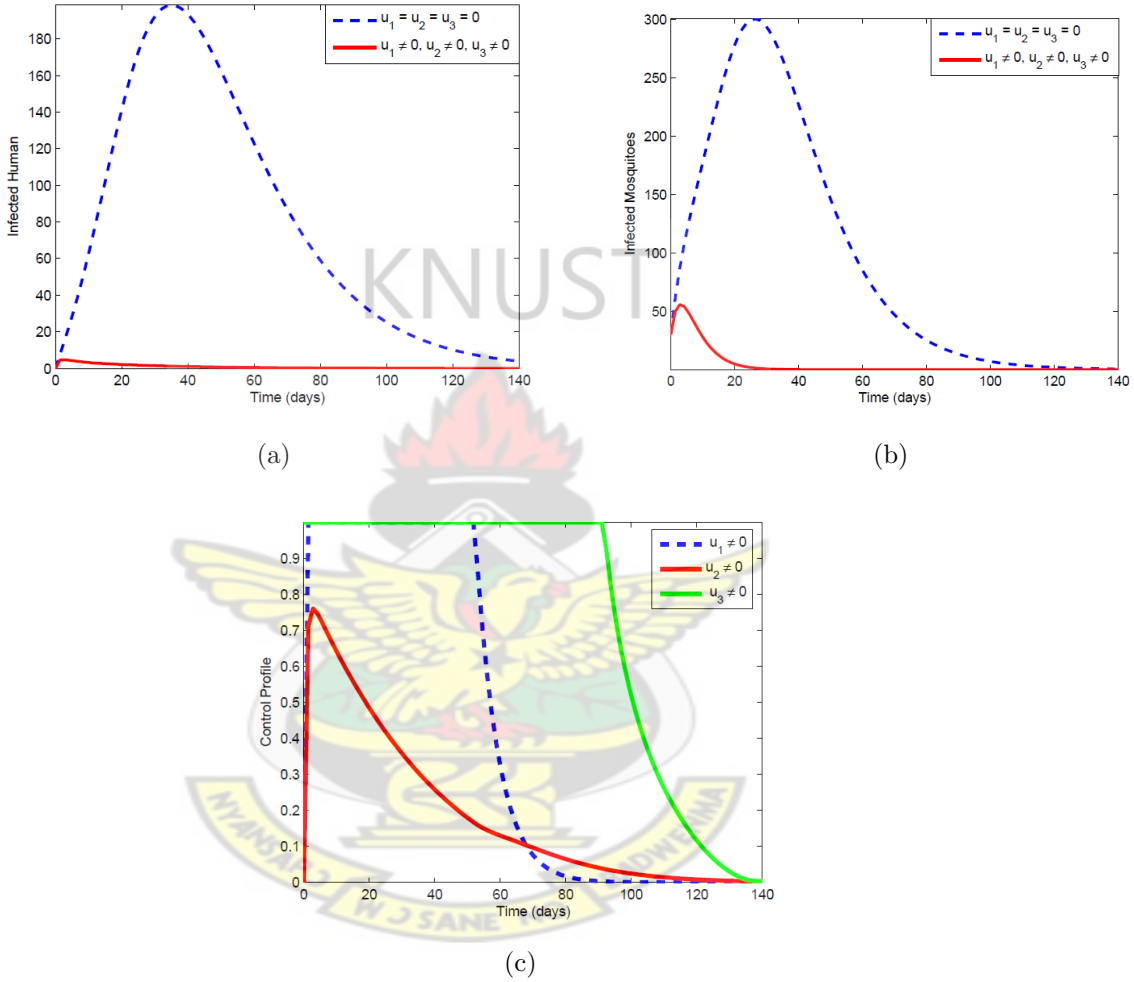



Figure 4.6: Simulations showing the effect of treated bednets and treatment only on infected human and mosquitoes populations

### 4.4.7 Simulation of treated bednets, treatment and insecticide spray

Here, all three controls ($u_1$, $u_2$ and $u_3$) are used. For this strategy in Figure 4.7, we observed in Figure 4.7(a) and 4.7(b) that the control strategies resulted in a decrease in the number of symptomatic humans ($I_h$) and infected mosquitoes ($I_v$) as against the increased number of symptomatic humans ($I_h$) and infected mosquitoes in the uncontrolled case. The control profile shown in Figure 4.7(c), shows that the control $u_1$ is at upper bound for $t = 60$ days, while control $u_2$, starts high at about 77% and reduces to the lower bound gradually over time. The control $u_3$ on the other hand is at upper bound for about 100 days before

reducing to the lower bound.



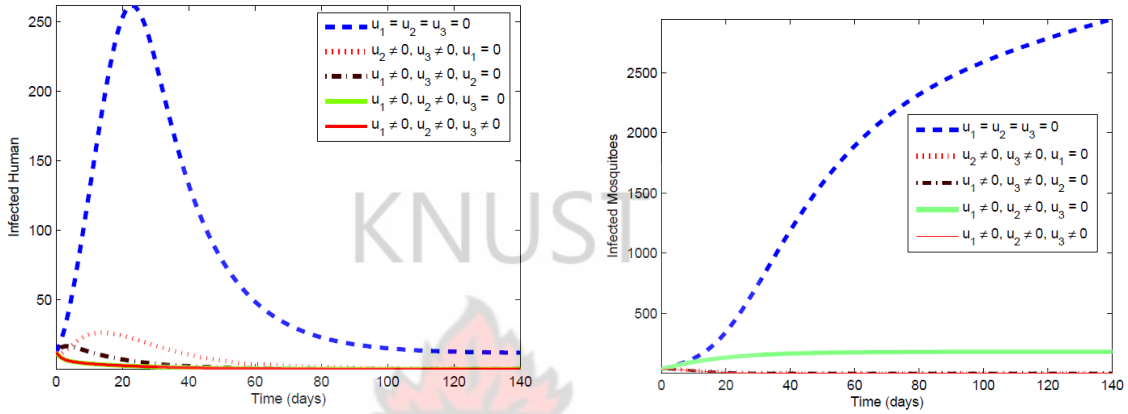

(a) (b)

(c)

Figure 4.7: Simulations showing the effect of treated bednets, treatment and insecticide spray only on infected human and mosquitoes populations

A comparison of all four control strategies in Figures 4.8(a) and 4.8(b) shows that while all four strategies lead to a decrease in the number of infected, both in human and in mosquitoes. The control strategy without treatment resulted in a higher number of infected humans, followed by the strategy without treated bednets. The strategy without the spray of insecticide even though, it gave a better result in reducing the infection in human, gave a poorer result in

reducing the mosquitoes population. This result shows that with individuals total adherence to effective use of treated bednets and spray of insecticide in the population, little treatment efforts will then be required by the nation Ghana in the control of the spread of the disease.




(a) (b)

Figure 4.8: Simulations showing the comparison of the effect of all four different control strategies

### 4.4.8 Simulation of insecticide spraying

A scenario with reducing different fraction of vector population is simulated, the result shows that the value of $p = 0.2$ gave the lowest number of susceptible ($S_v$) vectors while $p = 0.85$ gave the least value of infected ($I_v$) vectors, this is followed by $p = 0.6$, $p = 0.85$ and lastly by $p = 14$ (a case corresponding to no use or ineffective insecticide) as expected. This has the resultant effect (not depicted here) on total number of vectors susceptible to malaria $S_v$. When $p = 0.85$, the total number of vectors susceptible to malaria, $S_v$ is 4900, when $p = 0.6$, $S_v = 2000$, and lastly when $p = 0.2$, the total number of susceptible vectors to malaria, $S_v = 1000$.

# Chapter 5

# CONCLUSION AND RECOMENDATIONS

## 5.1 INTRODUCTION

In this chapter, we present the conclusion of our study. We also present some recommendations based on our findings and recommend some work for further research.



## 5.2 CONCLUSIONS

The malaria model is derived with four control parameters using a deterministic system of differential equations to effectively investigate the transmission dynamics of malaria in Ghana and to find out the most effective control measure. Mathematically, malaria was modelled as a 7-dimensional system of ordinary differential equations. It was first showed that there exists a domain where the model is epidemiologically and mathematically well-posed. The basic reproduction number,($R_0$) which is defined as the expected number of new infections (in mosquitoes or humans) from one infectious individual (human or mosquito) over the duration of the infectious period given that all other members of the population are susceptible and it was established that the model is locally asymptotically stable when the associated reproduction number is less than unity and the model is unstable when the reproduction number is greater than unit. That is to say if ($R_0 < 1$), the disease can not persist in Ghana and when ($R_0 > 1$) the disease can persist in Ghana. The stability analysis of the model was investigated and it proved that the disease-free equilibrium is locally asymptotically stable if ($R < 1$) and unstable when ($R > 1$) . The Centre Manifold theorem was used to show that the model has a unique endemic equilibrium which is locally asymp-

totically stable when ($R < 1$). The sensitivity analysis was applied to find which parameters impacts the basic reproduction number the most and it was observed that the most sensitive parameters are mosquitoes biting rate ($\epsilon$) and mosquitoes death rate ($\mu_v$). The reproductive number $R_0$ is directly related to the mosquitoes biting rate and inversely related to the mosquitoes death rate. It was realized that an increase (or decrease) in biting rate $\epsilon$ by 10% increases (or decreases) $R_0$ by 10%. Similarly increase (or decrease) in death rate $\mu_v$ of mosquitoes by 10% decreases (or increases) $R_0$ by 10%. Also numerical simulation using the fourth order Range-Kutta method in matlab was done to determine the effectiveness of all possible combinations of the four malaria control measures. In the control model considered, we use one control at a time and the combination of two controls at a time, while setting the other(s) to zero to investigate and compare the effects of the control strategies on malaria eradication in Ghana. Clinical malaria data from Ghana was used for the control analysis and our numerical results shows that the combination of the four (4) controls these are; the use of treated bednets ($u_1$), treatment of infective humans($u_2$), spray of insecticides($u_3$) and the intermittent preventive treatment for pregnant women ($u_4$) has the highest impact on the control of the disease. This is followed by the combination of treatment of infective human ($u_2$) and the use of treated bednets ($u_1$) among the human population and lastly by the combination involving the use of treated bednets ($u_1$) and spray of insecticide ($u_3$) . In communities where resources are scarce, it was suggested that the combination of treatment of infective human ($u_2$) and the use of treated bednets ($u_1$) should be adopted, having observed from the comparison of all four control strategies in Figure 4.8, that there is no significant difference between this strategy and the combination of the three (3) controls. Although, our recommendation agrees with the result obtained by Blayneh et al, our result however shows two possible control strategies, each with two combinations of control measures that are sufficient to effectively achieve and maintain interruption of transmission of malaria in Ghana. A result which addresses the

WHO concern about the insufficiency of only one control measure to achieve and maintain interruption of transmission of malaria.

## 5.3 RECOMMENDATIONS

(1) From the results it is observe that the best and effective way to eradicate malaria is the combination of all the four control strategies hence using one control strategy is not sufficient to eradicate malaria from Ghana. This addresses the WHO concern about the insufficiency of only one control measure to achieve and maintain interruption of transmission of malaria. Therefore it suggest that all the four control measures should be used at the same time for a minimum of 70 days to eradicate malaria from Ghana.

(2) From the sensitivity analysis it was realized that the mosquito biting rate, the mosquito contact rate with human and the mosquito death rate are the most sensitive parameters therefore it suggest that strategies that can be applied in controlling and eradicating malaria from Ghana are to target the mosquito biting rate and the mosquito death rate. These are; $u_1$ The use of insecticide-treated bed nets to prevent contact of the humans with the mosquitoes, $u_3$ Indoor residual spray and the use of other biochemical genetic methods to increase the mosquito death rate.

(3) In communities where resources are scarce, it was suggested that the combination of treatment of infective human ($u_2$) and the use of treated bednets ($u_1$) should be adopted, having observed from the comparison of all four control strategies in Figure 4.8, that there is no significant difference between this strategy and the combination of the three (3) controls.

(4) From the numerical results it suggest that the ministry of health should stop giving out only mosquito nets but give both mosquito nets and insecticide sprays since only one control measure cannot help to reduce malaria in Ghana.

### 5.3.1 FUTURE WORK

(1). The modelling of malaria together with another disease can be done to see the (mutual effects) or the rate at which a person with malaria becomes susceptible to other diseases.(Multi-morbidity)

(2). Optimal control theory can be applied to the model to see how far it agrees with simulation results of the present study.

# REFERENCES


Adams, B. M., Banks, H. T., and Tran, H. T. (2004). Dynamic multidrug therapies for hiv: optimal and sti control approaches. *Mathematical Biosciences*, 1(2):223–241.

Castilo-Chavez. and Song, B. (2004). Dynamical models of tuberculosis and their applications. *Mathematical Biosciences*, 1(2):361–404.

CDC (2013). Division of parasitic diseases,. *National Center for Infectious Diseases, Center for Disease Control and Prevention USA.*

Chiyaka, chuenche, Garira, and Dube (2008). Mathematical analysis of the effects of control strategies on the tramsmission dynamics of malaria. *Applied Mathematical Computation*, 195:641–662.

Felippe de Souza, Marco, A. L. and Takashi, Y. (2000). Optimal control theory applied to the anti-viral treatment of aids. *In Proc. Conference on Decision and Control Sydney.*

Gumel, A. B., Garba, S. M., and Abu, B. (2008). Backward bifurcations in dengue transmission dynamics. *Mathematical Bioscience*, 215:11–25.

Gupta, N. and Rink, R. (1973). Optimal control of epidemics. *Mathematical Bioscience*, 18:383–396.

Hyun (2001). A mathematical model for malaria transmission relating global warming and local socioeconomic conditions. *Rev. Saude Publica*, 35(3):224 – 231.

Isao, K., Akira, S., and Motoyoshi, M. (2004). Combing zooprophylaxis and insecticide spraying: a malaria-control strategy limiting the development of insecticide resistance in vector mosquitoes. *Proceedings - Electrochemical Society London.*, 271:301 – 309.

Joshi, H. (2002). Optimal control of an hiv immunology model. *Control Applied Mathematics*, 23:199–213.

Joshi, H., Lenhart, S., Li, M. Y., and Wang, L. (2006). Optimal control methods applied to diseae models. *Contemporary Mathematics*, 410:187–207.

Jung, E., Lenhart, S., and Feng, Z. (2002). Optimal control of treatments in a two-strain tuberculosis model. *Discrete Continuous Dynamical System*, B2 (4):473–482.

Kar, T. and Batabyal, A. (2011). Stability analysis and optimal control of an sir epidemic model with vaccination. *Biosystems*, 104(2-3),:127–135.

Karrakchou, J., Rachik, M., and Gourari, S. (2006). Optimal control and infectiology: application to an hiv/aids model. *Applied Mathematical Computation*, 177:807–818.

Kbenesh, B., Yanzhao, C., and C., Hee-Dae, K. (2009). Optimal control of vector-borne diseases: treatment and prevention. *Discrete Continuous Dynamical System*, B11 (3):587–611.

Kirschner, D., Lenhart, S., and Serbin, S. (1997). Optimal control of the chemotherapy of hiv. *Journal of Mathematical Biology*, 35:775–792.

Koella and Anita (2003). Epidemiological models for the spread of anti-malaria resistance. *Malaria Journal*, 2.

Macdonald, G. (1957). The epidemiology and control of malaria. *Oxford university Press, Oxford*.

Marco, A. L. and Takashi, Y. (2001). Optimal and suboptimal control in dengue epidemics. *Optimal Control Applied Methods*, 22:63–73.

Ngwa, G. (2006). On the population dynamics of the malaria vector. *Bull Mathematical Biology*, 68:2161–2189.

Ngwa, G.A. Shu, W. (2000). Amathematical model for endemic malaria with variable human and mosquito population. *Mathematical Computational model*, 32:747–763.

Oduro, F., T., Okyere, G., A., and Azu-Tungmah, G., T. (2012). Transmission dynamics of malaria in ghana. *Journal of Mathematics Research*, 4:6.

Okosun, K., Ouifki, R., and Marcus, N. (2011). Optimal control analysis of a malaria disease tramsmission model that includes vaccination with waning immunity. *Biosystems*, 106:136–145.

Okosun, K., Ouifki, R., and Marcus., N. (2013). Optimal control strategies and cost-effectiveness analysis of a malaria model. *BioSystems*, 111:83–101.

Pontryagin, L., Boltyanskii, V., Gamkrelidze, R., and Mishchenko, E. (1962). The mathematical theory of optimal processes. *Wiley, New York*.

Ross, R. (1911). The prevention of malaria. *Murray, London.*, 2nd ed.

Sachs, J. (2002). A new infected global effort to control malaria. *Journal of science*, doi:10.1126 /science:122 – 124.

Suresh, P. (1978). Optimal control of some simple deterministic epidemic models. *Pergamon Press*, 29(2):129–136.

WHO (2013). World malaria report. *World Health Forum*, page 213.

Xiefei, Y., Yun, Z., and Jianliang, L. (2007). Optimal quarantine and isolation strategies in epidemics control. *World Journal Model Simulation.*, 3(3):202–211.

# APPENDIX A

Matlab codes used for simulating the malaria model (1)

```
k1=0.04;k2=0.0032;k3=0.178;k4=0.13;k5=0.3;
h=0.001;
t=0:h:20;m=4;
n=length(t);
X=zeros(m,n);
for i=1:n-1
f=@(X)[-X(1)*(k1+k2+k3);k3*X(1)+k4*X(3)+k5*X(4);k2*X(1)-k4*X(3);k1*X(1)-
k5*X(4)];
X(:,1)=[46,0,0,0]';
k6=h*f(X(:,i));
k7=h*f(X(:,i)+0.5*k6);
k8=h*f(X(:,i)+0.5*k7);
k9=h*f(X(:,i)+k8);
X(:,i+1)=X(:,i)+1/6*(k6+2*k7+2*k8+k9);
end
disp(X)
plot(t,X(1,:),'-k','linewidth',3)
ylabel('Infected Human')
xlabel('time(days)')
hold on
plot(t,X(2,:),'–r','linewidth',3)
hold on
plot(t,X(3,:),'-.r','linewidth',2)
hold on
plot(t,X(4,:),':b','linewidth',3)
title('Simulation of control measures against time')
```

legend(u(1)= 0,u(2)=0,u(3)=0,u(4)=0)

(i) The M-function files

function dydt = malaria (t,y)

dydt = zeros (size(y));

a1=0.00005079;a2=0.071;b1=(1/14);b2=(1/11);c=(1/7);

d1=0.00004278;d2=(1/25);e1=(0.0000027);e2=(1/91.3125);

f1=0.42;f2=0.0655;f3=0.40;

Sh=y(1);

Eh=y(2);

Ih=y(3);



R=y(4);

Sm=y(5);

Em=y(6);

Im=y(7);

Nh = Sh + Eh + Ih + R;

k1=(f2*f3)/Nh; k2=(f1*f3)/Nh;

%The malaria model dydt(1) = a1 +e2*R - k1*Im*Sh - d1*Sh;

dydt(2) = k1*Im*Sh - (b1 + d1)*Eh;

dydt(3) = b1*Eh - (c + d1 + e1)*Ih;

dydt(4) = c*Ih - (e2 +d1)*R;

dydt(5) = a2 - k2*Ih*Sm - d2*Sm;

dydt(6) = k2*Ih*Sm - (b2 + d2)*Em

dydt(7) = b2*Em - d2*Im;

%The basic reproduction number for the malaria model

R(0) = sqrt(((f3$\hat{2}$)*a2*b1*b2*f1*f2*d1)/(a1*(d2$\hat{2}$)*(b1+d1)*(c + d1 + e1)*(b2 + d2)));

disp(R0)

(ii)The executable file for plotting the line graph of human population against time

tspan = [0 700];

y0 = [13413000 18000 3350000 3343000 16500000 500000 38000000];

(t,y) = 0de45(@malaria,tspan,y0);

plot(t,y(:,1),'r',t,y(:,2),'b',t,y(:,3),'g',t,y(:,4),'y','Linewidth',2)

title('Plot of human population against time')

xlabel('Time(days)')

ylabel('Infected Mosquitoes')

legend('Susceptible ','Exposed ','Infectious ','Recovered ',2)

(iii)The executable file for plotting the line graph of mosquito population against time



tspan = [0 700];

y0 = [13413000 18000 3350000 3343000 16500000 500000 38000000];

(t,y) = 0de45(@malaria,tspan,y0);

plot(t,y(:,5),'r',t,y(:,6),'b',t,y(:,7),'g','Linewidth',2)

title('Plot of mosquito population against time')

xlabel('Time(days)')

ylabel('Infected Mosquitoes')

legend(u(1) = 0 ,u(2) = 0,u(3) = 1)

(iv)The executable file for plotting the line graph of prevalence against time

tspan = [0 700];

y0 = [13413000 18000 3350000 3343000 16500000 500000 38000000];

(t,y) = ode45(@malaria,tspan,y0);

N1=(y(:,1)+y(:,2)+y(:,3)+y(:,4));

plot(t,(y(:,2)+y(:,3)+y(:,4))./N1,'r','Linewidth',2)

xlabel('Time (days)')

ylabel('Infected Humans')

(v)The executable file for plotting the line graph of Simulation of Biting Rate of Mosquitoes on the Model

tspan = [0 40];

y0 = [13413000 18000 3350000 3343000 1031250 31250 2375000];

(t,y) = ode45(@malaria,tspan,y0);

plot(t,y(:,1),'r',t,y(:,2),'b',t,y(:,3),'g',t,y(:,4),'y','Linewidth',2)

title('Plot of human population against time')

xlabel('Time(days)')

ylabel('Infected Mosquitoes')

legend('Susceptible ','Exposed ','Infectious ','Recovered ' , 2 )

(vi)The executable file for plotting the line graph of Simulation of Treatment Rate of Infectious Humans on the Model

tspan = [0 300];

y0 = [13413000 18000 3350000 3343000 16500000 500000 38000000];

(t,y) = ode45(@malaria,tspan,y0);

plot(t,y(:,1),'r',t,y(:,2),'b',t,y(:,3),'g',t,y(:,4),'y','Linewidth',2)

title('Plot of human population against time')

xlabel('Time(days)')

ylabel('Infected Humans')

legend('Susceptible ','Exposed ','Infectious ','Recovered ')

(vii)The executable file for plotting the line graph of Simulation of Biting and Treatment Rates of Infectious Humans on Model.

tspan = [0 40];

y0 = [13413000 18000 3350000 3343000 1031250 31250 2375000];

(t,y) = ode45(@malaria,tspan,y0);

plot(t,y(:,1),'r',t,y(:,2),'b',t,y(:,3),'g',t,y(:,4),'y','Linewidth',2)

title('Plot of human population against time')

xlabel('Time(days)')

ylabel('Infected Humans')

legend('u(1) = 1 ',u(2) = 1 ','u(3) = 1 ','u(4) = 1 ')