KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

MODELLING THE TRANSMISSION DYNAMICS OF MALARIA IN GHANA: A CASE STUDY OF THE GREATER ACCRA REGION

BY

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DECLARATION

Candidate's Declaration

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

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ABSTRACT

Malaria is hyper-endemic in Ghana, especially in the Greater Accra Region. It remains a major public health problem and requires prompt and effective case management. The Bulletin of Health Information: October 2004, 1 (1), reports that outpatient attendance over the last 19 years illustrates the increasing burden of malaria in the region. While there is an overall consistent decrease of other infectious and parasitic diseases (from 31.8% in 1985 to 19.5% in 2003), there has been an increase in malaria cases (from 37.1% in 1985 to 44.7% in 2003). Patterns of malaria morbidity and mortality in the region seem consistent with those observed in areas with high transmission in Ghana, emphasizing that the challenge of reducing malaria burden is still unmet.

The significance of the malaria burden in the region necessitated a formulation of a mathematical model to assess the impact of control strategies on malaria. Our model uses ordinary differential equations to simulate the spread of malaria. We performed stability analysis and numerical simulations on the model and the results show that the model has two equilibria: the disease-free equilibrium which is locally asymptotically stable when $R_o < 1$ and the endemic equilibrium that is locally asymptotically stable when $R_o > 1$.

TABLE OF CONTENTS

Contents	Page
DECLARATION	i
ABSTRACT	ii
TABLE OF CONTENTS	iii
LISTS OF TABLES	vi
LIST OF FIGURES	vii
LIST OF ABBREVIATIONS	viii
DEDICATION	ix
ACKNOWLEDGEMENTS	x
CHAPTER ONE: INTRODUCTION	1
1.1 Background to the study	1
1.2 Statement of the problem	10
1.3 Objectives of the study	11
1.4 Methodology	11
1.5 Justification	12
1.6 Organization of the study	13
CHAPTER TWO: REVIEW OF LITERATURE	14
2.1 Introduction	14
2.2 The Ross-MacDonald model	15
2.3 The Reproductive Number	16
2.4 Inclusion of acquired immunity in the model	18
2.5 Inclusion of the effects of environment on the model	20
2.6 Inclusion of the effects global warming	20
2.7 Inclusion of spread of drug-resistant Plasmodium	21

CHAPTER THREE: METHODOLOGY 24

3.0 Introduction 24

3.1 The malaria model 24

3.2 Model description and formulation 25

3.2.1 The state variables and model parameters 26

3.1.2 Equations of the model 28

3.3 Basic properties of the malaria model 29

3.3.1 Invariant region 29

3.3.2 Positivity of solutions 33

3.4 Analysis of the model 35

3.4.1 Existence and stability of steady-state solutions 35

3.4.2 Existence of disease-free equilibrium 35

3.4.3 The basic reproduction number 36

3.4.4 Local stability of the disease-free equilibrium 42

3.4.5 The endemic equilibrium point 46

3.4.6 Local stability of the endemic equilibrium point 52

3.4.6.1 Computation of *a* and *b* 57

3.5 Summary 59

CHAPTER FOUR: RESULTS AND DISCUSSION 60

4.1 Introduction 60

4.2 Data collection 60

4.2.1 Greater Accra population data 60

4.2.2 Lab-confirmed malaria cases and deaths 61

4.2.3 Data for mosquitoes population 61

4.2.4 Data for the human population 62

4.3 Estimation of parameters 63

4.4 Data processing 64

4.4.1 SEIR data of the Greater Accra region 64

4.5 Model for both human and mosquito populations: 65

4.5.1 Disease-free equilibrium point 66

4.5.2 Reproduction number 66

4.5.3 Local stability of the disease-free equilibrium 67

4.5.4 The endemic equilibrium point 68

4.5.5 Local stability of the endemic equilibrium point 70

4.6 Numerical solutions of the model 72

4.6.1 Simulation of the human population with time 73

4.6.2 Simulation of the behaviour of the vector population 74

4.6.3 Plot showing the prevalence in the model 75

4.6.4 Plot showing the behaviour of biting rate of vectors with time 76

4.7 Discussion 77

CHAPTER FIVE: CONCLUSION AND RECOMMENDATIONS 78

5.1 Introduction 78

5.2 Conclusion 78

5.3 Recommendation 79

5.4 Recommendations for future studies 79

REFERENCES 80

APPENDICES 90

Appendix A: The Next Generation Operator Method 90

Appendix B: Castillo-Chavez and Song 91

Appendix C: Matlab Code 92

LIST OF TABLES

Table		Page
3.1:	The state variables for the malaria model	27
3.2:	Parameters of the model	27
4.1:	Greater Accra population from 2000-2011	60
4.2:	Greater Accra lab-confirmed malaria cases and deaths	61
4.3:	Data for mosquitoes population	62
4.4:	Data for human population	62
4.5:	Parameter values of the model system	63
4.6:	SEIR data of the Greater Accra Region (2000-2011)	64

LIST OF FIGURES

Figure	Page
3.1: A diagrammatic representation of the model	24
4.6.1: Simulation of human population with time	72
4.6.2 Simulation of the behaviour of the vector population	73
4.6.3 Plot showing the prevalence in the model	75
4.6.4 Plot showing the behaviour of the biting rate of vectors with time	76

LIST OF ABBREVIATIONS

GHS	Ghana Health Service
AMDP	Anti-Malaria Drug Policy
UNICEF	United Nations Children's Fund
UNDP	United Nations Development Fund
NMCP	National Malaria Control Programme
RBM	Roll-Back Mosquito
MDGs	Millennium Development Goals
DDT	Dichloro-diphenyl-trichloroethane
ACT	Artemisinin-based Combination Therapy
ODEs	Ordinary Differential Equations
MOH	Ministry of Health
W.H.O	World Health Organization
IRS	Indoor Residual Spraying
RDT	Rapid Diagnostic Test
ITN	Insecticide-Treated bed Nets
CHIM	Center for Health Information Management

DEDICATION

To my dear wife, Naomi Agyeiwaa, and my lovely daughters, Afua Oppong Ankomah and Akosua Amankwah-Tia Ankomah for their moral and spiritual support.

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CHAPTER ONE

INTRODUCTION

1.1 Background to the study

Malaria is a mosquito-borne infectious disease of humans and other animals caused by a protozoan of the genus Plasmodium. According to the MOH 2009 "Guidelines for Case Management of Malaria in Ghana", there are four species of parasites that cause infections in humans but in Ghana, only three are found; these are P. falciparum, P. malariae and P. ovale. As noted by the WHO 2009 World Malaria Report, Ghana had an estimated 8.3 million malaria cases in 2006 and 3.2 million in 2008. It is reported that most cases are caused by P. falciparum; 26% of the reported cases were confirmed in 2008. The report further noted that there was no evidence of a reduction in the number of cases between 2001 and 2007, and the number of reported inpatient cases and deaths have increased. It is not known if the rise is due to better reporting or a change in the incidence of malaria.

In the year 1950, Ghana made an attempt to control the spread of malaria. Since the health sector alone was assumed to be incapable of controlling malaria, the other health-related sectors were involved. Some of the interventions that were put in place included indoor residual spraying (IRS), mass chemoprophylaxis with pyrimethamine medicated salt and draining of sewage system. With all these interventions, malaria continued to be the leading cause of death in Ghana. According to the Ghana Health Service 2010 Annual Report, the total number of malaria cases seen at the OPD showed an upward trend from 3,694,671 in 2009 to 3,740,055 for the year under review. The proportion of malaria to total OPD also increased from 32.5% to 34% during the year under review whilst the overall case fatality rate for malaria also worsened from 1.22 in 2009 to 1.44 in 2010.

The Ghana Health Service has been implementing strategies to improve on malaria case management. After successfully changing and revising the Anti-Malaria Drug Policy (AMDP), focus has been on early case detection and prompt treatment at all levels, especially cases in the most vulnerable groups, children under five, non-immune visitors and pregnant women. In Ghana, the diagnosis of malaria has been predominantly clinical. However, with the rapid scale up of proven interventions and their possible impact on malaria epidemiology, expert advice through the WHO recommends a parasitological confirmation of all cases prior to treatment. There has therefore been the need to scale up laboratory diagnosis either by microscopy or Rapid Diagnostic Tests (RDTs). To ensure that malaria cases are lab-confirmed before management is started, the training of laboratory staff on diagnosis which commenced in the previous year was continued with the training of 373 peripheral health workers on laboratory diagnosis (microscopy/RDTs).

According to Moore and Lanier (1961), resistance to chloroquine, an effective and safe anti-malarial that formed the first line of treatment, emerged more than 30 years ago, and since then malaria parasites have developed resistance against most of the widely used anti-malarials, including sulfadoxine-pyrimethamine, as noted by Hakim et al. (1996) and Smithius et al. (1997) and mefloquine, in the studies conducted by Mockenhaupt (1995), as well as quinine (Benito et al, 1995). Indeed, it is now generally believed that the widespread use of a new drug will inevitably be followed by the appearance of resistance in the parasite population.

One critical issue that has attracted the attention of donor agencies, especially WHO, World Bank, UNDP and UNICEF, in 1998, in response to the incidence of malaria led to the formation of a partnership to create the Roll Back Malaria movement, with the welcome and necessary goal of halving malaria deaths by the

year 2010 – the first major effort against the disease in four decades. Again, the Roll Back Malaria 2000 "Malaria in Africa" Factsheet 3, the need for such an effort is abundantly clear: malaria places a huge burden on Sub-Saharan Africa, with 300 million people suffering acute illness each year, and one million dying, at least 70% of whom are children or pregnant women. Reports indicate that in countries with a heavy malaria burden, the disease accounts for as much as 40% of public health expenditure, 30–50% of inpatient admissions, and up to 50% of outpatient visits. According to Holding and Snow (2001), those children who do not die can suffer brain damage or experience cognitive and learning deficiencies. In the view of Sachs and Malaney (2002), these events of illness and childhood retardation are so common in the tropics that entire countries fail to develop economically, cementing a future of desperation and poverty that spans generations.

According to the NMCP 2005 Annual Report, Ghana committed itself to the Roll Back Malaria (RBM) initiative in 1999 and developed a strategic framework to guide its implementation. Overall, the Ghana Roll Back Malaria emphasizes the strengthening of health services through multi and inter-sectoral partnerships and making treatment and prevention strategies more widely available. The goal was to reduce malaria specific morbidity and mortality by 50% by the year 2010. To achieve the goal, four main strategies were being pursued and these include:

i. Promote multiple prevention which includes promotion of insecticide-treated nets usage; chemoprophylaxis in pregnancy and environmental management.
ii. Improve malaria case management at all levels (from household to health facility);
iii. Encourage evidence-based research to come up with effective interventions
iv. Improve partnership with all partners at all levels.

The emerging and re-emerging diseases have led to a revived interest in infectious diseases. It is clear that human or animal invasions of new ecosystems, global warming, environmental degradation, increased international travel, and changes in economic patterns will continue to provide opportunities for new and existing infectious diseases (Martens, 1999).

Mathematical models have become important tools in analysing the spread and control of infectious diseases. The model formulation process clarifies assumptions, variables, and parameters; moreover, models provide conceptual results such as thresholds, basic reproduction numbers, contact numbers, and replacement numbers. Understanding the transmission characteristics of infectious diseases in communities, regions, and countries can lead to better approaches to decreasing the transmission of these diseases. As observed by Hethcote et al., (1989) and Hethcote and Van Ark (1992), epidemiology modeling can contribute to the design and analysis of epidemiological surveys, suggest crucial data that should be collected, identify trends, make general forecasts, and estimate the uncertainty in forecasts.

Mathematical models, according to Macdonald (1957) and Dietz (1974) have in the past provided a valuable framework for analysing the transmission dynamics of malaria. Moreover, MacDonald (1968) suggests that these models have been widely used to consider the effect of different strategies such as vector control whilst Halloran et al. (1992) and Gupta et al. (1996), emphasised on the use of future vaccines on the transmission dynamics of malaria. To produce relevant, robust findings, mathematical modelling should at the outset involve partnership and good communication between technical experts in mathematical modelling, experts in malaria field and laboratory science, and health policy decision-makers. Models produce the most useful data when they are formulated with important biological,

economic, and practical realities in mind and when their results are interpreted with care, making them another useful tool in the fight against malaria.

Gains in mathematical modelling of malaria:

Some of the benefits in malaria models include the following:

i. Models create the mathematical basis that could be used to guide policy formulation in the areas of public health. In the case of P. falciparum malaria, the policy decisions could be simply a matter of life and death. It is therefore important that the model is used to describe the aspects of the disease being well thought-out.

ii. Models have long been applied to malaria control and are particularly relevant today in light of rapid country progress in reaching high intervention coverage targets and given the intensifying global efforts to achieve the malaria-related Millennium Development Goals (MDGs).

iii. Modelling is especially well-suited to helping inform decision-making around malaria control because of the disease's complex biological systems, the considerable infrastructural and cost requirements of prevention and elimination, and the rapid pace of change in global planning and national programming to halt malaria.

iv. Epidemiology modelling can contribute to the design and analysis of epidemiological surveys, suggest crucial data that should be collected, identify trends, make general forecasts, and estimate the uncertainty in forecasts (Hethcote et al., 1989; Hethcote and Van Ark, 1992).

v. Mathematical models and computer simulations are useful experimental tools for building and testing theories, assessing quantitative conjectures,

answering specific questions, determining sensitivities to changes in parameter values, and estimating key parameters from data.

vi. Mathematical models are used in comparing, planning, implementing, evaluating, and optimizing various detection, prevention, therapy, and control programs.

Transmission of malaria:

According to the NMCP 2005 Annual Report, malaria is transmitted through the bite of an infected female Anopheles mosquito and three species transmit human malaria in Ghana: Anopheles gambiae, Anopheles arabiensis and Anopheles funestus. MacDonald (1957) and Smith & McKenzie (2004) found that a critical factor determining the successful transmission of malaria is the longevity of the adult mosquito relative to the incubation period of the parasite. The result of the study by Patz & Olson (2006), also show that the incubation period varies in the field from approximately 10 to more than 20 days, depending on temperature and only a relatively small fraction of mosquitoes naturally live long enough to infect humans. Thus, techniques that reduce adult survival further, such as indoor residual spraying (IRS) with insecticides and the deployment of insecticide-treated nets (ITNs), can cause substantial decreases in malaria transmission (Curtis & Mnzava 2000; Goodman et al. 2001; Guyatt & Snow 2002; Sharp et al. 2002).

Additionally, cases that are asymptomatic usually provide a necessary reservoir of parasites and they might become gametocyte carriers, which lead to malaria transmission (Bousema et al, 2004). Although reports indicate that the presence of asymptomatic cases is a big challenge for the management of the elimination programme in any malaria endemic area, evidence suggest that to achieve a successful elimination, detection of all parasite carriers by active case

detection and then treatment of all cases must be considered to interrupt the malaria transmission in endemic areas. Several studies have argued that asymptomatic malaria infections were frequently described in high and intermediate transmission areas including Ghana (Crookston et al., 2010; Owusu-Agyei et al., 2001), Kenya (Bousema et al., 2004) , Senegal (Males et al., 2008; Le Port et al., 2008), Gabon (Klein Klouwenberg et al., 2005; Nkoghe et al., 2011), Nigeria (Eke et al., 2006; Achidi et al., 1995), Uganda (Njama-Meya et al., 2004), Thailand (Coleman et al., 2002), Burma (Richards et al., 2007) and Yemen (Bin Mohanna et al., 2007).

As countries scale up malaria control efforts and reach high intervention coverage targets, they are faced with the question of what to do next. The strategy for maintaining and enhancing the achieved reductions in transmission is not obvious. It is often not clear whether maintaining current coverage levels would continue to reduce transmission, stabilize transmission at a new level, or slowly give way to an increase in transmission. Mathematical modelling can build on available data, test multiple scenarios and combinations of intervention strategies, and make verifiable predictions on what can be expected from these strategies.

Problems facing the control of malaria in Ghana:

The health sector, over the years, had been faced with some resource constraints, which had adversely affected the full and successful implementation of health interventions to accomplish preferred goals. The increased levels of partnerships in the area of malaria control provide a solid ground for sound coordination of malaria control within the context of planning and management. In order to achieve an impact and sustain the gains, emphasis needs to be laid on the use of proven cost effective interventions combined with needed local initiatives that will ensure success.

For instance, children under five years and pregnant women are known to be relatively more adversely affected. It contributes to the relatively high maternal mortality in Ghana as demonstrated by the estimates that 11% of mortality in pregnant women is due to malaria. Almost 30% of deaths in children below 5 years are caused by malaria. There are currently numerous obstacles to malaria control in Ghana. Many of these problems were responsible for the failure of the malaria eradication plan. Some of these obstacles include the following:

i. Resistance has developed to several antimalarial drugs, most notably chloroquine.
ii. There are also an increasing number of insecticide-resistant mosquitoes (including resistance to dichloro-diphenyl-trichloroethane (DDT)). Many mosquitoes have also now learned to altogether avoid insecticide treated surfaces, making their control even harder.
iii. Human activities continually create new breeding sites for mosquitoes and human populations have invaded mosquito habitats, thus increasing the number of contacts between mosquitoes and humans.
iv. Overpopulation and urbanization has significantly increased human population density in many parts of Ghana, again increasing the number of contacts between humans and mosquitoes.

In spite of the above obstacles, major advances have been made in malaria control as a result of the availability of key intervention strategies including insecticide-treated bed nets, indoor residual spraying and effective antimalarial therapy. However, control efforts remain inadequate, and malaria persists as a huge burden for many developing countries. To be most effective, the limited resources available for malaria control should be targeted at the populations in which they will

have the greatest impact (Caldas et al, 2004; Smith et al 2005; Woolhouse et al, 1997). Thus, detailed characterization of the risks for malaria among populations living in areas where the disease is endemic is an important priority.

Due to the widespread increase of chloroquine resistance in Africa, ACTs (Artemisinin-based Combination Therapies) have become the drugs of choice for uncomplicated malaria. According to the MOH's Revised Anti-Malaria Drug Policy for Ghana, 2 Revised Version (2009), Ghana began implementing an ACT-based Anti-Malaria Drug Policy (AMDP) in 2004. Prior to this time, Artesunate/Amodiaquine was the only ACT officially recommended for the treatment of uncomplicated malaria. The policy however faced challenges because no provision was made for those who could not tolerate the recommended drug. There was therefore the need for the policy to be revised to include alternate ACTs for uncomplicated malaria whilst the options for treatment of severe malaria and of malaria in pregnancy were also expanded.

Profile of the Greater Accra Region:

Accra, the capital city of Ghana, has a total land area of 201sq km. With a population of 4,010,054 million people (2010 National Population Census), Accra, Ghana's capital since 1877, is today one of the most populated and fast growing Metropolis in Africa with an annual growth rate of 3.22%. The gross population density for Accra Metropolitan Area is 10.03 persons per hectare as compared to 6.23 per hectare in 1970. Accra's population like that of most urban centres is very youthful with 58.3% of the population under the age of 24 years; 51.7% of the population are females. Accra is the second most industrialised city in Ghana, contributing over 10% to the GDP.

The state of sanitation in Accra is currently very unsatisfactory. The city is characterised by choked drains, indiscriminate waste disposal and uncollected refuse in central waste containers. Even though Accra generates between 1,500 – 1,800 tonnes of waste per day, it has the capacity to collect only 1,200 tonnes per day. Physical and settlement development in Accra is outstripping drainage network. This has culminated into seasonal flooding during the wet season the city authority spends 65-70% of its revenue on sanitation.

Although health facilities are within physical accessibility of the poor, the cost is beyond their scope. Most of them rely on traditional medication and self-medication for their health needs. The high-income groups rely on both public and private health facilities. There is high level private and non-governmental institutions participation in health delivery. There are 28 Hospitals in Accra. The major health problems of Accra are essentially communicable diseases due to poor environmental sanitation, ignorance, and poverty. Malaria has been the number one disease, accounting for about 53 per cent of outpatient cases. The major communicable diseases are malaria, sexually transmitted infection, diarrhoea, chicken pox, enteric fever. The transmission of the 5 major communicable diseases comes from poor sanitation, and the residents of the city over the years have been complaining about the poor sanitary conditions they are confronted with.

1.2 Statement of the Problem

Malaria disease is endemic in the Greater Accra Region. It accounts for as much as 40% of public health expenditure, 30–50% of inpatient admissions, and up to 50% of outpatient visits to an ever-increasing population with resource constraints. It continues to claim more lives despite the numerous interventions in

place. In order to address this problem and advise policy makers in the health sector, this study intends to investigate the effects of mathematical modelling on the transmission dynamics of malaria in the entire region.

1.3 Objectives of the study

The main aim of the study is to use mathematical models to analyse and describe the dynamics and spread of the malaria in the human population and how best it can be controlled.

The specific objectives are to:

i. Formulate a mathematical model to control the spread of malaria in the Greater Accra region.
ii. Perform stability analysis of the malaria model.
iii. Carry out numerical simulations on the model.

1.4 Methodology

The state of sanitation in Accra is currently very unsatisfactory. The city is characterised by choked drains, indiscriminate waste disposal and uncollected refuse in central waste containers. The major health problems of Accra are essentially communicable diseases due to poor environmental sanitation, ignorance, and poverty. Malaria has been the number one disease, accounting for about 53 per cent of outpatient cases and it is the highest among the region's top ten morbidity and mortality cases.

It is against this background that a malaria transmission model is being considered to investigate the effects of mathematical modelling on the transmission dynamics of malaria in the entire region. The model divides the human population

into four classes: susceptible, exposed, infectious and recovered whilst that for the mosquito population is divided into three classes: susceptible, exposed, and infectious. Thus, the human population follows a SEIR pattern whilst the mosquito vectors follow a SEI pattern. Our model is similar to that by Chitnis (2005), who described a compartmental model for malaria transmission, based on a model by Ngwa and Shu (2000). We also determine the reproductive number,R_o, which is the expected number of secondary cases that one infected individual would cause through the duration of the infectious period and show the existence and stability of disease-free equilibrium points, E_0, and endemic equilibrium points, E_1.

The data used in the analysis are secondary data and spans a period of twelve years; thus 2000 to 2011. The malaria cases and deaths data was obtained from the Ghana Health Service and the regional population data was obtained from the Ghana Statistical Service. Again, the method used for the numerical simulation was MATLAB's ode45.

1.5 Justification

Malaria is hyper-endemic and so many lives are lost every year especially in areas where people live in poor conditions and the successes of preventive strategies have been a dream. In view of the above, its study is valuable since it has had profound impact on social, political, cultural and economic development in the Greater Accra region. It remains a major public health problem and requires focused interventions including prompt and effective case management. It is hoped that the results of this study will provide relevant guidance for decision makers on which intervention to focus on.

1.6 Organisation of the study

The study is arranged into five chapters. The first chapter discusses the introductory background, problem statement, objectives, methodology and justification of the study. Chapter two covers the literature review. Chapter three explains the malaria model while the results of the numerical simulations of the model are discussed in chapter four. Chapter five covers the conclusion and recommendations as well as future work.

CHAPTER TWO

REVIEW OF LITERATURE

2.1 Introduction

Mathematical models are important tools for decision making in the control of infectious diseases, and malaria was one of the first infections for which such modeling was applied. However, there is still an urgent need for new models that can compare the potential impact of a comprehensive range of malaria interventions. The simulations of malaria infections are linked to models of interventions and health systems, epidemiology to predict the impacts of interventions on infection, morbidity, mortality, health services use and costs. An intervention is a method used to bring about a change in the state of the simulations (example to reduce transmission). Some of these are realistic strategies (e.g. vaccine treatment), some are unrealistic (e.g. “uninfect vectors”), whilst others don’t concern themselves with transmission (e.g. cohort selection).

This chapter presents the review of literature on the mathematical models for communicable diseases. The literature is vast for example, the survey by Hethcote et al. (1982). In most of these models, the assumption of constant total populations is often made. Mathematical modelling of malaria has flourished since the days of Ross (1911), who was the first to model the dynamics of malaria transmission, and Macdonald (1950; 1952; 1957) who expounded on Ross' work, introducing the theory of superinfection. Using data from the Garki project (1980), many studies have been carried out on the epidemiology of malaria and one of the most outstanding is the mathematical model proposed by Dietz (1975) which Nedelman (1982) analysed in detail. Further works on the subject include: Singer and Cohen

(1980), Gaton et. al. (1980), Aron and May (1982) and the review by Nedelman (1985).

2.2 The Ross-MacDonald model

Many people have developed malaria models and most of them are either directly related to the Ross-MacDonald model (Ross 1909; Macdonald 1957) or borrow many of their concepts from this model. Ross began mathematical modeling of malaria whilst Macdonald (1957) also made major extensions to the work done by Ross and the model later on became known as Ross-Macdonald model. It is defined as

$$\frac{dx}{dt} = \left(abM/N\right) y(1-x) - rx \tag{1.1a}$$

$$\frac{dy}{dt} = ax(1-y) - \mu y \tag{1.1b}$$

where x represents the fraction of infectious humans; y represents the fraction of infectious female mosquitoes; a represents the number of bites on humans by a single female mosquito per unit time (usually day); b is the probability of transmission of infection from an infected mosquito to a susceptible human per bite; M represents the total female mosquito population; N represents the total human population; r represents the rate of recovery for infectious humans ($1/r$) is the average duration of the infectious period); and μ represents the death rate of the female mosquito population ($1/\mu$) represents the average lifespan of an adult mosquito).

In the view of Aron and May (1982), the properties of this model, including the derivation of the reproductive number, R_o, could be described as

$$R_o = \frac{M}{N}\frac{a^2 b}{\mu r}. \tag{1.2}$$

2.3 The Reproductive Number, R_o

The reproductive number, R_o is defined as the number of secondary infections that one infectious person would produce in a fully susceptible population through the entire duration of the infectious period. In the study done by Heesterbeek (2002), he conducted a review on the history of R_o. Key studies in this area include those by Diekmann, Heesterbeek, and Metz (1990); Dietz (1993); Heesterbeek (1992); Heesterbeek and Dietz (1996); Roberts and Heesterbeek (2003); Simon and Jacquez (2003); Mathematical Biosciences, 180 (2002), which are devoted to the calculation of Ro for different models of various diseases, including malaria.

For simple homogeneous models, the reproductive number, R_o, can be defined as the product of the number of contacts that one individual has per unit time, the probability of transmission per contact and the duration of the infectious period. From equation (1.1) above, it can be deduced that R_o is simply the product of the number of mosquitoes that one infectious human infects and the number of humans that one infectious mosquito infects, through the duration of their infectious periods.

Considering equation (1.1a) above, $(^{aM}/_{N})$ represents the number of contacts with mosquitoes that one human has per unit time; the probability of transmission from an infectious human to a susceptible mosquito is assumed to be 1; and $^{1}/_{r}$ is the average duration of the infectious period of the human. It can therefore be deduced that $(^{M}/_{N})$ $(^{a}/_{r})$ is the number of mosquitoes that one human infects over the entire infectious period. Similarly, a represents the number of contacts with humans that one mosquito has per unit time; b is the probability of transmission from an infectious mosquito to a susceptible human; and $^{1}/_{\mu}$ is the average duration of the

infectious period of the mosquito (note that female mosquitoes are infectious till death). It can be deduced that (ab/μ) is the number of humans that one mosquito infects through its infectious lifetime. We can now prove from equation (1.2) that the product of the two, $\left(M/N\right)\left(a^2b/(r\mu)\right)$, forms the reproductive number: the number of humans that one infectious human will infect, through a generation of infectious mosquitoes.

The result of the studies by Aron and May (1982), also added various characteristics of malaria, such as an incubation period in the mosquito, a periodically fluctuating density of mosquitoes, super-infection and a period of immunity in humans, to the model. Also included was the continuum model for immunity where the dynamical variables are the population of asexual blood stages of Plasmodium in humans, the population of gametocytes (sexual stages of Plasmodium in humans), and the level of human immunity. In this system of partial differential equations, the variables depend on both time and age. The mosquitoes are modeled through V, the vectorial capacity, which is proportional to the mosquito density. The study resulted in a model which is a major deviation from the Ross-Macdonald model (1.1) as it does not keep track of the number of infected humans and mosquitoes. Instead, this continuum model measures the number of parasites and level of immunity in the average human. This is useful for malaria because there can be a large deference in the parasitemia load in different humans, that the Ross-Macdonald model ignores.

The studies as noted by Anderson and May (1991) revisit many of the ideas discussed by Aron and May (1982). In addition to the above, Anderson and May (1991) compile numerous data sets for parameter values, including the latent period in mosquitoes and humans, the rate of recovery for humans, the expected adult

lifespan of mosquitoes and malaria prevalence data across age distributions for humans. Additionally, Anderson and May (1991) study the effect of adding age structure to the basic Ross-Macdonald model (1.1). Finally, they look at different control strategies, discussing the effects of a vaccine and the reduction of transmission rates on the malaria age-prevalence profile of the human population.

Other reviews on mathematical modeling in malaria include Nedelman (1985) and Koella (1991). In the study done by Nedelman (1985), he surveys various data sets to statistically approximate parameters such as inoculation rates, rates of recovery and loss of immunity in humans, human-biting rates of mosquitoes and infectivity and susceptibility of humans and mosquitoes. Koella (1991) also begins with the Ross-Macdonald model (1.1) with an additional latent stage for the mosquitoes. He then studies the effect of variability of the parameters and adds an infection-rate dependent period of immunity. Using this model with immunity, he studies the effects of vaccines, comparing those that act on asexual blood stages and those that block transmission, to show that the asexual blood stage vaccines are more effective.

2.4 Inclusion of acquired immunity in the model

An important advance for the mathematical modeling of malaria was the inclusion of acquired immunity in the model proposed by Dietz, Molineaux and Thomas (1974). In the study by Dietz et al. (1974), he proposed a model with two different classes of humans: one without immunity to malaria and one class with some immunity. According to Dietz and his colleagues (1974), when the non-immune class falls sick, some people recover with immunity. The immune class can get infected, but does not fall clinically ill and cannot be infectious. The model by Dietz et al. (1974) also included super-infection, a phenomenon usually associated

with macro parasites. In the study done by Aron and May (1982) and Anderson and May (1991), they described that super-infection is a significant increase of the parasite load, when an infected person is reinfected from the outside. This is usually modeled by making the recovery rate (r in the above equation (1.1)) a (usually monotonically non-increasing) function of the inoculation rate. Various models, with super-infection, for the recovery rate, r, include:

Ross (1991): $$r = \gamma \tag{1.3a}$$

Dietz et al. (1974): $$r = \lambda / \left[\exp\left(\lambda / \gamma \right) - 1 \right] \tag{1.3b}$$

Macdonald (1957): $$r = \begin{cases} \gamma - \lambda, & \gamma > \lambda \\ 0, & \gamma \leq \lambda \end{cases} \tag{1.3c}$$

where λ is the inoculation rate (defined in (1.1) as , $\lambda = \lambda\left(abM / N \right) y$ and γ is the reinfection-free rate of recovery i.e. $1/\gamma$ is the average duration of the infectious period in the absence of further infection. In another study conducted by Bailey (1975), he also described the model for super-infection by Dietz (1993).

Another proposition put forward by Aron, (1988) reviews the compartmental and continuous models for temporary immunity in humans. In compartmental models, an additional recovered class is added. In the usual Susceptible-Infectious-Recovered-Susceptible (SIRS) or Susceptible-Exposed-Infectious-Recovered-Susceptible (SEIRS) model, the rate of loss of immunity, ρ is a constant parameter. However, sustained immunity to malaria requires continuous reinfection; thus in the absence of reinfection, immunity is lost quickly, while in the presence of a high infection rate, immunity is long-lived. This non-constant period of immunity can be modeled by making the rate of loss of immunity, ½, a function of the inoculation rate as in the equation below;

$$\rho(\lambda) = \frac{\lambda e^{-\lambda\tau}}{1 - e^{-\lambda\tau}}\ , \qquad (1.4)$$

where λ is the inoculation rate and τ is the average duration of the immune period in the absence of infection.

2.5 Inclusion of the effects of environment on the model

Some of the more recent papers on the mathematical modeling of malaria have included environmental effects, according to studies done by Li et al. (2002); Yang (2002) and Yang and Ferreira (2000). In the study of Yang (2002), he describes a compartmental model where humans follow an SEIRS-type (with more than one immune class for humans) pattern and mosquitoes follow a Susceptible-Exposed-Infectious (SEI) pattern. Additionally, some of the parameters related to mosquitoes are now a function of temperature. These include the time taken for mosquito eggs to develop into adults and the time taken for Plasmodium gametocytes ingested by the mosquito to develop into sporozoites and migrate to the salivary glands (the incubation time in the mosquito). Yang defines a reproductive number, R_o for this model and shows, through linear stability analysis, that the disease-free equilibrium is stable for $R_o < 1$. He also derives an expression for an endemic equilibrium that is biologically relevant only when $R_o>1$. He uses numerical simulations to support his proposition that for $R_o > 1$, the disease-free equilibrium is unstable and the endemic equilibrium is stable.

2.6 Inclusion of effects of global warming

Other studies, as noted by Yang and Ferreira (2002), use the model by Yang (2000) to study the effects of global warming. Using the estimated increase in temperature of 1.0^{o}C-3.5^{o}C by the year 2100, they show that it is possible in some areas of the world for R_o to increase above 1; for areas to change from a stable disease-free endemic state to one with low levels of endemicity and for other areas to

change from low levels of endemicity to high levels. They do, however, conclude by saying that economic and social effects are still more important than temperature effects and a good health care system with good malaria control techniques can overcome the negative effects of an increase in temperature.

In addition to the findings, Li et al. (2002) derive a model where humans move through multiple Susceptible-Exposed-Infectious-Recovered (SEIR) stages, where a history is kept of previous infections. They include a sub-model for the mosquito population with subdivisions for juveniles and adults. They use the steady state value for the adult mosquito population, from this sub-model, as the input into their model for malaria transmission. They introduce dependence of the parameters for the mosquito population sub-model on an environmental parameter (e.g. temperature or rainfall) and calculate the dependence of the reproductive number, for the full malaria model, on this environmental parameter.

2.7 Inclusion of spread of drug-resistant Plasmodium

Other recent models have included the spread of drug-resistant Plasmodium Koella and Antia (2003) and of the evolution of immunity Koella and BoÄete (2003). The study by Koella and Antia (2003) discuss a model where, starting with the Ross-Macdonald model (1.1) and moving to more complicated models, they include a strain of disease that is resistant to treatment. Their results show that in their simplest models, there is a threshold value of fraction of infectious humans treated, below which there is no resistance to drugs, and above which, resistance to treatment spreads. In the more complicated models, this kind of resistance is usually not fixed, but there is some level of sensitivity to drugs that is maintained in the population. Koella and BoÄete (2003) study a host-parasite evolution model of

malaria where the host invests in its immune system over time and the parasite invests in its ability to evade the host's immune response.

The model for malaria transmission that we analyse is an extension of the equations introduced by Ngwa and Shu (2000). In the Ngwa and Shu (2000) model, humans follow an SEIRS-like pattern and mosquitoes follow a SEI pattern, similar to that described by Yang (2000) but with only one immune class for humans. Humans move from the susceptible to the exposed class at some probability when they come into contact with an infectious mosquito, and then to the infectious class, as in conventional SEIRS models. However, infectious people can then recover with, or without, a gain in immunity; and either return to the susceptible class, or move to the recovered class. A new feature of this model is that although individuals in the recovered class are assumed to be “immune”, in the sense that they do not suffer from serious illness and do not contract clinical malaria, they still have low levels of Plasmodium in their blood stream and can pass the infection to susceptible mosquitoes. After some period of time these recovered individuals return to the susceptible class. Susceptible mosquitoes get infected and move to the exposed class, at some probability when they come into contact with either infectious humans or recovered humans. They then pass on to the infectious class. Both humans and mosquitoes leave the population through a density dependent natural death rate. This allows the model to account for changing human and mosquito populations. Variations in mosquito populations are crucial to the dynamics of malaria, and constant population models do not account for this. The model also includes human disease-induced death as mortality for malaria in areas of high transmission can be high, especially in infants.

Ngwa and Shu (2000) analyze this model assuming a linear per capita death rate. They convert the system to dimensionless quantities and in these new variables, define a reproductive number, R_o. They show that when $R_o > 1$, there exists an endemic equilibrium (non-negative solution distinct from the disease-free equilibrium), and furthermore, with no disease-induced death, this endemic equilibrium is unique. Using linear analysis, they also show that the disease-free equilibrium is locally asymptotically stable when $R_o=1$ and the unique endemic equilibrium (for no disease-induced death) is locally asymptotically stable when $R_o >1$. They conclude by using numerical simulations to support their proposition that the endemic equilibrium is stable for $R_o > 1$.

In a second paper Ngwa (2004) rewrites the reproductive number in terms of the original (with dimension) parameters. He also includes a small disease induced death rate, using perturbation analysis to evaluate a first order approximation to the endemic equilibrium with disease induced death. Finally, he conducts some numerical simulations on a stochastic expansion of the model. This profusion of models has been driven by the need to understand different aspects of the complex malaria epidemiology. In the model we analyze, we aim to capture some of the more important aspects of this epidemiology while still keeping it mathematically tractable. Some of the important factors that we include are the presence of an exposed state in mosquitoes and dynamically changing human and mosquito populations, including human immigration and disease-induced death.

CHAPTER THREE

METHODOLOGY

3.0 Introduction

This chapter investigates the dynamics of malaria in both human and vector populations. The model describes the dynamics of the two populations that interact with each other to cause the spread of the disease in the region. We derived threshold conditions to better understand the behaviour, trend and dynamics of the disease in the population. The model under study is similar to that by Chitnis, (2005) and Mwamtobe, (2010) and based on intervention strategies such as natural death, indoor residual spraying, and clinical treatment.

3.1 The malaria model:

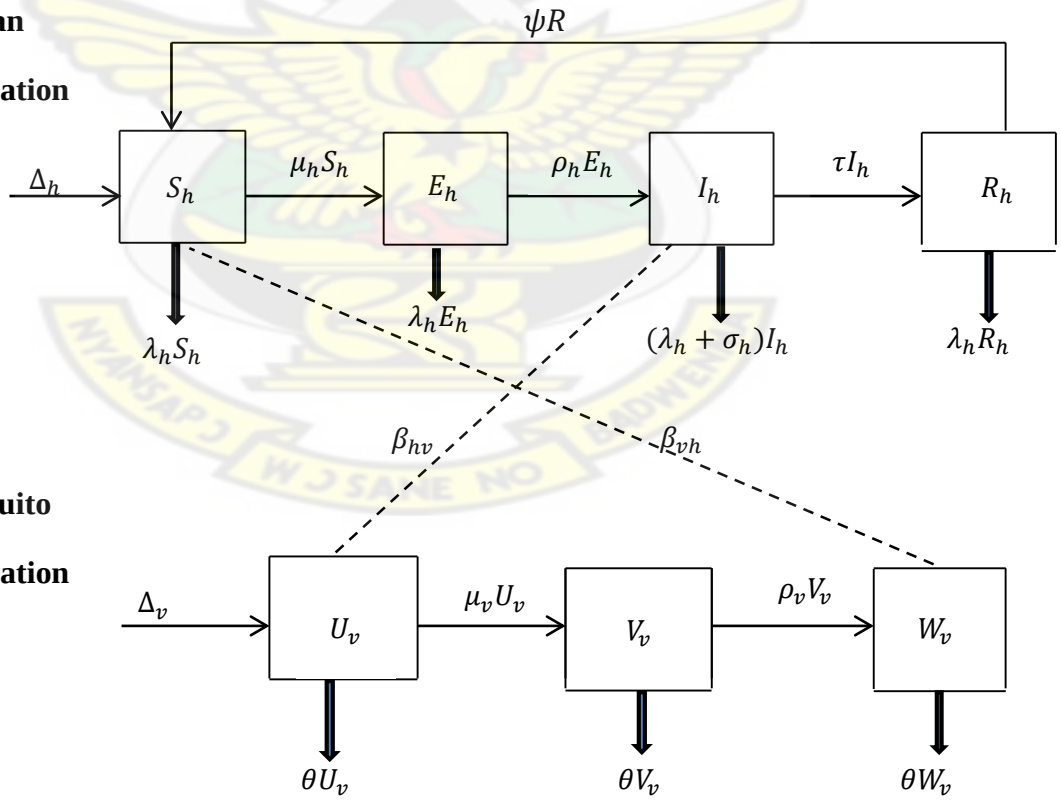

Figure 3.1: A diagrammatic representation of the model.

Susceptible humans, S_h, get infected when they are bitten by infectious mosquitoes. They then progress through the exposed, E_h, infectious, I_h, and recovered, R_h, classes, before returning to the susceptible class. Susceptible mosquitoes, U_v , also become infected when they bite infectious humans. The infected mosquitoes then move through the exposed, V_v , and infectious, W_v , classes.

3.2 Model description and formulation

This model describes the dynamics of two populations namely: human population and vector (mosquito) population, interacting with each other. The model divides both populations into compartments and with assumptions about the nature and time rate of transfer from one compartment to another. The human population (N_h) is divided into four compartments: susceptible or those at risk to infection (S_h), exposed (E_h), infected (I_h) and those who recover from infection (R_h). The vector population (N_v) is also divided into three compartments: susceptible vector (U_v), exposed vector (V_v) and infected vector (W_v).

In this model, the human population is recruited at a constant rate, Δ_h. When an infectious mosquito bites a susceptible human, the parasite is passed on to the human and that person will move to the exposed class at the rate μ_h. Again, the individual in the exposed class then move to the infectious class at a rate ρ_h. After some time, the infectious humans recover and move to the recovered class at the rate, τ. The recovered humans have some immunity to the disease and do not get clinically ill, but they still harbor low levels of parasite in their blood streams and can pass the infection to mosquitoes. After some period of time, they lose their immunity and return to the susceptible class. Humans leave the population through natural death at the rate, λ_h and the infected humans have an additional disease-

induced death rate constant, σ_h. Since most sick people do not travel, we do not include immigration of infectious humans. Again, since the number of exposed humans is insignificant, we exclude them given the short time of the exposed stage. We make the assumption that there is no immigration of recovered humans.

Female anopheles enters the susceptible class through birth at a rate Δ_v. The mosquito then moves from the susceptible to the exposed (incubating) class at the rate μ_v and after some time, depending on the humidity and temperature, the mosquito progresses at a rate ρ_v, from the exposed class to the infectious class. The mosquito remains infectious for life. Mosquitoes leave the population through a per capita natural death rate.

In other words, new infections occur in both populations where β_{vh} and β_{hv} are the respective rates of infection between susceptible human and infected vector, and susceptible vector and infected human. The effective contact rates between the two populations, which may be defined as the average number of contacts per day that will lead to the infection of one party if the other party was infectious, depends on a number of factors: the man biting rate of the mosquitoes, the transmission probabilities between the species and the number of individuals in both population.

We first describe the mathematical model including the definition of a domain where the model is mathematically and epidemiologically well-posed. We also define the reproductive number and then prove the existence and stability of both the disease-free equilibrium point and the endemic equilibrium point.

3.2.1 The state variables and model parameters

The state variables (Table 3.1) and parameters (Table 3.2) for the malaria model (Figure 3.1) satisfy the equations (3.1a and 3.1b). It is to be noted that all the

parameters are strictly positive with the exception of the disease-induced death rate, σ_h, which is nonnegative. Also, the mosquito birth rate must be greater than the mosquito death rate, to ensure that we have a stable positive mosquito population.

Table 3.1: The state variables for the malaria model

Parameter	Description
S_h	Number of susceptible humans
E_h	Number of exposed humans
I_h	Number of infectious humans
R_h	Number of recovered humans
U_v	Number of susceptible mosquitoes
V_v	Number of exposed mosquitoes
W_v	Number of infectious mosquitoes
N_h	Total human population
N_v	Total mosquito population

Table 3.2: Parameters of the model

Parameter	Description
Δ_h	Recruitment rate of humans.
Δ_v	Recruitment rate of mosquitoes.
μ_h	Progression rate of susceptible humans to exposed individuals.
μ_v	Progression rate of susceptible mosquitoes to exposed mosquitoes.

$\boldsymbol{\rho_h}$	Progression rate of exposed humans to infected individuals.
$\boldsymbol{\rho_v}$	Progression rate of exposed mosquitoes to infected mosquitoes.
$\boldsymbol{\tau}$	Rate of recovery of humans from the infectious state to the recovered state – clinical treatment.
$\boldsymbol{\lambda_h}$	Natural death rate for humans.
$\boldsymbol{\theta}$	Death of mosquitoes due to natural death and indoor residual spraying
$\boldsymbol{\sigma_h}$	Disease-induced death rate for humans.
$\boldsymbol{\psi}$	Rate of loss of immunity.
$\boldsymbol{\beta_{vh}}$	Probability that a bite results in transmission of infection from an infectious mosquito to a susceptible human.
$\boldsymbol{\beta_{hv}}$	Probability that a bite results in transmission of parasite from an infectious human to a susceptible mosquito.
$\boldsymbol{\vartheta}$	Mosquito biting rate.

3.1.2 Equations of the model:

The dynamics of the groups described above and as shown in the flow diagram (3.1) are described by the system of differential equations given by:

Human population:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Delta_h + \psi R_h - \left(\lambda_h + \mu_h\right) S_h \\
\frac{dE_h}{dt} &= \mu_h S_h - (\lambda_h + \rho_h) E_h \\
\frac{dI_h}{dt} &= \rho_h E_h - (\tau + \lambda_h + \sigma_h) I_h \\
\frac{dR_h}{dt} &= \tau I_h - (\psi + \lambda_h) R_h
\end{aligned}\right\} \qquad (3.1a)$$

Mosquito population:
$$\left.\begin{aligned} \frac{dU_v}{dt} &= \Delta_v - (\mu_v + \theta)U_v \\ \frac{dV_v}{dt} &= \mu_v U_v - (\rho_v + \theta)V_v \\ \frac{dW_v}{dt} &= \rho_v V_v - \theta W_v \end{aligned}\right\}$$

Total population:
$$\left.\begin{aligned} N_h &= S_h + E_h + I_h + R_h \\ N_v &= U_v + V_v + W_v \end{aligned}\right\}, \qquad (3.1b)$$

where $\mu_h = \frac{\beta_{vh}\vartheta W_v}{N_h}$ is the rate of infection between susceptible human and infected vector, and $\mu_v = \frac{\beta_{hv}\vartheta I_h}{N_h}$ is the rate of infection between susceptible vector and infected human.

3.3 Basic properties of the malaria model

The basic properties which are used in proving the stability of the system are the invariant region and positivity of solutions.

3.3.1 Invariant region

The invariant region describes the region in which the solution of the system makes biological sense**.** We can determine the total population sizes N_h and N_v from the differential equations of the model system.

Now, considering the human population in (3.1a), we have

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dE_h}{dt} + \frac{dI_h}{dt} + \frac{dR_h}{dt}$$

$$= \Delta_h - \lambda_h S_h - \lambda_h E_h - \lambda_h I_h - \lambda_h R_h - \sigma_h I_h$$

$$= \Delta_h - \lambda_h \left(S_h + E_h + I_h + R_h\right) - \sigma_h I_h$$

Hence, $$\frac{dN_h}{dt} = \Delta_h - \lambda_h N_h - \sigma_h I_h \tag{3.2}$$

Also, considering the vector population of the model system (3.1a), we have

$$\frac{dN_v}{dt} = \frac{dU_v}{dt} + \frac{dV_v}{dt} + \frac{dW_v}{dt}$$

$$= \Delta_v - \theta U_v - \theta V_v - \theta W_v$$

$$= \Delta_v - \theta(U_v + V_v + W_v)$$

Hence, $$\frac{dN_v}{dt} = \Delta_v - \theta N_v \tag{3.3}$$

We assume that all the variables and parameters of the model are positive for all $t \geq 0$. In the absence of the disease, ($\sigma_h = 0$), equation (3.2) becomes

$$\frac{dN_h}{dt} = \Delta_h - \lambda_h N_h - \sigma_h I_h \leq \Delta_h - \lambda_h N_h$$

Hence $$\frac{dN_h}{dt} \leq \Delta_h - \lambda_h N_h \tag{3.4}$$

When we apply both the Birkhoff and Rota (1989) theorem of differential inequality and separation of variables of differential inequality on equation (3.4), we get

$$\frac{dN_h}{\Delta_h - \lambda_h N_h} \leq dt.$$

Integrating both sides of the equation above, we have,

$$\int \frac{dN_h}{\Delta_h - \lambda_h N_h} \leq \int dt$$

$$\frac{-1}{\lambda_h}\ln\left(\Delta_h - \lambda_h N_h\right) \le t + c$$

$$\ln\left(\Delta_h - \lambda_h N_h\right) \ge -\lambda_h\left(t + c\right).$$

Hence, $$\Delta_h - \lambda_h N_h \ge Ae^{-\lambda_h t}, \tag{3.5}$$

where A is a constant. Now, if we apply the initial condition $N_h(0) = (N_h)_0$, we have

$$A = \Delta_h - \lambda_h (N_h)_0$$

Substituting $A = \Delta_h - \lambda_h (N_h)_0$ into equation (3.5), we have

$$\Delta_h - \lambda_h N_h \ge (\Delta_h - \lambda_h (N_h)_0)\, e^{-\lambda_h t}$$

Hence, $$N_h \le \frac{\Delta_h}{\lambda_h} - \left[\frac{\Delta_h - \lambda_h (N_h)_0}{\lambda_h}\right] e^{-\lambda_h t}. \tag{3.6}$$

where $(N_h)_0$ represents the value of the first equation of (3.1b) evaluated at the initial values of the respective variables. Thus as $t \to \infty$, we have $0 \le N_h \le \frac{\Delta_h}{\lambda_h}$.

This indicates that N_h is bounded and all the feasible solutions of the human only component of the model system starting in the region Ω_h approach, enter or stay in the region, where

$$\Omega_h = \left\{\left(S_h, E_h, I_h, R_h\right) \in \mathbb{R}_+^4 : N_h \le \frac{\Delta_h}{\lambda_h}\right\}. \tag{3.7}$$

Similarly, from equation (3.3) above, we can write

$$\frac{dN_v}{dt} \le \Delta_v - \theta N_v \tag{3.8a}$$

Applying both the Birkhoff and Rota (1989) theorem of differential inequality and separation of variables of differential inequality on equation (3.8a), we will have

$$\frac{dN_v}{\Delta_v - \theta N_v} \leq dt\,.$$

Integrating both sides of the equation above, we have

$$\int \frac{dN_v}{\Delta_v - \theta N_v} \leq \int dt$$

$$\frac{-1}{\theta}\ln\left(\Delta_v - \theta N_v\right) \leq t + c$$

$$\ln\left(\Delta_v - \theta N_v\right) \geq -\theta\left(t + c\right).$$

Hence, $$\Delta_v - \theta N_v \geq Be^{-\theta t}, \tag{3.8b}$$

where B is a constant. Now, applying the initial condition, $N_v(0) = (N_v)_0$ we have

$$B = \Delta_v - \theta(N_v)_0$$

Substituting $B = \Delta_v - \theta(N_v)_0$ into equation (3.8b), we have

$$\Delta_v - \theta N_v \geq (\Delta_v - \theta(N_v)_0)\, e^{-\theta t}$$

$$N_v \leq \frac{\Delta_v}{\theta} - \left[\frac{\Delta_v - \theta(N_v)_0}{\theta}\right] e^{-\theta t} \tag{3.9}$$

where $(N_v)_0$ represents the value of the second equation of (3.1b) evaluated at the initial values of the respective variables. Thus as $t \to \infty$, we have

$$0 \leq N_v \leq \frac{\Delta_v}{\theta}$$

This shows that N_v is bounded and all the feasible solutions of the mosquito only component of the model system starting in the region Ω_v approach, enter or stay in the region, where

$$\Omega_v = \left\{ \left(U_v, V_v, W_v \right) \in \mathbb{R}_+^3 : N_v \leq \frac{\Delta_v}{\theta} \right\}. \tag{3.10}$$

Finally, it follows from equations (3.7) and (3.10) that N_h and N_v are bounded and all the possible solutions of the model starting in Ω will approach, enter or stay in the

$$\Omega = \left\{ \left(S_h, E_h, I_h, R_h, U_v, V_v, W_v \right) \in \mathbb{R}_+^7 : N_h \leq \frac{\Delta_h}{\lambda_h}; N_v \leq \frac{\Delta_v}{\theta} \right\}, \tag{3.11}$$

which is a positively invariant set under the flow induced by the model (3.1). The solution of the system (3.1) remains in Ω for all $t > 0$ and thus the model is biologically meaningful and epidemiologically well posed in the domain Ω.

3.3.2 Positivity of solutions

The positivity of solutions describes non-negativity of solutions of system.

Theorem 1: Let the initial conditions for the model system (3.1) be $\left\{ \left(S_h(0), U_v(0) \right) > 0, \left(E_h(0), I_h(0), R_h(0), V_v(0), W_v(0) \right) \geq 0 \right\} \in \Omega$. Then, the solution set $\left\{ S_h(t), E_h(t), I_h(t), R_h(t), U_v(t), V_v(t), W_v(t) \right\}$ of the system (3.1) is positive for all $t > 0$.

Proof 1: Considering equation (3.1a) of the model,

$$\frac{dS_h}{dt} = \Delta_h + \psi R_h - \left(\lambda_h + \mu_h \right) S_h \geq -\left(\lambda_h + \mu_h \right) S_h$$

Hence, $$\frac{dS_h}{dt} \geq -\left(\lambda_h + \mu_h\right) S_h \tag{3.12}$$

Integrating equation (3.12) by separation of variables gives

$$\int \frac{dS_h}{dt} \geq -\int \left(\lambda_h + \mu_h\right) S_h$$

$$\int \frac{dS_h}{S_h} \geq -\int \left(\lambda_h + \mu_h\right) dt$$

$$lnS_h \geq -\int \left(\lambda_h + \mu_h\right) dt$$

$$S_h \geq e^{-\int (\lambda_h + \mu_h) dt} \tag{3.13}$$

Applying the initial conditions to equation (3.13), we will have

$$S_h(t) \geq S_h(0) e^{-\int (\lambda_h + \mu_h) dt} \geq 0$$

Similarly, from equation (3.1b) of the model,

$$\frac{dE_h}{dt} = \mu_h S_h - (\lambda_h + \rho_h) E_h \geq -(\lambda_h + \rho_h) E_h$$

$$\frac{dE_h}{dt} \geq -(\lambda_h + \rho_h) E_h \tag{3.14}$$

Integrating equation (3.14) by separation of variables leads to

$$\int \frac{dE_h}{dt} \geq -\int (\lambda_h + \rho_h) E_h$$

$$\int \frac{dE_h}{E_h} \geq -\int \left(\lambda_h + \rho_h\right) dt$$

$$lnE_h \geq -\int \left(\lambda_h + \rho_h\right) dt$$

$$E_h \geq e^{-\int (\lambda_h + \rho_h) dt} \tag{3.15}$$

Applying the initial conditions to (3.15) gives

$$E_h(t) \geq E_h(0)e^{-\int(\lambda_h+\rho_h)dt} \geq 0.$$

Therefore, it can be shown that the remaining equations of the model system (3.1) are positive for all $t > 0$.

3.4 Analysis of the model

3.4.1 Existence and stability of steady-state solutions

Let $E(S_h^{\diamond}, E_h^{\diamond}, I_h^{\diamond}, R_h^{\diamond}, U_v^{\diamond}, V_v^{\diamond}, W_v^{\diamond})$ be the equilibrium points of the model system (3.1). The equilibrium points can be obtained by setting the right hand side of (3.1) equal to zero. That is,

$$\left.\begin{aligned} \Delta_h + \psi R_h - (\lambda_h + \mu_h)S_h &= 0 \\ \mu_h S_h - (\lambda_h + \rho_h)E_h &= 0 \\ \rho_h E_h - (\tau + \lambda_h + \sigma_h)I_h &= 0 \\ \tau I_h - (\psi + \lambda_h)R_h &= 0 \\ \Delta_v - (\mu_v + \theta)U_v &= 0 \\ \mu_v U_v - (\rho_v + \theta)V_v &= 0 \\ \rho_v V_v - \theta W_v &= 0 \end{aligned}\right\} \quad (3.16)$$

3.4.2 Existence of Disease-Free Equilibrium point, E_o

The disease-free equilibrium points of a disease model are its steady-state solutions in the absence of disease or infection. We define the "diseased" classes as the human or mosquito populations that are either exposed or infectious. In the absence of disease, we have $(E_h^{\diamond} = 0,\ I_h^{\diamond} = 0,\ R_h^{\diamond} = 0,\ V_v^{\diamond} = 0 \, and \, W_v^{\diamond} = 0)$, and this reduces equation (3.16) to

$$\left.\begin{aligned} \Delta_h - \lambda_h S_h^{\diamond} &= 0 \\ \Delta_v - \theta U_v^{\diamond} &= 0 \end{aligned}\right\} \quad (3.17)$$

The positive disease-free equilibrium for human and vector populations for the model system are $N_h = \frac{\Delta_h}{\lambda_h}$ and $N_v = \frac{\Delta_v}{\theta}$.

Hence, $$E_o = \left[\frac{\Delta_h}{\lambda_h}, 0, 0, 0, \frac{\Delta_v}{\theta}, 0, 0 \right]. \quad (3.18)$$

This is the disease-free equilibrium point and there is virtually no disease in this state.

3.4.3 The Basic Reproduction Number, R_o

The basic reproduction number, according to Diekmann et al. (2000) and J.D. Murray (2002), is the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual. It helps us to set the threshold in the study of the disease both for predicting its outbreak and for evaluating its control strategies. Thus, the reproduction number, R_o, simply enables us to know whether a disease has died out or is persistent in a community.

We use $R_o = 1$ as a threshold below which the generation of secondary cases is insufficient to maintain the infection with human community. If $R_o < 1$ it implies that, on average an infected individual produces less than one new infected individual during the infectious period and the infection can be wiped out. Conversely, if $R_o > 1$, then infectious individuals can cause more than one secondary infection. Hence the disease will spread in the community whereas a large number of R_o is an indication of a major epidemic. Therefore it is advised that the effectiveness of health control strategies should lower R_o to less than zero.

The reproductive number R_o is computed using the next generation operator approach by van den Driessche and Watmough (2002) which is described in

Appendix A. From the system (3.1), we rewrite the equations starting with infectious classes for both the human and vector populations: E_h, I_h, V_v, W_v and the rest follow;

$$\left.\begin{aligned}
\frac{dE_h}{dt} &= \frac{\beta_{vh}\vartheta W_v}{N_h}S_h - (\lambda_h + \rho_h)E_h \\
\frac{dI_h}{dt} &= \rho_h E_h - (\tau + \lambda_h + \sigma_h)I_h \\
\frac{dV_v}{dt} &= \frac{\beta_{hv}\vartheta I_h}{N_h}U_v - (\rho_v + \theta)V_v \\
\frac{dW_v}{dt} &= \rho_v V_v - \theta W_v \\
\frac{dS_h}{dt} &= \Delta_h + \psi R_h - \left(\lambda_h + \frac{\beta_{vh}\vartheta W_v}{N_h}\right)S_h \\
\frac{dR_h}{dt} &= \tau I_h - (\psi + \lambda_h)R_h \\
\frac{dU_v}{dt} &= \Delta_v - (\frac{\beta_{hv}\vartheta I_h}{N_h} + \theta)U_v
\end{aligned}\right\} \quad (3.19).$$

The next generation matrix method was used to show the rate of appearance of new infection in compartments E_h and V_v, from the system (3.19);

$$F = \begin{bmatrix} \frac{\beta_{vh}\vartheta W_v S_h}{N_h} \\ 0 \\ \frac{\beta_{hv}\vartheta I_h U_v}{N_h} \\ 0 \end{bmatrix} \quad (3.20a)$$

The Jacobian matrix of $\mathcal{F}$ at $E_o = \left[\frac{\Delta_h}{\lambda_h}, 0, 0, 0, \frac{\Delta_v}{\theta}, 0, 0\right]$ where $N_h \le \frac{\Delta_h}{\lambda_h}$ and $N_v \le \frac{\Delta_v}{\theta}$ to form the Jacobian matrix,

$$F = \begin{bmatrix} 0 & 0 & 0 & \beta_{vh}\vartheta \\ 0 & 0 & 0 & 0 \\ 0 & \dfrac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\theta\Delta_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{3.20b}$$

Also, the transfer of humans out of the compartments of the model system by all other means

$$V = \begin{bmatrix} (\lambda_h + \rho_h)E_h \\ (\tau + \lambda_h + \sigma_h)I_h - \rho_h E_h \\ (\rho_v + \theta)V_v \\ \theta W_v - \rho_v V_v \end{bmatrix} \tag{3.21a}$$

Jacobian matrix of V is given by

$$V = \begin{bmatrix} (\rho_h + \lambda_h) & 0 & 0 & 0 \\ -\rho_h & (\tau + \lambda_h + \sigma_h) & 0 & 0 \\ 0 & 0 & (\rho_v + \theta) & 0 \\ 0 & 0 & -\rho_v & \theta \end{bmatrix} \tag{3.21b}$$

The inverse of matrix V is given by

$$V^{-1} = \begin{bmatrix} \dfrac{1}{(\rho_h + \lambda_h)} & 0 & 0 & 0 \\ \dfrac{\rho_h}{(\rho_h + \lambda_h)(\tau + \lambda_h + \sigma_h)} & \dfrac{1}{(\tau + \lambda_h + \sigma_h)} & 0 & 0 \\ 0 & 0 & \dfrac{1}{(\rho_v + \theta)} & 0 \\ 0 & 0 & \dfrac{\rho_v}{\theta(\rho_v + \theta)} & \dfrac{1}{\theta} \end{bmatrix} \tag{3.21c}$$

The product of $F \text{ and } V^{-1}$ is given by

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & \beta_{vh}\vartheta \\ 0 & 0 & 0 & 0 \\ 0 & \dfrac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\theta\Delta_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \dfrac{1}{(\rho_h+\lambda_h)} & 0 & 0 & 0 \\ \dfrac{\rho_h}{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)} & \dfrac{1}{(\tau+\lambda_h+\sigma_h)} & 0 & 0 \\ 0 & 0 & \dfrac{1}{(\rho_v+\theta)} & 0 \\ 0 & 0 & \dfrac{\rho_v}{\theta(\rho_v+\theta)} & \dfrac{1}{\theta} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \dfrac{\beta_{vh}\vartheta\rho_v}{\theta(\rho_v+\theta)} & \dfrac{\beta_{vh}\vartheta}{\theta} \\ 0 & 0 & 0 & 0 \\ \dfrac{\rho_h\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)} & \dfrac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta(\tau+\lambda_h+\sigma_h)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{3.22}$$

We let $s = \dfrac{\rho_h\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)}$, $t = \dfrac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta(\tau+\lambda_h+\sigma_h)}$, $q = \dfrac{\beta_{vh}\vartheta\rho_v}{\theta(\rho_v+\theta)}$, and $r = \dfrac{\beta_{vh}\vartheta}{\theta}$.

If we substitute s, t, q and r into equation (3.22), we have

$$FV^{-1} = \begin{bmatrix} 0 & 0 & q & r \\ 0 & 0 & 0 & 0 \\ s & t & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}. \tag{3.23}$$

We now calculate the eigenvalue of equation (3.23) to determine the reproduction number, R_0, defined as the spectral radius (dominant eigenvalue) of the matrix. The eigenvalues of FV^{-1} are computed from $D = \left|FV^{-1} - I\lambda\right| = 0$.

$$D = \begin{vmatrix} -\lambda & 0 & q & r \\ 0 & -\lambda & 0 & 0 \\ 0 & 0 & -\lambda & 0 \\ s & t & 0 & -\lambda \end{vmatrix} = 0 . \tag{3.24}$$

The eigenvalues of the matrix (3.24) is

$$\lambda_i = \begin{bmatrix} 0 \\ 0 \\ 0 \\ \sqrt{\frac{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)(\theta)(\frac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\theta\Delta_h})\beta_{vh}\vartheta\rho_h\rho_v}{(\lambda_h+\rho_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)\theta}} - \sqrt{\frac{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)\theta(\frac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\theta\Delta_h})\beta_{vh}\vartheta\rho_h\rho_v}{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)\theta}} \end{bmatrix}$$

(3.25)

The reproductive number, R_o is given by

$$R_o = \sqrt{\frac{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)(\theta)\beta_{hv}\beta_{vh}\vartheta^2\rho_h\rho_v\Delta_v\lambda_h}{(\rho_h+\lambda_h)^2(\tau+\lambda_h+\sigma_h)^2(\rho_v+\theta)^2\theta^2(\theta)\Delta_h}}$$

$$R_o = \sqrt{\frac{\beta_{hv}\beta_{vh}\vartheta^2\rho_h\rho_v\Delta_v\lambda_h}{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)\theta^2\Delta_h}} \tag{3.26}$$

where,

$\left[\frac{\rho_h}{\rho_h+\lambda_h}\right]$ – is the probability of survival of individual from exposed stage to infectious stage.

$\left[\frac{\rho_v}{\rho_v+\theta}\right]$ – is the probability of survival of mosquitoes from the exposed stage to infectious stage.

$\left[\frac{\beta_{vh}\rho_v\vartheta}{\theta(\rho_v+\theta)}\right]$ – is the number of humans that one mosquito infects during the lifetime it survives as infectious, when all humans are susceptible.

$\left[\frac{\beta_{hv}\vartheta\rho_h}{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)}\right]$ – is the number of mosquitoes that are infected through contacts with one infectious human, while the human survives as infectious, assuming no infection among vectors.

The threshold number, R_o is the product of R_{oh} and R_{ov}. We define R_{oh} as the number of humans that one mosquito infects through its infectious lifetime, assuming all humans are susceptible and R_{ov} is also defined as the number of mosquitoes that one human infects through the duration of the infectious period, assuming all mosquitoes are susceptibles. Our reproductive number is a square root since it includes the generation of infections of two populations. We manipulate R_o to get

$$R_o = \sqrt{\left(\frac{\beta_{vh}\rho_h\vartheta\lambda_h}{\Delta_h(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)}\right)\left(\frac{\beta_{hv}\rho_v\vartheta\Delta_v}{\theta^2(\rho_v+\theta)}\right)}$$

Hence, $$R_o = \sqrt{R_{oh}xR_{ov}}$$

where

$$R_{oh} = \frac{\beta_{vh}\rho_h\vartheta\lambda_h}{\Delta_h(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)} \tag{3.27}$$

and

$$R_{ov} = \frac{\beta_{hv}\rho_v\vartheta\Delta_v}{\theta(\rho_v+\theta)(\theta)}. \tag{3.28}$$

The number of latent infections produced by an infectious human during the average infectious period is

$$\frac{\beta_{vh}\vartheta\lambda_h}{\Delta_h(\tau+\lambda_h+\sigma_h)}.$$

Also, the number of latent infections produced by an infectious vector during the average infectious period is

$$\frac{\beta_{hv}\vartheta\Delta_v}{\theta^2}.$$

Infection of malaria occurs in a community owing to contact between the humans and mosquitoes. In this regard, it can be seen from (3.26) that the mosquito biting rate, ϑ, appears twice since it controls the spread from mosquitoes to humans and from humans to mosquitoes. The magnitude of the basic reproduction number, R_0 determines whether the disease still persists or is wiped out.

3.4.4 Local stability of the disease-free equilibrium, E_o

We now examine the stability of the disease-free equilibrium point, $E_o = \left(\frac{\Delta_h}{\lambda_h}, 0, 0, 0, \frac{\Delta_v}{\theta}, 0, 0\right)$. The local stability of E_o is determined based on the signs of the eigenvalues of the Jacobian matrix. The disease-free equilibrium point, (E_o) is locally asymptotically stable if the real parts of these eigenvalues are all negative, otherwise it is unstable.

Theorem 3: The disease-free equilibrium point, E_o for the system (3.1) is locally asymptotically stable if $R_o < 1$ and unstable if $R_o > 1$.

Proof: We differentiate each equation in the model system (3.1) with respect to the state variables $E_h, I_h, R_h, U_v, V_v, W_v$. We redefine the system as

$$\left.\begin{aligned}
a(E_h, I_h, R_h, U_v, V_v, W_v) &= \mu_h S_h - (\lambda_h + \rho_h)E_h \\
b(E_h, I_h, R_h, U_v, V_v, W_v) &= \rho_h E_h - (\tau + \lambda_h + \sigma_h)I_h \\
c(E_h, I_h, R_h, U_v, V_v, W_v) &= \tau I_h - (\psi + \lambda_h)R_h \\
d(E_h, I_h, R_h, U_v, V_v, W_v) &= \Delta_v - (\mu_v + \theta)U_v \\
e(E_h, I_h, R_h, U_v, V_v, W_v) &= \mu_v U_v - (\rho_v + \theta)V_v \\
f(E_h, I_h, R_h, U_v, V_v, W_v) &= \rho_v V_v - \theta W_v
\end{aligned}\right\}$$

Hence, at the steady states, the Jacobian a, b, c, d, e, f with respect to $E_h, I_h, R_h, U_v, V_v, W_v$ is given by

$$\begin{bmatrix} \frac{\partial a}{\partial E_h} & \cdots & \frac{\partial a}{\partial W_v} \\ \vdots & \ddots & \vdots \\ \frac{\partial f}{\partial E_h} & \cdots & \frac{\partial f}{\partial W_v} \end{bmatrix}$$

which becomes

$$\begin{bmatrix} -(\rho_h + \lambda_h) & 0 & 0 & 0 & 0 & \beta_{vh}\vartheta \\ \rho_h & -(\tau + \sigma_h + \lambda_h) & 0 & 0 & 0 & 0 \\ 0 & \tau & -(\psi + \lambda_h) & 0 & 0 & 0 \\ 0 & \frac{-\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta} & 0 & -\theta & 0 & 0 \\ 0 & \frac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta} & 0 & 0 & -(\rho_v + \theta) & 0 \\ 0 & 0 & 0 & 0 & \rho_v & -\theta \end{bmatrix} \tag{3.29}$$

The third and fourth columns have diagonal entries $-(\psi + \lambda_h)$ and $-\theta$ which are two of the eigenvalues of the Jacobian. We exclude these columns and the corresponding rows to calculate the remaining eigenvalues.

$$A = \begin{bmatrix} -(\rho_h + \lambda_h) & 0 & 0 & \beta_{vh}\vartheta \\ \rho_h & -(\tau + \sigma_h + \lambda_h) & 0 & 0 \\ 0 & \frac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta} & -(\rho_v + \theta) & 0 \\ 0 & 0 & \rho_v & -\theta \end{bmatrix} \tag{3.30}$$

If we let λ be the eigenvalues of matrix A, then $|A - \lambda I| = 0$ where I is a 4x4 identity matrix. Then,

$$|A - \lambda I| = \begin{vmatrix} -(\rho_h + \lambda_h + \lambda) & 0 & 0 & \beta_{vh}\vartheta \\ \rho_h & -(\tau + \sigma_h + \lambda_h + \lambda) & 0 & 0 \\ 0 & \frac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta} & -(\rho_v + \theta + \lambda) & 0 \\ 0 & 0 & \rho_v & -(\theta + \lambda) \end{vmatrix} = 0 \tag{3.31}$$

These eigenvalues are the solutions of the characteristic equation of the reduced matrix of dimension four which is given by

$$(\theta+\lambda)(\rho_h+\lambda_h+\lambda)(\rho_v+\theta+\lambda)(\tau+\sigma_h+\lambda_h+\lambda)-\frac{\vartheta^2\beta_{hv}\beta_{vh}\rho_h\rho_v\Delta_v\lambda_h}{\Delta_h\theta}=0 \qquad (3.32)$$

Now, letting $p_0=\theta$, $p_1=(\rho_h+\lambda_h)$, $p_2=(\rho_v+\theta)$ and $p_3=(\tau+\sigma_h+\lambda_h)$, we substitute into

$$R_o^2=\frac{\beta_{hv}\beta_{vh}\vartheta^2\rho_h\rho_v\Delta_v\lambda_h}{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)\theta^2\Delta_h}$$

to get

$$R_o^2=\frac{\beta_{hv}\beta_{vh}\vartheta^2\rho_h\rho_v\Delta_v\lambda_h}{p_0p_3p_2\ p_1\theta\Delta_h}.$$

We can expand and simplify (3.32) to get

$$\lambda^4+q_3\lambda^3+q_2\lambda^2+q_1\lambda+q_0=0 \qquad (3.33)$$

where

$$\left.\begin{aligned} q_3&=p_1+p_3+2p_0+\rho_v\\ q_2&=(p_3+p_1)(2p_0+\rho_v)+p_0p_2+p_1p_3\\ q_1&=p_0p_3p_2+p_1p_3(2p_0+\rho_v)+p_0p_1p_2\\ q_0&=p_0p_1p_2p_3-\rho_h\rho_v\beta_{hv}\beta_{vh}\vartheta^2\frac{\Delta_v\lambda_h}{\Delta_h\theta} \end{aligned}\right\} \qquad (3.34)$$

The Routh-Hurwitz conditions (Murray, 1991), ensure that all roots of the polynomial given by (3.33) have negative real parts. For this polynomial, the Routh-Hurwitz conditions are

$q_0 > 0,\ q_1 > 0, q_2 > 0,\ q_3 > 0$ and $H_1 = q_3 > 0$

$$H_n = \begin{bmatrix} q_3 & 1 & 0 & 0 & \cdots & 0 \\ q_1 & q_2 & q_3 & 1 & \cdots & 0 \\ 0 & q_0 & q_1 & q_2 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & q_n \end{bmatrix},$$

where $q_j = 0\ if\ j > n.$

$$|H_1| = q_3 > 0$$

$$|H_2| = \begin{vmatrix} q_3 & 1 \\ q_1 & q_2 \end{vmatrix} > 0$$

$$|H_3| = \begin{vmatrix} q_3 & 1 & 0 \\ q_1 & q_2 & q_3 \\ 0 & q_0 & q_1 \end{vmatrix} > 0$$

$$|H_4| = \begin{vmatrix} q_3 & 1 & 0 & 0 \\ q_1 & q_2 & q_3 & 1 \\ 0 & q_0 & q_1 & q_2 \\ 0 & 0 & 0 & q_0 \end{vmatrix} > 0$$

We can clearly see that $H_4 = q_0 H_3$. Since $p_0 > 0,\ p_1 > 0, p_2 > 0,\ p_3 > 0$ we have $q_i > 0,\ i = 1,2,3.$ Again, if $R_o < 0,$ it follows that $q_0 > 0$ and therefore $H_2 > 0$ and $H_3 > 0.$

Clearly,

$$H_3 = q_1 (q_3 q_2 - q_1) - q_0 q_3^2$$

and

$$H_2 = q_3 q_2 - q_1.$$

Using Maple, we can see that

$$H_2 = q_3 q_2 - q_1$$

$$H_2 = p_3^2\left(p_0 + p_2 + p_1\right) + p_2 p_3\left(2p_0 + p_2 + 2p_1\right) + p_0^2(p_3 + p_1 + p_2) + p_1^2\left(p_0 + p_2 + p_3\right) + 2p_0 p_1\left(p_3 + p_2\right) + p_2^2(p_1 + p_0) \tag{3.35}$$

$H_2 > 0$

and

$$H_3 = q_1\left(q_3 q_2 - q_1\right) - q_0 q_3^2$$

$$H_3 = \left(p_3 + p_0\right)\left(p_0 + p_2\right)\left(p_3 + p_2\right)\left(p_1 + p_0\right)\left(p_3 + p_1\right)\left(p_1 + p_2\right) + \rho_h \rho_v \beta_{hv} \beta_{vh} \vartheta^2 \frac{\Delta_v \lambda_h}{\Delta_h \theta}) > 0$$

which is clearly a positive quantity. (3.36)

Therefore, all of the eigenvalues of the Jacobian matrix have negative real parts when $R_o < 1$. On the other hand, $R_o > 1$ means that $q_o < 0$, and since all the coefficients $(q_1,\ q_2\ and\ q_3)$ of the polynomial (3.33) are positive, not all roots of this polynomial can have negative real roots. Hence, when $R_o > 1$, the disease-free equilibrium point is unstable.

3.4.5 Endemic equilibrium point, E_1

In the presence of infection, that is, $E \neq 0$ and $I \neq 0$, the model system (3.1) has non-trivial equilibrium point, E_1, called the endemic equilibrium point which is given by

$$E_1 = \left(S_h^{\varepsilon}, E_h^{\varepsilon}, I_h^{\varepsilon}, R_h^{\varepsilon}, U_m^{\varepsilon}, V_m^{\varepsilon}, W_m^{\varepsilon}\right) \neq 0$$

where

$$\left(S_h^{\varepsilon},\ E_h^{\varepsilon},\ I_h^{\varepsilon},\ R_h^{\varepsilon},\ U_m^{\varepsilon},\ V_m^{\varepsilon},\ W_m^{\varepsilon}\right) > 0.$$

According to Mwamtobe (2010), for the existence and uniqueness of endemic equilibrium, its coordinates should satisfy the following conditions

$$\left.\begin{aligned}
\Delta_h + \psi R_h^{\varepsilon} - \left(\lambda_h + \mu_h\right) S_h^{\varepsilon} &= 0 \\
\mu_h S_h^{\varepsilon} - \left(\lambda_h + \rho_h\right) E_h^{\varepsilon} &= 0 \\
\rho_h E_h^{\varepsilon} - \left(\tau + \lambda_h + \sigma_h\right) I_h^{\varepsilon} &= 0 \\
\tau I_h^{\varepsilon} - \left(\psi + \lambda_h\right) R_h^{\varepsilon} &= 0 \\
\Delta_v - \left(\mu_v + \theta\right) U_v^{\varepsilon} &= 0 \\
\mu_v U_v^{\varepsilon} - \left(\rho_v + \theta\right) V_v^{\varepsilon} &= 0 \\
\rho_v V_v^{\varepsilon} - \theta W_v^{\varepsilon} &= 0
\end{aligned}\right\} \tag{3.37}$$

We derive the endemic equilibrium point by solving equation (3.37) in terms of the forces of infection, $\mu_h = \frac{\beta_{vh} \vartheta W_v^{\varepsilon}}{N_h}$ and $\mu_v = \frac{\beta_{hv} \vartheta I_h^{\varepsilon}}{N_h}$.

From equation the second equation of (3.37), we have

$$E_h^{\varepsilon} = \frac{\mu_h S_h^{\varepsilon}}{\left(\lambda_h + \rho_h\right)} = \frac{\beta_{vh} \vartheta W_v^{\varepsilon} S_h^{\varepsilon}}{N_h \left(\lambda_h + \rho_h\right)} \tag{3.38}$$

From the sixth equation of (3.37), we have

$$V_v^{\varepsilon} = \frac{\mu_v U_v^{\varepsilon}}{\left(\rho_v + \theta\right)} = \frac{\beta_{hv} \vartheta I_h^{\varepsilon} U_v^{\varepsilon}}{N_h \left(\rho_v + \theta\right)} \tag{3.39}$$

and from the seventh equation of (3.37), we can write

$$W_v^{\varepsilon} = \frac{\rho_v V_v^{\varepsilon}}{\theta} \tag{3.40}$$

Substituting (3.39) into (3.40), we get

$$W_v^{\varepsilon} = \frac{\rho_v \beta_{hv} \vartheta I_h^{\varepsilon} U_v^{\varepsilon}}{\theta\left(\rho_v + \theta\right) N_h} \tag{3.41}$$

From the fifth equation of (3.37), we have

$$U_v^{\varepsilon} = \frac{\Delta_v N_h}{\left(\beta_{hv} \vartheta I_h^{\varepsilon} + \theta N_h\right)} \tag{3.42a}$$

Substituting (3.42a) into (3.41), we have

$$W_v^{\varepsilon} = \frac{\beta_{hv}\ \rho_v \vartheta \Delta_v I_h^{\varepsilon}}{\theta\left(\rho_v + \theta\right)\left(\beta_{hv}\vartheta I_h^{\varepsilon} + \theta N_h\right)} \tag{3.42b}$$

From equation (3.27), we have $R_{ov} = \frac{\beta_{hv}\rho_v \vartheta \Delta_v}{\theta^2(\rho_v + \theta)}$. Substituting into (3.42b), we have

$$W_v^{\varepsilon} = \frac{R_{ov}\theta I_h^{\varepsilon}}{\left(\beta_{hv}\vartheta I_h^{\varepsilon} + \theta N_h\right)} \tag{3.43}$$

From the second equation of (3.37), we can write

$$\frac{\beta_{vh}\vartheta W_v^{\varepsilon}}{N_h} S_h^{\varepsilon} - \left(\lambda_h + \rho_h\right) E_h^{\varepsilon} = 0 \tag{3.44}$$

Substituting equation (3.43) into equation (3.44), we have

$$\frac{R_{ov}\theta I_h^{\varepsilon}}{\left(\beta_{hv}\vartheta I_h^{\varepsilon} + \theta N_h\right)} \frac{\beta_{vh}\vartheta}{N_h} S_h^{\varepsilon} - \left(\lambda_h + \rho_h\right) E_h^{\varepsilon} = 0 \tag{3.45}$$

From the third equation of (3.37), we have

$$\rho_h E_h^{\varepsilon} - \left(\tau + \lambda_h + \sigma_h\right) I_h^{\varepsilon} = 0$$

It implies that $E_h^{\varepsilon} = \frac{\left(\tau + \lambda_h + \sigma_h\right) I_h^{\varepsilon}}{\rho_h}$.

Substituting $E_h^{\varepsilon} = \frac{\left(\tau + \lambda_h + \sigma_h\right) I_h^{\varepsilon}}{\rho_h}$ into equation (3.45), we have

$$\frac{R_{ov}\theta I_h^{\varepsilon}}{\left(\beta_{hv}\vartheta I_h^{\varepsilon} + \theta N_h\right)} \frac{\beta_{vh}\vartheta}{N_h} S_h^{\varepsilon} - \left(\lambda_h + \rho_h\right) \frac{\left(\tau + \lambda_h + \sigma_h\right) I_h^{\varepsilon}}{\rho_h} = 0 \tag{3.46a}$$

Multiplying through (3.46a) by $\left(\beta_{hv}\vartheta I_h^{\varepsilon}+\theta N_h\right)(\rho_h N_h)$ we get,

$$\left(R_{ov}\theta\beta_{vh}\vartheta S_h^{\varepsilon}\rho_h\right)I_h^{\varepsilon}-\left[\left(\lambda_h+\rho_h\right)\left(\beta_{hv}\vartheta I_h^{\varepsilon}+\theta N_h\right)\left(\tau+\lambda_h+\sigma_h\right)N_h\right]I_h^{\varepsilon}=0$$

Hence, $\left(R_{ov}\theta\beta_{vh}\vartheta S_h^{\varepsilon}\rho_h-\left(\lambda_h+\rho_h\right)\left(\beta_{hv}\vartheta I_h^{\varepsilon}+\theta N_h\right)\left(\tau+\lambda_h+\sigma_h\right)N_h\right)I_h^{\varepsilon}=0$

It implies that either

$$I_h^{\varepsilon}=0$$

or

$$R_{ov}\theta\beta_{vh}\vartheta S_h^{\varepsilon}\rho_h-\left(\lambda_h+\rho_h\right)\left(\tau+\lambda_h+\sigma_h\right)N_h\left(\beta_{hv}\vartheta I_h^{\varepsilon}+\theta N_h\right)=0 \qquad (3.46b)$$

From equation (3.46b) above, we can write

$$\frac{R_{ov}\theta\beta_{vh}\vartheta S_h^{\varepsilon}\rho_h}{\left(\lambda_h+\rho_h\right)\left(\tau+\lambda_h+\sigma_h\right)N_h}-\left(\beta_{hv}\vartheta I_h^{\varepsilon}+\theta N_h\right)=0 \qquad (3.46c)$$

But $R_{oh}=\dfrac{\beta_{vh}\rho_h\vartheta\lambda_h}{\Delta_h(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)}$, $N_h\le\dfrac{\Delta_h}{\lambda_h}$ and $R_o^2=R_{oh}xR_{ov}$

Rewriting equation (3.46c) by substituting the values we have

$$\left[\frac{\beta_{vh}\rho_h\vartheta\lambda_h}{\Delta_h(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)}\right]R_{ov}\theta S_h^{\varepsilon}-\left(\beta_{hv}\vartheta I_h^{\varepsilon}+\theta\frac{\Delta_h}{\lambda_h}\right)=0$$

It implies that $R_{oh}R_{ov}\theta S_h^{\varepsilon}-\beta_{hv}\vartheta I_h^{\varepsilon}-\theta\dfrac{\Delta_h}{\lambda_h}=0$

$$R_o^2\theta S_h^{\varepsilon}-\beta_{hv}\vartheta I_h^{\varepsilon}-\theta\frac{\Delta_h}{\lambda_h}=0$$

Solving for S_h^{ε} of the equation above, we have

$$S_h^{\varepsilon} = \frac{\beta_{hv}\vartheta\lambda_h I_h^{\varepsilon} + \theta\Delta_h}{\lambda_h \theta R_o^2} \tag{3.47}$$

From the fourth equation of (3.37), we have

$$\tau I_h^{\varepsilon} - (\psi + \lambda_h) R_h^{\varepsilon} = 0$$

Solving for R_h^{ε} we have $R_h^{\varepsilon} = \frac{\tau I_h^{\varepsilon}}{(\psi + \lambda_h)}$ (3.48a)

We also have $\lambda_h = \frac{\beta_{vh}\vartheta R_{ov}\theta I_h^{\varepsilon}}{N_h(\beta_{hv}\vartheta I_h^{\varepsilon} + \theta N_h)}$ (3.48b)

From the first equation of (3.37), we have

$$\Delta_h + \psi R_h^{\varepsilon} - (\lambda_h + \mu_h) S_h^{\varepsilon} = 0 \tag{3.49}$$

Now, substituting equations (3.47), (3.48a) and (3.48b) into (3.49), we can solve for I_h^{ε} as follows:

$$\Delta_h + \psi\left[\frac{\tau I_h^{\varepsilon}}{(\psi + \lambda_h)}\right] - \left[\left(\frac{\beta_{vh}\vartheta R_{ov}\theta I_h^{\varepsilon}}{N_h\left(\beta_{hv}\vartheta I_h^{\varepsilon} + \theta N_h\right)}\right) + \left(\frac{\beta_{vh}\vartheta W_v^{\varepsilon}}{N_h}\right)\right]\left[\frac{\beta_{hv}\vartheta\lambda_h I_h^{\varepsilon} + \Delta_h\theta}{\lambda_h\theta R_o^2}\right] = 0 \tag{3.50}$$

The endemic equilibrium (3.50) satisfy the equation

$$A(I_h^{\varepsilon})^2 + BI_h^{\varepsilon} + C = 0, \tag{3.51}$$

where

$$A = \left[\beta_{hv}\vartheta\tau\psi N_h - \frac{\beta_{vh}\vartheta^2\beta_{hv}R_{ov}(\psi + \lambda_h)}{R_0^2}\right] \tag{3.51a}$$

$$B = \left[\beta_{hv} \vartheta \Delta_h N_h \left(\psi + \lambda_h \right) - \frac{\beta_{vh} \vartheta \theta \Delta_h R_{ov} \left(\psi + \lambda_h \right)}{\lambda_h R_o^2} + \psi \tau \theta N_h^2 - \left(p_1 + p_3 + 2p_0 + \rho_v \right) \right]$$

(3.51b)

$$C = \lambda_h \theta^2 N_h^2 \Delta_h \left(\psi + \lambda_h \right) \left(R_o^2 - 1 \right) \tag{3.51c}$$

Solving (3.51) as a quadratic in I_h^{ε}, we have

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

Hence, $I_h^{\varepsilon} = \Omega$ (3.52)

It is to be noted that I_h^{ε} is positive because we cannot have the rate of infection as negative epidemiologically.

Now, substituting equation (3.52) into equation (3.47), we have

$$S_h^{\varepsilon} = \frac{\beta_{hv} \vartheta \lambda_h \Omega + \Delta_h \theta}{\lambda_h \theta R_o^2} \tag{3.53}$$

Also, substituting equation (3.52) into the third equation of (3.37), we get

$$E_h^{\varepsilon} = \frac{\left(\tau + \lambda_h + \sigma_h \right) \Omega}{\rho_h} \tag{3.54}$$

Substituting equation (3.52) into the fourth equation of (3.37), we have

$$R_h^{\varepsilon} = \frac{\tau \Omega}{\left(\psi + \lambda_h \right)} \tag{3.55}$$

Moreover, solving for the susceptible, exposed and infected mosquitoes in a malaria endemic area using equation (3.52), using equation (3.42), we can write

$$U_v^{\varepsilon} = \frac{\Delta_v N_h}{\left(\beta_{hv}\vartheta\Omega + \theta N_h\right)} \tag{3.56}$$

From equation (3.39), we have

$$V_v^{\varepsilon} = \frac{\beta_{hv}\vartheta I_h^{\varepsilon}\Delta_v N_h}{\left(\rho_v + \theta\right)N_h\left(\beta_{hv}\vartheta\Omega + \theta N_h\right)}$$

It implies that $$V_v^{\varepsilon} = \frac{R_{ov}\Omega\theta^2}{\rho_v\left(\beta_{hv}\vartheta\Omega + \theta N_h\right)} \tag{3.57}$$

From equation (3.43) $$W_v^{\varepsilon} = \frac{R_{ov}\theta\Omega}{\left(\beta_{hv}\vartheta\Omega + \theta N_h\right)} \tag{3.58}$$

When we examine (3.51) critically, we can show that there is a unique endemic equilibrium point if $B < 0$ and $C = 0 or B^2 - 4AC = 0$. There are two endemic equilibria if $C > 0$, B<0 and $B^2 - 4AC > 0$, otherwise there is none. It is also to be noted that the coefficient A is always positive and C is positive if and negative if. This leads to the following result:

a. There is a unique endemic equilibrium if $C < 0 \Leftrightarrow R_o > 1$,
b. There is a unique endemic equilibrium $B < 0 and C = 0 or B^2 - 4AC = 0$,
c. There are two endemic equilibria $C > 0$, $B < 0$ and $B^2 - 4AC > 0$,
d. No endemic equilibrium otherwise.

3.4.6 Local Stability of the Endemic Equilibrium E_1

We can determine the stability of the endemic equilibrium by computing the eigenvalues of the Jacobian matrix and then evaluate it at the endemic equilibrium. This can be done by using Centre Manifold Theory as presented in Chavez and

Song, 2004. The system (3.1) is rewritten by introducing the dimensionless state variables of the basic malaria model as follows; let

$$l_1 = S_h, l_2 = E_h, l_3 = I_h, l_4 = R_h, l_5 = U_v, l_6 = V_v, l_7 = W_v$$

Rewriting equation (3.1) in vector form, we have

$$\frac{dL_i}{dt} = G(L_i)$$

where

$$L_i = (l_1, l_2, \ldots, l_7)^T, \; G = (g_1, g_2, \ldots, g_7)^T, \; \Gamma = \beta_{vh} \text{ from equation (3.26).}$$

The system of equations (3.1) becomes

$$\left.\begin{aligned}
\frac{dl_1}{dt} &= \Delta_h - \frac{\lambda_h \Gamma \vartheta l_7 l_1}{\Delta_h} + \psi l_4 - \lambda_h l_1 = g_1 \\
\frac{dl_2}{dt} &= \frac{\Gamma \vartheta \lambda_h l_7 l_1}{\Delta_h} - (\lambda_h + \rho_h) l_2 = g_2 \\
\frac{dl_3}{dt} &= \rho_h l_2 - (\tau + \lambda_h + \sigma_h) l_3 = g_3 \\
\frac{dl_4}{dt} &= \tau l_3 - (\psi + \lambda_h) l_4 = g_4 \\
\frac{dl_5}{dt} &= \Delta_v - \frac{\beta_{hv} \vartheta \lambda_h l_3 l_5}{\Delta_h} - \theta l_5 = g_5 \\
\frac{dl_6}{dt} &= \frac{\beta_{hv} \vartheta \lambda_h l_3 l_5}{\Delta_h} - (\rho_v + \theta) l_6 = g_6 \\
\frac{dl_7}{dt} &= \rho_v l_6 - \theta l_7 = g_7
\end{aligned}\right\} \quad (3.59)$$

where,

$$N_h = l_1 + l_2 + l_3 + l_4,$$

$$N_v = l_5 + l_6 + l_7$$

$$\Gamma = \beta_{vh},$$

where Γ is the bifurcation parameter.

We linearise (3.59) at disease-free equilibrium point E_o when $\Gamma = \Gamma^*$ with $R_o = 1$.

Substituting $R_o = 1$ into (3.26), we have

$$\mathcal{R}_o = \sqrt{\frac{\beta_{hv}\beta_{vh}\vartheta^2\rho_h\rho_v\Delta_v\lambda_h}{(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)\theta^2\Delta_h}}$$

Hence, $$\Gamma^* = \frac{\theta^2(\rho_h+\lambda_h)(\tau+\lambda_h+\sigma_h)(\rho_v+\theta)\Delta_h}{\Delta_v\rho_h\rho_v\beta_{hv}\lambda_h\vartheta^2}$$

We have zero being the simple eigenvalue of the following Jacobian matrix, with the application of the bifurcation parameters.

$$\begin{bmatrix} -\lambda_h & 0 & 0 & \psi & 0 & 0 & -\Gamma\vartheta \\ 0 & K & 0 & 0 & 0 & 0 & \Gamma\vartheta \\ 0 & \rho_h & G & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau & -(\psi+\lambda_h) & 0 & 0 & 0 \\ 0 & 0 & H & 0 & -\theta & 0 & 0 \\ 0 & 0 & J & 0 & 0 & -(\rho_v+\theta) & 0 \\ 0 & 0 & 0 & 0 & 0 & \rho_v & -\theta \end{bmatrix} \tag{3.60}$$

where

$$G = -(\tau+\lambda_h+\sigma_h),\quad H = -\frac{\beta_{hv}\vartheta\lambda_h\Delta_v}{\Delta_h\theta},\quad J = \frac{\beta_{hv}\vartheta\lambda_h\Delta_v}{\Delta_h\theta} \quad \text{and} \quad K = -(\rho_h+\lambda_h)$$

.

The association between the right eigenvector with the eigenvalue zero is

$x = (x_1, x_2, ..., x_7)$.

Solving gives the system

$$
\left.
\begin{aligned}
-\lambda_h x_1 + \psi x_4 - \Gamma \vartheta x_7 &= 0 \\
-(\rho_h + \lambda_h) x_2 + \Gamma \vartheta x_7 &= 0 \\
\lambda_h x_2 - (\tau + \lambda_h + \sigma_h) x_3 &= 0 \\
\tau x_3 - (\psi + \lambda_h) x_4 &= 0 \\
-\frac{\beta_{hv} \vartheta \lambda_h \Delta_v}{\Delta_h \theta} x_3 - \theta x_5 &= 0 \\
\frac{\beta_{hv} \vartheta \lambda_h \Delta_v}{\Delta_h \theta} x_3 - (\rho_v + \theta) x_6 &= 0 \\
\rho_v x_6 - \theta x_7 &= 0
\end{aligned}
\right\} \qquad (3.61)
$$

We get a right eigenvector by solving the system (3.61)

$$
\left.
\begin{aligned}
x_1 &= \frac{\psi x_4 - \Gamma \vartheta x_7}{\lambda_h} \\
x_2 &= \frac{\Gamma \vartheta x_7}{(\rho_h + \lambda_h)} \\
x_3 &= \frac{\lambda_h x_2}{(\tau + \lambda_h + \sigma_h)} \\
x_4 &= \frac{\tau x_3}{(\psi + \lambda_h)} \\
x_5 &= -\frac{\beta_{hv} \vartheta \lambda_h \Delta_v x_3}{\Delta_h \theta^2} \\
x_6 &= \frac{\beta_{hv} \vartheta \lambda_h \Delta_v x_3}{\Delta_h \theta (\rho_v + \theta)} \\
x_7 &= x_7 > 0
\end{aligned}
\right\} \qquad (3.62)
$$

The left eigenvector satisfying $u * x = 1$ is $u = (u_1, u_2, \ldots, u_7)$.

Now, we transpose matrix (3.60) to find the left eigenvector associated with the eigenvalue 0. This will give us the matrix J_{left},

$$\begin{bmatrix} -\lambda_h & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & K & \rho_h & 0 & 0 & 0 & 0 \\ 0 & 0 & G & \tau & H & J & 0 \\ \psi & 0 & 0 & -(\psi+\lambda_h) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\theta & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\rho_v+\theta) & \rho_v \\ -\Gamma\vartheta & \Gamma\vartheta & 0 & 0 & 0 & 0 & -\theta \end{bmatrix} \tag{3.63}$$

where

$$G = -(\tau + \lambda_h + \sigma_h),\ H = -\frac{\beta_{hv}\vartheta\lambda_h\Delta_v}{\Delta_h\theta},\ J = \frac{\beta_{hv}\vartheta\lambda_h\Delta_v}{\Delta_h\theta} \quad and \quad K = -(\rho_h + \lambda_h).$$

We then calculate the following system

$$\left.\begin{aligned} -\lambda_h u_1 &= 0 \\ -(\rho_h + \lambda_h)u_2 + \rho_h u_3 &= 0 \\ -(\tau + \lambda_h + \sigma_h)u_3 + \tau u_4 - \frac{\beta_{hv}\vartheta\lambda_h\Delta_v}{\Delta_h\theta}u_5 + \frac{\beta_{hv}\vartheta\lambda_h\Delta_v}{\Delta_h\theta}u_6 &= 0 \\ \psi u_1 - (\psi + \lambda_h)u_4 &= 0 \\ -\theta u_5 &= 0 \\ -(\rho_v + \theta)u_6 + \rho_v u_7 &= 0 \\ -\Gamma\vartheta u_1 + \Gamma\vartheta u_2 - \theta u_7 &= 0 \end{aligned}\right\} \tag{3.64}$$

From the left eigenvector we have the following results

$$\left.\begin{aligned} u_1 &= 0 \\ u_2 &= u_2 > 0 \\ u_3 &= \frac{(\rho_h + \lambda_h)u_2}{\rho_h} \\ u_4 &= 0 \\ u_5 &= 0 \\ u_6 &= \frac{\rho_v u_7}{\rho_v + \theta} \\ u_7 &= \frac{\Gamma\vartheta u_2}{\theta} \end{aligned}\right\} \tag{3.65}$$

We have provided the theorem in Chavez and Song, (2004), in Appendix B to prove the local stability of the endemic equilibrium point near $R_o = 1$.

3.4.6.1 Computation of *a* and *b*

We use the same procedure as shown in Driessche and Watmough to determine the conditions at which the endemic equilibrium point is stable or unstable. The associated non-zero second order partial derivatives (at DFE) for the system (3.59) are given by

$$a = \sum_{k,i,j=2}^{3} u_k x_i x_j \frac{\partial^2 g_k}{\partial l_i \partial l_j}(0,0) + \sum_{k,i,j=6}^{7} u_k x_i x_j \frac{\partial^2 g_k}{\partial l_i \partial l_j}(0,0)$$

and

$$b = \sum_{k,i=2}^{3} u_k x_i \frac{\partial^2 g_k}{\partial l_i \partial \Gamma}(0,0) + \sum_{k,i=6}^{7} u_k x_i \frac{\partial^2 g_k}{\partial l_i \partial \Gamma}(0,0) \tag{3.66}$$

Now, $u_1 = u_4 = u_5 = 0$ for $k = 1, 4, 5$.

Considering $k = 2, 3, 6, 7$, we can compute a and b from the system (3.59), to get

$$g_2 = \frac{\Gamma \vartheta \lambda_h l_7 l_1}{\Delta_h} - (\rho_h + \lambda_h) l_2$$

$$= \frac{\Gamma \vartheta \lambda_h l_7}{\Delta_h}(N_h - l_2 - l_3) - (\rho_h + \lambda_h) l_2$$

Hence, $$g_2 = \frac{\Gamma \vartheta \lambda_h l_7 N_h}{\Delta_h} - \frac{\Gamma \vartheta \lambda_h l_7 l_2}{\Delta_h} - \frac{\Gamma \vartheta \lambda_h l_7 l_3}{\Delta_h} - (\rho_h + \lambda_h) l_2$$

Again,

$$g_6 = \frac{\beta_{hv} \vartheta \lambda_h l_3 l_5}{\Delta_h} - (\rho_v + \theta) l_6$$

$$= \frac{\beta_{hv}\vartheta\lambda_h l_3}{\Delta_h}\left(N_v - l_6 - l_7\right) - (\rho_v + \theta)l_6$$

Hence, $$g_6 = \frac{\beta_{hv}\vartheta\lambda_h l_3 N_m}{\Delta_h} - \frac{\beta_{hv}\vartheta\lambda_h l_3 l_6}{\Delta_h} - \frac{\beta_{hv}\vartheta\lambda_h l_3 l_7}{\Delta_h} - (\rho_v + \theta)l_6$$

Hence, the non-zero partial derivatives at the disease-free equilibrium are

$$\frac{\partial^2 g_2}{\partial l_2 \partial l_7} = -\frac{\Gamma\vartheta\lambda_h}{\Delta_h},$$

$$\frac{\partial^2 g_2}{\partial l_3 \partial l_7} = -\frac{\Gamma\vartheta\lambda_h}{\Delta_h},$$

$$\frac{\partial^2 g_6}{\partial l_6 \partial l_3} = -\frac{\beta_{hv}\vartheta\lambda_h}{\Delta_h}$$

$$\frac{\partial^2 g_6}{\partial l_7 \partial l_3} = -\frac{\beta_{hv}\vartheta\lambda_h}{\Delta_h}$$

Therefore,

$$a = u_2 x_2 x_7 \frac{\partial^2 g_2}{\partial l_2 \partial l_7} + u_2 x_3 x_7 \frac{\partial^2 g_2}{\partial l_3 \partial l_7} + u_6 x_6 x_3 \frac{\partial^2 g_6}{\partial l_6 \partial l_3} + u_6 x_7 x_3 \frac{\partial^2 g_6}{\partial l_7 \partial l_3}$$

$$= u_2 x_2 x_7 \left(-\frac{\Gamma\vartheta\lambda_h}{\Delta_h}\right) + u_2 x_3 x_7 \left(-\frac{\Gamma\vartheta\lambda_h}{\Delta_h}\right) + u_6 x_6 x_3 \left(-\frac{\beta_{hv}\vartheta\lambda_h}{\Delta_h}\right) + u_6 x_7 x_3 \left(-\frac{\beta_{hv}\vartheta\lambda_h}{\Delta_h}\right)$$

$$= -\frac{\vartheta\lambda_h}{\Delta_h}\left[u_2 x_7 \Gamma\left(x_2 + x_3\right) + u_6 x_3 \beta_{hv}\left(x_6 + x_7\right)\right]$$

$$a = -\frac{\vartheta\lambda_h}{\Delta_h}\left[u_2 x_7^2 \Gamma_7^2 \vartheta\left(\frac{\tau + \lambda_h + \sigma_h + \rho_h}{\left(\rho_h + \lambda_h\right)\left(\tau + \lambda_h + \sigma_h\right)}\right) + u_6 x_3 \beta_{hv}\left(\frac{\beta_{hv}\vartheta^2\lambda_h\Delta_v\rho_h\Gamma}{\psi\omega\left(\beta_v + \theta\right)\left(\tau + \lambda_h + \sigma_h\right)\left(\rho_h + \lambda_h\right)} + 1\right)\right] \quad (3.67)$$

Since the sign of a is negative, it implies that $a < 0$.

For the sign of b, we can show that the associated non-vanishing partial derivatives are

$$\frac{\partial g_2}{\partial \Gamma} = \frac{\vartheta \lambda_h l_7 l_1}{\Delta_h}$$

$$\frac{\partial^2 g_2}{\partial l_7 \partial \Gamma} = \frac{\vartheta \lambda_h l_1}{\Delta_h} = \frac{\vartheta \lambda_h}{\Delta_h}\left(\frac{\Delta_h}{\lambda_h}\right) = \vartheta.$$

We can find from the above expression that

$$b = u_2 x_7 \frac{\partial^2 g_2}{\partial l_7 \partial \Gamma} = u_2 x_7 \, \vartheta > 0 \tag{3.68}$$

It implies that the sign of b is positive, thus $b > 0$.

In view of the above, the theorem holds that the model system (3.1) has unique endemic equilibrium which is locally asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$.

Summary

We formulated a model of the transmission dynamics of malaria which have changing human population with recruitment of new individuals in the susceptible class. The model was analysed to show the existence of a domain in which the model is epidemiologically meaningful and mathematically well-posed. In addition, the existence and stability of the disease-free and endemic equilibrium points were analysed.

Moreover, the next generation method was used to calculate the reproduction number, R_o as an important parameter that plays an immense role in the control of malaria infection. We also proved that the disease-free equilibrium E_0 is locally asymptotically stable if $R_o < 1$, and when $R_o > 1$, the endemic equilibrium E_1 appeared.

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1 Introduction

This chapter presents the results and discussion of the study. The presentation follows the order of the study objectives as written in chapter one. They include formulating a mathematical model for the region, performing stability analysis of the model and carrying out numerical simulations on the model.

4.2 Data collection

Data was obtained mainly from secondary sources. The secondary data was obtained from both the Centre for Health Information Management of the Ghana Health Service and the Statistical Service as well as published materials from books, journals and related studies on mathematical modelling of malaria.

4.2.1 Greater Accra population data:

Table 4.1 presents the data on population of the Greater Accra region from the year 2000 to 2011. The data was obtained from the Ghana Statistical Service. However, the 2000 and 2010 population values for the region were obtained from the population and housing census conducted in 2000 and 2010 respectively. The rest were projected using the regional growth rate of 3.22.

Table 4.1: Greater Accra population from 2000 - 2011

Year	Population	Year	Population	Year	Population
2000	2905726	2004	3298607	2008	3744608
2001	2999326	2005	3404862	2009	3865230

2002	3095940	2006	3514540	2010	4010054
2003	3195667	2007	3627750	2011	4139226

Source: Ghana Statistical Service

4.2.2 Lab-confirmed malaria cases and deaths:

The data on lab-confirmed malaria cases and deaths of Greater Accra region is illustrated in Table 4.2. It was obtained from the Centre for Health Information Management of the Ghana Health Service. It spans a period of twelve years.

Table 4.2: Greater Accra lab-confirmed malaria cases and deaths

Year	Cases	Deaths	Year	Cases	Deaths
2000	374015	2548	2006	492658	4028
2001	398524	2719	2007	512087	4653
2002	420115	2987	2008	559653	4963
2003	458025	3018	2009	629537	5167
2004	478254	3529	2010	702599	6572
2005	479985	3897	2011	928220	7389

Source: CHIM, Ghana Health Service

4.2.3 Data for mosquitoes' population:

The data for the mosquito population are as presented in Table 4.3. The number constituting the dwelling units in Accra was obtained from the 2010 Population and Housing Census whilst the latent and incubation periods were obtained from the study done by Chitnis (2005). The other values were estimated.

Table 4.3: Data for mosquitoes' population

Parameter	Value	Source
Total number of dwelling units in the Greater Accra Region	1,090,397	GSS (2010)
Estimated number of female Anopheles mosquitoes in each dwelling unit	15	Estimated
Total female Anopheles mosquitoes population, N_v	16356000	Estimated
Mosquito life expectancy	25	Esteva and Vargas (2000)
Latent period in mosquitoes	11	Chitnis (2005)
Incubation period of malaria	14	MOH (2009)

4.2.4 Data for the human population:

Table 4.4 presents the data for the human population. The initial population and life expectancy were obtained from the 2000 and 2010 Population and Housing Census respectively by the Ghana Statistical Service.

Table 4.4: Data for human population

Parameter	Value	Source
Initial Population, N_h	2906000	GSS (2000)
Life expectancy	64	UNICEF (2012)
Number of days for humans to recover from malaria infection	7	MOH (2009)
Number of days for humans to lose immunity	90	Blayneh, et al. (2009)

4.3 Estimation of parameters

Table 4.5 presents the parameter of the model system and their corresponding values. These are estimated average values of the population and the rates are given per day.

Table 4.5: Parameter values of the model system

Description	Symbol	Value	Source
Humans recruitment rate	Δ_h	$\frac{0.0322}{365}$	GSS (2010)
Natural death rate for humans	λ_h	$\frac{1}{(64x365)}$	UNICEF (2012)
Progression rate of exposed humans to infected individuals	ρ_h	$\frac{1}{14}$	MOH (2009)
Rate of loss of immunity	ψ	$\frac{1}{90}$	Blayneh, et al. (2009)
Probability of a susceptible human being infected	β_{vh}	0.0655	Niger et al. (2008)
Recruitment rate of mosquitoes	Δ_v	0.071	Niger et al. (2008)
Natural death rate of mosquitoes	θ	$\frac{1}{25}$	Esteva and Vargas (2000)
Disease-induced death rate for humans	σ_h	0.0000027	World Malaria Report (2010) Ghana
Progression rate of exposed mosquitoes to infected mosquitoes	ρ_v	$\frac{1}{11}$	Chitnis (2005)
Probability of a susceptible mosquito being infected	β_{hv}	0.42	Miranda et al. (2009)
Rate of recovery of humans	τ	$\frac{1}{7}$	MOH (2009)
Mosquito biting rate	ϑ	0.4	Chitnis (2005)

4.4 Data processing

4.4.1 SEIR data of the Greater Accra Region:

Table 3 provides the overview of the SEIR data of the human population. The infected data represents the number of lab-confirmed malaria cases. Data of the columns labelled susceptible, exposed and recovered were computed as shown:

a. $Recovered = Infected - Deaths$

b. $Exposed = Infected \times \frac{2}{365}$

c. $Susceptible = Total\ population - (Infected + Recovered + Exposed)$

Using the year 2000 as an example, we can compute the recovered, exposed and susceptible data as follows:

a. $Recovered = 374015 - 2548 = 371467$

b. $Exposed = 374015 \times \frac{2}{365} = 2049$

c. $Susceptible = 2905726 - (374015 + 371467 + 2049) = 2158195$

Table 4.6: SEIR data of the Greater Accra Region

Year	Total population	Deaths	Susceptible	Exposed	Infected	Recovered
2000	2905726	2548	2158195	2049	374015	371467
2001	2999326	2719	2202813	2184	398524	395805
2002	3095940	2987	2256395	2302	420115	417128
2003	3195667	3018	2280126	2510	458025	455007
2004	3298607	3529	2343007	2621	478254	474725
2005	3404862	3897	2446159	2630	479985	476088
2006	3514540	4028	2530552	2699	492658	488630
2007	3627751	4653	2605424	2806	512087	507434
2008	3744608	4963	2627199	3067	559653	554690

2009	3865230	5167	2607873	3450	629537	624370
2010	4010054	6572	2607578	3850	702599	696027
2011	4139226	7389	2285089	5086	928220	920831

Source: GHS, GSS and other calculated values

4.5 Model for both human and mosquito populations:

The initial conditions are: $S_h(0) = 2159000,\ E_h(0) = 2000,\ I_h(0) = 374000,\ R_h(0) = 371000,\ U_v(0) = 10750000,\ V_v(0) = 350000,\ W_v(0) = 5256000$ and the total population sizes are $N_h = 2906000$ people and $N_v = 16356000$ mosquitoes.

Substituting the parameter values into the model systems (3.1a) and (3.1b), we respectively have

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= 0.000088 + 0.011111R_h - \left(0.000043 + \frac{0.344W_v}{N_h}\right)S_h \\
\frac{dE_h}{dt} &= \frac{0.344W_v}{N_h}S_h - (0.000043 + 0.071429)E_h \\
\frac{dI_h}{dt} &= 0.071429E_h - 0.142903I_h \\
\frac{dR_h}{dt} &= 0.142857I_h - 0.011154R_h \\
\frac{dU_v}{dt} &= 0.071 - \left(\frac{0.0332I_h}{N_h} + 0.04\right)U_v \\
\frac{dV_v}{dt} &= \left(\frac{0.0332I_h}{N_h}\right)U_v - 0.130909V_v \\
\frac{dW_v}{dt} &= 0.090909V_v - 0.04W_v
\end{aligned}\right\} \quad (3.69)$$

And the model for total human and mosquito populations are as follows:

$$\left.\begin{aligned}\frac{dN_h}{dt} &= 0.000088 - 0.000043N_h - 0.0000027I_h \\ \frac{dN_v}{dt} &= 0.071 - 0.04N_v\end{aligned}\right\} \tag{3.70}$$

4.5.1 Disease-free equilibrium point

From Table 4.5, we have $\Delta_h = 0.000088, \lambda_h = 0.000043, \ \Delta_v = 0.071$ and $\theta = 0.04$. If we substitute the into the expression, $E_o = \left[\frac{\Delta_h}{\lambda_h}, 0, 0, 0, \frac{\Delta_v}{\theta}, 0, 0\right]$ and multiply through by the initial conditions, we have the disease-free equilibrium point of the model system in the region to be

$$E_0 = \left(4449290,\ 0,\ 0,\ 0,\ 19081250,\ 0,\ 0\right).$$

4.5.2 Basic reproductive number

The basic reproductive number, R_o, which enables us to know whether a disease has died out or is persistent in the region, is computed as follows:

$$R_o = \sqrt{(R_{oh})(R_{ov})}$$

$$= \sqrt{\left(\frac{\beta_{vh}\rho_h \vartheta\lambda_h}{\Delta_h(\rho_h + \lambda_h)(\tau + \lambda_h + \sigma_h)}\right)\left(\frac{\beta_{hv}\rho_v \vartheta\Delta_v}{\theta^2(\rho_v + \theta)}\right)}$$

Substituting the parameter values into the above expression, we have

$$R_o = \sqrt{\left(\frac{(0.0655)(0.07143)(0.4)(0.000043)}{(0.000088219)(0.07147)(0.1429)}\right)\left(\frac{(0.42)(1/11)(0.4)(0.071)}{(0.04^2)(0.1309)}\right)}$$

$$= \sqrt{(0.088916915)\left(5.177442878\right)}$$

Hence, $R_o = 0.6785$

Since $R_o = 0.6785 < 1$, we can conclude that malaria can be wiped out of the Greater Accra Region.

4.5.3 Local stability of the disease-free equilibrium

From equation (3.31), we have

$$|A - \lambda I| = \begin{vmatrix} -(\rho_h + \lambda_h + \lambda) & 0 & 0 & \beta_{vh}\vartheta \\ \rho_h & -(\tau + \sigma_h + \lambda_h + \lambda) & 0 & 0 \\ 0 & \frac{\beta_{hv}\vartheta\Delta_v\lambda_h}{\Delta_h\theta} & -(\rho_v + \theta + \lambda) & 0 \\ 0 & 0 & \rho_v & -(\theta + \lambda) \end{vmatrix} = 0$$

If we substitute the parameter values into the above matrix, we have

$$|A - \lambda I| = \begin{vmatrix} -(0.07147 + \lambda) & 0 & 0 & 0.0262 \\ 0.07143 & -(0.1429 + \lambda) & 0 & 0 \\ 0 & 0.1447 & -(0.1309 + \lambda) & 0 \\ 0 & 0 & 0.091 & -(0.04 + \lambda) \end{vmatrix} = 0$$

The characteristic equation of the matrix is given by

$$(0.07147 + \lambda)(0.1429 + \lambda)(0.1309 + \lambda)(0.04 + \lambda) - 0.000024643 = 0$$

Solving the above quartic equation, we got the real parts of the eigenvalues to be $\lambda = \{-0.178209, \ -0.012728\}$. Now, since the real parts of the eigenvalues are all negative, the disease-free equilibrium point is asymptotically stable.

4.5.4 Endemic equilibrium point

From equation (3.51a), we have

$$A = \left[\beta_{hv} \vartheta \tau \psi N_h - \frac{\beta_{vh} \vartheta^2 \beta_{hv} R_{ov} (\psi + \lambda_h)}{R_0^2} \right]$$

Substituting the parameter values into the above equation, we have

$$A = \left[0.42x0.4x0.1429x0.01111x2906000 - \frac{0.0655x0.16x0.42x5.177443x0.11154}{0.46036} \right]$$

$$A = 775.083$$

Also, from equation (3.51b), we have

$$B = \left[\beta_{hv} \vartheta \Delta_h N_h (\psi + \lambda_h) - \frac{\beta_{vh} \vartheta \theta \Delta_h R_{ov} (\psi + \lambda_h)}{\lambda_h R_o^2} + \psi \tau \theta N_h^2 - (p_1 + p_3 + 2p_0 + \rho_v) \right]$$

Substituting the parameter values into the above equation, we have

$$B = [0.42x0.4x0.000088x2906000x0.011154] - \left[\frac{0.0655x0.4x0.04x0.000088x5.177442878x0.011154}{0.000043x0.46036225} \right]$$
$$+ \left[0.011111x0.142857x0.04x2906000^2 \right] - [0.385279]$$

$$B = 5.36174x10^8$$

Finally,

$$C = \lambda_h \theta^2 N_h^2 \Delta_h (\psi + \lambda_h)(R_o^2 - 1)$$

Substituting the parameter values into the above equation, we have

$$C = 0.000043x0.16x2906000^2 x0.000088x0.011154x(0.6785 - 1)$$

$$C = -18.3347$$

Now, substituting the values of A, B and C into $A(I_h^\varepsilon)^2 + BI_h^\varepsilon + C = 0$, we have

$$775.083(I_h^\varepsilon)^2 + 5.36174 * 10^8 I_h^\varepsilon - 18.3347 = 0$$

Solving the above equation as a quadratic in I_h^ε, we have

$$I_h^{\varepsilon} = (-691763,\ 3.41954\text{x}10^{-8})$$

$$\Longrightarrow \qquad I_h^{\varepsilon} = 3.41954\text{x}10^{-8}$$

Again, we compute the susceptible, exposed and recovered humans as well as the susceptible, exposed and infected mosquitoes in the malaria endemic area as follows:

$$S_h^{\varepsilon} = \frac{\beta_{hv}\vartheta\lambda_h\Omega + \Delta_h\theta}{\lambda_h\theta R_o^2}$$

$$= \frac{\left(0.42x0.4x0.000043x3.41954*10^{-8}\right) + \left(0.000088x0.04\right)}{\left(0.000043x0.04x0.46036225\right)}$$

$$= 4.44544$$

$$E_h^{\varepsilon} = \frac{\left(\tau + \lambda_h + \sigma_h\right)\Omega}{\rho_h}$$

$$= \frac{0.1429x3.41954*10^{-8}}{0.071429} = 6.84109x10^{-8}$$

$$R_h^{\varepsilon} = \frac{\tau\Omega}{\left(\psi + \lambda_h\right)}$$

$$= \frac{0.142857x3.41954*10^{-8}}{0.011154} = 4.37964*10^{-7}$$

$$U_v^{\varepsilon} = \frac{\Delta_v N_h}{\left(\beta_{hv}\vartheta\Omega + \theta N_h\right)}$$

$$= \frac{0.071x2906000}{\left(0.42x0.4x3.41954x10^{-8} + 0.04x2906000\right)} = 1.775$$

$$V_v^{\varepsilon} = \frac{R_{ov}\Omega\theta^2}{\rho_v\left(\beta_{hv}\vartheta\Omega + \theta N_h\right)}$$

$$= \frac{5.177442878x3.41954x10^{-8}\,x0.04^2}{0.090909\left(0.42x0.4x3.41954x10^{-8} + 0.04x2906000\right)} = 2.68065x10^{-14}$$

$$W_v^{\varepsilon} = \frac{R_{ov}\theta\Omega}{\left(\beta_{hv}\vartheta\Omega + \theta N_h\right)}$$

$$= \frac{5.177442878x0.04x3.41954x10^{-8}}{\left(0.42x0.4x3.41954x10^{-8} + 0.04x2906000\right)} = 6.09239x10^{-14}$$

Therefore the endemic equilibrium point is given by

$$E_1 = \left(4.44544,\ 6.84109x10^{-8},\ 3.41954x10^{-8},\ 4.37964x10^{-7},\ 1.775,\ 2.68065x10^{-14},\ 6.09239x10^{-14}\right)$$

If we multiply through by the initial conditions, the endemic equilibrium point is given by

$$E_1 = \left(9.5977x10^{6},\ 0.000137,\ 0.012789,\ 0.162485,\ 1.90813x10^{7},\ 9.38228x10^{-9},\ 3.20216x10^{-7}\right)$$

Also, since the sign of C is negative, i.e. $C = -18.3347 < 0$, it implies that the Greater Accra Region has precisely one unique endemic equilibrium.

4.5.5 Local stability of the endemic equilibrium

Using the bifurcation parameter, $\Gamma^* = \dfrac{\theta^2\left(\rho_h + \lambda_h\right)\left(\tau + \lambda_h + \sigma_h\right)\left(\rho_v + \theta\right)\Delta_h}{\Delta_v\rho_h\rho_v\beta_{hv}\lambda_h\vartheta^2} = 14.1927$

we can compute the right eigenvectors as follows:

$$
\left.
\begin{aligned}
x_1 &= \frac{\psi x_4 - \Gamma \vartheta x_7}{\lambda_h} = \frac{0.011111x0.30613 - (14.1927x0.4x1)}{0.000043} = -131946 \\
x_2 &= \frac{\Gamma \vartheta x_7}{(\rho_h + \lambda_h)} = \frac{14.1927x0.4x1}{0.07147} = 79.433 \\
x_3 &= \frac{\lambda_h x_2}{(\tau + \lambda_h + \sigma_h)} = \frac{0.000043x79.433}{0.1429} = 0.023902 \\
x_4 &= \frac{\tau x_3}{(\psi + \lambda_h)} = \frac{0.142857x0.023902}{0.011154} = 0.30613 \\
x_5 &= -\frac{\beta_{hv} \vartheta \lambda_h \Delta_v x_3}{\Delta_h \theta^2} = -\frac{0.42x0.4x0.000043x0.071x0.023902}{0.000088x0.04^2} = -0.08707 \\
x_6 &= \frac{\beta_{hv} \vartheta \lambda_h \Delta_v x_3}{\Delta_h \theta(\rho_v + \theta)} = \frac{0.42x0.4x0.000043x0.071x0.023902}{0.000088x0.04x0.1309} = 0.026607 \\
x_7 &= x_7 > free
\end{aligned}
\right\}
$$

Using equation (3.65), we can compute the left eigenvector as follows:

$$
\left.
\begin{aligned}
u_1 &= 0 \\
u_2 &= u_2 > 0 \\
u_3 &= \frac{(\rho_h + \lambda_h)u_2}{\rho_h} = \frac{0.07147x1}{0.071429} = 1.00057 \\
u_4 &= 0 \\
u_5 &= 0 \\
u_6 &= \frac{\rho_v u_7}{\rho_v + \theta} = \frac{0.090909x141.927}{0.1309} = 98.5673 \\
u_7 &= \frac{\Gamma \vartheta u_2}{\theta} = \frac{14.1927x0.4x1}{0.04} = 141.927
\end{aligned}
\right\}
$$

Finally, we now determine the signs of *a* and *b* to find out the local stability of the endemic region. Using equation (3.67) we have,

$$
a = -\frac{\vartheta \lambda_h}{\Delta_h}\left[u_2 x_7^2 \Gamma_7^2 \vartheta \left(\frac{\tau + \lambda_h + \sigma_h + \rho_h}{(\rho_h + \lambda_h)(\tau + \lambda_h + \sigma_h)} \right) + u_6 x_3 \beta_{hv} \left(\frac{\beta_{hv} \vartheta^2 \lambda_h \Delta_v \rho_h \Gamma}{\psi \omega (\rho_v + \theta)(\tau + \lambda_h + \sigma_h)(\rho_h + \lambda_h)} + 1 \right) \right]
$$

Substituting the parameter values into equation above, we have

$$
a = -0.194582\left[80.5731(20.9858) + 0.989501(0.014002 + 1) \right]
$$

Hence, $a = -329.212$

Also, from equation (3.68), we have

$$b = u_2 x_7 \frac{\partial^2 g_2}{\partial l_7 \partial \Gamma} = u_2 x_7 \, \vartheta > 0$$

Substituting the parameter values into equation (3.68) above, we have

$$b = u_2 x_7 \frac{\partial^2 g_2}{\partial l_7 \partial \Gamma} = 1x1x0.4$$

Hence, $b = 0.4$

We conclude that the model system (3.1) has a unique endemic equilibrium which is locally asymptotically stable. It implies that malaria would persist in the region.

NUMERICAL SOLUTION OF THE MODEL

In this section, we illustrate the analytical results of the work by carrying out numerical simulations of the model using a set of parameters values given in Table 4.5. The model system is simulated using ODE solvers coded in Matlab programming language. We simulate the malaria model with intervention strategies, and find out the effects of varying each intervention parameter. All figures are plotted using the parameter values presented in Table 4.5 and the following initial conditions: $S_h(0) = 2159000$, $E_h(0) = 2000$, $I_h(0) = 374000$, $U_v(0) = 10750000$, $R_h(0) = 371000$, $V_v(0) = 350000$ and $W_v(0) = 5256000$. Also, the total population sizes are $N_h = 2906000$ people and $N_v = 16356000$ mosquitoes.

Numerical results:

4.6.1 Simulation of the human population with time

The simulation of the susceptible, exposed, infected and recovered human populations are conducted to find out the dynamics of the disease in the population in order to ascertain whether we can reduce or eradicate the disease.

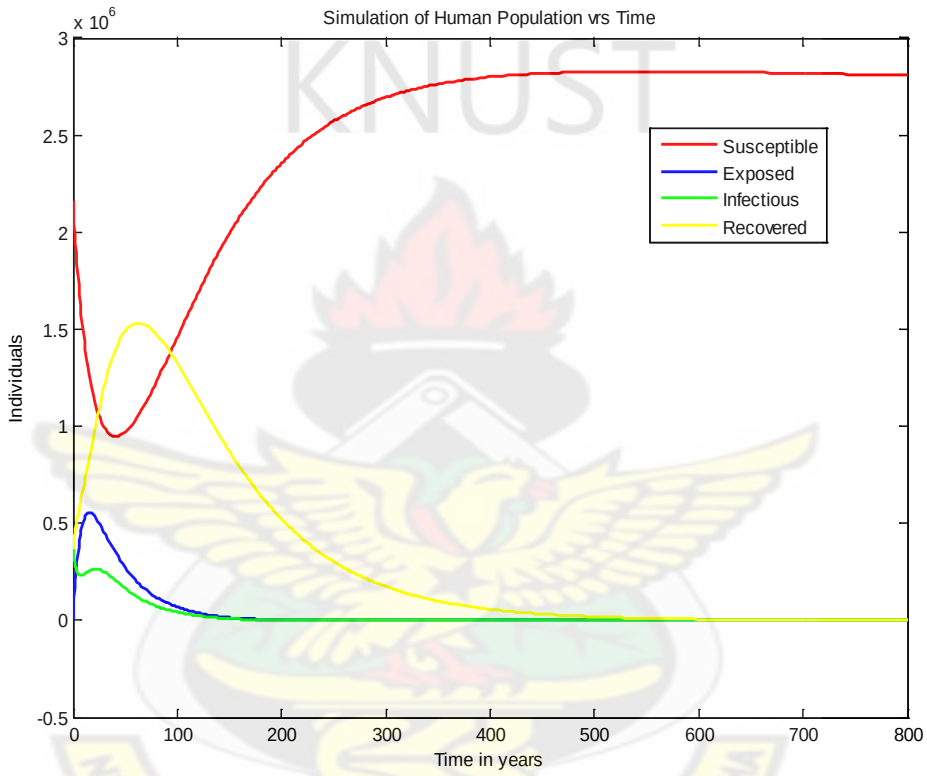

Figure 5.1: Illustrates the behaviour of the human population with time.

From Figure (5.1), we can observe that the susceptible population decreases with time and then increases exponentially due to the interventions being practised. This shows that the susceptible population will be free from the disease. With R_o<1, the plasmodium cannot multiply since there is a means of reducing or eradicating it. Also, the infected population decreases due to a decrease in the exposure to the

disease. We conclude that the control measures in place have positive impact in reducing or eradicating the spread of malaria disease.

4.6.2 Simulation of the behaviour of the vector population

The relationship of the susceptible, exposed and infected vector populations are considered in the figure below.

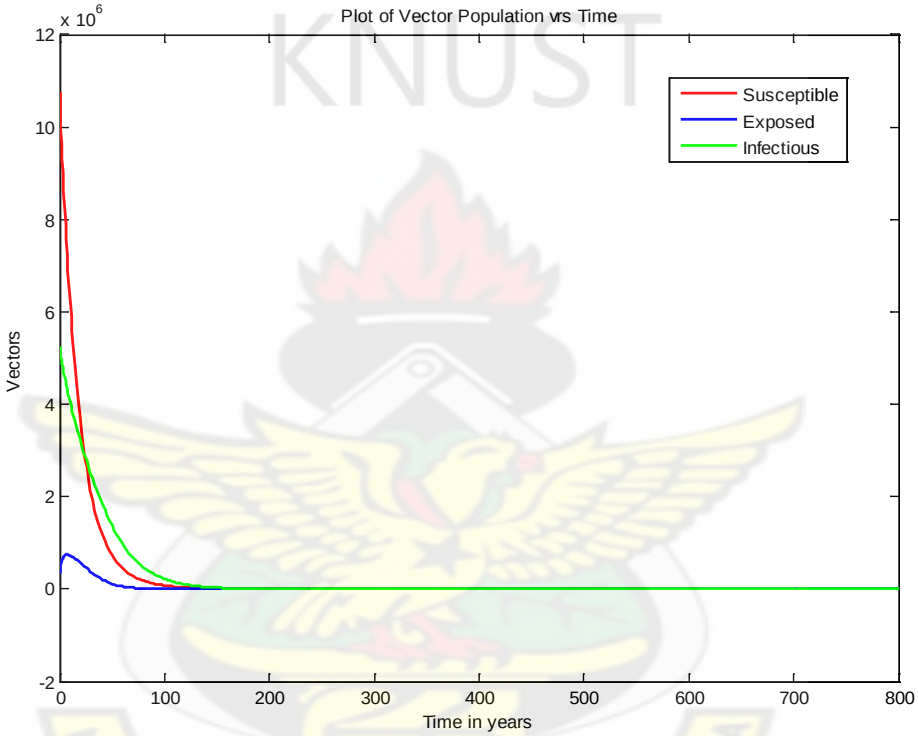

Figure 5.2: Illustrates the changes in the three state variables of the vector population in the model with time.

From figure (5.2) above, we can observe that there is an exponential decrease in all the vector populations with time. The susceptible population will decrease and as such, a lot of the population will not be exposed to the disease. In view of this, the exposed population will decrease. This implies that the plasmodium cannot multiply since there is a means of reducing or eradicating it. This is an

indication that with the current preventive measures, the disease can be eradicated from the region.

4.6.3 Plot showing the prevalence in the model

We now take a look at the prevalence in the population. We define prevalence as the ratio of the number of cases of a disease in a population to the number of individuals in the population at a given time.

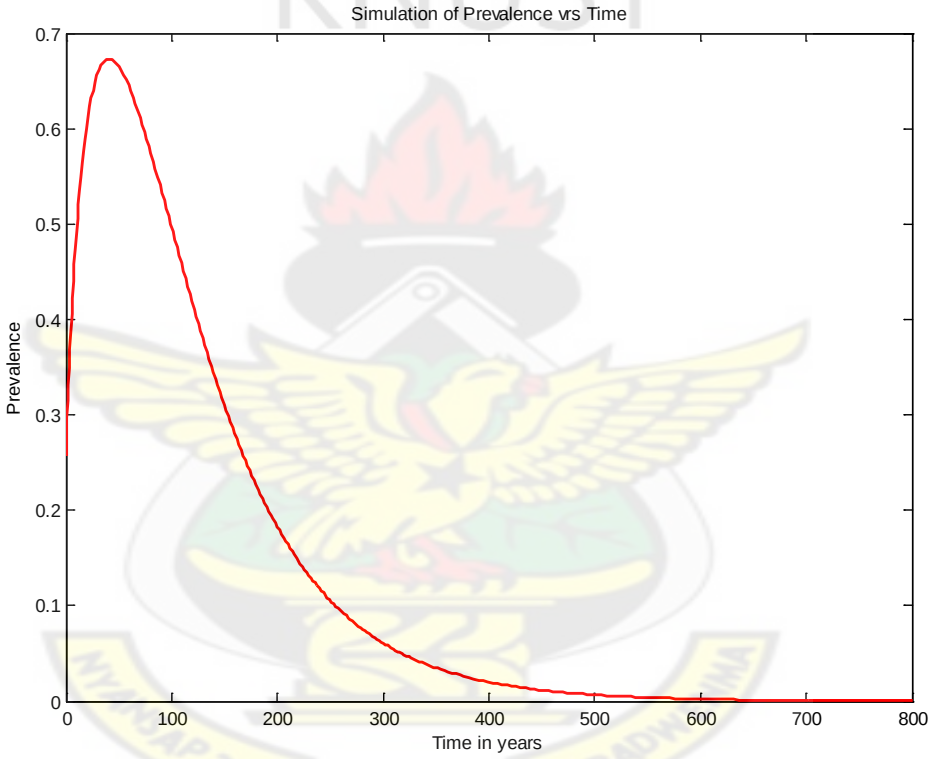

Figure 5.3: Represents changes of prevalence with time

The graph just increases slightly for a while and then drops asymptotically to 0 in the year 2600. This happens as a result of a reduction in the number of susceptible individuals who are affected by the disease with time. Subsequently, this leads to a reduction in the exposed mosquito population and then a corresponding decrease in the infectious vector population. This reduces the prevalence of the disease in the region with time.

4.6.4 Plot showing the behaviour of the biting rate of vectors with time

The susceptible mosquito population, the exposed mosquito population and the infected mosquito population graph, are shown below. This is to enable us to know whether a reduction in the biting rate leads to decrease in the spread of malaria.

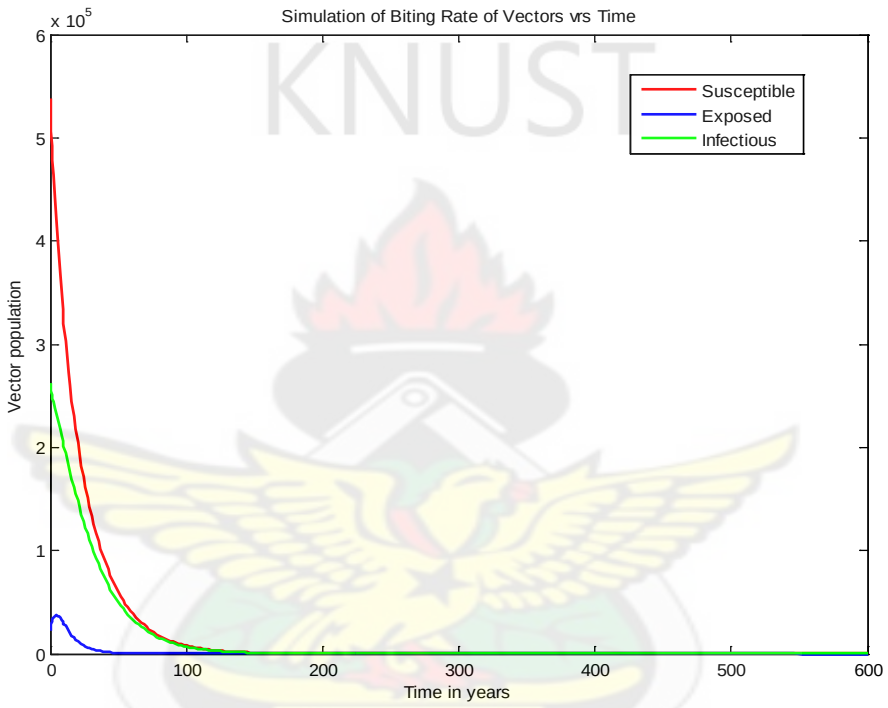

Figure (5.4): Illustrate the dynamics of vector population with time

The susceptible mosquito population, the exposed mosquito population and the infected mosquito population graph, Figure (5.4), shows the decreasing survival probability of a mosquito as more humans are covered by insecticide-treated bed nets and indoor residual spraying. These control measures reduce the availability of hosts, and kill mosquitoes that are attempting to feed, in such way reducing the spread of malaria.

4.7 Discussion

Our main objective was to analyse and describe the dynamics and spread of the malaria in the human population and how best it can be controlled in the Greater Accra Region. We formulated a malaria model to control the spread of malaria and performed stability analysis of the model. We used Matlab ode45 to simulate the model which enabled us know the dynamics of the disease in the region.

The basic reproduction number, R_o, was computed and we did a qualitative analysis of the model which showed that model has both a disease-free and endemic equilibria, and the two equilibrium points are locally asymptotically stable. We computed the disease-free-equilibrium to be $E_0 = (4449290,\ 0,\ 0,\ 0,\ 19081250,\ 0,\ 0)$, the reproduction number, $R_o = 0.6785$ and the endemic equilibrium point was found to be $E_1 = (9.5977x10^6,\ 0.000137,\ 0.012789,\ 0.162485,\ 1.90813x10^7,\ 9.38228x10^{-9},\ 3.20216x10^{-7})$

Numerical results showed that if more people tend to reduce the contact rate of the human and mosquito populations through the use of insecticide-treated bed nets and indoor residual spraying, then the region can reduce or eradicate malaria disease. It can therefore be concluded that if we really want to control the spread of the disease, then we must focus our attention on reducing the biting rate through the use of insecticide-treated bed nets and indoor residual spraying.

CHAPTER FIVE

CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

The summary of the findings as well as the conclusions and recommendations of the study are presented in this chapter. The study sought to analyse and describe the dynamics and spread of the malaria in the human population and how best it can be controlled in the Greater Accra Region.

5.2 Conclusions

We considered a malaria model to know the transmission dynamics of the disease in the Greater Accra region. The human population was varied to include recruitment of new individuals through birth or immigration, into the susceptible (vulnerable) class. Our model was shown to be epidemiologically and mathematically well-posed. We also computed the reproduction number, R_o, and the model was analysed for the existence and stability of disease-free and endemic equilibria. The disease-free equilibrium was proven to be locally asymptotically stable. Numerical analysis of the model recommended a two-pronged approach based on

a. vector control through indoor residual spraying (IRS) and insecticide-treated bed nets.
b. effective case management (diagnosis and treatment).

This is a strategic approach to reduce the transmission of the parasite from infected to uninfected individuals. Malaria case management is based on early detection and effective treatment to control the parasite

5.3 Recommendations

Based on the conclusions of the study, the following recommendations are made:

a. People who are exposed to malaria should be encouraged to use insecticide mosquito treated bednets (ITNs) and indoor residual spray (IRS) since this lead to a decreasing survival probability of a mosquito as more humans are covered.
b. It is recommended that prevention measures must be maintained to reduce or eradicate the disease. This can be achieved by lowering the exposed and infected members of each population.
c. More health centres should be established in many parts of the region to ensure that many people can easily attend hospital for diagnosis and treatment.

5.4 Recommendations for further studies

In view of the fact that this study was limited to only the Greater Accra region, future research should examine similar study countrywide to expand the evidence base and support informed decision-making in this area. Furthermore, it is important to have a comprehensive research done in order to explore new control strategies and access the impact of the existing ones.

REFERENCES

1. Achidi, E. A., Perlmann, H. and Berzins, K. (1995). Asymptomatic Malaria Parasitaemia and Seroreactivities to Plasmodium Falciparum Antigens: In Blood Donors from Ibadan, South-Western Nigeria. Ann Trop Med Parasitol, 89:601–610.
2. Anderson, R.M. and May, R.M. (1991). Infectious diseases of humans: dynamics and control, Oxford University Press, Oxford.
3. Aron, J. L. and May, R. M. (1982). The population dynamics of malaria: In Population dynamics of infectious diseases: theory and applications (ed. R. M. Anderson). Chapman and Hall. London, UK. pp. 139–179
4. Aron, J.L. (1988). Mathematical modeling of immunity to malaria, Mathematical Biosciences, 90:385-396.
5. Bailey, N.J.T. (1975). The mathematical theory of infectious diseases and its application, Griffin, London.
6. Benito, A., Roche, J., Molina, R., Amela, C. and Alvar, J. (1995). In vitro susceptibility of Plasmodium falciparum to chloroquine, amodiaquine, quinine, mefloquine, and sulfadoxine/pyrimethamine in Equatorial Guinea. Am J Trop Med Hyg. 53:526-531.
7. Bin Mohanna, M.A., Bin Ghouth, A.S. and Rajaa, Y.A. (2007). Malaria signs and infection rate among asymptomatic schoolchildren in Hajr Valley, Yemen. East Mediterr Health J. 13:35–40.
8. Blayneh, K.W. and Jang, S.R. (2006). “A discrete SIS-model for a vector-transmitted disease”, Applicable Analysis. 85(10):1271-1284.

9. Blayneh, K.W., Cao, Y. and Kwon, H. (2009). “Optimal Control of Vector-borne Diseases: Treatment and Prevention”, Discrete and Continuous Dynamical Systems Series B. 11(3):1-xx.
10. Blayneh, W.K., Kwon, H. and Cao, Y. (2007). “A model for vector-borne diseases: Optimal treatment and prevention”, Discrete and Continuous Dynamical Systems B. 11(3):587-611.
11. Bousema, J.T., Gouagna, L.C., Drakeley, C.J., Meutstege, A.M., Okech, B.A., Akim, I.N., Beier, J.C., Githure, J.I., Sauerwein, R.W. (2004). Plasmodium falciparum gametocyte carriage in asymptomatic children in western Kenya. Malar J. 3:18.
12. Caldas de Castro, M., Yamagata, Y., Mtasiwa, D. et al. (2004). Integrated Urban Malaria Control: A Case Study in Dar-es Salaam, Tanzania. AmJ Trop Med Hyg. 71:103–17.
13. Castillo-Chavez, C. and Song, B. (2004). Dynamical models of tuberculosis and their applications, Mathematical Biosciences and Engineering, 1:361-404.
14. Coleman, R.E., Maneechai, N., Rachaphaew, N., Kumpitak, C., Miller, R.S., Soyseng, V., Thimasarn, K. and Sattabongkot, J. (2002). Comparison of field and expert laboratory microscopy for active surveillance for asymptomatic Plasmodium falciparum and Plasmodium vivax in western Thailand. Am J Trop Med Hyg, 67:141–144.
15. Curtis, C. F. and Mnzava, A. E. P. (2000). Comparison of house spraying and insecticide-treated nets for malaria control. Bull. World Health Org. 78:1389–1410.

16. Diekmann, O. and Heesterbeek, J.A.P. (2000): Mathematical Epidemiology of Infectious Diseases. Model Building, Analysis and Interpretation Wiley Series in Mathematical and Computational Biology, John Wiley and Sons, La, Chichester.
17. Diekmann, O., Heesterbeek, J.A.P. and Metz, J.A.J. (1990). On the definition and the computation of the basic reproduction ratio Ro in models for infectious diseases in heterogeneous populations, Journal of Mathematical Biology, 28:365-382.
18. Dietz, K. (2008). The estimation of the basic reproduction number for infectious diseases. Stat Methods Med Res. 2:23-41.
19. Dietz, K. (1975). Transmission and Control of Arbovirus Diseases in Epidemiology. (K. L. Cooke, ed.). SIAM, Philadelphia. 104–121.
20. Dietz, K., Molineaux, L. and Thomas, A. (1974). A malaria model tested in the African savannah, Bulletin of the World Health Organisation, 50:347-357.
21. Dietz, K. (1993). The estimation of the basic reproductive number for infectious diseases. Statistical Methods in Medical Research. 2:23-41.
22. Dietz, K. (1975). Models for parasitic disease control. Bull. Intern. Statist. Inst. 46:531-544
23. Eke, R.A., Chigbu, L.N. and Nwachukwu, W. (2006). High prevalence of asymptomatic Plasmodium infection in a suburb of Aba Town, Nigeria. Ann of Afr Med. 5:42–45.
24. Esteva, L and Vargas, C. (2000). Influence of vertical and mechanical transmission on the dynamics of dengue disease. *Mathematical Biosciences*. 167.

25. Ghana Health Service (2010) Annual Report
26. Ghana Health Service (2004). Bulletin of Health Information. 1 (1).
27. Goodman, C. A., Mnzava, A. E. P., Dlamini, S. S., Sharp, B. L., Mthembu, D. J. and Gumede, J. K. (2001). Comparison of the cost and cost-effectiveness of insecticide-treated bednets and residual house-spraying in KwaZulu-Natal, South Africa. Trop. Med. Int. Health. 6:280–295.
28. Guyatt, H.L. and Snow, R.W. (2002). The cost of not treating bednets. Trends Parasitol. 18.
29. Hakim, S.L., Roohi, S.W.A.S., Zurkurnai, Y., Rain, A.N., Mansor, S.M., Palmer, K., Navaratnam, V. and Mak, J.W. (1996). Plasmodium falciparum – increased proportion of severe resistance (RII and RIII) to chloroquine and high rate of resistance to sulfadoxine-pyrimethamine in peninsular Malaysia after 2 decades. Trans R Soc Trop Med Hyg. 90:294-297
30. Heesterbeek, J. A. P. and Dietz, K. (1996). The concept of Ro in epidemic theory. Statistica Neerlandica. 50:89-110.
31. Heesterbeek, J.A.P. (1992). Reproduction number. PhD thesis. University of Leiden. Leiden, The Netherlands.
32. Hethcote, H. W. (2000). The mathematics of infectious diseases. SIAM Review. 42:599-653.
33. Hethcote, H.W., Gross, L., Hallam, T.G. and Levin, S. A. (1989). Three basic epidemiological models in Applied Mathematical Ecology eds. Springer-Verlag, Berlin. 119–144.
34. Hethcote, H.W., Stech, H.W, and van den Driessche, P. (1982). Periodicity and stability in epidemic models: A Survey In Differential equations and

Applications in Ecology, epidemics, and population Problems (S. Busenberg and K.L Cooke, Eds.), Academic Press, San Diego. 65-82

35. Holding, P.A. and Snow, R.W. (2001). Impact of Plasmodium falciparum malaria on performance and learning: review of the evidence. Am J Trop Med Hyg. Suppl 1–2:68–75.
36. http://www.who.int/inf-fs/en/fact094.html. (Retrieved on Wednesday, 17th June, 2009).
37. Klein Klouwenberg, P.M., Oyakhirome, S., Schwarz, N.G., Gläser, B., Issifou, S., Kiessling, G., Klöpfer, A., Kremsner, P.G., Längin, M., Lassmann, B., Necek, M., Pötschke, M., Ritz, A. and Grobusch, M.P. (2005). Malaria and asymptomatic parasitaemia in Gabonese infants under the age of three months. Acta Trop. 95:81–85.
38. Koella, J.C. and Antia, R. (2003). Epidemiological models for the spread of anti-malarial resistance, Malaria Journal, 2
39. Koella, J.C. and BoÄete, C. A model for the coevolution of immunity and immune evasion in vector-borne disease with implications for the epidemiology of malaria, The American Naturalist, 161 (2003), pp. 698-707.
40. Koella, J.C. (1991). On the use of mathematical models of malaria transmission, Acta Tropica. 49:1-25.
41. Le Port, A., Cot, M., Etard, J.F., Gaye, O., Migot-Nabias, F., Garcia, A. (2008). Relation between Plasmodium falciparum asymptomatic infection and malaria attacks in a cohort of Senegalese children. Malar J. 7:193.
42. Li, J., Welch, R. M., Nair, U. S., Sever, T. L., Irwin, D. E., Cordon-Rosales, C. and Padilla, N. (2002). Dynamic malaria models with environmental

changes, in Proceedings, Thirty-Fourth Southeastern Symposium on System Theory, Huntsville, AL, USA, pp. 396-400.

43. Macdonald, G. (1950). The analysis of infection rates in diseases in which superinfection occurs. trop. Dis. bull. 47:907-915.
44. Macdonald, G. (1952). The analysis of sporozoite rate. Trop. Dis. Bull. 49:569-585.
45. Macdonald, G. (1968). The dynamics of malaria. Bull World Health Organisation. 38:743–755.
46. Macdonald, G.: The epidemiology and control of malaria, Oxford University Press, London, 1957.
47. Males, S., Gaye, O. and Garcia, A. (2008). Long-term asymptomatic carriage of Plasmodium falciparum protects from malaria attacks: a prospective study among Senegalese children. Clin. Infect Dis. 46:516–522.
48. Martens, P. (1999). How will climate change affect human health? American Scientist. 87
49. Miranda, I., Teboh-Ewungkem, Chandra, N. Podder and Abba, B. G. (2009). Mathematical Study of the Role of Gametocytes and an Imperfect Vaccine on Malaria Transmission Dynamics", Bulletin of Mathematical Biology DOI 10. 1007(S11):538-009-9437-3.
50. Mockenhaupt, F. (1995) Mefloquine resistance in Plasmodium falciparum. Parasitol Today 11:248-253
51. Ministry of Health, (2009). Guidelines for Case Management of Malaria in Ghana.
52. Ministry of Health, (2009). Revised Anti-Malaria Drug Policy for Ghana, 2 Revised Version.

53. Molineaux, L. and Gramiccia, G. (1980). The Garki Project: Research on the Epidemiology and Control of Malaria in the Sudan Savanna of West Africa. WHO, Geneva.
54. Moore, D.V. and Lanier, J.E. (1961). Observations on two Plasmodium falciparum infections with abnormal response to chloroquine. Am J Trop Med Hyg. 10:5-9
55. Murray, J.D. (1991). Mathematical Biology Volume 19. Springer-Verlag, New York.
56. Murray, J.D.: (2002): Mathematical Biology, An Introduction. Springer, New York, third edition. Volume 17
57. Mwantobe, P.M.M., (2010): Modelling the Effects of Multi-Intervention Campaigns for the Malaria Epidemic in Malawi, M.Sc. (Mathematical Modelling) Dissertation, University of Dar-es Salaam, Tanzania.
58. National Malaria Control Programme (2005), Annual Report
59. Nedelman, J. (1985). Introductory review some new thoughts about some old malaria models. Math. Biosci. 73:158-182.
60. Ngwa, G.A. and Shu, W.S. (2000). A mathematical model for endemic malaria with variable human and mosquito populations. Mathematical and Computer Modelling. 32:747-763.
61. Ngwa, G.A. (2004). Modelling the dynamics of endemic malaria in growing populations, Discrete and Continuous Dynamical Systems Series B. 4:1173-1202.
62. Niger, A.M. and Gumel, A.B. (2008). Mathematical Analysis of the Role of Repeated Exposure on Malaria Transmission Dynamics. Differential Equations and Dynamical Systems. 16(3)251-287.

63. Njama-Meya, D., Kamya, M.R. and Dorsey, G. (2004). Asymptomatic parasitaemia as a risk factor for symptomatic malaria in a cohort of Ugandan children. Trop Med Int Health. 9:862–868.

64. Nkoghe, D., Akue, J.P., Gonzalez, J.P. and Leroy, E.M. (2011). Prevalence of Plasmodium falciparum infection in asymptomatic rural Gabonese populations. Malar J. 10:33.

65. Owusu-Agyei, S., Koram, K.A., Baird, J.K., Utz, G.C., Binka, F.N., Nkrumah, F.K., Fryauff, D.J. and Hoffman, S.L. (2001). Incidence of symptomatic and asymptomatic Plasmodium falciparum infection following curative therapy in adult residents of Northern Ghana. Am J Trop Med Hyg. 65:197–203.

66. Patz, J. A. and Olson, S. H. (2006). Malaria risk and temperature: influences from global climate change and local land use practices. Proc. Natl Acad. Sci. USA. 103:534–541.

67. Richards, A.K., Smith, L., Mullany, L.C., Lee, C.I., Whichard, E., Banek, K., Mahn, M., Shweo, E.K. and Lee, T.J. (2007). Prevalence of Plasmodium falciparum in active conflict areas of eastern Burma: a summary of cross-sectional data. Confl Health. 1:9.

68. Roberts, M.G. and Heesterbeek, J.A.P. (2003). A new method for estimating the effort required to control an infectious disease. Proceedings of the Royal Society of London Series B. 270:1359-1364.

69. Ross, R. (1909). Report on the Prevention of Malaria in Mauritius. Churchill, London.

70. Ross, R. (1911). The prevention of Malaria. John Murray. London.

71. Sachs, J. and Malaney, P. (2002). The economic and social burden of malaria. Nature. 415:680–685.
72. Sharp, B., Van Wyk, P., Sikasote, J. B., Banda, P. and Kleinschmidt, I. (2002). Malaria control by residual insecticide spraying in Chingola and Chililabombwe, Copperbelt Province, Zambia. Trop. Med. Int. Health. 7:732–736.
73. Smith, D. L. and McKenzie, F. E. (2004). Statics and dynamics of malaria infection in Anopheles mosquitoes. Malar. J. 3:13.
74. Smith, D.L., Dushoff, J., Snow, R.W. and Hay, S.I. (2005). The entomological inoculation rate and Plasmodium falciparum infection in African children. Nature. 5:438-492.
75. Smithius FM, Monti, F., Grundl, M., Kyaw, T.T., Phe, O. and White, M.J. (1997). Plasmodium falciparum: sensitivity in vivo to chloroquine, pyrimethamine/sulfadoxine and mefloquine in western Myanmar. Trans R Soc Trop Med Hyg. 91:468-472.
76. Tumwiine, J., Mugisha, J.Y.T. and Luboobi, L.S. (2007). On oscillatory pattern of malaria dynamics in a population with temporary immunity. Computational and Mathematical Methods in Medicine. 8(3):191-203.
77. United Nations, (2010). The Millennium Development Goals Report, accessed online at http:www.who.int/inf-fs/en/1. Information in Ghanaian Children. Malar J. 9:39
78. Van den Driessche, P. and Watmough, J. (2002): Reproduction numbers and Sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical Bio-sciences, 180: 29-48.

79. Van den Driessche, P. and Watmough, J. (2000). A simple SIS epidemic model with a backward bifurcation, Journal of Mathematical Biology, 40:525-540.
80. Wellems, T.E. (2002). Plasmodium chloroquine resistance and the search for a replacement antimalarial drug. Science Magazine. 298 (5591):124–6. http://www.sciencemag.org/cgi/pmidlookup?
81. Woolhouse, M.E., Dye, C. and Etard, J.F. (1997). Heterogeneities in the transmission of infectious agents: implications for the design of control programs. Proc Natl Acad Sci U.S.A. 94(3):38–42.
82. World Health Organization, (2010). Global Report on Malaria
83. World Health Organization, (2009): World Malaria Report.
    a. http://www.who.int/health topics/malaria/en/.
    b. http;//www.un.org/millenniumgoals retrieved on Sunday, 3th May, 2009.
84. Yang, H.M. (2000): Malaria transmission model for different levels of acquired immunity and temperature-dependent parameters (vector). Re Saude Public, 34:223-231.
85. Yang, H.M. and Ferreira, M.U. (2000). Assessing the effects of global warming and local social economic conditions on the malaria transmission. Re Saude Public. 34:214-222.

APPENDICES

Appendix A

The Next Generation Operator Approach

Let $\mathcal{F}_i$ equals the rate of appearance of new infections in compartment i;

$\mathcal{V}_i = \mathcal{V}_i^- - \mathcal{V}_i^+$ be the difference between the rate of transfer of individuals out of compartment *i*, ($\mathcal{V}_i^-$), by all other means and the rate of transfer of individuals in the compartment *i*, ($\mathcal{V}_i^+$) by all other means; and x_0 be the disease-free equilibrium point. According to Diekmann and Heesterbeek (2000), we call $\mathcal{F}\mathcal{V}^{-1}$ the next generation matrix for the model and we set,

$$R_o = \rho(\mathcal{F}\mathcal{V}^{-1}),$$

where $\mathcal{F} = \left[\frac{\partial \mathcal{F}_i(x_o)}{\partial x_j}\right]$ and $\mathcal{V} = \left[\frac{\partial \mathcal{V}_i(x_o)}{\partial x_j}\right]^{-1}$ with $1 \leq i, j \leq m$ for the infected compartments only. $\rho(A)$ denotes the spectral radius of a matrix *A*, $\mathcal{F}$ is nonnegative and $\mathcal{V}$ is non-singular M-matrix and both are $m\ x\ m$ matrices, where m is the number of infected classes.

Consider an infected individual introduced into compartment *k* of a disease-free population. The (i, j) entry of $\mathcal{F}$ is the rate at which an infected individual in compartment *j* produces new infections in compartment *i* and the (j, k) entry of V^{-1} is the average time an infected individual spends in compartment *j* during its lifetime in compartment *k*. Hence, the (i, k) entry of the product FV^{-1} is the expected number of new infections in compartment i produced by the infected individual originally introduced into compartment *k*, (van den Driessche and Watmough, 2002).

Appendix B

Castillo-Chavez and Song

Consider the following general system of ordinary differential equations with a parameter Γ.

$$\frac{dx}{dt} = h(x, \Gamma) \ , h: \mathbb{R}^n \times \mathbb{R} \longrightarrow \mathbb{R} \ \ and \ \ h \in \mathbb{C}^2(\mathbb{R}^n \times \mathbb{R})$$

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

- $A = D_x h(0,0) = \left(\frac{\partial h_i}{\partial x_i}(0,0)\right)$ is the linearization matrix of the system around the equilibrium 0 with Γ evaluated at 0.
- Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts.
- 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

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

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

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

2) $a < 0$, $b < 0$, when $\Gamma < 0$ with $|\Gamma| << 1$, 0 is unstable; when $0 < \Gamma << 1$, 0 is locally asymptotically stable, and there exists a positive unstable equilibrium.

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

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

Appendix C

Matlab Code

a) The M-function files

```
function dydt = malmod(t,y)
dydt=zeros(size(y));
a1=(0.0322/365);a2=0.000042808;a3=(1/14);a4=(1/90);a5=0.0655;a6=0.071;
b1=0.04;b2=0.0000027;b3=(1/11);b4=0.42;b5=(1/7);b6=0.4;
Sh=y(1);
Eh=y(2);
Ih=y(3);
Rh=y(4);
Uv=y(5);
Vv=y(6);
Wv=y(7);
Nh=Sh+Eh+Ih+Rh;
%The rates of infection are as follows
r1=a5*b6/Nh; r2=b4*b6/Nh;
%The equations of the malaria model system
dydt(1)=a1+a4*Rh-a2*Sh-r1*Wv*Sh;
dydt(2)=r1*Wv*Sh-(a2+a3)*Eh;
dydt(3)=a3*Eh-(b5+a2+b2)*Ih;
dydt(4)=b5*Ih-(a4+a2)*Rh;
dydt(5)=a6-r2*Ih*Uv-b1*Uv;
dydt(6)=r2*Ih*Uv-(b3+b1)*Vv;
dydt(7)=b3*Vv-b1*Wv;
%The reproduction number for the malaria model is
Ro=sqrt((a5*a3*b6*a2*b4*b3*b6*a6)/(a1*(a3+a2)*(b5+a2+b2)*b1*b1*(b3+b1)))
```

b) The executive file for behaviour of susceptible, exposed, infected and recovered individuals

```
tspan=[0 800];
y0=[2159000 2000 374000 371000 10750000 350000 5256000]
[t,y]=ode45(@malmod,tspan,y0);
plot(t,y(:,1),'r',t,y(:,2),'b',t,y(:,3),'g',t,y(:,4),'y','Linewidth',2)
title('Simulation of Human Population vrs Time')
xlabel('Time in years')
ylabel('Individuals')
legend('Susceptible','Exposed','Infectious','Recovered',2)
```

c) The executive file to determine the behaviour of susceptible, exposed and infected vector populations

```
tspan=[0 800];
y0=[2159000 2000 374000 371000 10750000 350000 5256000]
[t,y]=ode45(@malmod,tspan,y0);
plot(t,y(:,5),'r',t,y(:,6),'b',t,y(:,7),'g','Linewidth',2)
title('Plot of Vector Population vrs Time')
xlabel('Time in years')
ylabel('Vectors')
legend('Susceptible','Exposed','Infectious',2)
```

d) The executive file for prevalence in the model

```
tspan=[0 800];
y0=[2159000 2000 374000 371000 10750000 350000 5256000];
[t,y]=ode45(@malmod,tspan,y0);
T1=(y(:,1)+y(:,2)+y(:,3)+y(:,4));
plot(t, (y(:,2)+y(:,3)+(y(:,4))./T1,'r','Linewidth',2)
title('Simulation of Prevalence vrs Time')
xlabel('Time in years')
ylabel('Prevalence')
```

e) Executive file for biting rate of vectors

```
tspan=[0 600];
y0=[2159000 2000 374000 371000 537500 21880 262800]
[t,y]=ode45(@malmod,tspan,y0);
plot(t,y(:,5),'r',t,y(:,6),'b',t,y(:,7),'g','Linewidth',2)
title('Simulation of Biting Rate of Vectors vrs Time')
xlabel('Time in years')
ylabel('Vector population')
legend('Susceptible','Exposed','Infectious',2)
```