KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY,

KUMASI

MODELLING THE IMPACT OF **PROTECTION AND TREATMENT STRATEGIES** ON TRANSMISSION DYANAMICS OF MALARIA IN GHANA

A THESIS SUBMITTED TO THE DEPARTMENT OF MATHEMATICS IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTER OF PHILOSOPHY DEGREE IN APPLIED MATHEMATICS

BY

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CERTIFICATION

I herein certify that, this work was carried out solely by Paddy Jonathan (PG1099913) in the department of Mathematics, in partial fulfilment of the requirement for the award of Master of philosophy Degree in Applied Mathematics.

…… ……..

Dr. F.T. Oduro Date

(Supervisor)

DECLARATION

I hereby declare that this thesis is the result of my own work towards the Master of Philosophy (MPhil) and that, to the best of my knowledge, it contains no material previously published by another person or group of people or material which has been accepted for the award of any other degree of the University, except where the acknowledgement has been made in the text.

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DEDICATION

This thesis is dedicated to my wife, children, and parents. It is also dedicated to the memory of the founders and pioneers of mathematics whose fundamental theorems have made mathematics what it is today and lastly to every individual (both alive and yet to be born) who may have interest in the study of mathematics.

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My primary debt of gratitude goes to Almighty God for his grace, mercy and protection all these years of my educational life. Glory be unto his name.

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I am also thankful to my parents, relatives and friends who in diverse ways contribute to the success of our education. I wish them in returns abundance of love, peace, success and prosperity.

ABSTRACT

Eradicating malaria from Ghana has proven to be a difficult challenge not only to the researchers and health organizations but also to government .Despite great advances over the last decade, including the training of all health staff to control the disease, Ghana remains one of the countries worst affected by malaria. The goal of this thesis is to develop a mathematical model to help to assess the potential impact of protection and treatment strategies on the dynamics of malaria in Ghana. A basic deterministic malaria model SEIR model was first formulated. The model consists of seven non-linear differential equations which describe the dynamics of malaria with 4 variables for humans and 3 variables for mosquitoes. Analysis of the model showed that there exists a domain where the model is epidemiologically and mathematically well-posed. Key to the analysis is the definition of the basic reproductive number R_0, which was derived by use of next generation method. The basic reproduction number for Ghana is found to be

$R_0 \approx 0.7397$ hence malaria can be eliminated from Ghana. The disease-free equilibrium point is asymptotically stable. This means that malaria free society can be achieved.

In order to assess the potential impact of protection and treatment strategies on the transmission dynamics of malaria, two intervention strategies ,the protected and treated classes were added to the basic malaria model to formulate SPEITR model which consists of nine non-linear differential equations. The effective reproductive number was computed and was found to be $R_e \approx 0.0060183$.When the protection is not practiced and hence treatment is the only intervention strategy, then effective reproduction number R_e becomes

$R_{et} \approx 0.7151$. If protection is the only intervention strategy being practiced, the effective reproduction number becomes $R_{ep} \approx 0.006019$. The threshold for effective reproduction number and the basic reproduction number in the absence of the disease was compared. R_e is the useful indication of the effort required to eliminate an infection. It was also noted that $R\ R\ R\ R_e \square\ \square\ \square_{ep\ et\ 0}$ which implied that increasing preventive and control measures has a great effect on reduction of R_e. Numerical simulation of the model suggests that the most effective strategy for controlling or eradicating malaria is not only to reduce the biting rate of the female anopheles mosquito through the use of insecticide-treated bed nets and indoor residual spraying but to include prompt and effective diagnosis and treatment of infected individuals.

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CHAPTER ONE

INTRODUCTION

This chapter deals with the background of the study which includes Economic burden of malaria and life cycle of the malaria parasite.It also states the objectives of the thesis ,methodology that will use and how the chapters are organization in the thesis.

1.0 Background of the Study

Malaria disease has been of a great concern to human kind since the very beginning of our history. It is economic and social disease that burdens many nations globally with a mortality rate that is unmatched by any other modern disease other than tuberculosis (Sudhakar and subramani., 2007). In terms of lives lost and economic burden, malaria has had a very profound impact worldwide (Larry et al, 2005).World malaria report (2013) stated that one of the greatest tragedies of the 21st century is the fact that so many people are dying from mosquito bites.

According to world malaria report (2013), 3.4 billion people (almost half the world's population) are at risk of getting malaria, of which 1.2 billion are at high risk. In highrisk areas, more than one malaria case occurs per every 1000 population. Pregnant women and their unborn children are particularly vulnerable to malaria: it causes low birth weight and maternal anaemia. Infants born to mothers with malaria are likely to have low birth weight which has been the single greatest risk factor for death during the first three months of life. Another groups of people in the population that are at a high risk of getting the disease are travelers and migrants with no or partial immunity and are coming from areas with partial or no immunity.

According to the world health organization (2013), 207 million people felt sick from the disease and an estimated 627 000 deaths were recorded in 2012, with most of the people

from the poorest parts of the world such as, Sub-Saharan Africa, parts of Latin America and Asia .Thirty thousand (1300) children die from malaria every day (one child die almost every minutes) .In 2012, malaria killed an estimated 483 000 children under five years of age accounting for 77% of related death cases.

Houeto et al., (2007) agreed that malaria was the fourth leading cause of death among children under five years in developing countries including Africa and accounts for over one million deaths each year in areas with high malaria transmission, (WHO, 2007).

Indeed, sub-Saharan Africa alone in 2012 accounts for 80% of the world's estimated 207 million case. In the same year, 90% of the estimated 627 000 global malaria deaths occurred in Africa.

In Ghana, 11.3 million people contracted malaria in the year 2013 with the majority of cases being undocumented since they occur in areas where there are no health centers. Due to lack of transportation and the rural location, many people suffer from the disease without been treatment. Many of these people are too poor to afford access to hospitals and pharmacies or chemical stores even if they were within a walking distance.

According to Pattanayak et al., (2003) many of the world's poorest people live in areas of high rates of malaria. These People do not have access to effective health care due to financial constraint. It said that on the average 30,300 of such cases were seen each day in the county's health facilities in 2013. Malaria is known as a major cause of child death in Africa, but a recent Report has revealed that the reality is much worse than what has been reported. (WHO, 2013). In Ghana alone, between 3.1 and 3.5 million annual cases of clinical malaria were reported in public health facilities, of which 900,000 cases were children under the age of five. UNICEF (2007) reported that children die from Malaria every year (25 per cent of the deaths of children under the age of five). Even if a child

survives, the consequences from severe malaria such as convulsions or brain dysfunction can hamper long-term development and schooling.

1.1.1 Economic Burden of malaria

Malaria has been an important public health problem in sub-Saharan Africa (SSA) and continues to have a severe socioeconomic impact on our populations. It imposes substantial costs to not only the individual but the society and the nation as a whole. The Nobel prize-winning economist Jeffrey Sachs said malaria is first and foremost a disease of poverty. It is a disease of poverty and a cause of poverty in SSA. This disease is frequently called disease of the poor because its prevalent rate is very high in the poorest continent and in the poorest countries (Worral et al., 2003)

For developing economies, the gap in prosperity between countries with malaria and countries without malaria has become wider every single year. Annual economic growth in countries with high malaria transmission has historically been lower than in countries without malaria. Economists believe that malaria is responsible for a 'growth penalty' of up to 1.3% per year in some African countries. In a 2004 survey, nearly three-quarters of companies in the Africa region reported that malaria was negatively affecting their business.

Malaria also continues to prevent many school children from attending school due to illness, diminishing their capacity to realize their full potential (World malaria report 2013). Roll Back Malaria (2011) reported that Malaria caused economic losses of more than 12 billion USD annum and over 40% of public expenditure,30-50% of hospital admissions and over 50% of hospital visits mainly in poor countries in sub-Saharan Africa (O'Meara.,2010).

Roll Back Malaria report (2011) found that in sub-Saharan Africa, 72% of companies reported a negative malaria impact, with 39% perceiving these impacts to be serious.

International disbursements for malaria control rose from US$ 100 million in 2000 to US$ 1.94 billion in 2012 and US$ 1.97 billion in 2013. National government funding for malaria programmes has also increased since 2004 but not at the same pace; the total for 2012 was US$ 522 million.

The currently available funding is far below the resources required to reach universal coverage of interventions. An estimated US$ 5.1 billion is needed every year for this purpose. In 2012, the global total of international and domestic funding for malaria was US$ 2.5 billion which is less than half of what is needed.

1.1.2 Malaria parasite

Malaria is caused by a protozoan parasite of the genus Plasmodium. Malaria parasites are eukaryotic single-celled microorganisms that belong to the genus *Plasmodium* (Tuteja, 2007).Plasmodium spp. that cause malaria require two hosts throughout their lifecycle. They include man (vertebrate host) and mosquitoes (invertebrate female Anopheles spp.), with mosquitoes being the primary host. Anopheles gambiae is known to be the world's most efficient malaria vector larry etal (2005).

It is spread in three ways. The most common one is by the bite of an infected female Anopheles mosquito. Human malaria could only be transmitted by *Anopheles* mosquitoes because they feed on blood meal.The parasites are transmitted from person to person by a mosquito, of the genus Anopheles, each time the infected insect takes a blood meal. However, malaria could also be spread through a transfusion of infected blood and by sharing needle with an infected person. The symptoms of the disease are fever, chills, sweats, headache, nausea and vomiting, body aches, and general malaise.

Of the approximately 400 species of *Anopheles* throughout the world, about 60 are malaria vectors under natural conditions, 30 of which are of major importance (Tuteja, 2007). Only 5 of the species of plasmodia are infectious to humans (Tuteja, 2007).

These five species of Plasmodium parasites are Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and plasmodium knowlesi.

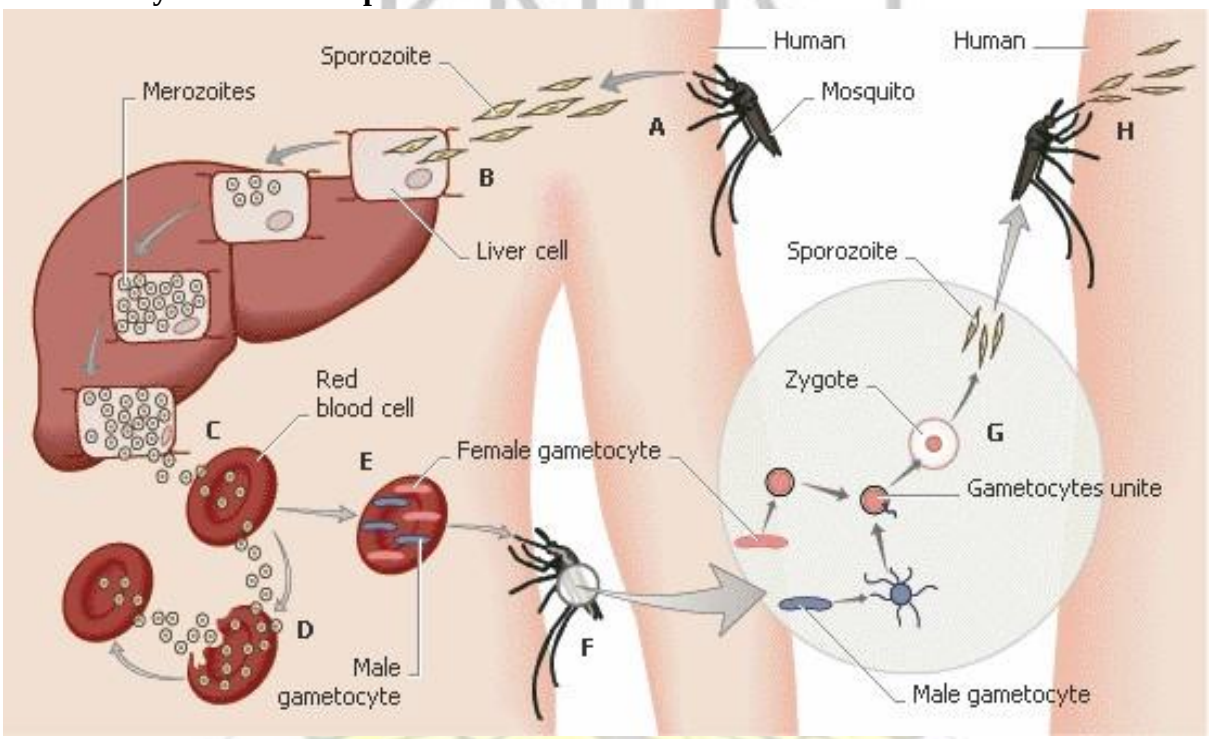
Plasmodium falciparum are found worldwide. P. falciparum is known to cause the deadliest form of malaria. Majority of cases and almost all deaths are caused by Plasmodium falciparum (Snow et al., 2004). It is the agent of severe, potentially fatal malaria and is the principal cause of malaria deaths in young children in Africa (Snow et al., 2004) and generally 90% of all cases in Africa (Suh et al., 2004). The incubation period for this parasite is 5-12 days. They are resistant to most of the drugs used to treat or prevent malaria.

Plasmodium vivax, Plasmodium ovale and Plasmodium malariae cause less severe disease (Suh et al., 2004). P. vivax are found worldwide but most commonly in India, Central and South America. The incubation period in the human body is approximately 8-13 days for the symptoms of the disease to become apparent. Infection by this parasite can sometimes lead to life-threatening rupture of spleen. They hide in liver and can return later once a person is infected.

P. ovale are found mostly in Africa. This form of malaria has an incubation period of 817 days in the infected person and can hide in the liver of partially treated people and return later.

P. malariae are found in most part of the world but are less frequent than other forms of the malaria parasite. The incubation period for this parasite is 2-4 weeks in the infected person. If the disease is untreated, it can last for many years.

1.1.3 Life cycle of malaria parasite



Picture Courtesy: MSN Encarta

Figure 1.0 Life cycle of malaria parasite

Figure 1.0 above explains the development phase of the malaria parasite. The infection begins when the malaria parasite enters the human body through the bite of the infected female *Anopheles* mosquito from its blood meal. The sporozoites are transferred to a human host with the mosquito bite, injecting its saliva into the tiny blood vessels (A).The sporozoite travels with the blood to the liver and enters the liver cells (B). In the liver some of the sporozoites divide and become thousands of merozoites. The merozoites enters the blood after being released from the liver cell and are taken by the red blood cells (C). In the red blood cells some of the merozoites turn into a ring formed trophozoites , which

splits again to form schizonts . The schizonts burst the red blood cells (D) at a certain moment, releasing the merozoite which in turn infects more red blood cells.

Each burst of red blood cells is associated with violent rise of temperature and severe body chill as seen during the attacks in malaria. The trophozoites that were left over during the division will develop into a sexual form, the male and female gametocyte (E) in the course of few days. The gametocyte is the form that infects mosquito and reproduces itself. When the uninfected mosquito has sucked blood (F) containing gametocytes, they pass into the salivary glands of the mosquito, where they develop into a new form, the sporozoites (G). The parasite matures inside the mosquito until it reaches the stage where it can again infect a human host when the mosquito takes her next blood meal (H), 10 to 14 or more days later. The incubation period (time from mosquito bite to development of the disease) is usually about 10 to 15 days. This period can be much longer depending on whether any antimalarial medication has been taken. *Plasmodium ovale* and *Plasmodium vivax* can stay in dormant form known as hypnozoite in liver cell, which can cause relapses of the disease months and even years after the original disease (relapsing malaria) (E. Schwartz,2003)

1.2 Statement of Problem

Good health is not only a basic human need but also a fundamental human right and a prerequisite for economic growth (Streeten, 1981). It is both a cause and consequence of under-development in any nation. The 2013 World Malaria Report commissioned by the WHO, shows malaria claimed 627,000 lives globally in 2012. In Ghana, malaria is the number one cause of morbidity and mortality accounting for 40-60% of outpatient. In Ghana alone, between 3.1 and 3.5 million annual cases of clinical malaria were reported in public health facilities, of which 900,000 cases were children under the age of five.

Malaria is hyperendemic in all parts of the country, with the entire population of 25 million at risk. The Government of Ghana is committed to spending $86,217,602 between 2009 and 2013 on malaria control, mainly on human resources and IPTp but yet malaria is number one killer among children. Several control programmes as such Intermittent Preventive Treatment in Infants (IPTI) by UNICEF, Roll Back Malaria (RBM) and Integrated Malaria Control Programme by AngloGold

Ashanti have been initiated in Ghana. Despite great advances over the last decade, Ghana remains one of the country's worst affected by malaria. The Yendi Municipal Director of Heath Service, Mrs. Denisia Agong Kara, on may 26, 2011 lamented that even though effective measures were being taken, including the training of all health staff to control malaria, the disease still continued to affect some people. Since all this strategies alone have not been able to eradicate malaria to our satisfaction, there is therefore the need to include a mathematical modelling to assist decision makers to formulate the best ideas to prevent, control and eradicate the disease upright.

1.3 Objectives

The objectives of this thesis are the following**;**

i. To formulate and analyze the basic malaria model (SEIRS) ii. To formulate and analyze the basic malaria model with interventions (SPEITR) iii. Investigate the

transmission dynamics of malaria and assess the effects of control measures in terms of the basic reproduction number.

iv. To simulate the impact of some of the intervention strategies of the models with numerical values.

1.4 Methodology

The data use for the analysis is a secondary data obtained from literature. Computations and Analysis were performed using mapple and matix laboratory (matlab).The basic SEIRS model was used to create the malaria model with interventions.

1.5 Justification

Good health is not only a basic human need but also a fundamental human right and a prerequisite for economic growth (Streeten, 1981). It is both a cause and consequence of under-development in any nation. This mathematical model in the thesis will help decision makers and stakeholders to understand the transmission and spread of malaria in order to make precise policy interventions.

It will also help to measure the performance of the interventions the nation has made so far in controlling the malaria disease. Finally, it will help researchers to further develop suitable models to help Ghana Health service make better strategies for controlling the disease.

1.6 Organization of the Thesis

Chapter One is the introduction which highlights on the background of the study, statement of the problem, objectives of the study, justification and the organization of the study. Chapter Two deals with the review of literature. Literature on malaria and some malaria intervention programme were reviewed. Highlights on the works of some of its

contributors that lead to the study of this thesis topic are also considered. Literature on SIR and SEIR models were also discussed in this chapter. In Chapter Three, the methodology used to achieve the objectives under study would be clearly stated. The basic malaria model without any intervention strategies and the model modified with intervention strategies were considered. The basic reproductive numbers were also considered in this chapter. Numerical simulations of the basic malaria model in the absence of any intervention and the malaria model with intervention strategies were discussed in Chapter Four. Summary of findings, recommendation and conclusion would also appear in Chapter Five.

CHAPTER TWO

2.0 LITERATURE REVIEW

This chapter deals with the review of literature. Literature on malaria, malaria models such as SIR and SEIR models and some malaria intervention programme are reviewed.

Highlights on the works of some of its contributors that lead to the study of this thesis topic are also considered.

2.1 Related Work on Malaria

Vries (2000) used LEMRA (Local Eco-Epidemiological Malaria Risk Assessment) model to examine the disease (malaria) dynamics in the population in the context of spatial setting where the local condition determines the risk for the population to be exposed to malaria. He found that disease risk is mainly influenced by social-economic and social cultural factors like human migration and circulation patterns. The researcher selected Kenya as a case study to assess malaria risk, and found that humans traveling from the valley to the highlands and vice versa might significantly influence the malaria dynamics in the area. On the other hand people who travel can spread malaria in two ways. In the first case the traveler harbours the malaria parasite and transmits the disease through its movements to areas of low or sporadic transmission. In the second case, the travellers initiate from these areas of low and sporadic transmission and expose themselves to the disease through their movements to areas of high transmission.

Also Yang (2001), developed a mathematical model for malaria that incorporates global warming and local socioeconomic conditions. The main objective was to apply sensitivity analysis to a mathematical model describing malaria transmission relating global warming and local socioeconomic conditions which represent the level of malaria infection in a community.

Their work was mainly based on the infection and none of the interventions were tackled. Lee et al (2001) evaluated the factors that determine the transmission level of vivax malaria using vectorial capacity, by conducting entomological surveys from June to August, 2000. From 6 nights of human-bait collection in Paju, the human biting rate (ma)

was counted as 87.5 bites/man/night. The parity of *Anopheles sinensis* from human baiting collections fluctuated from 41% to 71% (average 48.8%) of which the rate gradually increased as time passed on: 35.2% in Jun.; 55.0% in July; 66.2% in Aug. From this proportion of parous, they could estimate the probability of daily survival rate of An. sinensis to be 0.79 assumed with 3 days gonotrophic cycle and the expectancy of infective life through 11 days could be defined as 0.073. Blood meal analysis was performed using ELISA to determine the blood meal source. Only 0.8% of blood meals were from human hosts. They could conclude that *An. sinensis* is highly zoophilic (cow 61.8%). Malaria is highly unstable (stability index < 0.5) in this area. From these data, vectorial capacity (VC) was determined to be 0.081. In spite of a high human biting rate (ma), malaria transmission potential is very low due to a low human blood index. They concluded that malaria transmission by *An. sinensis* is causes by high population density, not by high transmission potential. They recommended that in order to eradicate malaria in Korea more effort is needed to decrease vector population and vector-human contact.

Li et al (2002), formulated a dynamic model for the transmission of malaria in both host human and vector mosquito populations. They included incubation periods for both infected human hosts and mosquitoes. The researchers further divided the infected human population into subgroups based on their infection history. Threshold conditions which determine whether the disease spreads in the human and vector populations or dies out were obtained. An explicit formula for the reproductive number is derived. The reproductive number is composed of key parameters in the disease transmission and those parameters are functional of environmental variables.

Impact of environmental changes on the disease transmission was then discussed through the sensitivity of the reproductive number with respect to the environmental variable.

Gomez-Elipe et al, (2003) studied a mathematical model involving malaria incidence based on monthly case reports and environmental factors. They predicted malaria incidence in an area of unstable transmission by studying the association between environmental variables such as rainfall, temperature and vegetation density, and disease dynamics. Malaria control measures were not mentioned.

Koella and Antia (2003) presented an epidemiological framework to investigate the spread of anti-malarial resistance. In examining the processes and parameters that are critical in determining the spread of resistance, several mathematical models, based on the Macdonald-Ross model of malaria transmission was used. They concluded with their simplest model that, resistance does not spread if the fraction of infected individuals treated is less than a threshold value; if drug treatment exceeds this threshold, resistance will eventually become fixed in the population. They determined threshold value only by the rates of infection and the infectious periods of resistant and sensitive parasites in untreated and treated hosts, whereas the intensity of transmission has no influence on the threshold value. In more complex models, where hosts can be infected by multiple parasite strains or where treatment varies spatially, resistance is generally not fixed, but rather some level of sensitivity is often maintained in the population

Teklehaimanot et al., (2004) found that malaria was associated with rainfall and minimum temperature (with the strength of the association varying with altitude) in Ethiopia. Chitnis (2005) derived and analyzed a mathematical model to better understand the transmission and spread of malaria disease. Their research was to use this model (which was obtained using ordinary differential equations) to compare intervention strategies for malaria control for two representative areas of high and low transmission. They analyzed the existence and stability of disease-free and endemic (malaria persisting in the population) equilibria. Global bifurcation theory was used to show the bifurcation of endemic

equilibria at $R_0 = 1$. They then compile two reasonable sets of values for the parameters in the model: for areas of high and low transmission. They computed sensitivity indices of R_0 and the endemic equilibrium to the parameters around the baseline values. R_0 is most sensitive to the mosquito biting rate in both high and low transmission areas. The fraction of infectious humans at the endemic equilibrium is most sensitive to the mosquito biting rate in low transmission areas, and to the human recovery rate in high transmission areas. This sensitivity analysis allows us to compare the effectiveness of different control strategies. According to their model, the most effective methods for malaria control are the use of insecticide-treated bed nets and the prompt diagnosis and treatment of infected individuals.

In view of the ongoing discussion on phasing out DDT in India, Gunasekaran,(2005) et al investigated the impact of dichlorodiphenyl trichloroethane (DDT) indoor residual spraying on two districts of Orissa State which are endemic for *Plasmodium falciparum* transmitted by *Anopheles fluviatilis* and *A. culicifacies*, This Based on their high annual parasite incidence and logistical considerations, 26 villages in Malkangiri and 28 in Koraput district were selected for DDT spraying. For comparison, six and four unsprayed villages were chosen from the same districts. In each district, the prevalence of malaria infection and incidence of malaria fever, indoor resting density and parous rate of the vectors, and their susceptibility to DDT were monitored in six and three villages selected randomly from the sprayed and unsprayed groups respectively. *Anopheles fluviatilis* was susceptible to DDT while *A. culicifacies* was resistant. DDT residual spraying with 1 g/m^2, was carried out in October–November 2001. Spraying 74– 86% of human dwellings and 100% of cattle sheds brought down the indoor resting density of *A. fluviatilis* by 93–95%. This was associated with a significant reduction of incidence of malaria fever as well as prevalence of malaria infection from November to February in both districts. The spraying

also seemed to impact on vector longevity, and a residual effect of DDT on the sprayed walls was observed up to 10–12 weeks despite replastering. They concluded that DDT spraying can still be an effective tool for controlling *fluviatilis*-transmitted malaria. They further argued that, although this species is exophilic, its nocturnal resting behaviour facilitates its contact with the sprayed surfaces. DDT is still useful for residual spraying in India, particularly in areas where the vectors are endophilic and not resistant.

In addition, Nakul et al., 2006, presented an ordinary differential equation mathematical model for the spread of malaria in human and mosquito populations. They assumed that both species follow logistic population model, with immigration and disease-induced death of humans. The sophistication of the epidemiological modelling efforts has grown steadily. A container-inhabiting mosquito simulation model was developed by Focks et al., (1993).

Worall et al., (2007) used rainfall and maximum temperature at a lag of four months to successfully fit a biological transmission model to malaria case data in a district in Zimbabwe.

Ruan et al (2008) argued that the feedback dynamics from mosquito to human and back to mosquito involve considerable time delays due to the incubation periods of the parasites. In this paper,taking explicit account of the incubation periods of parasites within the human and the mosquito, they first proposed a delayed Ross–Macdonald model and then calculated the basic reproduction number R_0 and carry out some sensitivity analysis of R_0 on the incubation periods. It was shown that the basic reproduction number is a decreasing function of both time delays. Thus, prolonging the incubation periods in either humans or mosquitos (via medicine or control measures) could reduce the prevalence of infection.

Li (2008) formulated and studied continuous-time models, based on systems of ordinary differential equations, for interacting wild and transgenic mosquito populations. He assume that the mosquito mating rate is either constant, proportional to total mosquito population size, or has a Holling-II-type functional form. The focus is on the model with the Holling-II-type functional mating rate that incorporates Allee effects, in order to account for mating difficulty when the size of the total mosquito populations is small. He investigated the existence and stability of both boundary and positive equilibria. He concluded that the Holling-II-type model is the more realistic and, by means of numerical simulations, it exhibits richer dynamics.

Brigitte(2008) developed a matrix model integrating climate fluctuations in order to describe the dynamics of mosquito populations. The population was structured in five stages: two egg stages (immature and mature), one larval stage and two female flying stages (nulliparous and parous). The water availability in breeding sites were considered as the main environmental factor affecting the mosquito life-cycle. Thus, the model represents the evolution of the mosquito abundance in each stage over time, in connection with water availability.

The model was used to simulate the abundance trends over 3 years of two mosquito species, *Aedes africanus* (Theobald) and *Aedes furcifer* (Edwards), vectors of the yellow fever virus in Ivory Coast. As both these species breed in tree holes, the water dynamics in the tree hole was reproduced from daily rainfall data. The results we obtained showed a good match between the simulated populations and the field data over the time period considered.

In addition, another project was done by Li (2008) who formulated a mathematical model for malaria transmission that includes incubation periods for both infected human hosts

and mosquitoes. It was demonstrated that models having the same reproductive number but different number of progression stages can exhibit different transient transmission dynamics. He concluded that humans acquire partial immunity to malaria after infection, although the mechanisms of immunity are not fully understood. The acquired immunity appears to depend on both the duration and the intensity of past exposure to infection.

Robert and Hove-Musekwa (2008) said indoor residual spraying (spraying insecticide inside houses to kill mosquitoes) is an important method for controlling malaria vectors in sub-Saharan Africa. They proposed a mathematical model for both regular and nonfixed spraying, using impulsive differential equations. First, they determined the stability properties of the nonimpulsive system. Next, they derived minimal effective spraying intervals and the degree of spraying effectiveness required to control mosquitoes when spraying occurs at regular intervals. If spraying is not fixed, then they determined the "next best" spraying times. They also considered the effects of climate change on the prevalence of mosquitoes. They concluded that both regular and nonfixed spraying will result in a significant reduction in the overall number of mosquitoes, as well as the number of malaria cases in humans. They recommend that the use of indoor spraying be re-examined for widespread application in malaria-endemic areas.

Craig and colleagues linked inter-annual differences in malaria to rainfall and temperature in South Africa. In Malawi, the main malaria vector Anopheles culicifacies breeds primarily in river bed pools (WHO, 2009) which occur during dry periods, but also in other breeding sites such as seepage areas next to irrigation tanks, hoof prints, and abandoned pits

Adams and Kapan (2009) investigates the impact of human movement and mosquito patchiness' on the dynamics and persistence of vector-borne diseases at the city scale.

They examined how migrants, tourists and commercial travelers can affect the occurrence and persistence of vector-borne diseases. A series of metapopulation models was developed and analyzed. They have shown that in those models, the human population was assumed to live in a home patch free of mosquitoes but moves to and from patches with immobile (static) mosquito subpopulations. They pinpointed out that people play a key role in the spatial spread of dengue in urban areas, carrying the infection between patchily distributed mosquito communities. They concluded that even low transmission areas are prone to dengue epidemics if local residents visit high risk area.

Chiyaka(2009) presented a mathematical model for malaria treatment and spread of drug resistance in an endemic population. The model considers treated humans that remain infectious for some time and partially immune humans who are also infectious to mosquitoes although their infectiousness is always less than their non immune counterparts. The model was formulated by considering delays in the latent periods in both mosquito and human populations and in the period within which partial immunity is lost. Qualitative analysis of the model including positivity and boundedness of solutions was performed. Analysis of the reproductive numbers shows that if the treated humans become immediately uninfectious to mosquitoes then treatment will always reduce the number of sensitive infections. If however treated humans are infectious then for treatment to effectively reduce the number of sensitive infections, the ratio of the infectious period of the treated humans to the infectious period of the untreated humans multiplied by the ratio of the transmission rate from a treated human to the transmission rate of an untreated human should be less than one. They concluded that the spread of drug resistance with treatment as a control strategy depends on the ratio of the infectious periods of treated and untreated humans and on the transmission rates from infectious humans with resistant and

sensitive infections. Numerical analysis is performed to assess the effects of treatment on the spread of resistance and infection.

The study provides insight into the possible intervention strategies to be employed in malaria endemic populations with resistant parasites by identifying important parameters.

Li (2009) formulated and studied discrete-time stage-structured models, based on systems of differential equations, for wild and transgenic mosquito populations. He divided the mosquito population into two classes: the larvae class which consists of the first three aquatic stages in a mosquito's lifetime, and the adult class. Due to the intraspecific competition among larvae, they assumed that the density dependence is based on larvae not on adults. He investigated the existence and stability of fixed points and positive or synchronous 2-cycles of the model systems. He found out that the models, by means of numerical simulations, exhibit rich dynamics.

Malaria creates serious health and economic problems which call for integrated management strategies to disrupt interactions among mosquitoes, the parasite and humans. In order to reduce the intensity of malaria transmission, malaria vector control may be implemented to protect individuals against infective mosquito bites (Lou and Zhao, 2011). As a sustainable larval control method, the use of larvivorous fish was promoted in some circumstances. To evaluate the potential impacts of this biological control measure on malaria transmission, the researchers proposed and investigated a mathematical model describing the linked dynamics between the host–vector interaction and the predator–prey interaction. The model, which consists of five ordinary differential equations, was rigorously analyzed via theories and methods of dynamical systems. They derived four biologically plausible and insightful quantities (reproduction numbers) that completely determined the community composition. Their results suggested that the introduction of

larvivorous fish can, in principle, have important consequences for malaria dynamics, but also indicatde that this would require strong predators on larval mosquitoes. Integrated strategies of malaria control are analysed to demonstrate the biological application of their developed theory.

Calistus (2012) developed and analyzed a deterministic ordinary differential equation model for the dynamics of malaria transmission that explicitly integrates the demography and life style of the malaria vector and its interaction with the human population. The model is different from standard malaria transmission models in that the vectors involved in disease transmission are those that are questing for human blood. The model captures oscillations that are known to exist in the dynamics of malaria transmission without recourse to external seasonal forcing. Additionally, their model exhibits the phenomenon of backward bifurcation. Two threshold parameters that can be used for purposes of control were identified and studied, and possible reasons why it has been difficult to eradicate malaria were advanced.

chitnis et al (2012) described and analyzed a periodically-forced difference equation model for malaria in mosquitoes that captures the effects of seasonality and allows the mosquitoes to feed on a heterogeneous population of hosts. They numerically show the existence of a unique globally asymptotically stable periodic orbit and calculate periodic orbits of field-measurable quantities that measure malaria transmission. They integrated this model with an individual-based stochastic simulation model for malaria in humans to compare the effects of insecticide-treated nets (ITNs) and indoor residual spraying (IRS) in reducing malaria transmission, prevalence, and incidence. They found that ITNs are more effective than IRS in reducing transmission and prevalence though IRS would achieve its maximal effects within 2 years while ITNs would need two mass distribution campaigns over several years to do so. Furthermore, the combination of both interventions

is more effective than either intervention alone. However, although these interventions reduce transmission and prevalence, they can lead to increased clinical malaria; and all three malaria indicators return to preintervention levels within 3 years after the interventions were withdrawn.

Briet et al., (2008) explained that the extreme south west of Sri Lanka has always been virtually free of malaria. It is attributed to the wet climate in which rivers flow year round without pooling. This brings to our attention that some areas will affect our assumptions of the model because the continuous flow of rivers reduces the availability of mosquitoes hence reducing the rate of mosquito-human contacts. Interventions to prevent or reduce the transmission of malaria are currently being used, with a degree of success, in some parts of the world. Some of the methods include: the situation of irrigated lands far from residential areas and cities, house spraying with residual insecticides and most recently the use of mosquito treated bed nets. The methods operate by reducing the contact rates (and hence exposure to infection) between the mosquitoes and humans. Other measures that employ the use of antimalarial drugs as a control measure may not be very effective when compared with control measures that directly affect the dynamics of transmission of the parasite (that is based on the human mosquito interaction).

This is because in endemic areas, drug coverage can only be effective if permanent prophylaxis is employed across an entire endemic human population. In most developed countries, where malaria has been eradicated but the mosquito vector is still present, changes in world climate through global warming indicate that these malaria free zones risk being re-colonised by malaria (Martens et al, 1999). Given these challenges be it in endemic areas or otherwise, predictive mathematical modelling and computer simulations remain our greatest hope (Carter, 2002; Ritchie and Montague, 1995). Ngwa (2004),

formulated a variable humans and mosquitoes mathematical model consisting of susceptible-exposed-infectious-recovered-susceptible (SEIRS) pattern for humans and susceptible-exposed-infectious (SEI) pattern for mosquitoes. The primary objective was to study endemic malaria and the consequent disease related deaths in endemic regions. The importance of including demographic effects with net population growth was seen to enable the model to predict the number of fatalities that may arise as a result of malaria. This type of prediction is not evident in the constant population model and hence has been overlooked in previous models for malaria. However, no control measure was mentioned to contain the epidemic in any region. Malaria affects the health and wealth of nations and individuals alike. In Africa today, malaria is understood to be both a disease of poverty and a cause of poverty (Greenwood and Mutabingwa, 2002; Sachs and Malaney, 2002). Malaria has significant measurable direct and indirect costs, and has been shown to be a major constraint to economic development (Sacks and Malaney, 2002). This means the gap in prosperity between countries with malaria and countries without malaria has become wider every single year. Gallup and Sachs (2003) showed that where malaria has been eliminated, economic growth has increased substantially. Hence we need to find cost effectiveness of the intervention strategies.

The Global Malaria Control Strategy is a concerted effort meant to bring about changes in the way malaria problem is addressed. As a result, this strategy stresses the selective use of preventive measures wherever they can lead to sustainable results (WHO, 1993). The measures are aimed at halting the deteriorating effects of the malaria situation, minimizing the wasteful use of resources and contributing appropriately to the development of health services, intersectoral cooperation and community participation. The ultimate goal of malaria control will be to prevent mortality and reduce morbidity and social and economic loss through the progressive improvement and strengthening of local and national

capacities (WHO, 1993; FMoH,2000). Several interventions have been recommended to curb the rising burden of the disease in endemic regions. These interventions form the pillar of the global campaign for effective malaria intervention, particularly in sub-Saharan Africa. In April 25, 2000, African Heads of State and Government at the Abuja, Nigeria summit on Roll Back Malaria expressed their political will to vigorously pursue the interventions.

The target set at the Summit was that by 2005 at least 60% of those at risk of malaria particularly pregnant women and children under five years of age will benefit from the most suitable combination of personal and community protective measures such as insecticide-treated mosquito nets and other interventions which are accessible and affordable to prevent infection and suffering (FMoH, 2000).

Oduro et al (2012) investigated the transmission dynamics of malaria in Ghana taking into account human and mosquito populations. Stability analysis of the model was performed and the basic reproduction number for Ghana was found to be $R0$ = 0.8939.The disease-free and endemic equilibria were locally asymptotically stable. Numerical simulations indicate that reducing current biting rate of female Anopheles mosquitoes by 1/16 could assist Ghana to achieve malaria free status by the year 2037.If, in addition, the number of days it takes to recover from malaria infection were reduced to three 3 days malaria free status could be achieved by the year 2029.

Chaves et al, (2008) suggested that the intervention using insecticide-treated bed nets represents an excellent example of implementing an infectious disease control programme. The results emphasize the need to implement infectious disease control programmes focusing on the most vulnerable populations which is the basis of this study. In addition, Morel et al, (2005) used a cost-utility analysis to examine the costs and the effects of

scaling-up seven interventions strategies against malaria and their promising combinations. They used efficacy data which came from the literature and researchers calculations supported by expert opinion. The results showed that high coverage with artemisinin based combination treatments was found to be the most cost effective strategy for control of malaria in most countries in sub-Saharan Africa. Since the researchers pointed out that, on the cost-effectiveness grounds, in most areas in subSaharan Africa, greater coverage with highly effective combination treatment should be the cornerstone of malaria control, this study will also determine the cost-effectiveness of the selected malaria control interventions using the estimated primary data obtained in Malawi.

Compartmental SEIR (susceptible-exposed-infected-recovered) differential equations models including asymptomatic immune humans were studied by (Ngwa et al., 2004). SEIR differential equations models with different levels of acquired immunity and the loss of immunity among human host population were formulated in Yang (2000) and the effects of social and economic conditions and temperature on the transmission were investigated by using numerical simulations in some of these studies. However, it seems that gradual partial immunity is induced by infections and hence multiple interventions have not been considered. Similarly, the prospects for the success of malaria control depend on the reproductive number for malaria, R_0 .Smith et al., (2007) explained that the large number of R_0 estimates strongly supports the long-held notion that malaria control presents variable challenges across its transmission spectrum. Therefore strategic planning malaria control should consider R_0 , the special scale of transmission, human population density and heterogeneous biting. Most commonly used practices of combating vector-borne diseases focus on the reduction of vectors and raising the public′s awareness about prevention of host-vector contacts. A number of field and laboratory research have been

conducted about vector control to find the most effective approaches to reduce vector population. This includes practicing and monitoring the efficacy of larvaciding, adulticiding, spraying pesticide (Peterson, 2005).

2.2 Overview of Mathematical Model of Malaria

Models have played great roles in the development of the epidemiology of a disease. A mathematical model is a mathematical description of a real world system or event. Mathematical models for transmission dynamics of malaria are useful in providing a better knowledge of the disease, to plan for the future and consider appropriate control measures. The study on malaria using mathematical modeling originated from the works of Ross .Nobel Prize winner Sir Ronald Ross (1911) was the first to attempt to provide a quantitative understanding of the mathematical model of malaria. His model is made up of few differential equations which describes the changes in densities of susceptible and infected people, and susceptible and infected mosquitoes. Base on his modeling Ross (1911, cited in Ruan et al., 2008) introduced the concept of a threshold density and concluded that in order to counteract malaria anywhere we need not banish *Anopheles* there entirely but only to reduce their numbers below a certain figure. Lotka extended the analysis of Ross.

Macdonald (1957) extended Ross' basic model, analyzed several factors contributing to malaria transmission, and concluded that "the least influence is the size of the mosquito population, upon which the traditional attack has always been made" (Macdonald, 1956). The results from Macdonald's model were what led to the WHO campaign to eradicate malaria worldwide between 1955 and 1978.

Ross-Macdonald model is defined as

$$\frac{dx}{dt} = \frac{abM}{N}y(1-x) - rx \qquad 2.1a$$

$$\frac{dy}{dt} = ax(1-y) - \mu y \qquad 2.1b$$

where x is the fraction of infectious humans; y is the fraction of infectious female mosquitoes; a is 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 is the size of the total female mosquito population; N is the size of the total human population; r is the rate of recovery for infectious humans such that $1/r$ is the duration of the disease in humans(the average duration of the infectious period) ;and μ is the death rate of the female mosquito population such that $1/\mu$ is the life expectancy of mosquitos (the average lifespan of an adult mosquito)

Aron and May (1982) in a survey, describe the properties of this model, including the derivation of the reproductive number, R_0, as

$$R_0 = \frac{M a^2 b}{N r} \qquad 2.2$$

The reproductive number, R_0, 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. The idea is derived from the idea of a reproductive number in population dynamics which is defined as the expected number of R_0 spring that one organism will produce over its lifespan. Heesterbeek in (2002) conducts a review on the history of R_0 .For simple homogeneous models, the reproductive number 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.

For Ross model 2.1, R_0 is defined as 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. The number of contacts with mosquitoes that one human has per unit time is (aM/N).

Chitnis (2005) said for simple homogeneous models, the reproductive number 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.

According to the Ross-Macdonald model as stated in equation 2.1, the reproductive number, R_0 is defined as 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. $\left(\frac{aM}{N}\right)$ is 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 r^{-1} is the average

duration of the infectious period of the human. This means that (M/N) ($_a$/r) is the number of mosquitoes that one human infects over the entire infectious period.

In the same way, *a* is 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 $\frac{1}{\square}$ is the average duration of the infectious period of the mosquito (female mosquitoes are infectious till death). Thus, $\frac{ab}{\square}$ is the number of humans that one mosquito infects through its infectious lifetime. The product of the two,

$(M/N)(_a/r)(\frac{\square}{\square}) = \frac{\square MN\square\square a}{\square r\square\square\square}$, forms the reproductive number: the number of humans that one infectious human will infect, through a generation of infectious mosquitoes. 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 were added to the model (Aron and May, 1928). In addition to the various characteristics of malaria, they also include a 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. The variables in this system of partial differential equations depend on both time and age.

The mosquitoes are modeled through V, the vectorial capacity, which is proportional to the mosquito density. There is a significant deviation of this model from the

RossMacdonald model (2.1) since 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 difference in the parasitemia load in different humans, that the Ross-Macdonald model ignores.

Anderson & May (1991) revisit many of the ideas discussed by Aron and May and also 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. They also study the effect of adding age structure to the basic Ross-Macdonald model (2.1) and 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.

Nedelman (1985) 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 (2.1) 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. Dietz, Molineaux and Thomas (1974) went further in the mathematical modelling by proposing inclusion of acquired immunity in the model.

Dietz et al added two classes of humans in their mathematical model, namely those with low recovery rate (more infections, greater susceptibility) and high recovery rate (less infections, less susceptibility).

The model by Dietz *et al*. also included superinfection, a phenomenon usually associated with macroparasites. Superinfection is a significant increase of the parasite load, when an infected person is re infected from the outside (Aron and May 2003).This is usually modeled by making the recovery rate (*r* in the above equation (2.1)) a (usually monotonically nonincreasing) function of the inoculation rate. Various models, with superinfection, for the recovery rate, *r*, include:

Ross (1911): r □□ (2.3a)

Dietz (1974): □/□□□exp□□□□□□□□□1□□□ (2.3b)

Macdonald [49]: r □□□□ when □□□ and r □ 0 when □□□ (2.3c)

Where □ is the inoculation rate □ $\frac{abM}{N}$ □ y and □ is the reinfection-free rate of recovery, i.e. □^{1} is the average duration of the infectious period in the absence of further infection.

Another important feature of malaria is the transient nature of acquired immunity. Aron (1982) 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-ExposedInfectious-Recovered-Susceptible (SEIRS) model, the rate of loss of immunity,□, 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,□, a function of the inoculation rate as in equation below.

$$\square(\square) \square \frac{\square e_{\square\square\square}}{1\square e_{\square\square\square}} \qquad 2.4$$

Where ¸□ is again the inoculation rate and □ is the average duration of the immune period in the absence of infection. Some of the more recent papers on the mathematical modeling of malaria have included environmental effects (Li et al, 2002). Yang (2000) describes a compartmental model where humans follow an SEIRS-type (with more than one immune class for humans) pattern and mosquitoes follow a Susceptible-ExposedInfectious (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_0 for this model and shows, through linear stability analysis, that the disease-free equilibrium is stable for $R_0 < 1$. He also derives an expression for an endemic equilibrium that is biologically relevant only when $R_0 > 1$. He uses numerical simulations to support his proposition that for $R_0 > 1$, the disease-free equilibrium is unstable and the endemic equilibrium is

stable.

Yang and Ferreira (2000) use the model by Yang (2000) to study the effects of global warming. Using the estimated increase in temperature of 1.0 ^{0} C -- 3.5^{0}C by the year

2100, they show that it is possible in some areas of the world for R_0 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.

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

Other recent models have included the spread of drug-resistant *Plasmodium* and of the evolution of immunity. Koella and Antia (2003) discuss a model where, starting with the Ross-Macdonald model 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 Boete (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 analyze, is an extension of the equations introduced by Ngwa and Shu(2000). In the Ngwa and Shu 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 (albeit at a much lower probability). 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 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_0

They show that when $R_0 > 1$, 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 $R_0 < 1$ and the unique endemic equilibrium (for no disease-induced death) is locally asymptotically stable when $R_0 > 1$. They conclude by using numerical simulations to support their proposition that the endemic equilibrium is stable for $R_0 > 1$.

In a second paper (2004), Ngwa 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 The Basic Malaria Model

This chapter deals with the formulation and analysis of the basic malaria model without Protection and treatment (without any intervention strategies) using the SEIRS model.

3.1 Formulation of the Basic Malaria Model

In the formulation of the basic malaria model, the total population sizes of human (host) is denoted by $N_H(t)$ and total population size of female Anopheles mosquitoes(vector) is denoted by $N_M(t)$.The total population of the model is divided into compartments and with assumptions about the nature and time rate of transfer from one compartment to another. The human population is divided into the SEIR compartmental model which consists of four classes: susceptible S_H, exposed E_H, infectious I_H and recovered R_H. In SEIR model the individual starts from the susceptible class, S, to the exposed class, E, then to infective class, I, and finally to the recovery class, R. $S_H(t)$ represents those individuals who are susceptible to the disease or the number of individuals who are not yet infected with the malaria parasite at time t, Blood meal taken by an infectious female Anopheline mosquito on a susceptible individual will cause sporozoites to be injected into the human bloodstream and will be carried to the liver. The individual will then move to the exposed class E_H. At the exposed class E (t), the individual is said to be infected but not infectious: after the latent period, humans who are exposed will be transferred to the infectious class as they are with gametocytes in their blood stream making them infectious to female *Anopheles* mosquitoes. R(t) denotes the number of individuals who have been infected and then removed from the possibility of being infected again or of spreading infection. Brauer

and Castillo-Chavez (2001) explain that R(t) denotes the number of individuals who have successfully recovered and gained immunity from the disease.

The mosquito population is divided into three epidemiological classes, the susceptible class S_M, the Exposed class E_M and infective class I_M. The vector population does not include immune class as mosquitoes never recover from infection; that is, their infective period ends with their death due to their relatively short life-cycle. Anopheles male mosquitoes are not included in the model because only female mosquitoes bite humans for blood meals.

3.2.1 Assumptions of the Model

The following assumptions are made to characterize the model:

(i) All newborns are susceptible to the disease.

(ii) The infectious period of mosquitoes ends when they die.

(iii) Susceptible individuals get infected through contact with infected mosquitoes (iv) The model do not include immigration of infectious humans.

(v) There is no immigration of the recovery human

In this model, each sub compartment in both human host and malaria vector are link with epidemiological parameters representing the transfer rate.

People enter the susceptible compartment through birth and immigration. The susceptible increases at a constant rate, Λ.When female anopheles mosquito carrying the parasite bites a susceptible human, there is some finite probability, β_{MH} that the parasite which is in the form of sporozoites will be transfer on to the human. The infected person (human) will then move to the exposed class at a rate α_H.people also leaves the susceptible class through nature death. The parasite (in the form of thousands of merozoites) enters the blood stream

after a certain period of time, usually leaving signs like violent rise of temperature and severe body chill. Then the exposed individuals become infectious and moves to infected class at a constant rate $\square_H$. After some time, individuals who have been infected may recover with natural immunity at a constant rate $\square$ and move to the recovered class. Some of the people in the infected class die through natural death and other related diseases at a constant rate $\square_H$.

The recovered individuals have some immunity to the disease and do not get clinically ill. Since disease-induced immunity due to malaria is temporary, this immunity is lost and a fraction $\square$ of individuals leave the recovered state to the susceptible state. We make the simplifying assumptions that there is no immigration of the recovered humans. Humans leave the population through natural death, $\square_H$. The disease-induced rate is very small in comparison with the recovery rate. Female anopheles mosquitoes enter the susceptible class through birth at a rate $\square$. Susceptible mosquitoes that feed on infectious human become infected by biting the infectious humans at a rate $\square$.The parasites enter the mosquito with probability β_{HM}, susceptible mosquitoes that feed on infectious human through biting moves from the susceptible to the exposed class. Depending on the ambient temperature and humidity, the parasite develops into sporozoites and enters the mosquito's salivary glands, and the mosquito moves from the exposed class to the infectious class at a rate of $\square$.Some of the mosquitoes die through nature death at a rate $\square_M$ while others also die through other means at the rate $\square_M$

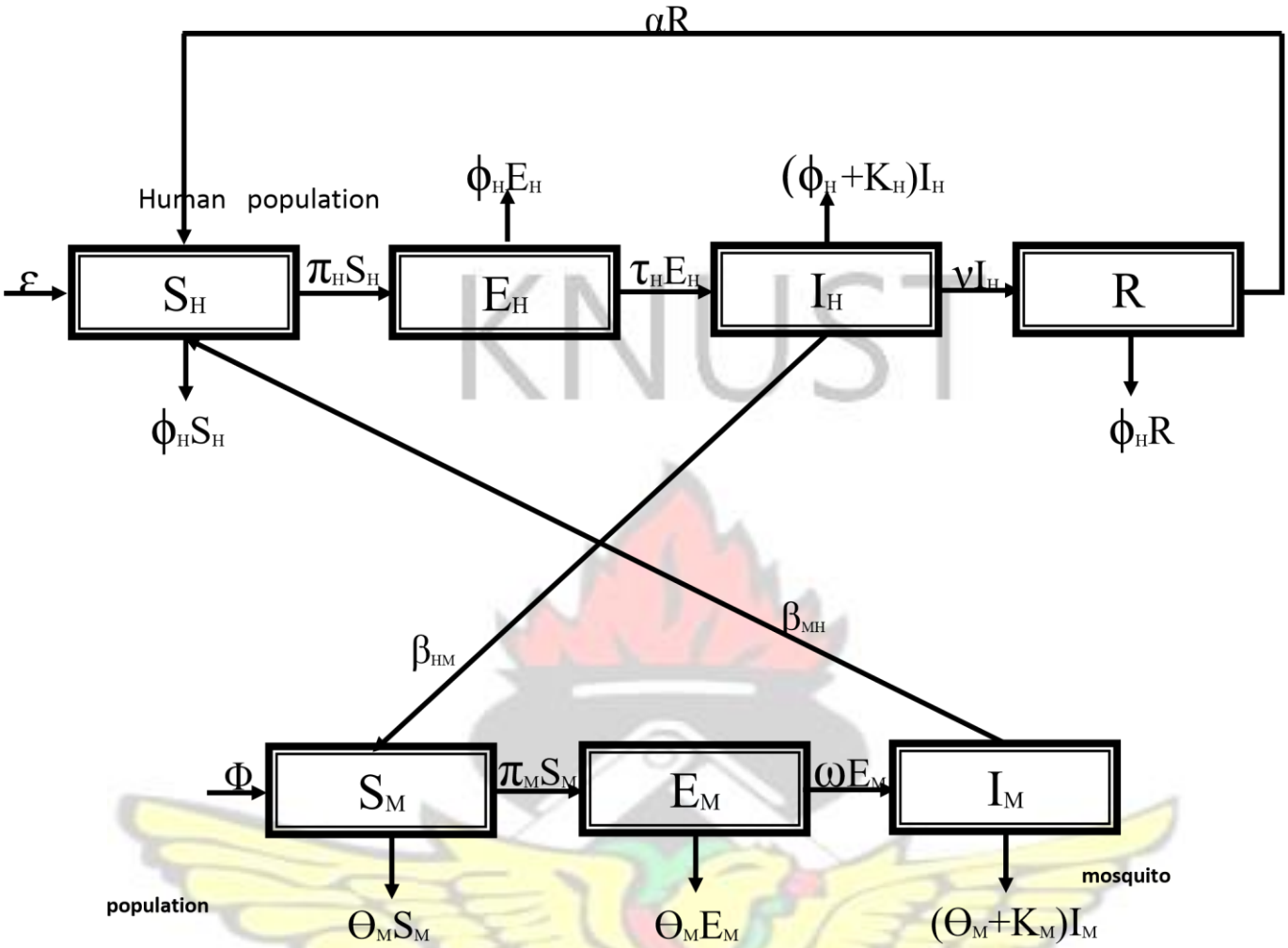


Figure 3.1: The basic malaria flowchart Table 3.1 The state variables for the basic malaria model

parameters	Description
$S_H(t)$	Number of susceptible humans host at time *t*
$E_H(t)$	Number of exposed humans host at time *t*
$I_H(t)$	Number of infectious humans host at time *t*
$R(t)$	Number of recovered humans at time *t*
$S_M(t)$	Number of susceptible mosquitoes vector at time *t*
$E_M(t)$	Number of exposed mosquitoes vector at time *t*
$I_M(t)$	Number of infectious mosquitoes vector at time *t*
$N_H(t)$	Total human population at time *t*
$N_M(t)$	Total mosquito population at time *t*

Table 3.2. Parameters and their meaning for the basic malaria model

parameters	Description
□	Recruitment rate of humans

Λ	Birth rate of mosquitoes
μ_H	Per capita natural death rate for humans
μ_M	Per capita natural death rate for mosquitoes
τ_H	Progression rate of humans from the exposed state to the infectious state
α_H	Per capita disease-induced death rate for humans
α_M	Per capita disease-induced death rate for mosquito
γ	Per capita rate of loss of immunity
σ	Progression rate of exposed mosquitoes to infected mosquitoes
δ	Recovery rate for humans from the infected state to the recovered state with natural immunity
λ_H	Force of infection for susceptible humans to exposed individuals
λ_M	Force of infection for susceptible mosquitoes to exposed mosquitoes
β	biting rate of mosquito
β_{MH}	Probability that a bite results in transmission of infection to the human
β_{HM}	Probability that a bite results in transmission of the parasite from an infectious human to the susceptible mosquito

The parameters in Table 3. 1 and the state variables in Table 3.2 are used in Figure 3.1 to formulate the malaria model.

3.3 Equations of the Basic Malaria Model

Following the compartmental model in Figure 3.1 , applying the assumptions, definitions of state variables ,parameters above and according to the Balance Law, the system of differential equations (non-linear differential equations) describing the transmission of the disease are as follows :

$$\frac{dS}{dt_H} = \Lambda_H + \gamma R - \lambda_H S - \mu_H S$$

$$\frac{dE}{dt_H} = \lambda_H S - (\mu_H + \tau_H) E_H$$

$$\frac{dI_H}{dt} = E_H - (\gamma_H + \mu_H)I_H$$

$$\frac{dR}{dt} = \gamma_H I_H - \mu_H R \qquad (3.1)$$

$$\frac{dS_M}{dt} = \mu_M - \beta_{MH} S_M I_H - \mu_M S_M$$

$$\frac{dE_M}{dt} = \beta_{MH} S_M I_H - (\mu_M + \gamma_M)E_M$$

$$\frac{dI_M}{dt} = \gamma_M E_M - (\mu_M + \alpha_M)I_M$$

with initial conditions

$S_H(0) = S_{H0}, E_H(0) = E_{H0}, I_H(0) = I_{H0}, R(0) = R_0, S_M(0) = S_{M0}, E_M(0) = E_{M0}, I_M(0) = I_{M0}$ where

$$\beta_{MH} = \beta_M \qquad \beta_{HM} = \beta_H$$

$$\beta_H = \frac{\beta_{HM}}{N_H}, \quad \beta_M = \frac{\beta_{MH}}{N_H}$$

The rate at which the human hosts S_H get infected by infected mosquitoes S_M and the rate at which the susceptible mosquitoes S_M are infected by the infected human hosts

I_M is denoted by $\beta_{MH} S_H I_M$, and $\beta_{HM} S_M I_H$ respectively.

N_H N_H

It indicates that the rate of infection of susceptible human S_H by infected mosquito I_M is dependent on the total number of humans N_H available per vector(Mwamtobe,2010).

The total population sizes (total number of humans N_H and total number of mosquitoes N_M) are $N_H = S_H + E_H + I_H + R$ and $N_M = S_M + E_M + I_M$ with their respective differential equation

$\frac{dN_H}{dt} = \frac{dS_H}{dt} + \frac{dE_H}{dt} + \frac{dI_H}{dt} + \frac{dR}{dt}$ are $\frac{dN_M}{dt} = \frac{dS_M}{dt} + \frac{dE_M}{dt} + \frac{dI_M}{dt}$

3.4 Analysis of Basic Malaria Model

3.4.1 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_M from the differential equations

$$\frac{dN_H}{dt} = \frac{dS_H}{dt} + \frac{dE_H}{dt} + \frac{dI_H}{dt} + \frac{dR}{dt}$$

$$\frac{dN_H}{dt} = \Lambda_H - \mu_H S_H - \mu_H E_H - \mu_H I_H - \mu_H R$$

$$\frac{dN_H}{dt} = \Lambda_H - \mu_H (S_H + E_H + I_H + R)$$

It can be further simplify to obtain

$$\frac{dN_H}{dt} = \frac{dS_H}{dt} + \frac{dE_H}{dt} + \frac{dI_H}{dt} + \frac{dR}{dt} \qquad (3.2)$$

$$\frac{dN_H}{dt} = \Lambda_H - \mu_H N_H - \mu_H I_H$$

and similarly

$$\frac{dN_M}{dt} = \frac{dS_M}{dt} + \frac{dE_M}{dt} + \frac{dI_M}{dt} \tag{3.3}$$

$$\frac{dN_M}{dt} = \Lambda_M - \mu_M N_M - \alpha_M I_M$$

Assuming the disease does not kill $(\alpha_H = 0)$, ie if the Per capita disease-induced death rate for humans is zero, we have

$$\frac{dN_H}{dt} = \Lambda_H - \mu_H N_H - \alpha_H I_H - \gamma_H N_H \tag{3.4a}$$

$$\frac{dN_H}{dt} = \Lambda_H - \mu_H N_H \tag{3.4b}$$

$$\frac{dN^H}{dt} \leq \Lambda_H - \mu_H N_H \tag{3.5}$$

this

Theorem 1

The solution set to model system (1) are feasible for all $t > 0$if they enter the Invariant region $\Omega = \{(S_H, E_H, I_H, R_H, S_M, E_M, I_M) \in R^7$.

Proof: Let $(S_H, E_H, I_H, R_H, S_M, E_M, I_M) \in R^7$ be any solution of the system with non-negative initial conditions.

Using the differential inequality $\frac{dN_H}{dt} \leq \Lambda_H - \mu_H N_H$ as stated in (3.5) and solving for N_H we have $N_H \leq \frac{\Lambda_H}{\mu_H} + Ke^{-\mu_H t}$.

ie $\Rightarrow Ke^{-\mu_H t} \Rightarrow \mu_H N_H$ where K is constant (3.6) using the initial condition at $t = 0, N_H(0) = N_{H0}$

$$N_{H0} = \frac{K}{\mu_H}$$

$$N_{H0} = \frac{1}{\mu_H} K$$

$$N_{H0}\mu_H = K$$

$$K = N_H\mu_{H0}$$

$$N_{H0} = \frac{1}{\mu_H}(\mu_H N_{H0})$$

$$N_{H0} = \frac{\mu_H}{\mu_H} N_{H0} = \frac{\mu_H}{\mu_H} e^{-\mu_H t}$$

At $t = 0$and Applying the theorem of differential inequality (Birkhof & Rota, 1982), we have

$$0 < N_H < \frac{\Lambda}{\mu_H}$$

Therefore, as $t \to \infty$, the human population N_H approaches $C = \frac{\Lambda}{\mu_H}$, the parameter $C = \frac{\Lambda}{\mu_H}$ is usually called the carrying capacity (Namawejje, 2011)

Hence all feasible solution set of the human population only of the model system (1) are in the region.

$$\Omega_H = \{(S_H, E_H, I_H, R) \in \mathbb{R}^4 : N_H \leq \frac{\Lambda_H}{\mu_H}\} \quad (3.7)$$

Similarly, the feasible solutions of the mosquito population only are in the region

$$\Omega_M = \{(S_M, E_M, I_M) \in \mathbb{R}^3 : N_M \leq \frac{\Lambda_M}{\mu_M}\}. \quad (3.8)$$

Thus, the feasible set for model system (1) is given by

$$\Omega = \Omega_H \times \Omega_M \subset \mathbb{R}^7 : (S_H, E_H, I_H, R_H, S_M, E_M, I_M) \in \mathbb{R}^7 : (S_H, E_H, I_H, R_H, S_M, E_M, I_M) \geq 0; N_H \leq \frac{\Lambda_H}{\mu_H}; N_M \leq \frac{\Lambda_M}{\mu_M}$$

Therefore, the feasible solutions set for model system (1) given by $\Omega = \Omega_H \times \Omega_M$ is positive invariant and hence it is biologically meaningful and mathematically well-posed in the domain Ω.

Therefore, in this domain it is sufficient to consider the dynamics of the flow generated by the model (1). In addition, the usual existence, uniqueness and continuation of results hold for the system.

3.4.2 Positivity of Solutions

Lemma 1 Let the initial data be

$$\{(S_H(0), S_M(0)) \in \mathbb{R}^2_+ : (E_H(0), I_H(0), R(0), E_M(0), I_M(0)) \in \mathbb{R}^5_+\}.$$

then the solution set $\{S_H, E_H, I_H, R, S_M, E_M, I_M\}(t)$ of the model system (1) is positive for all $t \geq 0$.

Proof: Using the first equation of the model (1) we obtain

$$\frac{dS_H}{dt} = \Lambda_H - \beta_H S_H - \mu_H S_H + \gamma_H R - \lambda_H S_H \geq -\lambda_H S_H - \mu_H S_H$$

$$\geq -(\lambda_H + \mu_H + \gamma_H) S_H$$

$$\frac{1}{S_H} dS_H \geq -(\lambda_H + \mu_H + \gamma_H) dt$$

$$S_H(t) \geq S_H(0) e^{-(\lambda_H + \mu_H + \gamma_H)t} \geq 0.$$

Also the second equation of model (1) gives

$$\frac{dE_H}{dt} = \lambda_H S_H - (\mu_H + \gamma_H) E_H \geq -(\mu_H + \gamma_H) E_H dt$$

$$\frac{1}{E_H} dE_H \geq -(\mu_H + \gamma_H) dt$$

$$E_H(t) \geq E_H(0) e^{-(\mu_H + \gamma_H)t} \geq 0$$

From the third equation of the model(1) we obtain

$$\frac{dI_H}{dt} = \gamma_H E_H - (\mu_H + \alpha_H) I_H \geq -(\mu_H + \alpha_H) I_H dt$$

$$\int \frac{1}{I_H}\, dI_H = \int (\beta + \alpha_H - \gamma_H)\, dt \qquad .$$

$$I_H(t) = I_H(0)\, e^{(\beta + \alpha_H - \gamma_H)t} > 0$$

From fourth equation of model (1) we obtain the following

$$\frac{dR}{dt} = \alpha_H I_H + (\beta + \gamma_H) R + (\beta + \gamma_H) R$$

$$\int \frac{1}{dR}\, dR = \int (\beta + \gamma_H)\, dt \qquad .$$

$$R(t) = R(0)\, e^{(\beta + \gamma_H)t} > 0$$

To solve for $S_M(t)$, we take into consideration the fifth equation of model (1) which gives

$$\frac{dS_M}{dt} = \Lambda_M - \beta_M S_M I_M - \mu_M S_M + \alpha_M S_M I_M + \gamma_M S_M$$

$$= \Lambda_M - (\beta_M I_M + \mu_M) S_M$$

$$\int \frac{1}{S_M}\, dS_M = \int (\beta_M I_M + \mu_M)\, dt$$

$$S_M(t) = S(0)\, e^{\int \beta_M dt + \mu_M t} > 0$$

We obtain the following from the six equation of model (1)

$$\frac{dE_M}{dt} = S_M \beta_M (\beta_M I_M) E_M + \alpha_M (\beta_M I_M) E_M - (\mu_M + \varepsilon_M) E_M$$

$$\int \frac{1}{E_M}\, dE_M = \int (\beta_M I_M - \mu_M - \varepsilon_M)\, dt \qquad .$$

$$E_M(t) = E_M(0)\, e^{(\beta_M I_M - \mu_M - \varepsilon_M)t} > 0$$

The seventh equation of mode (1) gives

$$\frac{dI_M}{dt} \leq E_M - (\mu + \alpha_M + \gamma_M) I_M \leq -(\mu + \alpha_M + \gamma_M) I_M$$

$$I_M \leq -(\mu + \alpha_M + \gamma_M) dt$$

$$I_M(t) \leq I_H(0) e^{-(\mu + \alpha_M + \gamma_M)t} \to 0$$

To show that the region Ω is positively invariant so that it suffices the dynamics of the above system, we use fact that the right hand sides of equations (3.2) and (3.3) are both bounded by $\Lambda - \mu N_H$ and $\Lambda_M - \mu_M N_M$, respectively. It then follows that

$$\frac{dN_H}{dt} \geq 0 \text{ if } N_H(t) \leq \frac{\Lambda}{\mu} \text{ and } \frac{dN_M}{dt} \geq 0 \text{ if } N_M(t) \leq \frac{\Lambda_M}{\mu_M}.$$

With a help of standard comparison theorem (Zhang, 1988), it has been shown above that

$$N_H(t) \leq \frac{\Lambda}{\mu}\left(1 - e^{-\mu t}\right) + N_H(0) e^{-\mu t}$$

and

$$N_M(t) \leq \frac{\Lambda_M}{\mu_M}\left(1 - e^{-\mu_M t}\right) + N_M(0) e^{-\mu_M t}.$$

In particular, if $N_H(0) \leq \frac{\Lambda}{\mu}$ then $N_H(t) \leq \frac{\Lambda}{\mu}$ and if $N_M(0) \leq \frac{\Lambda_M}{\mu_M}$ then $N_M(t) \leq \frac{\Lambda_M}{\mu_M}$.

Therefore Ω is positively invariant. If $N_M(0) \leq \frac{\Lambda_M}{\mu_M}$ and $N_H(0) \leq \frac{\Lambda_H}{\mu_H}$, then either the solution enters Ω in finite time, or $N_M(t)$ approaches $\frac{\Lambda_M}{\mu_M}$ and $N_H(t)$ approaches $\frac{\Lambda_H}{\mu_H}$ asymptotically, and the infected state variables E_H, I_H, E_M and I_H approaches zero.

3.4.3 Existence and Stability of Steady-state Solutions

Steady state solutions or equilibrium points $E^* = (S_H^*, E_H^*, I_H^*, R^*, S_M^*, E_M^*, I_M^*)$ are the roots or solutions of the system of equations when the right-hand side of a nonlinear system is set to zero.

At the steady state $\frac{dS_H}{dt} = 0, \frac{dE_H}{dt} = 0, \frac{dI_H}{dt} = 0, \frac{dR}{dt} = 0, \frac{dS_M}{dt} = 0, \frac{dE_M}{dt} = 0, \frac{dI_M}{dt} = 0.$

To calculated the steady state, the right hand side of the model (1) is equated to zero to give

$$\begin{aligned}
&\Lambda_H - \beta_H S_H I_M - \mu_H S_H = 0 \\
&\beta_H S_H I_M - (\mu_H + \varepsilon_H) E_H = 0 \\
&\varepsilon_H E_H - (\gamma + \alpha + \mu_H) I_H = 0 \\
&\gamma I_H - (\mu_H + \delta) R = 0 \\
&\Lambda_M - \beta_M S_M I_H - \mu_M S_M = 0 \\
&\beta_M S_M I_H - (\varepsilon_M + \mu_M) E_M = 0 \\
&\varepsilon_M E_M - (\mu_M + \delta) I_M = 0
\end{aligned} \tag{3.10}$$

Equation (3.10) is then solve to obtain $E^* = (S_H^*, E_H^*, I_H^*, R^*, S_M^*, E_M^*, I_M^*)$.

3.4.4 The Existence of the Trivial Equilibrium Point

So far as the mosquito recruitment term and the human recruitment term are not zero, the population will not be extinct. This implies that there is no trivial equilibrium point, thus.

$$(S_H, E_H, I_H, R, S_M, E_M, I_M) \neq (0,0,0,0,0,0,0)$$

3.4.5 Disease-free Equilibrium Point E_0

Disease-free equilibrium points (DFE) are steady-state solutions where there is no malaria (disease) in the human population or plasmodium parasite in the mosquito population. We define the "diseased" classes as the human or mosquito populations that are either exposed, or infectious, that is; E_H, I_H, E_M, and I_M in the system (1).

In absence of the disease, $E_H = I_H = E_M = I_M = 0$.
To obtain disease -free equilibrium point, the right-hand side of a system (1) is set to zero and we substitute $E_H = I_H = E_M = I_M = 0$. we have

$$S_H = \frac{\Lambda_H}{\mu_H}$$

$$S_M = \frac{\Lambda_M}{\mu_M}$$

Hence, the DFE of the basic malaria model (1) is given by,

$$E_0 = (S_H, E_H, I_H, R, S_M, E_M, I_M)$$

$$= \left(\frac{\Lambda_H}{\mu_H}, 0, 0, 0, \frac{\Lambda_M}{\mu_M}, 0, 0\right) \quad (3.11)$$

that represents the state in which there is no infection in the society and is known as the disease-free equilibrium point (DFE).

3.4.6 The Reproduction Number R_0

The next generation operator approach as described by Diekmann, (1990) was used to define the basic reproductive number, R_0, as the number of secondary infections that one infectious individual would create over the duration of the infectious period, provided that everyone else is susceptible. It is an important parameter that plays a big role in the control of the malaria infection.

$R_0 \square 1$ is a threshold below which the generation of secondary cases is insufficient to maintain the infection within human community. If $R_0 \square 1$, each individual produces, on average, less than one new infected individual and hence the disease dies out while if $R_0 \square 1$, each individual produces more than one new infected individual and hence the disease is able to invade the susceptible population. It is therefore a useful quantity in the study of a disease as it sets the threshold for its establishment.

The basic reproduction number cannot be determined from the structure of the mathematical model alone, but depends on the definition of infected and uninfected compartments. We define X_s to be the set of all disease free states. That is

$$X_s \square \square \square x0 | x_i \square \square 0, i1,...,m \square .$$

In order to compute R_0, it is important to distinguish new infections from all other changes in the population. Let

F_i be the rate of appearance of new infections in compartment i ,

V_i □ □V_i□ V_i□ is the difference between the rate of transfer of individuals out of compartment i ,$(V_i$□$)$, by all other means and the rate of transfer of individuals in the compartment$i$,$(V_i$□$)$ by all other means.

x_0 be the disease-free equilibrium point.

It is assumed that each function is continuously differentiable at least twice in each variable. The disease transmission model consists of non-negative initial conditions together with the following system of equations:

$$\chi$□ □ $f\, x_i(\,)$ □ $F\, x_i(\,)$□$V\, x\, i_i(\,)$, □1,..., .n .

□

Let F □□___□$F_i\,(x_0)$□□ and V□□□___□$V_i\,(x_0)$□□ with 1□ $i\, j,$ □ m .

□□□x_j □□ □□□x_j □□

Since F is nonnegative, V is a nonsingular then □$^{\square 1}$ is nonnegative and also $FV^{\square 1}$ is nonnegative.

Hence R_0 is the largest eigenvalue of FV^{-1}, where the $(i\, j,)$ entry of F is the rate at which infected individuals in compartment j produce new infections in compartment$i$,the $(\, j\, k,)$ entry of $V^{\square 1}$ is the average length of time this individual spends in compartment j during it's lifetime, assuming that the population remains near the DFE and barring reinfection.

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 . Following Diekmann et al., (2000), FV^{-1} is called the next generation matrix for the model and we set

$$R_0 = \rho(FV^{-1}),$$

where $\rho(A)$ denotes the spectral radius of a matrix A .

Rewriting the system (1) starting with the infected compartments for both populations; E_H, I_H, E_M, I_M, and then followed by uninfected classes; S_H, R, S_M also from the two populations, gives

$$\begin{aligned}
\frac{dS^H}{dt} &= \Lambda_H - \beta_H S_H I_M - \mu_H R \\
\frac{dE_H}{dt} &= \beta_H S_H I_M - \varepsilon_H E_H - \mu_H E_H \\
\frac{dI^H}{dt} &= \varepsilon_H E_H - \gamma_H I_H - \mu_H I_H - \alpha_H I_H - R \\
\frac{dS_M}{dt} &= \Lambda_M - \beta_M S_M I_H - \mu_M S_M \\
\frac{dE_M}{dt} &= \beta_M S_M I_H - \varepsilon_M E_M - \mu_M E_M \\
\frac{dI_M}{dt} &= \varepsilon_M E_M - \gamma_M I_M - \mu_M I_M
\end{aligned} \tag{3.12}$$

The method of next generation matrix has been used to show the rate of appearance of new infection in compartments; E_H and E_M, from the system (3.12);

$$\beta_{MH} I S_{MH}$$

$$\begin{pmatrix} N_H \\ 0 \\ f \\ \beta_{HM} I S_{HM} \\ N_H \\ 0 \end{pmatrix}$$

The Jacobian matrix of f at the disease-free equilibrium point E_0 (3.11) where

N_H and N_M to form the Jacobian matrix;

Calculating the transfer of individuals out of

$$F = \begin{pmatrix} 0 & 0 & 0 & \beta_{MH} \\ 0 & 0 & 0 & 0 \\ \beta_{HM} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad (3.13)$$

the compartments of the system (3.12) by all other means

$$\begin{pmatrix} \beta_H \\ \beta_H \\ E_H \\ \beta_{HH} I + \beta_{HH} E \\ \beta_M \\ E_M \\ \beta_M \\ \beta_{MM} I + \beta_M E_M \end{pmatrix}$$

The Jacobian matrix of is

$$V = \begin{bmatrix} -(\beta_H I_H + \mu_H) & 0 & 0 & 0 \\ \beta_H I_H & -(\gamma + \mu_H) & 0 & 0 \\ 0 & \gamma & -(\mu_H + \alpha) & 0 \\ 0 & 0 & \alpha & -(\beta_M I_M + \mu_M) \end{bmatrix} \quad (3.14)$$

The inverse of the Jacobian matrix (3.14) is obtain as

$$V^{-1} = \begin{bmatrix} -\frac{1}{\mu_H} & 0 & 0 & 0 \\ -\frac{\beta_H}{\mu_H(\gamma+\mu_H)} & -\frac{1}{(\gamma+\mu_H)} & 0 & 0 \\ -\frac{\beta_H}{\mu_H(\gamma+\mu_H)} & -\frac{1}{(\gamma+\mu_H)} & -\frac{1}{(\mu_H+\alpha)} & 0 \\ -\frac{\beta_H\beta_M}{\mu_H(\gamma+\mu_H)(\mu_M+\alpha)} & -\frac{\beta_M}{(\gamma+\mu_H)(\mu_M+\alpha)} & -\frac{\alpha}{(\mu_H+\alpha)(\mu_M+\alpha)} & -\frac{1}{(\mu_M+\alpha)} \end{bmatrix} \quad (3.15)$$

To obtain FV^{-1} ,we have to calculate the product of the equations (3.13) and (3.15) which gives

$$FV^{-1} = \begin{bmatrix} 0 & 0 & a & b \\ 0 & 0 & 0 & 0 \\ c & d & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}. \quad (3.16)$$

where

$$a = \frac{\beta_{MH}\alpha_H}{}, b = \frac{\beta_{MH}}{}, c = \frac{\beta_{HM}\alpha_H\alpha_H}{}$$

$$\alpha_M\alpha_M\alpha_M \quad \alpha_M\alpha_M \quad \alpha_M\alpha_H\alpha_H\alpha_H\alpha_H\alpha_H$$

and

$$d = \frac{\beta_{HM}\alpha_H}{\alpha_M\alpha_H\alpha_H}$$

The eigenvalues of FV^{-1} are calculated from $M = FV^{-1} = 0$

$$\begin{vmatrix} -\lambda & 0 & a & b \\ 0 & -\lambda & 0 & 0 \\ 1 & 0 & -\lambda & 0 \\ 0 & c & d & -\lambda \end{vmatrix} = 0$$

We calculate the eigenvalues from the matrix (3.16), and obtain

$$\begin{matrix} 0 \\ 0 \\ \\ 0 \end{matrix}$$

$$\alpha_H\alpha_H \quad \alpha_{HM}\alpha_H\alpha_{MH}\alpha_H$$

$$\alpha_H\alpha_H\alpha_H\alpha_M\alpha_M\alpha_M$$

$$\alpha_i = \pm\sqrt{\frac{\alpha_M\alpha}{}} \qquad (3.17)$$

$$\sqrt{\frac{}{\alpha_H\alpha_H\alpha_H\alpha_H\alpha_H\alpha_M\alpha_M\alpha_M}}$$

$$\sqrt{\frac{\alpha_{HM}\alpha_H}{\alpha_H\alpha_H\alpha_H\alpha_H\alpha_H\alpha_M\alpha_M\alpha_M}}$$

$$\alpha_H\alpha_H\alpha_H\alpha_H\alpha_H\alpha_M\alpha_M\alpha_M$$

Matrix (3.17) is further simplify to obtain

[illegible]

λ_i = [illegible] (3.18)

The (spectral radius) dominant eigenvalue of FV^{-1} from equation (3.18) is the reproduction number, R_0 ,and is giving by

R_0 = [illegible]

R_0 = [illegible] (3.19)

□□$_H$ □□$_H$ □□□□□$_H$ □□$_H$ □□□□□$_M$ □□□$_M$ □□$_M$ □□$_M$□

where

□$_H$
_____ is the probability of survival of individuals from latent (exposed) stage into the □$_H$ □□$_H$

infectious stage.

□
_____ is the probability of survival of mosquitoes from the exposed stage into the □□□$_M$

infectious stage of the mosquito population.

The term _____□^{MH}□□ describes the number of humans that one mosquito infects □□$_M$ □□$_M$ □□□□□$_M$ □

(through contact) during the lifetime it survives as infectious, when all humans are

susceptibles. On the other hand, the term, _____ □□$_H$

□□□$_{HHM}$□□□□□□□□$_{HH}$ □□$_H$ □describes the number of mosquitoes that are infected

through contacts with one infectious human, while the human survives as infectious, assuming no infection among vectors.

R_0, is the product of R_{0H} defined as the number of humans that one mosquito infects through its infectious lifetime, assuming all humans are susceptible, and R_{0M} defined as the number of mosquitoes that one human infects through the duration of the infectious period,

assuming all mosquitoes are susceptible. Our reproductive number includes the generation of infections of two populations, so is the square root.

Therefore, manipulation of the R_0, gives

$$R_0 = \sqrt{\frac{\beta_{MH}\beta_H N_H}{\gamma_H(\mu_H+\gamma_H)(\mu_M+\gamma_M)(\mu_M+\gamma_M)} \cdot \frac{\beta_{HM}\beta_M N_M}{\mu_M(\mu_M+\gamma_M)}}$$

$$R_0 = \sqrt{R_{0H} \cdot R_{0M}}$$

where

$$R_{0H} = \frac{\beta_{MH}\beta_H N_H}{\gamma_H(\mu_H+\gamma_H)} \quad (3.20)$$

and

$$R_{0M} = \frac{\beta_{HM}\beta_M N_M}{\mu_M(\mu_M+\gamma_M)} \quad (3.21)$$

$\frac{\beta_{MH}\beta_H N_H}{\gamma_H(\mu_H+\gamma_H)}$ is the number of latent infections produced by a typical infectious individual during the mean infectious period.

$\frac{\beta_{HM}\beta_M N_M}{\mu_M(\mu_M+\gamma_M)}$ is the number of latent infections produced by a typical infectious mosquitoes during the mean infectious period.

Since the mosquito biting rate controls transmission from humans to mosquitoes and from mosquitoes to humans, β therefore appears twice in the expression.

Malaria infection exists in a community due to contact between the humans and mosquitoes.

The magnitude of the basic reproduction number determines whether the disease becomes persistent or dies out. The basic reproduction number, R_0 can be used to determine the local stability of the disease free equilibrium point.

3.4.7 Local Stability of the Disease-free Equilibrium E_0

The local stability of the disease-free equilibrium can be discussed by examining the linearized form of the system (1) at the steady state E_0. Referring to the results of Van den Driessche and Watmough (2002), the following theorem holds.

Theorem 2 The disease-free equilibrium point E_0 for the system (1) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: The Jacobian matrix of the model (1) with $S_H = N_H, E_H = I_H = R = 0$ evaluated at the disease-free equilibrium point is given by

$$\begin{bmatrix} -(\mu_H + \lambda_H) & 0 & 0 & 0 & -\beta_{MH} \\ \lambda_H & -(\varepsilon + \mu_H) & 0 & 0 & 0 \\ 0 & \varepsilon & -(\gamma + \mu_H) & 0 & 0 \\ 0 & 0 & \gamma & -\mu_H & 0 \\ 0 & 0 & 0 & 0 & -(\lambda_M + \mu_M) \end{bmatrix} \quad (3.22)$$

The third and the fourth columns have diagonal entries. Therefore, the diagonal entries $-(\gamma + \mu_H)$ and $-\mu_M$ are the two of the eigenvalues of the Jacobian.

Thus, excluding these columns and the corresponding rows, we calculate the remaining eigenvalues. These eigenvalues are the solutions of the characteristic equation of the reduced matrix of dimension four which is given by

$$\left(x+\mu_M+\alpha_M\right)\left(x+\mu_H+\alpha_H\right)\left(x+\mu_H+\alpha_M\right)\left(x+\mu_M+\alpha_H\right)-\frac{\beta_{MH}\beta_{HM}}{\mu_M}\alpha_H\alpha_H=0 \quad (3.23)$$

To simplify the notation, we let $B_0=\mu_M\mu_M,\ B_1=\mu_H\mu_H,\ B_2=\mu_H^2\mu_H$

This reduces (3.19) to $R_{02}=\mu_{MH}\mu_{HM}B_0B_1B_2B_3\alpha_H^2$ and (3.23) to

$$x^4+A_3x^3+A_2x^2+A_1x+A_0=0, \quad (3.24)$$

where

$$\begin{aligned}
A_3&=B_1+B_3+2B_0+\mu_M\\
A_2&=B_3B_1+2B_0\mu_M+B_0B_2+B_1B_3\\
A_1&=B_0B_3B_2+B_1B_3+2B_0\mu_M+B_0B_1B_2\\
A_0&=B_0B_1B_2B_3+\mu_H^2\mu_{HM}\mu_{MH}+\mu_H^2\mu_M
\end{aligned} \quad (3.25)$$

The Routh-Hurwitz conditions (Murray, 1991), which usually have different forms are the sufficient and necessary conditions on the coefficients of the polynomial (3.24). These conditions ensure that all roots of the polynomial given by (3.24) have negative real parts. For this polynomial, the Routh-Hurwitz conditions are

$A_2>0,\ A_3>0,\ A_0>0,\ A_1>0, and\ H_1=A_3>0$,

$$H_2 = \begin{vmatrix} A_3 & 1 \\ A_1 & A_2 \end{vmatrix} > 0,$$

$$H = \begin{vmatrix} A_3 & 0 & 0 \\ A_1 & A_3 & 1 \\ 0 & A_1 & A_2 \end{vmatrix} > 0,$$

$$\begin{vmatrix} A_3 & 0 & 0 \\ A_1 & 1 & 0 \\ 0 & A_2 & A_3 \\ 0 & A_0 & A_1 \end{vmatrix} > 0$$

$$H_4 = \begin{vmatrix} A_3 & 1 & 0 & 0 \\ A_1 & A_2 & A_3 & 1 \\ A_0 & A_1 & A_2 & A_3 \\ 0 & 0 & A_0 & A_1 \end{vmatrix} > 0$$

Clearly $H_4 = A H_0$ $_3$. Since $B_0 > 0, B_1 > 0, B_2 > 0, B_3 > 0,$ we have $A_i > 0, i = 1,2,3$.

Moreover, if $R_0 > 0,$ it follows that $A_0 > 0$. Thus, it is enough to prove that

$H_2 > 0$ and $H_3 > 0$. Clearly $H_3 = A A A_1(_{3\,2} - A_1) A A_{0\,3}^2$ and $H_2 = A A_{3\,2} - A_1$.

Using Maple, it is observe that

$$H AA A_2 = _{3\,2} - _1 \qquad =$$

$$= B B B B BB B B^{32}(_0 - _2 - _1) - _{2\,3}(2_0 - _2 - 2B^1) - \qquad (3.26)$$

$$^2($$

$$- B B B B B B B B_0 \; _3 - _1 - _2) - _{12}(_0 - _2 - _3) \quad -$$

$$- 2BB B B B B B B_{0\,1}(_3 - _2) - _{22}(_1 - _0) \qquad --$$

which is positive.

Using Maple again, we observe that

$H_3 = A_1 A_3 A_2 - A_1 - A_0 A_3^2$

$= -(B_3 - B_0 - B_0 B_3 - B_2 - B_2 B_3 - B_2 - B_1 - B_0 - B_3 - B_1 - B_1 B_3 - B_2 - \beta_H - \beta_2 - \beta_{HM} - \beta_{MH} - \beta_H \beta_M$ (3.27)

which is clearly a positive quantity. Therefore, all of the eigenvalues of the Jacobian matrix have negative real parts when $R_0 < 1$.

However, $R_0 < 1$ implies that $A_0 > 0$, and since all of coefficients (A_1, A_2, A_3) of the polynomial (3.24) are positive, not all roots of this polynomial can have negative real parts. This means, when $R_0 < 1$, the disease-free equilibrium point is unstable.

Note that the result in theorem (2) is local, that is, we could only conclude that solutions with fairly small initial size in the invariant set Ω are attracted to the disease-free equilibrium point. We can also use $S_M + N_M = E_M + I_M$ and $S_H + N_H = E_H + I_H + R$ to reduce the dimension of the Jacobian in the proof of theorem (2) easily.

3.4.8 The Endemic Equilibrium Point(E_1)

Endemic equilibrium point E_1 is a steady-state solution where the disease persists in the population. All state variables are positive .That is, malaria infection will persists in the population and the endemic equilibrium point (EEP) of the model is given by

EEP= $E_1 = (S_H^*, E_H^*, I_H^*, R^*, S_M^*, E_M^*, I_M^*) > 0$.

For the existence and uniqueness of endemic equilibrium

$E_1 = (S_H^*, E_H^*, I_H^*, R^*, S_M^*, E_M^*, I_M^*)$, where the co-ordinates endemic equilibrium should satisfied the condition $S_H^* > 0, E_H^* > 0, I_H^* > 0, R^* > 0, S_M^* > 0, E_M^* > 0, I_M^* > 0$

To derive EEP, we need to solve the basic malaria model by equating to zero, at an arbitrary equilibrium

$$E_1 = (S_H, E_H, I_H, R, S_M, E_M, I_M).$$

When we solve second equation f (3.1) for E we get

$$E_H = \frac{\beta_{MH} I_M}{N_H(\mu_H + \kappa + \mu_H)} S_M \quad (3.28)$$

The sixth and seventh equations of (3.1) gives

$$E_M = \frac{\beta_{HM} I_H}{N_H(\mu_H + \kappa + \mu_H)} S_M \quad (3.29)$$

and

$$I_M = \frac{1}{\mu_M} E_M \quad (3.30)$$

respectively. putting (3.29) into (3.30) for E_M, we obtain

$$I_M = \frac{\beta_{HM} I_M}{N_H(\mu_M + \mu_H + \kappa + \mu_M)} \quad (3.31)$$

But from fifth equation of model (3.1), we recall that

$$S_M = \left(\frac{N^H}{I_M(\mu_H N_H)}\right) \quad (3.32)$$

β_{HM}

We than substitute the equation (3.32) into (3.31) to get

I_M β_{HM} I_H with equation (3.21) we get

$\beta\beta_M \beta\beta_M \beta\beta\beta\beta\beta_M \beta\beta\beta_{HM} I_M \beta\beta_M N_H \beta$

$R^0{}_M \beta_M \quad I_H$

(3.33)

β

$(\beta_{HM} I_H \beta\beta_M N_H)$

Furthermore, from the second equation of (3.1), we have

$\beta_{HM} I_M S_H \beta\beta\beta_H \beta\beta_H \beta E_H \beta 0$ (3.34) N_H

We can now substitute equation (3.33) into (3.34) to get

$\beta_{MH} R_{0M} \beta_M I_H \quad S$

$N_H \beta\beta_{HM} I_H \beta\beta_M N_H \beta \quad _H \beta\beta\beta_H \beta\beta_H \beta E_H \beta 0$ (3.35)

But from the third equation of (1) we get

$E_H \beta$ $\beta\beta\beta\beta^H \beta\beta_H \beta I_H \beta$ which can be substituted into (3.34) to give β_H

$\beta_{MH} R_{0M} \beta_M I_H \beta S_H \beta \beta\beta_H \beta\beta_H \beta\beta\beta\beta\beta_H \beta\beta_H \beta I_H \beta 0$ (3.36)

$\beta \quad N \beta$

$N_H \beta_{HM} I_H \beta\beta_M \quad _H \quad \beta_H$

Where $I_H \beta$ 0 or

□*MH*□ *ROM*□*M*□*HSH*□ □*NH*□□*H* □□*H*□□□□□*H* □□*H*□□□*HM*□*IH*□ □□*MNH*□□ 0
which means by

algebraic manipulation with N_H □ ___ □ and R_0^2 □R_{0H} □R_{0M} we have □*H*

□_____□*MH*□□*H*□*H*□*ROM*□*M SH*□ □□□□*HM*□ *I H*□ □□*M* ___□ □□ □ 0 with equation (3.20)

□□□□□*H* □□*H* □□□□□*H* □□*H* □□□ □ □*H* □

*R*0*HR*0*M*□*MSH*□ □□*HM*□ *IH*□ □□*M*□□ 0 □*H*

□*M R*02*SH*□ □□*HM*□ *IH*□ □□*M*□□0 which gives □*H*

SH□ □ □*HM*□□*H I H*□*R*02 □□□*M*. (3.37) □*H*□*M*

We can solve for I_M□ by considering equation (3.34), (3.37) and (3.33), with a lengthy algebraic manipulation, to get the following

□□ □*MH*□□*M*□*R*0*M IH*□ *SH*□ □ □□ *IH*□ □□*HSH*□ □ 0 *NH*□□*HM*□ *IH*□□*M*

NH□ □□□□*H*□

NH□□□□□*H* □□□*HM*□ *IH*□ □□*M NH* □□□*MH*□ *R*0*M*□*M* □□□□*H* □*IH*□ □ *NH*□□*IH*□ □□*HM*□ *IH*□ □□*M NH* □□

□*H NH*□□□□*H* □□□*HM*□ *IH*□ □□*M NH* □□ 0

Lastly we get

$$A\,I_H^{\,2} + BI_H + C = 0, \tag{3.38 a}$$

$$\beta_{HM}\,\gamma_2\,\gamma_{HM}\,R_{0M}\,\gamma_H \tag{3.38 b}$$

$$A = \beta_{MH}\,\gamma_H\,R_{02}$$

$$B = \beta_{HM}\,\gamma_H\,\gamma_{MH}\,\gamma_M\,R_{0M2}\,\gamma_H\,\gamma_M N_{H2} H_1, \tag{3.38 c}$$

$$\gamma_H R_0$$

$$C = \beta_{HM}(\gamma_M)^2 N_H^2 + \gamma_H R_0^2$$

$$\gamma^1 \quad (3.38)$$

with $H_1 = \beta_{HM}\beta_H N_H \gamma_H$, which gives

$$I_H = \frac{-B \pm \sqrt{B^2 - 4AC}}{2A} \tag{3.39}$$

Hence,

$$I_H = \quad 3.40$$

We can now solve equation (3.37) using (3.40) to get

$$S_H = \frac{\beta_{HM}\,\gamma_H}{\beta_{H M}} R_{02}\,\gamma_M \tag{3.41}$$

from the third and fourth equations of (3.1), and the substitution of (3.40) we get

$$E = \frac{\quad}{\quad}\,\gamma_H^{\,H}\,\gamma_H \tag{3.42}$$

$_H$ $\square_H$

and

$$R\square \frac{\square\square}{\square\square\square\square_H\square} \quad (3.43)$$

.

In addition we are required to solve the $S_M\square$ and $E_M\square$ for the susceptible and exposed mosquitoes in a malaria endemic area using (3.40) and $N_H \frac{\square}{\square_H}$, we get

$$S_M\square \frac{\square\square}{\square\square_{HM}\square\square_H\square\square\square_M\square\square}, \quad (3.44)$$

$$E_M\square \frac{\square\square^{\underline{M}}\square\square_{\underline{M}}\square^{\square_{\underline{M}}\square_{\underline{H}}R_{0M}\square}}{\square\square_{HM}\square\square_H\square\square\square_M\square\square} \quad (3.45)$$

We now consider the possibility of multiple endemic equilibria for the quadratic. The equation may indicate three distinct situations which we have to consider depending on the signs of B and C since A is always positive. The letter C is negative if $R_0\square 1$and positive if $R_0\square 1$. Hence, we have established the following result:

Remark 1 The basic malaria model (1) has

(1). precisely one unique endemic equilibrium if $B\square 0$, and $C\square 0$ or $B^2\square 4AC\square 0$,

(2). precisely one unique endemic equilibrium if $C\square\square 0\ R_0\square 1$,

(3). precisely two endemic equilibria if $C\square 0, B\square 0$ *and* $B^2\square 4AC\square 0$,

(4). no endemic otherwise.

3.5 Summary

A basic deterministic malaria model SEIR model was formulated. The model took into consideration a varying total human population that includes recruitment of new individuals into the susceptible class through either birth or immigration. The result from the analysis of the model proved that there exists a domain where the model is epidemiologically and mathematically well-posed. The model has been qualitatively analyzed for the existence and stability of the disease-free equilibrium and endemic equilibrium points. The reproduction number R_0 was then calculated using the next generation method. It was shown that disease-free equilibrium E_0 is locally asymptotically stable if $R_0 \square 1$, and unstable when $R_0 \square 1$.

THE MALARIA MODEL WITH PREVENTION AND TREATMENT STRATEGIES

3.6 Formulation of the Model.

Due to the use of insecticide treated bed nets (ITN) and indoor residual spraying (IRS) as the preventive measures, and treatment as a control measure, two different epidemiological compartments of individuals in the protected class denoted by $P\,t(\,)$ and treated class $T\,t(\,)$ are added to the human population system (1). The transfer rates between the subclasses are composed of several epidemiological parameters.

The fraction $\square$ of the susceptible recruited individuals, stated in the basic malaria model (1), are taken to be under preventive control and join the protected class. The likelihood of infection is assumed to be reduced by a factor of $\square$. Since this parameter is defined as the reduction of likelihood of infection by protection, the protection is ineffective if $\square\square 1$ and

effective if □□0. According to Mwamtobe(2010), for the protection to be effective there should be no progression of individuals from the protected class to the exposed individuals. This happens when □□0. Since we have the protected class, susceptible individuals who migrate to malaria free-areas, and thus become partially protected, but become exposed once they return to the malaria endemic areas by the force of infection□$_{HP}$ is represented by the proportion $Lwhere$ 0□ □L 1.The proportion L is due to the use of the protected mosquito bed nets and indoor residual spray.

In order that there is a nonzero flow of humans into the protected class, we assume that □L □□□□□ 0. The exposed individuals as discussed in the system (1) progress to infected class at a constant rate□$_H$. Individuals who have experienced infection may be treated at a constant rate □ and they enter a treated class. After they have been treated successfully, they recover temporarily at acquired immunity rate□. Since diseaseinduced immunity due to malaria is temporary, a fraction □ of individuals leave the recovered state to the susceptible state while the complementary fraction □1□□□ move to the protected class due to noncompliance to treatment. They did not comply fully and their recovery is temporal. The rate of infection of susceptible individual is□$_H$, and the rate at which the infected individuals infect the susceptible mosquito is □$_M$, see Figure (3.2)

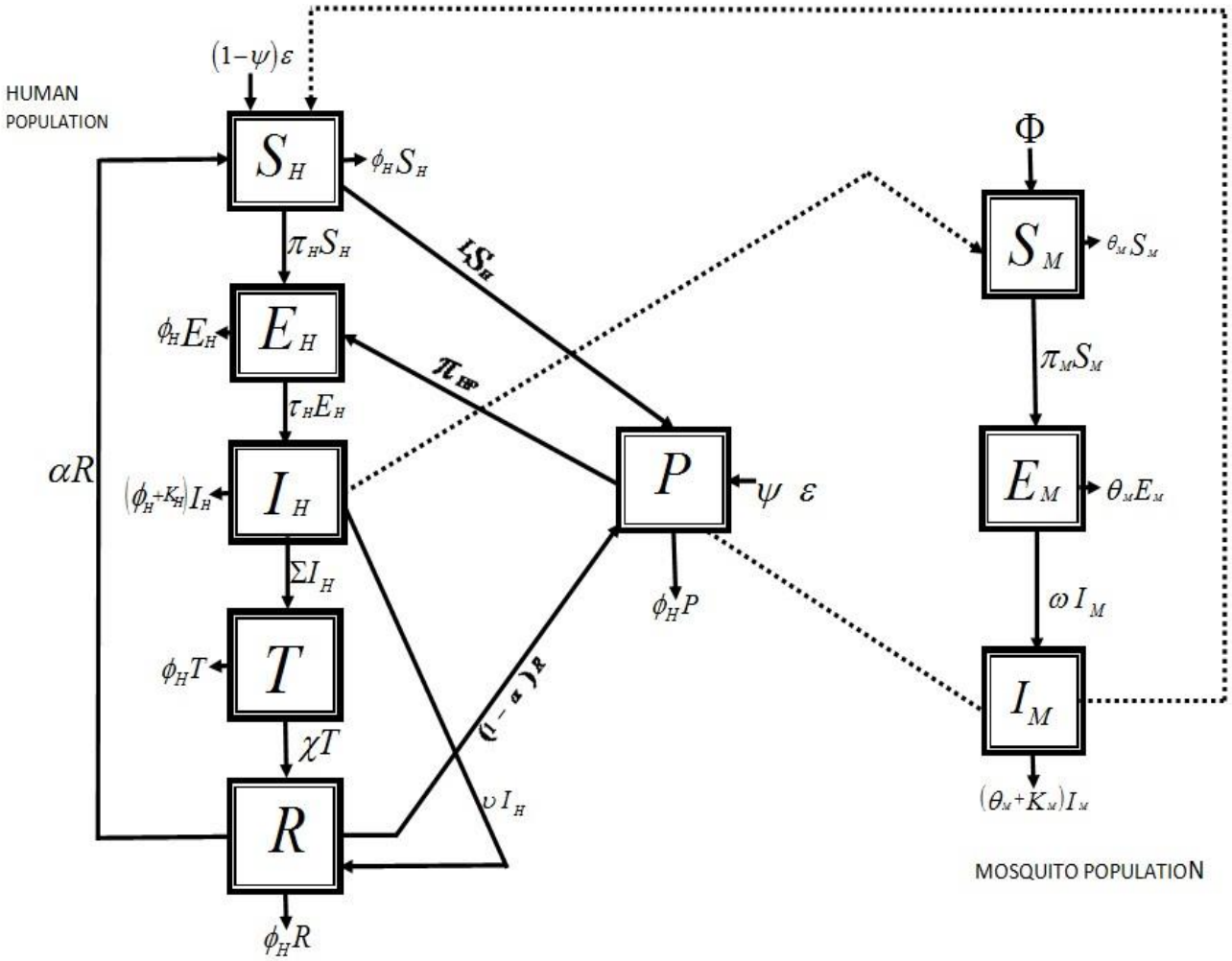


Figure 2 The malaria model with prevention and treatment flow chat

The flow-diagram of the model is shown in Figure (3.2). The malaria model with prevention and treatment strategies has additional state variables in Table 3.3 and parameters in Table 3.4 which satisfy the system of equations (3.46).

Table 3.3: State variables of the model with prevention and treatment strategies

Symbol	Description
P(t)	Number of protected humans at time *t*
T(t)	Number of treated humans at time *t*

Table 3.4: Parameters of the model with prevention and treatment strategies

Symbol	Description
□	Fraction of the susceptible recruited individuals who are protected
□	Reduction of likelihood of infection by protection
L	Progression rate of susceptible humans to protected class
□	Treatment rate for humans from infected state to treated class
□	Recovery rate for humans from the treated state to the recovered state

The following deterministic system of nonlinear ordinary differential equations which describe the progress of the disease with prevention and treatment strategies are obtain below.

$$
\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H(1-\rho) - \beta_{HH} S_H \frac{I_H}{N_H} + \gamma R_H - (L+\mu_H)S_H \\
\frac{dE_H}{dt} &= \beta_{HH} S_H \frac{I_H}{N_H} + \beta_{Hp} P_H \frac{I_H}{N_H} - (\varepsilon_H + \mu_H + \alpha_H)E_H \\
\frac{dI_H}{dt} &= \varepsilon_H E_H - (\tau_H + \mu_H + \sigma_H + K_H)I_H \\
\frac{dT_H}{dt} &= \tau_H I_H - (\mu_H + \delta_H)T_H \\
\frac{dR_H}{dt} &= \rho\Lambda_H + \sigma_H I_H + \delta_H T_H - (1-\rho)\gamma R_H - \mu_H R_H \\
\frac{dS_M}{dt} &= \Lambda_M - \beta_{MM} S_M \frac{I_M}{N_M} - \mu_M S_M
\end{aligned}
\tag{3.46}
$$

$$\frac{dP}{dt} \quad \mu_M$$

$$LS_H \quad 1$$

$$R \quad {}_{Hp}P \quad {}_{H}P \quad \frac{dE_M}{dt} \quad S_M \quad \mu_M E_M$$

Where.

$$\frac{dI_M}{dt} \quad E_M \quad (\mu_M \quad K_M) I_M$$

$$\pi_H = \frac{\delta I_M}{N_H} \quad , \pi_M = \frac{\delta I_H}{N_H} \quad , and \ \pi_{Hp} = \frac{I_M}{N_H}$$

$\delta \quad I_M P$ denotes the rate at which the protected individuals P , get infected by infectious mosquitoes I_M. It indicates that the rate of infection for the protected individuals is reduced by a factor

3.7 Mathematical Analysis of the Model with prevention and treatment Strategies

When we add the first six equations of the model (3.46), and if there is no disease-induced death, that is, $K_H = K_M = 0$, gives $\frac{dN_H}{dt} = \varepsilon - \phi_H N_h$, so that $N_h(t) \to \frac{\varepsilon}{\phi_H}$ as $t \to \infty$. Thus, $\frac{\varepsilon}{\phi_H}$ is an upper bound of $N_H(t)$ provided that $N_H(0) \leq \frac{\varepsilon}{\phi_H}$. Also, if

$N_H(0) = \frac{\Lambda_H}{\mu_H}$, then $N_H(t)$ will decrease to this level, $\frac{\Lambda_H}{\mu_H}$.

Using the same calculation for the vector equations, it is shows that $N_v \to \frac{\Phi}{\theta_M}$ as $t \to \infty$.

As a result of this, the following feasible region;

$$\Omega_1 = \{(S_H, P, E_H, I_H, R, S_M, E_M, I_M) \in \mathbb{R}^9 : N_H \leq \frac{\Lambda_H}{\mu_H}, N_M \leq \frac{\Phi}{\theta_M}\}$$

is positive-invariant and attracting.

3.7.1 Disease-free Equilibrium E_2

The disease-free equilibrium E_2 of the mathematical model with prevention and treatment strategies (46) is given by

$$E_2 = (S_H^*, P^*, E_H^*, I_H^*, T^*, R^*, S_M^*, E_M^*, I_M^*)$$

If we Set the system (3.46) equal to zero, we obtain $S_M^* = \frac{\Phi}{\theta_M}$, which is defined as the asymptotic carrying capacity of the mosquito population. Solving for S_M^* and P^* from the following equations

$$\begin{aligned} \Lambda_1 \alpha \rho (1-\varepsilon) - \mu_H S_H^* &= 0 \\ \varepsilon L S_H^* - \mu_H P^* &= 0 \end{aligned} \tag{3.47}$$

From first equation of (47), making S_H and setting $m_1 = \frac{1-\psi}{L+\phi_H}$, We obtain

$$S_{H^*} = \frac{1}{L+\phi_H} = m_1\varepsilon$$

Substituting in the second equation of (3.47), we obtain

$$\psi\varepsilon + Lm_1\varepsilon - \phi_H P^* = 0$$

Making P_* the subject,

$$P^* = \frac{(\psi + Lm_1)\varepsilon}{\phi_H} = m_2\varepsilon$$

Where

$$m_2 = \frac{(\psi + Lm_1)}{\phi_H} = \frac{\varepsilon\phi_H + L}{\phi_H(L+\phi_H)}$$

$$\Rightarrow \quad P^* = \frac{\varepsilon(\psi\phi_H+L)}{\phi_H(L+\phi_H)}$$

$$E_2 = \{S_H, P, E_H, I_H, T, R, S_M, E_M, I_M\}$$

$$= \begin{pmatrix} 1 & \frac{L}{L+\phi_H} & \frac{L}{L+\phi_H} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\psi}{L+\phi_H} & \frac{\psi}{L+\phi_H} & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad (3.48)$$

3.7.2 The Effective Reproduction Number, R_e

The associated next generation matrices F_2 and V_2 can be found from f_2 and v_2 respectively, where f_2 and v_2 gives the next generation matrices of F_2 and V_2 respectively

□□E^{I}_{H1H1} □□□□□□□□ □$_{MH}N_{H}I\ S_{M\,H}$□0□ □□$_{MH}N_{H}I\ P_{M}$____□□□□

□

f_2□ □E_{M1}□ □ □ □

□□TI_{M1} □□□ □□□□□ (□ □$_{HM}$ I S_H

$_M$00) / N_H □□□□ □

□ $_1$□ □ □

□ (□$_H$ □□$_H$)E_H □

□□(□$_H$ □□□□$_H$ □□$_H$)I_H

=

□□$_H E$□□ v_2□□ (□$_M$

(□□□□$_M$□)$_M I_M$)E□$_M$□E_M □□

□□ (□□□$_H$)T □□I_H □□

The Jacobian matrix of f_2 is given by

$$F_2 = \begin{bmatrix} 0 & 0 & 0 & m & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & n & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \quad (3.49)$$

Where

$$m = \frac{\rho_{MH}\, v_{MH}}{\rho_H\, v_H}, \text{ and } n = \frac{\rho_{HM}\, v_H}{(1-\phi)\,\rho_H\,(1-\phi)}$$

The Jacobian matrix of v_2 is given by

$$V_2 = \begin{bmatrix} a & 0 & 0 & 0 & 0 \\ b & c & 0 & 0 & 0 \\ 0 & 0 & e & 0 & 0 \\ 0 & r & f & q & 0 \\ 0 & 0 & 0 & 0 & j \end{bmatrix} \quad (3.50)$$

Where

$a = (\rho_H - \rho_H), b = \rho_H, c = \rho_H - \rho_H, e = \rho_M, f = \rho, q = \rho_M - \rho_M, r = \rho, j = \rho_H$

Then the inverse matrix of V_2 is given by

$$V_2^{-1} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ -\frac{a}{b} & \frac{1}{c} & 0 & 0 & 0 \\ \frac{ac}{} & -\frac{}{c} & 1 & 0 & 0 \\ 0 & 0 & -\frac{}{e} & 0 & 0 \\ 0 & 0 & \frac{f}{eq} & -\frac{1}{q} & 0 \end{bmatrix}. \quad (3.51)$$

$$\begin{bmatrix} \frac{rb}{ajc} & \frac{r}{jc} & 0 & 0 & \frac{1}{j} \end{bmatrix}$$

The product of matrices (3.49) and (3.51) gives

$$FV_{2\,2\square 1} = \begin{bmatrix} 0 & 0 & \frac{mf}{eq} & \frac{m}{q} & 0 \\ 0 & 0 & 0 & 0 & 0 \\ nb & n & 0 & 0 & 0 \\ \frac{}{ac} & \frac{}{c} & & & \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

While the eigenvalues are

$$\square_i = \begin{bmatrix} 0 \\ 0 \\ \\ 0 \\ \\ \sqrt{aceqnbmf} \\ aceq \\ \sqrt{\frac{}{aceqnbmf}} \\ aceq \end{bmatrix}. \qquad (3.52)$$

Hence the effective reproduction number for the model (3.46), which is denoted by R_e is given by

$$R_e = (FV_2 2 1)$$

$$= \sqrt{\frac{aceqnbmf}{(aceq)_2 nbmf}}$$

$$aceq$$

Substituting the original values back and after lengthy algebraic manipulation, the effective reproductive number R_e is obtain as

$$R_e = \sqrt{\frac{MH HM 2 H H 1 H m_2}{M H H H M M M}} \quad (3.53)$$

With $m_2 = 0$,

Where

$$R_{eM} = \frac{HM}{M M M M}$$

is the contribution of mosquito population when it infects the humans, while

$$R_{eH} = \frac{MH H H 1 H m_2}{H H H H}$$

is the human contribution when they infect the mosquitoes.

Substituting m_2 in the R_e, we get

$$R_e = \sqrt{\frac{MH HM ^2 H H L 1 H 1 M L H H H H}{H M M M}} \quad (3.54)$$

The expression for the effective reproduction number, R_e has a biological meaning that is readily interpreted from terms under the square root. The term

$$\frac{\square_{HM}\square\square\square\ \square_{M}\square\square\square\square_{M}\square\square\square_{M}\square\square_{M}\square}{}$$

represents the number of secondary human infections caused by one infected mosquito vector. The second term

$$\frac{\square_{MH}\square\square_{H}\square_{H}[L\square 1\square\square\square\square\square_{H}\square 1\square\square\square\square]}{\square\square\square_{H}\square\ L\square\square\square_{H}\square\square_{H}\square\square\square\square\square\square\square_{H}\square\square_{H}\square}$$

represents the number of secondary mosquito infections caused by one infected humans host. The square root represents the geometric mean R_e for an average individual of both species combined. This effective reproduction number serves as an invasion threshold both for predicting outbreaks and evaluating control strategies that would reduce the spread of the disease in the country through the reduction of the effective reproduction number and the parameters that enhance the spread of the disease due to the increase in the effective reproduction number.

The main control measures that have been in place include use of insecticide treated bed nets (ITN), indoor residual spraying (IRS) and treatment.

For the population to be below the threshold is to reduce the number of susceptible by providing them protection from the disease. From the expression for the effective reproduction number R_e, we note that the parameters□, and □ play important roles in the spread of the disease. The following cases can be considered:

We can obtain the value of the basic reproduction number from the value of the effective reproduction number when control measures are effective $\square\square 0$ since this is the reduction of likelihood of infection by protection in a sense that $\square\square 0$. Thus the basic reproduction number of the model (3.46) without control measures is given by

$$R_0 \square \sqrt{\frac{\square_{MH}\square_{HM}\square^2\square\square\square_H\square_H}{\square_M\square\square_H\square\square_H\square\square\square\square\square_H\square\square_H\square\square\square\square\square_M\square\square\square_M\square\square_M\square}}$$

From the two reproduction numbers, we notice that

$$R_e \square R_0$$

For $\square\square 0$, due to reduction of likelihood of infection by protection. This shows that control intervention strategies (prevention and treatment) have a positive impact on reduction of the spread of malaria.

The Jacobian matrix, J_E , of the model (3.46) evaluated at the disease-free equilibrium

$$\begin{bmatrix} \square\square b & 0 & 0 & 0 & 0 & \square & 0 & 0 & \square\square\square_{MH}\square & \\ \square & \square\square_H & 0 & 0 & 0 & d & 0 & 0 & & \\ \square L & 0 & \square a & 0 & 0 & 0 & 0 & 0 & \square\square & \\ \square 0 & 0 & \square_H & 0 & \square c & 0 & 0 & 0 & f & \\ \square & 0 & 0 & \square\square j & \square\square & & 0 & 0 & 0 & \\ \square 0 & 0 & 0 & \square\square 0 & & \square h & 0 & 0 & 0 & \\ \square 0 & 0 & 0 & \square 0\ 0 & & 0 & \square\square_M & 0 & 0 & \\ \square & 0 & 0 & 0 & & 0 & 0 & \square e & \square & \\ \square 0 & 0 & 0 & 0 & & & & & \square q & \\ \square 0 & & & & & & & & & \end{bmatrix} \quad (3.55)$$

point (3.48) is given by

where

whose trace and determinant are given by

$$T(D) = -(\mu_H + \mu_H) - (\mu_H + \gamma_H + \mu_M) - (\mu_M + \mu_M) < 0$$

$$D = (\mu_H + \mu_H)(\mu_H + \gamma_H + \mu_M)(\mu_M + \mu_M)(1 - R_e^2) > 0$$

$$\text{if } R_e < 1$$

where

$$R_e = \sqrt{\frac{\beta_M \beta_H \Lambda_M \Lambda_H (\mu_H + \gamma_H + \mu_M)}{(\mu_H + \mu_H)(\mu_H + \gamma_H + \mu_M)(\mu_M + \mu_M)}}.$$

Hence we establish the following results

Lemma 2 The disease-free equilibrium E_2, of the malaria model with prevention and treatment strategies (3.46), given by (3.48) is locally asymptotically stable if $R_e < 1$, and unstable if $R_e > 1$.

The threshold quantity, R_e, measures the average number of secondary cases generated by a single infected individual in a susceptible human population, where a fraction of the susceptible human population is under prevention and the infected class is under treatment. When the protection is not practiced and hence treatment is the only intervention strategy, then effective reproduction number R_e becomes

$$R_{et} = \sqrt{\frac{\beta_{MH}\beta_{HM}\Lambda^2\Lambda_H\Lambda_H}{(\mu_H + \gamma_H + \mu_M)(\mu_H + \gamma_H + \mu_M)(\mu_M + \mu_M)(\mu_M + \mu_M)}}$$

$$\square_M\square\square_H\square\square_H\square\square\square\square\square\square_H\square\square_H\square\square\square\square_M\square\square_M\square\square_M\square$$

Similarly, if the protection is the only intervention strategy being practiced, the effective reproduction number becomes

$$R_{ep}\square\sqrt{\frac{\square_{MH}\square_{HM}\square^2\square\square\square_H\square_H\square L\square 1\square\square\square\square\square_H\square 1\square\square\square\square}{\square_M\square\square L\ \square\square_H\square\square\square_H\square\square_H\square\square\square\square\square\square_H\square\square_H\square\square\square\square_M\square\square\square_M\square\square_M\square}}$$

3.7.3 Existence and Stability of Endemic Equilibrium Point E_3

System (3.46) is analyze to obtain the endemic equilibrium point E_3 of the system and its stability.

We take into consideration the equations for the proportions. Here new variables are use to scale the subpopulations for N_H and N_M first.

Using fractions of population, we let:

$$S^H=\frac{S}{N_H},\ P=\frac{\square p}{N_H},\ E^H=\frac{\square e}{N_H},\ I^H=\frac{\square i}{N_H},\ T=\frac{\square\square}{N_H},\ R=\frac{\square r}{N_H},\ S^M=\frac{\square x}{N_H},\ E^H=\frac{\square y}{N_H},\ I^M=\frac{\square z}{N_H}$$

Where $\frac{dN_H}{dt}=\square\square\square\square_H N_H\square\square_H I_H$, $\frac{dN_M}{dt}=\square\square\square\square_M N_M\square\square_M I_M$, and $N_H\square N_M\square 1$ in the classes $S_H,P,E_H,I_H,T,R,S_M,E_M,I_M$ in the populations and then differentiating each class with respect to time respectively. This is done by differentiating the fractions with respect to time t and simplifying as follows:

$$\frac{ds}{dt}=\frac{1}{N_H}\left(\frac{dS_H}{dt}-s\frac{dN_H}{dt}\right)\square\square\square$$

$$\frac{dt}{dt} \quad N_H$$

$$\frac{1}{N} \quad \frac{s}{sN_H} \quad \beta_{MH} z s N_H \quad \mu_H N_H \quad L \quad \mu_H \quad sN_H \quad \mu_H N_H$$

$$\mu_H \quad \mu_H \quad \mu_H iN_H$$

$$\frac{dP}{dt} \quad \frac{dp}{dt} \quad \frac{dN}{dt} \quad N_H$$

$$\frac{dt}{dt} \quad N_H$$

$$\frac{1}{N} \quad \frac{p}{\mu_H pN_H} \quad \mu_H pN_H \quad \mu_H iN_H$$

$$\frac{Ls}{N_H} \quad \frac{N_H}{N_H} \quad \beta_{MH} zp$$

$$\frac{de}{dt} \quad \frac{1}{N_H} \frac{de}{dt} \quad \frac{dN_H}{dt} \quad e$$

$$\frac{1}{N} \quad \frac{e}{\beta_{MH} zsN_H} \quad \mu_H eN_H \quad \mu_H eN_H \quad \mu_H N_H \quad \mu_H iN_H$$

$$\frac{N_H}{N_H}$$

$$\frac{}{N_H} \quad \mu_H \quad \mu_H i \quad e \quad \beta_{MH} zs \quad \beta_{MH} zp$$

$\frac{}{dt}di \square \frac{}{N1} \square\square \frac{}{dI_H} \square i \frac{}{dN_H} \square\square$

$\square\, dt \qquad dt$

$_H \qquad \square$

$\frac{1}{\quad} \qquad \square \qquad \frac{i}{\quad}$

$\square\square_H eN_H \qquad \square\square_H iN_H \square\square iN_H \square\square_H iN_H$

$\square\square\square\square\square\square_H N_H \square\square_H iN_H \square$

$N_H \qquad\qquad\qquad N_H$

$\square\,\square \qquad\qquad \square$

$\frac{}{\quad}$

$\square\square_H e \qquad \square\square\square N_H \square\square\square\square\square\square_H i \square\square i$

$\frac{d}{dt}\square \frac{}{N1} \square\square \frac{}{dT} \; t \frac{}{dN_H} \square\square$

$\square \qquad \square\, dt \square \qquad dt \square$

$_H$

$\frac{1}{\quad} \qquad\qquad t$

$\square \square\square iN$

$\frac{}{\quad}$

$N_H \quad _H \square\square_H tN_H \square\square tN_H \square\square \; N_H \qquad \square\square\square\square_H N_H \square\square_H iN_H \square$

$\frac{}{\quad} \qquad \square \quad \square$

$\square \qquad \square\square i \qquad \square\square\square N_H$

$\square\square\square\square_H i \square\square t$

$\frac{dr}{} \quad \frac{}{\quad} \quad \frac{}{\quad} \; 1 \frac{\square dR}{}$

dN

$_H \square\, r$

$dt \square N_H \square\square \, dt \square \qquad dt \square\square$

$1 \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad r$

$\square \frac{}{\quad} \square\square tN_H \square\square iN_H \square\square rN_H \square \square 1 \square\square \square rN_H \square\square_H rN_H \square\square \; \frac{}{\quad} \square\square\square\square_H N_H \square\square_H iN_H$

$\square$

$N_H \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad N_H$

$\square\,\square \qquad\qquad\qquad \square$

$\square\square t \square\square i \square\square \frac{}{\quad} N_H \square 1 \square\square_H i \square\square r$

$\square$

$dx \qquad 1 \square dX \qquad dN_M \square$

$$\frac{dt}{N_M} = \frac{dt}{x\,dt}$$

$$\frac{1}{N_M} = \frac{x}{N_{HM} i x N_M - N_H - N_{HM} N_M - N_M z N_M}$$

$$\frac{1}{N_M} = \frac{1 - x}{N_{HM} i x - N_M xz}$$

$$\frac{dy}{dt} = \frac{1}{N_M}\frac{dY}{dt} - \frac{y}{N_M}\frac{dN_M}{dt}$$

$$\frac{1}{N_M} = \frac{y}{N_{HM} i x N_M - N_{HM} y N_M} - \frac{y}{N_M N_M - N_M z N_M}$$

$$N_{HM} i x \frac{N_M}{N_M N_M z} y$$

$$\frac{dz}{dt} = \frac{1}{N_M}\frac{dZ}{dt} - \frac{z}{dt}\frac{dN_M}{dt}$$

$$\frac{1}{N_M} = \frac{z}{y N_M - N_M z N_M - N_M z N_M} - \frac{z}{N_M N_M - N_M z N_M}$$

$$y \frac{N_M}{N_M N_M z} z$$

$$\frac{dN}{dt_H} = N_H - N_H i N_H$$

and

$$\overline{dNdt_M} = \overline{} - \mu_H N_M - \alpha z N_M$$

$$N_M \qquad \square$$

Thus we have the following reduced system of equations

$$\frac{dS}{dt_H} = \mu_H(1 - N) - \beta_{HM} S z - \mu_H S \qquad \square\square\square$$

$$_H \square$$

$$\frac{dP}{dt} = N_H - \mu N_H \qquad \square$$

$$\frac{de}{dt} = \beta_{HM} S z - (\mu_H + \varepsilon)e - \mu_{MH} z s - \mu_{MH} z p \square\square$$

$$\frac{di}{dt} = \varepsilon e - (\mu_H + \gamma_H + \alpha_H) i \square\square$$

$$\frac{d\square}{dt} = \square\square N_H - \square\square - \mu_H \square\square \qquad \square\square$$

$$\frac{dr}{dt} = \gamma_H i - (\mu_H + \alpha_H) r \square\square$$

$$\frac{dx}{dt} = \square(1 - x) - \beta_{HM} i x - \mu_M x z \qquad (3.56)$$

$$\frac{dy}{dt} = \beta_{HM} i x - (\mu_M + \alpha_M) y \square\square$$

$$\frac{dz}{dt} = \square\square y - (\mu_M + \alpha_M) z \square\square$$

$Ls\square\square\_\_\square\ \square\ \square\square 1\ \square\square\square\ \square\square\square\ \_\_\square\ \square\square_H i\ p\square\square\ \square\square\ \square\square_{MH} zp\square$

together with total population sizes N_H and N_M satisfying

$$\frac{dN}{dt_H} = \square\square\square N\square_H \square\square_H \square\square_H i\square\square\square N_H$$

$$\frac{dN}{dt_M} = \square\square N\square_M \qquad z\square\square\square N_M$$
$$\square\ \square \qquad \square\square_H \square\square_M$$

The system of proportions involves the total human population size N_H in the proportions for human population and the total mosquito population size N_M in the proportions for mosquito population. We can now reduced the system to a ninedimensional system by eliminating s and x since $s = 1 - p - e - i - r$ and

$x = 1$ y z, respectively in the feasible region where the model makes biological sense

$$\Omega_2 = \left\{ \begin{pmatrix} P \\ e \\ i \\ \xi \\ r \\ N_H \\ y \\ z \\ N_M \end{pmatrix} \in R_+^9 \middle| \begin{matrix} P \geq 0, \\ e \geq 0, \\ i \geq 0, \\ \xi \geq 0, \\ r \geq 0, \\ p + e + i + \xi + r \leq 1, \\ N_H \leq \frac{\Phi}{\phi_H} \\ y \geq 0, \\ z \geq 0, \\ y + z \leq 1, \\ N_M \leq \frac{\Phi}{\theta_M} \end{matrix} \right\}$$

that can be shown to be positively invariant with respect to the system (3.57) where R_+^9 denotes the non-negative cone of R_+^9 including its lower dimensional faces. Thus, we have the following system of equations

— *dP* □ □ □ □ □ □ *L*□1□ — □ □ □ □*p* — *e i* □ *r*□□□ □ □□1 □□*r* □□ □□$_H$ *i p*□ □□ □□$_{MH}$ *zp*□

$$H \qquad H \qquad (3.57)$$

$$\frac{de}{dt} = N_H - \mu_H N_H - {}_H i e - \mu_{MH} z - p e - r e - \mu_{MH} e$$

$$\frac{di}{dt} = {}_H e - \mu_H i - i dt$$

$$\frac{d}{dt} = {}_H i - \mu_H i - dt$$

$$\frac{dr}{dt} = t - \mu_H r - dt$$

$$\frac{dN_H}{dt} = N_H - \mu_H N_H$$

$$\frac{dy}{dt} = {}_{HM} i - \mu_M y \qquad z - N_M - \mu_M z$$

$$\frac{dz}{dt} = N_M - \mu_M z - y$$

$$\frac{dN_M}{dt} = N_M - \mu_M z N_M$$

$$\frac{dt}{dt} \qquad N \qquad N$$

The steady states of the system (3.57) is calculated, by setting the derivatives with respect to the time in (3.57) to zero. Below results are obtain after simplifying it.

(3.58)

Hence the dimensionless proportions are calculated in terms of i as follows:

$$t = c\,i_2 \qquad (3.59)$$

$$r = c\,i_3$$

y □ □ □ □□ □ □ □□ □$_{HM}$ i[$_{HM}$ i□($_{HM}$ i□)($_{M}$□ $_{M}$)]□□□ □$_{HM^2}$ $_2i$ □

(□ □ □ □ □□ □ □ □ □ □ □ □$_{HM}$ i□ $_{M}$□)[$_{HM}$ i□□ $_{HM}$ i□ $_{M}$□ □($_{M}$□ $_{M}$)]□

$\overline{q\ i_1}$ □

z □ q i_6□q_5 □□

□□

for

c_1 □_____□□□□□$_H$ □□$_H$,c_2 □ _____□ ,c_3 □

_____□□ , □$_H$ □$_H$ □□ (□$_H$ □□)(□$_H$ □1)

d_1 □ □L □□□$_H$ □q_6 □ (□□$_H$ □ (1□□)c_3 □c_1L □ L □c_2L

□c_3L)q_5 d_2 □□□$_H$ □ (1□□)c_3 □c_1L □ L □c_2L □c_3L,

d_3 □ [L(1□□) □□$_H$(1□□□)](□$_M$ □□$_M$)(□$_M$ □□) d_4 □□$_{MH}$□□q_1 □ (□$_H$ □ L)q_6,

d_5 □ (□$_H$ □ L)q_5,q_1 □□$_{HM}$□□,q_5 □ (□$_M$ □□$_M$)(□$_M$ □□),q_6 □□$_{HM}$□(□□□$_M$ □□$_M$),

where i can be obtained by substituting for e into the equation two of the system (3.58) gives

$$c_1 i \square c_4 i \square c_4 p i \square c_5 i\ c_7 i \square c_8$$

It is clear that either i □0 (for the disease-free equilibrium point E_0) or

$$p \square \frac{d\ i^6 \square d_7}{c_4} \qquad (3.60)$$

(endemic equilibrium point E_3) for

c_4 □□$_{MH}$□$_{HM}$□$_2$□,c_5 □□$_{MH}$□q_1,c_7 □□$_{MH}$□$_{HM}$□$_2$□□ (□$_H$ □□$_H$)(□□□$_M$ □□$_M$)□$_{HM}$□,

$c_8 = (\beta_H \mu_H)(\beta_M \mu_M)(\beta_M \mu)$, $d_6 = c_6 c_7 - c_5$ *and* $d_7 = c_1 c_8 - c_4$

is the equations for p in (3.59) and (3.60) will be used.

Equating (3.59) and (3.60) we get

$$Ai^2 + Bi + C = 0 \quad (3.61)$$

where

$$A = d_4 d_6 - c_4 d_2$$

$$k[(\beta_H \mu_H)(\beta_2(\beta_{MH}\beta_{HM} + \mu_H \mu_H + \mu_H \mu_M + \mu_M \mu_{HM}) + \mu_H)$$

$$\beta_1 \beta_{MH}\beta_{HM} + \mu_H \mu_H + \mu_H \mu_M + \mu_M \mu_{HM}$$

$$\beta_1 \beta_{MH}\beta_{HM} + \mu_H \mu_H + \mu_H \mu_M + \mu_M \mu_{HM}$$

We make more realistic assumption that the protective control measures may not be totally effective in order to establish whether the unique endemic equilibria exist, and

thus $0 \leq \beta_1 \leq 1$.

3.7.4 Existence and Uniqueness of Endemic Equilibrium E_3

The existence of the endemic equilibrium in β_2, can be obtained by assuming $i \neq 0$, that

$$k_3(\mu_H + \mu_H)(\mu_H + \mu_H + \mu_H)(1 - \beta_2)(\beta_{HH} - \mu_H)L + H(\mu_H + \mu_H) = 0$$

$$B = d_4 d_7 + a_5 a_6 - c_4 d_1$$

$$k_1[(\beta_1(\mu_H + \mu_H)(\mu_H + \mu_H)\beta_{MH}\beta_{HM} + \mu_H(\mu_H + \mu_H)(\mu_M + \mu_M)(\mu_M + \mu)](\mu_H + L)(\mu_M + \mu_M)(\mu_M + \mu) k_2 \mu_H$$

$$\beta_2 \mu_H(\mu_H + (\mu_H + 1)(\mu_H + 1)(\mu_H + \mu_H)$$

$$(\mu_H + \mu_H)\beta_{MH}\beta_{HM} + \mu_H(\mu_H + \mu_H + \mu_H)(1 - \beta_2)$$

$$\mu_H \beta_{MH}\beta_{HM} + \mu_H(\mu_H + \mu_H + \mu_H)(1 - \beta_2) + \mu_H \mu_H + \mu_H \mu_M + \mu_M \mu_{HM} + \mu_H \mu_M + \mu_M \mu_{HM} + k_4(\mu_M + \mu_M)(\mu_M + \mu_M + \mu_M) = 0$$

with

$H \square L \square$ $\frac{\square L}{\square}$ $\square$ $\frac{\square\square L}{\square}$,

$\square\square_H \square\square\square$ $\square\square_H \square\square\square\square\square_H \square 1\square$ $k_1 \square\square_{MH} \square_{HM} \square_2 \square\square\square\square\square_H \square L \square\square\square\square_M$

$\square\square_M$ $\square\square_{HM}\square$, k_2 $\square\square\square\square\square$ $\frac{\square\square\square\square\square\square\square_{HH}}{\square}$ $\square\square_H$

$\square\square\square\square\square_{MH} \square_{HM} \square_2 \square\square\square\square_H \square\square_H \square\square\square\square\square_M \square\square_M \square\square_{HM} \square\square$, $k_3 \square\square_{MH} \square_{HM} \square_2 \square$

$k_4 \square\square\square_H \square$ $\frac{\square\square_H \square 1 \square\square\square\square\square\square\square\square\square 1 \square\square\square\square\square\square\square\square\square\square\square\square_{HH} \square\square_H \square\square\square\square L \square L \square\square_H \square\square L \square\square}{\square\square_H}$

$\square\square\square\square\square\square L \square_H \square 1 \square$,

$C \square d_5 d_7 \square c_4 d_3$

$\square$ $\frac{\square\square_H \square L \square\square\square_M \square\square_M \square_2 \square\square_M \square\square\square_2 \square\square_M \square\square\square_2 \square\square\square\square}{\square}$ $\square\square\square\square\square\square_{HH} \square\square_H \square\square\square\square\square_H \square\square_H$

$\square$

$\square$

$\square\square_{MH} \square_{HM} \frac{\square\square_2 \square L \square 1 \square\square\square\square\square_H \square 1 \square\square\square\square\square\square\square\square_M \square\square_M \square\square\square_M \square\square\square}{\square}$

$\square$ $\frac{\square\square_H \square L \square\square\square_M \square\square_M \square_2 \square\square_M \square\square\square_2 \square\square\square\square}{\square}$ $\square\square\square\square\square\square\square_{HH} \square\square_H \square\square\square\square\square_H \square\square_H$

$\square\square 1 \square R_{e2} \square$

For $R_e > 1$, the existence of endemic equilibria is determined by the presence in $(0,1]$ of positive real solutions of the quadratic expression (3.61).

C [illegible] $(L$ [illegible] $)$[illegible] R_{e2} [illegible] 0

From the quadratic theorem, if x x_1, $_2$ are the roots of equation (61), then their product

$$xx_{1\,2} = \frac{C}{A}.$$

Since $C > 0$ and $A > 0$, then $\frac{C}{A}$. Hence, there exists exactly one positive endemic A equilibrium for $i \in (0,1]$ whenever $R_e > 1$. This gives the threshold for the endemic persistence.

Therefore, we have proved the existence and uniqueness of the endemic equilibrium E_3 for the system (3.56). This result is summarized in the following theorem:

Theorem 3. If $R_e > 1$, the system (3.56) has a unique endemic equilibrium E_3.

3.8 Summary

We have maintained that the transfer rates between the subclasses are composed of several epidemiological parameters.

Due to the control measures, prevention and treatment two distinct epidemiological compartments of populations who are in the protected class ($P\,t(\,)$) and treated ($(\,)T\,t$ were added to the basic malaria model. The transfer rates between the subclasses are still composed of several epidemiological parameters.

Mathematical analysis of the model has proven that the existing domain is positive invariant and attracting. The model was analyzed qualitatively for the existence and stability of the disease-free equilibrium points.

Effective reproduction number, R_e, was identify as a tool for effective disease management after comparing it R_{ep} (if the protection is the only intervention strategy being practiced), R_{et} (if the treatment is the only intervention strategy being practiced), If $R_e \square 1$, the disease cannot persist in a country, hence R_e is the useful indication of the effort required to eliminate an infection. It has been noted that $R\ R\ R\ R_e \square\ \square\ \square_{ep\ et\ 0}$ which implied that the increasing preventive and control measures has a great effect on the reduction of R_e

CHAPTER FOUR

RESULT AND DISCUSSION

4.1 Introduction

This chapter presents the results and discussion of the study. Mathematical model is formulated for both the basic malaria model in the absence of any intervention and the malaria model with intervention strategies, stability analysis of the models are performed and numerical simulations carrying out on the models.

4.2 Estimation of Parameters

Clinical malaria data, demographic statistics of Ghana and that of world health organisation were used to estimate the parameters in the malaria model. Those that were not available were obtained from literature published by researchers in malaria endemic countries which have similar environmental conditions compared to Ghana. According to the Ghana Living Standards Survey Report of the six Round (GLSS 6), 2013, the estimated number of households in Ghana is 6.6015 million.it is assumed that there are 10 female Anopheles mosquitoes per household in Ghana. The female Anopheles mosquito population is then approximately given by: 6,601,500×10 = 66,015,000 mosquitoes.

4.3 Parameter Values Of The Model

Table 4.1: Parameter values of the Model

	PARAMETER	VALUE	SOURCE
Recruitment rate of humans	Π	0.00005079	(2010 est.) by 2011 CIA World Factbook
Birth rate of mosquitoes	Λ	0.071	Niger, 2008
Per capita natural death rate for humans	μ_H	1/(60×365)	At a glance: Ghana, UNICEF, 2012
Per capita natural death rate for mosquitoes	μ_M	0.03	estimated
Progression rate of humans from the exposed state to the infectious state	σ_H	1/14	Malaria.com, 2011
Per capita disease-induced death rate for humans	α_H	0.0000027	World Malaria Report 2010 for Ghana
Per capita disease-induced death rate for mosquito	α_M	0.06	estimated

Per capita rate of loss of immunity	$\square$	1/90	Blayneh, et al. (2009)
Progression rate of exposed mosquitoes to infected Mosquitoes	$\square$	1/11	Chitnis, 2005
Recovery rate for humans from the infected state to the recovered state with natural immunity	$\square$	1/7	MOH (2009)
biting rate of mosquito	$\square$	0.4	Chitnis (2005)
Probability that a bite results in transmission of infection to the human	$\square_{MH}$	0.42	Estimated
Probability that a bite results in transmission of the parasite from an infectious human to the susceptible mosquito	$\square_{HM}$	0.0655	Niger et al. (2008)
Fraction of the susceptible recruited individuals who are protected	$\square$	0.11	Miranda, 2009
Reduction of likelihood of infection by protection	$\square$	0.475	Estimated
Progression rate of susceptible humans to protected class	L	0.0833	NSO, 2008
Treatment rate for humans from infected state to treated class	$\square$	0.01	NSO, 2008
Recovery rate for humans from the treated state to the recovered state	$\square$	0.00722	Gumel, 2009

4.4 SEIR data of Ghana from 2004-2014:

Table 4.2 provides the overview of the SEIR data of the human population. The infected data represents the number of confirmed malaria cases. Data of the columns labelled susceptible, exposed and recovered were calculated as shown:

Recovered=infected – death

Exposed=infected$\square\frac{2}{365}$

Susceptible=Total population - (Infected + Recovered +Exposed)

Using the year 2004 as an example, we can calculate the recovered, exposed and susceptible data as follows

(i) Recovered=3,416,033-1,575=3,414,458

(ii) Exposed=3,416,033$\frac{2}{365}$ =18,718

(iii) Susceptible=21,119,910-(3,416,033+3,414,458+18,718) = 14270701

Table 4.2: SEIR data of the Year 2004-2012

Table 4.2: SEIR data of the Year 2004-2012						Total population
Year	Total population	Deaths	Susceptible	Exposed	Infected	Recovered
2004	21,119,910	1,575	14270701	18,718	3,416,033	3,414,458
2005	21,639,810	2,037	14716989	18,920	3,452,969	3,450,932
2006	22,170,560	3,125	15131540	19,241	3,511,452	3,508,327
2007	22,712,560	4,622	16453775	17,113	3,123,147	3,118,525
2008	23,264,180	3,889	16927976	17,535	3,200,147	3,196,258
2009	23,837,261	3,378	18542201	10,408	1,899,544	1,896,166
2010	24,391,823	3,859	19096763	14,477	2,642,221	2,638,362
2011	24,965,816	3,259	18469735	17,758	3,240,791	3,237,532
2012	25,366,462	2,855	7772205	48,080	8,774,516	8,771,661

4.5 Equations of the Basic Malaria Model

After substituting the estimated parameter values in table 4.1 into model (3.1), we have the following system of non-linear differential equations

$$\frac{dS_H}{} = 0.00005079 - 0.168\frac{I}{}S_{MH} - 0.011111R - 0.000045662S_H$$

$$\frac{dt}{N} \qquad H$$

$$\frac{dE_H}{dt} = 0.168\, I\, \frac{S_{MH}}{N_H} - 0.0714742E_H$$

$$\frac{dI_H}{dt} = 0.071429E_H - 0.1429055I_H$$

With initial conditions

$$\frac{dS_M}{dt} = 0.142857I - 0.071 - 0.0262\, I\, \frac{S_{HM}}{N_H} - 0.04S_M$$

$$\frac{dR}{dt} = 0.0262\, I\, \frac{S_{HM}}{N_H} - 0.01115677R \qquad (4.1)a$$

$$\frac{dE_M}{dt} = 0.0262\, I\, \frac{S_{HM}}{N_H} - 0.12091E_M$$

$$\frac{dI_M}{dt} = 0.0909091E_M - 0.09I_M$$

$$S_H(0) = 14270701, E_H(0) = 18718, I_H(0) = 3416033, R(0) = 3414458,$$

$$S_M(0) = 24878462, E_M(0) = 927401, I_M(0) = 40209136$$

$$\frac{dN_H}{dt} = 0.00005079 - 0.00004566N_H - 0.0000027I_H \qquad (4.1)b$$

$$\frac{dN_M}{dt} = 0.071 - 0.04N_M - 0.07I_M$$

4.5.1 Disease-free equilibrium point

If we substitute the values from table 4.1 into the expression

E_0 and multiply through by the initial conditions, we have the

disease-free equilibrium point of the model system to be

$$E_0 = (15873315, 0, 0, 0, 58879027, 0, 0)$$

4.5.2 Basic reproduction number R_0

The basic reproduction number is given by:

$$R_0 = \sqrt{\frac{\beta_{MH}\beta_{HM}\Lambda_H}{\mu_H(\mu_H+\gamma_H)(\mu_M+\gamma_M)\mu_M}}$$

$$= \sqrt{\frac{0.42(0.0655)(0.4)^2}{(1/14)(1/11)(0.071)(1/60/365)}}$$

$$R_0 = \frac{(1/14)(1/60/365)}{(1/14+1/60/365)}\cdot\frac{(1/7)(1/60/365)}{(1/11+0.03)(0.03+0.06)(0.03+0.00005079)}$$

$$R_0 = 0.7397$$

Since, $R_0 = 0.7397 < 1$, we can conclude that malaria can be wiped out from Ghana.

4.5.3 Local stability of the disease-free equilibrium E_0

The Jacobian matrix of V from equation (3.22) is

$$\begin{pmatrix} -(\mu_H+\gamma_H) & 0 & 0 & 0 & -\beta_{MH} \\ \gamma_H & -(\mu_H+\gamma_H) & 0 & 0 & 0 \\ 0 & \gamma_H & -(\mu_H+\gamma_H) & 0 & 0 \\ 0 & \frac{\beta_{HM}\gamma_H}{\mu_M} & 0 & -\mu_M & 0 \\ 0 & 0 & 0 & 0 & -\mu_M \end{pmatrix}$$

□□ 0 □ □ □HM□□□M H 0 0 □(□ □□ M) 0 □□

□ □

□□ 0 0 0 0 □ □□□ □M□ M□□□

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

2

□x□□ □M□ M□□x□□ □H□ H□□x□ □□ □ □M□ H□□x□ □□ □M□□□ □ □□ □□MH HM

□ H H□0

□□M

□x□0.09□□x□0.07147□□x□0.2029□□x□0.12091□□0.00006081□0

$x^4 \square 0.48521x^3 \square 0.0832x^2 \square 0.00604x \square 0.00009684 \square 0$

The solution has two negative real part -0.021769 and -0.228736

Also since the coefficients of the polynomial

0.48521, 0.0832, 0.00604, 0.00009684 □0 by the Routh-Hurwitz stability criteria the disease-free equilibrium point is asymptotically stable. This means that malaria free society can be achieved.

4.5.4 The endemic equilibrium point

From equation (3.38) $A\square I_H^{\square} \square^2 \square BI_H^{\square} \square C \square 0$,

A □□□□ □□□HM N_H□□ □ □MH 2 HM MRR_{02}0 □□ □□ H□□□□ ,

Where

□

B □ □□□$_{HM}$□□N_H □□□□$_H$ □□□$_{\underline{MH}}$□□$_{\underline{M}}$□RR_{0M02}□□□□$_{\underline{H}}$□□□□□$_M$ N_{H2} □ H_1□□□ ,

□ □$_H$

C □□□□ □ □ □ □ □ □$_{H\,M}$(□ $_M)^2$ $N_H{}^2$ □ □ $_H$ □□$R_0{}^2$ □^{1}□□□

R_{0M} □ _____ □$_{HM}$□□□

□$_M$ □□□□$_M$ □□□$_M$ □□$_M$ □

□0.0655□□0.09091□□0.4□□0.071□

□ R_{0M} □ _____ □ 0.518017,and

□0.03□□0.09091□0.03□□0.03□0.06□

H_1 □□ □□ □ □$_{HMH\,H}N$ □ □ $_H$ □

H =0.0655 0.4$_1$□ □(1/(60 365))□□21119910□((1/(60 36□ 5))+(1/90))

H_1 □ 0.12819

Substituting the values of R_{OM} ,*H and* R_{10} into A, B and C where necessary

□ □0.42□□0.4□^{2}□0.0655□□0.518017 □□0.0111□0.0000456621□□

A□□□0.0655□□0.4□□0.14286□□0.0111□□21119910□□

_____□

□□ 0.54716 □□

A□867.55

B □[0.0655□□□0.4□□0.00005079□□21119910□□0.0111□0.0000456621□

□0.42□□0.4□□0.03□□0.00005079□□0.518017□□0.011□0.0000456621□ ^{2}

□_____$_2$ □□ 0.0111□□

0.1429□□0.03□□21119910□ □0.000012819]

□0.0000456621□□0.7397□

B □ □2.1 10^{10}

$C = (0.000045662)(0.09)^2 (0.00005079)(21119910)^2$

$(0.0111)(0.000045662)(0.7397)^2 (1)$

$C = 42.334$

Substituting the parameter values of A, B and C into equation (3.38)

$867.55(I_H)^2 - 2.1 \times 10^{10} I_H + 42.334 = 0$

$I_H = 2.0159 \times 10^{-9}$

$I_H = 2.0159 \times 10^{-9}$

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

$$S_H = \Lambda_H - \frac{\beta_{HM} \beta_H \Lambda_M}{\mu_M (\mu_H + \gamma_H) R_0}$$

$$S_H = \frac{(0.0655)(0.4)(0.0000456621) - (2.0159 \times 10^{-9})(0.03)(0.00005079)}{(0.0000456621)(0.03)(0.7397)}$$

$S_H = 2.0329$

$$E_H = \frac{\beta_H \beta_H \Lambda_H}{\mu_H (\mu_H + \gamma_H)(\mu_H + \alpha_H)}$$

$$E_H = \frac{(1/7)(1/(60 \times 365))(0.0000027)(2.0159 \times 10^{-9})}{(1/14)}$$

$E_H = 4.03312 \times 10^{-9}$

$R_0 = \frac{\quad}{\quad}$.

$$\square\square\square_H\square$$

$$\square \quad \square 1/7\square\square 2.0159\ 10\square^{\square 9}\square$$

$$R\square \quad \frac{}{\square 0.011\square 0.0000456621\square}$$

$$R\square\square 2.6072\ 10\square^{\square 8}$$

$$S_M\square\square \frac{}{}\square\square \quad ,$$

$$\square\square_{HM}\square\square_H\square\square\square_M\square\square$$

$$S_M\square\square \frac{}{}0.0655\square\ \square 0.4$$

$$0.0000456621\ 2.0159\ 10\ )\square 0.071\square\square\square 0.00005079\square^{\square 9}\square\ \square(003\ 0.0000\square\quad 5079\square,$$

$$\square$$

$$S_M\square\square 2.3667$$

$$\square$$

$$E_M\square\ \square\ \square_M\square\square_M\square\square_M\square_H R_{0M}\square$$

$$\square\square_{HM}\square\square_H\square\square\square_M\square\square$$

$$\square \quad \square 0.03\square 0.06\ (0.03\ 0.0000456621\ 0.518017\square\quad\square\quad\square 2.0159\ 1\square\ 0^{\square 9})$$

$$E_M\square\ \square 0.0655\square 0.4\square 0.0000456621\ 2.0159\ 10\square\square^{\square 9})\square(0.03\ 0.000\square\quad 05079)\square$$

$$\square E_M\square\ \square 8.4495\ 10\square^{\square 11}$$

$$\frac{}{}\ \square\quad R_{0\square M\ M}\square\quad I_{H\square}$$

$$I_M\square$$

$$(\square\ \square\ \square_{HM} I_H\square_{\ M\ H} N\ )$$

$$\square 0.518017\square\square 0.03\square\square 2.0159\ 10\square^{\square 9}\square$$

$$I_M\square\ \square\ (0.0655\ 0.4\square\quad\square 2.0159\ 10\ )\square^{\square 9}\square(0.03\ 21119910)\square$$

$$I_M \approx 4.944 \times 10^{-17}$$

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

$$2.901 \times 10^{-7}, 7.5492 \times 10^{-4}, 6.8864 \times 10^{-3}, 0.08902, 5.888 \times 10^{-7}, 0, 7.8361 \times 10^{-8}, 1.988 \times 10^{-5}, 0$$

Since $C \approx 42.334$ and $R \approx 1$, it implies that the malaria model for Ghana has one unique endemic equilibrium point.

4.6 Equations of the model with prevention and treatment strategies

After substituting the estimated parameter values in table 4.1 into model (3.46), we have the following system of non-linear differential equations as the malaria with prevention and treatment strategies.

$$\frac{dS_H}{dt} = 0.0000452 - 0.168 \frac{I}{N_H} S_M S_H - 0.011R - 0.08335 S_H$$

$$\frac{dP}{dt} = \frac{I}{N_H} P_M - 0.00004566P + 0.000005587 - 0.0833 S_H - 0.99R - 0.1995$$

$$\frac{dE_H}{dt} = 0.168 \frac{I}{N_H} S_M S_H - 0.1995 \frac{I}{N_H} P_M - 0.07147 E_H$$

$$\frac{dI_H}{dt} = 0.07143 E_H - 0.15291 I_H$$

$$\frac{dT}{dt} = 0.01 I_H - 0.007266T$$

$$\frac{dR}{dt}$$

$\frac{dT}{dt} = 0.00722T - 0.14286I_H - 1.001157R$

$\frac{dS_M}{dt} = 0.071 - 0.0262 I S_{HH} - 0.03S$

$\frac{dS_M}{dt} = 0.0262 I S_H - 0.12091E_M$

$\frac{dE_M}{dt} = 0.09091E - 0.09 I_M$

4.6.1 Disease-free equilibrium point

$E_2 = (S_H, P, E_H, I_H, T, R, S_M, E_M, I_M)$

$= (1L, 0, 0, 0, 0, L, 0, 0, 0)$

$= (0.11 - 0.00004566 - 0.00005079 - 0.00005079)(0.11 - 0.00004566 - 21) - 0.0833$

0.071

$E_2 = (0.0833 - 0.0000456621)' - 0.0000456621 - 0.0833 - 0.0000456621$

$0.03, 0, 0, 0, 0, 0, 0, 0, 0, 7739.81, 12468008.65, 0, 0, 0, 0, 58879027, 0, 0$

4.6.2 Effective reproduction number R_e

$$R_{et} = \sqrt{\frac{\beta_{MH}\beta_{HM}\Lambda_H^2}{\mu_M(\mu_H+\nu_H)(\mu_H+\gamma_H)(\mu_M+\nu_M)(\mu_M+\gamma_M)}}$$

$$R_{et} = \sqrt{\frac{[0.42][0.0655][0.4^2][1/11][0.071/(60\times365)][1/14]}{[0.03][0.00005079+(1/14)][1/60\times365][(1/7)+0.01][1/60\times365][0.0000027][1/11+0.03][0.03+0.06]}}$$

$$R_{et} = 0.7151$$

Similarly, if the protection is the only intervention strategy being practiced, the effective reproduction number becomes

$$R_{ep} = \frac{\Lambda_H\beta_{MH}\beta_{HM}\Lambda_H}{\sqrt{\mu_M(L\mu_H+\mu_H+\nu_H)(\mu_H+\nu_H+\gamma_H)(\mu_M+\nu_M)(\mu_M+\gamma_M)}}$$

$$R^{ep} = \sqrt{\frac{[0.42][0.0655][0.4^2][1/11][0.071/(60\times365)][1/14][0.0833]}{[1-0.475][(1/(60\times365))+1-(0.11)0.475]}}$$

$$[0.03][0.00005079+0.0833][1/60\times365][1/60\times365][1/14][(1/7)+0.01][0.0000027][1/11+0.03][0.03+0.06]$$

$$R_{ep} = 0.006019$$

$$R_e = \sqrt{\frac{L\mu_H(\mu_H+\nu_H+\gamma_H)(\mu_M+\nu_M)}{\Lambda_H\beta_{MH}\beta_{HM}\Lambda_H\mu_M(L\mu_H+\mu_H+\nu_H)(\mu_H+\nu_H+\gamma_H)(\mu_M+\nu_M)}}$$

$$R_e = 0.0060183$$

This implies that control intervention strategies have a positive impact on reduction of the spread of malaria.

4.7 Numerical Simulations

Numerical analysis of the model is presented in this section using ODE solvers coded in Matlab programming language. This is conducted to find out the dynamics of the disease in the human population. The malaria model is simulated without any intervention and then with intervention strategies, and find out the effects of varying intervention parameter. The figures are plotted using the initial conditions and the parameter values presented in Table 4.1

S_H 0 14270701, P_0 11214672, E_H 0 1 8718, I_H 0 3416033, T_0 8194525, R 0 3414458,

S_M 0 24878462, E_M 0 927401, I_M 0 40209136

The rates are given per year. The time-axes in all the phase portraits start from the year 2004.

4.7.1 Dynamics of Human Population State Variables of the Basic Model

To find out the dynamics of the disease in the population when there is no intervention to reduce or eradicate the disease,the simulation of basic model has been conducted. The susceptible populations will initially decreases with time and then increases exponentially as shown in Figure 4.1 when there is no intervention strategies in the model.This explains that the susceptible population will continue being exposed to the disease, because of that, the exposed population will increase. The infected population increases small due to the increase in the exposure to the disease. Without any intervention strategies it will take the country about five hundred and fifty years from now to attain malaria free nation; since the infectious human population ends somewhere 2565 on time-axis in figure 4. 1.

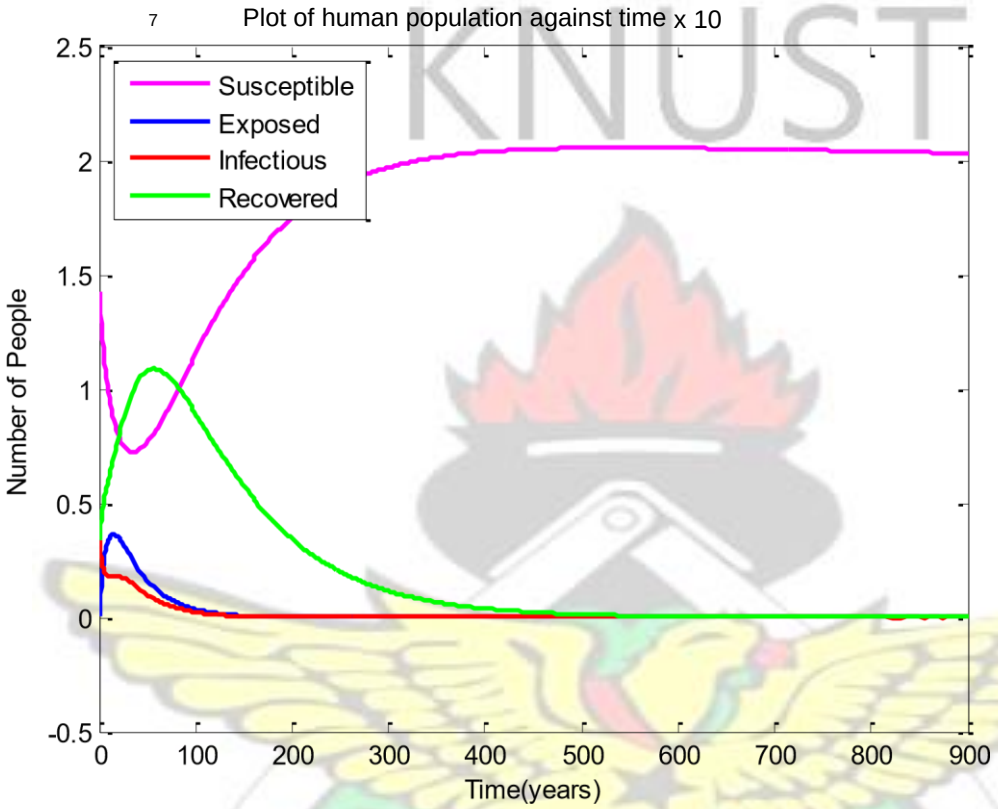


Figure 4.1: Illustrates the changes in the four state variables of the basic malaria model showing the dynamics, with time, of susceptible human individuals, exposed human individuals, infected human individuals and shows the dynamics of recovered human individuals.

4.7.2 Prevalence in the Basic Malaria Model

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. The prevalence graph, increases with bigger gradient 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 as most of the individuals in the society become affected with the disease.

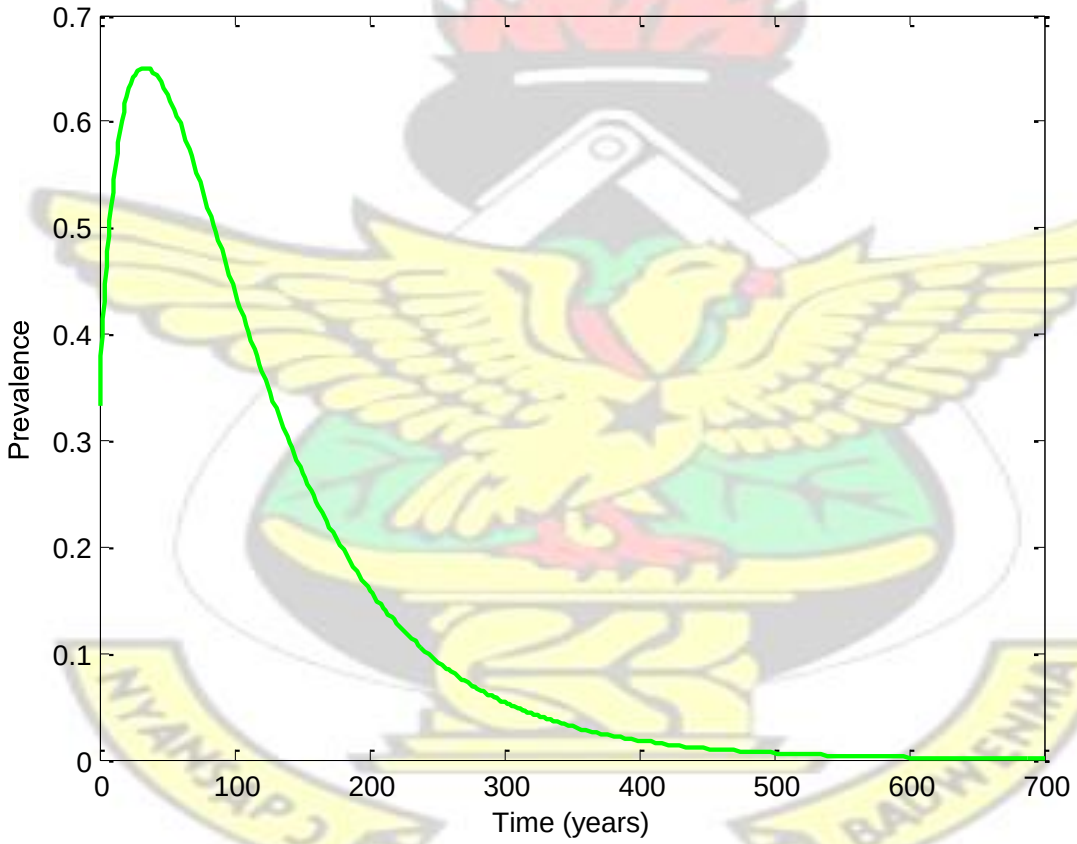


Figure 4.2: Represents changes of prevalence with time.

4.7.3 Simulation of the behavior of mosquito population

From figure (4.3) below that there is an exponential decrease in all the mosquitos' populations with time. The susceptible population will decrease and as such, a lot of the population will not be exposed to the disease. As a result of this, the exposed population will decrease. This implies that the plasmodium parasite cannot multiply .This is proof that the disease can be eradicated from the nation but will take a longtime since more work have to be done.

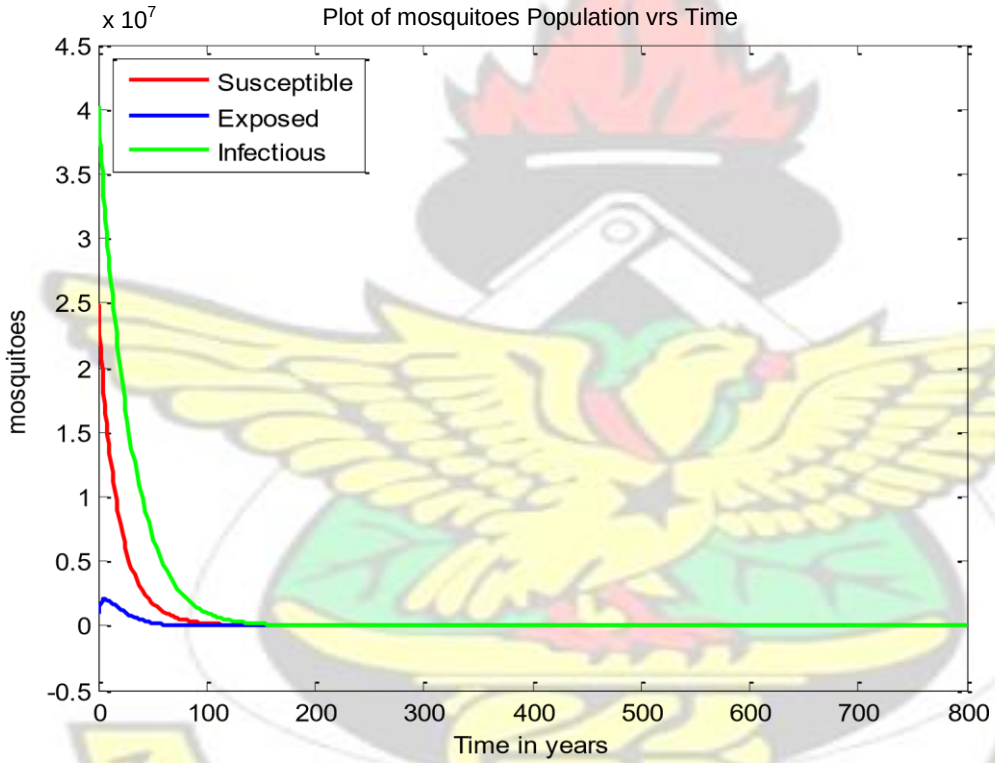


Figure 4.3: Illustrates the changes in the three state variables of the mosquito population in the model with time.

4.7.4 Simulation of biting rate of mosquitoes on the model

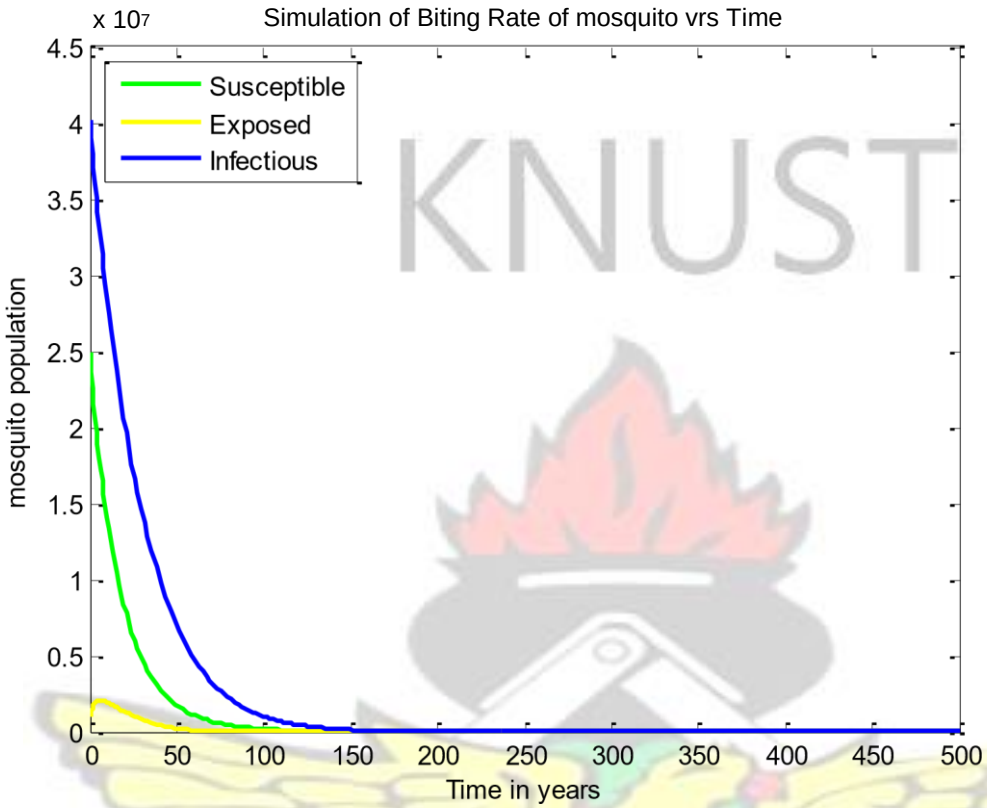


Figure (4.4): Illustrate the dynamics of vector population with time

The Figure (4.4) contains the plot of the susceptible mosquito population, the exposed mosquito population and the infected mosquito population.The graph 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.

4.7.5 Simulation of Protected and Treated Human Populations

Protected and treated individuals graph in figure (4.5) show that treatment has more effect at early stage compare to prevention. The trend changes with time as prevention measure plays a bigger part in reducing the spread of malaria disease. More evidence has been shown further with the variation in the prevention rate L as in Figure (4.6) and the treated rate. Treatment is highly needed when there are more infected individuals, In perspective, one could conclude from the controls in Figure (4.6) and Figure (4.7) that we should give full prevention effort in the beginning of emergence of the disease while giving full treatment effort in the middle of time interval when control efforts are practiced. This means that prevention is more important in the beginning of the disease outbreak.

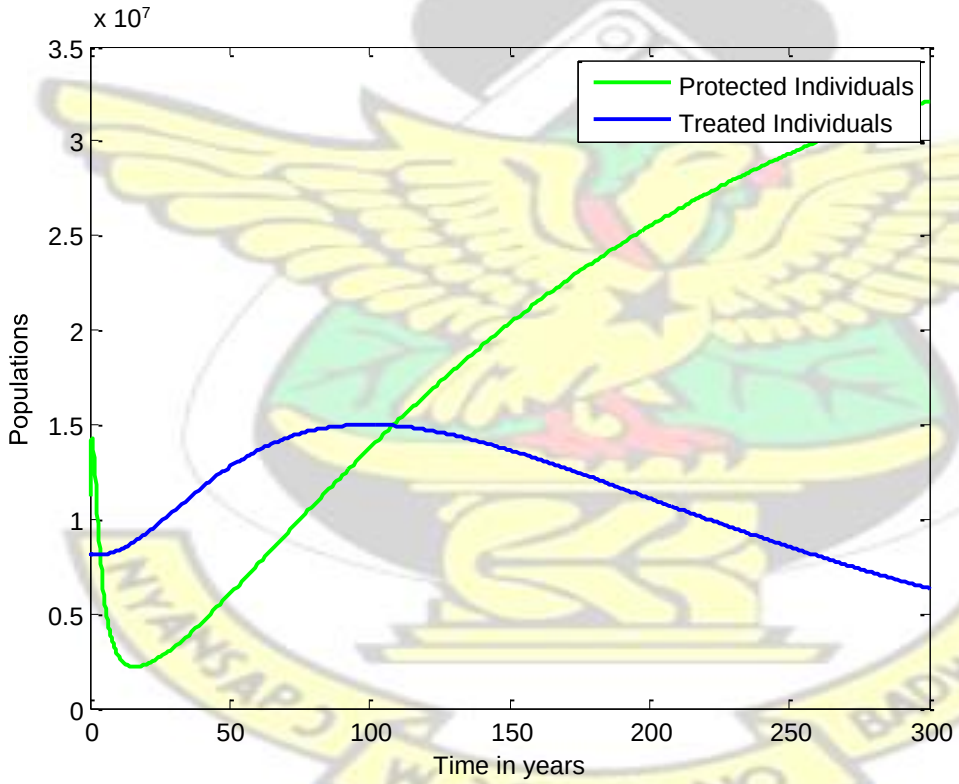
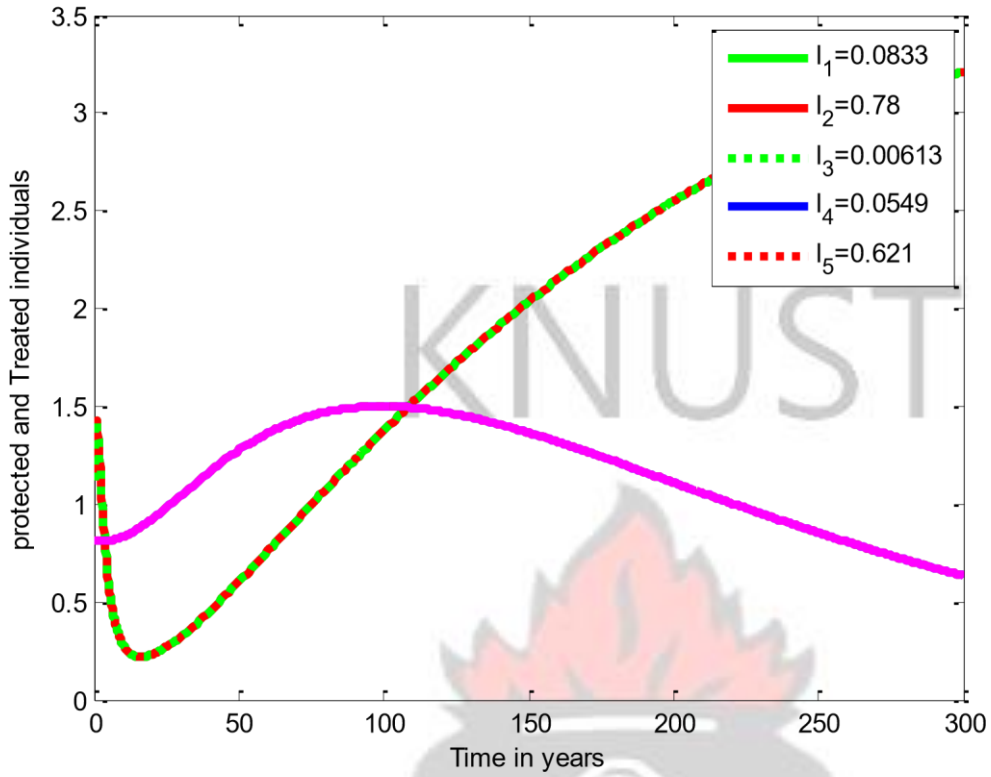


Figure 4.5: Shows the graphs of the protected human individuals and treated human individuals with time.

x 10^7



Treatment programs must be added to other interventions (such as vector reduction strategies and personal protection) to have a realistic chance of effectively controlling the disease spread. We can therefore conclusion that intervention practices that involve both prevention and treatment controls produces a relatively better result. Combination of these interventions can play a positive role in reducing or eradicating the disease in Ghana. This can be achieved by prompt provision of effective prevention measures and anti-malaria drug for treatment to reduce transmission and morbidity.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

A basic deterministic malaria model SEIR model was first formulated .The model took into consideration a varying total human population that includes recruitment of new individuals into the susceptible class through either birth or immigration. In order to assess the potential impact of protection and treatment strategies on the transmission dynamics of the disease, protected and treated classes were added to the basic model to formulate the malaria model with intervention strategies (SPEITR model).

Features that will be useful to control the transmission of malaria disease in the country was included in the model. The result from the analysis of the model proved that there exists a domain where the model is epidemiologically and mathematically well-posed.

The basic reproduction number, R_0 ,which is used to determine the seriousness of the disease and measures how fast the disease will be spread through a population was calculated to be 0.7397. This result confirmed that malaria can be eliminated from Ghana. The model was then analyzed qualitatively for the existence and stability of their associated equilibria. It was showed that under the condition that $R_0 < 1$ the disease-free equilibrium E_0 is locally asymptotically stable, and when $R_0 > 1$ the endemic equilibrium E_1, appeared.

The threshold for effective reproduction number and the basic reproduction number in the absence of the disease was compared. The effective reproductive number was computed and was found to be $R_e = 0.0060183$.When the protection is not practiced and hence treatment is the only intervention strategy, then effective reproduction number R_e becomes $R_{et} = 0.7151$.If protection is the only intervention strategy being practiced, the effective

reproduction number becomes $R_{ep} \approx 0.006019$. R_e is the useful indication of the effort required to eliminate an infection. It was also noted that

$R R R R_e \propto \propto \propto_{ep\ et\ 0}$ which implied that increasing preventive and control measures has a great effect on reduction of R_e.Thus, malaria can be eradicated out of Ghana by combination of strategies such as effective mass drug administration (treatment measure) and vector control(protection measure) that are of important in its fight.

Numerical simulation of the model also suggests that the most effective strategy for controlling or eradicating malaria is not only to reduce the biting rate of the female anopheles mosquito through the use of insecticide-treated bed nets and indoor residual spraying but to include prompt and effective diagnosis and treatment of infected individuals.

This study concurs with the Chavez (2008) suggestion that the intervention using insecticide-treated bed nets represents an excellent example of implementing an infectious disease control programme, and Smith et al, (2008)′s study, which showed that both regular and non-fixed spraying resulted in a significant reduction in the overall number of mosquitoes, as well as the number of malaria case in humans. Therefore, the combination of these interventions can play a bigger role in reducing or eradicating the transmission of the disease and malaria relate death cases in the Ghana. This study provides useful tools for assessing the potential impact of prevention and treatment strategies on the dynamics of malaria in Ghana.

5.2 Recommendations to stakeholders

1. Since most of the reductions in transmission come from the protection of a few humans, it is very important to improve the killing effects of insecticide mosquito treated bednets (ITNs) and indoor residual spray (IRS) around those who are mostly exposed to

the disease. however, complete coverage and improved killing effects may be necessary to reach control goals.

2. Vector control interventions such as insecticide-treated nets (ITNs) and indoor residual spraying (IRS) are proving effective to combat and prevent the disease in Ghana. ITNs and IRS, with insecticidal and diversionary properties, would reduce the availability of hosts, and kill mosquitoes that are attempting to feed on human's blood, and reducing malaria transmission.

3. For the protection strategy to be more effective,reduction of likelihood of infection by protection should be reduce to a number close to zero.

5.3 Recommendations for future work

The following recommendations should be considered in:

(1) Future models to include the effects of the environment on the spread of malaria. Some parameters, such as the incubation period in mosquitoes and mosquito birth rate depend on seasonal environmental factors such as rainfall, temperature, and humidity. We can include these effects by modelling these parameters as periodic functions of time. This would provide a more accurate picture of malaria transmission.

(2) Cost-utility analysis can be used to determine the costs and effects of protection and treatment strategies against malaria and their combinations.

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