MODELING OF MALARIA TRANSMISSION USING DELAY DIFFERENTIAL EQUATIONS

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A Thesis Submitted to the Board of Graduate Studies in Partial Fulfillment of the Requirements for the Conferment of the Degree of Master of Science in Applied Mathematics of the University of Kabianga

UNIVERSITY OF KABIANGA

MARCH, 2021

DECLARATION AND APPROVAL

Declaration

This thesis is my original work and has not been presented for the conferment of a degree or for the award of a diploma in this or any other University:

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DEDICATION

To my wife Risper Mibei and children Castro, Dorine and Sandra.

ACKNOWLEDGMENTS

First and foremost, I would like to thank our almighty father God for sufficient health and the far he has taken care of me. I wish to express my sincere gratitude to University of Kabianga Department of Mathematics and Computer Science for offering me a chance to pursue MSc. Applied Mathematics studies. My sincere thanks go to my supervisors Dr. Wesley Kirui and Dr. Daniel Adicka for their tireless efforts in guiding and ensuring that I succeed in my research and not forgetting their overwhelming support in my entire research work. I want to extend my appreciation to my lecturers who taught me in my first and second semester of first year in MSc. Applied mathematics program especially Prof. Michael Okoya, Prof. Maurice Oduor Ag. DVC (Planning, Research & Development), Dr. John Rotich, Dr. Job Bonyo and Mr. Richard Wachana. I would like to thank my family, my relatives, my wife for their support and love. Above all, I thank God for his guidance and mighty favors upon me.

ABSTRACT

Malaria is one of the major causes of deaths and ill health in endemic regions of sub-Saharan Africa and beyond despite efforts made to prevent and control its spread. Epidemiological models on how malaria is spread have made a substantial contribution on the understanding of disease changing aspects. Previous researchers have used Susceptible –Exposed-Infectious-Recovered (SEIR) model to explain how malaria is spread using ordinary differential equations. The main goal of this research was to develop mathematical SEIR epidemiology model to define the dynamics of the disease spread using delay differential equations with four control measures such as long lasting treated insecticides bed nets, intermittent preventive treatment of malaria in pregnant women (IPTP), intermittent preventive treatment of malaria in infancy (IPTI) and indoor residual spraying.The model would help health professionals to appreciate the dynamics of the spread of malaria and use the control measures above as intervention measures in controlling malaria spread. The model is then analysed and reproduction number derived using next generation matrix method and its stability is checked by jacobian matrix. Positivity of solutions and boundedness of the model is proved. We show that the disease free equilibrium is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. Numerical simulations results shows that basic reproduction number $R_0 = 0.2004$ and with proper treatment and control measures put in place the disease is controlled.

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LIST OF SYMBOLS

S	Susceptible class
E	Exposed class
I	Infectious class
R	Recovered class
S_h	Susceptible humans
E_h	Exposed humans
I_h	Infectious humans
R_h	Recovered humans
N_h	Total human population
S_m	Susceptible mosquitoes
E_m	Exposed mosquitoes
I_m	Infectious mosquitoes

$\boldsymbol{R_m}$	Recovered mosquitoes
$\boldsymbol{N_m}$	Total mosquitoes population
$\boldsymbol{R_0}$	Basic Reproductive number/ratio
$\boldsymbol{F_i(x)}$	Rate of appearance of new infections entering compartment i
$\boldsymbol{V_i^-(x)}$	Rate of transfer of individuals out of compartment i
$\boldsymbol{V_i^+(x)}$	Rate of transfer of individuals into compartment i by other means
$\boldsymbol{FV^{-1}}$	Next generation matrix
$\boldsymbol{x_\tau}$	Value of x at previous times
$\boldsymbol{t}$	Time
$\boldsymbol{x(t)}$	Value of x at current time
$\frac{\boldsymbol{d}}{\boldsymbol{dt}}$	Derivative at a definite period
$\boldsymbol{\Lambda_h}$	Humans birth rate
$\boldsymbol{\Lambda_m}$	Mosquitoes birth rate
$\boldsymbol{\alpha_h}$	Natural death rate of humans
$\boldsymbol{\alpha_m}$	Natural death rate of mosquitoes
$\boldsymbol{\beta_h}$	Disease induced deaths of humans
$\boldsymbol{\beta_m}$	Disease induced deaths of mosquitoes
$\boldsymbol{\mu}$	Recovered individuals loss of immunity
$\boldsymbol{\gamma}$	Human progression rate from susceptible to exposed
$\boldsymbol{\rho}$	Human progression rate from exposed to infected class
$\boldsymbol{\sigma}$	Human progression rate from infected class to exposed class
$\boldsymbol{\theta}$	Mosquito progression rate from susceptible class to exposed class
$\boldsymbol{\omega}$	Mosquito progression rate from exposed to infected class

LIST OF ABBREVIATIONS AND ACRONYMS

DDEs	Delay Differential Equations
DDT	Dichlorodiphenyltrichloroethane
LBW	Low Birth weight
WHO	World Health Organization
LLINS	Long Lasting Insecticides Treated Nets
IRS	Indoor Residual Spraying
SEIR	Susceptible class-Exposed class-Infectious class- Recovered class
IPT$_I$	Intermittent Preventive Treatment of Malaria in Infancy
IPT$_P$	Intermittent Preventive Treatment of Malaria in Pregnant Women

CHAPTER ONE

INTRODUCTION

1.1 Overview

The World health organization (WHO) estimated that there were 405,000 deaths from malaria worldwide in the year 2018 compared with 416,000 estimated in 2017 and 585,000 in the 2010 respectively.From the above statistics,malaria remains a major public health problem which requires immediate attention.

1.2 Background of the Study

Malaria is one of the most pandemic disease that remains arguably the greatest threat in our society and has remained the main cause of deaths in Africa and many regions of the world. Malaria was a major bottleneck in military camps in the United States where they initiated malaria campaigns (Nyangera, 2013). In the Second World War and war in Vietnam, more employees died as a result of malaria than those who died as a result of war. The discovery that malaria is transmitted by mosquitoes and was killing many people, they sought for ways on to control the spread. The measures that were designed targeted the life cycle of mosquito, at both larval stages and adult stages of the insect. During these two stages mosquitoes could be controlled by spraying using insecticides .In some regions such as the southern United States, they were able to drain swamps to reduce mosquito infestation. Substantial measures were taken when insecticide dichlorodiphenyltrichloroethane (DDT) and drug chloroquine were introduced. The insecticide DDT became very effective in controlling the infestation of

adult Anopheles mosquitoes. The drug Chloroquine was highly effective medicine for handling and preventing malaria. After some time, problems soon arose where cases of malaria increased rapidly as a result of new strains of female Anopheles mosquitoes developing resistance to DDT and other insecticides, and the environment impact assessment of DDT was realized. Meanwhile, malaria parasite became resistant to the drug chloroquine (Nyangera, 2013).

Malaria remains a leading cause of deaths and ill health in endemic regions of the world and has been a threat in many developing countries. Although previous researchers have looked into how to reduce its spreads, the disease continues to be the cause of mortality in many regions. In 2015 World Health organization (WHO) estimated the cases of malaria to be 214 million resulting in 438,000 deaths, majority of these were from Africa. Sub-Saharan Africa continues to exhibit a considerably high number of epidemics of malaria which results to many deaths. Furthermore, WHO (2016) estimates that there were 216 million quantifiable cases of malaria and 445,000 people perished of whom 306,000 were children under the age of 5 years and were mainly from Africa.

Severe malaria can lead to cerebral malaria, which is associated with unconsciousness, seizures, or other neurological anomalies. Risks associated with malaria in expectant mothers include maternal anaemia, low weight in infants (LBW), immature delivery and increased infant and maternal deaths (WHO, 2016).

The prevalence of malaria has been on the rise owing to malaria parasite developing resistance to drugs, mosquito-insecticide resistance and weak malaria intervention measures. This therefore warrants efficient and effective control measures on the spread of malaria.

1.2.1 Transmission of malaria

Malaria is transmitted by Plasmodium parasite. One gets malaria by being bitten by infected female anopheles mosquito. The mosquito must have been infected from blood meal of infected persons. Blood of infected person has microscopic malarial parasite that can be passed onto a mosquito when it bites such an individual. The malarial parasite incubates for about seven days after which it becomes infectious and if a mosquito bites a new individual the parasite from the blood meal will mix with mosquito's saliva and can be transmittable to the person being bitten. Malaria symptoms appears within 9-14 days. The most common symptoms are headache, fever and vomiting. Other ways through which malaria can be spread is by through blood transfusion or even by sharing used needles or syringes from blood which is contaminated. Also During delivery or before delivery of the new born baby, the mother may pass over the disease to the baby child. The various plasmodium parasite which causes malaria in individuals include:

(i) *Plasmodium falciparum* – Malarial deaths worldwide is brought about by this parasite specifically in Africa.

(ii) *Plasmodium Vivax*- Less severe symptoms is observed in this parasite as compared to Plasmodium falciparum though it may end at relapses as it can remain in the liver even for three years. It is common in Asia and Latin America.

(iii) *Plasmodium ovale* – It is rare though it may be found in West Africa. Its incubation period take years in the liver.

(iv) *Plasmodium malariae* – It is found in Africa though rarely.

(v) *Plasmodium knowlesi* – This is common in south East Asia though it is very rare.

Of all these, *Plasmodium falciparum* is the type of malaria parasite that usually causes severe deaths in many countries in Africa.

1.2.2 Signs and symptoms of malaria

Signs and symptoms may include fever, joint pains, Shaky chills, headache, muscle pains and drowsiness. Biliousness vomiting and diarrhoea could take place. Anaemia and jaundice may be as a result of malaria because red blood cells are reduced.

1.2.3 Asymptomatic malaria

Human host is considered asymptomatic when it is a carrier for malaria or infection, but experiences no symptoms. Countries infected by malaria in great percentage of *Plasmodium falciparum* contagions are asymptomatic. Microscopy detected levels of asymptomatic carriage as high as 39% have been reported by (WHO). Always, this concealed pool of parasites is crucial for keeping infection cycle. In areas vulnerable to the disease exposing continuously to the parasites results in limited invulnerability and subsequently form carriers the populace given. Furthermore, asymptomatic cases provide an important pool of parasites which may result in gametocyte carriers, contributing in the continuous spread of malaria. Consequently incidence of asymptomatic case in any malaria endemic area has been a big problem in the management and eradication program. Interrupting malaria transmission in prone area could be effective in eliminating, detection of carrier parasite by active case and even in full treatment.

1.2.4 Mosquito life cycle

Mosquitoes are pests that feed on blood and often spread the diseases that affect human health and affect our day to day activities. Nonetheless, the adult stage of the mosquito's

life cycle is the stage that is harmful to the human and animal health. Mosquito life cycle has varied morphology even though all the stages go from a common cycle of life.

1.2.4.1 Egg stage

Eggs are laid one at a time and they float on the surface of water or places where there are floods. Most eggs hatch into larvae within 48 hours.

1.2.4.2 Larval stage

Once mosquito larvae have hatched from the eggs they go through four instars changing in size after moulting in each stage. During this stage, the species display great variation in morphology and it is at this stage where they can be identified .Larvae take in oxygen from the atmosphere through a tube popping through the water surface, while the rest of the body align horizontally with the water surface so as to make it easier to breathe.

1.2.4.3 Pupa stage

This stage involves transition from water stages of mosquito's life cycle to surface-dwelling adult stage. They also live in water but mobile without feeding and escape from predators using a sinking motion in a maximum of two days where it moults into adult.

1.2.4.4 Adult stage

The newly emerged adult rests on the surface of water for a short time to allow itself to dry and all its parts to harden. Female mosquitoes are mated immediately they are capable. Mosquitoes maintain their energy from carbohydrate sources (nectar) which will be used for mating, flying and seeking host for blood meal. Female mosquito

develop eggs therefore require to take a blood meal so that she gets the extra-protein. Taking blood meal from malarial infected individual is a way of malarial transmission.

1.2.5 Delay differential equations

Delay differential equations (DDEs) are equations that involves the derivative of the unidentified function at a definite period given in relations to values of the function at preceding times. It takes the form:

$$\frac{d}{dt}x(t) = f(x(t), x_\tau, t) \tag{1.1}$$

where $x \in \mathbb{R}^n$ and τ is a positive integer.

1.3 Statement of the Problem

Although impressive preventive measures have been put in place in some tropical regions for example use of anti-malarial drugs,(prophylaxis of high risk groups e.g infants and pregnant mothers) early and prompt treatment of suspected cases with the use of drugs ,the spread of the disease was still a serious threat and the causes that maintain the spread remained to be a significant test with half of population still at risk of malaria with no effective vaccine available and with many anti-malarial drugs losing effectiveness due to evolved resistance and there is need to understand the spread of malaria. Consequently, in the study we developed a delay SEIR model, where in the model we determined the equilibrium state and incorporated control and preventive measures so as to understand the spread of malaria.

1.4 General Objective

The general objective of the study was to develop a delay differential equation model and to investigate the most effective control intervention measures of malaria.

1.5 Specific Objectives

The specific objectives for this study were:

(i) formulate a mathematical SEIR-SEI model to describe the spread of malaria.

(ii) determine the steady states of the SEIR-SEI model and their local stabilities.

(iii) carry out sensitivity analysis of the Basic reproduction number R_0 with respect to the SEIR- SEI model parameters.

(iv) carry out numerical simulations with MATLAB to verify analytic results

1.6 Justification of the Study

In this study we have addressed the importance of the model in the transmission dynamics of malaria. We have considered SEIR-SEI malaria transmission model with control measures with prime purpose of controlling malaria.We have addressed the parameters that impact the most on the reproduction number and the control measures that are responsible in reducing the spread of malaria.

1.7 Significance of the Study

Despite encouraging declines in disease over the past decades, malaria remains a leading cause of deaths and ill health in all endemic regions of sub Saharan Africa and beyond. The significance of this study would help the stakeholders in the public health

ministry to appreciate the dynamics of the spread of malaria and be able to devise realistic targets for intervention, since the results on control measures would provide relevant guidance on which interventions to focus on. The study would also assist scholars, scientist and mathematicians to improve on earlier developed models and include better and cost-effective control and preventive measures so as to reduce spread of malaria.

1.8 Scope of the Study

The study focused on developing malaria transmission SEIR-SEI model for human and mosquito population. The model was analysed by developing equations and determining reproduction number using next generation matrix and employed the use of delay differential equations in explaining malaria transmission dynamics. The study was modelled for a period of 350 days so as to know the extent of malaria transmission in a year. In the model, the intervention measures such long lasting treated bed nets, indoor residual spraying and intermittent preventive treatment for malaria for infants and expectant mothers and treatment by use of a drug were included .

1.9 Limitations of the Study

Analysis of the model was limited to the use of next generation matrix to generate reproduction number which measures the extent of malaria spread. The study incorporated all the four interventions measures mentioned in the scope of study above to model malaria transmission. Simulation analysis was done using MATLAB software.

1.10 Assumptions of the Study

The study assumed that mosquitoes and humans become susceptible at birth and that the infected humans and mosquitoes move into the exposed class if they escape death.

Mosquitoes and humans enters infectious class after latent period. Since lifespan of mosquitoes is relatively smaller as compared to humans, mosquitoes die after infection. On the other hand if humans receive treatment they recover from the disease and move to the recovered class where after a short while they become susceptible again and hence the SEIR-SEI model.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

There are a number of considerable literature on various mathematical malaria models from various scholars that were used to pronounce blow-out of malaria and various strategies to control malaria in pandemic regions of the world.

2.2 Review of Related Literature

Jessicca (2018) studied malaria spread dynamics for human and mosquito populations by considering vectorial transmission, vertical transmission of disease and a force of infection which measure the influence that occurs in the disease transmission rate which an infected human is introduced into mosquito population. The study examine a SEIR model for humans and SIR model for mosquitoes but fail to incorporate preventive and control measures to reduce malaria prevalence. The analysis revealed the existence of three steady states, the disease free equilibrium and two endemic equilibrium and that when $R_0 < 1$, then disease is controlled and when $R_0 > 1$, the disease persists. In the study ordinary differential equation were used ,which in this research is addressed by introducing delay differential equations to gather for the latency period that take place between when a mosquito bites and human becoming infected.

Sunita (2017), Studied SEIR model for human and SI model for mosquito population. SEIR model took into account new immigrants in the population who are susceptible, exposed and infective. Impressed by Sunita's work, Nisha (2017), analyzed

the steadiness of SEIR model for malaria with infectious migrants but failed to carry out simulation and sensitivity analysis of the given model which was necessary so as to understand the effect of infective immigrants on the spread of malaria in a population. Similar studies were carried by Mojeeb (2017) who used a SEIR mathematical model using ordinary differential equations with four control measures such as reducing contact rate between humans and mosquitoes, reducing the infection rate between humans, use of active malaria drugs and treated mosquito nets.

Agyingi (2016) ,studied the dynamics of several species and strains of malaria. In the model four species of the malaria parasite was considered and from the study it was found out that some species of the parasite have evolved into strains that are resistant to treatment. The model found out that all species or strains persist for some time for the reproduction number greater than one, however the species or strain with the highest reproduction number eventually displace the other species. In the model factors such as seasonality, age structure of humans and mosquitoes' incubation period and spatial distribution were not considered.

Abay (2015) ,looked at the important parameters in the transmission and the spread of endemic malaria disease. The model was developed using ordinary differential equations,carried out qualitative analysis which include dimensional analysis, scaling and perturbation technique in addition to stability theory for ODE systems. In the the study control measures were not incorporated as well as most sensitive parameters which affect the reproduction number. Fatima (2015), in the model studied about imported population. Compared malaria cases between the local population and non-local population (immigrants), where the locals was represented by SEIRS model, non- local SEI model and mosquito population represented by SI model structure. From the model re-

covery was not included in non-locals but assumes that once infected will be deported or isolated from the population.

Xiao (2013) ,derived a nonlocal and time delayed reaction- diffusion model. From the model positivity and invariance of travelling wave solutions of the resulting Cauchy problem in an unbounded domain was considered.In the study delay differential equations was used to analyze the model however,control measures were not incorporated in understanding disease changing aspects.

Tumwiine (2014) ,considered a model that looks at the emergence of drug resistance against the most common and affordable antimalarial as an obstacle to malaria control. From the model treatment as a preventive strategy was incorporated and used ordinary differential equation to analyze the model. Existence and stability of disease free equilibrium and endemic equilibrium was determined and increased treatment efforts on individuals with sensitive strains making sure that evolution of drug resistance was kept to the minimum.The study did not include the time delays which represents the incubation periods of vectors and human population as this will assist significantly in computation of reproduction number as time delays reduces reproduction number.

Shigui (2008), considered the response dynamics from mosquito to human and back to mosquito to involve substantial time delays due to the latency periods of the parasites.The effect latency on the basic reproduction number was considered and it was pointed out that prolonging incubation period in either humans or mosquitoes by use of control measures would result in decreasing the incidence of infection.However, sensitivity analysis was not carried out to find out the parameters that affect the reproduction number the most.

In his Ph.D. dissertation, Chitnis (2005) analyzed a comparable model for malaria

spread, where in this model, divided human population into four classes SEIR, where people from the exposed class enter the transmissible class at a rate that was give-and-take of the duration of the latent period. After some time the infectious humans recover and move to the recovered class and recovered humans have some immunity to the disease. In the model humans leave the population through a dependent per capita emigration and natural death rate and also through a per capita disease-induced death rate.The effects of the environment on the spread of malaria such as temperature, rainfall and humidity was considered which showed that the human or mosquito population approaches the locally asymptotically stable endemic equilibrium point depending on the number in the susceptible class.

Ngwa and Gumel (2010) ,the model described a compartmental model where humans follow Susceptible S_h-Exposed E_h-Infected I_h-Immune R_h and mosquitoes follow: Susceptible S_m-Exposed E_m-Infected I_m.They defined a reproductive number R_0 and shows that disease free equilibrium is stable for $R_0 \leq 1$ and unstable when $R_0 \geq 1$.The model also included net population growth in predicting the number of death rate that arose as a result of the disease.In the analysis they used ordinary differential equation but fail to capture time delays between when the mosquito bites and one becoming sick.

Koella (1991) investigated the reasons for the prevalence of the disease and nature and causes of its variation.It also looks at the dynamics of malaria transmission by considering life cycle of mosquito.From the study it was found out that malaria exists in a population only if mosquito density exceeds a certain critical threshold,continuity of malaria is most sensitive to changes in mosquito survival rate.The study used ordinary differential equations and fail to capture time delays between mosquito biting human

host and one becoming sick. Nedelman (1984) ,reviewed a study by Dietz *et al.* (1974) and included vaccination rate.It was shown that the rate of vaccination rely on virtual equilibrium estimate to the differential equation defining the mosquito changing aspects in the malarial model.Survey was conducted on 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, infection and susceptibility of humans and mosquitoes.

Dietz *et al.* (1974) ,investigated on two different types of immunity in individuals, some with invulnerability to malaria and some class with insusceptibility. As the non-immune class falls sick some people recover with immunity. The immune class got the disease but were asymptomatic and could not transmit the disease.The model also included super infection, a phenomenon usually associated with macro- parasites.

Aron and May (1982) made further modifications and improvement to the Macdonald (1957) model by considering various malaria characteristics such as latency period in mosquitoes, a periodically changing density of mosquitoes, super infection and a period of human's immunity. The age-specific resistance model was considered with a new compartment invulnerable class (R_h) being introduced. So that humans consist of three compartments, Susceptible (S_h),Infected (I_h) and Immune (R_h) classes to form (SIR model) a model for immunity was included, where the variables are the population of asexual blood stages of plasmodium in humans and the level of human immunity. Therefore the variables depend on time and age.

Macdonald (1957) ,developed a model that incorporated biological facts of latency in the mosquito due to malarial parasite growth and well thought-out adult female mosquito as the weakest element in malaria cycle.From the model the Exposed class was

introduced in the mosquitoes, so that three compartments of mosquito population is factored in (SEI) and the model studies the time evolution of the (S_h) and disease-ridden (I_h) classes.

Ross (2011) ,studied deterministic model of malaria by adopting a SIS structure model for population of individual and SI structure for mosquito population. Human population move from susceptible (S_h) class to Infectious (I_h) class where susceptible class is joined by the infected individuals again resulting to SIS structure. The parasite takes only two compartment (S_m,I_m) moving from susceptible class to infectious class where short life span followed makes them not recover from contagion and hence follow SI structure. Ross directed from the study on how mosquito could be controlled and showed that for disease to be reduced the mosquito population should be brought below a certain threshold. Ross fails to consider the incubation period of a parasite and their survival during the period.

2.3 Identification of Knowledge Gap

From the above reviews the use of delay differential equations with control measures has not been used, which our findings have used to explain the dynamics of disease transmission. The delay differential equation has been used because of time lag between when a mosquito bites and the time one becomes sick.

CHAPTER THREE

METHODOLOGY

3.1 Introduction

This chapter outlines the methodology used in the thesis. The standard model for malaria spread was a slight modification to those considered by Chitnis (2005), Agyingi (2016) and Jessicca (2018) where constant control factors and stability properties are analysed. The standard model for SEIR for humans and SEI for mosquitoes was considered using delay-differential equations. Preventive measures were taken into considerations in our model. For instance ,intermittent preventive treatment of malaria in pregnant mothers, Long- Lasting Insecticides Treated Nets (LLINS), indoor residual spraying (IRS) also their effects based on the fact that the methods are recommended for prevention by (WHO) and intermittent preventive treatment of malaria in infancy. In this model human population was sub divided into four classes while mosquito population into three classes. Human population follows the following classes namely:,the susceptible class (S_h) which represents the part of population that was vulnerable to infection ,Exposed class (E_h) which represents the part of population who are diseased, but not infective and they could not transmit the infection, next was infectious class (I_h), part of population who have been infected and are capable of spreading the disease, finally the Recovered class (R_h), the part of population who recover from infection through treatment with temporary immunity. The total human population is expressed as;

$$N_h = S_h + E_h + I_h + R_h \tag{3.1}$$

The female anopheles mosquito population was divided into 3 classes, susceptible (S_m), Exposed (E_m) and Infectious class (I_m).So that the total vector population is $N_m = S_m + E_m + I_m$. Because the lifespan of humans is higher as compared to the life expectancy of mosquito, our model assumed mosquitoes dies after infection.

3.2 Model Assumptions

The following are the assumptions of our model

i) Individuals are moved directly into the susceptible class at birth

ii) Infected individuals move into the exposed class after latent period, if they escape death they move to infectious class.

iii) Since the lifespan of mosquito is relatively small compared to the lifespan of humans, mosquitoes will die from infection.

iv) No recovery for infected mosquitoes

v) There is homogeneous interactions in the human population

vi) Human beings have natural immunity to malaria.

vii) A fraction of exposed class move to infectious class after losing natural immunity.

viii) All parameters in the model are non-negative

ix) The parameter *k* and *l* are respective rates for removal of mosquitoes from different classes by the use of LLINS and IRS.

x) LLINS and IRS are denoted by the letters x and y respectively.

xi) Total human population varies with time

xii) Humans and mosquitoes enter the population at specific birth rates, Λ_h and Λ_m respectively, die from natural causes at specific rates α_h and α_m,respectively, and die from disease induced death rates at specific rates, β_h and β_m respectively.

xiii) We allowed individuals to move from susceptible human population to the exposed human at a rate which was proportional to both size of susceptible human population and infected mosquito population and inversely proportional to total human population $\frac{\gamma S_h I_m}{N_h}$

xiv) Members of exposed class (E_h) move to infected human class (I_h) at a rate proportional to the number of individuals in the exposed class, ρE_h,

xv) Individuals in the infected class move to recovered class at a rate proportional to the number of individuals in the infected class, σI_h.

xvi) Lastly, individuals in the recovered class move to susceptible class at a rate proportional to size of individuals in the recovered class, μR_h.

xvii) Similarly, for mosquito population susceptible mosquitoes move to exposed class at a rate $\frac{\theta S_m I_h)}{N_m}$.

xviii) Finally mosquitoes in the exposed class move to infectious class at the rate proportional to the size of individuals in the exposed mosquito population ωE_m.

In addition to considering various stages of the disease, we modelled the effects of malaria preventive measures which includes;

i) Long lasting treated bed nets (LLINS)

ii) Intermittent preventive treatment of pregnant women and infants(P_T) (using prophylaxis)

iii) Indoor residual spraying

3.3 Model Formulation

The following is the Human-Mosquito model diagram;

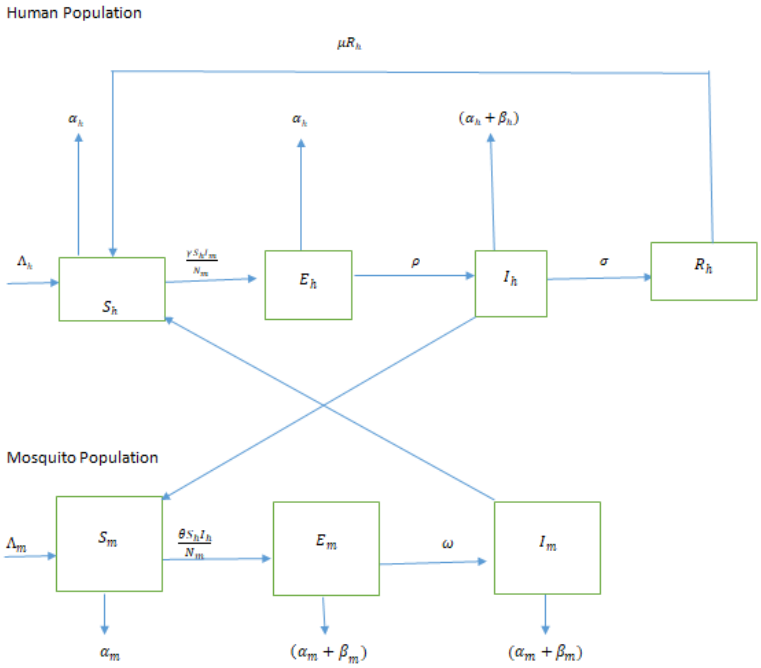

Figure 3.1: *Human-Mosquito model Flow Diagram*

3.4 Model Equations

From the assumptions made, the following are the model equations:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \mu R_h - \alpha_h S_h - \frac{(\gamma S_h I_m(t-\tau)(1-x))}{N_h} \\
\frac{dE_h}{dt} &= \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} - \rho E_h(t-\tau) - \alpha_h E_h(t-\tau) \\
\frac{dI_h}{dt} &= \rho E_h(t-\tau) - (\alpha_h + \beta_h) I_h - \sigma(1-z) I_h(t-\tau) \\
\frac{dR_h}{dt} &= \sigma(1-z) I_h(t-\tau) - \alpha_h R_h - \mu R_h \\
\frac{dS_m}{dt} &= -\frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} + \Lambda_m - (\alpha_m + \beta_m + Kx + Ly) S_m \\
\frac{dE_m}{dt} &= \frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} - \omega E_m(t-\tau) - (\alpha_m + \beta_m + Kx + Ly) E_m \\
\frac{dI_m}{dt} &= \omega E_m(t-\tau) - (\alpha_m + \beta_m + Kx + Ly) I_m
\end{aligned}\right\} \quad (3.2)$$

where $\tau > 0$ is the time delay.

3.5 Positivity and Boundedness of Solutions

3.5.1 Positivity of solutions

The following theorem is used in determining positivity of our solutions.

Theorem 3.1

Let the initial data be

$$\{(S_h(0), S_m(0) \geq 0, (E_h(0), I_h(0), R_h(0), E_m(0), I_m(0)\}$$

Then the solution set

$$\{S_h, E_h, I_h, R_h, S_m, E_m, I_m\}(t)$$

of the system is non-negative for all $t \geq 0$

Proof:

From the system of equation 3.2, we have;

$$\frac{dS_h}{dt} = \Lambda_h + \mu R_h - \alpha_h S_h - \frac{(\gamma S_h I_m(t-\tau)(1-x))}{N_h} \geq -\alpha_h S_h - \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h}$$

$$\implies \frac{dS_h}{dt} \geq -\left(\alpha_h + \frac{(\gamma I_m(t-\tau)(1-x))}{N_h}\right) S_h \tag{3.3}$$

Using separation of variables and integrating both sides

$$\int \frac{1}{S_h} dS_h \geq -\int \left(\alpha_h + \frac{\gamma I_m(t-\tau)(1-x)}{N_h}\right) dt$$

$$\ln S_h \geq -\left(\alpha_h + \frac{\gamma I_m S_h(t-\tau)(1-x)}{N_h}\right) t + c \tag{3.4}$$

$$S_h(t) = e^{(\alpha_h+\gamma I_m(t-\tau)(1-x))t} \times e^c$$

If we let $e^c = K$, then we have

$$S_h(t) = Ke^{(\alpha_h+\gamma I_m(t-\tau)(1-x))t} \tag{3.5}$$

When $t = 0, S_h(0) \geq KS_h(t) \geq S_h(0)e^{(\alpha_h+\gamma I_m(t-\tau)(1-x))t} \geq 0$

From the second equation of system (3.2)

$$\frac{dE_h}{dt} = \frac{(\gamma S_h I_m(t-\tau)(1-x))}{N_h} - \rho E_h(t-\tau) - \alpha_h E_h(t-\tau)$$

$$\implies \frac{dE_h}{dt} = \frac{(\gamma S_h I_m(t-\tau)(1-x))}{N_h} - \rho E_h(t-\tau) - \alpha_h E_h(t-\tau) \geq -(\rho+\alpha_h)E_h(t-\tau)$$

$$\implies \frac{dE_h}{dt} \geq -(\rho+\alpha_h)E_h(t-\tau) \tag{3.6}$$

Integrating both sides we have

$$\int \frac{1}{E_h} dE_h \geq -\int (\rho+\alpha_h)(t-\tau)dt$$

$$\text{In } E_h \geq -(\rho(t-\tau) + \alpha_h(t-\tau)t) + c$$

$$E_h(t) = e^{-(\rho(t-\tau)+\alpha_h(t-\tau)t)} \times e^c \tag{3.7}$$

Let $e^c = K$

When $t = 0, E_h(0) \geq e^c$

$$E_h(t) \geq E_h(0)e^{-(\rho(t-\tau)+\alpha_h(t-\tau)t)} \geq 0 \tag{3.8}$$

Similarly, it can be shown that the remaining equations of the model are positive for all $t > 0$, because $e^{\aleph} > 0$, for all $\aleph \in \mathbb{R}$.

This confirms that our model has both invariant and positivity of solutions.

3.5.2 Boundedness of solutions

The total population in our model are;

$$N_h = S_h + E_h + I_h + R_h$$

$$N_m = S_m + E_m + I_m$$

And their respective differential equations are:

$$\frac{N_h}{dt} = \frac{S_h}{dt} + \frac{E_h}{dt} + \frac{I_h}{dt} + \frac{R_h}{dt} = \Lambda_h - \beta_h I_h - \alpha_h N_h \tag{3.9}$$

And

$$\frac{N_m}{dt} = \frac{S_m}{dt} + \frac{E_m}{dt} + \frac{I_m}{dt} + \frac{R_m}{dt} = \Lambda_m - (\alpha_m + \beta_m + Kx + Ly)N_m \tag{3.10}$$

All state variables are assumed to be positive since the model is dealing with population. The positive invariant region can be obtained by the following theorem.

Theorem 3.2

The solution of system of equation (3.2) are feasible for all $t < 0$ if they enter invariant region

$$D = D_h \times D_m$$

Proof

Let $D_h = (S_h, E_h, I_h, R_h) \in \mathbb{R}^4_+$ be any solution of equation, (3.2) with nonnegative

initial conditions. Assuming that malaria does not kill ($\beta = 0, I_h = 0$), equation (3.9) becomes

$$\frac{dN}{dt} \leq \Lambda_h - \alpha_h N_h$$

$$\implies \frac{dN}{dt} + \alpha_h N_h \leq \Lambda_h \tag{3.11}$$

Using differential equation of the form $y' + p(t)y = q(t)$, we have $p(t) = \alpha_h$ and $q(t) = \Lambda_h$.

Therefore the integrating factor (IF) for equation (3.11) is given by;

$$e^{\int p(t)dt} = e^{\int \alpha_h dt} = e^{\alpha_h(t)}$$

Multiplying both sides of equation (3.11) by $e^{\alpha_h(t)}$ gives

$$\frac{dN}{dt}e^{\alpha_h(t)} + \alpha_h N_h e^{\alpha_h(t)} \leq \Lambda_h e^{\alpha_h(t)}$$

$$\frac{d}{dt}(N_h e^{\alpha_h t}) \leq \Lambda_h e^{\alpha_h t} \tag{3.12}$$

Integrating both sides of the inequality (3.12) w.r.t t , we have $N_h e^{\alpha_h t} \leq \frac{\Lambda_h e^{\alpha_h}}{\alpha_h} + c$, where c is a constant.

$$\implies N_h \leq \frac{\Lambda_h}{\alpha_h t} + ce^{-\alpha_h t} \tag{3.13}$$

Using the initial conditions at $t = 0, N_h(0) = N_h(0)$, we have;

$$N_h(0) \leq \frac{\Lambda_h}{\alpha_h t} + c$$
$$\implies N_h(0) - \frac{\Lambda_h}{\alpha_h t} \leq c$$
$$\implies N_h \leq \frac{\Lambda_h}{\alpha_h} + (N_h(0) - \frac{\Lambda_h}{\alpha_h})e^{-\alpha_h t}$$
$$\implies 0 \leq N_h \leq \frac{\Lambda_h}{\alpha_h} \text{ as } t \to \infty$$

Thus the total human population is given as;

$$N_h \leq \frac{\Lambda_h}{\alpha_h} \tag{3.14}$$

Hence

$$D_h = \left((S_h, E_h I_h, R_h) \in \mathbb{R}^4_+, S_h > 0, E_h \geq 0, I_h \geq 0, R_h \geq 0, N_h \leq \frac{\Lambda_h}{\alpha_h} \right) \tag{3.15}$$

Similarly, the feasible solutions of the vector (mosquito) population enters the region

$$D_m = \left((S_m, E_m, I_m) \in \mathbb{R}^3_+, S_m > 0, E_m \geq 0, I_m \geq 0 \geq 0, N_m \leq \frac{\Lambda_m}{\alpha_m} \right) \tag{3.16}$$

Therefore, the feasible solutions set for the model is given by,

$$\left. \begin{array}{c} D = \big((S_h, E_h I_h, R_h, S_m, E_m, I_m) \in \mathbb{R}^7_+, (S_h, S_m) > 0, (E_h, I_h, R_h, E_m, I_m) \geq 0 \big) \\ \left(N_h \leq \frac{\Lambda_h}{\alpha_h}, N_m \leq \frac{\Lambda_m}{\alpha_m} \right) \end{array} \right\} \tag{3.17}$$

Therefore the region D is positively invariant and therefore the model is biologically well posed in the domain D.

3.6 Basic Reproduction Number R_0

Diekmann (2000) defined Basic reproduction number as expected number of secondary cases produced by a single infection in a completely susceptible population. That is, it is a measure of how fast a disease spreads through a population.

Basic reproduction number is obtained by taking the largest dominant eigenvalue of FV^{-1} or spectral radius of FV^{-1} $\left(\frac{\partial F_i E_0}{\partial x_j}\right)\left(\frac{\partial V_i E_0}{\partial x_j}\right)$

Let $F = \left(\frac{\partial F_i E_0}{\partial x_j}\right)$, $V = \left(\frac{\partial V_i E_0}{\partial x_j}\right)$ and E_0 be disease free equilibrium.

From the system, F_i and V_i are defined as

F_i is the rate of appearance of new infections in compartment i.

V_i is the transfer of individuals into compartment i.

$$V_i = v_i^-(x) - v_i^+(x)$$

For computation of F We have,

$$F_i = \begin{bmatrix} \frac{\gamma S_h I_m (t-\tau)(1-x)}{N_h} \\ 0 \\ \frac{\theta S_m I_h (t-\tau)(1-x)}{N_m} \\ 0 \end{bmatrix} \tag{3.18}$$

Taking partial derivatives $\frac{\partial F_i}{\partial E_h}$, $\frac{\partial F_i}{\partial I_h}$,$\frac{\partial F_i}{\partial E_m}$, $\frac{\partial F_i}{\partial I_m}$, we get the 4×4 matrix below;

$$F = \begin{bmatrix} 0 & 0 & 0 & \frac{\gamma S_h(1-x)e^{-\lambda\tau}}{N_h} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\theta S_m(1-x)e^{-\lambda\tau}}{N_m} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{3.19}$$

For computation of V, we have,

$$V_i = \begin{bmatrix} (\rho + \alpha_h)E_h(t-\tau) \\ (\alpha_h + \beta_h)I_h + \sigma(1-z)I_h(t-\tau) - \rho E_h(t-\tau) \\ \omega E_m(t-\tau) + (\alpha_m + \beta_m + Kx + Ly)E_m \\ (\alpha_m + \beta_m + Kx + Ly)I_m - \omega E_m(t-\tau) \end{bmatrix} \tag{3.20}$$

Taking partial derivatives $\frac{\partial V_i}{\partial E_h}$, $\frac{\partial V_i}{\partial I_h}$,$\frac{\partial V_i}{\partial E_m}$, $\frac{\partial V_i}{\partial I_m}$, we get the 4×4 matrix below;

$$V = \begin{bmatrix} A & 0 & 0 & 0 \\ B & C & 0 & 0 \\ 0 & 0 & D & 0 \\ 0 & 0 & E & F \end{bmatrix} \tag{3.21}$$

where

$$A = (\rho + \alpha_h)e^{-\lambda\tau}$$

$$B = -\rho e^{-\lambda\tau}$$

$$C = (\alpha_h + \beta_h) + \sigma(1 - z)e^{-\lambda\tau}$$

$$D = \omega e^{-\lambda\tau} + (\alpha_m + \beta_m + Kx + Ly)$$

$$E = -\omega e^{-\lambda\tau}$$

$$F = (\alpha_m + \beta_m + Kx + Ly)$$

The inverse of matrix V is the given by;

$$V^{-1} = \begin{bmatrix} \frac{1}{A} & 0 & 0 & 0 \\ \frac{-B}{AC} & \frac{1}{C} & 0 & 0 \\ 0 & 0 & \frac{1}{D} & 0 \\ 0 & 0 & \frac{-E}{DF} & \frac{1}{F} \end{bmatrix} \tag{3.22}$$

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

$$FV^{-1} = \begin{bmatrix} 0 & 0 & a & b \\ 0 & 0 & 0 & 0 \\ c & d & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{3.23}$$

where

$$a = \frac{-E\gamma S_h(1-x)e^{-\lambda\tau}}{N_h DF}$$

$$b = \frac{\gamma S_h(1-x)e^{-\lambda\tau}}{N_h F}$$

$$c = \frac{-B\theta S_m(1-x)e^{-\lambda\tau}}{N_m AC}$$

$$d = \frac{B\theta S_m(1-x)e^{-\lambda\tau}}{N_m C}$$

The characteristic equation of matrix (3.23) is computed by:

$$\left|FV^{-1} - I\lambda_*\right| = 0$$

where I is a 4×4 identity matrix.

$$\implies \begin{vmatrix} -\lambda_* & 0 & a & b \\ 0 & -\lambda_* & 0 & 0 \\ c & d & -\lambda_* & 0 \\ 0 & 0 & 0 & -\lambda_* \end{vmatrix} = 0 \tag{3.24}$$

$$\implies -\lambda_* \begin{vmatrix} -\lambda_* & 0 & a \\ 0 & -\lambda_* & 0 \\ c & d & -\lambda_* \end{vmatrix} + a(0) - b(0) = 0 \tag{3.25}$$

$$\implies \lambda^{*2}(\lambda_*^2 - ac) = 0$$

$$\implies \lambda^{*2}(\lambda^{*2} - ac) = 0$$

$$\implies \lambda_* = 0, \text{ or } \lambda_* = \pm\sqrt{ac}$$

This implies the eigenvalues are given by:

$$\lambda_{*1} = \lambda_{*2} = 0, \lambda_{*3} = -\sqrt{ac}, \lambda_{*4} = \sqrt{ac} \tag{3.26}$$

The dominant eigenvalue is clearly λ_{*4}. Thus the reproductive ratio R_0, which is given

by the dominant eigenvalue, is;

$$R_0 = \sqrt{\frac{-E\gamma S_h(1-x)e^{-\lambda\tau}}{N_h DF}\frac{-B\theta S_m(1-x)e^{-\lambda\tau}}{N_m AC}}$$

$$= \sqrt{\frac{\omega e^{-\lambda\tau}\theta(1-x)e^{-\lambda\tau}S_m}{N_m\left\{[\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)]\,(\alpha_m+\beta_m+Kx+Ly)\right\}}}\sqrt{\frac{\rho e^{-\lambda\tau}(1-x)e^{-\lambda\tau}S_h}{N_h\left[(\alpha_h\beta_h)+\sigma(1-z)e^{-\lambda\tau}\right]}} \tag{3.27}$$

3.7 Existence of Disease Free Equilibrium

In the absence of disease in the population we have, $(E_h = I_h = 0, E_m = I_m = 0 = R_h)$ Here, $R_h = 0$, since there will be no disease to recover from, hence from the system of equation (3.2) we have,

$$\Lambda_h + \mu R_h - \alpha_h S_h - \frac{(\gamma S_h I_m(t-\tau)(1-x))}{N_h} = 0 \tag{3.28}$$

$$-\frac{(\theta I_h(t-\tau)S_m(1-x))}{N_h} + \Lambda_m - (\alpha_m + Kx + Ly)S_m = 0 \tag{3.29}$$

Substituting $I_m = R_h = 0 =$ in (3.28) we have;

$$S_h = \frac{\Lambda_h}{\alpha_h} \tag{3.30}$$

Substituting I_h in (3.29) we have;

$$S_m = \frac{\Lambda_m}{\alpha_m + Kx + Ly} \tag{3.31}$$

Similarly, when $(E_h = I_h = 0, E_m = I_m = 0 = R_h)$, then the remaining equations becomes

$$E_h^0 = 0, I_h^0 = 0, R_h^0 = 0, S_m^0 = \frac{\Lambda_m}{\alpha_m + Kx + Ly}, E_m^0 = 0, I_m^0 = 0 \tag{3.32}$$

Therefore disease free equilibrium point of our malaria model is given by

$$E_0 = (S_h^0, E_h^0 I_h^0, R_h^0, S_m^0, E_m^0, I_m^0) = \left(\frac{\Lambda_h}{\alpha_h}, 0, 0, 0, \frac{\Lambda_m}{\alpha_m + Kx + Ly}, 0, 0\right) \tag{3.33}$$

This is the state when there is no malaria in the society.

3.8 Stability of Disease Free Equilibrium

The stability of the disease free equilibrium state can be tested using eigenvalues of a Jacobian matrix obtained at DFE. This is where $R_0 < 1$.

$$J = \begin{bmatrix} a & 0 & 0 & \mu & 0 & 0 & b \\ 0 & c & 0 & 0 & 0 & 0 & d \\ 0 & e & f & 0 & 0 & 0 & 0 \\ 0 & 0 & g & h & 0 & 0 & 0 \\ 0 & 0 & i & 0 & j & 0 & 0 \\ 0 & 0 & k & 0 & 0 & l & 0 \\ 0 & 0 & 0 & 0 & 0 & m & n \end{bmatrix} \tag{3.34}$$

where

$$a = -\alpha_h$$

$$b = -\frac{\gamma S_h(1-x)e^{-\lambda\tau}}{N_h}$$

$$c = -(\rho + \alpha_h)e^{-\lambda\tau}$$

$$d = \frac{\gamma S_h(1-x)e^{-\lambda\tau}}{N_h}$$

$$e = \rho e^{-\lambda\tau}$$

$$f = -(\alpha_h + \beta_h) - \sigma(1-z)e^{-\lambda\tau}$$

$$g = \sigma(1-z)e^{-\lambda\tau}$$

$$h = -(\alpha_h + \mu)$$

$$i = -\frac{\theta S_m(1-x)e^{-\lambda\tau}}{N_m}$$

$$j = -(\alpha_m + \beta_m + Kx + Ly)$$

$$k = \frac{\theta S_m(1-x)e^{-\lambda\tau}}{N_m}$$

$$l = -\omega e^{-\lambda\tau} - (\alpha_m + \beta_m + Kx + Ly)$$

$$m = \omega e^{-\lambda\tau}$$

$$n = \alpha_m + \beta_m + Kx + Ly$$

The system of equations (3.2) is stable if all the eigenvalues of linearization matrix are negative. The characteristic equation of the Jacobian matrix J is given by:

$$|J - I\lambda_*| = 0$$

Thus the eigenvalues of Jacobian matrix (3.34) are $-(a+d)$, $-(j+d)$, $-(h+d)$ and the remaining eigenvalues can be obtained as follows:

$$\Longrightarrow \begin{vmatrix} -(c+\lambda_*) & 0 & 0 & d \\ e & -(c+\lambda_*) & 0 & 0 \\ 0 & k & -(l+\lambda_*) & 0 \\ 0 & 0 & m & -(n+\lambda_*) \end{vmatrix} = 0 \tag{3.35}$$

$$\Longrightarrow (c+\lambda_*)(n+\lambda_*)(f+\lambda_*)(l+\lambda_*) - dmek = 0 \tag{3.36}$$

To simplify the equation (3.36), let $A_1 = n, A_2 = l, A_3 = f, A_4 = c$ and $Q = dmek$ This implies

$$(\lambda_* + A_1)(\lambda_* + A_2)(\lambda_* + A_3)(\lambda_* + A_4) - Q = 0 \tag{3.37}$$

$$\Longrightarrow \lambda_*^4 + \lambda_*^3 B_1 + \lambda_*^2 B_2 + \lambda_* B_3 + B_4 = 0 \tag{3.38}$$

where,

$$B_1 = A_4 + A_3 + A_2 + A_1$$

$$B_2 = A_4(A_3 + A_2 + A_1) + A_3(A_2 + A_1) + A_2 A_1$$

$$B_3 = A_4 A_3 A_2 + A_4 A_3 A_1 + A_3 A_2 A_1$$

$$B_4 = A_4 A_3 A_2 A_1 - Q$$

Therefore R_0 in equation (3.27) can be written in terms of A_i where $i = 1, 2, 3, \ldots, n$ as

$$R_0^2 = \frac{e^{-\lambda\tau}\theta(1-x)e^{-\lambda\tau}S_m)(\rho e^{-\lambda\tau}(1-x)e^{-\lambda\tau}S_h)}{N_m N_h A_3 A_2 A_1^2} \tag{3.39}$$

Using the Routh-Hurwitz criteria on equation (3.38) we can show that all roots have negative real parts. Rourth –Hurwitz criteria (Flores, 2011) gives necessary and

sufficient conditions for all the roots of characteristic polynomial and lies on the left half of the complex plane.

Theorem 3.3: Routh-Hurwitz criteria

Given the polynomial

$$P(\lambda_*) = \lambda_*^n + \lambda_*^{n-1} B_1 + \cdots + + \lambda_* B_{n-1} + \lambda_* B_n$$

where the coefficients B_i are real constants $i = 1, \ldots, n$, define the n Hurwitz matrices using the coefficients B_i of the characteristic polynomial where $\boldsymbol{H_1}$=(B_1),

$$\boldsymbol{H_2} = \begin{bmatrix} B_1 & 1 \\ B_3 & B_2 \end{bmatrix}, \boldsymbol{H_3} = \begin{bmatrix} B_1 & 1 & 0 \\ B_3 & B_2 & B_1 \\ B_5 & B_4 & B_3 \end{bmatrix},$$

,

$$\boldsymbol{H_n} = \begin{bmatrix} B_1 & 1 & 0 & 0 & 0 & \ldots & 0 \\ B_3 & B_2 & B_1 & 1 & 0 & \ldots & 0 \\ B_5 & B_4 & B_3 & B_2 & B_1 & \ldots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ldots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ldots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ldots & 0 \\ 0 & 0 & 0 & 0 & 0 & \ldots & B_n \end{bmatrix}$$

where $B_j = 0$ if $j > n$, all the roots of the polynomial $P(\lambda_*)$ are negative if and only if the determinants of Hurwitz matrices are positive. That is, $det(H_j) > 0, j = 1, \ldots, n$.

For the equation (3.38), when $n = 4$, the Routhz-Hurwitz criteria are $B_1 > 0, B_2 >$

$0, B_3 > 0, B_4 > 0$ and the determinants of Hurwitz matrices are:

$$det(\boldsymbol{H_1}) = B_1 > 0$$

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

$$det(\boldsymbol{H_3}) = \begin{bmatrix} B_1 & 1 & 0 \\ B_3 & B_2 & B_1 \\ 0 & 0 & B_3 \end{bmatrix} = 0, B_1 B_2 B_3 - B_3^2 > 0$$

$$det(\boldsymbol{H_4}) = \begin{bmatrix} B_1 & 1 & 0 & 0 \\ B_3 & B_2 & B_1 & 1 \\ 0 & B_4 & B_3 & B_2 \\ 0 & 0 & 0 & B_4 \end{bmatrix} = 0, B_1(B_2 B_1 - B_3) - B_4 B_1^2 > 0$$

Clearly, from Hurwitz matrices all the determinants are positive, which means that all the eigenvalues of the Jacobian matrix have negative real part and therefore disease free equilibrium point is stable and $R_0 < 1$.

$$\left.\begin{array}{c} R_0 = \sqrt{\frac{\omega e^{-\lambda\tau}\theta(1-x)e^{-\lambda\tau}S_m}{N_m\left\{\left[\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)\right](\alpha_m+\beta_m+Kx+Ly)\right\}}} \times \\ \sqrt{\frac{\rho e^{-\lambda\tau}(1-x)e^{-\lambda\tau}S_h}{N_h\left[(\alpha_h\beta_h)+\sigma(1-z)e^{-\lambda\tau}\right]}} < 1 \end{array}\right\} \tag{3.40}$$

3.9 Endemic Equilibrium Point

To establish the endemic equilibrium point (EEP) of the model we equate the system of equations (3.2) to zero. That is;

$$\left.\begin{array}{c}
\Lambda_h + \mu R_h - \alpha_h S_h - \frac{(\gamma S_h I_m(t-\tau)(1-x))}{N_h} = 0 \\
\frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} - \rho E_h(t-\tau) - \alpha_h E_h(t-\tau) = 0 \\
\rho E_h(t-\tau) - (\alpha_h + \beta_h) I_h - \sigma(1-z) I_h(t-\tau) = 0 \\
\sigma(1-z) I_h(t-\tau) - \alpha_h R_h - \mu R_h = 0 \\
-\frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} + \Lambda_m - (\alpha_m + \beta_m + Kx + Ly) S_m = 0 \\
\frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} - \omega E_m(t-\tau) - (\alpha_m + \beta_m + Kx + Ly) E_m = 0 \\
\omega E_m(t-\tau) - (\alpha_m + \beta_m + Kx + Ly) I_m = 0
\end{array}\right\} \tag{3.41}$$

From 7th equation of system of equations (3.41) we have,

$$I_m^* = 0 = \frac{\omega E_m^*(t-\tau)}{(\alpha_m + \beta_m + Kx + Ly)} \tag{3.42}$$

From 6th equation of system of equations (3.41) we have,

$$E_m^* = \frac{\theta S_m^* I_h^* e^{-\lambda\tau}(1-x)}{N_m(\omega e^{-\lambda\tau} + (\alpha_m + \beta_m + Kx + Ly)))} \tag{3.43}$$

Substituting (3.43) into (3.42) we have

$$I_m^* = \frac{\omega e^{-\lambda\tau}}{(\alpha_m + \beta_m + Kx + Ly)} \frac{\theta S_m^* I_h^* e^{-\lambda\tau}(1-x)}{N_m(\omega e^{-\lambda\tau} + (\alpha_m + \beta_m + Kx + Ly)))} \tag{3.44}$$

From 5th equation of system of equations (3.41) we have,

$$S_m^* = \frac{N_m \Lambda_m}{N_m \left[(\alpha_m + \beta_m + Kx + Ly) + \theta I_h e^{-\lambda\tau}(1-x)\right]} \tag{3.45}$$

Substituting (3.45) into (3.44) we have

$$I_m^* = \left(\frac{\omega e^{-\lambda\tau}}{(\alpha_m+\beta_m+Kx+Ly)}\right)\left(\frac{\theta I_h^* e^{-\lambda\tau}(1-x)}{N_m(\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly))}\right) \left(\frac{N_m\Lambda_m}{N_m\left[(\alpha_m+\beta_m+Kx+Ly)+\theta I_h^* e^{-\lambda\tau}(1-x)\right]}\right) \tag{3.46}$$

Substituting (3.46) into the 2nd equation of the system of equations (3.41), we have

$$\left(\frac{\gamma S_h e^{-\lambda\tau}(1-x)}{N_h(\theta I_h^* e^{-\lambda\tau}(1-x))}\right)\left(\frac{R_{0m}(\alpha_m+\beta_m+Kx+Ly)I_h^*}{N_m(\alpha_m+\beta_m+Kx+Ly)+\theta I_h^* e(1-x)}\right) - (\rho+\alpha_h)E_h(t-\tau) = 0 \tag{3.47}$$

From the 3rd equation of the system of equations (3.41) we have,

$$E_h^* = \frac{(\alpha_h+\beta_h)I_h^* + \sigma(1-z)I_h^*(t-\tau)}{\rho} \tag{3.48}$$

Substituting (3.48) into (3.47) we have

$$\left(\frac{\gamma S_h e^{-\lambda\tau}(1-x)}{N_h(\theta I_h^* e^{-\lambda\tau}(1-x))}\right)\left(\frac{R_{0m}(\alpha_m+\beta_m+Kx+Ly)I_h^*}{N_m(\alpha_m+\beta_m+Kx+Ly)+\theta I_h^* e(1-x)}\right) - (\rho+\alpha_h)\frac{(\alpha_h+\beta_h)I_h^*+\sigma(1-z)I_h^*(t-\tau)}{\rho} = 0$$

$$\frac{\gamma S_h e^{-\lambda\tau}(1-x)R_{0m}(\alpha_m+\beta_m+Kx+Ly)I_h^*}{N_h(\alpha_h+\beta_h)e^{-\lambda\tau}} - (\theta I_h^* e^{-\lambda\tau}(1-x) + N_m(\alpha_m+\beta_m+Kx+Ly)) = 0$$

$$N_h \leq \frac{\Lambda_h}{\alpha_h}$$

$$R_{0h}R_{0m}(\alpha_m+\beta_m+Kx+Ly)S_h^*e^{-\lambda\tau}$$

$$-(\theta I_h^*e^{-\lambda\tau}(1-x)+N_m(\alpha_m+\beta_m+Kx+Ly))=0$$

$$\implies S_h^*=\frac{\alpha_h(\theta I_h^*e^{-\lambda\tau}(1-x)+(\alpha_m+\beta_m+Kx+Ly))\Lambda_h}{R_0^2(\alpha_m+\beta_m+Kx+Ly)\alpha_h} \tag{3.49}$$

From the 4th equation of the system of equations (3.41) we have,

$$R_h^*=\frac{\sigma(1-z)I_h^*(t-\tau)}{(\alpha_h+\mu)} \tag{3.50}$$

To solve I_h^*, we substitute (3.49) and (3.50), in the 1st equation of the system of equations (3.41). That is;

$$\begin{aligned}\Lambda_h+\mu\left(\tfrac{\sigma(1-z)I_h^*(t-\tau)}{(\alpha+\mu)}\right)-\alpha_h\left(\tfrac{\alpha_h(\theta I_h^*e^{-\lambda\tau}(1-x)+(\alpha_m+\beta_m+Kx+Ly))\Lambda_h}{R_0^2(\alpha_m+\beta_m+Kx+Ly)\alpha_h}\right)\\-\left(\tfrac{\gamma I_m(t-\tau)(1-x)}{N_h}\right)\left(\tfrac{\alpha_h(\theta I_h^*e^{-\lambda\tau}(1-x)+(\alpha_m+\beta_m+Kx+Ly))\Lambda_h}{R_0^2(\alpha_m+\beta_m+Kx+Ly)\alpha_h}\right)=0\end{aligned} \tag{3.51}$$

We get

$$M(I_h^*)^2+N(I_h^*)+C=0 \tag{3.52}$$

Where

$$M=R_0^2T(\alpha_m+\beta_m+Kx+Ly)\mu\sigma(1-z)I_h^*\theta e^{-\lambda\tau}-\theta^2\sigma(1-z)I_h^*(\tau)(\alpha_h+\mu)(T+P)$$

$$N=R_0^2\alpha_h(\alpha_m+\beta_m+Kx+Ly)^2N_h^2\alpha_h\sigma(1-z)I_h^*\theta e^{-\lambda\tau}$$

$$-(\alpha_m+\beta_m+Kx+Ly)(\gamma e^{-\lambda\tau}(1-x)(\alpha_h+\mu)T(\Lambda_hR_0^2-\Lambda_h-\alpha_hN_h)-P\Lambda_h)$$

$$Q=\alpha_h(\alpha_m+\beta_m+Kx+Ly)^2N_h^2\Lambda_h(\alpha_h+\mu)(R_0^2-1)$$

where,

$$T = N_h \alpha_h \gamma e^{-\lambda\tau}(1-x)$$

$$P = (\alpha_m + \beta_m + Kx + Ly) R_{0m} \gamma e^{-\lambda\tau}(1-x)$$

Using the quadratic formula

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

$$\implies I_h^* = \frac{\sqrt{B^2} - 4AC - B}{2A} = \psi, I_h^* \geq 0 \tag{3.53}$$

Using equations (3.49), (3.48),(3.53), (3.50), (3.45), (3.43) and (3.46), we have respectively;

$$S_h^* = \frac{\alpha_h(\psi\theta e^{-\lambda\tau}(1-x) + (\alpha_m + \beta_m + Kx + Ly))\Lambda_h}{R_0^2(\alpha_m + \beta_m + Kx + Ly)\alpha_h} \tag{3.54}$$

$$E_h^* = \frac{(\alpha_h + \beta_h)\psi + \sigma(1-z)I_h^*(t-\tau)}{\rho} \tag{3.55}$$

$$I_h^* = \psi \tag{3.56}$$

$$R_h^* = \frac{\sigma(1-z)e^{-\lambda\tau}\psi}{(\alpha + \mu)} \tag{3.57}$$

$$S_m^* = \frac{N_m \Lambda_m}{N_m\left[(\alpha_m + \beta_m + Kx + Ly) + \theta\psi e^{-\lambda\tau}(1-x)\right]} \tag{3.58}$$

$$E_m^* = \frac{\theta\psi S_m^* e^{-\lambda\tau}(1-x)}{N_m(\omega e^{-\lambda\tau} + (\alpha_m + \beta_m + Kx + Ly)))} \tag{3.59}$$

$$I_m^* = \left(\frac{\omega e^{-\lambda\tau}}{(\alpha_m+\beta_m+Kx+Ly)}\right)\left(\frac{\theta\psi e^{-\lambda\tau}(1-x)}{N_m(\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly))}\right) \left(\frac{N_m\Lambda_m}{N_m\left[(\alpha_m+\beta_m+Kx+Ly)+\theta\psi e^{-\lambda\tau}(1-x)\right]}\right) \tag{3.60}$$

3.10 Stability of Endemic Equilibrium Point

The asymptotic stability of the system of equations (3.2) islocally asymptotically stable established by examining the signs of the eigenvalues obtained at Endemic Equilibrium

Point (EEP) from the Jacobian matrix. If all the eigenvalues of linearization matrix about EEP are negative, then the system of equation (3.2) is locally asymptotically stable.

For stability analysis the equilibrium points of system of equations (3.2) are centered at EEP $E(S_h^*, E_h^*, R_h^*, S_m^*, E_m^*, I_m^*)$ by introducing new variables:

$$\begin{gathered} A_1 = S_h - S_h^*, A_2 = E_h - E_(h)^*, A_3 = I_h - I_(h)^*, \\ A_4 = R_h - R_h^*, A_5 = S_m - S_m^*, A_6 = E_m - E_m^*, A_7 = I_m - I_m^* \end{gathered} \tag{3.61}$$

Therefore

$$\begin{gathered} S_h^e = m_1 + S_h, E_h^e = m_2 + E_h, I_h^e = m_3 + I_h, R_h^e = m_4 + R_h, \\ S_m^e = m_5 + S_m, E_m^e = m_6 + E_m, I_m^e = m_7 + I_m \end{gathered} \tag{3.62}$$

We then rewrite the model equation (3.2) in terms of the new variables to get

$$\left.\begin{gathered} (\dot{S}_h^e) = \Lambda_h + \mu R_h - \alpha_h(m_1 + S_h) - \frac{(\gamma S_h I_m(t-\tau)(1-x))}{N_h} \\ (\dot{E}_h^e) = \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} - \rho(m_2 + E_h)(t-\tau) - \alpha_h(m_2 + E_h)(t-\tau) \\ (\dot{I}_h^e) = \rho E_h(t-\tau) - (\alpha_h + \beta_h)(m_3 + I_h) - \sigma(1-z)(m_3 + I_h)(t-\tau) \\ (\dot{R}_h^e) = \sigma(1-z) I_h(t-\tau) - \alpha_h(m_4 + R_h) - \mu(m_4 + R_h) \\ (\dot{S}_m^e) = -\frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} + \Lambda_m - (\alpha_m + \beta_m + Kx + Ly)(m_5 + S_m) \\ (\dot{E}_m^e) = \frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} - \omega(m_6 + E_m)(t-\tau) - (\alpha_m + \beta_m + Kx + Ly)(m_6 + E_m) \\ (\dot{I}_m^e) = \omega E_m(t-\tau) - (\alpha_m + \beta_m + Kx + Ly)(m_7 + I_m) \end{gathered}\right\} \tag{3.63}$$

Differentiating the system of equations (3.63) partially with respect to state variables

we obtain the Jacobian matrix below:

$$J = \begin{bmatrix} p & 0 & 0 & \mu & 0 & 0 & b \\ a & -c & 0 & 0 & 0 & & b \\ 0 & e & -f & 0 & 0 & 0 & 0 \\ 0 & 0 & g & -h & 0 & 0 & 0 \\ 0 & 0 & -d & 0 & -r & 0 & 0 \\ 0 & 0 & d & 0 & j & -l & 0 \\ 0 & 0 & 0 & 0 & 0 & m & -n \end{bmatrix} \tag{3.64}$$

where

$$a = \frac{\gamma I_m^e (t-\tau)(1-x)}{N_h}$$

$$b = -\frac{\gamma S_h^e (1-x) e^{-\lambda\tau}}{N_h}$$

$$c = -(\rho + \alpha_h) e^{-\lambda\tau}$$

$$d = \frac{\theta S_m^e (1-x) e^{-\lambda\tau}}{N_m}$$

$$e = \rho e^{-\lambda\tau}$$

$$f = -(\alpha_h + \beta_h) - \sigma(1-z)e^{-\lambda\tau}$$

$$g = \sigma(1-z)e^{-\lambda\tau}$$

$$h = \alpha_h - \mu$$

$$j = \frac{\theta I_h^*(1-x)e^{-\lambda\tau}}{N_m}$$

$$k = \frac{\theta S_m(1-x)e^{-\lambda\tau}}{N_m}$$

$$l = -\omega e^{-\lambda\tau} - (\alpha_m + \beta_m + Kx + Ly)$$

$$r = -\frac{\theta I_h^*(1-x)e^{-\lambda\tau}}{N_m} - n$$

$$m = \omega e^{-\lambda\tau}$$

$$n = -(\alpha_m + \beta_m + Kx + Ly)$$

$$p = -\alpha_h - \frac{\gamma}{N_h}$$

The system of equations (3.63) will be stable if all the eigenvalues of linearization matrix are negative. The characteristic equation of the Jacobian matrix J is given by:

$$|J - I\lambda_*| = 0$$

where I is a 7×7 identity matrix.

$$[J - I\lambda_*] = \begin{bmatrix} p-\lambda_* & 0 & 0 & \mu & 0 & 0 & b \\ a & -c-\lambda_* & 0 & 0 & 0 & & b \\ 0 & e & -f-\lambda_* & 0 & 0 & 0 & 0 \\ 0 & 0 & g & -h-\lambda_* & 0 & 0 & 0 \\ 0 & 0 & -d & 0 & -r-\lambda_* & 0 & 0 \\ 0 & 0 & d & 0 & j & -l-\lambda_* & 0 \\ 0 & 0 & 0 & 0 & 0 & m & -n-\lambda_* \end{bmatrix} = 0 \tag{3.65}$$

$$\Longrightarrow \begin{vmatrix} -(c+\lambda_*) & 0 & 0 & b \\ e & -(r+\lambda_*) & 0 & 0 \\ c & j & -(l+\lambda_*) & 0 \\ 0 & 0 & m & -(n+\lambda_*) \end{vmatrix} = 0 \tag{3.66}$$

Clearly, $\lambda_{*1} < 0$. Since c, r, l and n are negative we have;

$$(c+\lambda_*)(r+\lambda_*)(l+\lambda_*)(n+\lambda_*) - bmej = 0 \tag{3.67}$$

This implies

$$(\lambda_* + A_1)(\lambda_* + A_2)(\lambda_* + A_3)(\lambda_* + A_4) - Q = 0 \tag{3.68}$$

Where $Q = bmej$ by expanding we get,

$$\lambda_*^4 + \lambda_*^3 B_1 + \lambda_*^2 B_2 + \lambda_* B_3 + B_4 = 0 \tag{3.69}$$

where,

$$B_1 = A_4 + A_3 + A_2 + A_1$$

$$B_2 = A_4(A_3 + A_2 + A_1) + A_3(A_2 + A_1) + A_2A_1$$

$$B_3 = A_4A_3A_2 + A_4A_3A_1 + A_3A_2A_1$$

$$B_4 = A_4A_3A_2A_1 - Q$$

Therefore R_0 in equation (3.27) can be written in terms of A_i where $i = 1, 2, 3, \ldots, n$ as

$$R_0^2 = \frac{(\omega e^{-\lambda\tau}\theta(1-x)e^{-\lambda\tau}S_m)(\rho e^{-\lambda\tau}(1-x)e^{-\lambda\tau}S_h)}{N_m N_h A_3 A_2 A_1^2} \tag{3.70}$$

Using the Routh-Hurwitz criteria on equation (3.38) we can show that all roots have negative real parts. Rourth –Hurwitz criteria (Flores, 2011) gives necessary and sufficient conditions for all the roots of characteristic polynomial and lies on the left half of the complex plane.

Theorem 3.3: Routh-Hurwitz criteria

Given the polynomial

$$P(\lambda_*) = \lambda_*^n + \lambda_*^{n-1}B_1 + \cdots + +\lambda_* B_{n-1} + \lambda_* B_n$$

where the coefficients B_i are real constants $i = 1, \ldots, n$, define the n Hurwitz matrices using the coefficients B_i of the characteristic polynomial where $\boldsymbol{H_1}$=(B_1),

$$\boldsymbol{H_2} = \begin{bmatrix} B_1 & 1 \\ B_3 & B_2 \end{bmatrix}, \boldsymbol{H_3} = \begin{bmatrix} B_1 & 1 & 0 \\ B_3 & B_2 & B_1 \\ B_5 & B_4 & B_3 \end{bmatrix},$$

,

$$\boldsymbol{H_n} = \begin{bmatrix} B_1 & 1 & 0 & 0 & 0 & \ldots & 0 \\ B_3 & B_2 & B_1 & 1 & 0 & \ldots & 0 \\ B_5 & B_4 & B_3 & B_2 & B_1 & \ldots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ldots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ldots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ldots & 0 \\ 0 & 0 & 0 & 0 & 0 & \ldots & B_n \end{bmatrix}$$

where $B_j = 0$ if $j > n$, all the roots of the polynomial $P(\lambda_*)$ are negative if and only if

the determinants of Hurwitz matrices are positive. That is, $det(H_j) > 0, j = 1, \ldots, n$.

For the equation (3.38), when $n = 4$, the Routhz-Hurwitz criteria are $B_1 > 0, B_2 > 0, B_3 > 0, B_4 > 0$ and the determinants of Hurwitz matrices are:

$$det(\boldsymbol{H_1}) = B_1 > 0$$

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

$$det(\boldsymbol{H_3}) = \begin{bmatrix} B_1 & 1 & 0 \\ B_3 & B_2 & B_1 \\ 0 & 0 & B_3 \end{bmatrix} = 0, B_1 B_2 B_3 - B_3^2 > 0$$

$$det(\boldsymbol{H_4}) = \begin{bmatrix} B_1 & 1 & 0 & 0 \\ B_3 & B_2 & B_1 & 1 \\ 0 & B_4 & B_3 & B_2 \\ 0 & 0 & 0 & B_4 \end{bmatrix} = 0, B_1(B_2 B_1 - B_3) - B_4 B_1^2 > 0$$

Clearly, from Hurwitz matrices all the determinants are positive, which means that all the eigenvalues of the Jacobian matrix have negative real part and therefore disease free equilibrium point is stable and $R_0 < 1$.

3.11 Sensitivity Analysis of Basic Reproduction Number R_0

There are a number of factors responsible for disease transmission and prevalence. Therefore we need to calculate the sensitivity indices of the reproductive number with

respect to model parameters. By analysis of these indices we could determine which parameter is more crucial for disease transmission and prevalence.

$$R_0 = \sqrt{\frac{\omega e^{-\lambda\tau}\theta(1-x)e^{-\lambda\tau}S_m}{N_m\left\{[\omega e^{-\lambda\tau} + (\alpha_m + \beta_m + Kx + Ly)]\,(\alpha_m + \beta_m + Kx + Ly)\right\}}}\sqrt{\frac{\rho e^{-\lambda\tau}(1-x)e^{-\lambda\tau}S_h}{N_h\left[(\alpha_h\beta_h) + \sigma(1-z)e^{-\lambda\tau}\right]}}$$

where, $\frac{\omega e^{-2\lambda\tau}}{\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)}$ is the probability that a mosquito will survive the exposed state to become infectious and $\frac{\rho e^{-\lambda\tau}}{(\alpha_h+\beta_h)+\sigma(1-z)e^{-\lambda\tau}}$ is the probability that a human will survive the exposed state to become infectious

Therefore differentiating partially with respect to the reproduction number R_0 we have.

$$\frac{\partial R_0}{\partial \tau} = \frac{\omega^2\lambda e^{-3\lambda\tau}+2\omega e^{-2\lambda\tau}(\alpha_m+\beta_m+Kx+Ly)}{\left[\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)\right]^2}$$

$$\frac{\partial R_0}{\partial \alpha_m} = \frac{\omega e^{-2\lambda\tau}}{\left[\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)\right]^2}$$

$$\frac{\partial R_0}{\partial \beta_m} = \frac{\omega e^{-2\lambda\tau}}{\left[\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)\right]^2}$$

$$\frac{\partial R_0}{\partial x} = \frac{K\omega e^{-\lambda\tau}}{\left[\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)\right]^2}$$

$$\frac{\partial R_0}{\partial y} = \frac{L\omega e^{-\lambda\tau}}{\left[\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+Kx+Ly)\right]^2}$$

$$\frac{\partial R_0}{\partial \rho} = \frac{-e^{-\lambda\tau}\left[(\alpha_h+\beta_h)+\sigma(1-z)e^{-\lambda\tau}\right]}{\left[(\alpha_h+\beta_h)+\sigma(1-z)e^{-\lambda\tau}\right]^2}$$

$$\frac{\partial R_0}{\partial \alpha_h} = \frac{\rho e^{-\lambda\tau}}{\left[(\alpha_h+\beta_h)+\sigma(1-z)e^{-\lambda\tau}\right]^2}$$

$$\frac{\partial R_0}{\partial \beta_h} = \frac{\rho e^{-\lambda\tau}}{\left[(\alpha_h+\beta_h)+\sigma(1-z)e^{-\lambda\tau}\right]^2}$$

CHAPTER FOUR

RESULTS AND DISCUSSIONS

4.1 Introduction

In this chapter, numerical simulations were carried out using MATLAB to verify the analytic results on the stability of system of equations (3.2) presented in Chapter Three. The parameter values were obtained from the literature. Analytic solutions on the previous chapters were clarified through illustrations with specific numerical examples.

4.2 Results and Discussions

Numerical simulations of the model equations were obtained using the list of parameters as shown in Table 4.1.

Table 4.1: *Parameter values of the malaria model*

Parameter	Value	Source
Λ_h	0.028 per day	Chiyaka *et al.* (2008)
Λ_m	6 per day	Estimated
ρ	1/14	Malaria.com (2011)
α_h	0.00004 per day	Hyun (2001)
α_m	0.04 per day	Chiyaka *et al.* (2008)
β_h	0.0004 per day	Prince Harvim(2014)
β_m	0.01 per day	Chiyaka *et al.* (2008)
K	1/365	Estimated
L	1/365	Estimated
γ	0.0025	Estimated
μ	0.04	Estimated
ω	1/12	Chiyaka *et al.* (2008)
θ	0.415	Estimated
σ	0.005	Estimated
λ	0.06	Estimated
x	0.5	Estimated
y	0.5	Estimated
z	0.2 per day	Estimated
τ	14	Estimated

The initial conditions used are: $S_h = 300, E_h = 200, I_h = 100, R_h = 50, S_m = 400, E_m = 300, I_m = 200$ and $t = 350$ days.

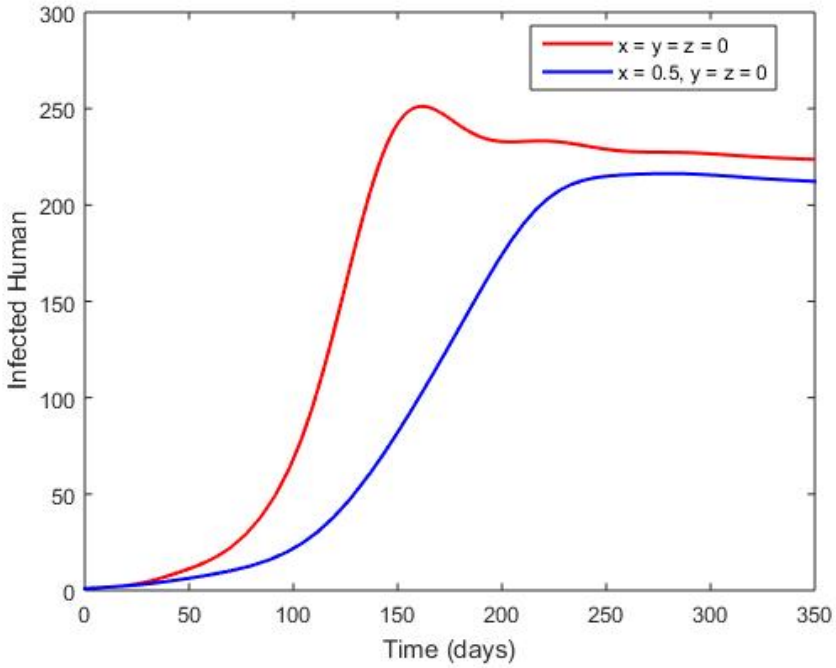

Figure 4.1: *Simulation of Long Lasting Insecticides Treated Nets (LLINS)*

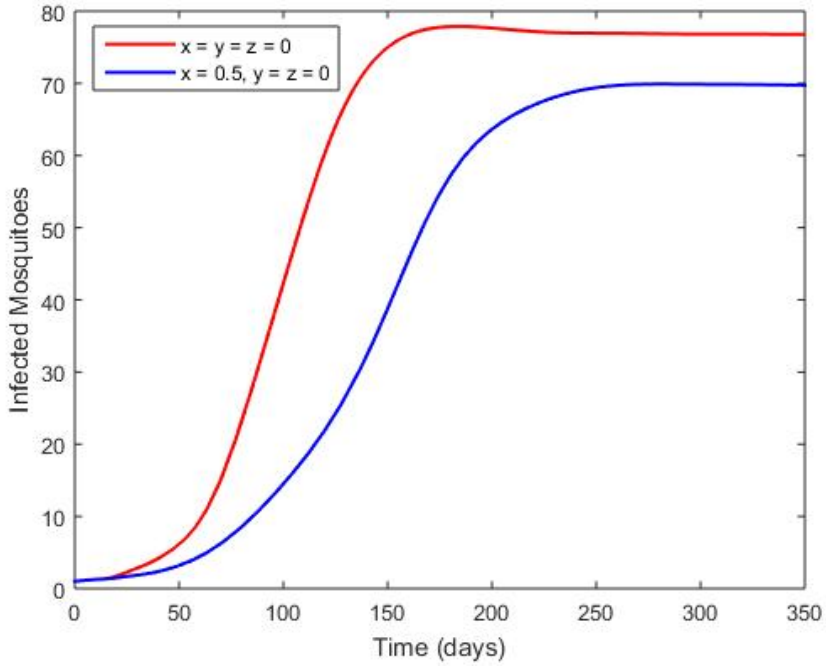

Figure 4.2: *Simulation of Long Lasting Insecticides Treated Nets (LLINS)*

Figure 4.1 and Figure 4.2 show simulations to determine the effects of Long Lasting

Insecticides Treated Nets (LLINS). It is evident that when the control strategies are not used, that is at points $x = y = z = 0$, the number of infective humans was high, and when only LLINS(x) was used the number of infective humans and mosquitoes dropped.

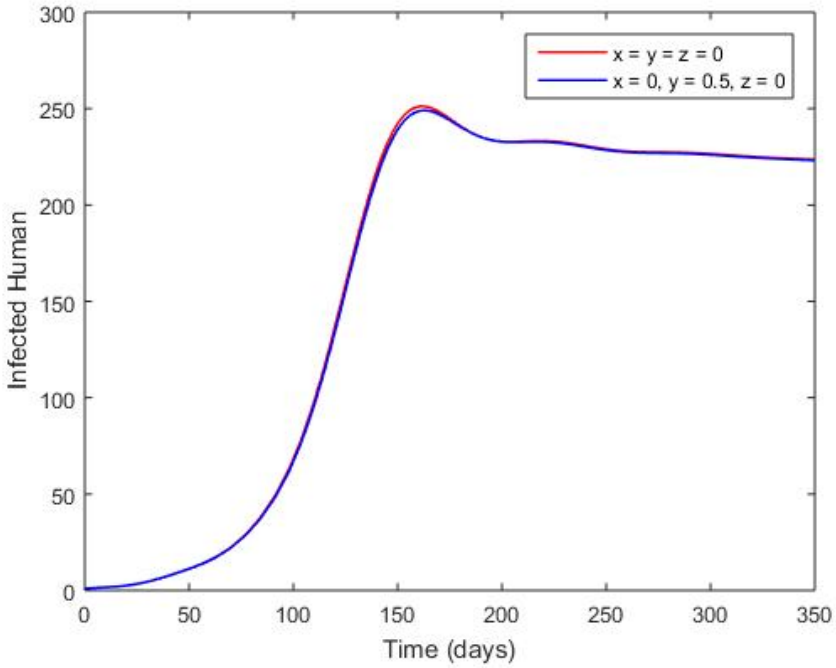

Figure 4.3: *Simulation of Indoor Residual Spraying (IRS)*

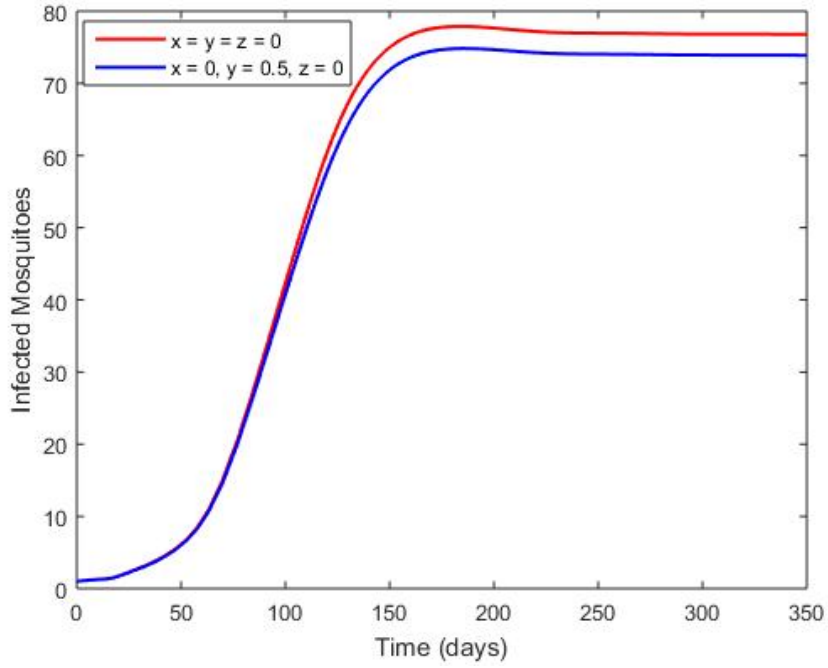

Figure 4.4: *Simulation of Indoor Residual Spraying (IRS)*

Figure 4.3 and Figure 4.4 show simulations to determine the effects of Indoor Residual Spraying (IRS). It is evident that indoor residual spraying reduced the number of mosquitoes, while it did not have any significance on the infected human population.

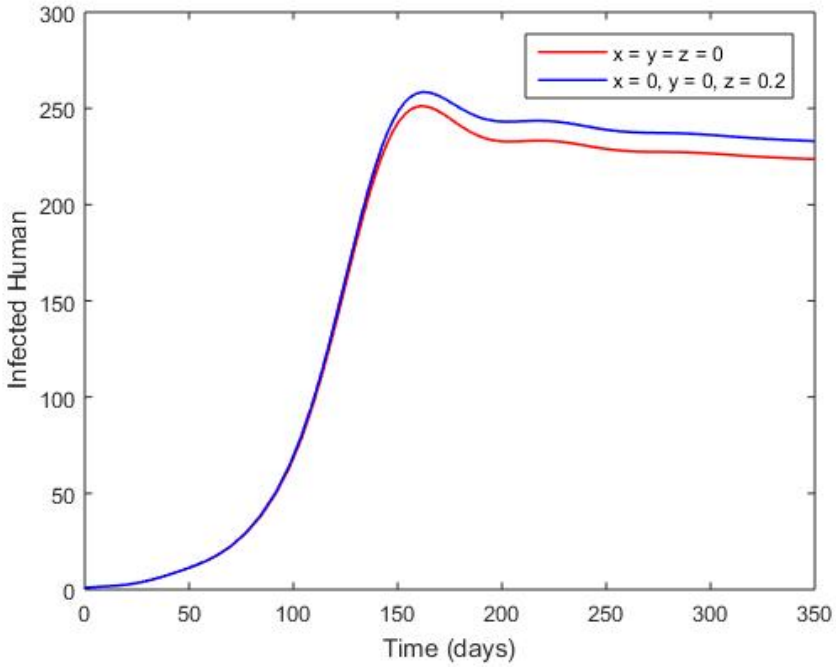

Figure 4.5: *Simulation of Treatment (with drug)*

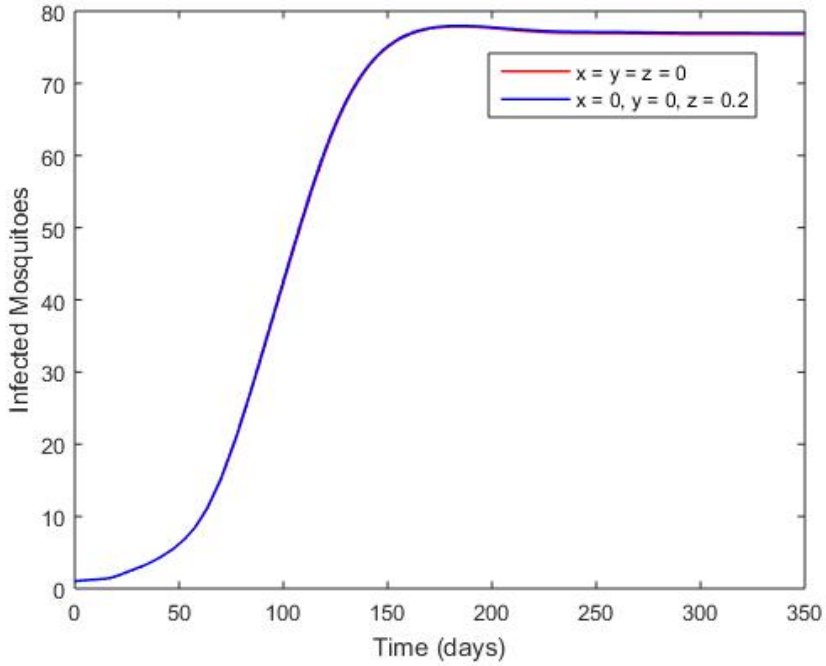

Figure 4.6: *Simulation of Treatment (with drug)*

Figure 4.5 and Figure 4.6 show simulations to determine the effects of treatment with a drug. It shows that with the use of drugs for treatment of malaria, it reduced the number of infected humans with time but does not have any effect on the infected mosquitoes.

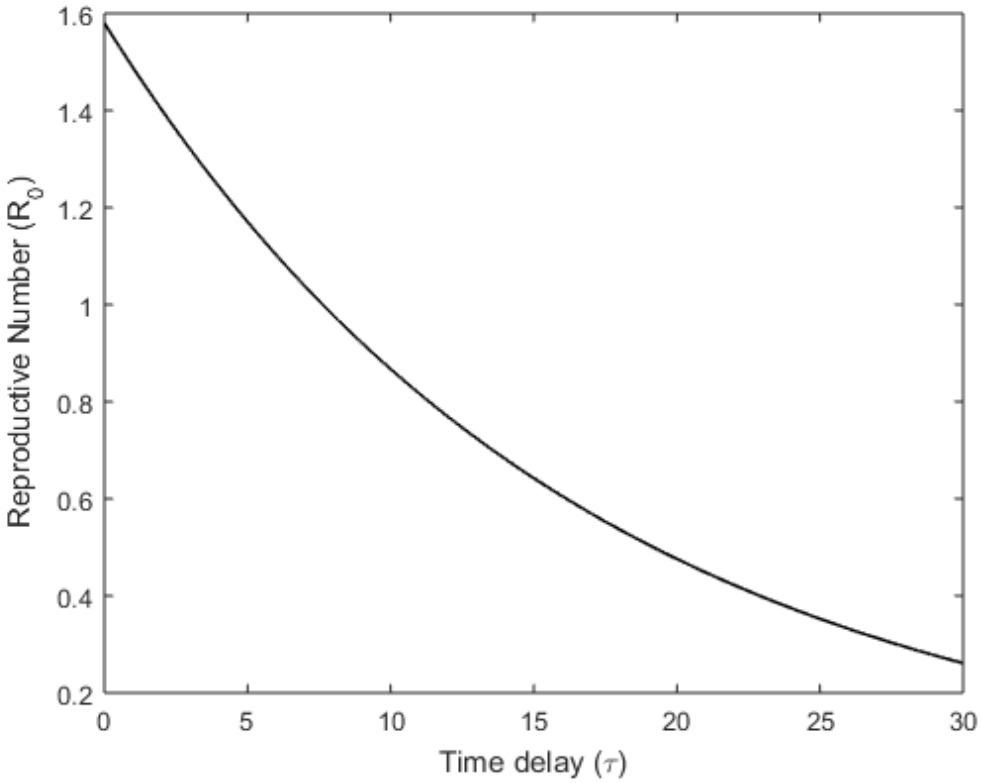

Figure 4.7: *Effects of Time delay on Basic Reproduction Number*

Figure 4.7 shows a plot of basic reproduction number against time delay. From the graph, it is evident that the longer the time delay between when mosquito bites and one becoming sick, the lower the basic reproduction number and vice versa.

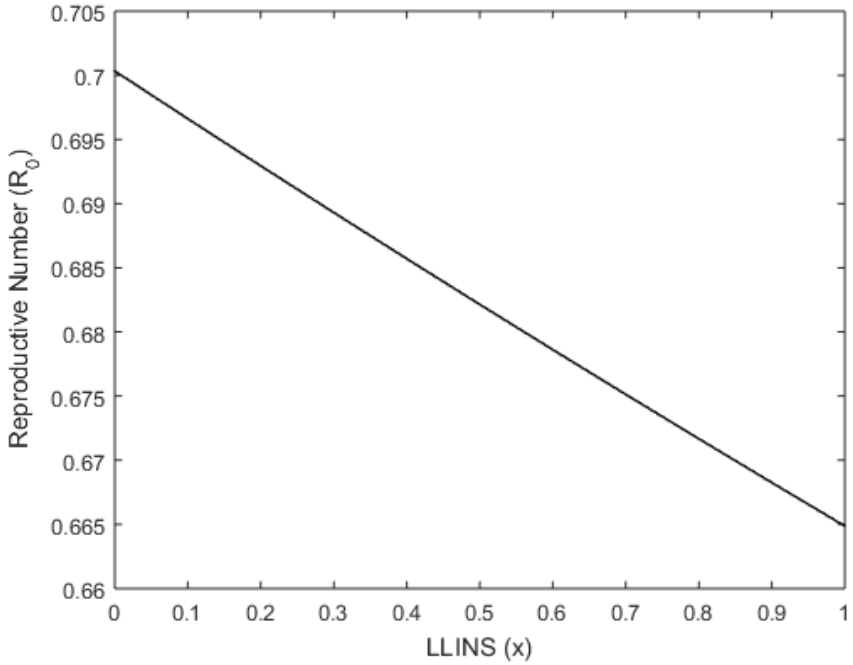

Figure 4.8: *Effects of LLINS (x) on Basic Reproduction Number*

Figure 4.8 shows a plot of basic reproduction number against LLINS (x). From the graph, it is clear that as one increase the use of control strategy (LLINS) the infectious mosquitoes are reduced and subsequently the number of infectious humans reduced and hence reproduction number also reduced.

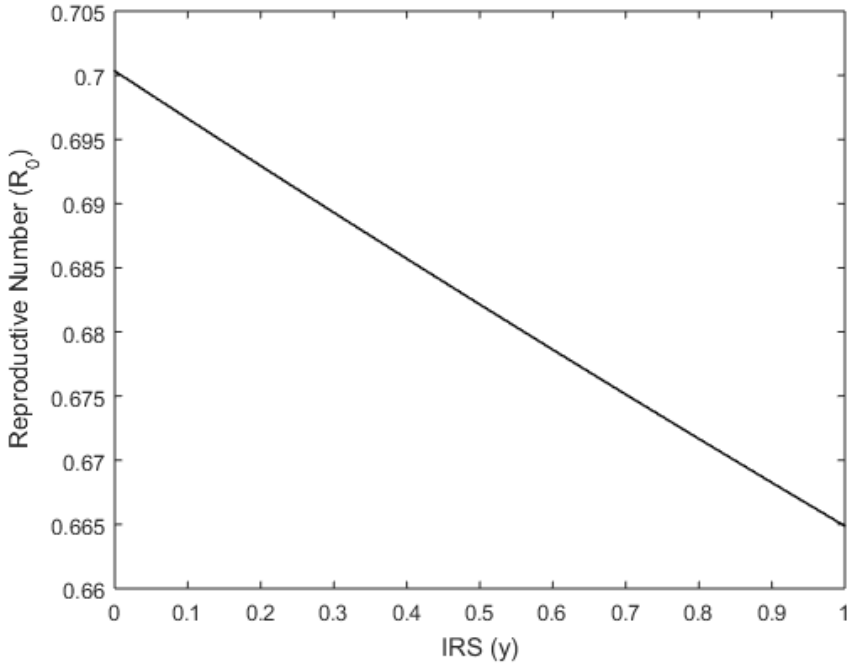

Figure 4.9: *Effects of IRS(y) on Basic Reproduction Number*

Figure 4.9 shows a plot of basic reproduction number against IRS(y) . From the graph, it is clear that as you increase the use of IRS(y) the number of mosquitoes who are infectious reduces and subsequently the reproduction number reduces significantly.

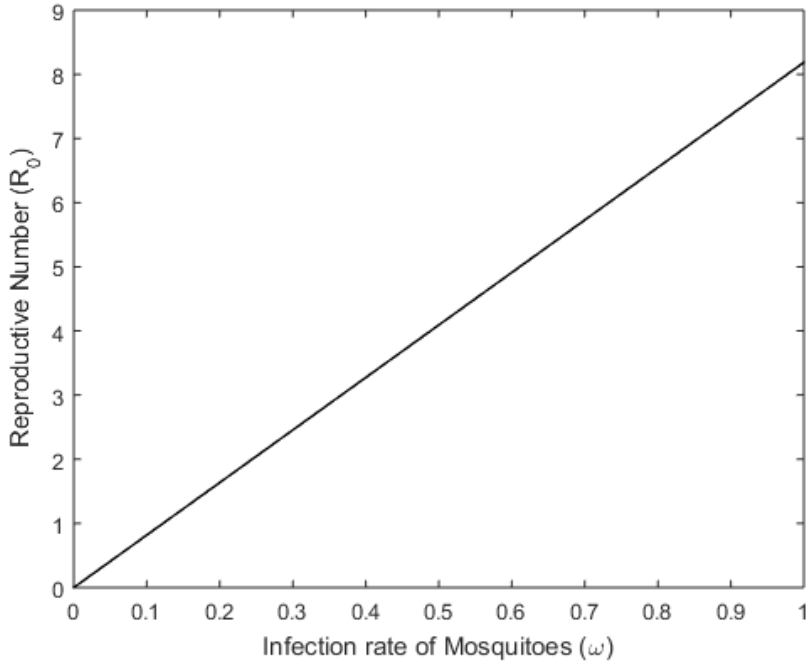

Figure 4.10: *Effects of Infection rate (ω) on Basic Reproduction Number*

Figure 4.10 shows a plot of basic reproduction number against the infection rate (ω). From the graph, it is evident that as progression rate of mosquitoes from exposed class to infectious class increases, the number of infections increases and the reproduction number also increases proportionally.

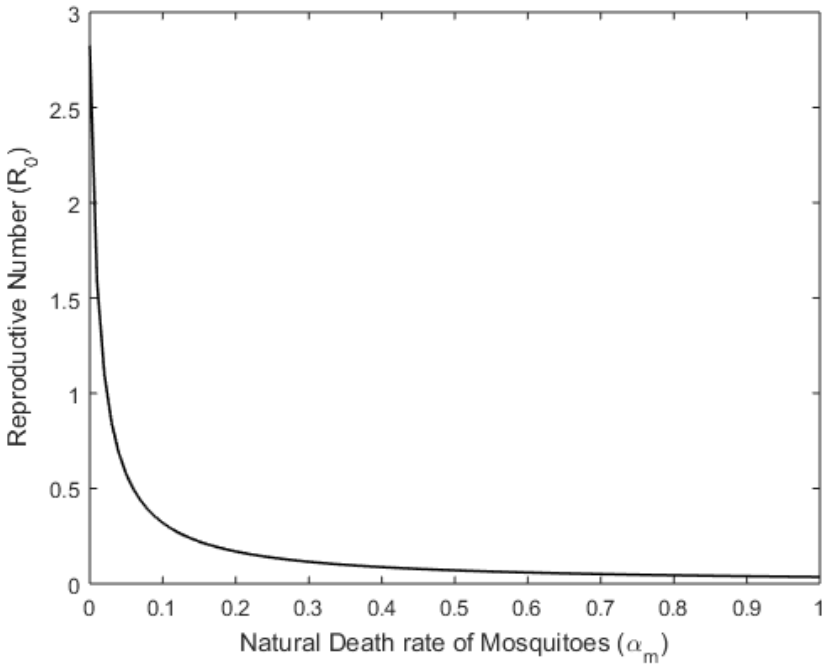

Figure 4.11: *Effects of Natural Death rate of Mosquitoes (α_m) on Basic Reproduction Number*

Figure 4.11 shows a plot of basic reproduction number against natural death rate of mosquitoes (α_m). From the graph, it is clear that as the rate of natural deaths of mosquitoes increases,mosquitoes biting rate and transmission reduces and subsequently reproduction number reduces significantly.

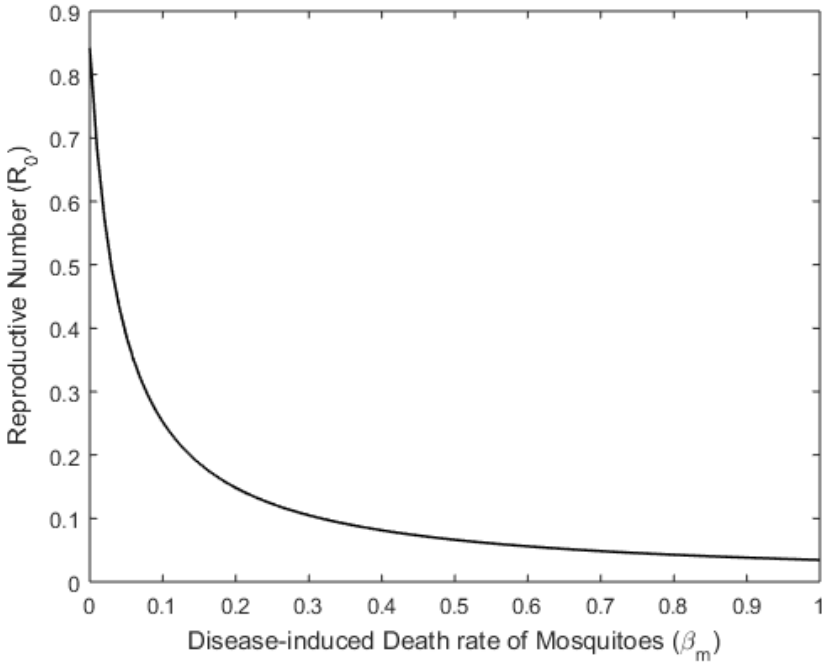

Figure 4.12: *Effects of Disease-induced Death rate of Mosquitoes (β_m) on Basic Reproduction Number*

Figure 4.12 shows a plot of basic reproduction number against disease-induced death rate of Mosquitoes (β_m). From the graph, it is evident that as the number of induced death rate of mosquitoes increases, the number of infectious mosquitoes reduces and hence infections reduces and subsequently reproduction number reduced.

CHAPTER FIVE

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

In this chapter we present summary of the findings. We also present conclusion and recommendations and suggestions for future work based on the findings

5.2 Summary

The model formulated is seven dimensional system of equations which considered four classes of transmission of human hosts and three classes of mosquitoes, SEIR and SEI respectively. We analyzed the model using delay differential equations because of the time lag between when a mosquito bites and one becoming sick. Reproduction number was derived using next generation matrix method and its stability checked by Jacobian matrix. We showed that the disease free equilibrium is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

The numerical analysis of the model shows that use of control measures like the use of insecticides treated bed nets, indoor residual spraying and use of malaria drugs for infants and expectant mothers are the most effective measures for controlling mosquito spread. Sensitivity analysis was done to find out which parameters influence the basic reproduction number the most and it was found out that time delay, mosquitoes infection rate, mosquitoes natural deaths and mosquitoes disease-induced deaths were most sensitive as seen in **Figures 4.7**, **4.10**, **4.11** and **4.12**, respectively. It was realized that control measures meant to reduce mosquitoes population and reduce human infec-

tion rate were effective for instance use of treated insecticides bed nets, indoor residual spraying and use of malaria preventive drugs.

5.3 Conclusions

Deterministic SEIR-SEI model for humans and mosquitoes was developed.The SEIR-SEI model equations were formulated from the four classes of humans and three classes of mosquitoes. Delay differential equations were used to analysed the equations.Disease free equilibrium was attained when $R_0 < 1$.Reproduction number is affected by time delay, mosquitoes infection rate, mosquitoes natural deaths and mosquitoes disease-induced deaths and are found to be most sensitive to reproduction number. Therefore control measures aimed at lowering the infective humans to mosquito vector will greatly contribute to lowering malaria transmission prevalence. All these can be achieved through prompt provision of preventive malaria drugs, use of treated bed nets and indoor residual spraying.

5.4 Recommendations

The model developed recommend that intervention measures be put in place by ministry of health for instance use of prophylaxis for infants and pregnant mothers,indoor residual spraying and long lasting treated bed nets.It is clear that with the use of intervention measures reproduction number was 0.2004 which at this point disease free equilibrium is stable and malaria transmission is low.The research can be used by public health department especially through sensitizing the public on the use of bed nets to control mosquito bites and even distributing the nets and also spraying insecticides to remove mosquito infestation which causes malaria.

5.5 Suggestions For Further Research

The model in our research has not exhausted all the strategies, like developing a malaria vaccine to check on malaria spread. Future models should consider the effects of environment on the number of infective mosquitoes.

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APPENDICES

A.1: MATLAB Codes

```
function sol = Mibei_Fig_1_8
global tau
tau = 14;
sol = dde23(@ddes,tau,[300; 1; 1; 0; 300; 1; 1],[0,350]);
figure(1)
plot(sol.x,sol.y(1,:),'k',sol.x,sol.y(2,:),'b',sol.x,sol.y(3,:),
'r',sol.x,sol.y(4,:),'g','Linewidth',1.5)
xlabel('Time (days)'); ylabel('Human Population');
title('Plot of Human population against time')
legend('Susceptible ','Exposed ','Infectious ','Recovered ')
figure(2)
plot(sol.x,sol.y(5,:),'k',sol.x,sol.y(6,:),'b',sol.x,sol.y(7,:),
'r','Linewidth',1.5)
xlabel('Time (days)'); ylabel('Mosquito Population');
title('Plot of Mosquito population against time')
legend('Susceptible ','Exposed ','Infectious')
figure(3)
plot(sol.x,sol.y(3,:),'r','Linewidth',1.5)
hold on
plot(sol.x,sol.y(3,:),'b','Linewidth',1.5)
```

```
xlabel('Time (days)'); ylabel('Infected Human');
legend('x = y = z = 0','x = 0.5, y = z = 0')
figure(4)
plot(sol.x,sol.y(7,:),'r','Linewidth',1.5)
hold on
plot(sol.x,sol.y(7,:),'b','Linewidth',1.5)
xlabel('Time (days)'); ylabel('Infected Mosquitoes');
legend('x = y = z = 0','x = 0.5, y = z = 0')
figure(5)
plot(sol.x,sol.y(3,:),'r','Linewidth',1)
hold on
plot(sol.x,sol.y(3,:),'b','Linewidth',1)
xlabel('Time (days)'); ylabel('Infected Human');
legend('x = y = z = 0','x = 0, y = 0.5, z = 0')
figure(6)
plot(sol.x,sol.y(7,:),'r','Linewidth',1.5)
hold on
plot(sol.x,sol.y(7,:),'b','Linewidth',1.5)
xlabel('Time (days)'); ylabel('Infected Mosquitoes');
legend('x = y = z = 0','x = 0, y = 0.5, z = 0')
figure(7)
plot(sol.x,sol.y(3,:),'r','Linewidth',1)
hold on
plot(sol.x,sol.y(3,:),'b','Linewidth',1)
```

```
xlabel('Time (days)'); ylabel('Infected Human');
legend('x = y = z = 0','x = 0, y = 0, z = 0.2')
figure(8)
plot(sol.x,sol.y(7,:),'r','Linewidth',1)
hold on
plot(sol.x,sol.y(7,:),'b','Linewidth',1)
xlabel('Time (days)'); ylabel('Infected Mosquitoes');
legend('x = y = z = 0','x = 0, y = 0, z = 0.2')
%================================================
function dydt = ddes(t,v,Z)
global tau
% Parameters:
Lambda_h=0.028;Lambda_m=6;alpha_h=0.00004;alpha_m=0.04;
beta_h=0.0004;beta_m=0.01;gamma=0.25;theta=0.415;rho=1/14;
omega=1/12;sigma=0.005;mu=0.04; K=1/365; L=1/365;
lambda=0.06; x=0.5;y=0.5;z=0.2;
% Variable names used in stating the DDEs:
Sh = v(1); Eh = v(2); Ih = v(3); Rh = v(4); Sm = v(5);
Em = v(6); Im = v(7);
vlag = Z(:,1); % Z(:,1) corresponds to the lag tau.
Nh = Sh + Eh + Ih + Rh; Nm = Sm + Em + Im;
dShdt = Lambda_h+mu*v(4)-alpha_h*v(1)-((gamma*v(1)*
vlag(7)*(1-x))/Nh);
dEhdt = ((gamma*v(1)*vlag(7)*(1-x))/Nh)-rho*vlag(2)-
```

```
alpha_h*vlag(2);

dIhdt = rho*vlag(2)-(alpha_h+beta_h)*v(3)-sigma*

(1-z)*vlag(3);

dRhdt = sigma*(1-z)*vlag(3)-alpha_h*v(4)-mu*v(4);

dSmdt = -((theta*vlag(3)*v(5)*(1-x))/Nm)+Lambda_m-

(alpha_m+K*x+L*y)*v(5);

dEmdt = ((theta*vlag(3)*v(5)*(1-x))/Nm)-omega*vlag(6)-

(alpha_m+K*x+L*y)*v(6);

dImdt = omega*vlag(6)-(alpha_m+beta_m+K*x+L*y)*v(7);

dydt = [dShdt; dEhdt; dIhdt; dRhdt; dSmdt; dEmdt; dImdt];

%.................................................

R0=(omega*exp(-lambda*tau))/(alpha_m+beta_m+K*x+L*y)
```

Mathematical Modelling and Applications
2020; 5(3): 167-175
http://www.sciencepublishinggroup.com/j/mma
doi: 10.11648/j.mma.20200503.15
ISSN: 2575-1786 (Print); ISSN: 2575-1794 (Online)

Modelling of Malaria Transmission Using Delay Differential Equation

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To cite this article:

Kipkirui Mibei, Kirui Wesley, Adicka Daniel. Modelling of Malaria Transmission Using Delay Differential Equation. *Mathematical Modelling and Applications*. Vol. 5, No. 3, 2020, pp. 167-175. doi: 10.11648/j.mma.20200503.15

Received: May 10, 2020; **Accepted**: July 14, 2020; **Published**: August 4, 2020

Abstract: Malaria is one of the major causes of deaths and ill health in endemic regions of sub-Saharan Africa and beyond despite efforts made to prevent and control its spread. Epidemiological models on how malaria is spread have made a substantial contribution on the understanding of disease changing aspects. Previous researchers have used Susceptible – Exposed-Infectious-Recovered (SEIR) model to explain how malaria is spread using ordinary differential equations. In this paper we develop mathematical SEIR model to define the dynamics of the spread of malaria using Delay differential equations with four control measures such as long lasting treated insecticides bed nets, intermittent preventive treatment of malaria in pregnant women (IPTP), intermittent preventive treatment of malaria in infancy (IPTI) and indoor residual spraying. The model is analyzed and reproduction number derived using next generation matrix method and its stability is checked by Jacobean matrix. Positivity of solutions and bounbedness of the model is proved. We show that the disease free equilibrium is locally asymptotically stable if $R_0<1$ (R_0 – reproduction number) and is unstable if $R_0>1$. Numerical simulation shows that, with proper treatment and control measures put in place the disease is controlled.

Keywords: Stability, Basic Reproduction Number, Delay Differential Equations

1. Introduction

Malaria is one of the most pandemic disease that remains arguably the greatest threat in our society and has remained the main cause of deaths in Africa and many regions of the world. Malaria was a major bottleneck in military camps in the United States where they initiated malaria campaigns to control the menace. In 2015 World Health organization (WHO) estimate on the cases of malaria to be 214 million resulting in 438,000 deaths, majority of these were from Africa. Sub-Saharan Africa continues to exhibit a considerably high number of epidemics of malaria which results to many deaths. Furthermore, WHO (2016) estimates that there were 216 million quantifiable cases of malaria and 445,000 people perished of whom 306,000 were children under 5 years and were mainly from Africa [1, 2].

Malaria is transmitted by Plasmodium parasite. One gets malaria by being bitten by infected female anopheles mosquito. The mosquito must have been infected from blood meal of infected persons. Blood of infected person has microscopic malarial parasite that can be passed onto a mosquito when it bites such an individual. The malarial parasite incubates for about seven days after which it becomes infectious and if a mosquito bites a new individual again the parasite from the blood meal will mix with mosquito's saliva and can be transmittable to the person being bitten. Malaria symptoms appears within 9-14 days. The most common symptoms are headache, fever and vomiting. Other ways through which malaria can be spread is by blood transfusion or sharing used needles or syringes of the blood which is contaminated. Also delivery or before delivery of the new born baby, the mother may pass over the disease to the baby. Severe malaria can lead to cerebral malaria, which is associated with unconsciousness, seizures, or other neurologic anomalies. Risks associated with malaria in expectant mothers include maternal anaemia, low weight in infants, immature delivery and increased infant and

maternal deaths [14]. The prevalence of malaria has been on the rise owing to malaria parasite developing resistance to drugs, mosquito-insecticide resistance and weak malaria intervention measures [3, 9]. This therefore warrants efficient and effective control measures on the spread of malaria through mathematical modelling. SEIR differential model for humans and SEI for mosquitoes was developed to study the dynamics of spread of malaria and incorporate Preventive measures. For instance, intermittent preventive treatment of malaria in pregnant mothers, Long- Lasting Insecticides Treated Nets (LLINS), indoor residual spraying (IRS).

2. Review of Related Literature

Jessica [7] studied malaria spread dynamics for humans and mosquito populations by considering vectorial transmission, vertical transmission of disease and a force of infection which measure the influence that occurs in the disease transmission rate which an infected human is introduced into mosquito population. The study examine a SEIR model for humans and SIR model for mosquitoes and fail to incorporate preventive and control measures to reduce malaria prevalence. In the analysis revealed the existence of three steady states, the disease free equilibrium and two endemic equilibrium and that when $R_o < 1$, then disease is controlled and when $R_o > 1$, the disease persists. In the study ordinary differential equations were used, which in this paper is addressed by introducing delay differential equations to cater for latency period that take place between when a mosquito bites and human becoming infected.

Sunita [5], Studied SEIR model for human and SI model for mosquito population. SEIR model took into account new immigrants in the population who are susceptible, exposed and infective.

Impressed by Sunita's work [5], Nisha [12] analysed the steadiness of SEIR model for malaria with infectious migrants but failed to carry out simulation and sensitivity analysis of the given model which was necessary so as to understand the effect of infective immigrants on the spread of malaria in a population. Similar studies were carried by Mojeeb [9] who used a SEIR mathematical model using ordinary differential equations with four control measures such as reducing contact rate between human and mosquito's, reducing the infection rate between humans, use of active malaria drugs and treated mosquito nets.

Ephraim [10] studied the dynamics of several species and strains of malaria. In the model analyzed four species of the malaria parasite and found out that some species of the parasite have evolved into strains that are resistant to treatment, he made assumption that there was no immunity to disease. The model found out that all species or strains persist for some time for the reproduction number greater than one, however the species or strain with the highest reproduction number eventually displace the others. In the model did not consider factors such as seasonality, age structure of humans and mosquitoes' incubation period and spatial distribution.

From the above literature malaria transmission was modelled using ordinary differential equation. In this paper we have modelled the spread of malaria using delay differential equations because of time lags between when a mosquito bites and one becoming sick. We have incorporated four control measures so as to control the spread.

2.1. The Method of Solution

In this section we formulate the model, generate the model equations, and find the reproduction number and study existence of disease free equilibrium and its stability.

2.2. The Model

In this model, the variables h and m denotes humans and mosquitoes population respectively and t is time.

The SEIRS model is used to develop human population and the sum of the entire population is given as:

$$N_h = S_h + E_h + I_h + R_h$$

Where; subscripts h-represents human population

$\mathrm{N_h} - \text{total human population}$

S_h-susceptible humans

E_h-exposed humans

I_h-infectious humans

R_h-recovered humans respectively.

Similarly, Susceptible-Exposed-Infected (SEI) model is used to develop mosquito population and the Sum total of population is given as;

$$N_m = S_m + E_m + I_m$$

Where; subscript m-represents mosquito population

$\mathrm{N_m} - \text{total mosquito population}$

S_m-susceptible mosquitoes

E_m-exposed mosquitoes

I_m-infectious mosquitoes

Some of the assumptions of our model include;

$[i]$ Mosquito will die after infection

$[ii]$ The rate at which humans and mosquito enter the population and die are respectively given by $\wedge_h$, $\wedge_m$ and α_h, α_m,

$[iii]$ The rate at which human and mosquito die from disease induced deaths are respectively given as β_h, β_m

$[iv]$ Individuals are allowed to move from susceptible human population to the exposed human population at a rate which is proportional to both size of susceptible human population and infected mosquito population and inversely proportional to total human population $\frac{\gamma S_h I_m}{N_h}$

$[v]$ Members of exposed class (E_h) move to infected human class (I_h) at a rate proportional to the number of individuals in the exposed class, ρE_h,

$[vi]$ Individuals in the infected class move to recovered class at a rate proportional to the number of individuals in the infected class, σI_h.

$[vii]$ Individuals in the recovered class move to susceptible class at a rate proportional to size of individuals in the recovered class, μR_h.

$[viii]$ For mosquito population, susceptible mosquitoes move to exposed class at a rate $\frac{\theta S_m I_h}{N_h}$

$[ix]$ Mosquitoes in the exposed class move to infectious class at the rate proportional to the size of individuals in the exposed mosquito population ωE_m

2.3. Model Formulation

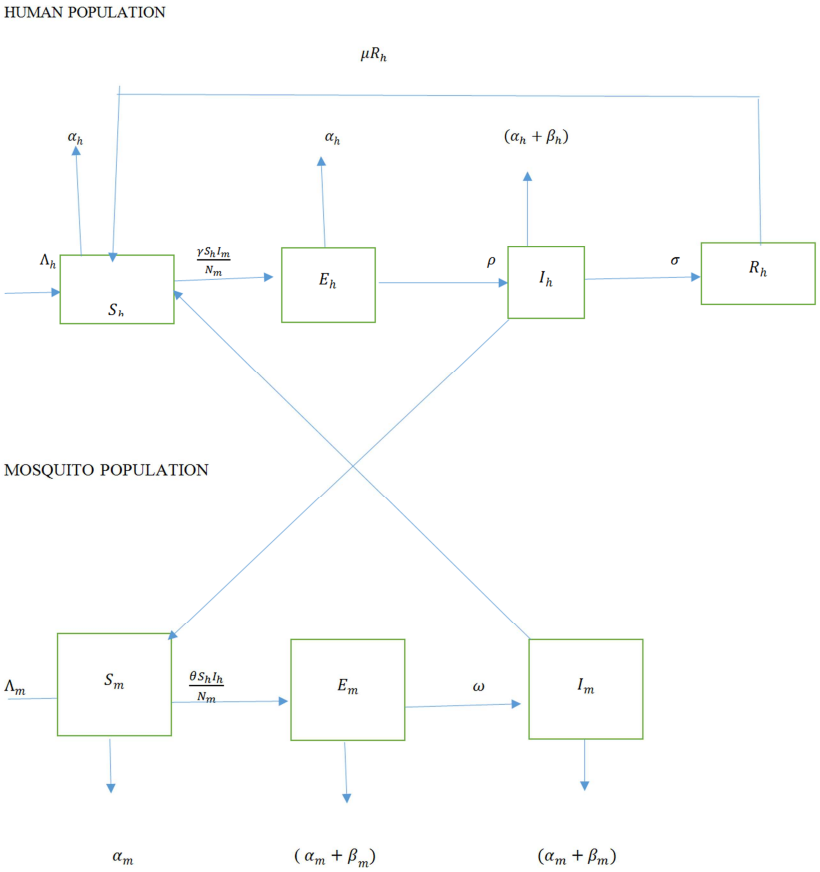


Figure 1. *Human-mosquito flow diagram.*

2.4. Model Equations

From the assumptions made, the following are equations from the model:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \mu R_h - \alpha_h S_h - \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} \\
\frac{dE_h}{dt} &= \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} - \rho E_h(t-\tau) - \alpha_h E_h(t-\tau) \\
\frac{dI_h}{dt} &= \rho E_h(t-\tau) - (\alpha_h + \beta_h) I_h - \sigma(1-z) I_h(t-\tau) \\
\frac{dR}{dt} &= \sigma(1-z) I_h(t-\tau) - \alpha_h R_h - \mu R_h \\
\frac{dS_m}{dt} &= -\frac{\theta I_h(t-\tau) S_m(1-x)}{N_h} + \Lambda_m - (\alpha_m + \beta_m + Kx + Ly) S_m \\
\frac{dE_m}{dt} &= \frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} - \omega E_m(t-\tau) - (\alpha_m + \beta_m + Kx + Ly) E_m \\
\frac{dI_m}{dt} &= \omega E_m(t-\tau) - (\alpha_m + \beta_m + Kx + Ly) I_m
\end{aligned}\right\} \quad (1)$$

2.5. Positivity of Solutions

The following theorem is used in determining positivity of our solutions.

Theorem

Let the initial data be

$$\{(S_h(0), S_m(0) \geq 0, (E_h(0), I_h(0), R_h(0), E_m(0), I_m(0)\}$$

Then the solution

$$\{S_h, E_h, I_h, R_h, S_m, E_m, I_m\}(t)$$

Of the system is non-negative for all t ≥ 0

Proof

From the system of equation (1) in the model

$$\frac{dS_h}{dt} = \Lambda_h + \mu R_h - \alpha_h S_h - \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h}$$

$$\geq -\alpha_h S_h - \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h}$$

$$\frac{dS_h}{dt} \geq -(\alpha_h + \frac{\gamma I_m(t-\tau)(1-x)}{N_h})S_h \quad (2)$$

Using separation of variables and integrating both sides

$$\int \frac{1}{S_h} dS_h \geq -\int \left(\alpha_h + \frac{\gamma I_m(t-\tau)(1-x)}{N_h}\right) dt$$

$$lnS_h \geq -(\alpha_h + \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} + c$$

$$S_h(t) = e^{-(}\alpha_h + \gamma I_m(t-\tau)(1-x)t \times e^c \quad (3)$$

Let $e^c = K$

$$S_h(t) = e^{-(}\alpha_h + \gamma I_m(t-\tau)(1-x)t \times K$$

$$S_h(t) = Ke^{-(}\alpha_h + \gamma I_m(t-\tau)(1-x)t \quad (4)$$

When $t = 0, S_h(0) \geq k$

$$S_h(t) \geq S_h(0)e^{-(}\alpha_h + \gamma I_m(t-\tau)(1-x)t \geq 0$$

From the second equation of system of equation (1)

$$\frac{dE_h}{dt} = \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} - \rho E_h(t-\tau) - \alpha_h E_h(t-\tau)$$

$$\frac{dE_h}{dt} \geq -(\rho + \alpha_h)E_h(t-\tau) \quad (5)$$

Integrating both sides we have

$$\int \frac{1}{E_h} dE_h \geq -\int -(\rho + \alpha_h)(t-\tau)dt$$

$$lnE_h \geq -(\rho(t-\tau) + \alpha_h(t-\tau)t + c$$

$$E_h(t) = e^{-(}\rho(t-\tau) + \alpha_h(t-\tau)t \times e^c \quad (6)$$

Let $e^c = K$

When $t = 0, E_h(0) \geq e^c$

$$E_h(t) \geq E_h(0)\, e^{-(}\rho(t-\tau) + \alpha_h)t \geq 0 \quad (7)$$

Similarly, it can be shown that the remaining equations of the model are positive for all $t > 0$, because $e^{\aleph} > 0$, for all $\aleph \in \mathbb{R}$.

Therefore our model has positivity of solutions.

2.6. Reproduction Number R_0

Basic reproduction number is defined as expected number of secondary cases produced by a single infection in a completely susceptible population i.e. it is a measure of how fast a disease spreads through a population [3].

R_0 Is obtained by taking the largest dominant Eigen value of FV^{-1} or spectral radius of FV^{-1}

Let $F = \frac{\partial F_i E_0}{\partial x_j}$ and $V = \frac{\partial V_i E_0}{\partial x_j}$ and $E_0 -$ Disease free equilibrium

$F_i -$ Is the rate of appearance of new infections in compartment i

$V_i^+ -$is the transfer of individuals into compartment i

$V_i^- -$is the transfer of individuals out of compartment i

$$\mathcal{V}_i = \upsilon_i^-(x) - \upsilon_i^+(x)$$

From the system of equation (1) we obtain F_i as,

$$F_i = \begin{bmatrix} \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} \\ 0 \\ \frac{\theta S_m I_h(t-\tau)(1-x)}{N_m} \\ 0 \end{bmatrix} \quad (8)$$

Taking partial derivatives of

$$\frac{\partial F_i}{\partial E_h}, \frac{\partial F_i}{\partial I_h}, \frac{\partial F_i}{\partial E_m}, \frac{\partial F_i}{\partial I_m}$$

To get

$$F = \begin{bmatrix} 0 & 0 & 0 & \frac{\gamma S_h(1-x)e^{-\lambda\tau}}{N_h} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\theta S_m(1-x)e^{-\lambda\tau}}{N_m} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \quad (9)$$

Also from system of equation (1) we obtain V_i as

$$V_i = \begin{bmatrix} (\rho - \alpha_h)E_h(t-\tau) \\ (\alpha_h + \beta_h)I_h + \sigma(1-z)I_h(t-\tau) - \rho E_h(t-\tau) \\ \omega E_m(t-\tau) + (\alpha_m + \beta_m + kx + ly)E_m \\ (\alpha_m + \beta_m + kx + ly)I_m - \omega E_m(t-\tau) \end{bmatrix} \quad (10)$$

Taking partial derivatives of

$$\frac{\partial V_i}{\partial E_h} \frac{\partial V_i}{\partial I_h} \frac{\partial V_i}{\partial E_m} \frac{\partial V_i}{\partial I_m}$$

$$V = \begin{bmatrix} (\rho - \alpha_h)e^{-\lambda\tau} & 0 & 0 & 0 \\ -\rho e^{-\lambda\tau} & (\alpha_h + \beta_h) + \sigma(1-z)e^{-\lambda\tau} & 0 & 0 \\ 0 & 0 & \omega e^{-\lambda\tau} + (\alpha_m + \beta_m + kx + ly) & 0 \\ 0 & 0 & -\omega e^{-\lambda\tau} & (\alpha_m + \beta_m + kx + ly) \end{bmatrix} \quad (11)$$

Let $A = (\rho - \alpha_h)e^{-\lambda\tau}$

$$B = -\rho e^{-\lambda\tau}$$

$$C = (\alpha_h+\beta_h) + \sigma(1-z)e^{-\lambda\tau}$$

$$D = \omega e^{-\lambda\tau} + (\alpha_m + \beta_m + kx + ly)$$

$$E = -\omega e^{-\lambda\tau}$$

$$F = (\alpha_m + \beta_m + kx + ly)$$

$$\text{Then, } V^{-1} = \begin{bmatrix} \frac{1}{A} & 0 & 0 & 0 \\ \frac{-B}{AC} & \frac{1}{C} & 0 & 0 \\ 0 & 0 & \frac{1}{D} & 0 \\ 0 & 0 & \frac{-E}{DF} & \frac{1}{F} \end{bmatrix} \quad (12)$$

And so,

$$FV^{-1} = \begin{bmatrix} 0 & 0 & -\frac{E\gamma S_h(1-x)e^{-\lambda\tau}}{N_h DF} & \frac{\gamma S_h(1-x)e^{-\lambda\tau}}{N_h F} \\ 0 & 0 & 0 & 0 \\ \frac{-B\theta S_m((1-x)e^{-\lambda\tau}}{N_m AC} & \frac{\theta S_m((1-x)e^{-\lambda\tau}}{N_m C} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \quad (13)$$

Let

$$a = -\frac{E\gamma S_h(1-x)e^{-\lambda\tau}}{N_h DF}$$

$$b = \frac{\gamma S_h(1-x)e^{-\lambda\tau}}{N_h F}$$

$$c = \frac{-B\theta S_m((1-x)e^{-\lambda\tau}}{N_m AC}$$

$$d = \frac{\theta S_m((1-x)e^{-\lambda\tau}}{N_m C}$$

Then (13) becomes,

$$FV^{-1} = \begin{bmatrix} 0 & 0 & a & b \\ 0 & 0 & 0 & 0 \\ c & d & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \quad (14)$$

then the characteristic equation of (14) is given by,

$$|FV^{-1} - \lambda I| = 0$$

Which implies that,

$$\begin{vmatrix} -\lambda & 0 & a & b \\ 0 & -\lambda & 0 & 0 \\ c & d & -\lambda & 0 \\ 0 & 0 & 0 & -\lambda \end{vmatrix} = 0 \quad (15)$$

Therefore

$$-\lambda \begin{vmatrix} -\lambda & 0 & a \\ 0 & -\lambda & 0 \\ c & d & -\lambda \end{vmatrix} + a(0) - b(0) = 0 \quad (16)$$

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

$$\lambda^2 = 0 \text{ or } \lambda^2 = ac, \Longrightarrow \lambda = \pm\sqrt{ac} \quad (17)$$

The dominant Eigen value or reproductive ratio is $\lambda = \sqrt{ac}$

Therefore,

$$R_0 = \sqrt{\frac{\omega e^{-\lambda\tau} S_h(1-x)e^{-\lambda\tau}}{N_h\left(\left(\omega e^{-\lambda\tau}+(\alpha_m+\beta_m+kx+ly)\right)(\alpha_m+\beta_m+kx+ly)\right)}} \times \sqrt{\frac{\rho e^{-\lambda\tau}\theta S_m((1-x)e^{-\lambda\tau}}{N_m((\alpha_h+\beta_h)+\sigma(1-z)e^{-\lambda\tau}))}} \quad (18)$$

2.7. Existence of Disease Free Equilibrium

In the absence of disease in the population we have;

$$(E_{h,} = I_h =, E_m = I_m = 0 = R_h).$$

Here, $R_h = 0$ since there will be no disease to recover from, hence from the system of equation (1) we have,

$$\Lambda_h + \mu R_h - \alpha_h S_h - \frac{\gamma S_h I_m(t-\tau)(1-x)}{N_h} = 0 \quad (19)$$

$$-\frac{\theta I_h(t-\tau)S_m(1-x)}{N_h} + \Lambda_m - (\alpha_m + Kx + Ly)S_m = 0 \quad (20)$$

Since $I_m = 0$ in (19)
We have,

$$S_h = \frac{\Lambda_h}{\alpha_h}$$

Since $I_h = 0$ in (20) then,

$$\frac{\Lambda_m}{\alpha_m+kx+ly} = S_m \quad (21)$$

Similarly, when $(E_{h,} = I_h =, E_m = I_m = 0 = R_h)$ in the

remaining equations becomes

$$E_h^0 = 0,, I_h^0 = 0,, R_h^0 = 0,, S_m^0 = \frac{\Lambda_m}{\alpha_m + kx + ly}, E_m^0 = 0, I_m^0 = 0 \quad (22)$$

Where E_h^0 , -at disease free equilibrium and likewise $I_h^0,, R_h^0,, S_m^0, E_m^0$ and, I_m^0 respectively

Therefore disease free equilibrium point of our malaria model is given by

$$E_0 = \left(S_h^0, E_h^0, I_h^0, R_h^0, S_m^0, E_m^0, I_m^0\right) = \left(\frac{\Lambda_h}{\alpha_h}, 0,0,0\, \frac{\Lambda_m}{\alpha_m + kx + ly}, 0, 0\right)$$

This is the state where there is no malaria in the population.

2.8. Stability of Disease Free Equilibrium

The stability of the disease free equilibrium state can be tested using Eigen values of a jacobian matrix obtained at DFE, this is where $R_0 < 1$. The linearization matrix of system of equation (1) at disease free equilibrium is given by

$$\boldsymbol{J} = \begin{bmatrix} -\alpha_h & 0 & 0 & \mu & 0 & 0 & -\gamma \frac{s_h(1-x)e^{-\lambda\tau}}{N_h} \\ 0 & -\rho e^{-\lambda\tau} - \alpha_h e^{-\lambda\tau} & 0 & 0 & 0 & 0 & \gamma \frac{s_h(1-x)e^{-\lambda\tau}}{N_h} \\ 0 & \rho e^{-\lambda\tau} & -(\alpha_h + \beta_h) - \sigma(1-z)e^{-\lambda\tau} & 0 & 0 & 0 & 0 \\ 0 & 0 & \sigma(1-z)e^{-\lambda\tau} & -\alpha_h - \mu & 0 & 0 & 0 \\ 0 & 0 & -\frac{\theta s_m(1-x)e^{-\lambda\tau}}{(\alpha_m + kx + ly)N_m} & 0 & -\alpha_m - \beta_m - kx - ly & 0 & 0 \\ 0 & 0 & \frac{\theta s_m(1-x)e^{-\lambda\tau}}{(\alpha_m + kx + ly)N_m} & 0 & 0 & -\omega e^{-\lambda\tau} - \alpha_m - \beta_m - kx - ly & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega e^{-\lambda\tau} & -\alpha_m - \beta_m - kx - ly \end{bmatrix} \quad (23)$$

The system of equation [1] is stable if all the Eigen values of linearization matrix are negative.

In solving the eigen values we let,

$$\text{a}=-\alpha_h, \text{b}=-\gamma \frac{s_h(1-x)e^{-\lambda\tau}}{N_h}, \text{c}=-\rho e^{-\lambda\tau} - \alpha_h e^{-\lambda\tau},$$

$$\text{d}=\gamma \frac{s_h(1-x)e^{-\lambda\tau}}{N_h}, \text{e}=\rho e^{-\lambda\tau}$$

$$\text{f}=-(\alpha_h + \beta_h) - \sigma(1-z)e^{-\lambda\tau}, \text{g}=\sigma(1-z)e^{-\lambda\tau}, \text{h}=-\alpha_h - \mu,$$

$$\text{i}=-\frac{\theta s_m(1-x)e^{-\lambda\tau}}{N_m}, \text{j}=-\alpha_m - \beta_m - kx - ly$$

$$\text{k}=\frac{\theta s_m(1-x)e^{-\lambda\tau}}{N_m}, \text{l}=-\omega e^{-\lambda\tau} - \alpha_m - \beta_m - kx - ly, \text{m}=\omega e^{-\lambda\tau},$$

$$\text{n}=-\alpha_m - \beta_m - kx - ly$$

Solving the eigen values of the jacobian matrix $|\text{J} - \lambda\text{I}| = 0$

$$\begin{bmatrix} c+\lambda & 0 & 0 & d \\ e & f+\lambda & 0 & 0 \\ c & k & l+\lambda & 0 \\ 0 & 0 & m & n+\lambda \end{bmatrix} = 0 \quad (24)$$

We have

$$(c+\lambda)(n+\lambda)(f+\lambda)(l+\lambda) - dmek = 0 \quad (25)$$

To simplify the equation (25)

Let

$$A_1 = n, A_2 = l, A_3 = f, A_4 = c \text{ and } Q = dmek$$

This implies

$$(\lambda + A_1)(\lambda + A_2)(\lambda + A_3)(\lambda + A_4) - Q = 0 \quad (26)$$

$$\lambda^4 + \lambda^3 B_1 + \lambda^2 B_2 + \lambda B_3 + B_4 = 0 \quad (27)$$

Where,

$$B_1 = A_4 + A_3 + A_2 + A_1$$

$$B_2 = A_4(A_3 + A_2 + A_1) + A_3(A_2 + A_1) + A_2 A_1$$

$$B_3 = A_4 A_3 A_2 + A_4 A_3 A_1 + + A_3 A_2 A_1$$

$$B_4 = A_4 A_3 A_2 A_1 - Q$$

Therefore R_0 in equation (18) can be written in terms of A_i where i=1,2,3,----n

As

$$R_0^2 = \frac{(\omega e^{-\lambda\tau}\theta((1-x)e^{-\lambda\tau}S_m)(\rho e^{-\lambda\tau}(1-x)e^{-\lambda\tau}S_h)}{N_m N_h A_3 A_2 A_1^2} \quad (28)$$

Using the Routh-Hurwitz criteria on equation (27) we can show that all roots have negative real parts.

Routh –Hurwitz criteria[15] gives necessary and sufficient conditions for all the roots of characteristic polynomial and lies on the left half of the complex plane.

Theorem 2.8 Routh-Hurwitz criteria.

Given the polynomial

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

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

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

$$H_n = \begin{bmatrix} B_1 & 1 & 0 & 0 & 0 & ' & 0 \\ B_3 & B_2 & B_1 & 1 & 0 & ' & 0 \\ B_5 & B_4 & B_3 & B_2 & B_1 & ' & 0 \\ ' & ' & ' & ' & ' & ' & 0 \\ ' & ' & ' & ' & ' & ' & 0 \\ ' & ' & ' & ' & ' & ' & 0 \\ 0 & 0 & 0 & 0 & 0 & ' & B_n \end{bmatrix}$$

Where $B_j = 0$ if $j > n$, all the roots of the polynomial $P(\lambda)$ are negative if and only if the determinants of Hurwitz matrices are positive

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

For the equation (27), when n=4, the Routh-Hurwitz criteria are

$B_1 > 0, B_2 > 0, B_3 > 0, B_3 > 0$ and the determinants of Hurwitz matrices are:

$$\det(H_1) = B_1 > 0$$

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

$$\det(H_3) = \begin{bmatrix} B_1 & 1 & 0 \\ B_3 & B_2 & B_1 \\ 0 & 0 & B_3 \end{bmatrix} = 0, B_1 B_2 B_3 - B_3^2 > 0$$

$$\det(H_4) = \begin{bmatrix} B_1 & 1 & 0 & 0 \\ B_3 & B_2 & B_1 & 1 \\ 0 & B_4 & B_3 & B_2 \\ 0 & 0 & 0 & B_4 \end{bmatrix} = 0, B_1(B_2 B_1 - B_3) - B_4 B_1^2 > 0$$

Clearly, from Hurwitz matrices all the determinants are positive, which means that all the Eigen values of the jacobian matrix have negative real part. Moreover, if $R_0 < 1$, it follows that from (28) that $A_i > 0$ and therefore disease free equilibrium point is stable when $R_0 < 1$.

3. Numerical Simulations and Results

The simulations were performed using MATLAB'S built in dde 23 solver. In the analysis, initial population sizes and other parameters were obtained from literature as shown from the table below.

Table 1. *Description of variables and parameters of malaria model.*

PARAMETER	VALUE	REFERENCE
Λ_h	0.028 per day	Chiyaka et al (2008)
Λ_m	6	Estimated
ρ	1/14	Malaria.com (2011)
α_h	0.00004 per day	Hyun (2001)
β_h	0.0004per day	Prince Harvim (2014)
β_m	0.01 per day	Chiyaka et al (2008)
α_m	0.04 per day	Chiyaka et al (2008)
Z	0.2 per day	Estimated
K	1/365	Estimated
L	1/365	Estimated
γ	0.0025	Estimated
μ	0.04	Estimated
ω	1/12	Chiyaka etal (2008)
θ	0.0415	Estimated
σ	0.005	Estimated
λ	0.06	Estimated
x	0.5	Estimated
y	0.5	Estimated

The initial conditions used are:

$$S_h = 300, E_h = 200, I_h = 100, R_h = 50, S_m = 400, E_m = 300, I_m = 200 \text{ t=350 days}$$

Numerical simulation.

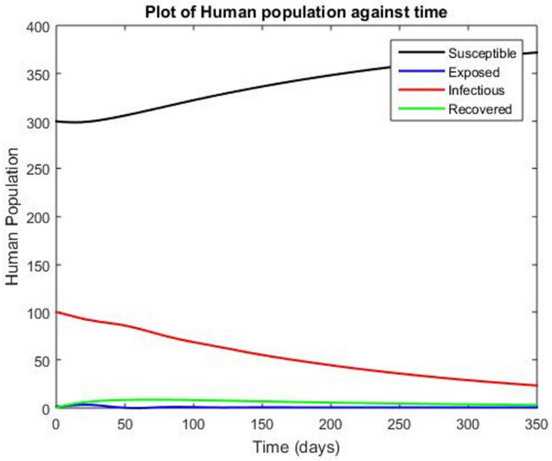


Figure 2. *Shows human population against time in days.*

From the graph it shows that the number of infective humans reduces considerably because of the use of control strategies, while the number of humans susceptible also increases because the disease is under control.

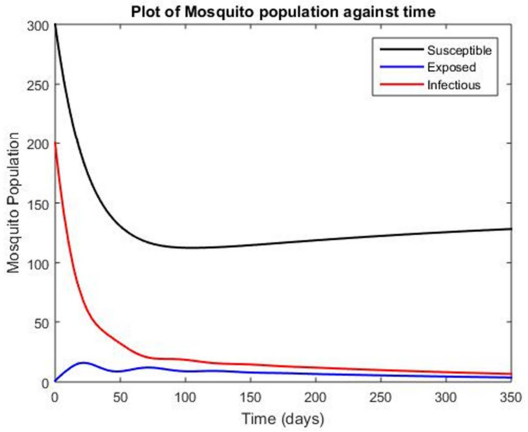
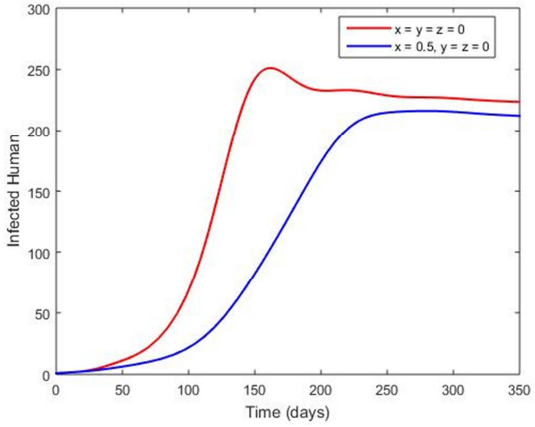


Figure 3. *Shows mosquito population with time.*

From the figure it is evident that the number of infective mosquitoes went down significantly with time as a result of a combination of control strategies and treatment used, while those exposed to disease dropped significantly.



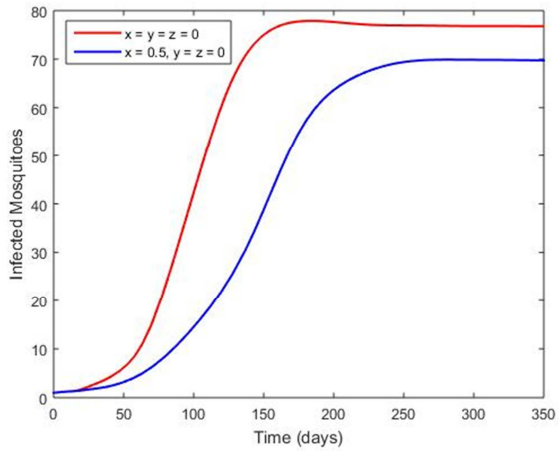
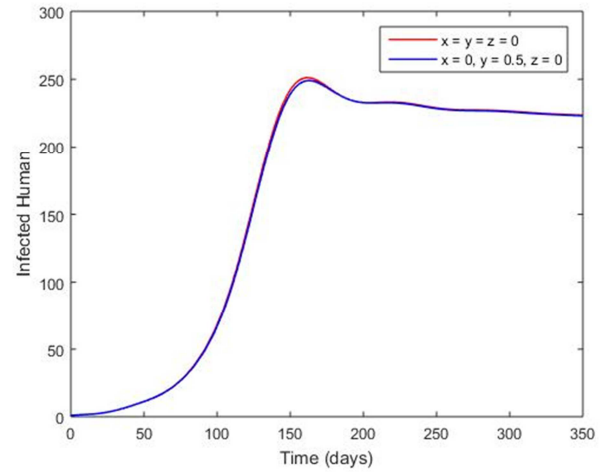


Figure 4. *Simulation of Long Lasting Insecticides Treated Nets (LLINS).*

From figure 4. above when the contol strategies are not used x=y=z=0 the number of infective humans was high, and when only LLINS (x) was used the number of infective humans and mosquitoes dropped.



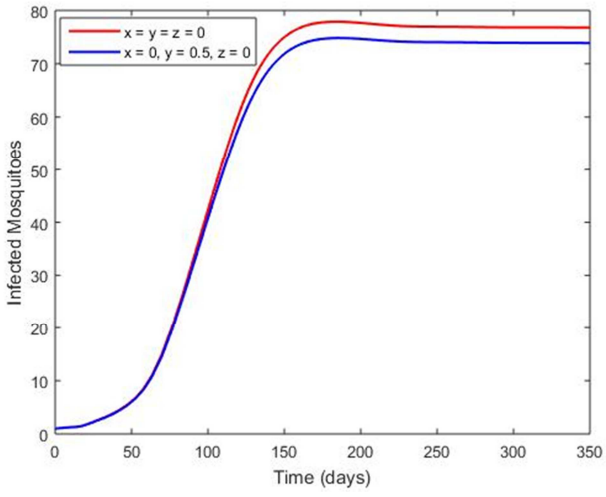
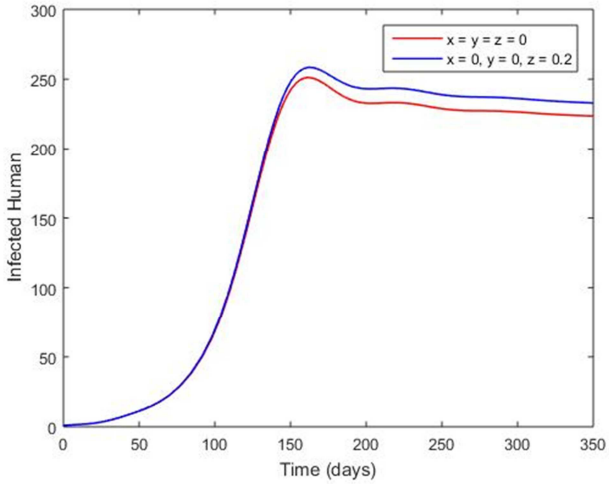


Figure 5. *Simulation of Indoor Residual Spraying (IRS).*

Figure 5 From the above figure it is evident that indoor residual spraying reduced the number of mosquitoes, while it didn't have any impact on infected human population



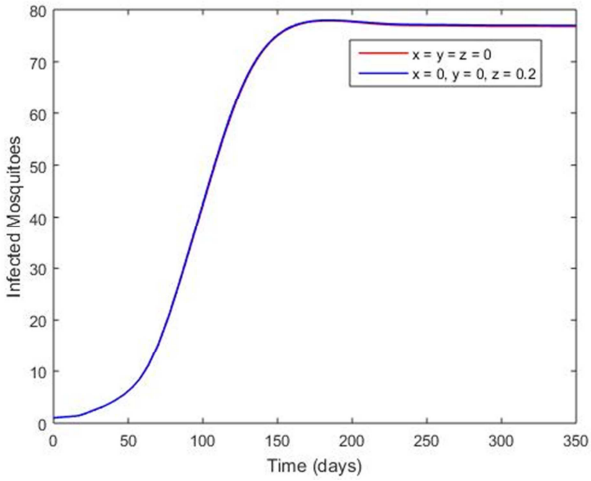


Figure 6. *Simulation ofTreatment (with drug).*

From figure 6. It shows that with the use of drugs for treatment of malaria, it reduced the number of infected humans with time.

4. Conclusion

From the study, SEIR and SEI model for humans and mosquitoes were used to study malaria transmission dynamics. The model is achieved with control strategies such as; use of long lasting treated bed nets (LLINS), indoor residual spraying, intermittent preventive treatment for infants and pregnant mothers.

The model equations generated were used to calculate reproduction number using the next generation matrix. From the results it was found out that when $R_0 < 1$ the model was locally stable and the disease was controlled and when

$R_0 > 1$, the disease persists because number of infective humans increased.

Therefore with the combination of control strategies and treatment, the malaria spread is put on control.

5. Future Research and Suggestions

The model in our research has not exhausted all the strategies, like developing a malaria vaccine to check on malaria spread. Future model should be developed to include the effects of environment on the number of infective mosquitoes.

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