A MATHEMATICAL MODEL FOR THE TRANSMISSION DYNAMICS OF MALARIA IN EASTERN UGANDA: A CASE STUDY OF BUTALEJA DISTRICT

A thesis presented to the College of Higher Degrees and Research Kampala International University Kampala, Uganda

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In partial fulfillment of the requirements for the degree of Master of Science in Applied Mathematics (MSc-AM)

BY

WAKHATA ROBERT
(MSC-AM/45499/143/DU)

May, 2016

Declaration A

This thesis is my original work and has never been presented for the award of a degree or any other academic award in any University or institution of learning.

WAKHATA ROBERT
(MSC-AM/45499/143/DU)

20-05-2016

Date

Acknowledgements

I would like to grately thank the almighty God for the gift of life and wisdom.

I wish to extend my sincere gratitude to my supervisor, Dr. Godwin Kakuba, lecturer for Applied Mathematics, Kampala International University for his inexhaustible support, help, guidance and advice rendered to me.

Thanks go to the staff, Head of department of Physical Sciences and the College of Higher degrees and Research Kampala International University specifically Dr.Muhammad Kibuuka, Dr. Mundu Musitafa, Dr.Maria Mbatudde, Dr.Sudi Balimutajjo and Dr.Winston Tumps Ereeta for teaching and guiding me.

Special thanks go to Belgium Technical Cooperation (BTC-Uganda) who have contributed immensely towards my education by sponsoring research and the whole programme.

I appreciate the head teacher of Mbale Secondary School Mr.Sam Kuloba for his coorperation during my studies.

I wish to acknowledge and appreciate the valuable support from the staff of Ministry of Health and Butaleja district Health Personnel in terms of reading materials and part of the data used in this research.

Lastly, I am equally very grateful for the support, cooperation, collaboration, encouragement and teamwork exhibited by my dear friends and classmates during the course.

May the almighty God bless you mightily.

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Abstract

A deterministic mathematical model for studying the transmission dynamics of malaria in Butaleja district was developed using ordinary differential equations (ODEs) where humans and mosquitoes interact and infect each other. The model has five non - linear differential equations with two state variables for mosquitoes (S_m and I_m) and three state variables for humans (S_h, I_h and A_h). The available literature on previous work in this area was reviewed.

Susceptible humans (S_h) are infected when they are bitten by infectious mosquitoes (I_m). They then progress through infectious and asymptomatic classes before re-entering susceptible class. Susceptible mosquitoes (S_m) become infected when they bite Infectious (I_h) and Asymptomatic (A_h) humans. They move to infectious class but do not recover due to their short life span.

Following ideas advanced by Ross, [Chapter 2] [41], the model can be applicable to other infectious diseases of humans such as yellow fever, typhoid. sleeping sickness, cholera etc: using specific model parameters.

Model Analysis was done, equilibrium points analyzed to establish their local and global stability. The important threshold in this research called the basic reproduction number (R_o) was obtained using the method of next-generation matrix to determine whether the disease dies out or persists. The rule of thumb is that; the disease- free equilibrium is locally asymptotically stable if $R_o \leq 1$ and the endemic equilibrium exist provided that $R_o > 1$. Using parameter values, R_o for Butaleja district was found to be $= 0.00000345 < 1$; an indication that malaria will be rolled out of the district after a certain period of time.

Numerical simulations show that there is a strong positive relationship between the number (proportion) of infected mosquitoes and infected humans in the same locality. Reducing the current rate of female anopheles mosquito bites could assist Butaleja district to achieve malaria free status by the year 2030 [26], [25]. Therefore, I recommend control methods such as ITNs and IRS that increase mosquito death rate and reduce mosquito birth rate/mosquito bites; as well as treating asymptomatic hosts using ACTs, and IPT. Hence, the formulated model, provides a framework for studying and designing effective intervention strategies for prevention and control of malaria in the district.

Chapter 1

1 Introduction

1.1 Background

Malaria is a vector borne infectious disease caused by *Plasmodium Parasites*. It is very high in Uganda and one of the most common infections in the world today that spreads to humans through the bites of infected female anopheles mosquitoes when they feed on blood for their developing eggs [6], [68]. Children under the age of 5 and expectant women are mostly affected due to low immunity against malaria as in [68] and [31]. The disease causes significant morbidity, mortality and economic loss; discourages foreign direct investment and hurts trade and tourism as in [31].

In Uganda (2011-2015), hospital records show that malaria was responsible for (30-50)% of outpatient visits, (15-20)% of all hospital admissions, (9-14)% of inpatient deaths and $\approx$ 20% of all hospital deaths. A significant percentage of deaths occur at home and are not reported by the facility-based Health Management Information System [16], [17], [18], [19], [20], [26], [38] and [55].

Of the 18 countries accounting for over 90% of *Plasmodium falciparum* infections in sub-Saharan Africa (SSA), Uganda was ranked 6th, world wide in the number of malaria cases and 3rd in the number of malaria deaths after Democratic Republic of Congo (DRC) and Nigeria [61], [67] with the overall malaria - specific mortality estimated to be 100,000 child deaths annually, and a death toll exceeding that of HIV/AIDS, [12], [31].

An estimated 3.3 billion people worldwide with more than 80% living in sub-Saharan Africa are at a risk of contracting malaria. Globally, malaria kills $\approx 1,000,000$ people annually yet it is a preventable and treatable mosquito-borne illness [31], [67],[68].

The four human species of *Plasmodium parasites* that occur and cause malaria in Uganda are: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium Ovale* and *Plasmodium Malariae*. *Plasmodium falciparum* accounts for over 90% of all malaria infections [49]. Other species appear to each account for $< 5\%$ of cases, with less percentage of infections due to mixed species. Determinations based on blood smears revealed that 99% of infected children had *P. falciparum*, 2% *P. vivax*, 2% *P. malariae*, and $< 1\%$ *P. ovale*; 3% carried mixed species infections, [48].

Malaria vectors are mosquitoes of the anopheles family which breed in fresh waters, temporary pools such as footprints and road cuts especially after rainfall and irrigation. *Anopheles gambiae*, a highly efficient vector, along with *Anopheles funestus* are the two main vectors. These vectors are predominantly *anthropophagic* (feed exclusively on humans), *endophilic* (rest indoor) and *endophagic* (feed indoor).

Although malaria transmission occur year-round (stable malaria) with transmission intensity varying according to seasons; Peak transmission occur at the end of the rainy seasons and ≈ 4 weeks after the end of rains in different geographic areas of the country [25]. Stable malaria is in $\approx$ (90 - 95)% of Ugandans. The (5 - 10)% of the country's population consists of unstable and epidemic-prone transmission areas especially in the highlands of South- and mid-west, along the eastern border with Rwanda, north-eastern border with Sudan, Mt. Rwenzori, Mt. Elgon and areas with altitudes above 1,800 Metres. Very high transmission areas (> 100 infective bites per person per year) account for 70%, those with medium to high transmission levels (10 - 100 infective bites per person per year) accounts for 20% and areas of low transmission (< 10 infective bites per person per year) accounts for 10%.

The symptomatic infections in a cohort study in Kampala

(2004 - 2008) where infecting parasites were speciated by molecular means, 94% of episodes of malaria were caused by *P. falciparum* (including mixed infections), 4.6% solely by *P. malariae*, 0.8% by *P. ovale*, and 0.5% by *P. vivax* as in [5].

The most common symptoms of malaria is on and off fever (temperatures $\geq 37.5^0C$) and can be detected by a thermometer or touch or a history of fever. Other Symptoms for *P. falciparum* arise (9 - 30) days after infection. However, they may occur later in those who have taken anti-malarial medications. These include loss of appetite, body weakness, nausea, muscle aches, headache, shivering, joint pain, vomiting, hemolytic anemia, jaundice, hemoglobin in urine, retinal damage, and convulsions.

A survey by Uganda Bureau of Statistics(UBOS) see [20] showed a general decrease in malaria cases throughout the country, with prevalence dropping to 19% in children under 5 years, from 42% in 2009; but the outbreak in Northern Uganda slowed this gain. According to the [31]; [22], a total of 22,873 malaria cases had been registered in the northern districts of Uganda (Lamwo, Gulu, Kitgum, Oyam, Agago, Apac, Amuru, Kole, Nwoya and Pader), with 162 confirmed deaths. Further more, a study by Ministry of health see [54], showed high malaria incidence (burden) in Butaleja district as shown.

YEAR	QUARTER	MALARIA INCIDENCE
2013	4	215
2014	3	196
2014	4	193

Table 1: Extracted from Malaria Quarterly Bulletin: Issue 8: Oct-Dec 2014

Source: Uganda MOH, National Malaria Control Program

YEAR	QUARTER	MALARIA INCIDENCE
2014	2	219
2015	1	179
2015	2	168

Table 2: Extracted from Malaria Quarterly Bulletin: Issue 10: Apr-Jun 2015

Source: Uganda MOH, National Malaria Control Program

Also, global malaria cases fell from an estimated 262 million in 2000 to 214 million in 2015, a decline of 18%. These estimates occurred in the WHO African Region (88%), followed by the WHO South-East Asia Region (10%) and the WHO Eastern Mediterranean Region (2%). Malaria incidence is estimated to have decreased by 37% between 2000 and 2015 as in [68]. Despite large malaria burden faced by Ugandans, an epidemiological report showed that 25 of 112 districts achieved $>$ a 20% reduction in malaria prevalence between 2000 and 2010 [54]. Countries with the highest death rate per 100,000 of population were Ivory Coast (86.15), Angola (56.93) and Burkina Faso (50.66) [62]. Also, Burkina Faso, Mozambique and Mali fell victims [67]. Others were Nigeria (11%), Democratic Republic of Congo (26%), Mozambique, Burkina Faso and Sierra Leone (25%) [67], [52].

According to WHO, Countries in Malaria Elimination phase are Algeria, Argentina, Azerbaijan, Islamic Republic of Iran, the Republic of Korea, Saudi Arabia, Srilanka, Tajikistan and Turkey.

It is important to note that despite the global malaria burden, four countries namely the United Arab Emirates, Morocco, Turkmenistan and Armenia were certified Malaria free within their borders since 2007.

In the process of eliminating Malaria, World Health Organization (WHO), states that sustained political commitment, adequate resourcing, and effective partnerships are all key and fundamental to the success of malaria elimination.

1.2 The Research Problem

In spite of the recent successes by the government of the Republic of Uganda and International Organizations in the struggle against malaria that have led to a substantial reduction of reported malaria cases and deaths, there is high malaria incidence and prevalence in Butaleja district as in [39], [54], [32], [33].

Malaria is endemic in $\approx 95\%$ of the country, affecting over 90% of the population , notably children below the age of 5 [20], [21].

Different studies about the transmission dynamics of malaria in vectors and humans have been done in Uganda and other parts in the world. However, no study has been done in Butaleja district. Therefore, there is need to formulate a mathematical model for studying parameters in the transmission dynamics of malaria in the district and design effective intervention strategies for prevention and control.

1.3 Objectives:

1.3.1 Major objective

To formulate a mathematical model and establish the dynamics of how malaria spreads in Butaleja district

1.3.2 Specific Objectives

Specifically, this study is intended to:

1. Formulate a model to represent the transmission of malaria
2. Determine the basic reproduction number (R_o) for the model
3. Establish the disease free equilibrium state for the model
4. Establish, analyze stability conditions for disease free equilibrium and predict malaria prevalence with time

1.4 Scope

The study was done in Butaleja district. The district has one county (Bunyole), twelve (12) Sub-counties (Budumba, Busaba, Busabi, Busolwe, Buswolwe town council, Butaleja, Butaleja town council, Himutu, Kachonga, Mazimasa, Nawanjofu and Naweyo) with a total population of 245,873 people and a population growth rate of 3.71 as in [53]. The district is bordered to the east by Namutumba, to the north by Budaka, to the north west by Mbale, to the west by Tororo, and to the south by Bugiri.

Secondary data and parameter estimates for establishing and analyzing stability conditions was got from the reviewed literature, Butaleja district health personnel and Health Management and Information System (HMIS) housed at the resource centre, Ministry of Health headquarters, Kampala.

Butaleja district was selected due to the highest malaria incidence and prevalence as in [54].

This study was based on a Mathematical Model that originated from the work of Ross, see [41]; This model outlines the basic features of malaria transmission i.e., if mosquito population can be reduced below a certain threshold, malaria can be eradicated. He therefore agitated for mosquito-based malaria control programmes.

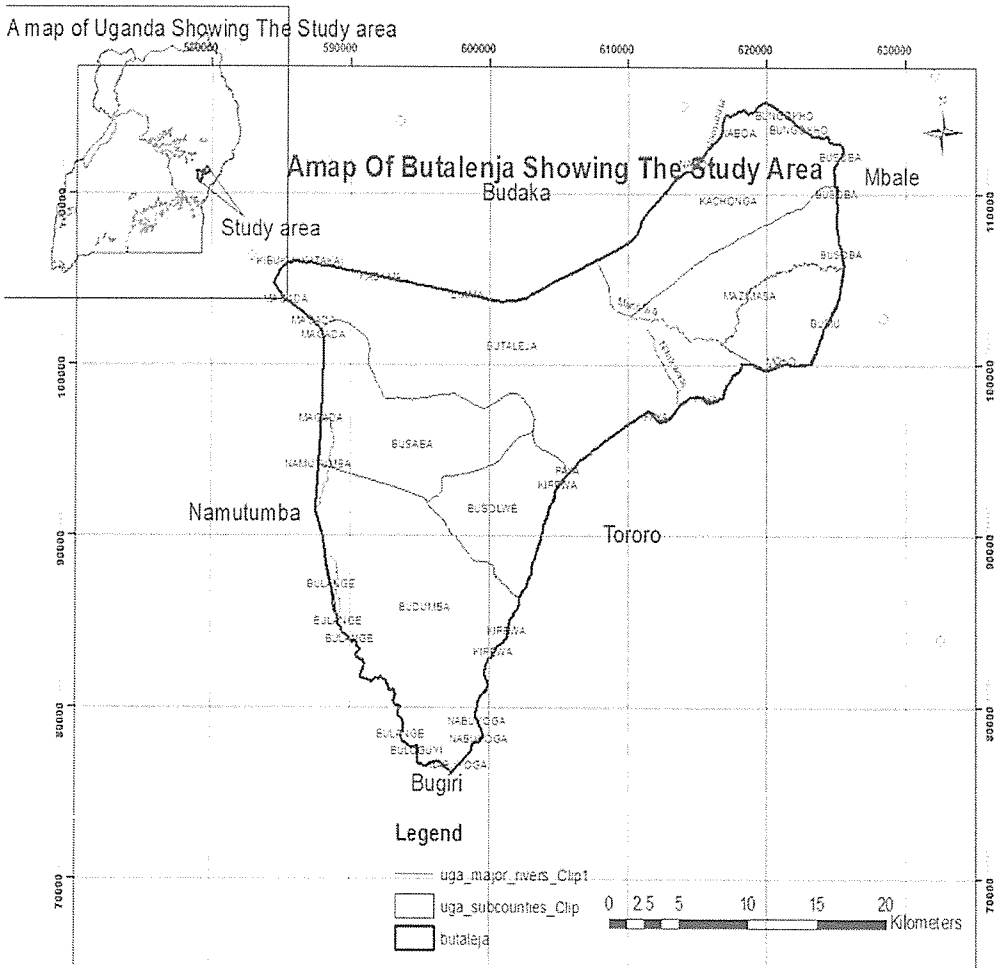

Figure 1: A sketch map showing Sub-counties of Butaleja District

1.5 Methods of the study

In this study, deterministic non-linear ordinary differential equations were formulated using the compartmental diagram. Their stability and equilibria were analyzed. Numerical simulations of the model to demonstrate theories were performed using MATLAB R2007b. LaTeX (WinEdt 5.5) was used for the write up.

1.6 Significance

Research findings will help the government through the Ministry of health, International Organizations, communities and health workers in Butaleja district to:-

1. Embrace the preventive measures (Example LLITNs, IRS, ACTs, IPT) needed in controlling further spread of malaria.
2. Use the mathematical model formulated in identifying parameters and remedies to malaria transmission.
3. Show case to the disease so that they continue lobbying for funding from the Government or international organizations in increasing health facilities in every Sub-county.
4. Increase funding for preventing malaria transmission and malaria mortality within the population especially in infants of 0-5 years and expectant women.

1.7 Structure of the dissertation

In Chapter 1, the background of malaria was covered; types of vectors that cause malaria in Uganda i.e., *P. falciparum, P. vivax, P. Ovale and P.Malariae* outlined and areas in Uganda where they are prevalent, stated. Also, mosquito vectors and how they spread malaria is explained. Symptoms of malaria in human population have been outlined. The rationale for the study is captured in the Research problem statement; Objectives, scope and significance of this research to the people of Butaleja district and the surrounding areas are all outlined there in.

In Chapter 2, articles from various scholars who did similar research about the dynamics of the spread of malaria in different parts of the world were reviewed. Statistics of the disease prevalence in Butaleja district has been summarised in tabular form. Suggested methods to eradicate or reduce disease incidence and prevalence such as ITNs, IRS, ACTs, and IPT were stated.

In Chapter 3, the research area, methods of data collection and analysis are mentioned. The model was analyzed qualitatively and the disease free equilibrium obtained and analyzed.

In Chapter 4, numerical analysis of the model using parameter values obtained from various publications, district health personnel and Health Management and Information System; Ministry of health has been carried out using MATLAB (R2007b) software. These show the variation of the number of susceptible, infected and asymptomatic human population with time.

In Chapter 5, further discussions on the results is done here, conclusions on this research, suggested recommendations as well as areas for further model development are outlined.

Chapter 2

2 Literature Review

2.1 Management Strategies

The health and development of a country are interrelated. Uganda's population has experienced a fair improvement in health indicators. However, child malnutrition, high prevalence of malaria and HIV/AIDS and high rates of maternal morbidity and mortality remain a challenge to the country's development as in [46], [53]. The most common malaria vectors in Uganda are *Anopheles gambiae* and *Anopheles funestus*, with *Anopheles gambiae* being the dominant species in most locations [34]. *Anopheles funestus* is common in high altitude areas and during the short dry seasons, when permanent water bodies are the most common breeding sites. In some areas of Northern Uganda, *Anopheles funestus* is the most common vector. Within *Anopheles gambiae* complex, the predominantly anthropophilic (prefering humans to other animals) *Anopheles gambiae* is most common. *Anopheles gambiae* and *Anopheles funestus* are highly endophagic (feeding indoors) and endophilic (resting indoors).

Efforts to reduce the burden of malaria have intensified recently through the use of effective tools for malaria control, notably Long-Lasting Insecticide Treated Nets (ITNs), Indoor Residual Spraying (IRS), treatment with Artemisinin-based Combination Therapies (ACTs), and Intermittent Preventive Therapy (IPT) for high-risk groups like expectant women [67]. These efforts have been made possible by recent focused policy recommendations and increased support from government and international organizations. Increased resources for control have come with ambitious targets and expectations of significant reductions

in disease burden. Subsequently, calls have been made for elimination of malaria from endemic areas and eventually, there will be complete eradication of the disease.

The tables below show that malaria is still a serious burden in Uganda despite control measures put in place by the government of Uganda (Ministry of Health) and international organizations.

Annual Sector Performance Report FY 2012/2013

Diagnosis	2008/2009	2009/2010	2010/2011	2011/2012	2012/2013
Malaria	37.0%	38.0%	36.0%	36.0%	36.8%

Table 3: Top ten causes of morbidity among all ages (2008 - 2012/2013)

Rank	IPD diagnosis	Total	Under 5	5 and over	%
1	Malaria	5079	2623	2456	20.6

Table 4: Top ten causes of hospital based morbidity for all ages (2012 - 2013)

Source: *MOH, HMIS, National Malaria Control Program*

Weekly epidemiological Bulletin, 2016

Weeks (2016)	1	2	3	4
Number of malaria cases	504 (0)	562 (0)	1092 (0)	787 (0)
Uganda	144370 (31)	206777 (43)	226696 (64)	213308 (39)

Table 5: Malaria morbidity and (mortality) in Butaleja district. 2016

Source: *MOH, Epidemiological Surveillance Division (ESD)*

2.2 Reduction of Malaria endemic

The findings demonstrate that the world is continuing to make impressive progress in reducing malaria cases and deaths, see [67], [68]. Each year, more people are reached with core malaria interventions to save more lives. The malaria target under Millennium Development Goal 6 has been met, and 55 countries are on track to reduce malaria burden by 75%, in line with the World Health Assembly's target, 2015 as in [42] and [59].
Major progress has been documented in vector control as well; In 2014, a record number of Long-Lasting Insecticidal Nets were delivered to endemic countries in Africa. The report showed that malaria mortality rates decreased by 47% between 2000 and 2013 globally, and by 54% in the WHO African Region. It also reveals that these trends are accompanied by a gradual and substantial reduction in parasite prevalence rates across Africa. This means that every year, fewer people get infected or carry asymptomatic infections.

The National Health Strategic Plan, as in [33], [26] and [25], is based on the principles and aims of the global Roll Back Malaria Partnership, aims as in [1], and United Nations Millennium Development Goals [49]. Also, [25] and [26] aims at controlling malaria such that it is no longer the major cause of illness and death in Uganda, ensure universal access to malaria prevention and treatment, and reduce mortality rate in children below the age 5 as in [47] and [50].

Principal intervention strategies and markers of implementation, primarily garnered from [47] and [16] are:- Integrated vector management, effective diagnosis and treatment, prevention of malaria in pregnancy, and attention to malaria epidemics [16].

2.3 Modeling and control of Malaria

Mathematical models for malaria plays a unique role in comparing the effects of control strategies. used individually or in packages. This is done by determining the relative importance of model parameters in malaria transmission and prevalence levels.

Mathematical modeling of malaria transmission was introduced by Ross, see [41]. He introduced the first deterministic differential equation model of malaria by dividing the human population into susceptible (S_h) and infected (I_h) compartments, with the infected class returning to susceptible class again leading to the SIS structure.

The mosquito population also had two compartments (S_m; I_m), but they do not recover from infection due to their short life span, thereby following the SI structure. Time evolution of the fraction of individuals in the infected classes ($I_h; I_m$) is studied for human and mosquitoes. The parameters that contribute to the increase of R_0 in the model, are related to mosquitoes and humans, and any change in them significantly affect malaria transmission. Increasing mosquito mortality (μ_m) and reducing mosquito biting rate (b) reduces R_0 other parameters being held constant.

The Ross model outlines the basic features of malaria transmission; and according to him, if mosquito population can be reduced to below a certain threshold, malaria can be eradicated.

The Ross model did not consider latency period of the parasite in mosquitoes and their survival. The model predicted a rapid progress of the epidemic in human, and a higher equilibrium prevalence of infectious mosquitoes. Macdonald (1957) considered this latency period (t_m), and introduced the Exposed (E_m) class in mosquitoes and divided mosquito population into three compartments (SEI). The model studies the time evolution

of the exposed (E_m) and infected (I_m) classes in mosquitoes. R_0 for the model was consequently scaled down with increasing latency period.

In a natural extension to [14] and [41], [4] considered 21 days latency period of parasite in humans, and introduced the Exposed (E_h) class in human population in their model. They divided the host population into three compartments(S_h, E_h and I_h), along with that in the mosquito population (S_m, E_m and I_m). This becomes a SEIS model for the human population. Time evolution of exposed and infected classes for humans and mosquitoes(E_h, I_h, E_m and I_m) was included. The R_0 for this model was further reduced due to inclusion of human latency period.

Immunity should be included during modeling for the transmission of malaria in a population. This is described by [13]. That is; "Incorporating immunity can help in making models more realistic." Also, even the recovered individuals become Susceptible to the infection as in [35].

The [2] consists of four compartments in humans. i.e., Susceptible (S_h), Exposed (E_h), Infected (I_h) and Immune (R_h) - and three compartments in mosquitoes - Susceptible (S_m), Exposed (E_m), and Infected (I_m).

Mathematical analysis of the model showed that the basic reproductive number (R_0), can describe malaria transmission dynamics; where a globally stable disease-free equilibrium exists if $R_0 < 1$, while for $R_0 > 1$, the endemic equilibrium becomes globally stable. The model explicitly shows the role of inclusion of demographic effects in predicting the number of fatalities that may arise as a result of the disease.

Similarly, [24], [28] and [8] did a bifurcation analysis of a malaria model. He included constant immigration of susceptible human population. Considering immigration of people and excluding direct human recovery from the infectious to suscepti-

ble class, the results showed that the population approaches the locally asymptotically stable endemic equilibrium point depending on the initial size of the susceptible class.

[10] and [69] divided the immune class (R_h) in human population into immune (R_{h1}), partially immune (R_{h2}) and non-immune but with immunologic memory (R_{h3}), with each class having differential immunity. Mathematical analysis of the model showed that the effects of three types of immune responses lead to delay in the reappearance of individuals who had experienced malaria, to the Susceptible population. Hence, the community under high threat of malaria (high R_0) shows low prevalence of individuals with asexual blood-stage infection and without infectious gametocytes, whereas, the same community is relatively free of severe infection due to the increase in immunity by re-infection.

[30] and [11] introduced three age-specific "immunity-functions" in their SEI Model. The infected human hosts are divided into three classes i.e., infected with severe disease (I_{h1}), asymptomatic patient infection (I_{h2}), and infected with undetectable parasite density (R_{h3}). The effect of mosquito density was incorporated through the force of infection.

In conclusion, strategies for controlling epidemiology of many infectious diseases such as malaria include models that result into a rapid reduction in both infected and asymptomatic population via treatment [45]. This calls for collective responsibility in using control measures like ITNs, IRS, ACTs, and IPT for high-risk groups especially children under the age of 5 and expectant women [67], [68].

Chapter 3

3 Mathematical Models for Malaria

3.1 The Mathematical Model

In this chapter, SIA-S model for transmission of Malaria is formulated. Model parameters, variables are explained and assumptions they satisfy are stated. The model is analyzed qualitatively for stability of steady states. The basic reproduction number (R_o); the important threshold in this research is obtained using the next generation matrix technique. Analysis of model parameters is done using the trace and determinant of the Jacobian matrix for the system of equations of the formulated model. To predict malaria transmission with time, simulations are performed to show the relationship between different classes of human and mosquito population.

The spread of malaria is modeled using ordinary differential equations (ODEs) where humans and mosquitoes interact and infect each other. In this model, N_h denotes total population size for human hosts which is divided into three classes; i.e., Susceptible
(S_h), Infectious (I_h) and Asymptomatic (A_h).

Human hosts are said to be susceptible if they are not infected and are capable of being infected. They are infectious if they have been infected and can infect others and asymptomatic when they are a carrier for malaria but experiences no symptoms. Arrows on the compartmental diagram either indicate population loss or transfer of population from one class to another.

3.1.1 Model Variables

Total human population (N_h) is given by: $N_h = S_h + I_h + A_h$

Where

S_h: Number of Susceptible human population at time t

I_h: Number of Infected human population at time t

A_h: Number of Asymptomatic human population at time t

I_m: Number of Infected mosquito population at time t

The Model is described with the following initial value equations:-

$$\acute{S} = \frac{dS_h}{dt} = f(S) = \lambda_h - bpI_m\frac{S_h}{N_h} - \mu_h S_h + \gamma(I_h + A_h);$$
$$S_h(0) = S_{h(0)} \geq 0$$

$$\acute{I} = \frac{dI_h}{dt} = f(I) = bpI_m\frac{S_h}{N_h} - I_h(\mu_h + \alpha + \delta + \gamma);$$
$$I_h(0) = I_{h(0)} \geq 0$$

$$\acute{A} = \frac{dA_h}{dt} = f(A) = \delta I_h - A_h(\mu_h + \gamma);$$
$$A_h(0) = A_{h(0)} \geq 0$$

$$\acute{S_m} = \frac{dS_m}{dt} = f(S_m) = \lambda_m - bqS_m\frac{I_h}{N_h} - brS_m\frac{A_h}{N_h} - \frac{\mu_m}{S_m}$$
$$S_m(0) = S_{m(0)} \geq 0$$

$$\acute{I_m} = \frac{dI_m}{dt} = f(I_m) = bqS_m\frac{I_h}{N_h} + brS_m\frac{A_h}{N_h} - \mu_m I_m;$$
$$I_m(0) = I_{m(0)} \geq 0$$

But; $N_h = S_h + I_h + A_h$

3.1.2 Model Parameters

Parameter	Definition
λ_h	Birth rate of humans
λ_m	Birth rate of mosquitoes
μ_h	Death rate of humans
μ_m	Death rate of mosquitoes
b	Biting rate on humans
p	Proportion of bites on humans at time t
q	Proportion of S_m bites on I_h at time t
r	Proportion of S_m bites on A_h at time t
δ_h	Rate of symptom's development
γ_h	Recovery rate of humans
α	Malaria mortality rate
$N_h(0)$	Number of Susceptible humans at time t
$N_m(0)$	Number of Susceptible mosquitoes at time t
$I_h(0)$	Number of Infectious humans at time t
$A_h(0)$	Number of Asymptomatic humans at time t
$I_m(0)$	Number of Infectious mosquitoes at time t

Table 6: Model Parameters

3.1.3 Model Assumptions

1. The total human and mosquito population varies with time.
2. The infectious period of mosquitoes ends when they die.
3. There is homogenous interaction in the population.
4. No recovery for infected mosquitoes since they die naturally.
5. The birth and death rates are exactly balanced.
6. The size of each class is treated as a continuous variable.
7. Asymptomatic humans have temporal immunity. However, they later become susceptible to re-infection.

3.1.4 Compartmental Diagram

A compartmental diagram below has been developed based on model variables, model assumptions and model parameters.

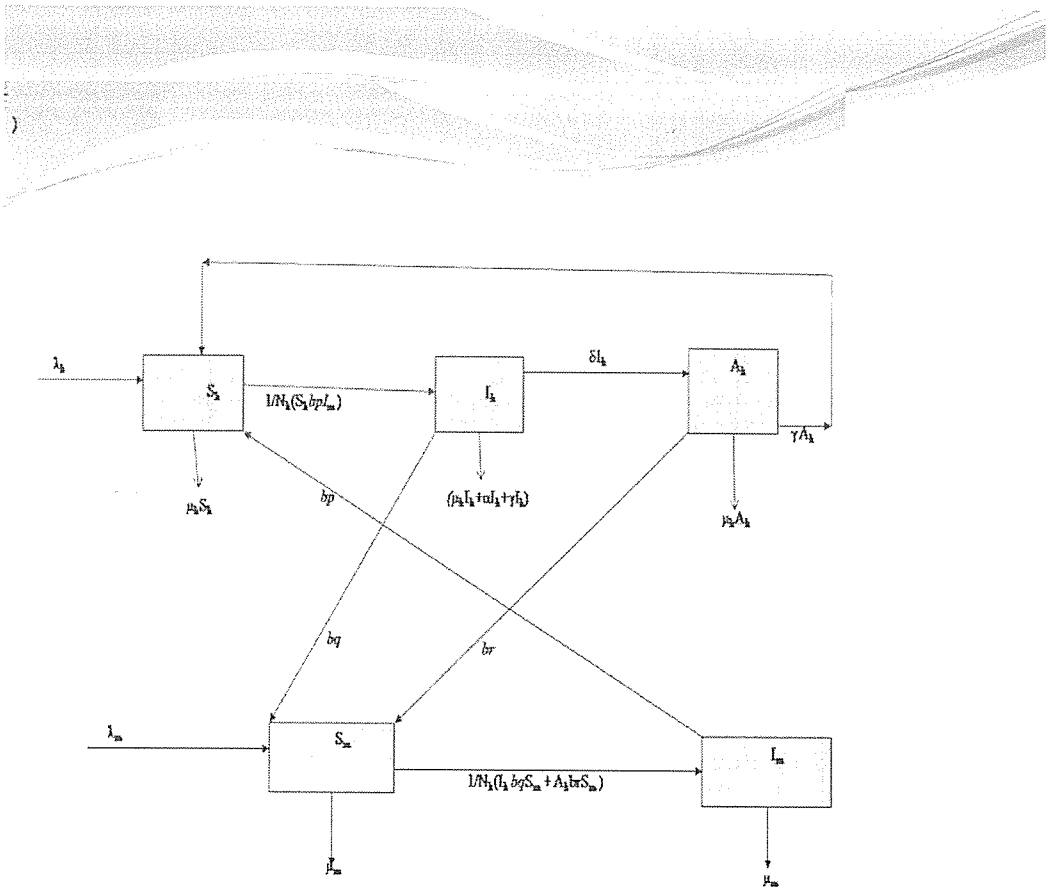

Figure 2: Compartmental diagram for transmission dynamics of malaria in mosquito and human population

Adopted from Ross and Ngwa Models, as in [2]

The transmission term $bpI_m\frac{S_h}{N_h}$ corresponds to frequency dependent infection of susceptible hosts by infectious mosquitoes, on infection, they move to infectious compartment.

The infected (γI_h) and asymptomatic (γA_h) hosts who recover become susceptible again.The terms $\mu_h S_h$, $\mu_h I_h$ and $\mu_h A_h$ represent per capita deaths of Susceptible, Infectious and Asymptomatic hosts respectively. The terms αI_h represents deaths due to infection, γI_h represents deaths after recovery while δI_h represents the number of infectious humans which gain immunity and move to asymptomatic compartment.

3.1.5 Model Equations

The above variables and parameters are illustrated in the model equations below:

$$\acute{S} = \frac{dS_h}{dt} = f(S_h) = \lambda_h - bpI_m\frac{S_h}{N_h} - \mu_h S_h + \gamma(I_h + A_h)$$

$$\acute{I} = \frac{dI_h}{dt} = f(I_h) = bpI_m\frac{S_h}{N_h} - I_h(\mu_h + \alpha + \delta + \gamma)$$

$$\acute{A} = \frac{dA_h}{dt} = f(A_h) = \delta I_h - A_h(\mu_h + \gamma)$$

$$\acute{S_m} = \frac{dS_m}{dt} = f(S_m) = \lambda_m - bqS_m\frac{I_h}{N_h} - brS_m\frac{A_h}{N_h} - \frac{\mu_m}{S_m}$$

$$\acute{I_m} = \frac{dI_m}{dt} = f(I_m) = bqS_m\frac{I_h}{N_h} + brS_m\frac{A_h}{N_h} - \mu_m I_m$$

3.2 The Basic Reproduction Number (R_o)

The quantity R_o is the measure of the average number of (new) secondary infections infected by a single infected vector or host. It is an important threshold parameter that plays a big role in the control of malaria infection. The reduction of the infection targets the parameters that brings the value of $R_o < 1$. i.e., the

disease free equilibrium becomes locally asymptotically stable and the disease dies out after some period of time.

To analyze the stability of equilibrium points, the basic reproduction number (R_o), for the model is computed.
It is an important parameter that shows whether an infection will either spread through the population or not.

Intuition suggest that malaria can spread in a population only if $R_0 > 1$ (epidemic). A disease free population is possible when $R_0 < 1$. However,these threshold conditions of R_0 may not hold for stochastic models. In such a case, the disease may go extinct even for $R_0 > 1$, depending on the magnitude of stochastic fluctuations around the endemic equilibrium state. R_o is obtained using the next-generation matrix technique as in [7], [37] and [56].

Let K represent the next generation matrix, F denote the matrix for new infection term and V, the matrix for transmission term.

Using the fact that $S_h = N_h - (A_h + I_h)$; and Since the human population is not constant due to disease induced death;

$$\acute{I_h} = \frac{dI_h}{dt} = f(I) = bpI_m\frac{S_h}{N_h} - I_h(\mu_h + \alpha + \delta + \gamma)$$
$$\acute{A_h} = \frac{dA_h}{dt} = f(A) = \delta I_h - A_h(\mu_h + \gamma)$$
$$\acute{I_m} = \frac{dI_m}{dt} = f(I_m) = bqS_m\frac{I_h}{N_h} + brS_m\frac{A_h}{N_h} - \mu_m I_m$$
$$\acute{N_h} = \frac{dN_h}{dt} = f(N_h) = \lambda_h - \mu_h N_h - \alpha I_h$$

$$\begin{bmatrix} \acute{I_h} \\ \acute{A_h} \\ \acute{I_m} \\ \acute{N_h} \end{bmatrix} = \begin{bmatrix} -(\mu_h + \alpha + \delta + \gamma) & 0 & bpI_m\frac{S_h}{N_h} & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{bqS_m}{N_h} & \frac{brS_m}{N_h} & -\mu_m & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix} \begin{bmatrix} I_h \\ A_h \\ I_m \\ N_h \end{bmatrix}$$

Equivalently,

$$\begin{bmatrix} \acute{I_h} \\ \acute{A_h} \\ \acute{I_m} \\ \acute{N_h} \end{bmatrix} = \left[\begin{bmatrix} 0 & 0 & \frac{bpS_h}{N_h} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{bqS_m}{N_h} & \frac{brS_m}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} - \begin{bmatrix} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & \mu_m & 0 \\ \alpha & 0 & 0 & \mu_h \end{bmatrix} \right] \begin{bmatrix} I_h \\ A_h \\ I_m \\ N_h \end{bmatrix}$$

Hence,

$$\begin{bmatrix} \acute{I_h} \\ \acute{A_h} \\ \acute{I_m} \\ \acute{N_h} \end{bmatrix} = [F - V] \begin{bmatrix} I_h \\ A_h \\ I_m \\ N_h \end{bmatrix}$$

where, [F - V] = J is the Jacobian matrix.
On linearizing;

$$F = \begin{bmatrix} 0 & 0 & \frac{bpS_h}{N_h} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{bqS_m}{N_h} & \frac{brS_m}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & \mu_m & 0 \\ \alpha & 0 & 0 & \mu_h \end{bmatrix}$$

Linearizing at disease free equilibrium, $E_o = (0, 0, 0, N_h^*)$.

$N_h^* = S_h^* = \dfrac{\lambda_h}{\mu_h}$; Similarly; $A_h^* = I_h^* = I_m^* = 0$. $N_m^* = S_m^* = \dfrac{\lambda_m}{\mu_m}$.

Therefore;

$$F = \begin{bmatrix} 0 & 0 & \frac{bpS_h^*}{N_h^*} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{bqS_m^*}{N_h^*} & \frac{brS_m^*}{N_h^*} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$F = \begin{bmatrix} 0 & 0 & bp & 0 \\ 0 & 0 & 0 & 0 \\ \frac{bq\lambda_m\mu_h}{\mu_m\lambda_h} & \frac{br\lambda_m\mu_h}{\mu_m\lambda_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & \mu_m & 0 \\ \alpha & 0 & 0 & \mu_h \end{bmatrix}$$

From Diekman and Heesterbeek as in [9], $R_o = \rho(K)$. At disease free equilibrium, $K = (FV^{-1})$ is the next generation matrix.

Theorem 1 *From* $s|F - V| < 0 \Leftrightarrow \rho(FV^{-1}) < 1$.
$K = (FV^{-1})$ *is the next generation matrix and its spectoral radius* $R_o = \rho(K) = \rho(FV^{-1})$ *is the basic reproduction number.*

Using Gauss Jordan method of matrix inversion to find V^{-1};

$$V^{-1} = \begin{bmatrix} \frac{1}{(\mu_h+\alpha+\delta+\gamma)} & 0 & 0 & 0 \\ \frac{\delta}{(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{1}{(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_m} & 0 \\ \frac{-\alpha}{\mu_h(\mu_h+\alpha+\delta+\gamma)} & 0 & 0 & \frac{1}{\mu_h} \end{bmatrix}$$

From $K = (FV^{-1})$;

$$K = \begin{bmatrix} 0 & 0 & bp & 0 \\ 0 & 0 & 0 & 0 \\ \frac{bq\lambda_m\mu_h}{\mu_m\lambda_h} & \frac{br\lambda_m\mu_h}{\mu_m\lambda_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{(\mu_h+\alpha+\delta+\gamma)} & 0 & 0 & 0 \\ \frac{\delta}{(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{1}{(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_m} & 0 \\ \frac{-\alpha}{\mu_h(\mu_h+\alpha+\delta+\gamma)} & 0 & 0 & \frac{1}{\mu_h} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{bp}{\mu_m} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{b\lambda_m\mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{br\lambda_m\mu_h}{\mu_m\lambda_h(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The characteristic Polynomial of K is $P(\lambda) = |K - \lambda I| = 0$

$$P(\lambda) = |K-\lambda I| = \begin{vmatrix} -\lambda & 0 & \frac{bp}{\mu_m} & 0 \\ 0 & -\lambda & 0 & 0 \\ \frac{b\lambda_m\mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{br\lambda_m\mu_h}{\mu_m\lambda_h(\mu_h+\gamma)} & -\lambda & 0 \\ 0 & 0 & 0 & -\lambda \end{vmatrix} = 0$$

Expanding along the forth row/column;

$$P(\lambda) = |K-\lambda I| = (-\lambda)\left[\begin{vmatrix} -\lambda & 0 & \frac{bp}{\mu_m} \\ 0 & -\lambda & 0 \\ \frac{b\lambda_m\mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{br\lambda_m\mu_h}{\mu_m\lambda_h(\mu_h+\gamma)} & -\lambda \end{vmatrix}\right] = 0$$

Expanding along the second row;

$$P(\lambda) = |K - \lambda I| = (-\lambda)\left[-\lambda\begin{vmatrix} -\lambda & \frac{bp}{\mu_m} \\ \frac{b\lambda_m\mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & -\lambda \end{vmatrix}\right] = 0$$

$$P(\lambda) = \lambda^2\left\{\lambda^2 - \frac{b^2p\lambda_m\mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m^2\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)}\right\} = 0$$

The eigen values of K are:

$\lambda^2 = 0$

$\Rightarrow \lambda_1 = \lambda_2 = 0$

$$\lambda_3 = -\left[\frac{b^2 p\lambda_m \mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)}\right]^{\frac{1}{2}}$$

$$\lambda_4 = \left[\frac{b^2 p\lambda_m \mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)}\right]^{\frac{1}{2}}$$

Since all parameters are positive,

$$\lambda_4 = \left[\frac{b^2 p\lambda_m \mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)}\right]^{\frac{1}{2}} > 0$$

But ρ is the spectoral radius of K, and considering the human and mosquito population (i.e., Squaring λ_4 above),

$$\lambda_4 = \left[\frac{b^2 p\lambda_m \mu_h[(\mu_h+\gamma)(q+\delta r)]}{\mu_m^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)}\right]$$

Substituting $N_h^* = \frac{\lambda_h}{\mu_h} and N_m^* = \frac{\lambda_m}{\mu_m}$;

$$\rho = R_o = \lambda_4 = \left[\frac{b^2 pN_m^*[(\mu_h+\gamma)(q+\delta r)]}{\mu_m N_h^*(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)}\right];$$

Since R_o is the dominant eigenvalue/maximum modulus eigenvalue (spectral radius) of the Jacobian of $K = (FV^{-1})$,

$R_o = Max|K-\lambda I| = Max|FV^{-1} - \lambda I| = Max\{|\lambda_1|, |\lambda_2|, |\lambda_3|, |\lambda_4|\}$.

Hence, the basic reproduction number $(R_o) = \lambda_4 = \left[\frac{b^2 pN_m^*[(\mu_h+\gamma)(q+\delta r)]}{\mu_m N_h^*(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)}\right]$.

Which can be reduced to $(R_o) = \lambda_4 = \frac{b^2 pN_m^*[q+\delta * r]}{\mu_m N_h^*(\mu_h+\alpha+\delta+\gamma)}$.

3.3 Model Analysis at Disease Free Equilibrium (DFE)

In this section, the model is qualitatively analyzed to investigate the existence and stability of its associated equilibria.
Human population varies with time due to disease induced death.

$\acute{N_h} = \acute{S_h} + \acute{I_h} + \acute{A_h} = \frac{dS}{dt} + \frac{dI}{dt} + \frac{dA}{dt} \Longleftrightarrow N_h - (S_h + I_h + A_h) = 0$

Substituting $\acute{S_h}$, $\acute{I_h}$ and $\acute{A_h}$,

$\acute{N_h} = \lambda_h - bpI_m\frac{S_h}{N_h} - \mu_h S_h + \gamma(I_h + A_h) + bpI_m\frac{S_h}{N_h} - I_h(\mu_h + \alpha + \delta + \gamma) + \delta I_h - A_h(\mu_h + \gamma)$

Writing in the form $\acute{N_h} = \frac{dN_h}{dt} = f(N_h)$,

$\acute{N_h} = \lambda_h - \mu_h(S_h + I_h + A_h) - \alpha I_h$

But $(S_h + I_h + A_h) = N_h$

Substituting N_h above,

$\acute{N_h} = \lambda_h - \mu_h N_h - \alpha I_h$

Hence $\acute{N_h}(t) = f(N_h) = \lambda_h - \mu_h N_h - \alpha I_h$

The above equation is autonomous because N_h is a function of the independent variable t and f(N_h) does not depend on t explicitly; but the only t dependence is through $N_h = N_h(t)$
An indication that the human population varies with time [40].

All state variables and model parameters are considered to be positive at time t = 0. In absence of the disease, $I_h = 0$ and $N_h = \frac{\lambda_h}{\mu_h}$. Meaning that the human population is constant. From which;

$\frac{dN_h}{dt} = (\lambda_h - \mu_h N_h) = (\lambda - \mu N) \Longrightarrow \frac{dN_h}{dt} + \mu_h N_h = \lambda_h$

Using the method of integrating factor to solve the above equation, $e^{\int \mu_h dt} = e^{\mu_h t}$

$\Longleftrightarrow \frac{dN_h}{dt}e^{\mu_h t} + \mu_h N_h e^{\mu_h t} = \lambda_h e^{\mu_h t}$

$= \frac{d}{dt}[(N_h)e^{\mu_h t}] = \lambda_h e^{\mu_h t}$

$\Longrightarrow d[N_h e^{\mu_h t}] = \lambda_h e^{\mu_h t} dt$

$$\int d(N_h e^{\mu_h t}) = \int (\lambda_h e^{\mu_h t}) dt$$

$$\int d(N_h e^{\mu_h t}) = \lambda_h \int e^{\mu_h t} dt$$

$\Longrightarrow N_h e^{\mu_h t} = \frac{\lambda_h}{\mu_h} e^{\mu_h t} + c_1$

Dividing through by $e^{\mu_h t}$; $N_h(t) = \frac{\lambda_h}{\mu_h} + c_1 e^{-\mu_h t}$.

This is the human population at disease free equilibrium.

As t $\rightarrow$ 0 $N_h(0) = \frac{\lambda_h}{\mu_h} + c_1$. c_1 is a constant of integration. But

$$\lim_{t \to \infty} N_h(t) = \frac{\lambda_h}{\mu_h}$$

It is the carrying capacity of human population and remains constant in the absence of the disease.

Using the similar approach, $N_m(t) = \frac{\lambda_m}{\mu_m} + c_2 e^{-\mu_m t}$

It is also the mosquito population at disease free equilibrium.

As t $\rightarrow$ 0 $N_m(0) = \frac{\lambda_m}{\mu_m} + c_2$. c_2 is a constant of integration. But

$$\lim_{t \to \infty} N_m(t) = \frac{\lambda_m}{\mu_m}$$

Called the carrying capacity of mosquito population that is also constant in the absence of malaria.

Theorem 2 *(Barrier theorem)*

A compact positively invariant set

$T = \{(I_h, A_h, I_m, N_h, N_m | 0 \leq A_h \leq I_h \leq N_h \leq \frac{\lambda_h}{\mu_h}, 0 \leq I_m \leq N_m \leq \frac{\lambda_m}{\mu_m})\}$

is a positively invariant compact set for the system. Moreover T is a global attractor on the non-negative orthant ${R_+}^5$ as in [15]. Since the ODE is Lipschitz, the vector field induced by the system is either tangent or entering T on its boundary of T .

Hence, the following are implications of theorem 1

- $N_m = 0$, $\acute{N_m} > 0$ *and* $N_m \geq \frac{\lambda_m}{\mu_m}$, $\acute{N_m} \leq 0$;
- $I_h = 0$ *and* $\acute{I_m} \geq 0$;

- $A_h = 0$ *and* $\acute{A}_h \geq 0$;
- *Since* $I_m \leq N_m$, $I_m = 0$, *then,* $\acute{I_m} \geq N_m$
- $N_h = 0$, $\acute{N_h} > 0$ *and* $N_h \geq \frac{\lambda_h}{\mu_h}$; $\acute{N_h} \leq 0$
- *When* $N_m = I_m$ *and* $N_m \geq \frac{\lambda_m}{\mu_m}$,

  then, $\acute{N_m} - \acute{I_m} = \lambda_m - 2\mu_m N_m \leq 0$
- *When* $N_h = (I_h + A_h)$ *and* $N_h \geq \frac{\lambda_h}{\mu_h}$,

  then, $\acute{N_h} - (\acute{I_h} + \acute{A_h}) = \lambda_h - (2\mu_h + 2\alpha + \gamma)N_h \leq 0$

This proves that all trajectories tends to T *and are forward bounded. The demographic equilibria are given by*
$N_h^* \geq \frac{\lambda_h}{\mu_h}$ *and* $N_m^* \geq \frac{\lambda_m}{\mu_m}$

3.3.1 Disease Free Equilibrium

They are also called fixed points. These are values of N_h for which there is no epidemic. i.e., when $\acute{N_h}(t) = \frac{dN_h}{dt} = f(N_h) = 0$ Disease-free equilibrium points are steady-state solutions where there is no malaria infection. From $\acute{N_h}(t) = \lambda_h - \mu_h N_h - \alpha I_h$,

Equating to zero, $\acute{N_h} = \lambda_h - \mu_h N_h - \alpha I_h = 0$

i.e., Steady state solutions occur when $\frac{d\acute{N_h}}{dt} = 0$

At disease free equilibrium; $I_h^* = A_h^* = I_m = 0$. This gives $N_h^* = \frac{\lambda_h}{\mu_h}$. Similary, $N_m^* = \frac{\lambda_m}{\mu_m}$. Hence, the system of equations give the steady states $E_o = (I_h, A_h, I_m, N_h) = (0, 0, 0, \frac{\lambda_h}{\mu_h})$.

From $\acute{N_h} = \lambda_h - \mu_h N_h - \alpha I_h = 0$

and $A_h = I_h = I_m = 0$

$\implies \acute{N_h} = (\lambda_h - \mu_h N_h) = 0 \implies (\lambda_h - \mu_h N_h) = 0$

Hence $N_h^* = \frac{\lambda_h}{\mu_h}$ for $\mu_h \neq 0$ is an equilibrium point. Meaning that the ODEs at disease free equilibrium ≥ 0 hence the compartmental model is well-posed.

3.4 Establishing and Analyzing Stability Conditions

In the absence of the disease in the population,

$I_h^* = A_h^* = I_m^* = 0$,

$N_h = \frac{\lambda_h}{\mu_h}$.

From f(N_h) = λ_h - $\mu_h N_h$,

For $\frac{\lambda_h}{\mu_h} < 0$, eg $(\frac{-\lambda_h}{\mu_h})$

$f(N_h) = \lambda_h + \frac{\mu_h}{\mu_h} * \lambda_h = 2\lambda_h > 0$

For $\frac{\lambda_h}{\mu_h} > 0$, eg $(\frac{3\lambda_h}{\mu_h})$

$f(N_h) = \lambda_h - \frac{\mu_h}{\mu_h} * 3\lambda_h = -2\lambda_h < 0$

Using the knowledge of linear stability analysis and phase portrait, the point $\frac{\lambda_h}{\mu_h}$ is asymptotically stable meaning that malaria infection will not grow in the population.

Hence, the disease free equilibrium is set at $E_o = (0, 0, 0, \frac{\lambda_h}{\mu_h})$

Also, from $\frac{dN_h}{dt} = f(N_h) = \lambda_h - \mu_h N_h$; λ_h and μ_h are constants, $\acute{f}(N_h) = -\mu_h < 0$; (Stable disease free equilibrium state).

3.4.1 Local Stability Analysis

Local stability analysis is examined at disease free equilibrium using eigenvalues($\lambda_s < 0$), trace(< 0) and determinant(> 0) of the Jacobian matrix as in [45] or using *Routh-Hurwitz criterion.*

Let $\bar{\gamma} = (\mu_h + \alpha + \delta + \gamma)$ and consider the following reduced form of the system of equations arranged to have the infection classes come first;

$\acute{I}_h = \frac{dI_h}{dt} = (-\bar{\gamma})I_h + bpI_m\frac{S_h}{N_h}$

$\acute{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma)A_h$

$\acute{I}_m = \frac{dI_m}{dt} = bqS_m\frac{I_h}{N_h} + brS_m\frac{A_h}{N_h} - \mu_m I_m$

$\acute{N}_h = \frac{dN_h}{dt} = -\alpha I_h + \lambda_h - \mu_h N_h$

Hence,
$\acute{I}_h = \frac{dI_h}{dt} = -\bar{\gamma} I_h + bpI_m \frac{S_h}{N_h}$
$\acute{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma) A_h$
$\acute{I}_m = \frac{dI_m}{dt} = bqS_m \frac{I_h}{N_h} + brS_m \frac{A_h}{N_h} - \mu_m I_m$
$\acute{N}_h = \frac{dN_h}{dt} = -\alpha I_h + \lambda_h - \mu_h N_h$
Linearizing the above system of differential equations;

$$J = \begin{bmatrix} -(\bar{\gamma}) & 0 & \frac{bpS_h}{N_h} & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{bqS_m}{N_h} & \frac{brS_m}{N_h} & -\mu_m & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix}$$

The Jacobian at the disease free equilibrium is given by:

$$J_{DFE} = \begin{bmatrix} -(\bar{\gamma}) & 0 & bp & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{bq\lambda_m \mu_h}{\mu_m \lambda_h} & \frac{br\lambda_m \mu_h}{\mu_m \lambda_h} & -\mu_m & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix}$$

with the characteristic polynomial P (λ) at disease free equilibrium given by P $(\lambda) = |J_{DFE} - \lambda I| = 0$
Hence,

$$\begin{vmatrix} -(\bar{\gamma} + \lambda) & 0 & bp & 0 \\ \delta & -(\mu_h + \gamma + \lambda) & 0 & 0 \\ \frac{bq\lambda_m \mu_h}{\mu_m \lambda_h} & \frac{br\lambda_m \mu_h}{\mu_m \lambda_h} & -(\mu_m + \lambda) & 0 \\ -\alpha & 0 & 0 & -(\mu_h + \lambda) \end{vmatrix} = 0$$

Expanding along the forth column;

$$-(\mu_h + \lambda) \begin{vmatrix} -(\bar{\gamma} + \lambda) & 0 & bp \\ \delta & -(\mu_h + \gamma + \lambda) & 0 \\ \frac{bq\lambda_m \mu_h}{\mu_m \lambda_h} & \frac{br\lambda_m \mu_h}{\mu_m \lambda_h} & -(\mu_m + \lambda) \end{vmatrix} = 0$$

Giving $-(\mu_h + \lambda) = 0 \Rightarrow \lambda_1 = -\mu_m$
Or

$$P(\lambda) = \begin{vmatrix} -(\bar{\gamma} + \lambda) & 0 & bp \\ \delta & -(\mu_h + \gamma + \lambda) & 0 \\ \frac{bq\lambda_m\mu_h}{\mu_m\lambda_h} & \frac{br\lambda_m\mu_h}{\mu_m\lambda_h} & -(\mu_m + \lambda) \end{vmatrix} = 0$$

From above,

$$P(\lambda) = -(\bar{\gamma}+\lambda)\begin{vmatrix} -(\mu_h + \gamma + \lambda) & 0 \\ \frac{br\lambda_m\mu_h}{\mu_m\lambda_h} & -(\mu_m + \lambda) \end{vmatrix} + (bp)\begin{vmatrix} \delta & -(\mu_h + \gamma + \lambda) \\ \frac{bq\lambda_m\mu_h}{\mu_m\lambda_h} & \frac{br\lambda_m\mu_h}{\mu_m\lambda_h} \end{vmatrix} = 0$$

$\Longrightarrow [-(\bar{\gamma}+\lambda)(\mu_h+\gamma+\lambda)(\mu_m+\lambda)] + (bp)[\delta][\frac{br\lambda_m\mu_h}{\mu_m\lambda_h}] - [(\frac{bq\lambda_m\mu_h}{\mu_m\lambda_h})(-(\mu_h + \gamma + \lambda))] = 0$

On expansion,

$P(\lambda) = \lambda^3 + \lambda^2[2(\mu_h + \gamma) + \alpha + \delta + \mu_m] + \lambda\{\bar{\gamma}(\mu_h + \gamma + \mu_m) + (\mu_h+\gamma)\mu_m - [\frac{(bpq\lambda_m\mu_h)}{(\mu_m\lambda_h)}]\} + \{(\mu_h+\gamma)\mu_m\bar{\gamma} - \frac{(b^2p\lambda_m\mu_h[q(\mu_h+\gamma)+r\delta]}{\mu_m\mu_h})\} = 0$

Which is equivalent to the polynomial $b_o\lambda^3 + b_1\lambda^2 + b_2\lambda^3 + b_3 = 0$

Where

$b_o = 1 > 0$

$b_1 = 2(\mu_h + \gamma) + \alpha + \delta + \mu_m > 0$

$b_2 = \bar{\gamma}(\mu_h + \gamma + \mu_m) + (\mu_h + \gamma)\mu_m - \frac{b^2pq\lambda_m\mu_h}{\mu_m\lambda_h}$

$= \bar{\gamma}(\mu_h+\gamma) + (\mu_h+\gamma)\mu_m + \bar{\gamma}\mu_m - \frac{(b^2pq\lambda_m\mu_h)(\mu_h+\gamma)}{(\mu_m\lambda_h)(\mu_h+\gamma)} - \frac{(b^2pr\lambda_m\mu_h)(\mu_h+\gamma)}{(\mu_m\lambda_h)(\mu_h+\gamma)} + \frac{(b^2pr\lambda_m\mu_h)(\mu_h+\gamma)}{(\mu_m\lambda_h)(\mu_h+\gamma)}$

$= (\mu_h + \gamma)(\mu_m + \bar{\gamma}) + \frac{(b^2pr\lambda_m\mu_h\delta}{\mu_m\lambda_h(\mu_h+\gamma)} + \bar{\gamma}\mu_m\left[1 - \frac{b^2p\lambda_m\mu_h[(\mu_h+\gamma)q+\delta r]}{\mu_m^2\lambda_h(\mu_h+\gamma)\bar{\gamma}}\right]$

$= (\mu_h + \gamma)(\mu_m + \bar{\gamma}) + \frac{(b^2pr\lambda_m\mu_h\delta}{\mu_m\lambda_h(\mu_h+\gamma)} + (\mu_h + \alpha + \delta + \gamma)\mu_m[1 - R_o]$

The above equation is positive when $(\mu_h+\alpha+\delta+\gamma)\mu_m[1-R_o] > 0$ i.e., iff $(R_o) \leq 1$

$p_3 = (\mu_h + \gamma)\mu_m\bar{\gamma} - \frac{(b^2pr\lambda_m\mu_h)[q(\mu_h+\gamma)+\delta r]}{\mu_m\lambda_h}$

$$= (\mu_h + \gamma)\mu_m\bar{\gamma}\left[1 - \frac{b^2 p\lambda_m\mu_h[(\mu_h+\gamma)q+\delta r]}{\mu_m^2\lambda_h(\mu_h+\gamma)\bar{\gamma}}\right]$$
$$= (\mu_h + \gamma)\mu_m\bar{\gamma}[1 - R_o] > 0 \qquad iff \qquad R_o \leq 1$$

Remark:
Solving the above characteristic polynomial for eigenvalues is tedious. The *Routh-Hurwitz criterion* is used to determine whether all roots have negative real parts and thus establish the stability of the system without solving the characteristic equation itself as in theorem 3..

Theorem 3 *(The Routh-Hurwitz criterion): The roots of the characteristic equation have negative real parts iff all the principal diagonal minors of the Hurwitz matrix are positive provided that* $b_o > 0$ *as in [43].*

The above equation is of order three.

The stability criterion is defined by the inequalities: $b_1 > 0$, $b_2 > 0$, $b_3 > 0$ *and* $(b_1b_2 - b_0b_3) > 0$

Hence;

$$b_1b_2 - b_0b_3 = [2(\mu_h + \gamma) + \alpha + \delta + \mu_m]\left[(\mu_h + \gamma)(\mu_m + \bar{\gamma}) + \frac{b^2 pr\lambda_m\mu_h\delta}{\mu_m\lambda_h(\mu_h+\gamma)} + \bar{\gamma}\mu_m[1 - R_o]\right] - \left[(\mu_h + \gamma)\mu_m\bar{\gamma}[1 - R_o]\right]$$

$$= [2(\mu_h + \gamma) + \alpha + \delta + \mu_m]\left[(\mu_h + \gamma)(\mu_m + \bar{\gamma}) + \frac{b^2 pr\lambda_m\mu_h\delta}{\mu_m\lambda_h(\mu_h+\gamma)}\right] + [2(\mu_h + \gamma) + \alpha + \delta + \mu_m]\bar{\gamma}\mu_m[1 - R_o] - \left[[\mu_h + \gamma]\bar{\gamma}\mu_m[1 - R_o]\right]$$

$$= [2(\mu_h + \gamma) + \alpha + \delta + \mu_m]\left[(\mu_h + \gamma)(\mu_m + \bar{\gamma}) + \frac{b^2 pr\lambda_m\mu_h\delta}{\mu_m\lambda_h(\mu_h+\gamma)}\right] + \bar{\gamma}\mu_m[1 - R_o][\mu_m + \bar{\gamma}]$$

The above equation is positive *iff* $R_o \leq 1$.

Since all coefficients are positive, $(b_1 b_2 - b_0 b_3) > 0$ *iff* $R_o \leq 1$.

Hence from *Routh-Hurwitz criterion*, all the real parts of eigen values of the Routh-Hurwitz matrix are negative showing that the system is stable.

Theorem 4 *The disease free equilibrium, E_o is locally asymptotically stable if $R_o \leq 1$, and becomes unstable if $R_o > 1$ [56]*

The quantity R_o is the measure of the average number of secondary infections infected by a single infected vector or host. It is an important threshold parameter that plays a big role in the control of malaria infection. The reduction of the infection targets the parameters that brings the value of $R_o < 1$. i.e., the disease free equilibrium becomes locally asymptotically stable and the disease dies out after some period of time.

3.4.2 Global Stability Analysis

This is established using theorem 5. i.e.,

Theorem 5 *The disease free equilibrium, $E_o = (0, 0, 0, \frac{\lambda_h}{\mu_h})$ of the system of differential equations is globally asymptotically stable if $R_o \leq 1$ and unstable if $R_o > 1$ as in [56].*

Considering the Lyapunov function of system of equations,

$L = \mu_m I_h(\mu_h + \gamma) + \frac{b^2 pr\lambda_m \mu_h A_h}{\mu_m \lambda_h} + bpI_m(\mu_h + \gamma)$

$\acute{L} = \mu_m \acute{I_h}(\mu_h + \gamma) + \frac{b^2 pr\lambda_m \mu_h \acute{A_h}}{\mu_m \lambda_h} + bp\acute{I_m}(\mu_h + \gamma)$

$= \mu_m(\mu_h + \gamma)\left[\frac{bpS_h I_m}{N_h} - \bar{\gamma} I_h\right] + \frac{b^2 pr\lambda_m}{\mu_m \lambda_h}\left[\delta I_h - A_h(\mu_h + \gamma)\right]$

$+ bp(\mu_h + \gamma)\left[\frac{brA_h S_m}{N_h} + \frac{bqI_h S_m}{N_h} - \mu_m I_m\right]$

$$\leq \mu_m(\mu_h+\gamma)\left[bpI_m - \bar{\gamma}I_h + \left[\frac{b^2pr\lambda_m\mu_h}{\mu_m\lambda_h} - A_h(\mu_h+\gamma)\right]\right.$$

$$+ bp(\mu_h+\gamma)\left[\frac{bq\lambda_m\mu_h I_h}{\mu_m\lambda_h} - \mu_m I_m\right]$$

$$= I_h\left[\frac{b^2pq\lambda_m\mu_h(\mu_h+\gamma)}{\mu_m\lambda - h} + \frac{b^2pr\delta\lambda_m\mu_h}{\mu_m\lambda_h - \mu_m\bar{\gamma}}(\mu_h+\gamma)\right]$$

$$+ A_h\left[\frac{b^2pr\lambda_m\mu_h(\mu_h+\gamma)}{\mu_m\lambda_h} - \frac{b^2pr\lambda_m\mu_h(\mu_h+\gamma)}{\mu_m\lambda_h}\right]$$

$$+ I_m\left[bp\mu_m(\mu_h+\gamma) - bp\mu_m(\mu_h+\gamma)\right]$$

$$= I_h\left[\frac{b^2pq\lambda_m\mu_h[q(\mu_h+\gamma)+r\delta]}{\mu_m\lambda_h} - \mu_m\bar{\gamma}(\mu_h+\gamma)\right] + 0A_h + 0I_m$$

$$= I_h\left[\frac{b^2pq\lambda_m\mu_h[q(\mu_h+\gamma)+r\delta]}{\mu_m\lambda_h} - \mu_m\bar{\gamma}(\mu_h+\gamma)\right]$$

$$= \mu_m\bar{\gamma}I_h(\mu_h+\gamma)\left[\frac{b^2pq\lambda_m\mu_h[q(\mu_h+\gamma)+r\delta]}{\mu_m^2\lambda_h\bar{\gamma}(\mu_h+\gamma)} - 1\right]$$

$$= \mu_m\bar{\gamma}I_h(\mu_h+\gamma)[R_o - 1] \leq 0 \text{ iff } R_o \leq 1.$$

Hence, $\acute{L} \leq 0$ if $R_o \leq 1$; $\acute{L} = 0$ iff $R_o = 1$; $I_h = A_h = I_m = 0$

If $R_o > 1$, $\acute{L} > 0$ when S_h(t) and S_m(t) is sufficiently close to $\frac{\lambda_h}{\mu_h}$ and $\frac{\lambda_m}{\mu_m}$ respectively except when $I_h = A_h = I_m = 0$.

The largest compact invariant set $D = \{I_h^*, A_h^*, I_m^*, N_h^*, N_m^* \in D : \acute{L} = 0\}$, When $R_o \leq 1$ is a singleton E_o.

On the boundary when $I_h = A_h = I_m = 0$, $\acute{N_h}(t) = \lambda_h - \mu_h N_h$; $\acute{N_m}(t) = \lambda_m - \mu_m N_m$ and $N_h(t) \to \frac{\lambda_h}{\mu_h}$, $N_m(t) \to \frac{\lambda_m}{\mu_m}$ as $t \to \infty$.

Theorem 6 *Lasalle Lyapunov*

Every solution that starts in the region D approaches E_o as $t \to \infty$. when $R_o \leq 1$ as in [36]. Hence, the DFE is globally asymptotically stable.

Chapter 4

4 Numerical Simulations

4.1 Introduction

In this chapter, numerical simulations of the model is done to demonstrate and analyze the dynamics of the system of the model and the qualitative results obtained in chapter three using MATLAB R2010a (ODE45).

4.2 Model Parameter Values

Parameter	Value	Reference
λ_h	0.00011997 Biths/Person/day	[6]
λ_m	0.071@day	[23]
μ_h	0.00002929 Deaths/Person/day	[6]
μ_m	0.40@day	Estimated
b	0.40	[8]
p	0.066	Estimated
q	0.42	Estimated
r	0.55	Estimated
δ_h	0.143	[45]
γ_h	0.011	Estimated
α	0.00022466 Deaths/Person/day	[66][68]
N_h	37,101,745	[6]
N_m	15000	Estimated
$I_h(0) = 100$	213308	[57],[10]
$A_h(0)$	1000	Estimated
$S_h(0)$	245,873	[27]
$I_m(0)$	1000	Estimated
$S_m(0)$	9000	Estimated

Table 7: Parameter estimates for malaria model

Parameter values were obtained from epidemiological and demographic literature, the district health personnel, Health Management and Information System (HMIS) housed at the resource centre; Ministry of Health Headquarters, Kampala, while other parameters were estimated.

Substituting parameter values in the model equations,

$\acute{S} = \frac{dS_h}{dt} = f(S_h) = \lambda_h - bpI_m\frac{S_h}{N_h} - \mu_h S_h + \gamma(I_h + A_h)$

$= 0.00011997 - (0.0264)\frac{I_m S_h}{N_h} - (0.00002929)S_h + 0.011(I_h + A_h)$

$\acute{I} = \frac{dI_h}{dt} = f(I_h) = bpI_m\frac{S_h}{N_h} - I_h(\mu_h + \alpha + \delta + \gamma)$

$= 0.0264\frac{S_h}{N_h} - I_h(0.15425395)$

$\acute{A} = \frac{dA_h}{dt} = f(A_h) = \delta I_h - A_h(\mu_h + \gamma)$

$= (0.143)I_h - (0.01102929)A_h$

$\acute{S_m} = \frac{dS_m}{dt} = f(S_m) = \lambda_m - bqS_m\frac{I_h}{N_h} - brS_m\frac{A_h}{N_h} - \frac{\mu_m}{S_m}$

$= 0.071 - (0.168)\frac{S_m I_h}{N_h} - (0.22)\frac{S_m A_h}{N_h} - \frac{0.40}{S_m}$

$\acute{I_m} = \frac{dI_m}{dt} = f(I_m) = bqS_m\frac{I_h}{N_h} + brS_m\frac{A_h}{N_h} - \mu_m I_m$

$= (0.168)\frac{S_m I_h}{N_h} + (0.22)\frac{S_m A_h}{N_h} - (0.40)I_m$

The initial conditions for $S_h(0)$, $I_h(0)$, $A_h(0)$, $S_m(0)$ and $I_m(0)$ are shown in the table above.

It is evident that when the above variables are substituted in the equation $R_o = \frac{b^2 pN_m^*[q+\delta*r]}{\mu_m N_h^*(\mu_h+\alpha+\delta+\gamma)}$,

$R_o = \frac{(0.4)^2*(0.066)(15000)[0.42+0.143*0.55]}{(0.4)(37101745)(0.00002929+0.00022466+0.143+0.011)}$,

$R_o = \frac{(0.16)*(0.066)(15000)(0.49865)}{(0.4)(37101745)(0.15425395)}$,

$R_o = \frac{(7.898616)}{(2289236.287)}$,

$R_o = 0.00000345 < 1$,

In conclusion, the basic reproduction number for Butaleja district is less than one since less people die from malaria meaning that malaria can be eliminated from the district considering the recommendations and control measures put in place.

4.3 Numerical Simulation Results

Model simulations illustrating the outcome of interaction between Susceptible (S_h), Infected (I_h) and Asymptomatic (A_h) humans; Susceptible (S_m) and Infected (I_m) mosquitoes; against time were done using parameter values in Table.7 and MATLAB 7.5.0 (R2007b) Package; the language of technical computing. These figures were exported to Latex (WinEdt) and interpreted.

4.3.1 The effect of varying b on R_o

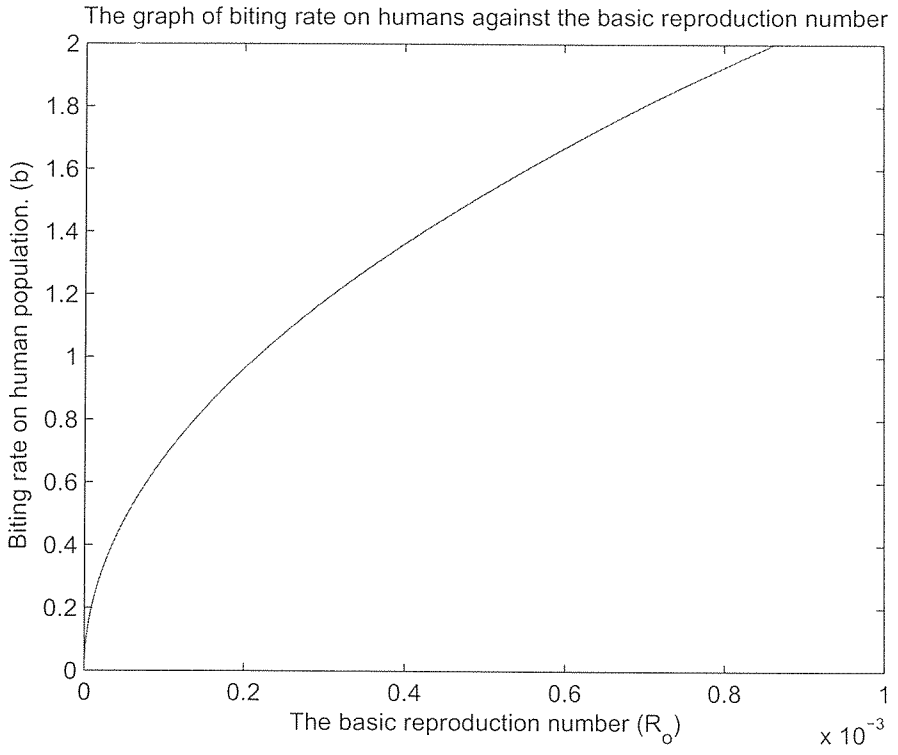

Figure 3: The effect of varying b on R_o

From **figure 3** above, increase in mosquito biting rate on humans **(b)** increases the basic reproduction number (R_o) other parameters being held constant. The converse is also true; implying that reducing **b** can be used as a control strategy for malaria. The parameter value for **b is 0.40.** To maintain $R_o < 1$, **b** has to be reduced by more than 40% as supported by [67] and [41].

4.3.2 The effect of varying b on S_h

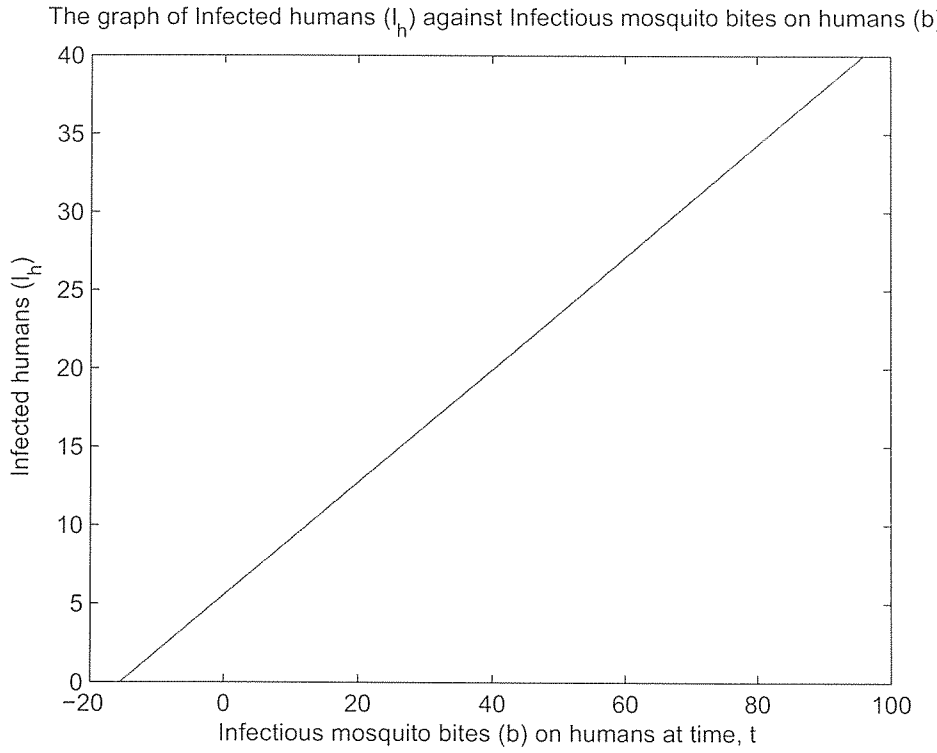

Figure 4: The effect of varying **b** on S_h

From **figure 4**, there is a strong positive correlation between infected mosquito bites and the number of infected humans in the same locality. As the number of infected mosquito bites on humans (**b**) increase, the number of infected humans increases too resulting into an increase in R_o holding other parameters constant. The converse is true; thus, reducing **b** is paramount in controlling the transmission of malaria to Susceptible humans.

4.3.3 The effect of varying p on S_h

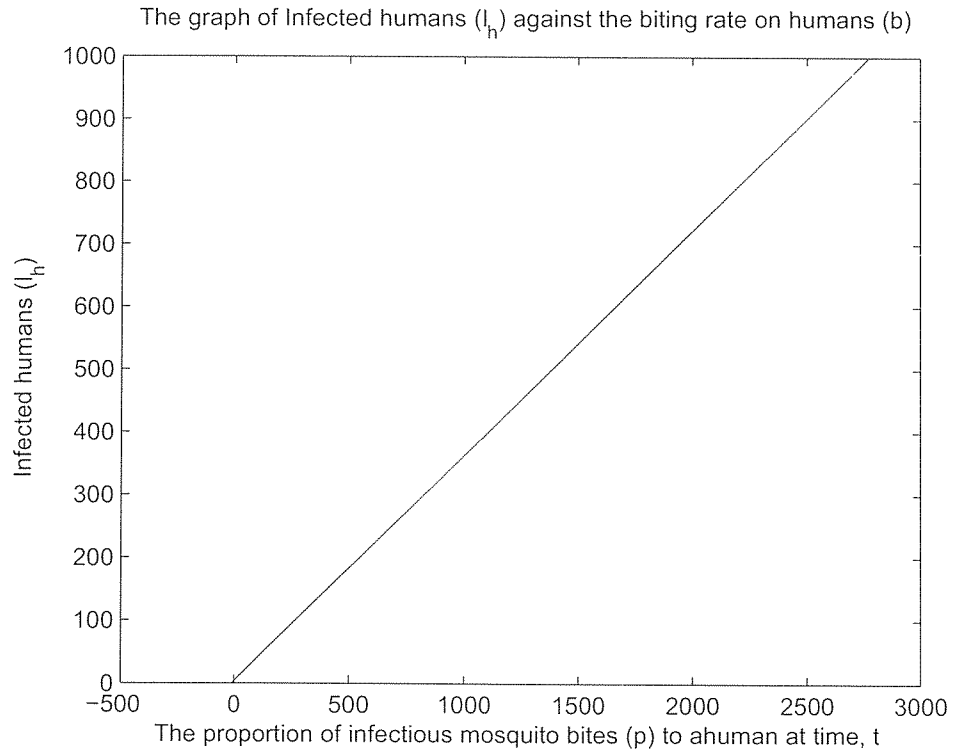

Figure 5: The effect of varying **p** on S_h

From **figure 5**, there is a strong relationship between the percentage of infected mosquito bites (p) and the number of infected humans. As the proportion of infected mosquito bites on humans (p) increase, the number of infected humans increase resulting into an increase in R_o holding other parameters constant. Reducing p by more than 7% can reduce the transmission of malaria in the district.

4.3.4 The effect of A_h with time

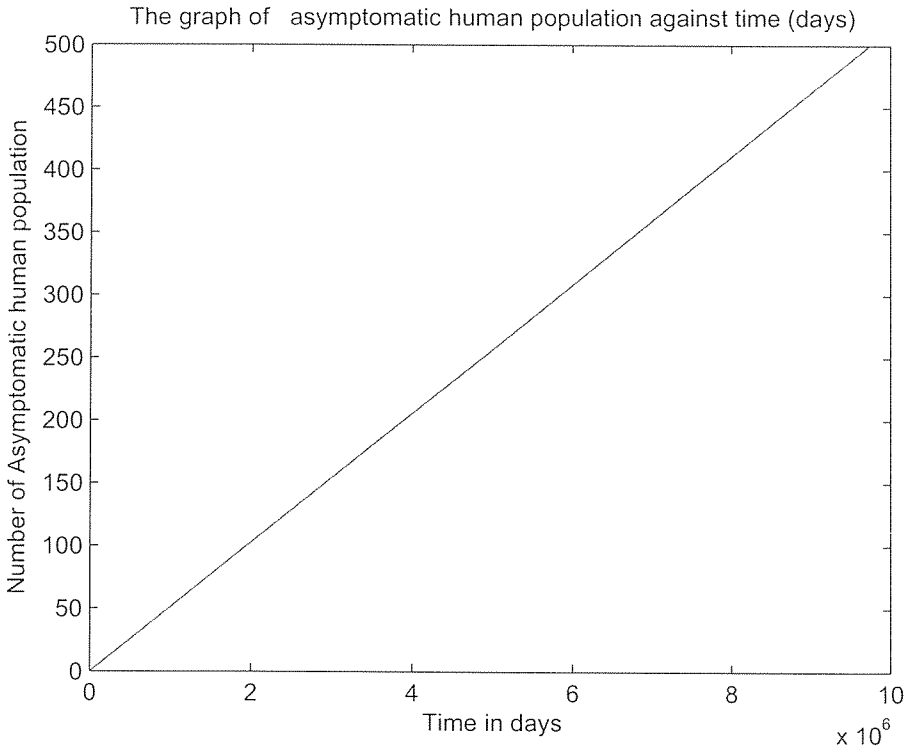

Figure 6: The effect of A_h with time

The number of asymptomatic humans increases with time and in turn affects the R_o unless control measures are put in place.

4.3.5 The effect of I_m on S_h

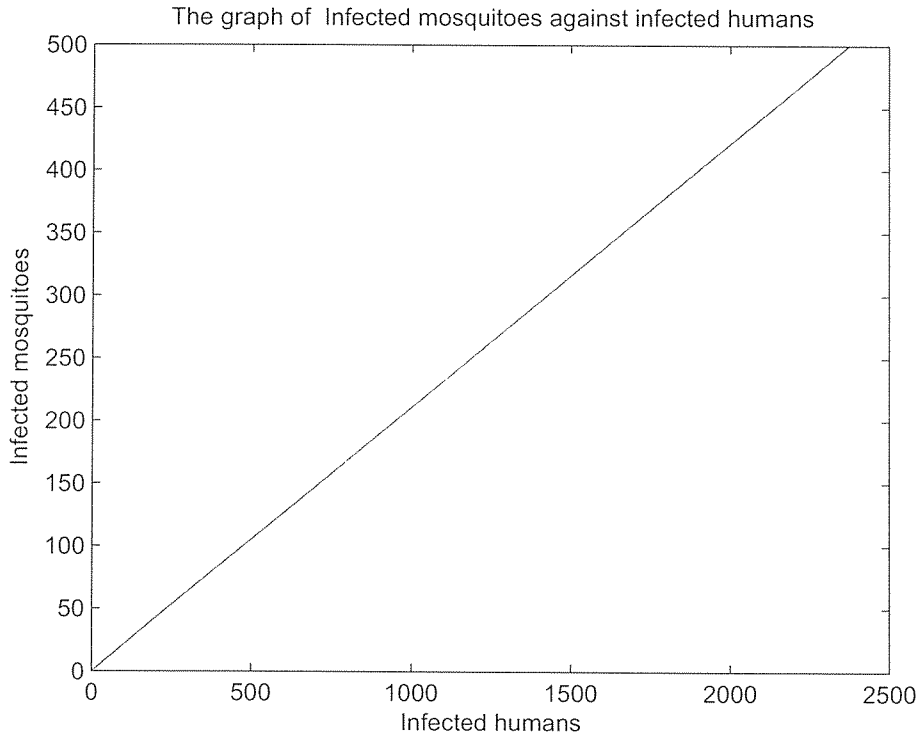

Figure 7: The effect of I_m on S_h

From **figure 7** above, it is clear that there is a positive linear relationship between the number of infected mosquitoes and infected humans in the same locality. Unless infected and asymptomatic humans are treated, Susceptible mosquitoes will continue being infected by infected and asymptomatic humans in the same locality given the assumption that there is free interaction between the two groups. The susceptible mosquitoes which later become infected will transmit malaria to susceptible humans and the circle continues.

Chapter 5

5 Discussion, Conclusion, Recommendations

5.1 Introduction

In this chapter, outcomes of research are discussed, conclusions made and recommendations as well as areas for further research have been outlined.

5.2 Discussion

In this study, a mathematical model was proposed for the transmission dynamics of malaria between human and mosquito population in which the reservoir of the Susceptible human hosts (S_h) is re-filled by individuals who join the Susceptible population by birth (λ_h) and those that are Asymptomatic (A_h) after losing their immunity to the disease.

The model was then reformulated in terms of the total number of classes of the respective populations. Model analysis and simulations were carried out. The disease free equilibrium was obtained and its stability analyzed.

It was established that when the basic reproduction number $R_o \leq 1$, the disease free equilibrium is globally asymptotically stable so that the disease always dies out. When $R_o > 1$, the disease free equilibrium points become unstable.

From simulation results above, as the number of infected mosquitoes increase, the number of infected humans increase concurrently; an indication that there is a strong positive correlation between the number of infected mosquitoes and infected humans in the same locality. This is because increase in the number of infected mosquitoes (q and r) increases the number of infectious bites to humans (p) at time t holding other parameters constant.

Therefore, control measures that aim at lowering the infectivity of infected mosquito and human populations; for instance, treatment of asymptomatic humans and eradicating mosquito population would contribute greatly to the lowering of the transmission of malaria in Butaleja district.

5.3 Conclusion

Malaria was modeled as a 4-dimensional system of ordinary differential equations. The existence and uniqueness of a domain was shown where the model is epidemiologically and mathematically well-posed. The model was analyzed for the disease free equilibrium since malaria mortality rate for Butaleja is low.

The basic reproduction number was defined in terms of model parameters. It was established that for the basic reproduction number, $R_o \leq 1$, the disease free equilibrium point is asymptotically stable and the disease dies out after some period of time. However, when $R_o > 1$, then the endemic equilibrium is locally asymptotically stable, and unstable if $R_o < 1$.

It is evident from numerical simulations that human and mosquito populations increase with time and finally leveling off in the long run when there is malaria transmission between the two groups.

It is therefore necessary for people of Butaleja district to adopt preventive measures to reduce mosquito bites hence malaria spread. Thus, the knowledge of the disease transmission dynamics will help to control the disease.

5.4 Recommendations

In this study, Susceptible (S_h), Infected (I_h) and Asymptomatic (A_h) classes for human population were considered. Also, Susceptible (S_m) and Infected classes (I_m) for mosquito population were considered too. The interaction between the two groups helps to identify intervention measures needed to have a lasting solution to malaria problem in the district.

From research findings, the control methods that reduce mosquito birth rate (λ_m) and increase mosquito death rate (μ_m) can be adopted to reduce the spread of malaria as in [41].

Therefore, collective responsibility by all the people of Butaleja district and Uganda in general; the government of the Republic of Uganda through the Ministry of Health and International bodies is needed in achieving the following [68], [26], [12], [25] and [54]:-

1. People who are ill should quickly seek treatment at health centres for effective diagnosis and treatment in order to avoid malaria transmission within the population hence $R_o < 1$.

2. Building capacity for mosquito larval source management in rural and urban areas by clearing breeding places around homesteads to reduce mosquito birth rate (λ_m).

3. Scale up and sustain Indoor Residual Spraying (IRS) in all villages and Sub-counties of Butaleja district to increase mosquito death rate (μ_m).

4. Sustain universal access to Long Lasting Insecticidal Nets (LLINs) to all household members in Butaleja. These LLINs provide protection against mosquito bites as well as transmission cf parasites and also kill mosquitoes or repel them hence increasing mosquito death rate (μ_m) and reducing **b**.

5. Strengthen capacity in entomology, epidemiological surveillance, insecticide resistance monitoring, vector behaviour and bionomics. These are fundamental in implementing a cost effective and efficient Indoor Residual Spraying (IRS) to increase mosquito death rate (μ_m).

6. Patients of all age groups should adopt and receive Rapid Diagnostic Tests (RDTs). Malaria diagnosis and Artemisinin-based mono-Therapies (ACTs) should be given free of charge to patients in both private and public health facilities. This will help in reducing R_o further.

5.5 Areas for further model development

This study was based on a mathematical model for transmission dynamics of malaria in Butaleja district. The study was carried out between July and December. Thus, Future models to include the effects of the environment on the spread of malaria could be developed. Some parameters, such as the incubation period in mosquitoes and mosquito birth rate depend on seasonal environmental factors such as rainfall, temperature, and humidity. These effects can be included by modeling these parameters as periodic functions with time. Also, further research in the district is needed when developing mathematical models to include:

1. Anaemia and malaria prevalence in children of (0-5) years and expectant women.

2. The effect of Long Lasting Insecticidal Nets (LLINs).

3. The effect of sustained Indoor Residual Spraying (IRS).

4. Weekly epidemiological data as time series data collected by Butaleja district health personnel and submitted to MOH.

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6 Appendices

6.1 MATLAB codes

6.1.1 The effect of varying b on R_o

clear
clc
close all
b = 0:0.001:2;
% b is the biting rate on human population.
$\gamma = 0.011$; $\mu_m = 0.40$; $N_h = 37101745$; $N_m = 15000$; $p = 0.066$,
$q = 0.42$; $r = 0.55$; $mu_h = 0.00002929$; $\alpha = 0.00022466$;
$\delta = 0.143$;...
$R_o = (b.^2 * p * N_m * [(q + delta * r)])/((mu_m * N_h) * (mu_h + alpha + delta + gamma))$;
% R_o is the basic reproduction number
plot(R_o, b,'r')
xlabel('The basic reproduction number (R_o)')
ylabel('Biting rate on human population. (b)')
title('The graph of b against R_o')

6.1.2 The effect of varying b on S_h

clear
clc
close all
$p = 0 : 0.001 : 40$;
% b is the biting rate of infectious mosquito bites (p) on humans.
$\gamma = 0.011$; $\mu_h = 0.00002929$; $N_h = 37101745$; $S_h = 245873$;
$b = 0.42$; $\alpha = 0.00022466$; $\delta = 0.143$; $I_m = 1000$; $I_h = 100$;...
$I_h =$
$(b * p * I_m * S_h)/N_h - (I_h) * (mu_h + alpha + delta + gamma)$;...

% I_h is the number of infectious humans
plot(I_h, p,'r')
xlabel('Biting rate of infectious mosquito bites on humans at time t')
ylabel('Infected humans (I_h')
title('The graph of (I_h) against b')

6.1.3 The effect of varying p on S_h

clear
clc
close all
p = 0:0.001:1000;
% p is the proportion of infectious mosquito bites (p) on humans.
$\gamma = 0.011$; $\mu_h = 0.00002929$; $N_h = 37101745$; $S_h = 245873$;
$b = 0.42$; $\alpha = 0.00022466$; $\delta = 0.143$; $I_m = 1000$; $I_h = 500$;
$I_h =$
$(b * p * I_m * S_h)/N_h - (I_h) * (mu_h + alpha + delta + gamma)$;...
% I_h is the number of infected humans
plot(I_h, p,'r')
xlabel('Proportion of infectious mosquito bites on humans at time t')
ylabel('Infected humans (I_h)')
title('The graph of (I_h) against p')

6.1.4 The effect of A_h with time

clear
clc
close all
t = 0:50:500;
% t is the time in days.

$\delta = 0.143$; $\mu_h = 0.00002929$; $A_h = 1000$; $I_h = 213308$;
$\gamma = 0.011$;...
$A_h = t * delta * I_h - A_h.^2 * (\mu_h + \gamma)$;
% A_h Is the total number of asymptomatic humans at time t
plot(A_h, t,'r')
xlabel('Time in days')
ylabel('Number of Asymptomatic human population')
title('The graph of asymptomatic human population against
time (days)')

6.1.5 The effect of I_m on S_h

clear
clc
close all
t = 0:50:500;
% t is the time in days.
$A_h = 1000$; $N_h = 37101745$; $S_m = 9000$; $\mu_m = 0.4$; $q = 0.42$;...
$I_m = 1000$; $I_h = 213308$; $b = 0.4$; $r = 0.55$;...
$I_m = t * (b * q * I_h * S_m)/(N_h) + t * (b * r * S_m * A_h)/(N_h) - t *$
$(\mu_m * I_m)$;...
% I_m represents infected mosquitoes
plot(I_m, t,'r')
xlabel('Time in days')
ylabel('Infected mosquitoes')
title('The graph of I_h against time')