Determination of the Risk of Malaria Using Different Models for Mosquito Biting and Mortality Rates

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Determination of the Risk of Malaria Using Different Models for Mosquito Biting and Mortality Rates

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A project submitted to the school of Mathematics in partial fulfillment for a degree of Master of Science in Applied Mathematics

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Declaration

I the undersigned declare that this project report is my original work and to the best of my knowledge has not been presented for the award of a degree in any other University.

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This project report has been submitted for examination with my approval as Supervisor

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Statement

This dissertation has been submitted in partial fulfilment of requirements for a Master of Science Degree at the University of Nairobi and is deposited in the University library to be made available to borrowers under the rules of the library.

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Dedication

To my parents Mr and Mrs Ongowe and my beloved fiance Grace Nabuala for her patience when I had to be away.

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Abstract

Malaria is a serious and sometimes a fatal epidemic affecting nearly half of the world's population. In this project, we analyse a non-linear deterministic model to assess the relation between rainfall, temperature, relative-humidity as climatic variables and malaria incidence. The seven equations from the compartmental model were reduced to two of which was used to derive the reproduction number as a function of the climatic variables. We analysed both the local and global stability of the disease-free equilibrium points and also the local stability of the endemic equilibrium.

We settled on two different biting rates and two different mortality rates so as to accommodate the different climatic variables under study. Our scope to analyse different biting and mortality rates was achieved by simultaneously substituting two models; one biting rate and one mortality rate into the reproduction number after which numerical simulations are provided to determine the correlation between climatic variables and malaria incidence.

Apart from reproduction number, the other index used in the analysis of the relation between temperature and future risk of malaria is the epidemic potential which showed qualitatively that an increase or decrease in temperature will lead to a corresponding behaviour in malaria incidence. Our findings in this study confirm that indeed there is some correlation between climatic variables and the dynamics of both total and confirmed malaria incidence.

Definition of Terms

The following terms are used in the project;

Gonotrophic Cycle

Time from blood feeding to oviposition.

Extrinsic Incubation Period *EIP*

The length of time it takes the malaria parasite to complete its development within the mosquito and migrate to the salivary glands ready for transmission.

Reproduction Number, R_0

The average number of secondary infections produced when one infected individual is introduced into host population where everyone is susceptible

Epidemic Potential, *EP*

This is the reciprocal of the host density threshold, i.e a comparative index that can be used to estimate the effect that change in temperature can have on the risk of malaria.

Latent Period

The period from the point of infection to the state of being infectious, i.e period in which individuals stay in exposed class.

Different biting and mortality rate models

The models for biting rate 1 and biting rate 2 are given by (3.36) and (3.37) respectively while the models for mortality rate 1 and mortality rate 2 are given by (3.39) and (3.41) respectively.

Zones sampled

Zone 1 is Kisumu and the entire Lake Victoria basin while zone 4 is Nairobi and its environs.

Chapter 1

INTRODUCTION

1.1 Background of Malaria

Malaria is a mosquito-borne illness caused by a parasite transmitted by a female anopheles mosquito in the process of seeking a blood meal for egg formation. Malaria has prevailed for more than a century and has a huge social, economic and health burden. According to [1], the total expenditure on malaria control including insecticide-spraying, supply and use of insecticide treated bed nets and access to rapid diagnosis and medicine amounted to 1.8 billion U.S Dollars. Malaria is predominantly present in the tropical countries. With the effort and investment which has been put in its investigation for hundreds of years, it still remains a major public health problem.

Persons most vulnerable to the disease are those with no, or little, protective immunity against the disease. High transmission areas such as sub-Saharan Africa have the following categories of people as the most vulnerable:

- Children under the age of five years due to undeveloped immunity.
- Expectant women as a result of lowered (weakened) immunity more so for first and second pregnancies.
- Travellers and immigrants from areas with low or no transmission and luck of immunity

WHO [1], estimates that in 2013, there were 198 million cases of malaria worldwide with an uncertainty interval of 124-283 million resulting in 584,000 deaths. Eighty

percent of the cases occur in sub-Saharan Africa and 40 million cases were confirmed in 2012 by 103 countries. Ninety percent of malaria deaths occur in Africa region and children under the age of 5 accounts for 78 % of the total deaths [1].

Malaria incidence has grown due to increasing parasite drug resistance and mosquito insecticide resistance. Malaria is believed to be one of the major vector-borne diseases most sensitive to climate change. Climate change plays a big role in increasing malaria incidence since climatic variables such as temperature, rainfall and relative-humidity have an effect on both the vector and malaria parasite cycles.

There is still much uncertainty regarding the effects of climate change on malaria due to limited attempts to incorporate environmental variables into mathematical models describing malaria transmission. Developing a reliable modelling framework is a challenge due to many factors influencing the transmission of malaria.The exact role played by climate in driving malaria epidemics also remains a substantial debate to most researchers [2].

Current methods of malaria eradication and control rely on the use of insecticide treated bed nets (ITNs), indoor residual spraying (IRS), chemo-prevention to prevent the blood stage infection and case management which includes diagnosis and use of drugs for prevention and disease treatment[1].

Among the above methods, ITNs are regarded as the standard tools for malaria control. They do this by reducing the intensity of malaria transmission. This is evident through the reduced average number of infectious bites received by a person over some period of time i.e the Entomological Inoculation Rate (EIR). According to [3], ITNs reduce EIR by a factor of 10.

Malaria is prevalent in tropical and subtropical regions because of availability of rainfall, consistent high temperatures and high humidity along with stagnant waters in which mosquito larvae readily mature. These environmental factors affect the incidence of malaria either through changes in the duration of mosquito and parasite life cycle or influences on human, vector or parasite behaviour. Thus climate change can affect malaria prevalence pattern by mosquitoes moving away from lower latitudes to regions where populations have not developed immunity to the disease [2].

1.2 Causes of malaria

Malaria is caused by a protozoan parasite called *Plasmodium* which can be spread to humans through the bites of an infected mosquito of genus Anopheles. The Plasmodium is a single-celled organism that cannot survive outside of the host(s). There

are about 400 different species of Anopheles but only 30 are of major importance. There are various types of Plasmodium parasites, out of these only five cause malaria in humans [1, 4, 22]. These are:

(i) *Plasmodium falciparum* - mainly found in Africa and responsible for most malaria deaths globally.

(ii) *Plasmodium vivax* - mainly found in Asia and Latin America. This parasite is the second most significant species after Plasmodium falciparum. It has less severe symptoms, but it can hide in the liver for upto three years.

(iii) *Plasmodium Ovale* - fairly rare and usually found in west Africa. It can remain in human Liver for several years without showing symptoms.

(iv) *Plasmodium malarie* - its quite rare and usually found in Africa.

(v) *Plasmodium Knowlesi* - this causes malaria among monkeys and occurs in rare forested parts of South-East Asia.

Of these five types, Plasmodium falciparum is the most common cause of infection in Africa and South East Asia. It accounts for approximately 80% of all malaria causes and approximately 90% of deaths [5].

1.3 Life cycle of the malaria parasite

As shown in figure (1.2), the malaria parasite has two main stages of life: one requires a human host (secondary host) which acts as a transmission vector and the other requires a female Anopheles mosquito (definite host). During a blood meal, the parasites which is in the form of sporozoites in the saliva of the infected female Anopheles mosquito enter the human through bite, into the blood system and travels to the liver.

Once in the liver, the malaria parasites invade the hepatic cells and undergo a sexual multiplication. After some days, the sporozoites invade the red blood cells and mature into schizonts, rapturing the red blood cells and releasing 8 to 24 new infective merozoites, see figure (1.1). The rapture is what frees the parasites and cause them to affect other blood cells [6, 39]. The toxin released (sporozoites) after the rapture is what causes the malaria symptoms. Some of the merozoites differentiate into sexual immature forms known as gametocytes which are the precursors of male (microgametocytes) and female (macrogametocytes) gametes.

In the mosquito (definite host), the cycle is known as sporogonic cycle whereby the parasites multiply in the mosquito host. When a mosquito bites and takes a blood meal from an infected human being (host), it ingests the gametocytes which mature in the mosquito gut. As shown in figure (1.1), these gametocytes fuse to form zygots that mature into motile and elongated ookinetes. The ookinetes invade the stomach (midgut) wall of the mosquito where they develop into oocysts. The oocysts grow, rapture and in a week or so, release sporozoites. This proces is ambient temperature dependent [7]. The sporozoites migrate into the insect's salivary glands ready to infect a new vertebrate host. When a mosquito bites a human, the sporozoites in the saliva are injected into the skin and the cycle continues [8].

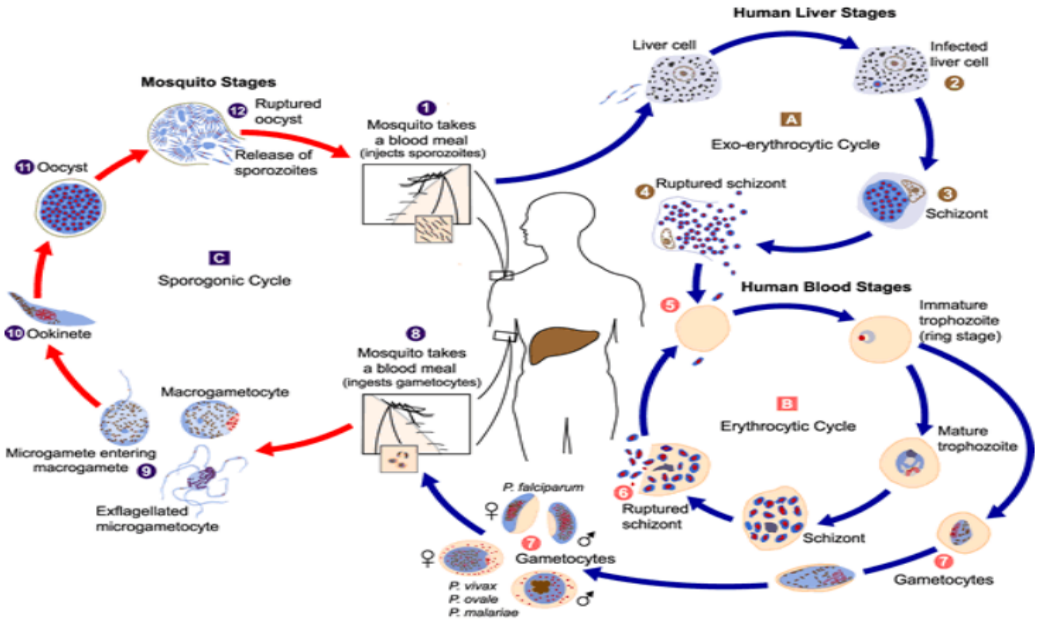
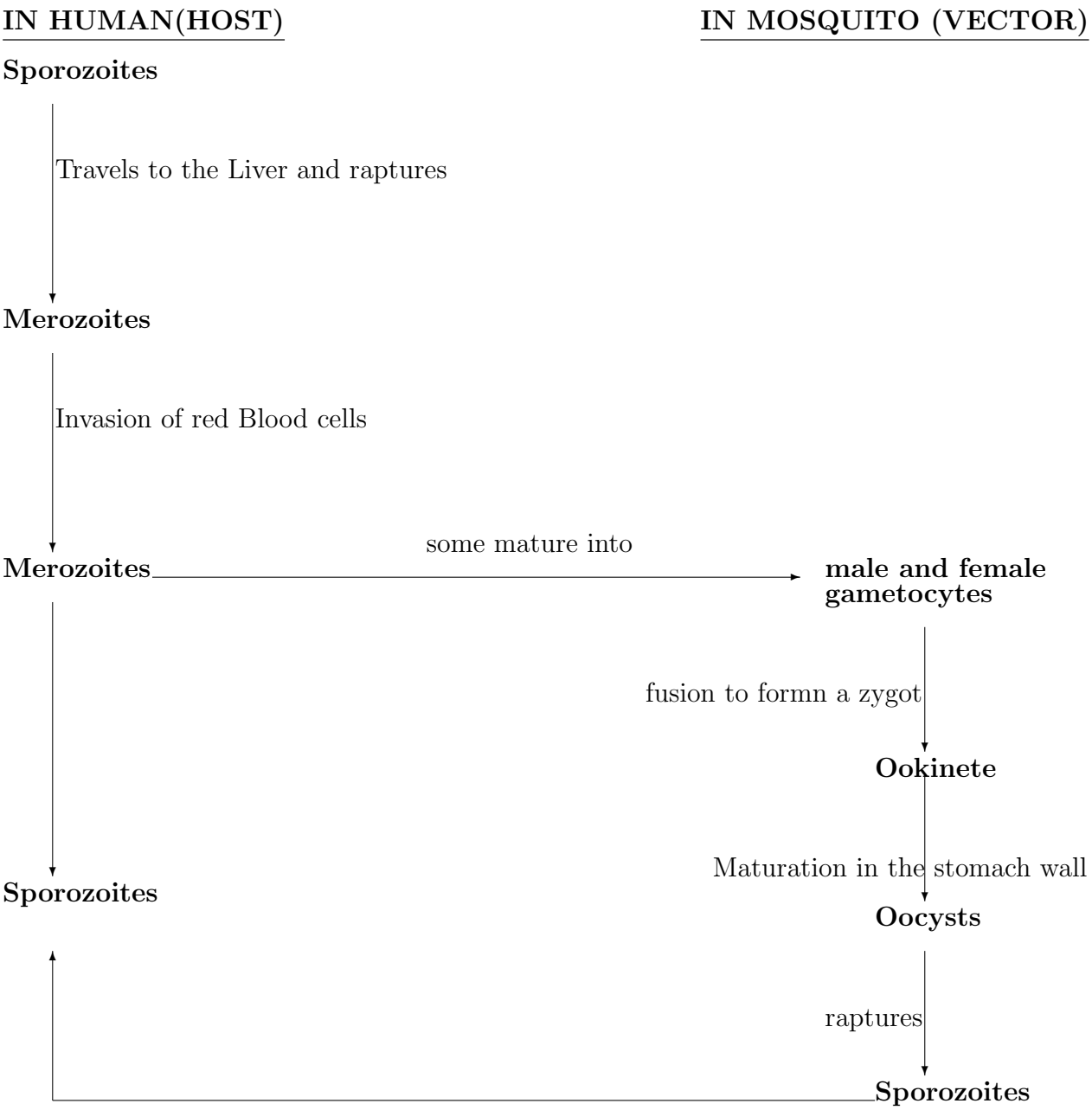


Figure 1.1: Life cycle of plasmodium [42]

Figure 1.2: Life cycle of parasites



The incubation period for the gametocytes to form new sporozoites usually takes 7 - 12 days but this period varies greatly depending on the environmental temperature, relative-humidity and the species of plasmodium. The optimal conditions for development of sporozoites are temperatures between 20^0 C and 30^0 C and relative humidity greater than 60% [9].

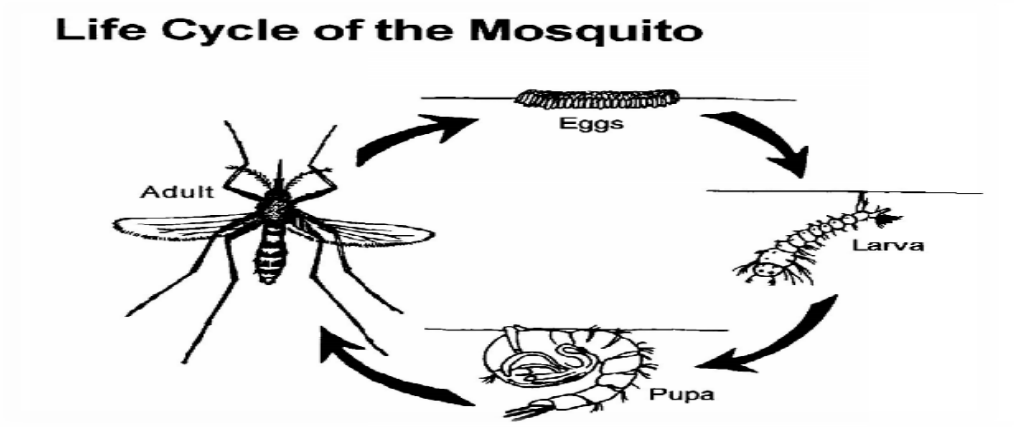
Only female mosquitoes feed on blood; male mosquitoes feed on plant nectar and hence do not transmit malaria. The females of the Anopheles genus prefer to feed at dusk to dawn whereby the search for a meal usually start at dusk and continue throughout the night [10].

1.4 Life cycle of the mosquito

The life cycle of a mosquito can be prolonged or shortened by the type of species and also depends upon the environmental conditions such as temperature and moisture. The mosquito has four separate and distinct stages of its life cycle.
Egg: The eggs are laid in water since they require water for successful hatching. They hatch into larvae in 24-48 hours depending on water temperature and availability of food. In cold weather, the hatching may be prolonged into weeks.
Larvae: This stage also lives in water and requires food. They feed on algae, bacteria and other micro-organisms. They live in water for 7-14 days depending on water temperature.
Pupa: It also requires water and may take 1-4 days depending on the species and temperature. This stage does not require food.

As shown in figure (1.3), the egg, larvae and pupa stage belong to the immature stage which do not participate in the infection cycle but requires the availability of stagnant water bodies for development.
Adult: Both the male and female adult mosquitoes are sexually active 2 days after mosquito emergence from its aquatic breeding sites or pupal stage [11, 12]. The average life span of an adult male is about one week while the female can live up to a month. The adult female requires a blood meal for provision of protein needed for egg development. After blood meal, it rests until the eggs develop and this process is temperature dependent and usually lasts for 2-3 days in tropical conditions. The lifespan of the adult mosquito depends on temperature, relative-humidity, sex of mosquito and season.

Figure 1.3: Life cycle of mosquito [42]



Temperature and moisture, in the form of precipitation and relative humidity can hasten or slow down cycle transition since they are crucial regulators of the growth and development within each stage in determining the end of one stage and the beginning of the next stage.These environmental factors also regulate the length of gonotrophic cycle [13]. Thus the transition usually occurs in 10-14 days in tropical conditions. The development time of mosquito depends on the environmental conditions and the species of the mosquito with warmer temperature catalysing development.

1.5 Transmission of the disease

According to [14] for malaria parasites to be transmitted from human to human, it requires at least two mosquito bites. To become infected, the mosquito needs to first feed (bite) an infected human host, then on the completion of the Extrinsic Incubation Period (EIP), the mosquito is infectious and needs a second bite to transmit the parasite to another human host.

The EIP is the length of time it takes the malaria parasite to complete its development within the mosquito and migrate to the salivary glands; it is one of the key rate limiting steps in transmission of malaria and it is known to be strongly temperature sensitive. EIP takes between 10 to more than 30 days depending on environmental factors such as temperature and humidity [14, 9].

The mosquito transmitting malaria has discrete feeding cycles in which blood feeding only occurs at the begining of a gonotrophic cycle and then not again until the blood has been digested, a batch of eggs has matured and oviposition is completed [15]. However there is the possibility of a small proportion of Anopheles mosquitoes taking multiple blood feeds within a cycle due to energy depletion after emergence from their breeding site.

In most cases, blood feeding is coupled with reproduction (egg formation) [14] and therefore the frequency of possible transmission events (i.e acquiring the parasite in an early feeding event and then passing it on in a later feed) depends on the duration of this gonotrophic cycle.

Gonotrophic cycle is the time between blood feeding and oviposition and is temperature dependent [18]. Under warmer conditions, about 30^0 C, the gonotrophic cycle can be completed in just 2-3 days [16] resulting in high frequency of blood feeding. Under cooler conditions (15 - 20^0 C), blood feeding might occur only once every 6-13 days.

The availability of moisture in the form of precipitation and relative-humidity can catalyse the cycle transition [2, 12]. The breeding sites comes to existence in the form of pools of stagnant waters after rainfall. The stagnant water bodies provide conducive environment for the immature stages of mosquito which can be hastened or slowed down by water temperature.

1.6 Signs and symptoms of malaria

Between 8-25 days after being bitten by an infectious parasite, the signs and symptoms of malaria begin to occur. For individuals who have taken antimalarial drugs, the symptoms might occur later [5]. The malaria parasites enter the blood stream and affect the red blood cells. These cells are essential and their destruction leads to presentation of symptoms. Presentation of the signs and symptoms may include fever and flu-like symptoms such as chills, headache, muscle aches, tiredness, nausea, shivering, diarrhoea and vomiting [17, 22].

Severe malaria is usually caused by Plasmodium falciparum. Its symptoms arise 9-30 days after infection [17]. Individuals with cerebral malaria frequently exhibit neurological symptoms including abnormal posturing, eyes facing in different directions and coma. If not treated it can lead to death [17].

The classic symptoms of malaria is paroxysm- an occurrence of sudden coldness followed by shivering, fever and then sweating occurring every two days in P. vivax and every three days for P. malariae. P. falciparum infection can cause recurrent fever every 36-38 hours or less pronounced and almost continuous fever [18].

1.7 Mathematical models and Epidemiology

The importance of mathematics and mathematical models dates back to early biologist and researchers in infectious diseases. Mathematical models provide an explicit framework for understanding the disease transmission dynamics within (intra) and between hosts and parasites. In mathematical modelling and expression, several known biological and clinical information are included in a simplified form by selecting features that seem to be significant to the problem being investigated.

A model is *a mathematical approximation* of the complex reality and its structure depends upon the process being studied its extension into the real world. Based on the question being investigated, a model can help fit empirical observations and can be applied to make theoretical predictions on lesser known situations. Mathematical models have been applied for example: by epidemiologists as tools to predict the occurrence of epidemics of infectious diseases and also currently it is applied as a tool to eradicate malaria [19]

Malaria is one of the oldest diseases which has been explored through research and has vast rich literature describing modelling approach, stages of the disease and economic impact to the human settlement. According to [19], combining different

approaches rather than a single type of modelling may have long term usefulness in eradication and control.

Mathematical models that study transmission of malaria are based on the *reproduction number* R_0, defining the important aspects of transmission for any infectious disease. The reproduction number R_0 is the number of secondary infections that result due to a single infection in a completely susceptible population. Control of the disease is arrived at when R_0 is expressed in such a way that the disease-free state can be established and maintained [20].

Previous studies used ordinary differential equations to model the transmission of malaria in which human population are classified into susceptible, exposed, infected and recovered while mosquito population are divided into susceptible, exposed and infectious.

1.8 Rationale of the study

Effects of climate change and global warming on malaria are of particular interest to researchers due to the sensitive nature of the transmission of malaria to environmental conditions. Since 1950s, the near surface global temperature of the earth has increased by about 0.5 - 0.6^0 C [21] and it is expected that the same will rise by 2^0 C by the year 2100 [30]. Most environmental variables such as temperature, rainfall, relative-humidity and windspeed affect the incidence of malaria either through changes in the duration of mosquito and parasite life cycles or influence on human, vector or parasite behaviour.[3, 9]

According to [9], a lot is known about how parasite development is influenced by temperature but the same cannot be said for mosquitoes. Increase in temperature accelerates larval development, the frequency of blood feeding (biting rate) by adult female mosquitoes on humans and reduces the time it takes the malaria parasite to mature in female mosquitoes (E.I.P). The malaria parasite needs a minimum temperature of 16^0 C for development [21]. Increase in rainfall not only creates additional breeding sites for mosquitoes but also increases the relative-humidity. Therefore the development of parasites in the mosquitoes is sensitive to external temperature while the rate of larval development is dependent upon water temperature and availability of breeding sites in terms of quality and quantity.

1.9 Problem statement

How temperature, rainfall and relative-humidity relate to malaria transmission.

1.10 Objective of the study

Asses the relation between climatic variables and malaria incidence.

1.10.1 Specific Objetives

The specific objectives of this study are:

(i) Examine deterministic model which represent the transmission of the disease in different environment .

(ii) Expressing the reproduction number as a function of temperature, rainfall and relative-humidity.

(iii) Express the dependence of various mortality and biting rates on temperature and relative-humidity.

(iv) To determine how different mortality and biting rates influence the dynamics of malaria.

(v) Determine the correlation between the observed meteorological variables and malaria incidence.

(vi) Determine the malaria risk through variation of reproduction number in the event of changes in climatic variables.

Chapter 2

LITERATURE REVIEW

2.1 History of malaria

The term malaria originates from medical Italian word, *mala aria* meaning *bad air*. The disease was formerly associated with swamps and marshland, hence derived its name *marsh fever* [23]. Malaria took effect in the Roman empire and was known as *Roman fever*. The favourable conditions such as stagnant waters, irrigated gardens, run-off from agriculture and drainage problems in Rome provided a good environment for the impact of malaria [22].

Plasmodium falciparum is the most prevalent and lethal of the malaria parasites infecting humans, yet the origin and evolutionary history of this important pathogen remain controversial. The population size of P. falciparum increased due to increased agricultural practice and advancing in human settlement. Some evidence suggests that humans may originally have caught plasmodium falciparum from gorillas [23].

During the second world war, in south Pacific, about 500,000 U.S troops encountered health hazard due to malaria infection and about 60,000 America soldiers died of malaria during the Africa and south Pacific campaigns. Scientific study on malaria began in 1880 by Charles Louis Alphause Laveren a French army doctor who discovered parasites in the red blood cells of patients. He was awarded the 1907 Nobel prize for philosophy or medicine. In 1881, Charles Finlay from Cuba, treated people with yellow fever in Hava and this provided strong evidence to show that mosquitoes were transmiting diseases to and fro humans [24].

In 1894, Sir Ronald Ross a Scottish Physician made a visit to Sir Patrick Manson in London after which the collaboration and earnest research four years later resulted

into Ross Ronald proving the complete life-cycle parasite in mosquitoes which earned him a Nobel prize in medicine in 1902. He proved that the mosquito was the vector for malaria in humans by showing that certain mosquito species transmit malaria to birds, by isolating malaria parasites from the salivary glands of mosquitoes that had fed on infected birds. These findings were later confirmed by a medical board headed by Walter Reed in 1900 and later implemented by William C. Gorgas. The recomendations in the public health work saved lives of thousands of workers and helped in developing the methods used in future public-health campaigns against the disease.

The very first effective treatment of malaria came from the bark of Cinchona tree which contained quinine. The indigenous people of Peru used Cinchona to control fever. In 1820, the active ingredient quinine was extracted from the bark of Cinchona tree and named by Pierre Joseph and Joseph Bienaim. Until 1920's, quinine predorminated malarial medication after which other medications developed. In 1940's chloroquine replaced quinine. In 1950, resistance to chloroquine emerged first in south-east Asia and south America then spread globally in 1980's [25].

The first pesticide used for indoor residual spraying was DDT. It was initially used exclusively to combat malaria after which its use spread quickly to agriculture for pest control rather than disease control. This wide spread use of DDT lead to its resistance by mosquitoes. In 1960, the use of DDT was banned due to the negative consequences of its indiscriminate use. Before DDT, malaria was eliminated in Brazil and Egypt by draining away or poisoning breeding grounds of the mosquitoes or aquatic habitats of the larvae stage.

Another area which has been of interest to researchers is the vaccination. In 1967, a study on malaria vaccine was demonstrated by immunizing mice with live, radiation-attenuated sporozoites which provided significant protection. Since 1970, there has been a considerable effort to develop similar vaccination strategies within humans.

2.2 Mathematical modelling of malaria

Mathematical models have been used to provide an explicit framework for understanding malaria transmission dynamics in human population for over 100 years.

2.2.1 Sir Ronald Ross model.

Around 1911, Sir Ronald Ross introduced the first deterministic differential equation model of malaria by dividing the human population into two compartments i.e Sus-

ceptible S_h and infected I_h with the infected class returning to susceptible class again leading to SIS structure. The mosquito population also has only two compartments i.e Susceptible S_m and Infectious I_m but do not recover from from infection due to their short life span hence follow the SI structure.

Time evolution of the fraction of individuals in the infected class (I_h, I_m) is studied using two differential equations one each for the human and mosquito as given below.

The equations that describe the model are:

$\frac{dI_h}{dt} = abmI_m(1 - I_h) - rI_h$

$\frac{dI_m}{dt} = acI_h(1 - I_m) - \mu_2 I_m$

with the reproduction number as:

$$R_0 = \frac{ma^2bc}{r\mu_2}$$

with the parameters and their values as:

a: man biting rate [0.01-0.5 day^{-1}]

b: proportion of bites that produce infection in human [0.2-0.5]

c: proportion of bites by which one susceptible mosquito becomes infected [0.5]

m: Ratio of number of female mosquitoes to that of humans [0.5-40]

r: average recovery rate of humans [0.005-0.05 day^{-1}]

μ_1: per capita rate of human mortality [0.017 year^{-1}]

μ_2: per capita rate of mosquito mortality [0.05-0.5 day^{-1}]

τ_m: Latent period of mosquito [5-15 days]

τ_h: Latent period of human [10-100 days]

Latent period is the period from the point of infection to the begining of the state of infectiousness during which infected individuals stay in the exposed class.

It is clear that the parameters m, a, b and c that contribute to the change of R_0 in this model are related to mosquitoes and humans and any change in them can significantly affect malaria transmission. Increasing mosquito mortality and reducing mosquito biting rate can reduce R_0. The Ross model outlines the basic features of malaria transmission and puts the main burden of transmission on mosquito-specific features, thereby paving the way for mosquito-based malaria control programmes.

Malaria parasite spends approximately 10 days inside a mosquito during its life cycle. The simple Ross model did assume this latency (incubation) period of the parasite of mosquito and their survival during that period. This resulted in the model predicting a rapid progress of the epidemic on human and higher equilibrium prevalence of infectious mosquito.

Ronald Ross in his classical mathematical model of malaria used the word *pathometry* to mean *quantitative* study of disease either on the individual or in the community [26]. Ross through his model showed that reduction of mosquito numbers below a certain figure, *trasmission threshold*, was significant to counter malaria.

2.2.2 MacDonald model

In 1950, McDonald modified Ross's model by integrating biological information of latency period (τ_m) and he introduced the exposed class of mosquitoes (E_m) [27]. He divided the mosquito population into SEI. The model studies the time evolution of the exposed (E_m) and infected (I_m) classes in mosquitoes. The increasing latency period scaled down the R_0.

The equations that describe the model are:

$$\frac{dI_h}{dt} = abmI_m(1 - I_h) - \gamma I_h$$

$$\frac{dE_m}{dt} = acI_h(1 - E_m - I_m) - acI_h(t - \tau_m)[1 - E_m(t - \tau_m) - I_m(t - \tau_m)]e^{-\mu_2\tau_m} - \mu_2 E_m$$

$$\frac{dI_m}{dt} = acI_h(t - \tau_m)[1 - E_m(t - \tau_m) - I_m(t - \tau_m)]e^{-\mu_2\tau_m} - \mu_2 I_m$$

with the reproduction number as:

$$R_0 = \frac{ma^2bc}{\gamma\mu_2}e^{-\mu_2\tau_m}$$

2.2.3 Anderson and May model

In an extension to Ross and MacDonald models, Anderson and May considered the 21 days latency period of the parasite in humans and introduced the exposed (E_h) class in human population in their model [28]. This divided the host population into three compartments ($S_hE_hI_h$) along with that of the mosquito population ($S_mE_mI_m$). This, therefore is a SEIS model for the human population and the model consists of four differential equations describing the time evolution of both the exposed and the

infected classes for humans and mosquitoes ($E_hI_hE_mI_m$). The R_0 for this model is further reduced due to inclusion of human latency period.

The equations that describe the model are:

$$\frac{dE_h(t)}{dt} = abmI_m[1 - E_h(t) - I_h(t)] - abmI_m(t - \tau_h[1 - E_h(t - \tau_h) - I_h(t - \tau_h)]e^{-(\gamma+\mu_1)\tau_h} - \gamma E_h(t) - \mu_1 E_h(t)$$

$$\frac{I_h(t)}{dt} = abmI_m(t - \tau_h)[1 - E_h(t - \tau_h) - I_h(t - \tau_h)]e^{-(\gamma+\mu_1)\tau_h} - \gamma I_h(t) - \mu_1 I_h(t)$$

$$\frac{dE_m}{dt} = acI_h(1 - E_m - I_m) - acI_h(t - \tau_m)[1 - E_m(t - \tau_m - I_m(t - \tau_m))]e^{-\mu_2\tau_m} - \mu_2 E_m$$

$$\frac{dI_m}{dt} = acI_h(t - \tau_m)[1 - E_m(t - \tau_m - I_m(t - \tau_m))]e^{-\mu_2\tau_m} - \mu_2 I_m$$

with the reproduction number as;

$$R_0 = \frac{ma^2bc}{\gamma\mu_2}e^{-\mu_2\tau_m}e^{-\mu_1\tau_h}$$

2.2.4 Review of Other Models

Continuous exposure to the disease results to development of immunity hence immunity comes in handy as one of the inter-related factors for transmission of the disease in a population. According to Koella [31], incorporating immunity into malaria models is significant because it makes models more realistic. Koella studied the effect of variability of the parameters and added an infection rate which depends on immunity by additional latent stage for the mosquitoes to the Ross-MacDonald model. Approximation of recovery rate, loss of immunity, biting rate, rate of infection and susceptibility of humans and mosquitoes were also surveyed.

The research and development of climate models done later were to focus on the improvement and understanding of the likely impact of climate on malaria transmission. Martens [30] used an integrated mathematical model to examine how climate change might affect global malaria transmission. The study assessed the effects of projected changes in temperature and precipitation on mosquito and parasite characteristics and their potential impact on malaria risk. The first sought to estimate the possible spatial shift in areas suitable for malaria transmission using the critical vector density threshold as a comparative index whereas the second approach considered possible changes in world malaria disease burden due to climate change. This model by Martens only generates broad estimates of future trends and does not include all relevant factors which would influence the distribution of malaria.

To understand the dynamic system, more studies were required using statistical techniques of modelling so as to provide decision makers with probability distribution. The use of larger and more complex model complicates and cripples the analysis of the results. Apart from this, another dilemma in an attempt to relate malaria to climatic variables was lack of data for comprehensive analysis as this leads to a lot of assumptions.

Use of simple mathematical models to look at the effects of temperature on the ability of Anopheles Maculipennis to transmit plasmodium vivax malaria came into focus. Lindsey and Martens [32] looked at the implications of climate change scenarios on highland malaria in Africa and more specifically in Zimbabwe. He also observed that all regions of the world indicated an increase in malaria transmission as climate changed with a varying magnitude depending on the climate scenario and specific characteristics of the malaria vector in question. They showed that rise in temperature is likely to increase the risk of epidemics in the highlands.

Yang [33] described a compartmental model where humans follow SEIRS type pattern and mosquitoes follow the SEI pattern. Parameters used in this model, like the time taken for mosquitoes eggs to develop into adults and the time taken for plasmodium gametocytes ingested by the mosquito to develop into sporozoites and migrate to the salivary glands (EIP), are functions of temperature. He defined a reproductive number R_0 for this model and showed through linear stability that the disease free equilibrium was stable for $R_0 < 1$. He also showed that for $R_0 > 1$, and endemic equilibrium was biologically relevant and used numerical simulation to support his proposition that for $R_0 > 1$, the disease free equilibrium was unstable and the endemic equilibrium was stable.

The potential effect of climate change on highland malaria was analysed by Hay et al [34] using a regression approach. This was done with a focus on four sites in East Africa highlands. They suggested that the increase in malaria incidence in Kericho (Kenya) and Usambara (Tanzania), was pegged on the rise in antimalarial drug resistance. In southern Uganda, the changes were related to El nino while in Muhanga, they attributed the change in land use and related temperatures.

Zhau et al [35] used time series techniques to analyse retrospectively outpatients data to asses the link between climate variability and transmission of malaria in highlands of Kenya. They observed that there was an association between increase of outpatient malaria cases and changes in climate conditions. Higher temperatures catalyse the egg to adult development and thus shorten the mosquito life cycle and the end result is production of more mosquitoes [36]. Horsheu and Morse [37] described in detail the development of weather driven dynamic mathematical malaria

model which captured both the seasonality and inter annual variability of infection at their test site in Zimbabwe.

From the models discussed above, it is prudent to relate the malaria transmission to climatic factors such as temperature, rainfall and relative-humidity. Malaria incidence is determined by a variety of factors among them are abundance of mosquito species, human behaviour and the prescence of malaria parasites [38, 30]. Climate change affects malaria incidence directly or indirectly. Directly climate change affects the behaviour (e.g biting rate) and geographical distribution of mosquitoes and the life cycle of the parasite (by prolonging or shortening) while indirectly it could have an effect by influencing environmental factors such as vegetation and the availability of breeding sites.

Reproductive number, R_0 is a measure that summarises many important processes in transmission of infectious diseases. How severe the disease can be, or whether the disease will lead to an epidemic or die out eventually is quantified through this number. For malaria microparasite, R_0 is defined as *the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible* [14, 30, 38]. The basic reproduction number is a measure of an individual parasites reproductive potential and enables one to simplify the epidemiology of malaria i.e if $R_0 > 1$, the disease will spread indefinitely while if $R_0 < 1$, the disease will die out eventually.

Our research will be drawn from Parham and Michael [2] who developed a model framework for modelling the effect of temperature and rainfall. They included the effect of weather on the biting rate, demographic (net population growth) parameters and duration of Plasmodium life cycle on temperature. Demographic effects were included to predict the number of fatalities that may arise as a result of the disease. They also found out that the effect of temperature on vector abundance had a strong physiological basis and thus could be meaningfully captured by the deterministic population model. However, the effect of rainfall was less predictable and more difficult to quantify.

The authors, [2, 14] found out that the rate of malaria spread increases significantly within a temperature window of $32 - 33^0$ C . They concluded that in addition to temperature and rainfall, the transmission rate depended more strongly on vector density than on parasite species. Changes in temperature can lead to negative or positive impact as far as distribution of malaria is concerned, i.e it can cause an increase or decrease in malaria cases depending on the initial temperature of the region.

According to [14], the parasite development time and feeding patterns (the gonotrophic cycle) exhibit different thermal sensitivities. Delays in infection and transmission

can reduce vectorial capacity by $20 - 60\%$. The delays have important implications for disease epidemiology and control for future transmission models. The authors, [2, 30] stressed on the use of mathematical models to conceptualize the effect of climate change on malaria transmission and argued that mathematical models are superior because they can address multiplicative exposure effects, non-linear feedback pathways, spatio-temporal heterogeneities and transmission outcome for dynamic complex processes.

Chapter 3

MODEL DESCRIPTION

3.1 Model Formulation

This mathematical model is to help understand better the effects of climate change on transmission of malaria. The disease is modelled using ordinary differential equations (O.D.E's) where humans and mosquitoes interact and infect each other. We used different biting and mortality rates to show the relationship between R_0 and climatic variables such as temperature, rainfall and relative-humidity.

As given by Parham and Michael [2], the compartmental model in figure (3.1) was considered;

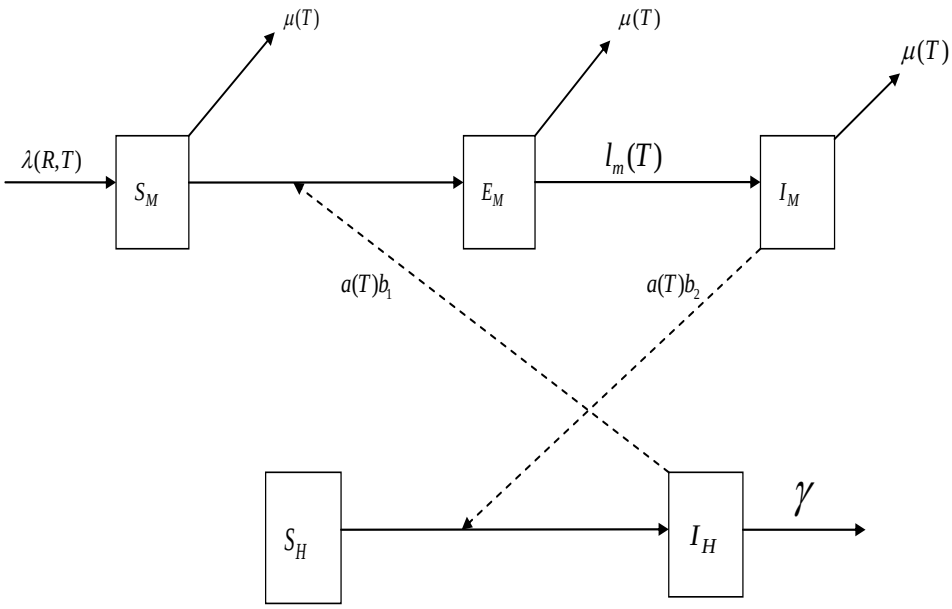


Figure 3.1: Compartmental Representation

The model in figure (3.1) divides the human population into two classes: the susceptible (S_H) and infected (I_H). The recovered class of infected human is assumed to acquire full immunity hence enter the removed class. According to [2, 39], susceptible humans get infected at a rate a when they are bitten by an infectious mosquito. As shown in figure (3.1), the mosquito population is divided into three classes: the susceptible (S_M), the exposed but not infectious (E_M), and those that are infectious(I_M). Mosquitoes never recover from infection; that is, their infective period ends with their death due to their short life cycle which is not significant compared to the period of investigation [39].

The susceptible compartment contains either the human host or mosquito vector all of which are not infectious but are susceptible. The human and mosquito infectious compartments contains the collection of infected human host or infectious mosquito vector respectively. The individuals in this compartment are infected and can infect others.

For transmission of malaria parasite to take place from one human to the other, the mosquito has to bite twice [14]. To become infected, the mosquito needs to first feed (bite) on infected human host then on the completion of the Extrinsic Incubation Period (E.I.P), the mosquito is infectious and needs a second bite to transmit the parasite to another susceptible human host. The E.I.P is the length of time it takes the malaria parasite to complete its development within the mosquito and migrate to the salivary glands ready for transmission.

The governing equations are:

$$
\begin{aligned}
\frac{dS_M}{dt} &= \lambda(R,T) - a(T)b_1\frac{I_H}{N}S_M - \mu(T)S_M \\
\frac{dE_M}{dt} &= a(T)b_1\frac{I_H}{N}S_M - \mu(T)E_M - a(T)b_1\frac{I_H}{N}S_M l_m(T) \\
\frac{dI_M}{dt} &= a(T)b_1\frac{I_H}{N}S_M l_m(T) - \mu(T)I_M \\
\frac{dS_H}{dt} &= -a(T)b_2\frac{I_M}{N}S_H \\
\frac{dI_H}{dt} &= a(T)b_2\frac{I_M}{N}S_H - \gamma I_H \\
\frac{dM(t)}{dt} &= \lambda(R,T) - \mu(T)M(t) \\
\frac{dN(t)}{dt} &= -\gamma I_H
\end{aligned}
\tag{3.1}
$$

Table (3.1) and (3.2) summarises the variables and constants used in the model equations (3.1) and the compartmental model figure (3.1). The total population sizes for the female mosquitoes and human hosts are denoted by M(t) and N(t) respectively. The transmission terms $a(T)b_2S_H\frac{I_M}{N}$ corresponds to frequency dependent infection of susceptible human hosts S_H by infectious mosquitoes I_M and $a(T)b_1S_M\frac{I_H}{N}$ for the rate at which susceptible mosquitoes S_M get infected by the infected human host I_H.

Variable	**Definition**
S_M	Susceptible Mosquitoes
E_M	Exposed and not infectious mosquitoes
I_M	Infectious mosquitoes
S_H	Susceptible humans
I_H	Infected humans
$N(t)$	Total number of humans
$M(t)$	Total number of mosquitoes

Table 3.1: Table of variables and their definitions

Parameter	**Definition**
$\lambda(R,T)$	Adult mosquito birth rate
$a(T)$	Mosquito biting rate
b_1	Proportion of bites by susceptible mosquitoes on infected humans that successfully produce infection
$\mu(T)$	Adult mosquito per capita death rate
$l_m(T)$	Survival probability of infected mosquitoes over the incubation period of the parasite.
b_2	proportion of bites by infectious mosquitoes on susceptible humans that successfully produce infection
γ	Rate at which infectious humans recover and acquire immunity.

Table 3.2: Table of Parameters against their definitions

Assumptions in the model;

(i) The recovered class of infected humans acquires full immunity

(ii) No recovery for infected mosquito

(iii) All parameters and variables in the model are non negative.

(iv) The human population is constant.

3.2 Model Analysis.

For analysis of the model, we transform the system of populations into a system of proportions of the individuals in each class.

The proportions of the classes S_H, I_H, S_M, E_M and I_M are defined as $s_h = \frac{S_H}{N}$, $i_h = \frac{I_H}{N}$, $s_m = \frac{S_M}{M}$, $e_m = \frac{E_M}{M}$ and $i_m = \frac{I_M}{M}$ respectively.

If the female vector-host ratio is given by:

$$k = \frac{M(t)}{N(t)}$$

where k is the number of female mosquitoes per human host.

Differentiating the proportions above with respect to time, we have:

$$\begin{aligned}
\frac{ds_h}{dt} &= -a(T)b_2 k s_h i_m + \gamma s_h i_h \\
\frac{di_h}{dt} &= \gamma i_h^2 - \gamma i_h + a(T)b_2 k i_m s_h \\
\frac{ds_m}{dt} &= (1 - s_m)\frac{\lambda(R,T)}{M(t)} - a(T)b_1 i_h s_m \\
\frac{de_m}{dt} &= a(T)b_1 i_h s_m - a(T)b_1 i_h s_m l_m(T) - \frac{\lambda(R,T)}{M(t)} e_m \\
\frac{di_m}{dt} &= a(T)b_1 i_h s_m l_m(T) - \frac{\lambda(R,T)}{M(t)} i_m
\end{aligned} \tag{3.2}$$

The new system (3.2) contains the total mosquito vector population M. Given that $i_h + s_h = 1$ and $s_m + e_m + i_m = 1$, we reduce the five equations to three equations by eliminating s_h and e_m.

Making s_h and e_m subject, we have; $s_h = 1 - i_h$ and $e_m = 1 - (s_m + i_m)$

Substituting s_h and e_m into the system (3.2), we have;

$$\begin{aligned}
\tfrac{di_h}{dt} &= \gamma i_h^2 - (\gamma + a(T)b_2 k i_m)i_h + a(T)b_2 k i_m \\
\tfrac{ds_m}{dt} &= (1 - s_m)\tfrac{\lambda(R,T)}{M} - a(T)b_1 i_h s_m \\
\tfrac{di_m}{dt} &= a(T)b_1 i_h s_m l_m(T) - \tfrac{\lambda(R,T)}{M(t)} i_m
\end{aligned} \tag{3.3}$$

Since the mosquito population is assumed to be constant at any time, we equated the second last equation in (3.1) to zero;

$$\tfrac{dM(t)}{dt} = \lambda(R,T) - \mu(T)M(t) = 0$$

Making $\mu(T)$ subject, we have, $\mu(T) = \frac{\lambda(R,T)}{M(t)}$ and substituting into the system (3.3) which depends on the total mosquito population M, the system thus reduces to three equations;

$$\frac{ds_m}{dt} = (1 - s_m)\mu(T) - a(T)b_1 i_h s_m \tag{3.4}$$

$$\frac{di_m}{dt} = a(T)b_1 i_h s_m l_m(T) - \mu(T) i_m \tag{3.5}$$

$$\frac{di_h}{dt} = \gamma i_h^2 - (\gamma + a(T)b_2 k i_m)i_h + a(T)b_2 k i_m \tag{3.6}$$

3.3 A compact positively invariant set.

Theorem 1. *The set*
D=$\{(s_m, i_m, i_h) \in \mathbb{R}^3_+; s_m \geq 0, i_m \geq 0, i_h \geq 0; s_m + i_m \leq 1; 0 \leq i_h \leq 1\}$
is positive invariant with respect to the model.

Proof: The model is monitoring human and mosquito population, therefore it is assumed that all the state variables are non-negative. From (3.4), when $s_m = 0 \Longrightarrow \dot{s}_m > 0$ and if $s_m = 1 \Rightarrow \dot{s}_m < 0$, from (3.5), when $i_m = 0 \Longrightarrow \dot{i}_m > 0$ and if $i_m = 1 \Rightarrow \dot{i}_m < 0$, also from (3.6), when $i_h = 0 \Longrightarrow \dot{i}_h > 0$ and if $i_h = 1 \Rightarrow \dot{i}_h = 0$. The right hand side of the equations is continuous with continuous partial derivatives

in the given region thus there is a unique solution. Since the solutions remain in D, they are continuous for all $t \geq 0$. If $B \in C^1[0,1]$, then the right hand side is globally lipschitzian in D so that the initial value problem has a unique solution for all $t \geq 0$. In the interior of D, the right side is locally lipschizian since for every closed bounded subset, there exists lipschitz constant.

Thus, for all points in the interior of D, the initial value problem has a unique solution for all $t \geq 0$. Thus solutions on the boundary of D eventually enter the interior and those starting in D remain there. Thus, the initial value problem is well posed in the closed set D. Therefore, in D the model is well posed epidemiologically and mathematically.

3.4 Reproduction Number R_0

The reproduction number R_0 is obtained using the next generation matrix i.e FV^{-1} where F and V denote the matrices for new infection and transmission terms respectively.

The two disease compartments responsible for transmission are i_h and i_m, thus from (3.6) and (3.5) we have;

$$\begin{aligned} \tfrac{di_h}{dt} &= \gamma i_h^2 - (\gamma + a(T)b_2 k i_m)i_h + a(T)b_2 k i_m \\ \tfrac{di_m}{dt} &= a(T)b_1 i_h s_m l_m(T) - \mu(T) i_m \end{aligned} \tag{3.7}$$

According to [29], we define the transmission vector $\mathcal{F}$ and the vector of infected components $\mathcal{V}$ from system above as;

$$\mathcal{F} = \begin{bmatrix} \gamma i_h^2 + a(T)b_2 k i_m \\ a(T)b_1 l_m(T) i_h s_m \end{bmatrix}, \mathcal{V} = \begin{bmatrix} -(\gamma + a(T)b_2 k i_m)i_h \\ -\mu(T) i_m \end{bmatrix} \tag{3.8}$$

The Jacobian of the two vectors above gives F and V as the matrices for the new infection and transmission terms

$$F = \begin{bmatrix} 2\gamma i_h & a(T)b_2 k \\ a(T)b_1 l_m s_m & 0 \end{bmatrix}, \tag{3.9}$$

$$V = \begin{bmatrix} -(\gamma + a(T)b_2 k i_m) & -a(T)b_2 k i_h \\ 0 & -\mu(T) \end{bmatrix} \tag{3.10}$$

When computed at the DFE ; $i_h = 0$, $i_m = 0$ and $s_m^* = 1$ the two equations above reduce to ;

$$F = \begin{bmatrix} 0 & a(T)b_2k \\ a(T)l_m(T)b_1 & 0 \end{bmatrix}, V = \begin{bmatrix} -\gamma & 0 \\ 0 & -\mu(T) \end{bmatrix} \tag{3.11}$$

Hence;

$$V^{-1} = \begin{bmatrix} -\frac{1}{\gamma} & 0 \\ 0 & -\frac{1}{\mu(T)} \end{bmatrix}$$

Thus FV^{-1} will be given by;

$$FV^{-1} = \begin{bmatrix} 0 & -\frac{a(T)b_2k}{\mu(T)} \\ -\frac{a(T)b_1l_m(T)}{\gamma} & 0 \end{bmatrix} \tag{3.12}$$

Let $K = -FV^{-1}$ be the next generation matrix, namely

$$K = -FV^{-1} = \begin{bmatrix} 0 & \frac{a(T)b_2k}{\mu(T)} \\ \frac{a(T)b_1l_m(T)}{\gamma} & 0 \end{bmatrix} \tag{3.13}$$

where the entries of K are interpreted as the number of secondary infections produced by the infected vectors and hosts during the course of their infection.

It follows that the R_0 is given by

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

.

where ρ-is the spectral radius of the next generation matrix $-FV^{-1}$

The eigenvalues of K above are

$$\lambda_{1,2} = \pm\sqrt{\frac{a^2(T)b_1b_2l_m(T)}{\gamma\mu(T)}k}$$

R_0 is given by the eigenvalue with the greatest magnitude, We have;

$$R_0 = \sqrt{\frac{a^2(T)b_1b_2l_m(T)}{\gamma\mu(T)}k}$$

Recall, $k = \frac{M(t)}{N(t)}$, substituting this into the R_0 above, the result becomes:

$$R_0^2 = \frac{M(R,T)a^2(T)b_1b_2l_m(T)}{\gamma\mu(T)N}$$

The square arises since, according to [14], it takes two generations for infected hosts to produce new infected hosts, i.e the mosquito bites twice for transmission to take place, once to acquire the parasite and again to transmit to a new host. Thus we have;

$$R_0 = \frac{M(R,T)a^2(T)b_1b_2l_m(T)}{\gamma\mu(T)N} \tag{3.14}$$

From [2, 14, 29], R_0 is known to provide the necessary condition for the eradication of an epidemic, in that if $R_0 < 1$, the disease can be eradicated and if $R_0 > 1$, the disease will persist in the population.

$a(T)$ is the number of mosquito bites per individual per day and it is dependent on the mosquito feeding (biting) rate which is highly affected by temperature as seen in (3.38) and (3.39), [2, 14, 40].

$a(T)b_1$ and $a(T)b_2$ are a measure of the conservation of bites through the biting rate a

$\frac{l_m(T)}{\mu(T)}$ is the fraction of vectors that progress from exposed to infected class.

$\frac{1}{\gamma}$ is the human average duration of infectiousness

3.5 Equilibrium States

The equilibria are obtained by equating the left hand side of equations (3.4), (3.5) and (3.6) to zero thus yielding

$$\begin{aligned}
&(1-s_m)\mu(T) - a(T)b_1s_mi_h = 0\\
&a(T)b_1l_m(T)i_hs_m - i_m\mu(T) = 0\\
&\gamma i_h^2 - (\gamma + a(T)b_2ki_m)i_h + a(T)b_2ki_m = 0
\end{aligned} \tag{3.15}$$

For easy analysis of the steady states, the solutions of the system (3.15) are expressed in terms of i_h.

Making s_m the subject from (3.15), we have;

$$s_m = \frac{\mu(T)}{\mu(T)+a(T)b_1 i_h} \tag{3.16}$$

Also, making i_m subject from (3.15) and substituting s_m from (3.16) above, we end up with;

$$i_m = \frac{ab_1 l_m(T) i_h}{\mu(T)+a(T) i_h} \tag{3.17}$$

3.6 Stability Analysis

In this section we establish the **local** and **global** stability of the disease-free equilibria (DFE) and endemic equilibria.

3.6.1 Disease-free equilibrium points, (DFE), E_0

At the disease-free equilibrium, we have an absence of disease in the population i.e $i_h = i_m = 0$ and thus $s_m = 1$. Substituting this into the system (3.15) gives the steady state $E_0 = (1, 0, 0)$

3.6.2 Local stability analysis of the disease free equilibrium

Analysis of the above is done by linearising the reduced system of differential equations in (3.4) to give the Jacobian matrix as;

$$J = \begin{bmatrix} -\mu(T) - a(T)b_1 i_h & 0 & -a(T)b_1 s_m \\ a(T)b_1 l_m(T) i_h & -\mu(T) & a(T)b_1 l_m(T) s_m \\ 0 & -a(T)b_2 k i_h + a(T)b_2 k & 2\gamma i_h - (\gamma + a(T)b_2 k i_m) \end{bmatrix} \tag{3.18}$$

At the DFE, $E_0 = E_0(1, 0, 0)$, the above Jacobian reduces to;

$$J_{DFE} = \begin{bmatrix} -\mu(T) & 0 & -a(T)b_1 \\ 0 & -\mu(T) & a(T)b_1 l_m(T) \\ 0 & a(T)b_2 k & -\gamma \end{bmatrix}$$

with the characteristic polynomial $P(\lambda)$ at DFE given by,

$$P(\lambda) = \left| J_{DEF} - \lambda I \right| = 0$$

or

$$P(\lambda) = \left|J_{DEF} - \lambda I\right| = \begin{vmatrix} -\mu(T) - \lambda & 0 & -a(T)b_1 \\ 0 & -\mu(T) - \lambda & a(T)b_1 l_m(T) \\ 0 & a(T)b_2 k & -\gamma - \lambda \end{vmatrix} = 0$$

Expanding the above along the first column gives;

$$-(\mu(T) + \lambda)[\lambda^2 + (\mu(T) + \gamma)\lambda + \mu\gamma - a^2(T)b_1 b_2 k l_m(T)] = 0$$

Since $k = \frac{M}{N}$, we have $R_0\gamma\mu(T) = a^2(T)b_1 b_2 k l_m(T)$. Substituting this into the expanded characteristic polynomial, $P(\lambda)$, we have

$$-(\mu(T) + \lambda)[\lambda^2 + (\mu(T) + \gamma)\lambda + \mu(T)\gamma(1 - R_0)] = 0$$

The roots of the above equation will have negative real parts provided:

$$\mu(T)\gamma(1 - R_0) > 0$$

The resulting eigenvalues of the characteristic polynomial are;

$$\lambda_1 = -\mu(T)$$

and

$$\lambda_{2,3} = -(\mu(T) + \gamma) \pm \sqrt{(\mu(T) + \gamma)^2 - 4\mu(T)\gamma(1 - R_0)}$$

The three eigenvalues have negative real parts for $R_0 < 1$. Thus, according to [39], E_0 is locally asymptotically stable if and only if $R_0 < 1$ and we have thus established the following Lemma:

Lemma 1: *The disease-free equilibrium E_0 is locally stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

3.6.3 Global stability analysis of the disease free-equilibrium.

As in [39], we use the following theorem to prove the global stability of the disease-free equilibrium point.

Theorem 2: *The disease-free equilibrium is globally asymptotically stable if $R_0 \leq 1$ and unstable if $R_0 > 1$*

Proof: Consider the following Lyapunov function;

$$L = \frac{\mu(T)}{a(T)} i_h + b_2 k i_m$$

Its derivative along the solution of the system is;

$$L' = \frac{\mu(T)}{a(T)} i_h' + b_2 k i_m' \tag{3.19}$$

$$= \frac{\mu(T)}{a(T)}[\gamma i_h^2 - (\gamma + a(T) b_2 k i_m) i_h + a(T) b_2 k i_m] + b_2 k [a(T) b_1 l_m(T) i_h s_m - i_m \mu(T)] \tag{3.20}$$

$$= a(T) b_1 b_2 k l_m(T) i_h s_m - \frac{\mu(T)}{a(T)} \gamma i_h + \frac{\mu(T)}{a(T)} \gamma i_h^2 - b_2 \mu(T) k i_m i_h + \mu(T) b_2 k i_m - b_2 \mu(T) k i_m \tag{3.21}$$

$$= \frac{\mu(T)}{a(T)} \gamma i_h [\frac{a^2(T) b_1 b_2 k l_m s_m}{\mu(T)\gamma} - 1] + \frac{\mu(T)}{a(T)} \gamma i_h^2 - b_2 \mu(T) k i_m i_h \tag{3.22}$$

$$= \frac{\mu(T)}{a(T)} \gamma i_h [R_0 s_m - 1] + \frac{\mu(T)}{a(T)} \gamma i_h^2 - b_2 \mu(T) k i_m i_h \tag{3.23}$$

$$= \frac{\mu(T)}{a(T)} \gamma i_h [R_0 s_m - 1] + \frac{\mu(T)}{a(T)} i_h [\gamma i_h - a(T) b_2 k i_m] \tag{3.24}$$

$$\leq \frac{\mu(T)}{a(T)} \gamma i_h [R_0 s_m - 1] \tag{3.25}$$

Since $s_m \leq 1$, then $L' \leq 0$ if $R_0 \leq 1$. $L' = 0$ if and only if $R_0 = 1$ and $i_h = i_m = 0$. By Lyapunov-Lesalle's Theorem, [39], every solution that starts in D=$\{s_m, i_m, i_h\}$ approaches the largest positive invariant subset of the set where $L' = 0$. Thus every solution that starts in the feasible region where the solutions have biological meaning approaches E_0 as $t \longrightarrow +\infty$. This shows that the disease eventually disappears from the community. Hence the disease-free equilibrium point is globally asymptotically stable hence the theorem is proved.

3.6.4 Local Stability of endemic equilibrium E_1

In this section, we will prove that when $R_0 > 1$, then the endemic equilibrium is asymptotically stable.

For existence and uniqueness of endemic equilibrium $EE = (s_m^*, i_m^*, i_h^*) > 0$
Theorem 3:
If $R_0 > 0$, the endemic equilibrium of the system is locally asymptotically stable.

Proof: We consider the Jacobian of system (3.16) given by;

$$J_{E_1} = \begin{bmatrix} -\mu(T) - a(T)b_1 i_h^* & 0 & -a(T)b_1 s_m^* \\ a(T)b_1 l_m(T) i_h^* & -\mu(T) & a(T)b_1 l_m(T) s_m^* \\ 0 & -a(T)b_2 k i_h^* + a(T)b_2 k & 2\gamma i_h^* - (\gamma + a(T)b_2 k i_m^*) \end{bmatrix} \tag{3.26}$$

The characteristic polynomial of the Jacobian above is given by;

$$p(\lambda) = \left| J_{E_1} - \lambda I \right| = 0$$

or

$$p(\lambda) = \begin{vmatrix} -\mu(T) - a(T)b_1 i_h^* - \lambda & 0 & -a(T)b_1 s_m^* \\ a(T)b_1 l_m(T) i_h^* & -\mu(T) - \lambda & a(T)b_1 l_m(T) s_m^* \\ 0 & -a(T)b_2 k i_h^* + a(T)b_2 k & 2\gamma i_h^* - (\gamma + a(T)b_2 k i_m^*) - \lambda \end{vmatrix} = 0$$

Expanding along the first raw, we have;

$$\begin{aligned} &\lambda^3 + [2\mu + ab_1 i_h^* + \gamma(1 - 2i_h^*) + ab_2 k i_m^*]\lambda^2 + \\ &[\mu^2 + 2\gamma\mu - 4\gamma\mu i_h^* + 2ab_2 k\mu i_h^* + ab_1\gamma i_h^*(1 - 2i_h^*) + a^2 b_1 b_2 k i_m^* i_h^* + a^2 b_1 b_2 k l_m s_m^*(i_h^* - 1)]\lambda + \\ &\qquad a^2 b_1 b_2 k\mu i_m^* i_h^* + ab_1\gamma\mu i_h^* + a^2 b_1 b_2 k\mu l_m i_h^* s_m^* + ab_2 k\mu^2 i_m^* + \\ &\qquad \gamma\mu^2 - 2\mu^2\gamma i_h^* - a^2 b_1 b_2 k\mu l_m s_m^* - 2ab_1\mu\gamma i_h^* = 0 \end{aligned} \tag{3.27}$$

If the characteristic polynomial of the matrix (3.26) is given by

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

then from (3.25), we have;

$$a_0 = 1$$

$$a_1 = 2\mu + ab_1 i_h^* + \gamma(1 - 2i_h^*) + ab_2 k i_m^*$$

$$a_2 = \mu^2 + 2\gamma\mu - 4\gamma\mu i_h^* + 2ab_2 k\mu i_h^* + ab_1\gamma i_h^*(1 - 2i_h^*) + a^2 b_1 b_2 k i_m^* i_h^* + a^2 b_1 b_2 k l_m s_m^*(i_h^* - 1)$$

$$a_3 = a^2 b_1 b_2 k\mu i_m^* i_h^* + ab_1\gamma\mu i_h^* + a^2 b_1 b_2 k\mu l_m i_h^* s_m^* + ab_2 k\mu^2 i_m^* + \gamma\mu^2 - 2\mu^2\gamma i_h^* - a^2 b_1 b_2 k\mu l_m s_m^* - 2ab_1\mu\gamma i_h^*$$

From the expression of R_0 derived previously, we have $R_0 = \frac{a^2 b_1 b_2 k l_m}{\mu\gamma} > 1$ or $a^2 b_1 b_2 k l_m > \mu\gamma$ thus we can deduce that $a_1 > 0$, $a_2 > 0$, $a_3 > 0$.

We need to show that $a_1a_2 > a_0a_3$ or $a_1a_2 - a_0a_3 > 0$:

$$\begin{aligned} a_1a_2-a_0a_3 = {} & 2\mu^3+4\mu\gamma(1-2i_h^*)[\mu+ab_2ki_m^*]+4ab_2k\mu^2i_m^*+3ab_1\mu^2i_h^*+2ab_1\gamma\mu i_h^*(1-3i_h^*) \\ & + a^2b_1b_2k\gamma(2i_m^*i_h^* + 3s_m^*i_h^*l_m - l_ms_m^* - 4i_m^*i_h^{2*} - 2l_ms_m^*i_h^{2*}) \\ & + 2a^2b_2^2k^2\mu i_m^{2*} + a^3b_1^2b_2ki_h^*(i_m^*i_h^* + l_ms_m^*i_h^* - l_ms_m^*) \\ & + a^3b_1b_2^2k^2i_m^*(i_m^*i_h^* + l_ms_m^*i_h^* - l_ms_m^*) + 8\gamma^2\mu i_h^*(i_h^* - 1) \\ & + ab_1\gamma^2i_h^*(4i_h^{2*} - 2i_h^* - 1) + a^2b_1^2i_h^{2*}(\mu + \gamma - 2\gamma i_h^*) \end{aligned} \quad (3.28)$$

If $R_0 > 1$ and $a_1a_2 > a_0a_3$, then by Routh-Hurwitz Criterion, the eigenvalues of the matrix have negative real parts and thus the endemic equilibrium is locally stable.

3.7 Adult mosquito birth rate.

According to Parham and Michael [2], the adult mosquito birth rate $\lambda(R,T)$, which is a function of rainfall and temperature is the parameter most affected by climate change. The birth rate can be expressed as:

$$\lambda(R,T) = \frac{B_E P_E(R) P_L(R) P_L(t) P_P(R)}{\tau_E + \tau_L(T) + \tau_P} \quad (3.29)$$

where

- R is rainfall
- T is temperature
- B_E is number of eggs laid per oviposition
- P_E is daily survival probability of eggs
- P_L is daily survival probability of larvae
- P_P is daily survival probability of pupa
- τ_E is duration of egg stage
- τ_L is duration of larvae stage
- τ_P is duration of the pupa stage

- α, β and γ are constants

The **assumptions** in above model are:

- B_E is independent of environmental conditions.
- Duration of each stage depends only on temperature if there is sufficient rainfall to sustain development.
- Eggs have the highest daily survival probability.

The daily survival probabilities of eggs, larvae and pupae are given by

$$\begin{aligned} P_E(R) &= 4\frac{P_{ME}}{R_{LE}^2}R(R_{LE}-R) \\ P_L(R) &= 4\frac{P_{ML}}{R_{LL}^2}R(R_{LL}-R) \\ P_P(R) &= 4\frac{P_{MP}}{R_{LP}^2}R(R_{LP}-R) \end{aligned} \tag{3.30}$$

The effect of temperature on larvae duration in days can be expressed as;

$$\tau_L(T) = \frac{1}{\alpha T+\beta} \tag{3.31}$$

and the daily survival probability of larvae on temperature as;

$$P_L(T) = e^{-(\alpha T+\beta)} \tag{3.32}$$

and the identical wash out limits as

$$R_{LE} = R_{LL} = R_{LP} = R_L \tag{3.33}$$

Substituting (3.30), (3.31), (3.32), and (3.33) into (3.29) gives rise to;

$$\lambda(R,T) = 64\frac{B_E P_{ME} P_{ML} P_{MP} R^3 (R_L-R)^3 (\alpha T+\beta) e^{-(\alpha T+\beta)}}{R_L^6[1+\tau_E(\alpha T+\beta)+\tau_P(\alpha T+\beta)]} \tag{3.34}$$

3.8 R_0 as a function of temperature, rainfall and Relative Humidity

According to Martens [30], to get the survival probability $l_m(T)$ of infected mosquitoes over the incubation period of the parasite in relation to the ambient temperature and latent period, the relation below was used:

$$l_m(T) = P^n$$

where the incubation period of the parasite in the vector, n, is in days and is given by [30, 2];

$$n = \frac{DD}{T - T_{min}}$$

where DD is the total degree days required for the development of the parasite and T_{min} is the minimum temperature required for parasite development. The incubation period of the parasite in the malarial mosquito must have elapsed before the infected vector can transmit the parasite. Thus;

$$l_m(T) = p^{\frac{DD}{T - T_{min}}} \tag{3.35}$$

If $P(T)$ is the survival probability of mosquito and $\mu(T)$ is the mortality rate, then according to Lunde et al [9], the survival probability is related to the mortality by;

$$\mu(T) = -lnp(T), or, p(T) = e^{-\mu(T)} \tag{3.36}$$

Substituting (3.36) into (3.35) gives

$$l_m(T) = e^{-\mu(T)\left[\frac{DD}{T - T_{min}}\right]} \tag{3.37}$$

Definition of Biting and Mortality Rates

To be able to analyse the dependence of R_0 on temperature and rainfall, we explored more into equations of the biting and mortality rates as a function of temperature.

Biting 1 and **Biting 2** given by (3.38) and (3.39) are the two models representing biting rate of the female Anopheles mosquito i.e, the number of mosquito bites per individual per day [14, 40].
Mortality 1 and **Mortality 2** given by (3.41) and (3.43) are the two models representing mortality rate of the female mosquito [9].

According to [30, 2], the mosquito biting rate per day was given by the frequency with which the vector takes a blood meal. The frequency of feeding depends on the speed at which the blood meal is digested. The belief is that as temperature rise, the frequency of biting increases. This can be measured by;

$$\frac{D_1}{T - T_1}$$

where D_1 is the number of degree days required for the digestion of a portion of blood ingested, T is the actual average temperature and T_1 is the minimum temperature required for the digestion of the blood meal. Thus according to [40], the number of mosquito bites per individual per day is given by;

$$a(T) = \frac{T - T_1}{D_1} \tag{3.38}$$

which shows that the frequency of feeding by a female mosquito $a(T)$ increases as temperature increases.

Also according to Paajmans [14], the biting rate of *Anopheles Pseudopunctipennis* one of the main malaria vectors in South Africa was described as:

$$a(T) = \eta T(T - \omega)\sqrt{(\rho - T)} \tag{3.39}$$

where $\eta = 0.000203$, $\omega = 11.7$ and $\rho = 42.3$ are constants.

We were motivated to pick on (3.36) and (3.37) because;

(i) The research was done within a mean temperature range of 18^0C to 35^0C which covers the thermal limits for transmission of *Plasmodium falciparum* which is the main cause of malaria in Kenya

(ii) The temperature range in (i) above is applicable to the Kenyan scenario.

Lunde *et al* [9], expressed the survival probability $p(T)$, as a function of temperature given by (3.40) which prolonged the daily survival probability at higher temperatures.

$$p(T) = e^{\frac{-1}{AT^2 + BT + C}} \tag{3.40}$$

Substituting (3.40) into (3.36) gives the mortality rate as;

$$\mu(T) = \frac{1}{AT^2 + BT + C} \tag{3.41}$$

where A, B and C are constants.

Parham [9] took a different approach from Martens by formulating a model in which he included the effects of relative humidity, (RH) in the survival probability $p(T)$. His model resembles (3.40) only that the constants A, B and C are replaced by expressions, β_0, β_1 and β_2 which are functions of RH. The survival probability $p(T)$ was expressed as a function of temperature T and RH as;

$$p(T, RH) = e^{\frac{-1}{\beta_2 T^2 + \beta_1 T + \beta_0}} \tag{3.42}$$

Substituting (3.42) into (3.36), gives the mortality rate as;

$$\mu(T) = \frac{1}{\beta_2 T^2 + \beta_1 T + \beta_0} \tag{3.43}$$

where,

$$\beta_0 = U_1(RH)^2 + V_1 RH + W_1$$
$$\beta_1 = U_2(RH)^2 + V_2 RH + W_2$$
$$\beta_2 = U_3(RH)^2 + V_3 RH + W_3$$

and $U_1, U_2, U_3, V_1, V_2, V_3, W_1, W_2$ and W_3 are constants.

In order to obtain the effect of rainfall, temperature and relative-humidity on R_0 we substitute the vector population $M(R, T)$; i.e

$$M(R, T) = \frac{\lambda(R,T)}{\mu(T)} \tag{3.44}$$

Substituting (3.37) and (3.44) into (3.14) results in

$$R_0 = \frac{\lambda(R,T) b_1 b_2}{\gamma N \mu^2(T)} a^2 e^{-\mu(T)\left[\frac{DD}{T - T_{min}}\right]} \tag{3.45}$$

Substituting biting 1, (3.38) and mortality 1, (3.41) into (3.45) yields

$$R_0 = \frac{\lambda(R,T) b_1 b_2}{\gamma N} \left(\frac{T - T_1}{D_1}\right)^2 [AT^2 + BT + C]^2 exp\left[\frac{-DD}{(AT^2 + BT + C)(T - T_{min})}\right] \tag{3.46}$$

Substituting biting 1, (3.38) and mortality 2, (3.43) into (3.45) yields

$$R_0 = \frac{\lambda(R,T) b_1 b_2}{\gamma N} \left(\frac{T - T_1}{D_1}\right)^2 [\beta_2 T^2 + \beta_1 T + \beta_0]^2 exp\left[\frac{-DD}{(\beta_2 T^2 + \beta_1 T + \beta_0)(T - T_{min})}\right] \tag{3.47}$$

Substituting biting 2, (3.39) and mortality 1, (3.41) into (3.45) yields

$$R_0 = \frac{\lambda(R,T) b_1 b_2}{\gamma N} \left[\eta T (T - \omega)\sqrt{(\rho - T)}\right]^2 [AT^2 + BT + C]^2 exp\left[\frac{-DD}{(AT^2 + BT + C)(T - T_{min})}\right] \tag{3.48}$$

Substituting biting 2, (3.39) and mortality 2, (3.43) into (3.45) yields

$$R_0 = \frac{\lambda(R,T)b_1b_2}{\gamma N}\left[\eta T(T-\omega)\sqrt{(\rho-T)}\right]^2 [\beta_2T^2+\beta_1T+\beta_0]^2 exp\left[\frac{-DD}{(\beta_2T^2+\beta_1T+\beta_0)(T-T_{min})}\right] \tag{3.49}$$

3.9 Epidemic Potential, *EP(T)*.

Apart from the use of the reproduction number to determine the endemic nature of malaria, we also use the *epidemic potential (EP)* as an index to project the future risk of malaria in the event of change in temperature due to global climate change. The EP serves as a summary parameter that can be used as a comparative index to estimate the effect that change in ambient temperature can have on the risk of malaria [41].

The disadvantage of this index is that unlike the R_0 which is an integrated link system model, it incorporates temperature as the only climatic variable in the form of mortality rate. Epidemic potential EP, is derived from R_0 (3.14), by factoring out $\frac{1}{\gamma}$ the average duration of human infectiousness.

$$R_0 = \frac{1}{\gamma}\left[\frac{M(R,T)a^2(T)b_1b_2P^n}{N(-lnP)}\right] = \frac{1}{\gamma}\left[\frac{ma^2(T)b_1b_2P^n}{(-lnP)}\right] = \frac{VC}{\gamma}$$

where the vectorial capacity VC is the number of potential infectious bites that can occur per unit time per infectious host and the mosquito vector density m is the number of female mosquitoes per human.

If we let VC = 1, i.e assume that 1 potential contact is infected by a mosquito per infectious person per unit time, then;

$$m_{CT} = \frac{(-lnP)}{a^2b_1b_2P^n}$$

where m_{CT} is the *critical threshold density* and represents the average number of female mosquitoes per person necessary for an infectious human to give rise to one new case of malaria in a susceptible population.

Thus the epidemic potential (EP) is the reciprocal of (m_{CT}) .

$$EP = \frac{1}{m_{CT}} = \frac{a^2b_1b_2P^n}{(-lnP)} \tag{3.50}$$

According to [30], an increase in EP indicates that conditions are suitable for *fewer* vectors to effectively potentiate epidemic spread in a given area where *P. falciparum* exist. As EP rises, conditions favour a greater chance of parasite development per mosquito, i.e, a high EP indicates that despite a smaller vector population, a given degree of endemicity may be maintained. The direct effect of temperature is on n, the development time of the parasite and the host mortality rates.

Substituting biting 1, (3.38) and mortality 1, (3.41) into (3.50) yields

$$EP = b_1 b_2 \left(\frac{T-T_1}{D_1}\right)^2 [AT^2 + BT + C] exp\left[\frac{-DD}{(AT^2+BT+C)(T-T_{min})}\right] \quad (3.51)$$

Substituting biting 1, (3.38) and mortality 2, (3.43) into (3.50) yields

$$EP = b_1 b_2 \left(\frac{T-T_1}{D_1}\right)^2 [\beta_2 T^2 + \beta_1 T + \beta_0] exp\left[\frac{-DD}{(\beta_2 T^2+\beta_1 T+\beta_0)(T-T_{min})}\right] \quad (3.52)$$

Substituting biting 2, (3.39) and mortality 1, (3.41) into (3.50) yields

$$EP = b_1 b_2 \left[\eta T(T-\omega)\sqrt{(\rho - T)}\right]^2 [AT^2 + BT + C] exp\left[\frac{-DD}{(AT^2+BT+C)(T-T_{min})}\right] \quad (3.53)$$

Substituting biting 2, (3.39) and mortality 2, (3.43) into (3.50) yields

$$EP = b_1 b_2 \left[\eta T(T-\omega)\sqrt{(\rho - T)}\right]^2 [\beta_2 T^2 + \beta_1 T + \beta_0] exp\left[\frac{-DD}{(\beta_2 T^2+\beta_1 T+\beta_0)(T-T_{min})}\right] \quad (3.54)$$

Chapter 4

RESULTS AND ANALYSIS

4.1 Numerical Simulation

Here we use MATLAB to run simulations in order to illustrate the behaviour and relationships between the confirmed and total malaria incidence and the climatic variables. We considered two regions in Kenya for analysis; i.e Lake Victoria region named Zone 1 and Nairobi and its environs named Zone 4 where the analysis was done on both monthly and seasonal values.

The parameters in Table (4.1) were used in simulation to compute the values of R_0 as temperature, rainfall and relative-humidity change.

4.2 Confirmed Malaria

This is the percentage of individuals who are confirmed medically to have malaria using the data between the year 2009-2011 for zone 1 and 4. Here we used the reproduction number, R_0 and epidemic potential, EP as the indices used to determine the risk of malaria and the future trends in malaria incidence and prevalence respectively.

For a better understanding of the relationship between climatic variables and malaria, we plotted graphs of temperature and rainfall against confirmed unlagged-malaria, figures (4.2), (4.3), and (4.1) perspectively both seasonally and monthly and also the reproduction number and epidemic potential against confirmed unlagged-malaria, figures (4.6), (4.10) and (4.12) seasonally. We also quantitatively calculated the cor-

relation co-efficient between the climatic variables, R_0, EP and confirmed malaria.

For further comparison and analysis, we computed graphs for confirmed-lagged malaria both in seasons and months as shown in figures (4.4, 4.5). The lagging was done by comparing the effects of climatic variables, R_0 and EP in one season (or month) to malaria incidence in the next season (or month). The analysis of unlagged and lagged malaria were done using the two biting rates (3.38) and (3.39) which are functions of temperature and also the two mortality rates (3.41) and (3.43) which are functions of temperature, rainfall and relative-humidity.

From figure (4.1), we observe that as rainfall peaks in one season, malaria does not peak immediately in the same season and similarly if rainfall reduces in one season, malaria drops after sometime .i.e. a change in rainfall pattern will lead to a corresponding change in malaria whose effect will be felt after sometime. The same behaviour is observed when we plotted temperature against confirmed malaria for the same zone. The effects of climatic variables are much clearer under seasonal analysis as compared to monthly analysis because of the fact that a change in climatic variable does not simultaneously cause a change in malaria but in most cases, the effect comes after one or more months.

As shown in figure (4.5) the computations of lagged-malaria, we observed that as R_0 and temperature peaks, lagged-malaria peaks almost immediately and a reduction in the climatic variable relates to a reduction in malaria incidence.

A similar observation was made when we computed reproduction number and epidemic potential against malaria, figures (4.7, 4.8). This is because the two indices are functions of climatic variables. A change in climatic variables, R_0 and EP does not correspond to a sudden change in malaria due to transmission dynamics in malaria which includes; the fact that the mosquito needs to bite twice, incubation period and four stages of mosquito growth to maturity before malaria transmission occurs, figure (1.3). Thus, during analysis this transmission dynamics are taken into account by lagging malaria data by one season or month.

4.3 Total Malaria

This data is obtained from the percentage of individuals who are reported to have suffered from malaria-like signs and symptoms prior to medical tests for confirmation.

As seen in the analysis of confirmed malaria, there is a similar relationship between climatic variables and total malaria both in seasons and monthly, figure (4.14, 4.15

and 4.20). This is to ascertain that, changes in climatic variables leads to unpleasant change in the functions of the body system. In the process the human body might succumb to the extreme sudden changes in climatic variables thus leading to manifestation of malaria-like symptoms.

Since the malaria-like symptoms does not manifest immediately, we lagged the data for total malaria so as to show clearly the relationship as seen in the peaks and troughs in the graphs of epidemic potential, reproduction number, climatic variables and total malaria, see figures (4.15, 4.17 and 4.19). Quantitatively, the high correlation co-efficient; 0.6747, 0.6599 and 0.6767 computed in figures (4.15, 4.17 and 4.19) respectively also confirm that there is a high correlation between climatic variables and total malaria.

From the graphs shown in figures (4.10 - 4.13), the biting rate models (3.38, 3.39) and mortality rate models (3.41, 3.43) shows the same relation with the confirmed malaria incidence when the analysis is done in the same zone. On the other hand, when a comparison is done from one zone to another, we found out that the relation does vary for both reproduction number and epidemic potential.

Parameter	**Value**	**Units**
T_1	19.9	${}^0C$
D_1	36.5	${}^0Cdays$
T_{min}	16	${}^0C$
DD	111	${}^0Cdays$
B_E	200	Dimensionless
P_{ME}	0.9	Dimensionless
P_{ML}	0.25	Dimensionless
P_{MP}	0.75	Dimensionless
R_L	50	mm
τ_E	1	$days$
τ_p	1	$days$
α	0.00554	$({}^0C^2days)^{-1}$
β	-0.06737	$(days)^{-1}$
b_1	0.04	Dimensionless
b_2	0.09	Dimensionless
γ	1/120	$days^{-1}$
η	0.000203	Dimensionless
ω	11.7	Dimensionless
ρ	42.3	Dimensionless
A	-0.03	$({}^0C^2days)^{-1}$
B	1.31	$({}^0Cdays)^{-1}$
C	-4.4	$days^{-1}$
U_1	0.00113	Dimensionless
V_1	-0.158	Dimensionless
W_1	-6.61	Dimensionless
U_2	-2.32 x 10^{-4}	Dimensionless
V_2	0.051	Dimensionless
W_2	1.06	Dimensionless
U_3	4 x 10^{-6}	Dimensionless
V_3	-1.09 x 10^{-3}	Dimensionless
W_3	-0.0255	Dimensionless

Table 4.1: Table of parameters estimates and their Units

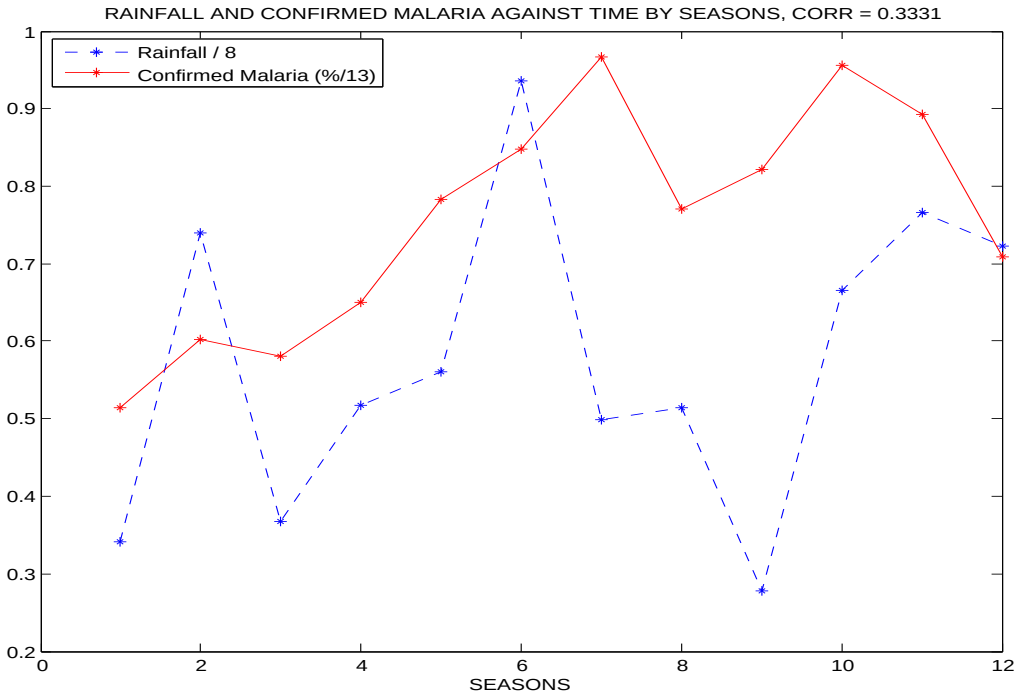


Figure 4.1: Rainfall and Confirmed Malaria for Zone 1

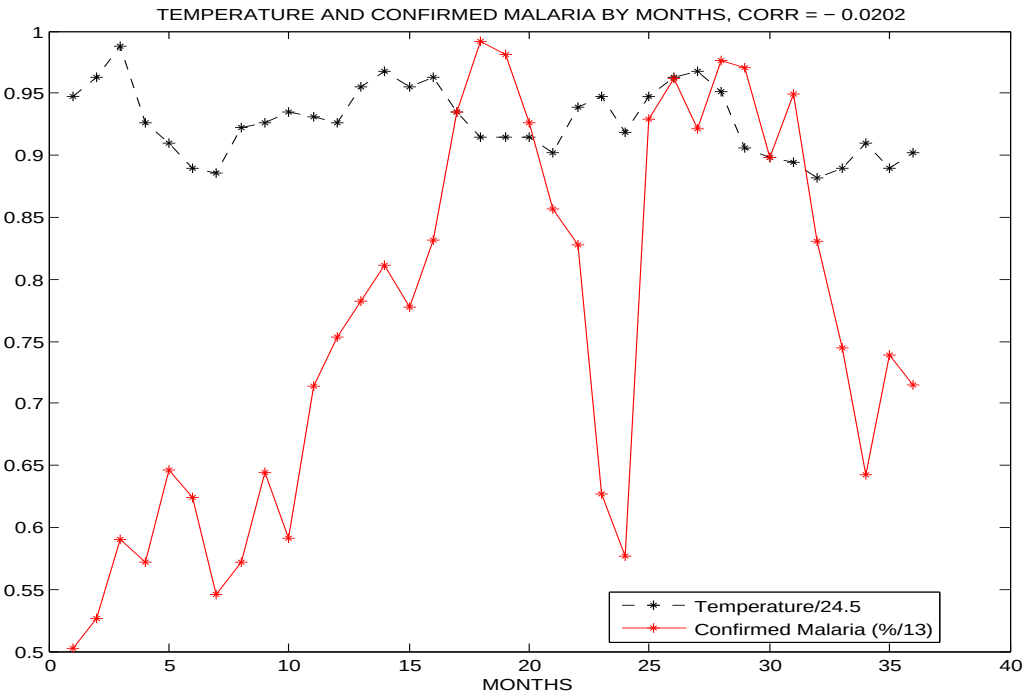


Figure 4.2: Temperature and Confirmed Malaria for Zone 1

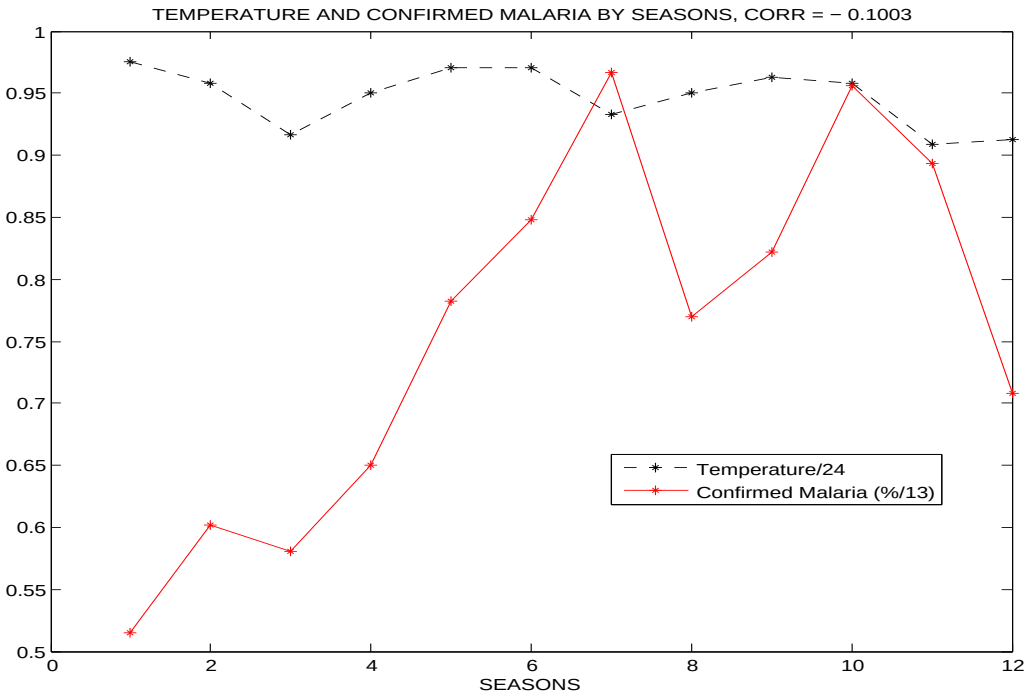


Figure 4.3: Temperature and Confirmed Malaria for Zone 1

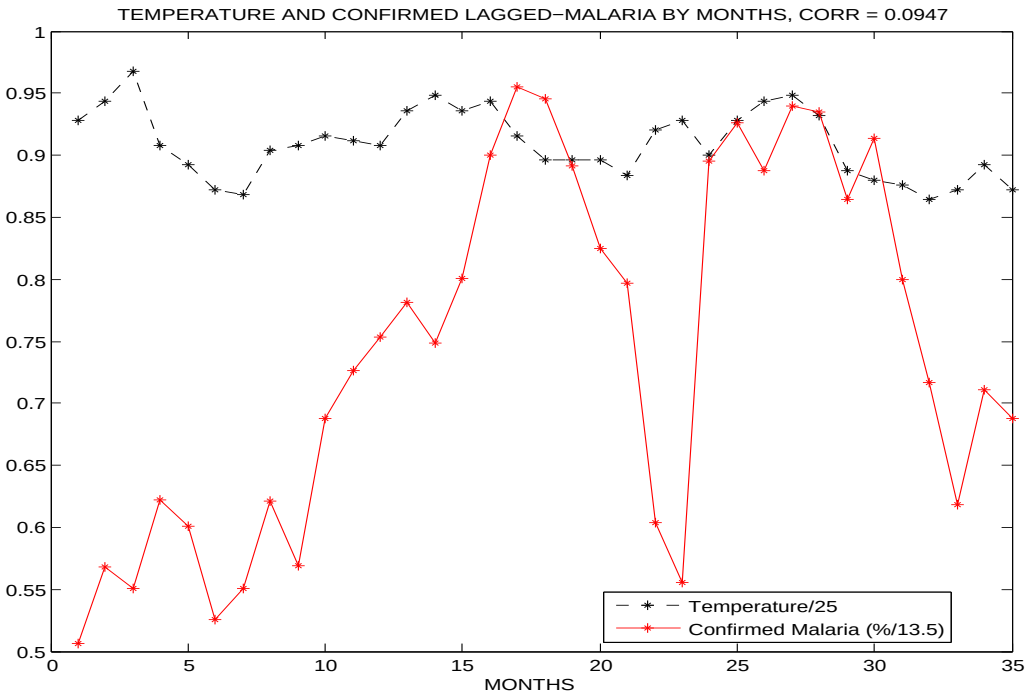


Figure 4.4: Temperature and Lagged-malaria for Zone 1

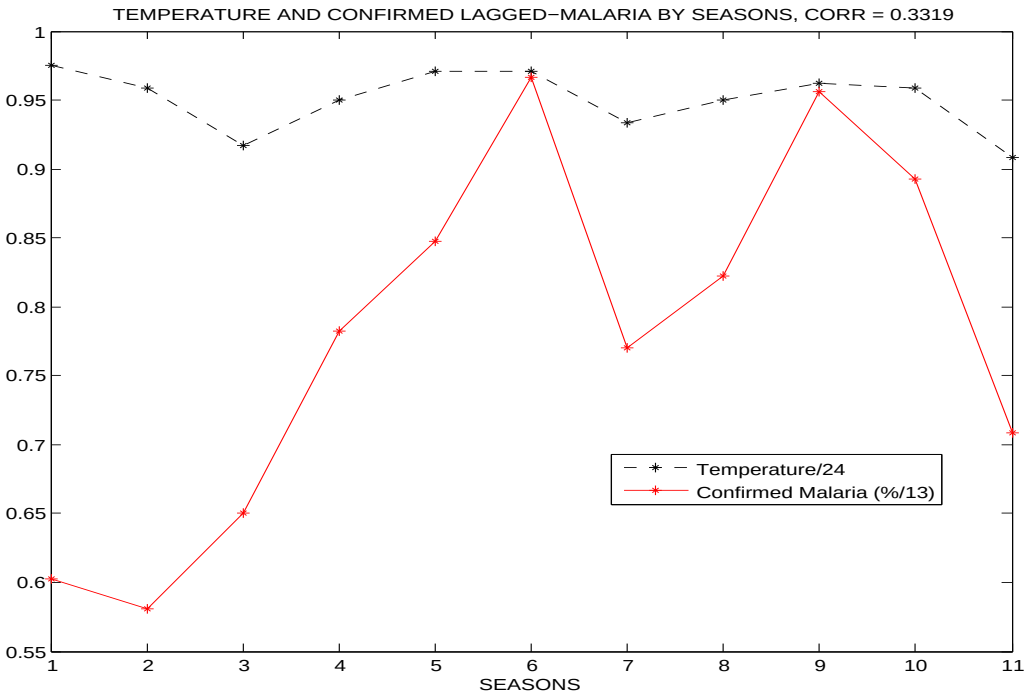


Figure 4.5: Temperature and lagged-Malaria Zone 1

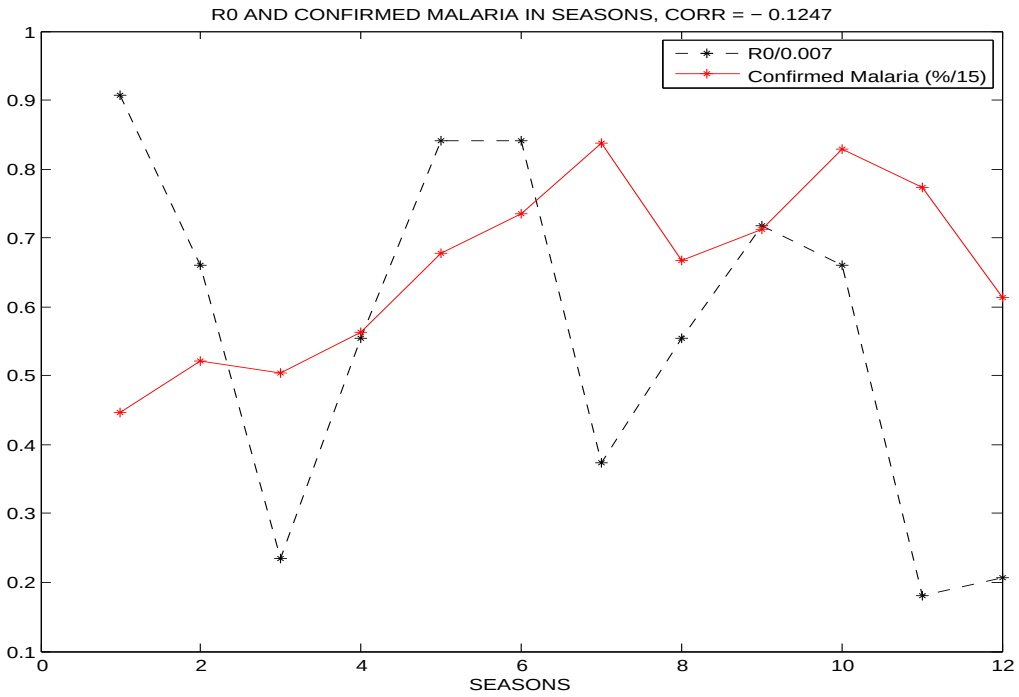


Figure 4.6: R_0 and Confirmed Malaria for Zone 1 using (3.38); (3.41)

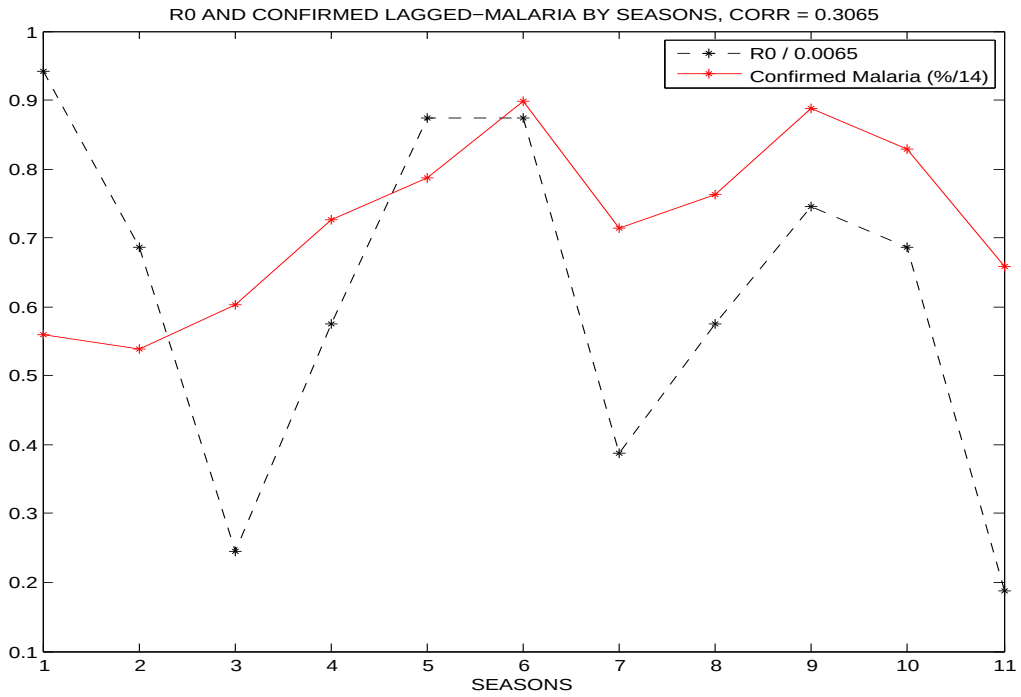


Figure 4.7: R_0 and Lagged-Malaria for Zone 1 using (3.38); (3.41)

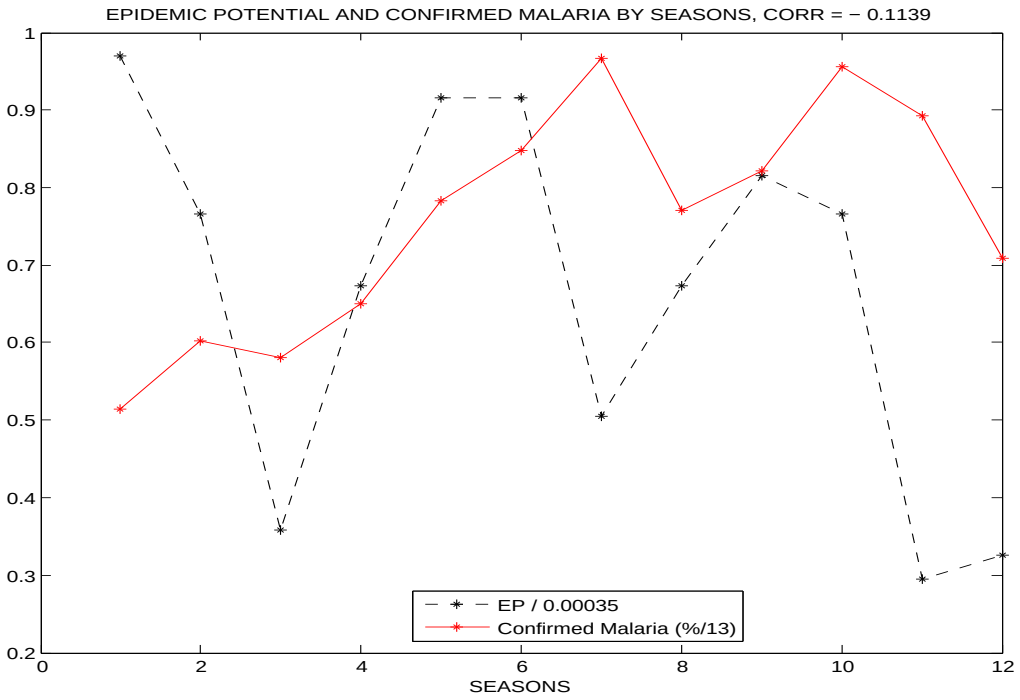


Figure 4.8: Epidemic potential and Confirmed Malaria for Zone 1, using (3.38); (3.41)

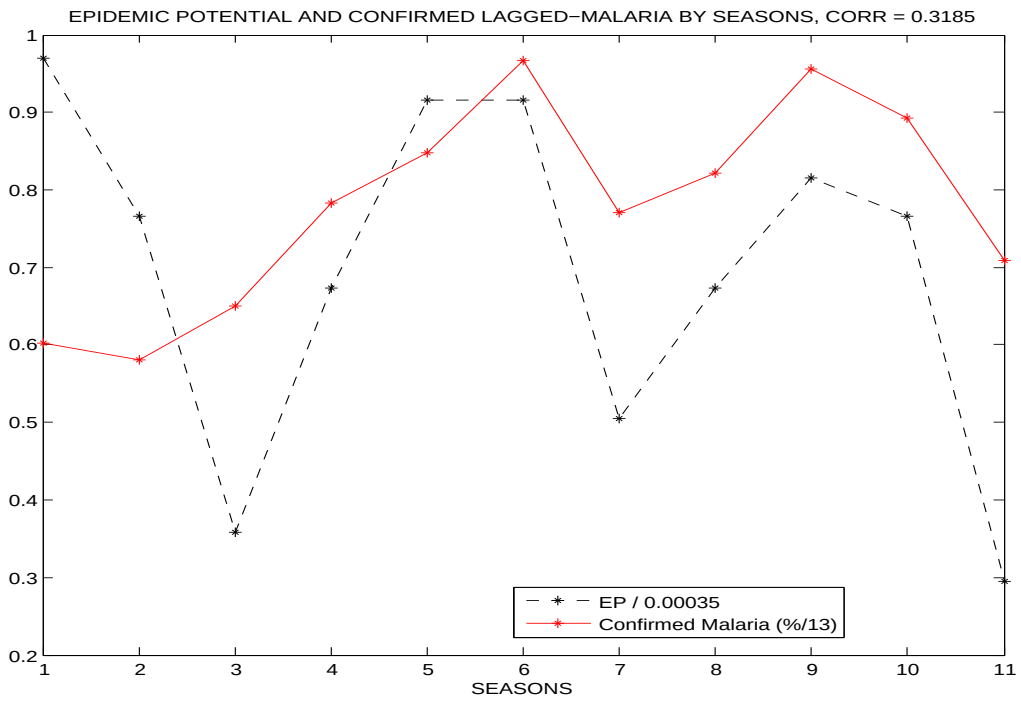


Figure 4.9: Epidemic potential and Lagged-Malaria for Zone 1, using (3.38); (3.41)

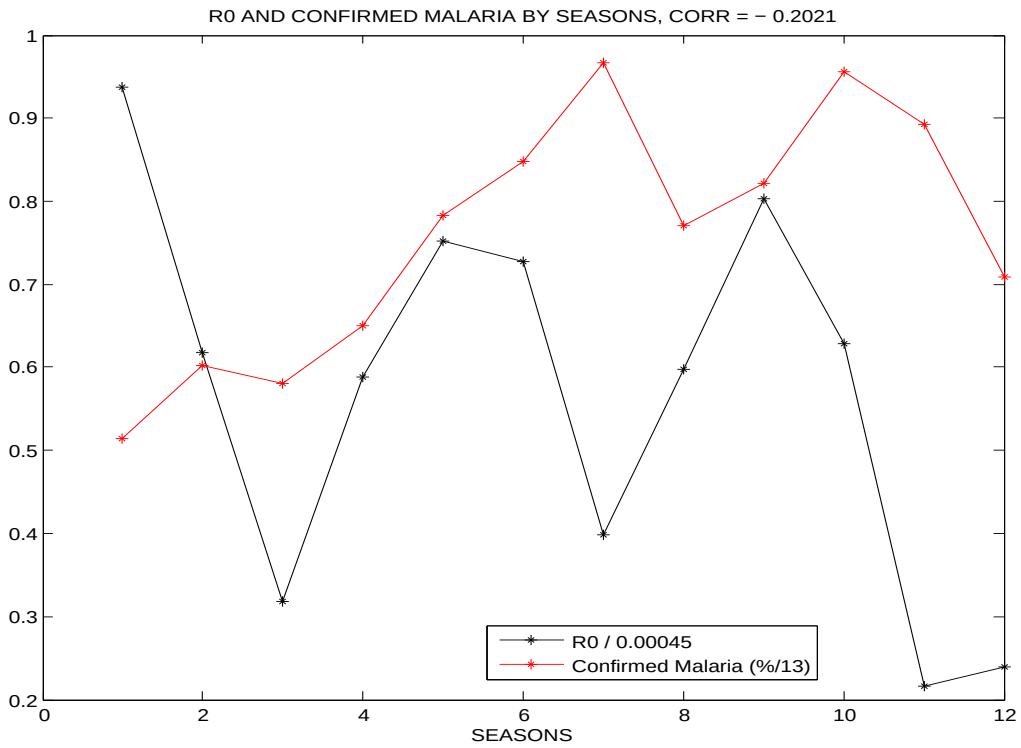


Figure 4.10: R_0 and Confirmed Malaria for Zone 1, using (3.39); (3.43)

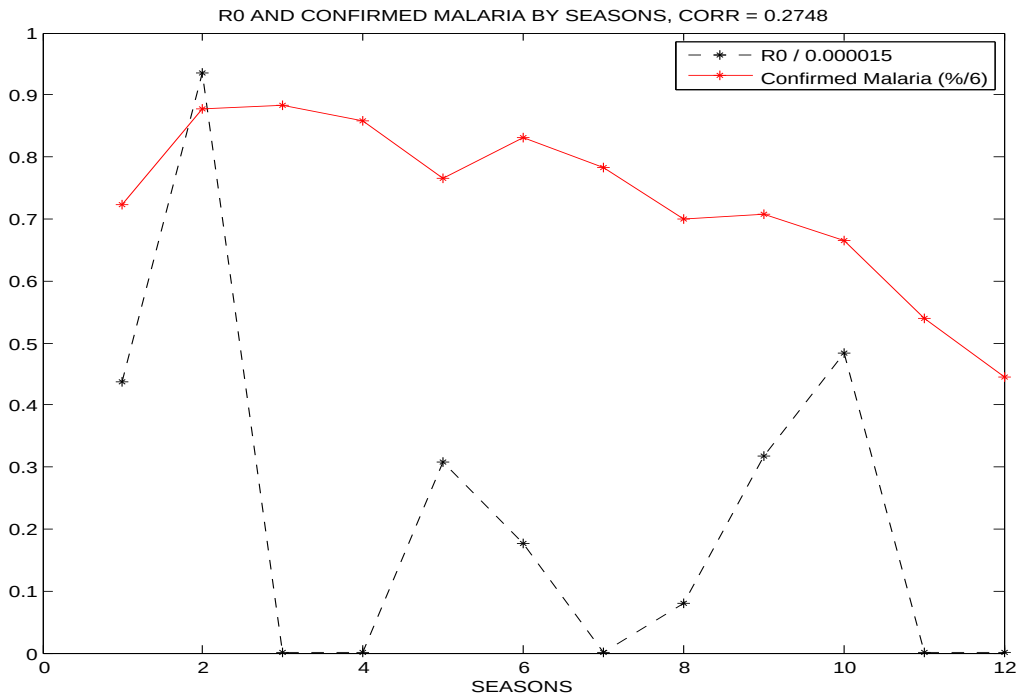


Figure 4.11: R_0 and Confirmed Malaria for Zone 4, using (3.39); (3.43)

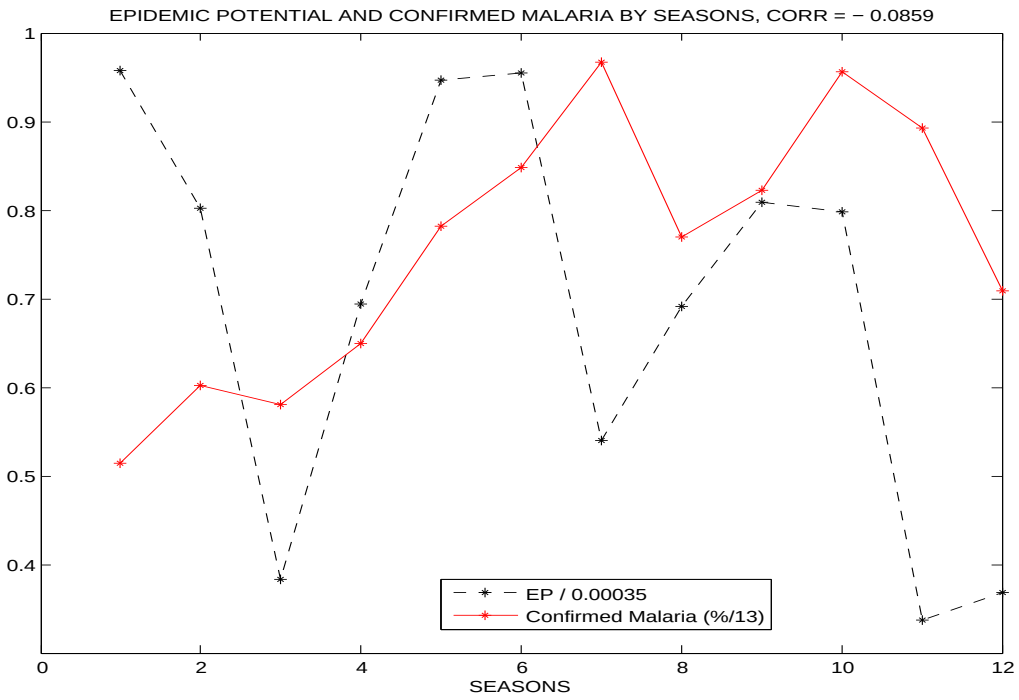


Figure 4.12: EP and Confirmed Malaria for Zone 1, using (3.39); (3.43)

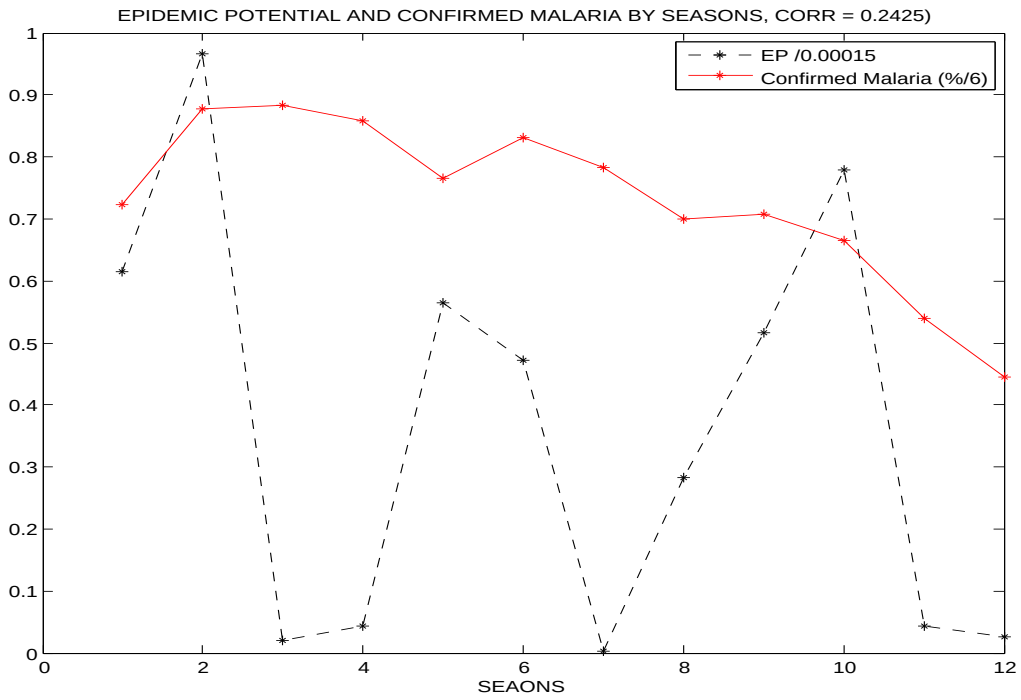


Figure 4.13: EP and Confirmed Malaria for Zone 4, using (3.39); (3.41)

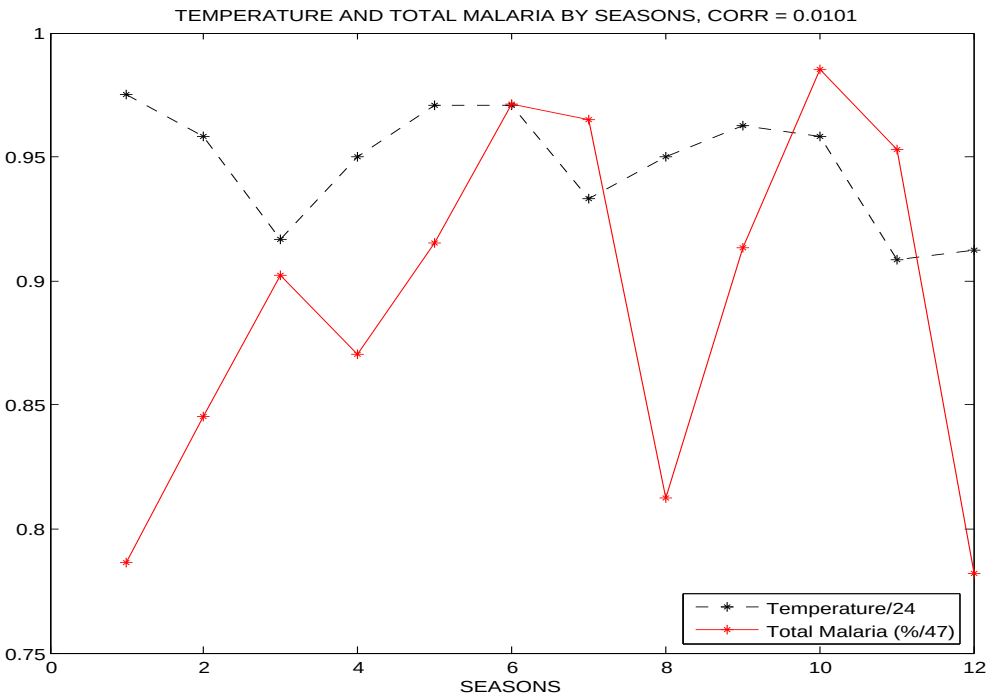


Figure 4.14: Temperature and Total Malaria for Zone 1, using (3.38); (3.41)

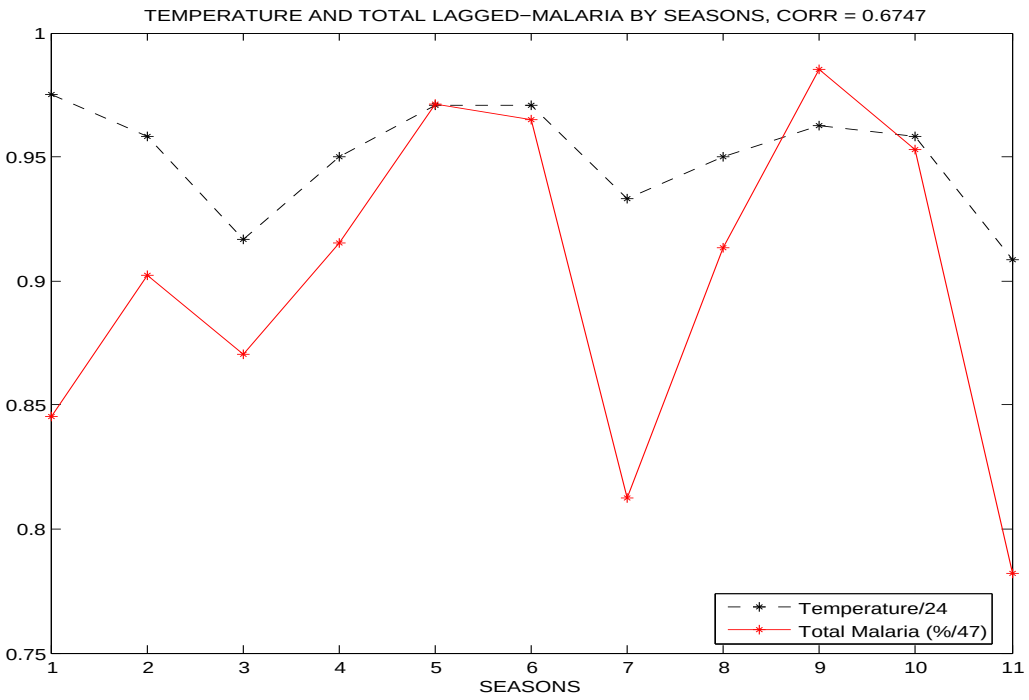


Figure 4.15: Temp and Total Lagged Malaria for Zone 1, using (3.38); (3.41)

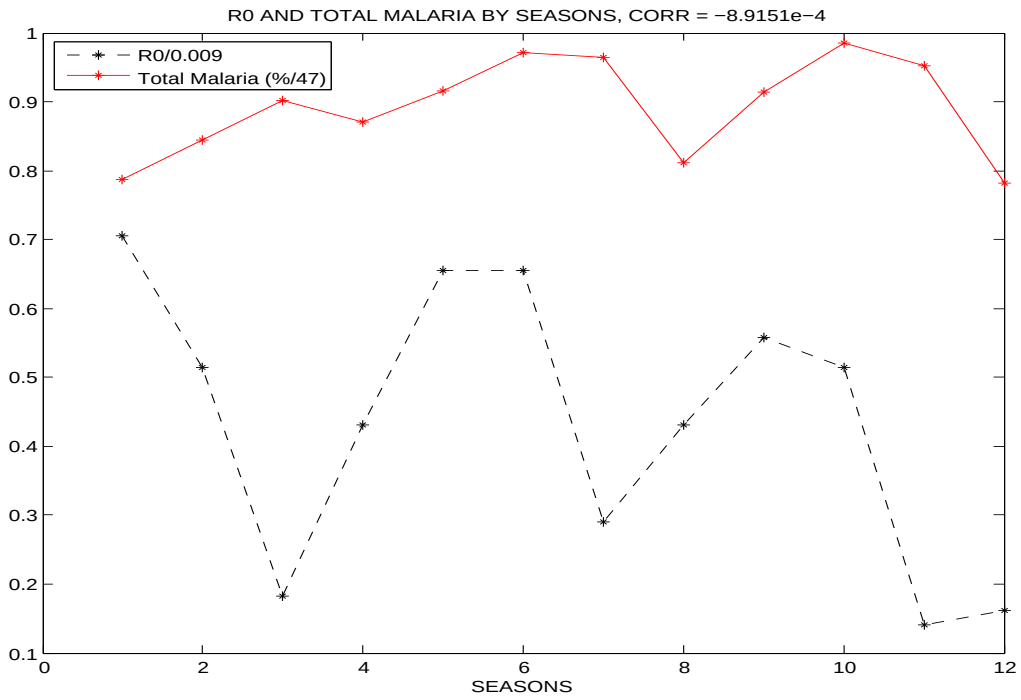


Figure 4.16: R_0 and Total Malaria for Zone 1, using (3.38); (3.41)

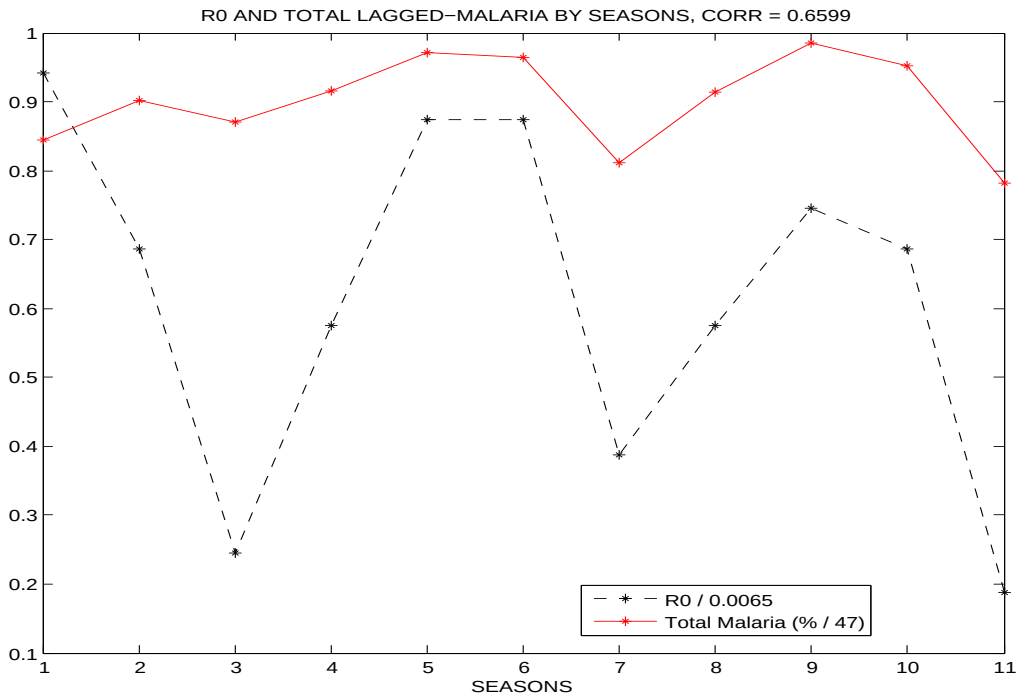


Figure 4.17: R_0 and Total Lagged Malaria for Zone 1, using (3.38); (3.41)

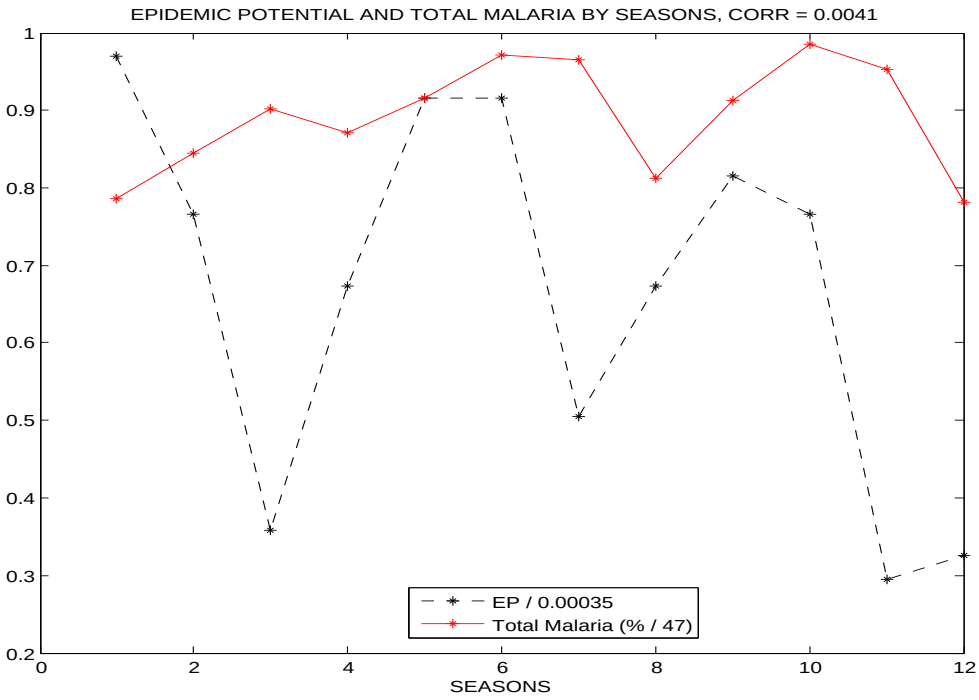


Figure 4.18: EP and Total Malaria for Zone 1, using (3.38); (3.41)

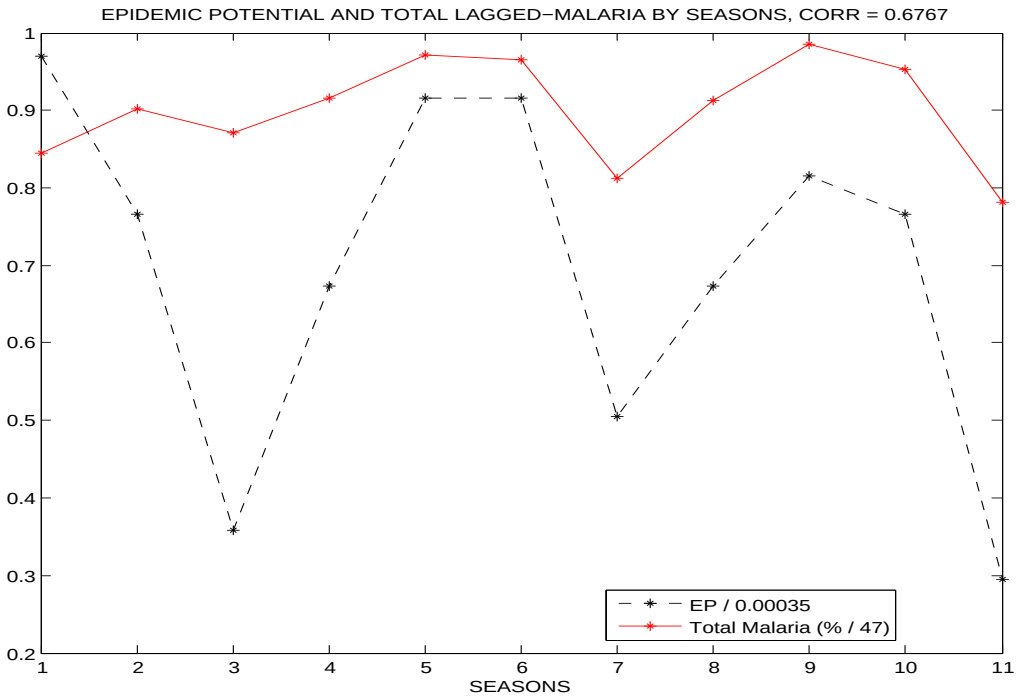


Figure 4.19: EP and Total Lagged Malaria for Zone 1, using (3.38); (3.41)

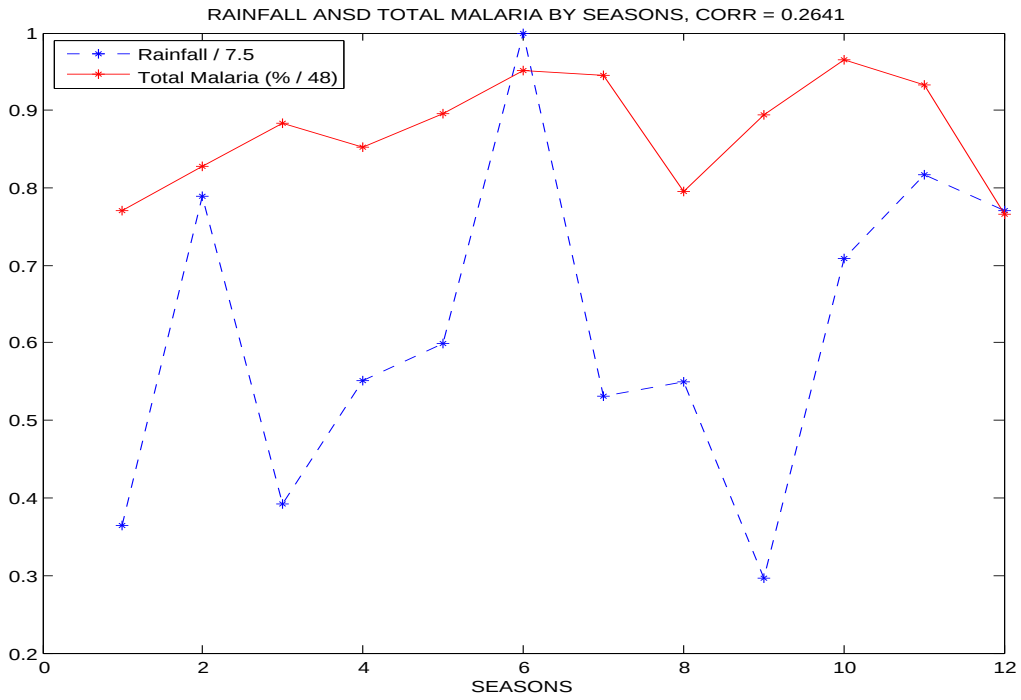


Figure 4.20: Rain and Total Malaria for Zone 1, using (3.38); (3.41)

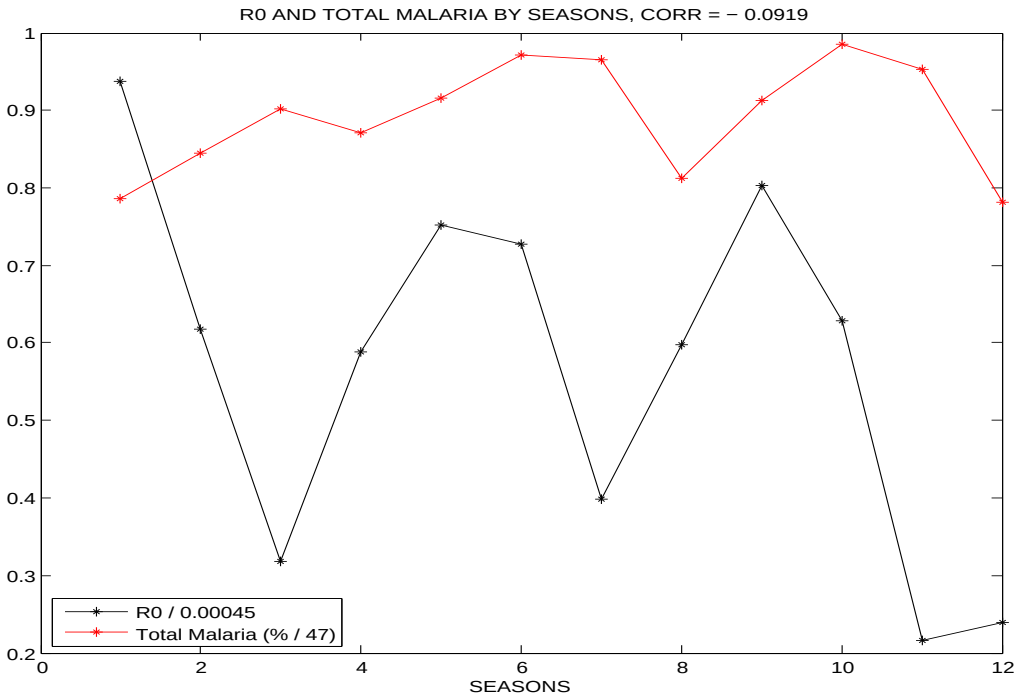


Figure 4.21: R_0 and Total Malaria for Zone 1, using (3.39); (3.43)

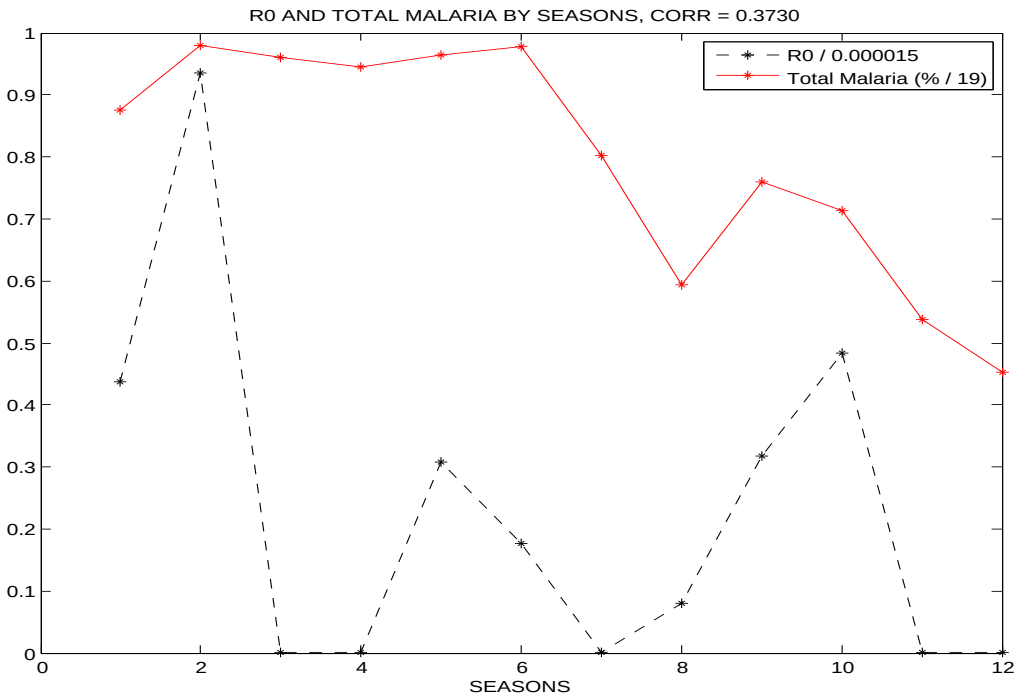


Figure 4.22: R_0 and Total Malaria for Zone 4, using (3.39); (3.43)

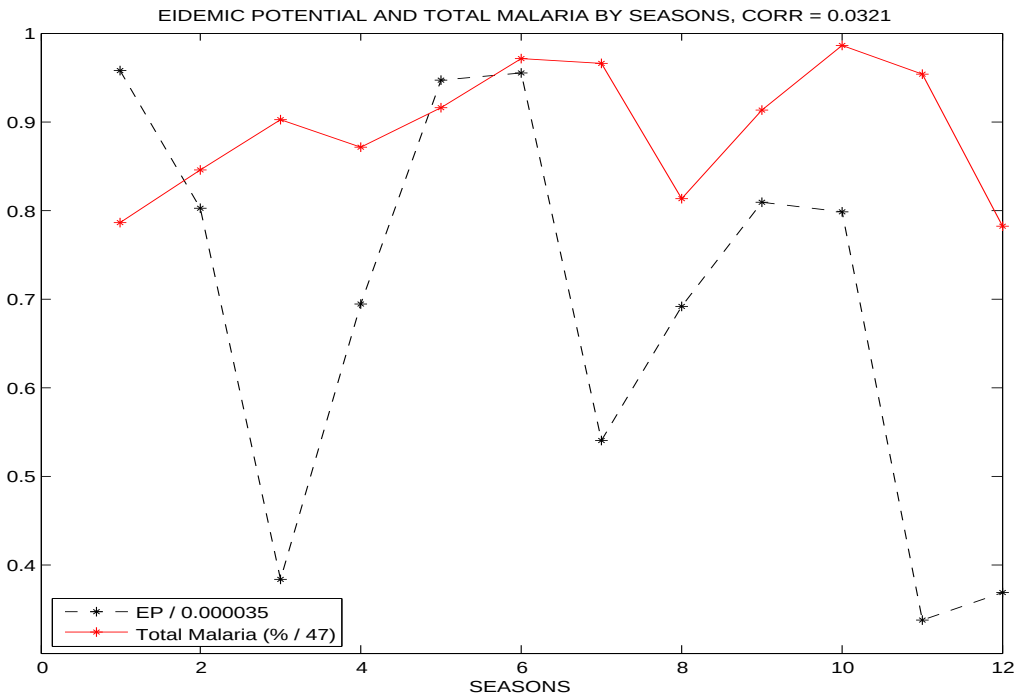


Figure 4.23: EP and Total Malaria for Zone 1, using (3.39); (3.43)

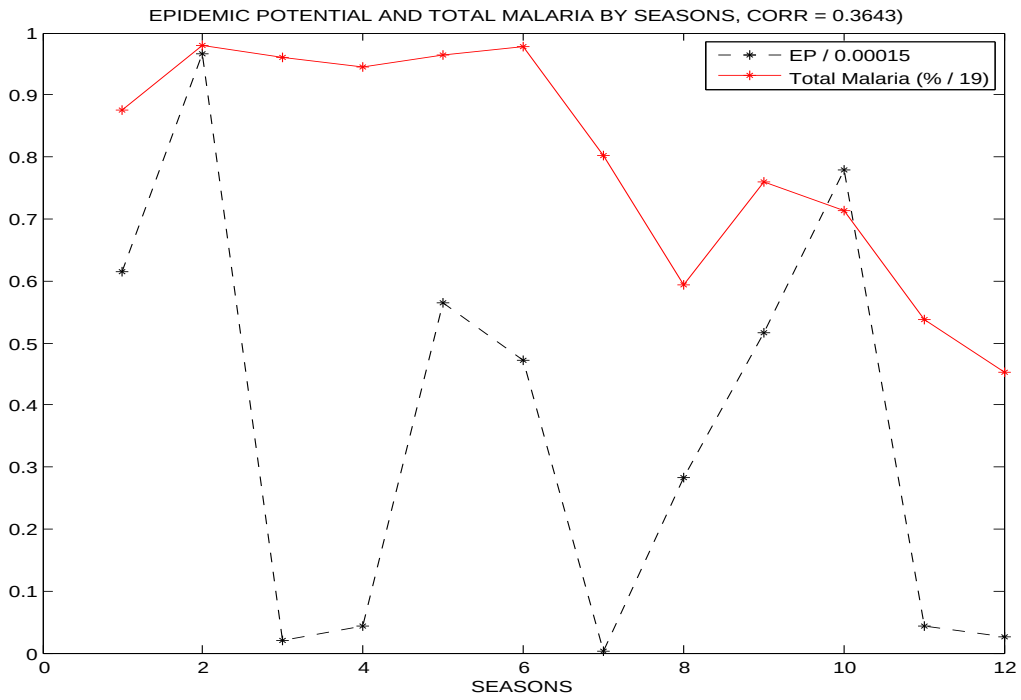


Figure 4.24: EP and Total Malaria for Zone 4, using (3.39); (3.41)

Chapter 5

CONCLUSION AND RECOMMENDATIONS

In this study, we modelled malaria as a 5-Dimensional system of ODEs where the model was reformulated in terms of the proportions of the classes of the respective populations. We reduced the system to a 3-dimensional system of ODEs which were used to carry out stability analysis, derive the reproduction number and express it as a function of climatic variables: rainfall, temperature and relative-humidity.

From the stability analysis,we found that DFE is locally asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$ and globally asymptotically stable when $R_0 \leq 1$ and unstable if $R_0 > 1$. We also found that when $R_0 > 1$, then the endemic equilibrium is locally asymptotically stable and that for the basic reproduction number $R_0 \leq 1$ the disease free equilibrium is globally stable so that the disease dies out with time but if $R_0 > 1$ the disease free equilibrium point is unstable and the disease persists.

We defined the indices (R_0 and EP) used in gauging malaria risk and determination for future trends as a function of the climatic variables. Computation of confirmed and total malaria shows that qualitatively, seasonal values are more reliable in showing clear relationship between malaria and climatic variables as compared to the monthly values which has scattered information. A change in climatic variable does not correspond to an immediate change in malaria incidence.

Following are some suggestions and recommendations for future investigation;

(i) Improving the model to capture important features of malaria transmission that our model does not include such as incubation period and mosquito develop-

ment.

(ii) A part from rainfall, temperature and relative-humidity as the climatic variables affecting malaria incidence, also incorporate altitude, wind speed, daylight, snow and clouds.

(iii) Predict future climate by using long-term average data consolidated for 30 years giving normal trends in meteorological behaviour which can be used to predict future malaria risk.

Mathematical models can provide an important approach to understanding the disease risk and planning for its control. In particular, the reproduction number R_0, is a threshold parameter which provides a quantitative framework to determine the risk of malaria. The epidemic potential EP, is also an index which can be used to predict the future trend of malaria prevalence so as to help the decision makers in planning.

If the EP is computed over 30 years period coupled with indication of an increase or decrease in value, then it implies qualitative increase or decrease in malaria. Since EP is an index which incorporates temperature as a climatic variable, computations of its values showing the future trends is helpful in gauging qualitatively the future malaria risk in the event of climate change.

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