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SEIR Model and Simulation for Controlling Malaria Diseases Transmission without Intervention Strategies

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ABSTRACT

In this study we have develop a basic deterministic mathematical model to investigate SEIR Model and Simulation for controlling malaria Diseases Transmission without Intervention Strategies. The model has seven non-linear differential equations which describe the spread of malaria with three state variables for mosquitoes populations and four state variables for humans population and to introduce the model without intervention strategies.

The models are analyzed qualitatively to determine criteria for control of a malaria transmission, and are used to calculate the basic reproduction R_0. The equilibria of malaria models are determined. In addition to having a disease-free equilibrium, which is locally asymptotically stable when the R_0<1, the basic malaria model manifest one's possession of (a quality of) the phenomenon of backward bifurcation where a stable disease-free equilibrium co-exists(at the same time) with a stable endemic equilibrium for a certain range of associated reproduction number less than one. The results also designing the effects of some model parameters, the infection rate and biting rate. The numerical analysis and numerical simulation results of the model suggested that the most effective strategies for controlling or eradicating the spread of malaria were suggest to use insecticide treated bed nets, indoor residual spraying, prompt effective diagnosis and treatment of infected individuals.

KEYWORDS: *Malaria, Basic reproduction number, Stability analysis, Existence of Backward bifurcation analysis, Endemic equilibrium point*

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1. INTRODUCTION

Malaria is an infectious disease and is life threatening for human beings worldwide. Parasite is an organism that lives on or inside a human body from which it gets its food. Malaria is caused due to a parasite called Plasmodium. Plasmodium parasite is transmitted into human body when an infected female anopheles mosquito makes bites. Plasmodium parasites making the human liver as their home multiply their population and start infecting red blood cells of the human. A variety of plasmodium parasites exist. Mainly four types of plasmodium cause malaria disease among the human viz., falciparum, vivax, ovale and plasmodium malaria [60].

Malaria is an infectious disease and is life threatening for human beings having a huge social, economic, and health burden. Malaria transmission occurs in all over the worldwide. Globally, an estimated 3.2 billion people are at risk of being infected with malaria and developing disease, and 1.2 billion are at high risk (>1 in 1000 chance of getting malaria in a year). According to the latest estimates, 198 million cases of malaria occurred globally in 2013 (uncertainty range 124-283 million) and the disease led to 584,000 deaths (uncertainty range 367,000-755,000).The burden is heaviest in the WHO African Region, where an estimated 90% of all malaria deaths occur, and in children aged under 5 years, WHO account for 78% of all deaths [45].

In our country Ethiopia is a major public health problem and has been reported the last five years (2002-2008) the proportion of malaria in outpatient department, admission and in-patient deaths has been increasing with the highest being recorded in 2003 and 2004. In 2008 malaria was still the first leading cause of health problem accounting for 48% of outpatient consultations, 20% admissions and 24.9% inpatient deaths. According to FMOH reports, approximately 70,000 people die of malaria each year in Ethiopia [10].

Malaria is a life threatening infectious disease caused by a parasite called Plasmodium which is transmitted through the bites of infected female anopheles mosquitoes. There are four different species causing the human malaria disease plasmodium falciparum, plasmodium vivax, plasmodium ovale and plasmodium malaria ([44],[50]). The plasmodium parasite is injected into the human bloodstream in the form or stage or life cycle known as sporozoite. The parasites go through a complex life cycle inside the hosting human body and they live at various stages both in liver and red blood cells. From time to time

the parasites pass through various stages of their life cycle and during which numerous human red blood cells are destroyed. From the listed four plasmodium parasites in our country Ethiopia are plasmodium falciparum and plasmodium vivax, accounting for 60% and 40% cases respectively present in country Ethiopia widely [11].

At this stage the disease generates and develops its symptoms in the infected human body. Eventually, the parasites become gametocytes which are in turn taken by mosquitoes that bite the human host. Inside the mosquito, the gametocytes mature, reproduce sexually, and migrate into the mosquito's salivary glands, at which stage the life cycle is repeated. For some species of Plasmodium, the parasites may persist in the liver for months or years, resulting in chronic and recurring eruptions of merozoites that correspond to episodes of fever and sickness.

The effect of malaria disease varies with the infecting variety species of Plasmodium and also with prior health and immune status of the individual. Typically malaria disease causes fever and chills together with headaches, vomiting and diarrhea. It may also cause long-term anemia, liver damage and neurological damage. The most dangerous falciparum parasite can cause cerebral malaria which causes frequently a fatal condition involving damaging the brain and central nervous system. The survived people from the cerebral malaria may too experience brain damage.

Now a days, although malaria deaths do not occur as often as previously, but still it remains a major public health problem and it is too early to reach any firm conclusion about the possibility of achieving MDGs, because of resistance of the parasite to antimalarial drugs, the complexity of disease, expensiveness of the control program, seasonal variability nature of the disease [44].

In the recent time, significant resources and control programs have been made available worldwide. The aim is to reduce malaria infected cases and prevalence or gain upper hand over the disease. Different strategies and programs with varying effectiveness and efficiency are being adopted to control malaria disease. Comparative knowledge of these existing programs is necessary to design and organize any new and useful and cost effective procedure to control malaria epidemic ([44],[52]).

The National Strategic Plan for Malaria Control and Prevention in Ethiopia (NSP) 2006-2010 aimed to rapidly scale-up malaria control interventions to achieve a 50% reduction of the malaria burden, in line with global Roll Back Malaria (RBM) [35] partnership objectives. The status of coverage of the major interventions was measured in the Malaria Indicator Survey (MIS) 2007. The MIS 2007 results show tremendous achievements by Ethiopia's malaria control program. Thus, between 2005 and 2007, insecticide-treated net (ITN) coverage increased 15 fold, with ITN use by children under five years of age and pregnant women increasing to nearly 45% in malaria-endemic areas and to over 60% in households that owned at least one ITN. Overall, 68% of households in malaria-endemic areas were protected by at least one ITN and/or indoor residual spraying of households with insecticide (IRS). It is believed that the vector control interventions have contributed greatly to a reduction in the burden of the disease. More than 20 million LLINs have been distributed to 10 million households between 2005 and 2007. With respect to IRS activities, evidence shows that 30% of IRS-targeted areas were sprayed in 2007 and in 2008 the coverage increased to 50%. So far, the main vector control activities implemented in Ethiopia include IRS, LLINs and mosquito larval source reduction.

The Malaria Vector Control Guidelines also addresses vector control interventions found to be effective in past decades. The insecticides commonly used in the country include dichloro-diphenyl-trichloroethane (DDT), Malathion and deltamethrin. Due to resistance of malaria vectors to DDT, the use of this Insecticide for IRS has been discontinued in 2009. Deltamethrin is currently being used as an interim substitute insecticide for DDT in IRS operations. However, the selection of insecticides for IRS use in Ethiopia will be determined annually based on the insecticide resistance pattern of the vectors and other factors. Environmental management, supported by active participation of the community and use of larvicides are other preventive measures addressed in this guideline. The guideline incorporates the three major vector control measures, namely environmental management, IRS, and LLINs [11].

Efforts to reduce malaria transmission have led to the development of efficient vector control interventions, particularly insecticide treated nets (ITNs), indoor residual spraying(IRS),and larvicide ([53],[54]). The ITNs include conventional nets treated with a WHO recommended insecticide and long-lasting insecticidal nets. Note that larva is an immature form of an insect and larvicide is a chemical used to kill larvae. These interventions are used in malaria endemic countries especially those in sub-Saharan Africa and have led to reduction in malaria morbidity and mortality substantially. However, malaria epidemic continues to claim hundreds of thousands of lives every year, thus necessitating a continued control effort to fight against the disease ([55], [56]).

Malaria has been considered as a global issue. Epidemiologists together with other scientists invest their efforts to understand the dynamics of malaria and to control transmission of the disease. From interactions with these scientists, mathematicians have developed tools called mathematical models. These models are used significantly and effectively for giving an insight into the interaction between the humans and mosquito population, the dynamics of malaria disease, control mechanisms of malaria transmission and effectiveness of eradication techniques.

Mathematical models are particularly helpful as they consider and include the relative effects of various sociological, biological and environmental factors on the spread of disease. The models have played a very important role in the development of malaria epidemiology. Analysis of mathematical models is important because they help in understanding the present and future spreads of malaria so that suitable control techniques can be adopted.

The SEIR is a simplest mathematical model and has four classes or compartments Susceptible, Exposed, Infected and Recovered. The effect of controlling technique in the spread of malaria is analyzed. Using these notations, eight classes of compartmental models are possible, SI, SIS, SEI, SEIS, SIR, SIRS, SEIR and SEIRS ([14],[29],[57]). For example, in an SEIRS model, a fraction of the susceptible (S) population gets exposed (E) to infection, a part of which then becomes infectious (I). Some from the I class recover from the disease, and become part of the R class with temporary immunity. When immunity is lost, they become susceptible to pathogen attack again, and enter the S class. The simulation studies of the model with variable values of sensitive parameter of the spread of malaria are performed and the results are incorporated. The necessary conclusions have been drawn.

2. The SEIR Malaria Model without Intervention Strategies

2.1. The model formulation

In this study we formulate that of similar model [58] and [60] describing the transmission of malaria. The malaria model divides the human population into four classes and with assumptions about the nature and time rate of transfer from one classes to another. We consider the total population sizes denoted by $N_h(t)$ and $N_m(t)$ for the human hosts and female mosquitoes, respectively. We will use the SEIRS framework to describe a disease with temporary immunity on recovery from infection. SEIRS model indicates that the passage of individuals is from the susceptible class, S, to the exposed class,E, then to infective class , I, and finally to the recovery class, R. $S(t)$ contains humans those do not have malaria disease but are likely to be bitten by infected female anopheles mosquitoes causing malaria parasite at time t, or those susceptible to the disease.

Many diseases like malaria have what is termed a latent or exposed phase, $E(t)$, during which an individual is said to be infected but not infectious. $I(t)$ contains humans those are already infected and got malaria disease. People come into infected class from susceptible class. This is done through infecting the susceptible mosquitoes. The dynamic transmission of the malaria parasite between and among individuals in both species is driven by the mosquito biting habit of the humans. $R(t)$ contains the people who recover from the malaria disease and return to normal status of health or individuals who have recovered from the disease. These humans cannot transmit the infection to mosquitoes as we assume that they have no plasmodium parasites in their bodies.

The transfer rates between the subclasses are composed of several epidemiological parameters. we explained that susceptible human bitten by an infectious anopheles mosquito may become infected with a finite probability that depends on the abundance of infectious mosquitoes and human populations [20]. The model assumes straight forward to the occurrence of the same kind that susceptible individuals get infected through biting with infected mosquitoes. The susceptible human population is increased by recruitment (birth and immigration) at a constant rate **y**.

All the recruited individuals are assumed to be naive when they join the community. Infected immigrants are not included because we assume that most people who are sick will not travel. When an infectious female anopheles mosquito bites a susceptible human, there is some probability of transmission of infection from an infectious mosquito to a susceptible human $\boldsymbol{\theta_{mh}}$.

The parasite then moves to the liver where it develops into its next life stage. The infected person will move to the exposed class. After a certain period of time, the parasite (in the form of merozoites) enters the blood stream, habitually the indication of malaria disease recognizable when the symptoms begin on the human body. Then the exposed individuals become infectious and progress to infected state at a constant rate $\boldsymbol{\beta_m}$. We exclude the direct infectious-to-susceptible recovery by assuming that the individuals do not recover by natural immunity. This is a true life to simplifying assumption because most people have some period of immunity before becoming susceptible again. After some time, individuals who have experienced infection may recovered with natural immunity at a constant rate **t** and move to the recovered class. The recovered individuals have some immunity to the disease and do not get clinically ill. Since disease-induced immunity due to malaria is temporary a fraction **ϕ** of individuals leave the recovered state to the susceptible state. We make the simplifying assumptions that there is no immigration of the recovered humans. Humans leave the population through natural death **m** and the infected humans have an additional disease-induced death rate constant **δ.** The disease-induced rate is very small in equivalent with the recovery rate.

We divide the mosquito population into three classes: susceptible S_m exposed E_m and infectious I_m. Female anopheles mosquitoes (male anopheles mosquito is not included in the model because only female mosquito bites humans for blood meals) enter the susceptible class through natural birth at a rate **ρ**. Susceptible mosquitoes become infected by biting infectious humans at a . The parasites (in the form of gametocytes) enter the mosquito with probability $\boldsymbol{\theta_{hm}}$, when the mosquito bites an infectious human, and the mosquito moves from the susceptible to the exposed class. After some period of time, dependent on the ambient temperature and humidity, the parasite develops into sporozoites and enters the mosquito's salivary glands, and the mosquito progresses at rate $\boldsymbol{\beta_m}$, from the exposed class to the infectious class. We assume that the infective period of the vector ends with its death, and therefore the vector does not recovered from being infective [1]. The mosquitoes leave the population through natural death. Its caused by natural death rate and insecticides is **ω**. The rate of infection of susceptible individual is α_h, and the rate of infecting a susceptible mosquito is α_m.

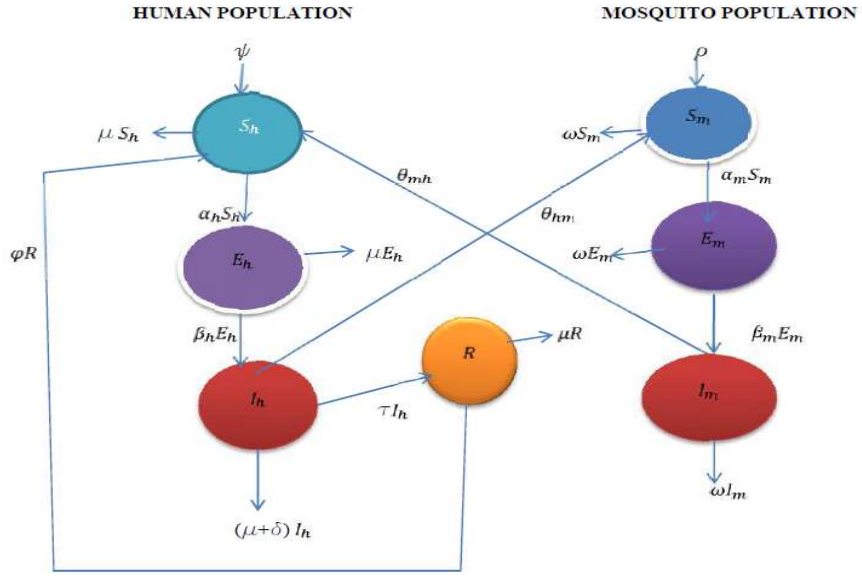
Table 1 Variables of the basic malaria model

Variables	Description
$S_h(t)$	Number of humans insusceptible compartment at time t
$E_h(t)$	Number of humans in exposed class at time t
$I_h(t)$	Number of humans in infected compartment at time t
$R(t)$	Number of humans in recovered compartment at time t
$S_m(t)$	Number of mosquitoes in susceptible compartment at time t
$E_m(t)$	Number of mosquitoes in exposed class at time t
$I_m(t)$	Number of mosquitoes in infected class at time t
$N_h(t)$	Total human population at time t
$N_m(t)$	Total mosquito population at time t

Table 2 Parameters and their interpretations for the malaria model

Parameter	Description
ψ	Natural birth rate of humans
ρ	Natural birth rate of mosquitoes
α_h	Transfer rate of humans from susceptible to infected compartment
α_m	Transfer rate of mosquitoes from susceptible to infected compartment
μ	Natural death rate for humans
δ	Death rate of humans due to disease-induced
ω	Death of mosquitoes caused by natural death rate and insecticides
β_h	Transfer rate of humans from the exposed class to the infected class
t	Transfer rate of humans from Infected to recovered class
φ	Transfer rate of humans from recovered to susceptible compartment
θ_{mh}	Probability of transmission of infection from an infectious mosquito to a susceptible human
θ_{hm}	Probability of transmission of infection from an infectious human to a susceptible mosquito
β_m	Transfer rate of mosquitoes from the exposed class to the infected class
$\emptyset$	Susceptible mosquitoes bite infected humans with this rate. Also, infected mosquitoes bites susceptible humans with the same rate

Figure 1 The flow chart for transmission of malaria disease



2.2. Mathematical formulation of SEIR model

Applying the assumptions, definitions of compartmental variables and parameters described in tables 1 and 2, the system of non-linear differential equations which describe the dynamics of malaria transmission with controlling measures are formulated and presented in this section.

$$
\begin{aligned}
&\mathrm{d}S_h/dt = \psi + \varphi R - \mu S_h - \alpha_h S_h \\
&dE_h\ /\ dt = \alpha_h S_h + \beta_h E_h - \mu E_h \\
&d\mathrm{I}_h/\mathrm{dt} = \beta_h E_h - \tau \mathrm{I}_h - (\mu + \delta_h)\mathrm{I}_h \\
&d\mathrm{R}/\mathrm{dt} = \tau \mathrm{I}_h - \varphi \mathrm{R} - \mu \mathrm{R} \\
&dS_m/dt\ = \rho - \alpha_m S_m - \omega S_m \\
&dE_m\ /\ dt = \alpha_m S_m + \beta_m E_m - \omega E_m \\
&d\mathrm{I}_m/dt = \beta_m\ S_m - \omega \mathrm{I}_m
\end{aligned}
\qquad (1)
$$

The initial conditions of the system of equations (1) are given by $S_h(0) = S_{h0}$,$E_h(0) = E_{h_0}$, $I_h(0) = I_{h0}$,$\mathrm{R}(0) = \mathrm{R}_0$, $S_m(0) = S_{m0}$, $E_m(0) = E_{m_0}$ and $I_m(0) = I_{m0}$. Also, we have used in equation (1) that $\alpha_h = (\theta_{mh}\emptyset\ \mathrm{I_m}/N_h)$ and $\alpha_m = (\theta_{hm}\emptyset\ \mathrm{I_h}/N_h)$. The term α_h denotes the rate at which the susceptible humans become infected by infectious female mosquitoes. Similarly, the term α_m denotes the rate at which the susceptible mosquitoes become infected by infectious humans. The rate of infection propagated to susceptible humans by infected mosquitoes is dependent on the total number of humans. Similarly, the rate of infection propagated to susceptible mosquitoes by infected humans is dependent on the total number of humans ([18], [60]).

2.3. Analysis of SEIR model (Analysis of the Model without intervention strategies)

We now analyze the SEIR model in order to show the two controlling methods considered here have substantial impact on controlling the transmission dynamics of malaria disease. In fact, the disease will be completely eradicated if the controlling methods are implemented effectively. The two controlling mechanisms proposed here have such a big potential. We consider now the solutions of the system of non-linear differential equation (1). We understand that the interpretations of these solutions must be biologically meaningful. Hence it is easy to identify that the feasible region of system (1) is $\mathbb{R}_+^7$. The seven dimensional solution space shows that all the solutions are positive. Hence, the feasible region containing all the solutions of the system of equations (1) is given by the set $\Omega = \{(S_h, E_h, I_h, R, S_m, E_m, I_m) \in \mathbb{R}_+^7\}$. Here the quantities $S_h, E_h, I_h, R, S_m, E_m, I_m$ are all non–negatives. Further the total human and mosquito populations are represented by N_h and $N_m$they have the upper asymptotic values (ψ/μ) and (ρ/ω) respectively. Therefore, the region Ω is positively invariant i.e. solutions remain positive for all the temporal values. Thus, the model (1) is biologically meaningful and mathematical well-posed or well present in the domain Ω.

On summing up all the individual equations from (1) of the system (1), it is straight forward to get $(dN_h/dt) = (\psi - \mu N_h - \delta_h I_h)$. Here the notation $N_h = (S_h + E_h + I_h + R$ represents the total human population contained in all the five compartments. We consider the solution of the system of equations (1) when the term $\delta_h I_h$ vanishes. In case if the death rate of humans due to malaria disease is considered to be free, i.e., $\delta_h = 0$ then we obtain$(dN_h/dt) = (\psi - \mu N_h)$. The solution of this differential equation is found to be $N_h(t) = (\psi/\mu) + [N_{h0} - (\psi/\mu)]\, e^{-\mu t}$showing that $N_h(t) \to \psi/\mu$ as $t \to \infty$. The termN_{h0} denotes the initial total human population. It can be interpreted that the total human population grows and asymptotically converges to a positive quantity given by (ψ/μ) under the condition that humans do not die due to malaria infection. Thus ψ/μ is an upper bound of the total human population$N_h(t)$ i.e.$N_h(\infty) \leq \psi/\mu$. Whenever the initial human population starts off low below (ψ/μ) then it grows over time and finally reaches the upper asymptotic value (ψ/μ). Similarly, whenever the initial human population starts off high above (ψ/μ) then it decays over time and finally reaches the lower asymptotic value (ψ/μ) [3].

Similarly on summing up all the individual equations from the system (1), it is straight forward to get $dN_m/dt = \rho - \omega N_m$. Here the notation $N_m = (S_m + E_m + I_m)$ represents the total mosquito population contained in all the two compartments. The solution of this differential equation is found to be $N_m(t) = (\rho/\omega) + [N_{m0} - (\rho/\omega)]\, e^{-\omega t}$ showing that $N_m(t) \to (\rho/\omega)$as $t \to \infty$. The term N_{m0}denotes the initial total mosquito population. It can be interpreted that the total mosquito population grows and asymptotically converges to a positive quantity given by (ρ/ω).Thus (ρ/ω) is an upper bound of the total mosquito population$N_m(t)$ i.e. $N_m(\infty) \leq (\rho/\omega)$. Whenever the initial mosquito population starts off low below (ρ/ω) then it grows over time and finally reaches the upper asymptotic value(ρ/ω). Similarly, whenever the initial mosquito population starts off high above (ρ/ω) then it decays over time and finally reaches the lower asymptotic value(ρ/ω) [26].

Hence all feasible solutions set of the human population and mosquito population of the model (1) enters the region.

$\Omega = \{(S_h, E_h, I_h, R, S_m, E_m, I_m) \in \mathbb{R}_+^7 ; (S_h, S_m) \geq 0, Eh, Ih, R, Em, Im \geq 0, Nh \leq \psi\mu, Nm \leq \rho\omega\}$.

Therefore, the region Ω is positively invariant (i.e solutions remain positive for all times t) and in the model (1) is biologically meaningful and mathematically well-posed in the domain Ω.

3. Existence of Disease free equilibrium point E_o

Disease free equilibrium points are steady state solutions when there is no malaria in the human population and there is no plasmodium parasite in the mosquito population. That is, absence of malaria causing infections occurs in both populations at the disease free equilibrium point. The disease free equilibrium point is denoted by $E_0 = (S_h^*, E_h{}^*, I_h^*, R^*, S_m^*, E_m{}^* I_m^*)$. The equilibrium point is obtained on setting the right-hand side of the non-linear system (1) to zero. Thus, at the equilibrium point the quantities satisfy the condition $E_h{}^* = I_h^* = R^* = E_m{}^* = I_m^* = 0, S_h^* = (\psi/\mu)$ and $S_m^* = (\rho/\omega)$.Also, Overhead star represents the values of the functions at the disease free equilibrium point. The disease free equilibrium point represents $E_0$the disease free situation in which there is no malaria infection either in the society or in the environment. Therefore, the diseases free equilibrium point is given by

$$E_0 = (\psi/\mu, 0, 0, 0, \rho/\omega, 0, 0) \qquad (2)$$

4. Basic Reproduction Number R_0

Reproduction number, denoted by R_o , is the threshold or a level for many epidemiological models. It determines whether a disease can attack the population or not. The threshold quantity R_0 indicates the number of new infected individuals is produced by one infected individual. When $R_0 < 0$ each infected individual propagates the infection and produces on average less than one new infected individual so that the disease is expected to die out completely over time. On the other hand if $R_0 > 1$,each individual produces more than one new infected individual so we would expect the disease to spread more and grow in the population. This means that the value of threshold quantity R_0 in order to eradicate the disease must be reduced by less than one.

The following steps are followed to compute the basic reproduction number R_0. The basic reproduction number cannot be determined from the structure of the mathematical model alone, but depends on the definition of infected and uninfected compartments. Assuming that there are n compartments of which the first m compartments to infected individuals. That is the parameters may be vary compartment to compartment, but are the identical for all individuals within a given compartment. Let

$X_i = (x_1, x_2, \ldots\ldots x_n), X_i \geq 0$ for all, $i = 1,2, \ldots \ldots m$

Be the vector of human and mosquito individuals in each compartment. Let us sort the compartments so that first m compartments infected individuals.

Let $F_i(x)$ be the rate of appearance of new infections in compartment i.

$V_i(x) = V^-{}_i(x) - V^+{}_i(x)$ Where $V^+{}_i(x)$ is rate of transfer of individuals into compartment i by all other means and $V^-{}_i(x)$ is the rate of transfer of individual out of the i^{th} compartment.

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

$\frac{dx_i}{dt} = f_i(x) = F_i(x) - V_i(x), i = 1,2,3 \ldots\ldots n$

Where $\frac{dx_i}{dt}$ is the rate of change of x. The next is the computation of the square matrices F and V of order (mxm), where m is the number of infected classes, defined by $F = [\frac{dF_i(x)}{dxj}(x_{0)})]$ and $V = [\frac{dV_i(x)}{dxi}(x_{0})]$ with $1 \leq i, j \leq m$, such that F is non- negative, V is non-singular matrix and x_0 is the disease-free equilibrium point (DFE). Since F is non-negative and V is non-singular, then V^{-1} is non-negative and also FV^{-1} is non-negative. Hence the of FV^{-1} is called the next generation matrix for the model. Finally the basic reproduction number R_0 is given by

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

Where $\gamma(A)$ denotes the spectral radius of matrix A and and the spectral radius is the biggest non-negative eigenvalue of the next generation matrix. Rewriting model system (1) starting with the infected compartments for both populations; $S_h, E_h, I_h, R, S_m, E_m, I_m$ and then following by uninfected classes; S_h, R, S_m also from the two populations, then the model system becomes

$$\begin{aligned}
dE_h/dt &= \frac{\theta_{mh}\emptyset\, \mathrm{I_m} S_h}{N_h} - (\beta_h + \mu)E_h \\
d\mathrm{I}_h/\mathrm{dt} &= \beta_h E_h - (\tau + \mu + \delta_h)\mathrm{I}_h \\
dE_m/dt &= \frac{\theta_{hm}\emptyset\, \mathrm{I_h} S_m}{N_h} - (\beta_m + \omega)E_m \\
d\mathrm{I}_m/dt &= \beta_m\, S_m - \omega \mathrm{I}_m \\
\mathrm{dS}_h/dt &= \psi + \varphi R - \frac{\theta_{mh}\emptyset\, \mathrm{I_m} S_h}{N_h} - \mu S_h \\
d\mathrm{R}/\mathrm{dt} &= \tau \mathrm{I_h} - (\varphi + \mu)\mathrm{R} \\
dS_m/dt &= \rho - \frac{\theta_{hm}\emptyset\, \mathrm{I_h} S_m}{N_h} - \omega S_m
\end{aligned} \tag{3}$$

Since $\alpha_h = \left(\frac{\theta_{hm}\emptyset\, \mathrm{I_h}}{N_h}\right)$ and $\alpha_m = \left(\frac{\theta_{mh}\emptyset\, \mathrm{I_h}}{N_h}\right)$ (1) malaria model. From the system of equation (3) F_i and V_i are defined as

$$F(x) = \begin{bmatrix} \frac{\theta_{mh}\emptyset\, \mathrm{I_m} S_h}{N_h} \\ 0 \\ \frac{\theta_{mh}\emptyset\, \mathrm{I_m} S_h}{N_h} \\ 0 \end{bmatrix} \quad V(x) = \begin{bmatrix} (\beta_h + \mu)E_h \\ (\tau + \mu + \delta_h)\mathrm{I}_h - \beta_h E_h \\ (\beta_m + \omega)E_m \\ \beta_m\, S_m - \omega \mathrm{I}_m \end{bmatrix}$$

The partial derivatives of (3) with respect to (I_h, I_m) and the jacobian matrix of F_i at the disease-free equilibrium point (2) is:-

$$F = \begin{bmatrix} 0 & 0 & 0 & \theta_{mh}\emptyset\, \mathrm{I_m} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\theta_{hm}\emptyset\mu\rho}{\omega\psi} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Similarly, the partial derivatives of (3) with respect to (E_h, I_h, E_m, I_m) and the jacobian matrix $V_i$is:-

$$v = \begin{bmatrix} (\beta_h + \mu) & 0 & 0 & 0 \\ -\beta_h & (\tau + \mu + \delta_h) & 0 & \\ 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_m & \omega \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{(\beta_h + \mu)} & 0 & 0 & 0 \\ \frac{1}{(\tau + \mu + \delta_h)(\beta_h + \mu)} & \frac{1}{(\tau + \mu + \delta_h)} & 0 & 0 \\ 0 & 0 & \frac{1}{(\beta_h + \mu)} & 0 \\ 0 & 0 & \frac{\beta_m}{\omega(\beta_h + \omega)} & \frac{1}{\omega} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & \frac{\beta_m\, \theta_{mh}\emptyset}{\omega(\beta_h + \omega)} & \frac{1}{\omega} \\ 0 & 0 & 0 & 0 & \\ \frac{\beta_h \theta_{hm}\emptyset\mu\rho}{\omega\psi(\tau + \mu + \delta_h)(\beta_h + \mu)} & \frac{\theta_{hm}\emptyset\mu\rho}{(\tau + \mu + \delta_h)} & 0 & 0 & \\ 0 & 0 & \frac{\beta_m}{\omega(\beta_h + \omega)} & 0 & \end{bmatrix}$$

From FV^{-1},we can determine the eigenvalues of the basic reproduction number R_0 by taking the spectral radius (dominant eigenvalue) of the matrix FV^{-1}. Thus it is calculated by $|A - \lambda A| = 0$. We determine the expression for R_0 using the next generation matrix approach [18] as $R_0 = \sqrt{\frac{\rho\, \theta_{mh}\, \theta_{hm}\, \emptyset^2 \mu}{\omega^2\, \psi\, (\tau+\lambda+\mu_h+\delta_h)}}$. Further, it can be verified that the disease free equilibrium point E_0 given by (4) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Local Stability of the Disease-Free Equilibrium

The local stability of the disease-free equilibrium can be analyzed using the Jacobian matrix of the malaria model (1) at the disease free equilibrium point. Using [40], the following theorem contains

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

Proof: The Jacobian matrix (J) of the malaria model (1) with
$S_h = (E_h + I_h + R \;\&\; S_m = (E_m + I_m)$ at the disease-free equilibrium point is given by:

$$dE_h/_{dt} = \frac{\theta_{mh} \emptyset\, \mathrm{I_m} S_h}{N_h} - (\beta_h + \mu) E_h$$
$$d\mathrm{I}_h/\mathrm{dt} = \beta_h E_h - (\tau + \mu + \delta_h)\mathrm{I}_h$$
$$d\mathrm{R}/\mathrm{dt} = \tau \mathrm{I_h} - (\varphi + \mu)\mathrm{R}$$
$$dE_m/_{dt} = \frac{\theta_{hm} \emptyset\, \mathrm{I_h} S_m}{N_h} - (\beta_m + \omega) E_m$$
$$d\mathrm{I}_m/dt = \beta_m\, S_m - \omega \mathrm{I}_m \qquad (4)$$

From the equation (4) the jacobian matrix

$$(J) = \begin{bmatrix} -(\beta_h + \mu) & 0 & 0 & 0 & \theta_{mh}\emptyset \\ \beta_h & -(\tau + \mu + \delta_h) & 0 & 0 & 0 \\ 0 & \tau & -(\varphi + \omega) & 0 & 0 \\ 0 & \frac{\theta_{hm}\emptyset\mu\rho}{\omega\psi} & 0 & -(\beta_m + \omega) & 0 \\ 0 & 0 & 0 & \beta_m & -\omega \end{bmatrix}$$

Let $a = (\beta_h + \mu)\,, b = \theta_{mh}\emptyset,\ c = \beta_h\ , d = (\tau + \mu + \delta_h)\ , e = \tau\,, f = (\varphi + \omega), g = \frac{\theta_{hm}\emptyset\mu\rho}{\omega\psi}\,,\quad h = (\beta_m + \omega), i = \beta_m\ and\ j = \omega$

Thus

$$(J) = \begin{bmatrix} -a & 0 & 0 & 0 & b \\ c & d & 0 & 0 & 0 \\ 0 & e & -f & 0 & 0 \\ 0 & g & 0 & -h & 0 \\ 0 & 0 & 0 & i & -j \end{bmatrix}$$

The eigenvalues of jacobian matrix are:-

$$|J - \lambda I| = 0$$

$$(J) = \begin{bmatrix} -(a+\lambda) & 0 & 0 & 0 & b \\ c & d & 0 & 0 & 0 \\ 0 & e & -f & 0 & 0 \\ 0 & g & 0 & -(h+\lambda) & 0 \\ 0 & 0 & 0 & i & -(j+\lambda) \end{bmatrix}$$

The third column has diagonal entry, therefore one of the eigenvalues of the jacobian matrix is$-(\varphi + \omega)$ or$f$. By using Routh-Hurwitz, stability criterion.

${R_0}^2 = \frac{\rho\, \theta_{mh}\, \theta_{hm}\, \emptyset^2 \mu}{\omega^2\, \psi\, (\tau+\lambda+\mu_h+\delta_h)}$ the proof end.

Using the Routh-Hurwitz criterion is a method for determining whether a linear system is stable or be examining the locations of the characteristic equation of the system. In fact, the method determines only if there are roots that put outside of the left half plane; it does not actually compute the roots Routh-Hurwitz criteria [12].

We can determine whether this system is stable or not, checking the following conditions:- Two necessary but not sufficient conditions that all the roots have negative real parts are

- All the polynomial coefficients must have the same sign.
- All the polynomial coefficients must be nonzero.

The necessary condition that all roots have negative real parts is that all the elements of the first column of the array have the same sign. The number of changes of sign equals the number of roots with positive real parts. All the elements of a particular row are zero. In this case, some of the roots of the polynomial are located symmetrically about the origin of the λ plane, e.g.,a pair of purely imaginary roots. The zero row will always occur in a row associated with an odd power of λ. The row just above the zero row holds the coefficients of the auxiliary polynomial. The roots of the auxiliary polynomial are the symmetrically placed roots. Be careful to remember that the coefficients in the array skip powers of λ from one coefficient to the [2].

5. Existence of Backward Bifurcation

We intend to determine the stability of the endemic equilibrium and to carry out the possibility of the existence of backward bifurcation due to existence of multiple equilibrium and reinfection. As a disease attacks it reduces the number of susceptible individuals in the population, which tends to reduce its reproductive rate. For a backward bifurcation to occur, this means that when $R_0 < 0$ the endemic equilibrium point can exist as well as when $R_0 > 1$.

we would expect the disease to be able to attack at $R_0 = 1$ in the case of a backward bifurcation with the properties of unstable equilibrium bifurcating from the disease-free equilibrium when $R_0 < 1$,giving rise to multiple stable states. But not in the case of a forward bifurcation, in which in the absence of a low-level unstable equilibrium when $R_0 < 1$ and a stable equilibrium bifurcating from the disease-free equilibrium when $R_0 > 1$ arise naturally when the disease does not attack when $R_0 = 1$. A simple criterion for a backward bifurcation, then, is one in which the disease can attack when $R_0 = 1$. This implies that the disease-free equilibrium may not be globally asymptotically stable even if $R_0 < 1$.

6. Numerical simulation

In this section we consider the simulation study of the system of differential equations given in (1). As stated earlier these equations describe the dynamics of human and mosquito populations of the malaria model that includes intervention strategies. The simulation study is performed using ode45 solver of MATLAB software. The Runge – Kutta fourth-order method based on a variable step-size is used for the purpose. The parametric values have been collected from the literature and used here. Those were not available were not obtained from literatures published by researchers in malaria endemic countries which have similar environmental conditions. we present the numerical analysis of the model(1). The initial conditions used were $S_h(0) = 47186$, $E_h(0) = 16987, I_h(0) = 47473, R(0) = 47470, S_m(0) = 17500, E_m(0) = 8750, I_M(0) = 26{,}250$. We simulate the basic malaria model in the absence of any intervention and the malaria model without intervention strategies, and find out the effects of varying each intervention parameter [60],[59].

6.1. Estimation of Parameters

We estimate that it will take 3 times a day for 7 days to recovery from malaria infection through Chemotherapy and the incubation period of malaria in humans was considered [9],[39]and [59].

Table 3: Estimated Parameter Value of the Malaria Modal without Intervention Strategies and with Intervention

Symbol	Values	sources
ψ	0.000027	Calculated
θ_{hm}	0.0655	[60]
ρ	0.071	Niger,2008 [24]
θ_{mh}	0.42	Estimated
β_h	1/14	FMOH,2004 [9]
ϕ	0.40	chitnis 2005 [58]
β_m	1/11	chitnis 2008 [24]
λ	0.01	Miranda, 2009 [30]
τ	1/7	FMOH,2004 [9] and Tamwiine et al 2004 [18]
ϵ	0.00722	Gumel,2008 [12]
μ	0.0000548	Calculated
g	0.78	Mwamtobe,2010 [34]
ω	1/25	Blayneh,2009 [4]
η	0.457	[59] and [46]
δ	0.00000071	World malaria report 2014 [45]
γ	0.11	Mwamtobe,2010 [34]
φ	1/121.75	Estimated

6.2. The System of Human Population State Variables of the Basic Model without Intervention

The simulation of basic model has been conducted to find out the dynamics of the disease in the population when there is no intervention to reduce or eradicate the disease. In the absence of interventions strategies, the susceptible populations in Figure 2 as shown below red colored that the change in state variables of malaria model shows the dynamics with time of susceptible humans with $R_0 = 1.3874$.

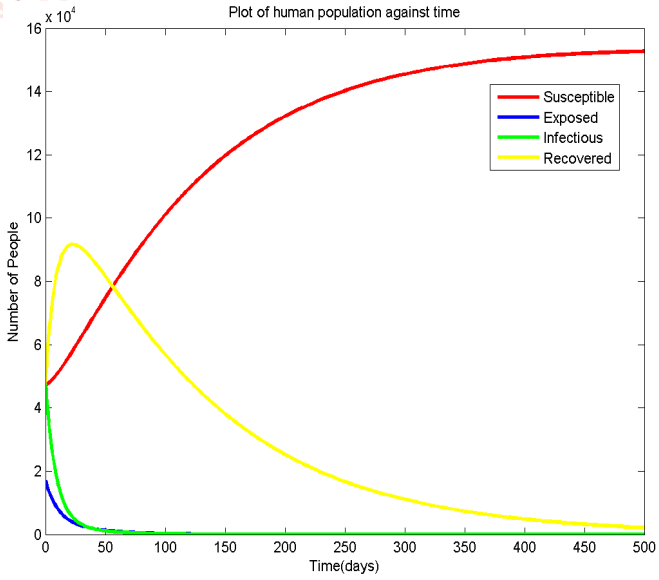


Figure 2:- A phase portrait illustrating the changes in the four state variables of the malaria model showing the system with time, of susceptible humans, exposed humans, infected humans and shows the system of recovered humans with $R_0 = 1.3874$.

This susceptible population increases then remained constant within the three years. The Figure 2 were blue colored showing the system with time of exposed humans initially was high but progress it reduces as some of population enters infections class and other recover. The green colored also were indicated in the Figure 2 showing the dynamics with time of infectious humans the infection population reduced as some recovers and other die within this three years. Finally, the yellowed color in Figure 2 the dynamics with time of recovered humans the recovered population initially was high as time goes by the recovered people reduced or to goes back to susceptible class.

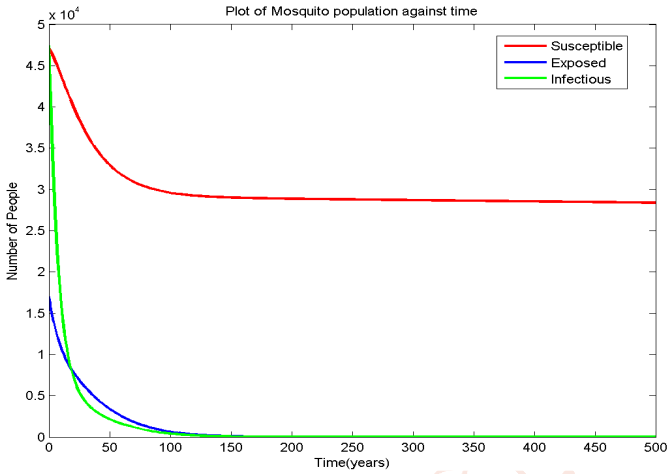


Figure3:-Illustrates the changes in the three state variables of the malaria model showing the dynamics with time, of susceptible mosquitoes, exposed mosquitoes and infectious mosquitoes with $R_0 = 1.3874$.

In Figure 3 shows all the three curves are decreasing as time increases which are positive for the current interventions in the mosquito population, but there is still more work to be done in the human population. Therefore, we will consider the effects of varying the main parameters responsible control malaria after considering malaria prevalence rate in the population now.

Prevalence the Basic malaria model without Intervention Strategies

Prevalence is defined as the ratio of which the number of cases of a disease in a population and with the number of individuals in a population at a given time.

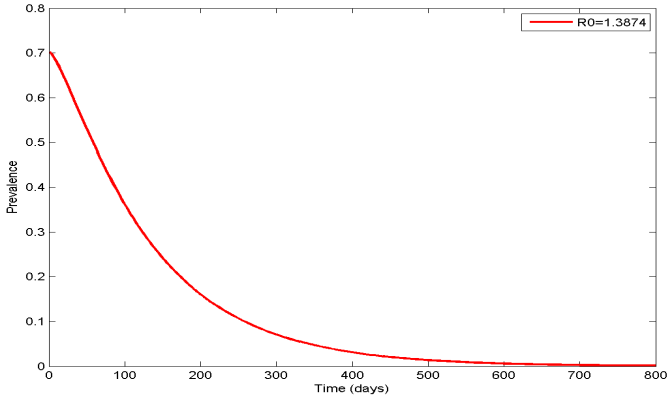


Figure 4:- Represents changes of prevalence with time with $R_0 = 1.3874$.

The prevalence graph shows that the prevalence rate as of now is high which confirms the Figure 2 as shown above that there is more work to be done if we want to achieve malaria free society, because the prevalence rate reduces asymptotically to zero as possible to increasing the intervention strategies time to time.

6.3. Simulation of Biting Rate of Mosquitoes on the Basic malaria model without Intervention Strategies

We now consider the effects of varying the main parameters responsible for controlling the spread of malaria disease. The values of the biting rate of mosquitoes, transmission rate of infection from an infectious mosquito to a susceptible human, rate of loss of immunity for humans and the mosquito population were reduced by constant fraction 1/8 , while the values of the other parameters are maintained. This important to showing the relationship of the susceptible and infected human populations was considered.

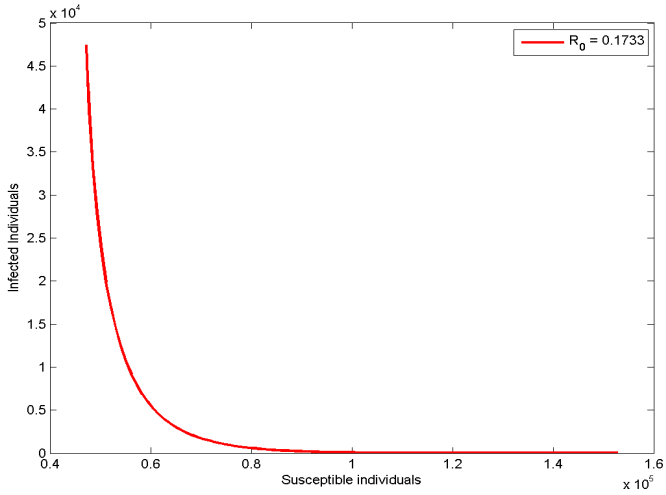


Figure 5:-Illustrates the system of infected human population against susceptible human population with R_0 =0.1733

The Figure 5 with R_0 =0.1733 shows that at an initial stage, the susceptible human population was free from the disease. The infection in the population is shown that it increases with time when there is no intervention being practiced. As most of the susceptible individuals were getting infected with time, the infected individuals increases. This is evidenced further when the parameter of mosquito biting rate varied.

7. Conclusion and Recommendation

7.1. Conclusion

Analysis of the model showed that there exists a domain where the model is epidemiologically and mathematically well-posed. The important parameter in our model, the basic reproduction number R_0 as an improved control intervention measure was computed. The model was then qualitatively analyzed for the existence and stability of their associated equilibria. It was proved that under the condition that $R_0 < 1$ the disease-free equilibrium E_0 is locally asymptotically stable, and when $R_0 < 1$ the endemic equilibrium E_1 appeared. The model exhibits the phenomenon of backward bifurcation where a stable disease-free equilibrium co-exists with a stable endemic equilibrium for a certain range of associated reproduction number less than one.

The numerical analysis of the model suggested that the most effective strategies for controlling or eradicating the spread of malaria disease. The use of insecticide-treated bed nets and indoor residual spraying and prompt and effective diagnosis and treatment of infected individuals. This study agree [7] suggestion that the intervention using insecticide-treated bed nets represents an excellent example of implementing an infectious disease control programme, and [38] study, which showed that both regular and non-fixed spraying resulted in a significant reduction in the overall number of mosquitoes, as well as the number of malaria case in humans.

7.2. Recommendation

So, far no really effective vaccine has been developed against malaria, so we cannot protect ourselves against the disease. For many years there have been few effective treatments for malaria, but things are getting better. In a country like ours, drugs alone are the answer. Many peoples live a long way from medical centers and cannot reach them easily, and medicines can be expensive. Mathematical modeling of spread of malaria disease can provide understanding of underlying techniques or strategies for the disease spread, help to pinpoint key factors in the disease transmission process, suggest effective controlling and prevention measures, and provide estimate for the severity and potential scale of the endemic and epidemic. The following recommendations should be considered:

- Individuals should be award about severity of malaria and increasing personal protection measures are highly recommended to prevent malaria (to control the reproduction number $R_0 < 1$).
- using methods of controlling malaria must involve controlling the *Anopheles* mosquitoes. Whenever possible avoid contact with mosquitoes.
- Using mosquito repellents, having screens on doors, windows to prevent mosquitoes, wearing clothes that protect the skin against mosquito's long sleeves and trousers are all effective measures that can protect you against malaria.
- Well-made insecticide-treated bed nets and indoor residual spraying and prompt and effective diagnosis make a big difference and they are cheap treatment effective way to control malaria transmission.
- Minimize any opportunities for the mosquito breed. They will lay eggs in any standing water in garden pond, old trees, flower pots, old drink cans,...etc.
- Removing the mosquitoes breeding places by removing as much as standing water as possible. The simplest way to do this to make sure you store rubbish out of the rain and dispose of your rubbish properly.
- Proper disposal of sewage again, managing human waste so that foul water is not left around will reduce the breeding places for the mosquitoes.
- Biological control (where an organism that feeds on the larva is introduced to the water) and chemical control (pesticides or IRS) spraying on to the water where the mosquitoes breed will kill the eggs and larvae, this in turn reduces the number of mosquitoes and slower the infection rate.
- Because of the complications of measuring malaria at different levels with different immunological status prevalent in different age and gender groups, and across different locations, some guidelines should be developed to give researchers and health professionals a more accurate foundation on which to select their indicators.
- There should be administration of drugs to these malaria case encountered individuals irrespective of whether symptoms show up or not in order to decrease the natural birth rate of mosquito and increase the rate mosquito using Indoor-Residuals Sprays (IRS).

References

[1] Aron, J. L (1988), "Mathematical modeling of immunity to malaria, Non-linearity in biology and medicine (Los Alamos, NM, 1987)", *Math. Biosc.,* Volume 90,pp385396.

[2] A. Hurwitz, "On the conditions under which an equation has only roots with negative real parts," *Mathematische Annelen*, vol.46, pp.273-284, 1895.

[3] Birkhoff, G and Rota, G.C (1982), *Ordinary Differential Equations, Ginn.*

[4] Kbenesh, Cao Yanzhao, and Kwon Hee-Dae (2009), "Optimal Control of Vector-borne Diseases: Treatment and Prevention", *Discrete and Continuous Dynamical Systems Series B*, Volume 11, No.3, pp 1-xx.

[5] Bupa UK (2009), *Malaria symptoms, causes and treatment of disease,* http://hcd2.bupa.co.uk/factsheets/html/malariadisease retrieved on Friday, 19th June, 2009.

[6] Carr J (1981), *Applications centre manifold theory,* Springer-Verg, New York.

[7] Chavez-Castillo C and Song B (2004), "Dynamical models of tuberculosis and their applications", *Math. Biosci*. Eng., No. 2, pp 361-404

[8] E. Danso-Addo (2009), "Mathematical Model for the Control of Malaria", *MPhil Thesis, University of Cape Coast, Cape Coast*, Ghana.

[9] Federal Democratic Republic of Ethiopia Ministry Of Health Ethiopia National Malaria Diagnosis and Treatment Guidelines for Health Workers in Ethiopia 2nd Edition Addis Ababa, 2004

[10] Federal Democratic Republic of Ethiopia Ministry Of Health Ethiopia National Malaria Indicator Survey, Addis Ababa, 2008.

[11] Federal Democratic Republic of Ethiopia Ministry Of Health Ethiopia National Malaria Guideline Third Edition Addis Ababa, 2012.

[12] Flores J. D. (2011). Math-735: Mathematical Modelling, Routh-Hurwitz criteria. Department of Mathematical Sciences, The University of South Dakota, jflores@usd.edu.

[13] Garba S. M, Gumel A. B and Abu Bakar M. R (2008), "Backward bifurcation in dengue transmission dynamics", *Math.Biosci*, Volume 215, pp 11-25.

[14] G. A. Ngwa and W. S. Shu (2000), "Mathematical Computational Modeling", Vol. 32, Pp.747-763.

[15] G. A. Ngwa, *Modelling the dynamics of endemic malaria in growing populations*, Discrete Contin. Dyn. (2004), pp.1173? 1202.

[16] Greenwood B, and Mutabingwa T (2002), Malaria in 2002, *Nature*, Volume 415, pp 670-672.

[17] Gimnig J, Ombok M, Kamau L, Hawley W (2003) Characteristics of larval *anopheline* (Diptera: Culicidae) habitats in Western Kenya. J. Med. Entomol. 38: 282-288.

[18] J. Y. T. Tumwiine, Mugisha and L. S. Lubobi (2007), "Applied Mathematics and Computation", Vol.189, Pp. 1953-1965.

[19] K. Dietz (1993), "The Estimation of the Basic Reproduction Number for Infectious Diseases", *Statistical Methods in Medical Research*, Vol. 2, Pp. 23?41.

[20] Killeen G. F, Mckenzie F. E, Foy B. D, Bogh C and Beier J. C (2001), "The availability of potential hosts as a determinant of feeding behaviors and malaria transmission by African mosquito populations", Trans. R. Soc. Trop. Med.Hyg., Volume 95, pp 469-47

[21] Lalloo D. G, Shingadia D, Pasvol G, Chiodini P. L, Whitty C. J and Beeching N.J(2008), UK malaria treatment guidelines, J. *Infect* 2007, Volume 54, pp 111-121.

[22] L. Perko, *Differential Equations and Dynamics Systems in Applied Mathematics*, vol.7, Springer, Berlin, Germany, 2000.1

[23] N. Chitins, J. M. Cushing and J. M. Hyman (2006), "Bifurcation Analysis of a Mathematical Model for Malaria Transmission", *Submitted: SIAM Journal on Applied Mathematics.*

[24] N. Chitnis, J. M. Hyman and J. M. Cushing (2008), "Determining Important Parameters in the Spread of Malaria through the Sensitivity Analysis of a Mathematical Model", In Preparation

[25] O. Diekmann and J. A. P. Heesterbeek (1999), "Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation", *Wiley-Blackwell*.

[26] Namawejje H.(2011). Modeling the Effect of Stress on the Dynamics and Treatment of Tuberculosis. M.Sc.(Mathematical Modelling) Dissertation, University of Dares Salaam, Tanzania.

[27] Niger Ashrafi M and Gumel Abba B (2008), "Mathematical Analysis of the Role of Repeated Exposure on Malaria Transmission Dynamics", *Differential Equations and Dynamical Systems*, Volume 16, No. 3, pp 251-287.

[28] Ngwa G. A (2004), Modeling the dynamics of endemic malaria in growing population, *Discrete and Continuous Dynamic System*. Ser. B, Volume 4, pp 1173-1202.

[29] Nita. H. Shah and Jyoti Gupta (2013),"SEIR Model and Simulation for Vector Borne Diseases", *Applied Mathematics*, Vol. 4, Pp. 13-17.

[30] Martens P, Kovats R. S, Nijhof S, Vries P. de, Livermore M. T. J, Bradley D. J, Cox J and McMichael A. J (1999), Climate change and future populations at risk of malaria, *Global Environmental Change*, Volume 9, pp S89-S107.

[31] Miranda I. Teboh-Ewungkem, Chandra N. Podder and Abba B. Gumel (2009),"Mathematical Study of the Role of Gametocytes and an Imperfect Vaccine on Malaria Transmission Dynamics", *Bulletin of Mathematical Biology* DOI 10,Volume 1007, No. S11, pp 538-009-9437-3.

[32] O. J. Diekmann (1990), "Mathematical Biology", Vol.28, Pp. 365-382.

[33] O. Diekmann, J. A. Heesterbeek, and J. A. Metz, "On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations," Journal of Mathematical Biology, vol.28, no.4, pp.365-382,1990.J

[34] P. M. M. Mwamtobe (2010), "Modeling the Effects of MultiIntervention Campaigns for the Malaria Epidemic in Malawi", M. Sc*. (Mathematical Modeling) Dissertation, University of Dar es Salaam, Tanzania*

[35] RollbackMalaria. What is malaria? http://www.rollbackmalaria.pdf. (2010-05-10).

[36] Sandip Mandal, Ram Rup arkar and Somdatta Sinha (2011), "Mathematical Models of Malaria A Review", *Malaria Journal*, Vol. 10, Pp.

[37] Samwel Oseko Nyachae, Johana K. Sigey, Jeconiah A. Okello, James M. Okwoyo and D. Theuri (2014),"A Study for the Spread of Malaria in Nyamira Town - Kenya, The *SIJ Transactions on Computer Science Engineering and its Applications (CSEA), The Standard International Journals (The SIJ),* Vol. 2, No. 3 (1), Pp. 53-60.

[38] Smith R.J and Hove-Musekwa D.S (2008), "Determining effective spraying periods to control malaria via indoor residual spraying in sub-Saharan Africa", *Appled Math and Deci Sc.,* doi:10, Volume 1155, No. 745463, pp 1-19.

[39] Turuse, E.A., et al. (2014) Determinants of Delay in Malaria Prompt Diagnosis and Timely Treatment among Under-Five Children in Shashogo Woreda, Hadiya Zone, Southern Ethiopia: A Case Control Study. Health, 6, 950-959.

[40] Van den Driessche, P., and Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission *Mathematical Biosciences*, 180, 29-48 http://dx.doi.org/10.4236/health.2014.610120.

[41] WHO (1993), Implementation of the global malaria control strategy. Reports of the World Health Organization Study Group on The Implementation of the Global Plan of Action for malaria control 1993-20002, *WHO Technical Report Series,* Number 839.

[42] WHO (1999), The WHO *Report 1999Making a difference*, Geneva.

[43] WHO/UNICEF: World malaria report 2008, Report series: WHO/HTM/MAL/2008.1102

[44] WHO (2009), "Global Malaria Programme: Position Statement on ITNs".

[45] World Malaria Report (2014) (www.who.int/malaria).

[46] Fekadu Tadege et.al controlling the spread of malaria with intervention strategies 'the book was released by LAP LAMBERT Academic Publishing in 2016 and ISBN 978-3-659-77730-1.

[47] M. Gatton, W. Hogarth, A. Saul and P. Dayananda (1996),"A Model for Predicting the Transmission Rate of Malaria from Serological Data", *Journal of Mathematical Biology,* Vol. 84, Pp. 878-888.

[48] J. Nedelman (1983), "Inoculation and Recovery Rates in the Malaria Model of Dietz, Molineaux, and Thomas", *Mathematical Biosciences*, Vol. 69, No. 2, Pp. 209-233.

[49] R. Ross (1911),"The Prevention of Malaria", John Murray, London.

[50] WHO Global Malaria Programme (2010), World Malaria Report 2010.

[51] Macdonald G. The epidemiology and control of malaria. London: Oxford University Press; 1957.

[52] WHO (2007) Insecticide treated mosquito nets: a WHO position statement. Technical report, World Health Organization.

[53] Bayoh MN, Mathias DK, Odiere MR, Mutuku FM, Kamau L, et al.. (2010) Anopheles gambiae: historical population decline associated with regional distribution of insecticide-treated bed nets in western Nyanza province, Kenya. Malaria Journal 9.

[54] WHO (2004) Global strategic framework for integrated vector management. Technical report, World Health Organization, Geneva.

[55] WHO (2011) World Malaria Report. Technical report, World Health Organization, Geneva.

[56] RBM (2013) Minutes of roll back malaria vector control working group 8th annual meeting. Technical report, Roll Back Malaria. Available: http://www.rollbackmalaria.org/mechanisms/vcwg.html.

[57] Hethcote HW. In: Frontiers in mathematical biology. Lecture notes in Bio mathematics. Simon A Levin, editor. Vol. 100. Springer; 1984. A thousand and one epidemic models; pp. 504-515.

[58] Chitnis N. (2005), "Using Mathematical Models in Controlling the Spread of Malaria", Ph.D. Thesis, *Program in Applied Mathematics, University of Arizona*, Tucson, AZ.

[59] Fekadu Tk. et al(2015) "a mathematical model to control the spread of malaria with intervention campaigns in Shashogo Woreda, Hadiya zone, Southern Ethiopia," Msc *unpublished Thesis, program in computational mathematics, Hawassa university*

[60] Fekadu Tadege Kobe and Purnachandra Rao Koya, "Controlling the Spread of Malaria Disease Using Intervention Strategies" *Journal of Multidisciplinary Engineering Science and Technology (JMEST) ISSN*: 3159-0040 Vol. 2 Issue 5, May 2015, pp 1068-1074. www.jmest.org JMESTN4235074567