IOSR Journal of Mathematics (IOSR-JM)
e-ISSN: 2278-5728, p-ISSN: 2319-765X. Volume 15, Issue 4 Ser. I (Jul – Aug 2019), PP 25-41
www.iosrjournals.org

Mathematical Modeling the Dynamics of Endemic Malaria Transmission with Control Measures

Dereje Gutema Edossa, and Purnachandra Rao Koya
Department of Mathematics, Wollega University, Nekemte, Ethiopia

Abstract: *Malaria is an infectious disease caused by the Plasmodium parasite and is transmitted between humans through bites of female anopheles' mosquitoes. The disease continues to emerge in developing countries and remains as a global health challenge. In this paper, a mathematical model is formulated that insights in to some essential dynamics of malaria transmission with environmental management strategy for malaria vector control, insecticide treated bed net, indoor residual spray and treatment with antimalaria drugs as control strategies for humans so as to minimize the disease transmission or spread. The reproduction numbers with single and combined control strategies are calculated and they were compared with each other so as to find the one that benefits more the communities. Numerical simulation shows that among single controls strategies, insecticide treated bed net yields the best result. Furthermore, controlling results of two strategies are better than one; those of three are far better than two and so on. Also, the simulations with all four interventions showed that those results are the best among all possible combinations of intervention strategies. Furthermore, sensitivity analysis is performed and identified important parameters that drive the disease dynamics. Also, their relative importance to disease transmission as well as its prevalence is measured.*

Key Words: *Endemic malaria, Infectious diseases, Numerical simulation, Plasmodium parasite, Reproduction number*

Date of Submission: 24-06-2019 Date of acceptance: 06-07-2019

I. Introduction

Malaria is an infectious disease caused by the Plasmodium parasite and is transmitted among humans through bites of female Anopheles mosquitoes. And also, it is transmitted more infrequently, by blood transfusion (needle sharing, surgery, birth) [1].The infection has been one of the most global health challenges throughout the world. About 40% of the world's population specially, Africans and some other developing countries live in malaria endemic area. Africa shares 80% of the cases and 90% of deaths [2].

The environmental conditions of the tropics are the prime factors for the malaria to be endemic. The moderate-to-warm temperatures, high humidity and water collection in low land in the tropics area are the main factors that allow mosquitoes to reproduce there. The epidemiological patterns of malaria usually vary with season because of its dependence on transmission by mosquitoes. Malaria infection can lead to dangerous complications such as affecting lungs, brain, kidneys and other organs. Clinical symptoms such as pain, chills, fever and sweats may develop some days after infected mosquito bites J. Tumwiine, J.Y.T. Mugisha and L.S. Luboobi [3].

The main challenging factors of malaria control include: cost of the control programs; complexity of disease control process; resistance of the parasite to antimalarial drugs; and resistance of vectors to insecticides. There is a variation in disease patterns and transmission dynamics from place to place together with changing seasons as well as varying environmental circumstances. The approaches of planning and implementation of prevention and control activities also vary based on local realities. Communities have poor sanitation and poor drainage, mostly because of poverty. These two factors allow mosquitoes to breed in ever greater numbers. Also, people will not be able to afford the simple protection strategies like mosquito nets or even screens for their windows.

World Health organization WHO recommended malaria intervention strategies include the use of long-lasting insecticide treated bed nets (LLINs), indoor residual spray (IRS), chemoprevention for the most vulnerable such as intermittent preventive treatment for pregnant women (IPTP), confirmation of malaria diagnostics through rapid diagnostics tests (RDTs) and microscopy for every suspected case, and timely treatment with artemisinin-based combination therapies (ACTs) [4,5].Controlling malaria only by drugs and insecticides are not sufficient since their sustainability has been undermined by the development of resistance and growing concerns about the long-term environmental impact of some insecticides. Environmental Management Strategy (EMS) for vector control would strengthen malaria control activities and is the cost-effective[4,6].

Malaria has for many years been considered as a global issue, and many epidemiologists and other scientists invest their effort in learning the dynamics of malaria and to control its transmission. From interactions with those scientists, mathematicians have developed a significant and effective tool. Mathematical models of malaria, gives an insight into the interaction between the host and vector population, as well as how to control malaria transmission.

II. Literature Review

Mathematical modeling of malaria has flourished since the days of Ronald Ross in 1911 who was awarded the Nobel Prize for his work [7].He developed a simple SIS-model (Susceptible -Infected - Susceptible) with the assumption that at any time, the total population can be divided into distinct human compartments. He used a mathematical model to show that bringing a mosquito population below a certain threshold was sufficient to eliminate malaria. This threshold naturally depended on biological factors such as the biting rate and vectors capacity. For the purpose of estimating infection and recovery rates, Macdonald G. [8] used a model in which he assumed the amount of infective material to which a population is exposed remains unchanged. His model shows that reducing the number of mosquitoes is an inefficient control strategy that would have little effect on the epidemiology of malaria in areas of strong transmission. Ferreira, M. U., H. M. Yang, [9] "Assessing the effects of global warming and local social and economic conditions on the malaria transmission The Ross-Macdonald [7, 8] mathematical model involves an interaction between infected human hosts and infected mosquito vectors. Aron [10,11] models considered that acquired immunity to malaria depends on exposure (i.e. that immunity is boosted by additional infections).Yang,H.M[12]"Malaria transmission model for different levels of acquired immunity and temperature-dependent parameters(vector)",Bacaer N. and C. Sokhna.[13] "A reaction-diffusion system modeling the spread of resistance to an antimalarial drug Tumwiin et al [3] used SIS and SI models in the human hosts and mosquito vectors for the study of malaria epidemics that last for a short period in which birth and immunity to the disease were ignored. They observed that the system was in equilibrium only at the point of extinction that was neither stable nor unstable. However, some important results were revealed numerically. Some recent papers have also included environmental effects and Ngwa, G. A. "Modelling the dynamics of endemic malaria in growing population [9, 14], and the spread of resistance to drugs [15].Addo, D.E., [16] "Mathematical model for the control of Malaria", Master Thesis. Recently, Tumwiine, Mugisha and Luboobi [3, 17] developed a compartment model for the spread of malaria with susceptible-infected-recovered-susceptible (SIRS) pattern for human and susceptible-infected (SI) pattern for mosquitoes. , Mugisha and Luboobi [3] .Yang, Wei, and Li [18], define the reproduction number, R_0 and show the existence and stability of the disease-free equilibrium and an endemic equilibrium and proposed SIR for the human and SI for the vector compartment model. Abadi Abay Gebremeskel, Harald Elias Krogstad, "Mathematical Modeling of Malaria Transmission", American Journal of Applied Mathematics [19], Fekadu Tadege Kobe and Purnachandra Rao Koya "Modeling Controlling of the Spread of malaria disease using intervention Strategies'' [20]. In the previous model that is, [18], [19] and [20] the relative impact of individual disease control measure or combined disease control measures on the specific important parameter for the diseases transmission or spread, is not taken into consideration.

In this paper, for the control of dynamics of endemic malaria transmission, environmental management strategy for malaria vector control is incorporated on the existing models as a control strategy. Therefore; the objective of this study is to understand the impact of incorporate control strategy on dynamics of endemic malaria transmission and to investigate the effect of environmental management strategies for malaria vector control as base for other control strategy such as indoor residual spray, insecticide treated bed nets and treatment with antimalaria drugs as intermittent prophy active for Infants or intermittent preventive treatment for pregnant women or treatment with artemisinin-based combination therapies [6].So, we have four types of controls: environmental management strategy (EMS), indoor residual spraying (IRS), insecticide treated bed nets and treatment with drugs for all human population according to their age's categories and others. In general, these control measures are functions of time. For the special case with constant controls, we are able to rigorously analyze the stabilities of the corresponding autonomous dynamical system. We will then use numerical simulation to explore various optimal control solutions involving single and multiple controls.

2. Model Formulation and Mathematical Analysis

2.1 Model Formulation

In this study transmission and spread of malaria disease between two interacting populations of humans (the host) and mosquitoes (the vector) has been considered. The model considers that the total human population at time t denoted by$N_h(t)$is divided into three classes: susceptible humans$S_h(t)$, infectious humans$I_h(t)$,and recovered humans$R_h(t)$.Hence, the total human population is given by: $N_h(t) = S_h(t) + I_h(t) + R_h(t)$.Similarly, the mosquito population is divided into two classes: Susceptible mosquitoes $S_v(t)$ and infectious mosquitoes$I_v(t)$.Thus, the total mosquito population at any time t is denoted and given by: $N_v(t) =$

$S_v(t) + I_v(t)$. Since, the infected mosquitoes remain infectious for whole life and thus the mosquitoes do not have any recovered class. Individuals are recruited into the susceptible class with a rate of Λ_h. An infectious female anopheles 'mosquito usually attacks susceptible human with a probability β_h [21]. In the process, the parasite in the form of sporozoites is injected into the blood and move to the infectious$I_h(t)$. It is considered that appropriate active antimalaria drugs are provided to the infectious human population. As a result, after some time, infectious humans recover due to immunity resistance and treatment with anti-malaria drugs and then move to the recovered class $R_h(t)$with respective rates γ and σ. It is also assumed that these recovered individuals with little permanent immunity move to the susceptible class again with respective rate θ .Every class of humans' population is decreased by natural death and except for the infectious class additionally which has disease-induced death with respective rates$\mu_h$and δ_h.

In a similar manner, susceptible individuals of mosquitoes are recruited into the mosquito population by input rate $\Lambda_v$when a susceptible mosquito$S_v$bites an infectious human $I_h(t)$, the susceptible mosquito becomes infected with probability$\beta_v$from infectious human $I_h(t)$, and the mosquito moves from the susceptible to the infectious $I_v(t)$ after a given time. Mosquitoes leave the population due to: natural death rate, action taken on environmental modification and manipulation, action of indoor residuals praying, insecticide-treated bed nets are used and disease-induced death with respective rates $\mu_v, \varepsilon, \alpha, \psi$ and $\delta_v$respectively.

2.1.1 Model Assumptions

The formulation of the present model is guided by the following assumptions:

(i) The total population of individuals is not constant.
(ii) Controls are implemented continuously.
(iii) Insecticide treated bed net (ITN) is continuously provided as protection to the susceptible human population.
(iv) Treatment with anti-malaria drugs is continuously applied to the infected individuals.
(v) Spraying insecticide chemicals on the place where mosquitoes reproduce and on the human home walls, leads to the death of mosquito populations.
(vi) On recovery, there is temporary immunity as well as permanent immunity.
(vii) Environmental modifications and manipulations support other control measures as base for control of outbreak of malaria disease.
(viii) The populations in compartments of both humans and vectors are non-negative and so are all the parameters involved in the model
(ix) malaria is active in a population for a long period of time

Table 1 Description of state variables

State variable	Description
$\mathbf{S_h(t)}$	Number of susceptible humans
$\mathbf{I_h(t)}$	Number of infected humans
$\mathbf{R_h(t)}$	Number of recovered humans
$\mathbf{S_v(t)}$	Number of susceptible mosquitoes
$\mathbf{I_v(t)}$	Number of infected mosquitoes

Table 2Descriptionof model parameters

Parameter	Description
$\mathbf{\Lambda_h}$	Recruitment rate of susceptible humans
$\mathbf{\Lambda_v}$	Recruitment rate of susceptible mosquitoes
$\mathbf{\mu_h}$	Natural death rate of humans
$\mathbf{\delta_h}$	Disease-induced death rate of humans
$\mathbf{\beta_h}$	Contact rate of infective vector and susceptible humans
$\boldsymbol{\gamma}$	Recovery rate of infective humans
$\mathbf{\mu_v}$	Natural death rate of mosquitoes
$\mathbf{\delta_v}$	Disease-induced death rate of humans
$\boldsymbol{\theta}$	Rate of loss of immunity in human per capita
$\mathbf{\beta_v}$	Contact rate of susceptible mosquitoes and infective humans

Table 3 Description of Prevention and control parameters

L.N	Prevention / Control Parameter	Description
1	$\boldsymbol{\sigma}$	Rate of control effort or treatment using drugs on infectious humans
2	$\boldsymbol{\varepsilon}$	Rate of malaria vector using environmental management strategy(EMS)
3	$\boldsymbol{\alpha}$	Rate of prevention of malaria vector using Indoor Residual Spraying Insecticide(IRS)

4	ψ	Rate of prevention of malaria vector measure using insecticide treated bed nets (ITN)

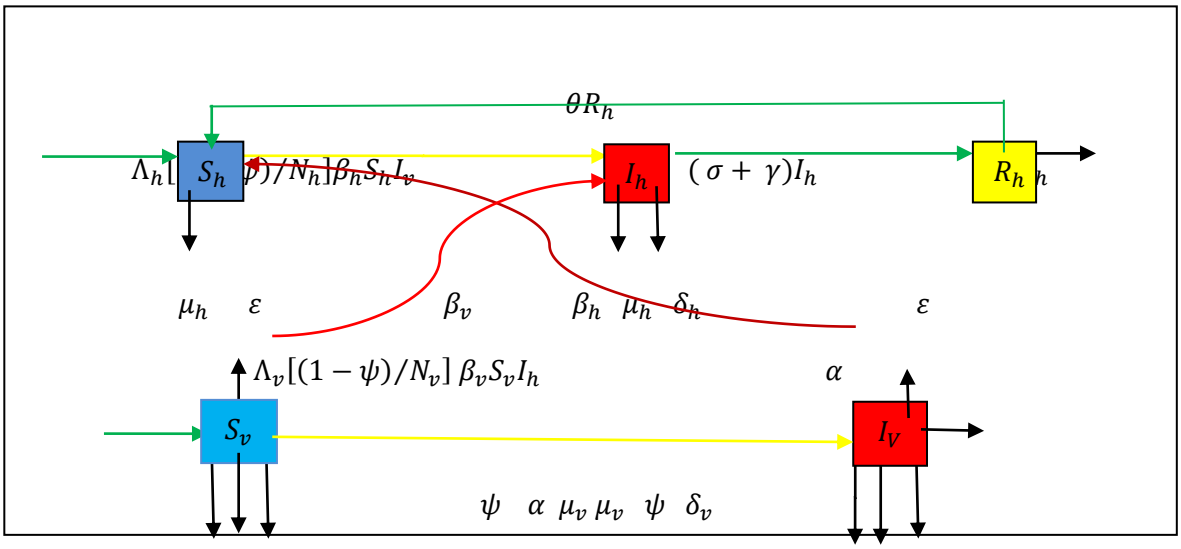

Figure 1: Flow of malaria parasite transmission between humans and mosquitoes

2.1.2Model equations

$$dS_h/dt = \Lambda_h + \theta R_h - [(1-\psi)/N_h]\beta_h S_h I_v - \mu_h S_h \quad 2.1a$$
$$dI_h/dt = [(1-\psi)/N_h]\,\beta_h S_h I_v - (\sigma + \gamma + \mu_h + \delta_h)I_h \quad 2.1b$$
$$dR_h/dt = (\sigma + \gamma)I_h - (\mu_h + \theta)R_h \quad 2.1c$$
$$dS_v/dt = \Lambda_v - [(1-\psi)/N_v]\,\beta_v S_v I_h - (\alpha + \psi + \varepsilon + \mu_v)S_v \quad 2.1d$$
$$dI_v/dt = [(1-\psi)/N_v]\,\beta_v S_v I_h - (\varepsilon + \alpha + \psi + \mu_v + \delta_v)I_v \quad 2.1e$$

With initial conditions:

$$S_h(0) = S_0 h,\ I(0) = I_0 h,\ R_h(0) = R_0 h, S_v(0) = S_0 v,\ I_v(0) = I_0 v \quad 2.2$$

2.2 Model Analysis

2.2.1 Existence and Positivity of Solutions

In this section, it is shown that the malaria model governed by the system of equations (2.1a-e) is epidemiologically and mathematically well posed. Specifically, the feasible region is identified as

$$\Pi = \{\Pi_h \times \Pi_v\} \subset \{\mathbb{R}^3_+ \times \mathbb{R}^2_+\}$$

where $\Pi_h = \{(S_h,\ I_h,\ R_h) \in \mathbb{R}^3_+ : N_h \leq (\Lambda_h/\mu_h)\}$

and

$$\Pi_v = \{(S_v,\ I_v) \in \mathbb{R}^2_+ : N_v \leq [\Lambda_v/(\alpha + \psi + \varepsilon + \mu_v)]\}.$$

Theorem 2.1: A domainΠ existsin which the solution $\{S_h,\ I_h,\ R_h,\ S_v,\ I_v\}$is contained and bounded.

Proof: Let the solutions of the system of equations (2.1) together with positive the initial conditions equation (2.2) are $\{S_h,\ I_h,\ R_h,\ S_v,\ I_v\}$. And also, let $N_h(t) = S_h(t) + I_h(t) + R_h(t)$and $N_v(t) = S_v(t) + I_v(t)$. Now, in order to show that both the human and mosquito populations are bounded it is enough to show that the respective two total populations i.e., $N_h(t)$and $N_v(t)$are bounded.

Boundedness of $N_h(t)$: Addition of human compartments of the system of equations (2.1) leads to$dN_h/dt = \Lambda_h - \mu_h N_h(t) - \delta_h I_h(t)$. After dropping the negative term $-\delta_h I_h(t)$ appearing on the right-hand side the fore going equation can be expressed without loss of generality as an inequality as$d\ N_h/dt \leq \Lambda_h - \mu_h N_h(t)$. Equivalently, it can be expressed as $dN_h/dt + \mu_h N_h(t) \leq \Lambda_h$. It is a first order linear ordinary differential equation and has the general solution $N_h(t) \leq (\Lambda_h/\mu_h) + A\,exp(-\mu_h t)$.Here, the integral constant A takes the form, on applying the initial condition, as $A = [N_0 - (\Lambda_h/\mu_h)]$. And hence, the complete solution is $N_h(t) \leq (\Lambda_h/\mu_h) + [N_{0h} - (\Lambda_h/\mu_h)]exp(-\mu_h t)$. Now, clearly it can be observed that $N_h(t) \leq (\Lambda_h/\mu_h)$as $t \to \infty$ and also, according to the initial conditions $N_h(t) = N_h$at the initial time $t = 0$. Hence, the total human population is bounded i.e., $N_{0h} \leq N_h(t) \leq (\Lambda_h/\mu_h)$.

Boundedness of $N_v(t)$: Addition of mosquito compartments of the system of equations (2.1a-e) leads to$dN_v/dt = \Lambda_v - (\alpha + \psi + \varepsilon + \mu_v)N_v(t) - \delta_v I_v(t)$.After dropping the negative term $-\delta_v I_v(t)$ appearing on the right-hand side, the fore going equation can be expressed without loss of generality as an inequality as.$dN_v/dt \leq \Lambda_v - (\alpha + \psi + \varepsilon + \mu_v)N_v(t)$. Equivalently, it can be expressed as $dN_v/dt + (\alpha + \psi + \varepsilon +$

$\mu_v)N_v(t) \leq \Lambda_v$. It is a first order linear ordinary differential equation and has the general solution $N_v(t) \leq \left[\Lambda_v/(\alpha+\psi+\varepsilon+\mu_v)\right] + A\ exp\left[-(\alpha+\psi+\varepsilon+\mu_v)t\right]$. Now, clearly it can be observed that $N_v(t) \leq \left[\Lambda_v/(\alpha+\psi+\varepsilon+\mu_v)\right]$ as $t \to \infty$ and also according to the initial conditions, $N_0(t) = N_{v0}$at the initial time $t = 0$. Hence, the total mosquito population is bounded i.e., $N_{0v} \leq N_v(t) \leq \left[\Lambda_v/(\alpha+\psi+\varepsilon+\mu_v)\right]$.

Thus, the solutions of the model variables representing human populations$\{S_h(t),\ I_h(t),\ R_h(t)\}$ are confined in the feasible region $\Pi_h = \{(S_h,\ I_h,\ R_h) \in \mathbb{R}_+^3 : N_h \leq (\Lambda_h/\mu_h)\}$. Similarly, the solutions of the model variables representing mosquito populations$\{S_v(t),\ I_v(t)\}$only confined in the feasible region

$\Pi_v = \{(S_v,\ I_v) \in \mathbb{R}_+^2 : N_v \leq [\Lambda_v/(\alpha+\psi+\varepsilon+\mu_v)]\}$.

This shows that the feasible region for the model equations (2.1) exists and is given by: $\Pi = \{S_h(t),\ I_h(t),\ R_h(t),\ S_v(t),\ I_v(t)\} \in \mathbb{R}_+^5$orequivalently$\Pi = \{\Pi_h \times \Pi_v\} \subset \{\mathbb{R}_+^3 \times \mathbb{R}_+^2\}$.

Theorem 2.2: (**Positivity of equations (2.1))**The solutions $\{S_h(t),\ I_h(t),\ R_h(t),\ S_v(t),\ I_v(t)\}$ of the malaria model given in equations (2.1a-e) together with the non-negative initial conditions given in equation(2.2) are all non–negative for all $t \geq 0$.

Proof: Consider the equation for susceptible humans, from the system equations (2.1). That is,

(i) $dS_h/dt = \Lambda_h + \theta R_h - [(1-\psi)\beta_h I_v/N_h] - \mu_h S_h$; after dropping the positive termsΛ_h and θR_h appearing on the right-hand side the fore going equation can be expressed without loss of generality as an inequality $dS_h/dt \geq -S_h\left[[(1-\psi)\beta_h I_v/N_h] + \mu_h\right]$, but from theorem 2.1 we have also $N_h \leq (\Lambda_h/\mu_h)$.Thus, it can be equivalently expressed as: $dS_h/dt \geq -S_h\left[\left[(1-\psi)\mu_h\beta_h I_v/\Lambda_h\right] + \mu_h\right]$. It is a first order linear ordinary differential equation and has the general solution$S_h(t) = A\ exp\left[-\left[[\mu_h(1-\psi)\beta_h I_{0v}/\Lambda_h] + \mu_h t\right]\right] \geq 0$. Where $A = S_{0h}$is constant of integration. Therefore; $S_h(t) \geq 0$ for all $t \geq 0$.

(ii) $dI_h/dt = [(1-\psi)\beta_h S_h I_v/N_h] - (\sigma + \gamma + \mu_h + \delta_h)I_h$after dropping the positive term $(1-\psi)\beta_h S_h I_v/N_h$appearing on the right-hand side the fore going equation can be expressed without loss of generality as an inequality $dI_h/dt \geq -[\sigma + \gamma + \mu_h + \delta_h]I_h$). It is a first order linear ordinary differential equation and has the general solution .$I_h(t) = B\ exp[-(\sigma + \gamma + \mu_h + \delta_h)t] \geq 0$. Where $B = I_{0h}$is constant of indefinite integration. Therefore; $I_h(t) \geq 0$ for all $t \geq 0$.

(iii) $dR_h/dt = (\sigma + \gamma)I_h - (\mu_h + \theta)R_h$ after dropping the positive terms$(\sigma + \gamma)I_h$appearing on the right-hand side the fore going equation can be expressed without loss of generality as an inequality $dR_h/dt \geq -(\mu_h + \theta)R_h$. It is a first order linear ordinary differential equation and has the general solution $R_h(t) = Cexp[-(\mu_h + \theta)t] \geq 0$, WhereC= $R_{0h}$is constant of indefinite integration . Therefore; $R_h(t) \geq 0$ for all $t \geq 0$

(iv) $dS_v/dt = \Lambda_v - [(1-\psi)\beta_v S_v I_h]/N_v - (\alpha + \psi + \varepsilon + \mu_v)S_v$after dropping the positive term $\Lambda_v$appearing on the right-hand side the fore going equation can be expressed without loss of generality: $dS_v/dt \geq -S_v\left[[\ \beta_v(\alpha+\psi+\varepsilon+\mu_v)\ (1-\psi)I_h/N_v] + (\alpha + \psi + \varepsilon+\mu_v\right]$.

Since$N_v \leq \Lambda_v/[\alpha+\psi+\varepsilon+\mu_v]$and hence, it can be equivalently expressed as:

$dS_v/dt \geq -S_v\left[[\ \beta_v(\alpha+\psi+\varepsilon+\mu_v)\ (1-\psi)I_h/\Lambda_v] + [\alpha + \psi + \varepsilon + \mu_v]\right]$. It is a first order linear ordinary differential equation and has the general solution:

$S_v(t) = D\ exp\left[-\left[[\ \beta_v(\alpha+\psi+\varepsilon+\mu_v)\ (1-\psi)I_{0h}/\Lambda_v] + [(\alpha + \psi + \varepsilon + \mu_v)t]\right]\right] \geq 0$WhereD= $S_{0v}$is constant of integration Therefore; $S_v(t) \geq 0$ for all $t \geq 0$.

(v) $dI_v/dt = [(1-\psi)\beta_v S_v I_h/N_v] - (\varepsilon + \alpha + \psi + \mu_v + \delta_v)I_v$,after dropping the positive term $(1-\psi)\beta_v S_v I_h/N_v$ appearing on the right-hand side the fore going equation can be expressed without loss of generality as: $dI_v/dt \geq -(\varepsilon + \alpha + \psi + \mu_v + \delta_v)I_v$. It is a first order linear ordinary differential equation and has the general solution:

$I_v(t) = k\exp[-(\varepsilon + \alpha + \psi + \mu_v + \delta_v)t] \geq 0$. Where $K = I_{0V}$ is constant of integration .

Therefore; $I_v(t) \geq 0$ for all $t \geq 0$.

2.3 Existence of Equilibrium solutions

The point at which differential equations(2.1a-e) is equal to zero is known as equilibrium Points or steady state solutions. From the proof of theorem 2.2 above ,it is important to have as remark that there is no trivial equilibrium Points since the requirement $\Lambda_h \neq 0\ and\ \Lambda_v \neq 0$ for human population and mosquito population respectively, this implies that,$\{S_h^0, I_h^0, S_v^0, I_v^0\} \neq \{0,0,0,0\}$.andpopulation will not be exist.

2.3.1 Existence of Disease Free- Equilibrium solutions

Disease free-equilibrium points are solutions where there is no malaria infection. Thedisease free-equilibrium points $\boldsymbol{E_0}$ for the malaria model equations (2.1a-e) implies that $I_h^0 = 0$, I_v^0=0 and solving the following from the model equations (2.1a-e) that is,

$dS_h/dt = 0 \Rightarrow S_h^0 = \Lambda_h/\mu_h$, $dS_v/dt = 0 \Rightarrow S_v^0 = \Lambda_v/[\alpha + \psi + \varepsilon + \mu_v]$.Thus,

$$E_{0,} = \{\Lambda_h/\mu_h, 0, \quad \Lambda_v/[\alpha + \psi + \varepsilon + \mu_v] \quad , 0\} \qquad 2.3$$

2.3.2Reproduction Number

The basic reproduction number denoted by R_0 is the average number of secondary infectious infected by an infective individual during his or her whole cause of disease in case that all numbers of the population are susceptible [22].And which helps us to check whether an infection will spread through the population or die out from the population. To obtain $R_0$of the model equations (2.1) we use the next generation matrix techniques designed in [23, 24].Let $X = (\mathrm{I_h}, \ \mathrm{I_v}, \ \mathrm{S_h}, \ \mathrm{S_v})^T$, then the model equation (2.1a-e) can be rewritten as

$$F(X) = \begin{bmatrix} (1-\psi)\beta_h S_h I_v/N_v \\ (1-\psi)\,\beta_v S_v I_h/N_v \\ 0 \\ 0 \end{bmatrix} \qquad and \ V(X) = \begin{bmatrix} (\sigma + \gamma + \mu_h + \delta_h) I_h \\ (\varepsilon + \alpha + \psi + \mu_v + \delta_v) I_v \\ \mu_h S_h - \Lambda_h - \theta R_h \\ (\alpha + \psi + \varepsilon + \mu_v) S_v - \Lambda_v \end{bmatrix}$$

Now, the matrices$F$ and V at the disease-free equilibrium point E_0 are defined as

$$F = \begin{bmatrix} (\partial/\partial I_h)[(1-\psi)\beta_h S_h I_v/N_h] & (\partial/\partial I_v)[(1-\psi)\beta_h S_h I_v/N_h] \\ (\partial/\partial I_h)[(1-\psi)\beta_v S_v I_h/N_v] & (\partial/\partial I_h)[(1-\psi)\beta_v S_v I_h/N_v] \end{bmatrix}_{E_0}$$

$$V = \begin{bmatrix} (\partial/\partial I_h)(\sigma + \gamma + \mu_h + \delta_h) I_h & (\partial/\partial I_v)(\sigma + \gamma + \mu_h + \delta_h) I_h \\ (\partial/\partial I_h)(\varepsilon + \alpha + \psi + \mu_v + \delta_v) I_v & (\partial/\partial I_v)(\varepsilon + \alpha + \psi + \mu_v + \delta_v) I_v \end{bmatrix}_{E_0}$$

After computed we have

$$F = \begin{bmatrix} 0 & (1-\psi)\beta_h \\ (1-\psi)\beta_v & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} \sigma + \gamma + \mu_h + \delta_h & 0 \\ 0 & \varepsilon + \alpha + \psi + \mu_v + \delta_v \end{bmatrix}$$

Also, after computing the inverse$V^{-1}$and finding the product i.e., FV^{-1}, then we have

$$V^{-1} = \begin{bmatrix} \dfrac{1}{\sigma + \gamma + \mu_h + \delta_h} & 0 \\ 0 & \dfrac{1}{\varepsilon + \alpha + \psi + \mu_v + \delta_v} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & \dfrac{(1-\psi)\beta_h}{\varepsilon + \alpha + \psi + \mu_v + \delta_v} \\ \dfrac{(1-\psi)\beta_V}{\sigma + \gamma + \mu_h + \delta_h} & 0 \end{bmatrix}$$

Now, the largest eigenvalue λ of $FV^{-1}$is given by evaluating the corresponding characteristic equation $\det(FV^{-1} - \lambda \mathrm{I}) = 0$and it can be represented by R_c. Thus,

$$\lambda = \sqrt{(1-\psi)^2 \ \beta_h \beta_V/[(\sigma + \gamma + \mu_h + \delta_h)(\varepsilon + \alpha + \psi + \mu_v + \delta_v)]}$$

$$R_c = \sqrt{(1-\psi)^2 \ \beta_h \beta_V/[(\sigma + \gamma + \mu_h + \delta_h)(\varepsilon + \alpha + \psi + \mu_v + \delta_v)]} \qquad (2.4)$$

Here, R_c is known as the basic effective reproduction number since it is the basic reproduction number that depends on all control measures. If there are no any control measures i.e.,$\sigma = \varepsilon = \alpha = \psi = 0$, then the basic effective reproduction number $R_c$for the model equations (2.1) reduces to the basic reproduction number $R_0$and is given by

$$R_0 = \sqrt{\beta_h \beta_V/[(\gamma + \mu_h + \delta_h)(\mu_v + \delta_v)]} \qquad (2.5)$$

2.4 Analysis of Basic Effective Reproduction Number R_c

2.4.1 Analysis of Basic Effective Reproduction Number R_c with Single Control Strategy

Here, the effective reproduction number R_c given in equation (2.4) is used to compute a variety of reproduction numbers for various combinations of individual control strategies or interventions.

(i) Suppose treatment of humans with anti-malaria drugs is the only control strategy considered i.e. $\sigma \neq 0,\ \varepsilon = \alpha = \psi = 0$. Then the basic reproduction number with treatment using anti-malaria drugs is given by

$$R_1 = \sqrt{\beta_h \beta_V / [(\sigma + \gamma + \mu_h + \delta_h)(\mu_v + \delta_v)]} \quad 2.6$$

(ii) Suppose environmental management strategy EMS is the only control strategy considered to control malaria vector i.e. $\varepsilon \neq 0,\ \sigma = \alpha = \psi = 0$. Then the basic reproduction number with environmental management strategy EMS for malaria vector control is dented and given by

$$R_2 = \sqrt{\beta_h \beta_v / [(\gamma + \mu_h + \delta_h)(\varepsilon + \mu_v + \delta_v)]} \quad 2.7$$

(iii) Suppose indoor residual spray IRS is the only control strategy that is used to control vector i.e., $\alpha \neq 0,\ \varepsilon = \sigma = \psi = 0$. Then the basic reproduction number within door residual spray IRS is denoted and given by

$$R_3 = \sqrt{\beta_h \beta_v / [(\gamma + \mu_h + \delta_h)(\alpha + \mu_v + \delta_v)]} \quad 2.8$$

(iv) Suppose insecticide treated bed nets is the only control strategy that is used to control vector i.e. $\psi \neq 0,\ \varepsilon = \sigma = \alpha = 0$. Then the basic reproduction number with insecticide treated bed net ITN is denoted and given by

$$R_4 = \sqrt{(1-\psi)^2 \beta_h \beta_v / [(\gamma + \mu_h + \delta_h)(\psi + \mu_v + \delta_v)]} \quad 2.9$$

2.4.2. Analysis of Basic Effective Reproduction Number R_c with Two Control Strategies

Here, the effective basic reproduction number given in equation (2.4) is further analyzed by computing the corresponding reproduction numbers for the combination of two control strategies or interventions.

(i) Suppose that a combination of environmental management and insecticide treated bed net strategies for controlling malaria vector is the only intervention strategy that is considered i.e., $\varepsilon \neq 0, \psi \neq 0,\ \sigma = \alpha = 0$. Then the basic reproduction number with environmental management strategy and insecticide treated bed nets are applied to control malaria vector is denoted and given by

$$R_2 R_4 = \sqrt{(1-\psi)^2 \beta_h \beta_v / [(\gamma + \mu_h + \delta_h)(\psi + \varepsilon + \mu_v + \delta_v)]} \quad 2.10$$

(ii) Suppose that the combination of environmental management strategy and indoor residual spray is the only intervention strategy that is considered to control the vector i.e. $\varepsilon \neq 0,\ \alpha \neq 0,\ \sigma = \psi = 0$. Then the basic reproduction number with environmental management strategy and indoor residual spray for controlling malaria vector is denoted and given by

$$R_2 R_3 = \sqrt{\beta_h \beta_v / [(\gamma + \mu_h + \delta_h)(\alpha + \varepsilon + \mu_v + \delta_v)]} \quad 2.11$$

(iii) Suppose that the combination of environmental management strategy for controlling malaria vector and treatment of humans with anti-malaria drugs is the only intervention strategy that is considered i.e. $\varepsilon \neq 0,\ \sigma \neq 0,\ \alpha = \psi = 0$. Then the basic reproduction number with environmental management strategy for controlling malaria vector and treatment of humans with anti-malaria drugs is denoted and given by

$$R_2 R_1 = \sqrt{\beta_h \beta_v / [(\gamma + \sigma + \mu_h + \delta_h)(\varepsilon + \mu_v + \delta_v)]} \quad 2.12$$

(iv) Suppose that the combination of insecticide treated bed net and indoor residual spray for controlling malaria vector is the only intervention strategy that is considered i.e. $\alpha \neq 0,\ \psi \neq 0,\ \sigma = \varepsilon = 0$. Then the basic reproduction number with insecticide treated bed net and indoor residual spray is denoted and given by

$$R_4 R_3 = \sqrt{(1-\psi)^2 \beta_h \beta_V / [(\gamma + \mu_h + \delta_h)(\alpha + \psi + \mu_v + \delta_v)]} \quad 2.13$$

(v) Suppose that the combination of insecticide treated bed nets to control malaria vector and anti-malaria drugs for treatment of humans is the only intervention strategy that is considered i.e. $\psi \neq 0,\ \sigma \neq 0,\ \sigma = \varepsilon = 0$. Then the basic reproduction number with treatment with anti-malaria drugs for treating humans and insecticide treated bed net to control malaria vector is denoted and given by

$$R_4 R_1 = \sqrt{(1-\psi)^2 \beta_h \beta_v / [(\sigma + \gamma + \mu_h + \delta_h)(\psi + \mu_v + \delta_v)]} \quad 2.14$$

(vi) Suppose that the combination of treatment of humans with anti-malaria drugs and indoor residual spray to control malaria vector is the only intervention strategy that is considered i.e. $\sigma \neq 0,\ \alpha \neq 0,\ \psi = \varepsilon = 0$. Then the basic reproduction number with treatment with anti-malaria drugs and indoor residual sprays is denoted and given by

$$R_1 R_3 = \sqrt{\beta_h \beta_v / [(\gamma + \sigma + \mu_h + \delta_h)(\alpha + \mu_v + \delta_v)]} \quad 2.15$$

2.4.3. Analysis of Basic Effective Reproduction Number R_c with Three Control Strategies

Here, the effective basic reproduction number given in equation (2.4) is further analyzes by computing corresponding reproduction numbers for various combinations of three control strategies or interventions.

(i)Consider the combination of three control strategies for controlling malaria vector: environmental management strategy, insecticide treated bed nets and indoor residual spray i.e. $\varepsilon \neq 0,\ \psi \neq 0\ , \alpha \neq 0,\ \sigma = 0$. Then the basic reproduction number with environmental management strategy, insecticide treated bed net and indoor residual spray for controlling malaria vector is denoted and given by

$$R_2R_4R_3 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\psi+\varepsilon+\alpha+\mu_v+\ \delta_v)]} \quad 2.16$$

(ii)Consider the combination of environmentalmanagementstrategy and Insecticide Treated bed net for controlling malaria vector andtreatment of humans with anti-malaria drugs is the only intervention strategy that is considered i.e.$\varepsilon \neq 0,\ \psi \neq 0\ , \sigma \neq 0,\ \alpha = 0$. Then the basic reproduction number with environmental management strategy and insecticide treated bed nets for controlling malaria vector and treatmentof humans with anti-malaria drugs is denoted and given by

$$R_2R_4R_1 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\gamma+\sigma+\mu_h+\delta_h)(\psi+\varepsilon+\mu_v+\ \delta_v)]} \qquad 2.17$$

(iii)Consider the combination of environmental management strategy and indoor residual spray for controlling malaria vector and treatment of humans with anti-malaria drugs is the only intervention strategy that is considered i.e.$\varepsilon \neq 0,\ \psi \neq 0\ , \sigma \neq 0,\ \alpha = 0$. Then the basic reproduction number with environmental management strategy and indoor residual spray for controlling malaria vector, and treatment of humans with anti-malaria drugs is denoted and given by

$$R_2R_3R_1 = \sqrt{\beta_h\beta_v/[(\gamma+\sigma+\mu_h+\delta_h)(\varepsilon+\alpha+\mu_v+\ \delta_v)]} 2.18$$

(iv)Consider the combination of insecticide treated bed nets and indoor residual spray to control malaria vector and treatment of humans with anti-malaria drugs i.e. $\alpha \neq 0,\ \psi \neq 0,\ \sigma \neq 0,\ \varepsilon = 0$. then the basic reproduction number with insecticide treated bed nets, and indoor residual spray for controlling malaria vector and treatment of humans with anti-malaria drugs is denoted and given by

$$R_4R_3R_1 = \sqrt{(1-\psi)^2\beta_h\beta_V/[(\gamma+\sigma+\mu_h+\delta_h)(\psi+\alpha+\mu_v+\ \delta_v)]} \qquad 2.19$$

Table 1 List of Reproduction Numbers with various combinations of control strategies

Malaria control Strategies	Reproduction Number
Anti-malaria drugs	$R_1 = \sqrt{\beta_h\beta_v/[(\sigma\ +\gamma+\mu_h+\delta_h)(\mu_v\ +\ \delta_v)]}$
Environmental management	$R_2 = \sqrt{\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\varepsilon+\mu_v\ +\ \delta_v)]}$
Indoor residual spray IRS	$R_3 = \sqrt{\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\alpha+\mu_v\ +\ \delta_v)]}$
Insecticide treated bed nets	$R_4 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\psi+\mu_v\ +\ \delta_v)]}$
Environmental management Insecticide treated bed nets	$R_2R_4 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\psi+\varepsilon+\mu_v\ +\ \delta_v)]}$
Environmental management Indoor residual spray	$R_2R_3 = \sqrt{\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\alpha+\varepsilon+\mu_v\ +\ \delta_v)]}$
Environmental management Anti-malaria drugs	$R_2R_1 = \sqrt{\beta_h\beta_v/[(\gamma+\sigma+\mu_h+\delta_h)(\varepsilon+\mu_v\ +\ \delta_v)]}$
Insecticide treated bed net Indoor residual spray	$R_4R_3 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\alpha+\psi+\mu_v\ +\ \delta_v)]}$
Insecticide treated bed nets Anti-malaria drugs	$R_4R_1 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\sigma+\gamma+\mu_h+\delta_h)(\psi+\mu_v\ +\ \delta_v)]}$
Anti-malaria drugs and Indoor residual spray	$R_1R_3 = \sqrt{\beta_h\beta_v/[(\gamma+\sigma+\mu_h+\delta_h)(\alpha+\mu_v\ +\ \delta_v)]}$
Environmental management Insecticide treated bed nets Indoor residual spray	$R_2R_4\ R_3 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\gamma+\mu_h+\delta_h)(\psi+\varepsilon+\alpha+\mu_v+\ \delta_v)]}$
Environmental management Insecticide Treated bed net Anti-malaria drugs	$R_2R_4\ R_1 = \sqrt{(1-\psi)^2\beta_h\beta_v/[(\gamma+\sigma+\mu_h+\delta_h)(\psi+\varepsilon+\mu_v+\ \delta_v)]}$
Environmental management Indoor residual spray Anti-malaria drugs	$R_2R_3\ R_1 = \sqrt{\beta_h\beta_v/[(\gamma+\sigma+\mu_h+\delta_h)(\varepsilon+\alpha+\mu_v+\ \delta_v)]}$
Insecticide treated bed nets Indoor residual spray Anti-malaria drugs	$R_4R_3R_1\ = \sqrt{(1-\psi)^2\beta_h\beta_V/[(\gamma+\sigma+\mu_h+\delta_h)(\psi+\alpha+\mu_v+\ \delta_v)]}$
Environmental management Insecticide treated bed nets Indoor residual spray Anti-malaria drugs	$R_c = \sqrt{(1-\psi)^2\ \beta_h\beta_V/[(\sigma+\ \gamma+\mu_h+\delta_h)(\varepsilon+\alpha+\psi+\ \mu_v\ +\ \delta_v)]}$

2.5 Stability of the Disease-Free and Endemic Equilibrium points

2.5.1. Local stability of the Disease-Free Equilibrium point

Here, the stability analysis of the disease-free Equilibrium point$E_0 = \{S_h^0,\ \ I_h^0,\ \ S_v^0,\ \ I_v^0\}$of model equations (2.1) is investigated by computing its Jacobian matrix. The Jacobian matrix is computed by differentiating the left hand side function of each equation in the system with respect to the state variables$S_h,\ \ I_h,\ \ S_v,\ \ I_v$. However, the equation $dR_h/dt = (\sigma + \gamma)I_h - (\theta + \mu_h)R_h$is not included in this analysis since permanent immunity is assumed [25, 26]. That is, the following system of four model equations only will be considered to construct Jacobian matrix and to conduct further analysis.

$$dS_h/dt = \Lambda_h + \theta R_h - [(1-\psi)\beta_h S_h I_v]/N_h - \mu_h S_h \quad \text{2.20a}$$
$$dI_h/dt = [(1-\psi)\beta_h S_h I_v]/N_h - (\sigma + \gamma + \mu_h + \delta_h)I_h \quad \text{2.20b}$$
$$dS_V/dt = \Lambda_v - [(1-\psi)\beta_h S_v I_h]/N_v - (\alpha + \psi + \varepsilon + \mu_v)S_v \quad \text{2.20c}$$
$$dI_v/dt = [(1-\psi)\beta_v S_v I_h]/N_v - (\varepsilon + \alpha + \psi + \mu_v + \delta_v)I_v \quad \text{2.20d}$$

The stability analysis and the results are stated and proved in Theorem 2.3.

Theorem2.3: The Disease-free Equilibrium point E_0 is locally asymptotically stableif $R_c < 1$ but unstable if$R_c > 1$.

Proof: the Jacobian matrix of the system of equations(2.20a-d) can be constructed as

$$J = \begin{bmatrix} -(\beta_h(1-\psi)I_v/N_h) - \mu_h & 0 & 0 & \dfrac{-\beta_h(1-\psi)S_h}{N_h} \\ -\beta_h(1-\psi)I_v/N_h & -(\gamma + \sigma + \mu_h + \delta_h) & 0 & \dfrac{\beta_h(1-\psi)S_h}{N_h} \\ 0 & -\beta_h(1-\psi)S_v/N_v & -(\psi + \varepsilon + \alpha + \mu_v) & 0 \\ 0 & \beta_h(1-\psi)S_v/N_v & 0 & -(\psi + \varepsilon + \alpha + \mu_v + \delta_v) \end{bmatrix}$$

The Jacobian matrix of the system of equations (2.20) evaluated at the disease-free equilibrium point $E_0$is given by

$$J(E_0) = \begin{bmatrix} -\mu_h & 0 & 0 & -(1-\psi)\beta_h \Lambda_h/N_h\mu_h \\ 0 & -(\gamma + \sigma + \mu_h + \delta_h) & 0 & (1-\psi)\beta_h \Lambda_h/N_h\mu_h \\ 0 & -(1-\psi)\beta_v \Lambda_v/[N_v(\psi + \varepsilon + \alpha + \mu_v)] & -(\psi + \varepsilon + \alpha + \mu_v) & 0 \\ 0 & (1-\psi)\beta_v \Lambda_v/N_v(\psi + \varepsilon + \alpha + \mu_v) & 0 & -(\psi + \varepsilon + \alpha + \mu_v + \delta_v) \end{bmatrix}$$

In order to prove the statement it is required to show that all the eigenvalues of $J(E_0)$are negative. Since the first and third columns contain only diagonal terms they give two negative eigenvalues$\lambda_1 = -\mu_h$, $\lambda_2 = -(\psi + \varepsilon + \alpha + \mu_v)$. The other two eigenvalues can be computed from the sub-matrix$J_1(E_0)$ formed by excluding the first and the third rows and columns of $J(E_0)$. Hence $J_1(E_0)$ is given by

$$J_1(E_0) = \begin{bmatrix} -(\gamma + \sigma + \mu_h + \delta_h) & (1-\psi)\beta_h \Lambda_h/N_h\mu_h \\ -(1-\psi)\beta_v \Lambda_v/N_v(\psi + \varepsilon + \alpha + \mu_v) & -(\psi + \varepsilon + \alpha + \mu_v + \delta_v) \end{bmatrix}$$

Now, the characteristic equation$\det[J_1(E_0) - \lambda \mathrm{I}] = 0$takes the form as

$$\begin{vmatrix} -(\gamma + \sigma + \mu_h + \delta_h) - \lambda & [(1-\psi)\beta_h \Lambda_h]/N_h\mu_h \\ -[(1-\psi)\beta_v \Lambda_v/N_v][(\psi + \varepsilon + \alpha + \mu_v)] & -(\psi + \varepsilon + \alpha + \mu_v + \delta_v) - \lambda \end{vmatrix} = 0$$

Also, the characteristic equation can be expressed in a quadratic form as

$$\lambda^2 + (a+b)\lambda + ab + c^2 d = 0$$

Here, the three quantities$a,\ b,\ c$ represent the following parametric expressions: $a = \gamma + \sigma + \mu_h + \delta_h$;
$b = \psi + \varepsilon + \alpha + \mu_v + \delta_v$; $c = \psi + \varepsilon + \alpha + \mu_v$; $d = (1-\psi)^2 \beta_h \beta_v$ and $N_h \approx \Lambda_h/\mu_h$, $N_v \approx \Lambda_v/c$
Here it can be observed that the quantities $a,\ b,\ c,\ and\ d$ areall positives i.e. $a > 0,\ b > 0,\ c > 0,$ d > 0.
Upon solving the quadratic equation, the3rdand 4th eigenvalues λ_3 andλ_3 are obtained as

$$\lambda_3 = -\left\{(a+b) + \sqrt{[(a+b)^2 - 4(ab + c^2 d)]}\right\}/2$$
$$\lambda_4 = -\left\{(a+b) - \sqrt{[(a+b)^2 - 4(ab + c^2 d)]}\right\}/2$$

Here, it can be observed that the eigenvalue $\lambda_3$is absolutely a negative quantity.However, the eigenvalue $\lambda_4$is a negative quantity if the condition $ab + c^2 d > 0$ is valid.
Thus, all the eigenvalues of the Jacobian matrix at the disease-free equilibrium $J(E_0)$ arenegative provided that the condition $ab + c^2 d > 0$ or equivalently $R_c < 1$ is valid.
Therefore,the disease-free equilibrium point is locally asymptotically stableif $R_c < 1$ and unstableif$R_c > 1$.

2.5.2. Local Stability of the Endemic Equilibrium Solution

A disease is endemic in a given population if it continues to persist in thatpopulation. The stability of endemic equilibrium of the model is studied in Theorem 2.4.

Theorem2.4: The endemic equilibrium solution $E^*$of the model equations (2.20a-d) is locally asymptotically stable if $R_c > 1$ and unstable if$R_c < 1$.

Proof: let $E^* = (S_h^*,\ I_h^*,\ S_v^*,\ I_v^*)$be non-trivial equilibrium of the model equations (2.20a-d). That is, all components of E^* are obtained by setting the left hand sides of all equations (2.20 a-d) equal to zero i.e. $(dS_h/dt) = (dI_h/dt) = (dS_v/dt) = (dI_v/dt) = 0$. Solutions of the resultant equations are the components of E^* and they are obtained as

$S_h^* = \{b\Lambda_v\Lambda_h(1-\psi)(\Lambda_h - a)\}/\{\Lambda_v\beta_h\beta_v(1-\psi)^2(\Lambda_h - a) + b\Lambda_h[\beta_v(1-\psi)(\Lambda_h - a) - abc\Lambda_v]\}$ 2.21a

$I_h^* = \{[\beta_h\Lambda_v(\Lambda_h - a)]/ba\Lambda_h\} - \{\Lambda_v/[\beta_v(1-\psi)]\}$2.21b

$S_v^* = ba\Lambda_v\Lambda_h/[b\beta_h\beta_v(1-\psi)^2(\Lambda_h - a)]$2.21c

$I_v^* = \{\Lambda_v\beta_v\beta_h(1-\psi)^2(\Lambda_h - a) - ab\Lambda_h\Lambda_V\}/\{b\beta_h\beta_v\mu_h(1-\psi)^2(\Lambda_h - a)\}$2.21d

Here the quantities $a,\ b,\ c$ represent the following parametric expressions: $a = \sigma + \gamma + \mu_h + \delta_h,\ b = \alpha + \psi + \varepsilon + \mu_v + \delta_h,\ c = \alpha + \psi + \varepsilon + \mu_v$,

Now, the Jacobian matrix of model equations (2.20a-d)at endemic equilibriumE^*reduces to the form as

$$J(E^*) = \begin{pmatrix} -\frac{ab\Lambda_v\Lambda_h}{c\beta_v(1-\psi)(\Lambda_h - a)} - \mu_h - \frac{\mu_h(1-\psi)}{b} & 0 & 0 & \frac{ca\Lambda_h}{\beta_h(1-\psi)(\Lambda_h - a)} - \frac{\Lambda_h\beta_v(1-\psi)}{b\Lambda_v} \\ \frac{\mu_h\beta_h(1-\psi)}{b} & -a & 0 & \frac{c\beta_v(1-\psi)}{b} \\ 0 & -\frac{ab\Lambda_h}{\beta_h(1-\psi)(\Lambda_h - a)} & \frac{c\beta_h(1-\psi)}{\Lambda_v} - c & -\frac{ac\Lambda_h}{\beta_h(1-\psi)(\Lambda_h - a)} \\ 0 & \frac{ab\Lambda_h}{\beta_h(1-\psi)(\Lambda_h - a)} & 0 & -b \end{pmatrix}$$

Recall that the endemic equilibrium solution $E^*$of the model equations (2.20a-d) is locally asymptotically stable if the trace of the Jacobian matrix at that solution is negative and its determinant is positive i.e. $TrJ(E^*) < 0$ and $det(J(E^*)) > 0$. Now, let us show that the trace is negative and the determinant is positive as follows:

The trace of theJacobian matrix at endemic equilibrium $J(E^*)$is given by

$$TrJ(E^*) = -\left[\frac{ab\Lambda_v\Lambda_h}{c\beta_v(1-\psi)(\Lambda_h - a)} + \mu_h + \frac{\mu_h(1-\psi)}{b}\right] - \left[\frac{ab\Lambda_h}{\beta_h(1-\psi)(\Lambda_h - a)}\right] + \left[\frac{b\beta_h(1-\psi)}{\Lambda_v} - (c+b)\right]$$

Now, the negative trace i.e. $TrJ(E^*) < 0$ leads to the following condition:

$$\left[\frac{b\beta_h(1-\psi)}{\Lambda_v}\right] < \left[\frac{ab\Lambda_v\Lambda_h}{c\beta_v(1-\psi)(\Lambda_h - a)} + \mu_h + \frac{\mu_h(1-\psi)}{b}\right] + \left[\frac{ab\Lambda_h}{\beta_h(1-\psi)(\Lambda_h - a)}\right] + (c+b)$$

This condition is equivalent to $R_c > 1$ If $(a_1 - a_0) > a_2$ and $R_c < 1$ if $(a_1 - a_0) < a_2$ Here, $a_0 = [ab\Lambda_v\Lambda_h/c\beta_v(\Lambda_h - a)],\ a_1 = (c + b + \mu_h)\left(\sqrt{ab/\beta_h\beta_v}\right),\ a_2 = (ab/\beta_h\beta_v)[b\beta_h/\Lambda_v - \mu_h/b]$ and $R_c = \sqrt{(1-\psi)^2\ \beta_h\beta_V/[(\sigma + \gamma + \mu_h + \delta_h)(\varepsilon + \alpha + \psi + \mu_v + \delta_v)]}$.

The determinant of Jacobian matrix at endemic equilibrium of the model equation (2.20a-d) is given by

$$\det\ J(E^*) = \begin{vmatrix} -(m + \mu_h + n) & 0 & 0 & r - s \\ \beta_h n & -a & 0 & s - r \\ 0 & -p & -(q + c) & 0 \\ 0 & p & 0 & -b \end{vmatrix}$$

The positive quantities $m,\ n,\ p,\ q,\ r,\ s$ appearing in the $\det\ J(E^*)$ represent the following parametric expressions:

$$m = a\Lambda_v\Lambda_h/[\beta_v(1-\psi)(\Lambda_h - a)]$$
$$n = \mu_h(1-\psi)/b$$
$$p = ab\Lambda_h/[\beta_h(1-\psi)(\Lambda_h - a)]$$
$$q = c\beta_h(1-\psi)/\Lambda_v$$
$$r = ca\Lambda_h/[\beta_h(1-\psi)(\Lambda_h - a)] > 0$$
$$s = c\Lambda_h\beta_v(1-\psi)/b\Lambda_v$$

$det(J(E^*)) = abq + abcn + pqnr\beta_h + pnrc\beta_h + abqm + abq\mu_h + bccm + abc\mu_h + (-pqns\beta_h pnsc\beta_h) > 0$ if $abq + abcn + pqnr\beta_h + pnrc\beta_h + abqm + abq\mu_h + bccm + abc\mu_h > pqns\beta_h + pnsc\beta_h$.This is true for $R_c > 1$ if $-(b_1 + b_0) > b_2$ and $R_c < 1$ if $-(b_1 + b_0) < b_2$; where, $b_0 = (ac\Lambda_h)^2$,

$$b_1 = [a^2bc\beta_h\Lambda_h/\beta_v(\Lambda_h - a)] + abc\mu_h + (ac\Lambda_h)^2/\Lambda_v\ (\Lambda_h - a)^2$$
$$b_2 = [a^2bc/\beta_v][(b/\Lambda_v + \mu) - (\beta_h\Lambda_h\mu_h/\Lambda_v(\Lambda_h - a))]$$

Since, the conditions for $Tr\,J(E^*) < 0$ and $\det\ J(E^*) > 0$ above are satisfied $R_c > 1$ it can be concluded that the model equations (2.20a-d) has locally asymptotically stableendemic equilibrium solution if $R_c > 1$ 1 and unstable if$R_c < 1$.

III. Simulation and Discussion

In the present study an **SIR-SI** model has been formulated and mathematically analyzed. The main objective of this study is to understand the impact of the incorporated control strategies on the transmission dynamics of the malaria disease. Here, simulation study is conducted in support of mathematical analysis. Numerical simulation of model system equations (2.1a-e) is carried out using a set of parameter values given in Table 5using DEDiscover. Graphical representations showing the variations in reproduction numbers with respect to contact rate between the infected humans and the infected mosquitoes are provided in Figures (5) – (7). Since values of the most parameters are not available in the real world, data from literature is used for some parameters and for others estimated values are assigned. Tables 4 and 5 show the values assigned to state variables and parameters respectively and these values have been used in conducting Simulation study.

Table4 Estimated values of state variables

State variable	Initial value	Source
$\mathbf{S}_h$	631	Estimated
$\mathbf{I}_h$	276	Estimated
$\mathbf{R}_h$	40	Estimated
$\boldsymbol{S}_v$	924	Estimated
$\mathbf{I}_v$	560	Estimated

Table 5 Estimated values of parameters

Parameter	Value	Source
Λ_h	0.0280	[20]
μ_h	0.0000391	[20]
δ_h	0.0040	[20]
β_h	0.115	Estimated
Λ_v	6.000	[20]
μ_v	0.0010	Estimated
δ_v	0.0014	Estimated
β_v	0.0200	Estimated
θ	0.014	Estimated
γ	0.0035	[20]
α	0.0270	Estimated
ψ	0.1030	Estimated
ε	0.009	Estimated
σ	0.0200	Estimated

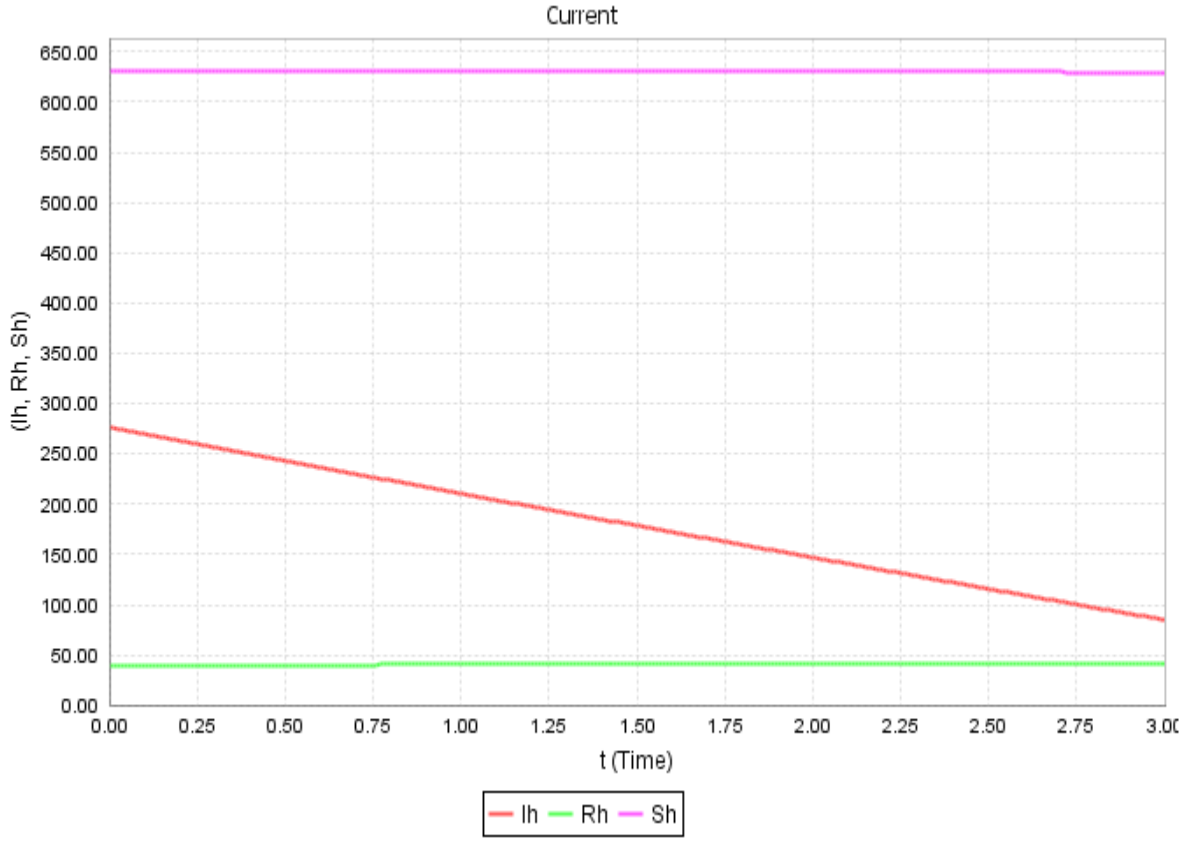

Figure2: Time graph of Human populations

In Figure 2, it is observed that the population size of susceptible humans slightly decreases while that of recovered humans slightly increases, as time progresses. However, the population size of infected humans drops down drastically.

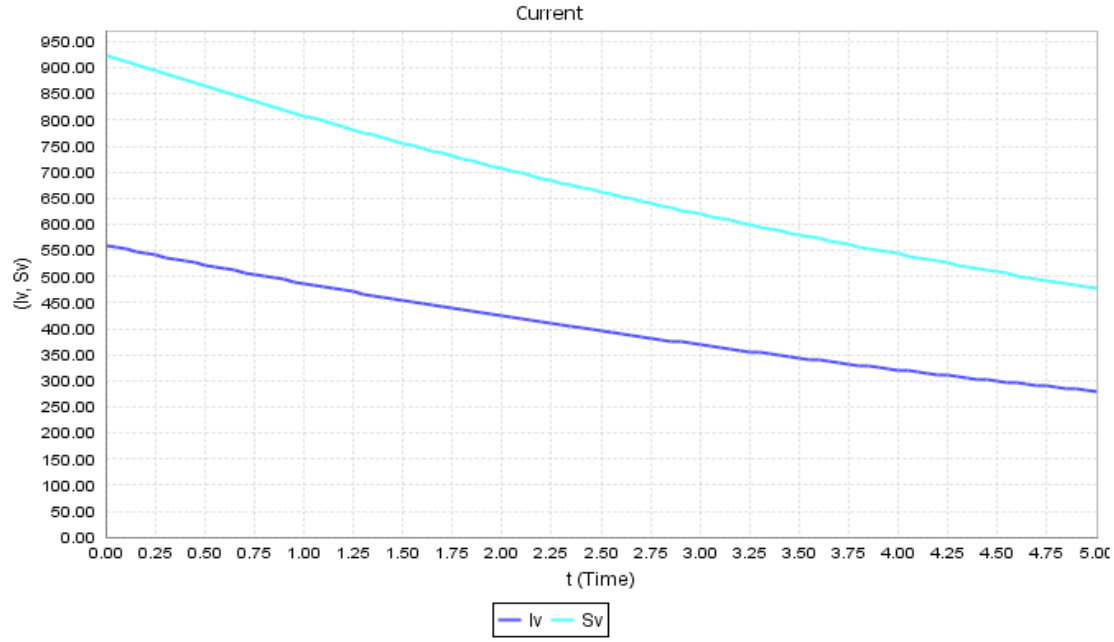

Figure3: Time graph of Mosquitoes populations

In Figure 3, it can be shown that the population sizes of both susceptible and infected vectors decrease as time progresses.

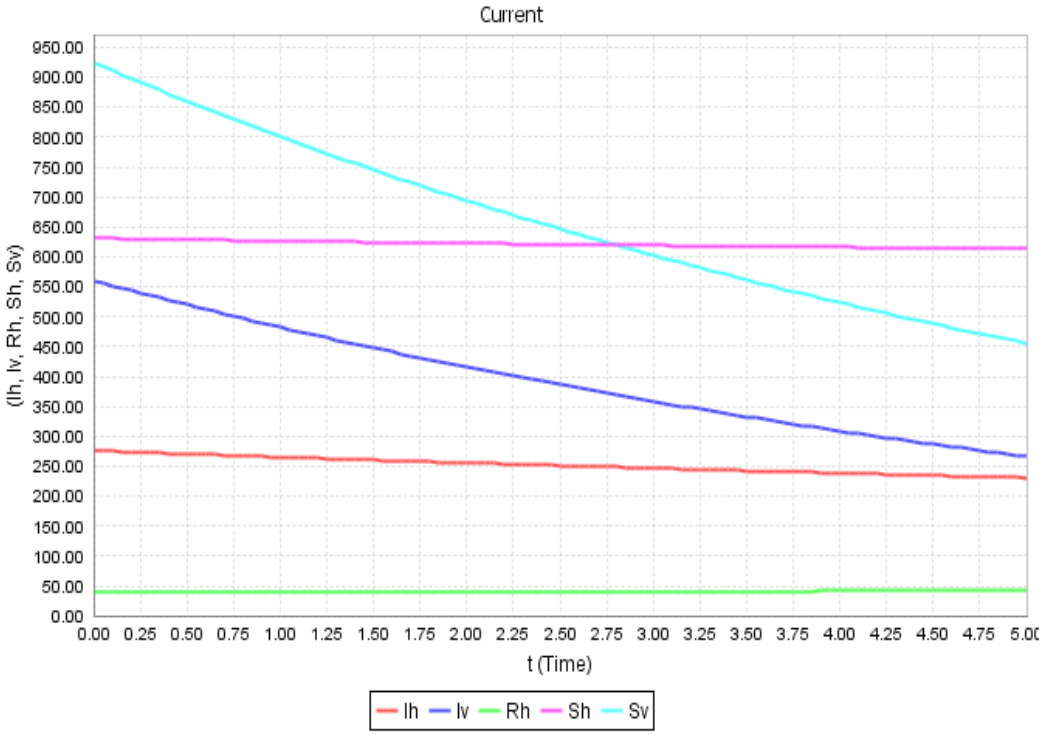

Figure 4: Temporal variations of state variables of human and mosquito populations after control measures are implemented

In Figure 4, it is observed that when control measures are continuously used with time, each class of human and mosquito populations are decreased relatively except the recovery class of human population. The population size of recovered class increases by some constant rate. The mosquito populations are exponentially decreased. This simulation study implies that when malaria vector control measures are used continuously with time the speed of transmission or spread of malaria disease among the communities will become slower.

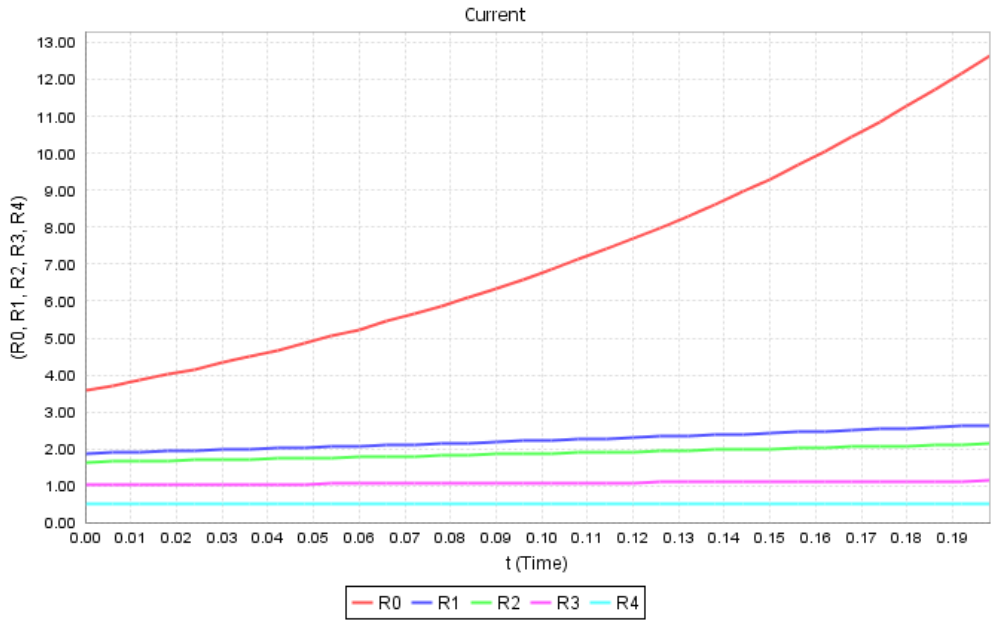

Figure 5: Comparison of single control reproduction numbers with respect to human-mosquito contact rate at time t

Recall here that the reproduction numbers with no or one control strategy are given by R_0, R_1, R_2, R_3, R_4. Here, R_0 for no control; R_1 for Anti-malaria drugs; R_2 for Environmental management; R_3 for Indoor residual spray IRS; and R_4 for Insecticide treated bed nets.

Figure 5 shows the increasing order of the reproduction numbers as$R_4 < R_3 < R_2 < R_1 < R_0$.It can be classified from these graphs that the numbers R_0, $R_1$and $R_2$are the worst cases. These numbers R_0, $R_1$and R_2 occur when there is no any control, only treatment with anti-malaria drugs and only environmental management strategy for malaria vector control respectively.

Particularly, graph of the basic reproduction numberR_0grows exponentially with respect to an increase in human-mosquito contact rate. Such an increase in R_0 above one unit implies that there is a high spread or eruption of malaria in the community.

The best case occurs when the strategy called Insecticide treated bed nets (ITN) is used as shown in the graph of R_4. It is the only intervention strategy offered to susceptible human individuals. It can be noticed that the reproduction number with ITN is less than unity. ITNs can reduce the number mosquito-bites as they provide physically a barrier between mosquitoes and the humans. Furthermore, ITNs can reduce population size of the mosquitoes by killing them after they land on the treated bed nets.

The next case occurs at the graph of R_3which corresponds to the control strategy known as indoor residual spray. Its effect reflects in killing the mosquito population as the latter interact with the sprayed walls and reducing the mosquito population.

The next case occurs as shown by the graph of R_2, which corresponds to the strategy known as environmental management strategy for malaria vector control.

Since the environmental management strategy for malaria vector control provides only a base for other control measures, it has the lowest power in reducing malaria vector compared to other control measures. In similar way intervention with treatment with anti-malaria drugs has little impact to reduce malaria disease transmission compared to other control strategy.

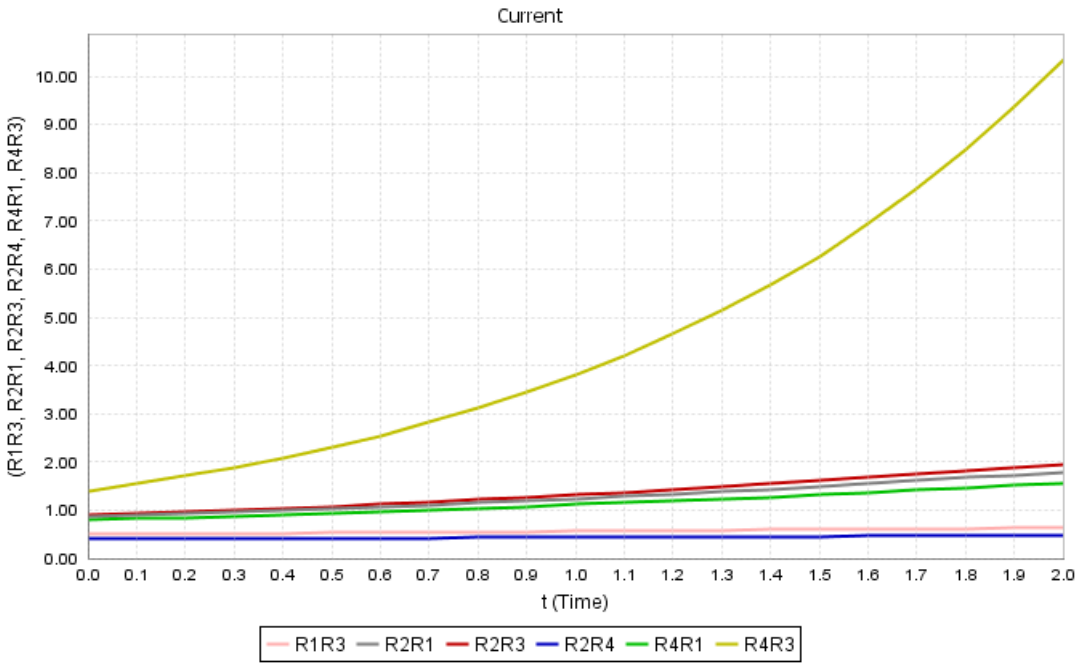

Figure 6: Comparison of reproduction numbers of two-control-strategies with respect to human-mosquito contact rate

Clearly, we observe in Figure 6 that, there is a reduction in disease as compared to simulations with single control and which leads to the inequality:$R_2R_4 < R_1R_3 < R_4R_1 < R_2R_1 < R_2R_3 < R_4R_3$.

It is obvious thatR_4R_3, R_2R_3, R_2R_1, and $R_4R_1$are the worst case, it occurs when a combination of insecticide treated bed net and indoor residual spray, environmental management strategy for malaria vector control and indoor residual spray, environmental management strategy for malaria vector control and treatment with anti-malaria drugs , and insecticide treated bed net and treatment with anti-malaria drugs respectively, this increasing reproduction number shows the eruption of malaria in the community. The best case occurs at graph R_2R_4 here, the twostrategyareenvironmental management strategy for malaria vector control and

insecticide treated bed net incorporated. The next to best case occurs at graph R_1R_3in which the combination of treatment with anti-malaria drugs and indoor residual spray were considered, from this we conclude that increasing the number of controls together with their associated parameters values yields rapid decay of the reproduction number curves.

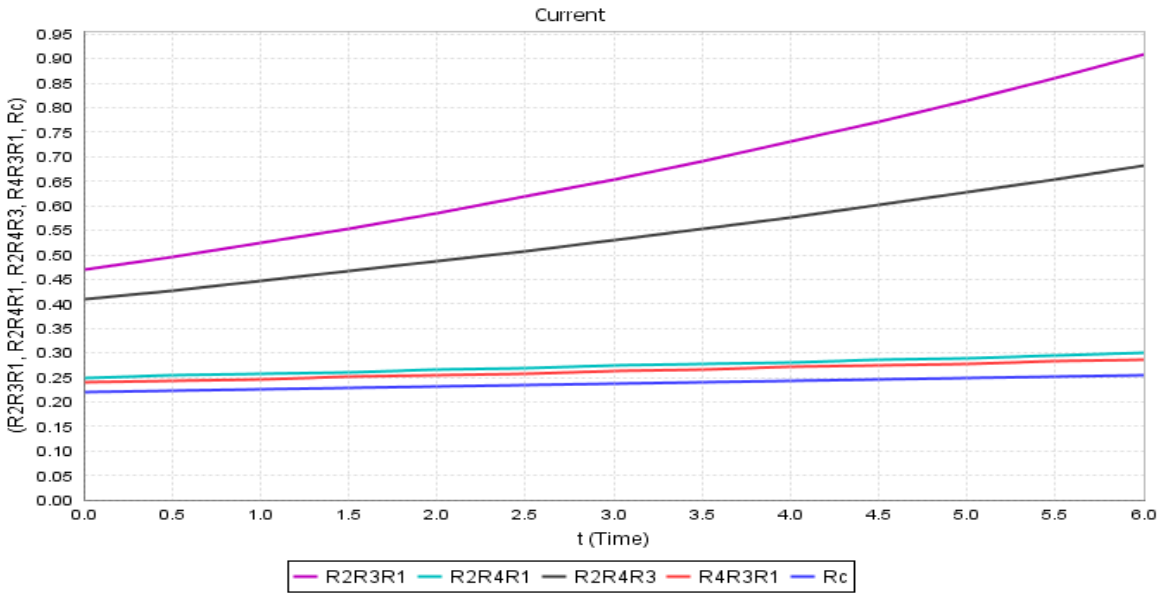

Figure 7: Variations of tri-control reproduction number with respect to human-mosquito contact rate at time$t$

Clearly, we observe in Figure 7 that there is a drastic reduction in disease as compared to both Figure 5 and Figure 6, where all of the reproduction numbers are far less than unity. This implies that there is a control of the disease. The simulations with tri-controls and with all four control measures lead to the inequality:
$R_C < R_4R_3R_1 < R_2R_4R_1 < R_2R_4R_3 < R_2R_3R_1$.Threecontrols give results that a remarked obtained with single control and a combination of two interventions. Therefore, increasing the number of controls together with their associated parameters values yield a rapid decay of the reproduction number curves

IV. Sensitivity Analysis

Sensitivity analysis is helps to determine extent to what "sensitive" a model is to vary in the value of the given parameters of the model and to changes in the base of the model. Sensitivity analysis to rises up confidence in the model dealing with the uncertainties that are often related with parameters in models is conducted. Sensitivity indices enable us to measure the relative change in a state variable while a parameter change. Thus, we use it to deal parameters that have a high degree impact on the reproduction number$R_c$and should be emphasized by intervention strategies. If the result is negative, then the relationship between the parameters and R_c isinversely proportional. In this case, we will take the modulus of the sensitivity index so that we can reduce the size of the effect of changing that parameter. On the other hand, a positive sensitivity index means an increase in the value of a parameter. The parameter values displayed in Table 5 are taken as the baseline values and they are used to evaluate the sensitivity indices of some parameters which are responsible for the transmission and management of malaria disease to four places of decimal in relation to the effective reproduction number, using equation(2.4) as a guide, the result of which is presented in Table 6.Since R_c depends only on six parameters, we derive an analytical expression for its sensitivity to each parameter using the normalized sensitivity indices by Chitins [27]
as follows:

$$\Upsilon_{\beta_h}^{R_c} = \frac{\partial R_c}{\partial \beta_h} \times \frac{\beta_h}{R_c} = +0.5$$

$$\Upsilon_{\beta_v}^{R_c} = \frac{\partial R_c}{\partial \beta_v} \times \frac{\beta_v}{R_c} = +0.5$$

The other sensitivity induces for all parameters used are computed in similar approach and their values given in the following Table 6.

Table6: Sensitivity index of R_c with respect to each parameter

Parameter	sensitivity index
β_h	+0.5000
β_v	+ 0.5000
σ	-0.3636
ε	-0.0318
α	-0.3636
ψ	-0.3642
γ	-0.0630
μ_h	-0.0007
δ_h	-0.0720
μ_v	-0.0053
δ_v	-0.0037

From Table 6 it is obtained that $\Upsilon_{\beta_h}^{R_c} = \frac{\partial R_c}{\partial \beta_h} \times \frac{\beta_h}{R_c} = +0.5$. This means that an increase in β_h or β_v will cause an increase of exactly the same proportion in R_c. Similarly, a decrease in β_h or β_v will cause a decrease in R_c, as they are directly proportional. It can also be noted that $\Upsilon_{\sigma}^{R_c} = -0.36$ this means that an increase in σ will cause a decrease of exactly the same proportion in R_c. Similarly, a decrease in σ will cause an increase in R_c, as they are inversely proportional. We also note that $\sigma < 0,\ \psi < 0,\ \alpha < 0\ , \varepsilon < 0,\ \gamma < 0$ hence these parameters are inversely proportional to R_c. We can arrange these parameters in the order of their magnitude from the smallest to the largest as follows: $\psi,\ \sigma,\ \alpha,\ \varepsilon,\ \gamma,\ \beta_h = \beta_v$.This implies that insecticide treated bed net has high power of reducing mosquitoes or transmission of malaria than the other control measures.

V. Conclusion and Recommendation

In this paper, we have formulated a deterministic mathematical model for transmission dynamics of malaria that incorporates four control strategies namely, environmental management strategy for malaria vector control, insecticide treated bed net, indoor residual spray and treatment with antimalaria drugs. The effective reproduction number for the model is calculated from which the basic reproduction number, and the reproduction numbers with combination of two, and three control strategies are also deduced. The effective reproduction number has been used to measure the relative impact for individual or combined intervention for effective disease control.

Both the disease-free equilibrium E^0 and the endemic equilibrium E^* for the model are derived. Also, proved that the disease-free equilibrium E^0 is locally asymptotically stable when $R_c < 1$ and the endemic equilibrium point E^* is locally asymptotically stable when $R_c > 1$.

Numerical simulations of the model have been conducted and the observations include the following: (i) if the control strategies are introduced independently then the insecticide treated bed nets is the best alternative to reduce the malaria vectors and also to increase the number of susceptible human populations, (ii) if combinations two strategies are considered then the best combination is environmental management strategy for malaria vector control and insecticide treated bed net, (iii) Among the combinations of three control strategies the best one comprises of insecticide treated bed nets, indoor residual spray and treatment with anti-malaria drugs (iv) Furthermore, it has been noted that the best of all possible combinations is the one that is incorporated all four control strategies. Thus, it can be concluded that more the number of control strategies that are used quicker it will be to eradicate the malaria from the community.

Also, sensitivity analyses have been performed on the basic reproduction number with respect to all the individual control strategies, from which it is noted that the most sensitive parameter is the insecticide treated bed net. Therefore, in order to reduce malaria transmission in a population, this study recommends that insecticide treated bed nets should be given high emphasis which reduces mosquito to human contact rate and so is advisable.

Reference

[1]. Centers for Disease Control and Prevention. *CDC - Malaria* (accessed August 8, 2011) http: //www.cdc.gov/MALARIA.
[2]. WHO, "Investing in health research for development", Technical Report, *World Health Organization*, Geneva, 1996.
[3]. Tumwiine J., Mugisha J., Luboobi L., "A mathematical model for the dynamics of malaria in a human host and mosquito vector with temporary immunity", *Journal of Applied Mathematics and Computation*, vol. 189, pp. 1953-1965, 2005.
[4]. Global Strategic framework for Integrated Vector Management. *Geneva*, WHO, 2004.
[5]. DOMC, National Guidelines for Diagnosis, Treatment and Prevention of Malaria in Kenya, Division of Malaria Control, Ministry of public health and sanitation, Nairobi, Kenya,3rd edition, 2010.

[6]. Lindsay S et al. Environmental Management for malaria control in the East Asia and Pacific (EAP) Region Washington., DC, *World Bank/WHO,* 2004.
[7]. Ross R. "The Prevention of Malaria", John Murray, 1911.
[8]. Macdonald G., "The Epidemiology and Control of Malaria", *Oxford university press*, 1957.
[9]. Ferreira, M. U., H. M. Yang, "Assessing the effects of global warming and local social and economic conditions on the malaria transmission", *Revista de Saude Publica*, vol. 34, pp.214-222, 2000.
[10]. Aron J. L., "Acquired immunity dependent upon exposure in a SIRS epidemic model", *Journal of Mathematical Biosciences*, vol. 88, pp. 37-47, 1988.
[11]. Aron J. L., "Mathematical modeling of immunity to Malaria", Journal of Mathematical Bio- sciences, vol. 90, pp. 385-396, 1988.
[12]. Yang, H. M., "Malaria transmission model for different levels of acquired immunity and temperature-dependent parameter (vector)", *Revista de Saude Publica*, vol. 34, pp. 223-231, 2000. 96-400.
[13]. Bacaer N. and C. Sokhna. "A reaction-diffusion system modeling the spread of resistance to an anti-malarial drug", Math. *Bio-sci. Engrg*, vol. 2, pp. 227-238, 2005.
[14]. Ngwa, G.A. and W.S. Shu, "A Mathematical model for endemic malaria with variable human and mosquito populations", *Mathematical and Computer Modeling* Journal. 32, pp. 747-763, 2000.
[15]. Ngwa, G. A. "Modeling the dynamics of endemic malaria in growing populations", *Discrete Contin. Dyn. Syst*. Ser. B, vol. 4, pp. 1173-1202, 2004.
[16]. Addo, D. E., "Mathematical model for the control of Malaria", Master Thesis, University of Cape Coast, 2009.
[17]. Tumwiine J., L. S. Luboobi, J.Y.T. Mugisha, "Modeling the effect of treatment and mosquitoes' control on malaria transmission", *International Journal of Management and Systems*, vol. 21, pp. 107-124, 2005.
[18]. Yang H., Wei H., Li X., "Global stability of an epidemic model for vector borne disease", J Syst Sci Complex Journal, vol. 23, pp. 279-292, 2010.
[19]. Abadi Abay Gebremeskel, Harald Elias Krogstad, "Mathematical Modelling of Endemic Malaria Transmission", *American Journal of Applied Mathematics*, Vol. 3, No. 2, 2015, pp. 36-46. Doi: 10.11648/j.ajam.20150302.12.
[20]. Fekadu Tadege Kobe & Purnachandra Rao Koya, 'Spread of Malaria Disease Using Intervention Strategies ''*Journal of multi disciplinary Engineering Science and Technology (JMEST),* vol.2, Issse5, May-2015.
[21]. E. C. Ibezim and U. odo, Current trends in malarial chemotherapy, *African Journal of Biotechnology*, 7 No.4 (2008), 349-356, 2014.
[22]. M. Zhien, Z. Yicang and W. Jianhong, Modeling and Dynamics of Infectious disease, *World Scientific Publishing Co Pte Ltd*. Singapore (2009).
[23]. O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz, on the definition and computation of the basic reproduction ratio in models for infectious diseases in heterogeneous populations, *J. Math. Biol*, 28 (1990), 365-382, doi: 10.1007/BF00178324.156 S. Olaniyi, O.S. Obabiyi.
[24]. P. Van den Driessche and J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Bios, 180 (2002), 29-48, doi: 10.1016/S0025-5564(02)00108-6.
[25]. Wang, J. and Modnak C. (2011). Modeling Cholera Dynamics with Controls *Canadian Applied Mathematics Quarterly*. 19 (3), 255-273.
[26]. Tian J. P., Liao, S. and Wang, J. Dynamical Analysis and Control Strategies in Modelling Cholera. *Retrieved from*, (2010).
[27]. Chitins N., Hyman, J.M., and Cusching, J. I. Determining important Parameters in the spread of malaria through the sensitivity analysis of a mathematical *Model. Bulletin of Mathematical Biology*, (2008), 70 (5):1272–12.

Dereje Gutema Edossa. " Mathematical Modeling the Dynamics of Endemic Malaria Transmission with Control Measures." IOSR Journal of Mathematics (IOSR-JM) 15.4 (2019): 25-41