AN OPTIMAL CONTROL ANALYSIS OF MALARIA HBV COINFECTION MODEL

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Abstract
Malaria and Hepatitis B Virus (HBV) are diseases that poses serious challenges health wise in the world especially in countries that are developing. Both diseases belong to the most widespread diseases, and therefore, a major public health concerns in tropical developing countries. In this research, a mathematical model showing dynamics of co-infection of Malaria and HBV diseases was developed using ordinary differential equations which consists of 9 compartments. The study covers the model's future solution positivity, model invariant region and disease-free points. The next generation matrix method was used to compute the basic reproduction number,$\mathcal{R}_0$, for the coinfection model using and the disease free equilibrium point and was shown to be Locally Asymptotically Stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. Then, the coinfection model was extended to optimal control by incorporating four control interventions. The optimality system was obtained using the Pontryagin's maximum principle. Simulation of the optimality system was done and five strategies was proposed to check the effect of the controls. First, prevention only for both diseases was considered, and the result shows that, applying prevention control has a great impact in bringing down the expansion of malaria, HBV infection, and their coinfection in the specified period of time. Other approaches are prevention effort for malaria and treatment effort for HBV infection, prevention effort for HBV infection and treatment effort for malaria, treatment effort for both diseases, and using all interventions. We obtained that the listed strategies were effective in minimizing the expansion of Malaria HBV coinfectious population in the specified period of time.
Keywords*: Co-Infection, Malaria, Hepatitis B Virus.*

Introduction

Infectious diseases have produced enormous destruction and death of humans through the ages, most recently, they become threats to countries that are developing (Greenhalgh, Samanta, Sardar, Bhattacharya, & Chattopadhyay, 2015). Malaria disease is vector borne which is treatable and also can be prevented. Even though malaria can be prevented, deaths of over 627,000 people of which most of them are children in Africa have been caused by it in the year 2012 (WHO W. H., 2013). There was an appeal in October 2007 for effort to be increased globally towards the eradication of Malaria and over 25 countries that are previously endemic have entered either the elimination or pre-elimination phase of this global eradication. Malaria spread is extensive in tropical and subtropical regions which include Asia, Africa, Latin America, some parts of Europe and the Middle East. Though, death cases due to Malaria are generally reported in the sub-Saharan Africa especially 30 countries within sub-Saharan Africa which are responsible for 90% of malaria deaths globally. In Africa, after every 30 seconds the disease causes the death of a child and globally, above 2,000 lives of young people are lost every day. Amid the outpatient visits, malaria is responsible for 60%, and 30% of children below 5 years who are hospitalized in Nigeria (Olaniyi & Obabiyi, 2013). Hepatitis B is a potentially life-threatening infection of the liver caused by the hepatitis B virus (HBV) and as well a major health problem globally. HBV, an hepadnavirus with a circular genome composed of partially double-stranded

DNA, replicates through an RNA intermediate form by reverse transcription. The infection has caused epidemics in parts of Asia and Africa. About 2 billion infections have been recorded globally and about 360 million people are living with chronic HBV infection. An estimated deaths of about 600,000 is recorded each year due to the acute or chronic consequences of hepatitis B. HBV mono infection is a serious and common infectious disease of the liver. World Health Organization (WHO) in 2009 reported HBV to infect nearly 2 billion people around the world. Activities that cause it include unprotected sex, blood transfusion, tattoo, and sharing unprotected needles and blades predisposed by individuals with the infection (Gideon K. H., et al., 2018). The hepatitis B virus is spread through the blood, semen, or other body fluid of infected individual get into the body of a person who is not infected. The aim of this study is to develop a mathematical model to study the dynamics of Malaria-HBV co-infection.

Model Formulation

The model is a compartmental model with sub compartments. The total human population (N_h) which is divided into; susceptible humans (S_h), individuals infected with Malaria only (I_{hm}), individuals that are infected with HBV only (I_{hH}), individuals that are infected with both Malaria and HBV (I_{hmH}), and those that have recovered from Malaria, HBV, and both Malaria and HBV, respectively, (R_{hm}), (R_{hH}), and (R_{hmH}). The total vector population (N_v) which is divided int; susceptible mosquitos (S_v) and infected mosquitos (I_v). These two different classes of population therefore give us the following equations:

$$N_h = S_h + I_{hm} + I_{hH} + I_{hmH} + R_{hm} + R_{hH} + R_{hmH} \quad \ldots (1)$$

$$N_v = S_v + I_v \quad \ldots (2)$$

For the human population, the susceptible compartment increase by recruitment rate of Λ_h and also from Malaria recovered compartment with rate of γ_1, HBV recovered compartment with rate of γ_2 and from co-infectious recovered compartment with rate of γ_3. Forces of infection of Malaria and HBV are α_1 and α_2 respectively where $\alpha_1 = \frac{\alpha_{mh} b_m I_v}{N_h}$ and $\alpha_2 = \alpha_H(I_{hH} + I_{hmH})$. Since the liver condition in malaria infected humans increase the susceptibility of humans to HBV infection, it means that, the rate of infection of humans in I_{hm} is higher than those in S_h, so we introduce a parameter $\psi > 1$ to change the HBV infection rate of I_{hm} from α_2 to $\psi\alpha_2$. Malaria – only recovered compartment is increased by the rate, β_1. HBV – only compartment is increased by the rate, β_2 while the coinfection recovered compartments increase with a rate of δ. In the coinfectious recovered compartment, individuals either recovered only from Malaria, HBV, or from both diseases with a probability of δe,$\delta f(1-e)$ or $\delta(1-f)(1-e)$, respectively, where $0 \leq e \leq 1$ and $0 \leq f \leq 1$. The natural death rate is denoted by μ_h and Malaria – causing death rate and HBV – causing death rate are represented by d_1 and d_2, respectively.

For the mosquito population, the susceptible compartment increase by a constant recruitment rate of Λ_v and decrease by the mosquito death rate represented by μ_v. While new infected mosquitoes are generated at a rate of $\xi_v = \frac{\alpha_{hm} b_m}{N_h}(I_{hm})$, and are removed from the compartment through the mosquito death rate. All parameters described in this model are assumed to be nonnegative.

Malaria – HBV Co-infection Model Equation

The following system of Ordinary Differential Equations (ODEs) capture the dynamics of the coinfection model.

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \gamma_1 R_{hm} + \gamma_2 R_{hH} + \gamma_3 R_{hmH} - (\alpha_1 + \alpha_2 + \mu_h) S_h \\
\frac{dI_{hm}}{dt} &= \alpha_1 S_h - \psi \alpha_2 I_{hm} - (\mu_h + d_1) I_{hm} - \beta_1 I_{hm} \\
\frac{dI_{hH}}{dt} &= \alpha_2 S_h - \alpha_1 I_{hH} - (\mu_h + d_2) I_{hH} - \beta_2 I_{hH} \\
\frac{dI_{hmH}}{dt} &= \psi \alpha_2 I_{hm} + \alpha_1 I_{hH} - (\mu_h + d_1 + d_2) I_{hmH} - \delta I_{hmH} \\
\frac{dR_{hm}}{dt} &= (\beta_1) I_{hm} + (\delta e) I_{hmH} - (\mu_h + \gamma_1) R_{hm} \\
\frac{dR_{hH}}{dt} &= (\beta_2) I_{hH} + (\delta f(1-e)) I_{hmH} - (\mu_h + \gamma_2) R_{hH} \\
\frac{dR_{hmH}}{dt} &= (\delta(1-f)(1-e)) I_{hmH} - (\mu_h + \gamma_3) R_{hmH} \\
\frac{dS_v}{dt} &= \Lambda_v - (\mu_v + \xi_v) S_v \\
\frac{dI_v}{dt} &= \xi_v S_v - \mu_v I_v
\end{aligned} \quad \ldots (3)$$

Initial conditions of system (3) are

$$\begin{aligned}
S_h(0) &\geq 0 \\
I_{hm}(0) &\geq 0 \\
I_{hH}(0) &\geq 0 \\
I_{hmH}(0) &\geq 0 \\
R_{hm}(0) &\geq 0 \\
R_{hH}(0) &\geq 0 \\
R_{hmH}(0) &\geq 0 \\
S_v(0) &\geq 0 \\
I_v(0) &\geq 0
\end{aligned} \quad \ldots (4)$$

From the above system of differential equations, the following flow diagram (Figure 1) of the model is obtained:

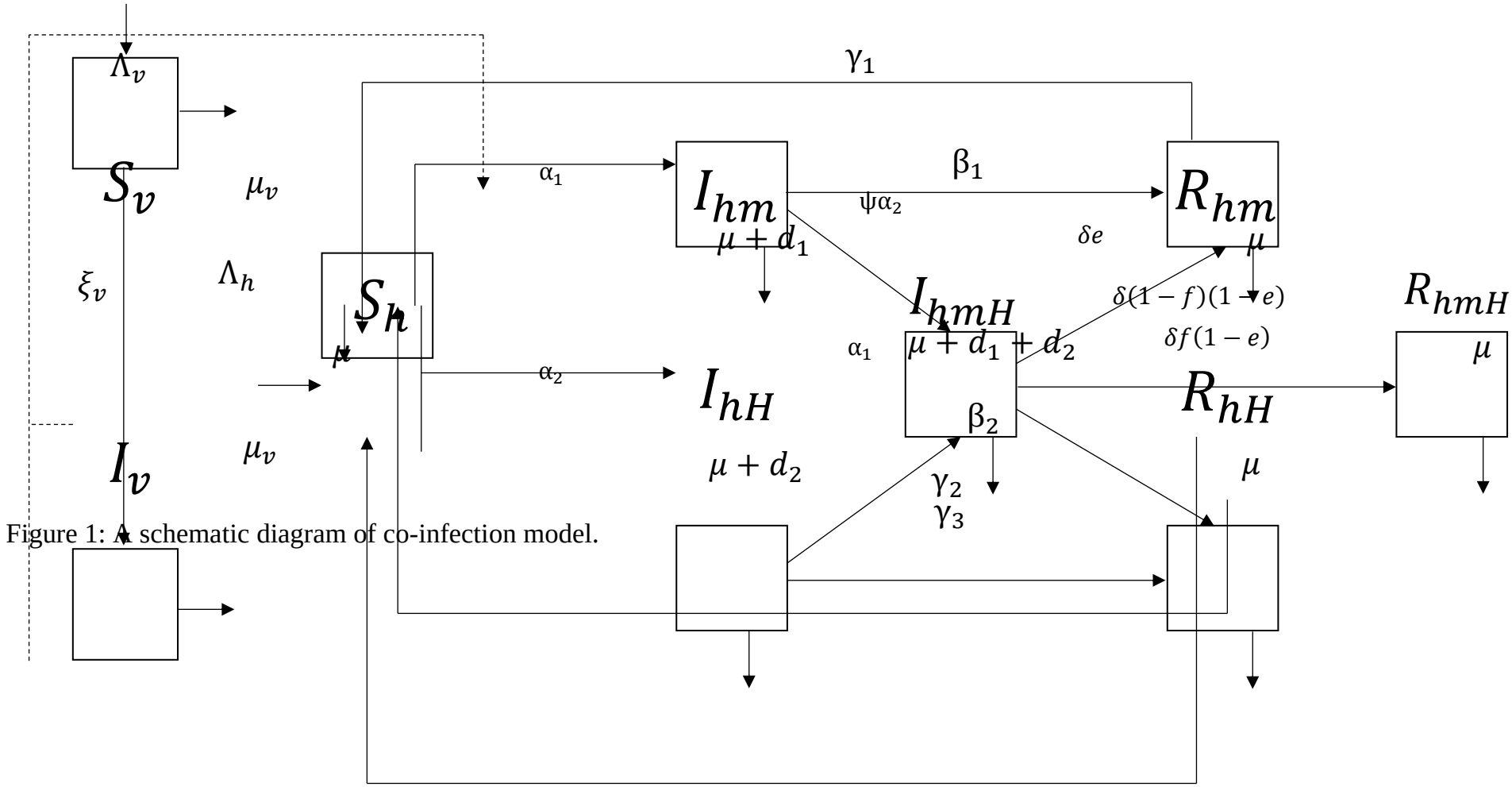


Figure 1: A schematic diagram of co-infection model.

Malaria HBV Coinfection Model Invariant Region

Here, it is shown that the Malaria HBV coinfection model is epidemiologically and mathematically well-posed and such a solution exist and is positive in an invariant region. To get the invariant region in which the solution of the model is bounded, we consider the total population

$N_h = S_h + I_{hm} + I_{hH} + I_{hmH} + R_{hm} + R_{hH} + R_{hmH}$ and $N_v = S_v + I_v$ . . . (5)

Now,

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_{hm}}{dt} + \frac{dI_{hH}}{dt} + \frac{dI_{hmH}}{dt} + \frac{dR_{hm}}{dt} + \frac{dR_{hH}}{dt} + \frac{dR_{hmH}}{dt}$$
$$= \Lambda_h - \mu_h N_h - d_1(I_{hm} + I_{hmH}) - d_2(I_{hH} + I_{hmH}) \quad \ldots (6)$$

Similarly

$$\frac{dN_v}{dt} = \Lambda_v - \mu_v N_v \quad \ldots (7)$$

Assuming $d_1 = d_2 = 0$ and letting $= \begin{pmatrix} N_h \\ N_v \end{pmatrix}$, $\Lambda = \begin{pmatrix} \Lambda_h \\ \Lambda_v \end{pmatrix}$ and $\mu_a = \begin{pmatrix} \mu_h & 0 \\ 0 & \mu_v \end{pmatrix}$, we obtain

$$\frac{dN}{dt} \leq \Lambda - \mu_a N \quad \ldots (8)$$

Solving equation (8) we obtain

$$\Omega = \left\{(S_h, I_{hm}, I_{hH}, I_{hmH}, R_{hm}, R_{hH}, R_{hmH}, S_v, I_v) \in \mathbb{R}^9, 0 \leq N \leq \frac{\Lambda}{\mu_a}\right\} \quad \ldots (9)$$

which is the invariant region of the model.

Theorem 1 (Positivity of Solution): If

$$S_{h0} > 0, I_{hm_0} > 0, I_{hH_0} > 0, I_{hmH_0} > 0, R_{hm_0} > 0, R_{hH_0} > 0, R_{hmH_0} > 0, S_{v_0} > 0, I_{v_0} > 0,$$

then all the solution sets

$$(S_h(t), I_{hm}(t), I_{hH}(t), I_{hmH}(t), R_{hm}(t), R_{hH}(t), R_{hmH}(t), S_v(t), I_v(t))$$

are positive for future time.

Proof: To prove by contradiction, firstly, take t_a as

$$t_a = \sup\{t > 0: S_h(\tau) > 0,\ I_{hm}(\tau) > 0, I_{hH}(\tau) > 0, I_{hmH}(\tau) > 0,\ R_{hm}(\tau) > 0,\ R_{hH}(\tau) > 0, R_{hmH}(\tau) > 0, S_v(\tau) > 0, I_v(\tau) > 0\ for\ all\ \tau \in [0, t]\}$$
. . . (10)

Now consider

$$S_{h_0} \geq 0, I_{hm_0} \geq 0, I_{hH_0} \geq 0, I_{hmH_0} \geq 0, R_{hm_0} \geq 0, R_{hH_0} \geq 0, R_{hmH_0} \geq 0, S_{v_0} \geq 0, I_{v_0} \geq 0;$$

thus, $t_a > 0$.

If $t_a < \infty$, then necessarily,

$S_h\ or\ I_{hm}\ or\ I_{hH}\ or\ I_{hmH}\ or\ R_{hm}\ or\ R_{hH}\ or\ R_{hmH}\ or\ S_v\ or\ I_v$ is equal to zero at t_a.

From equation (3), we have

$$\frac{dS_h(t)}{dt} = \Lambda_h + \gamma_1 R_{hm} + \gamma_2 R_{hH} + \gamma_3 R_{hmH} - (\alpha_1 + \alpha_2 + \mu_h) S_h(t) \quad \ldots (11)$$

Equation (11) can be solved using variation formula at t_a:

$$S_h(t_a) = S_h(0) exp\left[-\int_0^{t_a} (\alpha_1 + \alpha_2 + \mu_h)(s) ds\right] + \int_0^{t_a} (\Lambda_h + \gamma_1 R_{hm} + \gamma_2 R_{hH} + \gamma_3 R_{hmH}) exp\left[-\int_0^{t_a} (\alpha_1 + \alpha_2 + \mu_h)(\tau) d\tau\right] ds \quad \ldots (12)$$

Accordingly, all the variables are nonnegative in $[0, t_a]$; then $S_h(t_a) > 0$.

In a similar manner, we can show

$I_{hm}(t_a) > 0, I_{hH}(t_a) > 0, I_{hmH}(t_a) > 0, R_{hm}(t_a) > 0, R_{hmH}(t_a) > 0, R_{hmH}(t_a) > 0\ , S_v(t_a) > 0\ and\ I_v(t_a) > 0$ which is a contradiction. Hence $t_a = \infty$. ■

Existence of Disease – Free Equilibrium (DFE) Point for the Coinfection Model.

At Disease – Free Equilibrium point, (E_0), none of the diseases exists. The disease-free equilibrium point there is no Malaria HBV coinfection. At Disease-free Equilibrium E_0; $I_{hm} = I_{hH} = I_{hmh} = I_v = 0$. Therefore, eliminating I_{hm}, I_{hH}, I_{hmh} and I_v from equation (1). Thus, equating the right hand side of the system of equation (1) to zero, we get

$$\Lambda_h + \gamma_1 R_{hm} + \gamma_2 R_{hH} + \gamma_3 R_{hmH} - (\alpha_1 + \alpha_2 + \mu_h) S_h = 0 \quad \ldots (13)$$

$$-(\mu_h + \gamma_1) R_{hm} = 0 \quad \ldots (14)$$

$$-(\mu_h + \gamma_2) R_{hH} = 0 \quad \ldots (15)$$

$$-(\mu_h + \gamma_3) R_{hmH} = 0 \quad \ldots (16)$$

$$\Lambda_v - (\mu_v + \xi_v) S_v = 0 \quad \ldots (17)$$

From equations (14), (15) and (16) we get $R_{hm} = R_{hH} = R_{hmh} = 0$, and since $\alpha_1 = \alpha_2 = \xi_v = 0$ at DFE point we have

$$E_0 = \left(S_{h_0}, I_{hm_0}, I_{hH_0}, I_{hmH_0}, R_{hm_0}, R_{hH_0}, R_{hmH_0}, S_{v_0}, I_{v_0}\right) = \left(\frac{\Lambda_h}{\mu_h}, 0,0,0,0,0,0, \frac{\Lambda_v}{\mu_v}, 0\right) \quad \ldots (18)$$

Basic Reproduction Number for the Malaria HBV Coinfection Model

The basic reproduction number usually denoted by $\mathcal{R}_0$ for the Malaria HBV Coinfection Model was obtained using the next generation method as applied by (Diekmann, Hoesterbeek, & Roberts, 2010), (Agusto & Khan, 2018) and (Van den Driessche &

Watmough, 2002). From the model equations, using their approach we first rearrange the model equations beginning with the infective classes to obtain the following equations

$$\frac{dI_{hm}}{dt} = \alpha_1 S_h - \psi\alpha_2 I_{hm} - (\mu_h + d_1)I_{hm} - \beta_1 I_{hm}$$
$$\frac{dI_{hH}}{dt} = \alpha_2 S_h - \alpha_1 I_{hH} - (\mu_h + d_2)I_{hH} - \beta_2 I_{hH}$$
$$\frac{dI_{hmH}}{dt} = \psi\alpha_2 I_{hm} + \alpha_1 I_{hH} - (\mu_h + d_1 + d_2)I_{hmH} - \delta I_{hmH}$$

$$\frac{dI_v}{dt} = \xi_v S_v - \mu_v I_v$$

Using their approach, we have;

$$F = \begin{pmatrix} 0 & 0 & 0 & \frac{\alpha_{mh} b_m S_v}{N_h} \\ 0 & \alpha_H S_h & \alpha_H S_h & 0 \\ \psi\alpha_H(I_{hH} + I_{hmH}) & \frac{\alpha_{mh} b_m I_v}{N_h} & \psi\alpha_H I_{hm} & \frac{\alpha_{mh} b_m I_{hH}}{N_h} \\ \frac{\alpha_{hm} b_m S_v}{N_h} & 0 & \frac{\alpha_{hm} b_m S_v}{N_h} & 0 \end{pmatrix}; \qquad \ldots (20)$$

$$V = \begin{pmatrix} \beta_1 + \mu_h + d_1 & \psi\alpha_H I_{hm} & \psi\alpha_H I_{hm} & 0 \\ 0 & \frac{\alpha_{hm} b_m I_v}{N_h} + \beta_2 + \mu_h + d_2 & 0 & \frac{\alpha_{mh} b_m I_{hH}}{N_h} \\ 0 & 0 & \delta + \mu_h + d_1 + d_2 & 0 \\ 0 & 0 & 0 & \mu_v \end{pmatrix} \qquad \ldots (21)$$

We now obtain F and V at the DFE point $E_0 = \left(\frac{\Lambda_h}{\mu_h}, 0,0,0,0,0,0, \frac{\Lambda_v}{\mu_v}, 0\right)$

$$F|_{E_0} = \begin{pmatrix} 0 & 0 & 0 & \alpha_{mh} b_m \\ 0 & \frac{\alpha_H \Lambda_h}{\mu_h} & \frac{\alpha_H \Lambda_h}{\mu_h} & 0 \\ 0 & 0 & 0 & 0 \\ \alpha_{hm} b_m \frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h} & 0 & \alpha_{hm} b_m & 0 \end{pmatrix}; \qquad \ldots (22)$$

$$V|_{E_0} = \begin{pmatrix} \beta_1 + \mu_h + d_1 & 0 & 0 & 0 \\ 0 & \beta_2 + \mu_h + d_2 & 0 & 0 \\ 0 & 0 & \delta + \mu_h + d_1 + d_2 & 0 \\ 0 & 0 & 0 & \mu_v \end{pmatrix} \qquad \ldots (23)$$

And we have

$$V^{-1}|_{E_0} = \begin{pmatrix} \frac{1}{\beta_1+\mu_h+d_1} & 0 & 0 & 0 \\ 0 & \frac{1}{\beta_2+\mu_h+d_2} & 0 & 0 \\ 0 & 0 & \frac{1}{\delta+\mu_h+d_1+d_2} & 0 \\ 0 & 0 & 0 & \frac{1}{\mu_v} \end{pmatrix} \quad \ldots (24)$$

and,

$$FV^{-1}|_{E_0} = \begin{pmatrix} 0 & 0 & 0 & \frac{\alpha_{mh}b_m}{\mu_v} \\ 0 & \frac{\alpha_H\frac{\Lambda_h}{\mu_h}}{\beta_2+\mu_h+d_2} & \frac{\alpha_H\frac{\Lambda_h}{\mu_h}}{\delta+\mu_h+d_1+d_2} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{\alpha_{hm}b_m}{(\beta_1+\mu_h+d_1)}\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h} & 0 & \frac{\alpha_{hm}b_m}{\delta+\mu_h+d_1+d_2} & 0 \end{pmatrix} \quad \ldots (25)$$

Therefore, $\mathcal{R}_0 = \rho(F\,V^{-1})$ is spectral radius of $F\,V^{-1}$.

$$\mathcal{R}_0 = \rho(FV^{-1}) = \sqrt{\frac{\alpha_{mh}b_m}{\mu_v}.\frac{\alpha_{hm}b_m}{(\beta_1+\mu_h+d_1)}\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h}} \quad \ldots (26)$$

Stability Analysis of the DFE Point for Malaria HBV Coinfection Model

The following theorem describes the local asymptotical stability at the disease free case:

Theorem 2. *If* $\mathcal{R}_0 < 1$, *then the equilibrium point* E_0 *of the model (3) is Locally Asymptotically Stable* (*LAS*) *and unstable if* $\mathcal{R}_0 > 1$.

Proof. Assume $\mathcal{R}_0 < 1$,

Evaluating the Jacobian matrix for the model (3) at the DFE point we get,

$$J_0 = \begin{pmatrix} j_{11} & 0 & 0 & 0 & \gamma_1 & \gamma_2 & \gamma_3 & 0 & \alpha_{mh}b_m \\ 0 & j_{22} & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_{mh}b_m \\ 0 & 0 & j_{33} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & j_{44} & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_1 & 0 & \delta e & j_{55} & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 & \delta f(1-e) & 0 & j_{66} & 0 & 0 & 0 \\ 0 & 0 & 0 & -\delta(1-f)(1-e) & 0 & 0 & j_{77} & 0 & 0 \\ 0 & -\alpha_{hm}b_m\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h} & 0 & -\alpha_{hm}b_m\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h} & 0 & 0 & 0 & j_{88} & 0 \\ 0 & \alpha_{hm}b_m\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h} & 0 & 0 & -\alpha_{hm}b_m\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h} & 0 & 0 & 0 & j_{99} \end{pmatrix} \quad \ldots (27)$$

Where

$j_{11} = -(\mu_h + \alpha_1 + \alpha_2)$ . . . (28)

$j_{22} = -(\beta_1 + \mu_h + d_1)$ . . . (29)

$j_{33} = -(\beta_2 + \mu_h + d_2)$ . . . (30)

$j_{44} = -(\delta + \mu_h + d_1 + d_2)$ . . . (31)

$j_{55} = -\gamma_1$ . . . (32)

$j_{66} = -(\gamma_2 + \mu_h)$ . . . (33)

$j_{77} = -\mu_h$ . . . (34)

$j_{88} = -\mu_v$ . . . (35)

$j_{99} = -\mu_v$ . . . (36)

For the DFE to be LAS, all eigenvalues of the Jacobian matrix evaluated at the DFE point must have negative real parts. To find the eigenvalues, we need the characteristics equation which is,

$(j_{11} - \lambda)(j_{33} - \lambda)(j_{44} - \lambda)(j_{55} - \lambda)(j_{66} - \lambda)(j_{77} - \lambda)(j_{88} - \lambda)(a_2\lambda^2 + a_1\lambda + a_0) = 0$ . . . (37)

Where

$a_2 = 1;\ a_1 = -(j_{22} + j_{99});\ a_0 = \left(j_{22}j_{99} - \alpha_{hm}b_m\frac{\Lambda_v\mu_h}{\mu_v\Lambda_h}\cdot\alpha_{mh}b_m\right)$ . . . (38)

We will now show that all the eigenvalues have negative real parts.

Seven eigenvalues are obtained from the seven linear factors of the characteristics equation, these are:

$\lambda = j_{11} = -(\mu_h + \alpha_1 + \alpha_2) < 0$ since $(\mu_h + \alpha_1 + \alpha_2) > 0$ . . . (39)

$\lambda = j_{33} = -(\beta_2 + \mu_h + d_2) < 0$ since $(\beta_2 + \mu_h + d_2) > 0$ . . . (40)

$\lambda = j_{44} = -(\delta + \mu_h + d_1 + d_2) < 0$ since $(\delta + \mu_h + d_1 + d_2) > 0$ . . . (41)

$\lambda = j_{55} = -\gamma_1 < 0$ since $\gamma_1 > 0$ . . . (42)

$\lambda = j_{66} = -(\gamma_2 + \mu_h) < 0$ since $(\gamma_2 + \mu_h) > 0$ . . . (43)

$\lambda = j_{77} = -\mu_h < 0$ since $\mu_h > 0$ . . . (44)

$\lambda = j_{88} = -\mu_v < 0$ since $\mu_v > 0$ . . . (45)

The remaining 2 eigenvalues can be obtained from the quadratic equation

$(a_2\lambda^2 + a_1\lambda + a_0) = 0$ . . . (46)

Where

$a_2 = 1;\ a_1 = -(j_{22} + j_{99});\ a_0 = \left(j_{22}j_{99} - \alpha_{hm}b_m\frac{\Lambda_v\mu_h}{\mu_v\Lambda_h}\cdot\alpha_{mh}b_m\right)$ . . . (47)

We use the Routh – Hurwitz criteria.

The Routh – Hurtwiz array for $(a_2\lambda^2 + a_1\lambda + a_0)$ is

$$\begin{array}{l|ll} \lambda^2 & a_2 & a_0 \\ \lambda^1 & a_1 & 0 \\ \lambda^0 & a_0 & \end{array}$$

If the signs of a_2, a_1 and a_0 are the same, then we conclude that all eigenvalues for $(a_2\lambda^2 + a_1\lambda + a_0)$ have negative real parts.

To prove: $a_2 > 0$ and $a_1 > 0$:

Proof:

$a_2 = 1 > 0$ . . . (48)

$a_1 = -(j_{22} + j_{99})$

$= -[-(\beta_1 + \mu_h + d_1) + (-\mu_v)] = \beta_1 + \mu_h + d_1 + \mu_v > 0$ . . . (49)

To prove: $a_0 > 0$

Proof:

$$a_0 = (\beta_1 + \mu_h + d_1)\cdot\mu_v - \alpha_{hm}b_m\frac{\Lambda_v\mu_h}{\mu_v\Lambda_h}\cdot\alpha_{mh}b_m \quad \ldots (50)$$

$\mathcal{R}_0 < 1$,

$$\Longrightarrow \sqrt{\frac{\alpha_{mh}b_m}{\mu_v}\cdot\frac{\alpha_{hm}b_m}{(\beta_1+\mu_h+d_1)}\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h}} < 1$$

$$\Longrightarrow \frac{\alpha_{mh}b_m}{\mu_v}\cdot\frac{\alpha_{hm}b_m}{(\beta_1+\mu_h+d_1)}\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h} < 1$$

$$\Longrightarrow \alpha_{hm}b_m\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h}\alpha_{mh}b_m < (\beta_1 + \mu_h + d_1)\cdot\mu_v$$

$$\Longrightarrow \alpha_{hm}b_m\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h}\alpha_{mh}b_m - (\beta_1 + \mu_h + d_1)\cdot\mu_v < 0$$

$$\Longrightarrow (\beta_1 + \mu_h + d_1)\cdot\mu_v - \alpha_{hm}b_m\frac{\Lambda_v}{\mu_v}\frac{\mu_h}{\Lambda_h}\alpha_{mh}b_m > 0$$

$$\Longrightarrow a_0 > 0$$

Hence, all eigenvalues of the Jacobian matrix evaluated at the DFE point have negative real parts. This completes the proof that the DFE for the coinfection Model is LAS if $\mathcal{R}_0 < 1$ and it is unstable whenever $\mathcal{R}_0 > 1$ (since not all eigenvalues have negative real parts if $\mathcal{R}_0 > 1$).

Optimal Control Analysis

The co-infection model was extended to include four controls which have a major effect in the control of the infected population. The control intervention added to the co-infection model are:

1. u_m^1: Malaria prevention effort
2. u_H^1: HBV Infection prevention effort
3. u_m^2: Malaria Treatment prevention effort
4. u_H^2: HBV Infection Treatment effort

The above four controls are incorporated into the co-infection model and the following model is obtain:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \gamma_1 R_{hm} + \gamma_2 R_{hH} + \gamma_3 R_{hmH} - ((1-u_m^1)\alpha_1 + (1-u_H^1)\alpha_2 + \mu_h)S_h \\
\frac{dI_{hm}}{dt} &= (1-u_m^1)\alpha_1 S_h - \psi(1-u_H^1)\alpha_2 I_{hm} - (\mu_h + d_1)I_{hm} - (\beta_1 + u_m^2)I_{hm} \\
\frac{dI_{hH}}{dt} &= (1-u_H^1)\alpha_2 S_h - (1-u_m^1)\alpha_1 I_{hH} - (\mu_h + d_2)I_{hH} - (\beta_2 + u_H^2)I_{hH} \\
\frac{dI_{hmH}}{dt} &= \psi(1-u_H^1)\alpha_2 I_{hm} + (1-u_m^1)\alpha_1 I_{hH} - (\mu_h + d_1 + d_2)I_{hmH} - (\delta + u_m^2 + u_H^2)I_{hmH} \\
\frac{dR_{hm}}{dt} &= (\beta_1 + u_m^2)I_{hm} + (\delta e + u_m^2)I_{hmH} - (\mu_h + \gamma_1)R_{hm} \\
\frac{dR_{hH}}{dt} &= (\beta_2 + u_H^2)I_{hH} + (\delta f(1-e) + u_H^2)I_{hmH} - (\mu_h + \gamma_2)R_{hH} \\
\frac{dR_{hmH}}{dt} &= (\delta(1-f)(1-e) + u_m^2 + u_H^2)I_{hmH} - (\mu_h + \gamma_3)R_{hmH} \\
\frac{dS_v}{dt} &= \Lambda_v - (\mu_v + \xi_v)S_v \\
\frac{dI_v}{dt} &= \xi_v S_v - \mu_v I_v
\end{aligned} \quad \ldots (51)$$

We now consider the following objective functional for the above model

$$\begin{aligned}
J(u_m^1, u_H^1, u_m^2, u_H^2) &= \int_0^{t_F} \Big[a_1 I_{hm} + a_2 I_{hH} + a_3 I_{hmH} + \frac{1}{2} b_1 (u_m^1)^2 + \frac{1}{2} b_2 (u_H^1)^2 + \frac{1}{2} b_3 (u_m^2)^2 \\
&\quad + \frac{1}{2} b_4 (u_H^2)^2 \Big] dt
\end{aligned} \quad \ldots (52)$$

Where u_m^1, u_H^1, u_m^2 and u_H^2 are the control functions and are bounded, Lebesgue – integrable functions. The control functions are consistent with other studies like (Bonyah, Khan, Okosun, & Gómez-Aguilar, 2019) and (Getachew, 2019). The controls u_m^1 and u_H^1 deal with the wanted amount of effort made in the prevention of Malaria and HBV infections respectively while controls u_m^2 and u_H^2 deals with the treatment effort made on Malaria – Infected individuals and HBV Infected individuals respectively. u_m^1 and u_H^1 satisfy $0 \leq u_m^1 \leq M_1$ and $0 \leq u_H^1 \leq H_1$ where M_1 deal with the efficacy of insecticide used against mosquitoes and H_1 denotes the efficacy of HBV infection vaccine use for the prevention of HBV infection in susceptible individuals.

u_m^2 and u_H^2 satisfy $0 \leq u_m^2 \leq M_2$ and $0 \leq u_H^2 \leq H_2$ where M_2 and H_2 deal with the efficacy of drugs used in treatment against Malaria and the efficacy of HBV infection drugs use for the treatment of HBV infection in infected individuals respectively.
$U = \{(u_m^1(t), u_H^1(t), u_m^2(t), u_H^2(t)): 0 \leq u_m^1 \leq M_1, 0 \leq u_H^1 \leq H_1, 0 \leq u_m^2 \leq M_2, 0 \leq u_H^2 \leq H_2, 0 \leq t \leq t_F\}$ being Lebesgue Measurable is crucial for the study of optimal level. We assume $M_1 = M_2 = H_1 = H_2 = 1$. The target here is to find a set of controls $U = \{(u_m^1(t), u_H^1(t), u_m^2(t), u_H^2(t))\}$ and I_{hm}, I_{hH}, I_{hmH} that will minimize the objective function

$$J(u_m^1, u_H^1, u_m^2, u_H^2) = \int_0^{t_F} \left[a_1 I_{hm} + a_2 I_{hH} + a_3 I_{hmH} + \frac{1}{2} b_1 (u_m^1)^2 + \frac{1}{2} b_2 (u_H^1)^2 + \frac{1}{2} b_3 (u_m^2)^2 + \frac{1}{2} b_4 (u_H^2)^2\right] dt \quad \ldots (53)$$

Where $a_i, i = 1, 2, 3$ and $b_i, i = 1, 2, 3, 4$ are positive. The expression $\frac{1}{2} b_1 (u_m^1)^2 + \frac{1}{2} b_2 (u_H^1)^2 + \frac{1}{2} b_3 (u_m^2)^2 + \frac{1}{2} b_4 (u_H^2)^2$ denotes costs. The aim is to minimize the compartments that are infected and costs which means that we want to obtain optimal controls set $\left(u_m^{1\,*}, u_H^{1\,*}, u_m^{2\,*}, u_H^{2\,*}\right)$ where,

$$J\left(u_m^{1\,*}, u_H^{1\,*}, u_m^{2\,*}, u_H^{2\,*}\right) = \min \{(u_m^1, u_H^1, u_m^2, u_H^2): (u_m^1, u_H^1, u_m^2, u_H^2) \in U\} \quad \ldots (54)$$

The vital criterion for an optimal solution to be made to satisfy can be derived from Pontryagin's maximum principle (PMP). This principle essentially converts equations (51) and (53) to a problem of minimizing a Hamiltonian, with regards to u_m^1, u_H^1, u_m^2 and u_H^2 (Bonyah, Khan, Okosun, & Gómez-Aguilar, 2019). The Hamiltonian for the problem is given as,

$$H\left(S_h(t), I_{hm}(t), I_{hH}(t), I_{hmH}(t), R_{hm}(t), R_{hH}(t), R_{hmH}(t), S_v(t), I_v(t)\right) = L(I_{hm}(t), I_{hH}(t), I_{hmH}(t), u_m^1, u_H^1, u_m^2, u_H^2, t) + \lambda_1 \frac{dS_h(t)}{dt} + \lambda_2 \frac{dI_{hm}(t)}{dt} + \lambda_3 \frac{dI_{hH}(t)}{dt} + \lambda_4 \frac{dI_{hmH}(t)}{dt} + \lambda_5 \frac{dR_{hm}(t)}{dt} + \lambda_6 \frac{dR_{hH}(t)}{dt} + \lambda_7 \frac{dR_{hmH}(t)}{dt} + \lambda_8 \frac{dS_v(t)}{dt} + \lambda_9 \frac{dI_v(t)}{dt} \quad \ldots (55)$$

Where

$$L(I_{hm}(t), I_{hH}(t), I_{hmH}(t), u_m^1, u_H^1, u_m^2, u_H^2, t\ ) = a_1 I_{hm} + a_2 I_{hH} + a_3 I_{hmH} + \frac{1}{2} b_1 (u_m^1)^2 + \frac{1}{2} b_2 (u_H^1)^2 + \frac{1}{2} b_3 (u_m^2)^2 + \frac{1}{2} b_4 (u_H^2)^2 \quad \ldots (56)$$

And

$\lambda_i, i = 1, 2, 3, 4, 5, 6, 7, 8, 9$ ... (57)

Are the adjoint variable functions (Getachew, 2019).

Theorem 3: For the optimal control set $u_m^1, u_H^1, u_m^2, u_H^2$ which minimizes J over U, there exist some adjoint variables, $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8, \lambda_9$ such that:

$$\frac{d\lambda_1}{dt} = -\lambda_1\big((1-u_m^1)\alpha_1 + (1-u_H^1)\alpha_2 + \mu_h\big) - \lambda_2\big((1-u_H^1)\alpha_2\big) - \lambda_3((1-u_H^1)\alpha_2\big)$$

$$\frac{d\lambda_2}{dt} = -a_1 - \lambda_1\big(\psi(1-u_H^2)A_1 - (\mu_h + d_1 + \beta_1 + u_m^2)) - \lambda_4(\psi(1-u_H^2)A_1)\big) - \lambda_5(\beta_1 + u_m^2) + \lambda_8 A_2 - \lambda_9 A_2$$

$$\frac{d\lambda_3}{dt} = -a_2 - \lambda_1(1-u_H^1)B_1 S_h - \lambda_2(1-u_H^1)B_1 I_{hm} - \lambda_3\big((1-u_H^1)B_1 S_h - \alpha_1(1-u_m^1) - (\mu_h + d_2 + \beta_2 + u_H^2)\big) - \lambda_4\big((1-u_H^1)B_1 I_{hm} - \alpha_1(1-u_m^1)\big) - \lambda_6(\beta_2 + u_H^2)$$

$$\frac{d\lambda_4}{dt} = -a_3 - \lambda_1(1-u_H^1)B_1 S_h - \lambda_2\psi(1-u_H^1)B_1 I_{hm} - \lambda_3(1-u_H^1)B_1 S_h - \lambda_4\big(\psi(1-u_H^1)B_1 I_{hm} - (\mu_h + d_1 + d_2 + \delta + u_m^2 + u_H^2)\big) - \lambda_5(\delta e + u_m^2) + \lambda_6(\delta f(1-e) + u_H^2) + \lambda_7(\delta(1-f)(1-e) + u_m^2 + u_H^2)$$

$$\frac{d\lambda_5}{dt} = -\lambda_1\gamma_1 + \lambda_5(\mu_h + \gamma_1)$$

$$\frac{d\lambda_6}{dt} = -\lambda_1\gamma_2 + \lambda_6(\mu_h + \gamma_2)$$

$$\frac{d\lambda_7}{dt} = -\lambda_1\gamma_3 + \lambda_7(\mu_h + \gamma_3)$$

$$\frac{d\lambda_8}{dt} = \lambda_8(\mu_v + \xi_v) - \lambda_9\xi_v$$

$$\frac{d\lambda_9}{dt} = -\lambda_1(1-u_m^1)C_1 S_h - \lambda_2(1-u_m^1)C_1 S_h + \lambda_1(1-u_m^1)C_1 I_{hH} - \lambda_4(1-u_m^1)C_1 I_{hH} + \lambda_9\mu_v \quad \ldots (58)$$

where $A_1 = \frac{\alpha_H(I_{hH}+I_{hmH})}{N_h}, A_2 = \frac{S_v\alpha_{hm}b_m}{N_h}, B_1 = \frac{\alpha_H}{N_h}, C_1 = \frac{\alpha_{mh}b_m}{N_h}$

With transversality conditions $\lambda_i(t_F) = 0, i = 1,2,3,4,5,6,7,8,9.$

And the following controls,

$$u_m^{1\,*} = \frac{\alpha_1 S_h(\lambda_2-\lambda_1) + \alpha_1 I_{hH}(\lambda_4-\lambda_3)}{b_1} \quad \ldots (59)$$

$$u_H^{1\,*} = \frac{\alpha_2 S_h(\lambda_3-\lambda_1)+\psi\alpha_2 I_{hm}(\lambda_4+\lambda_2)}{b_2} \quad \ldots (60)$$

$$u_m^{2\,*} = \frac{I_{hm}(\lambda_2-\lambda_5)+I_{hmH}(\lambda_4-\lambda_5-\lambda_7)}{b_3} \quad \ldots (61)$$

$$u_H^{2\,*} = \frac{I_{hH}(\lambda_3-\lambda_6)+I_{hmH}(\lambda_4-\lambda_6-\lambda_7)}{b_4} \quad \ldots (62)$$

Proof: We will apply the Pontryagin's Maximum Principle used in (Getachew, 2019), that is the adjoint system must satisfy

$$\frac{d\lambda_i}{dt} = -\frac{dH}{di} \quad \ldots (63)$$

Where $i = S_h,\ I_{hm},\ I_{hH}, I_{hmH}, R_{hm}, R_{hH}, R_{hmH}, S_v, I_v$ and H is the Hamiltonian. The Hamiltonian for the system is given by,

$$H = L + \lambda_1\frac{dS_h(t)}{dt} + \lambda_2\frac{dI_{hm}(t)}{dt} + \lambda_3\frac{dI_{hH}(t)}{dt} + \lambda_4\frac{dI_{hmH}(t)}{dt} + \lambda_5\frac{dR_{hm}(t)}{dt} + \lambda_6\frac{dR_{hH}(t)}{dt} + \lambda_7\frac{dR_{hmH}(t)}{dt} + \lambda_8\frac{dS_v(t)}{dt} + \lambda_9\frac{dI_v(t)}{dt} \quad \ldots (64)$$

Where

$$L = a_1 I_{hm} + a_2 I_{hH} + a_3 I_{hmH} + \frac{1}{2}b_1(u_m^1)^2 + \frac{1}{2}b_2(u_H^1)^2 + \frac{1}{2}b_3(u_m^2)^2 + \frac{1}{2}b_4(u_H^2)^2 \quad \ldots (65)$$

We obtain the following adjoint systems after applying the PMP,

$$\frac{d\lambda_1}{dt} = -\frac{dH}{dS_h} = -\lambda_1\big((1-u_m^1)\alpha_1 + (1-u_H^1)\alpha_2 + \mu_h\big) - \lambda_2\big((1-u_H^1)\alpha_2\big) - \lambda_3\big((1-u_H^1)\alpha_2\big) \quad \ldots (66)$$

$$\frac{d\lambda_2}{dt} = -\frac{dH}{dI_{hm}} = -a_1 - \lambda_1\big(\psi(1-u_H^2)A_1 - (\mu_h + d_1 + \beta_1 + u_m^2)\big) - \lambda_4(\psi(1-u_H^2)A_1)\big) - \lambda_5(\beta_1 + u_m^2) + \lambda_8 A_2 - \lambda_9 A_2 \quad \ldots (67)$$

$$\frac{d\lambda_3}{dt} = -\frac{dH}{dI_{hH}} = -a_2 - \lambda_1(1-u_H^1)B_1 S_h - \lambda_2(1-u_H^1)B_1 I_{hm} - \lambda_3\big((1-u_H^1)B_1 S_h - \alpha_1(1-u_m^1) - (\mu_h + d_2 + \beta_2 + u_H^2)\big) - \lambda_4\big((1-u_H^1)B_1 I_{hm} - \alpha_1(1-u_m^1)\big) - \lambda_6(\beta_2 + u_H^2) \quad \ldots (68)$$

$$\frac{d\lambda_4}{dt} = -\frac{dH}{dI_{hmH}}$$
$$= -a_3 - \lambda_1(1-u_H^1)B_1S_h - \lambda_2\psi(1-u_H^1)B_1I_{hm} - \lambda_3(1-u_H^1)B_1S_h - \lambda_4\left(\psi(1-u_H^1)B_1I_{hm} - (\mu_h + d_1 + d_2 + \delta + u_m^2 + u_H^2)\right) - \lambda_5(\delta e + u_m^2) + \lambda_6(\delta f(1-e) + u_H^2) + \lambda_7(\delta(1-f)(1-e) + u_m^2 + u_H^2))$$
. . . (69)

$$\frac{d\lambda_5}{dt} = -\frac{dH}{dR_{hm}} = -\lambda_1\gamma_1 + \lambda_5(\mu_h + \gamma_1) \quad \ldots (70)$$

$$\frac{d\lambda_6}{dt} = -\frac{dH}{dR_{hH}} = -\lambda_1\gamma_2 + \lambda_6(\mu_h + \gamma_2) \quad \ldots (71)$$

$$\frac{d\lambda_7}{dt} = -\frac{dH}{dR_{hmH}} = -\lambda_1\gamma_3 + \lambda_7(\mu_h + \gamma_3) \quad \ldots (72)$$

$$\frac{d\lambda_8}{dt} = -\frac{dH}{dS_v} = \lambda_8(\mu_v + \xi_v) - \lambda_9\xi_v \quad \ldots (73)$$

$$\frac{d\lambda_9}{dt} = -\frac{dH}{dI_v} = -\lambda_1(1-u_m^1)C_1S_h - \lambda_2(1-u_m^1)C_1S_h + \lambda_1(1-u_m^1)C_1I_{hH} - \lambda_4(1-u_m^1)C_1I_{hH} + \lambda_9\mu_v$$
. . . (74)

where $A_1 = \frac{\alpha_H(I_{hH}+I_{hmH})}{N_h}, A_2 = \frac{S_v\alpha_{hm}b_m}{N_h}, B_1 = \frac{\alpha_H}{N_h}, C_1 = \frac{\alpha_{mh}b_m}{N_h}$

Now, we get the controls, we apply the equation,

$$\frac{\partial H}{\partial u_i} = 0, u_i = u_m^1, u_H^1, u_m^2, u_H^2 \quad \ldots (75)$$

Thus we obtain the following equations,

$$\frac{\partial H}{\partial u_m^1} = 0 \quad \ldots (76)$$

$$\frac{\partial H}{\partial u_H^1} = 0 \quad \ldots (77)$$

$$\frac{\partial H}{\partial u_m^2} = 0 \quad \ldots (78)$$

$$\frac{\partial H}{\partial u_H^2} = 0 \quad \ldots (79)$$

Solving for $u_m^1, u_H^1, u_m^2, u_H^2$ we obtained the following:

$$u_m^{1\,*} = \frac{\alpha_1 S_h(\lambda_2-\lambda_1) + \alpha_1 I_{hH}(\lambda_4-\lambda_3)}{b_1} \quad \ldots (80)$$

$$u_H^{1\,*} = \frac{\alpha_2 S_h(\lambda_3-\lambda_1) + \psi\alpha_2 I_{hm}(\lambda_4+\lambda_2)}{b_2} \quad \ldots (81)$$

$$u_m^{2\,*} = \frac{I_{hm}(\lambda_2-\lambda_5)+I_{hmH}(\lambda_4-\lambda_5-\lambda_7)}{b_3} \quad \ldots (82)$$

$$u_H^{2\,*} = \frac{I_{hH}(\lambda_3-\lambda_6)+I_{hmH}(\lambda_4-\lambda_6-\lambda_7)}{b_4} \quad \ldots (83)$$

now, the optimality system obtained is

. . . (84)

$$\frac{dS_h}{dt} = \Lambda_h + \gamma_1 R_{hm} + \gamma_2 R_{hH} + \gamma_3 R_{hmH} - ((1-u_m^1)\alpha_1 + (1-u_H^1)\alpha_2 + \mu_h)S_h$$

$$\frac{dI_{hm}}{dt} = (1-u_m^1)\alpha_1 S_h - \psi(1-u_H^1)\alpha_2 I_{hm} - (\mu_h + d_1)I_{hm} - (\beta_1 + u_m^2)I_{hm}$$

$$\frac{dI_{hH}}{dt} = (1-u_H^1)\alpha_2 S_h - (1-u_m^1)\alpha_1 I_{hH} - (\mu_h + d_2)I_{hH} - (\beta_2 + u_H^2)I_{hH}$$

$$\frac{dI_{hmH}}{dt} = \psi(1-u_H^1)\alpha_2 I_{hm} + (1-u_m^1)\alpha_1 I_{hH} - (\mu_h + d_1 + d_2)I_{hmH} - (\delta + u_m^2 + u_H^2)I_{hmH}$$

$$\frac{dR_{hm}}{dt} = (\beta_1 + u_m^2)I_{hm} + (\delta e + u_m^2)I_{hmH} - (\mu_h + \gamma_1)R_{hm}$$

$$\frac{dR_{hH}}{dt} = (\beta_2 + u_H^2)I_{hH} + (\delta f(1-e) + u_H^2)I_{hmH} - (\mu_h + \gamma_2)R_{hH}$$

$$\frac{dR_{hmH}}{dt} = (\delta(1-f)(1-e) + u_m^2 + u_H^2)I_{hmH} - (\mu_h + \gamma_3)R_{hmH}$$

$$\frac{dS_v}{dt} = \Lambda_v - (\mu_v + \xi_v)S_v$$

$$\frac{dI_v}{dt} = \xi_v S_v - \mu_v I_v$$

$$\frac{d\lambda_1}{dt} = -\lambda_1\big((1-u_m^1)\alpha_1 + (1-u_H^1)\alpha_2 + \mu_h\big) - \lambda_2\big((1-u_H^1)\alpha_2\big) - \lambda_3((1-u_H^1)\alpha_2\big)$$

$$\frac{d\lambda_2}{dt} = -a_1 - \lambda_1\big(\psi(1-u_H^2)A_1 - (\mu_h + d_1 + \beta_1 + u_m^2)) - \lambda_4(\psi(1-u_H^2)A_1)\big) - \lambda_5(\beta_1 + u_m^2) + \lambda_8 A_2 - \lambda_9 A_2$$

$$\frac{d\lambda_3}{dt} = -a_2 - \lambda_1(1-u_H^1)B_1 S_h - \lambda_2(1-u_H^1)B_1 I_{hm} - \lambda_3\big((1-u_H^1)B_1 S_h - \alpha_1(1-u_m^1) - (\mu_h + d_2 + \beta_2 + u_H^2)\big) - \lambda_4\big((1-u_H^1)B_1 I_{hm} - \alpha_1(1-u_m^1)\big) - \lambda_6(\beta_2 + u_H^2)$$

$$\frac{d\lambda_4}{dt} = -a_3 - \lambda_1(1-u_H^1)B_1 S_h - \lambda_2\psi(1-u_H^1)B_1 I_{hm} - \lambda_3(1-u_H^1)B_1 S_h - \lambda_4\big(\psi(1-u_H^1)B_1 I_{hm} - (\mu_h + d_1 + d_2 + \delta + u_m^2 + u_H^2)\big) - \lambda_5(\delta e + u_m^2) + \lambda_6(\delta f(1-e) + u_H^2) + \lambda_7(\delta(1-f)(1-e) + u_m^2 + u_H^2)$$

$$\frac{d\lambda_5}{dt} = -\lambda_1\gamma_1 + \lambda_5(\mu_h + \gamma_1)$$

$$\frac{d\lambda_6}{dt} = -\lambda_1\gamma_2 + \lambda_6(\mu_h + \gamma_2)$$

$$\frac{d\lambda_7}{dt} = -\lambda_1\gamma_3 + \lambda_7(\mu_h + \gamma_3)$$
$$\frac{d\lambda_8}{dt} = \lambda_8(\mu_v + \xi_v) - \lambda_9\xi_v$$
$$\frac{d\lambda_9}{dt} = -\lambda_1(1-u_m^1)C_1S_h - \lambda_2(1-u_m^1)C_1S_h + \lambda_1(1-u_m^1)C_1I_{hH} - \lambda_4(1-u_m^1)C_1I_{hH} + \lambda_9\mu_v$$

With $\lambda_i(t_F) = 0, i = 1,2,3,4,5,6,7,8,9$

And

$$\begin{aligned} S_h(0) &= S_{h_0} \\ I_{hm}(0) &= I_{hm_0} \\ I_{hH}(0) &= I_{hH_0} \\ I_{hmH}(0) &= I_{hmH_0} \\ R_{hm}(0) &= R_{hm_0} \\ R_{hH}(0) &= R_{hH_0} \\ R_{hmH}(0) &= R_{hmH_0} \\ S_v(0) &= S_{v_0} \\ I_v(0) &= I_{v_0} \end{aligned} \quad \ldots (85)$$

Numerical Solution of the Optimality System

In this section, we extend the co-infection model through the incorporation of control. The following sections, we present the optimality system numerical simulation using the forward fourth-order Runge–Kutta method in solving the system. The solution of the optimality system was obtained using a method called the forward – backward sweep method which was applied by (Haileyesus, Assefa, & Anteneh, 2021). We started by solving the equations of the state variables using an initial guess for the controls over the simulated time by applying the forward fourth – order Runge Kutta method. We then continued by solving the equations of the adjoint variables using the backward fourth – order Runge Kutta method with the solutions of the state variables of the current iteration and the tranversality condition. The control variables are then continuously updated by combining previous results of the control with the control characterization. After updating the control variables, the solutions of the state variables and adjoint variables are repeated. These iterations are repeated continuously until when consecutive iterations are close enough to each other (Haileyesus, Assefa, & Anteneh, 2021). Maple 17 and Matlab software were used for the simulation.

Numerical Experiment and Simulation of the Optimality System

The numerical simulations of the Malaria HBV co-infection model with controls i.e. model (3) and without controls were examined so as to demonstrate the effectiveness of the controls that have been considered. The following five approaches for the numerical simulation were offered:

1. Using only prevention effort for both diseases $(\boldsymbol{u_m^1 \neq 0, u_H^1 \neq 0, u_m^2 = 0, u_H^2 = 0})$.
2. Using prevention effort for Malaria and treatment effort for HBV infection disease $(\boldsymbol{u_m^1 \neq 0, u_H^1 = 0, u_m^2 = 0, u_H^2 \neq 0})$.
3. Using prevention effort for HBV infection disease and treatment effort for Malaria $(\boldsymbol{u_m^1 = 0, u_H^1 \neq 0, u_m^2 \neq 0, u_H^2 = 0})$.
4. Using only treatment effort for both diseases $(\boldsymbol{u_m^1 = 0, u_H^1 = 0, u_m^2 \neq 0, u_H^2 \neq 0})$.
5. Using all the intervention efforts $(\boldsymbol{u_m^1 \neq 0, u_H^1 \neq 0, u_m^2 \neq 0, u_H^2 \neq 0})$.

For the purpose of simulation, parameter values listed in table 3 were used together with the following initial conditions, $S_h(0) = 200, I_{hm}(0) = 600, I_{hH}(0) = 600, I_{hmH}(0) = 250, R_{hm}(0) = 60, R_{hH}(0) = 60, R_{hmH}(0) = 40, S_v(0) = 260, I_v(0) = 120, a_1 = 35, a_2 = 45, a_3 = 26, b_1 = 4, b_2 = 3, b_3 = 5, b_4 = 6$ (Getachew, 2019).

Control using only prevention effort for both diseases $(\boldsymbol{u_m^1 \neq 0, u_H^1 \neq 0, u_m^2 = 0, u_H^2 = 0})$

Here prevention for both Malaria and HBV infection diseases were applied as the intervention strategy. The following figures shows the simulation results, we see this prevention strategy has a great impact in controlling the coinfection population.

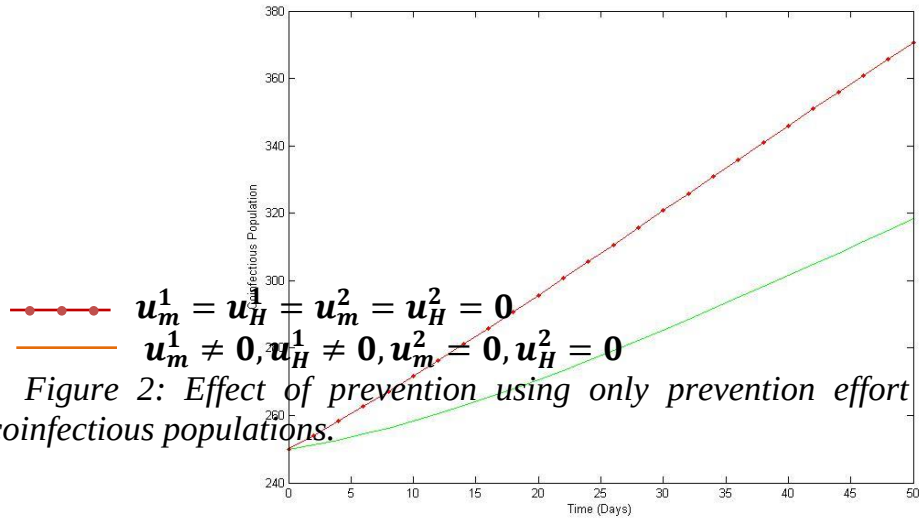


Figure 2: Effect of prevention using only prevention effort for both diseases on coinfectious populations.

Control using prevention effort for Malaria and treatment effort for HBV infection disease ($u_m^1 \neq 0, u_H^1 = 0, u_m^2 = 0, u_H^2 \neq 0$).

Here prevention effort for Malaria and treatment effort for HBV infection diseases were applied as the intervention strategy. The following figures shows the simulation results, we see this prevention strategy has a great impact in controlling the coinfection population.

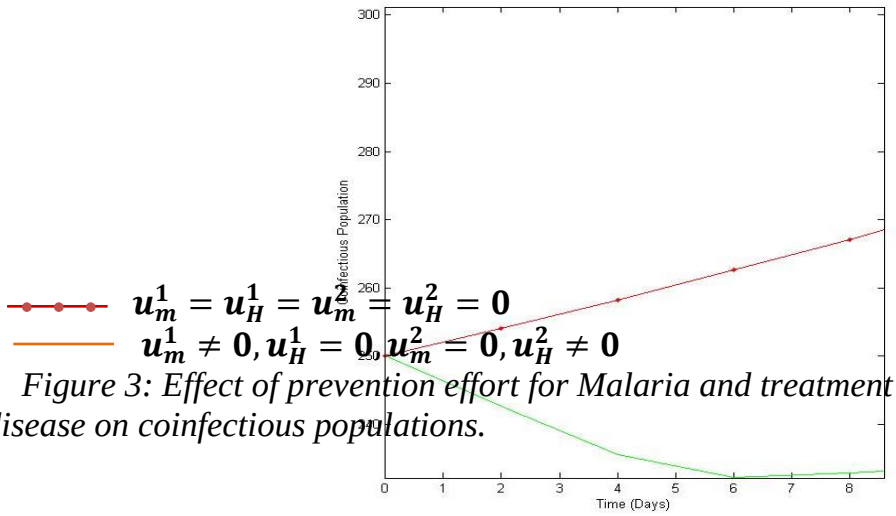
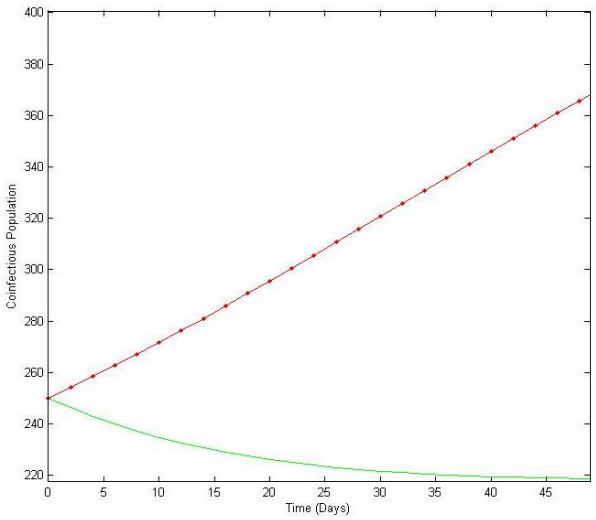


Figure 3: Effect of prevention effort for Malaria and treatment effort for HBV infection disease on coinfectious populations.

Control using prevention effort for HBV infection disease and treatment effort for Malaria ($u_m^1 = 0, u_H^1 \neq 0, u_m^2 \neq 0, u_H^2 = 0$).

Here prevention effort for HBV infection disease and treatment effort for Malaria were applied as the intervention strategy. The following figures shows the simulation results, we see this prevention strategy has a great impact in controlling the coinfection population.



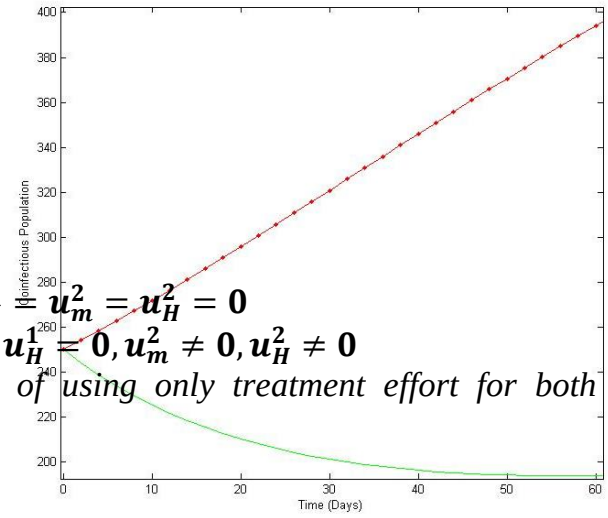
$u_m^1 = u_H^1 = u_m^2 = u_H^2 = 0$

$u_m^1 = 0, u_H^1 \neq 0, u_m^2 \neq 0, u_H^2 = 0$

Figure 4: Effect of prevention using prevention effort for HBV infection disease and treatment effort for Malaria on coinfectious populations.

Control using only treatment effort for both diseases ($u_m^1 = 0, u_H^1 = 0, u_m^2 \neq 0, u_H^2 \neq 0$).

Here only treatment effort for both Malaria and HBV infection diseases were applied as the intervention strategy. The following figures shows the simulation results, we see this prevention strategy has a great impact in controlling the coinfection population.



$u_m^1 = u_H^1 = u_m^2 = u_H^2 = 0$

$u_m^1 = 0, u_H^1 = 0, u_m^2 \neq 0, u_H^2 \neq 0$

Figure 5: Effect of using only treatment effort for both diseases on coinfectious populations.

Control using all the intervention efforts ($u_m^1 \neq 0, u_H^1 \neq 0, u_m^2 \neq 0, u_H^2 \neq 0$).
Here all intervention efforts were applied as the intervention strategy. The following figures shows the simulation results, we see this strategy has a great impact in controlling the coinfection population.

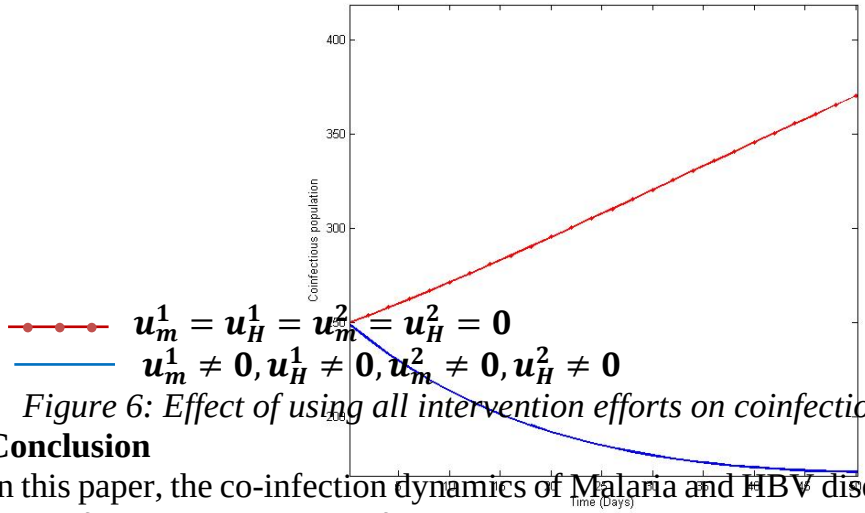


Figure 6: Effect of using all intervention efforts on coinfectious populations.

Conclusion

In this paper, the co-infection dynamics of Malaria and HBV diseases was developed. First, we performed the analysis of single disease sub models, which include the Malaria – only model and the HBV infection – only model. The compartmental model was analyzed to fully understand the transmission mechanism of Malaria and HBV coinfection. Our model revealed that the disease-free equilibrium of the Malaria and HBV coinfection model is locally asymptotically stable whenever the basic reproduction number $\mathcal{R}_0 < 1$ and unstable whenever basic reproduction number is greater than one. Optimal control analysis was carried out on the co-infection model incorporating some controls; the co-infection model was extended to include four controls which have a major effect in the control of the infected population. The control intervention added to the co-infection model are: Malaria prevention effort, HBV Infection prevention effort, Malaria Treatment prevention effort, and HBV Infection Treatment effort. The four controls are incorporated into the co-infection model and the model 77 was obtained. This lead to the optimality system, which was solved to obtain the optimal controls which minimizes the compartments that are

infected and costs (Theorem 3). Figures 2,3,4,5 and 6 illustrates the numerical simulations of the Malaria HBV co-infection model with controls (i.e. model 77) and without controls were examined so as to demonstrate the effectiveness of the controls that have been considered. Four different approaches for the numerical simulation were considered.

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Appendix I

Table 1: Description of Variables and Parameters

Variable	Description
$S_h(t)$	Number of susceptible humans at time t
$I_{hm}(t)$	Number of Malaria – only infectious humans at time t
$I_{hH}(t)$	Number of HBV – only infectious humans at time t
$I_{hmH}(t)$	Number of Malaria/HBV co infectious humans at time t
$R_{hm}(t)$	Number of Malaria – only recovered humans at time t
$R_{hH}(t)$	Number of HBV – only recovered humans at time t
$R_{hmH}(t)$	Number of Malaria/HBV recovered humans at time t
$S_v(t)$	Number of susceptible mosquitoes at time t
$I_v(t)$	Number of infectious mosquitoes at time t
Parameter	**Description**
Λ_h	Constant recruitment rate from N_h to S_h
μ_h	Natural death rate of human
d_1	Malaria induced death rate of humans
d_2	HBV induced death rate of humans
α_1	Malaria infection rate of humans
α_2	HBV infection rate of humans

β_1	Malaria recovery rate for humans from I_{hm} state to R_{hm} state
β_2	HBV recovery rate for humans from I_{hH} state to R_{hH} state
γ_1	Rate of recruitment from R_{hm} state to S_h
γ_2	Rate of recruitment from R_{hH} state to S_h
γ_3	Rate of recruitment from R_{hmH} state to S_h
$\delta(1-f)(1-e)$	Rate of recovery from I_{hmH} state to R_{hmH}
δe	Rate of recovery from I_{hm} state to R_{hm}
$\delta f(1-e)$	Rate of recovery from I_{hH} state to R_{hH}
Λ_v	Constant recruitment rate of mosquito into S_v
μ_v	Natural death rate of mosquito
ξ_v	Infection rate of mosquito
α_{hm}	Transmission probability for malaria in mosquitoes
α_{mh}	Transmission probability for malaria in humans
α_H	Transmission probability for HBV infection in humans
b_m	Maximum number of mosquito bites

Appendix 2

Table 2 Tables of parameter values and compartment initial population

S/N	Parameter	Value (day^{-1})	Source
1	Λ_h	9.6274 x 10^{-5}	(Onyango, Ogada, Thirika, & Lawi, 2018)
2	μ_h	0.00004	(Jones, Feng-Bin, & Naveen, 2015)
3	d_1	0.6	(Jones, Feng-Bin, & Naveen, 2015)
4	d_2	0.0141	(Ebenezer, Rahat, & Fatma, 2020)
5	α_1	0.02	(Segun, Michael, Michael, & Maba, 2020)
6	α_2	0.169	(Magaji, Mubarak, & Dauda, 2019)
7	β_1	0.038 – 0.38	(Jones, Feng-Bin, & Naveen, 2015)
8	β_2	0.09738 – 0.9738	(Hussam, et al., 2020)
9	γ_1	0.00156	(Onyango, Ogada, Thirika, & Lawi, 2018)
10	γ_2	0.01	(Hussam, et al., 2020)

11	γ_3	0.05	Assumed
12	δ	0.45	Assumed
13	e	0.5	Assumed
14	f	0.5	Assumed
15	Λ_v	0.071	(Onyango, Ogada, Thirika, & Lawi, 2018)
16	μ_v	0.1429	(Onyango, Ogada, Thirika, & Lawi, 2018)
17	ξ_v	0.312	Assumed
18	α_{hm}	0.025 – 0.5	(Onyango, Ogada, Thirika, & Lawi, 2018)
19	α_{mh}	0.0833 – 0.8333	(Onyango, Ogada, Thirika, & Lawi, 2018)
20	α_H	0.5	(Hussam, et al., 2020)
21	b_m	12	(Jones, Feng-Bin, & Naveen, 2015)
22	Ψ	1.2	Assumed
S/N	**Compartment**	**Initial Population**	
1	S_h	**200**	
2	I_{hm}	**250**	
3	I_{hH}	**250**	
4	I_{hmH}	**250**	
5	R_{hm}	**50**	
6	R_{hH}	**50**	
7	R_{hmH}	**40**	
8	S_v	**260**	
9	I_v	**120**	