Stability analysis and modeling the dynamics of Hepatitis B with vaccination compartment

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Abstract. Resources hinder control and prevention of diseases in a number of communities in Ghana and Africa in general. Some measures have been put in place in an attempt to combat infectious diseases. A model that explains the dynamics of hepatitis B was formulated and analysed. The local and global stability of the disease as well as the basic reproduction number were determined. It was established that the hepatitis B infection is locally asymptotically stable whenever the basic reproduction number is less than unity and unstable otherwise. The population dynamics of the susceptible, infectious and recovered were determined numerically. The effects of contact rate between the infectious and susceptible population was established numerically. It was evidence that as contact rate increases, the population infected increase with time. Moreover, as the contact rate between the treated and recovered populations increase, the population of recovery increases with time.

Keywords: Hepatitis B, vaccination, treatment, equilibrium points, stability analysis.

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1. Introduction

Hepatitis B is among the world's leading health complication [1]. It can cause chronic infection, and if not well managed, can result in death from cirrhosis and hepatocellular carcinoma [2]. Approximately, hepatitis B deaths in a year ranges between 500 to $1,200,000$ people annually, and it's among the top 10 causes of death worldwide [2]. An individual is infected when the virus gets into bloodstream either through vertical transmission or blood, semen and other bodily fluids of infected persons [3].

There are safe and effective vaccines since 1982 for the prevention of hepatitis B infection through vaccination [4]. The vaccines work by activating the body to produce antibodies that ensure protection against contracting the virus. Susceptible individuals who are predisposed to the infection or are at high risk because of their particular circumstances are candidates for vaccination. Therefore, it is necessary to screen people to ascertain whether they are candidates for vaccination or not.

Research is still in progress to find a cure for chronic hepatitis B infection. Reports estimate that about one percent of the chronically infected break free from the virus each year [5]. One goal of available antiviral therapies is to help bring down the viral load and thus reduce the chance of disease progression towards liver scarring and liver cancer that are both extremely life-threatening [2].

Contact with an infectious person leading to infection can occur through sex, sharing needles, syringes and contaminated equipment, sharing toothbrushes and razors. Direct contact with blood or open sore [6, 7].The virus, after it has left its host for some days, can still infect susceptible individuals [8]. Infected individuals who are not able to fight off the hepatitis B virus become chronically infected after about 180 days of infection [9]. This stage of contagiousness in the transmission model of the diseases is known as the chronic class. If left untreated, the chronically infected is very likely to die from liver cancer or hepatocellular carcinoma [10].

Disease models generally describe the transmission dynamics of diseases, determine the best optimal control mechanism and the most effective cost to be employed in fighting the infections [11, 12].

A real phenomenon is clearly translated into a disease model for optimal cost control and employ sensitivity analysis to determine the best control measure [13, 14, 15].

2. Model description and formulation

The model divides population under study into six compartments with respect to their disease status at any point in time t. Susceptible Humans $S(t)$, Expose Population $E(t)$, Infected Population $I(t)$, Treated Population $T(t)$, Vaccinated Population $V(t)$ and Recovered Population $R(t)$. The nutural birth and death

rates are given by μ_1 and μ_2 respectively. Vaccination rate of the susceptible is given by σ_1 and rate of unsuccessful vaccination is given by η. β_1 and β_2 are transmission rates for infectious and treated populations respectively. α is the rate at which the exposed are infected. p_1 is the probability that an infected person clears the virus and the probability of failing to clear the virus is $(1-p_1)$. p_2 is the probability of an infected mother gives birth to an infected baby. σ_3 is the rate at which the recovered loss immunity and return to the susceptible class. The rate at which the treated move to the recovered class is given by σ_4.

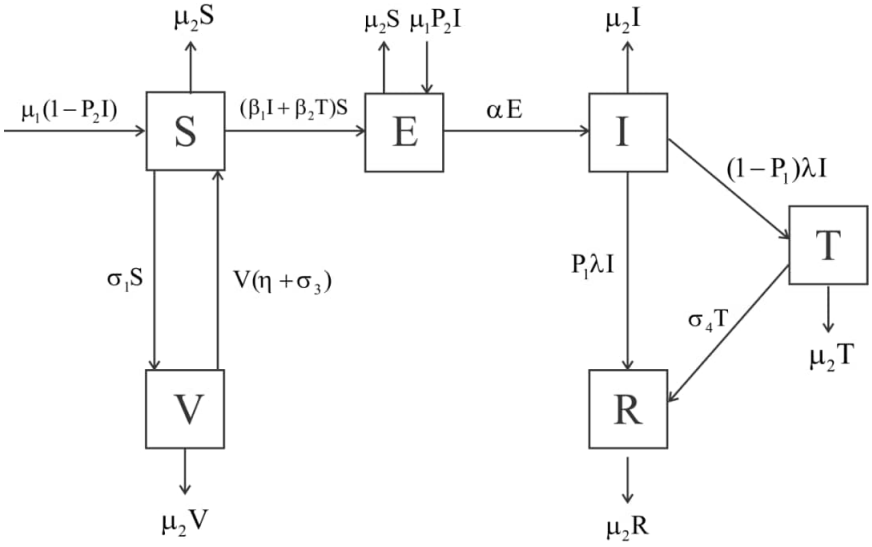

Figure 1: Hepatitis B Model flow chart

Total population, $N(t)$;

$$N = S(t) + E(t) + I(t) + T(t) + V(t) + R(t). \tag{1}$$

System of differential equation obtained from the model flow diagram in Figure (1)

$$\begin{cases} \frac{dS}{dt} &= \mu_1(1-p_2I) + \eta V + \sigma_3 R - [(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]S, \\ \frac{dE}{dt} &= (\beta_1 I + \beta_2 T)S + \mu_1 p_2 I - [\mu_2 + \alpha]E, \\ \frac{dI}{dt} &= \alpha E - [p_1\lambda + (1-p_1)\lambda + \mu_2]I, \\ \frac{dT}{dt} &= (1-p_1)\lambda I - [\sigma_4 + \mu_2]T, \\ \frac{dV}{dt} &= \sigma_1 S - [\eta + \mu_2]V, \\ \frac{dR}{dt} &= p_1\lambda I + \sigma_4 T - [\sigma_3 + \mu_2]R. \end{cases} \tag{2}$$

3. Model analysis

We provide evidence of well-posedness of hepatitis model by proving the boundedness and positivity of the model solution.

3.1 Feasible region

The invariant region is given by, $\Upsilon = \{(S(t)+E(t)+I(t)+T(t)+V(t)+R(t))) \in \mathbb{R}^6_+; S(t)+E(t)+I(t)+T(t)+V(t)+R(t) = N \leq \frac{\mu_1}{\mu_2}\}$. From model equation, the total population N is given by

$$\begin{cases} \frac{dN}{dt} & = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dT}{dt} + \frac{dV}{dt} + \frac{dR}{dt} \\ & = [\mu_1 - (S+E+I+T+V+R)\mu_2] \\ & = \mu_1 - N\mu_2, \end{cases} \tag{3}$$

$$\frac{dN}{dt} = \mu_1 - N\mu_2. \tag{4}$$

By solving

$$\begin{aligned} &\frac{dN}{\mu_1 - N\mu_2} = dt, \\ &\int \frac{dN}{\mu_1 - N\mu_2} = \int dt, \\ &\frac{-\ln|\mu_1 - N\mu_2|}{\mu_2} = t + c, \\ &-\ln|\mu_1 - N\mu_2| = \mu_2 t + c_1, \\ &\mu_1 - N\mu_2 = e^{-\mu_2 t + c_1}, \\ &\mu_1 - N\mu_2 = c_2 e^{-\mu_2 t}, \\ &N(t) = \frac{c_2 e^{-\mu_2 t} - \mu_1}{-\mu_2}, \\ &N(t) = \frac{\mu_1}{\mu_2} - c_2 e^{-\mu_2 t} \end{aligned}$$

as $t = 0, N(t) = N(0)$, $N(0) = \frac{\mu_1}{\mu_2} - c_2$, $c_2 = \frac{\mu_1}{\mu_2} - N(0)$. Therefore,

$$N(t) = \frac{\mu_1}{\mu_2} - \left(\frac{\mu_1}{\mu_2} - N(0)\right)e^{-\mu_2 t}. \tag{5}$$

Now, as t $\to \infty$, $N(t) \leq \frac{\mu_1}{\mu_2}$. Hence, Υ is positively invariant.

3.2 Positivity of model solutions

An epidemic model must epidemiologically meaningful. The positivity of the model solution must be established.

Let the initial values of the parameters be $\{S(t) \geq 0, E(t) \geq 0, I(t) \geq 0, T(t) \geq 0, V(t) \geq 0, R(t) \geq 0\} \in \Upsilon$ then the solution set $\{S(t), E(t), I(t), T(t), V(t), R(t)\} \geq 0$, $\forall\ t \geq 0$.

Proof. From

$$\frac{dS}{dt} = \mu_1(1 - p_2 I) + \eta V + \sigma_3 R - [(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]S, \tag{6}$$

we have

$$\frac{dS}{dt} \geq -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]S(t),$$
$$\frac{dS}{S(t)} \geq -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]dt.$$

Applying anti-derivate on both sides, we have

$$\int \frac{dS}{S(t)} \geq \int -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]dt,$$
$$\ln|S(t)| \geq -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]t + c,$$
$$S(t) \geq e^{-[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]t + c},$$

for $t \geq 0$

$$S(t) \geq S(0)e^{-[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]t} \geq 0.$$

Therefore $S(t) \geq 0$. Next,consider the second equation in the model

$$\frac{dE}{dt} = (\beta_1 I + \beta_2 T)S + \mu_1 p_2 I - [\mu_2 + \alpha]E. \tag{7}$$

Now, we have

$$\frac{dE}{dt} \geq -[\mu_2 + \alpha]E(t),$$
$$\frac{dE}{E(t)} \geq -[\mu_2 + \alpha]dt.$$

Taking anti derivative of both sides of the equation, we have

$$\int \frac{dE}{E(t)} \geq \int -[\mu_2 + \alpha]dt,$$
$$\ln|E(t)| \geq -[\mu_2 + \alpha]t + c,$$
$$E(t) \geq e^{-[\mu_2 + \alpha]t + c},$$

for non-negative values of t

$$E(t) \geq E(0)e^{-[\mu_2 + \alpha]t} \geq 0.$$

Hence, $E(t) \geq 0$ similarly, it can be proved that $I(t), T(t), V(t)$ and $R(t)$ are all positively invariant for all non-negative values of t. □

3.3 Disease free equilibrium

At disease free equilibrium, there are no infections and recovery, hence;

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dT}{dt} = \frac{dV}{dt} = \frac{dR}{dt} = 0. \tag{8}$$

The DFE of the model is obtained as;

$$\Big(A_1, 0, 0, 0, A_2, 0\Big), \tag{9}$$

where

$$A_1 = \frac{\mu_1[\eta + \mu_2]}{\big([\mu_2 + \sigma_1][\eta + \mu_2]\big) - \eta\sigma_1},$$
$$A_2 = \frac{\sigma_1\mu_1}{\big([\eta + \mu_2][\mu_2 + \sigma_1]\big) - \sigma_1\eta}.$$

3.4 Basic reproduction number, R_0

Using the next generation matrix approach as outlined in [16, 17]; Considering;

$$\begin{cases} \dfrac{dE}{dt} &= (\beta_1 I + \beta_2 T)S + \mu_1 p_2 I - [\mu_2 + \alpha]E, \\ \dfrac{dI}{dt} &= \alpha E - [\lambda + \mu_2]I, \\ \dfrac{dT}{dt} &= (1 - p_1)\lambda I - [\sigma_4 + \mu_2]T. \end{cases} \tag{10}$$

Let

$$F_i(x) = \begin{bmatrix} (\beta_1 I + \beta_2 T)S(t) \\ 0 \\ 0 \end{bmatrix}, \quad V_i(x) = \begin{bmatrix} -\mu_1 p_2 I + [\mu_2 + \alpha]E \\ -\alpha E + [\lambda + \mu_2]I \\ -(1 - p_1)\lambda I + [\sigma_4 + \mu_2]T \end{bmatrix}.$$

Taking the partial derivative of $F_i(x)$ and $V_i(x)$ at DFE;

$$F = \begin{bmatrix} 0 & S^0\beta_1 & S^0\beta_2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \tag{11}$$

and

$$V = \begin{pmatrix} [\mu_2 + \alpha] & -\mu_1 P_2 & 0 \\ -\alpha & [\lambda + \mu_2] & 0 \\ 0 & -\lambda(1 - p_1) & [\sigma_4 + \mu_2] \end{pmatrix} \tag{12}$$

finding the inverse of V

(13)
$$V^{-1} = \begin{pmatrix} \dfrac{\lambda+\mu_2}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2} & \dfrac{\mu_1P_2}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2} & 0 \\ \dfrac{\alpha}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2} & \dfrac{\alpha+\mu_2}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2} & 0 \\ \dfrac{(1-P_1)\alpha\lambda}{A_3} & \dfrac{(1-P_1)\lambda(\alpha+\mu_2)}{A_3} & \dfrac{1}{\sigma_4+\mu_2} \end{pmatrix},$$

where $A_3 = (\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2\big)$

(14)
$$FV^{-1}\begin{pmatrix} D_1 & D_2 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

where

$$D_1 = \frac{S^0\beta_1\alpha(\sigma_4+\mu_2)+S^0\beta_2\alpha(1-P_1)\lambda}{(\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2\big)}$$
$$D_2 = \frac{S^0\beta_1(\sigma_4+\mu_2)(\alpha+\mu_2)+S^0\beta_2\alpha(1-P_1)\lambda(\alpha+\mu_2)}{(\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2\big)}.$$

The spectral radius (largest eigen value) of the matrix FV^{-1} is the basic reproductive number [18, 19, 20]. Since FV^{-1} is a triangular matrix the eigen values are $D_1, 0$ and 0 therefore the spectral radius is D_1 hence $R_0 = D_1$

(15)
$$R_0 = \frac{S^0\beta_1\alpha(\sigma_4+\mu_2)+S^0\beta_2\alpha(1-P_1)\lambda}{(\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2\big)}.$$

Our model is epidemiologically meaningful if

(16)
$$[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2 > 0.$$

3.5 Local stability of disease-free equilibrium

Theorem 3.1. *The disease-free equilibrium point is locally asymptotically stable if $R_0 \leq 1$ and unstable if $R_0 > 1$.*

Proof. The Jacobian matrix is given by

(17)
$$J_{DFE} = \begin{bmatrix} -H_1 & 0 & -H_7 & -H_8 & \eta & \sigma_3 \\ 0 & -H_2 & H_7 & H_8 & 0 & 0 \\ 0 & \alpha & -H_3 & 0 & 0 & 0 \\ 0 & 0 & H_9 & -H_4 & 0 & 0 \\ \sigma_1 & 0 & 0 & 0 & -H_5 & 0 \\ 0 & 0 & H_{10} & \sigma_4 & 0 & -H_6 \end{bmatrix}$$

where $H_1 = [\sigma_1+\mu_2]$, $H_2 = [\mu_2+\alpha]$, $H_3 = [\lambda+\mu_2]$, $H_4 = [\sigma_4+\mu_2]$, $H_5 = [\eta+\mu_2]$, $H_6 = [\sigma_3+\mu_2]$, $H_7 = \mu_1 P_2 + \beta_1 S^0$, $H_8 = \beta_2 S^0$, $H_9 = \lambda(1-p_1)$, $H_{10} = \lambda p_1$, $S = S^0$.

The characteristics equation $P(\bar{\lambda}) = |\bar{\lambda} I - J_{DEF}| = 0$ becomes

$$P(\bar{\lambda}) = \begin{vmatrix} \bar{\lambda}+H_1 & 0 & H_7 & H_8 & -\eta & -\sigma_3 \\ 0 & \bar{\lambda}+H_2 & -H_7 & -H_8 & 0 & 0 \\ 0 & -\alpha & \bar{\lambda}+H_3 & 0 & 0 & 0 \\ 0 & 0 & -H_9 & \bar{\lambda}+H_4 & 0 & 0 \\ -\sigma_1 & 0 & 0 & 0 & \bar{\lambda}+H_5 & 0 \\ 0 & 0 & -H_{10} & -\sigma_4 & 0 & \bar{\lambda}+H_6 \end{vmatrix} = 0. \tag{18}$$

Let

$$\begin{aligned} P(\bar{\lambda}) &= P(\bar{\lambda_1}) \times P(\bar{\lambda_2}) = 0, \\ P(\bar{\lambda_1}) &= (\bar{\lambda}+H_6)[(\bar{\lambda}+H_1)(\bar{\lambda}+H_5) - \sigma_1\eta] - \sigma_1\sigma_3 = 0 \\ &= \bar{\lambda}^3 + (H_1+H_5+H_6)\bar{\lambda}^2 + (H_1H_5 + H_1H_6 + H_5H_6 - \sigma_1\eta)\bar{\lambda} \\ &\quad + H_1H_5H_6 - \sigma_1\eta H_6 - \sigma_1\sigma_3 = 0. \end{aligned} \tag{19}$$

For the other factor

$$\begin{aligned} P(\bar{\lambda_2}) &= (\bar{\lambda}+H_4)[(\bar{\lambda}+H_2)(\bar{\lambda}+H_3) - \alpha H_7] - \alpha H_8 H_9 = 0 \\ &= \bar{\lambda}^3 + (H_2+H_3+H_4)\bar{\lambda}^2 + (H_2H_3 + H_2H_4 + H_3H_4 - \alpha H_7)\bar{\lambda} \\ &\quad + H_2H_3H_4 - \alpha H_4H_7 - \alpha H_8H_9 = 0. \end{aligned}$$

Now, we analyze $P(\bar{\lambda_1}) = 0$ and $P(\bar{\lambda_2}) = 0$ separately for the nature of their roots by using the Routh-Hurwitz criteria. Let's begin with $P(\bar{\lambda_1}) = 0$. $P(\bar{\lambda_1})$ is in the form

$$P(\bar{\lambda_1}) = \bar{\lambda}^3 + m_1\bar{\lambda}^2 + m_2\bar{\lambda} + m_3 = 0 \tag{20}$$

and

$$\begin{aligned} m_1 &= H_1 + H_5 + H_6 \\ &= \sigma_1 + \mu_2 + \eta + \mu_2 + \sigma_3 + \mu_2 \\ &= \sigma_1 + \sigma_3 + \eta + 3\mu_2, \\ m_2 &= H_1H_5 + H_1H_6 + H_5H_6 - \sigma_1\eta \\ &= (\sigma_1+\mu_2)(\eta+\mu_2) + (\sigma_1+\mu_2) \\ &\quad (\sigma_3+\mu_2) + (\eta+\mu_2)(\sigma_3+\mu_2) - \sigma_1\eta \\ &= \mu_2\eta + (\sigma_1+\mu_2)(\mu_2) + (\sigma_1+\mu_2)(\sigma_3+\mu_2) \\ &\quad + (\eta+\mu_2)(\sigma_3+\mu_2), \end{aligned}$$

$$\begin{aligned} m_3 &= H_1H_5H_6 - \sigma_1\eta H_6 - \sigma_1\sigma_3 \\ &= (\sigma_1+\mu_2)(\eta+\mu_2)(\sigma_3+\mu_2) \\ &\quad - \sigma_1\eta(\sigma_3+\mu_2) - \sigma_1\sigma_3 \\ &= \sigma_1\mu_2 + \mu_2(\sigma_1+\eta+\mu_2)(\sigma_3+\mu_2). \end{aligned}$$

According to Routh-Hurwitz criteria, roots of $P(\bar{\lambda_1})$ will have negative real parts if the conditions below are satisfied

(i) $m_1 > 0$;

(ii) $m_2 > 0$;

(iii) $m_3 > 0$;

(v) $m_1m_2 > m_3$;

$$\begin{aligned} m_1 &= \sigma_1+\sigma_3+\eta+3\mu_2 > 0, \\ m_3 &= \sigma_1\mu_2 + \mu_2(\sigma_1+\eta+\mu_2)(\sigma_3+\mu_2) > 0. \end{aligned}$$

Now,

$$\begin{aligned} m_1m_2 &= (\sigma_1+\sigma_3+\eta+3\mu_2)\big[\mu_2\eta + (\sigma_1+\mu_2)(\mu_2) + (\sigma_1+\mu_2)(\sigma_3+\mu_2) \\ &\quad + (\eta+\mu_2)(\sigma_3+\mu_2)\big], \\ m_3 &= \sigma_1\mu_2 + \mu_2(\sigma_1+\eta+\mu_2)(\sigma_3+\mu_2). \end{aligned}$$

Notice that in expanded form , m_1m_2 contains all the terms in m_3 and will still be left with additional terms. Therefore $m_1m_2 > m_3$ is satisfied. By the Routh-Hurwitz criteria all the roots of $P(\bar{\lambda_1}) = 0$ are negative or have negative real parts.

Let's now analyze the second factor $P(\bar{\lambda_2})$. $P(\bar{\lambda_2})$ is in the form

$$P(\bar{\lambda_2}) = \bar{\lambda}^3 + c_1\bar{\lambda}^2 + c_2\bar{\lambda} + c_3 = 0, \tag{21}$$

where

$$\begin{aligned} c_1 &= H_2+H_3+H_4 = \alpha+\lambda+\sigma_4+3\mu_2, \\ c_2 &= H_2H_3 + H_2H_4 + H_3H_4 - \alpha H_7 = (\alpha+\mu_2)(\lambda+\mu_2) + (\alpha+\mu_2)(\sigma_4+\mu_2) \\ &\quad + (\lambda+\mu_2)(\sigma_4+\mu_2) - \alpha(\mu_1P_2+\beta_1S), \\ c_3 &= H_2H_3H_4 - \alpha H_4H_7 - \alpha H_8H_9 = (\alpha+\mu_2)(\lambda+\mu_2)(\sigma_4+\mu_2) - \alpha\mu_1P_2(\sigma_4+\mu_2) \\ &\quad - \alpha\beta_1S(\sigma_4+\mu_2) - \alpha\lambda\beta_2S(1-p_1). \end{aligned}$$

According to the Routh-Hurwitz criterion for $P(\bar{\lambda_2}) = 0$ to have negative real parts, $c_1 > 0, c_3 > 0$ and $c_1c_2 > c_3$, $c_1 = \alpha+\lambda+\sigma_4+3\mu_2 > 0, c_2 > 0 \implies$

$(\alpha+\mu_2)(\lambda+\mu_2)+(\alpha+\mu_2)(\sigma_4+\mu_2)+(\lambda+\mu_2)(\sigma_4+\mu_2)-\alpha\mu_1P_2>\alpha\beta_1S$ but from $R_0<1$ $(\alpha+\mu_2)(\lambda+\mu_2)-\mu_1P_2>\alpha\beta_1S$, $c_2>0$ holds

$$
\begin{aligned}
&c_3=(\alpha+\mu_2)(\lambda+\mu_2)(\sigma_4+\mu_2)-\alpha\mu_1P_2(\sigma_4+\mu_2)-\alpha\beta_1S(\sigma_4+\mu_2)\\
&-\alpha\lambda\beta_2S(1-p_1)>0,\\
&(\alpha+\mu_2)(\lambda+\mu_2)(\sigma_4+\mu_2)-\alpha\mu_1P_2(\sigma_4+\mu_2)>\alpha\beta_1S(\sigma_4+\mu_2)+\alpha\lambda\beta_2S(1-p_1)\\
&\alpha\beta_1S(\sigma_4+\mu_2)+\alpha\lambda\beta_2S(1-p_1)<(\alpha+\mu_2)(\lambda+\mu_2)(\sigma_4+\mu_2)-\alpha\mu_1P_2(\sigma_4+\mu_2),
\end{aligned}
$$

$$
\frac{\alpha\beta_1S(\sigma_4+\mu_2)+\alpha\lambda\beta_2S(1-p_1)}{(\alpha+\mu_2)(\lambda+\mu_2)(\sigma_4+\mu_2)-\alpha\mu_1P_2(\sigma_4+\mu_2)}<1. \tag{22}
$$

Since $R_0<1$, $m_3>0$ holds.

We now analyze $c_1c_2>c_3$ below

$$
\begin{aligned}
&(H_2+H_3+H_4)(H_2H_3+H_2H_4+H_3H_4-\alpha H_7)>H_2H_3H_4\\
&-\alpha H_4H_7-\alpha H_8H_9,\\
&(H_2+H_3)(H_2H_3+H_2H_4+H_3H_4-\alpha H_7)+H_2H_3H_4+H_2H_4H_4\\
&+H_3H_4H_4-\alpha H_4H_7>H_2H_3H_4-\alpha H_4H_7-\alpha H_8H_9,\\
&(H_2+H_3)(H_2H_3+H_2H_4+H_3H_4)-\alpha H_7(H_2+H_3)+H_4H_4(H_2+H_3)>-\alpha H_8H_9,\\
&(H_2+H_3)(H_2H_3+H_2H_4+H_3H_4+H_4H_4)>\alpha H_7(H_2+H_3)-\alpha H_8H_9,\\
&(H_2+H_3)(H_2+H_4)(H_3+H_4)>\alpha H_7(H_2+H_3)-\alpha H_8H_9,\\
&\alpha H_7(H_2+H_3)-\alpha H_8H_9<(H_2+H_3)(H_2+H_4)(H_3+H_4),
\end{aligned}
$$

substituting the model parameters

$$
\begin{aligned}
&\alpha(\mu_1P_2+\beta_1S)(\alpha+\lambda+2\mu_2)-\alpha\beta_2S\lambda(1-p_1)<\\
&(\alpha+\lambda+2\mu_2)(\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2),\\
&(\alpha+\lambda+2\mu_2)\beta_1S-\alpha\beta_2S\lambda(1-p_1)<(\alpha+\lambda+2\mu_2)(\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2)\\
&-\alpha(\alpha+\lambda+2\mu_2)\mu_1P_2\alpha\beta_1S-\frac{\alpha\beta_2S\lambda(1-p_1)}{\alpha+\lambda+2\mu_2}\\
&<(\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2)-\alpha\mu_1P_2,
\end{aligned}
$$

$$
\alpha\beta_1S<(\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2)-\alpha\mu_1P_2+\frac{\alpha\beta_2S\lambda(1-p_1)}{\alpha+\lambda+2\mu_2}. \tag{23}
$$

From $R_0<1$

$$
\begin{aligned}
&\alpha\beta_1S(\sigma_4+\mu_2)+\alpha\beta_2\lambda S(1-p_1)<(\sigma_4+\mu_2)\big[(\alpha+\mu_2)(\lambda+\mu_2)-\alpha\mu_1P_2\big],\\
&\alpha\beta_1S(\sigma_4+\mu_2)<(\sigma_4+\mu_2)\big[(\alpha+\mu_2)(\lambda+\mu_2)-\alpha\mu_1P_2\big],\\
&\alpha\beta_1S<(\alpha+\mu_2)(\lambda+\mu_2)-\alpha\mu_1P_2.
\end{aligned} \tag{24}
$$

Equation (24) is a true inequality when $R_0 < 1$, therefore equation (23) is also true because the right hand side of equation (23) is greater than right hand side of equation (24).

This proves that $c_1c_2 > c_3$. It follows that $P(\bar{\lambda}_2) = 0$ has its roots negative or negative real parts.

In conclusion, the roots of $P(\bar{\lambda}) = 0$ are all negatives or have negative real parts so the disease free-equilibrium is asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$ □

3.6 Global stability of the disease free equilibrium point (DFE)

Theorem 3.2. *If $R_0 > 1$, the disease free equilibrium Q^0 of the model is globally asymptotically stable*

Let F_i, V_i, F and V be defined as

$$f(x,y) = (F-V)x - F_i(x,y) + V_i(x,y), \tag{25}$$

where $x = (E, I, T)^T$,

$$\begin{aligned} f(x,y) &= \begin{bmatrix} -(\alpha+\mu_2) & \beta_1 S + \mu_1 P_2 & \beta_2 S \\ \alpha & -(\mu_2+\lambda) & 0 \\ 0 & \lambda(1-p_1) & -(\mu_2+\sigma_4) \end{bmatrix} \begin{bmatrix} E \\ I \\ T \end{bmatrix} \\ &+ \begin{bmatrix} -(\beta_1 I + \beta_2 T)S - \mu_1 P_2 I + (\alpha+\mu_2)E \\ (\lambda+\mu_2)I - \alpha E \\ (\sigma_4+\mu_2)I - \lambda(1-p_1)I \end{bmatrix} \\ &= \begin{bmatrix} -(\alpha+\mu_2)E + (\beta_1 S + \mu_1 P_2)I + \beta_2 ST \\ \alpha E - (\mu_2+\lambda)I \\ \lambda(1-p_1)I - (\mu_2+\sigma_4)T \end{bmatrix} \\ &+ \begin{bmatrix} -(\beta_1 I + \beta_2 T)S - \mu_1 P_2 I + (\alpha+\mu_2)E \\ (\lambda+\mu_2)I - \alpha E \\ (\sigma_4+\mu_2)I - \lambda(1-p_1)I \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}. \end{aligned}$$

Also, let $x' = (F-V)x - F(x,y)$ but $f(x,y) = 0 \therefore x' = (F-V)x$. Let $W^T \geq 0$ be defined as the left eigen vector of the nonnegative matrix $V^{-1}F$ corresponding to the eigen value $\rho(V^{-1}F) = \rho(FV^{-1}) = R_0$. We proceed to first find $V^{-1}F$ and $\rho(V^{-1}F)$

$$V^{-1} = \begin{bmatrix} \dfrac{\lambda+\mu_2}{[\alpha+\mu_2][\lambda+\mu_2] - \alpha\mu_1 P_2} & \dfrac{\mu_1 P_2}{[\alpha+\mu_2][\lambda+\mu_2] - \alpha\mu_1 P_2} & 0 \\ \dfrac{\alpha}{[\alpha+\mu_2][\lambda+\mu_2] - \alpha\mu_1 P_2} & \dfrac{\alpha+\mu_2}{[\alpha+\mu_2][\lambda+\mu_2] - \alpha\mu_1 P_2} & 0 \\ \dfrac{(1-P_1)\alpha\lambda}{D_0} & \dfrac{(1-P_1)\lambda(\alpha+\mu_2)}{D_0} & \dfrac{1}{\sigma_4+\mu_2} \end{bmatrix}$$

$$F = \begin{bmatrix} 0 & S^0\beta_1 & S^0\beta_2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

Now,

$$V^{-1}F = \begin{pmatrix} 0 & \dfrac{(\lambda+\mu_2)\beta_1 S}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1 P_2} & \dfrac{(\lambda+\mu_2)\beta_2 S}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1 P_2} \\ 0 & \dfrac{\beta_1 S\alpha}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1 P_2} & \dfrac{\beta_2 S\alpha}{[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1 P_2} \\ 0 & \dfrac{(1-P_1)\alpha\lambda\beta_1 S}{D_0} & \dfrac{(1-P_1)\alpha\lambda\beta_2 S}{D_0} \end{pmatrix}.$$

Define $g = \beta_1 S$, $h = \beta_2 S$, $j = \alpha+\mu_2$, $k = \lambda(1-p_1)$, $m = (\alpha+\mu_2)(\lambda+\mu_2)-\alpha\mu_1 P_2$, $n = \sigma_4+\mu_2$, $l = \lambda+\mu_2$, $S = S^0$. Hence

$$V^{-1}F = \begin{pmatrix} 0 & \dfrac{gl}{m} & \dfrac{hl}{m} \\ 0 & \dfrac{\alpha g}{m} & \dfrac{\alpha h}{m} \\ 0 & \dfrac{\alpha gk}{mn} & \dfrac{\alpha hk}{mn} \end{pmatrix}.$$

For $\rho(V^{-1}F)$, first determine eigenvalues, the characteristics equation $|(V^{-1}F)-\bar{\lambda}I| = 0$ is given by

$$\begin{aligned} &-\bar{\lambda}\left[(\frac{\alpha g}{m}-\bar{\lambda})(\frac{\alpha hk}{mn}-\bar{\lambda})-\frac{\alpha gk}{mn}\times\frac{\alpha h}{m}\right]=0, \\ &-\bar{\lambda}\left[\bar{\lambda}^2-\frac{\alpha g}{m}\bar{\lambda}-\frac{\alpha hk}{mn}\bar{\lambda}+\frac{\alpha^2 ghk}{m^2 n}-\frac{\alpha^2 ghk}{m^2 n}\right]=0, \\ &-\bar{\lambda}\left[\bar{\lambda}^2-(\frac{\alpha g}{m}+\frac{\alpha hk}{mn})\bar{\lambda}\right]=0, \end{aligned}$$

either

$$\begin{aligned} &-\bar{\lambda}=0, \quad or \quad \bar{\lambda}^2-\frac{\alpha gn+\alpha hk}{mn}\bar{\lambda}=0, \bar{\lambda}=\big(0,0,\frac{\alpha gn+\alpha hk}{mn}\big), \\ &\therefore V^{-1}F=\left(0,0,\frac{S^0\beta_1\alpha(\sigma_4+\mu_2)+S^0\beta_2\alpha(1-P_1)\lambda}{(\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1 P_2\big)}\right), \\ &\therefore \rho\big(V^{-1}F\big)=\rho(FV^{-1})=R_0. \end{aligned}$$

The left eigen vector of the matrix $V^{-1}F$ corresponding to the eigen value R_0 can be obtained from

$$\begin{pmatrix} x_1 & x_2 & x_3 \end{pmatrix} \begin{pmatrix} 0 & \frac{gl}{m} & \frac{hl}{m} \\ 0 & \frac{\alpha g}{m} & \frac{\alpha h}{m} \\ 0 & \frac{\alpha gk}{mn} & \frac{\alpha hk}{mn} \end{pmatrix} = R_0 \begin{pmatrix} x_1 & x_2 & x_3 \end{pmatrix},$$

$$\left(0, \quad (\frac{gl}{m}x_1 + \frac{\alpha g}{m}x_2 + \frac{\alpha gk}{mn}x_3 \quad), (\frac{hl}{m}x_1 + \frac{\alpha h}{m}x_2 + \frac{\alpha hk}{mn}x_3)\right)$$
$$= R_0 \begin{pmatrix} x_1R_0 & x_2R_0 & x_3R_0 \end{pmatrix}.$$

Equating corresponding entries we have

$$\begin{aligned} R_0x_1 &= 0, \\ \frac{gl}{m}x_1 + \frac{\alpha g}{m}x_2 + \frac{\alpha gk}{mn}x_3 &= R_0x_2, \\ \frac{hl}{m}x_1 + \frac{\alpha h}{m}x_2 + \frac{\alpha hk}{mn}x_3 &= R_0x_3. \end{aligned}$$

Simplifying, we have

$$\begin{aligned} x_1 &= 0, \\ gnlx_1 + \alpha gnx_2 + \alpha gkx_3 &= mnR_0x_2, \\ hlnx_1 + \alpha hnx_2 + \alpha hkx_3 &= mnR_0x_3, \end{aligned}$$

but $x_1 = 0$, therefore

$$\begin{aligned} \alpha gnx_2 + \alpha gkx_3 = mnR_0x_2 &= (\alpha gn + \alpha hk)x_2, \\ \alpha hnx_2 + \alpha hkx_3 = mnR_0x_3 &= (\alpha gn + \alpha hk)x_3. \end{aligned}$$

Simplifying further and expressing x_3 in terms of x_2 yields

$$x_3 = \frac{h}{g}x_2 = \frac{\beta_2 S x_2}{\beta_1 S} = \frac{\beta_2 x_2}{\beta_1}.$$

Let $x_2 = t$, $(x_1, x_2, x_3) = (0, t, \frac{\beta_2}{\beta_1}t) = t\big(0, 1, \frac{\beta_2}{\beta_1}\big)$. Therefore, the left eigen vector of the matrix $V^{-1}F$ corresponding to the eigen value R_0 is $W^T = \big(0, 1, \frac{\beta_2}{\beta_1}\big)$ or any scalar multiple of $(0, 1, \frac{\beta_2}{\beta_1})$.

The Lyapunov function to prove the disease free equilibrium of the model is given by

$$A = W^T V^{-1} x = (0, 1, \frac{\beta_2}{\beta_1}) V^{-1} \begin{pmatrix} E \\ I \\ T \end{pmatrix} = (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} \frac{l}{m} & \frac{\mu_1 P_2}{m} & 0 \\ \frac{\alpha}{m} & \frac{j}{m} & 0 \\ \frac{\alpha k}{mn} & \frac{\alpha j k}{mn} & \frac{1}{n} \end{pmatrix} \begin{pmatrix} E \\ I \\ T \end{pmatrix}$$

$$= \begin{pmatrix} \frac{\alpha}{m} + \frac{\beta_2 \alpha k}{\beta_1 mn} & \frac{j}{m} + \frac{\beta_2 j k}{\beta_1 mn} & \frac{\beta_2}{\beta_1 n} \end{pmatrix} \begin{pmatrix} E \\ I \\ T \end{pmatrix}$$

$$= \left(\frac{\alpha}{m} + \frac{\beta_2 \alpha k}{\beta_1 mn} \right) E + \left(\frac{j}{m} + \frac{\beta_2 j k}{\beta_1 mn} \right) I + \frac{\beta_2}{\beta_1 n} T$$

$$= \frac{\alpha \beta_1 n + \beta_2 \alpha k}{\beta_1 mn} E + \frac{\beta_1 n j + \beta_2 j k}{\beta_1 mn} I + \frac{\beta_2}{\beta_1 n} T$$

$$\therefore A = \frac{\beta_1 \alpha(\sigma_4 + \mu_2) + \beta_2 \alpha \lambda (1 - p_1)}{\beta_1 (\sigma_4 + \mu_2) \big[(\alpha + \mu_2)(\lambda + \mu_2) - \alpha \mu_1 P_2 \big]} E \tag{26}$$

$$+ \frac{\beta_1 (\sigma_4 + \mu_2)(\alpha + \mu_2) + \beta_2 (\alpha + \mu_2)(1 - p_1) \lambda}{\beta_1 (\sigma_4 + \mu_2) \big[(\alpha + \mu_2)(\lambda + \mu_2) - \alpha \mu_1 P_2 \big]} I + \frac{\beta_2}{\beta_1 (\sigma_4 + \mu_2)} T. \tag{27}$$

Form this it is obvious that

(i) $A(x) > 0$ for all $x \in \upsilon$;

(ii) $||A(x)|| \to \infty \implies ||x|| \to \infty$ (that is radially unbounded).

We can directly find the derivative of the Lyapunov function from A. (Refer to the Appendix). However, we chose to find it from the equation as shown as

$$\begin{aligned} A' &= W^T V^{-1} x' \\ &= W^T V^{-1} \big[(F - V) x - f(x, y) \big] \\ &= W^T V^{-1} (F - V) x - W^T V^{-1} f(x, y) \\ &= W^T V^{-1} F x - W^T V^{-1} V x - 0 \\ &= W^T V^{-1} f x - W^T x \\ &= (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} 0 & \frac{gl}{m} & \frac{hl}{m} \\ 0 & \frac{\alpha g}{m} & \frac{\alpha h}{m} \\ 0 & \frac{\alpha g k}{mn} & \frac{\alpha h k}{mn} \end{pmatrix} x - (0, 1, \frac{\beta_2}{\beta_1}) x \end{aligned}$$

$$= \begin{pmatrix} 0 & \frac{\alpha g}{m} + \frac{g\beta_2\alpha k}{\beta_1 mn} & \frac{\alpha h}{m} + \frac{\alpha\beta_2 hk}{\beta_1 mn} \end{pmatrix} \begin{pmatrix} E \\ I \\ T \end{pmatrix} - (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix}$$

$$= \begin{pmatrix} 0 & \frac{\beta_1 n\alpha g + g\beta_2\alpha k}{\beta_1 mn} & \frac{\beta_1 n\alpha h + \alpha\beta_2 hk}{\beta_1 mn} \end{pmatrix} \begin{pmatrix} E \\ I \\ T \end{pmatrix} - (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix}.$$

Substituting model parameter for values of g and h

$$A' = \begin{pmatrix} 0 & \frac{\beta_1 n\alpha\beta_1 S + \beta_2\alpha k\beta_1 S}{\beta_1 mn} & \frac{\beta_1 n\alpha\beta_2 S + \alpha\beta_2\beta_2 Sk}{\beta_1 mn} \end{pmatrix} \begin{pmatrix} E \\ I \\ T \end{pmatrix} - (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix}$$

$$= \frac{n\alpha\beta_1 S + \alpha k\beta_2 S}{mn} (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix} - (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix}.$$

Substituting values of m, n and k in terms of parameters for the model

$$A' = \frac{\beta_1\alpha S^0(\sigma_4 + \mu_2) + \beta_2\alpha\lambda S^0(1 - p_1)}{(\sigma_4 + \mu_2)\big[(\alpha + \mu_2)(\lambda + \mu_2) - \alpha\mu_1 P_2\big]} (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix} - (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix}$$

$$= R_0 (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix} - (0, 1, \frac{\beta_2}{\beta_1}) \begin{pmatrix} E \\ I \\ T \end{pmatrix}$$

$$= R_0\big(I + \frac{\beta_2}{\beta_1} T\big) - \big(I + \frac{\beta_2}{\beta_1} T\big)$$

$$= \big(R_0 - 1\big)\big(I + \frac{\beta_2}{\beta_1} T\big).$$

It is easy to see that if $R_0 \leq 1$ then $A' \leq 0$, thus A is a Lyapunov function for the system. In addition, $A' = 0$ if $I = T = 0$ and $S = S^0$. Therefore the largest compact invariant set in $\{S(t), E(t), I(t), T(t), V(t), R(t) \in R^6_+ : A' = 0\}$ is the singleton Q^0, the disease free equilibrium of the system. Hence , by La Salle's invariance principle Q^0 is globally asymptotically stable in Υ if $R_0 \leq 1$.

4. Endemic equilibrium

It is a constant solution of the model where the disease per exist in the system. In our model the endemic equilibrium is denoted by Q^e. To obtained the endemic equilibrium we set the system in (2) to zero. Therefore, the endemic equilibrium

points are given by

$$\begin{cases} S^e = k_1, \\ E^e = \dfrac{(\lambda+\mu_2)(\sigma_4+\mu_2)(k_1k_2k_3 - k_1k_4 + k_5)}{\alpha\lambda(1-p_1)(k_6 + k_1k_7 - k_8)}, \\ I^e = \dfrac{(\sigma_4+\mu_2)(k_1k_2k_3 - k_1k_4 + k_5)}{\lambda(1-p_1)(k_6 + k_1k_7 - k_8)}, \\ T^e = \dfrac{k_1k_2k_3 - k_1k_4 + k_5}{k_6 + k_1k_7 - k_8}, \\ V^e = k_1k_2, \\ R^e = \dfrac{\sigma_2k_1k_2(1-p_1)(k_6 + k_1k_7 - k_8) + D_6(k_1k_2k_3 - k_1k_4 + k_5)}{(\sigma_3+\mu_2)(1-p_1)(k_6 + k_1k_7 - k_8)}, \end{cases}$$

where $D_6 = [p_1(\sigma_4+\mu_2) + \sigma_4(1-p_1)]$

$$k_1 = \frac{(\sigma_4+\mu_2)\big[(\mu_2+\alpha)(\lambda+\mu_2) - \alpha P_2\mu_1\big]}{\alpha\big[\beta_1(\sigma_4+\mu_2) + \beta_2\lambda(1-p_1)\big]}, \qquad k_2 = \frac{\sigma_1}{\eta+\mu_2},$$

$$k_3 = \lambda(1-p_1)(\sigma_3+\eta), \qquad k_4 = \lambda(1-p_1)(\sigma_3+\mu_2)(\sigma_1+\mu_2),$$

$$k_5 = \mu_1\lambda(1-p_1), \qquad k_7 = \beta_1(\sigma_3+\mu_2)(\sigma_4+\mu_2) + \lambda\beta_2(\sigma_3+\mu_2)(1-p_1),$$

$$k_6 = \mu_1P_2(\sigma_3+\mu_2)(\sigma_4+\mu_2), \qquad k_8 = \lambda\sigma_3\big[p_1(\sigma_4+\mu_2) + \sigma_4(1-p_1)\big].$$

Hence, $Q^e = \{S^e, E^e, I^e, T^e, V^e, R^e\}$.

4.1 Global stability of the endemic equilibrium point

Theorem 4.1. *If $R_0 > 1$, the endemic equilibrium Q^e of the model is globally asymptotically stable.*

Proof. The global asymptotic stability of the endemic equilibrium can be prooved using the Lyapunov function define as;

$$G(S^e, E^e, I^e, T^e, V^e, R^e) = G_1 + G_2 + G_3 + G_4 + G_5 + G_6 \tag{28}$$

$$\begin{cases} G_1 = S - S^e - S^e\ln\frac{S}{S^e}, & G_2 = E - E^e - E\ln\frac{E}{E^e} \\ G_3 = I - I^e - I^e\ln\frac{I}{I^e}, & G_4 = T - T^e - T^e\ln\frac{T}{T^e} \\ G_5 = V - V^e - V^e\ln\frac{V^e}{V}, & G_6 = R - R^e - R^e\ln\frac{R}{R^e} \end{cases}.$$

By setting the system of equation in (2) to zereo and taking the derivative of G along the solution of the equations, we obtain

$$\frac{dG}{dt} = \frac{dG_1}{dt} + \frac{dG_2}{dt} + \frac{dG_3}{dt} + \frac{dG_4}{dt} + \frac{dG_5}{dt} + \frac{dG_6}{dt}. \tag{29}$$

By substituting and simplifying all terms

$$
\begin{cases}
\frac{dG}{dt}=\mu_2 S^e\Big[-\mathcal{M}\Big(\frac{S^e}{S}\Big)-\mathcal{M}\Big(\frac{S}{S^e}\Big)\Big]+\mu_2 E^e\Big[-\mathcal{M}\Big(\frac{E^e}{E}\Big)-\mathcal{M}\Big(\frac{E}{E^e}\Big)\Big] \\
+\mu_2 I^e\Big[-\mathcal{M}\Big(\frac{I^e}{I}\Big)-\mathcal{M}\Big(\frac{I}{I^e}\Big)\Big]+\mu_2 T^e\Big[-\mathcal{M}\Big(\frac{T^e}{T}\Big)-\mathcal{M}\Big(\frac{T}{T^e}\Big)\Big] \\
+\mu_2 V^e\Big[-\mathcal{M}\Big(\frac{V^e}{V}\Big)-\mathcal{M}\Big(\frac{V}{V^e}\Big)\Big]+\mu_2 R^e\Big[-\mathcal{M}\Big(\frac{R^e}{R}\Big)-\mathcal{M}\Big(\frac{R}{R^e}\Big)\Big] \\
+\mu_1 P_2 I^e\Big[-\mathcal{M}\Big(\frac{S^e I}{SI^e}\Big)+\mathcal{M}\Big(\frac{E^e}{E}\Big)-\mathcal{M}\Big(\frac{E^e I}{EI^e}\Big)+\mathcal{M}\Big(\frac{S^e}{S}\Big)\Big] \\
+\sigma_1 S^e\Big[-\mathcal{M}\Big(\frac{S^e}{S}\Big)-\mathcal{M}\Big(\frac{V^e S}{VS^e}\Big)+\mathcal{M}\Big(\frac{V^e}{V}\Big)\Big]+\eta V^e\Big[-\mathcal{M}\Big(\frac{V^e}{V}\Big) \\
-\mathcal{M}\Big(\frac{S^e V}{SV^e}\Big)+\mathcal{M}\Big(\frac{S^e}{S}\Big)\Big]+\sigma_3 R^e\Big[-\mathcal{M}\Big(\frac{R^e}{R}\Big)-\mathcal{M}\Big(\frac{S^e R}{SR^e}\Big)+\mathcal{M}\Big(\frac{S^e}{S}\Big)\Big] \\
+\beta_1 I^e S^e\Big[-\mathcal{M}\Big(\frac{ISE^e}{I^e S^e E}\Big)-\mathcal{M}\Big(\frac{S^e}{S}\Big)+\mathcal{M}\Big(\frac{I}{I^e}\Big)+\mathcal{M}\Big(\frac{E^e}{E}\Big)\Big] \\
+\beta_2 T^e S^e\Big[-\mathcal{M}\Big(\frac{TSE^e}{T^e S^e E}\Big)+\mathcal{M}\Big(\frac{E^e}{E}\Big)-\mathcal{M}\Big(\frac{S^e}{S}\Big)+\mathcal{M}\Big(\frac{T}{T^e}\Big)\Big]
\end{cases} \tag{30}
$$

$$
\begin{cases}
+\ \alpha E^e\Big[-\mathcal{M}\Big(\frac{E^e}{E}\Big)-\mathcal{M}\Big(\frac{EI^e}{IE^e}\Big)+\mathcal{M}\Big(\frac{I^e}{I}\Big)\Big]+p_1\lambda I^e\Big[-\mathcal{M}\Big(\frac{I^e}{I}\Big) \\
-\mathcal{M}\Big(\frac{R^e I}{RI^e}\Big)+\mathcal{M}\Big(\frac{R^e}{R}\Big)\Big]+(1-p_1)\lambda I^e\Big[-\mathcal{M}\Big(\frac{I^e}{I}\Big)-\mathcal{M}\Big(\frac{T^e I}{TI^e}\Big) \\
+\mathcal{M}\Big(\frac{T^e}{T}\Big)\Big]+\sigma_4 T^e\Big[-\mathcal{M}\Big(\frac{T^e}{T}\Big)-\mathcal{M}\Big(\frac{R^e T}{RT^e}\Big)+\mathcal{M}\Big(\frac{R^e}{R}\Big)\Big] \\
+V^e\Big[-\mathcal{M}\Big(\frac{V^e}{V}\Big)-\mathcal{M}\Big(\frac{R^e V}{RV^e}\Big)+\mathcal{M}\Big(\frac{R^e}{R}\Big)\Big]
\end{cases} \tag{31}
$$

Let

$$
\frac{dG}{dt}=L_1+L_2, \tag{32}
$$

where

$$
\begin{cases}
L_1 &= -\mu_2 S^e\mathcal{M}\Big(\frac{S}{S^e}\Big)-\mu_2 E^e\mathcal{M}\Big(\frac{E}{E^e}\Big)-\mu_2 I^e\mathcal{M}\Big(\frac{I}{I^e}\Big)-\mu_2 T^e\mathcal{M}\Big(\frac{T}{T^e}\Big) \\
&-\mu_2 V^e\mathcal{M}\Big(\frac{V}{V^e}\Big)-\mu_2 R^e\mathcal{M}\Big(\frac{R}{R^e}\Big)-\mu_1 P_2 I^e\mathcal{M}\Big(\frac{E^e I}{EI^e}\Big)-\sigma_1 S^e\mathcal{M}\Big(\frac{V^e S}{VS^e}\Big) \\
&-\eta V^e\mathcal{M}\Big(\frac{S^e V}{SV^e}\Big)-\sigma_3 R^e\mathcal{M}\Big(\frac{S^e R}{SR^e}\Big)-\beta_1 I^e S^e\mathcal{M}\Big(\frac{ISE^e}{I^e S^e E}\Big)-\beta_2 T^e S^e\mathcal{M}\Big(\frac{TSE^e}{T^e S^e E}\Big) \\
&-\alpha E^e\mathcal{M}\Big(\frac{I^e E}{IE^e}\Big)-p_1\lambda I^e\mathcal{M}\Big(\frac{R^e I}{RI^e}\Big)-(1-p_1)\lambda I^e\mathcal{M}\Big(\frac{T^e I}{TI^e}\Big)-\sigma_4 T^e\mathcal{M}\Big(\frac{R^e T}{RT^e}\Big) \\
&-V^e\mathcal{M}\Big(\frac{R^e V}{RV^e}\Big)
\end{cases} \tag{33}
$$

and

$$
\begin{cases}
L_2 &= (\beta_1 I^e S^e+\beta_2 T^e S^e+\mu_1 P_2 I^e)\mathcal{M}\Big(\frac{E^e}{E}\Big)+(V^e+\sigma_4 T^e+p_1\lambda I^e)\mathcal{M}\Big(\frac{R^e}{R}\Big) \\
&+(1-p_1)\lambda I^e\mathcal{M}\Big(\frac{T^e}{T}\Big)+\sigma_1 S^e\mathcal{M}\Big(\frac{V^e}{V}\Big)+\alpha E^e\mathcal{M}\Big(\frac{I^e}{I}\Big)-(\mu_2 E^e+\alpha E^e) \\
&\mathcal{M}\Big(\frac{E^e}{E}\Big)-(\sigma_3 R^e+\mu_2 R^e)\mathcal{M}\Big(\frac{R^e}{R}\Big)-(\sigma_4 T^e+\mu_2 T^e)\mathcal{M}\Big(\frac{T^e}{T}\Big) \\
&-(\eta V^e+V^e+\mu_2 V^e)\mathcal{M}\Big(\frac{V^e}{V}\Big)-(p_1\lambda I^e+(1-p_1)\lambda I^e+\mu_2 I^e)\mathcal{M}\Big(\frac{I^e}{I}\Big)
\end{cases} \tag{34}
$$

$$
\begin{cases}
+\mu_1 P_2 I^e\mathcal{M}\Big(\frac{S^e I}{SI^e}\Big)+\beta_1 I^e S^e\mathcal{M}\Big(\frac{I}{I^e}\Big)+\beta_2 T^e S^e\mathcal{M}\Big(\frac{T}{T^e}\Big).
\end{cases} \tag{35}
$$

Using endemic equilibrium relations

$$L_2 = \mu_1 P_2 I^e \mathcal{M}\left(\frac{S^e I}{S I^e}\right) + \beta_1 I^e S^e \mathcal{M}\left(\frac{I}{I^e}\right) + \beta_2 T^e S^e \mathcal{M}\left(\frac{T}{T^e}\right) \tag{36}$$

Observation; $|L_1|$ is greater than $|L_2|$.

Hence, $\frac{dG}{dt} = L_1 + L_2 \leq 0$.

Noting that $L_1 + L_2 = 0$ if $(S, E, I, T, V, R) = (S^e, E^e, I^e, T^e, V^e.R^e)$. By La Salle's invariance principle the endemic equilibrium, Q^e is globally asymptotically stable [21]. □

5. Sensitivity analysis

In this section, we conducted an analysis of the contributions of each parameter to the basic reproductive number [22, 23]. Sensitivity analysis helps determine which parameter contributes positively or negatively to the basic reproduction number. Sensitivity index of $\mathcal{R}_0$ with respect to some parameter, say ρ is given by: $\Lambda_\rho^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \rho} \frac{\rho}{\mathcal{R}_0}$

Table 1: parameter and sensitivity indices.

Parameter	Sensitivity Index
β_1	0.6058
β_2	0.3942
μ_1	1.0001
μ_2	-3.7908
σ_1	-0.9599
σ_3	0.1511
σ_4	-0.0832
α	0.1415
η	0.0755
λ	-0.5931

From Table 1, the parameters β_1,β_2,σ_3, α and η have positive sensitivity indices. They have a high impact on the transmission dynamics and prevalence of Hepatitis B.

However,μ_2,σ_1,σ_4 and λ have negative sensitivity indices. Hence, they have high influence on controlling and combating Hepatitis B infections.

6. Bifurcation analysis

In this section, we carried out the phenomenon of backward bifurcation by aplying the centre manifold theory on the sysyem of equations in (2) as outlined in [24]. The phenomenon of backward bifurcation exists only in situations where

disease free equilibrium (DFE) and disease endemic equilibrium (EE) coexists [25, 26]. The epidemiological implications is that the idea that whenever $R_0 < 1$, the disease can be controled is no longer a sufficient condition. Our model exhibited the phenomenon of backward bifurcation and the bifurcation diagram in 2 supports our theoretical analysis.

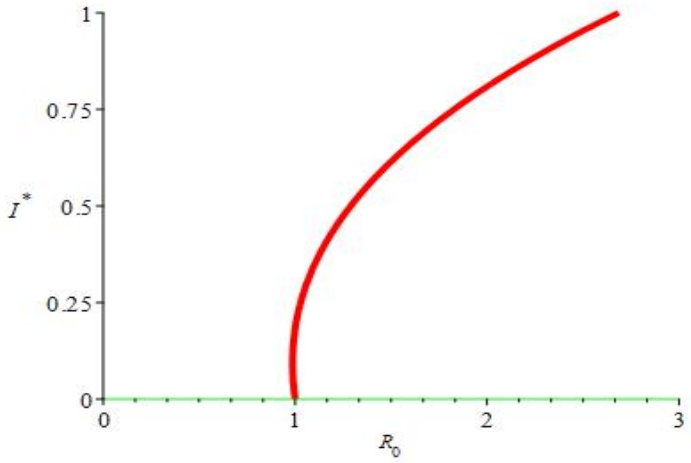

Figure 2: Backward Bifurcation

7. Numerical results

This section discusses the effect of limited medical resources on the spread of the disease. Controlling and preventing the spread of hepatitis B using treatment and vaccination require medical resources. The smaller the resources, the smaller the rates of vaccination and treatment. So in the simulation, we vary the rates of treatment and vaccination to determine the dynamics of the disease over time. The essence of controlling hepatitis B is to decrease the infectious population and increase recovery population. We examine the effects of different rates of vaccination and treatment on the performance criteria.

8. Population dynamics of susceptible, infectious and recovered

Figure 3 shows the population dynamics of susceptible, infectious and the recovered population with time. As the susceptible population decreases with, there is an increase in the number of people infected with hepatitis B. This implies that as the susceptible interact with the infected, the number of people getting infected with hepatitis B increases.

Moreover, as the number of infectious increases, there is a corresponding increase in the number of recovery. This shows that contact rate and recovery rate are directly proportional as shown in Figure 3.

Table 2: Numerical Values

Parameter	Value	Reference
β_1	0.0400	[27]
β_2	0.002	[28]
μ_1	0.0196	[28]
μ_2	0.0096	[28]
p_1	0.6500	Assumed
p_2	0.0025	Assumed
σ_1	0.2500	[27]
σ_3	0.0020	Assumed
σ_4	0.0025	[28]
α	0.0550	Assumed
η	0.0010	Assumed
λ	0.4500	Assumed

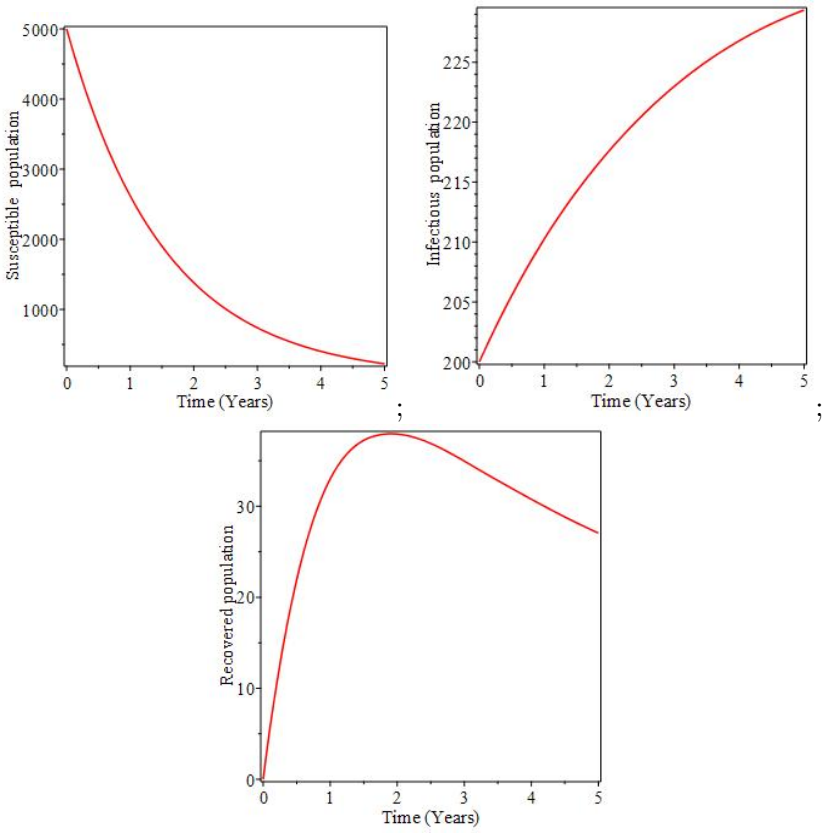

Figure 3: The population dynamics of susceptible, infectious and the recovered

8.1 Effects of contact rate on the infectious population

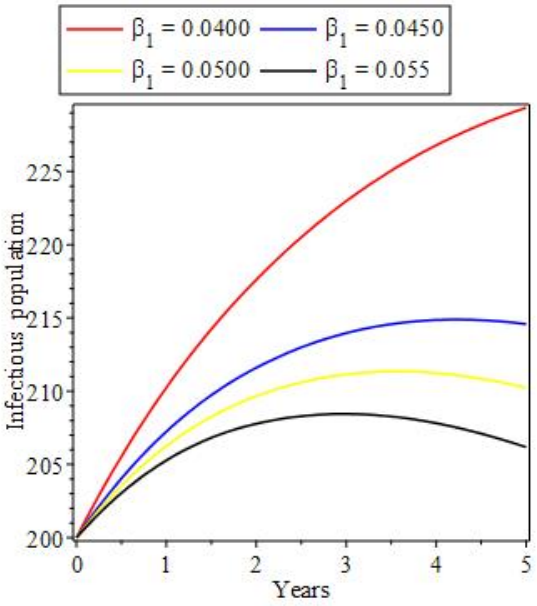

Figure 4: Model flow diagram

An analysis of the effects of interaction between the susceptible and infectious populations was investigated. This was done by varying the contact rate as shown in Figure 4.

As the value of the contact rate reduces, the population infected with hepatitis B decreases and vice versa. Hence, the infection can be controlled by ensuring that the contact rate reduces to the barest minimum as shown in Figure 4.

8.2 Effects of treatment rate on the recovered population

An analysis of the effects of treatment on the recovered populations was investigated. This was done by varying the contact rate as shown in Figure 5.

As the value of the treatment rate reduces, the population recovered from hepatitis B decreases and vice versa. Hence, the recovery can be achieved by ensuring that recovery rate increases to the barest minimum as shown in Figure 5.

9. Conclusion

A mathematical model of Hepatitis B with treatment and vaccination as compartments was developed and analysed as shown in Figure 1.

The local and global stability of the hepatitis B model was analysed using the Routh Hurwitz criteria. It was established that depending on the control

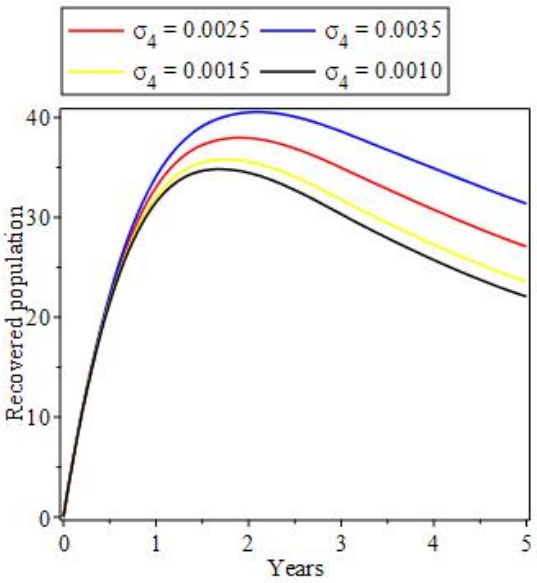

Figure 5: Model flow diagram

strategies authorities adopt, the disease can persist or get eliminated from the region.

The model was simulated to see the population dynamics of disease by plotting the susceptible, infectious and recovered populations inddividually. It was established the susceptible population decreases as the number of infected persons increases. Moreover, there is an increase in the number of persons recovered from hepatitis B as the number of infectious increases.

Additionally, the effects of treatment and contact rate was analysed numerically. As the value of the contact rate reduces, the population infected with hepatitis B decreases and vice versa. Hence, the infection can be controlled by ensuring that the contact rate reduces to the barest minimum as shown in Figure 4. As the value of the treatment rate reduces, the population recovered from hepatitis B decreases and vice versa. Hence, the recovery can be achieved by ensuring that recovery rate increases to the barest minimum as shown in Figure 5.

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References

[1] Mauro Manno, Calogero Cammà, Filippo Schepis, Fabio Bassi, Roberta Gelmini, Francesco Giannini, Francesca Miselli, Antonella Grottola, Ilva Ferretti, Chiara Vecchi, et al, *Natural history of chronic hbv carriers in northern Italy: morbidity and mortality after 30 years,* Gastroenterology, 127 (2004), 756-763.

[2] Resat Ozaras and Dominique Salmon-Ceron, *Viral hepatitis: chronic Hepatitis C*, Springer, 2019.

[3] Jia-Horng Kao, *Diagnosis of Hepatitis B virus infection through serological and virological markers,* Expert Review of Gastroenterology & Hepatology, 2 (2008), 553-562.

[4] NY Rots, AJ Wijmenga-Monsuur, W Luytjes, P Kaaijk, TW De Graaf, BAM van der Zeijst, and CJP Boog, *Hepatitis B vaccination strategies tailored to different endemicity levels: some considerations,* Vaccine, 28 (2010), 893-900.

[5] Peter A Revill, Francis V Chisari, Joan M Block, Maura Dandri, Adam J Gehring, Haitao Guo, Jianming Hu, Anna Kramvis, Pietro Lampertico, Harry LA Janssen, et al, *A global scientific strategy to cure Hepatitis B,* The Lancet Gastroenterology & Hepatology, 4 (2019), 545-558.

[6] Mehlika Toy, IK Veldhuijzen, MC Mostert, RA De Man, and Jan Hendrik Richardus, *Transmission routes of Hepatitis B virus infection in chronic Hepatitis B patients in the Netherlands,* Journal of Medical Virology, 80 (2008), 399-404.

[7] Yin-Chu Chien, Chyi-Feng Jan, Hsu-Sung Kuo, and Chien-Jen Chen, *Nationwide Hepatitis B vaccination program in Taiwan: effectiveness in the 20 years after it was launched,* Epidemiologic Reviews, 28 (2006), 126-135.

[8] Kevin M De Cock, Benoit Soro, Issa Malick Coulibaly, and Sebastian B Lucas, *Tuberculosis and hiv infection in sub-Saharan Africa,* Jama, 268 (1992), 1581-1587.

[9] Colin W Shepard, Edgar P Simard, Lyn Finelli, Anthony E Fiore, and Beth P Bell, *Hepatitis B virus infection: epidemiology and vaccination,* Epidemiologic Reviews, 28 (2006), 112-125.

[10] Rajani Ravi, Bijoyesh Mookerjee, Zaver M Bhujwalla, Carrie Hayes Sutter, Dmitri Artemov, Qinwen Zeng, Larry E Dillehay, Ashima Madan, Gregg L Semenza, and Atul Bedi, *Regulation of tumor angiogenesis by p53-induced degradation of hypoxia-inducible factor 1α,* Genes & development, 14 (2000), 34-44.

[11] Shaibu Osman and Oluwole Daniel Makinde, *A mathematical model for co-infection of listeriosis and anthrax diseases,* International Journal of Mathematics and Mathematical Sciences, 2018.

[12] Oluwole Daniel Makinde, *Adomian decomposition approach to a sir epidemic model with constant vaccination strategy,* Applied Mathematics and Computation, 184 (2007), 842-848.

[13] Shaibu Osman, Houenafa Alain Togbenon, and Dominic Otoo, *Modelling the dynamics of campylobacteriosis using nonstandard finite difference approach with optimal control,* Computational and Mathematical Methods in Medicine, 2020, 2020.

[14] Joan Kavuti Kanyaa, Shaibu Osman, and Mary Wainaina, *Mathematical modelling of substance abuse by commercial drivers,* Global Journal of Pure and Applied Mathematics, 14 (2018), 1149-1165.

[15] Dominic Otoo, Getachew Teshome Tilahun, Shaibu Osman, and Getinet Alemayehu Wole, *Modeling the dynamics of tuberculosis with drug resistance in north shoa zone, oromiya regional state, Ethiopia,* Commun. Math. Biol. Neurosci., 2021: Article-ID, 2021.

[16] Oluwole Daniel Makinde and Kazeem O Okosun, *Impact of chemo-therapy on optimal control of malaria disease with infected immigrants,* BioSystems, 104 (2011), 32-41.

[17] Getachew Teshome Tilahun, Oluwole Daniel Makinde, and David Malonza, *Modelling and optimal control of pneumonia disease with cost-effective strategies,* Journal of Biological Dynamics, 11 (2017), 400-426.

[18] Shaibu Osman, *Mathematical modelling of anthrax and listeriosisco-dynamics with optimal control*, PhD Thesis, PAUST, JKUAT, 2019.

[19] Kazeem Oare Okosun and Oluwole Daniel Makinde, *Optimal control analysis of Hepatitis C virus with acute and chronic stages in the presence of treatment and infected immigrants,* International Journal of Biomathematics, 7 (2014), 1450019.

[20] Getachew Teshome Tilahun, *Modeling co-dynamics of pneumonia and meningitis diseases,* Advances in Difference Equations, 2019 (2019), 149.

[21] Shaibu Osman, Dominic Otoo, and Charles Sebil, *Analysis of listeriosis transmission dynamics with optimal control,* Applied Mathematics, 11 (2020), 712-737.

[22] Shaibu Osman, Dominic Otoo, Charles Sebil, and Oluwole Daniel Makinde, *Bifurcation, sensitivity and optimal control analysis of modelling anthrax-listeriosis co-dynamics,* Commun. Math. Biol. Neurosci., 2020: Article-ID, 2020.

[23] Shaibu Osman, Oluwole Daniel Makinde, and David Mwangi Theuri, *Mathematical modelling of listeriosis epidemics in animal and human population with optimal control,* Tamkang Journal of Mathematics, 51 (2020), 261-287.

[24] Shaibu Osman, Dominic Otoo, Oluwole Daniel Makinde, et al, *Modeling anthrax with optimal control and cost effectiveness analysis,* Applied Mathematics, 11 (2020), 255.

[25] Shaibu Osman, Oluwole Daniel Makinde, and David Mwangi Theuri, *Stability analysis and modelling of listeriosis dynamics in human and animal populations,* Global Journal of Pure and Applied Mathematics, 14 (2018), 115-137.

[26] Shaibu Osman, Oluwole Daniel Makinde, and David Mwangi Theuri, *Mathematical modelling of transmission dynamics of anthrax in human and animal population,* Mathematical Theory and Modelling, 2018.

[27] Remigius Okeke Aja and David Omale, *Stability analysis of the transmission dynamics of Hepatitis B virus infection with controls in a population.*

[28] Reza Akbari, Ali Vahidian Kamyad, Aghileh Heydari, et al. *The analysis of a disease-free equilibrium of Hepatitis B model,* Sahand Communications in Mathematical Analysis, 3 (2016), 1-11.

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