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Modeling Anthrax with Optimal Control and Cost Effectiveness Analysis

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Abstract

Anthrax is an infection caused by bacteria and it affects both human and animal populations. The disease can be categorized under zoonotic diseases and humans can contract infections through contact with infected animals, ingest contaminated dairy and animal products. In this paper, we developed a mathematical model for anthrax transmission dynamics in both human and animal populations with optimal control. The qualitative solution of the model behaviour was analyzed by determining R_{hv}, equilibrium points and sensitivity analysis. A vaccination class was incorporated into the model with waning immunity. Local and global stability of the model's equilibria was found to be locally asymptotically stable whenever $R_{hv} < 1$ and unstable otherwise. Analysis of parameter contribution was conducted to determine the contribution of each to R_{hv}. It was revealed that reducing animal and human interaction rate, would decrease R_{hv}. We extended the model to optimal control in order to find the best control strategy in reducing anthrax infections. It showed that the effective strategy in combating the anthrax epidemics is vaccination of animals and prevention of humans.

Keywords

Anthrax Model, Stability Analysis, Sensitivity, Optimal Control, Cost Effectiveness

1. Introduction

Anthrax is an infectious disease that is caused by the bacteria *Bacillus anthracis*. The disease affects wild, domestic animals and humans. Susceptible individuals

contract the anthrax disease if they interact with infected animals or consumed contaminated dairy and animal products. Anthrax is a zoonotic disease found naturally in the soil and it affects both animal and human populations worldwide. Individuals can contract the disease from direct contact with animals or from contaminated animal products [1] [2].

Mathematical models are capable of describing a natural phenomenon and the transmission dynamics of infectious diseases. These models play a key role in combating infectious diseases in epidemiology. These models can explicitly explain the transmission mechanism and dynamics of disease [3] [4]. Complex models for transmission dynamics of diseases such as periodic orbits, Hoff bifurcations and multiple equilibrium have been proposed and worked on for some time now. They give a concise qualitative illustration of the disease dynamics and better analysis and implications for disease prediction of [5] [6].

[1] investigated the effects of constant vaccination on anthrax model but never considered effects of optimal control. From the theoretical results of their study under constant vaccination, the transmission of the disease model is similar to dynamics without vaccination. Moreover, [7] developed a model by considering vaccine impact and concluded by establishing the optimal vaccine coverage threshold required for disease eradication. However, [8] used optimal control in the study of a nonlinear SIR epidemic model with a vaccination strategy.

[9] considered the application of optimal control to investigate the impact of chemo-therapy on malaria disease with infection immigrants and [10] applied optimal control methods associated with preventing exogenous reinfection based on a exogenous reinfection tuberculosis model. Authors in [11], investigated the essential role of three basic controls: personal protection, treatment, and mosquito reduction strategies in combating an infectious disease.

However, [12] formulated a general epidemic model of a vector-borne disease
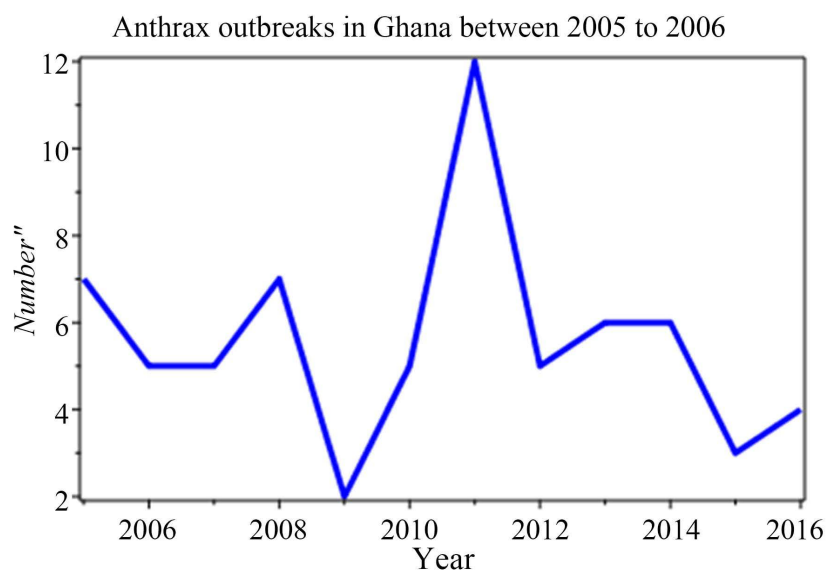
Figure 1. Cases of anthrax outbreaks in Ghana between 2005-2016.

consisting two vertebrate host species and one insect vector species. The qualitative analysis of the study revealed that model exhibited a multiple endemic equilibrium. The spread of anthrax has an impact on the life's of people and cost of treatment is of concern in every human endeavour. Many studies in literature have been performed to establish the role of vaccination and treatment on transmission of diseases [13].

Some studies reveal the complex nature of the anthrax disease. The transmission dynamics of the disease varies depending on the prevailing conditions of the country. There has not been any mathematical model developed to explain the transmission dynamics of anthrax with optimal control and cost effectiveness in Ghana. We therefore developed a model to investigate the dynamics of anthrax with optimal control and cost effectiveness analysis using the anthrax data between 2005 to 2016 as shown in Figure 1.

2. Model Formulation and Description

The model divides human and animal populations at any time, (t) into compartments with respect to their disease status as shown in Figure 2. Total animal population, $N_v(t)$, is subdivided into Susceptible animals, (S_v), Infectious animals, (I_v), Vaccinated animals, (V_v), and Recovered animals, (R_v).

Hence total animal population;

$$N_v(t) = S_v(t) + V_v(t) + I_v(t) + R_v(t). \tag{1}$$

Total human population denoted by N_h, is subdivided into Susceptible humans, (S_h), Infectious humans, (I_h), and Recovered, (R_h).

Hence, total human population:

$$N_h(t) = S_h(t) + I_h(t) + R_h(t). \tag{2}$$

Susceptible humans to are recruited at a rate Λ_h. Humans acquire anthrax through direct contact, inhalation and ingestion of contaminated animal products at a rate $(I_h + I_v)\beta$. Infected humans recover from anthrax disease at a rate γ. Humans infected with anthrax die at a rate δ_h and the recovered humans may loose immunity and return to the susceptible class at a rate σ_h. The entire human population has a natural death rate of μ_h.

Susceptible animals are recruited at a rate Λ_v, only a fraction of the animals are successfully vaccinated at a rate u_3, where $u_3 \in [0,1]$. The disease can be obtained through contacts with infectious animals and humans at a rate $(I_h + I_v)\lambda$. Natural death rate of all animal compartments is μ_v and death rate as a result of anthrax infections is δ_v. Animal recovery rate is α and vaccinated animals may move to the infected class at a rate $b\beta_m^*\lambda$ due to waning effect. Where $(1-b) \in [0,1]$ is the efficacy of the vaccine. Rate at which animals may loose immunity and join susceptible class is τ. Where $\beta_m^* = I_h + I_v$

The system of ordinary differential equations obtained from the model in Figure 2 are as follows:
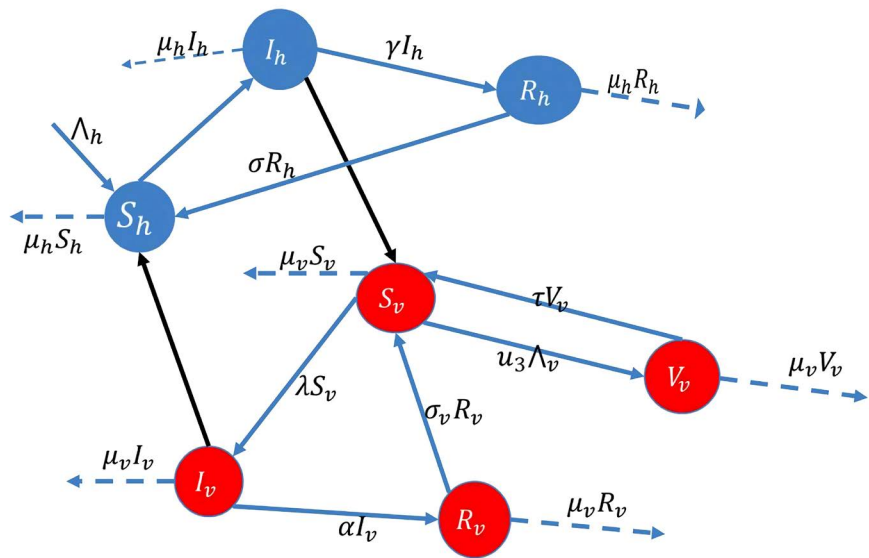
Figure 2. Flow diagram for the anthrax disease transmission dynamics.

$$\frac{\mathrm{d}S_h}{\mathrm{d}t} = \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h$$

$$\frac{\mathrm{d}I_h}{\mathrm{d}t} = \beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h$$

$$\frac{\mathrm{d}R_h}{\mathrm{d}t} = \gamma I_h - (\sigma_h + \mu_h) R_h$$

$$\frac{\mathrm{d}S_v}{\mathrm{d}t} = (1 - u_3)\Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v + \tau V_v \qquad (3)$$

$$\frac{\mathrm{d}I_v}{\mathrm{d}t} = \beta_m^* \lambda S_v + b\beta_m^* \lambda V_v - \alpha I_v - (\mu_v + \delta_v) I_v$$

$$\frac{\mathrm{d}R_v}{\mathrm{d}t} = \alpha I_v - (\sigma_v + \mu_v) R_v$$

$$\frac{\mathrm{d}V_v}{\mathrm{d}t} = u_3 \Lambda_v - (\tau + \mu_v) V_v - b\lambda \beta_m^* V_v$$

3. Model Analysis

3.1. Positivity and Boundedness of Solutions

In epidemiological models, conditions under which the system should have non-negative solutions is paramount. The model would be biologically meaningful if all the solutions with positive initial conditions remain positive at every point in time.

Theorem 1. *Let* $\Pi = \left\{ \left(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t) \right) \in \mathbb{R}_+^7 : \left(S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), V_v(0), R_v(0) \right) > 0 \right\}$,

then the solution of $\left\{ \left(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t) \right) \right\}$ are non-negative for all time $t \geq 0$.

Hence, if $S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), V_v(0), R_v(0)$, then $S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t)$ are also non-negative for all $t > 0$.

Human total population at any given time:

$$N_h(t) = S_h(t) + I_h(t) + R_h(t). \tag{4}$$

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_h}{dt} + \frac{dR_h}{dt}. \tag{5}$$

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h S_h - (\mu_h + \delta_h) I_h - (\sigma_h + \mu_h) R_h.$$

In the absence of mortality due to Anthrax infections, the above equation becomes;

$$\frac{dN_h}{dt} \leq \Lambda_h - \mu_h N_h. \tag{6}$$

Solving the equation and as $t \to \infty$, the population size, $N_h \to \dfrac{\Lambda_h}{\mu_h}$.

$$0 \leq N_h \leq \frac{\Lambda_h}{\mu_h} \quad \text{and} \quad N_h(t) \leq \frac{\Lambda_h}{\mu_h}.$$

Also, if

$$N_h(0) \leq \frac{\Lambda_h}{\mu_h}, \text{ then } N_h(t) \leq \frac{\Lambda_h}{\mu_h}.$$

$$\Pi_h = \left\{ (S_h, I_h, R_h) \in \mathbb{R}_3^3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\} \tag{7}$$

However, for total animal (vector) population at any given time:

$$N_v(t) = S_v(t) + V_v(t) + I_v(t) + R_v(t). \tag{8}$$

$$\frac{dN_v}{dt} = \frac{dS_v}{dt} + \frac{dV_v}{dt} + \frac{dI_v}{dt} + \frac{dR_v}{dt}. \tag{9}$$

$$\frac{dN_v}{dt} = \Lambda_v - \mu_v N_v - \delta_v I_v.$$

$$\frac{dN_v}{dt} \leq \Lambda_v - \mu_v N_v. \tag{10}$$

Solving the differential equation and as $t \to \infty$, the population size, $N_v \to \dfrac{\Lambda_v}{\mu_v}$.

$$0 \leq N_v \leq \frac{\Lambda_v}{\mu_v} \quad \text{and} \quad N_v(t) \leq \frac{\Lambda_v}{\mu_v}.$$

Also, if

$$N_v(0) \leq \frac{\Lambda_v}{\mu_v}, \text{ then } N_v(t) \leq \frac{\Lambda_v}{\mu_v}.$$

$$\Pi_v = \left\{ (S_v, I_v, R_v, V_v) \in \mathbb{R}_+^4 : S_v + I_v + R_v + V_v \leq \frac{\Lambda_v}{\mu_v} \right\}. \tag{11}$$

Hence, feasible region for the dynamical system in (1) is given by:

$$\Pi = \Pi_h \times \Pi_v \subset \mathbb{R}_+^3 \times \mathbb{R}_4^4. \tag{12}$$

$$\Pi_h = \left\{ (S_h, I_h, R_h) \in \mathbb{R}_3^3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\} \tag{13}$$

$$\Pi_v = \left\{ (S_v, I_v, R_v, V_v) \in \mathbb{R}_+^4 : S_v + I_v + R_v + V_v \leq \frac{\Lambda_v}{\mu_v} \right\}. \tag{14}$$

where Π is positively invariant.

3.2. Disease Free Equilibrium

The Disease Free Equilibrium (DFE) of the dynamical system in (3) only exists in the absence of infections. We can then compute DFE by setting the system of equations in (3) to zero and establish DFE points.

At DFE, there are no infections and recovery. Hence, $R_v^* = I_h^* = I_v^* = R_h^* = 0$.

$$\xi_0 = \left(S_h^*, I_h^*, R_h^*, S_v^*, I_v^*, R_v^*, V_v^* \right).$$

$$\left. \begin{aligned} \frac{dS_h}{dt} &= \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h = 0 \\ \frac{dV_v}{dt} &= u_3 \Lambda_v - (\tau + \mu_v) V_v - b\lambda \beta_m^* V_v = 0 \\ \frac{dS_v}{dt} &= (1 - u_3)\Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v + \tau V_v = 0 \end{aligned} \right\} \tag{15}$$

The DFE point is given by;

$$\xi_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v(\tau + \mu_v(1 - u_3))}{\mu_v(\tau + \mu_v)}, 0, 0, \frac{u_3 \Lambda_v}{\tau + \mu_v} \right). \tag{16}$$

3.3. The Basic Reproductive Number

Using the next generation matrix approach in [4], the reproductive rate can be established. The reproductive rate combines the biology of infections with the social and behaviour of the factors influencing contact rate.

The basic reproductive rate refers to the number of secondary cases one infectious individual will produce in a completely susceptible population [14] [15]. This is a threshold parameter that governs the spread of a disease.

Definition 2. *The spectral radius of a matrix A is defined as the maximum of the absolute values of the eigenvalues of the matrix A:* $\rho(A) = \sup\{|\lambda| : \lambda \in \rho(A)\}$, *where $\rho(A)$ denotes the set of eigenvalues of the matrix A.*

Considering only the infective compartments in the system of differential equations in (3):

$$\left. \begin{aligned} \frac{dI_h}{dt} &= (I_h + I_v)\beta S_h - \gamma I_h - (\mu_h + \delta_h)I_h \\ \frac{dI_v}{dt} &= (I_h + I_v)\lambda S_v + (I_h + I_v)b\lambda V_v - \alpha I_v - (\mu_v + \delta_v)I_v \end{aligned} \right\} \tag{17}$$

Let f be the number of new infection coming into the system and v be the number of infectives that are leaving the system either by death or birth.

$$f = \begin{bmatrix} (I_h + I_v)\beta S_h \\ (I_h + I_v)\lambda S_v + (I_h + I_v)b\lambda V_v \end{bmatrix},$$

$$v = \begin{bmatrix} \gamma I_h + (\mu_h + \delta_h) I_h \\ \alpha I_v + (\mu_v + \delta_v) I_v \end{bmatrix}.$$

The Jacobian matrix of f and v at DFE is obtained by F and V as follows:

$$F = \begin{bmatrix} \beta S_h^* & \beta S_h^* \\ \lambda S_v^* + b\lambda V_v^* & \lambda S_v^* + b\lambda V_v^* \end{bmatrix},$$

$$V = \begin{bmatrix} \gamma + (\mu_h + \delta_h) & 0 \\ 0 & \alpha + (\mu_v + \delta_v) \end{bmatrix}.$$

Computing the product of FV^{-1}.

$$FV^{-1} = \begin{bmatrix} \dfrac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} & \dfrac{\beta S_h^*}{\alpha + (\mu_v + \delta_v)} \\ \dfrac{\lambda S_v^* + b\lambda V_v^*}{\gamma + (\mu_h + \delta_h)} & \dfrac{\lambda S_v^* + b\lambda V_v^*}{\alpha + (\mu_v + \delta_v)} \end{bmatrix}$$

By computing the eigenvalues of FV^{-1} and selecting the dominant eigenvalue. The eigenvalues are as follows;

$$0 \text{ and } \left[\left(\frac{\lambda S_v^* + b\lambda V_v^*}{\alpha + (\mu_v + \delta_v)} \right) + \left(\frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} \right) \right].$$

The dominant eigenvalue is $\left(\dfrac{\lambda S_v^* + b\lambda V_v^*}{\alpha + (\mu_v + \delta_v)} \right) + \left(\dfrac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} \right).$

This implies that the basic reproductive rate is given by;

$$R_{hv} = \left[\left(\frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} \right) + \left(\frac{\lambda S_v^* + b\lambda V_v^*}{[\alpha + (\mu_v + \delta_v)]} \right) \right]. \tag{18}$$

At DFE, it becomes;

$$R_{hv} = \left(\frac{\beta \Lambda_h}{\mu_h [\gamma + (\mu_h + \delta_h)]} \right) + \frac{b\lambda \Lambda_v (\tau + \mu_v (1 - 2u_3))}{\mu_v (\tau + \mu_v) [\alpha + (\mu_v + \delta_v)]} \tag{19}$$

where;

$$R_h = \left(\frac{\beta \Lambda_h}{\mu_h [\gamma + (\mu_h + \delta_h)]} \right), R_v = \frac{b\lambda \Lambda_v (\tau + \mu_v (1 - 2u_3))}{\mu_v (\tau + \mu_v) [\alpha + (\mu_v + \delta_v)]}.$$

3.4. Global Stability of the Disease-Free Equilibrium

Proposition 3. *The disease-free equilibrium* (*DFE*) *of model* (3) *is locally asymptotically stable if* $R_{hv} < 1$ *and unstable if* $R_{hv} > 1$.

Theorem 4. *If* $R_{hv} \leq 1$, *the disease-free equilibrium is globally asymptotically stable in the interior of* Ω.

Proof. Considering the Lyapunov function below, □

$$P(t) = (\alpha + \mu_v + \delta_v) I_h + (\gamma + \mu_h + \delta_h) I_v \tag{20}$$

Taking time derivative of $P(t)$ along solutions of the differential equations in (3);

$$\begin{aligned}
\frac{\mathrm{d}P(t)}{\mathrm{d}t} &= (\alpha + \mu_v + \delta_v)\frac{\mathrm{d}I_h}{\mathrm{d}t} + (\gamma + \mu_h + \delta_h)\frac{\mathrm{d}I_v}{\mathrm{d}t} \\
&= (\beta S_h(I_h + I_v) - \gamma I_h - (\mu_h + \delta_h)I_h) + \lambda S_v(I_h + I_v) \\
&\quad + b(I_h + I_v)\lambda V_v - \alpha I_v - (\mu_v + \delta_v)I_v \\
&\le (\alpha + \mu_v + \delta_v)\frac{\beta\Lambda_h I_h}{\mu_h} + (\alpha + \mu_v + \delta_v)\frac{\beta\Lambda_h I_v}{\mu_h} \\
&\quad - (\alpha + \mu_v + \delta_v)(\gamma + \mu_h + \delta_h)I_h \\
&\quad + I_h(\gamma + \mu_h + \delta_h)\left(\frac{\lambda\Lambda_v(\tau + \mu_v(I - u_3))}{\mu_v(\tau + \mu_v)}\right) \\
&\quad + I_v(\gamma + \mu_h + \delta)\left(\frac{\lambda\Lambda_v(\tau + \mu_v(I - u_3))}{\mu_v(\tau + \mu_v)}\right) \\
&\quad + I_h(\gamma + \mu_h + \delta_h)\left(\frac{bu_3\lambda\Lambda_v}{\tau + \mu_v}\right) + I_v(\gamma + \mu_h + \delta)\left(\frac{bu_3\lambda\Lambda_v}{\tau + \mu_v}\right) \\
&\quad - I_v(\gamma + \mu_h + \delta)(\alpha + \mu_v + \delta_v) \\
&\le -I_h(\gamma + \mu_h + \delta_h)(\alpha + \mu_v + \delta_v)(1 - R_{hv}) \\
&\quad - I_v(\gamma + \mu_h + \delta_h)(\alpha + \mu_v + \delta_v)(1 - R_{hv}) \\
&= -(I_h + I_v)(\gamma + \mu_h + \delta_h)(\alpha + \mu_v + \delta_v)(1 - R_{hv})
\end{aligned} \tag{21}$$

Time derivative of P along the solutions of differential equations in (3) yields:

$$\left(\frac{\mathrm{d}P(t)}{\mathrm{d}t}\right) \le 0, \text{ if and only if } R_{hv} < 0$$

$$\left(\frac{\mathrm{d}P(t)}{\mathrm{d}t}\right) = 1, \text{ if and only if } I_h + I_v = 0 \text{ or } R_{hv} = 1.$$

The highest compact invariant set in $S_h, I_h, I_v \in \Omega$, $\frac{\mathrm{d}P(t)}{\mathrm{d}t} = 0$, if $R_{hv} \le 1$, is the singleton, ξ_0.

It shows that ξ_0 is globally asymptotically stable in Ω. By LaSalle's invariant principle [16].

3.5. Endemic Equilibrium

Considering the system in 3, at equilibrium, $\beta_m^* = I_h + I_v = 0$. This corresponds to the DFE or the relation:

$$H_0\beta_m^{*3} + H_1\beta_m^{*2} + H_2\beta_m^* + H_3 = 0. \tag{22}$$

Remark. The system of equations in (3) would have an EE, E^*, if $R_{hv} > 1$. This is satisfied by cases (2, 4, 6) in **Table 1**. The system would have more than one EE point if $R_{hv} > 1$. This is satisfied by case (8) as shown in **Table 1**. The system in Equation (2.3), would have more than one EE point if $R_{hv} < 1$, as satisfied by case (3, 5, 7).

From **Table 1**, multiple EE exists when (R_{hv}) is less than unity. This indicates the tendency of backward bifurcation. This is a situation where the DFE and EE coexists. The existence of backward bifurcation has significant implication

Table 1. Possible positive real roots of $P\left(\beta_m^*\right)$ for $R_{hv} > 1$ and $R_{hv} < 1$.

Cases	H_0	H_1	H_2	H_3	R_{hv}	No. of sign change	No. of positive real roots
1	+	+	+	+	$R_{hv} < 1$	0	0
1	+	+	+	−	$R_{hv} > 1$	1	1
2	+	+	−	+	$R_{hv} < 1$	2	0, 2
2	+	+	−	−	$R_{hv} > 1$	1	1
3	+	−	−	+	$R_{hv} < 1$	2	0, 2
3	+	−	−	−	$R_{hv} > 1$	1	1
4	+	−	+	+	$R_{hv} < 1$	2	0, 2
4	+	−	+	−	$R_{hv} > 1$	3	1, 3

for epidemiological control measures because an epidemic may persist at steady state even when $\left(R_{hv} < 1\right)$.

3.6. Global Stability of Endemic Equilibrium

In this section, the global behaviour of the system in Equation (3) is analysed. Considering the non-linear Lyapunov function.

Theorem 5. *The system in Equation* (3), *is said to have a unique endemic equilibrium if* $R_{hv} > 1$, *and it is globally asymptotically stable.*

The EE can only exists if and only if $R_{hv} > 1$. So by letting $R_{hv} > 1$, it implies that the EE exists.

Considering the non-linear Lyapunov function bellow;

$$
\begin{aligned}
L = {} & S_h^{**}\left(\frac{S_h}{S_h^{**}} - \ln\frac{S_h}{S_h^{**}}\right) + I_h^{**}\left(\frac{I_h}{I_h^{**}} - \ln\frac{I_h}{I_h^{**}}\right) + \frac{g_1 R_h^{**}}{\gamma}\left(\frac{R_h}{R_h^{**}} - \ln\frac{R_h}{R_h^{**}}\right) \\
& + S_v^{**}\left(\frac{S_v}{S_v^{**}} - \ln\frac{S_v}{S_v^{**}}\right) + I_v^{**}\left(\frac{I_v}{I^{**}} - \ln\frac{I_v}{I_v^{**}}\right) \\
& + R_v^{**}\left(\frac{R_v}{R_h^{**}} - \ln\frac{R_v}{R^{**}}\right) + V_v^{**}\left(\frac{Vv}{V_v^{**}} - \ln\frac{V_v}{V_v^{**}}\right).
\end{aligned}
\tag{23}
$$

where;

$$
g_1 = \left(\gamma + \mu_h + \delta_h\right),\ \ g_2 = \left(\sigma_2 + \mu_h\right),
$$
$$
g_3 = \left(\alpha + \mu_v + \delta_v\right),\ \ g_4 = \left(\sigma_v + \mu_v\right),
$$

when the above Lyapunov function is differentiated with respect to time, we obtain the equation;

$$
\begin{aligned}
\frac{\mathrm{d}L}{\mathrm{d}t} = {} & \left(1 - \frac{S_h^{**}}{S_h}\right)\frac{\mathrm{d}S_h}{\mathrm{d}t} + \left(1 - \frac{I_h^{**}}{I_h}\right)\frac{\mathrm{d}I_h}{\mathrm{d}t} + \frac{g_1}{\gamma}\left(1 - \frac{R^{**}}{R_h}\right)\frac{\mathrm{d}R_h}{\mathrm{d}t} \\
& + \left(1 - \frac{S_v^{**}}{S_v}\right)\frac{\mathrm{d}S_v}{\mathrm{d}t} + \left(1 - \frac{I_v^{**}}{I_v}\right)\frac{\mathrm{d}I_v}{\mathrm{d}t} \\
& + \left(1 - \frac{R_v^{**}}{R_v}\right)\frac{\mathrm{d}R_v}{\mathrm{d}t} + \left(1 - \frac{V_v^{**}}{V_v}\right)\frac{\mathrm{d}V_v}{\mathrm{d}t}.
\end{aligned}
\tag{24}
$$

Therefore, this implies that;

$$
\begin{aligned}
\frac{\mathrm{d}L}{\mathrm{d}t} &= \left(1-\frac{S_h^{**}}{S_h}\right)\left[\Lambda_h + \sigma_h R_h^{**} + \beta\beta_m^{**} S_h^{**} + \mu_h S_h^{**} - \Lambda_h - \sigma R_h - \beta\beta_m S_h - \mu_h S_h\right] \\
&+ \left(1-\frac{I_h^{**}}{I_h}\right)\left[\beta\beta_m S_h - g_1 I_h\right] + \frac{g_1}{\gamma}\left(1-\frac{R_h^{**}}{R_h}\right)\left[\gamma I_h - g_2 R_h\right] \\
&+ \left(1-\frac{S_v^{**}}{S_v}\right)\Big[\left(1-u_3\right)\Lambda_v + \lambda\beta\beta_m^{**} S_v^{**} + \mu_v S_v^{**} + \sigma_v R_v^{**} + \tau V_v^{**} \\
&\quad - \left(1-u_3\right)\Lambda_v - \lambda\beta_m S_v - \mu_v S_v - \sigma_v R_v - \tau V_v\Big] \\
&+ \left(1-\frac{I_v^{**}}{I_v}\right)\left[\lambda\beta_m S_v + b\lambda\beta_m V_v - g_3 I_v\right] + \frac{g_3}{\alpha}\left(1-\frac{R_v^{**}}{R_v}\right)\left[\alpha I_v - g_4 R_v\right] \\
&+ \left(1-\frac{V_v^{**}}{V_v}\right)\left[u_3\Lambda_v + b\lambda\beta_m^{**} V_v^{**} + \left(\tau+\mu_v\right)V_v^{**} - u_3\Lambda_v - b\lambda\beta_m V_v - \left(\tau+\mu_v\right)V_v\right]
\end{aligned}
\tag{25}
$$

By further simplification;

Arithmetic mean value exceeds the geometric mean value [17] [18]. This follows that;

$$2-\frac{S_h^{**}}{S_h}-\frac{S_h}{S_h^{**}}\leq 0$$

$$1-\frac{R_h}{R_h^{**}}\leq 0$$

$$1-\frac{R_h^{**}}{R_h}-\frac{g_1 g_2 S_h}{\gamma S_h^{**}}\left(1-\frac{R_h^{**}}{R_h}\right)\leq 0$$

$$1-\frac{\beta_m}{\beta_h^{**}}-\frac{S_h^{**}}{S_h}-\frac{S_h\beta_m I_h^{**}}{S_h^{**}\beta_m^{**}}\leq 0$$

$$1-\frac{I_h}{I_h^{**}}-\frac{\gamma I_h}{I_h^{**}}\left(1-\frac{R_h^{**}}{R_h}\right)\leq 0$$

$$2-\frac{S_v^{**}}{S_v}-\frac{S_v}{S_v^{**}}\leq 0$$

$$1-\frac{S_v^{**}}{S_v}-\frac{R_v}{R_v^{**}}+\frac{R_v S_v^{**}}{R_v^{**}S_v}\leq 0$$

$$1-\frac{S_v^{**}}{S_v}-\frac{V_v}{V_v^{**}}-\frac{V_v S_v^{**}}{V_v^{**}S_v}\leq 0$$

$$1-\frac{S_v^{**}}{S_v}+\frac{\beta_m}{\beta_h^{**}}-\frac{S_v\beta_m I_v^{**}}{S_v^{**}\beta_m^{**}I_v}\leq 0$$

$$1-\frac{I_v}{I_v^{**}}-g_3\alpha\frac{I_v}{I_v^{**}}-g_3\alpha\frac{I_v R_v^{**}}{I_v^{**}R_v}\leq 0$$

$$1-\frac{R_v}{R_v^{**}}\leq 0$$

$$2-\frac{V_v^{**}}{V_v}-\frac{V_v}{V_v^{**}}\leq 0$$

$$1 - \frac{V_v^{**}}{V_v} + \frac{\beta_m}{\beta_h^{**}} - \frac{V_v \beta_m I_v^{**}}{V_v^{**} \beta_m^{**} I_v} \tag{26}$$

Since all model parameters are non-negative, then the derivative of the Lyapunov function is less than zero $\left(\frac{\mathrm{d}L}{\mathrm{d}t} \leq 0 \right)$, if the R_{hv} of the system in Equation (3) is greater than one. $(R_{hv} > 1)$. By LaSalle's Invariant Principle [16], as t approaches infinity, all the solution of the system approach the EE point if $R_{hv} > 1$.

Backward Bifurcation and Multiple Equilibrium

In this section, we discuss the phenomenon of Backward Bifurcation. The bifurcating EE point exists only if $(R_{hv} < 1)$. The model has exhibited this property and backward bifurcation exists. When backward bifurcation occurs, the range of R_{hv} is between $R_{hv}^* < R_{hv} < 1$. There exits at least one EE. Usually, at least one is stable and the DFE is not globally stable when $(R_{hv} < 1)$. In this scenario, the infection would exist even when $R_{hv} < 1$.

4. Sensitivity Analysis

Basically, the essence of sensitivity analysis is to determine the contribution of each parameter to the reproductive rate. This is help to identify the parameters with high impact on R_{hv}. The basic reproductive rate is usually analysed to find out whether or not treatment of the infectives, mortality and vaccination could help in the control or eradication of the disease in the population [19] [20].

Definition 6. *The normalised forward sensitivity index of a variable, y, which depends differentially on a parameter, x, defined as:*

$$\Upsilon_x^y = \frac{\partial y}{\partial x} \times \frac{x}{y}. \tag{27}$$

Sensitivity Indices of R_{hv}

In epidemiological models, the value of R_{hv} determines the ability of the infection to spread within the population. We will determine the reduction in infection due to the diseases by computing the sensitivity indices of R_{hv}, with respect to the parameter values in the model. The sensitivity indices serve as determinants of the contribution of each parameter in the dynamics of the diseases. Considering all the parameters of the system in model (3), we derive the sensitivity of R_{hv} to each of the parameters in the model.

The sensitivity indices of R_{hv} with respect to each of the parameters of the system in model (3), are given in Table 2.

The detailed sensitivity analysis of (R_{hv}) showed that increasing α would decrease R_{hv}. Moreover, decreasing α would increase (R_{hv}). Also, an increase in the values of Λ_h, Λ_v, β and λ would cause an increase in R_{hv} and a decrease in the values of Λ_h, Λ_v, β and λ would cause a decrease in R_{hv}.

Table 2. Sensitivity indices of parameters to R_{hv}.

Parameter	Description	Sensitivity index (+ve/−ve)
Λ_h	recruitment rate of humans	+ve
Λ_v	recruitment rate of animals	+ve
μ_h	human natural death rate	−ve
μ_v	animal natural death rate	−ve
δ_h	disease induced death rate in humans	−ve
δ_v	disease induced death rate in animals	−ve
u_3	vaccinated proportion	−ve
α	recovery rate of animals	−ve
β	transmission rate of humans	+ve
γ	recovery rate of humans	−ve
τ	waning rate	+ve
λ	animals transmission rate	+ve
b	vaccine efficacy	+ve

5. Optimal Control of the Anthrax Model

The essence optimal control in disease modelling to to determine the best control strategy in fighting the spread of the infection and the costs associated with this strategy. This analysis is carried out to establish the impact of various intervention schemes. Optimal control problem is established by introducing controls into the Anthrax model (3) and the formation of an objective functional which seeks to minimise: (u_1, u_2, u_3, u_4).

Preventive control measure on susceptible humans, (u_1): This is to reduce the acquisition of the disease. Treatment control on infected humans, (u_2): This is to minimise infections. Vaccination as a control measure on susceptible animals, (u_3): By using antimicrobial drugs. Treatment control on infected animals, (u_4): This is to reduce infections.

The objective functional in achieving this purpose is as follows:

$$J = \min_{u_1, u_2, u_3, u_4} \int_0^{t_f} \left(A_1 I_v + A_2 I_h + A_3 u_1^2 + A_4 u_2^2 + A_5 m u_3^2 + A_6 u_4^2 \right) \mathrm{d}t. \tag{28}$$

subject to the system in (3). Where; $(A_1, A_2, A_3, A_4, A_5, A_5)$ are generally referred as balancing cost factors (weight constants) to help balance all terms in the integral thereby avoiding dominance of one over the other. $A_1 I_h, A_2 I_v$ are the costs associated with I_h and I_v. $A_3 u_1^2$ is the cost associated with S_h. $A_5 m u_3^2$ is the cost associated with vaccination of S_v and m is the number of I_v. $A_4 u_2^2$ is the costs of treatment of I_h. $A_6 u_4^2$ is the cost of treatment of I_v. t_f is intervention period. $A_1 I_h, A_2 I_v$ represents a linear function for cost of infection and $A_3 u_1^2, A_4 u_2^2, A_5 m u_3^2, A_6 u_4^2$ denotes a quadratic function for cost of controls.

Control efforts of model is by linear combination $u_i^2(t)$, $(i = 1, 2)$. A qua-

dratic in nature by assumption that cost is non-linear naturally [21] [22] [23]. The purpose is to reduce infection and cost of treatment.

This is finding the optimal functions; $\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t) \right)$ such that;

$$J\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t) \right) = \min_{u_1, u_2, u_3, u_4 \in \bigcup} J\left(u_1, u_2, u_3, u_4 \right) \tag{29}$$

where;

$\bigcup = \left\{ u : u, 0 \le u_i(t) \le 1, t \in \left[0, t_f \right], i = 1, 2, 3, 4 \right\}$ and is called the control set.

Pontryagin's Maximum Principle

This principle gives the necessary conditions that an optimal must satisfy. It changes the system in (3) and (29) into minimisation problem point-wise Hamiltonian, (*H*) with respect to $\left(u_1, u_2, u_3, u_4 \right)$.

$$\begin{aligned}
H = {} & A_1 I_v + A_2 I_h + A_3 u_1^2 + A_4 u_2^2 + A_5 m u_3^2 + A_6 u_6^2 \\
& + \lambda_1 \left\{ \Lambda_h + \sigma_h R_h - (1 - u_1) \beta (I_v + I_h) S_h - \mu_h S_h \right\} \\
& + \lambda_2 \left\{ (1 - u_1) \beta_m^* \beta S_h - (u_2 + \gamma) I_h - (\mu_h + \delta_h) I_h \right\} \\
& + \lambda_3 \left\{ (u_2 + \gamma) I_h - (\sigma_h + \mu_h) R_h \right\} \\
& + \lambda_4 \left\{ (1 - u_3) \Lambda_v - (1 - u_1) \lambda (I_v + I_h) S_v - (\mu_v S_v + \sigma_v R_v + \tau V_v) \right\} \\
& + \lambda_5 \left\{ (1 - u_1) \beta_m^* \lambda S_v + (1 - u_1) b \beta_m^* \lambda V_v - (u_4 + \alpha) I_v - (\mu_v + \delta_v) I_v \right\} \\
& + \lambda_6 \left\{ (u_4 + \alpha) I_v - (\sigma_v + \mu_v) R_v \right\} \\
& + \lambda_7 \left\{ u_3 \Lambda_v - (\tau + \mu_v) V_v - (1 - u_1) b \lambda (I_v + I_h) V_v \right\}
\end{aligned} \tag{30}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6$ and λ_7 are the adjoint variables.

The solutions of adjoint are system;

$$\left. \begin{aligned}
\frac{d\lambda_1}{dt} &= (1 - u_1)(I_v + I_h)\beta(\lambda_1 - \lambda_2) + \mu_h \lambda_1 \\
\frac{d\lambda_2}{dt} &= -A_2 + (1 - u_1)\beta S_h(\lambda_1 - \lambda_2) + (u_2 + \gamma)(\lambda_2 - \lambda_3) + \lambda_2(\mu_h + \delta_h) \\
&\quad + (1 - u_1)\lambda S_v(\lambda_4 - \lambda_5) + (1 - u_1)b\lambda V_v(\lambda_7 - \lambda_5) \\
\frac{d\lambda_3}{dt} &= -\sigma_h \lambda_1 + (\sigma_h + \mu_h)\lambda_3 \\
\frac{d\lambda_4}{dt} &= (1 - u_1)\lambda(I_v + I_h)(\lambda_4 - \lambda_5) + \mu_v \lambda_4 \\
\frac{d\lambda_5}{dt} &= -A_1 + (1 - u_1)\beta S_h(\lambda_1 - \lambda_2) + (1 - u_1)\lambda S_v(\lambda_4 - \lambda_5) \\
&\quad + b\lambda(\lambda_7 - \lambda_5)V_v + (\lambda_5 - \lambda_6)(u_4 + \alpha) + \lambda_5(\mu_v + \delta_v) \\
\frac{d\lambda_6}{dt} &= -\sigma_v \lambda_4 + (\sigma_v + \mu_v)\lambda_6 \\
\frac{d\lambda_7}{dt} &= -\tau \lambda_4 + (1 - u_1)b\lambda(I_v + I_h)(\lambda_7 - \lambda_5) + (\tau + \mu_v)\lambda_7
\end{aligned} \right\} \tag{31}$$

which satisfies the transversality condition;

$$\lambda_1(tf) = \lambda_2(tf) = \lambda_3(tf) = \lambda_4(tf) = \lambda_5(tf) = \lambda_6(tf) = \lambda_7(tf) = 0. \tag{32}$$

By combining the Pontryagin's Maximum Principle and the existence of optimal control [24] [25].

Theorem 7. *The optimal control vector* $\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)\right)$ *that maximizes the objective function* (J) *over* $\cup$, *given by*;

$$
u_1^*(t) = \max\left\{0, \min\left(1, \frac{\beta(\lambda_2 - \lambda_1)(I_v + I_h)S_h^*}{2A_3}\right.\right.
$$

$$
\left.\left. + \frac{\lambda(\lambda_5 - \lambda_4)(I_v + I_h)S_v^* + b\lambda(\lambda_5 - \lambda_7)(I_v + I_h)V_v^*}{2A_3}\right)\right\}
$$

$$
u_2^*(t) = \max\left\{0, \min\left(1, \frac{(\lambda_2 - \lambda_3)I_h^*}{2A_4}\right)\right\} \tag{33}
$$

$$
u_3^*(t) = \max\left\{0, \min\left(1, \frac{\Lambda_v(\lambda_4 - \lambda_7)}{2mA_5}\right)\right\}
$$

$$
u_4^*(t) = \max\left\{0, \min\left(1, \frac{\alpha(\lambda_5 - \lambda_6)I_v^*}{2A_6}\right)\right\}
$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6$ and λ_7 are the solutions of Equation (31) and Equation (32).

Proof. Optimal control exists as a result the convexity of the integral of J w.r.t u_1, u_2, u_3 and u_4, Lipschitz property of the state system with respect to the state variables and a priori boundedness of the state solutions [9]. The system in (31) was obtained by differentiating the Hamiltonian function evaluated at optimal control. By equating the derivatives of Hamiltonian with respect to the controls to zero, we obtained the following;

$$
u_1 = \tilde{u}_1 := \left\{\left(\frac{\beta(\lambda_2 - \lambda_1)(I_v + I_h)S_h^*}{2A_3}\right.\right.
$$

$$
\left.\left. + \frac{\lambda(\lambda_5 - \lambda_4)(I_v + I_h)S_v^* + b\lambda(\lambda_5 - \lambda_7)(I_v + I_h)V_v^*}{2A_3}\right)\right\}
$$

$$
u_2 = \tilde{u}_2 := \left\{\left(\frac{(\lambda_2 - \lambda_3)I_h^*}{2A_4}\right)\right\}
$$

$$
u_3 = \tilde{u}_3 := \left\{\left(\frac{\Lambda_v(\lambda_4 - \lambda_7)}{2mA_5}\right)\right\} \text{ and}
$$

$$
u_4 = \tilde{u}_4 := \left\{\left(\frac{(\lambda_5 - \lambda_6)I_v^*}{2A_6}\right)\right\}
$$

By standard control arguments which involve bounds on the controls, it can be concluded that;

$$
u_1^* = \begin{cases} 0, & \text{if } \tilde{u}_1 \leq 0 \\ \tilde{u}_1 & \text{if } 0 < \tilde{u}_1 < 1 \\ 1 & \text{if } \tilde{u}_1 \geq 1 \end{cases}, \quad u_2^* = \begin{cases} 0, & \text{if } \tilde{u}_2 \leq 0 \\ \tilde{u}_2 & \text{if } 0 \prec < \tilde{u}_2 < 1 \\ 1 & \text{if } \tilde{u}_2 \geq 1 \end{cases}
$$
$$
u_3^* = \begin{cases} 0, & \text{if } \tilde{u}_3 \leq 0 \\ \tilde{u}_3 & \text{if } 0 < \tilde{u}_3 < 1 \\ 1 & \text{if } \tilde{u}_3 \geq 1 \end{cases}, \quad u_4^* = \begin{cases} 0, & \text{if } \tilde{u}_4 \leq 0 \\ \tilde{u}_4 & \text{if } 0 < \tilde{u}_4 < 1 \\ 1 & \text{if } \tilde{u}_4 \geq 1 \end{cases} \tag{34}
$$

The system in (34) leads to the system in (33) in Theorem (7). Uniqueness of op-

timal of the system is guaranteed by imposing a condition on time interval [26]. □

6. Numerical Results

The numerical simulations of the effects of control strategies on disease dynamics is shown. This is done by solving the optimal system consisting of Equation (3), co-state Equation (31), transversality conditions (32) and characterisation (34). Optimal system were solved by applying an iterative scheme. A fourth order Range-Kutta scheme was applied to solve the state equations with a guess of controls over time. We also apply the current iterations solutions of state systems to solve adjoint equations by backward fourth order Range-Kutta scheme. Finally, an update of controls by using a convex combination of previous controls and value from (33). This process was repeated and iterations stops if values of unknowns at the previous iterations are very close to the ones at the present iterations [27].

Most effective strategies were presented as follows: Combination of u_1 and u_2. Combination of u_2, u_3 and u_4. Combination of u_2 and u_4. Combination of u_2 and u_3. Combination of u_1 and u_3. Combination of u_1, u_2 and u_3. Combination of u_3 and u_4. Combination of u_1, u_3 and u_4. Combination of u_1 and u_4. The plots of the three most effective strategies were selected and presented as follows;

Strategy 1: Optimal treatment of infectious animals and treatment of humans.

Using u_4 and u_2, we optimised the objective functional, (J) by setting u_1 and u_3 to zero. Due to these control strategies applied, from **Figure 3**, it can be seen that the number of I_v and I_h have reduced substantially. This implies spread of anthrax can be curbed through effective treatment of infectious animals and the treatment of infectious humans. This strategy can best be reached by treatment all infectious animals and humans in the system. **Figure 4** shows an exponential reduction in the number of recovered animals and humans the system.
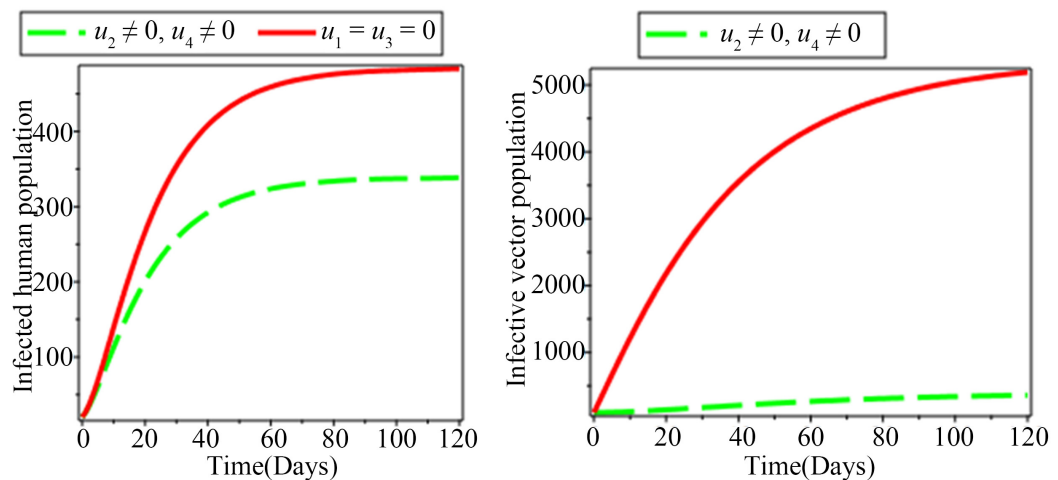
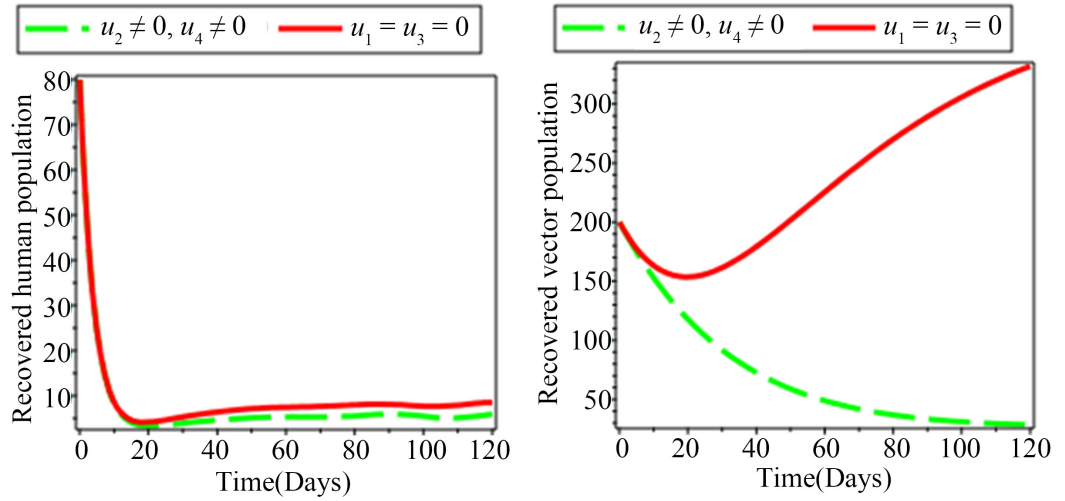**Figure 3.** Simulation of model indicating the effects of optimal strategies: u_4 and u_2.

Figure 4. Simulation of model indicating the effects of optimal strategies: u_4 and u_2.
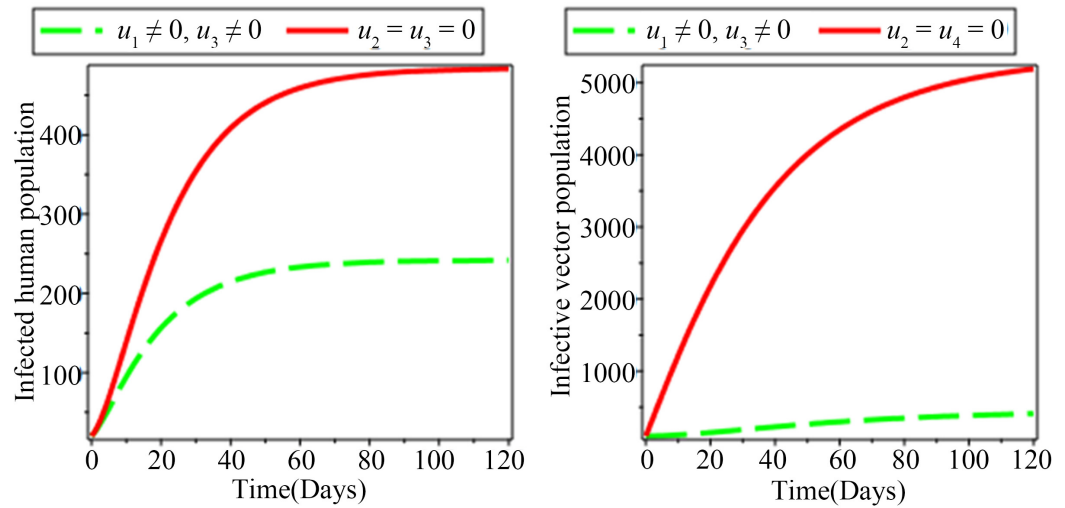

Figure 5. Simulation of anthrax model indicating the effects of optimal strategies: u_3 and u_1.
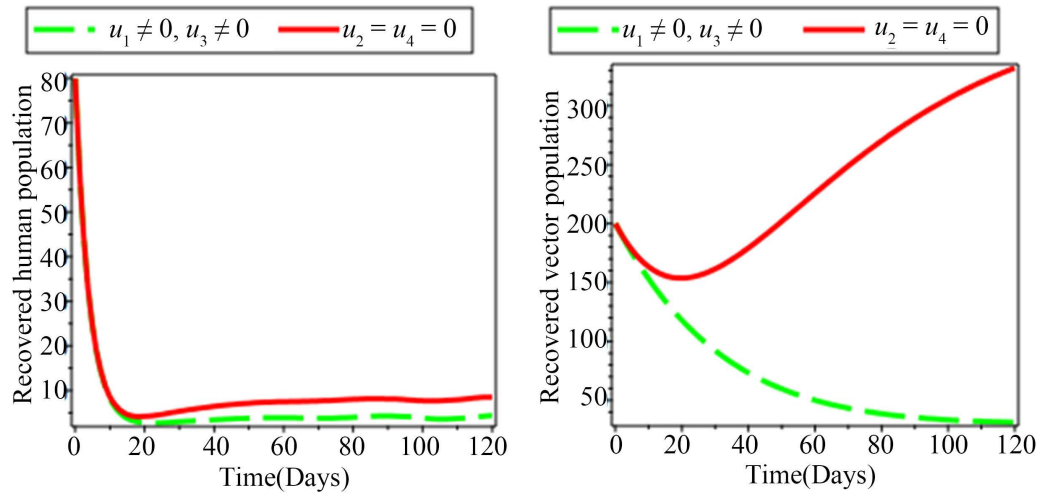

Figure 6. Simulation of Anthrax model indicating the effects of optimal strategies: u_3 and u_1.
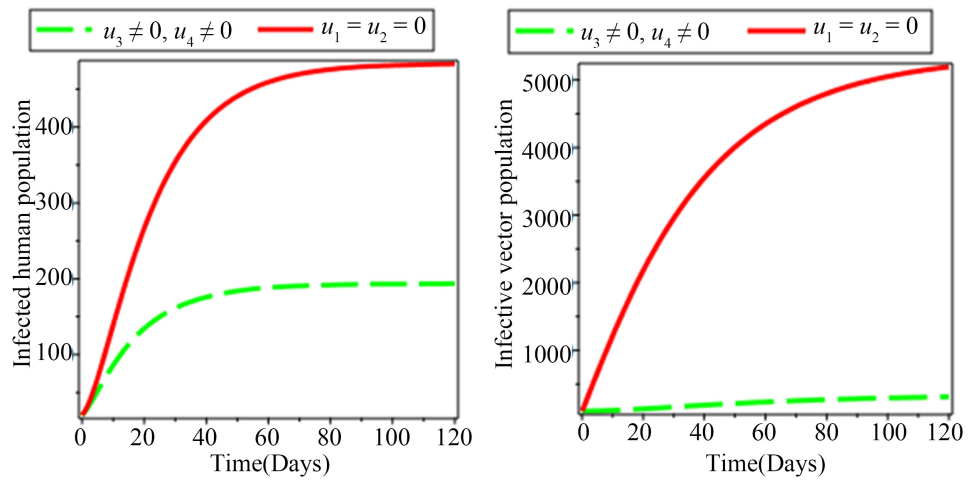
Figure 7. Simulation of model showing the effects of optimal strategies: u_3 and u_4.
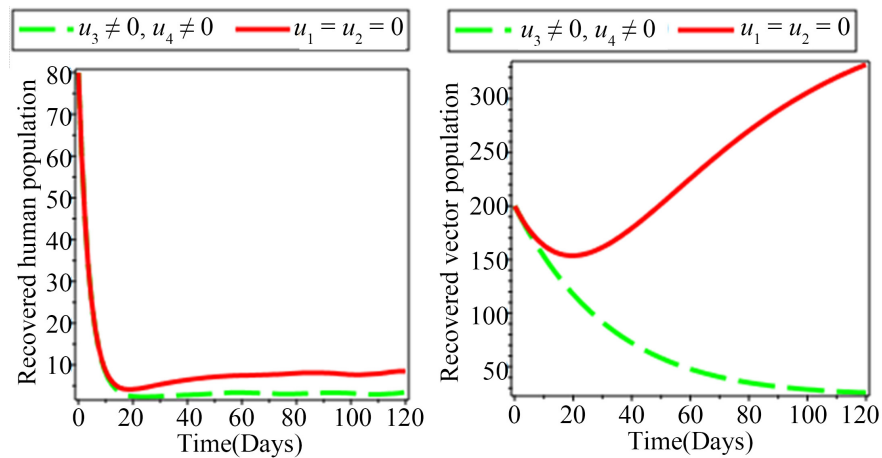

Figure 8. Simulation of model indicating the effects of optimal strategies: u_3 and u_4.

Strategy 2: Optimal vaccination of animals and prevention of humans.

Using u_3 and u_1, we optimise J by setting the controls u_2 and u_4 to zero. As a result of this control strategies used, it can be seen that the number of I_v and I_h have reduced considerably as shown in **Figure 5**. This means that anthrax spread can be tackled through u_3 and u_1. This can be done though education of farmers on vaccination of animals against anthrax. Also, educating the public on the dangers associated with consumption of infected meat and products from animals infected with anthrax. Moreover, there are some reductions in the populations of R_h and R_v as shown in **Figure 6**.

Strategy 3: Optimal vaccination of animals and treatment of infectious animals.

Using u_3 and u_4, we optimise the objective functional by setting u_1 and u_2 to zero. As a result of this, it can be observed that there have been a reduction in the population of I_v and I_h as indicated in **Figure 7**. This means anthrax spread can handled by effective vaccination of susceptible animals and treatment of infectious animals. In order to achieve this, proper vaccination of

animals and the treatment of all infectious animals should be conducted. **Figure 8** shows a considerable reduction in both human and animal population.

7. Cost Effectiveness Analysis

In this section, a cost-benefit analysis is conducted to determine the costs associated with prevention of susceptible humans, treatment of infectious humans, vaccination of susceptible animals and treatment of infectious animals. In this paper, we consider the Infection Averted Ratio, (IAR) approach.

Intervention Averted Ratio (IAR)

The intervention averted ratio is defined as the ratio of the number of infection averted to the number of recovered. Number of infection averted is the diffeences between infectious population without optimal control and infectious population with optimal control. The IAR for each strategy was determined using the model's parameter values. Generally, the strategy with the highest ratio is taken as the best and most effective strategy to be considered.

$$IAR = \frac{\text{Number of infection averted}}{\text{Number of recovered}} \tag{35}$$

The values in **Table 3** shows the intervention averted ratios of the various strategies. Strategy 2 has the highest ratio and hence, it is the most effective strategy. The second most highest ratio is strategy 3. Hence, anthrax spread can be tackled through u_1 and u_3. This can be done though education of farmers on vaccination of animals against anthrax. Also, educating the public on the dangers associated with consumption of infected meat and products from animals infected with anthrax. The diagram in **Figure 9** shows IAR plots on the effects of control strategies.
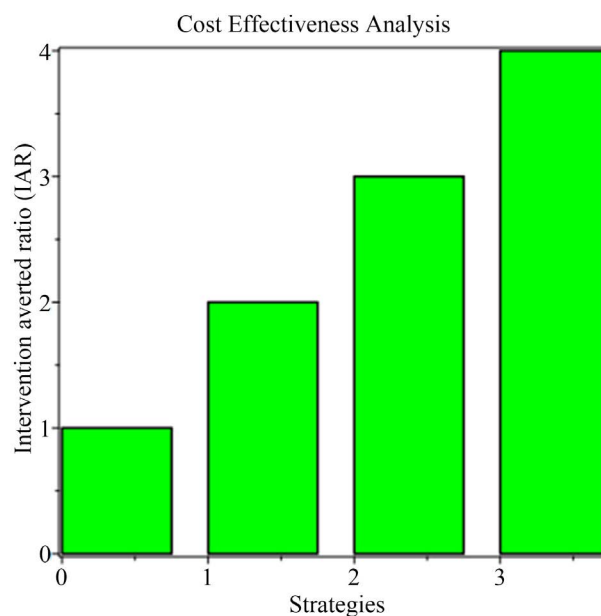
Figure 9. IAR plot showing control effects on strategies.

Table 3. Total infection averted ratio (IAR).

Strategy	Total infection averted	Infection Averted Ratio (IAR)
Strategy 1	155.3554	18.3781
Strategy 2	250.2184	38.3118
Strategy 3	315.1165	34.1349
Strategy 4	264.2318	30.8685

8. Conclusions

The model's qualitative analysis exhibited an existence of multiple endemic equilibria. Its biological implications are that, proper anthrax disease can best be done if $R_{hv} < 1$. Moreover, sensitivity analysis of R_{hv} showed that, an increase in animal recovery rate would decrease R_{hv}. However, a decrease in animal recovery rate would increase R_{hv}. Additionally, an increase in animal and human transmission rates would increase R_{hv} and a decrease in animal and human transmission rates decreases R_{hv}.

Analysis of optimal control and cost effectiveness of our model showed that the best and most effective strategy is vaccination of animals and prevention of susceptible humans in the system. Prevention control on humans and vaccination of animals should be considered as priority when fighting anthrax infections. There should be proper campaign on anthrax prevention and more animals should be vaccinated against the disease.

Data Availability Statement

Data supporting this model analysis are from previously published works and reported studies and all these have been cited in this paper. Some parameter values were assumed and others taken from published articles. These articles have also been cited accordingly at relevant places within the text as references.

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Conflicts of Interest

Authors declare that there is no conflict of interest regarding the publication of this paper.

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