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MODELLING ZOONOTIC DISEASES WITH TREATMENT IN BOTH HUMAN AND ANIMAL POPULATIONS

CHRISTOPHER SAAHA BORNAA[1,*], YAKUBU IBRAHIM SEINI[2], BABA SEIDU[3]

[1]Department of Science and Mathematics Education, University for Development Studies, P. O. Box 24, Navrongo Campus, UER, Ghana

[2]School of Engineering, University for Development Studies, P. O. Box 1350, Nyankpala Campus, NR, Ghana

[3]Department of Mathematics, University for Development Studies, P. O. Box 24, Navrongo Campus, UER, Ghana

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Abstract. This paper proposes and analyzes a nonlinear mathematical model to study the factors responsible for transmission of zoonotic diseases and how effectively the zoonotic diseases can be managed. The disease free equilibrium of the system is established and the effects of the model parameters on the disease transmission dynamics are equally assessed. We then modify the basic model into an optimal control problem by incorporating three control variables into the model which are categorized into curative and preventive strategies. Numerical simulations of the optimal control problem are also carried out to determine the most cost-effective of various options of combinations of the controls. The results indicate that the combined effort of curatives and preventives is the most cost-effective strategy to combat the spread of the zoonotic disease.

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*Corresponding author

E-mail address: chrisbornaa@gmail.com

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1. Introduction

Human health is inextricably linked to animal health because the two populations share the same environment. This is more so when in developing countries animals provide energy in the form of power for transport. Animals droppings such as cow dung also serve as fuel and the products are source of protein food supplement and raw materials for making clothing. It is estimated that about 75% of human infectious diseases are zoonotic and basically transmitted from both domestic and wildlife animals [1]. Cleaveland, Laurenson and Taylor [2], identified 1,415 species of infectious organisms as causing emerging infectious diseases known to be pathogenic to humans. These include 217 viruses and prions, 538 bacteria and rickettsia, 307 fungi, 66 protozoa and 287 helminths. Out of these, 868 infectious organisms representing about 61% were classified as zoonotic and 175 (about 12%) of the pathogenic species were considered to be associated with emerging diseases. Among the group of 175 pathogenic emerging diseases, 132 representing about 75% were zoonotic. These are diseases that are transmitted from both domestic and wild animals to human beings. This group of infectious diseases pose much threat to human life as the associated cost continue to increase. The up-front costs associated with preparing for and responding to epidemic-prone infectious diseases is always factored into planning to combat any epidemic. The financial burden of these preventable zoonotic epidemics from 1995 to 2008 exceed $120 billion globally[3]. The economic consequences are felt in many areas such as industry, agriculture, trade and tourism as well as health [3].

Despite the impact of zoonoses on human life, most infections go undiagnosed causing untold suffering and the death of thousands of people [4]. In sub-Saharan Africa, farming practices, culture and eating habits, increased movement of animals, low educational levels, inadequate disease control programs and lack of information about the disease have been reported to be the contributing factors for the persistence of zoonotic diseases [4, 5, 6, 7, 8, 9].

There is therefore the need to study the transmission dynamics of zoonotic diseases from one animal to the other and also to humans by employing mathematical modelling. This is a powerful tool that has brought revealing results in ecological studies [10, 11]. Hsieh and Hsiao [12] stated that the population of animals, including human beings, are significantly controlled by infectious diseases.

2. Model formulation

In this section, the mathematical model under discussion is developed through incorporation of the following assumptions into the model of Bornaa, Makinde and Seini, [13]:

(1) The susceptible human , $Y(T)$, and animal populations, $S(T)$, become infected through contact with the infective human population , $Z(T)$, and animal populations, $I(T)$.
(2) The contact process is assumed to follow the simple mass action kinetics with β as the rate of transmission.
(3) The infected animal population is also treated with a recovery rate of γ are incorporated.

All other assumptions pertaining to [13] remain constant. These assumption are as follows:

(i) In the absence of the disease, the susceptible animal (prey) population grows logistically with intrinsic growth rate r_1, environmental carrying capacity K, $(r_1, K \in R_+)$ and decreases in the population due to predation rate of n.
(ii) Only the susceptible S(T) can procreate. Logistic law is then use to model the birth process with the assumption that births should always be positive.
(iii) The infected animals I(T) is remove with a death rate c or by human predation before they can possibly reproduce. However, both the infected I(T) and susceptible S(T) animals populations contribute to the population growth towards the carrying capacity K.
(iv) Susceptible animals S(T) become infected through contact with an infected animals I(T) and this contact process is assumed to follow the simple mass action kinetics with β as the rate of transmission.
(v) Susceptible humans Y(T) become infected through contact with the infective population, $\{$I(T) and Z(T)$\}$, and this contact process is assumed to follow the simple mass action kinetics with β as the rate of transmission.
(vi) The disease can cross species barrier from the animal population $N_1(T)$ to the human population $N_2(T)$. Hence the susceptible predator(human), Y(T), adds up to the infected predator, Z(T), through predation and/or contact with the infected and it is not genetically inherited.

(vii) The infected human Z(T) population can recover by treatment at the rates γ and possesses a death rate of $(\sigma+\mu)$, where σ and μ are the death rates due to infection and nature respectively.

(viii) The predation functional response of the human being towards both susceptible S(T) and infected I(T) animals are assumed to follow Michaelis-Menten kinetics and is modeled using a Holling type-II functional form with predation coefficients b, $(b>0)$ and half-saturation constant a, $(a>0)$.

(ix) The efficiency at which the consumed susceptible S(T) and infected I(T) animals (prey) are converted into predator is given as p and q respectively, where $0<p<1$ and $0<q<1$.

The flow diagram of the model is presented in Figure 1.

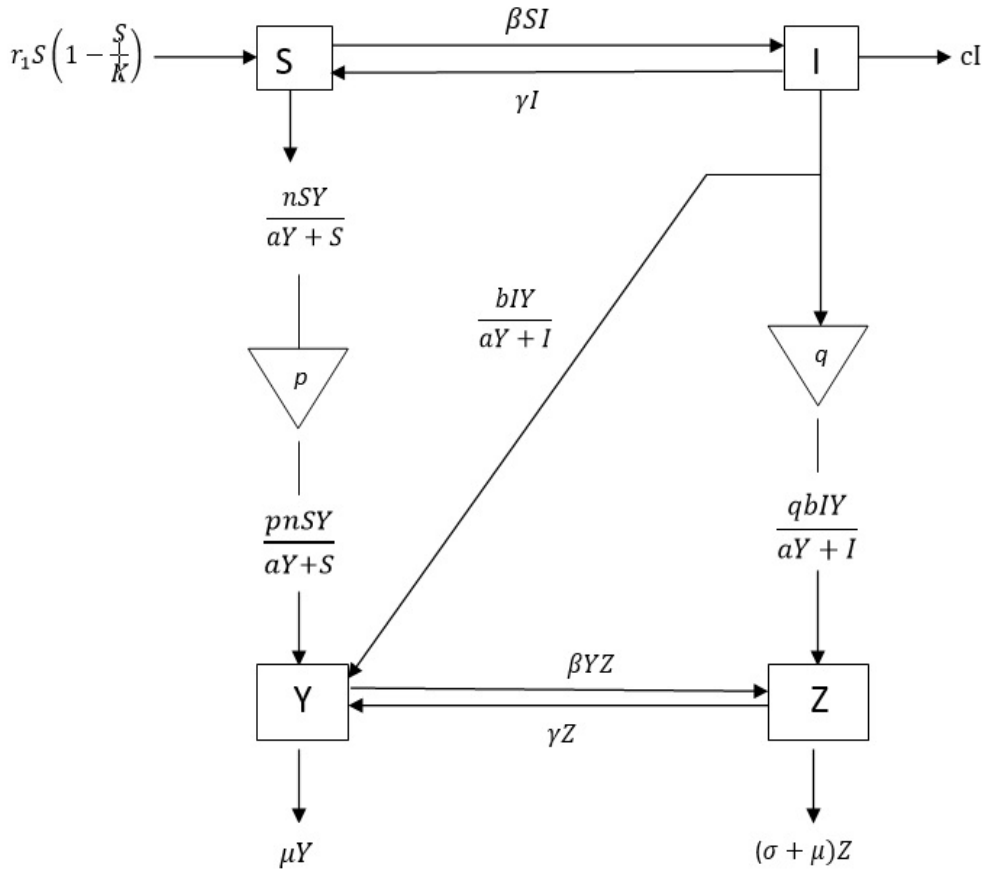

FIGURE 1. Flowchart of the model

The model equations are therefore as follows:

$$(1)\qquad \begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}T} = r_1 S(1-\dfrac{S}{K}) - \beta SI - \dfrac{nSY}{aY+S} + \gamma I \\ \dfrac{\mathrm{d}I}{\mathrm{d}T} = \beta SI - \dfrac{bIY}{aY+I} - cI - \gamma I \\ \dfrac{\mathrm{d}Y}{\mathrm{d}T} = \dfrac{pnSY}{aY+S} - \mu Y + \gamma Z - \beta YZ \\ \dfrac{\mathrm{d}Z}{\mathrm{d}T} = \dfrac{qbIY}{aY+I} - (\sigma+\mu)Z - \gamma Z + \beta YZ \end{cases}$$

With initial values $S(0) \geq 0, I(0) \geq 0, Y(0) \geq 0, Z(0) \geq 0$.

To non-dimensionalize the system (1),we set $s = \frac{S}{K}$, $i = \frac{I}{K}$, $y = \frac{aY}{K}$, $z = \frac{Z}{K}$ and $t = \beta KT$ so that the dimensionless model is given by.

$$(2)\qquad \begin{cases} \dfrac{\mathrm{d}s}{\mathrm{d}t} = rs(1-s) - si - \dfrac{msy}{a(y+s)} + \gamma il \\ \dfrac{\mathrm{d}i}{\mathrm{d}t} = si - \dfrac{giy}{a(y+i)} - (c+\gamma)il \\ \dfrac{\mathrm{d}y}{\mathrm{d}t} = \dfrac{pmsy}{(y+s)} - \mu yl + (a\gamma l - y)z \\ \dfrac{\mathrm{d}z}{\mathrm{d}t} = \dfrac{qgiy}{a(y+i)} - (\sigma+\mu+\gamma)zl + \dfrac{yz}{a} \end{cases}$$

where $r = \frac{r_1}{\beta K}, g = \frac{b}{\beta K}, m = \frac{n}{\beta K}$ and $l = \frac{1}{\beta K}$; with initial data values $s(0) \geq 0, i(0) \geq 0, y(0) \geq 0$ and $z(0) \geq 0$.

3. Positivity Test

Theorem 3.1. *Let $s(0) > 0$, $i(0) > 0$, $y(0) > 0$, and $z(0) > 0$. Then the solutions $s(t), i(t), y(t)$ and $z(t)$ of the system are positive $\forall t \geq 0$.*

It is required to prove theorem 3.1 on (2) to show that the model is epidemiologically meaningful and mathematically well posed (i.e, all the solutions of the system with positive initial data will remain positive $\forall t > 0$).

Proof. Consider the last equation of model (2).

$\frac{\mathrm{d}z}{\mathrm{d}t} = \frac{qgiy}{y+i} - (\sigma+\mu+\gamma)zl + \frac{yz}{a}$.

Implying $\frac{\mathrm{d}z}{\mathrm{d}t} \geq -(\sigma+\mu+\gamma)zl$

$\frac{\mathrm{d}z}{z} \geq -(\sigma+\mu+\gamma)l\,dt$

$\int \frac{\mathrm{d}z}{z} \geq -(\sigma+\mu+\gamma)l \int dt$

$\ln|z| \geq -(\sigma+\mu+\gamma)lt + C$, where C is a constant.

Let $\theta = (\sigma+\mu+\gamma)l$,

then $\ln|z| \geq -\theta t + C$

$z(t) \geq e^{(C-\theta t)}$

$z(t) \geq e^{C} e^{-\theta t}$

$\Rightarrow \lim_{t\to+\infty} z(t) \geq 0$

Therefore $\forall t \geq 0$, $z(t) \geq 0$. Implying that $z(t)$ is positive.

Similarly, the solutions of the other model equations can be shown to be positive.

4. Boundedness of the System

The biological validity and behaviour of model (2) depend on bounds of the model. All the solutions of must be within $\mathbb{R}^4_+$. Theorem 3.2 satisfies the condition if proven for model (2) .

Theorem 4.1. *All the solutions of the system (2) are uniformly bounded within* $\mathbb{R}^4_+$

Proof. Assume $\{s(t), i(t), y(t), z(t)\}$ to be any solution of system (2).

Consider $W = s + i + y + z$.

Therefore $\dfrac{\mathrm{d}W}{\mathrm{d}t} \leq \hat{k}(r+1) - hw$.

where $\hat{k} = \max\{s(0), k\}$ and $h = \min\{1, c, \mu, \sigma\}$.

The theorem of differential inequalities gives a solution of $\dfrac{\mathrm{d}W}{\mathrm{d}t} + hw \leq \hat{k}(r+1)$ to be

$W \leq \frac{\hat{k}}{h}(r+1)(1-e^{-ht})$.

As $t \to \infty$, $W \leq \frac{\hat{k}}{h}(r+1)$. This implies that the solution is confined for $0 \leq W \leq \frac{\hat{k}}{h}(r+1)$. It shows that all the solutions of model (2) in $\mathbb{R}^4_+$ are within the region $\tau = \{(s,i,y,z) \in \mathbb{R}^4_+ : W \leq \frac{\hat{k}}{h}(r+1) + \varepsilon\}$ for all $\varepsilon > 0$ and $t \to \infty$. Hence, the theorem is satisfied

The dynamics of the model within τ can now be studied and hence consider the model to be epidemiologically and mathematically well formed.

5. Equilibrium States of the Model

5.1. Disease Free Equilibrium State

The disease-free equilibrium point is $B(S^*,0,Y^*,0)$, where

$S^* = \frac{rap-pm+\mu l}{rap}$ and $Y^* = \frac{(rap-pm+\mu l)(pm-\mu l)}{rap\mu l} = \frac{pm-\mu l}{\mu l}S^*$.

Remark 5.1. *A necessary condition for existence of the disease-free equilibrium is* $\mu l < pm < rap + \mu l$ *(or equivalently* $\mu < pn < r_1 ap + \mu$*).*

5.2. Endemic equilibrium state

The endemic equilibrium state of the model (2) is given by $E_2(S^{**},I^{**},Y^{**},Z^{**})$.

where

$S^{**} = \frac{gY^{**}+lacY^{**}+lacI^{**}+la\gamma Y^{**}+I^{**}la\gamma}{a(Y^{**}+I^{**})}$,

$Y^{**} = \frac{pmS^{**}+\gamma Z^{**}al-Z^{**}S^{**}-\mu lS^{**}-\sqrt{\Pi}}{2(\mu l+Z^{**})}$

$Z^{**} = \frac{qgY^{**}I^{**}}{(Y^{**}+I^{**})(la\sigma+la\mu+a\gamma l-Y^{**})}$ and

$I^{**} = \frac{S^{**}\left(rS^{**}Y^{**}a+rS^{**2}a+mY^{**}-raY^{**}-arS^{**}\right)}{a(Y^{**}+S^{**})(\gamma l-S^{**})}$.

where

$$\begin{aligned}\Pi = \; & p^2m^2S^{**2} + 2\,pmS^{**}Z^{**}la\gamma - 2\,pmS^{**2}Z^{**} - 2\,pmS^{**2}\mu l + Z^{**2}l^2a^2\gamma^2 \\ & + 2Z^{**2}la\gamma S^{**} + 2Z^{**}l^2a\gamma\mu S^{**} + Z^{**2}S^{**2} + 2Z^{**}S^{**2}\mu l + \mu^2l^2S^{**2}\end{aligned}$$

Remark 5.2. *The existence of* S^{**} *and* Z^{**} *is dependent on* Y^{**} *and* I^{**}*. For* Y^{**} *to exist,* $l(\sigma+\mu+\gamma) < 0$ *in its positive root and for* I^{**} *to exist,* $Y^{**} < \frac{rS^{**}(1-S^{**})}{m-r(1-S^{**})}$.

6. Reproduction Number and Stability Analysis

6.1. Reproduction Number

The Reproduction number derived from the Next Generation Matrix method [14, 15] is given by:

$\mathscr{R}_0 = \frac{rap-pm+\mu l-grp}{rpa(c+\gamma)l}$.

Theorem 6.1. *The disease-free equilibrium state,$B(S^*,0,Y^*,0)$ of the model (2) is locally asymptotically stable if $\mathscr{R}_0 < 1$, otherwise it is unstable.*

It shows that with $\mathscr{R}_0 < 1$, the disease can be eradicated if the initial sub-population is within the restricted region.

A feature of the Reproduction Number from $\mathscr{R}_0 < 1$ is $S^* < \frac{lac+a\gamma l+g}{a}$.
From the original equation, $S^* < \frac{ac+a\gamma+b}{a\beta K}$.

This relation according portrays two important points [16]:

- The persistence of the disease depends on some parameters that measure the characteristics of the susceptible animals and infection.
- The requirement that the density of susceptible animals must not exceed a certain critical value for the disease not to persist.

6.2. Stability Analysis

The local stability condition can be establish with the Jacobian matrix (J) of the model equation (2),
where

$$J = \begin{bmatrix} J_{11} & \gamma l - s & -\frac{ms^2}{a(y+s)^2} & 0 \\ i & J_{22} & -\frac{gi^2}{a(y+i)^2} & 0 \\ \frac{pmy^2}{(y+s)^2} & 0 & J_{33} & (a\gamma l - y) \\ 0 & \frac{qgy^2}{a(y+i)^2} & \frac{qgi^2}{a(y+i)^2} + \frac{z}{a} & J_{44} \end{bmatrix} \tag{3}$$

$J_{11} = r(1-2s) - i - \frac{my^2}{a(y+s)^2}$
$J_{22} = s - \frac{gy^2}{a(y+i)^2} - (c+\gamma)l$
$J_{33} = \frac{pms^2}{(y+s)^2} - \mu l - z$, and
$J_{44} = \frac{y}{a} - (\sigma + \mu + \gamma)l$.

6.2.1. Local Stability of Disease - Free Equilibrium

The Jacobian (JB), evaluated at B is given by:

$$JB = \begin{bmatrix} r(1-s) - \frac{my^2}{a(y+s)^2} & \gamma l - s & -\frac{ms^2}{a(y+s)^2} & 0 \\ 0 & s - \frac{g}{a} - (c+\gamma) l & 0 & 0 \\ \frac{pmy^2}{(y+s)^2} & 0 & \frac{pms^2}{(y+s)^2} - \mu l & a\gamma l - y \\ 0 & \frac{qg}{a} & 0 & -(\sigma+\mu+\gamma) l + \frac{y}{a} \end{bmatrix}$$

$$JB = \begin{bmatrix} \xi & \frac{(\gamma l-1)rap+pm-\mu l}{rap} & -\frac{\mu^2 l^2}{p^2 am} & 0 \\ 0 & \frac{rap-pm+\mu l-grp}{rap} - (c+\gamma) l & 0 & 0 \\ \frac{(-pm+\mu l)^2}{pm} & 0 & \frac{(-pm+\mu l) l\mu}{pm} & \pi \\ 0 & \frac{qg}{a} & 0 & \eta \end{bmatrix}$$

where

$\xi = \frac{\left(r\left(\frac{pm-\mu l}{rap}\right) p^2 am - (pm-\mu l)^2\right)}{p^2 am}$,

$\eta = -\frac{a^2 l^2 pr\mu\sigma + a^2 l^2 pr\mu^2 + a^2\gamma l^2 pr\mu - rap^2 m + apr\mu l + p^2 m^2 - 2pm\mu l + \mu^2 l^2}{a^2 pr\mu l}$ and

$\pi = \frac{a^2\gamma l^2 pr\mu - rap^2 m + apr\mu l + (pm-\mu l)^2}{apr\mu l}$.

$$JB = \begin{bmatrix} \xi & \frac{(\gamma l-1)rap+pm-\mu l}{rap} & -\frac{\mu^2 l^2}{p^2 am} & 0 \\ 0 & (\mathscr{R}_0 - 1)(c+\gamma) l & 0 & 0 \\ \frac{(-pm+\mu l)^2}{pm} & 0 & \frac{(-pm+\mu l) l\mu}{pm} & \pi \\ 0 & \frac{qg}{a} & 0 & \eta \end{bmatrix}$$

where $\mathscr{R}_0 (c+\gamma) l = \frac{rap-pm+\mu l-grp}{rap}$

The eigenvalues of the Jacobian matrix are:

$$\lambda = \begin{bmatrix} 0 \\ \eta \\ (\mathscr{R}_0 - 1)(c+\gamma) l \\ -\frac{\mu l((pm-\mu l)ap-(pm-\mu l))}{p^2 am} \end{bmatrix}.$$

The disease free - equilibrium state is therefore stable if $\mathscr{R}_0 < 1$ and since $\eta < 0$. The zero eigenvalue indicates that the origin is stable but not asymptotically stable.

6.2.2. Local Stability of Endemic Equilibrium State

Let the Jacobean matrix for the endemic equilibrium state $E(S^{**}, I^{**}, Y^{**}, Z^{**})$ be:

$$JE = \begin{bmatrix} -C_1 & -C_2 & -C_3 & 0 \\ I^{**} & -C_4 & -C_5 & 0 \\ C_6 & 0 & C_7 & C_8 \\ 0 & C_9 & C_{10} & -C_{11} \end{bmatrix}$$

where

$$-C_1 = \frac{-raY^{**} - raI^{**} + 2rgY^{**} + 2rlacY^{**} + 2rla\gamma Y^{**} + 2rlacI^{**} + 2rla\gamma I^{**} + aY^{**}I^{**} + I^{**2}a}{a(Y^{**} + I^{**})} + \frac{mY^{**2}a(Y^{**} + I^{**})^2}{\left(aY^{**2} + aY^{**}I^{**} + gY^{**} + lacY^{**} + la\gamma Y^{**} + lacI^{**} + la\gamma I^{**}\right)^2}$$

$$-C_2 = \frac{gY^{**} + lacY^{**} + lacI^{**}}{a(Y^{**} + I^{**})}$$

$$-C_3 = \frac{m(gY^{**} + lacY^{**} + la\gamma Y^{**} + lacI^{**} + la\gamma I^{**})^2}{a\left(aY^{**2} + aY^{**}I^{**} + gY^{**} + lacY^{**} + la\gamma Y^{**} + lacI^{**} + la\gamma I^{**}\right)^2}$$

$$-C_4 = \frac{gY^{**}(Y^{**} - 1)}{a(Y^{**} + I^{**})}$$

$$-C_5 = \frac{gI^{**}}{a(Y^{**} + I^{**})^2}$$

$$C_6 = \frac{pmY^{**2}a^2(Y^{**} + I^{**})^2}{\left(aY^{**2} + aY^{**}I^{**} + gY^{**} + lacY^{**} + la\gamma Y^{**} + lacI^{**} + la\gamma I^{**}\right)^2}$$

$$C_7 = \frac{pm(gy + lacy + la\gamma y + laci + la\gamma i)^2}{\left(ay^2 + ayi + gy + lacy + la\gamma y + laci + la\gamma i\right)^2} - \frac{\mu l^2 ya\sigma + \mu^2 l^2 ya + \mu l^2 a\gamma y - l\mu y^2 + \mu l^2 ia\sigma + \mu^2 l^2 ia + \mu l^2 a\gamma i - \mu lyi + qgyi}{(y + i)(la\sigma + la\mu + la\gamma - y)}$$

$$C_8 = (a\gamma l - Y^{**})$$

$$C_9 = \frac{qgY^{**2}}{a(Y^{**} + I^{**})^2}$$

$$C_{10} = \frac{qgI^{**}\left(I^{**}la\sigma + I^{**}la\mu + la\gamma I^{**} + Y^{**2}\right)}{a(Y^{**} + I^{**})^2(la\sigma + la\mu + la\gamma - Y^{**})}$$

$$-C_{11} = \frac{la\sigma + la\mu + la\gamma - Y^{**}}{a}$$

$$det(JE) = \begin{vmatrix} -C_1 - \lambda & -C_2 & -C_3 & 0 \\ I^{**} & -C_4 - \lambda & -C_5 & 0 \\ C_6 & 0 & C_7 - \lambda & C_8 \\ 0 & C_9 & C_{10} & -C_{11} - \lambda \end{vmatrix} = 0$$

The characteristic equation is of the form:

$$\lambda^4 + b_1\lambda^3 + b_2\lambda^2 + b_3\lambda + b_4 = 0,$$

where

$$b_1 = C_{11} - C_7 + C_4 + C_1$$

$$b_2 = C_6C_3 - C_{10}C_8 - C_{11}C_7 + C_{11}C_4 + C_{11}C_1 - C_7C_4 - C_7C_1 + I^{**}C_2 + C_4C_1$$

$$b_3 = C_{11}C_6C_3 - C_9C_5C_8 - C_{10}C_8C_4 - C_{10}C_8C_1 - C_{11}C_7C_4 - C_{11}C_7C_1 + I^{**}C_{11}C_2 + C_{11}C_4C_1 + C_6C_2C_5 + C_6C_3C_4 - I^{**}C_7C_2 - C_7C_4C_1$$

$$b_4 = I^{**}C_9C_3C_8 - C_9C_5C_8C_1 - I^{**}C_{10}C_8C_2 - C_{10}C_8C_4C_1 + C_{11}C_6C_2C_5 + C_{11}C_6C_3C_4 - I^{**}C_{11}C_7C_2 - C_{11}C_7C_4C_1$$

From Routh-Hurwitz stability criterion, if the conditions

(a) $b_1 > 0$, $b_3 > 0$ and $b_4 > 0$

(b) $b_1b_2b_3 > b_1^2b_4 + b_3^2$

are satisfied, then the endemic equilibrium point is stable. Otherwise it is unstable.

7. Sensitivity Analysis

Using the estimated parameter values, $r = 10.00$, $l = 0.95$, $p = 0.10$, $\mu = 0.01$, $m = 0.42$, $\gamma = 1.12$, $a = 0.50$ and $\sigma = 0.02$, the sensitivity indexes are calculated and indicated in table 1.

TABLE 1. Sensitivity Indexes of $\mathscr{R}_0$

Parameter	Description	Value	Index
$l = \frac{1}{\beta K}$	K = Environmental carrying capacity of susceptible prey and		
	β = Disease transmission rate	0.95	-1.0017
p	Conversion rate of susceptible predator	0.10	-1.0828
γ	Recovery rate due to treatment	1.12	-0.9825
$m = \frac{n}{\beta K}$	n= Predation rate of susceptible prey	0.42	0.0076
$r = \frac{r_1}{\beta K}$	r_1= Logistic intrinsic growth rate of susceptible prey	10.00	-0.0059
c	Death rate of the infected prey	0.02	-0.0175
$g = \frac{b}{\beta K}$	Rate of predation of infected prey	1.20	1.0845
μ	Natural death rate of the predator	0.01	-0.0017
a	Half saturation constant	0.50	-0.0059

From Table 1, the most sensitive parameters are l, p and g (That is the rates of disease transmission, Conversion rate of susceptible predator and predation of the infected prey with K, the environmental carrying capacity remaining constant). An increase (decrease) in β, all other things remaining constant, or b by 10% leads to an approximate increase (decrease) in $\mathscr{R}_0$ by 10% and 11% respectively. An increase (decrease) in p by 10% will lead to an approximate decrease (increase) in $\mathscr{R}_0$ by 11%.

8. Optimal Controls Analysis

We consider the case where time dependent control variables are incorporated into the basic model as given:

$$
\begin{cases}
\dfrac{\mathrm{d}s}{\mathrm{d}t} = rs(1-s) - (1-u_1)si - \dfrac{msy}{a(y+s)} + \gamma il \\
\dfrac{\mathrm{d}i}{\mathrm{d}t} = (1-u_1)si - \dfrac{(1-u_2)giy}{a(y+i)} - (c+\gamma)il \\
\dfrac{\mathrm{d}y}{\mathrm{d}t} = \dfrac{pmsy}{(y+s)} - \mu yl + a\gamma zl - \{(1-u_3) - (1-u_2)y\}z \\
\dfrac{\mathrm{d}z}{\mathrm{d}t} = \dfrac{(1-u_2)qgiy}{a(y+i)} - (\sigma+\mu+\gamma)zl + \{(1-u_3) - (1-u_2)y\}\dfrac{z}{a}
\end{cases} \tag{4}
$$

The control interventions are:

- u_1 is the intervention variable based on quarantine of infected prey and vaccination of susceptible prey.
- u_2 is the intervention variable based on education and awareness of the disease by the predator as well as vaccination of susceptible predator for protection against the disease.
- u_3 is the intervention variable due to the efficacy of the drug used for the treatment of infected predator.

These interventions can be categorized into preventives and curatives. Interventions such as quarantine, vaccination and education are preventives whilst treatment is aimed at curing the infection. We therefore investigate the following control options to determine the best strategy:

- **Strategy A:** Implementing the control aim at curing the infection (i.e. $u_1 = u_2 = 0$, $u_3 \neq 0$).

- **Strategy B:** Implementing only the controls aim at preventing infection (i.e $u_1 \neq u_2 \neq 0$, $u_3 = 0$).
- **Strategy C:** Implementing all controls (i.e. $u_1 \neq u_2 \neq u_3 \neq 0$).

The major objective therefore is to find the optimal levels of the intervention strategies desired to reduce the cost of implementation and hence the prevalence of the disease in both the predator (Human)

The related objective functional J is given as:

$$J = \min_{u_i, i\in[1,3]} \int_0^{t_f} (i + z + \pi_1 u_1^2 + \pi_2 u_2^2 + \pi_3 u_3^2) dt \tag{5}$$

where $\pi_i, i \in [1,3]$ are non-negative weights associated with the controls. These measure the relative cost of implementing the interventions [11]. To minimize $J(u_1, u_2, u_3)$ over the set of admissible controls U given by:

$$U = \{(u_1, u_2, u_3) \,|\, 0 \leq u_i \leq 1 \text{ is measurable for } t \in [0, T]\}.$$

We find an optimal control triple $(u_1, u_2, u_3)$by minimizing J subject to model (2).

Pontryagin's maximum principle [17] converts the optimal control problem into a problem of point-wise minimization of the Hamiltonian function H with respect to u_1, u_2 and u_3.

$$H(u_i) = i + z + \pi_1 u_1^2 + \pi_2 u_2^2 + \pi_3 u_3^2 + \alpha_s \frac{\mathrm{d}s}{\mathrm{d}t} + \alpha_i \frac{\mathrm{d}i}{\mathrm{d}t} + \alpha_y \frac{\mathrm{d}y}{\mathrm{d}t} + \alpha_z \frac{\mathrm{d}z}{\mathrm{d}t} \tag{6}$$

That is;

$$\begin{aligned} H(u_i) \quad &= f(i,z,u,t) + \alpha \dot{X} = i + z + \pi_1 u_1^2 + \pi_2 u_2^2 + \pi_3 u_3^2 \\ &+ \alpha_s \left(rs(1-s) - (1-u_1)si - \tfrac{msy}{a(y+s)} + u_3 \gamma il \right) \\ &+ \alpha_i \left((1-u_1)si - \tfrac{(1-u_2)giy}{a(y+i)} - (c + u_3\gamma)il \right) \\ &+ \alpha_y a \left(\tfrac{pmsy}{y+s} - \mu yl + a u_3 \gamma z l - \{(1-u_3) - (1-u_2)y\} z \right) \\ &+ \alpha_z \left(\tfrac{(1-u_2)qgiy}{a(y+i)} - (\sigma + \mu + u_3\gamma) zl + \{(1-u_3) - (1-u_2)y\} \tfrac{z}{a} \right) \end{aligned}$$

Where $\alpha_s, \alpha_i, \alpha_y$ and α_z are the adjoint variables or co-state variables. By the Pontryagin's Maximum Principle we have;

Proposition 8.1. *If the optimal triple* (u_1^*, u_2^*, u_3^*) *minimizes* $J(u_1, u_2, u_3)$ *over* U *then there exists adjoint variables which satisfy the following:*

$$
\left\{
\begin{aligned}
\frac{\mathrm{d}\alpha_s}{\mathrm{d}t} &= -\frac{\partial H}{\partial s} = \alpha_s r(2s-1) + (\alpha_s - \alpha_i)(1-u_1)i + \frac{(\alpha_s/a + \alpha_y p)my^2}{(y+s)^2} \\
\frac{\mathrm{d}\alpha_i}{\mathrm{d}t} &= -\frac{\partial H}{\partial i} = (\alpha_s - \alpha_i)(1-u_1)s + \frac{(\alpha_i - \alpha_z q)(1-u_2)gy^2}{a(y+i)^2} + (\alpha_s + \alpha_i u_3)\gamma l \\
&\quad + \alpha_i c l - 1 \\
\frac{\mathrm{d}\alpha_y}{\mathrm{d}t} &= -\frac{\partial H}{\partial y} = \frac{(\alpha_s/a - \alpha_y p)ms^2}{(y+s)^2} + \frac{(\alpha_i - \alpha_z q)(1-u_2)gi^2}{a(y+i)^2} + \left(\frac{\alpha_z}{a} - \alpha_y\right)(1-u_3)z \\
&\quad + \alpha_y \mu l \\
\frac{\mathrm{d}\alpha_z}{\mathrm{d}t} &= -\frac{\partial H}{\partial z} = (\alpha_z - \alpha_y a)u_3\gamma l + (\alpha_y - \alpha_z)(1-u_2) + \left(\frac{\alpha_z}{a} - \alpha_y\right)(1-u_3)y \\
&\quad + \alpha_z(\sigma + \mu)l - 1
\end{aligned}
\right. \tag{7}
$$

Where $\alpha_s(t) = \alpha_i(t) = \alpha_y(t) = \alpha_z(t)$ are the transversality conditions. The state and adjoint systems give the solution of the optimal control problem [18]. From equation (6) and by the stationary condition, the optimal control triple is determined as:

$$
\left\{
\begin{aligned}
u_1^*(t) &= \min\left(1, \max\left(\frac{(\alpha_i - \alpha_s)si}{2\pi_1}, 0\right)\right) \\
u_2^*(t) &= \min\left(1, \max\left(\frac{\alpha_z qgiy + \alpha_z zy + \alpha_z zi - \alpha_i giy - \alpha_y zay - \alpha_y zai}{2\pi_2 a(y+i)}, 0\right)\right) \\
u_3^*(t) &= \min\left(1, \max\left(\frac{\alpha_i \gamma ila - \alpha_y za^2\gamma l + \alpha_y zay + \alpha_z za\gamma l - \alpha_z zy}{2\pi_3 a}, 0\right)\right)
\end{aligned}
\right. \tag{8}
$$

9. Numerical Simulation

The purpose of numerical simulation is to verify the analytical results [**?**]. Computer simulations of the solution of the system are presented with the following selected parameter values: $r = 10.00, l = 0.95, p = 0.10, c = 0.02, \mu = 0.01, m = 0,42, g = 1.20, \gamma = 1.12, \sigma = 0.02$, $q = 0.05, \pi_1 = 6 * 10^3, \pi_2 = 6 * 20^2, \pi_3 = 6 * 10$ and $a = 0.50$ with initial values scaled to $s(0) = 1.00, i(0) = 0.50, y(0) = 1.20, z(0) = 0.30$ per 10,000 individuals.

The simulation results are presented graphically as follows:

Strategy A: Implementing the Control Aim at Curing the Infection

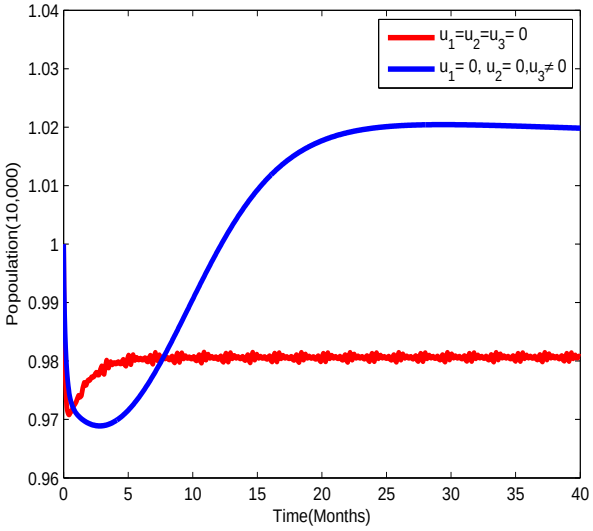

FIGURE 2. Susceptible Prey

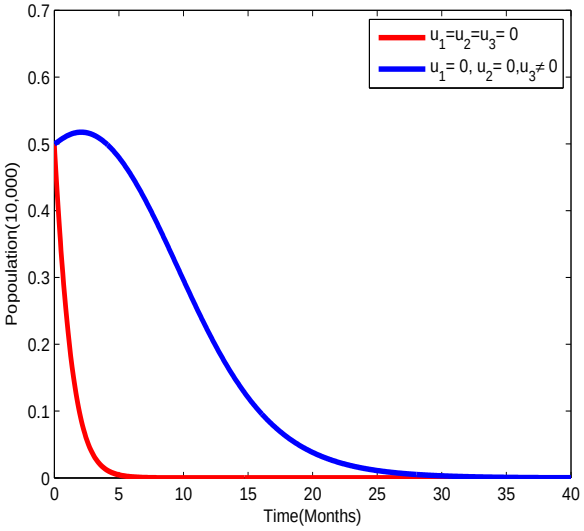

FIGURE 3. Infected Prey

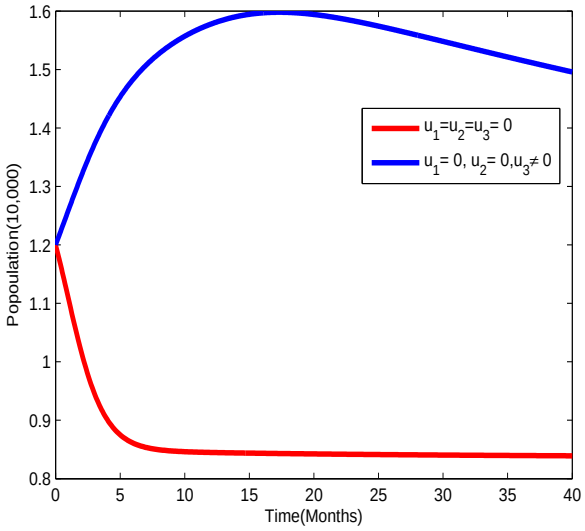

FIGURE 4. Susceptible Predator

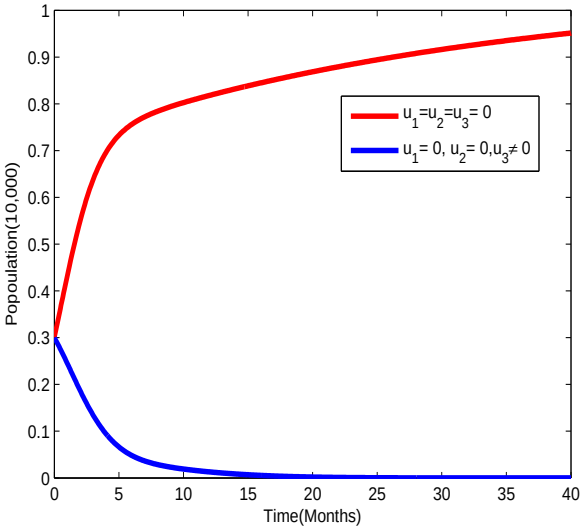

FIGURE 5. Infected Predator

The effect of strategy A is shown in figures 2, 3, 4, and 5.

Strategy B: Implementing the Controls Aim at Preventing Infection

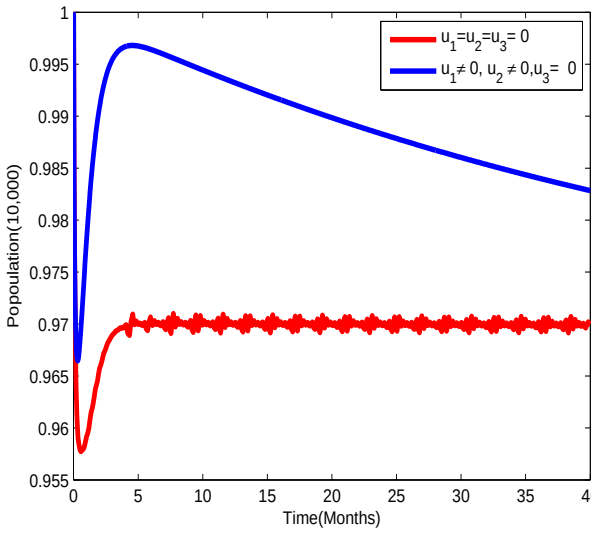

FIGURE 6. Susceptible Prey

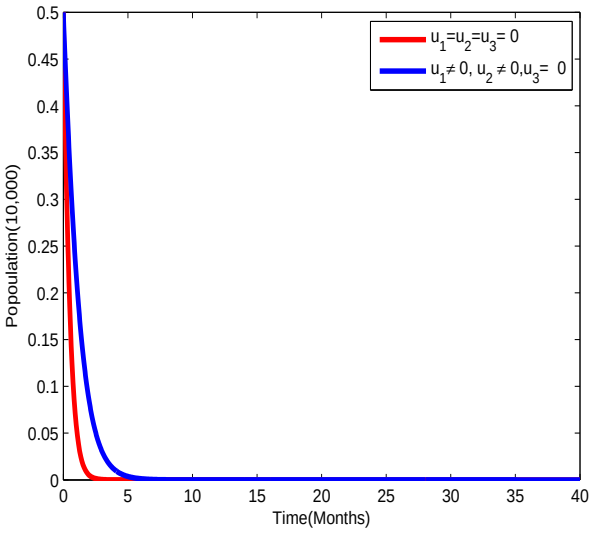

FIGURE 7. Infected Prey

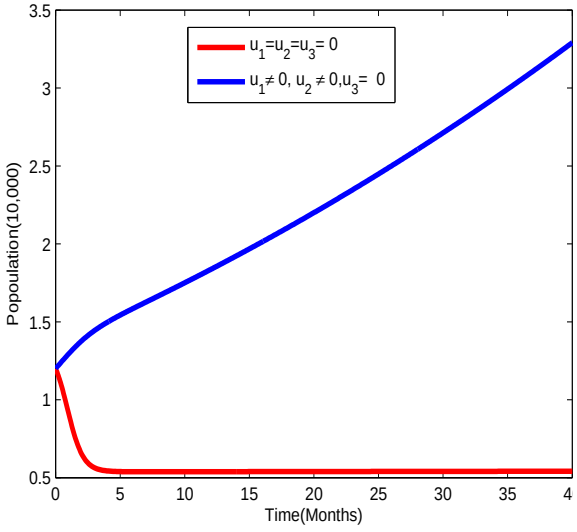

FIGURE 8. Susceptible Predator

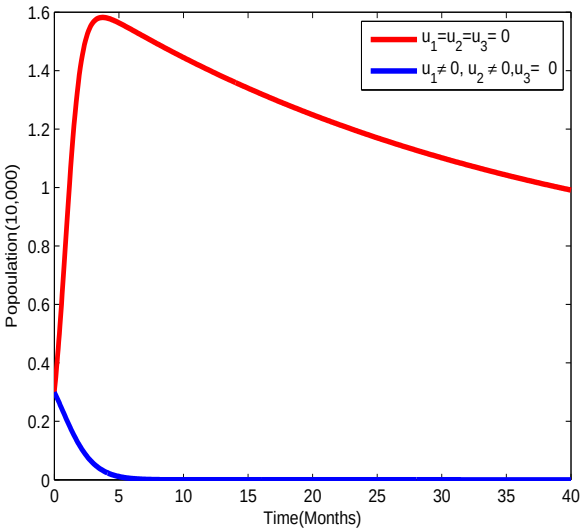

FIGURE 9. Infected Predator

By implementing strategy B, the profile is shown in figures 6, 7, 8 and 9.

Strategy C: Implementing all Controls

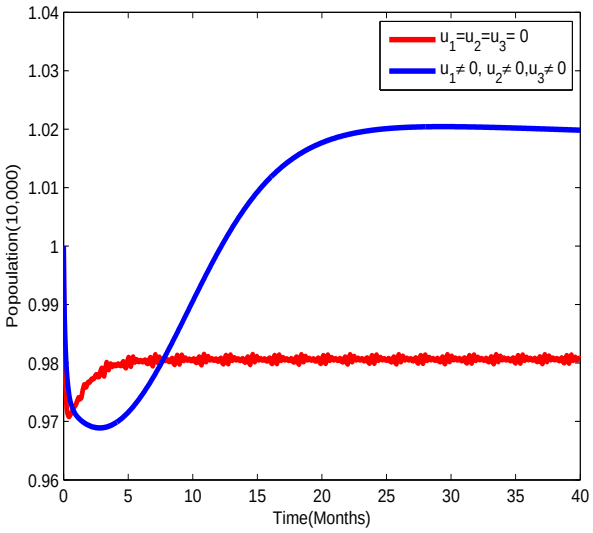

FIGURE 10. Susceptible Prey

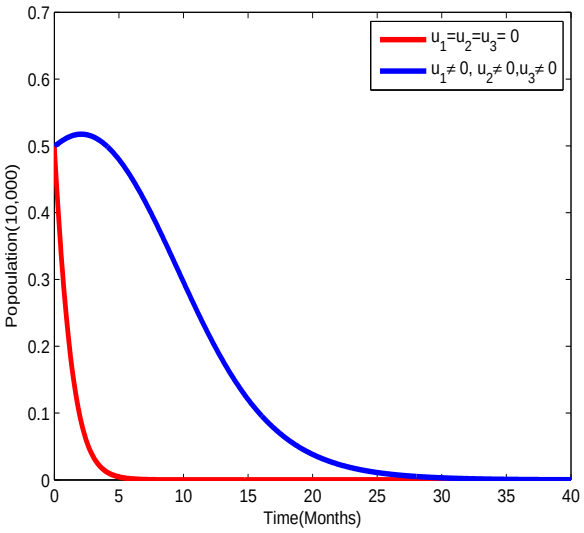

FIGURE 11. Infected Prey

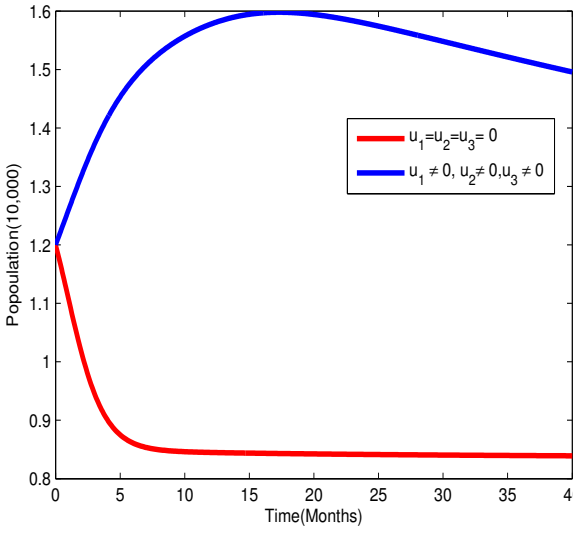

FIGURE 12. Susceptible Predator

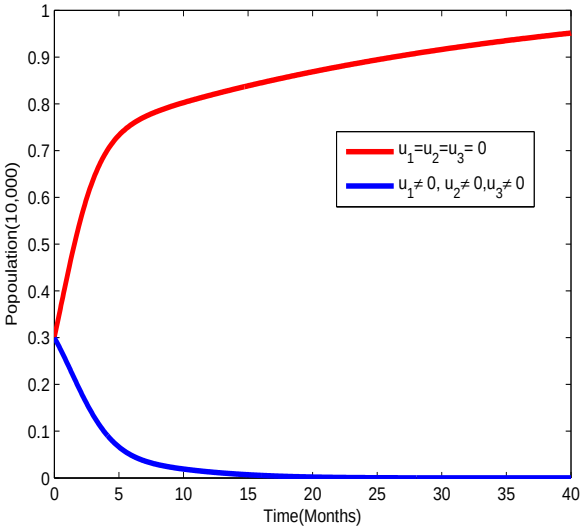

FIGURE 13. Infected Predator

Figures 10, 11, 12 and 13 show the profile of the effect of strategy C on the infection.

Comparing the Effects of the Strategies

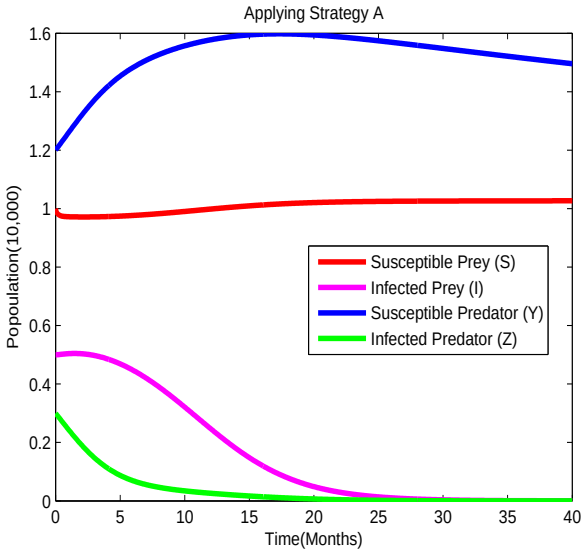

FIGURE 14. Strategy A

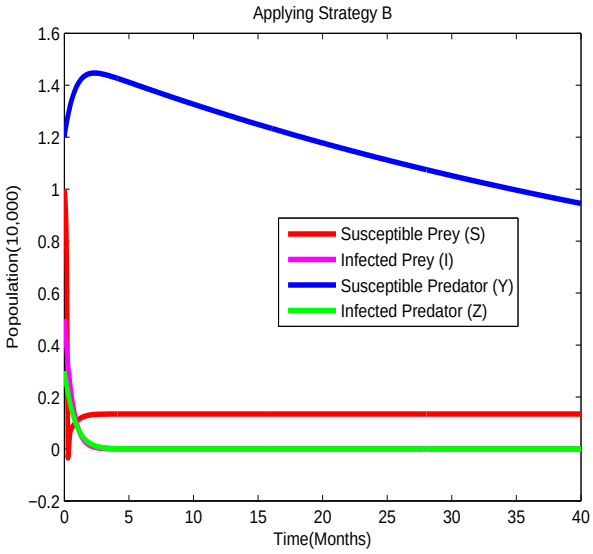

FIGURE 15. Strategy B

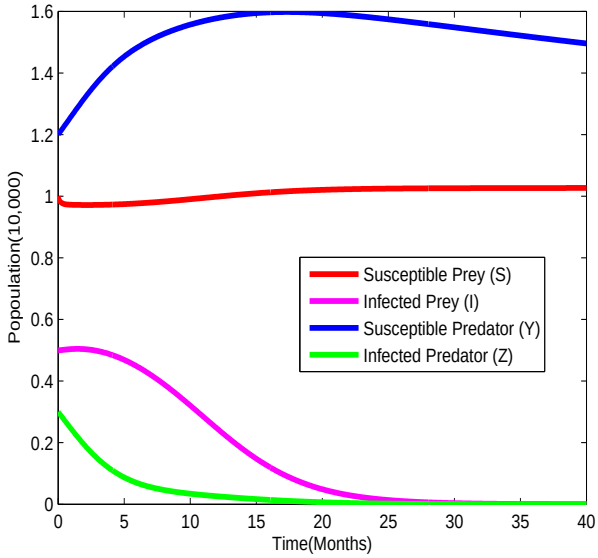

FIGURE 16. Strategy C

The effects of the control strategies on each class are compared in the figures 14, 15 and 16.

10. Cost-Effectiveness Analysis

TABLE 2. Incremental Cost-Effectives Analysis

Alternative Interventions	Total Cost($)	Total Effect	Change in Cost ($)	Change in Effect	ICER ($)
Strategy B (Preventive)	1.6986	0.9500	1.6986	0.9500	1.79
Strategy A (Curative)	2.7986	1.5000	1.1000	0.5500	2.00
Strategy C (Preventive and Curative)	2.1657	1.5003	-0.2329	0.0003	-776.33

From Table 2 Strategy A is excluded from the options because it produces less effect with high cost, hence the ICER is higher $1.79 as compared to $2.00 for strategy A and negative $776.33 for strategy C.

TABLE 3. Incremental Cost-Effectives Analysis

Alternative Interventions	Total Cost($)	Total Effect	Change in Cost($)	Change in Effect	ICER ($)
Strategy B (Preventive)	1.6986	0.9500	1.6986	0.9500	1.79
Strategy C (Preventive and Curative)	2.1657	1.5003	0.4671	0.5503	0.85

From Table 3, strategy C dominates strategy B in terms of lives saved and cost. The analysis revealed a cost saving of $0.85 for C over B as compared to $1.79 for B over C. In other words, it cost less ($0.85) to get an additional life-year gained with strategy C than with strategy B ($1.79).

11. Conclusions

The model is shown to have a stable disease free equilibrium when the basic reproduction number is less than unity. This shows a similar impression when the treatment is administered to only the human population with all other things remaining unchanged.

It is also noted that;

- The persistence of the disease depends on some parameters that measure the characteristics of the susceptible animals and infection.
- The second is the requirement that the density of susceptible animals must not exceed a certain critical value for the disease not to persist.

A sensitivity analysis of the basic reproduction number indicates that the rate of infection, Conversion rate of susceptible predator and the rate of predation of the infected prey are the most critical parameter to consider for fighting against the infection.

Conflict of Interests

The authors declare that there is no conflict of interests.

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