RESEARCH ARTICLE

COMPUTATIONAL DYNAMICS AND OPTIMAL CONTROL OF TOXOPLASMOSIS DISEASE IN HUMAN AND CAT POPULATIONS

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ABSTRACT

In this paper, a non-linear mathematical model for computational dynamics and optimal control of Toxoplasmosis disease in human and cat populations is formulated and analysed. The steady states of the equilibrium points are determined and found to be locally asymptotically stable if the threshold parameter is less than unity and unstable if it is greater than unity. However the analysis shows that the endemic equilibrium point is globally asymptotically stable if the threshold parameter is greater than unity. The basic reproduction number of the model is determined. Two control measures: (vaccination and quarantine of infected humans) and (vaccination and quarantine of infected cats) are incorporated to the model and analysed in order to determine the optimal control. Numerical simulations of the model in the presence of control measures are finally performed. The results show that in the presence of optimal control, the Toxoplasmosis Disease can be eliminated in the Society.

Key words: Toxoplasmosis, Optimal, Control, Cat, Human, gondii

INTRODUCTION

Toxoplasmosis is an infection of warm-blooded vertebrates caused by the obligate intracellular protozoan parasite, toxoplsama gondii. It is one of the most common parasitic human diseases which has infected approximately one-third of the world's population (Kistiah *et al.*, 2012). The protozoan toxoplasma gondii is a prevalent parasite in wild and domestic animals worldwide, especially in cats, being transmitted through the food chain by carnivorous feeding and scavenging (Beaver *et al.*, 1984). Its life cycle include asexual multiplication in various tissues of intermediate hosts and sexual reproduction in the intestine of definitive hosts. Intermediate hosts are probably all warm-blooded animals including all livestock and animals, while definitive hosts are members of the family felidae, for example, domestic cats (Tenter, 2009). The infection is mainly acquired by ingestion of undercooked or raw meat containing viable tissue cysts and/or by ingestion of food and water that are contaminated with oocysts shed by felis (Dubey and Jones, 2008). Also, humans can inadvertently ingest oocysts that cats have passed in their feces, either from a little box or from soil (soil from gardening, unwashed fruits or unfiltered water). Further, women can transmit the infection transplacentally to their unborn fetus (Jones *et al.*, 2003). To prevent toxoplasmosis and other food-borne illnesses, food should be cooked at a safe temperature ($\approx 71.1^0$C). Optimal Control is the process of determining control and state trajectories for a dynamic system, over a period of time, in order to optimize a given performance index (Rodrigues *et al.*, 2014). Since the financial resources are limited, optimal control is used to optimize investments for disease prevention. In dynamical systems, a typical optimal control problem for ordinary differential equations is described by the state equation

$$g_i'(t) = f\left(t,\ g_i,\ u(t)\right),$$

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where $u(t)$ is the control and g_i are the state variables which depend on the control variables in a time t, with $t_0 \leq t \leq t_f$. The main goal is to find a piecewise continuous control variable $u(t)$ and the associated state variables g_i in order to maximize or minimize the given objective functional subject to some constraints (Rodrigues *et al.*, 2012).

The basic optimal control problem used to minimize the objective function is given by,

$$J = \min_{u \in U} \int_{t_0}^{t_f} f\left(t, g_i, u(t)\right) dt, \qquad (1)$$

subject to

$$g_i'(t) = f\left(t, g_i, u(t)\right),$$
$$g(t_0) = g_0,$$
$$a \leq u(t) \leq b,$$

where a and b are fixed real constants and $a < b$, $g(t_f)$ is free, which implies that the value of $g(t_f)$ is unrestricted or fixed. Such a minimizing control is called an optimal control (Lenhart and Workman, 2007). The technique involved in the optimal control problem is to solve a set of necessary conditions that an optimal control and the corresponding state must satisfy. Pontryagin's maximum principle provides necessary conditions for the optimal control using Hamiltonian H (Pontryagin's *et al.*, 1962), which is defined as:

$$H\left(t, g_i, u(t), \}_i\right) = f\left(t, g_i, u(t)\right) + \sum_{i=1}^{n} \}_i g_i$$

subject to

$$\frac{d g_i}{dt} = f\left(t, g_i, u(t), \}_i\right) \qquad (2)$$

where $\}_i$ are the adjoint variables or co-state variable and n is the number of the ith state variables. If $u_i^*(t)$ are optimal for equation (2), subject to some ordinary differential equations defining the given dynamical systems, then there exists a piecewise differentiable adjoint variable $\}$ such that:

$$H\left(t, g_i, u(t), \}_i\right) \leq H\left(t, g_i, u^*(t), \}_i\right) \qquad (3)$$

for each control $u_i(t)$ at each time t. The necessary conditions for optimizing H with respect to u at u^* are,

$$\frac{\partial H}{\partial u_i} = 0, \text{ at } u_i^* \Rightarrow f_{u_i} + \left(\sum_{1}^{n} \}_i g_i \right),$$
$$\frac{d \}_i}{dt} = -\frac{\partial H}{\partial g_i} \Rightarrow \frac{d \}_i}{dt} = -\left(f_{g_i} + \sum_{1}^{n} \}_i g_i \right),$$
$$\}(t_f) = 0.$$

It is then intended to optimise the given objective functional, subject to some constraints (Evans, 2006, Lenhart and Workman, 2007).

Model Formulation

The Basic Model: Arena *et al.*, (2009) studied the dynamics of a toxoplasmosis disease in human and cat populations. Their results revealed that the dynamics of toxoplasmosis disease is strongly influenced by both the horizontal transmission and vertical transmission in human and cat populations respectively. Their results also revealed that the control strategy to reduce toxoplasmosis prevalence should focus on reducing the infection through vaccine program for cat populations. However Arena *et al.* (2009) analysed the dynamics of toxoplasmosis disease in human and cat populations without applying any control strategies. Hence this study intends to incorporate the optimal control strategies on the disease dynamics of toxoplasmosis infections through

vaccination and quarantine to both human and cat populations. Therefore a nonlinear mathematical model is proposed and analysed to study the dynamics of toxoplasmosis disease in human and cat populations.

Model Assumptions

The following assumptions are considered in model formulation:

- Toxoplasma gondii occurs in the population when there is a direct or indirect contact between the susceptible human and infected cats,
- There is no human to human transmission,
- Infected human enters the recovery class $R(t)$ at a rate of u,
- The susceptible cat is infected when there is a direct contact with infected vector (cat),
- The population is assumed to be constant to both human and cat since their birth rates and death rates are equal,
- The susceptible human population $S_1(t)$ and susceptible cat population $S_2(t)$ have the same probabilities of being infected.

The model divides the population into two sub populations: the human population and the vector (cat) population. Human population N_1 is divided into three groups: humans being at risk of being infected by toxoplasmosis disease (S_1), humans being infected by toxoplasmosis (I_1) and humans who have recovered from toxoplasmosis (R). The vector (cat) population is divided into two groups: the susceptible cats which have not yet been infected by toxoplasmosis disease ,(S_2) and cats already infected by toxoplasmosis disease (I_2) (Arena *et al.*, 2009). The new infection occurs in both populations when the susceptible human population and infected cat population come into contact. With, $N_2(t)$, the total cat population at time t, Q, recruitment rate of susceptible humans, f, recruitment rate of susceptible cats, s_1, disease transmission rate to the susceptible human by infected cats, s_2, disease transmission rate to the susceptible cat by infected cat, Γ, the rate of progression to susceptible human from recovery, $\sim_1$, human natural death rate, $\sim_2$, cat natural death rate, m_1, the human death rate due to disease, m_2, the cat death rate due to disease, u_1, the control measure to human due to vaccination and quarantine of infected human, u_2 the control measure to cat due to vaccination and quarantine of infected cat and taking into account of the above considerations and assumptions, we have the following schematic flow diagram:
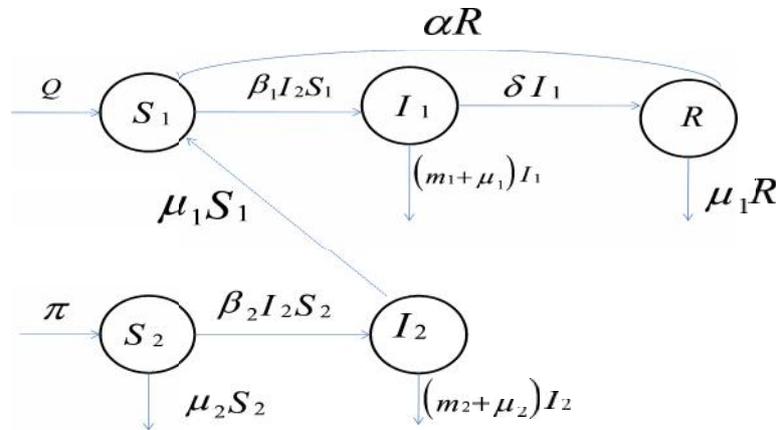

Figure 1. Compartmental Diagram for a Toxoplasmosis Model

From the above flow diagram, the dynamics of the disease is governed by the following system of nonlinear ordinary differential equations:

$$\frac{dS_1}{d_t} = Q - s_1 I_2 S_1 + \Gamma R - \sim_1 S_1$$

$$\frac{dI_1}{d_t} = s_1 I_2 S_1 - (u + m_1 + \sim_1) I_1$$

$$\frac{dR}{d_t} = u I_1 - (\Gamma + \sim_1) R$$

$$\frac{dS_2}{d_t} = f - s_2 I_2 S_2 - \sim_2 S_2$$

(4)

$$\frac{dI_2}{dt} = \text{s}_2 I_2 S_2 - (m_2 + \sim_2) I_2$$

with initial conditions $S_1(0) = S_0, I_1(0) = I_0, R(0) = R_0, S_2(0) = S_0, I_2(0) = I_0.$

The total populations for human and vector (cat) population are

$$N_1 = S_1 + I_1 + R, \tag{5}$$

$$N_2 = S_2 + I_2. \tag{6}$$

Model Analysis: The model system (4) will be analysed qualitatively to get insight to its dynamical features which give a better understanding of toxoplasmosis disease in human and cat populations.

Invariant Region: The model under consideration involves human population and vector (cat) populations. Therefore, it is assumed that all the variables and parameters in the model are positive for all $t \geq 0$. The total populations can be determined by $N_1 = S_1 + I_1 + R$ and $N_2 = S_2 + I_2$ respectively. Then we have the following Lemma.

Lemma 1: The solution set $\{S_1, I_1, R, S_2, I_2\} \in \sqcup_+^5$ of system (4) is contained in the feasible region Ω.

Proof:

If N is the total population size, then

$$N = S_1 + I_1 + R + S_2 + I_2.$$

It follows that

$$\frac{dN}{dt} = \frac{dS_1}{dt} + \frac{dI_1}{dt} + \frac{dR}{dt} + \frac{dS_2}{dt} + \frac{dI_2}{dt}$$

or

$$\frac{dN}{dt} = Q - \sim N + mI_1$$

For the human population, we have

$$\frac{dN_1}{dt} \leq Q - \sim N_1 \tag{7}$$

The differential equation (7) has a solution

$$-\frac{1}{\sim_1} \ln(Q - \sim_1 N_1) \leq t + c$$

or

$$N_1 \leq \frac{Q}{\sim_1} - \left(\frac{Q - \sim_1 N_0}{\sim_1}\right) e^{-\sim_1 t} \tag{8}$$

Similarly, for vector (cat) population, we have:

$$N_2 \leq \frac{f}{\sim_2} - \left(\frac{f - \sim_2 N_0}{\sim_2}\right) e^{-\sim_2 t} \tag{9}$$

As $t \to \infty$, we have

$$N_1 \le \frac{Q}{\sim_1} \text{ and } N_2 \le \frac{f}{\sim_2} \tag{10}$$

Since $N_1 \le \frac{Q}{\sim_1}$ and $N_2 \le \frac{f}{\sim_2}$, then the basic Mathematical model is well posed and it is mathematically relevant; hence it is sufficient to study the dynamics of the epidemiological system (4) in the region Ω.

Positivity of Solutions

Lemma 2: If the initial Solution of a dynamical model (4) is $\{S_1(0), I_1(0), R(0), S_2(0), I_2(0) \ge 0\} \in \Omega$, then the solution set $\{S_1(t), I_1(t), R(t), S_2(t), I_2(t)\}$ of the model system (4) is positive for all $t > 0$.

Proof:

From the first equation of the model system (4), we have

$$\frac{dS_1}{dt} = Q - \mathsf{s}_1 I_2 S_1 + \mathsf{r} R - \sim_1 S_1$$

or

$$\frac{dS_1}{dt} \ge -\left(\mathsf{s}_1 I_2 + \sim_1\right) S_1 \tag{11}$$

The inequality (11) has a solution

$$S_1(t) \ge e^{-\int (\mathsf{s}_1 I_2 + \sim_1) dt} \tag{12}$$

As $t \to \infty$, $S_1 > 0$.

Similarly using the other equations of system (4), positivity of solutions can be established. Hence, all the solutions of the system (4) are positive for all $t > 0$.

Disease free Equilibrium Point (DFE): The Equilibrium point of the system (4) can be established by setting

$$\frac{dS_1}{dt} = \frac{dI_1}{dt} = \frac{dR}{dt} = \frac{dS_2}{dt} = \frac{dI_2}{dt} = 0. \tag{13}$$

Then

$$0 = Q - \mathsf{s}_1 I_2 S_1 + \mathsf{r} R - \sim_1 S_1$$

$$0 = \mathsf{s}_1 I_2 S_1 - \left(\mathsf{u} + \sim_1 + m_1\right) I_1$$

$$0 = \mathsf{u} I_1 - \left(\mathsf{r} + \sim_1\right) R \tag{14}$$

$$0 = f - \mathsf{s}_2 I_2 S_2 - \sim_2 S_2$$

$$0 = \mathsf{s}_2 I_2 S_2 - \left(\sim_2 + m_2\right) I_2$$

At the steady state, $S_1 = I_1 = R = S_2 = I_2 = 0$. Therefore from the model system (14), the disease free equilibrium E_0 is

$$E_0 = \left(S_1^*, \ I_1^*, \ R^*, \ S_2^*, \ I_2^*\right) = \left(\frac{Q}{\sim_1}, \ 0, \ 0, \ \frac{f}{\sim_2}, \ 0\right). \tag{15}$$

The Basic Reproduction Number $\mathfrak{R}_0$: The basic reproduction number $\mathfrak{R}_0$, is defined as the average number of secondary cases produced by a "typical" infected (assumed infectious) individual during his/her entire life of infectious period when introduced in a population of susceptibles (Dierkman and Heesterbeek, 1990). Also, Dierkman *et al.* (1990) defined the basic reproduction number $\mathfrak{R}_0$, as the spectral radius $\left(\cdots\left(\mathbf{F}\mathbf{V}^{-1}\right)\right)$ of the next generation matrix.

This can be expressed by a threshold parameter such that, if the DFE is locally asymptotically stable, then the disease cannot invade the population and $\Re_0 < 1$, whereas, if the number of infected individuals grow, the disease can invade the population and $\Re_0 > 1$ (Driessche and Watmough, 2008).

$\Re_0$ can be obtained through computation of Eigen values of the Jacobian matrix using next generation operator matrix (Driessche and Watmough, 2002), which is obtained by taking the largest (dominant) eigenvalue (spectral radius) of

$$\left[\frac{\partial \mathbf{F}_i(E_0)}{\partial X_i}\right]\left[\frac{\partial \mathbf{V}_i(E_0)}{\partial X_i}\right]^{-1} \tag{16}$$

where $\mathbf{F}_i(x)$ is the rate of new infections entering compartment i, $\mathbf{V}_i^+(x)$ is the rate of transfer into compartment i by any other means and $\mathbf{V}_i^-(x)$ is the rate of transfer out of compartment i and E_0 is the disease free equilibrium. Also, it is assumed that each function $\left(\mathbf{F}_i, \mathbf{V}_i^+, \mathbf{V}_i^-\right)$ is continuously differentiable at least twice with respect to each variable and $\mathbf{V}_i = \mathbf{V}_i^- - \mathbf{V}_i^+$ (Driessche and Watmough, 2002).

Therefore

$$\mathbf{F}_i = \begin{bmatrix} F_1 \\ F_2 \\ F_3 \\ F_4 \\ F_5 \end{bmatrix} = \begin{bmatrix} Q + r R \\ s_1 I_2 S_1 \\ u R \\ f \\ s_2 I_2 S_1 \end{bmatrix}. \tag{17}$$

The transfer of individual out of compartments i is given by,

$$\mathbf{V}_i = \begin{bmatrix} V_1 \\ V_2 \\ V_3 \\ V_4 \\ V_5 \end{bmatrix} = \begin{bmatrix} s_1 I_2 S_1 + \sim_1 S_1 \\ (u + m_1 + \sim_1) I_1 \\ (r + \sim_1) R \\ s_2 I_2 S_2 + \sim_2 S_2 \\ (m_2 + \sim_2) I_2 \end{bmatrix}. \tag{18}$$

By linearization at the DFE, we have

$$\mathbf{F} = \begin{bmatrix} 0 & 0 & r & 0 & 0 \\ 0 & 0 & 0 & 0 & \dfrac{Q s_1}{\sim_1} \\ 0 & u & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \dfrac{f s_2}{\sim_2} \end{bmatrix}, \tag{20}$$

and

$$\mathbf{V} = \begin{bmatrix} \sim_1 & 0 & 0 & 0 & \dfrac{Q s_1}{\sim_1} \\ 0 & (u + m_1 + \sim_1) & 0 & 0 & 0 \\ 0 & 0 & 0 & r + \sim_1 & 0 \\ 0 & 0 & 0 & \sim_2 & \dfrac{f s_2}{\sim_2} \\ 0 & 0 & 0 & 0 & m_2 + \sim_2 \end{bmatrix}. \tag{21}$$

Then

$$
\mathbf{FV}^{-1} = \begin{bmatrix}
0 & 0 & r\left(u\,\tilde{}_1\tilde{}_2 + m_1\tilde{}_1\tilde{}_2 + \tilde{}_1^2\tilde{}_2\right) & 0 & 0 \\[2mm]
0 & 0 & 0 & 0 & \dfrac{Q s_1}{\tilde{}_1\left(m_2 + \tilde{}_2\right)} \\[3mm]
0 & \dfrac{u\left(r\,\tilde{}_1\tilde{}_2 + \tilde{}_1^2\tilde{}_2\right)}{\left(r + \tilde{}_1\right)\left(u\,\tilde{}_1 + m_1\tilde{}_1 + \tilde{}_1^2\right)\tilde{}_2} & 0 & 0 & 0 \\[3mm]
0 & 0 & 0 & 0 & 0 \\[2mm]
0 & 0 & 0 & 0 & \dfrac{f s_2}{\tilde{}_2\left(m_2 + \tilde{}_2\right)}
\end{bmatrix}.
$$

(22)

The Eigen values of (22) are given by

$$
\}_{1,\,2,\,3,\,4,\,5} = \left\{ 0,\ 0,\ 0,\ 0,\ \dfrac{f s_2}{\tilde{}_2\left(m_2 + \tilde{}_2\right)} \right\}
$$

(23)

Therefore the basic reproduction number $\Re_0$ is given by

$$
\Re_0 = \dfrac{f s_2}{\tilde{}_2\left(m_2 + \tilde{}_2\right)}.
$$

(24)

Stability Analysis of Disease Free Equilibrium Point

Lemma 3: If $\Re_0 < 1$, the disease free equilibrium point of the model is locally asymptotically stable and unstable if $\Re_0 > 1$ (Driessche and Watmough, 2008).

The stability of disease free equilibrium point is established by linearization of the system of ordinary differential equations. We linearize the model system (4) and compute its Jacobian matrix $\mathbf{J}_E$ as follows:

$$
\mathbf{J}_E = \begin{bmatrix}
\dfrac{\partial f_1}{\partial S_1} & \dfrac{\partial f_1}{\partial I_1} & \dfrac{\partial f_1}{\partial R} & \dfrac{\partial f_1}{\partial S_2} & \dfrac{\partial f_1}{\partial I_2} \\[3mm]
\dfrac{\partial f_2}{\partial S_1} & \dfrac{\partial f_2}{\partial I_1} & \dfrac{\partial f_2}{\partial R} & \dfrac{\partial f_2}{\partial S_2} & \dfrac{\partial f_2}{\partial I_2} \\[3mm]
\dfrac{\partial f_3}{\partial S_1} & \dfrac{\partial f_3}{\partial I_1} & \dfrac{\partial f_3}{\partial R} & \dfrac{\partial f_3}{\partial S_2} & \dfrac{\partial f_3}{\partial I_2} \\[3mm]
\dfrac{\partial f_4}{\partial S_1} & \dfrac{\partial f_4}{\partial I_1} & \dfrac{\partial f_4}{\partial R} & \dfrac{\partial f_4}{\partial S_2} & \dfrac{\partial f_4}{\partial I_2} \\[3mm]
\dfrac{\partial f_5}{\partial S_1} & \dfrac{\partial f_5}{\partial I_1} & \dfrac{\partial f_5}{\partial R} & \dfrac{\partial f_5}{\partial S_2} & \dfrac{\partial f_5}{\partial I_2}
\end{bmatrix}
$$

At the disease free equilibrium point, $\mathbf{E}_0 = \left(\dfrac{Q}{u_1},\ 0,\ 0,\ \dfrac{f}{u_2},\ 0 \right)$ and the Jacobian matrix becomes:

$$
\mathbf{J}_{E_0} =
\begin{bmatrix}
-\mu_1 & 0 & r & 0 & \dfrac{-Qs_1}{\mu_1} \\[2mm]
0 & -(u+m_1+\mu_1) & 0 & 0 & \dfrac{Qs_1}{\mu_1} \\[2mm]
0 & u & -(r+\mu_1) & 0 & 0 \\[2mm]
0 & 0 & 0 & -\mu_2 & \dfrac{-fs_2}{\mu_2} \\[2mm]
0 & 0 & 0 & 0 & \dfrac{fs_2}{\mu_2}-(m_2+\mu_2)
\end{bmatrix}
$$

$$(25)$$

Theorem 2: *The disease free equilibrium is locally asymptotic stable if the eigenvalues of the Jacobian matrix has negative real parts (Brauer et al.,2008).*

The eigenvalues of the matrix (25) are

$$
\left(-\mu_1,\ -\mu_2,\ -(r+\mu_1),\ -(u+m_1+u_1),\ -\left(\frac{m_2\mu_2+\mu_2^2+fs_2}{\mu_2}\right)\right).
$$

Since all the Eigen values of the Jacobian matrix above have negative real parts, then the disease free equilibrium of the model is locally asymptotically stable.

Existence and Global (Local) Stability of Endemic Equilibrium Point: Endemic equilibrium point (EEP) is a steady state in which the disease persists in the populations (Driessche and Watmough, 2008). That is $I_1, I_2 \neq 0$, which is given by $E_1 = \left(S_1^*, I_1^*, R^*, S_2^*, I_2^*\right) \neq 0$. Then, by solving the model systems (4), we express each equilibrium point at a steady state to get $S_1^*,\ I_1^*,\ R^*,\ S_2^*,\ I_2^*$ as an endemic equilibrium where:

$$
S_1^* = \frac{Qs_2\mu_2(r+\mu_1)(u+m_1+\mu_1)(R_0-1)}{s_1\mu_2(r+\mu_1)(u+m_1+\mu_1)(R_0-1)^2 - rs_1\mu_1(R_0-1)^2 + s_2\mu_1(r+\mu_1)(u+m_1+\mu_1)(R_0-1)}
$$

$$
I_1^* = \frac{Qs_1\mu_2(r+\mu_1)(R_0-1)}{s_1\mu_2(r+\mu_1)(u+m_1+\mu_1)(R_0-1) - rs_1\mu_2 u(R_0-1) + s_2\mu_1(r+\mu_1)(u+m_1+\mu_1)}
$$

$$
R^* = \frac{Qs_1\mu_2 u(R_0-1)}{s_1\mu_2(r+\mu_1)^2(u+m_1+\mu_1)(R_0-1) - rs_1\mu_2 u(r+\mu_1)(R_0-1) + s_2\mu_1(r+\mu_1)^2(u+m_1+\mu_1)}
$$

$$
S_2^* = \frac{f}{\mu_2}R_0
$$

$$
I_2^* = \frac{\mu_2}{s_2}(R_0-1)
$$

From the above equations of S_1^*, I_1^*, R^*, S_2^* and I_2^*, we conclude that the endemic equilibrium point E_1 is always non-negative and well-defined if and only if $R_0 > 1$. Therefore, we state the following lemma 3 as follows:

Lemma 3: The endemic equilibrium point E_1 exists and is always positive if and only if $\Re_0 > 1$ (Driessche and Watmough, 2002). Hence, the model system (4) will exhibit forward bifurcation.
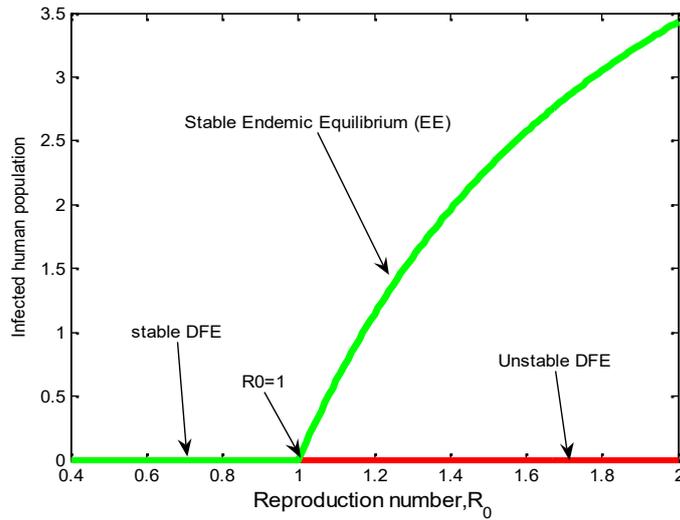
Figure 2: The Forward Bifurcation

From the figure above, it can be seen that, the forward bifurcation occurs at $\Re_0 = 1$, meaning that the disease is decreasing due to interventions and if $\Re_0 < 1$, no endemic exists while If $\Re_0 > 1$, the endemic equilibrium exists in the population

Global stability of the Endemic Equilibrium point E_1

Theorem 3: If $\Re_0 > 1$, the endemic equilibrium of the model system (4) is globally asymptotically stable.

Proof:

Using the constructed Lyapunov function as suggested by Cai and Li (2010), the global stability of Endemic equilibrium can be analysed by defining the Lyapunov function as

$$V\left(S_1^*, I_1^*, R^*, S_2^*, I_2^*\right) = \left(S_1 - S_1^* - S_1^* \log\frac{S_1^*}{S_1}\right) + \left(I_1 - I_1^* - I_1^* \log\frac{I_1^*}{I_1}\right)$$
$$+ \left(R - R^* - R^* \log\frac{R^*}{R}\right)\left(S_2 - S_2^* - S_2^* \log\frac{S_2^*}{S_2}\right) + \left(I_2 - I_2^* - I_2^* \log\frac{I_2^*}{I_2}\right).$$

It can be shown that

$$\frac{dV}{dt} = K - R \tag{25}$$

Where

$$K = \frac{\left(S_1 - S_1^*\right)}{S_1}\left[Q + r\left(R - R^*\right)\right] + s_1\left(I_2 - I_2^*\right)\left(S_1 - S_1^*\right)\frac{\left(I_1 - I_1^*\right)}{I_1} + u\frac{\left(R - R^*\right)}{R}\left(I_1 - I_1^*\right)$$
$$+ f\frac{\left(S_2 - S_2^*\right)}{S_2} + s_2\left(S_2 - S_2^*\right)\frac{\left(I2 - I_2^*\right)^2}{I_2},$$

$$R = \frac{\left(S_1 - S_1^*\right)^2}{S_1}\left[\sim_1 + s_1\left(I2 - I_2^*\right)\right] + \left(u + m_1 + \sim_1\right)\frac{\left(I_1 - I_1^*\right)^2}{I_1}$$

$$+\left(r+\sim_1\right)\frac{\left(R-R^*\right)^2}{R} + S_2\left(I_2-I_2^*\right)\frac{\left(S_2-S_2^*\right)^2}{S_2}$$

$$+\sim_2\frac{\left(S_2-S_2^*\right)^2}{S_2}+\left(m_2+\sim_2\right)\frac{\left(I_2-I_2^*\right)^2}{I_2}\,.$$

Thus, if $K<R$, then $\frac{dV}{dt}\leq 0$. But $\frac{dV}{dt}=0$ if and only if $S_1=S_1^*$, $I_1=I_1^*$, $R=R^*$, $S_2=S_2^*$ and $I_2=I_2^*$. Therefore, the largest compact invariant set in $\left\{\left(S_1^*,I_1^*,R^*,S_2^*,I_2^*\right)\in\Omega:\frac{dV}{dt}=0\right\}$ is the singleton $\{E_1\}$, where E_1 is the endemic equilibrium point of the model systems (4). Therefore, by LaSalle's invariant principle, E_1 is globally asymptotically stable in Ω if $K<R$.

Model with Control Variable

Introduction

In this section, the mathematical model system (4) is extended by incorporating two time- dependent controls u_1 and u_2 where
(i) $u_1 = $ Control measure due to vaccination and quarantine of infected humans,
(ii) $u_2 = $ Control measure due to vaccination and quarantine of infected cats.

Then the model becomes

$$\frac{dS_1}{dt}=Q-\left(1-u_1\right)S_1I_2S_1+rR-\sim_1S_1$$

$$\frac{dI_1}{dt}=\left(1-u_1\right)S_1I_2S_1-\left(u+\sim_1+m_1+m_2\right)I_1$$

$$\frac{dR}{dt}=uI_1-\left(r+\sim_1\right)R \tag{26}$$

$$\frac{dS_2}{dt}=f-\left(1-u_2\right)S_2I_2S_2-\sim_2S_2$$

$$\frac{dI_2}{dt}=\left(1-u_2\right)S_2I_2S_2-\left(\sim_2+m_2\right)I_2$$

where the control functions are bounded i.e. $0\leq u_1(t)\leq 1$ and $0\leq u_2(t)\leq 1$.

Optimal Control Problem: Here we aim at minimizing the Toxoplasmosis disease while optimizing $u_1(t)$ (control measure due to vaccination and quarantine of infected human) and $u_2(t)$ (the control measure due to vaccination and quarantine of infected cats). In order to minimize infection, it is required to minimize the objective function

$$J\left(u_i\right)=\int_{t_0}^{t_f}\left[B_1S_1(t)+B_2S_2(t)+B_3I_1(t)+B_4I_2(t)+\frac{1}{2}\sum_{i=1}^{2}c_iu_i^2\right]dt \tag{27}$$

subject to $x'(t) = g\big(t, x(t), u_1(t), u_2(t)\big)$, with $x(t_0) = x_0$ and $x(t_f)$ free variables. B_1, B_2, ..., B_4 are the balancing cost factors, while $\frac{c_1}{2}u_1^2$ is the cost of treatment and $\frac{c_2}{2}u_2^2$ is the cost associated with education campaigns, c_1 and c_2 are weights which depend on the relative importance of each of the control measures. It is then intended to find optimal controls u_1^* and u_2^*, such that $J\big(u_1^*, u_2^*\big) = \min J\big(u_1, u_2\big)$, where $0 \le u_1 \le 1$ and $0 \le u_2 \le 1$. The Pontryagin maximum principle will be used to suggest the necessary optimal conditions, by forming Hamiltonian function

$$H = B_1 S_1(t) + B_2 S_2(t) + B_3 I_1(t) + B_4 I_2(t) + \frac{1}{2}\sum_{i=1}^{2} c_i u_i^2 + \sum_{i=1}^{5} \}_i g_i \tag{28}$$

where $g_i\big(x, u_1(t), u_2(t), t\big)$ are the equations on the right hand side of the Ordinary differential equation of Control problem and $\}_i$ are co-state variables with $i = 1, 2, 3, 4, 5$.

Theorem 2: There exists a pair of optimal controls $\big(u_1^*, u_2^*\big)$ and optimal solution $\big(S_1^*, S_2^*, I_1^*, I_2^*, R^*\big)$ that minimizes $J\big(u_1, u_2\big)$ Furthermore there exist adjoint functions $\}_i(t)$ for $i = 1, 2, 3, 4, 5$ satisfying equation (28) for the Hamiltonian (H) (Okosun and Makinde, 2013b_3); such that

$$\frac{d\}_1}{dt} = -\frac{\partial H}{\partial S_1} = B_1\big((1-u_1)s_1 I_2 - \sim_1\big) - B_3(1-u_1)s_1 I_2$$
$$-\}_1\big((1-u_1)s_1 I_2 - \sim_1\big) - \}_2\big((1-u_1)s_1 I_2\big),$$
$$\frac{d\}_2}{dt} = -\frac{\partial H}{\partial I_1} = B_3\big(u + +m_1 + \sim_1\big) + \}_2\big(u + m_1 + \sim_1\big) - u\}_3$$
$$\frac{d\}_3}{dt} = -\frac{\partial H}{\partial R} = -r B_1 - r\}_1 + \}_3\big(r + \sim_1\big)$$
$$\frac{d\}_4}{dt} = -\frac{\partial H}{\partial S_2} = B_2\big((1-u_2)s_2 I_2 - \sim_2\big) - B_3(1-u_2)s_2 I_2$$

$$-B_4(1-u_2)s_2 I_2 - \}_4\big((1-u_2)s_2 I_2 - \sim_2\big) - \}_5(1-u_2)s_2 I_2 \tag{29}$$
$$\frac{d\}_5}{dt} = -\frac{\partial H}{\partial I_2} = B_1(1-u_1)s_1 S_1 + B_2\big(1-u_2\big)s_2 S_2$$
$$-B_3(1-u_1)s_1 S_2 - B_4\big((1-u_2)s_2 S_2 - (m_2 + \sim_2)\big)$$
$$+\}_1(1-u_1)s_1 S_1 - \}_2(1-u_1)s_1 S_1$$

$$+\}_4(1-u_2)s_2 S_2 - \}_5\big((1-u_2)s_2 S_2 - (m_2 + \sim_2)\big)$$

with the transversality conditions

$$\}_1(t_f) = \}_2(t_f) = \}_3(t_f) = \}_4(t_f) = \}_5(t_f) = 0. \tag{30}$$

The optimal controls u_1^* and u_2^* can be solved from the optimality conditions $\frac{\partial H}{\partial u_1} = 0$ and $\frac{\partial H}{\partial u_2} = 0$ as suggested by Lenhart and Workman (2007). Thus

$$\frac{\partial H}{\partial u_1} = s_1 I_2 S_1\big(B_1 - B_3 + \}_1 - \}_2\big) + c_1 u_1,$$

$$\frac{\partial H}{\partial u_2} = s_2 I_2 S_2\big(B_2 - B_4 + \}_4 - \}_5\big) + c_2 u_2. \tag{31}$$

This gives

$$u_1 = \frac{s_1 I_2 S_1\big(B_3 - B_1 - \}_1 + \}_2\big)}{c_1},$$

$$u_2 = \frac{S_2 I_2 S_2 (B_4 - B_2 - \}_4 + \}_5)}{c_2}.$$

(32)

Consequently

$$u_1^* = \max \left\{ 0, \ \min \left(1, \ \frac{S_1 I_2 S_1 (B_3 - B_1 - \}_1 + \}_2)}{c_1} \right) \right\}$$

and

$$u_2^* = \max \left\{ 0, \ \min \left(1, \ \frac{S_2 I_2 S_2 (B_4 - B_2 - \}_4 + \}_5)}{c_2} \right) \right\}$$

(33)

By standard control arguments as suggested by Makinde and Okusun (2013), we have

$$u_1^* = \begin{cases} 0 & if & u_1 \leq 0 \\ u_1 & if & 0 \leq u_1 \leq 1 \\ 1 & if & u_1 \geq 1 \end{cases}$$

and

$$u_2^* = \begin{cases} 0 & if & u_2 \leq 0 \\ u_2 & if & 0 \leq u_2 \leq 1 \\ 1 & if & u_2 \geq 1 \end{cases}.$$

(34)

Numerical Simulations of the Model with Control: In this section, we illustrate the analytical results of the study by carrying out numerical simulations of the model with controls i.e. model system (26) using the set of estimated parameter values given in the Table 1 below.

Table 1: Parameter Values Used for Model Simulation

Parameters	Value per month	Source
S_1	0.5	Estimated
S_2	0.1	Estimated
$\sim_1$	0.2	Estimated
$\sim_2$	0.275	Estimated
u	0.19	Estimated
m_1	0.3	Estimated
m_2	0.41	Estimated
f	1	Estimated
Q	25	Estimated
r	0.98	Estimated

Initial values are estimated as $S_1(0)=200$, $I_1(0)=100$, $R(0)=80$, $S_2(0)=50$, and $I_2(0)=5$. The weights $A_i = B_i = 100$, for $i = 1, 2, 3, 4$ and 5 are used, in order to show the effect of optimizing control measures in the control problem (26) when,

- Only a control measure due to quarantine of exposed and susceptible humans, u_1, is applied to the model equations,
- Only a control measure due to vaccination and quarantine of infected cats (u_2) is applied to the model equations,
- Both controls, u_1 and u_2 are applied to the model equations.

Figures 3 below show the behaviour of the control model when one control u_1 (Control measure of humans due to vaccination and quarantine of infected humans) is applied.
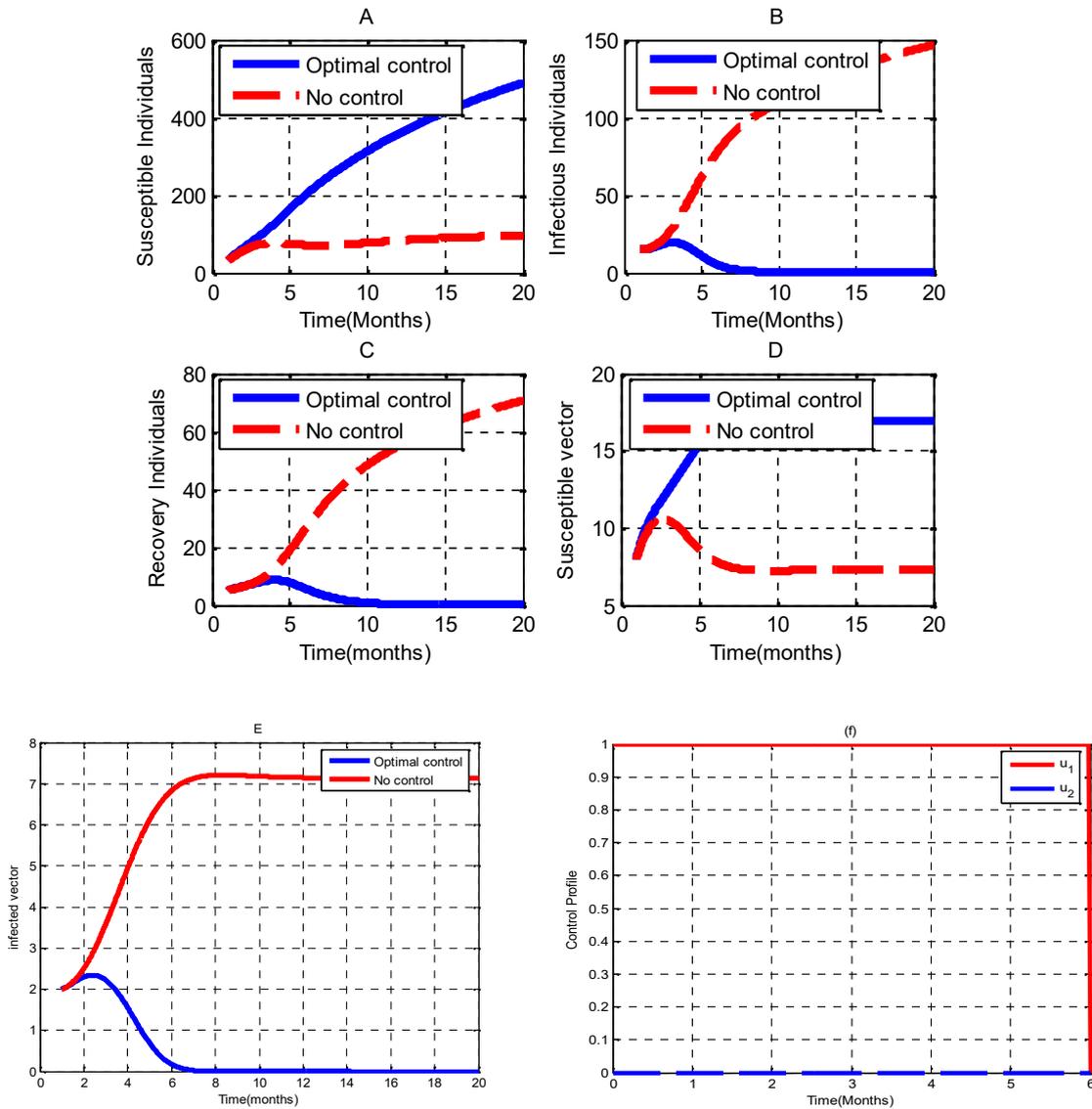
Figures 3. Behaviour of the Control Model When Only One Control, u_1 is Applied.

In figure 3A, it is seen that the susceptible individuals increase logistically with time when control u_1 is applied. This is because, as vaccination and quarantine are applied effectively to the susceptible individuals, large number of individuals increases continuously. On the contrary, when the control is not applied, the susceptible individuals increase with the increase in time. In figure 3B, it is seen that the application of control to the infected individuals results in reducing the number of infectious individuals with time. On the contrary, in the absence of vaccination and quarantine, the infectious individuals increase continuously since no supportive treatment is given to the group. In figure 3C, the numerical solution of recovered individuals with control and with no control is shown.

From the figure, it is seen that the number recovered individuals without control increase continuously than with control during the control period. On the contrary, the recovered individuals with control increase with time until the population develops immunity. Figure 3D shows that susceptible vectors with control increase to the maximum during the control period. The reason is, as vaccination is given to the susceptible vector, the number of susceptible individuals continues to increase with time. On the contrary, when vaccination is not given to the susceptible vectors, the number of susceptible individuals decrease with time. Figure 3E shows show that, in the absence of control u_1, the number of infected individuals increases to the maximum while with control u_1, the number of infected individuals decreases to zero.

Figures 4 below shows the behaviour of the control model when only the control u_2 (Control measure of vaccination and quarantine of infected cats) is applied
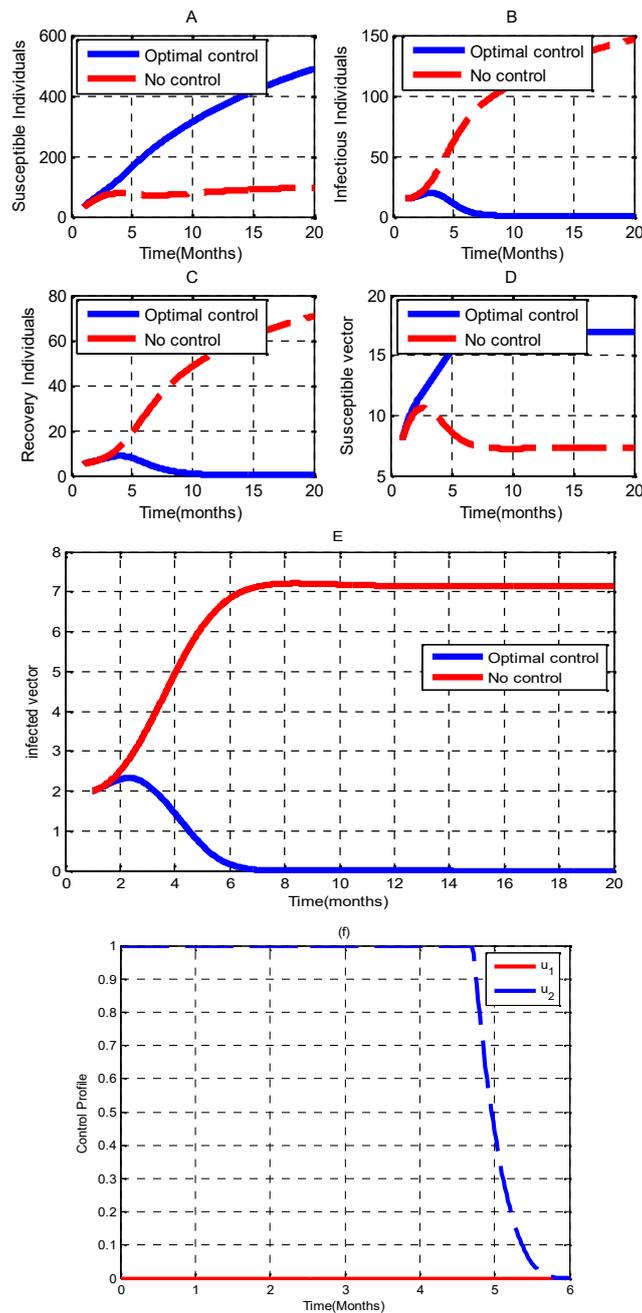
Figure 4. Behaviour of the Control Model When only the Control u_2 is Applied

Figure 4A shows that when control u_2 is applied, the number of susceptible individuals increase logistically with time. The same case occurs to susceptible vectors in figure 5.7 D, where the graph increases logistically to the maximum when vaccination is applied to susceptible vectors and decreases with time when no control is applied. Figure 4B shows that, if control measure of vaccination and quarantine is not applied, large number of infectious individuals increases logistically to the maximum. With the application of control, the infected individuals decrease with time The same happens in figure 4E where the infectious population increases logistically to the maximum when control is not applied to the group. On the contrary, when control measure is applied, the number of infectious decreases logistically with time. Figure 4C shows the recovery individuals with control and with no control. From the figure, it can be seen that the recovery class without control increases logistically with time. The reason is that large number of individuals from the susceptible and infectious groups who are not vaccinated, enter into this group. On the contrary, when we optimize the control u_2 the recovery individuals decrease with time until the population gets immunity. Figure 4F shows the control profile when u_2 (control measure of cat with vaccination and quarrantine of infected cat) is optimized. From the graph, the results show that, when control is optimized, the graph increases to the maximum and decreases with time until it drops to the final time where u_1 equals to zero.

Figures 5 below show the simulation of the model when both controls are optimized $\left(u_1, \ u_2 \neq 0 \right)$.
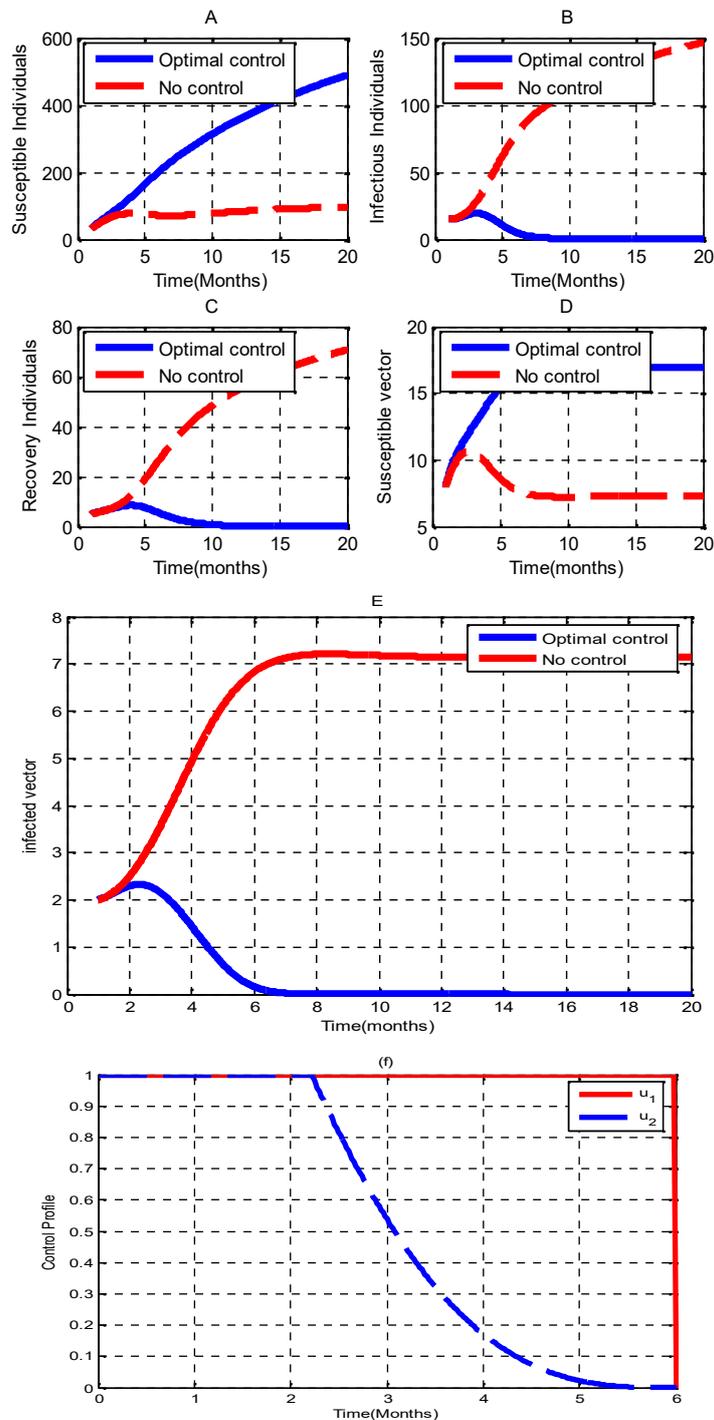
Figure 5. Simulation of the Model when both Control are Optimized $\left(u_1, \ u_2 \neq 0\right)$

Figures 5A and 5D, show that, in the presence of control strategies, susceptible individuals and susceptible vectors with control increase logistically with time, while if there is no control the related populations decrease with time. Figures 5B and 5E, show that, in the absence of control strategies, the populations of both infected individuals and infected vectors increase logistically with time. On the contrary, in the presence of control strategies, the infections decrease with time. Figure 5C shows the numerical solution of recovery individuals with control and with no control. The results show that, if no control strategies are used, the recovery class increases logistically with time, whereas the recovery class with control strategies increases with time until the population developed immunity. Figure 5F shows that using both controls, could minimize the rate of infection on the populations, where both controls are at the maximum and decrease to zero.

Conclusions

In this paper, a non-linear mathematical model for controlling toxoplasmosis infection to human and cat populations has been formulated and analysed to investigate the dynamical behaviour of the disease. Qualitative analysis was performed to the basic model. By applying stability theory of ordinary differential equations, the equilibrium points were found to be stable if the reproduction number was less than unity. Two control measures: control measure of humans due to vaccination and quarantine of

infected humans and control measure of cats due to vaccination and quarantine of infected cats were finally introduced to the model. Model simulation of the model revealed that application of control strategies of vaccination and quarantine may succeed in the elimination of toxoplasmosis infection in a society.

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