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Modelling and Optimal Control of Ebola Virus Disease in the Presence of Treatment and Quarantine of Infectives

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Abstract: In this paper, a non-linear mathematical model for the dynamics of Ebola virus diseases is formulated and analysed. The model has five classes namely susceptible human, exposed human, infected human, treated human and recovered human. Invariant region and positivity solution of the model are determined. Local stability analyses of disease free Equilibrium and endemic equilibrium are examined. The disease free equilibrium analysis is determined using Routh-Hurwitz criteria, whereby it is found to be locally stable if the reproduction number is less than one. Two control measures: control measure due to quarantine of exposed and susceptible individuals and control measure due to efficacy of treatment drug, used for treating Ebola virus disease Ebola victim are incorporated to the Ebola virus disease model. The control problem is then analysed in order to determine the optimal control. Numerical simulations for the model in the presence of control measures are finally performed. The results show that in the presence of optimal control, the Ebola virus disease can be eliminated in the Society. Furthermore, to minimize infections of Ebola virus disease, quarantine centres with skilled manpower must be prepared in advance so as to accommodate the significant number of exposed and susceptible individuals, in order to avoid further transmission in other areas out of quarantine centres. Also tracing of exposed and infected individuals must be efficiently done in order to quarantine the affected population and educate people on the transmission of the disease, symptoms and prevention measures in order to minimize human to human transmissions. Investing more on researches on new drugs which are effective in treating the Ebola virus disease victim is inevitable.

Keywords: Ebola, Control, Quarantine, Treatment, Infectives

1. Introduction

Ebola Virus Disease (formerly known as Ebola haemorrhagic fever) is a severe often fatal illness in humans. Ebola is a disease with haemorrhage bleedings. It usually affects human and non-human primates. Non-human primates include Monkeys, Gorillas and Chimpanzees [1]. Ebola virus comprises of five distinct species: Bundibugyo Ebolavirus (BDBV), Zaire Ebolavirus (EBOV), Reston Ebolavirus (RESTV), Sudan Ebolavirus (SUDV) and Tai Ebolavirus (TAFV) [2].

Ebola is characterized by flu like symptoms which rapidly progress to vomiting, diarrhoea, rash, internal and external bleeding [3]. Ebola is introduced into human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals. In Africa, infection has been spreading through the handling of infected chimpanzees, Gorillas, Fruitbats, Monkeys, Forest antelopes and porcupines found ill or dead in the Rain Forest. Ebola then spreads in the community through human to human transmission with infection resulting from direct contact (through scratched skin

or muscular membrane). Burial ceremonies in which mourners have direct contact with the body of the deceased can also play a role in Transmission of Ebola [4]. An incubation period, a time interval from infection with virus to onset of symptoms is 2 to 21 days [1].

Supportive car-rehydration with oral intravenous fluids and treatment of specific symptoms improve survival from Ebola virus disease [1] The treatment of Ebola hemorrhagic fever infected patient consists mainly of palliative treatment and treatment to avoid cardiovascular collapse and renal insufficiency [5]. Immediate quarantine, treatment and management by the hospital can halt the spread of the outbreak if one is quick to act on a person who has been in contact with Ebola patient, or patient suspected of Ebola fever [6].

In dynamical systems, optimal control is the process of determining control and state trajectories of dynamical system; over a period of time in order to maximize a given performance index [7]. Optimal Control Theory is applied to suggest the most effective mitigation theory to minimize number of individuals who become infected in the course of an infection while balancing vaccination and treatment applied to the models with various cost scenarios [8]. The control problem in dynamical systems is in the form of $\dot{x}(t) = g(t, x(t), u(t))$ where by, $t = \text{time}$, $u(t) = \text{the control}$ variable and $x(t) = $ state variable. The control is measurable with $0 \leq u(t) \leq 1$. Both control and the state usually affect the goal which is called objective function [9].

The basic optimal control problems involves a cost functional or performance criterion say $J(u)$. which is of the form,

$$J(u) = \int_0^T f(t, x, u)dt + \Phi(T)$$

subject to the above differential equations and initial conditions. Such a minimizing control is called an optimal control problem. f is a given real valued function and Φ is a continuous real-valued function. In the minimization case, the goal is to find an optimal control u^* such that,

$$J(u^*) = \underset{u}{Min} J(u).$$

The principle technique for such an optimal control problem is to solve a set of "necessary conditions" that an optimal control and corresponding state variables must satisfy [10]. The necessary conditions is generated from the Hamiltonian H, which is defined as

$$H = f(t, u(t), x(t)) + \lambda g(t, u(t), x(t)).$$

Subject to $\dfrac{dg_i}{dt} = q\big(g_i(t), u(t), t\big)$

where λ is an adjoint function [9].

The necessary conditions for maximizing/minimizing H with respect to u at u^* are,

$$\left.\frac{\partial H}{\partial u}\right|_{u=u^*} = 0, \rightarrow f_u + \lambda g_u = 0$$

$$\lambda' = -\frac{\partial H}{\partial x} = 0 \rightarrow \lambda' = -(f_x + \lambda g_x)$$

and

$$\lambda(T) = 0 \quad [9].$$

It is then intended to optimise the quarantine of exposed and infected individuals and to optimise the efficacy of drug used for treating Ebola virus disease victim in order to minimize the infections of Ebola virus disease.

2. Model Formulation

Chowell *et al.* developed a Mathematical model to investigate the epidemics of Ebola, the basic reproduction number of Ebola and the effects of public measures, using the cases of Congo and Uganda [11].

DiekMann *et al.* conducted a study on mathematical modelling, simulation and optimal control of the 2014 Ebola outbreak in West Africa, whereby they introduced the control on vaccination rate of Ebola [12].

In this paper, a Mathematical model for Ebola Virus Disease in the presence of treatment and quarantine of infectives will be formulated and analysed. It is intended to extend the mathematical model by Chowell *et al.* who established a simple SEIR-model to elaborate the dynamics of Ebola virus disease [11]. The process will include recruitment rate of susceptible population, disease transmission rate by exposed population to susceptible population, natural death rate in each class, death due to the disease and possibility of the recovered population to be susceptible again. All these inputs are significant in transmission of Ebola virus disease. In modelling the dynamics of the disease, the population is divided into five subclasses namely, $S(t)$: The Susceptible human, the number of people who are not yet affected by Ebola Virus Disease, $E(t)$: The Exposed Human beings, the number of individuals who are affected by Ebola Virus Disease but not yet infectious, $I(t)$: The Infected, number of individuals who are affected with Ebola Virus Disease who can spread that disease to the susceptible population, $T(t)$: The number of people who are subjected to treatment procedure at time t and $R(t)$: The number of people who have recovered from Ebola Virus Disease.

Ebola virus disease is transmitted from the exposed population and infected population at the rates of β_1 and β_2 respectively. Therefore, the susceptible population is recruited at the exposed class at the rate of $\beta_1 E + B_2 I$. The exposed group gets infected and joins the infectious group at the rate of δ, infectious joins the treated group at the rate of γ whereby m proportion of infectious group die due to Ebola virus disease, treated individuals get recovered at the rate of b, recovered population joins the susceptible class at rate of

a. Natural death rate is constant (μ) in each of the five classes.

In formulating the model, the following assumptions are taken into consideration:-

Recruitment rate of susceptible humans is constant,

The Ebola virus disease patient cannot get immunity after recovering from the disease,

Ebola virus disease infection is proportional to the number of infectives,

All people affected by virus disease pass through the same disease process,

Ebola virus disease infection is possible through Human to Human only.

With S the susceptible humans, E the exposed human to Ebola virus, I the infected human, T the treatment group, R the recovered group, Q the recruitment rate of susceptible human, β_1 the disease transmission rate to susceptible human by exposed human, β_2 the disease transmission rate to the susceptible human by the infected human, a the rate of progression to susceptible group from recovered group, μ the human natural death rate, b the rate of progression of treated group to recovered group, γ the rate of progression of infected to treated group, δ, the rate of progression of exposed group to infected group, m the death rate due to Ebola virus disease and taking into account the above considerations and assumptions, we have the following schematic flow diagram:
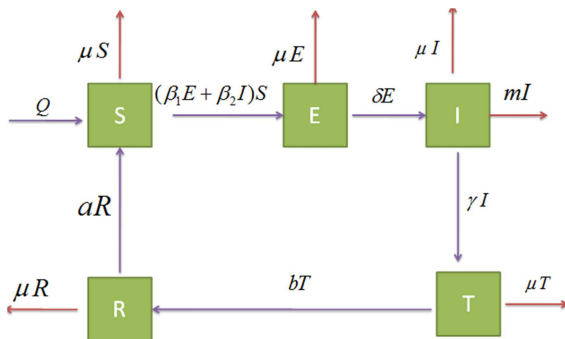

Figure 1. Compartmental representation of the model.

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

$$\frac{dS}{dt} = Q - (\beta_1 E + \beta_2 I)S + aR - \mu S$$

$$\frac{dE}{dt} = (\beta_1 E + \beta_2 I)S - (\delta + \mu)E$$

$$\frac{dI}{dt} = \delta E - (\gamma + m + \mu)I \qquad (1)$$

$$\frac{dT}{dt} = \gamma I - bT - \mu T$$

$$\frac{dR}{dt} = bT - (a + \mu)R$$

where $S(0) = S_0 \geq 0$, $E(0) = E_0 \geq 0$, $I(0) = I_0 \geq 0$, $T(0) = T_0 \geq 0$ and $R(0) = R_0 \geq 0$ are the initial conditions of the above model.

3. Model Analysis

The model system (1) will be analysed qualitatively to get insight to its dynamical features which give a better understanding of Ebola virus disease in the presence of treatment and quarantine of infectives. Threshold which governs elimination or persistence of Ebola virus disease in the presence of treatment and quarantine of infectives will be determined and analysed.

3.1. Invariant Region

Since the model (1) is Ebola model dealing with human population, we assume that all state variables and parameters of the model are positive. The model (1) will then be analysed in suitable feasible region where all state variables are positive. This region will be obtained by considering the following lemma:-

Lemma 1: The feasible region Ω, contains the solution set $(S, E, I, T, R) \in \mathbb{R}^5$.

Proof:

If N is the total population size, then

$$N = S + E + I + T + R \qquad (2)$$

It follows that,

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dT}{dt} + \frac{dR}{dt}$$

$$\frac{dN}{dt} = Q - \mu(N) - mI$$

$$\frac{dN}{dt} \leq Q - \mu N$$

$$N(t) \leq \frac{Q - (Q - \mu N(0))e^{-\mu t}}{\mu}$$

As $t \to \infty$, $N(t) \leq \frac{Q}{\mu}$

Since $N(t) \leq \frac{Q}{\mu}$, then the basic Mathematical model is well posed and it is mathematically relevant, therefore it is sufficient to study the dynamics of the epidemiological system (1) in the region Ω.

3.2. Positivity of the Solution

Lemma 2: If the initial Solution of a dynamical model (1) is

$\{S(t) \geq 0, E(t) \geq 0, I(t) \geq 0, T(t) \geq 0, R(t) \geq 0\} \in \Omega \frac{1}{2}$, then the

solution set of dynamical model (1) is positive for all $t \geq 0$.

Proof:

Consider $\dfrac{ds}{dt}$ in the system (1):

$$\frac{dS}{dt} = Q - (\beta_1 E + \beta_2 I)S + aR - \mu S$$

Then

$$\frac{dS}{dt} \geq -\mu S \tag{3}$$

The inequality (3) has a solution

$$S \geq e^{-\mu t}$$

As

$$t \to \infty, \quad S \geq 0 .$$

Similarly using the other equations of system (1), positivity of solutions can be established. Hence, all the solutions of the system (1) are positive for all $t > 0$.

3.3. Disease free Equilibrium Point

The Equilibrium point of the system (1) can be established by setting $\dfrac{dS}{dt} = \dfrac{dE}{dt} = \dfrac{dI}{dt} = \dfrac{dT}{dt} = \dfrac{dR}{dt} = 0$.
Then

$$Q - (\beta_1 E^* + \beta_2 I^*)S^* + aR^* - \mu S^* = 0$$

$$(\beta_1 E^* + \beta_2 I^*)S^* - (\delta + \mu)E^* = 0$$

$$\delta E^* - (\gamma + m + \mu)I^* = 0 \tag{4}$$

$$\gamma I^* - bT^* - \mu T^* = 0$$

$$bT^* - (a + \mu)R^* = 0$$

When there is no disease, the disease free equilibrium point can be established by setting $I = 0$ in the system (4) followed by solving the resulting system of simultaneous equations to get $E_0 = (E, I, T, R) = \left(\dfrac{Q}{\mu}, 0, 0, 0, 0\right)$. Thus the disease free equilibrium point is given by

$$E_0 = \left(\frac{Q}{\mu}, 0, 0, 0, 0\right). \tag{5}$$

3.4. The Basic Reproduction Number

The basic reproduction number R_0, defined as the number of Secondary cases which one case would produce in a completely susceptible population [12].

Next generation matrix method is the natural basis for the definition and calculation of R_0 , Where finitely many different categories of individuals are recognized [12] R_0 is the spectral radius of the next generation Matrix [16]. Next generation matrix (G) is given by:

$$G = FV^{-1} \tag{6}$$

where $F = \dfrac{\partial F_i(E_0)}{\partial x_j}$, $V = \dfrac{\partial V_i(E_0)}{\partial x_j}$ and E_0 is the disease free equilibrium point.

F_i is the rate at which new infections appears at compartment i and V_i is the removal of individuals among different classes. Also $V_i = V_i^- - V_i^+$ whereby V_i^+ is rate of movement of individuals into the compartment i and V_i^- is rate of movement of individuals out of compartment i .

Considering the equation (6),
Since,

$$F_i = \begin{pmatrix} (\beta_1 E + \beta_2 I)S \\ 0 \end{pmatrix},$$

then,

$$F = \frac{\partial F_i(E_0)}{\partial x_j} = \begin{pmatrix} \dfrac{\partial F_1}{\partial E} & \dfrac{\partial F_1}{\partial I} \\ \dfrac{\partial F_2}{\partial E} & \dfrac{\partial F_2}{\partial I} \end{pmatrix}. \tag{7}$$

This can be rewritten as

$$F = \begin{pmatrix} \beta_1 S & \beta_2 S \\ 0 & 0 \end{pmatrix} \tag{8}$$

If V_i is the movement of individuals out of each compartment i, then

$$V_i = \begin{pmatrix} (\delta + \mu)E \\ (\gamma + m + \mu)I - \delta E \end{pmatrix}$$

Let V be the Jacobian of V_i. Then

$$V = \frac{\partial V_i(E_0)}{\partial X_j} = \begin{pmatrix} \dfrac{\partial V_1}{\partial E} & \dfrac{\partial V_2}{\partial I} \\ \dfrac{\partial V_1}{\partial E} & \dfrac{\partial V_2}{\partial I} \end{pmatrix} = \begin{pmatrix} (\delta + \mu) & 0 \\ -\delta & (\gamma + m + \mu) \end{pmatrix} \tag{9}$$

Consequently

$$V^{-1} = \begin{pmatrix} \dfrac{1}{\delta + \mu} & 0 \\ \dfrac{\delta}{(\gamma + m + \mu)(\delta + \mu)} & \dfrac{1}{(\gamma + m + \mu)} \end{pmatrix} \tag{10}$$

Then

$$G = FV^{-1} = \begin{pmatrix} \dfrac{Q\beta_1}{\mu(\delta+\mu)} + \dfrac{Q\delta\beta_2}{\mu(\gamma+m+\mu)(\delta+\mu)} & \dfrac{Q\beta_2}{\mu(\gamma+m+\mu)} \\ 0 & 0 \end{pmatrix}$$

The eigenvalues of G are given by

$$\left(0, \; \frac{Q\beta_1}{\mu(\delta+\mu)} + \frac{Q\delta\beta_2}{\mu(\gamma+m+\mu)(\delta+\mu)}\right).$$

Therefore

$$R_0 = \frac{Q\beta_1}{\mu(\delta+\mu)} + \frac{Q\delta\beta_2}{\mu(\gamma+m+\mu)(\delta+\mu)}$$

or

$$R_0 = \frac{Q((\gamma+m+\mu)\beta_1+\delta\beta_2)}{\mu(\gamma+m+\mu)(\delta+\mu)} \qquad (11)$$

3.5. Local Stability Analysis of the Disease Free Equilibrium

Theorem 1: The disease free equilibrium point is locally asymptotic stable if the basic reproduction number is less than one and unstable if the basic reproduction number is greater than one $(R_0 > 1)$ [13].

In epidemiological point of view, it means that the spread of Ebola virus disease can be eradicated whenever the reproduction number is less than one $(R_0 < 1)$.

In order to determine the stability of the disease free equilibrium point, it is necessary to linearize the system of differential equation (1), so as to find an approximation of the system at the disease free equilibrium point.

We write the system as

$$g_1 = Q - (\beta_1 E + \beta_2 I)S + aR - \mu S$$

$$g_2 = (\beta_1 E + \beta_2 I)S - (\delta+\mu)E$$

$$g_3 = \delta E - (\gamma+m+\mu)I \qquad (12)$$

$$g_4 = \gamma I - bT - \mu T$$

$$g_5 = bT - (a+\mu)R$$

The Jacobian Matrix of the system (12) is

$$J = \begin{pmatrix} -(\beta_1 E+\beta_2 I)-\mu & -\beta_1 S & -\beta_2 S & 0 & a \\ (\beta_1 E+\beta_2 I) & \beta_1 S-(\delta+\mu) & \beta_2 S & 0 & 0 \\ 0 & \delta & -(\gamma+m+\mu) & 0 & 0 \\ 0 & 0 & \gamma & -b-\mu & 0 \\ 0 & 0 & 0 & b & -(a+\mu) \end{pmatrix} \qquad (13)$$

At the disease free equilibrium point $\left(\dfrac{Q}{\mu},0,0,0,0\right)$, the system (13) becomes

$$J = \begin{pmatrix} -\mu & \dfrac{-\beta_1 Q}{\mu} & \dfrac{-\beta_2 Q}{\mu} & 0 & a \\ 0 & \dfrac{\beta_1 Q}{\mu}-(\delta+\mu) & \dfrac{\beta_2 Q}{\mu} & 0 & 0 \\ 0 & \delta & -(\gamma+m+\mu) & 0 & 0 \\ 0 & 0 & \gamma & -b-\mu & 0 \\ 0 & 0 & 0 & b & -(a+\mu) \end{pmatrix}$$

If λ is an eigenvalue of the Jacobian matrix J, then the characteristic equation of Matrix J is

$$f(\lambda) = (\lambda+\mu)(a+\lambda+\mu)(-\lambda-\mu-b)\big(\mu(\mu+m+\gamma+\lambda)(\delta+\lambda+\mu)-Q((\mu+m+\gamma+\lambda)(\beta_1+\delta\beta_2))\big) = 0 \qquad (14)$$

Theorem 2: *The disease free equilibrium is locally asymptotic stable if the eigenvalues of the Jacobian matrix has negative real parts* [14].

The first three eigenvalues are:

$$\lambda_1 = -\mu < 0, \;\; \lambda_2 = -a-\mu < 0$$

and

$$\lambda_3 = -\mu-b < 0. \qquad (15)$$

Since the first three eigenvalues have negative real parts, Routh-hurwitz criteria will be used in the fourth factor, as follows:

$$\mu(\mu+m+\gamma+\lambda)(\delta+\lambda+\mu)-Q(\mu(\mu+m+\gamma+\lambda))(\beta_1+\delta\beta_2)=0 \qquad (16)$$

Equation (16) can be written as

$$\lambda^2 + A\lambda + B = 0,$$

where,

$$A = \mu(\mu+\gamma+m)+\mu(\delta+\mu)-Q$$

and

$$B = \mu(\mu+\gamma+m)(\delta+\mu)-Q(\mu(\mu+\gamma+m)\beta_1+\delta\beta_2)$$

$$A > 0 \;\; \text{if} \;\; \mu(\mu+\gamma+m)+\mu\delta+\mu(\delta+\mu)>Q \quad (17)$$

$$B > 0 \;\; \text{if}$$

$$\mu(\mu+\gamma+m)(\delta+\mu) > -Q(\mu(\mu+\gamma+m)\beta_1+\delta\beta_2) \quad (18)$$

or

$$\frac{Q(\mu(\mu+\gamma+m)\beta_1+\delta\beta_2)}{\mu(\mu+\gamma+m)(\delta+\mu)} < 1. \qquad (19)$$

But $R_0 = \dfrac{Q\left(\mu(\mu+\gamma+m)\beta_1 + \delta\beta_2)\right)}{\mu(\mu+\gamma+m)(\delta+\mu)}$.

Hence

$$R_0 < 1 . \qquad (20)$$

Therefore $R_0 < 1$ if $B > 0$ and $A > 0$. Then by Routh-Hurwitz criteria the disease free equilibrium of the system (1) is locally asymptotically stable.

3.5.1. Existence of Endemic Equilibrium

Lemma 3: There exists a positive endemic equilibrium point if and only if $R_0 > 1$.

Proof:

Endemic equilibrium point for the system (1) can be determined by setting, $\dfrac{dS}{dt} = \dfrac{dE}{dt} = \dfrac{dI}{dt} = \dfrac{dT}{dt} = \dfrac{dR}{dt} = 0$, if $I \neq 0$.

This gives the endemic equilibrium point $(S^*, E^*, I^*, T^*, R^*)$ as

$$S^* = \frac{Q}{\mu R_0}$$

$$E^* = \frac{Q(\gamma+m+\mu)(R_0-1)(a+\mu)(b+\mu)}{R_0\left((\delta+\mu)(\gamma+m+\mu)(a+\mu)(b+\mu)-ab\delta\gamma\right)}$$

$$I^* = \frac{Q(R_0-1)\delta(a+\mu)(b+\mu)}{R_0\left((\delta+\mu)(\gamma+m+\mu)(a+\mu)(b+\mu)-ab\delta\gamma\right)}$$

$$T^* = \frac{Q\gamma(R_0-1)\delta(a+\mu)}{R_0\left((\delta+\mu)(\gamma+m+\mu)(a+\mu)(b+\mu)-ab\delta\gamma\right)}$$

$$R^* = \frac{(R_0-1)Qb\gamma\delta}{R_0\left((\delta+\mu)(\gamma+m+\mu)(a+\mu)(b+\mu)-ab\delta\gamma\right)} .$$

Therefore there is only one positive endemic equilibrium point, which exists for $R_0 > 1$.

For I^*:

$$\frac{dI^*}{dR_0} = \frac{Q\delta(a+\mu)(b+\mu)}{R_0^2\left((\delta+\mu)(\gamma+m+\mu)(a+\mu)(b+\mu)-ab\delta\gamma\right)} \qquad (21)$$

Therefore $\dfrac{dI^*}{dR_0} > 0$. This implies that $R_0 > 1$ increases the value of positive I^* and at $R_0 = 1, I^* = 0$.

3.5.2. Global Stability Analysis of Endemic Equilibrium

Lemma 4: The endemic equilibrium of the mathematical model (1) is globally asymptotically stable if $R_0 > 1$ and unstable if $R_0 \leq 1$.

Proof:

Using the constructed Lyapunov function as suggested by [15], the global stability of Endemic equilibrium can be established by defining the Lyapunov function as

$$L(S^*,E^*,I^*,T^*,R^*) = \left(S - S^* - S^* Log\frac{S^*}{S}\right)$$
$$+ \left(E - E^* - E^* Log\frac{E^*}{E}\right)$$
$$+ \left(I - I^* - I^* Log\frac{I^*}{I}\right) + \left(T - T^* - T^* Log\frac{T^*}{T}\right)$$
$$+ \left(R - R^* - R^* Log\frac{R^*}{R}\right).$$

It can be shown that

$$\frac{dL}{dt} = X - Y$$

where

$$X = Q + \beta_1 E^* \frac{(S-S^*)^2}{S} + \beta_2 I^* \frac{(S-S^*)^2}{S} + aR^* + aR^* \frac{S^*}{S}$$
$$+ \beta_1 S^* \frac{(E-E^*)^2}{E} + \beta_2 IS + \beta_2 I \frac{E^* S^*}{E}$$
$$+ \beta_2 E^* S + \delta E + \frac{\delta I^* E^*}{I}$$
$$+ \gamma I + \gamma I^* \frac{T^*}{T} + bT + bT \frac{R^*}{R} , \qquad (22)$$

$$Y = Q\frac{S^*}{S} + \beta_1 E \frac{(S-S^*)^2}{S} + \beta_2 I \frac{(S-S^*)^2}{S} + aR\frac{S^*}{S} + aR^*$$
$$+ \mu \frac{(S-S^*)^2}{S} + \beta_1 S^* \frac{(E-E^*)}{E} + \beta_2 IS^* + \beta_2 I\frac{E^* S}{E}$$
$$+ \beta_2 IS + \beta_2 E^* S + (\delta+\mu)\frac{(E-E^*)^2}{E} + \delta E^* + \frac{\delta I^* E^*}{I}$$
$$-(\gamma+m+\mu)\frac{(I-I^*)^2}{I} + \gamma I^* \frac{T^*}{T} + \gamma I^* + bT \frac{R^*}{R} + (a+\mu)\frac{(R-R^*)^2}{R} . \qquad (23)$$

If $X < Y$ we obtain $\dfrac{dL}{dt} < 0$. $\dfrac{dL}{dt} = 0$ if and only if $S = S^*, E = E^*, I = I^*, T = T^*$ and $R = R^*$.

Then the largest compact invariant set $\left\{(S^*,E^*,I^*,T^*,R^*) \in \Omega : \dfrac{dL}{dt} = 0\right\}$ is the singleton $\{E^*\}$, where E^* is the endemic equilibrium. Therefore by Lassale Invariance principle, E^* is globally asymptotically stable if $X < Y$.

4. Model with Control

4.1. Introduction

In this section, the mathematical model (1) is extended by incorporating control variables $u_1(t)$ and $u_2(t)$, where

$u_1(t) =$ Control measure due to quarantine of exposed and

infected humans,

$u_2(t)$ = Control measure due to efficacy of treatment of drug used for Ebola virus victims.

Then the model becomes

$$\frac{dS}{dt} = Q - (1-u_1)(\beta_1 E + \beta_2 I)S + aR - \mu S$$

$$\frac{dE}{dt} = (1-u_1)(\beta_1 E + \beta_2 I)S - (\delta + \mu)E$$

$$\frac{dI}{dt} = \delta E - (\gamma + m + \mu)I \qquad (24)$$

$$\frac{dT}{dt} = \gamma I - (1-u_2)bT - \mu T$$

$$\frac{dR}{dt} = (1-u_2)bT - (a+\mu)R$$

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

4.2. Analysis of the Ebola Optimal Control Problem

Here we aim at minimizing the infections of Ebola Virus disease, while optimizing $u_1(t)$ (treatment and Quarantine of individuals) and $u_2(t)$ (efficacy of treatment drug used for treating Ebola virus disease victims). In order to minimize infection, it is required to minimize the objective function

$$J(u_1, u_2) = \int_{t_0}^{T} \left(A_1 S(t) + A_2 E(t) + A_3 T(t) + A_4 R(t) + \frac{1}{2}\sum_{i=1}^{2} B_i u_i^2 \right) dt \quad (25)$$

subject to control problem $x'(t) = g\left(t, x(t), u_1(t), u_2(t)\right)$, with $x(t_0) = x_0$ and $x(T)$ free variable. B_i's are relative costs of intervention over $[t_0, T]$, The constants A_1, A_2, A_3 and A_4 are positive weights. It is then intended to find optimal controls u_1^* and u_2^*, such that $J\left(u_1^*, u_2^*\right) = \min J\left(u_1, u_2\right)$, 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,

$$H = A_1 S(t) + A_2 E(t) + A_3 T(t) + A_4 R(t)$$

$$+ \frac{1}{2}\sum_{i=1}^{2} B_i u_i^2 + \sum_{i=1}^{5} \lambda_i g_i\left(x, u_1(t), u_2(t)\right) \quad (26)$$

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

Theorem 3: *There exists a pair of optimal controls $\left(u_1^*, u_2^*\right)$ and optimal solution $\left(S^*, E^*, I^*, T^*, R^*\right)$ that minimizes $J\left(u_1, u_2\right)$ also there exist adjoint functions $\lambda_i(t)$ for $i = 1, 2, 3, 4$ and 5 for Hamiltonian (H),*

$$H = A_1 S(t) + A_2 E(t) + A_3 T(t) + A_4 R(t) + \frac{1}{2}B_1 u_1^* + \frac{1}{2}B_1 u_2^* + \lambda_1\left(Q - (1-u_1)(\beta_1 E + \beta_2 I)S + aR - \mu S\right) + \lambda_2\left((1-u_1)(\beta_1 E + \beta_2 I)\right)S \quad (27)$$

$$-(\delta + \mu)E + \lambda_3\left(\delta E - (\gamma + m + \mu)I\right)$$

$$+\lambda_4\left(\gamma I - (1-u_2)bT - \mu T\right)$$

$$+\lambda_5\left((1-u_2)bT - (a+\mu)R\right)$$

Such that,

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S} = -A_1 + \lambda_1\left((1-u_1)(\beta_1 E + \beta_2 I) - \mu\right)$$

$$-\lambda_2\left(\beta_1 E + \beta_2 I\right),$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial E} = -A_2 + \lambda_1(1-u_1)\beta_1 S$$

$$-\lambda_2(1-u_1)\beta_1 S - \lambda_3 \delta,$$

$$\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial I} = \lambda_1(1-u_1)\beta_2 S - \lambda_2(1-u_1)\beta_2 S + \lambda_3(\gamma + m + \mu) - \lambda_4 \delta \quad (28)$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial T} = -A_3 + \lambda_4\left((1-u_2)b + \mu\right) - \lambda_5(1-u_1)b,$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial R} = -A_4 - \lambda_1 a + \lambda_5(a+\mu).$$

The Transversality conditions are

$$\lambda_i(T) = 0, \text{ for } i = 1, 2, 3, 4 \text{ and } 5. \quad (29)$$

The pair of Optimal controls $\left(u_1^*(t), u_2^*(t)\right)$ is obtained by solving for $u_1(t)$ and $u_2(t)$ in optimality conditions $\left(\frac{\partial H}{\partial u_1} = 0\right)$ and $\left(\frac{\partial H}{\partial u_2}\right)$ as suggested by [19].

$$\frac{\partial H}{\partial u_1} = B_1 u_1 + \lambda_1\left(\beta_1 E + \beta_2 I\right)S1$$

$$-\lambda_2\left(\beta_1 E + \beta_2 I\right)S = 0,$$

$$\frac{\partial H}{\partial u_2} = B_2 u_2 + \lambda_4 bT - \lambda_5 bT = 0. \tag{30}$$

Then

$$\bar{u}_1 = \frac{(\beta_1 E + \beta_2 I) S (\lambda_2 - \lambda_1)}{B_1}$$

$$\bar{u}_2 = \frac{bT (\lambda_5 - \lambda_4)}{B_2} \tag{31}$$

Consequently,

$$u_1^* = \max\left\{0, \ \min\left(1, \ \frac{(\beta_1 E + \beta_2 I) S (\lambda_2 - \lambda_1)}{B_1}\right)\right\},$$

$$u_2^* = \max\left\{0, \ \min\left(1, \ \frac{bT (\lambda_5 - \lambda_4)}{B_2}\right)\right\}. \tag{32}$$

By standard control arguments as suggested by [20], we have

$$u_1^* = \begin{cases} 0, \ if \ \bar{u}_1 \le 0 \\ \bar{u}_1, \ if \ 0 < \bar{u}_1 < 1 \\ 1, \ if \ \bar{u}_1 \ge 1 \end{cases} \quad u_2^* = \begin{cases} 0, \ if \ \bar{u}_2 \le 0 \\ \bar{u}_2, \ if \ 0 < \bar{u}_2 < 1 \\ 1, \ if \ \bar{u}_2 \ge 1 \end{cases} \tag{33}$$

5. 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 control i.e. model system (23) using the set of estimated parameter values given in the Table 1 below.

Table 1. *Parameter values used for Model Simulation.*

Parameter	Value(per month)	Source
β_1	0.16	[18]
β_2	0.12	Estimated
μ	0.1	Estimated
m	0.5	[18]
γ	0.3086	[18]
δ	0.83	[18]
b	0.063	[18]
a	0.82	Estimated
Q	40	Estimated

Initial values are estimated as
$S(0) = 30, \ E(0) = 20, \ I(0) = 18, \ T(0) = 17$ and $R(0) = 12$.
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 a control problem (23) when,

No control is applied to a system of equations,

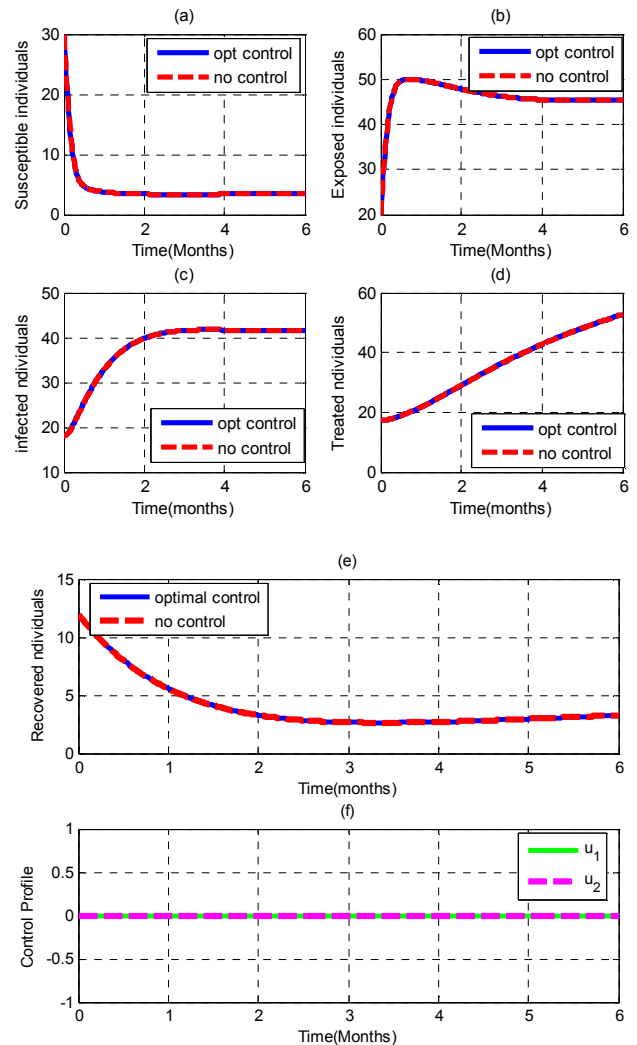Only a control measure due to efficacy drug used for treating an Ebola virus disease victim (u_2) is applied,

Only a control measure due to quarantine of exposed and susceptible individuals (u_1) is used,

Both controls, which are u_1 (control measure due to quarantine of exposed and susceptible individuals) and u_2 (control measure due to efficacy drug used for treating an Ebola virus disease victim) are used in control problem.

Figure 2 below shows the simulation of Ebola control problem, when there is no control applied, that is $u_1 = u_2 = 0$.

Figure 2(a), shows that when there is no control, the number of susceptibles is reduced with time due to removal by infections. Figure 2(b) shows that the exposed individuals increase with time before being reduced by removal of exposed individuals to infected population. Figure 2(c) shows that infected population increases with time. Figure 2(d) shows that treated population increases with time and figure 2(e) shows that recovered individuals are reduced with time.

Figure 2. *Simulation of Ebola control problem, when there is no control applied, that is* $u_1 = u_2 = 0$.

Therefore the disease will persist in the population for a long time, until some interventions strategies are introduced in the population.

Figures 3 below show the simulation of an objective function for Ebola virus disease when only a control

measure (u_1) due to quarantine of exposed and susceptible individuals is applied.

Figure 3(a) shows that susceptible population increases with time. Figure 3(b) shows that the exposed population decreases with time. Figure 3(c) shows that the infected population increases with time. Figure 3(d) shows that the treated population decreases with time due to reduction of infected population with time. Figure 3(e) shows that the recovered population will be decreases with time due to reduction of treated population with time. Figure 3(f) shows the control profile whereby u_1 (control measure due to quarantine of exposed and susceptible individuals) is set to the maximum and there is no control of efficacy drug used for treating Ebola virus disease victim $(u_2 = 0)$.
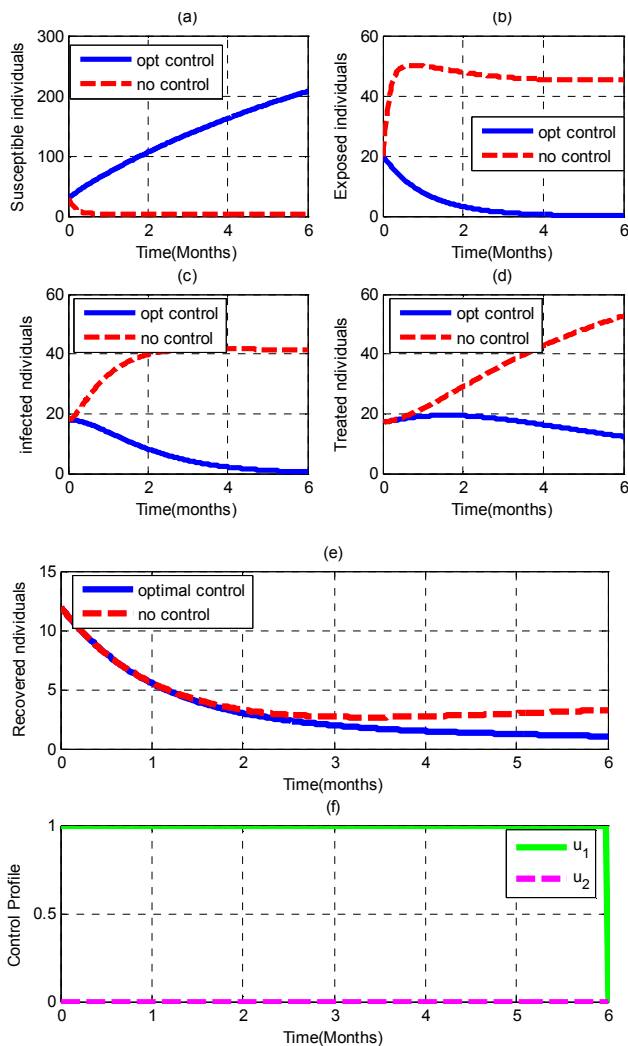

Figures 3. *Simulation of the objective function for Ebola virus disease when only a control measure (u_1) due to quarantine of exposed and susceptible individuals is applied.*

Therefore by quarantining the exposed and susceptible population only, there will be reduction of disease persistence in the population, due to reduction of population in exposed and infected classes.

Figures 4 below, show the simulation of control problem (23), when only the control measure due to efficacy of drug used for treating Ebola virus disease victim (u_2) is optimized.
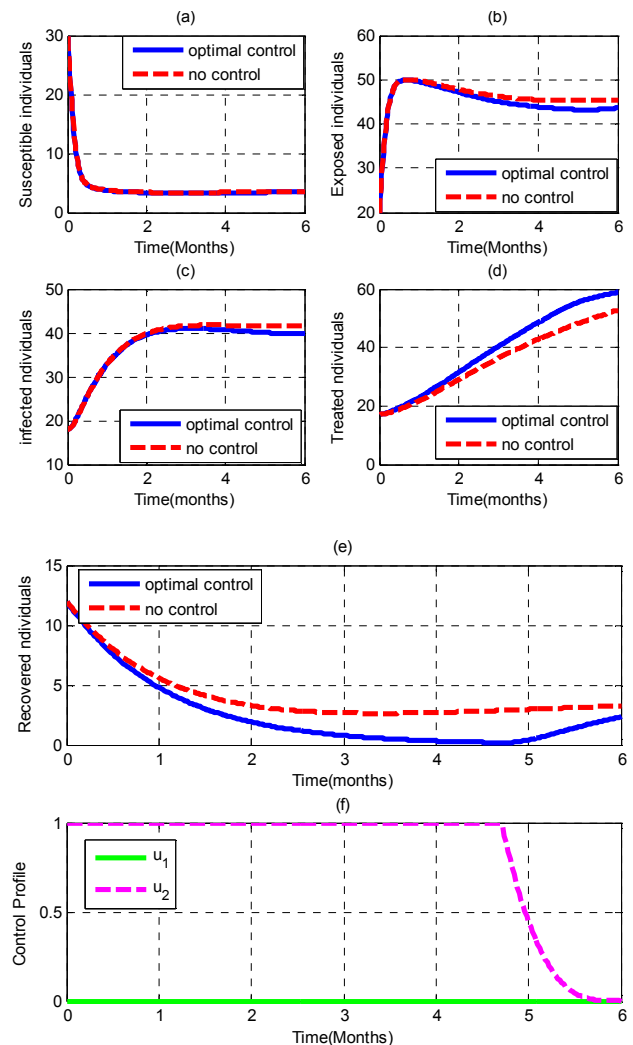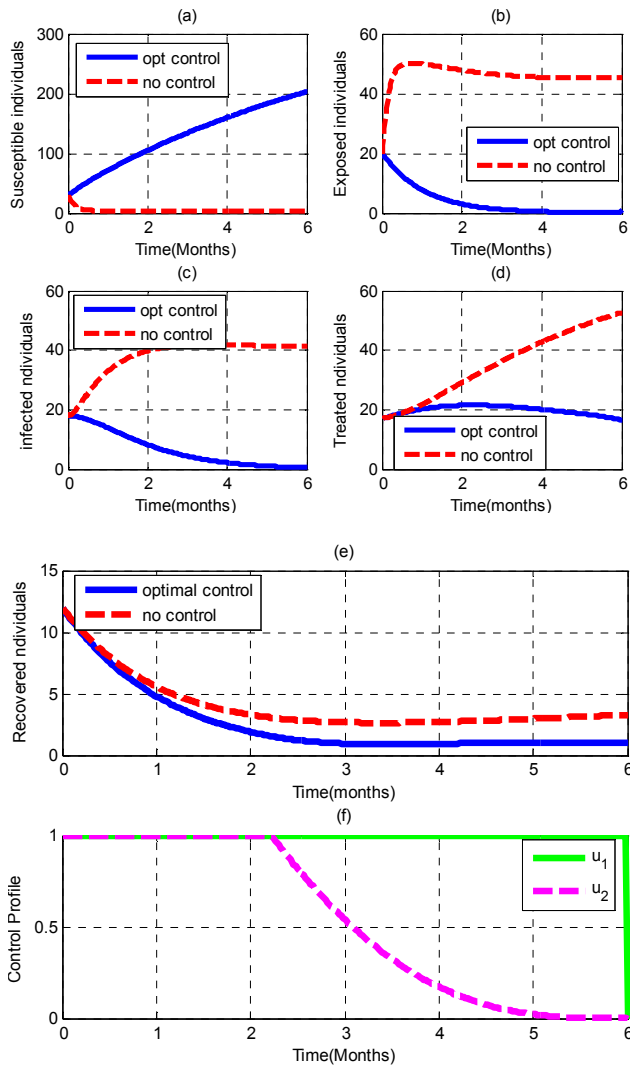

Figure 4 *Simulation of control problem (23), when only the control measure due to efficacy of drug used for treating Ebola virus disease victim is optimized*

Figure 4(a) shows that with one control, there will be no changes in susceptible population with time. Figures 4(b) and figure 4(c) show that there will be a slight reduction in exposed and infected populations with time. Figure 4(d) shows that there will be an increase in treated population with time. Figure 4(e) shows that there will be a decrease of recovered population with time due to the decrease in infected population with time.

Therefore optimizing the control measure due to efficacy of drug used for treating Ebola virus disease victim minimizes infections by reducing exposed and infected population while maximizing treatment.

Figure 5 below shows the simulation of control problem (23), when both controls u_1 (control measure due to quarantine of exposed and susceptible individuals) and u_2 (control measure due to efficacy of drug used for treating Ebola virus disease victim) are employed.

Figure 5. *Simulation of control problem (23), when both controls are employed.*

When both controls are employed, figure 5(a) shows that susceptible population increases with time. Figures 5(b) and figure 5(c) show that exposed and infected populations decrease with time respectively due to the decrease of number of people who acquire new infections. Figure 5(d) shows that treated population decreases with time due to reduction of the infected population. Figure 5(e) shows that recovered population are decreases with time due reduction of treated population with time. Figure 5(f) shows the control profile whereby u_1 (the control measure due to quarantine of exposed and susceptible individuals) remains at maximum up to the terminal time and u_2 (control measure due to efficacy drug used for treating Ebola virus disease victim) remains at maximum for at least two months before finally decreasing exponentially to the minimum.

From the simulations of the objective function, it can be seen that optimizing a control measure due to quarantine of exposed and susceptible individuals only (u_1) has a greater effect in reduction of Ebola virus disease than using a control measure due to efficacy drug used for treating Ebola virus disease victim only (u_2), since optimizing u_1 only reduces

the exposed and infected population more than optimizing u_2 only. Also the simulations show that optimizing both the two controls (u_1 and u_2) have a significant impact in reduction of disease transmission.

6. Conclusions

A mathematical model for the Ebola virus disease in the absence of control measures was developed and analysed. Using Routh Hurwitz criteria, it was established that the disease free equilibrium is locally asymptotically stable whenever the reproduction number is less than one $(R_0 < 1)$. The endemic equilibrium was determined and found to be locally asymptotically stable whenever the reproduction number is greater than one $(R_0 > 1)$. By applying two controls, i.e. treatment and Quarantine of individuals and efficacy of treatment drug used for treating Ebola virus disease victims, the optimal control problem was analysed so as to minimize the infections of Ebola Virus disease, while optimizing the controls. The control problem was finally simulated in order to examine the effect of one control or both controls in controlling Ebola virus disease. It was found that, optimizing a control measure due to quarantine of exposed and susceptible individuals only is more effective in reduction of Ebola virus disease than using a control measure due to efficacy drug used for treating Ebola virus disease victim only. However, simulations further showed that optimizing both of the two controls have a significant impact in reduction of disease transmission.

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