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MODELING OPTIMAL CONTROL OF ROTAVIRUS DISEASE WITH DIFFERENT CONTROL STRATEGIES

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Abstract. In this paper, we consider a rotavirus epidemic model with vaccination, treatment and health education campaigns as control variables. We derive and analyse the conditions for optimal control using the optimal control theory and the Pontryagin's Maximum Principle. We solve the optimal control problem numerically using fourth order Runge-Kutta scheme. Results show that multiple control strategies are more effective than a single control strategy.

Keywords: Pontryagin's maximum principle; rotavirus; optimal control; vaccination; treatment.

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1. Introduction

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Rotavirus is a virus that causes severe gastroenteritis infections (CDC, 2011) in infants and children below age of five. Rotavirus can be very harmful because it leads to dehydration which can be very dangerous especially for babies and young children (Roberts, 2004).

Rotaviruses are transmitted primarily by the fecal-oral route (Molholland, 2004) both through close person-to-person contact and through contaminated environment-to-person (CDC, 2013; WHO 2009).

Like any other infectious diseases (Rowthorny and Toxvaerdz, 2008) rotavirus also, remains the second deadly disease with high causes of morbidity and mortality especially in developing countries and are a major strain on most public budgets (WHO, 2009 ; Danovara *et al.,* 2002).

The dynamical sketch of rotavirus and its mathematical formulation has been done by many researchers for example: Offit *et al.,* 1998; Shim *et al.,* 2001; Matson *et al.,* 2003; CDC, 2009; Van *et al.,* 2010; Tate *et al.,* 2012; CDC, 2013 among other. However its study via application of optimal control using the Pontryagin Maximum Principle, little or nothing has been done yet. We are going to base this study on other infectious diseases that have similar characteristics where the optimal control theory has been applied.

The application of optimal control theory has become another interesting area in the field of mathematical modeling (Lenhart, 2007) in that it provides insightful understanding of many biomedical problems and its being used extensively in the controlling of infectious diseases (Kirschner *et al.,* 1997; Lenhart, 2007). It is mostly used in the control of the spread of numerous diseases for which control measures are in place, for example vaccination, treatment, isolation among other (Nanda *et al.,* 2007; Tunde *et al.*, 2012).

Tunde *et al.,* 2012, applied optimal control to find the optimal combination of vaccination and treatment strategies that will minimize the cost of the two control measures as well as the number of infectives. Kbenesh *et al.,* 2009, also applied optimal control when looking at time dependent prevention and treatment efforts.

Again the work of Neilan and Lenhart (2010) serves as an introduction to the theory of optimal control applied to systems of ordinary differential equations with emphasis on disease models. They outline the steps in formulating an optimal control problem and derive necessary

conditions. Several simple examples are provided with a detailed methodology in characterizing the optimal control through use of Pontryagin Maximum Principle.

Devipriya and Kalaivani (2012) presented their work on "optimal control of multiple transmission of water-borne disease". A controlled SIWR model was considered which was an extension of the simple SIR model by adjoining a compartment W that tracks the pathogen concentration in the water. The controls represented an immune boosting and pathogen suppressing drugs. Their objective function was based on a combination of minimizing the number of infected individuals and the cost of the drugs dose.

In this work, we consider a susceptible-infected-recovered and Environment pathogen (SIR-E) model to incorporate the epidemiological features that depict the rotavirus disease using a system of differential equations. We formulate an optimal control model of rotavirus with vaccination, treatment and health education campaign controls and solve the optimal control problem using the Pontryagin Maximum Principle (Pontryagin *et al.*, 1962). We finally perform numerical simulations and draw conclusions.

2. Model Formulation

We formulate an optimal control model for rotavirus disease in order to derive optimal vaccination, treatment and health education campaigns strategies with minimal implementation cost while we want to eradicate the disease after a defined period of time. The control functions used include, $u_1(t)$, $u_2(t)$, $u_3(t)$ to represent time dependent efforts of vaccination, treatment and education campaigns respectively and this is practiced on a time interval of $[0,T]$.

The efforts used in vaccination, can be the cost of different types of vaccines used, for example, RotaTeq and Rotatrix among other vaccines, the vaccine storage costs, other related overheads etc. The treatment efforts include: antibiotics, administration of drugs to patients, screening of the sick, hydration therapy, medical tests and diagnosis, drug costs, hospitalisation costs, surveillance and follow up of drug management plus any other related cost of treating children with various health complications among others. On the other hand health education

campaigns can be in the form of increasing knowledge and awareness of risks (through information and awareness-raising), social marketing, outreach services, etc. (Nanda *et al.,* 2007; Gaff *et al.,* 2009; Zaman *et al.,* 2008; Lee *et al.,* 2010).

Now we consider an *SIRSE* model, with S denoting the number of susceptibles, I denoting the number of infected children, R denoting the number of children who are removed on recovery from the disease but confers temporarily immunity and moves back to the susceptible class S and E denoting the pathogen infected environment (e.g a water reservoir contaminated with the virus).

In this model we assume recruitment rate Λ into $S(t)$ through birth by the adults. Children at $S(t)$ can get infected either through contact with infected children or through contacts with contaminated/unhygienic environment. The force of infection is denoted by $\psi(S,E,I)$, where

$$\psi(S,E,I) = \varepsilon SI + \frac{\nu SE}{K+E}$$

with ε being the contact rate of susceptible children with infected children and ν being the probability of exposure of susceptible children to an infected environment.

Infected children can join the recovery class R at a rate α_1. Children in I die due to the disease at per capita rate d. Due to the nature of the disease, children can lose immunity and become susceptible again at a rate ε_1. All human class experience natural death at per capital rate μ. We further note that, the pathogen infected population is generated at a rate γ while the contribution rate of infected children to pathogen growth in environment, this can be inform of feaces, is denoted by σ_1. The rotavirus pathogen die naturally at a rate μ_1.

The following model assumptions are made:

(i) We introduce vaccination to the susceptible children at a rate u_1, such that $u_1 S(t)$ children per time are removed from the susceptible class.

(ii) Treatment is given to the infectious children at a rate of u_2, such that $u_2(t)I(t)$ children per time are removed from the infectious class and on recovery they are joined to the recovered class, R.

(iii) Health education campaigns help to create awareness, this leads to the reduction of the virus at a rate u_3.

The main objective of the model to find the best optimal strategy in terms of combined efforts of vaccination, treatment and health education campaigns such that we minimise the number of infectious children while keeping the costs as low as possible as well as maximizing the number of susceptibles.

2.1. Equations of the Model

The rotavirus disease is modeled with a system of ordinary differential equations as stated below with the three controls embedded within the dynamical system.

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda - \varepsilon SI - \tfrac{\nu SE}{K+E} + \varepsilon_1 R - \mu S - u_1 S, \\
\frac{dI(t)}{dt} &= \varepsilon SI + \tfrac{\nu SE}{K+E} - (\alpha_1 + \mu + d)I - u_2 I, \\
\frac{dR(t)}{dt} &= \alpha_1 I - \mu R - \varepsilon_1 R + u_1 S + u_2 I, \\
\frac{dE(t)}{dt} &= \gamma E - \mu_1 E + \sigma_1 I - u_3 E
\end{aligned} \tag{1}$$

with initial conditions

$$S(0) \geq 0,\ I(0) \geq 0,\ R(0) \geq 0,\ E(0) \geq 0\ u_1(0) = u_{10},\ u_2(0) = u_{20},\ \textit{and}\ u_3(0) = u_{30}.$$

2.2. Existence and Stability of Equilibrium Points

We now analyze model (1) when all our control parameters are positive, that is, $u_1 > 0$, $u_2 > 0$ and $u_3 > 0$.

2.2.1. Disease Free Equilibrium Point, DFE, H_0

This is obtained when $I = E = 0$, that is, in absence of the disease. Thus H_0 is given by

$$H_0 = \left(\frac{\Lambda}{(\mu + u_1)}, 0, 0, 0 \right).$$

2.2.2. Effective Reproduction number, R_c

We compute the effective reproduction number R_c using the next generation approach method as described by Van de Driessche and Watmough (2002). We have:

$$\mathscr{F}_i = \begin{bmatrix} \varepsilon SI + \frac{\nu ES}{K+E} \\ 0 \end{bmatrix} \tag{2}$$

and

$$\mathscr{V}_i = \begin{bmatrix} (\alpha_1 + \mu + d + u_2)I \\ (\mu_1 - \gamma)E - \sigma_1 I + u_3 E \end{bmatrix}. \tag{3}$$

Obtaining the partial derivatives of (2) and (3) with respect to I and E, we obtain

$$\mathscr{F} = \begin{bmatrix} \varepsilon S & \frac{\nu S}{K} \\ 0 & 0 \end{bmatrix}$$

and

$$\mathscr{V} = \begin{bmatrix} (\alpha_1 + \mu + d + u_2) & 0 \\ -\sigma_1 & (\mu_1 - \gamma) + u_3 \end{bmatrix}.$$

The next step is to compute the inverse of V and this gives

$$V^{-1} = \begin{bmatrix} \frac{1}{(\alpha_1 + \mu + d + u_2)} & 0 \\ \frac{\sigma_1}{(\alpha_1 + \mu + d + u_2)((\mu_1 - \gamma) + u_3)} & \frac{1}{((\mu_1 - \gamma) + u_3)} \end{bmatrix}.$$

Thus FV^{-1} is given by

$$FV^{-1} = \begin{bmatrix} \frac{\varepsilon S}{(\alpha_1 + \mu + d + u_2)} + \frac{\nu S \sigma_1}{K(\alpha_1 + \mu + d + u_2)((\mu_1 - \gamma) + u_3)} & \frac{\nu S}{K((\mu_1 - \gamma) + u_3)} \\ 0 & 0 \end{bmatrix}.$$

The effective reproduction number is determined as a spectral radius of FV^{-1}, and this is given by

$$R_c = \frac{\varepsilon S}{(\alpha_1 + \mu + d + u_2)} + \frac{\nu S \sigma_1}{K(\alpha_1 + \mu + d + u_2)((\mu_1 - \gamma) + u_3)},$$

substituting for S, we have our R_c as

$$R_c = \frac{\Lambda}{(\mu + u_1)(\alpha_1 + \mu + d + u_2)} \left(\varepsilon + \frac{\nu \sigma_1}{K((\mu_1 - \gamma) + u_3)} \right). \tag{4}$$

We note that from (4) we can have our basic reproduction number as

$$R_0 = \frac{\Lambda}{\mu(\alpha_1 + \mu + d)} \left(\varepsilon + \frac{\nu \sigma_1}{K(\mu_1 - \gamma)} \right). \tag{5}$$

Logically, considering the three types of children controls, when we compare (4) and (5). We clearly note that (4) is reduced by $\frac{1}{\mu+u_1}$ and this implies that $R_c < R_0$. Thus, controls can reduce the value of R_c to a value lower than 1 so that the disease can be eliminated unless backward bifurcation occurs.

Let us further assume u_2 and u_3 are zeros, that is, $u_2 = u_3 = 0$ with $u_1 = u_{10}$. In this case we consider when only vaccination is implemented. Based on (4) we can see that $R_0 > 1$. This means that, there is a critical value for vaccination strength, say u_{10} such that

$$\frac{\varepsilon\Lambda}{(\mu+u_{10})(\alpha_1+\mu+d)} + \frac{\Lambda\nu\sigma_1}{K(\mu+u_{10})(\alpha_1+\mu+d)(\mu_1-\gamma)} = 1$$

solving for u_{10} and multiplying both sides by $(\mu+u_{10})$ we get

$$u_{10} = \frac{\Lambda}{(\alpha_1+\mu+d)}\left(\varepsilon + \frac{\nu\sigma_1}{K(\mu_1-\gamma)}\right) - \mu.$$

when $u_1 > u_{10}$, the disease will be eliminated if $R_c < 1$ and when $u_1 < u_{10}$, the disease will persist if $R_c > 1$. With the above analysis, the strength of each control strategy can be obtained. However, this would be limited by available resources in terms of social and economic factors, and the combination of different control approaches would possibly bring about the required result.

2.2.3. Local Stability of the Disease Free Equilibrium Point, H_0

Here, we compute the Jacobian matrix of model (1) by differentiating each equation in the system with respect to the state variables S, I, R, E. Thus, at steady state the Jacobian is given by

$$J = \begin{bmatrix} -(\mu+u_1) & -\varepsilon S & \varepsilon_1 & -\frac{\nu S}{K} \\ 0 & \varepsilon S - (\alpha_1+\mu+d+u_2) & 0 & \frac{\nu S}{K} \\ u_1 & (\alpha_1+u_2) & -(\varepsilon_1+\mu) & 0 \\ 0 & \sigma_1 & 0 & -(\mu_1-\gamma+u_3) \end{bmatrix}. \tag{6}$$

We note that matrix (6) can be reduced to

$$J = \begin{bmatrix} -(\mu+u_1) & -\frac{\varepsilon\Lambda}{(\mu+u_1)} & -\frac{\nu\Lambda}{K(\mu+u_1)} \\ 0 & \frac{\varepsilon\Lambda}{(\mu+u_1)} - (\alpha_1+\mu+d+u_2) & \frac{\nu\Lambda}{K(\mu+u_1)} \\ 0 & \sigma_1 & -(\mu_1-\gamma+u_3) \end{bmatrix}. \tag{7}$$

The disease free equilibrium point H_0 will be locally stable if all the eigenvalues of (7) have real negative values. We have already noted that one of the eigenvalues is negative, that is, $\lambda_1 = -(\mu+u_1)$ and matrix (7) reduces to a 2×2 matrix J_A as follows:

$$J_A = \begin{bmatrix} -\frac{\varepsilon\Lambda}{(\mu+u_1)} & -\frac{\nu\Lambda}{K(\mu+u_1)} \\ \frac{\varepsilon\Lambda}{(\mu+u_1)} - (\alpha_1+\mu+d+u_2) & \frac{\nu\Lambda}{K(\mu+u_1)} \end{bmatrix}.$$

From matrix J_A the remaining two eigenvalues give us the following characteristic equation

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

where

$$B = -\frac{\varepsilon\Lambda}{(\mu+u_1)} + (\alpha_1+\mu+d+u_2) + (\mu_1-\gamma+u_3),$$
$$C = -\frac{\varepsilon\Lambda}{(\mu+u_1)}(\mu_1-\gamma+u_3) - \frac{\nu\Lambda\sigma_1}{K(\mu+u_1)} - (\alpha_1+\mu+d+u_2)(\gamma-\mu_1-u_3).$$

The roots of the characteristic equation (eigenvalues) are negative if and only if both B and $C<0$. We clearly note that $C<0$ and $B<0$ if and only if B can be written as the following expression

$$-\left(\frac{\varepsilon\Lambda}{(\mu+u_1)} - (\alpha_1+\mu+d+u_2) - (\mu_1-\gamma+u_3)\right) < 0.$$

Hence, since the coefficients in the characteristic equation A and B have negative real parts with $R_c<1$, the H_0 is locally asymptotically stable. This leads to the following Theorem.

Theorem 2.1. *The disease free equilibrium point H_0 is locally asymptotically stable whenever $R_c<1$ and unstable whenever $R_c>1$.*

2.2.4. Endemic Equilibrium Point, H_1

Let $H_1^* = (S^*, I^*, R^*, E^*)$ be our endemic equilibrium point. This is obtained when we set the right hand side of equation (1) to zero. The endemic equilibrium shows the persistence of the

disease within the population. Thus expressing our state variables (S^*, R^*, E^*) in terms of I^* we get

$$
\begin{aligned}
S^* &= \frac{\Lambda(\mu+\varepsilon_1)K + [K\varepsilon_1(\alpha_1+u_2) + \Theta\Lambda(\mu+\varepsilon_1)]I^* + \varepsilon_1\Theta(\alpha_1+u_2)I^{*2}}{\mathbf{M}I^* + \varepsilon(\mu+\varepsilon_1)\Theta I^{*2} + ((\mu+\varepsilon_1)(\mu+u_1)K - K\varepsilon_1 u_1)}, \\
\mathbf{M} &= \varepsilon K(\mu+\varepsilon_1) + (\mu+\varepsilon_1)(\mu+u_1)\Theta + (\mu+\varepsilon_1)\nu\Theta - \varepsilon_1 u_1\Theta, \\
\Theta &= \frac{\sigma_1}{(\mu_1+u_3-\gamma)}, \qquad (8) \\
E^* &= \Theta I^*, \\
R^* &= \frac{1}{(\mu+\varepsilon_1)}[(\alpha_1+u_2)I^* + u_1 S^*].
\end{aligned}
$$

We compute the endemic equilibrium point $H_1^* = (S^*, I^*, R^*, E^*)$ in terms of force of infection ψ^*, where

$$\psi^* = \varepsilon S^* I^* + \frac{\nu S^* E^*}{K+E^*}.$$

Substituting S^*, I^*, E^* into ψ^* from (8) we get the following equation as:

$$\psi^*(A\psi^{*2} + B\psi^* + C) = 0,$$

where $\psi^* = 0$ corresponds to the disease free equilibrium point and $A\psi^{*2} + B\psi^* + C = 0$ corresponds to the endemic equilibrium point.

After computations:

$$
\begin{aligned}
A =& \frac{\varepsilon\sigma_1}{(\mu_1+u_3-\gamma)(\alpha_1+\mu+d+u_2)}, \\
B =& \varepsilon K + \frac{2\sigma_1(\mu+u_1)}{(\mu_1+u_3-\gamma)} - \frac{\varepsilon\Lambda\sigma_1}{(\mu_1+u_3-\gamma)(\alpha_1+\mu+d+u_2)}, \\
C =& K(\mu+u_1)(\alpha_1+\mu+d+u_2) - \left(\varepsilon K\Lambda + \frac{\Lambda\nu\sigma_1}{(\mu_1+u_3-\gamma)}\right).
\end{aligned}
$$

C can further be reduced as follows:

$$
\begin{aligned}
C &= \left\{1 - \left(\frac{\varepsilon\Lambda}{(\mu+u_1)(\alpha_1+\mu+d+u_2)} + \frac{\Lambda\nu\sigma_1}{K(\mu+u_1)(\alpha_1+\mu+d+u_2)(\mu_1+u_3-\gamma)}\right)\right\}, \\
&= (1-R_c)
\end{aligned}
$$

Hence when $C < 0 \Longrightarrow R_c > 1$ and when $C > 0 \Longrightarrow R_c < 1$.

Applying Routh-Hurwitz criterion (Gantmacher, 1959), all eigenvalues of $A\psi^{*2}+B\psi^{*}+C=0$ are negative if and only if $A>0, B>0, C>0$ and $AB>C$. Hence the following theorems hold.

Theorem 2.2. *If $C>0, B>0$ and $B^2-4AC>0$, then two endemic equilibria (two positive roots) exists, and therefore it's possible for backward bifurcation to occur, otherwise, there is none.*

Theorem 2.3. *The endemic equilibrium point H_1^* of (1) has precisely one unique endemic equilibrium if $C<0 \iff R_c>1$ otherwise none.*

3. Optimal Control

To describe the mathematical model presented in (1), we formulate an appropriate optimal control problem with the objective (cost) function given by

$$J(u_1,u_2,u_3)=\int_0^T A_1S(t)+A_2I(t)+\frac{1}{2}(B_1u_1^2+B_2u_2^2+B_3u_3^2)dt, \tag{9}$$

where A_1 and A_2 are the weight constants or balance factors of the susceptible and the infected group respectively, whereas B_1, B_2, and B_3 are constant relative cost weight parameters for vaccination, treatment and health education campaigns efforts respectively which regulate the optimal control.

We further assume that, due to technical reasons, the cost of vaccination, treatment and health education campaigns is non linear and quadratic as seen in the cost function (9). $B_1u_1^2$ represents the cost of vaccination, $B_2u_2^2$ represents the cost of treatment and $B_3u_3^2$ represents the cost of health education campaigns.

Our main objective is to characterize an optimal control $(u_1^*,u_2^*,u_3^*)\in\mathbb{U}$ which minimizes the cost of vaccination, treatment and health education campaigns as well as minimising the number of infectives at terminal time (T) such that the number of susceptibles in the children population increases. Thus, the Lagrange for the optimal control problem (9) is given by:

$$L(N_c,N_e,u)=A_1S(t)+A_2I(t)+\frac{1}{2}(B_1u_1^2+B_2u_2^2+B_3u_3^2), \tag{10}$$

where N_c is the population for the children and N_e is the free pathogen environment. Thus we define our Hamiltonian function H for our control problem as:

$$\begin{aligned} H((N_c,N_e,u;t)) =& A_1S(t)+A_2I(t)+\frac{1}{2}(B_1u_1^2+B_2u_2^2+B_3u_3^2) \\ &+\lambda_S\left(\Lambda-\varepsilon SI-\frac{\nu SE}{K+E}+\varepsilon_1R-\mu S-u_1S\right) \\ &+\lambda_I\left(\varepsilon SI+\frac{\nu SE}{K+E}-(\alpha_1+\mu+d)I-u_2I\right) \\ &+\lambda_R\left(\alpha_1I-\mu R-\varepsilon_1R+u_1S+u_2I\right) \\ &+\lambda_E\left(\gamma E-\mu_1E+\sigma_1I-u_3E\right). \end{aligned} \tag{11}$$

We therefore have to find numerically our optimal control functions u_1^*, u_2^*, and u_3^* that satisfy our optimal control set (u_1^*,u_2^*,u_3^*) such that

$$J(u_1^*,u_2^*,u_3^*)=min\{J(u_1,u_2,u_3)|u_1,u_2,u_3\in\Omega\}$$

subject to the dynamical system stated in (1) and the control set is given by

$$\begin{aligned} \Omega =&\{(u_1,u_2,u_3)|u_i(t)\ \textit{is Lebesgue measureable and piecewise continous on}\ [0,T], \\ &a_i\le u_i(t)\le b_i, i=1,2,3\} \end{aligned} \tag{12}$$

where a_i and b_i, $i=1,2,3$ are constants in the interval $[0,T]$ which represents both the lower and upper bounds for the control respectively. Therefore, due to the above results, using our optimal problem we are going to prove the existence of the optimal control and then characterize it through the optimality system.

3.1. Existence of Control Problem

Let $S(t),I(t),R(t)$ and $E(t)$ be the state variables representing susceptibles, infected, recovered and environment of pathogens respectively, with controls $u_1(t),u_2(t),u_3(t)$. We can rewrite the system (1) in the form.

$$X^{'}=AX+F(X)$$

with

$$X = \begin{bmatrix} S(t) \\ I(t) \\ R(t) \\ E(t) \end{bmatrix}$$

$$F = \begin{bmatrix} \Lambda - \varepsilon SI - \frac{\nu ES}{K+E} \\ \varepsilon SI + \frac{\nu ES}{K+E} \\ 0 \\ -u_3 \end{bmatrix}$$

and

$$A = \begin{bmatrix} -\mu - u_1 & 0 & \varepsilon_1 & 0 \\ 0 & -(\alpha_1 + \mu + d) - u_2 & 0 & 0 \\ u_1 & \alpha_1 + u_2 & -\mu - \varepsilon & 0 \\ 0 & \sigma_1 & 0 & \gamma - \mu_1 \end{bmatrix},$$

where $X^{'}$ represents the derivative with respect to time t. Thus, the system (1) is considered to be a non linear system with a bounded coefficient, we set

$$G(X) = A(X) + F(X). \tag{13}$$

From (13), $F(X)$ satisfies

$$\begin{aligned} |F(X_1) - F(X_2)| \leq C_1(|(S_{1c}(t) - S_{2c}(t))| + C_2|(I_{1c}(t) - I_{2c}(t))| + C_3|(R_{1c}(t) - R_{2c}(t))| + \\ C_4|(E_{1c}(t) - E_{2c}(t))|) \\ \leq C(|(S_{1c}(t) - S_{2c}(t))| + |(I_{1c}(t) - I_{2c}(t))| + |(R_{1c}(t) - R_{2c}(t))| + \\ |(E_{1c}(t) - E_{2c}(t))|), \end{aligned}$$

where the positive constant

$$C = max(C_1, C_2, C_3, C_4)$$

is independent of the state variables. Again we have

$$|G(X_1) - G(X_2)| \leq C|X_1 - X_2|,$$

where

$$C = C_1 + C_2 + C_3 + C_4 + ||H|| < \infty$$

so the function G is uniformly Lipschitz continuous.

Hence, a solution of system (13) exists (Birkhoff, G. and Rota, G.C., 1989) from the defination of control variables and non-negative initial conditions.

Theorem 3.1. *The optimal control exits for* $u^* = (u_1^*, u_2^*, u_3^*) \in \Omega$ *such that*

$$J(u_1^*, u_2^*, u_3^*) = min_{(u_1,u_2,u_3)\in\Omega} J(u_1, u_2, u_3),$$

subject to the control system (1) *with its initial conditions.*

Proof. The existence of an optimal control pair for system (1) can be obtained by using results from Fleming and Rishel (1978). In their work, the existence is guaranteed by compactness of the control and the state spaces, and convexity based on Fleming and Rishel's Theorem (see Fleming and Rishel, 1978 : 3.1 of Chapter 3).

From our system (1), we note that, the controls u_1, u_2, u_3 and state variables S, I, R, E are non negative values, hence the necessary convexity of our objective functional stated in terms of u_1, u_2, u_3 are satisfied. We further note that, by definition, our set Ω of control variables (u_1, u_2, u_3) is closed and convex.

Since our optimal system is bounded, this means that, the compactness required for the existence of optimal control is determined. Hence, the integrand of our objective function (9) is

$$A_1 S(t) + A_2 I(t) + \frac{1}{2}(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2)$$

is convex in the control set Ω.

Lastly, we note that, there exists a positive constant $\sigma > 1$ with positive constants ω_1 and ω_2 such that

$$\omega_1(|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\sigma}{2}} - \omega_2$$

which shows the existence of an optimal control problem.

3.2. The Optimal Control Solution

Here, we apply the Pontryagin's Maximum Principle (PMP) (Pontryagin *et al.,* 1962). The principle identifies the adjoint functions of the optimal system and represents an optimal control in terms of the state and adjoint functions. The main goal of this principle (PMP) is to minimize the objective function. Thus depending on the constraints in the objective function, we want to minimise the Hamiltonian with respect to the controls.

We define the adjoint functions as λ_S, λ_I, λ_R, and λ_E associated with state equations defined for S, I, R and E. From (11) the following Theorem 1.5 holds.

Theorem 3.2. *Let S, I, R and E be optimal state solutions with associated optimal control variables u_1, u_2, u_3 for optimal control (1). There exists adjoint variables λ_S, λ_I, λ_R and λ_E. Thus to achieve the optimal control, our adjoint functions must satisfy*

$$\begin{aligned}
-\frac{d\lambda_S}{dt} &= \frac{\partial H}{\partial S} \\
-\frac{d\lambda_I}{dt} &= \frac{\partial H}{\partial I} \\
-\frac{d\lambda_R}{dt} &= \frac{\partial H}{\partial R} \\
-\frac{d\lambda_E}{dt} &= \frac{\partial H}{\partial E},
\end{aligned}$$

where

$$\begin{aligned}
\frac{\partial H}{\partial S} &= A_1 - \lambda_S(\varepsilon I + \frac{\nu E}{K+E} + \mu + u_1(t)) + \lambda_I(\varepsilon I + \frac{\nu E}{K+E}) + \lambda_R u_1(t) \\
\frac{\partial H}{\partial I} &= A_2 + \lambda_S(-\varepsilon S) + \lambda_I(\varepsilon S - (\alpha_1 + \mu + d) - u_2(t)) + \lambda_R(\alpha_1 + u_2(t)) + \lambda_E \sigma_1 \\
\frac{\partial H}{\partial R} &= \lambda_S \varepsilon_1 - \lambda_R(\mu + \varepsilon_1) \\
\frac{\partial H}{\partial E} &= \lambda_S \frac{-K\nu S}{(K+E)^2} + \lambda_I \frac{K\nu S}{(K+E)^2} + \lambda_E(\gamma - \mu_1 - u_3(t)).
\end{aligned}$$

Thus

$$\frac{d\lambda_S}{dt} = \lambda_S(\varepsilon I + \frac{\nu E}{K+E} + \mu + u_1(t)) - A_1 - \lambda_I(\varepsilon I + \frac{\nu E}{K+E}) - \lambda_R u_1(t)$$
$$\frac{d\lambda_I}{dt} = \lambda_S \varepsilon S - A_2 - \lambda_I(\varepsilon S - (\alpha_1 + \mu + d) - u_2(t)) - \lambda_R(\alpha_1 + u_2(t)) - \lambda_E \sigma_1$$
$$\frac{d\lambda_R}{dt} = \lambda_R(\mu + \varepsilon_1) - \lambda_S \varepsilon_1$$
$$\frac{d\lambda_E}{dt} = \lambda_S \frac{K\nu S}{(K+E)^2} - \lambda_I \frac{K\nu S}{(K+E)^2} - \lambda_E(\gamma - \mu_1 - u_3(t))$$

with transversality conditions (or final time conditions)

$$\lambda_S(T) = 0,\ \lambda_I(T) = 0,\ \lambda_R(T) = 0 \text{ and } \lambda_E(T) = 0.$$

The characterizations of the optimal controls $u_1^*(t), u_2^*(t), u_3^*(t)$, that is, the optimality equations, are based on the conditions: $\frac{\partial H}{\partial u_1} = \frac{\partial H}{\partial u_2} = \frac{\partial H}{\partial u_3} = 0$ for

$$\frac{\partial H}{\partial u_1} = B_1 u_1(t) - S\lambda_S + \lambda_R S = 0$$
$$\frac{\partial H}{\partial u_2} = B_2 u_2(t) - I\lambda_I + \lambda_R I = 0$$
$$\frac{\partial H}{\partial u_3} = B_3 u_3(t) - \lambda_E E = 0$$

subject to the constraints $0 \le u_1(t) \le u_{1\ max}$, $0 \le u_2(t) \le u_{2\ max}$, $0 \le u_3(t) \le u_{3\ max}$

Hence we hav $u_1^* = \frac{(\lambda_S - \lambda_R)S}{B_1}$, $u_2^* = \frac{(\lambda_I - \lambda_S)I}{B_2}$ and $u_3^* = \frac{\lambda_E E}{B_3}$. Thus, using the bounds of the control $u_1(t)$, its optimal control is given by

$$u_1^* = \begin{cases} \frac{(\lambda_S - \lambda_R)S}{B_1} & \text{if } 0 \le \frac{(\lambda_S - \lambda_R)S}{B_1} \le 1, \\ 0 & \text{if } \frac{(\lambda_S - \lambda_R)S}{B_1} \le 0, \\ 1 & \text{if } \frac{(\lambda_S - \lambda_R)S}{B_1} \ge 1. \end{cases} \tag{14}$$

Equation (14) can be written in compact form as $u_1^* = min\{max\{0, \frac{(\lambda_S - \lambda_R)S}{B_1}\}, 1\}$. Also, using the bounds of the control $u_2(t)$, its optimal control is given by

$$u_2^* = \begin{cases} \frac{(\lambda_I - \lambda_S)I}{B_2} & \text{if } 0 \le \frac{(\lambda_I - \lambda_S)I}{B_2} \le 1, \\ 0 & \text{if } \frac{(\lambda_I - \lambda_S)I}{B_2} \le 0, \\ 1 & \text{if } \frac{(\lambda_I - \lambda_S)I}{B_2} \ge 1. \end{cases} \tag{15}$$

Equation (15) can be written in compact form as $u_2^* = min\{max\{0, \frac{(\lambda_I-\lambda_S)I}{B_2}\}, 1\}$. Again, using the bounds of the control $u_3(t)$, its optimal control is given by

$$u_3^* = \begin{cases} \frac{\lambda_E E}{B_3} & \text{if } 0 \leq \frac{\lambda_E E}{B_3} \leq 1, \\ 0 & \text{if } \frac{\lambda_E E}{B_3} \leq 0, \\ 1 & \text{if } \frac{\lambda_E E}{B_3} \geq 0. \end{cases} \tag{16}$$

Equation (16) can be written in compact form as $u_3^* = min\{max\{0, \frac{\lambda_E E}{B_3}\}, 1\}$. Referring to equations (14), (15), and (16), we obtain the following optimality system.

(17)

$$\frac{dS(t)}{dt} = \Lambda - \varepsilon SI - \frac{\nu SE}{K+E} + \varepsilon_1 R - \mu S - min\{max\{0, \frac{(\lambda_S-\lambda_R)S}{B_1}\}, 1\}S,$$

$$\frac{dI(t)}{dt} = \varepsilon SI + \frac{\nu SE}{K+E} - (\alpha_1 + \mu + d)I - min\{max\{0, \frac{(\lambda_I-\lambda_S)I}{B_2}\}I,$$

$$\frac{dR(t)}{dt} = \alpha_1 I_1 - \mu R - \varepsilon_1 R + min\{max\{0, \frac{(\lambda_S-\lambda_R)S}{B_1}\}, 1\}S + min\{max\{0, \frac{(\lambda_I-\lambda_S)I}{B_2}\}I,$$

$$\frac{dE(t)}{dt} = \gamma E - \mu_1 E + \sigma_1 I_1 - min\{max\{0, \frac{\lambda_E E}{B_3}\}E.$$

$$\frac{d\lambda_S}{dt} = \lambda_S(\varepsilon I + \frac{\nu E}{K+E} + \mu + u_1(t)) - A_1 - \lambda_I(\varepsilon I + \frac{\nu E}{K+E}) - \lambda_R min\{max\{0, \frac{(\lambda_S-\lambda_R)S}{B_1}\}, 1\}$$

$$\frac{d\lambda_I}{dt} = \lambda_S \varepsilon S - A_2 - \lambda_I(\varepsilon S - (\alpha_1 + \mu + d) - u_2(t)) - \lambda_R(\alpha_1 + min\{max\{0, \frac{(\lambda_I-\lambda_S)I}{B_2}\}, 1\}) - \lambda_E \sigma_1$$

$$\frac{d\lambda_R}{dt} = \lambda_R(\mu + \varepsilon_1) - \lambda_S \varepsilon_1$$

$$\frac{d\lambda_E}{dt} = \lambda_S \frac{K\nu S}{(K+E)^2} - \lambda_I \frac{K\nu S}{(K+E)^2} - \lambda_R(\gamma - \mu_1 - min\{max\{0, \frac{\lambda_E E}{B_3}\}, 1\})$$

with

$$S(0) = S_0, I(0) = I_0, R(0) = R_0, E(0) = E_0, \text{ and } \lambda_S(T) = \lambda_I(T) = \lambda_R(T) = \lambda_E(T) = 0.$$

We note that, the optimality system consists of the state equations with the initial conditions, the adjoint equations plus there transversity conditions, and the optimal control characterization. All these will be solved numerically in Section 4.

4. Numerical Results and Discussions of the Model

Under this Section, we present our model with control system in equation (1) being solved numerically. We applied the Forward Runge-Kutta order four schemes method (8) to compute the optimality control solution as well as the transversality conditions or boundary conditions under Section 3.2. The state equations are solved using initial guess values for the control variables as stated in Table. 1 for the different simulations.

Different values of the state and adjoint solutions are used in the process repeatedly until we achieve convegence of solutions. Various constant cost parameters used in the objective function are as stated: $A_1 = 0.02$, $A_2 = 10$, $B_1 = 10$, $B_2 = 10$, $B_3 = 20$.

The parameter values used in the simulation of this model are also stated in Table.1 with the set initial conditions and we consider the entire period $T = 100$ days.

4.1. Optimal Vaccination

Under this strategy, we use control u_1 to optimize the objective function while u_2 and u_3 are set to zero. In Figure 1 (a), control u_1 is maximum from $t = 0$ to $t = 55$ days and drops rapidly to zero. This implies that vaccination is effective from the beginning and should be fully implemented. When vaccination is applied, the susceptible children take 60 days to leave this class than when there is no vaccination which is almost $10 - 20$ days only as seen in Figure 1 (b).

4.2. Optimal health education campaigns

Under this strategy we use control u_3 to optimize the objective function while u_1 and u_2 are set to zero. In Figure 2 (a) control u_3 is maximum from $t = 36$ to $t = 60$ days when it gradually decreases to zero. This implies that in presence of disease health education campaigns should not be implemented alone because it is less effective at the beginning between $t = 0$ and $t = 36$ days. With health education campaigns are applied, the disease will disappear after 40 days

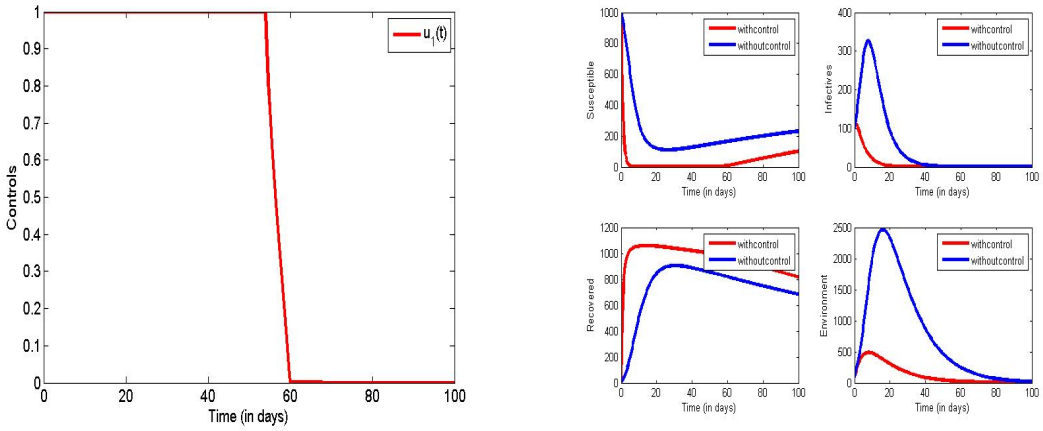
Table 1. state variables and parameters of the Model

state variables	Description	Value	Reference
$S(0)$	number of susceptible children at time $t = 0$	1000	Assumed
$I(0)$	number of infected children at time $t = 0$	100	Assumed
$R(0)$	number of recovered children at time $t = 0$	0	Assumed
$E(0)$	free pathogen environment at time $t = 0$	100	Assumed
Parameters			
Λ	birth rate	0.0018 per day	[9]
μ	natural death rate	0.0018 per day	[9]
ε	direct transmission rate	0.0005	Assumed
ν	indirect transmission rate	0.002	Assumed
α_1	recovery rate	0.2 per day	[12, 25]
ε_1	immunity waning rate	0.0027 per day	[24]
σ	shedding rate	1cell/ml/day	[18]
K	concetration of rotavirus in exposed environment	10000cell/ml/day	[18]
γ	pathogen contribution from the environment	0.0001 cell/ml/day	[18]
d	death rate due to rotavirus	0.000446 per day	[1]
μ_1	free pathogen death rate	0.0667 per day	[2]

as seen in Figure 2 (b). We further note that, in Figure 2b in case of susceptible, infected and recovered the graphs overlap to show that health education campaigns has no effect on these three classes except on the environment.

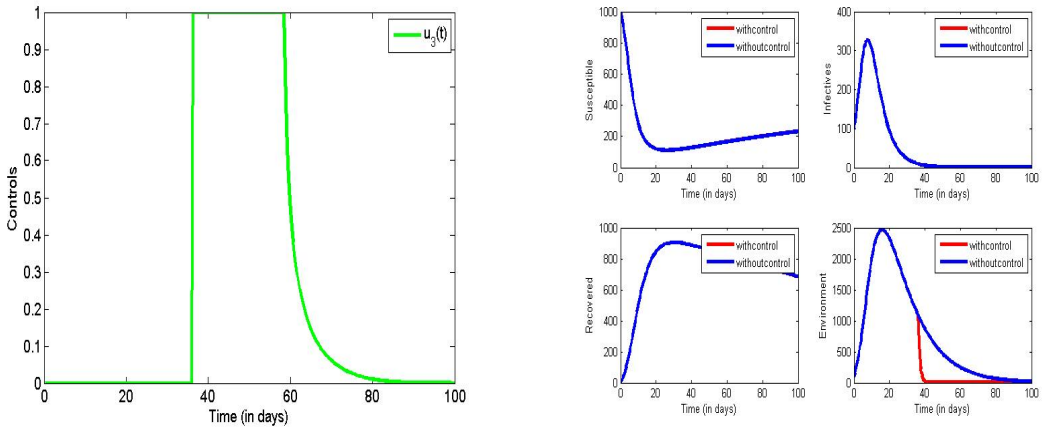
4.3. Optimal vaccination and health education campaigns

Under this strategy we use two controls u_1 and u_3 to optimize the objective function while u_2 is set to zero. Figure 3 (a) show the controls u_1 and u_2. u_1 is maximum from $t = 0$ to $t = 48$ days and drop rapidly to 0, while u_3 is maximum from $t = 12$ to $t = 38$ days when it gradually decreases to zero. This implies that vaccination should be implemented fully from the beginning



(a) u_1 control (b) u_1 profile

FIGURE 1. A plot represents optimal of vaccination only.



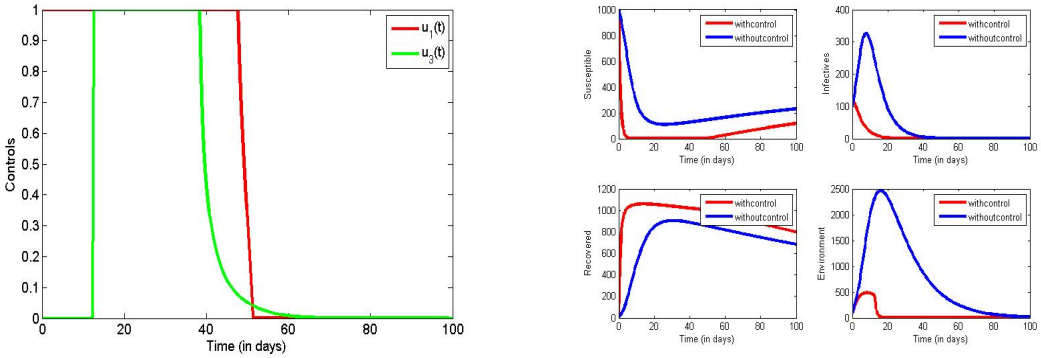
(a) u_3 control (b) u_3 profile

FIGURE 2. A plot represents optimal health education campaigns only.

followed by the educational campaigns. With treatment and health education campaigns applied the disease will also disappear within 20 days as shown in Figure 3 (b).

4.4. Optimal vaccination, treatment and health education campaigns

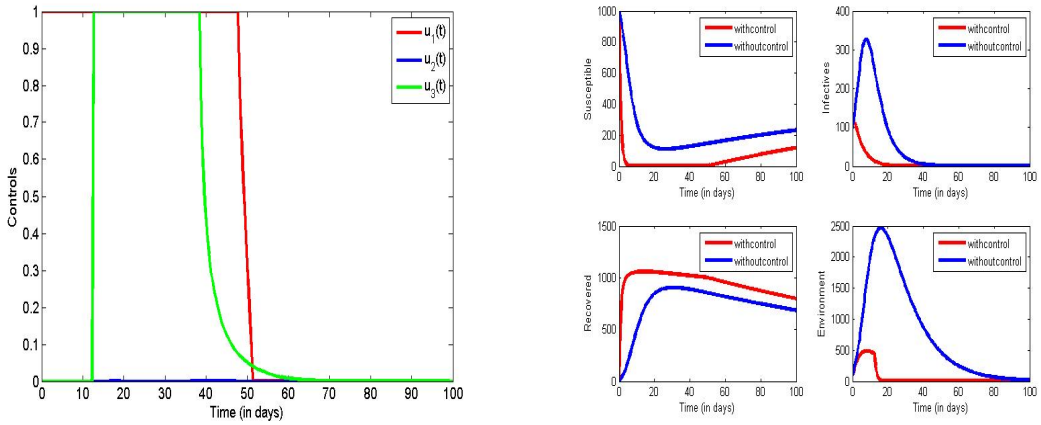
Under this strategy, we use all controls, that is, u_1, u_2 and u_3 to optimize the objective function. Figure 4 (a) show the controls u_1, u_2 and u_2. u_1 is maximum from $t = 0$ to $t = 48$ days and drop rapidly to 0. u_2 is low throughout the time. u_3 is maximum from $t = 12$ to $t = 38$ days when is gradually decreases to zero. This implies that vaccination should be implemented



(a) u_1 and u_3 controls (b) u_1 and u_3 profile

FIGURE 3. A plot represents optimal vaccination and health education campaigns only.

fully from the beginning followed by the educational campaigns. Treatment rate is low because if more kids are vaccinated only few individuals will get sick. With all controls applied the disease will disappear within 20 days as shown in Figure 4 (b). When there is no control, the infection will persist for about 40 days and the pathogens with persist for about 100 days.



(a) u_1, u_2 and u_3 controls (b) u_1, u_2 and u_3 profile

FIGURE 4. A plot represents optimal vaccination, treatment and health education campaigns.

5. Conclusion

A mathematical model with controls, u_1 for vaccination of susceptible children, u_2 for treatment of infected children and u_3 for health education campaigns has been formulated. We have computed the basic reproduction number R_0, the effective reproduction number R_c, as well as the disease free equilibrium and endemic equilibrium points. We have found that the disease free equilibrium is locally asymptotically stable whenever $R_c < 1$ and unstable whenever $R_c > 1$. We have also derived and analysed the conditions for optimal control of rotavirus and evaluate different control strategies. The results show that vaccination is the most effective, followed by health education campaigns then treatment.

Conflict of Interests

The authors declare that there is no conflict of interests.

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