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Optimal control of cholera incorporating the dynamics of the induced achlorhydria condition with cost-effective strategies

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Abstract: A nonlinear dynamical system is proposed and qualitatively analyzed to study the dynamics of cholera disease in a population. The basic model is extended to include; reduce infection rate (u_1), increase rate of seeking treatment (u_2), decrease development of achlorhydria condition (u_3), increase recovery rate from achlorhydria condition (u_4), increase recovery rate (improve efficacy of the drugs) (u_5). This leads to an optimal control problem which is qualitatively analyzed using Pontryaginâs maximum principle. Numerical simulation of the resulting optimal control problem is carried out to gain quantitative insights into the implications of the model and pertinent results are displayed graphically. The simulation reveals that a multifaceted approach to the fight against the disease is more effective than single control strategy.

Key Words: Cholera, optimal control, Pontryaginâs maximum principle, numerical simulation, multifaceted approach

1. Introduction

Modelling is a technique for simulating real-life situations with mathematical equations in order to predict future behavior by generating a simplified representation of a real system [1]. The modeling of infectious diseases is a tool that has been used to study the mechanisms by which diseases spread, predict the future course of an outbreak and evaluate strategies to control an epidemic [2]. The study of the emergence of infectious diseases is likely to become increasingly important with increase in human and livestock population and increasing stress placed on aquatic reservoirs [3]. Access to clean water through improved water network systems and sanitary facilities therefore remains the most effective means of preventing cholera outbreaks [4]. Studies of gastric acidity and cholera are of interest, *vibrio cholerae* is a very acid-labile organism and it has been proposed that normal gastric acidity presents a barrier to the establishment of intestinal infection [5]. Several models have been formulated and analysed to explain the dynamics of cholera transmission which include; [6] studied cholera dynamics with prevention and control. Therapeutic treatment was in the form of administration of antibiotics or rehydration salts, vaccination and therapeutic treatment were incorporated as prevention and control strategies against cholera transmission. According to this study availability and potency of these interventions were capable of averting 120 000 deaths due to cholera. [7] developed a model on mathematical assessment of the role of environmental factors on the dynamical transmission of cholera. The objective was to investigate the impact of environmental factors on the dynamical transmission of cholera within a human population on the persistence of the disease. [8] discussed a model on cholera with hyper infectious and hypo infectious *vibrios*, in which both humans and environment to humans transmissions were considered. A combination with quarantine, sanitation, vaccination and treatment strategy is most efficient to prevent, control and eradicate cholera. [9] developed a model considering optimal control of cholera on presence of asymptotic transmission and control interventions (social mobilization, drug/oral re-hydration solution and safe water). The goal was to develop (deterministic and stochastic) mathematical models of cholera transmission and control dynamics with the aim of investigating the effect of the three control interventions against cholera transmission in order to find optimal control strategies, it was advised that the use of multiple control interventions be adopted for cholera in areas where there were sufficient resources. However, in areas where there are limited or lack of resources, it was advised that treatment of the asymptomatic individuals with drug or administration of oral re-hydration solution to the infected should be used.

Achlorhydria refer to condition in which production of hydrochloric acid in the digestive system is respectively absent or reduced, it is usually secondary to an underlying medical condition. Stomach pH in fasting, healthy people is between pH 2.5 and serves as a barrier to food-borne pathogens [10]. *Vibrio cholerae* survived well in normal gastric juice when the pH was adjusted to neutrality but were rapidly killed at pH values less than 4.8 [5]. There is evidence that patients with hypochlorhydria

or achlorhydria or who have been treated with proton pump inhibitors or H-2 receptor antagonists are more susceptible to *Vibrio cholerae* than healthy persons [11]. Proton pump inhibitors are available increasingly without prescription, so that people can self-medicate without realizing that this might mean an increased risk of cholera disease. In a study conducted in the USA, adult volunteers experimentally challenged with virulent strains of *Vibrio cholerae* only developed cholera after the gastric pH in the volunteers was raised by antacid drugs [12]. Optimal control is a branch of mathematics developed to find optimal ways to control a dynamic system [13]. There are few papers that apply optimal control to cholera models [14]. Here we propose and analyze one such optimal control problem, where the control function represents the fraction of Susceptible(S), infected individuals I_c and where I_c will be submitted to treatment until complete recovery. The objective is to find the optimal control strategy that minimizes the number of infected individuals and increases the number of susceptible individuals.

2. Derivation of the Models and Their Analysis

2.1. Mathematical modelling of cholera incorporating the dynamics of the induced achlorhydria condition and treatment

We had earlier discussed in [15] the impact of the induced achlorhydria condition on their role in fueling cholera transmission. Model of cholera dynamics incorporating the dynamics of the induced achlorhydria condition and treatment was also developed.

2.2. Positivity of the Solution

Suppose that the initial data $S(0) \leq 0$, $I_c(0) \leq 0$, $I_{cr}(0) \leq 0$, $T_c(0) \leq 0$ and $R(0) \leq 0$ then the solutions (S(t), $I_c(t)$, I_{cr} $T_c(t)$, R(t)) of the cholera control model (1) are non-negative for all $t > 0$.
For the proof [15].

2.3. Boundedness of the Solution

All solutions (S(t), $I_c(t)$, $I_{cr}(t)$, $T_c(t)$ and R(t) of the cholera control model are bounded that is $0 \leq N < \frac{\pi}{\mu}$ and $N \leq \frac{\pi}{\mu}$, therefore $\Omega = \{S(t), I_c(t), I_{cr}(t), T_c(t), R(t) \in R_+^5; N \leq \frac{\pi}{\mu}\}$
For the proof [15].

2.4. Disease Free Equilibrium Point (DFE)

The disease-free equilibrium is obtained in [15] by setting the LHS (left hand side) of the model to zero and then we obtained the solution of the variables in the model.

2.5. Computation of basic reproduction number

The effective reproduction number R_0 is obtained using the next generation matrix method [15]. The effective reproduction number R_0 is given as

$$R_0^* = \frac{S^0\beta}{N\Omega_2} + \frac{S^0\beta\eta_1\Omega_1}{N\Omega_2\Omega_5} + \frac{S^0\alpha\beta\eta_2}{N\Omega_2\Omega_5} + \frac{S^0\beta\eta_2\Omega_1\Omega_3}{N\Omega_2\Omega_4\Omega_5} \tag{1}$$

For the proof [15].

2.6. Existence of Endemic Equilibrium Point

Theorem. If $R_0^* > 1$ which has biological sense.
For the proof [15].

3. Model Formulation

The model is adopted from the classical SIR model. The model describe the transmission of Cholera incorporating the dynamic of the induced achlorhydria condition and treatment. The total population is denoted as N which subdivide into the following classes, (S) as the susceptible individuals, (I_c) the cholera infected individuals, (I_{cr}) the cholera infected individual with induced achlorhydria condition, (T_c) those seeking treatment for cholera and (R) individual who have recovered from cholera (S, I_c, I_{cr}, T_c, R). The main feature of the model is that the force of infection, λ is obtained by mass-mixing of individuals in a population, β infection rate is also considered. Infected individuals

who joined the class I_c can progress into I_{cr} due to implications of the induced achlorhydria condition or may die out naturally. After progressing into this group and treatment of achlorhydria is done or correct mechanism by enhancing production of hydrochloric acid is done individual progress to (T_c) where they seek treatment for cholera at a rate α. Individuals recover from cholera and join class (R) and return to susceptible class (S) after gaining temporal immunity against cholera. The next-generation matrix is used to derive the basic reproduction number, for a compartmental model of the spread of infectious diseases, in population dynamics it is used to compute the basic reproduction number for structured population models.

3.1. Model Equation

$$\begin{aligned}
\frac{dS}{dt} &= \pi + \phi R - \mu S - \lambda S \\
\frac{dI_c}{dt} &= \lambda S - \mu I_c - \alpha I_c - \delta_1 I_c - V_{max}\frac{A_L}{K_M + A_L} I_c \\
\frac{dI_{cr}}{dt} &= V_{max}\frac{A_L}{K_M + A_L} I_c - \mu I_{cr} - \theta\delta_1 I_{cr} - V_{max}\frac{A_H}{K_M + A_H} I_{cr} \\
\frac{dT_c}{dt} &= V_{max}\frac{A_H}{K_M + A_H} I_{cr} + \alpha I_c - \delta_2 T_c - \mu T_c - \omega T_c \\
\frac{dR}{dt} &= \omega T_c - \mu R - \phi R
\end{aligned} \tag{2}$$

4. Extension of the model

In this section, we apply optimal control strategies on the model [15]. This help us to identify the best intervention strategies that helps to eradicate the disease in the specified time. The optimal control model is an extension cholera model by including the following five optimal controls defined as;

i. $u_1$is the prevention effort, that reduces the possibility of susceptible from contacting the disease.
ii. u_2 is the treatment effort, to minimize infection by treating infectious.
iii. u_3 is the prevention effort, that reduced development of achlorhydria condition on individuals during cholera outbreak.
iv. u_4 is the treatment effort, that reduces achlorhydria condition on individuals with problem of gastric acid secretion.
v. u_5 is the curative effort, that help to increase the number of recovered individuals from cholera (improving efficacy of the drugs).

After incorporating, u_1, u_2, u_3, u_4, u_5 in cholera model equations (2), we obtain the following optimal control model of cholera:

4.1. Model Equation

$$\begin{aligned}
\frac{dS}{dt} &= \pi + \phi R - \mu s - (1-u_1)S \\
\frac{dI_c}{dt} &= (1-u_1)S - \mu I_c - (1-u_2)I_c - \delta_1 I_c - V_{max}\frac{u_3}{K_M + u_3} I_c \\
\frac{dI_{cr}}{dt} &= V_{max}\frac{u_3}{K_M + u_3} I_c - \mu I_{cr} - \theta\delta_1 I_{cr} - V_{max}\frac{u_4}{K_M + u_4} I_{cr} \\
\frac{dT_c}{dt} &= V_{max}\frac{u_4}{K_M + u_4} I_{cr} + (1-u_2)I_c - \delta_2 T_c - \mu T_c - (1-u_5)T_c \\
\frac{dR}{dt} &= (1-u_5)T_c - \mu R - \phi R
\end{aligned} \tag{3}$$

To study the optimal levels of the controls, the control set $\cup$ is Lebesgue measurable and it is defined as $\cup = (u_1(t), u_2(t), u_3(t), u_4(t), u_5(t)$:

$0 \le u_1 < 1, 0 \le u_2 < 1, 0 \le u_3 < 1, 0 \le u_4 < 1, 0 \le u_5 < 1, 0 \le t \le T$. Our aim is to obtain a control u and S, I_c, I_{cr}, T_c and R that minimize the proposed objective function J and the form of the objective functional is taken in

line with literature on epidemic models [16] given by

$$J = \min_{u_1,u_2,u_3,u_4,u_5} \int_0^{t_f} (b_1 I_c + b_2 I_{cr} + b_3 T_c + \frac{1}{2}\sum_{i=1}^{3} w_i u_i^2)dt \tag{4}$$

where b_1, b_2, b_3 and w_i are positive. The expression $\frac{1}{2}w_i u_i^2$ represents cost which is associated with the controls u_i. The form is quadratic because we assume that costs are nonlinear in its nature. Our aim is to minimize the number of carriers, infectives and costs. Thus, we seek to find an optimal five controls $(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ such that

$J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*) = minJ(u_1, u_2, u_3, u_4, u_5)/u_i \in U,$
where U $= (u_1, u_2, u_3, u_4, u_5)/$ each u_i is measurable with $0 \leq u_i < 1$ for $0 \leq tâtf$.

5. The Hamiltonian and optimality system

By using the Pontryaginâs Maximum Principle [13] we got the necessary conditions which is satisfied by optimal pair. Therefore, by this principle, we obtained a Hamiltonian (H) defined as

$$H(S, I_c, I_{cr}, T_c, R, t) = L(I_c, I_{cr}, T_c, u_1, u_2, u_3, u_4, u_5, t) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dI_c}{dt} + \lambda_3 \frac{dI_{cr}}{dt} + \lambda_4 \frac{dT_c}{dt} + \lambda_5 \frac{dR}{dt}$$

where

$$L(I_c, I_{cr}, T_c, u_1, u_2, u_3, u_4, u_5, t) = b_1 I_c + b_2 I_{cr} + b_3 T_c + \frac{1}{2} 3i = 1 w_i u_i^2$$
$$\lambda_i, i = 1, 2, 3, 4, 5$$

are the adjoint variable functions to be determined suitably by applying Pontryaginâs maximal principle [13] and also using [17] for existence of the optimal control pairs.
Theorem: For an optimal control set u_1, u_2, u_3, u_4, u_5 that minimizes J over U, there is an adjoint variables, $\lambda_1, \ldots, \lambda_5$ such that:

$$\frac{d\lambda_1}{dt} = -[-\mu - (1-u_1)]\lambda_1 - (1-u_1)\lambda_2 \tag{5}$$
$$\frac{d\lambda_2}{dt} = -[-\mu - (1-u_2) - \delta_1 - V_{max}\frac{u_3}{K_M + u_3}]\lambda_2 - V_{max}\frac{u_3}{K_M + u_3}\lambda_3 - (1-u_2)\lambda 4 \tag{6}$$
$$\frac{d\lambda_3}{dt} = -[-\mu - \theta\delta_1 - V_{max}\frac{u_4}{K_M + u_4}]\lambda_3 - V_{max}\frac{u_4}{K_M + u_4}\lambda_4 \tag{7}$$
$$\frac{d\lambda_4}{dt} = -[(1-u_2) - \delta_2 - \mu - (1-u_5)]\lambda_4 - (1-u_5)\lambda_5 \tag{8}$$
$$\frac{d\lambda_5}{dt} = -\phi\lambda_1 - (-\mu - \phi)\lambda_5 \tag{9}$$
$$\tag{10}$$

With transversality conditions, $\lambda_i(t_f) = 0$, i = 1,....,5. Furthermore, we obtain the control set $(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ characterized by

$u_1^*(t) = max0, min(1, \Phi_1),$
$u_2^*(t) = max0, min(1, \Phi_2),$
$u_3^*(t) = max0, min(1, \Phi_3),$

$$\begin{aligned}
\Phi_1 =&(\lambda_2-\lambda_1)S\\
\Phi_2 =&(\lambda_4-\lambda_2)I_c\\
\Phi_3 =&(V_{max}\frac{K_M}{(K_M+u_3)^2}\lambda_2-V_{max}\frac{K_M}{(K_M+u_3)^2}\lambda_3)I_c\\
\Phi_4 =&(V_{max}\frac{K_M}{(K_M+u_4)^2}\lambda_3-V_{max}\frac{K_M}{(K_M+u_4)^2}\lambda_4)I_{cr}\\
\Phi_5 =&(\lambda_5-\lambda_4)T_c
\end{aligned}$$

Proof: The form of the adjoint equation and transversality conditions are standard results from Pontryaginâs maximum principle [13]. We differentiate Hamiltonian with respect to states S, I_c, I_{cr}, T_c and R, respectively, and then the adjoint system can be written as

$$\begin{aligned}
\frac{d\lambda_1}{dt} =&-[-\mu-(1-u_1)]\lambda_1-(1-u_1)\lambda_2\\
\frac{d\lambda_2}{dt} =&-[-\mu-(1-u_2)-\delta_1-V_{max}\frac{u_3}{K_M+u_3}]\lambda_2-V_{max}\frac{u_3}{K_M+u_3}\lambda_3-(1-u_2)\lambda 4\\
\frac{d\lambda_3}{dt} =&-[-\mu-\theta\delta_1-V_{max}\frac{u_4}{K_M+u_4}]\lambda_3-V_{max}\frac{u_4}{K_M+u_4}\lambda_4\\
\frac{d\lambda_4}{dt} =&-[(1-u_2)-\delta_2-\mu-(1-u_5)]\lambda_4-(1-u_5)\lambda_5\\
\frac{d\lambda_5}{dt} =&-\phi\lambda_1-(-\mu-\phi)\lambda_5
\end{aligned} \tag{11}$$

Similarly by following the approach of [13], to get the controls, we solved the equation, $\frac{\partial H}{\partial u_i}=0$ at u_i^* , for i = 1, 2, 3, 4, 5 and obtained:

$$\begin{aligned}
u_1^* =&(\lambda_2-\lambda_1)S\\
u_2^* =&(\lambda_4-\lambda_2)I_c\\
u_3^* =&(V_{max}\frac{K_M}{(K_M+u_3)^2}\lambda_2-V_{max}\frac{K_M}{(K_M+u_3)^2}\lambda_3)I_c\\
u_4^* =&(V_{max}\frac{K_M}{(K_M+u_4)^2}\lambda_3-V_{max}\frac{K_M}{(K_M+u_4)^2}\lambda_4)I_{cr}\\
u_5^* =&(\lambda_5-\lambda_4)T_c
\end{aligned}$$

When we write by using standard control arguments involving the bounds on the controls, we conclude

$$u_1^*=\begin{cases}\Phi_1 & if 0<\Phi_1<1,\\ 0 & if \Phi_1\leq 0,\\ 1 & if \Phi_1\geq 1.\end{cases}$$

$$u_2^*=\begin{cases}\Phi_2 & if 0<\Phi_2<1,\\ 0 & if \Phi_2\leq 0,\\ 1 & if \Phi_2\geq 1.\end{cases}$$

$$u_3^*=\begin{cases}\Phi_3 & if 0<\Phi_3<1,\\ 0 & if \Phi_3\leq 0,\\ 1 & if \Phi_3\geq 1.\end{cases}$$

$$u_4^*=\begin{cases}\Phi_4 & if 0<\Phi_4<1,\\ 0 & if \Phi_4\leq 0,\\ 1 & if \Phi_4\geq 1.\end{cases}$$

$$u_5^* = \begin{cases} \Phi_5 & if 0 < \Phi_5 < 1, \\ 0 & if \Phi_5 \leq 0, \\ 1 & if \Phi_5 \geq 1. \end{cases}$$

In compact notation

$$u_1^*(t) = max[0, min(1, \Phi_1)], \tag{12}$$
$$u_2^*(t) = max[0, min(1, \Phi_2)], \tag{13}$$
$$u_3^*(t) = max[0, min(1, \Phi_3)], \tag{14}$$
$$u_4^*(t) = max[0, min(1, \Phi_4)], \tag{15}$$
$$u_5^*(t) = max[0, min(1, \Phi_5)], \tag{16}$$

$$\begin{aligned}
\Phi_1 =& (\lambda_2 - \lambda_1)S \\
\Phi_2 =& (\lambda_4 - \lambda_2)I_c \\
\Phi_3 =& (V_{max}\frac{K_M}{(K_M + u_3)^2}\lambda_2 - V_{max}\frac{K_M}{(K_M + u_3)^2}\lambda_3)I_c \\
\Phi_4 =& (V_{max}\frac{K_M}{(K_M + u_4)^2}\lambda_3 - V_{max}\frac{K_M}{(K_M + u_4)^2}\lambda_4)I_{cr} \\
\Phi_5 =& (\lambda_5 - \lambda_4)T_c
\end{aligned}$$

The optimality system is formed from the optimal control system (the state system) and the adjoint variable system by incorporating the characterized control set, initial and transversal condition.

$$\begin{aligned}
\frac{dS}{dt} =& \pi + \phi R - \mu s - (1 - u_1^*)S \\
\frac{dI_c}{dt} =& (1 - u_1^*)S - \mu I_c - (1 - u_2^*)I_c - \delta_1 I_c - V_{max}\frac{u_3^*}{K_M + u_3^*}I_c \\
\frac{dI_{cr}}{dt} =& V_{max}\frac{u_3^*}{K_M + u_3^*}I_c - \mu I_{cr} - \theta\delta_1 I_{cr} - V_{max}\frac{u_4^*}{K_M + u_4^*}I_{cr} \\
\frac{dT_c}{dt} =& V_{max}\frac{u_4^*}{K_M + u_4^*}I_{cr} + (1 - u_2^*)I_c - \delta_2 T_c - \mu T_c - (1 - u_5^*)T_c \\
\frac{dR}{dt} =& (1 - u_5^*)T_c - \mu R - \phi R
\end{aligned}$$

$$\begin{aligned}
\frac{d\lambda_1}{dt} =& -[-\mu - (1 - u_1^*)]\lambda_1 - (1 - u_1^*)\lambda_2 \\
\frac{d\lambda_2}{dt} =& -[-\mu - (1 - u_2^*) - \delta_1 - V_{max}\frac{u_3^*}{K_M + u_3^*}]\lambda_2 - V_{max}\frac{u_3^*}{K_M + u_3^*}\lambda_3 - (1 - u_2^*)\lambda 4 \\
\frac{d\lambda_3}{dt} =& -[-\mu - \theta\delta_1 - V_{max}\frac{u_4^*}{K_M + u_4^*}]\lambda_3 - V_{max}\frac{u_4^*}{K_M + u_4^*}\lambda_4 \\
\frac{d\lambda_4}{dt} =& -[(1 - u_2^*) - \delta_2 - \mu - (1 - u_5^*)]\lambda_4 - (1 - u_5^*)\lambda_5 \\
\frac{d\lambda_5}{dt} =& -\phi\lambda_1 - (-\mu - \phi)\lambda_5
\end{aligned}$$

$\lambda_i(t_f) = 0$, i=1, 2, 3, 4, 5, $S(0) = S_0$, $I_c(0) = I_c$, $I_{cr}(0) = I_{cr}$,$T_c(0) = T_c$ and $R(0) = R_0$

6. Uniqueness of the optimality system

Due to the prior boundedness of the state, adjoint functions and the resulting Lipschitz structure of the ordinary differential equations, we can obtain the uniqueness of solutions of the optimality system for the small time interval. Using Pontryaginâs maximum principle, the adjoint or costate equations are obtained by differentiating the Hamiltonian partially with respect to the state variables. Thus,we have

$$\frac{d\lambda_1}{dt} = \frac{\partial H}{dS}, \frac{d\lambda_2}{dt} = \frac{\partial H}{dI_c}, \frac{d\lambda_3}{dt} = \frac{\partial H}{dI_{cr}}, \frac{d\lambda_4}{dt} = \frac{\partial H}{dT_c}, \frac{d\lambda_5}{dt} = \frac{\partial H}{dR} \tag{17}$$

with $\lambda_i T = 0$ for i = 1,..,5
Since the Hamiltonian is minimized at the optimal controls, the optimality conditions $\frac{\partial H}{\partial u_i} = 0$ $u_i = u_i^*$ are met. These optimality conditions can be used to obtain expressions for u_i^* By standard control arguments involving the bounds on the controls, 12-16 is obtained, concluding the proof.

7. Numerical simulations

In this section, we perform some numerical experimentation on the basic model equation (2) and the resulting optimality system consisting of the state equations (3) and the adjoint system(4). We make use of the parameter values given in Table 2 [15] for the simulation. An iterative scheme is used to find the optimal solution of the optimality system. Since the state system(2) has initial conditions and the adjoint systems (4) have final conditions, we solve the state system using a forward fourth-order RungeâKutta method and solve the adjoint system using a backward fourth-order RungeâKutta method. The solution iterative scheme involves making a guess of the controls and using that guess to solve the state system. The initial guess of the control together with the solution of the state systems is used to solve the adjoint systems. The controls are then updated using a convex combination of the previous controls and the values obtained using the characterizations. The updated controls are then used to repeat the solution of the state and adjoint systems. This process is repeated until the values in the current iteration are close enough to the previous iteration values. Using different combinations of the controls, such as one control only at a time, two controls at a time, three controls at a time, four controls at a time and also all controls at a time, that we analyse and compare numerical results from simulations with the following scenarios.

7.1. Control with preventive effort u_1 only

We simulate the model by preventive intervention only. Figure 1 and 2 we see that the increase in susceptible and decrease in infectious due to implementation of prevention. This can be attribute the fact that prevention minimizes the rate of joining of individuals in to infective compartments. This implies that optimized prevention reduces the burden of the infection of cholera.

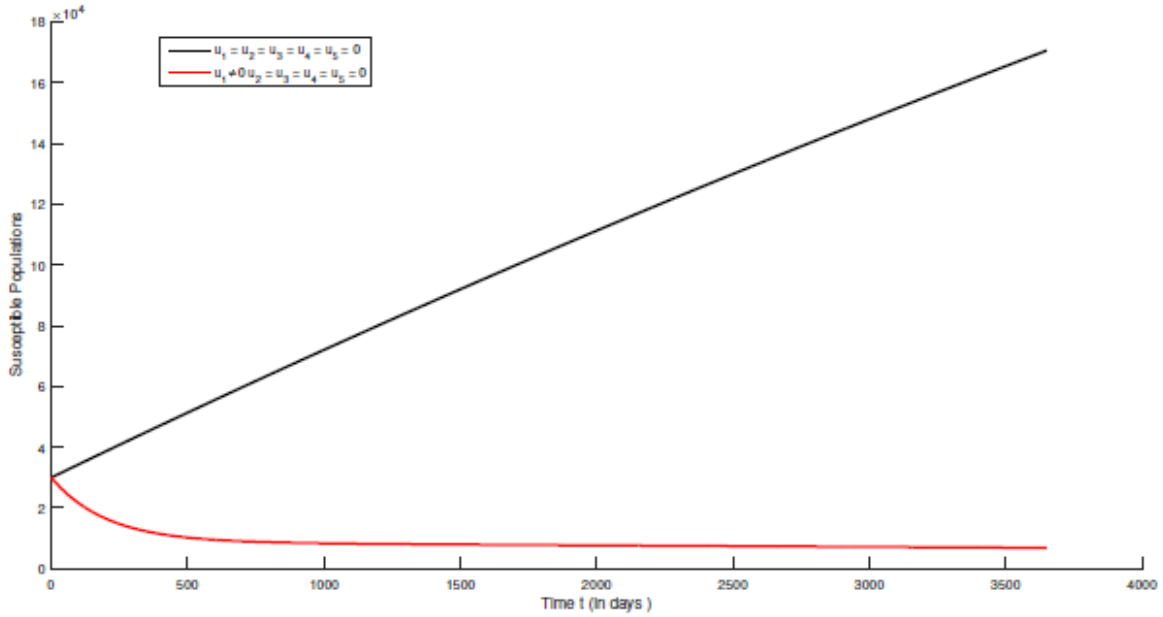

Figure 1. Simulations of optimal control with prevention only.

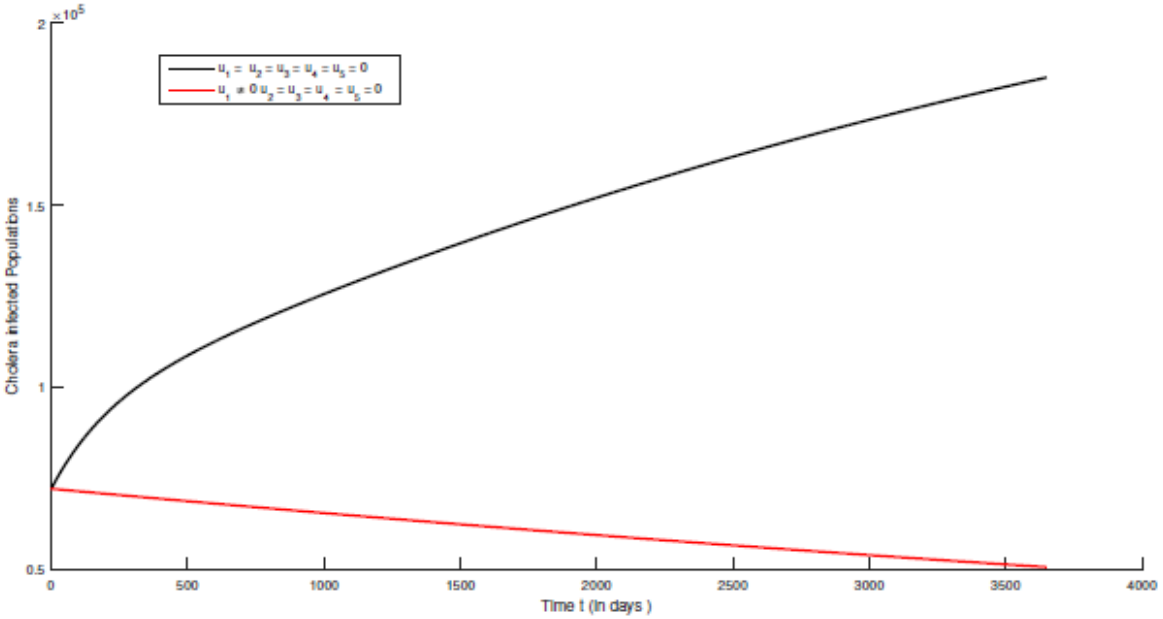

Figure 2. Simulations of optimal control with prevention only.

7.2. *Control with preventive u_1 and treatment effort u_2*

We used prevention and treatment as intervention strategy, the susceptible goes up as the infectious goes down. Therefore, this strategies is effective in eradicating the disease from the community in a specified period of time.

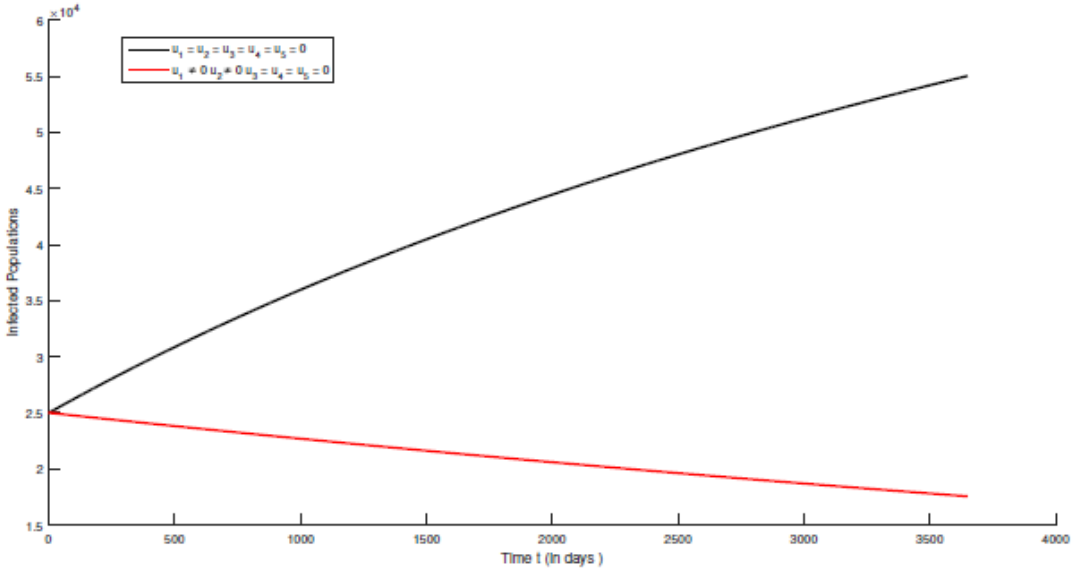

Figure 3. Simulations of optimal control with prevention u_1 and treatment u_2.

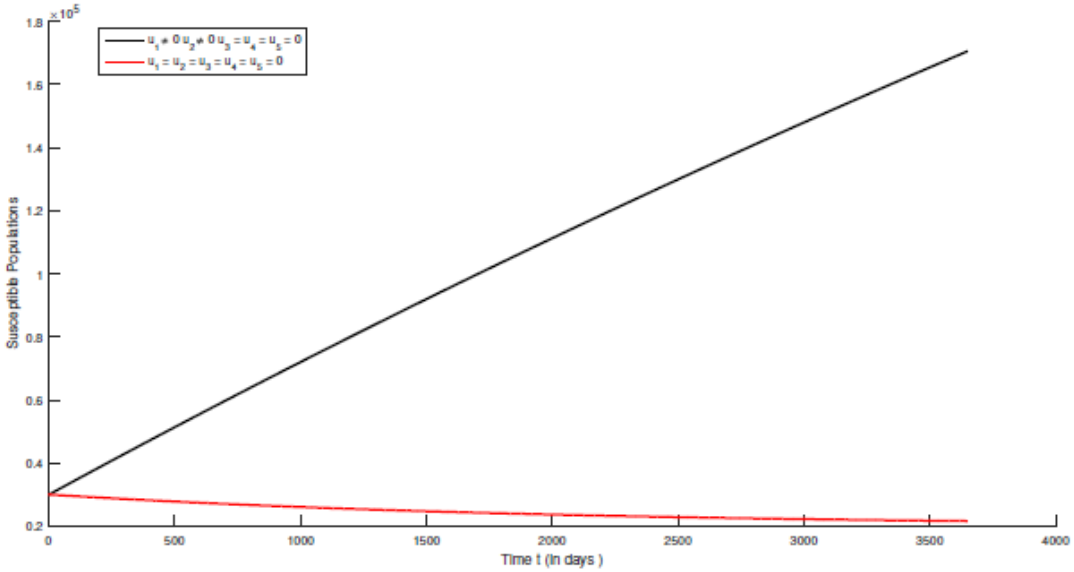

Figure 4. Simulations of optimal control with prevention u_1 and treatment u_2.

7.3. *Control with preventive u_1, treatment u_2, preventive u_3 and treatment effort u_4*

We used preventive and treatment strategy. Figure 5 and 6 we observe that optimal control of the combination of prevention and treatment helps to bring down the infectious as well as increasing the susceptible population which helps to eradicate the disease in the community.

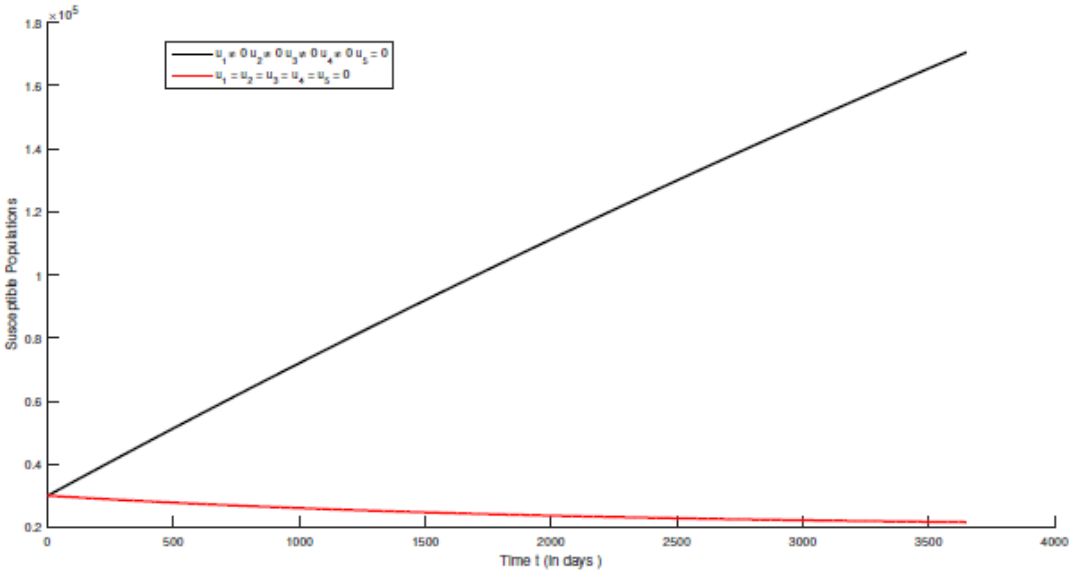

Figure 5. Simulations of optimal control with prevention u_1, treatment u_2, preventive u_3 and treatment u_4 effort.

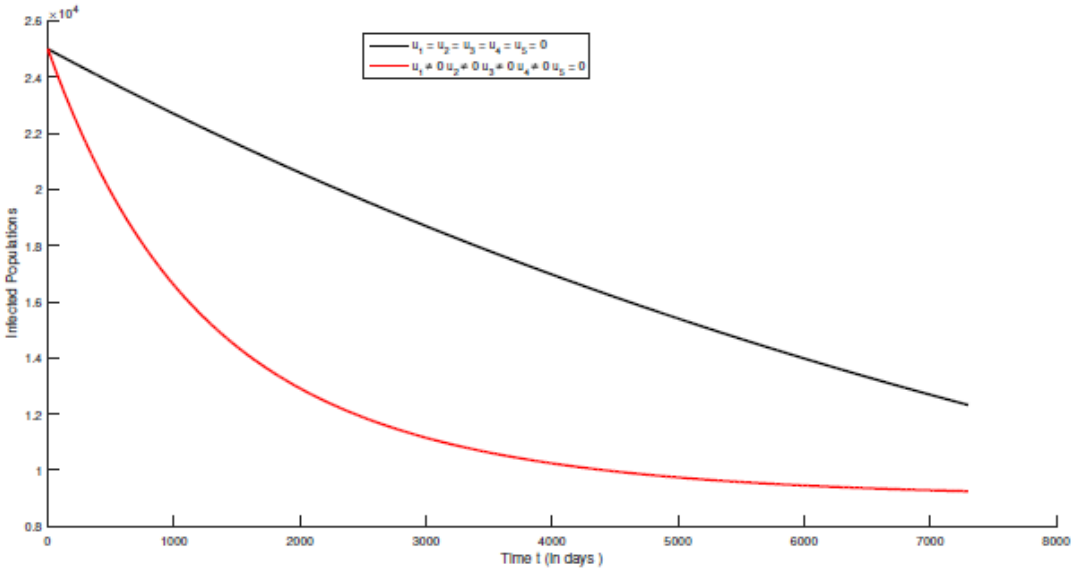

Figure 6. Simulations of optimal control with prevention u_1, treatment u_2, preventive u_3 and treatment u_4 effort.

7.4. Control with preventive u_1, treatment u_2, preventive u_3, treatment u_4 and curative effort u_5

We use preventive, treatment and curative strategy. Figure 7 and 8 shows an increase in susceptible and a decrease in infectious compartment as these control are optimized since more individuals will be treated and go back to susceptible after gaining temporal immunity.

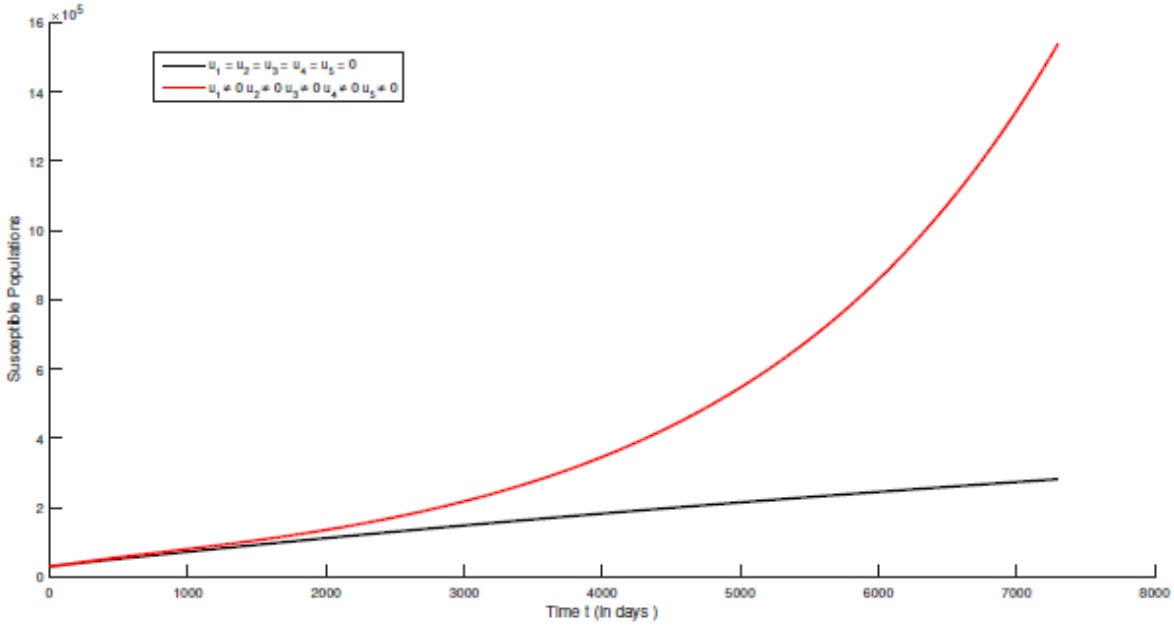

Figure 7. Simulations of optimal control with prevention u_1, treatment u_2, preventive u_3, treatment u_4 and curative u_5 effort.

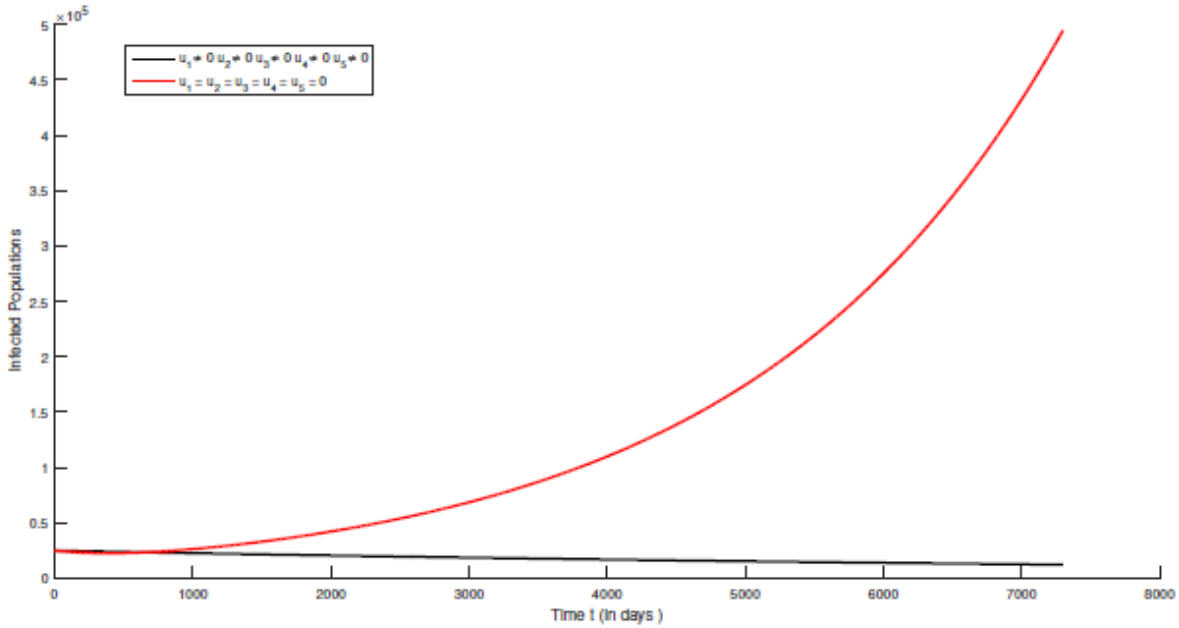

Figure 8. Simulations of optimal control with prevention u_1, treatment u_2, preventive u_3, treatment u_4 and curative u_5 effort.

7.5. Control with preventive u_1, treatment u_2 and curative effort u_5

We use preventive, treatment and curative strategy. Figure 9 and 10 show an increase in susceptible and a decrease in infectious individuals. This strategy is effective once the control is optimized in a given community.

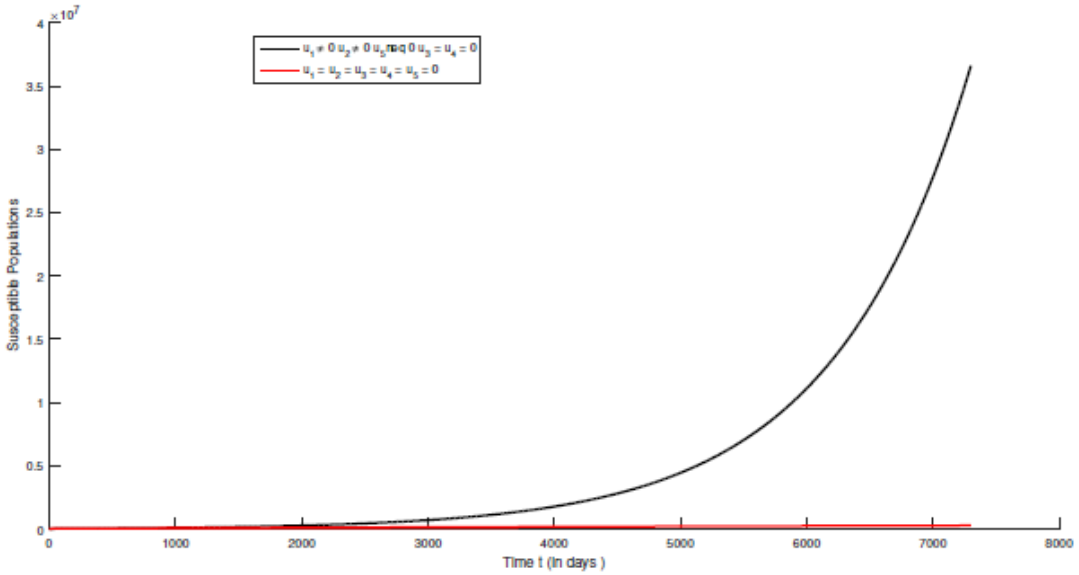

Figure 9. Simulations of optimal control with prevention u_1, treatment u_2 and curative u_5 effort.

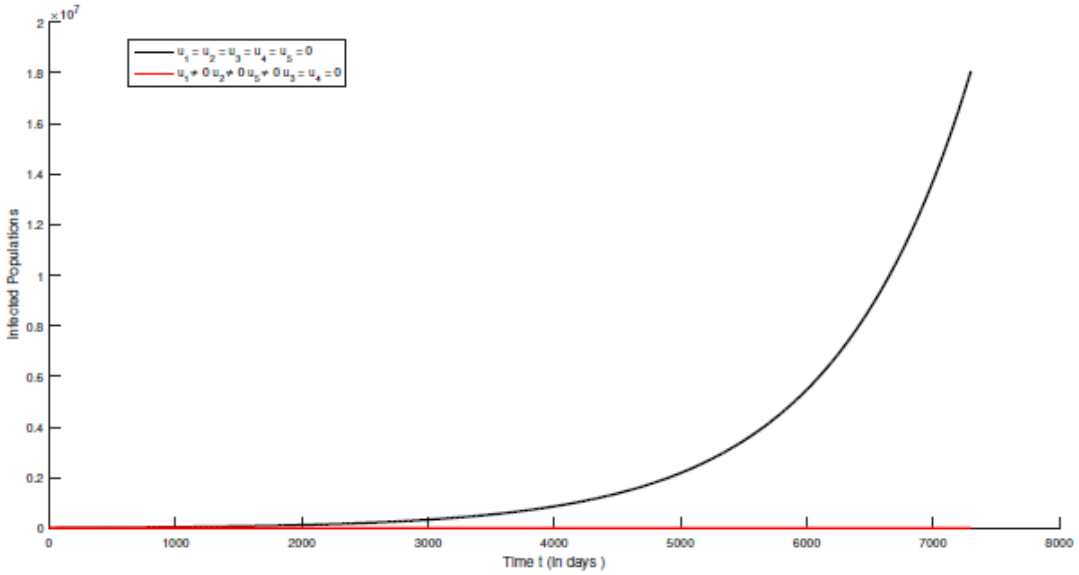

Figure 10. Simulations of optimal control with prevention u_1, treatment u_2 and curative u_5 effort.

7.6. Control with preventive u_1, treatment u_2, preventive u_3 and curative effort u_5

Preventive, treatment and curative strategy is applied in figure 11 and 12. Optimizing the controls leads to a great decrease in infectious individuals this strategy is effective in controlling cholera in a given community.

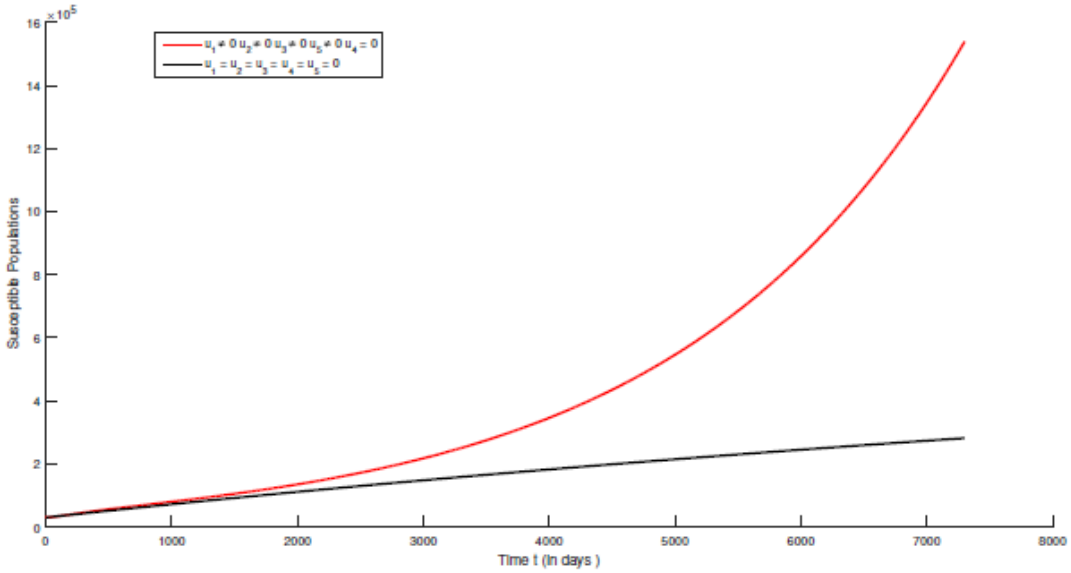

Figure 11. Simulations of optimal control with prevention u_1, preventive u_3 and curative u_5 effort.

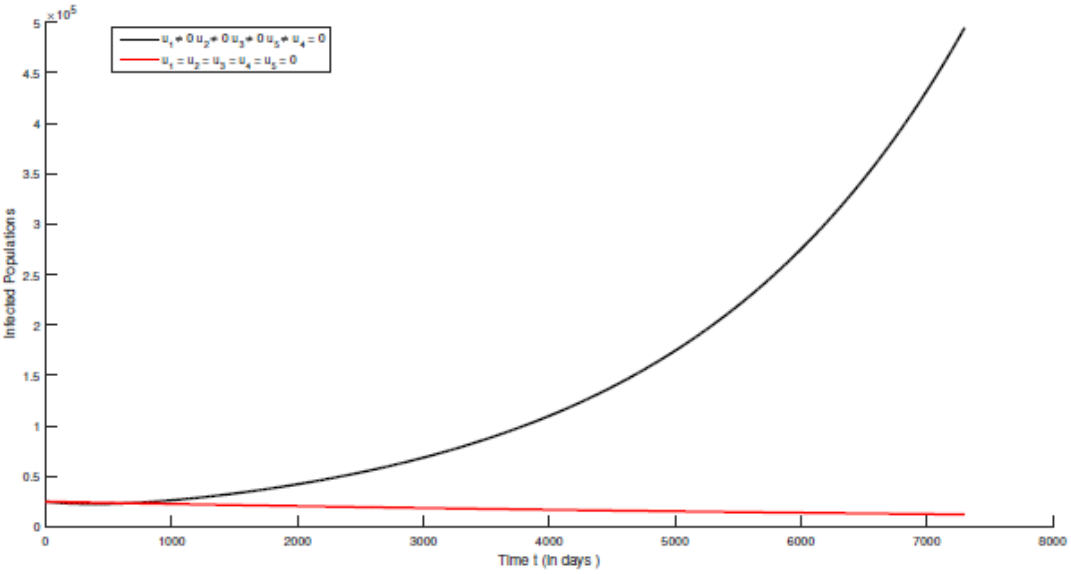

Figure 12. Simulations of optimal control with prevention u_1, preventive u_3 and curative u_5 effort.

7.7. *Control with preventive u_1, preventiveu_3 and treatment effort u_4*

Preventive and treatment as a control strategy is applied the susceptible increases while the infectious decrease which shows this strategy is effective in controlling cholera.

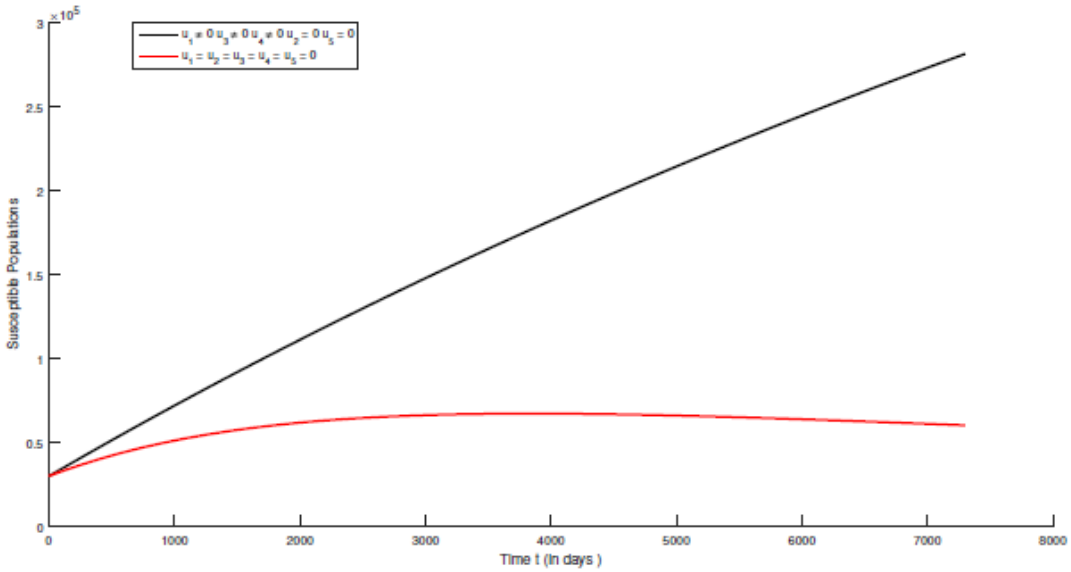

Figure 13. Simulations of optimal control with prevention u_1, preventive u_3 and treatment effort u_4 effort.

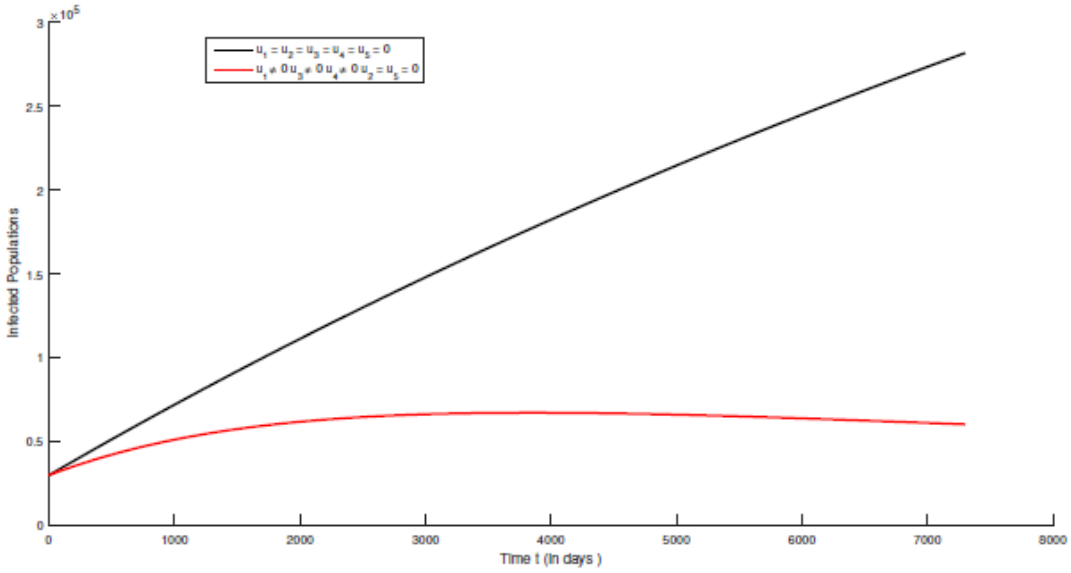

Figure 14. Simulations of optimal control with prevention u_1, preventive u_3 and treatment effort u_4 effort.

7.8. Control with treatment u_2, preventive u_3 and treatment u_4

We use treatment and preventive as control. The susceptible increase as more individuals receive treatment and go back to susceptible compartment while infectious decrease since treatment minimizes infectious class. This strategy is efficient in a community at a specified time.

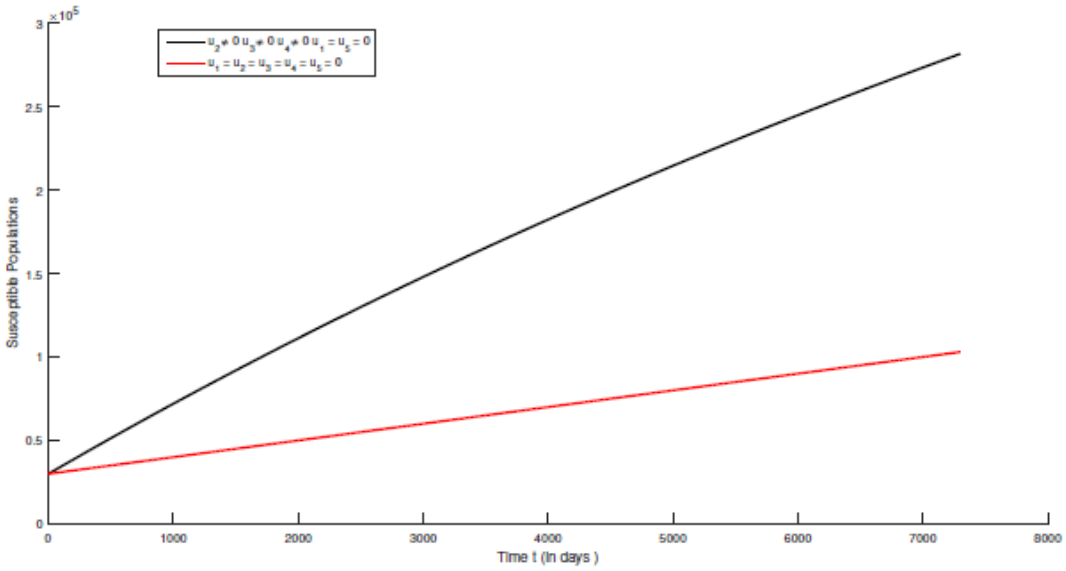

Figure 15. Simulations of optimal control with treatment u_2, preventive u_3 and treatment effort u_4 effort.

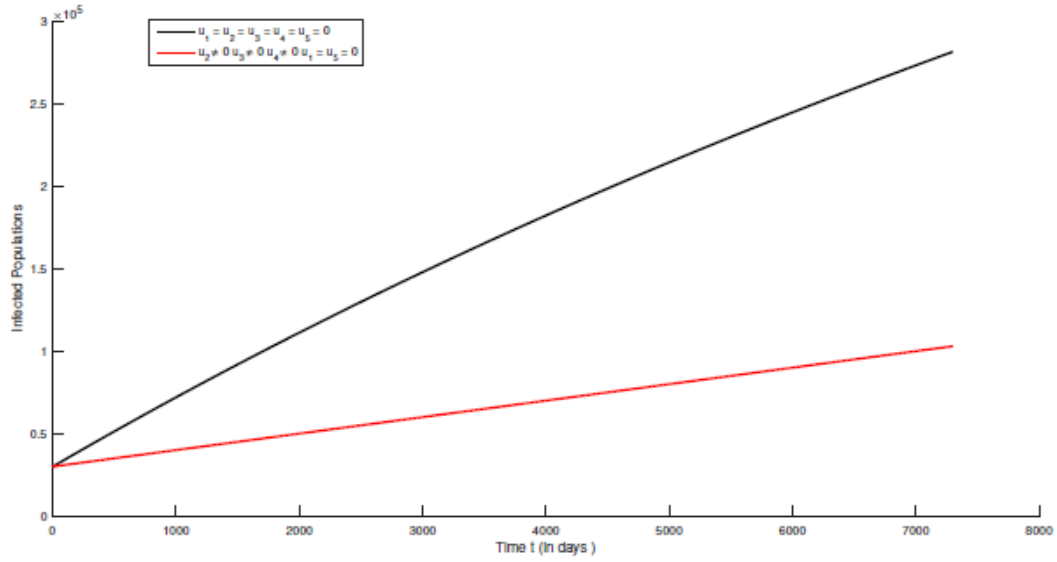

Figure 16. Simulations of optimal control with treatment u_2, preventive u_3 and treatment effort u_4 effort.

7.9. Control with preventive u_1 and curative effort u_5

We use prevention and curative on susceptible and infectious an increase in susceptible while a decrease in infectious is attributed by prevention and curative strategy. Optimizing these strategy in a given community are effective in controlling cholera.

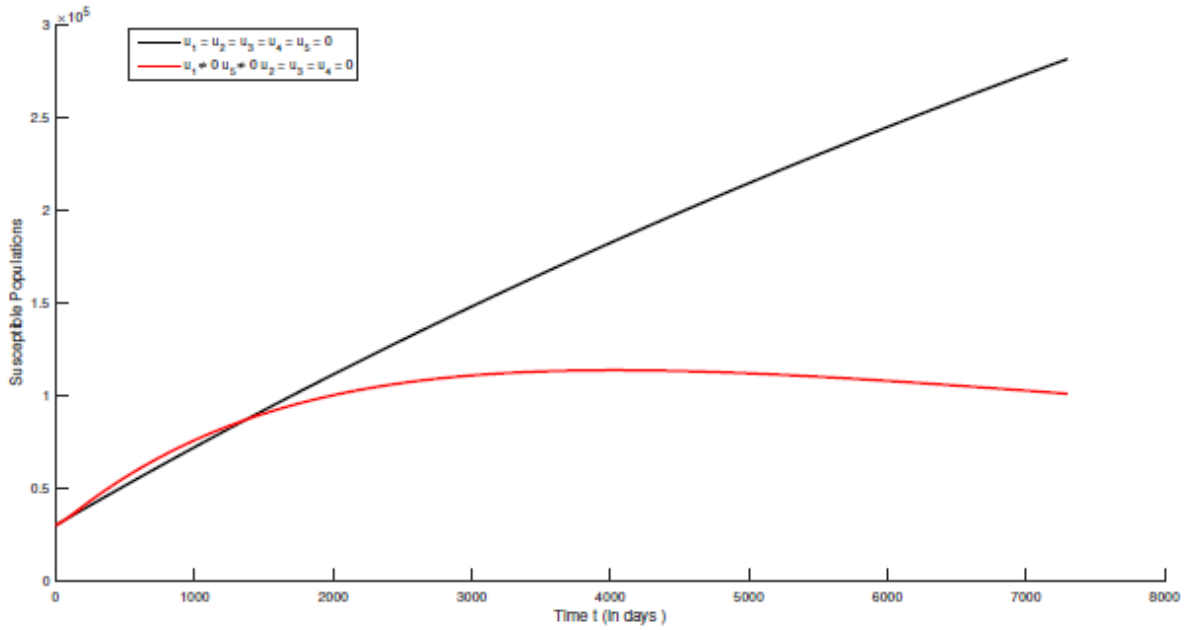

Figure 17. Simulations of optimal control with preventive u_1 and curative effort u_5.

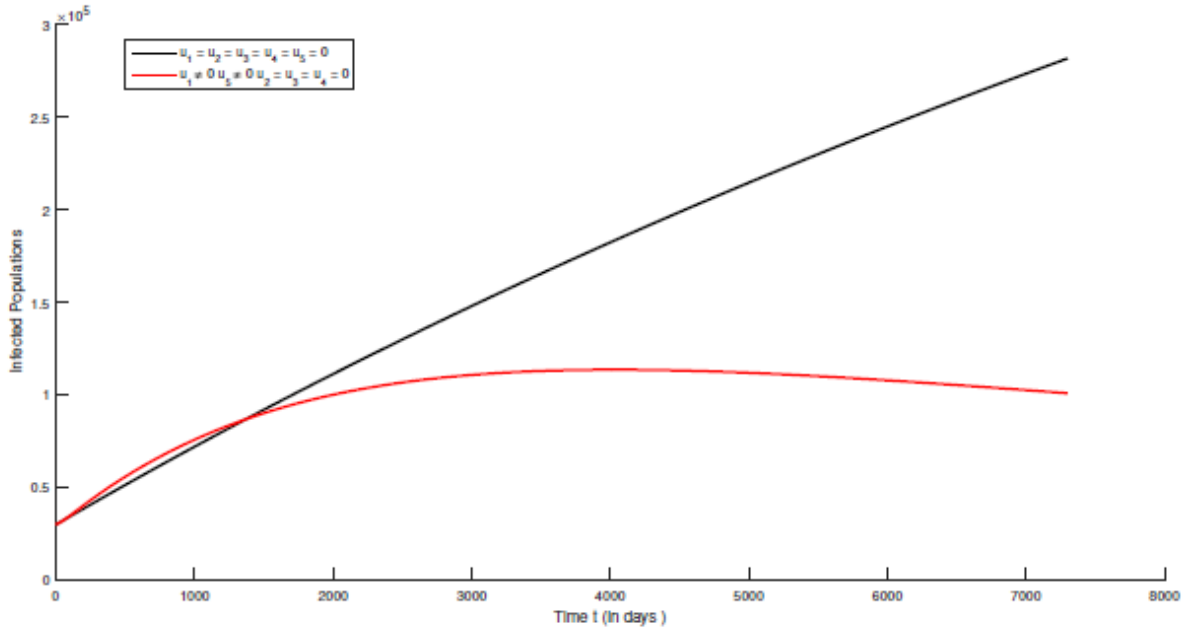

Figure 18. Simulations of optimal control with preventive u_1 and curative effort u_5..

8. Discussions and conclusions

In Section 3 we analysed the model by obtaining the feasible region, positivity of the solution set, effective reproductive number, equilibria points and their stability. In Section 4 we extended the model by applying optimal control interventions and we obtained the Hamiltonian, the adjoint variables, the characterization of the controls and the optimality system. In Section 5 we applied the optimality system by considering different strategies as follows:
By applying a single control
By applying two control, preventive u_1 and treatment u_2
By applying four control, preventive u_1, treatment u_2, preventive u_3 and treatment u_4.
By applying five control, preventive u_1, treatment u_2, preventive u_3, treatment u_4 and curative u_5.
By applying three control, preventive u_1, treatment u_2 and curative u_5.
By applying four control, preventive u_1, treatment u_2, preventive u_3 and curative u_5.
By applying three control, preventive u_1, preventive u_3 and treatment u_4.
By applying three control, treatment u_2, preventive u_3 and treatment u_4.
By applying two control, treatmentu_1 and curative u_5
In section 7 numerically we investigated cost effectiveness to determine, the least and the most efficient strategies. The purpose is to find the optimal control that will eliminate spread of cholera using by minimising cost of control. From the result in this study the simulation shows that a multifaceted approach to the fight against cholera disease is more effective than single control strategies.

8.1. Conflict of interest

The authors declare that they have no financial and personal relationships with other people or organizations that can inappropriately influence their work. There is no professional or other personal interest of any nature or kind in any product, service or company that could be construed as influencing the position presented in or the review of the paper.

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