Optimal Control Strategy of Cholera Epidemic Dynamics from Vibrio and Flies Transmission

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ABSTRACT

In this paper, we studied the spread of cholera in a mathematical model that incorporates data on public health interventions. We are interested in simulating cholera outbreaks from vibrio and flies transmission to populations. The population of humans is classified into three classes; susceptible humans (S_h), infected humans (I_h) and recovered human (R_h). The concentration of bacterial in the contaminated environment (B). The population of flies is divided into two groups; susceptible flies (S_F) and infected flies (I_F) individuals. Equilibrium analysis is conducted in the case with constant control for both epidemic and endemic dynamics. Numerical simulations are used to verify the analysis, and optimal solutions are computed by using an optimal control study

Keywords: Cholera, Mathematical model, Equilibrium, Optimal control theory

INTRODUCTION

In the past, there has been a worldwide outbreak of cholera, including one of the largest cholera outbreaks in modern history. Recent cholera in Haiti from 2010–2011 with more than 530,000 reported cases and over 7000 deaths. Major cholera outbreaks also include those in Sierra Leone (2012), Nigeria (2010), Vietnam (2009), Zimbabwe (2008) and India (2007), among others. Most outbreaks are caused came from public health management and strategies to control the disease are not adequate.

Mathematical modeling is a powerful tool which can test and compare different intervention strategies that might be useful in controlling or eliminating cholera, and mathematical modelling can be especially important to conserve limited resources. Various mathematical models can help people conceptualize the transmission dynamics in a quantitative way as well as enable the testing of different hypotheses to understand their importance. Numerous mathematical models have been published to analyze cholera outbreaks in an effort to better understand the complex disease transmission and determine adequate prevention and effective

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control strategies (see, examples, (Codeco, 2001; Hartley et al., 2006; Modnak, 2017; Neilan et al., 2010; Posny et al., 2015; Wang and Modnak, 2011; Thongtha and Modnak, 2017). In 2001, Claudia Torres Codeco proposed the reproduction rate of cholera is a function of social and environmental factors. It is necessary to determine the relative weights of each one of these components in order to develop appropriate control strategies (Codeco, 2001). In 2011, Jin Wang and Chairat Modnak (Wang and Modnak, 2011) presented and analyzed a cholera epidemiological model with control measures incorporated by vaccination, therapeutic treatment, and water sanitation. They have extended mathematical models of infectious diseases of Rachael L. Miller Neilan et.al. in (Neilan et al., 2010). In 2015, Drew Posny et al. (Posny et al., 2015), presented a new deterministic cholera epidemiological model with three types of control measures incorporated into a cholera epidemic setting: treatment, vaccination and sanitation. They used a mathematical model of infectious diseases that plays a critical role in predicting and understanding disease mechanisms. Later in few years, Chairat Modnak (Modnak, 2017) proposed and analyzed a cholera mathematical model with vaccine being incorporated. The results show that using vaccination during cholera outbreaks at the very beginning of the onset can reduce the number of infections significantly. In the same year, Adison Thongtha et al. (Thongtha and Modnak, 2017) proposed a new model that consider human-to-human and fly-to-human transmission while human-to-human transmission was defined in the context of infection by hyperinfertions vibrios (Hartley et al., 2006). As we all know that flies and bacteria can spread cholera, however, not many researchers are interested in considering flies as the main character. Actually, flies in Thailand can cause so many serious disease infectious. Therefore, in this study we will include fly population in our model to investigate cholera dynamics.

In this study, we also use mathematical modeling incorporated with control measures and simulation techniques to shed light on the value of optimal control measures in controlling ongoing cholera outbreaks. Particularly, we will formulate a new optimal control model and explore optimal times during epidemics for deploying cholera vaccines.

MATERIALS AND METHODS

We modify the model of Wang, J. et al. (Wang and Modnak, 2011) and Thongtha, A. et al. (Thongtha and Modnak, 2017) by adding vaccination control, treatment control, bacteria control and control by eliminating the flies. We let N_h and N_F represent the population of humans and flies, respectively. The population of humans is classified into three classes; susceptible humans (S_h), infected humans (I_h) and recovered humans (R_h). Let B be the concentration of bacterial in the contaminated environment. The population of flies is divided into two groups: Susceptible flies (S_F) and infected flies (I_F).

Ingestion rates from the environment, the human-human interaction and the fly-human interaction are defined as β_e, β_h and β_F, respectively. Natural death and birth rate of humans and flies are given by μ_h and μ_F respectively. δ is death rate of vibrio in the environment. κ is the half saturation concentration of environmental vibrio. Recovery from cholera is at a rate γ and human contribution to vibrio chalerae is at a rate ξ. We let ϕ_1 represents eliminating the flies, ϕ_2 represents for vaccination control, ϕ_3 represents for treatment control and ϕ_4 represents for bacteria control. The dynamic system equations are the following:

$$\frac{dS_h}{dt} = \mu_h N_h - \beta e S_h \frac{B}{\kappa + B} - \beta_h S_h I_h - \beta_F S_h I_F - \mu_h S_h - \phi_2 S_h, \quad (1)$$

$$\frac{dI_h}{dt} = \beta e S_h \frac{B}{\kappa + B} + \beta_h S_h I_h + \beta_F S_h I_F - (\gamma + \mu_h) I_h - \phi_3 I_h, \quad (2)$$

$$\frac{dR_h}{dt} = \gamma I_h + \phi_2 S_h + \phi_3 I_h - \mu_h R_h, \quad (3)$$

$$\frac{dB}{dt} = \xi I_h - \delta B - \phi_4 B, \quad (4)$$

$$\frac{dS_F}{dt} = \mu_F N_F - (\mu_F + \beta_F I_h) S_F - \phi_1 S_F, \quad (5)$$

$$\frac{dI_F}{dt} = \beta_F I_h S_F - \mu_F I_F. \quad (6)$$

Disease-free equilibrium

With constant controls and setting $I_h = B = I_F = 0$ the disease-free equilibrium (DFE) of the system (1) – (6) is given by

$$\varepsilon_0 = (S_{h0}, 0, R_{h0}, 0, S_{F0}, 0) \quad (7)$$

where $S_{h0} = \frac{\mu_h N_h}{\mu_h + \phi_2}$, $S_{F0} = \frac{\mu_F N_F}{\mu_F + \phi_1}$, $R_{h0} = \frac{\phi_2 N_h}{\mu_h + \phi_2}$.

Next-generation matrix analysis

We start our analysis by determining the basic reproduction number, R_0. R_0 is mathematically defined as the spectral radius of the next-generation matrix. To compute the basic reproduction number, we use the well-known method of Van den

Driessche and Watmough (Van den Driessche and Watmough, 2002). From system (1), I_h and B are directly related to the infection. We have

$$\begin{bmatrix} \frac{dI_h}{dt} \\ \frac{dB}{dt} \end{bmatrix} = \begin{bmatrix} \beta_e S_h \frac{B}{\kappa + B} + \beta_h S_h I_h + \beta_F S_h I_F \\ 0 \end{bmatrix} - \begin{bmatrix} \gamma I_h + \mu_h I_h + \phi_3 I_h \\ -\xi I_h + \delta B + \phi_4 B \end{bmatrix} = \mathrm{F} - \mathrm{V},$$

where $\mathcal{F}$ denotes the rate of appearance of new infections and $\mathcal{V}$ denotes the rate of transfer of individuals into or out of each population set. Then we have

$$F = \begin{bmatrix} \frac{\partial \mathrm{F}_1}{\partial I_h} & \frac{\partial \mathrm{F}_1}{\partial B} \\ \frac{\partial \mathrm{F}_2}{\partial I_h} & \frac{\partial \mathrm{F}_2}{\partial B} \end{bmatrix} = \begin{bmatrix} \beta_h S_h & \frac{\kappa \beta_e S_h}{(\kappa + B)^2} \\ 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \frac{\partial \mathrm{V}_1}{\partial I_h} & \frac{\partial \mathrm{V}_1}{\partial B} \\ \frac{\partial \mathrm{V}_2}{\partial I_h} & \frac{\partial \mathrm{V}_2}{\partial B} \end{bmatrix} = \begin{bmatrix} \gamma + \mu_h + \phi_3 & 0 \\ -\xi & \delta + \phi_4 \end{bmatrix}.$$

The next-generation matrix is defined as FV^{-1}, where F and V are the Jacobian matrices given by

$$F(\varepsilon_0) = \begin{bmatrix} \frac{\beta_h \mu_h N_h}{\mu_h + \phi_2} & \frac{\beta_e \mu_h N_h}{\kappa(\mu_h + \phi_2)} \\ 0 & 0 \end{bmatrix}, V(\varepsilon_0) = \begin{bmatrix} \gamma + \mu_h + \phi_3 & 0 \\ -\xi & \delta + \phi_4 \end{bmatrix}, \quad (8)$$

where ε_0 is DFE defined in Equation (7). By spectral radius, we have

$$R_0 = \sigma\left(FV^{-1}\right) = \frac{\mu_h N_h \left(\beta_h \kappa(\delta + \phi_4) + \xi \beta_e\right)}{\kappa(\mu_h + \phi_2)(\mu_h + \gamma + \phi_3)(\delta + \phi_4)}. \quad (9)$$

Consequently, based on the work in the paper proposed by Van den Driessche and Watmough (Van den Driessche and Watmough, 2002), we immediately have the following result:

Theorem 1. The disease-free equilibrium of the model is locally asymptotically stable if $R_0 < 1$, and unstable if $R_0 > 1$.

To study the global asymptotic stability of the DFE, we will apply the following result introduced by Castillo-Chavez et al (Chavez and Huang, 2002).

Lemma 1. Consider a model system written in the form

$$\frac{dX_1}{dt} = F(X_1, X_2)$$

$$\frac{dX_2}{dt} = G(X_1, X_2), \qquad G(X_1, 0) = 0$$

where $X_1 \in \mathbf{R}^m$ denotes (its components) the number of uninfected individuals and $X_2 \in \mathbf{R}^m$ denotes (its components) the number of infected individuals including latent, infections, etc.; $X_0 = \left(X_1^*, 0\right)$ denotes the disease-free equilibrium of the system. Also assume the conditions (H1) and (H2) below:

(H1) For $\frac{dX_1}{dt} = F\left(X_1, 0\right)$ is globally asymptotically stable.

(H2) $G\left(X_1, X_2\right) = AX_2 - \hat{G}\left(X_1, X_2\right)$, $\hat{G}\left(X_1, X_2\right) \geq 0$ for $\left(X_1, X_2\right) \in \Omega$, where the Jacobian $A = \left(\partial G / \partial X_2\right) G\left(X_1^*, 0\right)$ is an M-matrix (the off diagonal elements of A are nonnegative) and Ω is the region where the model makes biological sense. Then the DFE is globally asymptotically stable.

Theorem 2. The DFE of the model (1) is globally asymptotically stable.

Proof. We adopt the notations in Lemma1 and verify the conditions (H1) and (H2). In our model, $X_1 = \left(S_h, R_h, S_F\right)$, $X_2 = \left(I_h, B, I_F\right)$ and $X_1^* = \left(S_{h0}, R_{h0}, S_{F0}\right)$. We note that the system is linear and its solution can be easily found as:

$$\frac{dX_1}{dt} = F\left(X_1, X_2\right) = \begin{bmatrix} \mu_h N_h - \beta e S_h \dfrac{B}{\kappa + B} - \beta_h S_h I_h - \beta_F S_h I_F - \mu_h S_h - \phi_2 S_h \\ \gamma I_h + \phi_2 S + \phi_3 I - \mu_h R_h \\ \mu_F N_F - (\mu_F + \beta_F I_h) S_F - \phi_1 S_F \end{bmatrix}. \tag{10}$$

We have

$$\frac{dX_1}{dt} = F\left(X_1, 0\right) = \begin{bmatrix} \mu_h N_h - \mu_h S_h - \phi_2 S_h \\ \phi_2 S_h - \mu_h R_h \\ \mu_F N_F - \mu_F S_F - \phi_1 S_F \end{bmatrix}.$$

It follows from solving these differential equations that $S_h(t) = \frac{\mu_h N_h}{\mu_h + \phi_2} + C_1 e^{-(\mu_h + \phi_2)t}$, $R_h(t) = C_2 e^{-\mu_h t}$ and $S_h(t) = \frac{\mu_F N_F}{\mu_F + \phi_1} + C_3 e^{-(\mu_F + \phi_1)t}$. Thus, $S_h(t) \to S_{h0}$, $R_h(t) \to R_{h0}$ and $S_F(t) \to S_{F0}$, as $t \to \infty$. Hence, $X_1^* = \left(S_{h0}, R_{h0}, S_{F0}\right)$ is globally asymptotically stable for the subsystem (5).

Now, note that

$$G\left(X_1, X_2\right) = AX_2 - \hat{G}\left(X_1, X_2\right) \tag{11}$$

where $A=\frac{\partial G}{\partial X_2}\left(X_1^*,0\right)$. Substituting into (11) gives, $\hat{G}\left(X_1,X_2\right)=\left(0,0\right)^T \geq 0$. We complete the proof. □

Endemic equilibrium

When the disease is appears in the population, $I_h \neq 0$, there may be several critical points where $I_h \neq 0$, which are the endemic equilibrium points of the model.

$$S_h^* = \frac{\mu_h N_h - a_2 I_h^*}{a_1},\ B^* = \frac{\xi I_h^*}{a_3},\ S_F^* = \frac{\mu_F N_F}{\mu_F + \beta_F I_h^* + \phi_1},\ I_F^* = \frac{\beta_F I_h^* N_F}{\mu_F + \beta_F I_h^* + \phi_1}.$$

Hence, our endemic equilibrium point are $\varepsilon_1^* = \left(S_h^*, I_h^*, B^*, R_h^*\right)$ and $\varepsilon_2^* = \left(S_F^*, I_F^*\right)$.

Local stability

Next, we proceed to analyze the stability properties of the endemic equilibrium. First we prove the following result regarding the local stability.

Theorem 3. The positive endemic equilibrium ε_1^* is locally asymptotically stable.

Proof. The Jacobian matrix of the system (1) – (4) at $x=\varepsilon_1^*$ is given by

$$J\left(S_h^*, I_h^*, B^*\right) = \begin{bmatrix} -P-\left(\mu_h+\phi_2\right) & -\beta_h S_h^* & -Q \\ P & \beta_h S_h^* - (\gamma+\mu_h+\phi_3) & Q \\ 0 & \xi & -(\delta+\phi_4) \end{bmatrix}.$$

Where $P=\beta e\frac{B^*}{\kappa+B^*}+\beta_h I_h^*+\beta_F I_F^*$ and $Q=\frac{\kappa\beta_e S_h^*}{(\kappa+B^*)^2}$. The characteristic polynomial of $J\left(\varepsilon_1^*\right)$ is

$$\begin{aligned} 0 &= \det\left[J\left(\varepsilon_1^*\right)-\lambda I^*\right] \\ &= \lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 \end{aligned}$$

where

$$a_0 = (\mu_h+\phi_2)\left((\delta+\phi_4)(\gamma+\mu_h+\phi_3)-(\delta+\phi_4)\beta_h S_h^* - \xi Q\right) + P(\gamma+\mu_h+\phi_3)(\delta+\phi_4),$$

$$a_1 = \left((\delta+\phi_4)(\gamma+\mu_h+\phi_3)-(\delta+\phi_4)\beta_h S_h^* - \xi Q\right) + (\mu_h+\phi_2)(\gamma+\mu_h+\phi_3-\beta_h S_h^*) + (P+(\mu_h+\phi_2))(\delta+\phi_4) + P(\gamma+\mu_h+\phi_3),$$

$$a_2 = P + (\mu_h + \phi_2) + (\gamma + \mu_h + \phi_3 - \beta_h S_h^*).$$

Next, consider characteristic equation above by using the Routh-Hurwitz Criterion in the form of polynomial of degree 3. Therefore, the endemic equilibrium point is stable if $a_0 > 0, a_1 > 0, a_2 > 0$ and $a_1 a_2 > a_0$. Thus, ε_1^* is locally asymptotically stable. We complete the proof. □

RESULTS: OPTIMAL CONTROL

Now we turn to the more general model with time-dependent controls $\phi_1(t)$, $\phi_2(t)$, $\phi_3(t)$ and $\phi_4(t)$. We consider the system on a time interval [0,T]. The function $\phi_1(t)$, $\phi_2(t)$, $\phi_3(t)$ and $\phi_4(t)$ are assumed to be at least Lebesgue measurable on [0,T]. The control set is defined as

$$\Omega = \left\{ \begin{array}{l} \left(\phi_1(t), \phi_2(t), \phi_3(t), \phi_4(t)\right) \middle| \, 0 < \phi_1(t) < \phi_{1\max}, \\ 0 < \phi_2(t) < \phi_{2\max}, 0 < \phi_3(t) < \phi_{3\max}, 0 < \phi_4(t) < \phi_{4\max} \end{array} \right\}$$

where $\phi_{1\max}$, $\phi_{2\max}$, $\phi_{3\max}$ and $\phi_{4\max}$ denote the upper bounds for the eliminating the flies, vaccination, treatment and bacteria, respectively. The bounds reflect practical limitation on the maximum rate of control in given time period. The presence of time-dependent controls makes the analysis of our system difficult. In fact, the disease dynamics now depend on the evolution of control. In what follows we perform an optimal control study on this problem. We aim to minimize the total number of infections and the costs of control over the time interval $[0, T]$, i.e.;

$$\min_{\phi_{1,2,3,4} \in \Omega} \int_0^T \left[\begin{array}{c} I(t) + c_{11}\phi_1(t) S_F(t) + c_{12}\phi_1^2(t) + c_{21}\phi_2(t) S_h(t) + c_{22}\phi_2^2(t) \\ + c_{31}\phi_3(t) I_h(t) + c_{32}\phi_3^2(t) + c_{41}\phi_4(t) B(t) + c_{42}\phi_4^2(t) \end{array} \right] dt \quad (7)$$

Here, the parameters c_{11}, c_{12}, c_{21}, c_{22}, c_{31}, c_{32}, c_{41} and c_{42} with appropriate units, define the appropriate costs associated with these controls. Quadratic terms are introduced to indicate nonlinear costs potentially arising at high intervention level. The minimization process is subject to the differential equation of our system, which are now referred to as the state equations. Correspondingly, the unknown variables S_F, S_h, I_h and B are now called the state variables, in contrast to the control variables $\phi_1(t)$, $\phi_2(t)$, $\phi_3(t)$ and $\phi_4(t)$. Our goal is to determine the optimal controls $\phi_1^*(t)$, $\phi_2^*(t)$, $\phi_3^*(t)$ and $\phi_4^*(t)$, so as to minimize the objective functional in (7).

Let us first define the adjoint functions $\lambda_{S_h}, \lambda_{I_h}, \lambda_B, \lambda_{S_F}$ and λ_{I_F} associated with the state equations for S_h, I_h, B, S_F and I_F, respectively. We then form the Hamitonian, H, by multiplying state equation, and adding each of these products to the integrand of the objective functional. As a result, we obtain

$$\begin{aligned} H = {} & I(t) + c_{11}\phi_1(t)S_F(t) + c_{12}\phi_1^{\,2}(t) + c_{21}\phi_2(t)S_h(t) + c_{22}\phi_2^{\,2}(t) + c_{31}\phi_3(t)I_h(t) \\ & + c_{32}\phi_3^{\,2}(t) + c_{41}\phi_4(t)B(t) + c_{42}\phi_4^{\,2}(t) \\ & + \lambda_{S_h}\left(\mu_h N_h - \beta e S_h \frac{B}{\kappa + B} - \beta_h S_h I_h - \beta_F S_h I_F - \mu_h S_h - \phi_2(t)S_h\right) \\ & + \lambda_{I_h}\left(\beta e S_h \frac{B}{\kappa + B} + \beta_h S_h I_h + \beta_F S_h I_F - (\gamma + \mu_h)I_h - \phi_3(t)I_h\right) \\ & + \lambda_B\left(\xi I_h - \delta B - \phi_4(t)B\right) + \lambda_{S_F}\left(\mu_F N_F - (\mu_F + \beta_F I_h)S_F - \phi_1(t)S_F\right) \\ & + \lambda_{I_F}\left(\beta_F I_h S_F - \mu_F I_F\right). \end{aligned}$$

To achieve the optimal control, the adjoint functions must satisfy $\frac{d\lambda_{S_h}}{dt} = -\frac{\partial H}{\partial S_h}$, $\frac{d\lambda_{I_h}}{dt} = -\frac{\partial H}{\partial I_h}$, $\frac{d\lambda_B}{dt} = -\frac{\partial H}{\partial B}$, $\frac{d\lambda_{S_F}}{dt} = -\frac{\partial H}{\partial S_F}$ and $\frac{d\lambda_{I_F}}{dt} = -\frac{\partial H}{\partial I_F}$ with transversality conditions (or final time conditions): $\lambda_{S_h}(T) = 0$, $\lambda_{I_h}(T) = 0$, $\lambda_B(T) = 0$, $\lambda_{S_F}(T) = 0$ and $\lambda_{I_F}(T) = 0$. The characterization of the optimal control $\phi_1^*(t)$, $\phi_2^*(t)$, $\phi_3^*(t)$ and $\phi_4^*(t)$ are based on the conditions $\frac{\partial H}{\partial \phi_1} = 0$, $\frac{\partial H}{\partial \phi_2} = 0$, $\frac{\partial H}{\partial \phi_3} = 0$ and $\frac{\partial H}{\partial \phi_4} = 0$, respectively, subject to the constraints $0 \le \phi_1 \le \phi_{1\max}$, $0 \le \phi_2 \le \phi_{2\max}$, $0 \le \phi_3 \le \phi_{3\max}$ and $0 \le \phi_4 \le \phi_{4\max}$. Specifically, we have

$$\phi_1^*(t) = \max\left(0, \min\left(\phi_1(t), \phi_{1\max}\right)\right), \quad \phi_2^*(t) = \max\left(0, \min\left(\phi_2(t), \phi_{2\max}\right)\right),$$

$$\phi_3^*(t) = \max\left(0, \min\left(\phi_3(t), \phi_{3\max}\right)\right), \text{ and } \phi_4^*(t) = \max\left(0, \min\left(\phi_4(t), \phi_{4\max}\right)\right),$$

where

$\phi_1(t)=\frac{(\lambda_{s_F}-c_{11})S_F(t)}{2c_{12}}$, $\phi_2(t)=\frac{(\lambda_{s_h}-c_{21})S_h(t)}{2c_{22}}$, $\phi_3(t)=\frac{(\lambda_{I_h}-c_{31})I_h(t)}{2c_{32}}$ and $\phi_4(t)=\frac{(\lambda_B-c_{41})B(t)}{2c_{42}}$.

Due to the presence of both initial conditions (for the state equations) and final time conditions (for the adjoint equations), and the fact that most models of our interest are nonlinear, the optimal control system has to be solved numerically. We apply the forward-backward sweep method to solve the optimality system in an iterative manner. The control is then updated with the new values of the state and adjoint solutions, and the process is repeated until the solutions converge.

Table1: Symbols and Parameter values .

Parameter	Value	Reference	Parameter	Value	Reference
N_h	$10,000$	R.L.M. Neilan et al. (2010)	ξ	10	R.L.M. Neilan et al. (2010)
μ_h	$43.5\,\text{day}^{-1}$	R.L.M. Neilan et al. (2010)	β_e	0.075	R.L.M. Neilan et al. (2010)
κ	10^6	R.L.M. Neilan et al. (2010)	β_h	0.00011	R.L.M. Neilan et al. (2010)
γ	5	R.L.M. Neilan et al. (2010)	δ	30	R.L.M. Neilan et al. (2010)
N_F	$100,000$	Estimated	β_F	0.00001	Estimated
μ_F	0.4	Estimated			

We make use the initial conditions $S_h(0)=9990$, $I_h(0)=10$, $R_h(0)=0$, $B(0)=0$, $S_F(0)=99900$ and $I_F(0)=100$. The simulations were carried out using the parameter values in Table1.

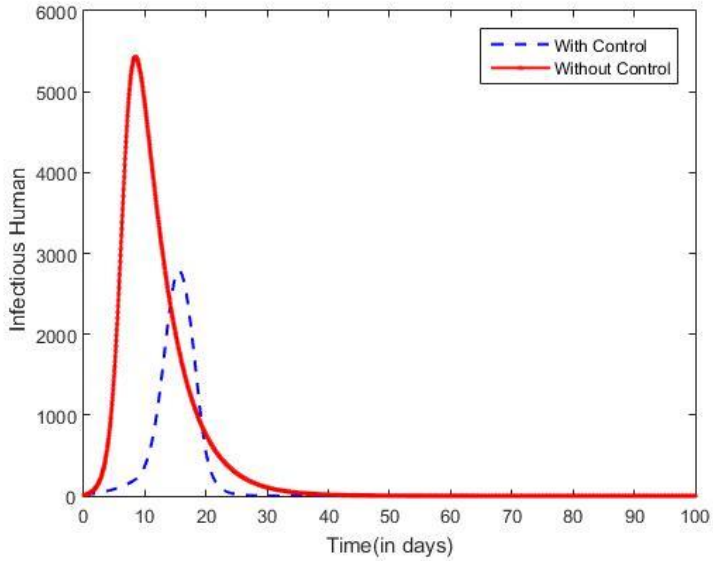


Figure 1: shows the human infection levels predicted by the model for the scenario with control (dashed line) and the scenario without control (solid line). It is clearly seen that the infection level has been reduced due optimal control.

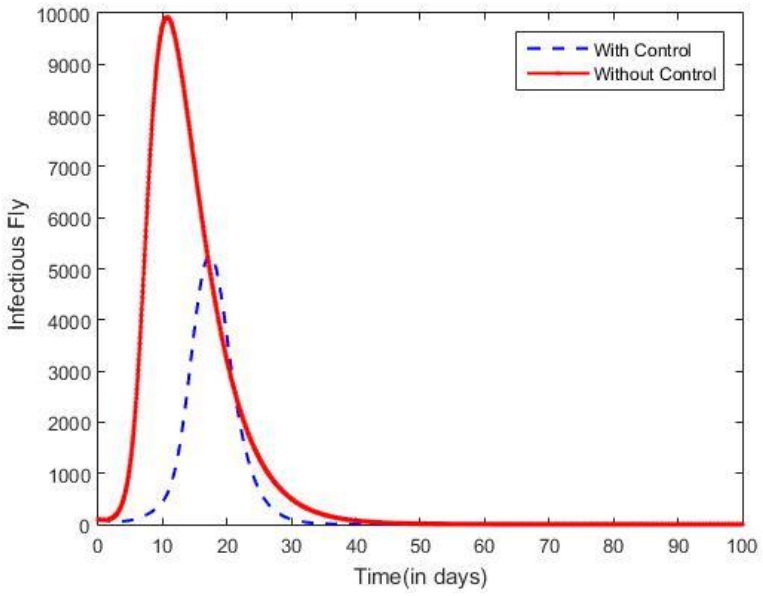
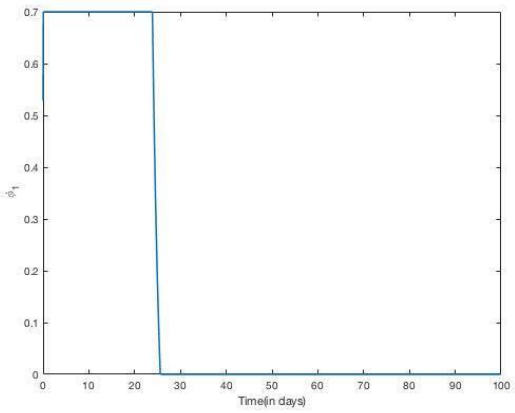
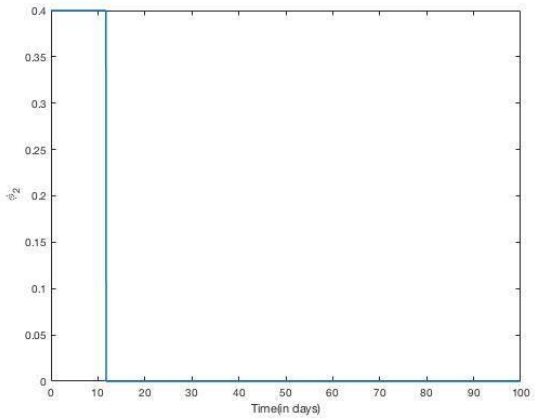


Figure 2: shows how the level of the infected house flies population by the model for the scenario with control (dashed line) and the scenario without control (solid line). It is clearly seen that the infection of house flies population level has been reduced due optimal control.

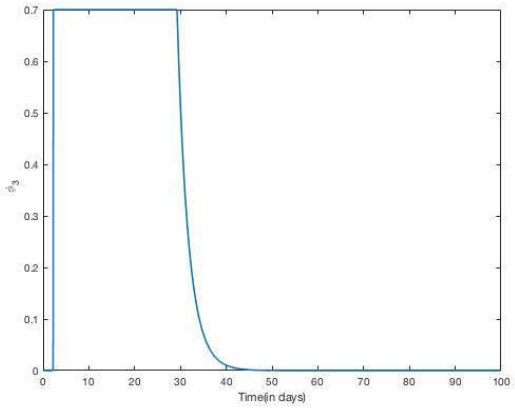
We first consider the following set of values for the cost parameters $c_{11}=0.00001,\ c_{12}=1,\ c_{21}=4,\ c_{22}=4,\ c_{31}=2,\ c_{32}=2,\ c_{41}=0.00001,$ $c_{42}=1,\ \phi_{\max 1}=0.7,\ \phi_{\max 2}=0.4,\ \phi_{\max 3}=0.7,$ and $\phi_{\max 4}=0.7.$ Figure1 shows the infection curves for the model with controls (dashed line) and that without the optimal controls (solid line). It is clearly seen the infection level has been reduced due to the incorporation of vaccine and other controls. Figure 2 shows that with elimination control in the model can reduce the number of infected flies that carry Vibrio Cholerae. Figures 3 show the optimal control proflier of each control. These plots are very useful to plan for deployments of the treatment in order to control cholera outbreaks.



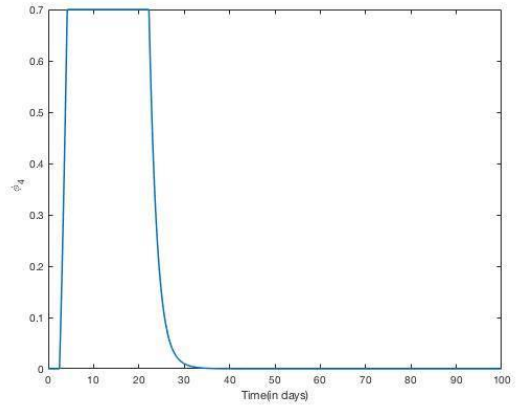
a) Rate of eliminating the flies controls



b) Rate of vaccination controls



c) Rate of treatment controls



d) Rate of bacteria controls

Figure 3: Rate of controls.

CONCLUSIONS

This study has presented a mathematical model of cholera which takes into account and analyzes both house flies, bacterium and human populations. In order to uncover the effects of the flies elimination rate, the bacteria elimination rate, the vaccinations rate and the medical treatment of infected people on the spread of the disease, and in order to find ways to control the outbreak of cholera, an optimal control study was carried out. The equilibrium analysis has been conducted. The stability of the disease-free equilibrium point and the endemic equilibrium point are controlled by the threshold number. If R_0 is less than one, then the disease dies out and the disease-free equilibrium is stable. If R_0 is greater than one, then the disease persists and the disease-free equilibrium is unstable. In conclusion, the numerical simulations and theories presented here have shown that attentive treatment of infected people, vaccination, thorough elimination of flies and bacteria can significantly reduce the number of people infected and harmed by cholera. We to show in Table1 and Table2.

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