

Optimal intervention strategies for cholera outbreak by education and chlorination

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Abstract. This paper discusses the control of infectious diseases in the framework of optimal control approach. A case study on cholera control was studied by considering two control strategies, namely education and chlorination. We distinct the former control into one regarding person-to-person behaviour and another one concerning person-to-environment conduct. Model are divided into two interacted populations: human population which follows an SIR model and pathogen population. Pontryagin maximum principle was applied in deriving a set of differential equations which consists of dynamical and adjoin systems as optimality conditions. Then, the fourth order Runge-Kutta method was exploited to numerically solve the equation system. An illustrative example was provided to assess the effectiveness of the control strategies toward a set of control scenarios.

1. Introduction

Cholera is still a major public health problem in underdeveloped and developing countries causing morbidity and mortality. According to WHO [12], a more than 190,000 cholera cases with more than 2,200 deaths were reported by 42 countries in 2014, resulting in an overall case fatality rate (CFR) of 1.17 per cent, a 47 per cent increase compared to 2013. Most of cholera outbreaks were caused by serogroup O1 of *Vibrio cholerae*. While serogroup O139 which first identified in Bangladesh in 1992, is confined to South-East Asia. Non-O1 and non-O139 *V. cholerae* can cause mild diarrhea but do not generate epidemics. Cholera outbreak in Haiti, appeared ten months after the devastating earthquake of 2010, claimed over 4,500 lives and sickened almost 300,000 people, was the first case in nearly a century; revealing that cholera is an ancient-fatal disease that continues to cause epidemic and pandemic infection. Another fact that cases were reported from all regions with 55 per cent of all reported cases originated from Africa, 30 per cent from Asia and 15 per cent from Hispaniola [12] indicates that cholera needs global awareness.

As an acute bacterial infection of the intestine caused by bacterium *V. cholerae*, cholera transmitted through sanitary channel, i.e., contaminated food and drinking-water, as well as by person-to-person contact through the fecal-oral route. Thus, the dynamics of cholera involve multiple interactions between the human host, the pathogen and the environment [6]. A number of mathematical models have been developed for gaining better knowledge of the complex dynamics of cholera, where a brief introduction to the basics of ordinary differential equation models and its modification was given by [2]. Several deterministic cholera epidemic models were introduced by [9] to analyze the global stability of the models. A general compartmental model is proposed by [8] by incorporating both direct and indirect transmission, non-linear incidence, multiple infectious states of the pathogen, and



multiple infection stages of infectious individuals. A study by [4] attempted to estimate the reproductive numbers for the 2008-2009 cholera outbreaks in Zimbabwe. In the framework of intervention model, a mathematical model that captures some essential dynamics of cholera transmission to study the impact of public health educational campaigns, vaccination and treatment as control strategies in curtailing the disease was formulated by [5]. In [11], a cholera epidemiological model with control measures including the effects of vaccination, therapeutic treatment, and water sanitation was investigated.

In this paper we discuss the control of cholera transmission in the framework of optimal control approach, where we take into account two intervention strategies, namely education and chlorination. The former is intended to educate the community about the importance of improving sanitation and hygienic practices in order to reduce direct and indirect contacts. The latter is referred to the use of chlorine to degrade *V. cholerae* concentration in the water source.

2. Mathematical model

2.1. Model

To assess the effectiveness of the control strategies we adopt a model introduced by [1], where a different approach of analysis was considered. Firstly, instead of analyzing the effects of education and chlorination as constant parameters of the model, we represent both efforts as dynamic variables. In the framework of optimal control, we consider two parameters as control variables should be determined optimally with respect to a certain performance index. Secondly, beyond the control by chlorination, we introduce two educational control variables to respectively quantify the effect of education on both direct human-to-human and indirect environment-to-human transmission pathways.

We consider a model with two interacted populations: human population which follows an SIR model and pathogen population (Figure 1). We denote by $S(t)$, $I(t)$, and $R(t)$, the number of susceptible, infected and recovered individuals at time t , respectively, and by $P(t)$ the concentration of pathogen *V. cholerae* in the aquatic environment, i.e., the contaminated water source, at time t . For a relatively short period of time and for low rate of mortality we assume that the total population N is constant, i.e., $N = S + I + R$. Susceptible individuals enter the model with constant recruitment rate Λ and are exposed to a force of infection λ , where $\lambda = \beta_1 P / (K_1 + P) + \beta_2 I / (K_2 + I)$. Here, K_1 and K_2 respectively denote the pathogen concentration level at which half of all contacts with contaminated water produce infection with per capita contact rate β_1 and the contact between susceptible and infected individuals with rate β_2 . Parameters μ_h , μ_d and μ_p denote the natural mortality rate of human, cholera-induced mortality rate of infected human and mortality rate of pathogen, respectively. The average contribution of each infected individual to the pathogen population is given by θ . Infected individuals may recover at rate δ and become susceptible at a rate α . We assume a logistic growth for pathogen with per capita growth rate b and carrying capacity K .

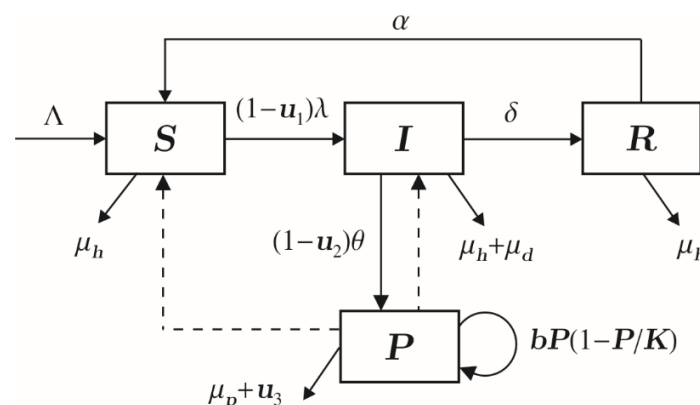


Figure 1. Compartmental model of cholera dynamics [1].

The compartmental model of cholera dynamics described by Figure 1 is then represented by the following ordinary differential equation system.

$$\frac{dS}{dt} = \Lambda + \alpha R - (1 - u_1) \left(\frac{\beta_1 P}{K_1 + P} + \frac{\beta_2 I}{K_2 + I} \right) S - \mu_h S, \quad (1)$$

$$\frac{dI}{dt} = (1 - u_1) \left(\frac{\beta_1 P}{K_1 + P} + \frac{\beta_2 I}{K_2 + I} \right) S - (\mu_h + \delta + \mu_d) I, \quad (2)$$

$$\frac{dR}{dt} = \delta I - (\alpha + \mu_h) R, \quad (3)$$

$$\frac{dP}{dt} = bP \left(1 - \frac{P}{K} \right) + \theta(1 - u_2)I - (\mu_p + u_3)P, \quad (4)$$

where the following initial values are applied: $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = R_0 > 0$ and $P(0) = P_0 > 0$. To intervene the model during the control period of $[0, T]$ we introduce three control variables $u_1(t)$, $u_2(t)$ and $u_3(t)$. If $u_1 = u_2 = u_3 = 0$, then we refer to a model without control, where its stability analysis has been undertaken by [1].

2.2. Control problem

A multidisciplinary approach is key for reducing cholera outbreaks, controlling cholera in endemic areas and reducing deaths. A series of prevention and control actions include water and sanitation interventions; treatment using oral rehydration salt, intravenous fluid, and antibiotic; surveillance as part of an integrated disease surveillance system that includes feedback at the local level and information-sharing at the global level; social mobilization through health education campaigns; and application of cholera vaccines.

In model (1)-(4), the first control u_1 refers to the direct cholera-related education aimed to behaviorally change the interaction among susceptible and infected individuals. This control strategy seems sensible since a cholera outbreak in a Singapore psychiatric hospital indicated that the direct human-to-human transmission was a driving force [3]. It is also discovered that the cholera outbreak in Papua, Indonesia, in 2008 primarily caused by misconduct during funeral of cholera victim, i.e., family members are hugging and kissing the dead-body [7]. The second control u_2 relates to the indirect education whose objective is to improve the person-to-environment conduct. This action comprises interventions at the household level such as the importance of water filtration, water chemical or solar disinfection, and safe water storage containers as well as advising community with the so-called Five Basic Cholera Prevention Messages (drink and use safe water, wash hands, use latrines or bury feces, cook food well and clean up safely). The third control u_3 represents the disinfection of the source of water by adding chlorine to kill harmful microorganisms such as bacteria, viruses, protozoa and helminths. In our setting, u_1 and u_2 can also be interpreted as the portion of human population which can be influenced by control actions. While, u_3 is the portion of *V. cholerae* which can be removed from the environment by adding chlorine.

We consider the following performance index:

$$J(u_1, u_2, u_3) := \int_0^T (A_0 I(t) + A_1 u_1^2(t) + A_2 u_2^2(t) + A_3 u_3^2(t)) dt, \quad (5)$$

where A_k ($k = 0, 1, 2, 3$) can be interpreted as balancing cost weights due to the size and relative importance of each term in (5). We aim to minimize the number of infected individual as well as the control efforts. Hence, we are interested in finding an optimal control pair (u_1^*, u_2^*, u_3^*) such that

$$J(u_1^*, u_2^*, u_3^*) = \min_{(u_1, u_2, u_3) \in \mathcal{U}} J(u_1, u_2, u_3), \quad (6)$$

where $\mathcal{U}$ is the set of all Lebesgue measurable control variables given by

$$\mathcal{U} := \{u_i(t) \mid 0 \leq u_i(t) \leq \bar{u}_i, 0 \leq t \leq T, i = 1, 2, 3\}. \quad (7)$$

The minimization process is subject to system (1)-(4), which is now referred to as the state system. Correspondingly, the unknowns S , I , R and P are now called the state variables, in contrast to the

control variables u_1, u_2, u_3 . In (7), bounds $\bar{u}_i$ ($i = 1, 2, 3$) reflect practical limitations on the maximum rates of controls in period $[0, T]$.

3. Optimality conditions

In this section we provide the necessary conditions for the existence of optimal control variables and corresponding state variables. Pontryagin maximum principle [10] was exploited by introducing the adjoint functions and represents an optimal control in terms of the state and adjoint functions. First we assign the problem of minimization (5) into one of minimization the following Hamiltonian:

$$\begin{aligned} \mathcal{H} = & A_0 I + A_1 u_1^2 + A_2 u_2^2 + A_3 u_3^2 + p_1 \left[\Lambda + \alpha R - (1 - u_1) \left(\frac{\beta_1 P}{K_1 + P} + \frac{\beta_2 I}{K_2 + I} \right) S - \mu_h S \right] \\ & + p_2 \left[(1 - u_1) \left(\frac{\beta_1 P}{K_1 + P} + \frac{\beta_2 I}{K_2 + I} \right) S - (\mu_h + \delta + \mu_d) I \right] \\ & + p_3 [I - (\alpha + \mu_h) R] + p_4 \left[bP \left(1 - \frac{P}{K} \right) + \theta(1 - u_2) I - (\mu_p + u_3) P \right], \end{aligned} \quad (8)$$

where p_i ($i = 1, 2, 3, 4$) are adjoint functions corresponding to S, I, R and P , respectively. According to Pontryagin maximum principle, optimality conditions for the control problem are given by the following set of requirements:

$$\frac{\partial \mathcal{H}}{\partial u_i} = 0, \quad i = 1, 2, 3, \quad (9)$$

$$\frac{\partial x_i}{\partial t} = \frac{\partial \mathcal{H}}{\partial p_i}, \quad i = 1, 2, 3, \quad x_i \in \{S, I, R, P\}, \quad (10)$$

$$\frac{\partial p_i}{\partial t} = -\frac{\partial \mathcal{H}}{\partial x_i}, \quad i = 1, 2, 3, \quad x_i \in \{S, I, R, P\}. \quad (11)$$

By considering that we have a bounded optimal control problem, i.e., $0 \leq u_i(t) \leq \bar{u}_i$, condition (9) provides the optimal control pair (u_1^*, u_2^*, u_3^*) as follows

$$u_1^* = \min \left\{ \bar{u}_1, \max \left\{ 0, \frac{1}{2A_1} (p_2 - p_1) \left(\frac{\beta_1 P}{K_1 + P} + \frac{\beta_2 I}{K_2 + I} \right) S \right\} \right\}, \quad (12)$$

$$u_2^* = \min \left\{ \bar{u}_2, \max \left\{ 0, \frac{\theta}{2A_2} p_4 I \right\} \right\}, \quad (13)$$

$$u_3^* = \min \left\{ \bar{u}_3, \max \left\{ 0, \frac{1}{2A_3} p_4 P \right\} \right\}. \quad (14)$$

Indeed, condition (10) provides the state system (1)-(4) alongside with its initial values. Further, condition (11) gives the following adjoint system:

$$\frac{dp_1}{dt} = (1 - u_1)(p_1 - p_2) \left(\frac{\beta_1 P}{K_1 + P} + \frac{\beta_2 I}{K_2 + I} \right) + \mu_h p_1, \quad (15)$$

$$\frac{dp_2}{dt} = (1 - u_1)(p_1 - p_2) \frac{\beta_2 K_2 S}{(K_2 + I)^2} + \delta p_3 - \theta(1 - u_1) p_4 + (\mu_h + \delta + \mu_d + A_0), \quad (16)$$

$$\frac{dp_3}{dt} = -\alpha p_1 + (\alpha + \mu_h) p_3, \quad (17)$$

$$\frac{dp_4}{dt} = (1 - u_1)(p_1 - p_2) \frac{\beta_1 K_1 S}{(K_1 + P)^2} - b \left(1 - \frac{2}{K} P \right) p_4 + (\mu_p + u_3) p_4. \quad (18)$$

Since in this control problem we assume a free terminal time, then the adjoint system (15)-(18) should satisfy the so-called transversality condition

$$p_1(T) = p_2(T) = p_3(T) = p_4(T) = 0. \quad (19)$$

Therefore, the optimality condition for the existence of optimal solution are represented by optimal controls (12)-(14), the state system (1)-(4) and adjoint system (15)-(18), which all should be solved simultaneously. Since the admissible control set $\mathcal{U}$ is closed and convex, and the integrand of performance index (5) is also convex in I and u_i , then the optimal controls (12)-(14) minimize (5), i.e., Pontryagin maximum principle constitutes both necessary and sufficient conditions for optimality.

4. Numerical solution

4.1. Iterative method

For a model without control, i.e., $u_1 = u_2 = u_3 = 0$ and thus the adjoint system is not exist, we applied a forward-in-time iterative method over state system (1)-(4) under initial conditions $S(0) = S_0$, $I(0) = I_0$, $R(0) = R_0$, dan $P(0) = P_0$. However, for a model with control whose optimality conditions include a set of differential equations with initial conditions and another set with terminal conditions, we implemented the forward-backward sweep method based on the fourth-order Runge-Kutta algorithm as did in [11]:

- Set an initial guess for the control variables u_i^0 ($i = 1, 2, 3$).
- Solve forward-in-time the initial value problem of state system (1)-(4).
- Solve backward-in-time the terminal value problem of adjoint system (15)-(18).
- Calculate the new controls (12)-(14) with the new values of the state and adjoint solutions and then update the controls. The update of the controls can be the average between old and new controls.
- Iterate the process until the solutions converge with a sufficiently small level of tolerance.

4.2. Control scenarios

A set of control strategies were examined to quantify the effectiveness of the control actions. The first three scenarios relate to the application of a single control action, i.e., we set either u_1 , u_2 or u_3 to be active, while the last scenario makes all controls active. For parameter values we followed those given in [1]. In addition, we also use following values: $A_0 = A_1 = A_2 = A_3 = 0.25$, $\bar{u}_1 = \bar{u}_2 = \bar{u}_3 = 1$, and $T = 60$ days.

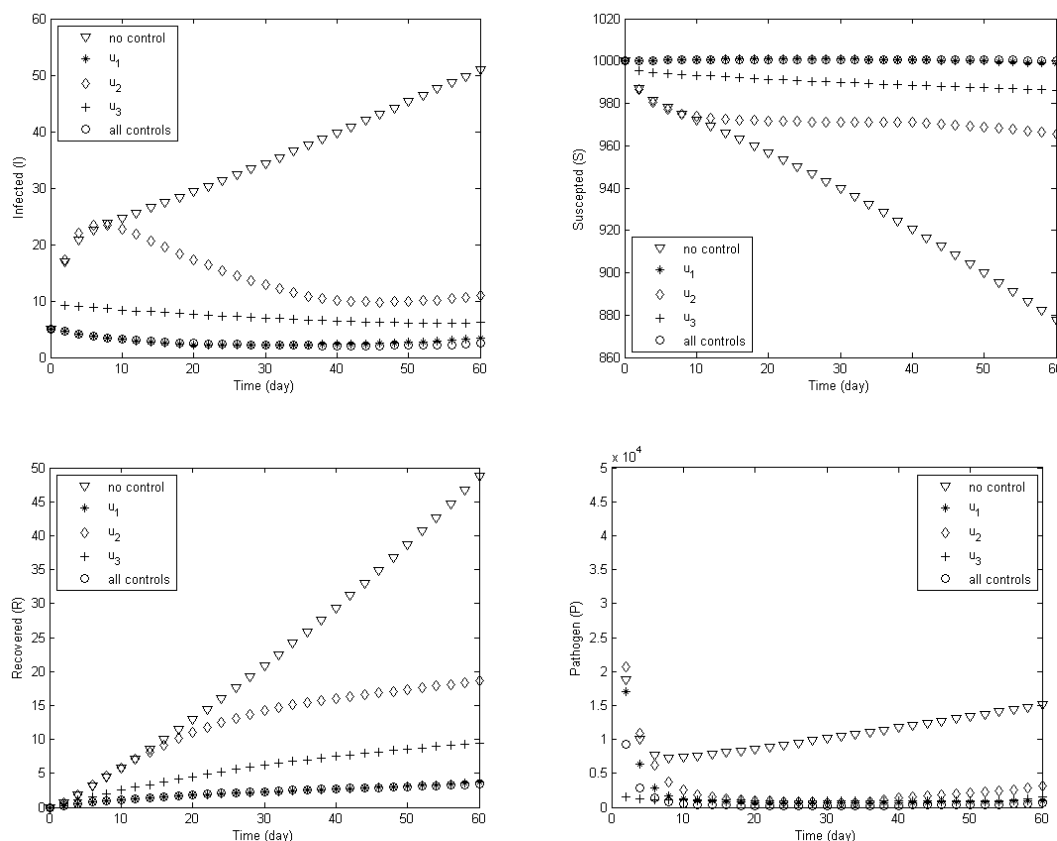


Figure 2. The dynmics of cholera transmission with and without controls.

Figure 2 provides the dynamics of cholera transmission in each compartment. It can be seen that without intervention a cholera outbreak occurs, where the number of infected individuals increase from 5 people in the beginning of period to more than 50 people in two months. An intervention in the form of human-to-human related education (u_1) prevents the occurrence of outbreak by maintaining the number of infected individuals no more than 5 people. Other types of intervention (u_2 and u_3) contributed the similar effect in avoiding the community from the outbreak, even though with lower level of effectivity. Surprisingly, when all control actions were simultaneously applied, the effect in infection reduction is not different with that of only single control u_1 was applied. This, however, indicates that the human-to-human related education is quite effective in directly controlling not only the cholera infection but also indirectly the biomass of pathogen in aquatic environment. In fact, the application of chlorine in reducing the concentration of *V. cholerae* is extremely effective as the number of pathogen reduced up to 96 per cent in few days.

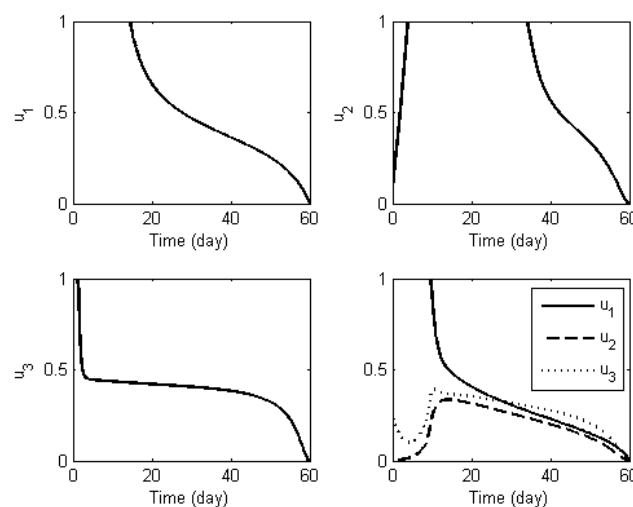


Figure 3. The optimal interventions.

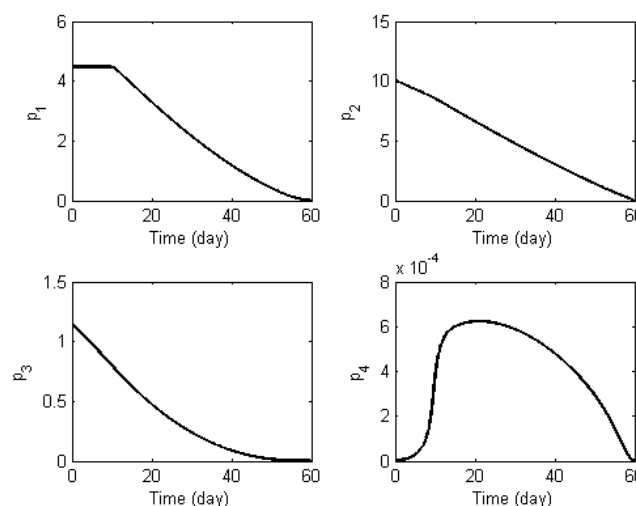


Figure 4. The adjoint functions.

Figure 3 shows that an intervention in the form of human-to-human related education should be implemented at maximum rate during the first 15 days in order to provide the optimal contribution. While that in the form human-to-environment related education should be maximally applied during a longer time, i.e., the 4-34th days. Chlorination needs to be implemented at maximum rate during the first two days. When all interventions were applied concurrently then the first control were active at

maximum rate during the first 10 days as there were additional contributions from others actions of control. Figure 4 illustrates the adjoin functions. It is confirmed that transversality conditions (19) are satisfied.

5. Conclusion

We have presented in this present work a cholera transmission model representing an interaction between human and pathogen populations. Three types of intervention were attached to the model, namely human-to-human related education, human-to-environment related education and chlorination. It is revealed that the first control performs the most effective contribution. In comparison with other controls, the effect of the first control dominates the action in reducing the number of infected individuals as well as the control effort during the period of two months. This result, however, exhibits similarities with that drawn by [1], where direct education is a critical factor in cholera control that has a greater and longer-lasting effect on disease management than technological interventions such as chlorination.

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