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Optimal Control Analysis of a Cholera Disease Transmission Model in Tanzania

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ABSTRACT

In this paper, a deterministic model with optimal control of cholera in Tanzania is proposed and analysed. Necessary conditions of optimal control problem were rigorously analysed using Pontryagin's maximum principle and the numerical values of model parameters were estimated using maximum likelihood estimator. Two control strategies were incorporated such as human education campaign and treatment of water (to reduce the growth of the organism) and its' impact were graphically observed. The goal is to minimize the spread of cholera disease in the community and to minimize the costs of control strategies. The results show that the effective use of optimal human education campaign and treatment of water has a significant impact in reducing the spread of the disease in the community.
Keywords: Modelling, Education Campaign, Treatment, Optimal Control

I. INTRODUCTION

Cholera is a severe water-borne infectious disease caused by the bacterium Vibrio cholerae (V. cholerae) (Al-Arydah et al., 2013). Cholera can either be transmitted through interaction between humans (i.e., fecal-oral) or through interaction between humans and their environment (i.e., ingestion of contaminated water and food from the environment).

The re-emergence of cholera is presenting unprecedented challenges. Africa reported 118,349 cases to the World Health Organization in 1997, for 80% of cases worldwide. Africa also had the highest overall case-fatality rate (4.9%), compared with 1.3% in the Americas and 1.7% in Asia (WHO, 1998). Cholera began spreading throughout the Dar es Salaam region and 12 other regions: Arusha, Dodoma, Geita, Morogoro, Kigoma, Mara, Mwanza, Shinyanga, Singida, Tabora, Tanga as well as the island of Zanzibar. Tanzania has consistently reported cholera cases; annual reports ranged from 1,671 cases in 1977 to 18,526 in 1992. During the last 2 decades, three major choleraepidemics have occurred: 1977-78, 1992, and 1997 (WHO, 2016). In 1997, Tanzania had one of the highest case-fatality rates in East Africa (5.6%), with 2,268 deaths in 40,226 cases (WHO,1998). We describe risk factors and pattern of spread of the 1997 cholera epidemic in a rural area in southern Tanzania. As of 19 November 2015, there were 8,954 reported cases and 129 deaths according to World Health Organization (WHO), and 19 out of 30 regions had detected and reported cholera cases on mainland Tanzania and Zanzibar (United Nations Resident Coordinator's Office (UNRCO) and Ministry of Health & Social Welfare (MoHSW). As of 20 April 2016, a total of 24,108 cases, including 378 deaths, had been reported nationwide.

Over the years, mathematical models have been used to provide important insights into disease behavior and intervention strategies. For instance, the study of an infectious disease model with population-dependent death rate using computer simulation was investigated by Greenhalgh (1992). Mathematical models provide results such as thresholds, basic reproduction numbers, contact numbers and replacement numbers (Benyah 2007). These results can help health workers understand and predict the spread of an epidemic and evaluate potential effectiveness of the different control measures to be used. They can improve our understanding of the relationship between social and biological factors that influence the spread of diseases.

Optimal control problems have generated a lot of interest from researchers all over the world, for instance (Imanov, 2011) examined application of the method of similar solutions in solving time optimal control problems with state constraints. Similarly, various techniques have been applied to study optimal control problems related to dynamical systems. In particular, Lemos-Paião, Silva and Torres (2017) proposed and analyzed an epidemic model for cholera with optimal control treatment. Hakim, Trisilowati and Darti (2015) investigated an optimal control model of the spread of cholera disease by vaccination. Fister, Gaff, Lenhart, Numfor, Schaefer and Wang (2016) analyzed optimal control of vaccination in an Age-Structured cholera model. However, none of these studies have considered the aspect of optimal control to reduce spread of cholera disease through the combination of the aspects of education campaign and treatment of water in a Tanzania.

This particular study is also motivated by large number of cases reported in Tanzania. The majority of cases had been reported from 23 regions in mainland Tanzania (20,961 cases, including 329 deaths) (WHO, 2016). From the middle of December 2015 to the end of March 2016, the number of new reported cases started to increase again in Tanzania. It becomes significant we carry out a scientific study of this disease that has become endemic, so as to enhance its control in Tanzania using a mathematical model with time dependent controls. It is against this background that this study is therefore undertaken as an attempt to apply the optimal control theory in minimizing the spread of cholera and minimize the cost of applying controls, in order to best combat the spread of cholera disease. Therefore, this study intends to apply optimal control theory to minimize the spread disease by some control strategies and minimize the cost of applying controls, in order to best combat the spread of cholera disease.

II. MODEL FORMULATION

In this section, we formulate and analysis a mathematics model of cholera in Tanzania. The modelled populations include human populations and the environmental component. The total human population is divided into three compartments depending on the epidemiological status of individuals. These compartments include: Susceptible (S (t)), symptomatically infected (I (t)) and the concentration of the vibrios in the environment (that is contaminated water) (B(t)). We assume that the total population is non-constant, which is a reasonable assumption for a relatively short period of time and for low-mortality diseases such as cholera. Furthermore, the susceptible population increases due to the incoming of immigrants at the rate Λ. On the other hand the susceptible population decreases due to the infection. k is the concentration of Vibrio Cholera in food and water that yields 50% chance of catching cholera disease and the infected people recovered from cholera at the rate β.

Human suffer from natural death and also dead due to cholera disease at the rates μ and d respectively. Let α be the net mortality rate of V. cholerae in the aquatic environment and also each infected person contribute to the population of V. cholera at the rate e. We assume that a is the rate of expose to contaminated water and K is the carrying capacity of V. cholera.

Table 1. Parameters used in the model formulation and their description

Parameter	**Description**
Λ	Constant human recruitment rate
μ	Natural human mortality rate
d	Disease related death rate
n	Loss of rate of V. cholerae in the aquatic environment
a	Rate of exposure to contaminated water
k	Concentration of V. cholerae in water that yields 50% chance of catching cholera.
K	The carrying capacity of V. cholerae.
β	Rate at which people recover from cholera
r	Growth rate of Per V. cholerae in the aquatic environment
e	Contribution of each infected person to the population of V. cholera
w	Net mortality rate of V. cholerae in the aquatic environment.

From the description of the dynamics of cholera, the following set of non-linear ordinary differential equations can be derived:

$$\begin{aligned}\frac{dS}{dt} &= \Lambda - a\left(\frac{B}{K+B}\right)S - \mu S\\ \frac{dI}{dt} &= a\left(\frac{B}{K+B}\right)S - (\mu + d + \beta)I\\ \frac{dB}{dt} &= rB\left(1-\frac{B}{K}\right) - nB + eI\end{aligned} \qquad (1)$$

We introduce the time dependent controls in the model (1) for the aim of controlling cholera and study the strategies that curtail the spread of the disease. For the optimal control problem, we consider the following model equations.

$$\begin{aligned}\frac{dS}{dt} &= \Lambda - a\left(1-u_1(t)\right)\left(\frac{B}{k+B}\right)S - \mu S\\ \frac{dI}{dt} &= \left(1-u_1(t)\right)a\left(\frac{B}{k+B}\right)S - (\mu + d + \beta)I\\ \frac{dB}{dt} &= rB\left(1-\frac{B}{K}\right) - u_2(t)nB + eI\end{aligned} \qquad (2)$$

where, the control functions $u_1(t)$ and $u_2(t)$ represent the reduction of contact between infected persons and the susceptible and treatment of water to reduce the growth of the organism respectively. We apply control theory as a mathematical tool that is used to make decision involving complex biological situations (Lenhart and Workman, 2007). The purpose of introducing controls in the model is to find the optimal level of the intervention strategy preferred to reduce the spreads and cost of implementation of the control. The control variables $u_1(t)$ and $u_2(t)$ are minimized subject to the differential equations (2). The control coefficients u_2 and $(1-u_1)$ reduce the organism growth and the contacts between the infected and susceptible accordingly. To investigate the optimal level of effort that would be needed to control the disease, first we formulate the objective functional J which is defined by choosing a quadratic cost on the controls. The objective is to minimize the spread of cholera disease and minimize the cost of interventions to the final time, with different relative weights applied toinfective populations. Therefore the objective functional J is defined over a feasible set of control $u_1(t)$ and $u_2(t)$ applied over the finite time interval $[0,T]$ which is

$$J = \min \int_0^T \left(B_1 B(t) + B_2 I(t) + \frac{A_1 u_1^2}{2} + \frac{A_2 u_2^2}{2} \right) dt \quad (3)$$

where B_1 and B_2 are the costs associated with infective populations and the concentration of the vibrios in the environment (that is contaminated water) respectively, while A_1 and A_2 , are the relative cost weights for each control measure. The true value of weights is not well known since they require extensive field work and data mining. The weights used here are intended only for theoretical purposes to investigate the effect of various control practices. The choice of quadratic cost on the controls is done in a similar way as in other epidemiological models with controls (Okosun et al. 2012, Lee et al. 2013, Lenhart and Neilan, 2010).

The target is to minimize the objective functional J defined in equation (3). Therefore we are required to find numerically optimal controls $u_1^*$and u_2^* such that

$$J\left(u_1^*, u_2^*\right) = \min\left\{J(u_1, u_2) \mid u_1, u_2 \in u\right\} \quad (4)$$

for $u = \{u_1, u_2\}$ such that u_1, u_2 are measurable with $0 \le u_1 \le 1$ and $0 \le u_2 \le 1$ for $t \in [0,T]$.

The necessary conditions that an optimal control problem must satisfy come from Pontryagin's maximum principle (Pontryagin et al., 1962). This principle converts (2)-(3) into a problem of minimizing pointwise a Hamiltonian H , with respect to u_1 and u_2 defined by;

$$H = B_1 B + B_2 I + \frac{A_1 u_1^2}{2} + \frac{A_2 u_2^2}{2} + \lambda_1 \left\{ \Lambda - a\left(1 - u_1(t)\right)\left(\frac{B}{k+B}\right) S - \mu S \right\} \quad (5)$$

where λ_1 and λ_2 are the adjoint variables or co-state variables. By applying Pontryagin's maximum principle (Pontryagin et.al., 1962) and the existence result for the optimal control (Fleming and Rishel, 1975), we obtain

Proposition 1: *For optimal control triple u_1^* and u_2^* that minimizes $J(u_1, u_2)$ over u , there exist adjoint variables λ_1, λ_2 and λ_3 satisfying*

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{dH}{dS} = (1-u_1)\lambda_1 \frac{aB}{k+B} + \lambda_1 \mu - (1-u_2)\lambda_2 \frac{aB}{k+B} \\
\frac{d\lambda_2}{dt} &= -\frac{dH}{dI} = (d+\mu+\beta)\lambda_2 - \lambda_3 e - B_2 \\
\frac{d\lambda_3}{dt} &= -\frac{dH}{dB} = (1-u_1)\frac{aKS}{(k+B)^2}\lambda_1 - (1-u_1)\lambda_2 \frac{aKS}{(k+B)^2} \\
&\quad - \frac{r(K-2B)}{K}\lambda_3 + u_2 n \lambda_3 - B_1
\end{aligned} \quad (6)$$

with transversality conditions

$$\lambda_1(T) = \lambda_2(T) = \lambda_3(T) = 0$$

(7)

The following characterization holds on the interior of the control set u

$$\begin{aligned}
u_1^* &= \max\left\{0, \min\left(1, (\lambda_2 - \lambda_1)\frac{aBS}{A_1(k+B)}\right)\right\} \\
u_2^* &= \max\left\{0, \min\left(1, \left(\frac{\lambda_3 n B}{A_2}\right)\right)\right\}
\end{aligned} \quad (8)$$

where λ_1, λ_2 and λ_3 are solutions of (5).

Proof. The form of adjoint (or co-state) system (6) and transversality conditions (7) are standard results from Pontryagin's Maximum Principle (Pontryagin *et al.* 1962). To obtain the co-state system (6), the partial derivatives of the Hamiltonian (H) (5) with respect to each state variable are computed as follows

$$\frac{d\lambda_S}{dt} = -\frac{\partial H}{\lambda_S};\ \lambda_S(tf) = 0,$$

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$$\frac{d\lambda_R}{dt} = -\frac{\partial H}{\lambda_R};\ \lambda_R(tf) = 0.$$

(9)

The optimality equations (9) are obtained by finding the partial derivative of the Hamiltonian equation (H) (5) with respect to each control variable and solving for

u_i^* (optimal control) where the derivative vanishes. That is,

$$\frac{\partial H}{\partial u_i} = 0 \text{ for } i = 1, 2$$

Solving for $u_1^*$and u_2^* , subject to the constraints, gives the characterization equation (8). Hence proved. Note that the state system (2) has initial time conditions and the co-state system (6) has final time conditions.

III. APPLICATION OF THE MODEL

In this section, we present the data of cholera cases and deaths from 1998 to 2010 in Tanzania as summarized in Table 2. The method used to estimate parameters in this section is maximum likelihood (ML) where real data of cholera cases and deaths were used.

Table 2: Cumulative Cholera Cases(C) and Deaths (D) from 1998 to 2010

YEAR	1998	1999	2000	2001	2002
C	296	12,266	4,637	2154	12,403
D	87	591	153	88	314
YEAR	**2003**	**2004**	**2005**	**2006**	**2007**
C	12,919	9,639	3,284	14,297	2,860
D	281	242	108	254	70
YEAR	**2008**	**2009**	**2010**		
C	1,619	6,295	5,566		
D	50	83	95		

Because of the unavailability of data on transmission and progression rates, we estimated most of the parameters, which makes the setting of initial conditions difficult for the purpose of the simulations and illustrating the usefulness of the model.

Many parameters are known to lie within limits. Only a few parameters are known exactly and it is thus important to estimate the others. The estimation process attempts to find the best accordance between the computed and observed data. Here, the fitting process involved the use of the least squares curve fitting method. A Matlab code was used where unknown parameter values were given a lower and upper bound from which the set of parameter values that produced the best fit were obtained. The parameter values obtained from the fitting are shown in Table 3.

Table 3. Parameter values that give the best fit to the data in the model

Parameters	Literature Value (range)	Literature Value	Estimated Parameter Values
Λ	(0.3,0.99)	10	9.865
μ	(0.001,0.8)	0.022	0.01745
d	0.5	0.015	0.03075
a	(0.0044,0.34)	0.5	0.3350
k	(0.020,.09)	0.000001	0.00000025
K	(0.002,0.5)	0.00000001	0.00000002
β	0.13,0.5	0.1	0.1814
r	0.03	(0-0.25)	0.2809
e	0.06	10	8.76

In this section we study numerically the effects of optimal control strategies such as education campaign and treatment of infected human in the spread of cholera. The solution of the optimal control problem was obtained by solving the optimality system of state and adjoint systems through forward–backward sweep method. The adjoint systems (6) were solved by fourth order Runge–Kutta scheme using the forward solution of the state equations. We describe the controls in the following strategies using the parameter values in Table 3.

Strategy A: Control with Education Campaign in Human Population (u_1)

The purpose of education campaign strategy is to explore the awareness of the disease, mode of transmission, prevention and control measures in community. Figure 1 describes the effect of implementing education campaign in human and the impact is visible in infected individuals and bacteria population.

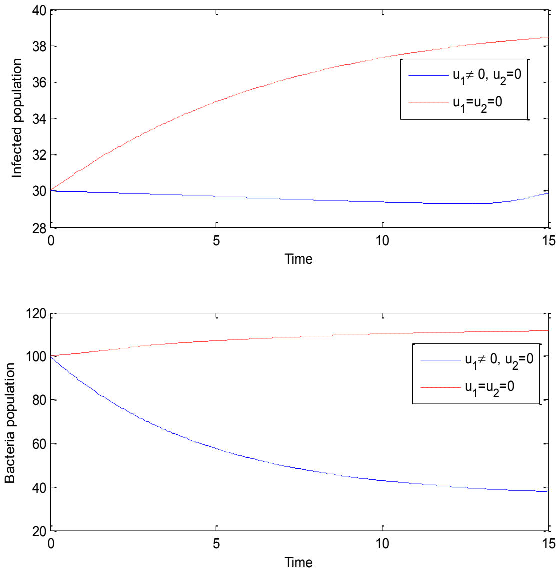

Figure 1. Simulations of the model showing the effects of education campaign on the spread of cholera

Strategy B: Control with Treatment of Water (u_2)

In Figure 2, the results show a significant difference in the number of infected humans with optimal strategy compared to case without controls. Specifically, it is observed that in Figure 2(A) the control strategy lead to reduce the growth of organism as against increase in the uncontrolled case. The treatment of water is minimizing the concentration of the bacteria population in water. Similarly in Figure 2(B), the uncontrolled case results in increased number of bacteria while the control strategy lead to a decrease in the number of bacteria population.

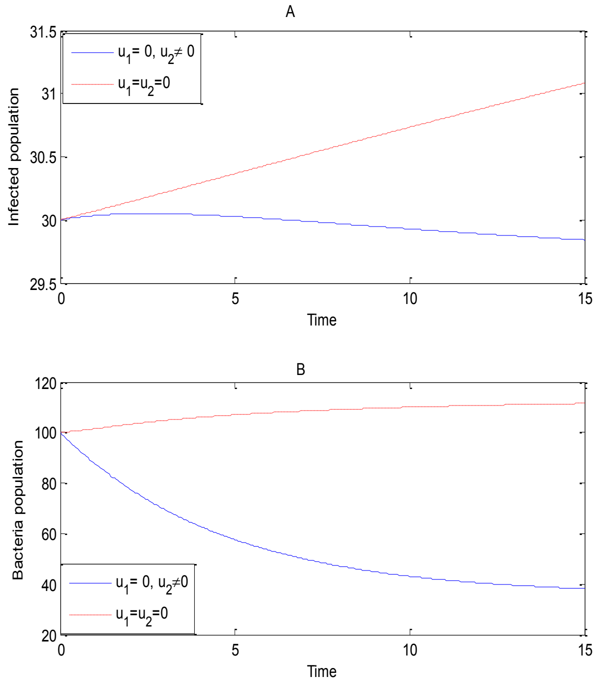

Figure 2. Simulations of the model showing the effects of treatment of water

Strategy C: Combination of Education Campaign in Human (u_1) and Treatment of Water (u_2)

The results in Figure 3(A-B) show a significant difference in the numbers of infectious humans and bactreria population with optimal strategy compared to the number without controls. Due to the control strategies, the number of infected individuals decreses while the infectiuos population increases when there is no control. In Figure 3 (B), the bacteria population decrease in the presence of control strategies while an incresed number is observed for the uncontrolled case. The presence of treatment of water and education in the community will somehow reduce the spread of disease.

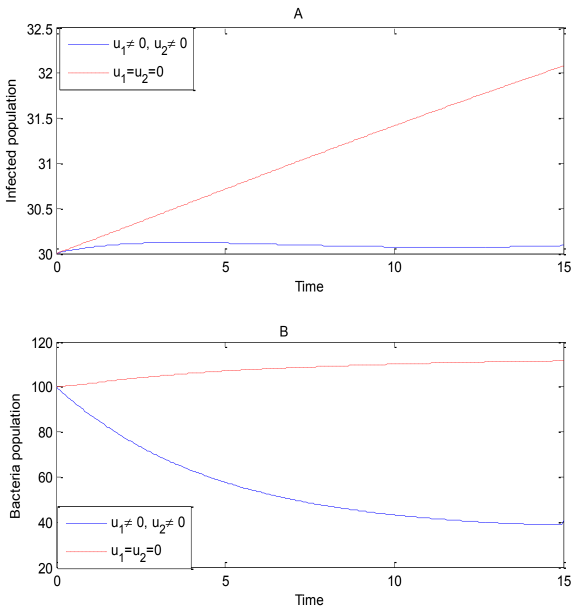

Figure 3. Simulations of the model showing the effects of education campaign in human and treatment of water

IV. CONCLUSION

This paper analysed the optimal control using Pontryagin's Maximum Principle where two control strategies were numerically studied. Our numerical simulation results show that the effective use of optimal education campaign in the population and treatment water has a significant impact in reducing the spread of the cholera disease in the community since it leads the decrease in the number of new infection cases in Tanzania compared to the case with no control.

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