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Optimal Control Problem for Cholera Epidemiology

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ABSTRACT

In this paper, the major objective was to theoretically investigate, proof the existence and local optimality state of singular control by applying L^1 type objective function. The objective function L^1 has been applied in a Compartmental model since it is linear in the control variables. Generalized Legendre-Clebsch Condition applied showed the existence of singular control for both vaccination and sanitation that are optimal. The condition for local stability of the model was also established and the basic reproductive number assimilated. The disease-free equilibrium of the model is locally asymptotically stable if R_O< 1, and unstable if R_O>1. This means that all interventions applied need to reduce the basic reproductive number to reduce the force of infection.

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1. Introduction

The control and elimination of organisms that cause diseases as well as the introduction of antibiotics and vaccinations has been the focus since 1950's in combating diseases. However, factors such as resistance to medicine by micro-organisms, demographic evolution and accelerated urbanization led to new infections and re-emergence of existing diseases such as cholera.

The application of mathematical models has therefore become an important tool in epidemiology of in providing control measures of epidemics. Using Compartmental models have been used to describe the dynamic behavior of populations exposed to diseases, leading to proposals of optimal control. These models differ on the choices of the dynamism, constraints and the cost of application.

Global incidence of cholera has significantly been reduced through control strategies such as vaccination, sanitation, treatment, and education though it remains a public health problem in many developing countries. Cholera is an acute diarrheal infection caused by ingestion of food or water contaminated with the bacterium Vibrio cholerae. According to [1] it is estimated that each year there are 1.3 million to 4.0 million cases of cholera, and 21 000 to 143 000 deaths worldwide due to cholera.

The disease dynamics depend on the interactions between human host, the pathogen, and the environment as stated by [2] which leads to two pathways that is environment to human and human - human transmission. The number of cholera cases reported by [1] has continued to be high over the last few years. During 2016; 132,121 cases were notified from 38 countries, including 2420 deaths. The discrepancy between these figures and the estimated burden of the disease is because

many cases are not recorded due to limitations in surveillance systems and fear of impact on trade and tourism.

In 1979, Capasso and Paveri – Fontana proposed a mathematical model where they studied cholera epidemic which occurred in Mediterranean in 1973 [3]. This model had components which included pathogen concentration in water and infected individual. The model was later extended in 2001 by Codeco [4] and considered the role of environment (water) and introduced susceptible compartment in the population model. Both models only assumed the environment to human mode of transmission. In 2011 [5], Mukandavire clarified the work done by [6] in 2005 in studying the 2008 to 2009 cholera outbreak in Zimbabwe where they explored two types of cholera transmission that is human to human (horizontal) and environment to human transmissions. In 2011, Wang and Modnak [7] extended the model to involve three interventions which are sanitation, treatment and vaccination and from their analysis, these controls applied are closely linked and that the power of one measure as an optimal strategy depended on its relative cost and the setting in the population.

Yusuf and Benyah [8] in 2012 presented optimal intervention for treatment and vaccination for a SIR model, where they applied on a variable size of the population and formulated the optimal problems for the controls. Their major goal was to get combined optimal interventions to minimize the force of infection and cost in a particular strategy. According to Gaff and Schaefer [9], they stated that optimal control theory was applied to give the most strategy that reduced the number of infected individuals while efficiently balancing the two strategies applied. Based on the dynamic's models by Hethcote [10], various strategic control schedules have been studied by applying techniques in the optimal. These models so far applied L2 objective function in measuring the weight of control strategy applied but according to [11], L2 objective are not suitable in biological approach because they lead to continuous control functions that are difficult to administer in practical applications and therefore, there is need to apply L1 objective function to establish if this can lead to a better intervention administration to help control the cholera infection. In 2011, [12] initiated the analysis of an optimal control problem for a SIR model with vaccination and treatment by applying geometric optimal control and based on their conclusion, they found out that only vaccination was singular. This propelled the application of vaccination and sanitation to check if both can be singular at the same time.

In this paper, we are majorly concerned with the state of singular control problem. Singular control is a challenging type of stochastic control problems. We theoretically investigate and proof the existence and local optimality of singular control, the role of combined basic reproductive number and to ascertain stability analysis and equilibrium point of the model by applying L1 type objective function which is linear in the control variables.

2. Methodology

a) Mathematical Model

The objective is to formulate a model for cholera that includes relevant biological details and accounts for the intervention strategies. We use this model of an epidemic, imposing vaccination, and sanitation on it and then determine an optimal strategy for rolling out the control strategies. We do this optimization for the case of SIR model with simple constraints. Since the control variables appear linearly in the Hamiltonian, the Pontryagin's Maximum Principle leads to either singular or bang-bang

controls. Let S(t) represent the number of susceptible at time t, I(t) the number of infective at t and R(t) the number of recovered individuals in time. We also denote the total number of individuals by N(t) = S(t) + I(t) + R(t) and assume that all births enter the susceptible class S(t).

b) The SIR Model Equation

The system of differential equations describing the dynamics of Cholera outbreak is formulated below with their initial conditions

S' = ΛN − (μ + v(t)) S(t) − βII(t)S(t) − βBB(t)S(t) + ωR(t), S (0) = S0 ≥ 0

I' = βII(t)S(t) + βBB(t)S(t) − γI(t) − μI(t) − ξ I(t), I (0) = I0 ≥ 0 R' = γI(t) − μR(t) − ωR(t) + v(t)S(t), R (0) = R0 ≥ 0 **(1)**

B' = ξ I(t) − mB(t) − δ B(t), B (0) =B0 ≥ 0

Where μ denotes the natural death rate, Λ is the rate of recruitment; β_I is the rate of transmission from human to human, β_B is the rate of transmission from the environment to human, γ is the rate of recovery, ω is the rate at which the recovered are susceptible, ξ is the rate at which the infectious shed, δ is the rate of *Vibrio cholerae*, v is the rate at which the susceptible are vaccinated, m is the rate of sanitation to the environment.

The solution of the model system (1) is biologically feasible for all times. The solution domain is

$\Omega = [(S,I,R,B) \in \Re_+^4 : S \geq 0, I \geq 0, R \geq 0, B \geq 0, S + I + R = N]$

Since $R(t) = N(t) - S(t) - I(t)$, we now consider a new system of differential equation (1):

$S' = \Lambda N - (\mu + v(t)) S(t) - \beta_I I(t)S(t) - \beta_B B(t)S(t) + \omega R(t), S(0) = S_0 \geq$

$I' =) - \gamma(t) - \mu I(t) - \xi I(t), I(0) = I_0 \geq 0$ **(2)**

$N' = \Lambda N - \mu N - \xi I, N(0) = N_0 \geq 0$

$B' = \xi I(t) - mB(t) - \delta B(t), B(0) = B_0 \geq 0$

The above model system has a disease-free equilibrium (DFE)

- DFE- is a point where disease is (i.e. *I=B=0)* absent in the population and thus it is given as.

$DFE = (S^O, I^O, B^O) = \left[\frac{\Lambda N}{\mu + v)}, 0, 0\right]$ **(3)**

To analyze the DFE, we first find the basic reproductive number.

c) Basic Reproduction Number

The basic reproduction number R_0 is the average number of secondary infections caused when a single infectious person is introduced into a susceptible population. R_0 is determined by applying the next generation method which is given by FV^{-1}.

Where: F- Rate at which new infected enter compartment,i

V- Denote the transfer of individuals into and out of compartment,i

Using equation (2), we obtain the following:

$$\boldsymbol{F} = \begin{bmatrix} \beta_I IS + \beta_B BS \\ 0 \end{bmatrix} \text{ and } \boldsymbol{V} = \begin{bmatrix} (\gamma + \mu + \xi)I \\ (\delta + m)B - \xi I \end{bmatrix} \quad \textbf{(4)}$$

Obtaining the derivatives of F and V about $\boldsymbol{x} = (I, B)$

$$\boldsymbol{F} = \begin{bmatrix} \beta_I S_0 & \beta_B S_0 \\ 0 & 0 \end{bmatrix} \text{ and } \quad \boldsymbol{V} = \begin{bmatrix} (\gamma + \mu + \xi) & 0 \\ -\xi & (\delta + m) \end{bmatrix} \quad \textbf{(5)}$$

We obtain V^{-1} given as

$$\boldsymbol{V^{-1}} = \frac{1}{(\gamma+\mu+\xi)(\delta+m)} \begin{bmatrix} (\delta + m) & 0 \\ \xi & (\gamma + \mu + \xi) \end{bmatrix} \quad \textbf{(6)}$$

Therefore FV^{-1} is then given as

$$\boldsymbol{FV^{-1}} = \begin{bmatrix} \frac{\beta_I S_0}{(\gamma+\mu+\xi)} + \frac{\beta_B S_0 \xi}{(\gamma+\mu+\xi)(\delta+m)} & \frac{\beta_B S_0}{(\delta+m)} \\ 0 & 0 \end{bmatrix} \quad \textbf{(7)}$$

From the characterization equation (7), we take the largest spectral radius of FV^{-1} to obtain R_0 as shown below

$$\boldsymbol{R_0} = \frac{\beta_I \Lambda N}{(\gamma+\mu+\xi)(\mu+v)} + \frac{\beta_B \Lambda N \xi}{(\gamma+\mu+\xi)(\delta+m)(\mu+v)} \quad \textbf{(8)}$$

d) Local Stability of DFE

Theorem: The disease-free equilibrium is locally asymptotically stable if $R_o < 1$ and is unstable if $R_o > 1$

Proof: The eigenvalues of the Jacobian matrix are the solutions of the characteristic equation

$$[J - \lambda I] = 0 \quad \textbf{(9)}$$

For the disease-free equilibrium to be asymptotically stable, then all eigenvalues are negative.

We obtain J from equation (2)

$$J = \begin{bmatrix} -(\mu + v) - \lambda & -\frac{\beta_I \Lambda N}{(\mu+v)} & -\frac{\beta_B \Lambda N}{(\mu+v)} \\ 0 & \frac{\beta_I \Lambda N}{(\mu+v)} - (\gamma + \mu + \xi) - \lambda & \frac{\beta_B \Lambda N}{(\mu+v)} \\ 0 & \xi & -(\delta + m) - \lambda \end{bmatrix} \quad \textbf{(10)}$$

Taking one of the eigenvalues to be $-(\mu + v)$, we apply Routh Hurwitz criterion as shown by [13] by checking the signs of the eigenvalues of the reduced matrix as show

$$\begin{bmatrix} \frac{\beta_I \Lambda N}{(\mu+v)} - (\gamma + \mu + \xi) & \frac{\beta_B \Lambda N}{(\mu+v)} \\ \xi & -(\delta + m) \end{bmatrix} \quad \textbf{(11)}$$

We obtain the determinant:

$$-(\delta + m)\left[\frac{\beta_I \Lambda N}{(\mu+v)} - (\gamma + \mu + \xi)\right] - \frac{\beta_B \Lambda N \xi}{(\mu+v)} = 0 \quad \textbf{(12)}$$

Making the determinant to be positive, we have:

$$(\delta + m)\ \frac{\beta_I \Lambda N}{(\mu+v)} + \frac{\beta_B \Lambda N \xi}{(\mu+v)} < (\delta + m)(\gamma + \mu + \xi) \quad \textbf{(13)}$$

Dividing both sides by $(\delta + m)(\gamma + \mu + \xi)$, we obtain

$$\frac{\beta_I \Lambda N}{(\gamma+\mu+\xi)(\mu+v)} + \frac{\beta_B \Lambda N \xi}{(\gamma+\mu+\xi)(\delta+m)(\mu+v)} < 1 \quad \textbf{(14)}$$

But

$$\frac{\beta_I \Lambda N}{(\gamma+\mu+\xi)(\mu+v)} + \frac{\beta_B \Lambda N \xi}{(\gamma+\mu+\xi)(\delta+m)(\mu+v)} = R_0 \quad \textbf{(15)}$$

Thus $R_0 < 1$ this therefore means that the model converges to DFE and hence there is no epidemic.

e) Optimal Control Strategies

The objective is to choose a combined strategy of vaccination and sanitation in such a way to minimize the value of objective function, the force of infection and to minimize the cost of vaccination and sanitation of the population. According to [14] they stated that a quadratic-control (L^2) cost function is not appropriate for problems with biological or biomedical background. Therefore, we consider a linear (L^1) cost function.

The objective function J given as:

$$J(v, m) = \int_{t_0}^{t_f} [a_0 I + a_1 v S + a_2 m B]\, dt \quad \textbf{(16)}$$

- $a_0 I$- This term represents the number of people who become infected and is also a measure of deaths associated with the outbreak
- $a_1 v S$ - This term, where a_1 is a positive parameter associated with the control $v(t)$, represents the cost of vaccination given to a susceptible.
- $a_2 m B$ - This term, where a_2 is a positive parameter associated with the control $m(t)$, represents the cost of sanitation in the bacterial concentration.
- With $a_0 > 0, a_1 > 0$ and $a_2 > 0$, where we minimize the infected group $I(t)$ by reducing the force of infection, while also minimizing the cost of vaccination and sanitation. The control function $v(t)$, with $0 \leq v(t) \leq 1$ (Representing fraction of susceptible that require vaccination). When $v(t)$ is close to 1, then vaccination failure is low but with high implementation costs (The value $v^*(t) = 1$ is a characteristic of a perfectly effective vaccine but cholera vaccines have low protective efficacy of about 85%. Therefore, the upper bound of this control may not be necessarily attainable). Let $m(t)$ denote the level of sanitation, scaled so that $0 \leq m(t) \leq 1$. The effect of sanitation efforts is modeled as a reduction in vibrio ingestion rates, thus the level of sanitation decreases the transmission rate of cholera $m^*(t) = 1$ would signify no transmission of pathogens, especially if there is good sanitation).

Necessary optimality conditions:
The basic control problem in compact form contains *OCP*

$$\begin{cases} J(v,m) = \int_{t_0}^{t_f} [a_0 I + a_1 vS + a_2 mB]\, dt \\ Subject\ to \\ S' = \Lambda N - (\mu + v)S - \beta_I IS - \beta_B BS + \omega R, S(0) = S_0 \geq 0 \\ I' = \beta_I IS + \beta_B BS - (\gamma + \mu + \xi)I, I(0) = I_0 \geq 0 \\ N' = (\Lambda - \mu)N - \xi I, N(0) = N_0 \geq 0 \\ B' = \xi I - (m + \delta)B, B(0) = B_0 \geq 0 \\ 0 \leq v(t) \leq 1 \\ 0 \leq m(t) \leq 1 \end{cases} \quad \textbf{(17)}$$

Introducing the state $x = (S, I, B, N)^{\mathsf{T}}$, the dynamics of the system is a multi-input control linear system of the form

$$x' = f(x) + g_1(x)v + g_2(x)m \quad \textbf{(18)}$$

With the drift vector field $f(x)$ given by

$$f(x) = \begin{bmatrix} \Lambda N - \mu S - \beta_I IS - \beta_B BS + \omega R \\ \beta_I IS + \beta_B BS + \omega R - (\gamma + \mu + \xi)I \\ \Lambda N - \mu N - \xi I \\ \xi I - \delta B \end{bmatrix} \quad \textbf{(19)}$$

And control vector fields g_1 and g_2 are given by

$$g_1(x) = \begin{bmatrix} -S \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad \text{and} \quad g_2(x) = \begin{bmatrix} 0 \\ 0 \\ 0 \\ -B \end{bmatrix} \quad \textbf{(20)}$$

The integrand of the objective is denoted
$L(x, v, m) = a_0 I + a_1 vS + a_2 mB$
The necessary optimality conditions of the Maximum Principle for the problem will be evaluated. Minimizing equation (2), the standard Hamiltonian function is given by:

$$H = L(x, v, m) + \lambda(f(x) + g_1(x)v + g_2(x)m$$
$$H = min_{v,m}[a_0 I + a_1 vS + a_2 mB + \lambda_S S' + \lambda_I I' + \lambda_N N' + \lambda_B B'] \quad \textbf{(21)}$$

The adjoint equations formed are:

$$\begin{bmatrix} \lambda'_S = -a_1 v + \lambda_S[\beta_I I + \beta_B S + \mu + v] - \lambda_I[\beta_I I + \beta_B B] \\ \lambda'_I = -a_0 + \lambda_S \beta_I S - \lambda_I[\beta_I S - (\gamma + \mu + \xi)I] + (\lambda_N - \lambda_B)\xi \\ \lambda'_N = -\lambda_S \Lambda - \lambda_N[\Lambda - \mu] \\ \lambda'_B = -a_2 m + \lambda_S \beta_B S - \lambda_I \beta_B S + \lambda_B(m + \delta) \end{bmatrix} \quad \textbf{(22)}$$

Where $\lambda_S(T) = 0, \lambda_I(T) = 0, \lambda_N(T) = 0$ and $\lambda_B(T) = 0$ are the transversality conditions.

The Hamiltonian is minimized with respect to the control variables. Since the Hamiltonian is linear in the controls, we consider the switching functions $\phi_v(t)$ and $\phi_m(t)$ and separate the minimization problem into two:

$$\begin{cases} \phi_v = H_v = a_1 S - \lambda_S S \\ \phi_m = H_m = a_2 B - \lambda_B B \end{cases} \quad \textbf{(23)}$$

The control is bang-bang if the switching function $\phi_i(t) = 0$ is not sustained over an interval of time but occurs at infinitely many points. It occurs at the extreme values of the control set. It is a piecewise constant function, switching between only the lower and upper bounds. The control is also said to be singular, if the switching function $\phi_i(t) = 0$ and its derivatives vanish over an open interval. The switch times are times when the optimal control switches from lower to upper boundary or switches to singular control. We theoretically investigate the existence and local optimality of singular or bang-bang control for the system as shown by [12]. Optimal controls then need to be synthesized from bang and singular controls through the analysis of the switching function. If $\phi(\tau) = 0$, but $\dot{\phi}(\tau) \neq 0$ then the control has a switch at time τ. To analyze the structure of the optimal controls, the switching function and its derivatives are analyzed first. In this paper, the existence and the local optimality of singular controls are analyzed.

Hamiltonian being linear in the controls, the minimum condition requires

$$v^*(t) = \begin{cases} 0 \; if \; \phi_v(t) > 0 \\ 1 \; if \; \phi_v(t) < 0 \\ singular \; if \; \phi_v(t) = 0 \end{cases} \quad \text{and}$$

$$m^*(t) = \begin{cases} 0 \; if \; \phi_m(t) > 0 \\ 1 \; if \; \phi_m(t) < 0 \\ singular \; if \; \phi_m(t) = 0 \end{cases} \quad \textbf{(24)}$$

f) Singular Extremals.

To investigate the singular case, let $\phi_i(t) = 0$ on some interval. In this case the minimum condition (21) does not determine the value of the controls. Instead, the singular controls can be computed by differentiating the switching functions in time until that point of time the control value appears in the derivative, say $\phi^{(k)}(t)$ and then using the obtained equation $\phi^{(k)}(t)$ to get the control. We will then define the singular optimal control if it has the value between 0 and 1. According to [15], he stated that for a single input system that is linear in the control, *k=2r*, and *r* is called the order of the singular arc. This is subjected to vary with time over an interval but when it is constant it forms the necessary condition for optimality of a singular arc of order *r*, which is termed as the Generalized Legendre-Clebsch condition that is given as:

$$(-1)^r = \frac{\partial}{\partial(u)} \frac{d^{2r}}{dt^{2r}} \frac{\partial H}{\partial u} \geq 0 \quad \textbf{(25)}$$

Along the extremals. $\frac{\partial H}{\partial u} = \phi$, Is the switching function for the problem? In summary we have:

$$\frac{d}{dt}\big(\phi_i(t)\big) = 0 \quad \textbf{(26)}$$

Further solving for the value of the singular control if it is not present in equation (26) by obtaining the *2r* derivative that will give optimal controls

$$\frac{d^{2r}}{dt^{2r}}(\phi_i(t)) = 0 \quad \textbf{(27)}$$

To check on the Generalized Legendre-Clebsch (GLC) for the singular control to be optimal, the derivative of $\frac{d^{2r}}{dt^{2r}}(\ \phi_i(t))$ with the respect to the control (v, m) needs to be negative as stated by [15].

$$\frac{\partial}{\partial(v,m)}\ [\frac{d^{2r}}{dt^{2r}}\ (\phi_i(t))] \quad \textbf{(28)}$$

Proof 1: Vaccination

The switching function is given as:

$$\phi_v = a_1 S - \lambda_S \mathrm{S} \quad \textbf{(29)}$$

The derivate is given by

$$\phi'_V = \lambda_I S[\beta_I I + \beta_B B] - a_1 S(\mu + \beta_I I + \beta_B B) \quad \textbf{(30)}$$

If the control variable does not appear in the first derivative, we check on the second derivative to obtain

$$\phi''_v = \lambda_S \beta_I S(\beta_I IS + \beta_B BS) + (\lambda_1 \beta_B S - a_1 \beta_b S)(\xi I - mB - \delta B) + (\lambda_I I\beta_I + \lambda_I \beta_B B - a_1\mu - a_1\beta_I I - a_1\beta_I S)(\Lambda N - \mu S - \beta_I IS - \beta_B BS + \omega R) - \beta_I IS(a_0 - \lambda_N \xi - a_1\xi) + \beta_B BS(a_0 - \lambda_I I(\gamma + \mu + \xi) - \lambda_N \xi - a_1\xi) + a_1\beta_1 S[(\gamma + \mu + \xi) - (\beta_I IS + \beta_B BS)] - vS(\lambda_I \beta_I SI + \lambda_I \beta_B BS - a_1\mu S - a_1\beta_I IS - a_1\beta_B BS) \quad \textbf{(31)}$$

The above equation can be written in the form:

$$\phi''_v = \psi_v(t)v(t) + \psi_1(t) = 0 \quad \textbf{(32)}$$

And solving for the singular control as

$$v_{sing}(t) = -\frac{\psi_1(t)}{\psi_v(t)} \quad \textbf{(33)}$$

If $\psi_v(t) \neq 0$ and $0 \leq -\frac{\psi_1(t)}{\psi_v(t)} \leq 1$

With

$\psi_v(t) = S(\lambda_I \beta_I SI + \lambda_I \beta_B BS - a_1\mu S - a_1\beta_I IS - a_1\beta_B BS$

(34)

And

$\Psi_v(t) = \lambda_S\beta_I S(\beta_I IS + \beta_B BS) + (\lambda_I\beta_B S + a_1\beta_B S)(\xi I - mB - \delta B) + (\lambda_I\beta_I I + \lambda_I\beta_B B - a_1\mu - a_1\beta_I I - a_1\beta_I S)(\Lambda N - \mu S - \beta_I IS - \beta_B BS + \omega R) - \beta_I IS(a_0 - \lambda_N\xi - a_1\xi) + \beta_B BS(-a_0 - \lambda_I\beta_I(\gamma + \mu + \xi) - \lambda_N\xi - a_1\xi) + a_1\beta_I S[(\gamma + \mu + \xi) - (\beta_I IS + \beta_B BS)]$ **(35)**

Thus, the Generalized Legendre-Clebsch Condition (GLC) requires that the following inequality holds for the singular control to be optimal:

$\frac{\partial}{\partial v}\left[\frac{d^2}{dt^2}\phi_v\right] = -S(\lambda_I\beta_I IS + \lambda_I\beta_B SB - a_1\mu - a_1\beta_B BS - a_1\beta_I IS)$ **(36)**

Therefore, the control characterization is given as:

$$v^*(t) = \begin{cases} 0 \; if \; \phi_v(t) > 0 \\ 1 \; if \; \phi_v(t) < 1 \\ singular \; if \; \phi_v(t) = -\frac{\Psi_1(t)}{\Psi_v(t)} \end{cases} \quad \textbf{(37)}$$

Thus, the control is optimal at t only if $\phi_v(t) = 0$ and $0 \leq -\frac{\Psi_1(t)}{\Psi_v(t)} \leq 1$

Proof 2: Sanitation

$\phi_m = a_2 B - \lambda_B B$

The derivative is

$\phi'_m = \lambda_I\beta_B BS - \lambda_S\beta_B BS - a_2\delta B$ **(38)**

Obtaining the second derivative

$\phi''_m = -mB(\lambda_I\beta_B S - \lambda_S\beta_B S - a_2\delta B) + (\lambda_I\beta_B S - \lambda_S\beta_B S)(\xi I + \Lambda N + \omega R) + \beta_B BS(a_0 + a_1 v + \lambda_S\beta_I S - \lambda_I\beta_I S + \lambda_S\beta_B S + \lambda_I\beta_B B + \lambda_I I(\gamma + \mu + \xi) + \lambda_N\xi - a_2\xi + a_2\xi\delta + \lambda_S\beta_B\delta SB)$ **(39)**

The above equation can be written in the form:

$\phi''_m = \psi_m(t)m(t) + \psi_2(t) = 0$ **(40)**

And solving for the singular control as

$m_{sing}(t) = -\frac{\psi_2(t)}{\psi_m(t)}$ **(41)**

If $\psi_m(t) \neq 0$ and $0 \leq -\frac{\psi_2(t)}{\psi_m(t)} \leq 1$

$\psi_m(t) = B(\lambda_I\beta_B S - \lambda_S\beta_B S - a_2\delta B)$ **(42)**

And

$\psi_2(t) = (\lambda_I\beta_B S - \lambda_S\beta_B S)(\xi I + \Lambda N + \omega R) + \beta_B BS(a_0 + a_1 v + \lambda_S\beta_I S - \lambda_I\beta_I S + \lambda_S\beta_B S + \lambda_I\beta_B B + \lambda_I I(\gamma + \mu + \xi) + \lambda_N\xi - a_2\xi + a_2\xi\delta + \lambda_S\beta_B\delta SB)$ **(43)**

Thus, the Generalized Legendre-Clebsch Condition (GLC) requires that the following inequality holds for the singular control to be optimal

$$\frac{\partial}{\partial m}\left[\frac{d^2}{dt^2}\phi_m(t)\right] = -B(\lambda_I\beta_B S - \lambda_S\beta_B S - a_2\delta B) \quad \textbf{(44)}$$

Therefore, the control characterization is given as:

$$m^*(t) = \begin{cases} 0 \; if \; \phi_m(t) > 0 \\ 1 \; if \; \phi_m(t) < 1 \\ singular \; if \; \phi_m(t) = -\frac{\Psi_2(t)}{\Psi_m(t)} \end{cases} \quad \textbf{(45)}$$

Thus, the control is optimal at t only if $\phi_m(t) = 0$ and $0 \leq -\frac{\Psi_2(t)}{\Psi_m(t)} \leq 1$

Proposition: As per the two cases of linear vaccination and sanitation models, it shows that singular controls are locally optimal.

3. Parameter Estimation

The parameter values used for the analysis are shown below:

Table 1. Parameter and Values

Parameter	Symbol	Values	Source
Recruitment and Natural death rate	Λ and μ	4.108 x 10^{-5}/day	[1]
Immunity waning rate	ω	0.005/day	[16]
Population	N	10000	Assumed
Transmission rate from environment	β_B	0.21/day	[6]
Transmission rate from human-human	β_I	0.02/day	[6]
Recovery rate	γ	0.2/day	[6]
Bacterial concentration in water	B	10^6 cells/ml	[4]
Shedding rate of bacteria by human	ξ	10 cells/ml-day	[6]
Bacterial death rate in the environment	δ	0.03/day	[4]

Using the above estimates in Table 1, the basic reproduction number is estimated:

$$R_0 = \frac{0.20536}{0.0000418+v}\left[0.021 + \frac{2.14}{0.033+m}\right] \quad \textbf{(46)}$$

The above results presented, shows that varying the values of v and m will alter the number of

susceptible and infected persons. For instance, if $v = m = 0$, then $R_O > 1$. Thus the endemic equilibrium is locally asymptotically stable. This implies that if there is no vaccination and sanitation, then the disease will persist and more infection will occur.

If $v = m = 1$, then $R_0 = 0.42973 < 1$,the disease-free equilibrium is locally asymptotically stable. Thus, the disease dies out. In conclusion, R_O decreases as the parameters v and m increases. This means that when more effort is put on vaccination and we also improve the sanitation, then we are lowering rate of infection.

4. Local Stability

Stability analysis of DFE

Applying Jacobian matrix in equation (5) and parameter values estimated, will give the below matrix

$$J = \begin{bmatrix} -(0.00004 + v) - \lambda & -\frac{0.0086}{(0.000041+v)} & -\frac{0.0879}{(0.00004+v)} \\ 0 & \frac{0.0086}{(0.00004+v)} - 10.2 - \lambda & \frac{0.0879}{(0.000041+v)} \\ 0 & 10 & -(0.033 + m) - \lambda \end{bmatrix} \quad \textbf{(47)}$$

One of the eigenvalue obtained from the above matrix is $-(0.00004 + v)$ and the other two roots are calculated as

$$0 = \lambda^2 + \left[\frac{0.0086}{(0.00004+v)} + m - 10.167\right]\lambda - \left(\frac{0.0086}{(0.00004+v)} - 10.2\right)(m + 0.033) - \frac{0.0879}{(0.00004+v)} \quad \textbf{(48)}$$

We apply quadratic method to solve forλ:

$$\lambda_{2,3} = \frac{-w \pm \sqrt{w^2 - 4rk}}{2r} \quad \textbf{(49)}$$

Where

$$\begin{cases} w = \frac{0.0086}{(0.00004+v)} + m - 10.167 \\ k = \left(\frac{0.0086}{(0.00004+v)} - 10.2\right)(m + 0.033) - \frac{0.0879}{(0.00004+v)} \\ r = 1 \end{cases} \quad \textbf{(50)}$$

Disease free equilibrium is asymptotically stable if all the eigenvalues are negative. Hence the disease-free equilibrium is locally asymptotically stable as long as $R_0 < 1$, whereas unstable if $R_0 > 1$

5. Conclusion

On applying Generalized Legendre-Clebsch Condition in equations (34) and (42) respectively, the two theorems for vaccination and sanitation showed that there exists singular control. The condition for the local stability of the model was established, basic reproductive number, and Pontryagin's Maximum Principle applied to characterize the interventions and derived the optimality of the

system. The singular control structures were analyzed though there was a desire to check on the feasible concatenations with bang-bang controls and the numerical analysis. Singular control is expected to lead to a simpler and efficient numerical solution method which when solved will assist scientists to develop appropriate models for a cholera control and to guide public health professionals to make better strategies for controlling the disease.

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REFERENCES

[1] Ali, M., Nelson, A. R., Lopez, A. L., & Sack, D. A. (2015). Updated global burden of cholera in endemic countries. PLoS neglected tropical diseases, 9(6), e0003832.

[2] Capasso, V. and Paveri-Fontana, S. (1979). A mathematical model for the 1973 cholera epidemic in the European Mediterranean region. Revue d'epidemiologie et de Sante' Publique, 27(2):121-132

[3] Codeço, C. T. (2001). Endemic and epidemic dynamics of cholera: the role of the aquatic reservoir. BMC Infectious diseases, 1(1):1.

[4] Gaff, H., & Schaefer, E. (2009). Optimal control applied to vaccination and treatment strategies for various epidemiological models. *Mathematical biosciences and engineering: MBE*, *6*(3), 469-492.

[5] Hartley, D. M., Morris Jr, J. G., & Smith, D. L. (2005). Hyperinfectivity: a critical element in the ability of V. cholerae to cause epidemics? *PLoS medicine*, *3*(1), e7.

[6] Hethcote, H. W. (2000). The mathematics of infectious diseases. *SIAM review*, *42*(4), 599-653.

[7] Krener, A. J. (1977). The high order maximal principle and its application to singular extremals. *SIAM Journal on Control and Optimization*, *15*(2), 256-293.

[8] Ledzewicz, U., & Schättler, H. (2011). On optimal singular controls for a general SIR-model with vaccination and treatment. *Discrete and Continuous Dynamical Systems*, *2*, 981-990.

[9] Li, M. Y., & Wang, L. (1998). A criterion for stability of matrices. *Journal of mathematical analysis and applications*, *225*(1), 249-264.

[10] Maurer, H., & De Pinho, M. D. R. (2014). Optimal Control of Epidemiological SEIR models with L1-Objectives and Control-State Constraints.

[11] Mukandavire, Z., Liao, S., Wang, J., Gaff, H., Smith, D. L., and Morris, J.G. (2011). Estimating the reproductive numbers for the 2008-2009 cholera outbreaks in Zimbabwe. Proceedings of the National Academy of Sciences, 108(21):8767-8772.

[12] Neilan, R. L. M., Schaefer, E., Gaff, H., Fister, K. R., & Lenhart, S. (2010). Modeling optimal intervention strategies for cholera. *Bulletin of mathematical biology*, *72*(8), 2004-2018.

[13] Nelson, E. J., Harris, J. B., Morris Jr, J. G., Calderwood, S. B., & Camilli, A. (2009). Cholera transmission: the host, pathogen, and bacteriophage dynamic. *Nature Reviews Microbiology*, *7*(10), 693.

[14] Schättler, H., Ledzewicz, U., & Maurer, H. (2014). Sufficient conditions for strong local optimality in optimal control problems with L^2 type objectives and control constraints.*Discrete & Continuous Dynamical Systems-Series B*, *19*(8).

[15] Wang, J., & Modnak, C. (2011). Modeling cholera dynamics with controls. *Canadian applied mathematics quarterly*, *19*(3), 255-273.

[16] Yusuf, T. T., & Benyah, F. (2012). Optimal control of vaccination and treatment for an SIR epidemiological model. *World journal of modelling and simulation*, *8*(3), 194-204.