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Optimal Control and Cost-Effectiveness Analysis for Dysentery Epidemic Model

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Abstract: In this paper, optimal control theory is applied to a system of ordinary differential equations representing a dysentery diarrhea epidemic. Optimal control strategies are proposed to reduce the number of infected humans and the cost of interventions. The Pontryagin's maximum principle is employed to find the necessary conditions for the existence of the optimal controls. Runge-Kutta forward-backward sweep numerical approximation method is used to solve the optimal control system. The incremental cost-effectiveness analysis technique is used to determine the most cost-effective strategy. We observe that the control measure implementing sanitation and education campaign is the most efficient and cost-effective.

Keywords: Dysentery diarrhea, Sensitivity index, Optimal control, Hamiltonian, Cost-effectiveness analysis.

1 Introduction

Mathematical modeling plays an important role in terms of understanding of the underlying mechanisms that influence the spread of the diseases and used as a crucial instrument for the implement of control strategies. Most of the existing epidemic models fall into autonomous and non-autonomous systems. In the first case, intervention strategies are modeled by a constant parameter and the aim is to understand how changes in the parameter values changes the dynamics of the system in the long term. Usually the aim is to determine the best parameter value for a given performance measure. In the second case, intervention strategies vary as a function of time and the aim is to find the best function for a given performance measure. Mathematical control theory is a basic principle which is applicable to solve the latter case [1]. It is developed to determine a control and a state values for a dynamical system in a specified period in order to minimize or maximize a certain goal.

Optimization and optimal control problems have got a lot of attention from researchers all over the globe. For instance, Hailay Berhe [2] have solved constrained optimization problems using penalty function methods and Blayneh, Kbenesh and Cao, Yanzhao [3] presented an autonomous ordinary differential equation model with vector control and treatment model, and a time-dependent counter part of the model involving an optimal control of vector-borne diseases with treatment and prevention as control measures. Furthermore, Makinde and Okosun [4] presented the impact of chemotherapy on optimal control strategies on malaria transmission with infective immigrants. Recently, the authors in [5] applied optimal control theory on HIV-TB co-infection model and Okosun and Makinde [6] studied the co-infection model of malaria and cholera diseases with optimal control. However, all of these studies failed to include a cost-effectiveness analysis of the intervention methods employed.

The present paper aims to develop an optimal control epidemic model of dysentery diarrhea. More specifically, the system is formulated as an optimal control problem by implementing continuous controls treatment, environmental sanitation and health education for changes in personal hygienic practices. Pontryagin's maximum principle is used to find the necessary condition for the controls to be optimal. The study compares different control strategies and recommends the best control strategy in terms of cost-effectiveness in a relatively short period.

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This paper is organized as follows. After this introduction Section 2 presents the system framework, and further formulated as an optimal control problem. The numerical method is given in Section 3. In Section 4, numerical simulation and discussion with given parameter values are performed. Brief conclusion is presented in the last Section.

2 Model formulation

In this section, we formulate and analyse a mathematical model of dysentery diarrhea. The modelled populations include pathogens and humans. The human population is subdivided into three classes. The class of individuals who are susceptible (S), infected humans who can transmit the disease (I), and the number of individuals who have recovered (R). The pathogen population (concentration of shigella dysenteriae) is represented by B. The formulation of the model is based on the following assumptions: disease transmission is multiple pathway. The population is homogeneously mixed. Then rate of recruitment of the susceptible humans by birth or immigration is Λ. The incidence in the human to human interaction is assumed to be standard incidence (frequency dependent) and environment to human is logistic. They are represented respectively by

$$\lambda_h = \frac{\beta_h I}{N} \quad \text{and} \quad \lambda_\beta = \frac{\beta_B B}{K+B}.$$

K is the shigella concentration that yields $25-50\%$ chance of catching dysentery diarrhea [7]. β_B and β_h represent rates of ingesting shigella from contaminated environment and through human to human interaction, respectively. $\beta_h = cq$, where c is the contact rate and q is probability of transmission per contact. Infected humans contribute to the concentration of shigella at a rate of ε. The pathogen population is growing at a rate of σ_1 and its natural death rate is σ_2. We assume that $\sigma_2 - \sigma_1 = \sigma > 0$ represents the net death rate of the pathogen population in the environment [8]. Recovered individuals lose immunity and return to the susceptible class at a rate of α. Infected ones are assumed to recover at a rate of γ, where γ is the rate of natural recovery. The natural death rate of all human classes is μ. The disease-induced death rate is represented by d. All parameters are assumed to be non-negative.

The corresponding systems of differential equations and the description of the parameters are respectively given in (1) and Table (1).

$$\begin{cases} \frac{dS}{dt} = \Lambda + \alpha R - (\lambda_h + \lambda_B + \mu)S, \\ \frac{dI}{dt} = (\lambda_h + \lambda_B)S - (\mu + \gamma + d)I, \\ \frac{dR}{dt} = \gamma I - (\mu + \alpha)R, \\ \frac{dB}{dt} = \varepsilon I - \sigma B, \\ S(0) \geq 0, I(0) \geq 0, R(0) \geq 0, B(0) \geq 0, \end{cases} \tag{1}$$

where $(S(0), I(0), R(0), B(0))$ is the initial value of individuals in each classes. We introduce the time-dependent controls in the model (1) for the aim of controlling dysentery diarrhea and study the strategies that eradicate dysentery epidemic in the community. The system is formulated as an optimal control problem with the following assumptions. The control treatment rate of infected individuals varies with time and denoted by u_1. The control sanitation rate varies with time and is denoted by u_2. We add a third control which is preventive control (Health education and hygiene) and is denoted by u_3. It is assumed that a fraction of susceptible population are being infectious at a rate of $(1-u_3)\lambda I$ and the remaining are still in the susceptible class. Time is specified and is relatively short and is given by $t \in [0, T]$, T is the terminal time.

Table 1: Description of parameters of model (1)

Parameters	Interpretation	Units
Λ	Recruitment rate of susceptible population	Humans Time $^{-1}$
μ	Natural death rate of humans	Time^{-1}
c	Average contact rate between susceptible and infected humans	Time^{-1}
q	Transmission probability per contact	Dimensionless
γ	Natural recovery rate of diarrhea	Time^{-1}
α	Relapse rate of the recovered ones to susceptible	Time^{-1}
d	Disease induced death rate of dysentery diarrhea	Time^{-1}
K	Concentration of Shigella	cells
β_h	Effective transmission rate of diarrhea due to human to human interaction	Time^{-1}
β_B	Effective transmission rate of dysentery diarrhea due to environment to human interaction	Time^{-1}
ε	Pathogen shedding rate	Cells Human^{-1}Time^{-1}
σ_1	Shigella Pathogen growth rate	Time^{-1}
σ_2	Shigella Pathogen death rate	Time^{-1}
σ	Net death rate of Shigella Pathogen	Time^{-1}.

The corresponding state system for the model (1) is given by:

$$\begin{cases} \frac{dS}{dt} = \Lambda + \alpha R - \big((1-u_3)(\lambda_h + \lambda_B) + \mu\big)S, \\ \frac{dI}{dt} = (1-u_3)(\lambda_h + \lambda_B)S - (\mu + \gamma + u_1 + d)I, \\ \frac{dR}{dt} = \big(\gamma + u_1\big)I - (\mu + \alpha)R, \\ \frac{dB}{dt} = \varepsilon I - (\sigma + u_2)B, \\ S(0) \geq 0, I(0) \geq 0, R(0) \geq 0, B(0) \geq 0. \end{cases} \tag{2}$$

It is also further assumed that there is limitations on the maximum rate of treatment, sanitation and prevention controls in a given time period T. Hence, a bounded Lebesgue measurable control set is represented as

$$\mathrm{U} = \left\{ u = (u_1, u_2, u_3),\ 0 \le u_i \le u_{i\max}, i = 1,2,3 \right\}.$$

The aim is to minimize the number of infected humans and pathogen population while minimizing the rate of interventions u_1, u_2 and u_3 in that period. Therefore, the optimal control problem for the model (2) is to minimize the objective functional:

$$J(u) := \int_0^T [g(\phi,u)]dt = \int_0^T [I+B+\frac{a_1u_1^2}{2}+\frac{a_2u_2^2}{2}+\frac{a_3u_3^2}{2}]dt \tag{3}$$

where $\phi = (S,I,R,B)$ solves equation (2) for the specified control u. In the intervention of controls the solution $\phi = (S,I,R,B)$ depends on the controls. $a_i \ge 0$ represents the weights on the benefit and cost. $\frac{a_1u_1^2}{2}$ is minimization of cost of treatment and treatment rate; $\frac{a_2u_2^2}{2}$ is minimization of cost of sanitation and sanitation rate and $\frac{a_3u_3^2}{2}$ is minimization of cost of protection and protection rate [11,12].

The goal is to find an optimal control pair $u^* = (u_1^*, u_2^*, u_3^*)$, such that

$$J(u^*) = \min_U J(u_1,u_2,u_3). \tag{4}$$

The basic setup of the optimal control problem is to check the existence and uniqueness of the optimal controls and to characterize them.

2.1 Existence of the optimal controls

Theorem 2.1 Given $J(u)$ subject to system (2) with $(S_0,I_0,R_0,B_0) \ge (0,0,0,0)$, then there exists an optimal control u^* and corresponding (S^*,I^*,R^*,B^*), that minimizes $J(u)$ over U. The proof is based on the following assumptions given in [9]:

1. The set of controls and corresponding state variables is nonempty.
2. The measurable control set is convex and closed.
3. Each right hand side of the state system is continuous, is bounded above by a sum of the bounded control and the state, and can be written as a linear function of u with coefficients depending on time and the state.
4. The integrand $g(\phi,u)$ of the objective functional is convex.
5. There exist constants $C_1, C_2 > 0$, and $\beta^* > 1$ such that the integrand of the objective functional satisfies $g \ge C_1\left(|u_1|^2+|u_2|^2+|u_3|^2\right)^{\frac{\beta^*}{2}} - C_2$.

Proof.

1. U is an nonempty set of measurable functions on $0 \le T$ with values in real numbers R. The system (2) has bounded coefficients and hence any solutions are bounded on [0,T]. The corresponding solutions for the system (2) exist [10].
2. It suffices to write $U = U_1 \times U_2 \times U_3$. So that $U = U_1 \times U_2 \times U_3$ is bounded and convex $\forall t \in [0,T]$.
3. By definition, each right hand side of system (2) is continuous. All variables S,I,R,B and u are bounded on [0, T]. To prove the boundedness we use the method in [13]. To do so we use the fact that the supersolutions of system (2) given by

$$\begin{cases} \frac{d\bar{S}}{dt} = \Lambda + \alpha\bar{R}, \\ \frac{d\bar{I}}{dt} = (\beta_h+\beta_B)\bar{S}, \\ \frac{d\bar{R}}{dt} = (\gamma+u_1)\bar{I}, \\ \frac{d\bar{B}}{dt} = \varepsilon\bar{I}. \end{cases} \tag{5}$$

are bounded on a finite time interval. System (5) can be written as

$$\phi = \begin{bmatrix} S' \\ I' \\ R' \\ B' \end{bmatrix} = \begin{bmatrix} 0 & 0 & \alpha & 0 \\ (\beta_h+\beta_B) & 0 & 0 & 0 \\ 0 & \gamma+u_1 & 0 & 0 \\ 0 & \varepsilon & 0 & 0 \end{bmatrix} \begin{bmatrix} \bar{S} \\ \bar{I} \\ \bar{R} \\ \bar{B} \end{bmatrix} + \begin{bmatrix} \Lambda \\ 0 \\ 0 \\ 0 \end{bmatrix}. \tag{6}$$

The system is linear in finite time with bounded coefficients, then the supersolutions $\bar{S}$, $\bar{I}$, $\bar{R}$, and $\bar{B}$ are uniformly bounded. Since the solution to each state equation is bounded, we see that,

$$\begin{aligned} \left| f(t,\phi,u) \right| &\le \left| \begin{bmatrix} 0 & 0 & \alpha & 0 \\ (\beta_h+\beta_B) & 0 & 0 & 0 \\ 0 & \gamma+u_1 & 0 & 0 \\ 0 & \varepsilon & 0 & 0 \end{bmatrix} \begin{bmatrix} \bar{S} \\ \bar{I} \\ \bar{R} \\ \bar{B} \end{bmatrix} \right| + \left| \begin{bmatrix} \Lambda \\ 0 \\ 0 \\ 0 \end{bmatrix} \right| + \left| I \begin{bmatrix} 0 \\ 0 \\ u_1 \\ 0 \end{bmatrix} \right| \\ &\le K_1|\phi| + I|u_1| + K_2 \end{aligned}$$

where K_1 depends on the coefficients of the system. Thus, the assumption holds.

4. Let $\varpi \in [0,1]$ and $v = (v_1,v_2,v_3) \in U$, and $w = (w_1,w_2,w_3) \in U$, we have

$$\begin{aligned} & g(\phi,(1-\varpi)v+\varpi w) - ((1-\varpi)g(\phi,v)+\varpi g(\phi,w)) \\ &= \frac{a_1}{2}\left((1-\varpi)^2v_1^2+2\varpi(1-\varpi)v_1w_1+\varpi^2w_1^2\right) \\ &+ \frac{a_2}{2}\left((1-\varpi)^2v_2^2+2\varpi(1-\varpi)v_2w_2+\varpi^2w_2^2\right) \\ &+ \frac{a_3}{2}\left((1-\varpi)^2v_3^2+2\varpi(1-\varpi)v_3w_3+\varpi^2w_3^2\right) \\ &- \left((1-\varpi)(\frac{a_1}{2}v_1^2+\frac{a_2}{2}v_2^2++\frac{a_3}{2}v_2^3)\right) \\ &- \varpi\left(\frac{a_1}{2}w_1^2+\frac{a_2}{2}w_2^2++\frac{a_3}{2}w_3^2\right) \\ &= (\varpi^2-\varpi)\left(\frac{a_1}{2}(v_1-w_1)^2+\frac{a_2}{2}(v_2-w_2)^2+\frac{a_3}{2}(v_3-w_3)^2\right) \\ &= \frac{(\varpi^2-\varpi)}{2}\left((v-w)^2\right) \le 0. \end{aligned}$$

Hence
$g(\phi,(1-\varpi)v+\varpi w) \le ((1-\varpi)g(\phi,v)+\varpi g(\phi,w))$.
Thus, the assumption holds.

5.Finally,

$$g(\phi,u) = I+B+\frac{a_1u_1^2}{2}+\frac{a_2u_2^2}{2}+\frac{a_3u_3^2}{2} \ge \frac{C_1}{2}\left(u_1^2+u_2^2+u_3^2\right)-C_2$$

where $C_1 = \min\{a_1,a_2,a_3\}$, $\beta^* = 2$, $C_2 > 0$. Thus, this assumption is justified. □

Therefore, the optimal control u exists.

2.2 Characterization of the optimal controls

The represntation of the optimal controls relies on Pontryagin's maximumum principle [14]. To apply this we need to convert the optimal control problem into a problem of minimizing point-wise a Hamiltonian, H, with respect to u. The Hamiltonian associated to our problem is:

$$\begin{aligned} H(\phi,u,\lambda) &= I+B+\frac{a_1u_1^2}{2}+\frac{a_2u_2^2}{2}+\frac{a_3u_3^2}{2} \\ &+ \lambda_1\Big(\Lambda+\alpha R-((1-u_3)(\lambda_h+\lambda_B)+\mu)S\Big) \\ &+ \lambda_2\Big((1-u_3)(\lambda_h+\lambda_B)S-(\mu+\gamma+u_1+d)I\Big) \\ &+ \lambda_3\Big((\gamma+u_1)I-(\mu+\alpha)R\Big) \\ &+ \lambda_4\Big(\varepsilon I-(\sigma+u_2)B\Big). \end{aligned} \tag{7}$$

Based on [15], if the control u^* and the corresponding state ϕ^* are an optimal couple, necessarily there exists a non-trivial adjoint vector $\lambda = (\lambda_1,\lambda_2,\lambda_3,\lambda_4)$ satisfying the following equality

$$\begin{cases} \frac{d\phi}{dt} = \frac{\partial H(\phi,u,\lambda)}{\partial\lambda}, \\ \frac{d\lambda}{dt} = -\frac{\partial H(\phi,u,\lambda)}{\partial\phi}, \ , \\ \frac{\partial H(\phi,u,\lambda)}{\partial u} = 0. \end{cases}$$

which gives after derivation

$$\begin{cases} u_i^* = 0, & \text{if} \quad \frac{\partial H}{\partial u_i} < 0, \\ 0 \le u_i^* \le u_{i\max}, & \text{if} \quad \frac{\partial H}{\partial u_i} = 0, \\ u_i^* = u_{i\max}, & \text{if} \quad \frac{\partial H}{\partial u_i} > 0. \end{cases}$$

Now we apply the necessary conditions to the Hamilton function, H.

Theorem 2.2. Given an optimal control u^* and a solution to the corresponding state (2), ϕ^*, then there exist an adjoint vector λ and this satisfies the following adjoint equation:

$$\begin{cases} \frac{d\lambda_1}{dt} = \big((1-u_3)f_1+\mu\big)\lambda_1-\big((1-u_3)f_1\big)\lambda_2, \\ \frac{d\lambda_2}{dt} = -1+\big((1-u_3)f_2S\big)\lambda_1 \\ -\big((1-u_3)f_2S-(\mu+d+\gamma+u_1)\big)\lambda_2-\big(\gamma+u_1\big)\lambda_3-\varepsilon\lambda_4, \\ \frac{d\lambda_3}{dt} = -\alpha\lambda_1+\big(\mu+\alpha\big)\lambda_3, \\ \frac{d\lambda_4}{dt} = -1+(1-u_3)Sf_3\lambda_1-(1-u_3)Sf_3\lambda_2+(\sigma+u_2)\lambda_4, \\ \text{where} \\ f_1 = \frac{(\lambda_h+\lambda_B)N-\lambda_hS}{N}, \quad f_2 = \frac{\beta_h-\lambda_h}{N}, \quad f_3 = \frac{\beta_BK}{(K+B)^2}, \\ \lambda_i(T) = 0, i = 1,\cdots,4. \end{cases} \tag{8}$$

$\lambda_i(T) = 0$ is the transvelsality condition. Moreover, the optimal control u^* is given by

$$\begin{aligned} u_1^* &= \min\left\{\max\left\{\frac{(\lambda_2-\lambda_1)I}{a_1},0\right\},u_{1\max}\right\}, \\ u_2^* &= \min\left\{\max\left\{\frac{\lambda_4B}{a_2},0\right\},u_{2\max}\right\}, \\ u_3^* &= \min\left\{\max\left\{\frac{S(\lambda_h+\lambda_B)(\lambda_2-\lambda_1)}{a_3},0\right\},u_{3\max}\right\}. \end{aligned} \tag{9}$$

Proof. The adjoint equation (refadjoint:eq) is found by differentiating the Hamiltonian (7) with respect to $\phi = (S,I,R,B)$. That is $\frac{d\lambda}{dt} = -\frac{\partial H(\phi,u,\lambda)}{\partial\phi}$.

Assuming that the final states $S(T),I(T),R(T),B(T)$ are free we get the transversality conditions $\lambda(T) = 0$. The optimal controls u are found from the optimality conditions and using the property of the control space U. The optimality condition of the Hamiltonian gives $\frac{\partial H}{\partial u} = 0$. That is

$$\frac{\partial H}{\partial u_1} = a_1u_1+\lambda_1I-\lambda_2I = 0 \Rightarrow u_1^* = \frac{(\lambda_2-\lambda_1)I}{a_1}.$$
$$\frac{\partial H}{\partial u_2} = a_2u_2-\lambda_4B = 0 \Rightarrow u_2^* = \frac{\lambda_4B}{a_2}.$$
$$\frac{\partial H}{\partial u_3} = a_3u_3+\lambda_1\lambda S-\lambda_2\lambda S = 0 \Rightarrow u_3^* = \frac{(\lambda_2-\lambda_1)(\lambda_h+\lambda_B)S}{a_3}.$$

And using the property of the control space U, the controls are given as

$$u_1^* = \begin{cases} 0, & \text{if} \quad (\lambda_2-\lambda_1)I < 0, \\ u_1^*, & \text{if} \quad 0 \le (\lambda_2-\lambda_1)I \le a_1u_{1\max}, \\ u_{1\max}, & \text{if} \quad (\lambda_2-\lambda_1)I > a_1u_{1\max}. \end{cases}$$

$$u_2^* = \begin{cases} 0, & \text{if} \quad \lambda_4B < 0, \\ u_2^*, & \text{if} \quad 0 \le \lambda_4B \le a_2u_{2\max}, \\ u_{2\max}, & \text{if} \quad \lambda_4B > a_2u_{2\max}. \end{cases}$$

and

$$u_3^* = \begin{cases} 0, & \text{if} \quad (\lambda_2-\lambda_1)(\lambda_h+\lambda_B)S < 0, \\ u_3^*, & \text{if} \quad 0 \le (\lambda_2-\lambda_1)(\lambda_h+\lambda_B)S \le a_3 u_{3\max}, \\ u_{3\max}, & \text{if} \quad (\lambda_2-\lambda_1)(\lambda_h+\lambda_B)S > a_3 u_{3\max}. \end{cases}$$

This can be rewritten in compact notation as equation (9). □

Next, we check the optimal control and we find that it is indeed a minimum one by checking the condition $\frac{\partial^2 H}{\partial u^2} > 0$. The second derivative of the Hamiltonian is:

$$\frac{\partial^2 H}{\partial u^2} = \begin{bmatrix} 2 & 0 & 0 \\ 0 & 2 & 0 \\ 0 & 0 & 2 \end{bmatrix}.$$

Since this matrix is positive definite the optimal control is a minimizer.

2.3 The optimality system

The optimality system consists of the state system (6) with its initial conditions coupled with the adjoint system (8) with its transversality conditions together with the characterization of the optimal controls. It is presented as follows.

$$\begin{cases} \frac{dS}{dt} = \Lambda + \alpha R - ((1-u_3)(\lambda_h+\lambda_B)+\mu)S, \\ \frac{dI}{dt} = (1-u_3)(\lambda_h+\lambda_B)S - (\mu+\gamma+u_1+d)I, \\ \frac{dR}{dt} = (\gamma+u_1)I - (\mu+\alpha)R, \\ \frac{dB}{dt} = \varepsilon I - (\sigma+u_2)B, \\ S(0) \ge 0, I(0) \ge 0, R(0) \ge 0, B(0) \ge 0 \\ \frac{d\lambda_1}{dt} = ((1-u_3)f_1+\mu)\lambda_1 - ((1-u_3)f_1)\lambda_2, \\ \frac{d\lambda_2}{dt} = -1 + ((1-u_3)f_2 S)\lambda_1 \\ -((1-u_3)f_2 S - (\mu+d+\gamma+u_1))\lambda_2 \\ -(\gamma+u_1)\lambda_3 - \varepsilon\lambda_4, \\ \frac{d\lambda_3}{dt} = -\alpha\lambda_1 + (\mu+\alpha)\lambda_3, \\ \frac{d\lambda_4}{dt} = -1 + (1-u_3)S f_3 \lambda_1 - (1-u_3)S f_3 \lambda_2 + (\sigma+u_2)\lambda_4, \\ \text{where} \\ f_1 = \frac{(\lambda_h+\lambda_B)N - \lambda_h S}{N}, \quad f_2 = \frac{\beta_h - \lambda_h}{N}, \quad f_3 = \frac{\beta_B K}{(K+B)^2}, \\ \lambda_i(T) = 0, i = 1, \cdots, 4 \end{cases} \tag{10}$$

2.4 Uniqueness of the optimality system

In order to successively discuss uniqueness of the optimality system we notice that the adjoint system (8) is also linear in λ_i for i = 1, 2, 3, 4 with bounded coefficients. Thus, there exists a $M > 0$ such that $|\lambda_i(t)| < M$ for i = 1, 2,3, 4 on [0,T].

Theorem 2.3. ([16]) For T sufficiently small the solution to the optimality system (2) is unique.

Solving equation (10) analytically is not practical. Consequently, we have to use numerical algorithm to find the optimal control pairs ϕ^* and u^*.

3 Numerical methods

To solve the optimal controls and states, we use the Runge-Kutta numerical method using MATLAB program. It needs to solve four-state equations and four adjoint equations. For that, first we solve system (2) with a guess for the controls forward in time and then using the transversality conditions as initial values; the adjoint system (8) is solved backward in time using the current iteration solution of the state system. The controls are updated by using a convex combination of the previous controls and the values from (9). The process continues until the solution of the state equations at the present is very close to the previous iteration values. The algorithm based on [17,5] is used in this paper.

Algorithm:
Result: The optimal solution ϕ^* that solves (2).
Initialization: Set N the number of subdivisions, h the step size, $t = [0, T]$, tolerance δ, ϕ_{old}=ϕ_0, $\lambda_{old} = \lambda = 0$, $\mathbf{u} = u_{old}$, $err = \frac{||\phi^k - \phi^{k-1}||}{||\phi^k||}$.
while *(err* $< \delta$*)* **do**
  $\phi_{old} \longleftarrow \phi$; $u_{old} \longleftarrow$u; $\lambda_{old} \longleftarrow \lambda$;
  for $i \leftarrow 1$ **to** N **do**
    Solve ϕ forward in time (using a 4th-order Runge-Kutta scheme) for (2) ;
    Using the transversality condition $\lambda = 0$ and the stored values for **u**, ϕ, solve λ backward in time (using a 4th order Runge-Kutta scheme) for (8) ;
  end
  Update $\phi \longleftarrow \phi_{old}$; $\frac{\mathbf{u}_{old}+\mathbf{u}}{2} \longleftarrow \mathbf{u}$; $\lambda \longleftarrow \lambda_{old}$.
end

4 Numerical simulations

In this section, we first present the numerical simulation of the autonomous system (1). Next, the sensitivity of the reproduction number R_0 to the assumed system parameters is analyzed. Finally, an optimal control strategy is designed and presented using different control strategies.

4.1 Numerical simulation of the autonomous system

Numerical simulations of the model (1) show that the disease-free equilibrium is globally stable for some

parameter values. In particular, Figure (1) shows all solution trajectories converge to the disease-free equilibrium $E_0 = (20468, 0, 0, 0)$ as time goes to infinity for $R_0 = 0.9928$. On the other hand, the endemic equilibrium $E^* = (1.7122, 0.0083, 0.0440, 0.0013) \times 10^8$ is globally stable for $R_0 = 768.1821 > 1$ (Figure 2).

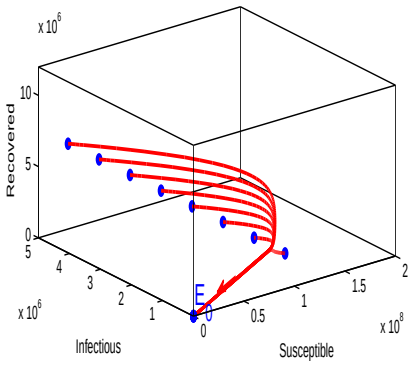

Fig. 1: Disease free solution trajectories. $(S_0, I_0, R_0, B_0) = (93803000, I(0), 2323000, 14000)$, $\Lambda = 325$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, and $I(0) = 100000 : 1000000 : 8000000$.

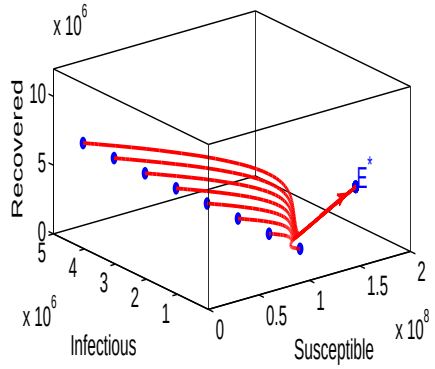

Fig. 2: Endemic solution trajectories. $(S_0, I_0, R_0, B_0) = (93803000, I(0), 2323000, 14000)$, $\Lambda = 3.25 \times 10^6$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, and $I(0) = 100000 : 1000000 : 8000000$.

4.2 Sensitivity analysis of R_0

In determining how best to reduce mortality and morbidity due to the diseases, it is necessary to know the relative importance of the different factors responsible for the transmission and prevalence. The sensitivity of the reproduction number to the given parameters is used to determine the robustness of system predictions to parameter values (since there are usually errors in data collection and presumed parameter values) [18]. Hence, studying its sensitivity is important in system dynamics. A highly sensitive parameter should be carefully estimated, because a small variation in that parameter will lead to large quantitative changes. Less sensitive parameter does not require as much effort to estimate since a small change in that parameter does not result in a big influence in the disease dynamics.

The sensitivity of a variable with respect to system parameters is usually measured by sensitivity index.

Definition 3.1. ([1,18]) The normalized forward sensitivity index of a variable Π that depends differentiably on a parameter θ is defined by

$$\gamma_\theta^\Pi = \frac{\partial \Pi}{\partial \theta} \frac{\theta}{|\Pi|}.$$

Notice that γ_θ^Π has a maximum value of magnitude 1. $\gamma_\theta^\Pi = 1$ implies an increase (decrease) of θ by y% increases (decreases) Π by y%. On the other hand, $\gamma_\theta^\Pi = -1$ indicates an increase (decrease) of θ by y% decreases (increases) Π by y%.

The normalized sensitivity of the reproduction number with respect to the assumed parameters is given in Table (2).

Table 2: Sensitivity indices of R_0

Parameter	Sensitivity indices of R_0
Λ	$\varphi_\Lambda^{R_0} = 0.8692$
β_h	$\varphi_{\beta_h}^{R_0} = 0.1308$
β_B	$\varphi_{\beta_B}^{R_0} = 0.8692$
K	$\varphi_K^{R_0} = -0.4996$
μ	$\varphi_\mu^{R_0} = -0.8692$
γ	$\varphi_\gamma^{R_0} = -0.9712$
d	$\varphi_d^{R_0} = -0.0102$
ε	$\varphi_\varepsilon^{R_0} = 0.8692$
σ	$\varphi_\sigma^{R_0} = -0.4996$

4.3 Numerical simulation of the optimal control problem

Next we discuss numerical results of system (2) to show the effect of various control strategies on the spread of dysentery diarrhea. We assume the following conditions: $(S(0), I(0), R(0), B(0)) = (93803000, 448000, 2323000, 14000)$, $a_1 = a_2 = a_3 = 500$, and $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

4.3.1 Strategy one: Implementing treatment (u_1), sanitation (u_2) and education campaign (u_3).

There is a pronounced difference in the number of infectious with and without controls (Figure 3). More precisely, the total number of infectious group with controls and without controls at the end of the period is 9530 and 502030 respectively. To achieve this, the control profiles u_2 and u_3 are implemented at a maximum rate for the whole period. The control u_1 is at a maximum level for 6.5 years and declines afterwards to zero (Figure 4).

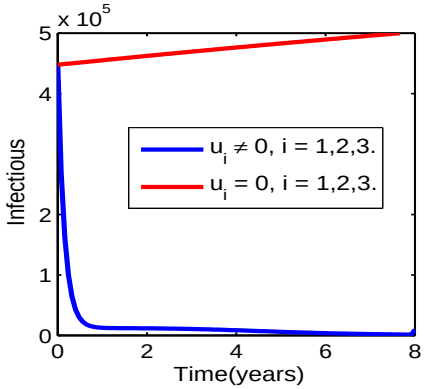

Fig. 3: Time series of infectious.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

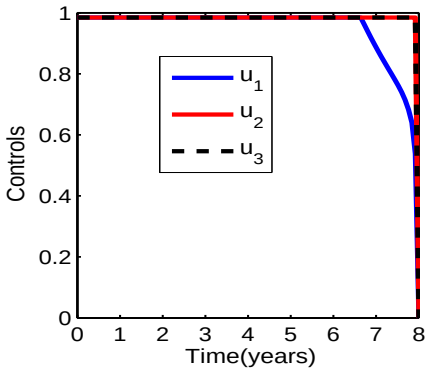

Fig. 4: Control profiles u_1, u_2, u_3.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

4.3.2 Strategy two: Implementing treatment (u_1), sanitation (u_2).

The number of infectious individuals at the end of the period is 429220 (Figure 5). There appears a marginal difference on the implementation of both controls. The implementation of both controls is decreased by 8% (Figure 6).

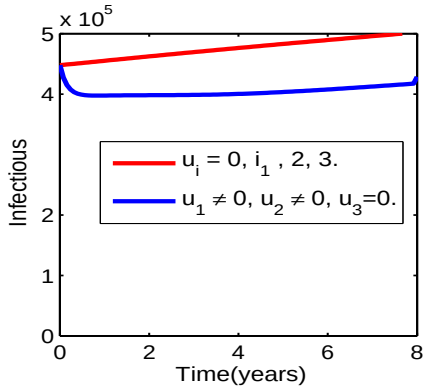

Fig. 5: Time series of infectious.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

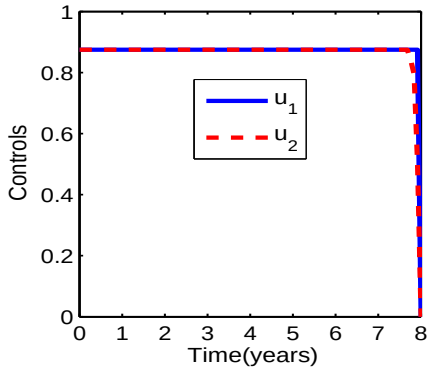

Fig. 6: Control profile when $u_3 = 0$. In this case the initial value is $(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

4.3.3 Strategy three: Implementing treatment (u_1) and education campaign (u_3).

The number of infectious individuals at the end of the period is decreased to 111390 (7). However, the implementation of u_1 is increased to the maximum capacity between 6.5 years and the end of the period (Figure 8).

4.3.4 Strategy four: Implementing sanitation (u_2) and education campaign (u_3).

The number of infectious individuals at the end of the period dramatically dropped to 11660 (Figure 9). There appears no pronounced difference on the implementation of both controls as compared to Strategy three (Figure 10).

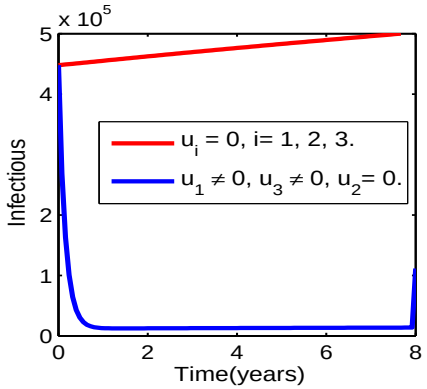

Fig. 7: Time series of infectious.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

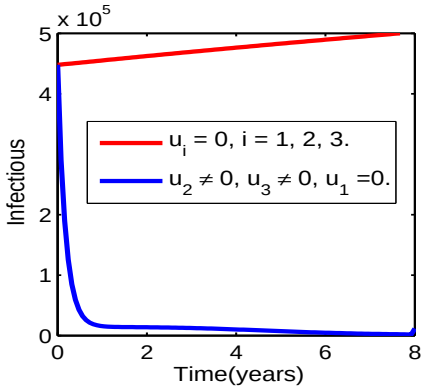

Fig. 9: Time series of infectious.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

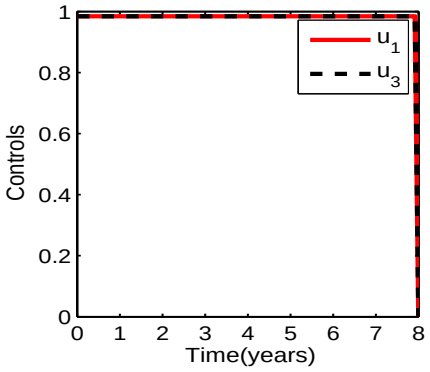

Fig. 8: Time series of infectious. Control profile when $u_2 = 0$.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

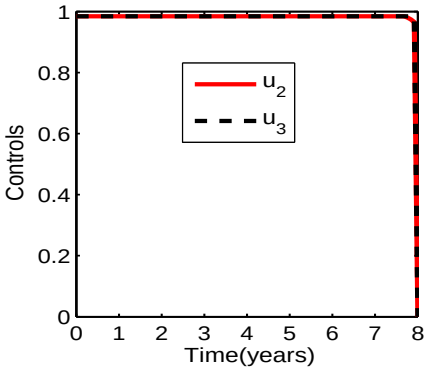

Fig. 10: Control profile when $u_1 = 0$.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

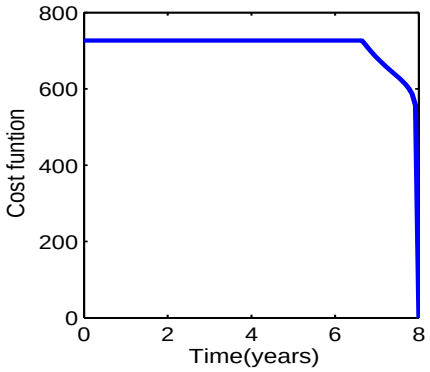

Fig. 11: Cost function with all controls.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

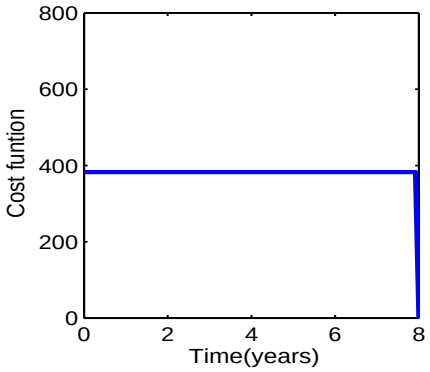

Fig. 12: Cost function when $u_3 = 0$.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

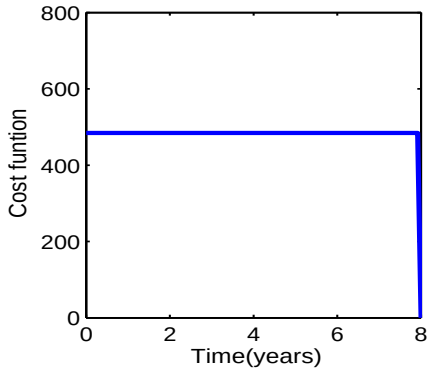

Fig. 13: Cost function when $u_2 = 0$.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

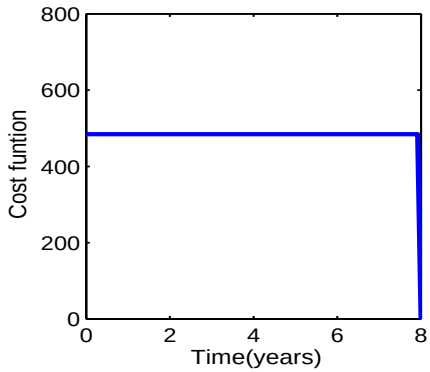

Fig. 14: Cost function when $u_1 = 0$.
$(S_0, I_0, R_0, B_0) = (93803000, 448000, 2323000, 14000)$, $\Lambda = 3246384.83297$, $\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$, $u_{1\max} = u_{2\max} = u_{3\max} = 1$.

4.3.5 Strategy five: the effect of other cost functional.

We see the effect of using other cost functional in the optimal control problem. We target minimization of the dysentery diarrhea infectious only equation (11). The objective functional considered is given as:

$$C(u_1, u_2, u_3) = \int_0^T [I + \frac{a_1 u_1^2}{2} + \frac{a_2 u_2^2}{2} + \frac{a_3 u_3^2}{2}]dt. \quad (11)$$

The number of dysentery diarrhea infectious humans when we consider equation (5) and (11) are 9500 and 9530 respectively. Thus, the objective functional in equation (5) relatively reduces the number of infected humans as compared to (11). For it is plainly demonstrable from (Figures 16,17,18) there is no significant difference on the implementation of the controls.

5 Cost-effectiveness analysis

Cost-effectiveness analysis is a method used to compare the cost benefits of implementing the control strategies implemented in Subsection (4.3). The total cost implemented during the entire period is:

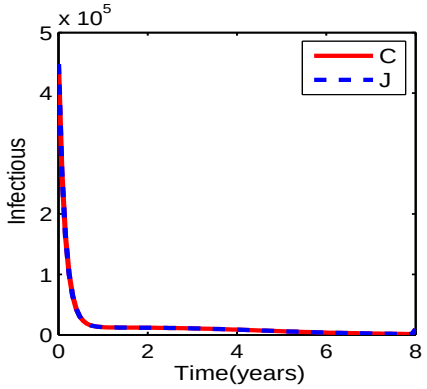

Fig. 15: Time series of infectious. $(S(0),I(0),R(0),B(0)) = (93803000,448000,2323000,14000)$, $\Lambda = 3246384.83297$, $c\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$.

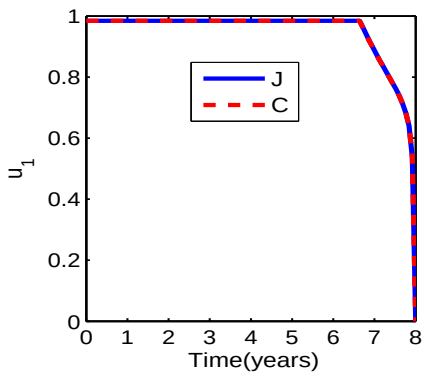

Fig. 16: Control profile u_1. $(S(0),I(0),R(0),B(0)) = (93803000,448000,2323000,14000)$, $\Lambda = 3246384.83297$, $c\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$.

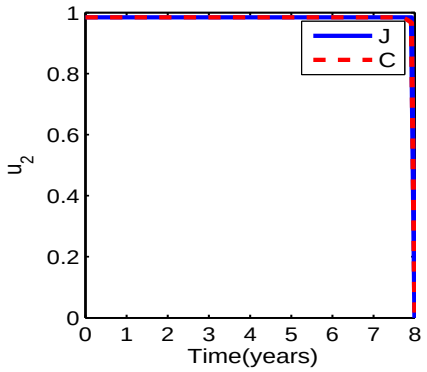

Fig. 17: Control profile u_2. $(S(0),I(0),R(0),B(0))$=$(93803000,448000,2323000,14000)$, $\Lambda = 3246384.83297$, $c\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$.

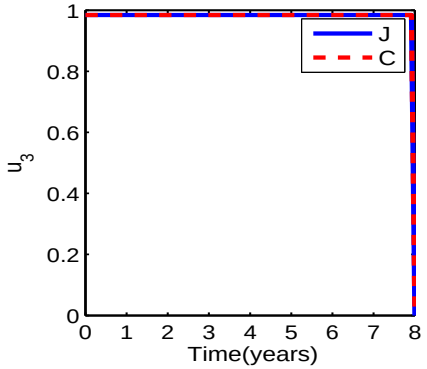

Fig. 18: Control profile u_3. $(S(0),I(0),R(0),B(0)) = (93803000,448000,2323000,14000)$, $\Lambda = 3246384.83297$, $c\beta_h = 0.08233$, $\beta_B = 0.02710$, $K = 196.41519$, $\gamma = 5.10986$, $d = 0.53777$, $\mu = 0.01587$, $\varepsilon = 0.00511$, $\alpha = 0.94871$, $\sigma = 0.03319$, $a_1 = 500$, $a_2 = 500$, $a_3 = 500$.

$$C(u) := \int_0^T [C(\phi,u)]dt = \int_0^T [\frac{a_1u_1^2}{2} + \frac{a_2u_2^2}{2} + \frac{a_3u_3^2}{2}]dt.$$

To calculate the cost-efectiveness analysis, we follow the method applied in [19]. It relies on calculating the incremental cost-effectiveness ratio(ICER). This is defined by the difference in cost between two possible interventions divided by the difference in their outcome, given that they compete for the same resource. Its economic interpretation is the average incremental cost associated with one additional unit of health outcome.

Mathematically

$$\text{ICER} = \frac{\text{Difference in costs in strategies i and j}}{\text{Difference in infected averted in strategies i and j}}.$$

The ICER numerator includes the differences in the costs of disease averted or cases prevented, the costs of intervention(s), and the costs of averting productivity losses among others. The denominator on the other hand is the differences in health outcomes which may include the total number of infections averted in this case.

To implement this, we simulate the model using four intervention strategies. Using these simulation results, the control strategies are ranked in increasing order of effectiveness in terms of the number of infection averted.

The number of infection averted in Strategy two, three, four, and one in an increasing order is given in Table (3).

Table 3: Total infection averted, total cost and ICER.

Strategies	Total infection averted	Total cost	ICER
Strategy two	72810	38281	0.526
Strategy three	390,640	48450	0.032
Strategy four	490410	48450	0
Strategy one	492500	71395	10.98.

$$\text{ICER(two)} = \frac{38281}{72810} = 0.526,$$
$$\text{ICER(one)} = \frac{71395 - 48450}{492500 - 490410} = 10.98,$$
$$\text{ICER(four)} = \frac{48450 - 48450}{490410 - 390640} = 0,$$
$$\text{ICER(three)} = \frac{48450 - 38281}{390,640 - 72810} = 0.032.$$

The comparison between strategies one and two shows a cost saving of 0.526 for strategy two over Strategy one. The lower ICER for Strategy two indicates that Strategy one is strongly dominated. That is, Strategy one is more costly and less effective than Strategy two. Strategy one has to be excluded from the set of alternatives since it consumes limited resources Table (4).

Table 4: ICER in increasing order of total infection averted.

Strategies	Total infection averted	Total cost	ICER
Strategy two	72810	38281	0.526
Strategy three	390,640	48450	0.032
Strategy four	490410	48450	0.

The comparison between strategies three and two shows a cost saving of 0.032 for Strategy three over Strategy two. Strategy two is strongly dominated by Strategy three. That is, Strategy two is more costly and less effective than Strategy three. Therefore, Strategy two is excluded from the set of alternatives so it does not consume limited resources Table (5).

Table 5: ICER in increasing order of total infection averted.

Strategies	Total infection averted	Total cost	ICER
Strategy three	390,640	48450	0.032
Strategy four	490410	48450	0.

With this result, we conclude that Strategy four implementing sanitation (u_2) and education campaign (u_3) has the least ICER and is more cost-effective than Strategy three and the rest strategies.

6 conclusion

We have developed a deterministic model to study the effects of implementing continuous controls on dysentery epidemic model. In this process, we have designed an optimal control problem that minimizes the cost for implementation of the controls while also minimizing the total infected individuals over the intervention interval. First, we have demonstrated that optimal control exists and that it can be portrayed in terms of the solution to the optimality system. We additionally establish the idea that the answer for the optimality system is unique for a sufficiently small time. Next, we have solved the system numerically in an attempt to understand how to eliminate dysentery diarrhea from the community more effectively in a cost-effective way.

Pontryagin's maximum principle is used to find the necessary conditions for the optimal values of the controls that minimize the spread of the disease and cost of implementing controls. The findings from the optimal control problem suggest that the disease may be eradicated by implementing continuous controls in a short period of time. This result shows that the optimal control measure is effective in human and environment and finally we may have disease-free population. In particular, the strategy implementing sanitation of the environment and education campaign is found to be the most cost-effective. However, control policies implementing either of the strategies presented in this paper can reduce the number of infectious in a community.

For future work, it would be interesting to investigate the effect of different objective functionals and variation of the weighting constants in the cost-effectiveness analysis.

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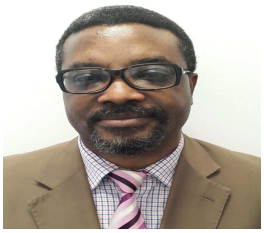

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