

Modelling Cholera Transmission Dynamics with Logistic Growth Through Optimal Vaccination, Treatment and Sanitation

Samson Olaniyi^{1,2}, Tolulope D. Ogunniyi¹, Kazeem O. Okosun³, Ramoshweu S. Lebelo²,
Furaha M. Chuma⁴, Sulaimon F. Abimbade^{1,5}

¹*Department of Pure and Applied Mathematics, Ladoke Akintola University of Technology, Ogbomoso, Nigeria*

²*Department of Applied Physical Sciences, Vaal University of Technology, Vanderbijlpark, South Africa*

³*Pure and Applied Analytics, North-West University, South Africa*

⁴*Department of Physics, Mathematics and Informatics, Dar Es Salaam University College of Education, Univeristy of Dar Es Salaam, Dar Es Salaam, Tanzania*

⁵*Institute of System Science, Durban University of Technology, Durban, South Africa*

*Corresponding author: sfabimbade81@lautech.edu.ng

Abstract. A novel mathematical model for the time-evolution of cholera incorporating pre-exposure vaccination of healthy individuals and logistic bacteria growth is presented and analysed. The nonlinear model is shown to be well-posed in the framework of positivity and boundedness of solutions. With next generation matrix approach, the effective reproduction number, $\mathcal{R}_e$, measuring the extent of cholera spread in an environment comprising susceptible and vaccinated individuals is obtained. The model has a unique cholera-present steady state, indicating possibility of eliminating cholera disease in the environment. Key sensitive parameters fueling transmission dynamics of cholera are identified through sensitivity analysis. Furthermore, three control intervention strategies representing pre-exposure vaccination, $v(t)$, treatment effort, $u_1(t)$, and environmental sanitation effort, $u_2(t)$, are considered in mitigating the transmission of cholera as a consequence of the insights gained from the sensitivity analysis. The existence of the optimal control triple is explicitly proved and characterized through Pontryagin's maximum principle. Consequently, the three control measures are further classified into four different intervention scenarios, namely Scenario Z_1 (implementation of vaccination strategy); Scenario Z_2 (implementation of treatment effort); Scenario Z_3 (implementation of environmental sanitation effort); and Scenario Z_4 (combination of all the three controls). In particular, in-depth efficiency and economic assessments show that Scenario Z_4 is the most efficient and most cost-effective intervention scenario. Therefore, the intervention scenario that significantly averts the cases of cholera disease is strongly recommended.

Received: Oct. 3, 2025.

2020 *Mathematics Subject Classification.* 92B05, 34D20, 34H05.

Key words and phrases. cholera; logistic growth; effective reproduction number; optimal control; efficiency index; cost-effectiveness ratio.

1. INTRODUCTION

Cholera is a severe bacterial infection that has been endangering human lives with a pronounced record of causalities over the years. Early writings from Sushruta, Hippocrates, and Aretaeus recounted the disease's occurrence with its origin from the Ganges Delta region of Asia [1]. It was John Snow's discovery in the 19th century that proved that cholera source was associated with the contaminated water supplied to the people. In 1883, during an epidemic in Egypt, a German biologist, Robert Koch, identified the disease's causative agent as *Vibrio cholerae* [2,3]. There are only two serotypes of *Vibrio cholerae*, namely 01 and 0139, that have caused all current cholera outbreaks and the bacteria are found in salty marine habitat [4,5]. Once ingested, the bacteria passes through the stomach acid barrier in the abdomen, penetrating the mucus lining to enter the intestinal epithelium to colonise it. The bacteria then produces enterotoxins that lead to the discharge of excessive fluids and electrolytes by the epithelial cells and other cholera symptoms in human body [6].

Cholera can be transmitted to human through fecal-oral route due to intake of contaminated water or food and poor sanitation [4,5,7,8]. The time window for the manifestation of the disease in the body system is between 12 hours to 5 days, which may lead to severe watery diarrhoea and ultimately death if left untreated [9–11]. The disease thrives in areas with lack of clean water, overpopulation, improper waste disposal, and poor hygienic environment. The transmission of the cholera disease can mainly be attributed to the interaction between humans and the environment where the pathogen resides [7,12,13]. According to World Health Organization (WHO), about 1.3 – 4 million cholera cases and nearly 21,000 to 143,000 global mortality are recorded annually [5]. In an effort to fully comprehend and efficiently control the transmission dynamics of the infectious disease in human population, mathematical modelling tools can be adopted.

In recent times, mathematical modelling has become an essential tool used by researchers to analyse and understand the mechanisms of cholera transmission dynamics in the population. Through comprehensive evaluation of mathematical models, effective intervention approaches are obtained to give insights into prevention and control of cholera transmission. Notably, in [14], a deterministic mathematical model was developed with control intervention policies to curb the spread of cholera in human population. The authors in [15] designed an optimal control framework for the dynamics of cholera using a simple Susceptible-Infected-Recovered model purposely to control susceptibility by vaccination. With the aid of a robust mathematical model, Maliki and associates [16] studied how the dynamics of cholera can be regulated in the population without spontaneous recovery.

In the same manner, a modified Susceptible-Infected-Recovered epidemic diffusion model was employed in [17] to examine the migration dynamics among susceptible humans within a meta-population structure of two remote cities. The authors in [18] formulated and analysed a mathematical model for cholera transmission integrating vaccination strategy with the main goal of contributing to the efforts in combating the dynamics of the disease. Issam and co-workers [19]

focused on adopting optimal control strategies for curtailing the spread of cholera using a discrete mathematical model. Logistic and Gompertz epidemic models were employed in [20] and fitted to real data of cholera cases in Iraq purposely forecast the future trend of the disease, and hamper its spread using effective control measures. In [21], the influence of medication and environmental sanitation on the transmission dynamics of cholera was studied using a mathematical model governed by a system of ordinary differential equations. Mushanyu and colleagues [22] investigated a multi-drug resistant (MDR) cholera model with stage-switching of two antibiotics to reduce the menace of cholera resistance. A continuous deterministic model was examined by authors in [23] to explore cholera transmission dynamics integrating Susceptible-Infectious-Centers-Recovered-Bacterial. The impact of temperature as a major factor influencing the disease transmission was studied in [24], while Chukwumela and co-workers in [25] stressed on the role of environmental factors and bacterial concentration in cholera transmission using a nonlinear delayed model. A mathematical model studied in [26] was analysed to understand cholera transmission dynamics in Nigeria, considering treatment mechanism as an intervention strategy. In [27], the authors considered a mathematical model that addressed the dynamics of *Vibrio cholerae* within a certain population, incorporating major factors like bacteria growth, treatment, sanitation, and vaccination rates.

At this point, it is noteworthy to state that despite plethora studies dedicated to gain insights into the cholera dynamics in the literature, no single mathematical model has up till this time, to the best of our knowledge, considered the combined effect of time-dependent optimal vaccination, treatment and environmental sanitation efforts on the transmission of cholera with logistic growth. Consequently, this study focuses on the analysis of a novel mathematical model featuring vaccination and logistic growth rate for the time-evolution of cholera with optimal control measures. This study is further organized as follows: Section 2 describes how the mathematical model is formulated for cholera transmission dynamics in the population. Fundamental qualitative properties and analysis of the autonomous nonlinear cholera model are shown in Section 3. In Section 4, rigorous analysis of the non-autonomous form of the model is explored. Efficiency and cost-effectiveness of the control strategies are examined in Section 5. While Section 6 gives the conclusion of the study.

2. CHOLERA MODEL

Let the total human population, represented by $N(t)$, be sub-divided into five compartments, namely susceptible population $S(t)$ (those who are not infected but are vulnerable to cholera disease), exposed human population $E(t)$ (individuals with cholera bacteria without clinical symptoms, i.e., inactive stage of the disease), infectious human population $I(t)$ (those who have contracted the *Vibro cholerae* and are capable of spreading it, i.e., active stage of the disease), class of vaccinated population $V(t)$ (individuals who have received the vaccine and build immunity against the bacteria), and recovered humans represented by $R(t)$ (those who have recovered from

the disease). Thus, the total human population governing the time-evolution of cholera is given by

$$N(t) = S(t) + E(t) + I(t) + V(t) + R(t). \quad (2.1)$$

The population of individuals vulnerable (i.e., susceptible human) to cholera infection is assumed to increase by recruitment of individuals at a rate Λ , and is further increased by loss of immunity from the recovered population at a rate θ . The population starts to diminish due to effective contact with infectious human and *Vibrio cholerae* from the environment, respectively at bilinear incidence rates βSI and βSB , where β is the effective contact rate. In an attempt to manage the threat posed by cholera in the population, a proportion of the susceptible class is vaccinated at a rate, ν , thus leading to a further reduction in the population. The population is finally reduced by natural mortality at a rate μ . As a consequence, the dynamics of the susceptible compartment over time is given by

$$\frac{dS}{dt} = \Lambda - \beta SI - \beta SB - \nu S - \mu S + \theta R. \quad (2.2)$$

The exposed population follows from the effective contact of susceptible humans with infectious human and contaminated environment at bilinear incidence rates βSI and βSB . This population is decreased at a rate α , which is the progression of individuals at the preclinical stage of cholera to the clinical stage of the infection. And the population is further reduced by natural death at a rate μ . Thus, the time-evolution of exposed population over time is given by

$$\frac{dE}{dt} = \beta SI + \beta SB - \alpha E - \mu E. \quad (2.3)$$

As a result of progression of exposed class, the infectious human population is populated. The infectious population reduces due to recovery at a rate τ , and is further reduced by death due to the disease and natural mortality rates δ and μ , respectively. Therefore, the time-evolution of infectious population is given by

$$\frac{dI}{dt} = \alpha E - \tau I - \delta I - \mu I. \quad (2.4)$$

The vaccinated population is generated by the rate ν at which susceptible humans are vaccinated, and reduces due to natural mortality at a rate μ . Thus, the time-evolution of vaccinated compartment is given by

$$\frac{dV}{dt} = \nu S - \mu V. \quad (2.5)$$

The recovered population is developed by recovery of the infectious humans at per capita rate τ . The loss of immunity of recovered humans at a rate θ and natural mortality rate μ reduce the recovered population. Thus, the evolution of this class is given by

$$\frac{dR}{dt} = \tau I - \theta R - \mu R. \quad (2.6)$$

Since the transmission of cholera requires the interaction between human, bacteria, and concentration of *Vibrio cholerae* in the environment at time t , denoted by $B(t)$. Then, the bacteria concentration compartment is developed by the shedding rate of *Vibrio cholerae* by infectious humans to the environment at a rate ϵ . The compartment is increased at a logistic growth rate

$rB(1 - B/c)$, where r is the intrinsic growth of the bacteria and c is the carrying capacity of the bacteria. And the class is reduced by the natural death or decay rate, σ , of the bacteria. Therefore, the rate of change of *Vibrio cholerae* concentration in the environment is given by

$$\frac{dB}{dt} = \epsilon I + rB \left(1 - \frac{B}{c}\right) - \sigma B. \quad (2.7)$$

As a consequence of these assumptions and connecting all the aforementioned equations together, a six-dimensional system of ordinary differential equations describing the time-evolution of cholera transmission dynamics in the presence of environmental contamination with logistic growth rate is obtained. Descriptions of variables and parameters associated with the cholera transmission dynamics are given in Table 1 and Table 2, respectively, while the schematic representation of the flow of cholera transmission via human and environmental routes is shown in Figure 1.

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \beta SI - \beta SB - \nu S - \mu S + \theta R, \\ \frac{dE}{dt} &= \beta SI + \beta SB - \alpha E - \mu E, \\ \frac{dI}{dt} &= \alpha E - \tau I - \delta I - \mu I, \\ \frac{dV}{dt} &= \nu S - \mu V, \\ \frac{dR}{dt} &= \tau I - \theta R - \mu R, \\ \frac{dB}{dt} &= \epsilon I + rB \left(1 - \frac{B}{c}\right) - \sigma B, \end{aligned} \quad (2.8)$$

with non-negative initial conditions,

$$S(0) = S_0, E(0) = E_0, I(0) = I_0, V(0) = V_0, R(0) = R_0, B(0) = B_0. \quad (2.9)$$

TABLE 1. The description of variables of the cholera model (2.8).

Variable	Description
$S(t)$	Population of susceptible humans
$E(t)$	Population of exposed humans
$I(t)$	Population of infectious humans
$V(t)$	Population of vaccinated humans
$R(t)$	Population of recovered humans
$B(t)$	Concentration of <i>Vibrio cholerae</i>

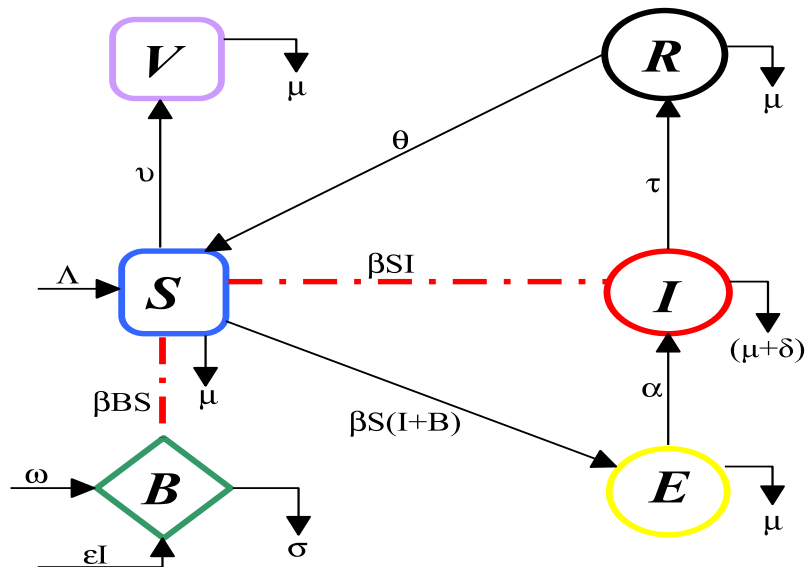


FIGURE 1. Schematic flow of cholera transmission via humans and environmental routes, where $\omega = rB\left(1 - \frac{B}{C}\right)$.

TABLE 2. The description of parameters of the cholera model (2.8).

Parameter	Description
Λ	Recruitment rate
β	Contact rate
ν	Per capita vaccination rate
μ	Per capita natural death rate
θ	Per capita loss of immunity rate
α	Per capita progression rate from exposed to infectious class
τ	Per capita recovery rate
δ	Per capita induced death rate by the infection
ϵ	Shedding rate of <i>Vibrio cholerae</i>
r	Per capita intrinsic growth rate of bacteria concentration
c	Carrying capacity of bacteria
σ	Death or decay rate of <i>Vibrio cholerae</i>

3. MODEL ANALYSIS

This section is dedicated to the qualitative properties and basic analysis of the autonomous nonlinear mathematical model (2.8) describing the transmission dynamics of cholera in the population.

3.1. Invariant region and positivity of solutions.

Lemma 3.1. *The biologically feasible region of the cholera model (2.8), given by*

$$\mathfrak{D} = \left\{ (S, E, I, V, R, B) \in \mathbb{R}_+^6 : S + E + I + V + R \leq \frac{\Lambda}{\mu}; B \leq Q \right\}$$

is positively-invariant and attracting.

Proof. It follows from the rate of change of the total human population, $N(t)$, that

$$\frac{dN}{dt} \leq \Lambda - \mu N.$$

So that

$$N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}),$$

implying that $N(t) \rightarrow \Lambda/\mu$ as $t \rightarrow \infty$. Since each of human compartments is bounded above by Λ/μ , it suffices that the rate of change of *Vibrio cholerae* concentration, $B(t)$, gives

$$\frac{dB}{dt} \leq \epsilon \frac{\Lambda}{\mu} + rB \left(1 - \frac{B}{c} \right) - \sigma B.$$

Using Bernoulli approach, the complementary and particular solutions are, respectively, given by

$$B_C \leq \frac{1}{\frac{r}{(r-\sigma)c} + \left(\frac{(r-\sigma)c - rB(0)}{B(0)(r-\sigma)c} \right) \exp(-(r-\sigma)t)},$$

and

$$B_P \leq \frac{c}{2r}((r-\sigma) \pm \omega), \text{ where } \omega = \left((r-\sigma)^2 + \frac{4r\epsilon\Lambda}{c\mu} \right)^{\frac{1}{2}}.$$

Since $B(t) = B_C + B_P$, the bound Q can be obtained based on the relation between the intrinsic growth rate and decay rate of bacteria concentration as shown hereunder:

- (i) if $r > \sigma$, then $B(t) \rightarrow \left(Q = \frac{3c(r-\sigma)}{2r} \right)$ as $t \rightarrow \infty$.
- (ii) if $r < \sigma$, then $B(t) \rightarrow \left(Q = \frac{c\omega}{2r} \right)$ as $t \rightarrow \infty$.

As a consequence of the bounds for total human population $N(t)$ and bacteria concentration $B(t)$, the biologically feasible region, $\mathfrak{D}$, of the cholera model (2.8) is positively-invariant and attracting, implying that all solutions initiated in $\mathbb{R}_+^6$ eventually enter $\mathfrak{D}$. $\square$

Hence, it is convenient to study the transmission dynamics of the cholera model (2.8) in the region $\mathfrak{D}$, where the model can be considered as being mathematically and epidemiologically well-posed [28].

Theorem 3.1. *The solution set, $\{S(t), E(t), I(t), V(t), R(t), B(t)\}$, of the cholera model (2.8) with positive initial conditions in $\mathfrak{D}$, remains positive in $\mathfrak{D}$ for all time, $t > 0$.*

Proof. The following differential inequality holds from the first equation of the cholera model (2.8)

$$\frac{dS(t)}{dt} \geq -(\beta(I(t) + B(t)) + \nu + \mu) S(t),$$

which by integrating factor approach gives

$$\frac{d}{dt} \left[S(t) \exp \left(\int_0^t (\beta(I(\vartheta) + B(\vartheta)) d\vartheta + (\nu + \mu)t \right) \right] \geq 0, \quad (3.1)$$

so that,

$$S(t) \geq S(0) \exp \left[- \left(\int_0^t (\beta(I(\vartheta) + B(\vartheta)) d\vartheta + (\nu + \mu)t \right) \right] > 0, \quad \text{for all } t > 0.$$

The remaining state variables, $E(t)$, $I(t)$, $V(t)$ and $R(t)$ can be shown following similar approach, while Bernoulli method can be used to show the positivity of $B(t)$ for all time, $t > 0$. $\square$

3.2. Equilibria and threshold quantity.

3.2.1. Disease-free equilibrium (DFE). By definition, disease-free or cholera-free equilibrium is a steady state where cholera is assumed not to exist in the population. So, the cholera-free state of the cholera model, denoted by $\mathcal{E}_0$, is obtained by solving system (2.8) simultaneously at $E(t) = I(t) = B(t) = 0$, so that the cholera-free equilibrium is obtained as

$$\mathcal{E}_0 = (S^*, E^*, I^*, V^*, R^*, B^*) = \left(\frac{\Lambda}{\nu + \mu}, 0, 0, \frac{\Lambda\nu}{\mu(\nu + \mu)}, 0, 0 \right). \quad (3.2)$$

In what follows, an important metric often used in epidemiological modelling to assess the extent of spread of diseases in the population is next explored. Since the cholera model considered in this study features protection of individuals with vaccination, therefore, the epidemiological threshold quantity called effective reproduction number, $\mathcal{R}_e$, of the cholera model (2.8) can be obtained using the next generation operator method [29]. Evaluating matrices F (of the new infection terms) and V (of the transition terms) at the cholera-free equilibrium (3.2), respectively, gives

$$F = \begin{pmatrix} 0 & \frac{\beta\Lambda}{\nu + \mu} & \frac{\beta\Lambda}{\nu + \mu} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} k_1 & 0 & 0 \\ -\alpha & k_2 & 0 \\ 0 & -\epsilon & k_3 \end{pmatrix},$$

where $k_1 = \alpha + \mu$, $k_2 = \tau + \delta + \mu$, and $k_3 = \sigma - r$. Then, the spectral radius of FV^{-1} is the effective reproduction number given by

$$\mathcal{R}_e = \frac{\beta\Lambda\alpha(k_3 + \epsilon)}{k_1k_2k_3(v + \mu)}. \quad (3.3)$$

It is important to note that the effective reproduction number, $\mathcal{R}_e$, of the cholera model (2.8) measures the transmission potential of cholera when an actively infectious human or environmental agent is introduced into a mixed population of susceptible and vaccinated humans [30]. Thus, it suffices to state that the intrinsic growth of bacteria must be less than its decay rate in order to achieve an epidemiologically reasonable effective reproduction number (see, [27]). Then, the next result due to Theorem 2 of [29] establishing the local asymptotic stability of the cholera-free equilibrium is theorized.

Theorem 3.2. *The cholera-free steady state $\mathcal{E}_0$, of the cholera model (2.8) is locally asymptotically stable in $\mathfrak{D}$ if $\mathcal{R}_e < 1$ and unstable otherwise.*

This means that the spread of cholera can be curtailed in the population if the initial sizes of the active cholera cases can be set to the basin of attraction of the cholera-free steady state, such that $\mathcal{R}_e$ is maintained below unity.

3.2.2. Cholera-present equilibrium. Here, the cholera-present or endemic steady state of system (2.8) is obtained in the presence of cholera infection in the population. Let the cholera-present steady state of the model be given by $\mathcal{E}_1 = (S^{**}, E^{**}, I^{**}, V^{**}, R^{**}, B^{**})$ and let the force of infection at steady state be represented by $\lambda^{**} = \beta(I^{**} + B^{**})$. By solving system (2.8) simultaneously in terms of λ^{**} yields

$$\left\{ \begin{array}{l} S^{**} = \frac{\Lambda k_1 k_2 (\theta + \mu)}{\lambda^{**} (k_1 k_2 (\theta + \mu) - \theta \tau \alpha) + k_1 k_2 (\theta + \mu) (v + \mu)}, \\ E^{**} = \frac{\Lambda k_2 (\theta + \mu) \lambda^{**}}{\lambda^{**} (k_1 k_2 (\theta + \mu) - \theta \tau \alpha) + k_1 k_2 (\theta + \mu) (v + \mu)}, \\ I^{**} = \frac{\Lambda \alpha (\theta + \mu) \lambda^{**}}{\lambda^{**} (k_1 k_2 (\theta + \mu) - \theta \tau \alpha) + k_1 k_2 (\theta + \mu) (v + \mu)}, \\ V^{**} = \frac{\Lambda v k_1 k_2 (\theta + \mu)}{\mu (\lambda^{**} (k_1 k_2 (\theta + \mu) - \theta \tau \alpha) + k_1 k_2 (\theta + \mu) (v + \mu))}, \\ R^{**} = \frac{\Lambda \alpha \tau \lambda^{**}}{\lambda^{**} (k_1 k_2 (\theta + \mu) - \theta \tau \alpha) + k_1 k_2 (\theta + \mu) (v + \mu)}, \\ B^{**} = \frac{(k_1 k_2 (\theta + \mu) - (\theta \tau \alpha)) (\lambda^{**})^2 + (k_1 k_2 (v + \mu) - \alpha \beta \Lambda) (\theta + \mu) \lambda^{**}}{\beta (\lambda^{**} (k_1 k_2 (\theta + \mu) - \theta \tau \alpha) + k_1 k_2 (\theta + \mu) (v + \mu))}. \end{array} \right.$$

By algebraic simplification, $k_1 k_2 (\theta + \mu) > \theta \tau \alpha$. It follows, using I^{**} and B^{**} in λ^{**} , that the non-trivial equilibria of the cholera model (2.8) satisfy the polynomial equation given by

$$a_1 (\lambda^{**})^3 + a_2 (\lambda^{**})^2 + a_3 \lambda^{**} + a_4 = 0, \quad (3.4)$$

where,

$$a_1 = r(k_1 k_2 (\theta + \mu) - \theta \tau \alpha)^2,$$

$$a_2 = c\beta k_3 (k_1 k_2 (\theta + \mu))^2 + 2rk_1 k_2 (\theta + \mu)(v + \mu)(k_1 k_2 (\theta + \mu) - \theta \tau \alpha) \times \left(1 - R_e + \frac{\beta \Lambda \alpha \epsilon}{k_1 k_2 k_3 (v + \mu)}\right),$$

$$a_3 = r(\theta + \mu)^2 (\beta \alpha \Lambda - k_1 k_2 (v + \mu))^2 + c\beta k_1 k_2 k_3 (\theta + \mu)(v + \mu)(k_1 k_2 (\theta + \mu) - \theta \tau \alpha)(2 - R_e),$$

$$a_4 = c\beta k_1^2 k_2^2 k_3 (\theta + \mu)^2 (v + \mu)^2 (1 - R_e).$$

It is important to note that the cubic polynomial (3.4) indicates the possibility of multiple endemic equilibrium states for the cholera model. However, it can be observed that the coefficient a_1 of the cubic polynomial is positive with non-negative parameters, whereas coefficients a_2 , a_3 and a_4 are negative whenever $R_e > 1$. Then, by applying Descartes' rule of signs [31], it follows that the cubic polynomial (3.4) has only one positive root whenever the associated effective reproduction number is greater than one. This underscores the importance of the threshold quantity $R_e > 1$ in achieving the existence condition for the cholera-present steady state. It should be mentioned that the existence of a single positive root implies that the cholera model (2.8) has a unique cholera-present steady state.

3.3. Sensitivity analysis. To examine how certain key epidemiological parameters associated with the effective reproduction number, R_e affect the dynamics of cholera in the population, the following normalized forward sensitivity index due to [32] is employed.

$$\Gamma_p^{R_e} = \left(\frac{\partial R_e}{\partial p}\right) \times \left(\frac{p}{R_e}\right), \quad (3.5)$$

where p is any given parameter that is associated with the effective reproduction number R_e . Analysing the sensitivity of parameters in epidemiological modelling of biological processes offers actionable and valuable insights to policymakers in designing effective control policies for combating the threat of infectious diseases in the population. Thus, with the aid of the parameter values provided in Table 3, the sensitivity indices of parameters of the cholera model (2.8) in relation to R_e , are outlined as depicted in Figure 2. One sees that there are parameters with positive and negative sensitivity indices. Notably, increase in parameter with a positive index yields an increase in the value of R_e , while increase in a negative-indexed parameter implies a decrease in R_e . In particular, increasing the value of transmission rate, β , by 10%, will yield a corresponding increase in the value of R_e by 10%. This is signaling prevalence of cholera in the population if

effort is not intensified to interrupt its potential spread, see Figure 3(a) where an increase in the contact rate beyond 2×10^{-4} makes $\mathcal{R}_e$ to go above unity, pushing the population out of the safe zone. In contrast, the effective reproduction number, $\mathcal{R}_e$, is a decreasing function of the parameter, ν , representing vaccination of susceptible individuals. This simply means increasing ν , by 100% will downsize the value of $\mathcal{R}_e$ by 99%. The practical implication of this is that, massive vaccination with potent vaccine capable of fighting against *Vibrio cholerae* will assist in hampering the menace of the disease in the population. This is supported by Figure 3(b), showing that the only condition to have a cholera-free environment is to increase the vaccination rate beyond 55% of the population and bring the value of the effective reproduction number down to the safe zone, where $\mathcal{R}_e$ is below unity.

Moreover, the effects of two important parameters, namely shedding rate of *Vibrio cholerae*, ϵ , and recovery rate, τ , are simultaneously assessed on the effective reproduction number in Figure 4. It can be seen that uninterrupted increase in *Vibrio cholerae* shedding rate will yield a corresponding spontaneous increase in the effective reproduction number, thereby contributing largely to the widespread of cholera. By implication, cholera will continue to persist as long as proper environmental management scheme is not enforced in the population. Whereas, an increase in τ brings down the value of the effective reproduction number, indicating the possibility of eliminating cholera in the population when effective treatment is proffered.

TABLE 3. Sensitivity indices of $\mathcal{R}_e$ relative to its parameters.

Parameters	Values	References	Sensitivity indices
Λ	10	[23,33]	+1.0000
β	0.00011	[34]	+1.0000
ν	0.2	[27]	-0.9997
μ	0.0000548	[33]	-0.0008
α	0.2	[5]	+0.0003
τ	0.2	[34]	-0.9299
δ	0.015	[33]	-0.06975
ϵ	50	[27]	+0.9901
r	0.2	[27]	+0.39604
σ	0.7	Assumed	-1.3861

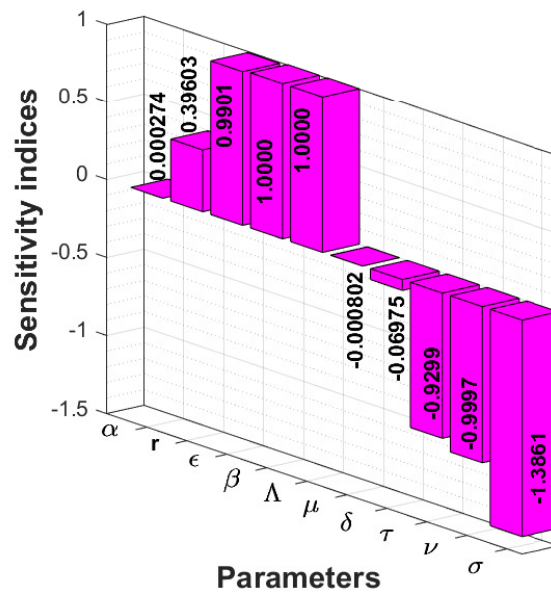


FIGURE 2. Bar plots showing the sensitivity indices of the effective reproduction number relative to its associated parameters.

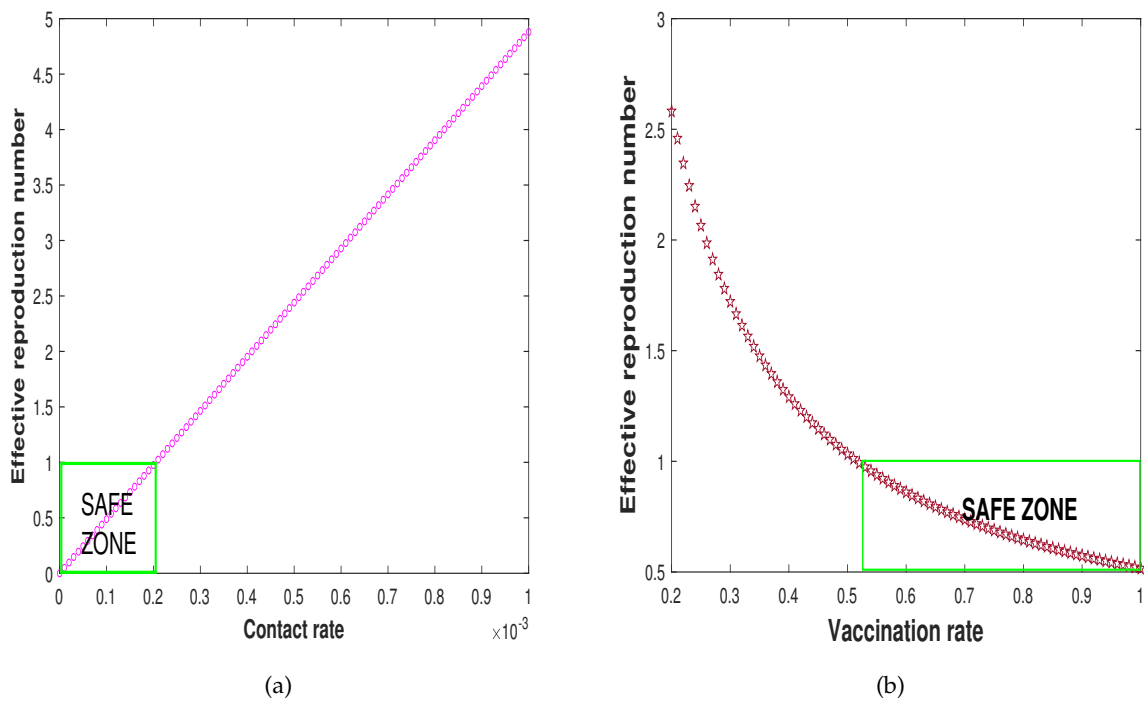


FIGURE 3. Plots showing how effective reproduction number of the cholera model (2.8) is affected by β and ν .

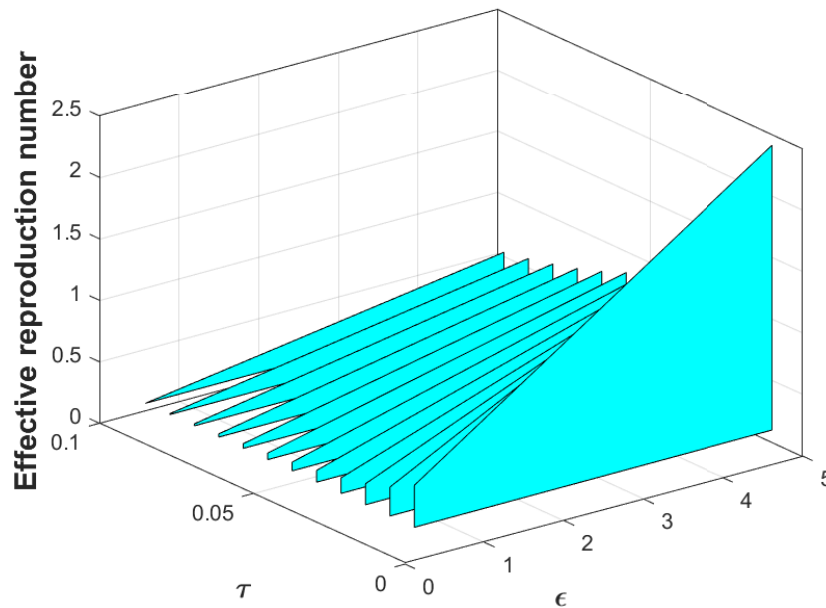


FIGURE 4. 3D plot showing how effective reproduction number of the cholera model (2.8) is affected by shedding rate of *Vibrio cholerae* denoted by ϵ , and recovery rate τ .

4. OPTIMAL CONTROL MODEL AND ANALYSIS

As a consequence of the insights gained from the sensitivity analysis, the autonomous system (2.8) describing the dynamics of cholera is expanded to accommodate time-varying intervention strategies $v(t)$, $u_1(t)$ and $u_2(t)$, leading to a control dynamical system of the form

$$\begin{aligned}
 \frac{dS}{dt} &= \Lambda - \beta SI - \beta SB - v(t)S - \mu S + \theta R \\
 \frac{dE}{dt} &= \beta SI + \beta SB - (\alpha + \mu)E \\
 \frac{dI}{dt} &= \alpha E - (\tau + c_0 u_1(t) + \delta + \mu)I \\
 \frac{dV}{dt} &= v(t)S - \mu V \\
 \frac{dR}{dt} &= (\tau + c_0 u_1(t))I - \theta R - \mu R \\
 \frac{dB}{dt} &= (1 - u_2(t))\epsilon I + rB \left(1 - \frac{B}{c}\right) - \sigma B,
 \end{aligned} \tag{4.1}$$

where $v(t)$ is the time-dependent vaccination for susceptible population, the control variable $u_1(t)$ represents the time-dependent treatment at the rate constant c_0 , and $u_2(t)$ is the time-dependent sanitation effort to fight against shedding rate of *Vibrio cholerae* from infectious humans into the environment.

The performance index also known as the objective functional required to minimize the populations of exposed class, $E(t)$, infectious class, $I(t)$ and concentration of bacteria, $B(t)$, together with the associated costs of applying the three control strategies $v(t)$, $u_1(t)$ and $u_2(t)$, is given by

$$J(u_i) = \int_0^{T_f} (A_1 E(t) + A_2 I(t) + A_3 B(t) + C_1 v^2(t) + C_2 u_1^2(t) + C_3 u_2^2(t)) dt, \quad (4.2)$$

where A_i and C_i , for $i = 1, 2, 3$, are the balancing weight constants and T_f is the proposed final time of the cost implementation. It is of great significance to find an optimal control triple, $u^* = (v^*, u_1^*, u_2^*)$ such that

$$J(u^*) = \min\{J(v, u_1, u_2) : (v, u_1, u_2) \in U\}, \quad (4.3)$$

subject to the non-autonomous system (4.1), where the control set, U , is given by

$$U = \{(v(t), u_1(t), u_2(t)) : 0 \leq v(t), u_1(t), u_2(t) \leq 1; t \in [0, T_f]\}. \quad (4.4)$$

4.1. Existence and characterization of optimal control. This aspect carefully explores the existence of optimal control u^* that simplifies the minimization problem described in (4.3) through the existence result theorized below.

Theorem 4.1. *Given the performance index (4.2) subject to the state system (4.1) with non-negative initial conditions at $t = 0$. Then, there exists an optimal control triple (v^*, u_1^*, u_2^*) such that $J(v^*, u_1^*, u_2^*) = \min\{J(v, u_1, u_2) : (v, u_1, u_2) \in U\}$, provided the following properties are satisfied.*

- (1) The control set U is closed and convex.
- (2) The right-hand side of system (4.1) is continuous and bounded above by a linear functional in state variables and controls.
- (3) The integrand of the performance index (4.2) is convex.
- (4) There exist constants $w_1, w_2 > 0$ and $w_3 > 1$ such that the Lagrangian is bounded below by $w_1(|v|^2 + |u_1|^2 + |u_2|^2)^{w_3/2} - w_2$.

Proof. Proof (1): By definition (4.4), the control set U is closed since each of the controls $v(t)$, $u_1(t)$ and $u_2(t)$ is defined on the interval $[0, 1]$. Now, for arbitrary points $m, n \in U$, where $m = (m_1, m_2, m_3)$ and $n = (n_1, n_2, n_3)$, it follows that

$$\psi m_i + (1 - \psi)n_i \in U, \quad \forall \psi \in [0, 1], \quad i = 1, 2, 3. \quad (4.5)$$

Hence, $\psi m + (1 - \psi)n \in U$, simply means that U is a convex set.

Proof (2): Let the right-hand side of the control dynamical system (4.1) be denoted by $f(t, x, u)$, so

that

$$f(t, x, u) = \begin{pmatrix} \Lambda - \beta SI - \beta SB - v(t)S - \mu S + \theta R \\ \beta SI + \beta SB - (\alpha + \mu)E \\ \alpha E - (\tau + c_0 u_1(t) + \delta + \mu)I \\ v(t)S - \mu V \\ (\tau + c_0 u_1(t))I - (\theta + \mu R) \\ (1 - u_2(t))\epsilon I + rB \left(1 - \frac{B}{c}\right) - \sigma B \end{pmatrix}, \quad (4.6)$$

where $x = (S, E, I, V, R, B)$ and $u = (v, u_1, u_2)$. Then, $f(t, x, u)$ can be written as

$$f(t, x, u) = g(t, x) + h(t, x)u,$$

where

$$g(t, x) = \begin{pmatrix} \Lambda - \beta SI - \beta SB - \mu S + \theta R \\ \beta SI + \beta SB - (\alpha + \mu)E \\ \alpha E - (\tau + \delta + \mu)I \\ -\mu V \\ \tau I - (\theta + \mu)R \\ \epsilon I + rB \left(1 - \frac{B}{c}\right) - \sigma B \end{pmatrix} \quad (4.7)$$

and

$$h(t, x) = \begin{pmatrix} -S & 0 & 0 \\ 0 & 0 & 0 \\ 0 & -c_0 I & 0 \\ S & 0 & 0 \\ 0 & c_0 I & 0 \\ 0 & 0 & -\epsilon I \end{pmatrix}. \quad (4.8)$$

Following the explicit approach given in [35], it can be established that

$$\begin{aligned} \|f(t, x, u)\| &\leq \|g(t, x)\| + \|h(t, x)\| \|u\| \\ &\leq q_1 + q_2 \|u\|, \quad (\text{where } q_1, q_2 > 0). \end{aligned} \quad (4.9)$$

Proof (3): The integrand of the performance index (4.2) also known as the Lagrangian is given as

$$L(t, x, u) = (A_1 E + A_2 I + A_3 B + C_1 v^2 + C_2 u_1^2 + C_3 u_2^2) = g_1(t, x) + h_1(t, u). \quad (4.10)$$

It is necessary to prove the convexity of $h_1(t, u) = (C_1 v^2 + C_2 u_1^2 + C_3 u_2^2)$ on the control variable u . Thus, define an analogous function $p(u) = Cu^2$, where $C > 0$. For any $m, n \in u$ and $\psi \in [0, 1]$, then, it follows from $h_1(t, u)$ that

$$\begin{aligned} p(\psi m + (1 - \psi)n) - (\psi p(m) + (1 - \psi)p(n)) &= C(\psi m + (1 - \psi)n)^2 - C(\psi m^2 + (1 - \psi)n^2) \\ &= C(\psi^2 - \psi)(m^2 + n^2 - 2mn) \\ &= C(\psi^2 - \psi)(m - n)^2 \leq 0, \quad \text{since } \psi \in [0, 1]. \end{aligned}$$

Hence,

$$p(\psi m + (1 - \psi)n) \leq (\psi p(m) + (1 - \psi)p(n)),$$

establishing the definition of a convex function. Therefore, the Lagrangian $L(t, x, u)$ is convex.

Proof (4):

$$\begin{aligned} L(t, x, u) &= (A_1E + A_2I + A_3B + C_1v^2 + C_2u_1^2 + C_3u_2^2) \\ &\geq (C_1v^2 + C_2u_1^2 + C_3u_2^2) \\ &\geq w_1(v^2 + u_1^2 + u_2^2) \frac{w_3}{2} - w_2, \end{aligned}$$

where $w_1 = \min\{C_1, C_2, C_3\}$, $w_2 > 0$ and $w_3 = 2$, completing the proof of the existence of optimal control. $\square$

4.2. Characterization of the optimal control. Herein, the necessary conditions needed to characterize the optimal control triple (v^*, u_1^*, u_2^*) that minimizes the performance index (4.10) are obtained using Pontryagin's maximum principle [36]. Thus, the Hamiltonian, $\mathbb{H}$, for the optimal control problem is given by

$$\begin{aligned} \mathbb{H} = & A_1E + A_2I + A_3B + C_1v^2 + C_2u_1^2 + C_3u_2^2 \\ & + \lambda_1(\Lambda - \beta SI - \beta SB - v(t)S - \mu S + \theta R) \\ & + \lambda_2(\beta SI + \beta SB - (\alpha + \mu)E) \\ & + \lambda_3(\alpha E - (\tau + c_0u_1(t) + \delta + \mu)I) \\ & + \lambda_4(v(t)S - \mu V) \\ & + \lambda_5((\tau + c_0u_1(t))I - (\theta + \mu)R) \\ & + \lambda_6\left((1 - u_2(t))\epsilon I + rB\left(1 - \frac{B}{c}\right) - \sigma B\right), \end{aligned} \quad (4.11)$$

where $\lambda_i, i = 1, 2, \dots, 6$, are referred to as co-state (adjoint) variables associated to the state variables S, E, I, V, R, B of the cholera model (4.1). Then, the following existence result is obtained.

Theorem 4.2. *Given an optimal control triple (v^*, u_1^*, u_2^*) satisfying the minimization problem (4.3), then there exist co-state variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ and λ_6 that preserve the co-state system given by*

$$\begin{aligned} \frac{d\lambda_1}{dt} &= \beta(I + B)(\lambda_1 - \lambda_2) + v(\lambda_1 - \lambda_4) + \mu\lambda_1, \\ \frac{d\lambda_2}{dt} &= \alpha(\lambda_2 - \lambda_3) + \mu\lambda_2 - A_1, \\ \frac{d\lambda_3}{dt} &= \beta S(\lambda_1 - \lambda_2) + (\tau + u_1c_0)(\lambda_3 - \lambda_4) + (\delta + \mu)\lambda_3 - (1 - u_2)\epsilon\lambda_6 - A_2, \end{aligned} \quad (4.12)$$

$$\frac{d\lambda_4}{dt} = v\lambda_4,$$

$$\frac{d\lambda_5}{dt} = \theta(\lambda_4 - \lambda_1) + \mu\lambda_4,$$

$$\frac{d\lambda_6}{dt} = \beta S(\lambda_1 - \lambda_2) + \left(\sigma + \frac{2rB}{c} - r\right)\lambda_6 - A_3,$$

with transversality conditions

$$\lambda_i(T_f) = 0, \quad i = 1, 2, \dots, 6, \quad (4.13)$$

and optimal control characterizations

$$\begin{aligned} v^* &= \max \left\{ 0, \min \left\{ \frac{S(\lambda_1 - \lambda_4)}{2C_1}, 1 \right\} \right\}, \\ u_1^* &= \max \left\{ 0, \min \left\{ \frac{c_0 I(\lambda_3 - \lambda_4)}{2C_2}, 1 \right\} \right\}, \\ u_2^* &= \max \left\{ 0, \min \left\{ \frac{\epsilon I \lambda_6}{2C_3}, 1 \right\} \right\}. \end{aligned} \quad (4.14)$$

Proof. The co-state equations in (4.12) are uniquely determined by partially differentiating the Hamiltonian (4.11) with respect to the associated state variables as follows

$$\frac{d\lambda_1}{dt} = -\frac{\partial \mathbb{H}}{\partial S}, \quad \lambda_1(T_f) = 0; \quad \frac{d\lambda_2}{dt} = -\frac{\partial \mathbb{H}}{\partial E}, \quad \lambda_2(T_f) = 0; \quad \frac{d\lambda_3}{dt} = -\frac{\partial \mathbb{H}}{\partial I}, \quad \lambda_3(T_f) = 0;$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial \mathbb{H}}{\partial V}, \quad \lambda_4(T_f) = 0; \quad \frac{d\lambda_5}{dt} = -\frac{\partial \mathbb{H}}{\partial R}, \quad \lambda_5(T_f) = 0; \quad \frac{d\lambda_6}{dt} = -\frac{\partial \mathbb{H}}{\partial B}, \quad \lambda_6(T_f) = 0.$$

Moreover, the optimal control characterization (4.14) is obtained by solving for $v^*(t)$, $u_1^*(t)$, and $u_2^*(t)$, respectively, from the optimality conditions

$$\begin{aligned} \frac{\partial \mathbb{H}}{\partial v} &= 2C_1 v^* - S(\lambda_1 - \lambda_4) = 0, \\ \frac{\partial \mathbb{H}}{\partial u_1} &= 2C_2 u_1^* - c_0 I(\lambda_3 - \lambda_4) = 0, \\ \frac{\partial \mathbb{H}}{\partial u_2} &= 2C_3 u_2^* - \epsilon I \lambda_6 = 0. \end{aligned} \quad (4.15)$$

Therefore, by standard arguments involving the bounds on controls [37,38], it is easy to see that

$$v^* = \begin{cases} \Psi_1^*, & \text{for } 0 < \Psi_1^* < 1 \\ 0, & \text{for } \Psi_1^* \leq 0 \\ 1, & \text{for } \Psi_1^* \geq 1, \end{cases} \quad u_1^* = \begin{cases} \Psi_2^*, & \text{for } 0 < \Psi_2^* < 1 \\ 0, & \text{for } \Psi_2^* \leq 0 \\ 1, & \text{for } \Psi_2^* \geq 1, \end{cases}$$

and

$$u_2^* = \begin{cases} \Psi_3^*, & \text{for } 0 < \Psi_3^* < 1 \\ 0, & \text{for } \Psi_3^* \leq 0 \\ 1, & \text{for } \Psi_3^* \geq 1, \end{cases}$$

where

$$\Psi_1^* = \frac{S(\lambda_1 - \lambda_4)}{2C_1},$$

$$\Psi_2^* = \frac{c_0 I(\lambda_3 - \lambda_4)}{2C_2},$$

$$\Psi_3^* = \frac{\epsilon I \lambda_6}{2C_3}.$$

This wraps up the proof. □

4.3. Simulation of the optimality system. Optimality system is generated by combining the state system (4.1) and the co-state system (4.12), together with their associated initial and transversality conditions. This optimality system is numerically solved using the 4th-order Runge-Kutta forward-backward method as explained in [39]. With the aid of the parameter values given in Table 3 for which the effective reproduction number is obtained as $\mathcal{R}_e = 2.5817 > 1$, and $c = 10^5$, simulations are performed over a time window $[0, 90]$ in days (i.e., the expected final time of implementation, $T_f = 90$), together with initial conditions $S(0) = 500, E(0) = 100, I(0) = 10, V(0) = 0, R(0) = 0$, and $B(0) = 1000$. In addition, the balancing weight and rate constants are chosen as $A_1 = A_2 = A_3 = 10, C_1 = C_2 = C_3 = 10$ and $c_0 = 1$.

The three time-dependent control interventions $v(t), u_1(t)$, and $u_2(t)$ are classified into four different intervention scenarios, Z_1, Z_2, Z_3 , and Z_4 with a view to examining the appropriate intervention to be adopted in fighting against the menace of cholera in the community. These intervention scenarios are explained as follows.

- (1) Scenario Z_1 : implementation of vaccination strategy ($v(t)$)
- (2) Scenario Z_2 : implementation of treatment ($u_1(t)$)
- (3) Scenario Z_3 : implementation of environmental sanitation effort ($u_2(t)$)
- (4) Scenario Z_4 : combination of all the three controls ($v(t), u_1(t), u_2(t)$)

Scenario Z_1 : Implementation of vaccination strategy $v(t)$. The impact of optimal implementation of Scenario Z_1 on the dynamics of cholera transmission is examined as presented in Figure 5, comparing the system trajectories with the case where there is no control. In the event that Scenario Z_1 is considered, one sees that the populations of exposed and infectious humans, together with the concentration of *Vibrio cholerae* pathogens in the environment reduce more significantly in contrast to the event where control is not considered. This implies that boosting healthy individuals immunity through pre-exposure vaccination helps in reducing further spread of cholera in the population. In the control profile given in Figure 5(d), it is observed that vaccination strategy, v ,

remains at maximum 100% for about 89 days of scenario implementation before declining to zero over time.

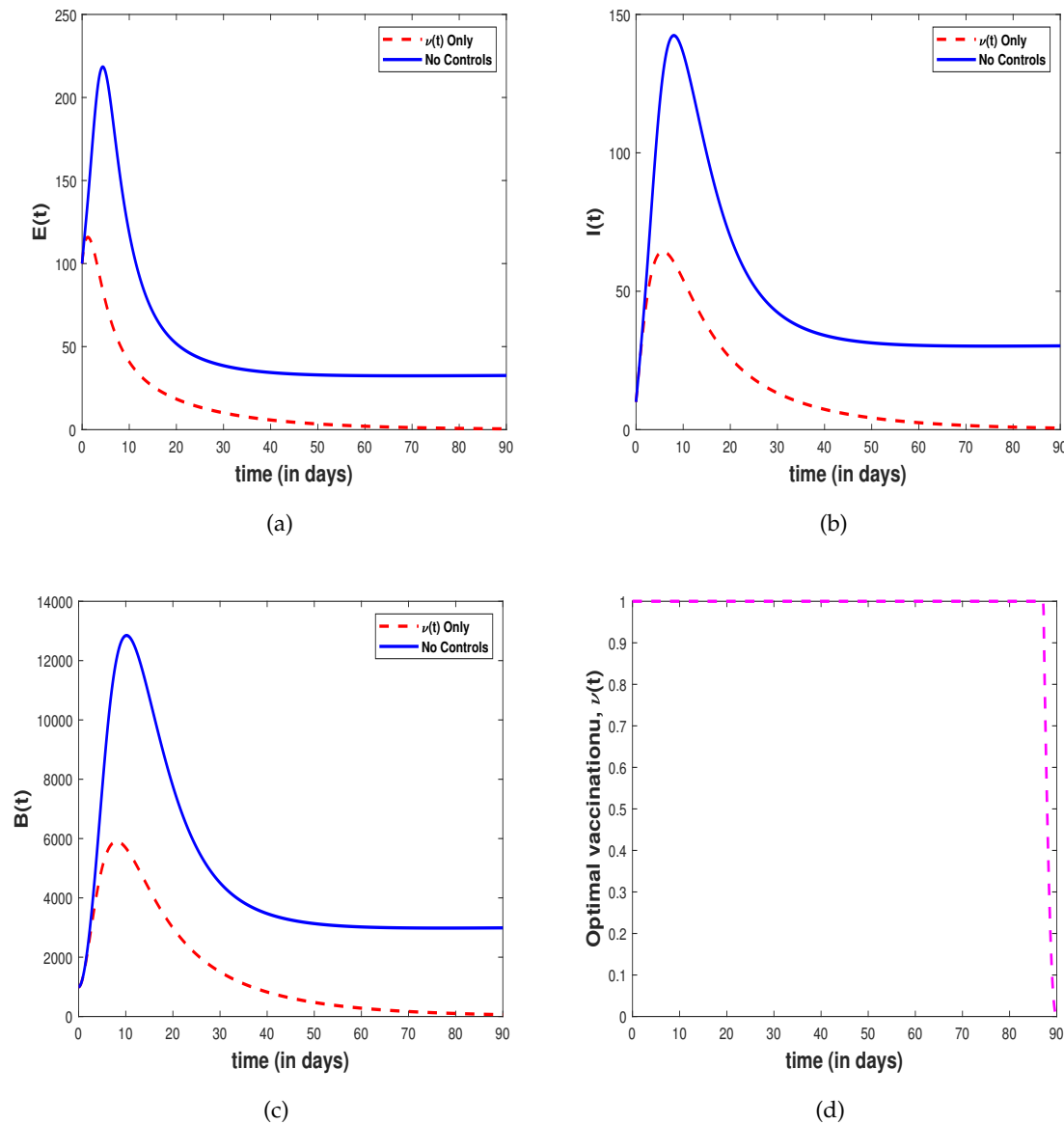


FIGURE 5. Effect of pre-exposure vaccination, ν , on the trajectories of the exposed, infectious classes and concentration of *Vibrio cholerae* in the environment.

Scenario Z_2 : Implementation of treatment strategy $u_1(t)$. In Figure 6, the behaviour of trajectories of infectious human population and concentration of *Vibrio Cholerae* pathogens in the environment is examined in the presence of optimal implementation of Scenario Z_2 . Reduction in the sizes of infectious human as well as in concentration of *Vibrio cholerae* in the environment is observed when Scenario Z_2 is optimally implemented. This biologically implies that treatment with effective anti-bacterial drugs will assist in stemming the transmission of cholera in the population. Figure 6(c)

exhibits the control profile for Scenario Z_2 encouraging optimal implementation of Scenario Z_2 maximally at 100% throughout the entire period of the control implementation.

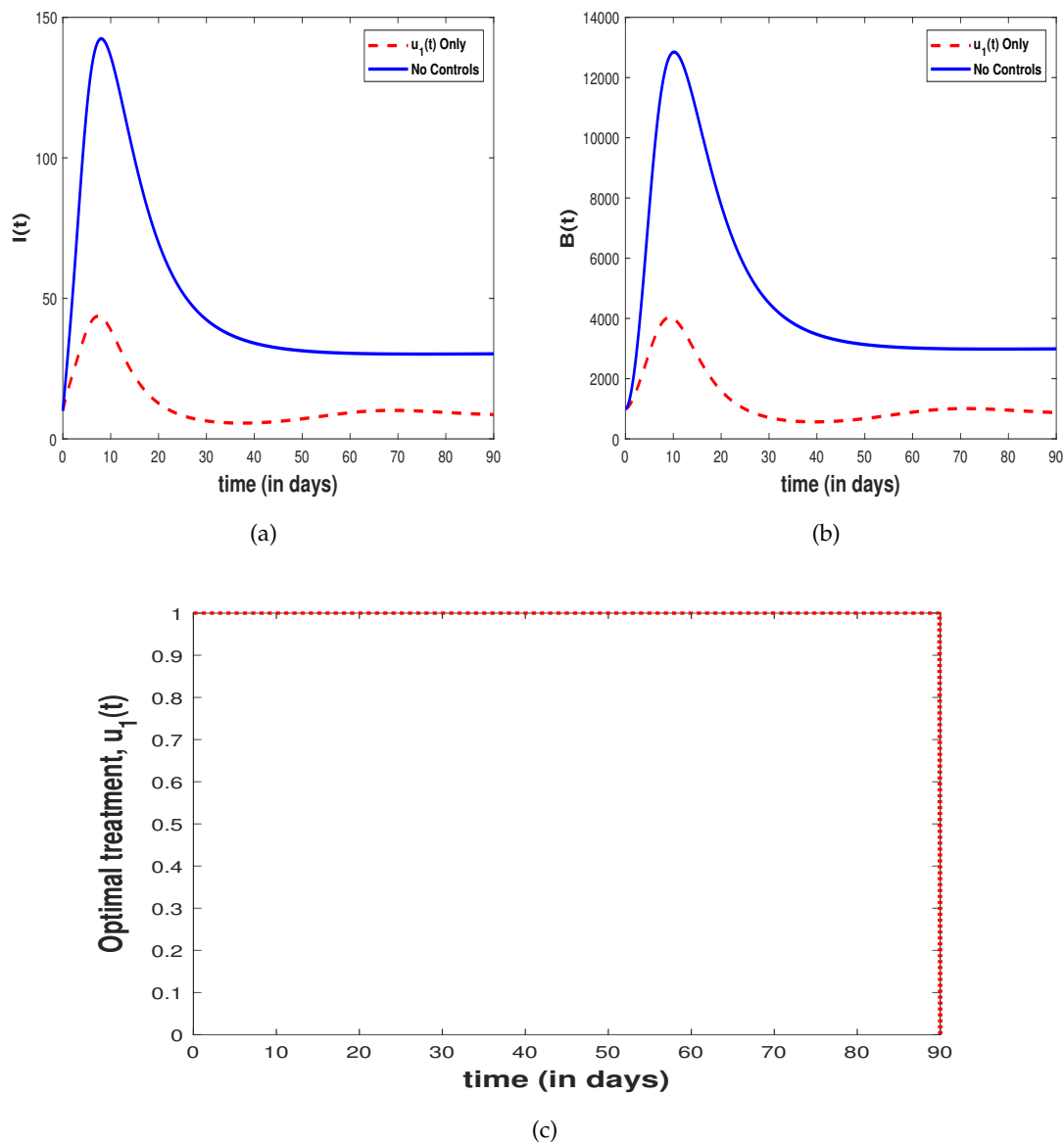


FIGURE 6. Effect of treatment strategy $u_1(t)$ on the trajectories of infectious class and concentration of *Vibrio cholerae* in the environment.

Scenario Z_3 : Implementation of environmental management effort $u_2(t)$. In the same vein, the population sizes of both exposed and infectious humans depicted in Figures 7(a) and (b), reduce substantially to the minimum level when Scenario Z_3 is maximally applied, while a tremendous reduction is observed in Figure 7(c) right from the inception of the implementation period. This is substantiating the need for effective environmental management efforts that could be enforced to minimize factors such as poor sanitation, open defecation, unavailability of portable water,

and inadequate waste management, contributing to the growth of pathogens in the environment. Moreover, maximum coverage is noticed in Scenario Z_3 representing proper environmental management efforts throughout the entire period of implementation before progressively dropping to zero in final time.

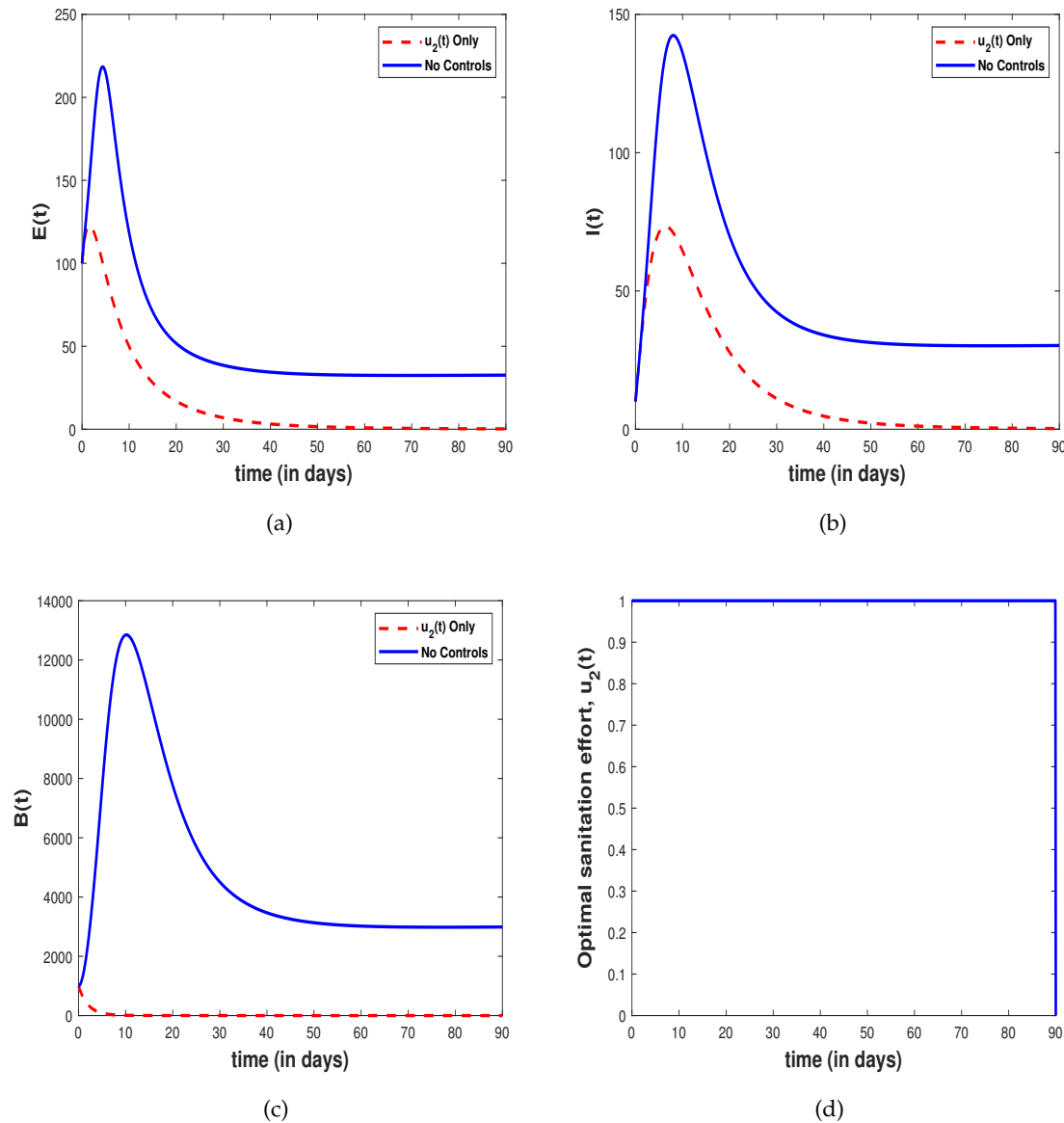


FIGURE 7. Effect of environmental sanitation effort, $u_2(t)$, on the trajectories of the exposed, infectious classes and concentration of *Vibrio cholerae* in the environment.

Scenario Z_4 : Combination of the three controls $v(t)$, $u_1(t)$ and $u_2(t)$. As expected, the populations of infected individuals and concentration of *Vibrio cholerae* in the environment shown in Figure 8 reduce most significantly when Scenario Z_4 is optimally considered to tackle the dynamics of cholera in the population. It is shown in the combined control profiles given in Figure 8(d) that

each of the given controls helps in minimizing the transmission of cholera in the population within the shortest period of implementation at maximum level. It is worth emphasizing that massive and prompt dissemination of these controls will contribute towards the elimination of cholera in the population.

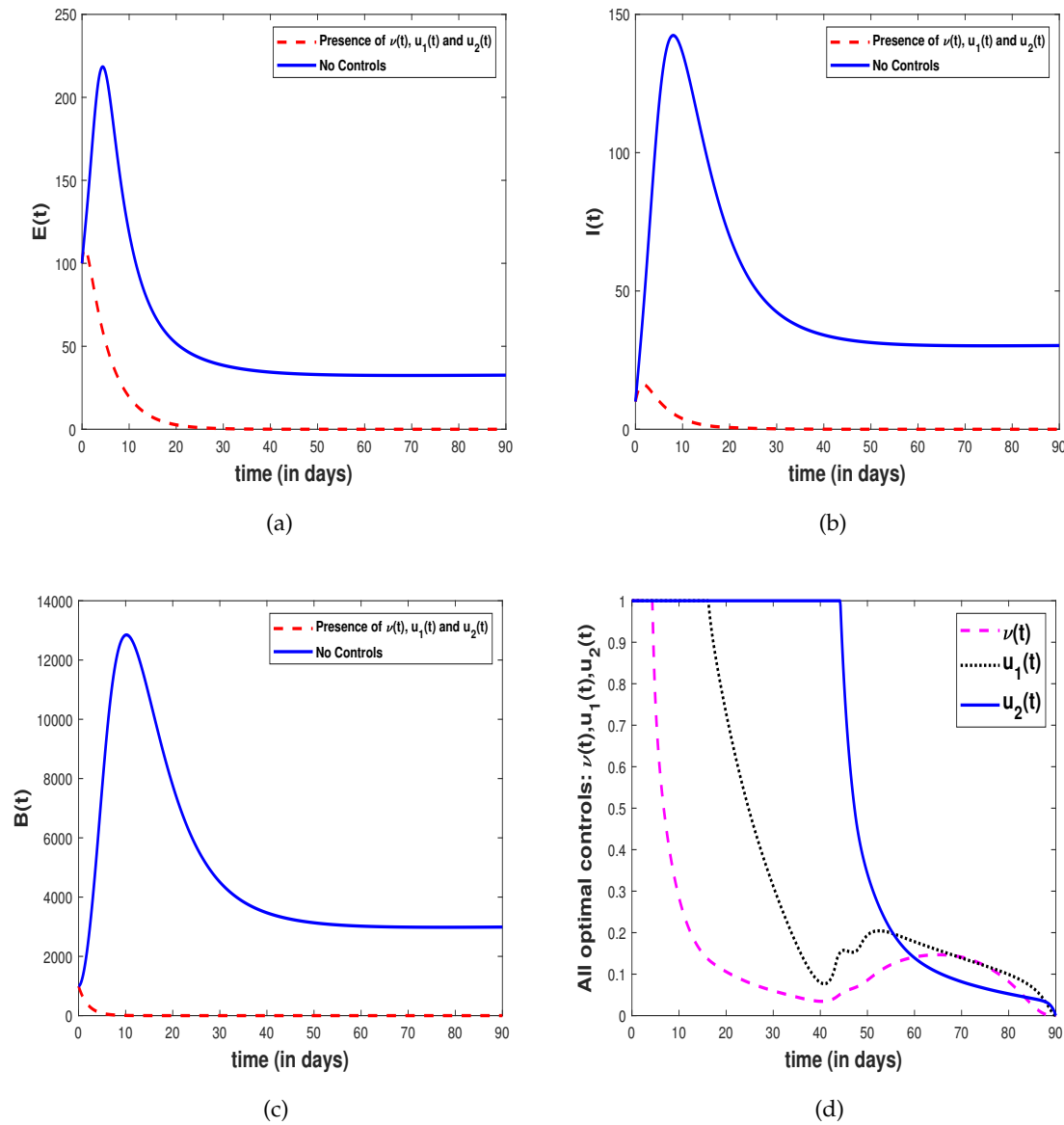


FIGURE 8. Effects of Scenario Z_4 on the trajectories of the exposed, infectious classes and concentration of *vibrio cholerae* in the environment.

5. ECONOMIC ANALYSIS

In an attempt to significantly avert cholera dynamics in the population, this section seeks to identify the most efficient and most economic scenario that can be used to successfully achieve this goal.

5.1. Efficiency analysis of the intervention scenarios. Efficiency analysis is employed to determine the intervention scenario that best prevent the highest number of cholera cases irrespective of the associated costs of implementation. Notably, intervention scenario with the highest efficiency index is the most efficient scenario. Following [40], the efficiency index, denoted by E_f , of each of the intervention scenarios can be obtained using

$$E_f = \frac{\text{Total number of cholera cases averted by scenario}}{\text{Total number of cholera cases averted without scenario}} \times 100. \quad (5.1)$$

It is shown in Table 4 that $E_f(Z_4) > E_f(Z_3) > E_f(Z_2) > E_f(Z_1)$ with each having the following values, indicating that Scenario Z_4 with the greatest efficiency index 99.35% is the most efficient intervention that prevents the largest infection cases among all other scenarios considered in combating the spread of cholera.

5.2. Cost-effectiveness analysis. Owing to the fact that the most efficient intervention may not be the most cost-effective intervention, cost-effectiveness analysis is used to investigate the control strategy that averts significant number of infection cases while minding the cost, especially in a resource-limited system. Three different methods, such as Average cost-effectiveness ratio (ACER), Incremental cost-effectiveness ratio (ICER) and Infection averted ratio (IAR) are adopted to conduct the economic and health benefits of the intervention scenarios.

Infection averted ratio (IAR). Infection averted ratio (IAR) is used to evaluate the ratio of the total number of infection cases prevented by control against the total number of recovered humans due to the control [41–43]. This is mathematically represented by

$$IAR = \frac{\text{Total cholera cases prevented by intervention scenario}}{\text{Total recovered due to intervention scenario}}. \quad (5.2)$$

In the context of IAR, the intervention scenario with the highest number of IAR value is considered the most economic intervention over other scenarios. Thus, Scenario Z_4 is the most cost-effective control since $IAR(Z_2) < IAR(Z_1) < IAR(Z_3) < IAR(Z_4)$, as seen in Table 4.

Average cost-effectiveness ratio (ACER). Average cost-effectiveness ratio is used basically to measure the ratio of total cost of implementing an intervention scenario to the total number of cholera cases averted by the intervention scenario [40,44]. It can be calculated using the following formula

$$ACER = \frac{\text{Total cost of control implementation}}{\text{Total number of cholera cases prevented by intervention scenario}}. \quad (5.3)$$

Incremental cost-effectiveness ratio (ICER). Incremental cost-effectiveness ratio (ICER) is used to quantify the ratio of difference in costs of two alternative intervention scenarios to the difference in the number of cholera cases prevented by such scenarios [45–48]. The ICER for any given strategies X_1 and X_2 is given by

$$ICER = \frac{\text{Difference in total costs between strategies } X_1 \text{ and } X_2}{\text{Difference in total number of infection averted by strategies } X_1 \text{ and } X_2}. \quad (5.4)$$

It is worth noting that the intervention with the lowest ACER value is regarded as the most cost-effective of all the interventions considered in stemming the spread of cholera in the population. The ACER for each of the intervention scenarios is examined using (5.3) and the results are summarized in Table 4. It can be deduced that Scenario Z_4 , combining all the three controls $v(t)$, $u_1(t)$, and $u_2(t)$, has the lowest ACER value. Therefore, the combination of pre-exposure vaccination, treatment and environmental management efforts is the most cost-effective intervention to be adopted in hampering the danger of cholera disease in the population. Moreover, the immediate first two ICER values outlined in Table 4 are compared and it is discovered that $ICER(Z_1)$ is greater than $ICER(Z_2)$, meaning that Z_1 is more expensive and less effective than Z_2 . This indicates that intervention scenario Z_2 dominates Z_1 . Thus, the single implementation of pre-exposure vaccination is removed from the list of intervention scenarios, and the remaining interventions are re-evaluated and summarized in Table 5.

TABLE 4. Ascending order of the cholera cases averted by interventions with efficiency, ACER, ICER and IAR.

Control	Cases averted	Total cost	$E_f(\%)$	ACER ($\times 10^3$)	ICER	IAR
Z_1	3.3732×10^6	9.7503×10^3	69.12	2.8905	0.0028905	16.16059
Z_2	3.5212×10^6	1×10^4	72.15	2.8399	0.0016872	4.16725
Z_3	4.8261×10^6	1×10^4	98.89	2.0721	0.00000	21.73821
Z_4	4.8486×10^6	8.5514×10^3	99.35	1.7637	-0.064382	36.54632

TABLE 5. ICER values without Scenario Z_1 .

Control	Cases averted	Total cost	ICER
Z_2	3.5212×10^6	1×10^4	0.0028399
Z_3	4.8261×10^6	1×10^4	0.00000
Z_4	4.8486×10^6	8.5514×10^3	-0.064382

It can also be seen by comparing Z_2 and Z_3 that $ICER(Z_3)$ is less than $ICER(Z_2)$, inferring that the intervention scenario Z_2 is dominated by Z_3 . Hence, Z_2 is more costly and less effective than the alternative. The implementation of intervention scenario Z_2 is consequently removed from the available list of intervention scenarios. The ICER values for the remaining controls Z_3 and Z_4 are re-evaluated as shown in Table 6.

TABLE 6. ICER values for Scenarios Z_3 and Z_4 .

Control	Cases averted	Total cost	ICER
Z_3	4.8261×10^6	1×10^4	0.00207
Z_4	4.8486×10^6	8.5514×10^3	-0.06438

It can be confirmed from Table 6 that Z_3 is strongly dominated by Z_4 . This implies that Z_3 is far less effective and more expensive than implementing scenario Z_4 . Hence, Z_3 is expunged from the

list of scenarios striving for the same resources, while scenario Z_4 is retained. In what follows, it can be concluded that scenario Z_4 , which combines vaccination of susceptible human, treatment with anti-bacterial drugs, and environmental sanitation strategy is the most cost-effective scenario based on ICER technique. Interestingly, the result of IAR aligns perfectly with the results obtained for both ACER and ICER. Hence, to successfully interrupt the transmission of cholera disease, intervention scenario Z_4 offers the optimum solution at minimal cost.

6. CONCLUSION

In this study, a novel deterministic mathematical model governed by both autonomous and non-autonomous systems has been presented to understand the intricacies associated with the transmission dynamics of cholera in the population. The study borders on exploring the influence of vaccination of susceptible individuals and concentration of *Vibrio cholerae* pathogens in the environment with logistic growth rate on the dynamics of cholera with optimal interventions. The following findings are obtained from various analyses carried out on the formulated model:

- i. Two different bounds for the concentration of *Vibro cholerae* are discovered depending on whether the intrinsic growth rate exceeds the decay rate of the bacteria in the environment, establishing the biologically feasible region for the well-posedness of the formulated cholera transmission model with logistic growth. However, it is confirmed that the decay rate of bacteria concentration must exceed its intrinsic growth rate for an effective reproduction number to exist.
- ii. Some key sensitive parameters that drive the dynamics of cholera in the population, including transmission rate, *Vibrio cholerae* shedding rate, decay rate, vaccination and recovery rates, are identified through sensitivity analysis. In particular, increasing the vaccination rate up to 55% of the population guarantees a safe zone at the effective reproduction number less than unity, where cholera dies out.
- iii. The presence of each of the time-dependent intervention scenarios (vaccination, treatment, environmental sanitation, and combination of all the three) through simulation of the optimality system shows significant reduction in the trajectories of the infectious classes and concentration of *Vibrio cholerae* in the environment when compared with the trajectories of the uncontrolled system.
- iv. Efficiency analysis reveals that Scenario Z_4 , which combines all the three control measures, having the efficiency index 99.35%, is the most efficient intervention to be adopted in curtailing the spread of cholera in the population.
- v. The three methods of economic analysis conducted, including infection averted ratio (IAR), average cost-effectiveness ratio (ACER) and incremental cost-effectiveness ratio (ICER), confirm that Scenario Z_4 , is the most cost-effective scenario to be considered in inhibiting the threat posed by cholera in the population.

Therefore, optimal implementation of integrated intervention comprising vaccination, prompt treatment and environmental management efforts through provision of adequate sanitation facilities and public awareness campaign against open defecation is highly recommended towards achieving cholera-free population.

Conflicts of Interest: The authors declare that there are no conflicts of interest regarding the publication of this paper.

REFERENCES

- [1] A. Onion, M. Sullivan, M. Mullen, C. Zapata, Cholera, HISTORY, 2022. <https://www.history.com/topics/inventions/history-of-cholera>.
- [2] National Institutes of Health, Cholera. <https://web.archive.org/web/20240809003333/https://history.nih.gov/display/history/Cholera>.
- [3] S. Handa, Cholera, Medscape, 2025. <https://emedicine.medscape.com/article/962643-overview>.
- [4] Centers for Disease Control and Prevention (CDC), Clinical Overview of Vibriosis, 2024. <https://www.cdc.gov/vibrio/hcp/clinical-overview/index.html>.
- [5] World Health Organization (WHO), Cholera, 2024. <https://www.who.int/news-room/fact-sheets/detail/cholera>.
- [6] M. Abdelghani, M. Bakheet, E. Bashier, A Mathematical Model of Cholera Outbreak with Type III Functional Response, Eur. Chem. Bull. 12 (2023), 4599–4625.
- [7] S.O. Gbodogbe, Harmonizing Epidemic Dynamics: A Fractional Calculus Approach to Optimal Control Strategies for Cholera Transmission, Sci. Afr. 27 (2025), e02545. <https://doi.org/10.1016/j.sciaf.2025.e02545>.
- [8] Z.O. Dere, A.O. Oladapo, Mathematical (SEIRB) Model Analysis for Evaluating Cholera Control Strategies in Remote Dry Season Region, J. Diferensial 6 (2024), 148–169. <https://doi.org/10.35508/jd.v6i2.17868>.
- [9] M.O. Onuorah, F.A. Atiku, H. Juuko, Mathematical Model for Prevention and Control of Cholera Transmission in a Variable Population, Res. Math. 9 (2022), 2018779. <https://doi.org/10.1080/27658449.2021.2018779>.
- [10] O.K. Jakob, O. Akinyi, F. Tireito, A Mathematical Model on the Dynamics of In-Host Infection Cholera Disease with Vaccination, Discret. Dyn. Nat. Soc. 2023 (2023), 1465228. <https://doi.org/10.1155/2023/1465228>.
- [11] M. Claeson, R. Waldman, Cholera Through History, Encyclopedia Britannica, 2025. <https://www.britannica.com/science/cholera/Cholera-through-history>.
- [12] S. Siddiqua, A. Chaturvedi, N.K. Goswami, A Simple Mathematical Model of Cholera Dynamics with Sensitivity Analysis, AIP Conf. Proc. 2516 (2022), 130002. <https://doi.org/10.1063/5.0108808>.
- [13] S. Cherotich, B. Khachiti, P. Khakali, R. Kendi, Mathematical Modeling of Cholera Mitigation Incorporating Handwashing, Afr. Sci. Annu. Rev. 1 (2024), 127–148. <https://doi.org/10.51867/Asarev.Maths.1.1.9>.
- [14] P.N. Okolo, A.S. Magaji, I. Joshua, P.F. Useini, Mathematical Modelling and Analysis of Cholera Disease Dynamics with Control, FUDMA J. Sci. 4 (2020), 363–381. <https://doi.org/10.33003/fjs-2020-0404-494>.
- [15] N. Hidayati, E.R. Sari, N.H. Waryanto, Mathematical Model of Cholera Spread Based on SIR: Optimal Control, Pythagoras J. Pendidik. Mat. 16 (2021), 70–83. <https://doi.org/10.21831/pg.v16i1.35729>.
- [16] O.S. Maliki, O.C. Chibuike, A Mathematical Model for the Control of Cholera Epidemic without Natural Recovery, Appl. Math. 12 (2021), 655–668. <https://doi.org/10.4236/am.2021.128046>.
- [17] M. Demir, The Effect of Population Migration on the Diffusion of Cholera Outbreaks in Metapopulations, medRxiv: 2022.04.12.22273810, (2022). <https://doi.org/10.1101/2022.04.12.22273810>.
- [18] N.S. Abdul, L. Yahya, R. Resmawan, A.R. Nuha, Dynamic Analysis of the Mathematical Model of the Spread of Cholera with Vaccination Strategies, Barekeng J. Ilmu Mat. Terapan 16 (2022), 281–292. <https://doi.org/10.30598/barekengvol16iss1pp279-290>.

- [19] I. Sahib, B. Khajji, A. Labzai, H. Gourram, M. Belam, Mathematical Modeling and Optimal Control Strategy for a Discrete-Time Cholera Model, *Commun. Math. Biol. Neurosci.* 2023 (2023), 135. <https://doi.org/10.28919/cmbn/8285>.
- [20] H.H. Hameed, H.M. Al-Saedi, M.H. Al-Mayyah, Mathematical Modelling for Cholera Epidemic in Iraq, in: 2023 5th International Conference on Problems of Cybernetics and Informatics (PCI), IEEE, 2023, pp. 1–4. <https://doi.org/10.1109/PCI60110.2023.10325918>.
- [21] R. Resmawan, L. Yahya, S.L. Mahmud, A.R. Nuha, N.H. Laita, Dynamic Analysis of the Mathematical Model for the Cholera Disease Spread Involving Medication and Environmental Sanitation, *Barekeng J. Ilmu Mat. Terapan* 17 (2023), 0341–0360. <https://doi.org/10.30598/barekengvol17iss1pp0341-0360>.
- [22] J. Mushanyu, L. Matsebula, F. Nyabadza, Mathematical Modeling of Cholera Dynamics in the Presence of Antimicrobial Utilization Strategy, *Sci. Rep.* 14 (2024), 30128. <https://doi.org/10.1038/s41598-024-77834-4>.
- [23] I. Sahib, M. Baroudi, H. Gourram, B. Khajji, A. Labzai, M. Belam, The Mathematical Modeling and Analysis of the Cholera Disease Model, *Commun. Math. Biol. Neurosci.* 2024 (2024), 93. <https://doi.org/10.28919/cmbn/8785>.
- [24] K.J. Owade, A. Okaka, F. Tireito, A Between-Host Cholera Mathematical Model Incorporating Temperature Dependence, *Afr. J. Empir. Res.* 5 (2024), 85–101. <https://doi.org/10.51867/ajernet.Mathematics.5.4.8>.
- [25] A. Chukwumela, D. Iyai, Effect of Time Delay in the Stability Analysis of Cholera Epidemic-Endemic Disease Model, *Eur. J. Theor. Appl. Sci.* 2 (2024), 281–297. [https://doi.org/10.59324/ejtas.2024.2\(3\).24](https://doi.org/10.59324/ejtas.2024.2(3).24).
- [26] B.C. Agbata, W. Obeng-Denteh, Q.O. Ahman, G.O. Acheneje, F. Asantemensa, D.J. Yahaya, D.G. Eshetu, P.A. Kwabi, A Mathematical Model for the Control of Cholera Outbreak in Nigeria, *J. Pharm. Allied Sci.* 21 (2024), 4360–4378.
- [27] K.W. Brhane, A.G. Ahmad, H. Hina, H. Emadifar, Mathematical Modeling of Cholera Dynamics with Intrinsic Growth Considering Constant Interventions, *Sci. Rep.* 14 (2024), 4616. <https://doi.org/10.1038/s41598-024-55240-0>.
- [28] H.W. Hethcote, The Mathematics of Infectious Diseases, *SIAM Rev.* 42 (2000), 599–653. <https://doi.org/10.1137/S0036144500371907>.
- [29] P. van den Driessche, J. Watmough, Reproduction Numbers and Sub-Threshold Endemic Equilibria for Compartmental Models of Disease Transmission, *Math. Biosci.* 180 (2002), 29–48. [https://doi.org/10.1016/S0025-5564\(02\)00108-6](https://doi.org/10.1016/S0025-5564(02)00108-6).
- [30] S. Olaniyi, I.A. Lawal, R.S. Lebelo, F.M. Chuma, S.F. Abimbade, Modelling and Optimal Control of Influenza Dynamics with Structured Populations Based on Education and Isolation, *Int. J. Anal. Appl.* 23 (2025), 81. <https://doi.org/10.28924/2291-8639-23-2025-81>.
- [31] O.S. Obabiyi, S. Olaniyi, Asymptotic Stability of Malaria Dynamics with Vigilant Human Compartment, *Int. J. Appl. Math.* 29 (2016), 127–144. <https://doi.org/10.12732/ijam.v29i1.10>.
- [32] N. Chitnis, J.M. Hyman, J.M. Cushing, Determining Important Parameters in the Spread of Malaria Through the Sensitivity Analysis of a Mathematical Model, *Bull. Math. Biol.* 70 (2008), 1272–1296. <https://doi.org/10.1007/s11538-008-9299-0>.
- [33] H. Namaweje, E. Obuya, L.S. Luboobi, Modeling Optimal Control of Cholera Disease under the Interventions of Vaccination, Treatment and Education Awareness, *J. Math. Res.* 10 (2018), 137–152. <https://doi.org/10.5539/jmr.v10n5p137>.
- [34] J. Wang, C. Modnak, Modeling Cholera Dynamics with Controls, *Can. Appl. Math. Q.* 19 (2011), 255–273.
- [35] A. Abidemi, S. Olaniyi, O.A. Adepoju, An Explicit Note on the Existence Theorem of Optimal Control Problem, *J. Phys.: Conf. Ser.* 2199 (2022), 012021. <https://doi.org/10.1088/1742-6596/2199/1/012021>.
- [36] L.S. Pontryagin, V.G. Boltyanskii, R.V. Gamkrelidze, E.F. Mishchenko, The Mathematical Theory of Optimal Processes, Interscience Publishers, 1962.
- [37] S. Barman, S. Jana, S. Majee, D.K. Das, T.K. Kar, Complex Dynamics of a Fractional-Order Epidemic Model with Saturated Media Effect, *Nonlinear Dyn.* 112 (2024), 18611–18637. <https://doi.org/10.1007/s11071-024-09932-x>.

- [38] N.K. Goswami, S. Olaniyi, S.F. Abimbade, F.M. Chuma, A Mathematical Model for Investigating the Effect of Media Awareness Programs on the Spread of COVID-19 with Optimal Control, *Healthc. Anal.* 5 (2024), 100300. <https://doi.org/10.1016/j.health.2024.100300>.
- [39] S. Lenhart, J.T. Workman, *Optimal Control Applied to Biological Models*, Chapman and Hall/CRC, 2007. <https://doi.org/10.1201/9781420011418>.
- [40] S. Olaniyi, S.F. Abimbade, O.A. Ajala, F.M. Chuma, Efficiency and Economic Analysis of Intervention Strategies for Recurrent Malaria Transmission, *Qual. Quant.* 58 (2024), 627–645. <https://doi.org/10.1007/s11135-023-01664-1>.
- [41] K.O. Okosun, R. Ouifki, N. Marcus, Optimal Control Strategies and Cost-Effectiveness Analysis of a Malaria Model, *Biosystems* 111 (2013), 83–101. <https://doi.org/10.1016/j.biosystems.2012.09.008>.
- [42] S. Al-Shanfari, I.M. Elmojtaba, N. Al-Salti, Cost-Effectiveness Analysis of a Cholera Model with Awareness Programs and Limited Resources, *J. Math. Comput. Sci.* 11 (2021), 5380–5416. <https://doi.org/10.28919/jmcs/6001>.
- [43] S. Olaniyi, F.M. Chuma, Lyapunov Stability and Economic Analysis of Monkeypox Dynamics with Vertical Transmission and Vaccination, *Int. J. Appl. Comput. Math.* 9 (2023), 85. <https://doi.org/10.1007/s40819-023-01572-w>.
- [44] J.K.K. Asamoah, Z. Jin, G.-Q. Sun, B. Seidu, E. Yankson, A. Abidemi, F.T. Oduro, S.E. Moore, E. Okyere, Sensitivity Assessment and Optimal Economic Evaluation of a New COVID-19 Compartmental Epidemic Model with Control Interventions, *Chaos Solitons Fractals* 146 (2021), 110885. <https://doi.org/10.1016/j.chaos.2021.110885>.
- [45] S.A. Rahmayani, D. Aldila, B.D. Handari, Cost-Effectiveness Analysis on Measles Transmission with Vaccination and Treatment Intervention, *AIMS Math.* 6 (2021), 12491–12527. <https://doi.org/10.3934/math.2021721>.
- [46] J.K.K. Asamoah, E. Okyere, A. Abidemi, S.E. Moore, G.-Q. Sun, Z. Jin, E. Acheampong, J.F. Gordon, Optimal Control and Comprehensive Cost-Effectiveness Analysis for COVID-19, *Results Phys.* 33 (2022), 105177. <https://doi.org/10.1016/j.rinp.2022.105177>.
- [47] S. Olaniyi, J.O. Olayiwola, O.S. Obabiyi, R.S. Lebelo, S.F. Abimbade, Mathematical Analysis of Non-Autonomous HIV/AIDS Transmission Dynamics with Efficient and Cost-Effective Intervention Strategies, *Contemp. Math.* 6 (2025), 1380–1400. <https://doi.org/10.37256/cm.6220256138>.
- [48] F.S. Tessema, P.R. Koya, B.K. Bole, Optimal Control and Cost-Effectiveness Analysis of Cholera with Vaccination, *J. Math.* 2022 (2022), 1705277. <https://doi.org/10.1155/2022/1705277>.