Modeling vaccination and environmental hygiene strategies: An ordinary differential equations approach for optimizing cholera interventions

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ABSTRACT

The objective of the study was to evaluate the effectiveness of vaccination and environmental hygiene interventions in controlling cholera outbreaks. We used an Ordinary Differential Equation model using MATLAB for the numerical simulations to examine the influence of varying vaccination rates and sanitation measures on cholera transmission within a population over a simulated period of 400 days. The results showed that increased vaccination rates significantly reduced the susceptible population, while improved sanitation measures led to a decrease in the environmental bacterial load. The computed basic reproduction number is $R_0 = 0.00081634$, which is significantly less than unity, indicates that, under the combined effects of vaccination and environmental sanitation interventions, cholera transmission is effectively eliminated. Sensitivity analysis revealed that transmission rate and the rate at which exposed individuals become infectious are the most influential parameters and that the vaccination rate exhibits a high sensitivity index, highlighting the substantial impact of vaccination coverage on cholera transmission dynamics. In contrast, the recovery rate and the waning rate of vaccine-induced immunity have negligible sensitivity indices, indicating a limited influence on the model outcome within the parameter ranges considered. Environmental parameters, including the bacterial decay rate, bacterial shedding rate, and sanitation intervention rate, exhibit relatively low sensitivity values. While their individual effects are modest, collectively, they contribute to reducing environmental contamination and complement direct human-targeted interventions. These findings suggest that a combined approach of heightened vaccination efforts and rigorous environmental hygiene practices is essential for the timely control of cholera outbreaks.

Keywords*:* Bacteria, Cholera, Environment, Hygiene, Vaccination, Waterborne

I. INTRODUCTION

Cholera, a severe diarrhea disease triggered by the bacterium *Vibrio cholerae*, is prevalent worldwide. Statistics show that in a year, there are approximately 1,300,000 to 4,000,000 cases of cholera and twenty-one thousand to one hundred forty-three thousand deaths across the globe (Mustapha et.al. 2024). According to UN Sustainable Development Goals 3 and 6, the world is assured of good health and sustainable management of water and sanitation, respectively (Clark & Wu, 2016), but the situation is still unmanageable. Cholera poses a great health challenge, especially in countries with poor sanitation and hygiene. It is a watery diarrhea disease and is generally regarded as a disease of the poor. It affects areas that lack access to safe drinking water and a sense of hygiene (Andam et. al., 2015).

Cholera remains a major public health threat globally, particularly in areas with limited access to safe water and sanitation. While previous modeling studies have explored vaccination or hygiene interventions separately, there is a lack of models that assess their combined impact on cholera transmission. To address this gap, we develop an ordinary differential equations (ODE) model that integrates both vaccination and environmental hygiene strategies. This integrated approach allows us to quantify their synergistic effects and identify optimal intervention combinations. The central research question is: How can vaccination and hygiene strategies be jointly optimized to effectively reduce cholera incidence in endemic regions? This dual-focus modeling framework represents the novelty of our study, providing insights beyond what single-intervention models can offer.

Mathematical modeling has appeared to be a vital tool in understanding disease spread dynamics and intervention strategies' impact (Anteneh et al., 2024; Bakare & Hoskova-Mayerova, 2021; Fakai et al., 2014). In their study, Bakare and Hoskova-Mayerova (2021) used an unidentified nonlinear mathematical model to study cholera control. They revealed that treatment with drugs and social mobilization are measures for cholera control. Also, Cai et al. (2017) used an age-structured cholera model that combines partial differential equations (PDEs) and ordinary differential equations (ODEs) coupled system to analyse the age-dependent cholera dynamics. In their analysis,

emphasis was placed on the complex interplay among environmental pathogens, human hosts with obvious age structure, and age-dependent immunization as a disease control measure. However, the implementation of these interventions often lacks a coordinated approach that maximizes collective efficiency. The interplay between vaccination and environmental hygiene practices is complex and multifaceted, and is influenced by factors such as population density, local infrastructure, cultural practices, and resource availability.

In current existing models, there is a notable scarcity of comprehensive models that integrate both vaccination and environmental hygiene strategies within a single framework, as this paper is set to do. As cholera control in endemic regions often requires a multifaceted approach (Brhane et al., 2024), there is a need to study the relationship between vaccination and environmental hygiene control to optimize cholera intervention. This will not only reveal the relationship, but also the understanding of their relationship will improve hygiene practices to have a synergistic effect on reducing cholera transmission (Ezeagu et. al., 2019). The rest of the paper is organized as follows. Section II presents the literature review and Section III presents the methods. Section IV presents the findings and discussion, and Section V consists of the conclusion and recommendations.

1.1 Research Objectives

The objective of the study was to evaluate the effectiveness of vaccination and environmental hygiene interventions in controlling cholera outbreaks, using ordinary differential equation model. Precisely, the study was guided by the following specific objectives:

i. To construct an ODE model that incorporates the dynamics of cholera transmission, vaccination coverage, and environmental hygiene practices
ii. To utilize the ODE model to explore different scenarios to investigate the impact of varying vaccination schedules and hygiene interventions.
iii. To use the ODE model to identify the effective combination of vaccination and sanitation measures that minimize cholera incidence and mortality rates.

II. LITERATURE REVIEW

2.1 Theoretical Review

The theoretical foundation of disease modeling using Ordinary Differential Equations (ODEs) is robust and multifaceted, providing a critical framework for understanding the dynamics of infectious diseases. ODEs are instrumental in capturing the continuous changes in various epidemiological states within a population over time. These models have been pivotal for epidemic prediction peaks in assessing the impact of public health interventions and understanding long-term disease behavior (David, 2020).

Ordinary Differential Equations models for infectious diseases, such as cholera, are constructed using the compartmentalization of the population into different epidemiological states, such as susceptible (S), exposed (E), infectious (I), and recovered (R). Then, the SEIR framework is used to formulate a set of ODES that describe the rate of movement of individuals between this compartment due to processes such as infection, recovery, and loss of immunity (Glass et al., 2021).

The strength of ODE models lies in their ability to offer insight into the spread dynamics of diseases. By incorporating parameters such as transmission rates, contact patterns, and duration of infection, these models can simulate the spread of an infection through a population over time. This allows the identification of potential intervention points where measures such as vaccination and improved environmental hygiene can be the most effective (Sundnes, 2024).

Furthermore, ODE models can be extended to include additional complexities such as age-structured populations, spatial heterogeneity, and stochastic elements. This extension enables a better understanding of disease transmission and control, particularly in diseases such as cholera, through environmental reservoirs and transmission pathways (Saravi & Saravi, 2020). The application of ODE models to the evaluation of control measures is significant. By simulating various intervention strategies, such as vaccination campaigns or improvements in water quality, researchers can predict the potential impact of these strategies on disease prevalence and incidence, which is crucial for both policymakers and public health when planning and implementing effective control measures (Rathee & Nilam, 2017)

2.2 The Conceptual Review

The conceptual framework for implementing the method involves a comprehensive Ordinary Differential Equation (ODE) model that serves as a basis for understanding and optimizing cholera intervention strategies. This model was designed to encapsulate the core aspects of cholera transmission and control, integrating vaccination coverage, environmental hygiene practices, and the natural history of the disease into a unified structure.

2.2.1 Vaccination Coverage

The model incorporates simulated vaccination data, including the fraction or percentage of the population immunized, efficacy of the vaccine, and duration of immunity provided. The impact of different vaccination coverage levels on the spread of cholera was simulated to determine the threshold required to achieve herd immunity.

2.2.2 Environmental Hygiene Practices

The model also included variables representing the level of environmental hygiene, which can significantly affect the transmission dynamics of cholera. Factors such as access to clean water, proper sanitation, and waste management will be modeled to assess their contribution to reducing the risk of cholera outbreaks.

2.2.3 Natural History of Cholera

The natural progression of cholera in individuals and populations was represented in the model. The model also considers the environmental persistence of vibrio cholera and its interaction with human hosts, including the incubation period, the period of infectiousness, and the rate of recovery or fatality. The conceptual framework for the implementation of this method is illustrated in Figure 1.

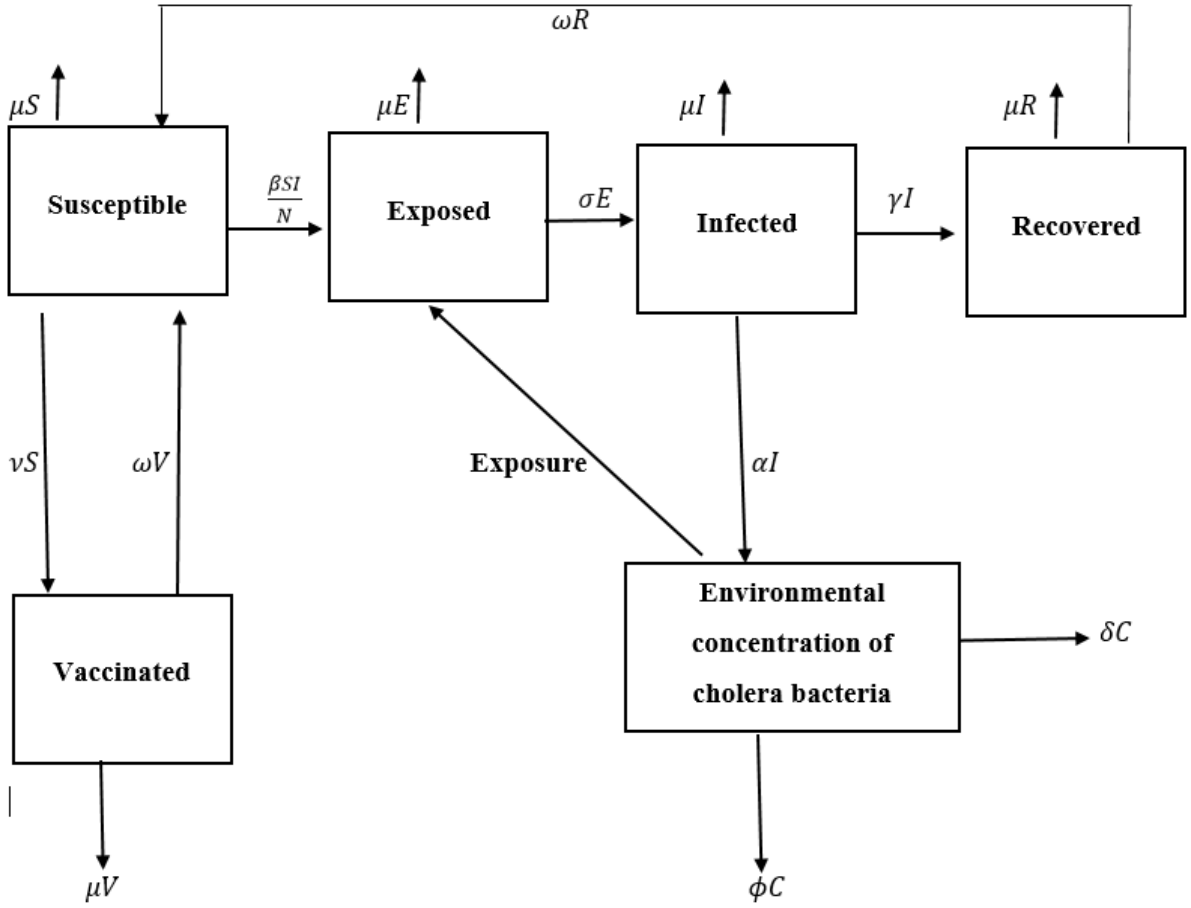


Figure 1

The Implementation of the Method

III. METHODOLOGY

The methods section provides the conceptualization of the model, which includes compartments of the model, transitions between compartments, model assumptions, model construction, parameter (s) estimation, and model equations. The model parameters, basic model properties including the non-negativity and boundedness, disease-free equilibrium (DFE), stability of the DFE, and sensitivity analysis of the basic reproduction number and optimal control shall form the model equations.

3.1 Conceptualization of the Model

This provides the groundwork for a mathematical model that defines the structure and interactions between different components. In this study, the model developed by Nyaberi and Malonza (2019) was revisited, which included vaccination and environmental hygiene strategies.

3.1.1 Compartments of the Model

This mathematical model for optimizing cholera incorporates intervention strategies by expanding the basic SIR model to include the effects of vaccination and environmental hygiene. Vaccination intervention involves introducing a vaccination rate (ν), which represents the rate at which susceptible individuals are vaccinated, and an environmental hygiene intervention that involves introducing a sanitation intervention rate ϕ, representing the rate at which environmental hygiene measures reduce the concentration of cholera bacteria.

Therefore, the formulated mathematical model for optimizing cholera control considers various compartments, such as susceptible individuals (S), who are at risk of contracting cholera but have not yet been exposed. Exposed individuals (E) who have been exposed to cholera bacteria but are not yet infectious can move to the exposed (E) compartment upon contact with the cholera bacteria. After the incubation period, there is a transition to the infectious (I) compartment, whereby infectious individuals (I) who are currently ill with cholera can spread the disease to others in the susceptible (S) compartment. Recovered individuals (R) who have recovered from cholera and gained immunity may return to the susceptible (S) compartment if immunity wanes over time. Vaccinated individuals (V) who have received the cholera vaccine are less likely to become infected and move to the exposed (E) compartment. The environmental concentration of cholera bacteria (C), which represents the concentration of cholera bacteria in the environment, can infect susceptible (S) individuals.

3.1.2 Transitions between Compartments

The transmission between compartments occurs in two ways: first, it can be a natural process such as being infected as susceptible individuals (S) become exposed (E) upon contact with the infectious (I) or the contaminated environment (C); incubation where the exposed individuals (E) become infectious (I) after the incubation period; recovery where transmittable individuals (I) recover and move to the recovered (R) compartment and loss of immunity where recovered individuals (R) lose immunity and become susceptible (S) again. In addition, it can be due to interventions such as vaccination of a certain rate of susceptible (S) individuals, moving to the vaccinated (V) compartment, and environmental hygiene measures that reduce the environmental concentration of cholera bacteria (C), thus lowering the infection rate.

3.1.3 Model Assumptions

The mathematical model assumes that:- An individual in the universal group, called a population, has an equal probability of coming into contact with others. The total population size remains constant, with births and deaths balanced, Direct Transmission through direct contact with infectious individuals (I) or indirectly through the environmental compartment(C), Post-infection immunity and vaccine-induced immunity are presumed to wane over time, following exponential decay. The effectiveness of interventions such as vaccination and environmental hygiene is assumed to reduce the transmission rate of cholera.

3.2 Model Equations

Given the above assumptions in Section 3.1.3 and the description of the variables and parameters in Table 1, the mathematical model can be described by the first-order nonlinear ordinary differential equations shown in Section 3.2.1. It is a system of differential equations that defines the rate of change of each compartment over time. These equations account for the interactions between compartments, transmission rates, recovery rates, and vaccination effects, and the model equations form the foundation for the analysis.

3.2.1 Equations

The equations are formulated based on the conceptual framework as provided in Figure 1.

Susceptible individuals (S)

To derive the equation for the rate of change of susceptible individuals ($\frac{dS}{dt}$), we considered all processes that affect the number of susceptible individuals in the population, such as births, which add new susceptibility to the population. Assuming that every newborn is susceptible and that the birth rate is equal to the natural death rate (μ), the rate of new susceptibility entering the population (N) becomes μN. Furthermore, individuals are exposed to infection through contact with infectious individuals. The rate at which susceptible individuals become exposed is proportional to the number of contacts between the susceptible and infectious individuals.

Further, if β represents the transmission rate per contact, then the rate of new exposures is βS , where S $denotes$ the number of susceptible individuals, I denotes the number of infectious individuals, and N is the total population. It further argued that, for vaccination, the susceptible are vaccinated at a rate ν, so the rate at which susceptible leave the S compartment due to vaccination is (νS). The susceptible leaves the S compartment through natural death at the rate of μS.

Therefore, combining the above, where the births add susceptibility by$+\mu N$, infection reduces susceptibility by $-\frac{\beta SI}{N}$, vaccination reduces susceptibility by $-\nu S$ and natural death reduces susceptibility by$-\mu S$, yielding the following results:

$\frac{dS}{dt} = \mu N - \beta\frac{SI}{N} - \nu S - \mu S$ ……. (1) where μ represents normal or natural birth as well as the mortality rate, N is the total population, β is the transmission rate, and ν is the vaccination rate.

Exposed individuals (E)

Consider exposed individuals who come from the susceptible class S when in contact with infectious individuals I. The rate at which susceptible individuals are exposed is given by $\frac{\beta SI}{N}$ where β is the transmission rate per contact, S is the number of susceptible individuals, I is the number of infectious individuals, and N is the total population. It follows that progression to infectious, where the exposed individuals become infectious at a rate σ, the degree to which the exposed class is likely to become infectious is σE. Natural death occurs when exposed individuals leave the E compartment through natural death at a rate μE.

Therefore, combining these factors, by adding an infection that increases the number of exposed individuals by $+\frac{\beta SI}{N}$, the progression to infection reduces exposed individuals by $-\sigma E$, and natural death reduces exposed individuals by $-\mu E$. This results in a differential equation for the exposed individuals, as shown in equation (2):

$\frac{dE}{dt} = \beta\frac{SI}{N} - (\sigma + \mu)E$ …… (2) and σ is the rate at which exposed individuals become infectious.

Infectious individuals (I)

To derive the equation for the rate of change of infectious individuals $\frac{dI}{dt}$, consider the rate at which infectious I recuperate from the disease, by the rate of γ, which will result in a reduction in the number of infectious individuals by γI. A natural death similar to equation (2) above, which focuses on the natural death rate of infectious individuals given by μI, reduces the number of infectious individuals. Therefore, combining these terms results in Equation 3:

$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$ …… (3)

Recovered individuals (R)

To derive the equation for the rate of change of recovered individuals$\frac{dR}{dt}$, recovery represents the rate at which infectious individuals I recover from the disease. This occurs at a rate γ, the term is γI. Natural Death is a term that accounts for the natural death rate of recovered individuals, which is μR, and this term reduces the number of recovered individuals. Combining the two processes, where recovery increases recovered individuals by $+\gamma I$ and Natural Death decreases recovered individuals by $-\mu R$; the differential equation for the recovered individuals is then.

$\frac{dR}{dt} = \gamma I - \mu R$ …… (4)

Vaccinated individuals (V)

To derive the equation for the rate of change of vaccinated individuals given by $\left(\frac{dV}{dt}\right)$. This equation represents individuals who have been vaccinated and are thus less likely to become infected. The first term in the equation represents the rate at which vulnerable or susceptible individuals (S) are immunized, which occurs at a rate ν, the term is expressed as νS. Further, for waning immunity, due to the protection provided by the vaccine, which decreases at a

rate ω, the term will be given as $-\omega V$ as it tends to reduce the number of individuals in the vaccinated compartment. Again, natural death is similar to the above, but the difference here is that it focuses on the natural death of vaccinated individuals, which is given by μV. This also reduces the number of vaccinated individuals. When combining these three processes by vaccination, which increases vaccinated individuals by $+\nu S$, waning immunity, which also decreases vaccinated individuals by $-\omega V$, and natural death decreases vaccinated individuals by $-\mu V$;

$$\frac{dV}{dt} = \nu S - (\mu + \omega)V \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

Where ω is the waning rate of vaccine immunity.

Environmental concentration of cholera bacteria (C)

To derive the equation for the rate of change in the environmental concentration of cholera bacteria, we used the derivative ($\frac{dC}{dt}$). This equation represents the bacteria present in the environment that can infect susceptible individuals. These bacteria can be due to a number of factors, including contributions by infectious individuals and the rate at which infectious individuals (I) contribute to the environmental load of cholera bacteria. This occurs at a rate α so that the term can be expressed as αI. The natural decay of the bacteria in the environment, whereby over time, the bacteria die at a rate δ so that the term will be $-\delta C$. This term reduces the environmental concentration of the bacteria. Finally, sanitation interventions, such as reduction in the environmental concentration of bacteria due to sanitation interventions, such as clean water supply and proper sewage disposal. This occurs at a rate ϕ, and the term is expressed as $-\phi C$.

Then, combining these three processes will result in a differential equation expressed as:

$$\frac{dC}{dt} = \alpha I - \delta C - \phi C \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (6)$$

where α is the rate at which infectious individuals contribute to the environmental load, δ is the natural decay rate of the bacteria, and ϕ is the rate of reduction due to sanitation interventions.

Therefore, the Cholera model as a system of ODEs is shown in Equation (7).

$$\left.\begin{aligned} \frac{dE}{dt} &= \beta\frac{SI}{N} - (\sigma + \mu)E \\ \frac{dI}{dt} &= \sigma E - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I - \mu R \\ \frac{dV}{dt} &= \nu S - (\mu + \omega)v \\ \frac{dC}{dt} &= \alpha I - \delta C - \phi C \end{aligned}\right\} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$

3.2.2 Model Parameters Estimation

Accurate parameter values are essential for realistic simulation. We estimated parameters such as transmission rates (β), recovery rates (γ), vaccination rate (ν), and environment decay rate (δ), $\mu, \sigma, \omega, \alpha, \phi$ as explained in the above sections, from available data and literature during the simulation period (in days).

Table 1

Description of Parameters

Parameter	Description	Dimension	Value	Source
N	Total population	2012-2022	471409	(Rugeiyamu, 2022)
μ	Natural birth and death rates	Day^{-1}	1/70/365	Assumed
β	Transmission rate	Day^{-1}	0.4	Assumed
ν	Vaccination rate	Day^{-1}	0.07	(Fung, I. C. H., 2014)
σ	The frequency at which exposed individuals become transmissible.	Day^{-1}	1/7	Assumed
γ	Recovery rate	Day^{-1}	γ = 0.20 day-1	(Fung, I. C. H., 2014)
ω	Waning rate of vaccine immunity	Day^{-1}	1/365	Assumed
α	The rate at which infectious individuals contribute to the environmental load	Cells/ ml-day	10	(Wang & Modnak, 2011)
δ	The natural decay rate of the bacteria	Day^{-1}	0.05	Assumed
ϕ	Rate of Cholera bacteria reduction due to sanitation interventions	Day^{-1}	0.02	(Grad et al., 2012)

Several model parameters were assumed due to the lack of setting-specific empirical estimates. These assumed values were chosen to ensure biological plausibility and consistency with previously published cholera transmission and environmental models. In particular, the transmission rate β was set to 0.4 day^{-1}, representing a moderate-to-high transmission scenario appropriate for cholera-prone settings. Sensitivity analyses were conducted to assess the robustness of the model outcomes to variations in assumed parameters.

3.3 Basic Model Properties

3.3.1 Non-Negativity and Boundedness

For the model to be biologically feasible, all state variables (S, E, I, R, V, and C) must remain non-negative for all $t \geq 0$. This is a standard requirement for epidemiological models because negative values do not have a biological interpretation.

Starting with the first equation for susceptible individuals (S) from Equation (1):

$$\frac{dS}{dt} = \mu N - \frac{\beta SI}{N} - \nu S - \mu S \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (8)$$

Solving Equation (8) by applying the integrating factor $\rho(t) = e^{\int(\nu+\mu)dt} = e^{(\nu+\mu)t}$ leads to the following solution:

$$S(t) = \frac{\mu N}{\nu + \mu} + Ce^{-(\nu+\mu)t}$$

Given that $S(0) \geq 0$, we can determine C such that $S(t) \geq 0$ for all $t \geq 0$.

The same was performed for the remaining (E, I, R, V, and C).

The sum of the compartments did not exceed the universal population (N), and the environmental concentration of cholera bacteria (C) remained within realistic limits.

Consider the universal population at any time (t), which is the sum of all individual compartments.

$$P(t) = S(t) + E(t) + I(t) + R(t) + V(t) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (9)$$

Upon differentiation of Equation (9) with respect to time (t), we obtain

$$\frac{dP}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt} + \frac{dV}{dt}$$

Substituting the given ODEs for each compartment, we have:-

$$\frac{dP}{dt} = (\mu N - \frac{\beta SI}{N} - \nu S - \mu S) + (\frac{\beta SI}{N} - (\sigma + \mu)E) + (\sigma E - \gamma I - \mu I) + (\gamma I - \mu R) + (\nu S - (\mu + \omega)V) \ldots\ldots.(10)$$

Simplifying equation (10) leads to:

$$\frac{dP}{dt} = \mu N - \mu(S + E + I + R + V) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (11)$$

Equating to zero, i.e. $\frac{dP}{dt} = 0$

This implies that $P(t)$ remains constant over time. If we assume non-negative initial conditions such as $(0) + E(0) + I(0) + R(0) + V(0) \leq N$, then $P(t) \leq N$ for all $t \geq 0$.

3.3.2 The Disease-Free Equilibrium

DFE involves analyzing the conditions under which a population can remain free of cholera, such that DFE is a state in the model where the number of infectious individuals is zero, and new cholera cases are not introduced.

In the context of the ODE model for cholera dynamics, the DFE is the state where the disease is absent from the population, as shown by the system of OD equations in equation (7).

Lemma 1. Assuming that there was no introduction of new infections ($E = 0$), the environment was free from cholera bacteria ($C = 0$). If $I = 0$, then system (7) has an equilibrium point.

$$\text{DFE} = \left(\frac{N}{1 + \frac{\nu}{\mu}}, 0, 0, \frac{\nu N}{\mu(1 + \frac{\nu}{\mu}) + \omega}, 0, 0 \right)$$

3.3.3 Basic Reproduction Number (R_0)

To calculate the basic reproduction number R_0 using the next-generation matrix method (NGM), F and V were used in the NGM, where F represents the new infection terms, and V represents the transition terms. For each element, F_{ij} represents the mean number of new infections in compartment (i) produced by an individual in compartment (j), and for each element, V_{ij} represents the rate at which individuals leave compartment (i) due to recovery, vaccination, or death. The NGM was then calculated as FV^{-1}, which represents the expected number of new infections produced by a single infected individual during their infectious period in a population where everyone else is susceptible.
That is:-

$$F = Jacobian\ of\ new\ infection\ terms\ at\ DFE$$
$$V = Jacobian\ of\ transition\ terms\ at\ DFE$$
$$NGM = FV^{-1}$$
$$R_0 = Spectral\ radius\ of\ NGM$$

$$F = \begin{bmatrix} 0 & \frac{\beta I}{N} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \sigma & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \nu & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha & 0 & 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \mu+\nu & 0 & 0 & 0 & 0 & 0 \\ -\sigma & \sigma+\mu & 0 & 0 & 0 & 0 \\ 0 & \sigma & \gamma+\mu & 0 & 0 & 0 \\ 0 & 0 & -\gamma & \mu & 0 & 0 \\ \nu & 0 & 0 & 0 & \mu+\omega & 0 \\ 0 & 0 & 0 & 0 & 0 & \delta+\phi \end{bmatrix}$$

The MATLAB result for the basic reproduction number using NGM is shown in Figure 2:

```
Command Window
>> BASIC_REPRODUCTION_NUMBER
The basic reproduction number R0 is: 0.00081634
```

Figure 2
Basic Reproduction Number

Interpretation of R_0
If $R_0 > 1$, the disease can spread; If $R_0 < 1$, the disease will die out.

Therefore, the basic reproduction number R_0 is 0.00081634, indicating a good average for the disease to die out over time. However, the computed basic reproduction number is R_0=0.00081634, which is significantly less than unity, indicates that, under the combined effects of vaccination and environmental sanitation interventions, cholera transmission is effectively eliminated. Consequently, the disease-free equilibrium is stable, and sustained outbreaks cannot occur within the modeled framework.

3.3.4 Stability of the DFE

DFE stability is crucial for understanding whether an infectious disease is likely to die or persist in a population. To determine the stability of the DFE, we analyzed the Jacobian matrix of the system at the DFE. An interesting result will be to deduce if all the eigenvalues of the Jacobian at the DFE have negative real parts. If this occurs, we conclude that the DFE is locally asymptotically stable.

From Lemma 1, we obtain the disease-free equilibrium point. The analysis of the stability around the DFE is stated in Theorem 1.

Theorem 1. If $R_0 < 1$, the DFE is asymptotically stable. If $R_0 > 1$, the DFE is not stable.
Proof:

The Jacobian matrix of the DFE from the system of equations, as denoted in equation (7), is denoted by the capital letter J. Solving the modulus $|J - \lambda I| = 0$, gives the eigenvalue λ. To obtain the Jacobian Matrix at the DFE, the partial derivatives of the right-hand side of each differential equation with respect to each state variable are used. For the cholera model, the state variables were S, E, I, R, V, and C. At the DFE, I assumed that $I = 0$, $E = 0$, and $C = 0$. Consider the system of ODEs, given as

$$\frac{dS}{dt} = \mu N - \beta \frac{SI}{N} - \nu S - \mu S$$

$$\frac{dE}{dt} = \beta\frac{SI}{N} - (\sigma + \mu)E$$
$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$
$$\frac{dR}{dt} = \gamma I - \mu R$$
$$\frac{dV}{dt} = vS - (\mu + \omega)v$$
$$\frac{dC}{dt} = \alpha I - \delta C - \phi C$$

The Jacobian Matrix is given by

$$J = \begin{bmatrix} \frac{\partial S}{\partial S} & \frac{\partial S}{\partial E} & \frac{\partial S}{\partial I} & \frac{\partial S}{\partial R} & \frac{\partial S}{\partial V} & \frac{\partial S}{\partial C} \\ \frac{\partial E}{\partial S} & \frac{\partial E}{\partial E} & \frac{\partial E}{\partial I} & \frac{\partial E}{\partial R} & \frac{\partial E}{\partial V} & \frac{\partial E}{\partial C} \\ \frac{\partial I}{\partial S} & \frac{\partial I}{\partial E} & \frac{\partial I}{\partial I} & \frac{\partial I}{\partial R} & \frac{\partial I}{\partial V} & \frac{\partial I}{\partial C} \\ \frac{\partial R}{\partial S} & \frac{\partial R}{\partial E} & \frac{\partial R}{\partial I} & \frac{\partial R}{\partial R} & \frac{\partial R}{\partial V} & \frac{\partial R}{\partial C} \\ \frac{\partial V}{\partial S} & \frac{\partial V}{\partial E} & \frac{\partial V}{\partial I} & \frac{\partial V}{\partial R} & \frac{\partial V}{\partial V} & \frac{\partial V}{\partial C} \\ \frac{\partial C}{\partial S} & \frac{\partial C}{\partial E} & \frac{\partial C}{\partial I} & \frac{\partial C}{\partial R} & \frac{\partial C}{\partial V} & \frac{\partial C}{\partial C} \end{bmatrix} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (12)$$

Taking $S = N$ and applying the partial derivatives, equation (12) becomes:

$$J = \begin{bmatrix} -\mu - \nu & 0 & -\beta & 0 & 0 & 0 \\ 0 & -(\sigma + \mu) & \beta & 0 & 0 & 0 \\ 0 & \sigma & -(\gamma + \mu) & 0 & 0 & 0 \\ 0 & 0 & \gamma & -\mu & 0 & 0 \\ \nu & 0 & 0 & 0 & -(\mu + \omega) & 0 \\ 0 & 0 & \alpha & 0 & 0 & -(\delta + \phi) \end{bmatrix} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (13)$$

Determining the determinant, $|J - \lambda I| = 0$, leads to the equation:

$$(-\mu - v - \lambda)(-(\sigma + \mu) - \lambda)(-(\gamma + \mu) - \lambda)(-\mu - \lambda)(-(\mu + \omega) - \lambda)(-(\delta + \phi) - \lambda) = 0$$

Therefore, the eigenvalues are:-

$$\lambda_1 = -\mu - \nu \lambda_2 = -(\sigma + \mu) \lambda_3 = -(\gamma + \mu) \lambda_4 = -\mu \lambda_5 = -(\mu + \omega) \lambda_6 = -(\delta + \phi)$$

The result for the eigenvalues calculated in the Jacobian matrix is shown in the snapshot of the MATLAB interface below:

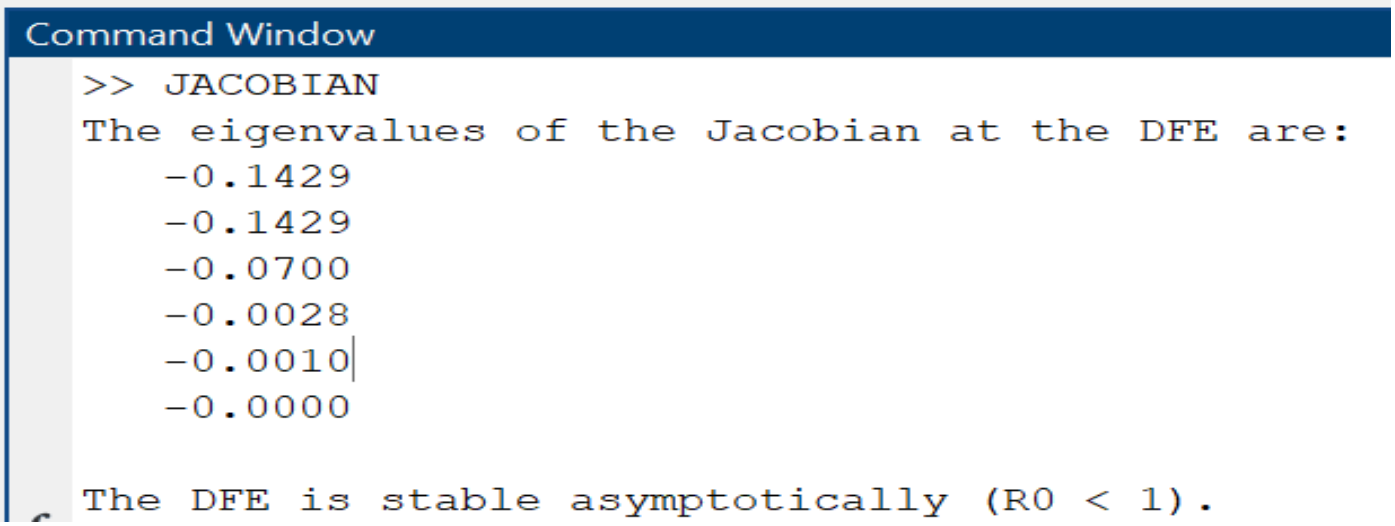


Figure 3

Eigenvalues of the Jacobian at the DFE

Thus, from Figure 3, according to the Routh-Hurwitz criterion, the eigenvalues of all Jacobians have negative real parts, indicating that this occurs when $R_0 < 0$, thus proving the stability of the DFE.
Therefore, the basic reproduction number calculation forms the basis of the sensitivity analysis described in Section 3.3.5.

3.3.5 Sensitivity Scrutiny of the Rudimentary Reproduction Number

Mathematically, sensitivity scrutiny involves calculating the partial derivatives of R_0 for each parameter to determine how a small change in parameter values would affect R_0. This can help to identify parameters that significantly impact disease transmission. It involves several steps: first, to calculate R_0 using a next-generation matrix, and then to calculate the partial derivatives of R_0 concerning (p). To compare the sensitivity of R_0 to different parameters on a similar scale, we calculated the normalized sensitivity coefficients, which are defined as $S_p = \frac{\partial R_0}{\partial p} \cdot \frac{p}{R_0}$, where S_p is the sensitivity coefficient for parameter p as shown in Table 2.

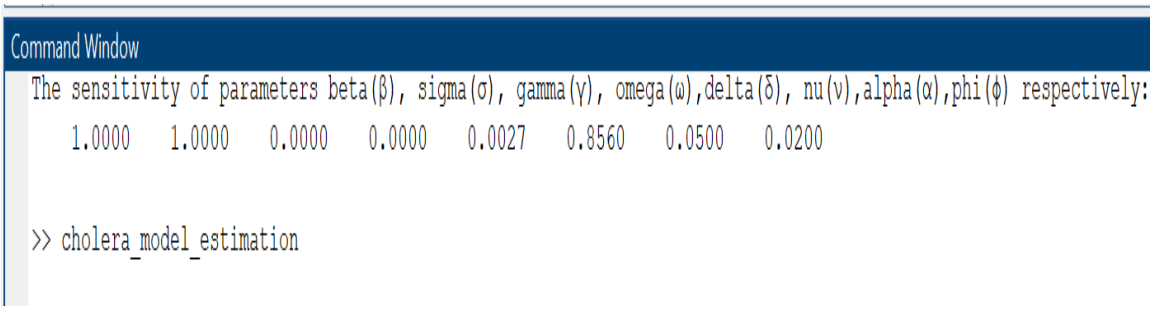


Figure 4
Matlab results for sensitivity analysis parameters

Table 2
Sensitivity Analysis for Parameters

Parameter	Description	Sensitivity index	Meaning
β	Transmission rate	1.0000	Highly sensitive; primary driver of transmission
ν	Vaccination rate	0.8560	Strong control leverage
σ	The frequency at which exposed individuals become transmissible.	1.0000	Strong influence on epidemic growth
γ	Recovery rate	0.0000	Negligible effect
ω	Waning rate of vaccine immunity	0.0000	Negligible effect
α	The rate at which infectious individuals contribute to the environmental load	0.0500	Low sensitivity
δ	The natural decay rate of the bacteria	0.0027	Minimal effect
ϕ	Rate of Cholera bacteria reduction due to sanitation interventions	0.0200	Low but supportive impact

The sign of S_p Indicates the direction of change (positive or negative), and the magnitude indicates the strength of the impact. Parameters with larger absolute values of S_p had a greater effect on R_0 . A normalized forward sensitivity analysis was conducted to assess the relative influence of model parameters on the model outcome (basic reproduction number/infection burden). The results indicate that the transmission rate (β) and the rate at which exposed individuals become infectious (σ) are the most influential parameters, each with a sensitivity index of 1. This implies that a 1% increase in either parameter results in a proportional 1% increase in the model outcome. The vaccination rate (ν) also exhibits a high sensitivity index (0.856), highlighting the substantial impact of vaccination coverage on cholera transmission dynamics. This result underscores the effectiveness of vaccination strategies as a control measure.

In contrast, the recovery rate (γ) and the waning rate of vaccine-induced immunity (ω) have negligible sensitivity indices, indicating a limited influence on the model outcome within the parameter ranges considered. Environmental parameters, including the bacterial decay rate (δ), bacterial shedding rate (α), and sanitation intervention rate (ϕ), exhibit relatively low sensitivity values. While their individual effects are modest, these parameters collectively contribute to reducing environmental contamination and complement direct human-targeted interventions.

3.4 Optimal Control

The mathematical framework for determining the best strategies for managing and controlling the spread of infectious diseases is well explained in optimal control theory. Diversities of the optimal control methods have been used to understand the dynamics of some diseases (Kumar et al., n.d.). In this study, we borrowed from Albalawi et al. (2023) to identify cost-effective cholera vaccinations and environmental hygiene interventions. The sensitivity analysis above suggests that the optimal control model is highly responsive to changes in key parameters, particularly transmission rate (β), vaccination rate (ν), and sanitation intervention rate (ϕ). After defining the two control measures, model (7) is rewritten as follows:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \mu N - \beta\frac{SI}{N} - w(t)S - \mu S \\
\frac{dE}{dt} &= \beta\frac{SI}{N} - (\sigma+\mu)E \\
\frac{dI}{dt} &= \sigma E - \gamma I - \mu I \\
\frac{dR}{dt} &= \gamma I - \mu R \\
\frac{dV}{dt} &= w(t)S - (\mu+\omega)V \\
\frac{dC}{dt} &= \alpha I - \delta C - \phi(t)C
\end{aligned}\right\} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (14)$$

The objective function includes the costs associated with each compartment and the control efforts.

$$K(w,\phi) = \int_0^{t_f}\left(C_1S(t) + C_2I(t) + C_3E(t) + C_4V(t) + C_5C(t) + \frac{1}{2}\tau\left(w^2(t) + \phi^2(t)\right)\right)dt$$

C_1, C_2, C_3, C_4, C_5 are the weights of the susceptible, infectious, exposed, vaccinated, and environmental compartments, respectively; τ is the cost parameter for the control measures; u(t) represents vaccination control; and $\phi(t)$ represents environmental hygiene intervention control.

The controls u^* and ϕ^* can be computed for which $J(u^*,\phi^*) = \min\{J(u,\phi),(u,\phi)\in U\}$. The set U is called the set of controls and is described as

$U = \{(u,\phi)|\left(u(t),\phi(t)\right)\ is\ Lebsgue\ measurable\ on\ the\ interval\ [0,0.9]$, such that

$0 \le \left(u(t),\phi(t)\right) \le 0.9\}$. Using the Pontryagin Maximum Principle (Chambers et al., 1965), we can obtain the necessary conditions and solutions for a system with ODE number (8).

The Hamiltonian H incorporates the objective function and state equations. To obtain the objective, we obtain Hamiltonian H as follows:

Let $X = (S,E,I,R,V,C), \lambda = (\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5,\lambda_6)$ and $U = (u,\phi)$ then we have

$$H(X,U,\lambda) = C_1S(t) + C_2I + C_3E(t) + C_4V(t) + C_5C(t) + \frac{1}{2}\tau\left(u^2(t) + \phi^2(t)\right)$$
$$+\lambda_{S(t)}\left(\mu N - \frac{\beta SI}{N} - \nu S - \mu S\right) + \lambda_{E(t)}\left(\beta\frac{SI}{N} - \sigma E - \mu E\right) + \lambda_{I(t)}(\sigma E - \gamma I - \mu I)$$
$$+\lambda_{R(t)}(\gamma I - \mu R) + \lambda_{V(t)}(\nu S - \mu V - \omega V) + \lambda_{C(t)}(\alpha I - \delta C - \phi C) \qquad (15)$$

The optimal control $u^*(t)$ and $\phi^*(t)$ result from setting the partial derivatives of the Hamiltonian for the control variables to zero.

$\frac{\partial H}{\partial u} = \tau u(t) + \lambda_{S(t)}(-S) + \lambda_{V(t)}(S) = 0 \Rightarrow u^*(t) = \frac{\lambda_{V(t)} - \lambda_{S(t)}}{\tau}$, and

$\frac{\partial H}{\partial \phi} = \tau\phi(t) + \lambda_{C(t)}(-C) = 0 \Rightarrow \phi^*(t) = \frac{\lambda_{C(t)}}{\tau}$

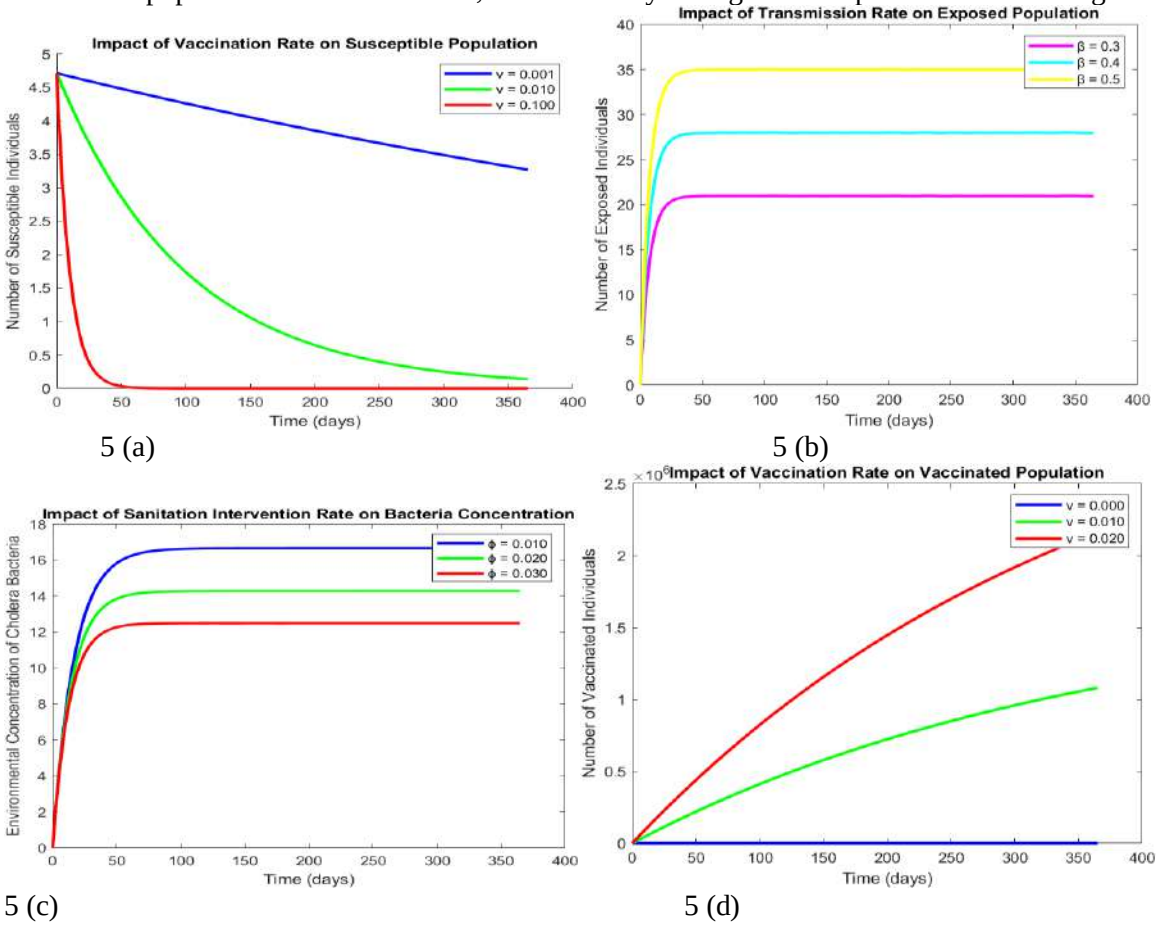
Then applying the constraints on the control functions will result in:

$u^*(t) = \max\{\min\left[\frac{\lambda_{V(t)} - \lambda_{S(t)}}{\tau}, 0.9\right], 0\}$ and $\phi^*(t) = \max\{\min\left[\frac{\lambda_{C(t)}}{\tau}, \phi_{max}\right], 0\}$

IV. FINDINGS & DISCUSSION

4.1 Findings

The simulation results are presented in a series of figures, each illustrating the impact of different intervention rates on the population and environment, and ultimately the figures for optimal control strategies.



5 (a) 5 (b)

5 (c) 5 (d)

Figure 5

Impact of Vaccination and Sanitation Intervention Rate

In Figure 5(a), the vaccination rate ($v = 0.001$) and the blue curve represent a low vaccination rate. We observed a gradual decline in the number of susceptible individuals over time. This suggests that, at a low vaccination rate, the population remains at risk for a longer period, and herd immunity is achieved more slowly. Similarly, the vaccination rate ($v = 0.010$) shown in the green curve indicates a moderate rate. The decline in susceptible individuals is more pronounced and occurs faster than the blue curve. This rate of vaccination leads to a quicker reduction in the number of persons at risk and suggests a more effective control of disease spread. Finally, the vaccination rate ($v = 0.100$) shown in the red curve indicates a high vaccination rate. There was a rapid and steep decline in the number of susceptible individuals, indicating that a high vaccination rate can significantly accelerate the achievement of herd immunity and effectively control the outbreak.

The general conclusion from the graphs is that increasing the vaccination rate has a substantial impact on reducing the number of susceptible individuals in the population. A higher immunization rate leads to a faster decrease in the number of individuals at risk of contracting cholera, which is crucial for timely control of an outbreak. On the other hand, Figure 5 (b) illustrates the effect of different transmission rates on the exposed population. Even small increases in the transmission rate can significantly affect the spread of the disease.

If the Transmission Rate ($\beta = 0.3$), as shown by the magenta curve, represents a low transmission rate. This shows a gradual increase in the number of exposed individuals, indicating that the disease spreads more slowly throughout the population. This peak was relatively low, suggesting that fewer individuals were exposed to cholera at this rate. Similarly, the transmission rate ($\beta = 0.4$) indicated by the curve indicates a slightly higher transmission rate. The number of exposed individuals increases more quickly and reaches a peak higher than the pink curve. This suggests that even a small increase in transmission rate can significantly affect the spread of the disease. Ultimately, the transmission rate ($\beta = 0.5$) indicated by the yellow curve represents a high transmission rate. The number of exposed

individuals skyrockets quickly, reaching the highest peak among all curves. This indicates that at high transmission rates, the disease can spread rapidly, leading to a large number of exposed individuals in a short time frame.

Figure 5 (c) highlights the influence of sanitation intervention rate on the environmental concentration of cholera bacteria. The sanitation intervention rate ($\varphi = 0.01$) represented by the blue curve indicates a low rate of sanitation intervention. This shows that the concentration of cholera bacteria gradually declined in the environment. This suggests that, at lower intervention rates, the reduction in bacteria is slower, and it takes longer to reach safer levels. The sanitation intervention rate ($\varphi = 0.020$) indicated by the green curve indicates a moderate sanitation intervention rate. The decrease in bacterial concentration was more pronounced compared to the blue curve, suggesting that increasing the intervention rate can lead to a more significant and faster reduction in environmental bacterial levels. The sanitation intervention rate ($\varphi = 0.030$) indicated by the red curve indicates a high rate of sanitation intervention. There was a rapid and steep decline in the concentration of bacteria, indicating that aggressive sanitation measures can quickly reduce the bacteria to minimal levels, greatly reducing the risk of transmission.

This graph illustrates the importance of sanitation interventions in controlling the spread of cholera. Effective sanitation measures, such as treating water sources and improving waste management, are crucial for reducing the presence of cholera bacteria and preventing outbreaks.

Finally, on figures, Figure 5 (d) highlights the impact of vaccination rates on the number of vaccinated individuals, and the vaccination rate ($v = 0.000$) is represented by a blue curve, indicating that if there are no vaccination campaigns that are conducted, it simply means that there are no vaccinated individuals, which is logically true. Similarly, the vaccination rate ($v = 0.010$) indicated by the green curve indicates that the provision of vaccination services to the population groups by 10% will slightly increase the number of vaccinated individuals with a curve of gentle slope in nature. Furthermore, the vaccination rate ($v = 0.020$) shown by the red curve indicates that an increase of 10% from the first increase will lead to a rapid increase in the number of vaccinated individuals. This implies that more vaccination campaigns conducted in populations with susceptible individuals will lead to an increase in the number of vaccinated persons, which then reduces the number of individuals who are at risk of cholera infection.

4.1.1 Result of Numerical Simulation on Optimal Control Measures

From the Optimal Control Problem, as explained in detail in the previous section, the simulation for the combined strategies for Cholera Optimal Control is as follows.

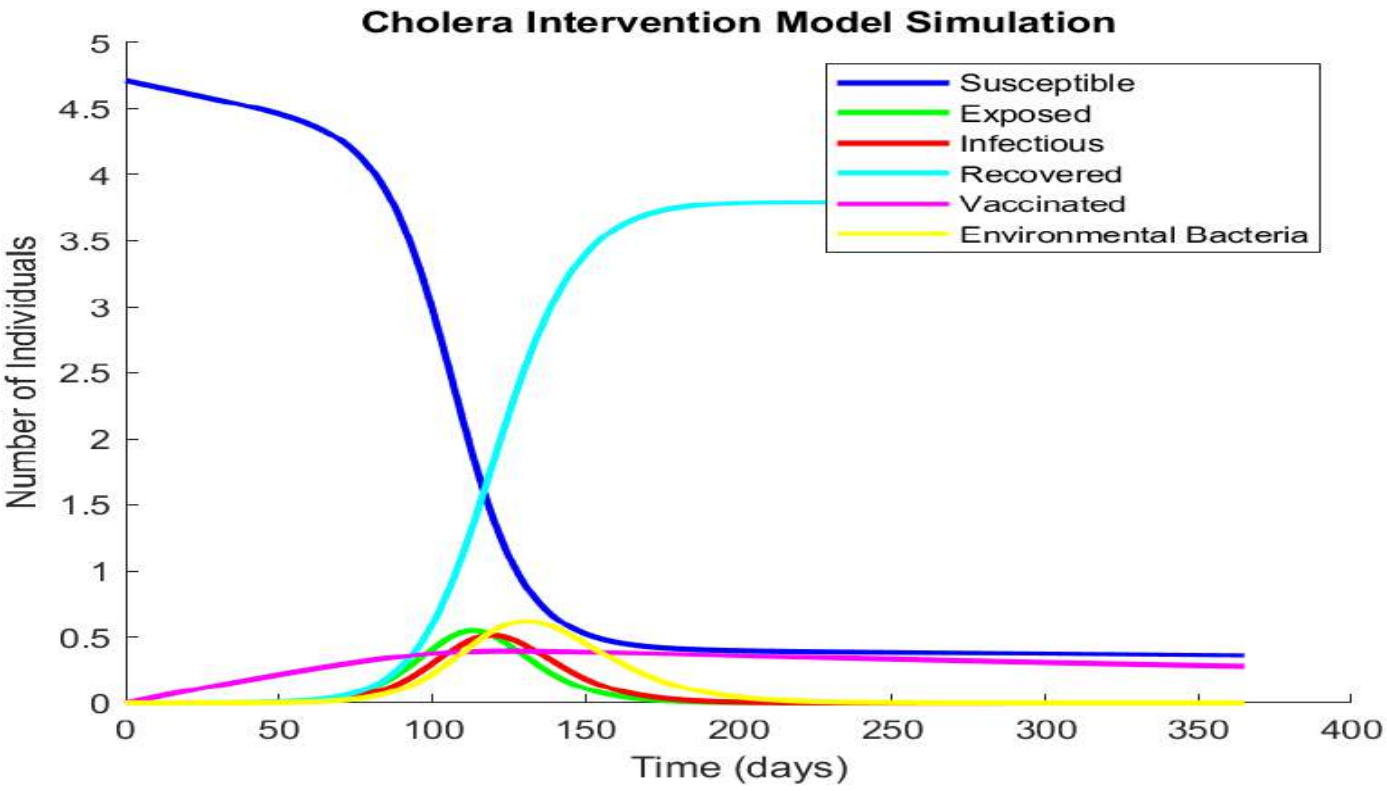


Figure 6
Cholera Intervention Model Simulation

Figure 6 shows the time evolution of susceptible, exposed, infectious, recovered, and vaccinated compartments. A notable observation is the peak in the infectious compartment, which indicates the height of the outbreak before

interventions take effect. The disease dynamics and influence of the intervention over a simulated period of 400 days, as shown above, are detailed below:

Susceptible (S): The susceptibility (S) of individuals starts at the highest point, indicating the total population at risk of infection. It decreases as individuals become exposed to cholera, either through direct contact with infectious individuals or through environmental bacteria.

Exposed (E): Exposed individuals initially rise as more susceptible individuals contact bacteria. However, it does not reach as high as the susceptible curve owing to the transition of exposed individuals to the infectious state after the incubation period. *Infectious (I):* It has a sharp peak near the 125-day mark, indicating a rapid increase in cholera cases. This peak represents the height of the outbreak before intervention, and natural recovery begins to reduce the number of infectious individuals. *Recovered (R):* The cyan curve for recovered individuals increases over time, reflecting those who have recovered from cholera and developed immunity. This curve continues to rise as more individuals recover from the infection. *Vaccinated (V):* Vaccinated individuals showed a steady increase, representing the rollout of the vaccination campaign. As more individuals are vaccinated, the rate of new infections slows down, contributing to the control of the outbreak.

Environmental Bacteria (C): The figure shows that the environmental bacteria concentration initially rises as the bacteria spread through the environment. However, it begins to decline as hygiene interventions take effect, reducing the presence of bacteria and the risk of transmission. Therefore, the simulation demonstrated the effectiveness of vaccination and environmental hygiene interventions in controlling cholera outbreaks. The early peak and subsequent decline in the infectious curve suggest that timely interventions can significantly reduce the transmission of the disease.

The Impact of effective vaccination and environmental hygiene measures can be extended further to smooth changes to reflect real-life situations on changes in each compartment. The interpretation of Figures 6 and 7 both emphasizes the effects of the implementation of control measures. The u^* represented by the cyan color, stands for vaccination control, and ϕ^* which is represented by black colors, stands for environmental hygiene intervention control; all of these control measures are implemented together in an effective way, which then reduces the state of other compartments and increases the number of recovered individuals.

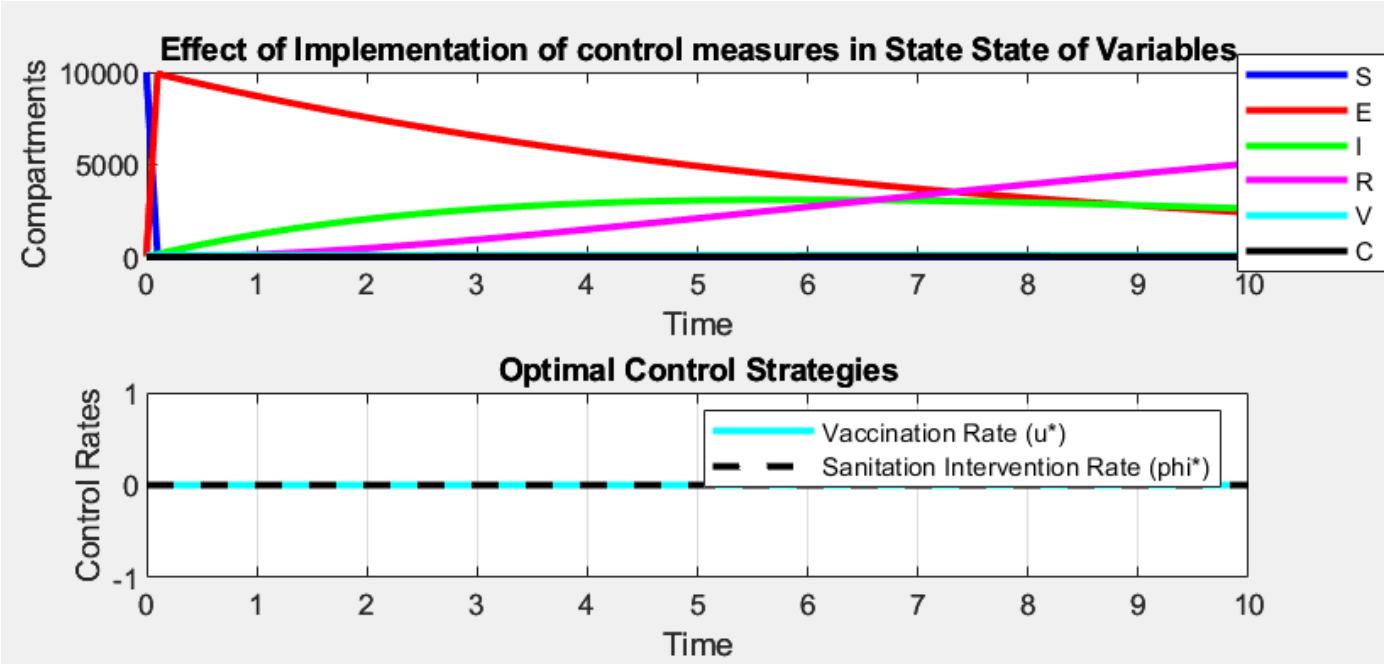


Figure 7
Effect of the Control Measures

Figures 6 and 7 collectively demonstrate the effectiveness of vaccination and environmental sanitation interventions in monitoring cholera transmission. The simulation results show a quick decline in the number of infectious individuals and environmental bacterial concentration over time when control measures are implemented, indicating a clampdown of disease transmission and stability of the disease-free equilibrium. Compared to scenarios without intervention, vaccination reduces the susceptible population while sanitation measures diminish environmental contamination, thereby weakening both direct and indirect transmission pathways. The combined application of these interventions produces a synergistic effect, leading to faster elimination of cholera and substantially lower infection levels, consistent with the analytically derived basic reproduction number being well below unity. From a public health perspective, these findings support the implementation of integrated cholera control strategies that simultaneously

prioritize mass vaccination campaigns and sustained investments in water, sanitation, and hygiene infrastructure to achieve effective and long-term disease prevention.

V. CONCLUSION & RECOMMENDATIONS

5.1 Conclusion

This study used the Ordinary Differential Equation (ODE) model to evaluate the effectiveness of vaccination and environmental hygiene interventions in governing cholera outbreaks. The study further utilized MATLAB for numerical simulations and explored the impact of varying immunization rates and sanitation measures on the dynamics of cholera transmission within a population over a simulated period of 400 days. The model attempted to optimize cholera interventions by combining vaccination strategies with environmental hygiene measures. The general idea was to make suggestions that would help to minimize the incidence of cholera cases and associated mortality within the population. The results showed that the spread of cholera disease largely depends on the contact rates with infected individuals in the set where a large number is at risk of acquiring the cholera pathogen (susceptible members), and the number of bacteria in the environment greatly contributes to the increase in the spread of diseases. The model also highlights the importance of immunity level among individuals, which can be boosted through vaccination campaigns. We conclude that if the proportion of the population that is immune exceeds the herd immunity level for cholera disease, then cholera disease can no longer persist in the population. Furthermore, the model showed the significance of environmental hygiene as an effective measure for reducing the concentration of cholera bacteria in the environment, which can greatly contribute to an increase in the spread of cholera. Therefore, the model underscores the importance of timely and combined interventions, including vaccination campaigns and improved sanitation, to control cholera outbreaks effectively. The observed trend suggests that such measures can lead to a significant decrease in the number of infections and environmental bacteria, thereby mitigating the spread of the disease and achieving the objectives of Goals 3 and 6 of the UN's Sustainable Development Goals.

5.2 Recommendations

Guided by the general objective which was to assess the effectiveness of vaccination and environmental hygiene interventions in controlling cholera outbreaks and based on the results obtained, this study recommends that public health authorities adopt a combined cholera control strategies that concurrently strengthen vaccination coverage and environmental hygiene interventions. Precisely, the implementation of sustainable and well-coordinated vaccination campaigns should be in place to guarantee that immunity levels within the population exceed the herd immunity edge, thereby interfering sustained cholera transmission. Along with this, the investments in improved sanitation, waste management systems, safe and effective water supply are vital to reduce the concentration of the bacterium in the environment, which the model identifies as a key driver of disease spread. Further, timely deployment of these combined interventions, particularly in high-risk and densely populated societies, is crucial for minimizing cholera incidence and associated mortality. Policy makers also have the role to play and should leverage mathematical modeling and numerical simulation tools, such as ODE-based models, to guide evidence-based planning, resource allocation, and early response strategies. Strengthening surveillance systems and promoting community level hygiene practices will further enhance the effectiveness of these interventions. Collectively, these recommendations support sustainable cholera control efforts and contribute directly to the attainment of Sustainable Development Goals 3 & 6 on good health and well-being as well as clean water and sanitation, respectively.

Declaration of Interest

The authors declare that they do not have any known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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