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The *SEIRS* Model Simulation of Cholera Transmission with Treatment and Vaccination

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ABSTRACT

Cholera is an acute diarrhoea infection caused by the bacterium 'Vibrio cholerae' ingestion of contaminated food or water. Cholera remains a global public health threat as well as an indicator of inequity and a lack of social development. This research aims to investigate the impact of treatment and vaccination on cholera disease transmission using the SEIRS model. In this research, the dynamic behaviour of susceptible, exposed, infected, and recovered populations are illustrated using three different simulation cases: the influence of treatment only, the influence of vaccination only, and the influence of a combination of treatment and vaccination on the SEIRS model, respectively. Additionally, this research also analyses the effects of treatment factors and vaccination variation on the infected populations. The basic reproductive number is also calculated with respect to the variation in vaccination rate. To illustrate the theoretical results, some numerical simulations are provided. The findings indicate that adequate vaccination and treatment levels are required to eradicate cholera from the population.

Keywords: Cholera transmission, Numerical simulation, *SEIRS* model, Treatment, Vaccination

1 INTRODUCTION

Cholera is an acute intestinal infectious disease caused by consuming food or water directly or indirectly contaminated with faeces or vomits from infected individuals carrying the Gram-negative bacterium Vibrio cholerae [1]. Severe diarrhoea is a lethal infection that can cause acute severe watery diarrhoea. It will usually take a person from 12 hours to 5 days to show the symptoms after ingesting infected food or water, the person may sweat excessively and become dehydrated over a few days [2]. This illness, a warning sign of acute diarrheal sickness, could be fatal if not treated promptly and thoroughly [3]. Some research and testing indicate that a person who has recovered may be immune to the illness for three to ten years. Current research indicates that immunity may be lost after a few weeks [4-8].

Cholera is still a significant public health problem in many countries today. Even though it has been a long time since its first outbreak, the disease is still present in several developing countries, particularly those with poor sanitation and insufficient clean drinking water. Case Fatality Rate (CFR) measures the severity of a particular disease by defining the total number of deaths as a proportion

of reported cases of a specific disease at a specific time. CFR is presented as a percentage (0%-100%) or a ratio (between 0-1) and measures the number of confirmed deaths among the number of confirmed diagnosed cases of a particular disease at a given time. As of 23rd March 2021, the cumulative number of suspected cholera cases is 780, including two associated deaths with a Case Fatality Ratio (CFR) of 0.3 [9].

Researchers have made numerous attempts over the years to stop the spread of the cholera epidemic, including using the mathematical model. Mathematical models have been developed and studied to understand how cholera outbreaks spread, primarily with the Haitian cholera epidemic of 2010–2011 [10]. The optimal control function, which is the proportion of ill persons that receive treatment through quarantine, and how to structure and solve an optimal control problem is determined [11]. The first-ever oral cholera vaccine program was started in Yemen on 6th May 2018, under guidelines from the World Health Organization (WHO); however, it was stopped on 15th May 2018[12-14].

A study was carried out to understand better how different control strategies interact with different cholera transmission pathways and to provide valuable recommendations for effective cholera prevention strategies. The modification adds three other types of controls to the original model: immunization, therapeutic treatment (such as hydration therapy, antibiotics, etc.), and water sanitation [14]. Other techniques utilize similar concepts in mathematical techniques to introduce mathematical models such as *SIR* and *SEIR* [15-19].

SEIRS model is an extension model from the *SIR* and *SEIR* models with a slight improvement as it considers both vaccination and treatment methods [20-24]. This study allows the researcher to determine the effect of different disease control strategies that effectively use the vaccination and water treatment approaches. This paper is organized as follows: Section 2 discusses the formulation of the *SEIRS* model, the existence of disease-free and endemic equilibrium points, as well as the basic reproductive number. Section 3 illustrates the findings of numerical simulations for various scenarios. Finally, in the final section, the conclusions and recommendations are highlighted.

2 *SEIRS* MODEL FORMULATION

This section highlights the formulation of mathematical modeling of cholera transmission with vaccination and treatment. In addition, the disease-free equilibrium points, endemic equilibrium points, and basic reproductive numbers are also discussed.

The transmission of cholera to the human population can be illustrated by the *SEIRS* model. The model in this paper was inspired by Side et al. [3]. However, some modifications are made to the model in terms of the treatment factor, which subsequently improved the rate of change for the infected and recovered groups. The *SEIRS* model divides the human population into four categories. The first group is the susceptible (S) population, which represents the number of cholera susceptible people. The second group is the exposed (E) population, which consists of humans who have been identified but have not yet been infected with the disease. The third group is the infected (I) population, including humans infected with the disease. Finally, the recovered (R) population is defined as individuals who have been cured of the disease but have no immunity, implying that they will return to a susceptible group.

All parameters are assumed to be positive. Parameter A denotes the number of healthy new-born humans per unit of time. μ is the rate of natural death that occurs in each susceptible, exposed, infected, or recovered group. β and α indicate the rate of disease transmission and infectivity, respectively. Individuals infected with cholera can recover from their illness at a rate of recovery, γ. The parameter σ refers to the proportion of recovered individuals who return to the susceptible group. The parameter q represents the proportion of infected individuals who received the treatment. Individuals who survive the treatment will subsequently be transferred to the recovered class. The parameter $v\epsilon(0,1)$ represents the proportion of susceptible individuals who received the vaccine. The vaccine is assumed to be initiated in response to an outbreak, indicating that vaccination provides immediate control.

With all these assumptions, the following flowchart describes cholera transmission with vaccination and treatment:

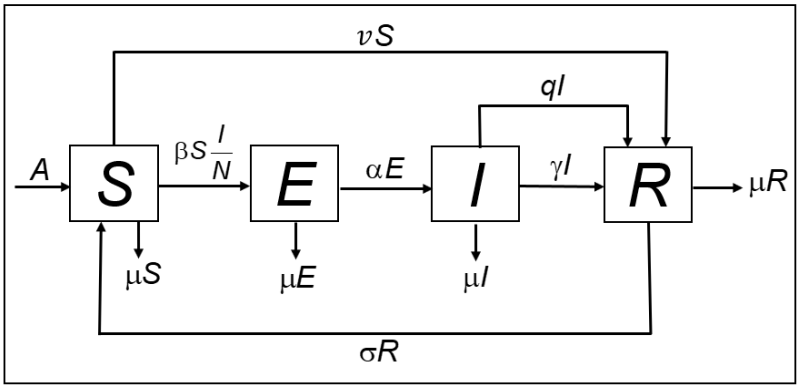


Figure 1: Schematic diagram of cholera transmission with vaccination and treatment.

Based on Figure 1, the mathematical model is expressed by a set of differential equations as follows:

$$\frac{dS}{dt} = A + \sigma R - \beta S\frac{I}{N} - vS - \mu S$$

$$\frac{dE}{dt} = \beta S\frac{I}{N} - \alpha E - \mu E$$

$$\frac{dI}{dt} = \alpha E - qI - \gamma I - \mu I \qquad (1)$$

$$\frac{dR}{dt} = \gamma I + vS + qI - \sigma R - \mu R$$

with $S(0) = S_0 \geq 0, E(0) = E_0 \geq 0, I(0) = I_0 \geq 0, R(0) = R_0 \geq 0,$

and $S(t) + E(t) + I(t) + R(t) = N.$

To find the equilibrium points, the model (1) assumable to be equal to zero. There are at most two equilibrium points in the system:

i) Free-disease equilibrium point,

$$\varepsilon_0 = (S^0, 0,0, R^0) = \left(\frac{A(\mu+\sigma)}{\mu(\mu+\sigma+v)}, 0,0, \frac{Av}{\mu(\mu+\sigma+v)}\right).$$

This equilibrium point indicates the absence of cholera disease in the populations.

ii) Endemic equilibrium point, $\varepsilon_1 = (S^*, E^*, I^*, R^*)$ where

$$S^* = \frac{N(\alpha+\mu)(\mu+\gamma+q)}{\alpha\beta}$$

$$E^* = \frac{\alpha\beta(A+\sigma R^*) - N(v+\mu)(\alpha+\mu)(\mu+\gamma+q)}{\alpha\beta(\alpha+\mu)}$$

$$I^* = \frac{\alpha\beta(A+\sigma R^*) - N(v+\mu)(\alpha+\mu)(\mu+\gamma+q)}{\beta(\alpha+\mu)(\mu+\gamma+q)}$$

and R^* satisfies

$$R^* = \frac{Nv(\mu+\gamma+q)}{\alpha\beta} + \frac{(v-q)[\alpha\beta(A+\sigma R^*) - N(v+\mu)(\alpha+\mu)(\mu+\gamma+q)]}{\alpha(\alpha+\mu)^2(\mu+\gamma+q)}.$$

This equilibrium point describes the presence of cholera disease in the populations.

Next, the basic reproductive number is calculated using the next generation matrix and represented as follows:

$$R_0 = \frac{\beta A\alpha(\mu+\sigma)}{N\mu(\mu+\sigma+v)(\alpha+\mu)(\mu+\gamma+q)}. \quad (2)$$

The R_0 value represents an average of infectious humans who spread to another number of n susceptible populations. The cholera disease occurs when the value of $R_0 > 1$. Meanwhile, the cholera disease does not occur for $R_0 < 1$. In other words, the disease is eradicated. When $R_0 = 1$, cholera disease occurs, and it is constant for one infected human to transmit another susceptible human.

The Jacobian matrix is then used to analyze the stability of these two equilibrium points:

$$J_{SEIRS} = \begin{bmatrix} -\frac{\beta I}{N} - v - \mu & 0 & -\frac{\beta S}{N} & \sigma \\ \frac{\beta I}{N} & -\alpha - \mu & \frac{\beta S}{N} & 0 \\ 0 & \alpha & -\gamma - \mu - q & 0 \\ v & 0 & \gamma + q & -\sigma - \mu \end{bmatrix}. \quad (3)$$

The stability analysis is carried out using Maple software, whereas MATLAB software is used to simulate and analyse the dynamical behaviour of susceptible, exposed, infected, and recovered populations based on model (1). The standard values for the parameters used in this project were

adapted from Aghdaoui et al. [24]. All simulations and analyses that required calculations were solved using the standard parameter values listed in Table 1 below.

Table 1: Parameter values used in *SEIRS* model

Parameter	Description	Standard value	Source
A	Newborns	20/day	[24]
σ	Rate of returning individuals vulnerable	0.1/day	[24]
β	Cholera transmission rate	0.8/day	[24]
α	Cholera infectivity rate	0.8/day	[24]
γ	Recovery rate	0.1/day	[24]
μ	Death rate	0.1/day	[24]
v	Vaccination rate	Varied	Assumed
q	Treatment rate	Varied	Assumed

3 RESULTS AND DISCUSSION

3.1 Dynamical Behaviour of Susceptible, Exposed, Infected, and Recovered Populations

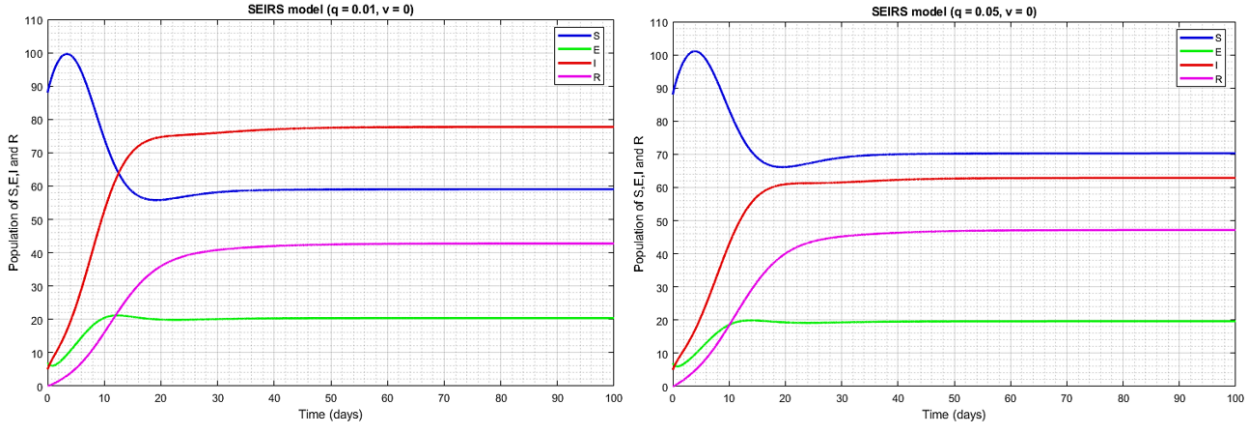
In this section, the dynamic behaviour of susceptible, exposed, infected, and recovered populations is illustrated using three different simulation cases: the influence of treatment only, the influence of vaccination only, and the influence of a combination of treatment and vaccination on the *SEIRS* model (1), respectively. The initial conditions for all the simulations are set to $(S_0, E_0, I_0, R_0) = (88,7,5,0)$.

3.1.1 Case I: The Influence of Treatment on the SEIRS Model

In this case, the model only considers the treatment factor and omits the vaccination parameter. We aim to compare the effects of treatments within 100 days with the treatment parameter values $q = 0.01$ and $q = 0.05$. These treatment parameter values refer to the proportion of infected populations who received the treatment factor, such as water treatment. Fluids and electrolytes are given to cholera patients in hospitals to prevent dehydration. This is essential for restoring fluid balance and avoiding death.

Figures 2(a) and 2(b) depict the behaviour of susceptible, exposed, infected, and recovered populations for treatment effects $q = 0.01$ and $q = 0.05$, respectively. According to our observations, on the 100^{th} day, the susceptible population increased from 59 to 70, while the infected population decreased from 78 to 63. The recovered population has increased from 43 to 48 people. This

demonstrates that by increasing the rate of treatment, the number of people who recover can be increased.

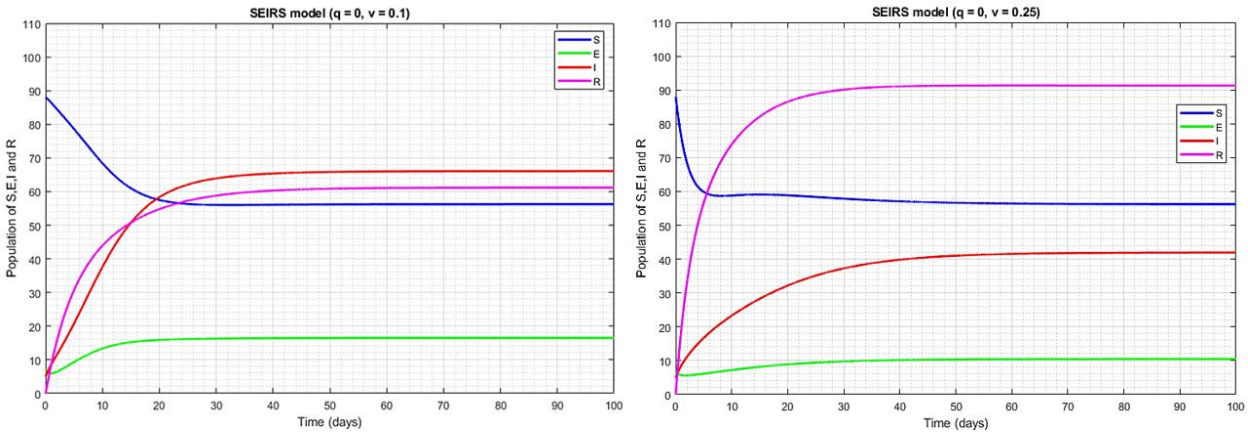


(a) (b)

Figure 2: The *SEIRS* simulations with the influence of treatment, (a) $q = 0.01$ and (b) $q = 0.05$.

3.1.2 Case II: The Influence of Vaccination on The SEIRS Model

In this case, the model investigates the vaccination effect while excluding the treatment parameter. Figures 3(a) and 3(b) demonstrate the behaviour of populations for the influence of vaccination parameters $v = 0.1$ and $v = 0.25$, respectively. The value of these parameters describes the proportion of the susceptible population that receives a cholera vaccination injection. For this analysis, we observed the behaviour of populations on the 100th day. As the vaccination proportion increases, the exposed and infected populations decrease from 17 to 11 and 68 to 42, respectively. In contrast, the recovered population increased from 61 to 91 people.

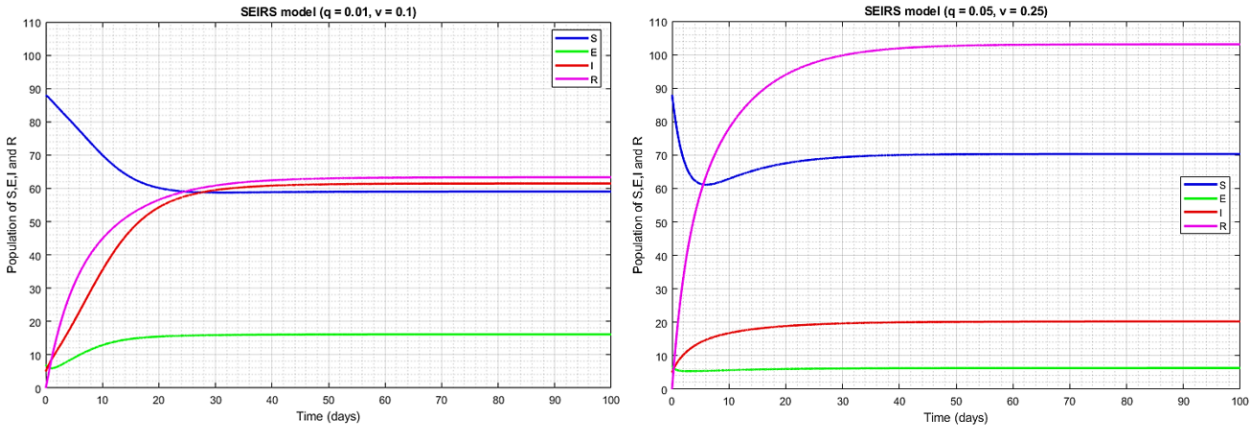


(a) (b)

Figure 3: The *SEIRS* simulations with the influence of vaccination, (a) $v = 0.1$ and $v = 0.25$.

3.1.3 Case III: The Influence of Treatment and Vaccination on the SEIRS Model

The combination of treatment factor and vaccination are considered in the simulation. Figure 4(a) depicts the behaviour of populations when infected populations are treated at a rate of $q = 0.01$, and susceptible populations are vaccinated at a rate of $v = 0.1$. In comparison, other infected and susceptible populations receive a treatment rate of $q = 0.05$ and a vaccination rate of $v = 0.25$, respectively. The findings indicate that as treatment and vaccination rates are increased simultaneously, there are significant increases and decreases for some populations. For example, compared to the results obtained in Figures 4(a) and 4(b), the infected population decreased dramatically to 20 people on day 100. On the other hand, the recovered population increased significantly from 65 to 103 people. This situation proves that the strategy of combining treatment and vaccination methods was effective in reducing cholera cases and increasing the recovery number among those infected.



(a) (b)

Figure 4: The *SEIRS* simulations with the influence of both treatment and vaccination, (a) $q = 0.01, v = 0.1$ and (b) $q = 0.05, v = 0.25$.

3.2 The Combine Influence of Treatment and Vaccination.

In this section, the effect of treatment or vaccination versus infected populations is studied. The simulation of different cases is shown in Figure 5 and Figure 6.

3.2.1 Case I: The Effect of Treatment Variation on Infected Populations

This is the simulation of the model when the vaccination rate is fixed at $v = 0.30$. For observing behavioural changes in infected populations, various treatment rates of $0.01, 0.02, 0.05, 0.1$, and 0.15 are considered. These values represent the proportion of total populations that have been given various treatment rates, q. It can be observed that as the value of the treatment rate increase, the value of infected people will reduce faster. From the simulation graph in Figure 5, we can see that over 100 days, when the treatment rate value increases to 15%, the infected population becomes 0. It means that if the infected population gets the full treatment, it is possible to fully recover in a short time.

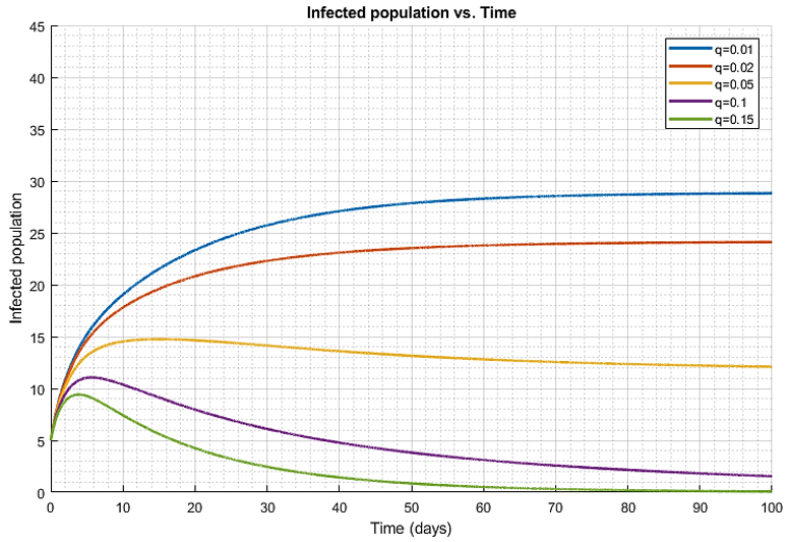


Figure 5: The effect of varying treatment rate, q on the infected populations.

3.2.2 Case II: The Effect of Vaccination Variation on Infected Populations

This is the simulation of the model when the treatment factor rate is fixed at $q = 0.15$. Different vaccination rates of $0.1, 0.15, 0.2, 0.35,$ and 0.65 are assumed for analysing behavioural changes in infected populations. Next, we explore the influence of the vaccination rate, v, on the infected population, as illustrated in Figure 6. These values represent the proportion of the total infected population that has been vaccinated. It can be observed that as vaccination rates increase, the number of infected people reduces. When the vaccination rate increases by 65%, the number of infected people decreases and eventually disappears after 30 days. As a result, vaccination appears to be an effective method for preventing the spread of cholera transmission.

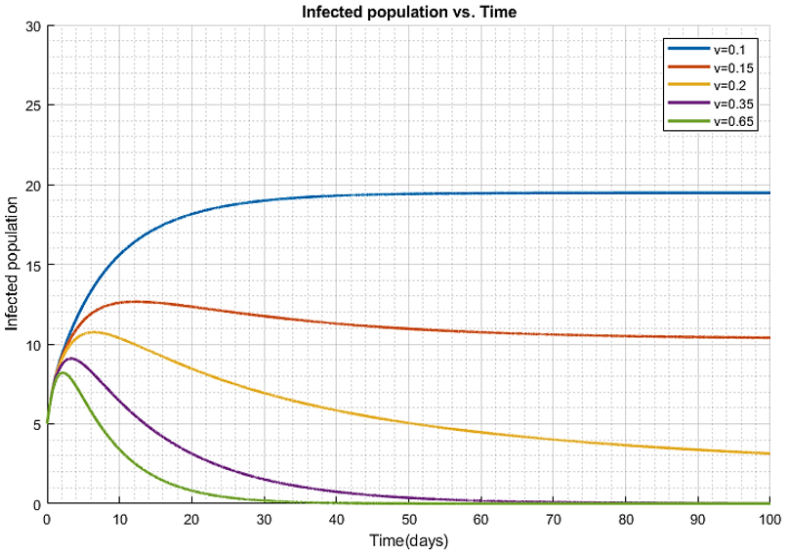


Figure 6: The effect of varying vaccination rate, v on the infected populations.

Table 2 shows a summary of vaccination rates, v and basic reproductive numbers, R_0. The basic reproductive number is calculated using equation (2) and parameter values from Table 1, with parameter q set to 0.15. We can see that as the vaccination rate rises, the basic reproductive number drops. Moreover, when the vaccination proportion reaches 65%, the basic reproductive number, $R_0 = 0.96$, is less than one. This value indicates that the cholera disease is being eradicated.

Table 2: The basic reproductive number with respect to the vaccination rate.

Variation of vaccination rate (v)	Basic reproductive number (R_0)
0.10	2.71
0.15	2.32
0.20	2.03
0.35	1.48
0.65	0.96

4 CONCLUSION

This research expands on a *SEIRS* model of cholera infection that incorporates treatment and vaccination. Based on our findings, we can conclude that the rate of vaccination and treatment will influence the spread of cholera disease. Adequate levels of vaccination and treatment are required to eradicate cholera from the population. As vaccination and treatment rates increase simultaneously, the percentage of infected people decreases, it shows from simulation when the vaccination reaches 65%, the basic reproductive number is less than 1 which implying that there will be no endemic cases of cholera, and the disease will eventually decline in prevalence. This research, on the other hand, is merely based on a previous study's data and parameter values. As a potential future research, we could investigate the real cholera problem in specific countries, such as Malaysia.

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