

## Research Article

# Analysis and Optimal Control Intervention Strategies of a Waterborne Disease Model: A Realistic Case Study

Obiora Cornelius Collins<sup>1,2</sup> and Kevin Jan Duffy<sup>1</sup>

<sup>1</sup>*Institute of Systems Science, Durban University of Technology, Durban 4000, South Africa*

<sup>2</sup>*School of Mathematics, Statistics and Computer Science, University of KwaZulu-Natal, Durban 4000, South Africa*

Correspondence should be addressed to Obiora Cornelius Collins; obiora.c.collins@gmail.com

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A mathematical model is formulated that captures the essential dynamics of waterborne disease transmission under the assumption of a homogeneously mixed population. The important mathematical features of the model are determined and analysed. The model is extended by introducing control intervention strategies such as vaccination, treatment, and water purification. Mathematical analyses of the control model are used to determine the possible benefits of these control intervention strategies. Optimal control theory is utilized to determine how to reduce the spread of a disease with minimum cost. The model is validated using a cholera outbreak in Haiti.

## 1. Introduction

Waterborne diseases which include Cholera, Hepatitis A and Hepatitis E, Giardia, Cryptosporidium, and Rotavirus are among the serious health problems of people globally. This is especially so in developing countries where there is limited access to clean water. Unsafe water supply, poor sanitation and poor hygiene are major causes of waterborne diseases [1]. According to WHO [2], approximately 1.1 billion people globally do not have access to sources of reliable water. About 700,000 children die every year from diarrhoea caused by unsafe water and poor sanitation [3]. The prevalence of waterborne diseases could be controlled especially in developing countries through access to safe water, provision of adequate sanitation facilities, and better hygiene practices [1]. Control measures such as water purification, vaccination, and treatment of infected individuals are among the most effective ways of reducing the spread of these diseases [4–6]. In this study, we investigate the impact of these types of control measures in reducing the spread of waterborne diseases.

Even with the availability of control measures, affordability is often the greatest obstacle for many communities where

diseases are endemic. The spread of waterborne diseases are often associated with poverty, limited resources, and low socioeconomic status [2, 7]. Optimal control theory can point to efficient approaches to reduce the spread of a disease with minimum costs [4, 8]. In this study, we consider optimal control theory to investigate how to reduce the spread of waterborne diseases with minimum costs.

Some of the essential factors that influence the dynamics of waterborne diseases include sanitation [9], different transmission pathways [10, 11], water treatment efforts [12, 13], pathogen ecology outside of human hosts [14], climatological factors or seasonal fluctuations [15–18], and heterogeneity in disease transmission [19, 20]. Understanding how these factors interact to influence the dynamics of waterborne diseases are challenging, making the dynamics of waterborne diseases complex. Several theoretical studies have taken some of these factors into account to improve the understanding of waterborne disease dynamics and subsequently investigate the possible means of reducing the diseases [7, 11, 19, 21–26]. Even though these studies have contributed immensely in improving the understanding of waterborne disease dynamics, theoretical studies for waterborne disease dynamics and control are not complete. In this study, we

consider mathematical models to investigate the dynamics and control of waterborne diseases. The findings complement existing results in the literature on the dynamics and control of waterborne diseases.

The remaining parts of this paper are organized as follows. In Section 2, a waterborne disease model, which underpins the essential dynamics, is presented and analysed. To determine the possible benefits of control measures a multiple control model (with all controls imposed simultaneously) is presented and analysed in Section 3. In Section 4, optimal control analyses are used to investigate how to reduce the spread of a disease with minimum costs. The model is validated by using it to study a cholera outbreak in Haiti in Section 5. We conclude the paper by discussing our results in Section 6.

## 2. Waterborne Disease Model and Analysis

In this section we present a waterborne disease model that underlies the dynamics for a homogeneous population without any control intervention measures. Analyses of this model are necessary as a comparison to understand the effects of the control intervention strategies included in subsequent sections.

**2.1. Formulation of the Control-Free Model.** We consider an extension of the standard SIR model under the assumption of constant human population size  $N(t)$  by adding a compartment  $W(t)$  that measures pathogen concentration in a water reservoir [11, 27]. As usually done, the total human population  $N(t)$  is partitioned into susceptible  $S(t)$ , infected  $I(t)$ , and recovered individuals  $R(t)$  such that  $N(t) = S(t) + I(t) + R(t)$ . Individuals enter the susceptible class  $S(t)$  through birth at a rate  $\mu$ . Susceptible individuals  $S(t)$  become infected with waterborne disease through contact with contaminated water at a rate  $b$ . Direct person-to-person transmissions are not considered because water-to-person transmissions have been shown to be the major route of waterborne disease transmissions [6, 23, 28]. Infected individuals  $I(t)$  shed pathogens into water at a rate  $\nu$  and recover naturally at a rate  $\gamma$ . Pathogens are generated naturally in the water at a rate  $\alpha$  and decay at a rate  $\xi$ . Natural human deaths occur at a rate  $\mu$ . With these assumptions we obtain the model

$$\begin{aligned}\dot{S}(t) &= \mu N(t) - bS(t)W(t) - \mu S(t), \\ \dot{I}(t) &= bS(t)W(t) - (\mu + \gamma)I(t), \\ \dot{W}(t) &= \nu I(t) - \sigma W(t), \\ \dot{R}(t) &= \gamma I(t) - \mu R(t),\end{aligned}\tag{1}$$

where  $\sigma = \xi - \alpha > 0$  is the natural decay rate of pathogens in the water reservoir. Note that our model (1) is in the form considered by Tien and Earn [11] to study the multiple transmission pathways for waterborne diseases. A difference is that they considered infections to be generated through both direct person-to-person and indirect water-to-person contacts. Our approach that considers infections through

indirect water-to-person contacts only is particularly relevant with waterborne diseases such as cholera which are primarily transmitted through contaminated water.

For the qualitative analyses of model (1), we consider a dimensionless version given by

$$\begin{aligned}\dot{s}(t) &= \mu - \beta s(t)w(t) - \mu s(t), \\ \dot{i}(t) &= \beta s(t)w(t) - (\mu + \gamma)i(t), \\ \dot{w}(t) &= \sigma(i(t) - w(t)), \\ \dot{r}(t) &= \gamma i(t) - \mu r(t),\end{aligned}\tag{2}$$

where  $s = S/N$ ,  $i = I/N$ ,  $r = R/N$ ,  $w = \sigma W/(\nu N)$ , and  $\beta = b\nu N/\sigma$ .

All parameters are realistically assumed positive and the initial conditions are as follows:

$$\begin{aligned}r(0) &> 0, \\ i(0) &\geq 0, \\ w(0) &\geq 0, \\ r(0) &\geq 0.\end{aligned}\tag{3}$$

All the solutions of model (2) considered are in the feasible region

$$\Phi = \{s, i, w, r > 0 : s + i + r = 1\}. \tag{4}$$

$\Phi$  is positively invariant and the existence and uniqueness of solutions of model (2) hold in this region. Thus, model (2) is well posed mathematically and epidemiologically in  $\Phi$ .

**2.2. Basic Reproduction Number.** The control-free model (2) has a unique disease-free equilibrium (DFE) given by

$$(s^0, i^0, w^0) = (1, 0, 0). \tag{5}$$

The basic reproduction number  $\mathcal{R}_0$  of the control-free model (2) is determined using the next generation matrix method [29]:

$$\mathcal{R}_0 = \frac{\beta}{(\gamma + \mu)}. \tag{6}$$

**2.3. Stability Analysis of the Disease-Free Equilibrium.** For a dynamical infectious disease model, stability about its disease-free equilibrium (DFE) describes the short-term dynamics of the disease [30]. Therefore to determine the short-term dynamics of the waterborne disease considered here, it is necessary to investigate the stability of the control-free model (2) about its DFE. From Theorem 2 in van den Driessche and Watmough [29], the following result holds.

**Theorem 1.** *The DFE of the control-free model (2) is locally asymptotically stable if  $\mathcal{R}_0 < 1$  and unstable if  $\mathcal{R}_0 > 1$ .*

Theorem 1 implies that waterborne disease can be eliminated from the entire population (when  $\mathcal{R}_0 < 1$ ) if the initial

size of the infected population is in the basin of attraction of the DFE (5). On the other hand, the disease will establish in the population if  $\mathcal{R}_0 > 1$ .

**Theorem 2.** *The DFE of the control-free model (2) is globally asymptotically stable provided that  $\mathcal{R}_0 < 1$ .*

This theorem can be established using a global stability result by Castillo-Chavez et al. [31]. This global stability ensures that disease elimination is independent of the initial size of the population of infected individuals if  $\mathcal{R}_0 < 1$ . The epidemiological implication is that in this case waterborne disease can be eradicated from the entire community irrespective of the initial number of infected people in the community.

**2.4. Outbreak Growth Rate.** If  $\mathcal{R}_0 > 1$ , then the DFE (5) becomes unstable and a disease outbreak occurs in the population. The positive (dominant) eigenvalue of the Jacobian at the DFE is typically referred to as the initial outbreak growth rate [11]. The eigenvalues of the Jacobian matrix of model (2) evaluated at the DFE (5) are

$$\begin{aligned} \lambda_1 &= -\mu, \\ \lambda_2 &= \frac{1}{2} \left[ -(\mu + \gamma + \sigma) \right. \\ &\quad \left. - \sqrt{(\mu + \gamma + \sigma)^2 + 4\sigma(\mu + \gamma)(\mathcal{R}_0 - 1)} \right], \\ \lambda_3 &= \frac{1}{2} \left[ -(\mu + \gamma + \sigma) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + \sigma)^2 + 4\sigma(\mu + \gamma)(\mathcal{R}_0 - 1)} \right]. \end{aligned} \quad (7)$$

Clearly,  $\lambda_1, \lambda_2 < 0$ . Thus, the positive (dominant) eigenvalue is given by

$$\lambda^+ = \lambda_3. \quad (8)$$

From the above results, when  $\mathcal{R}_0 = 1$  the outbreak growth rate  $\lambda^+$  vanishes. Also, if  $\mathcal{R}_0 < 1$  all three eigenvalues become negative confirming Theorem 1. So the outbreak growth rate ( $\lambda^+$ ) exists only when  $\mathcal{R}_0 > 1$ . Epidemiologically, this result demonstrates how for  $\mathcal{R}_0 > 1$  an outbreak will occur in the community and the growth rate of that outbreak is determined by  $\lambda^+$ . In particular, this might occur when there are no control measures. Next it is necessary to obtain the likely magnitude of an outbreak, often called the expected final size of the outbreak [32].

**2.5. Final Outbreak Size.** Our analyses have shown that when  $\mathcal{R}_0 > 1$  a waterborne disease outbreak occurs and grows at the rate  $\lambda^+$ . The final outbreak size of SIR epidemiological models and other similar models are given by the relation

$$Z = 1 - \exp(-\mathcal{R}_0 Z), \quad (9)$$

where  $Z$  denotes the proportion of the population who become infected at some point during the outbreak. This

relation applies to our control-free model (2) [11] and so if there is no control intervention and an outbreak occurs, with  $\mathcal{R}_0 > 1$  then the final outbreak size of the epidemic can be determined by (9).

**2.6. Stability Analysis of the Endemic Equilibrium.** The long-term dynamics of a dynamical system is characterized by the stability about its endemic equilibrium [30]. To determine the long-term dynamics of the control-free model (2) we investigate its stability about this endemic equilibrium (EE). Algebraically, it can be demonstrated that when  $\mathcal{R}_0 > 1$ , a unique EE occurs in model (2) given by

$$(s^e, i^e, w^e) = \left( \frac{1}{\mathcal{R}_0}, \frac{\mu(\mathcal{R}_0 - 1)}{\mathcal{R}_0(\gamma + \mu)}, i^e \right). \quad (10)$$

Obviously,  $i^e$  will vanish if  $\mathcal{R}_0 \leq 1$ . This confirms that the disease cannot be endemic when  $\mathcal{R}_0 \leq 1$ . The stability analyses of the EE (10) are summarized as follows using [11, 33–36].

**Theorem 3.** *The unique endemic equilibrium (10) is locally and globally asymptotically stable whenever  $\mathcal{R}_0 > 1$ .*

The proof of Theorem 3 can be established using the approach in [11] and implies that whenever  $\mathcal{R}_0 > 1$  any outbreak in the population will persist in the population (remain endemic). So, to minimize the chances of a disease outbreak the intervention of control measures can be used such that the basic reproduction number is kept below unity (i.e.,  $\mathcal{R}_0 < 1$ ).

### 3. Multiple Control Model and Analyses

In this section we present a control model to investigate the impact of introducing control measures in the spread of diseases. Three different types of control measure are considered: vaccination, water purification, and treatment. The impact of these control measures is investigated by extending the original control-free model (2) to include these control measures.

**3.1. Formulation of the Multiple Control Model.** A multiple control model is formulated as follows.

Vaccination is one control strategy for reducing the spread of waterborne diseases such as cholera. For example, a cholera vaccine can offer about 60–90% protection against the disease. Thus in the control model we assume that susceptible individuals are vaccinated at rate  $\phi$  with a vaccine whose efficacy is  $\varepsilon$ . Effectively the model now has new class of individual that are vaccinated.

Effective treatment of waterborne disease is also very important in reducing the spread of the disease. Some waterborne diseases like cholera can kill within hours of contracting the disease if there is no proper treatment. If people infected with cholera are treated quickly and properly, the mortality rate is less than 1% but if they are left untreated, the mortality rate rises to 50–60% [37, 38]. We introduce treatment in the control-free model (2) by assuming that infected

individuals are treated at rate  $\tau$  and treated individuals  $T(t)$  recover due to treatment at rate  $\gamma_\tau$ .

According to the World Health Organization [1], unsafe water, poor sanitation, and poor hygiene are the major causes of waterborne diseases. A significant number of cases of a disease could be reduced through access to clean water supplies, provision of adequate sanitation facilities, and better hygiene practices. Here we extend the model (2) by assuming that provision of clean water reduces pathogen concentrations at a rate  $d$ .

Based on these assumptions, and by introducing these control intervention strategies simultaneously, we obtain the multiple control model

$$\begin{aligned}\dot{s}(t) &= \mu - \beta s(t) w(t) - (\mu + \phi) s(t), \\ \dot{v}(t) &= \phi s(t) - (1 - \varepsilon) \beta v(t) w(t) - \mu v(t), \\ \dot{i}(t) &= \beta s(t) w(t) + (1 - \varepsilon) \beta v(t) w(t) \\ &\quad - (\mu + \gamma + \tau) i(t), \\ \dot{\zeta}(t) &= \tau i(t) - (\mu + \gamma_\tau) \zeta(t), \\ \dot{w}(t) &= \sigma i(t) - (d + \sigma) w(t), \\ \dot{r}(t) &= \gamma i(t) + \gamma_\tau \zeta(t) - \mu r(t),\end{aligned}\tag{11}$$

where  $V$  are vaccinated individuals,  $T$  are treated individuals,  $v = V/N$  are the proportion of vaccinated individuals, and  $\zeta = T/N$  are the proportion of treated individuals.

All the solutions of model (11) enter the feasible region

$$\Phi_c = \{s, v, i, \zeta, w, r > 0 : s + v + i + \zeta + r = 1\}.\tag{12}$$

The region  $\Phi_c$  is positively invariant; thus it is sufficient to consider the solutions of model (11) within it.

**3.2. Basic Reproduction Number for the Multiple Control Model.** The multiple control intervention strategy model (11) has a DFE given by

$$(s_c^0, v_c^0, i_c^0, \zeta_c^0, w_c^0) = \left( \frac{\mu}{\mu + \phi}, \frac{\phi}{\mu + \phi}, 0, 0, 0 \right),\tag{13}$$

and a basic reproduction number given by

$$\mathcal{R}_0^c = \mathcal{R}_0 E_c,\tag{14}$$

where

$$E_c = \frac{\sigma(\gamma + \mu)(\mu + (1 - \varepsilon)\phi)}{(d + \sigma)(\gamma + \mu + \tau)(\mu + \phi)}.\tag{15}$$

The basic reproduction number can be defined as the expected number of secondary infections that result from introducing a single infected individual into an otherwise susceptible population [29]. Thus, the threshold quantity  $\mathcal{R}_0^c$  is a measure of the number of secondary infections of the population in the presence of vaccination, treatment, and water purification. From (15) and (14), we have that

$$\begin{aligned}E_c < 1 &\iff \\ \mathcal{R}_0^c < \mathcal{R}_0.\end{aligned}\tag{16}$$

This implies that the multiple control measures in the model do have an impact in reducing the number of secondary infections.

**3.3. Stability Analysis of the DFE for Multiple Control Measures.** Again, to determine the short-term dynamics in the presence of the multiple control measures we investigate the stability of the multiple control model at the DFE. The results are summarized in the theorem below.

**Theorem 4.** If  $\mathcal{R}_0^c < 1$ , the DFE (13) of model (11) is globally asymptotically stable and unstable if  $\mathcal{R}_0^c > 1$ .

The epidemiological implication of this result is that waterborne diseases can be eradicated from the entire community using multiple control measures irrespective of the initial size of the infected people provided that  $\mathcal{R}_0^c < 1$ .

**3.4. Outbreak Growth Rate for Multiple Control Measures.** Suppose that the multiple control measures are not effective, then  $\mathcal{R}_0^c > 1$  and the DFE (13) becomes unstable and a disease outbreak occurs. The outbreak growth rate of the multiple control model is given by

$$\begin{aligned}\lambda_c^+ &= \frac{1}{2} \left[ -(\mu + \gamma + \tau + \sigma + d) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + \tau + \sigma + d)^2 + 4(\sigma + d)(\mu + \gamma + \tau)(\mathcal{R}_0^c - 1)} \right].\end{aligned}\tag{17}$$

Comparing the outbreak growth rate of the multiple control model with the no control model is summarized in the theorem below.

**Theorem 5.** If  $d \geq 0, \phi \geq 0, \tau \geq 0$ , and  $\varepsilon \geq 0$ , then  $\lambda_c^+ \leq \lambda^+$ . Furthermore,  $\lambda_c^+ = \lambda^+$  if and only if  $d = \phi = \tau = \varepsilon = 0$ .

The proof of this theorem can be established by simple algebraic manipulation. This shows that introducing multiple controls can reduce the outbreak growth rate.

**3.5. Single and Double Control Measures.** Waterborne disease outbreaks are often associated with poverty and limited resources to control the disease [1]. Often such communities cannot afford to introduce more than one control measure such as the three considered here. Thus, it is important to investigate the impact of introducing a single control or double controls. By comparing the impact of a single control, double control, and multiple controls, we determine the control (or combination of controls) that can yield the best results. These comparisons will be done at both the epidemic stage as well as the endemic stage of the outbreak. Theoretically, for the epidemic stage of the outbreak the basic reproduction number is used, while at the endemic stage the outbreak growth rate is used. These results can help in advising communities with limited resources.

### 3.5.1. Basic Reproduction Number for a Single Control Measure.

Suppose the community can afford vaccinations only, then the basic reproduction number is

$$\mathcal{R}_0^v = E_v \mathcal{R}_0, \quad E_v = \frac{\mu + (1 - \varepsilon) \phi}{\mu + \phi}. \quad (18)$$

This threshold quantity  $\mathcal{R}_0^v$  can be understood as a measure of the number of secondary infections in the presence of vaccination [11, 39]. By elementary algebraic manipulations, the equations

$$\begin{aligned} E_v < 1 &\iff \\ \mathcal{R}_0^v < \mathcal{R}_0, & \\ \forall 0 < \varepsilon, \phi \leq 1, & \end{aligned} \quad (19)$$

$$\begin{aligned} E_v = 1 &\iff \\ \mathcal{R}_0^v = \mathcal{R}_0, & \\ \varepsilon = \phi = 0 & \end{aligned} \quad (20)$$

hold. From (19) the number of secondary infections is less when vaccination is introduced provided  $0 < \varepsilon, \phi \leq 1$ , and this implies that introducing vaccination decreases the spread of the infection.

For communities that can afford only treatment the basic reproduction number is

$$\mathcal{R}_0^\tau = \mathcal{R}_0 E_\tau, \quad E_\tau = \frac{\mu + \gamma}{\mu + \gamma + \tau}. \quad (21)$$

Clearly, the equations

$$\begin{aligned} E_\tau < 1 &\iff \\ \mathcal{R}_0^\tau < \mathcal{R}_0, & \\ \tau \neq 0, & \\ E_i^\tau = 1 &\iff \\ \mathcal{R}_0^\tau = \mathcal{R}_0, & \\ \tau = 0 & \end{aligned} \quad (22)$$

hold. Epidemiologically, the treatment of infected individuals reduces the number of secondary infections in the population provided that  $0 < \tau \leq 1$ .

Finally, we investigate the impact of introducing water purification as the only control measure. The water purification induced basic reproduction number is

$$\mathcal{R}_0^w = \mathcal{R}_0 E_w, \quad (24)$$

where

$$E_w = \frac{\sigma}{\sigma + d}. \quad (25)$$

Again the following equations hold:

$$\begin{aligned} E_w < 1 &\iff \\ \mathcal{R}_0^w < \mathcal{R}_0, & \\ \forall d \neq 0, & \end{aligned} \quad (26)$$

$$\begin{aligned} E_w = 1 &\iff \\ \mathcal{R}_0^w = \mathcal{R}_0, & \\ d = 0, & \end{aligned} \quad (27)$$

and introducing water purification reduces the number of secondary infections in the community provided that  $0 < d \leq 1$ .

Having shown the impact of each of the single controls using the basic reproduction number, it is important to compare each of these single controls with the multiple control. Since,  $E_c$  is the product of  $E_v$ ,  $E_\tau$ , and  $E_w$  and each of these is less than 1, then using the calculations of each reproduction number (19), (22), (26), and (16) can be written in compact form as

$$\mathcal{R}_0^c < \mathcal{R}_0^v, \mathcal{R}_0^w, \mathcal{R}_0^\tau < \mathcal{R}_0. \quad (28)$$

These results show that even though each of the single controls has some influence in reducing the number of secondary infections, the multiple control always has at least the greatest influence. The above results agree with intuitive expectation and justify why multiple controls are encouraged whenever an outbreak occurs in any community.

### 3.5.2. Outbreak Growth Rate for a Single Control Measure.

For communities that consider only treatment as a control measure, our analyses show that, if infected individuals are not properly treated such that  $\mathcal{R}_0^\tau > 1$ , then an outbreak occurs in the community. The treatment-induced outbreak growth rate is given by

$$\begin{aligned} \lambda_\tau^+ &= \frac{1}{2} \left[ -(\mu + \gamma + \tau + \sigma) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + \tau + \sigma)^2 + 4\sigma(\mu + \gamma + \tau)(\mathcal{R}_0^\tau - 1)} \right]. \end{aligned} \quad (29)$$

To determine the strength of this outbreak, we compare it with the outbreak growth rate in the absence of control intervention. The result of the comparison is summarized in the theorem below.

**Theorem 6.** *If  $\tau \geq 0$ , then  $\lambda_\tau^+ \leq \lambda^+$ . Furthermore,  $\lambda_\tau^+ = \lambda^+$  if and only if  $\tau = 0$ .*

Theorem 6 can be established by algebraic manipulations. Thus, the outbreak growth rate in the presence of treatment is always lower than that with no control.

Similarly, for communities that can afford only vaccination or water purification the outbreak growth rates are given by

$$\begin{aligned}\lambda_v^+ &= \frac{1}{2} \left[ -(\mu + \gamma + \sigma) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + \sigma)^2 + 4\sigma(\mu + \gamma)(\mathcal{R}_0^v - 1)} \right].\end{aligned}\quad (30)$$

and

$$\begin{aligned}\lambda_w^+ &= \frac{1}{2} \left[ -(\mu + \gamma + d + \sigma) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + d + \sigma)^2 + 4(\sigma + d)(\mu + \gamma)(\mathcal{R}_0^w - 1)} \right],\end{aligned}\quad (31)$$

respectively.

Since  $\mathcal{R}_0^v \leq \mathcal{R}_0$  and  $d \geq 0$  then

$$\lambda_v^+ \leq \lambda^+.\quad (32)$$

and

$$\lambda_w^+ \leq \lambda^+.\quad (33)$$

This shows that vaccination or introducing water purification reduces the outbreak growth rate more than when no control is introduced.

Epidemiologically, these results demonstrate that even when a control does not prevent a disease from invading the population, the outbreak will be less compared to when no control is considered.

We have shown that each of the single control intervention strategies and the multiple control intervention strategy reduce the outbreak growth rate. Next, the multiple control intervention strategy is shown to reduce the outbreak growth rate more than each of the single control intervention strategy. The details are given in Theorem 7,

**Theorem 7.** Suppose that  $d \geq 0$ ,  $\phi \geq 0$ ,  $\tau \geq 0$ , and  $\varepsilon \geq 0$ , then

$$\begin{aligned}\lambda_c^+ &\leq \lambda_v^+, \\ \lambda_c^+ &\leq \lambda_\tau^+, \\ \lambda_c^+ &\leq \lambda_w^+.\end{aligned}\quad (34)$$

Furthermore,

$$\begin{aligned}\lambda_c^+ = \lambda_v^+ = \lambda_\tau^+ = \lambda_w^+ \iff \\ d = \phi = \tau = \varepsilon = 0.\end{aligned}\quad (35)$$

which is easily demonstrated.

**3.6. Two Control Measures.** Suppose a community can only afford two control intervention strategies which, for example, could be (i) vaccination + treatment, (ii) vaccination + treatment, and (iii) treatment + water purification. Qualitative analyses of these cases can be important for communities that can afford up to two control measures. Similar to the

single control, the basic reproduction number and outbreak growth rate are used to investigate the impact of introducing double control measures. Using the same approach, the basic reproduction numbers induced by vaccination + treatment  $\mathcal{R}_0^{vt}$ , vaccination + water purification  $\mathcal{R}_0^{vw}$ , and treatment + water purification  $\mathcal{R}_0^{tw}$  are, respectively, given by

$$\begin{aligned}\mathcal{R}_0^{vt} &= E_v E_\tau \mathcal{R}_0, \\ \mathcal{R}_0^{vw} &= E_v E_w \mathcal{R}_0, \\ \mathcal{R}_0^{tw} &= E_\tau E_w \mathcal{R}_0.\end{aligned}\quad (36)$$

By a similar reasoning, the outbreak growth rates associated with vaccination + treatment  $\lambda_{vt}^+$ , vaccination + water purification  $\lambda_{vw}^+$ , and treatment + water purification  $\lambda_{tw}^+$  are, respectively, given by

$$\begin{aligned}\lambda_{vt}^+ &= \frac{1}{2} \left[ -(\mu + \gamma + \tau + \sigma) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + \tau + \sigma)^2 + 4\sigma(\mu + \gamma + \tau)(\mathcal{R}_0^{vt} - 1)} \right], \\ \lambda_{vw}^+ &= \frac{1}{2} \left[ -(\mu + \gamma + \sigma + d) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + \sigma + d)^2 + 4(\sigma + d)(\mu + \gamma)(\mathcal{R}_0^{vw} - 1)} \right], \\ \lambda_{tw}^+ &= \frac{1}{2} \left[ -(\mu + \gamma + \tau + \sigma + d) \right. \\ &\quad \left. + \sqrt{(\mu + \gamma + \tau + \sigma + d)^2 + 4(\sigma + d)(\mu + \gamma + \tau)(\mathcal{R}_0^{tw} - 1)} \right].\end{aligned}\quad (37)$$

Again, we compare these results with the cases for no control, a single control, or multiple control measures. In each comparison, the case with less controls must be a subset of the case with more controls. Comparing these basic reproduction numbers and outbreak growth rates show that considering two control measures is always better than no control or a single control in reducing the disease. On the other hand, the multiple control is better than the two control measures. Thus, if an outbreak occurs in any community, multiple controls are highly recommended. However, if a community has limited resources to control an outbreak, then the double or single control methods can be recommended depending on availability of resources.

To compare other combinations of controls (one case not necessarily a subset of the other) we consider numerical simulations. The parameter values for the numerical simulations are given in Table 1. The results are presented in Figures 1(a)–1(d). Again, as expected, in each comparison the multiple control has the greatest impact in reducing infections while no control has the least impact. The multiple control can prevent close to 25% more people from the disease as compared with no control.

In each case introducing a single control is always better than introducing no control (control Figures 1(a)–1(d)). However, depending on the actual parametrisation, one of these single measures will have the best impact (for example water purification in Figure 1(d)). Thus, for a community that can afford only a single control these types of results

TABLE 1: Parameter values used for numerical simulations with reference.

Parameter	Symbol	Value	Reference
Contact rate	$\beta$	$0.1072 \text{ day}^{-1}$	[11]
Birth/death rate	$\mu$	$0.02 \text{ day}^{-1}$	[20]
Recovery rate	$\gamma$	$11.3 \text{ year}^{-1}$	[4, 24]
net decay rate of pathogen	$\sigma$	$0.0333$	[11]
Efficacy of vaccine	$\varepsilon$	$0.78$	[40]
Vaccination rate	$\phi$	$0.07 \text{ day}^{-1}$	[5]
Treatment rate	$\tau$	$0.005 \text{ day}^{-1}$	[5]
Recovery rate due treatment	$\gamma_\tau$	$0.003 \text{ day}^{-1}$	[5]
vaccination rate	$\phi$	$0.07 \text{ day}^{-1}$	[5]
Reduction in $w$ due to water purification	$d$	$2\sigma \text{ day}^{-1}$	Estimate

can inform their choices. These arguments also apply for communities that can afford a double control. For our results vaccination + water purification has the greatest impact in reducing infections (Figures 1(a) and 1(c)) and this would be recommended. Thus, these examples illustrate how the model could guide communities in choosing appropriate control measures. These findings are consistent with results using different models ([4, 5, 39]).

#### 4. Optimal Control Problem

Qualitative analyses of our model have revealed that multiple control intervention strategies are the best under uniform circumstances. Unfortunately, affordability of any multiple control intervention strategy is a major concern as many communities have limited resources. Thus, further analyses are used investigate possible multiple control intervention strategies with minimum costs. The results of these analyses can be helpful in advising communities with limited resources. Optimal control theory has been successfully used in analysing such problems [4, 8, 39, 41–45] and is used here.

To minimize the cost of implementing multiple controls we make the following assumptions. First, we assume that there are control parameters  $\phi$ ,  $\tau$ , and  $d$  that are measurable functions of time and formulate an appropriate optimal control functional that minimizes the cost of implementing model (11). For simplicity, we assume that  $\phi = u_1(t)$ ,  $\tau = u_2(t)$ , and  $d = u_3(t)$ .

The appropriate optimal control cost functional is

$$J(u_1, u_2, u_3) = \int_0^{t_f} [A_1 i(t) + B_1 w(t) + C_1 u_1^2(t) + C_2 u_2^2(t) + C_3 u_3^2(t)] dt \quad (38)$$

where the coefficients,  $A_1$ ,  $B_1$ ,  $C_1$ ,  $C_2$ , and  $C_3$ , are balancing cost factors that transform the integral into money expended over a finite time  $t_f$ . The aim is to minimize the number of infected individuals and pathogens in water source as well as the costs for applying the multiple controls. To account for the anticipated nonlinear costs that could arise from the multiple controls, we consider quadratic functions for measuring the control costs [4, 26, 39, 41–47].

The existence of optimal controls  $(u_1^*, u_2^*, u_3^*)$  that minimize the cost functional  $J(u_1, u_2, u_3)$  follows from [48, 49]. Pontryagin's Maximum Principle [50] introduces adjoint functions and enables us to minimize a Hamiltonian  $H$ , with respect to the controls  $(u_1(t), u_2(t), u_3(t))$  instead of minimizing the original objective functional. The Hamiltonian associated with the objective functional is given by

$$\begin{aligned} H = & A_1 i(t) + B_1 w(t) + C_1 u_1^2(t) + C_2 u_2^2(t) \\ & + C_3 u_3^2(t) + \lambda_s (\mu - \beta s(t) w(t) - (\mu + u_1) s(t)) \\ & + \lambda_v (u_1 s(t) - (1 - \varepsilon) \beta v(t) w(t) - \mu v(t)) \\ & + \lambda_i (\beta s(t) w(t) + (1 - \varepsilon) \beta v(t) w(t) \\ & - (\mu + \gamma + u_2) i(t)) + \lambda_\zeta (u_2 i(t) - (\mu + \gamma_\tau) \zeta(t)) \\ & + \lambda_w (\sigma i(t) - (u_3 + \sigma) w(t)) + \lambda_r (\gamma i(t) + \gamma_\tau \zeta(t) \\ & - \mu r(t)), \end{aligned} \quad (39)$$

where  $\lambda_s$ ,  $\lambda_v$ ,  $\lambda_i$ ,  $\lambda_\zeta$ ,  $\lambda_w$ , and  $\lambda_r$  are the associated adjoints for the states  $s$ ,  $v$ ,  $i$ ,  $\zeta$ ,  $w$ , and  $r$ , respectively.

Given optimal controls  $(u_1^*, u_2^*, u_3^*)$  together with the corresponding states  $(s^*, v^*, i^*, \zeta^*, w^*, r^*)$  that minimize  $J(u_1, u_2, u_3)$ , there exist adjoint variables  $\lambda_s$ ,  $\lambda_v$ ,  $\lambda_i$ ,  $\lambda_\zeta$ ,  $\lambda_w$ , and  $\lambda_r$  satisfying

$$\begin{aligned} \frac{d\lambda_s}{dt} = & \lambda_s (\beta w(t) + \mu + u_1(t)) - \lambda_v u_1(t) \\ & - \lambda_i \beta w(t), \\ \frac{d\lambda_v}{dt} = & \lambda_v ((1 - \varepsilon) \beta w(t) + \mu) - \lambda_i (1 - \varepsilon) \beta w(t), \\ \frac{d\lambda_i}{dt} = & -A_1 + \lambda_i (\mu + \gamma + u_2(t)) - \lambda_\zeta u_2(t) - \lambda_w \sigma \\ & - \lambda_r \gamma, \end{aligned}$$

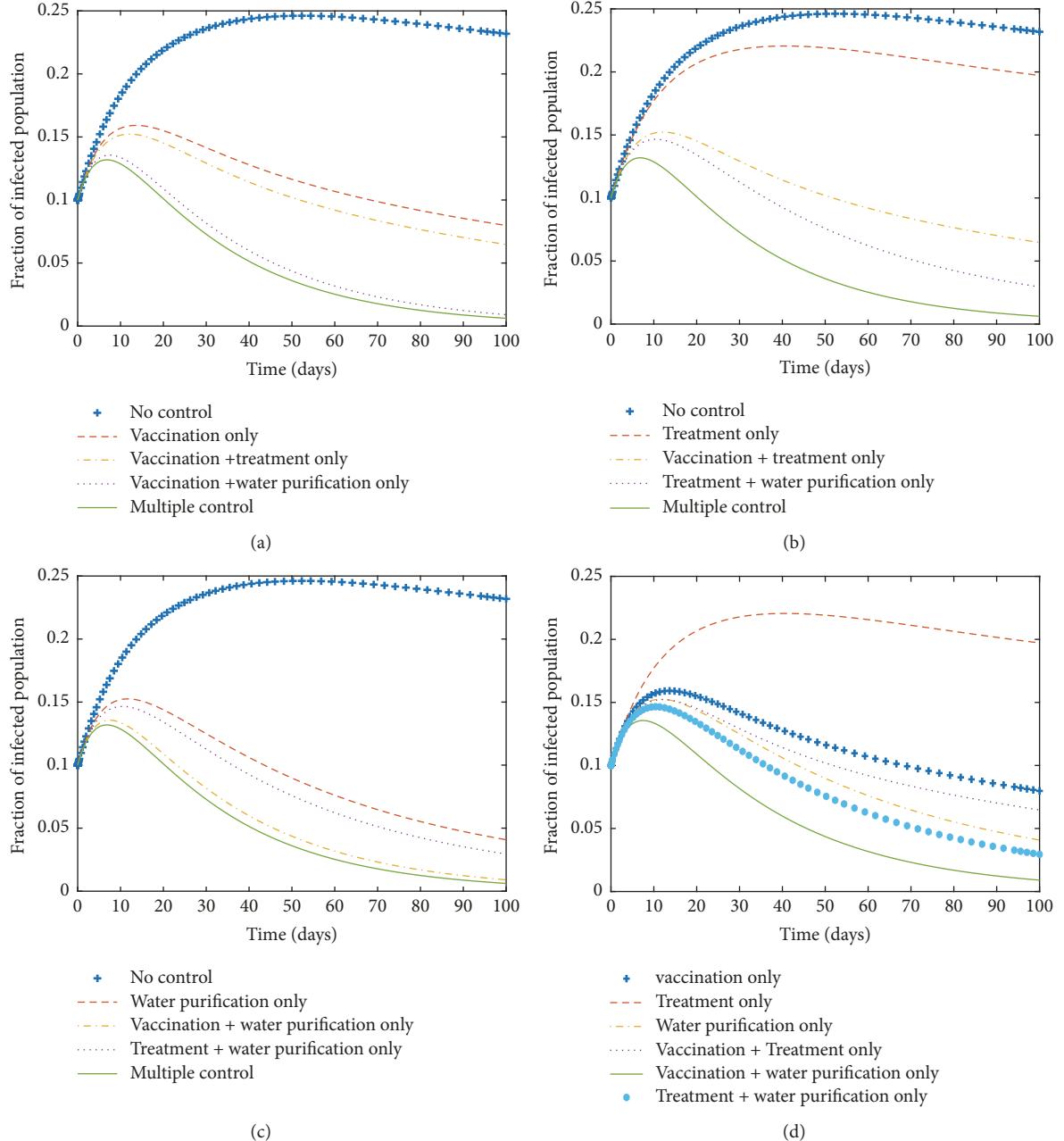


FIGURE 1: Graphical illustration of the impact of considering a single control, double control, or multiple (three) control measures in reducing the spread of waterborne diseases for different combinations of control (a-d).

$$\begin{aligned}
 \frac{d\lambda_\zeta}{dt} &= \lambda_\zeta (\mu + \gamma_\tau) - \lambda_r \gamma_\tau, \\
 \frac{d\lambda_w}{dt} &= -B_1 + \lambda_s \beta s(t) + \lambda_v (1 - \varepsilon) \beta v(t) \\
 &\quad - \lambda_i (\beta s(t) + (1 - \varepsilon) \beta v(t)) \\
 &\quad + \lambda_w (u_3(t) + \sigma), \\
 \frac{d\lambda_r}{dt} &= \lambda_r \mu,
 \end{aligned} \tag{40}$$

and transversality conditions:

$$\lambda_k(t_f) = 0 \tag{41}$$

where  $k = s, v, i, \zeta, w, r$ .

The differential equations (40) were obtained by differentiating the Hamiltonian function (39) with respect to the corresponding states as follows:

$$\frac{d\lambda_k}{dt} = -\frac{dH}{dk}. \tag{42}$$

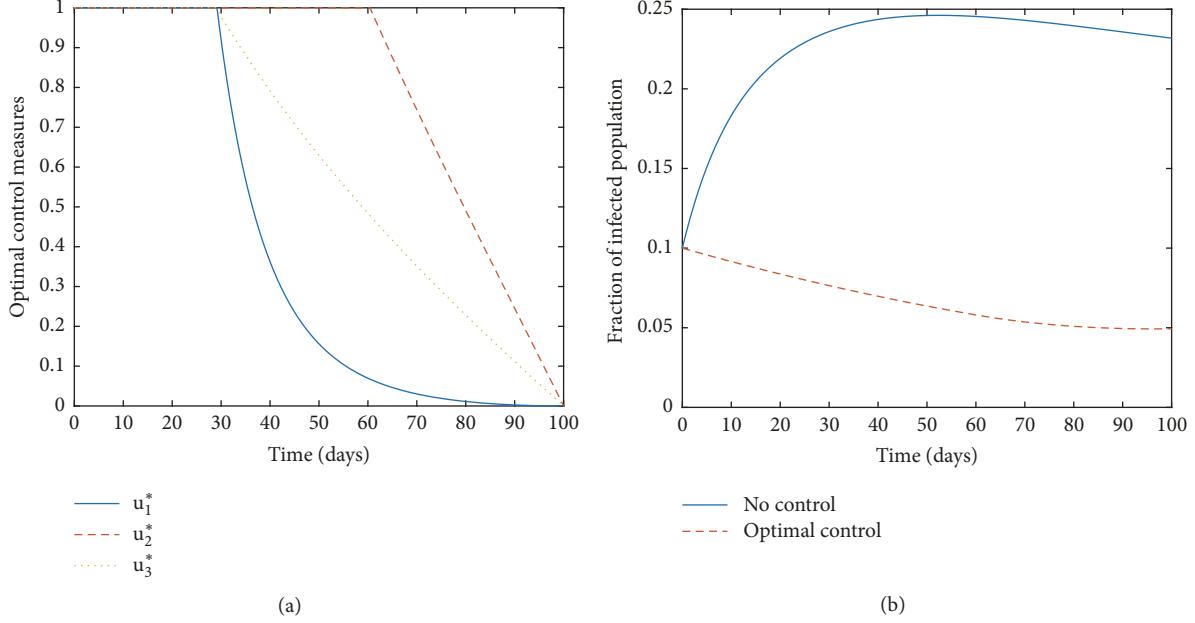


FIGURE 2: Graphical illustration of (a) the optimal control functions  $u_1^*, u_2^*, u_3^*$  and (b) impact of considering optimal control over no control in reducing the spread of waterborne disease.

The optimal conditions are

$$\begin{aligned} 0 &= \frac{dH}{du_1}, \\ 0 &= \frac{dH}{du_2}, \\ 0 &= \frac{dH}{du_3}. \end{aligned} \quad (43)$$

Solving for  $u_1(t)$  under these optimal conditions (43) and subsequently taking bounds into consideration, we obtain

$$u_1^* = \max \left\{ 0, \min \left\{ 1, \frac{s(t)(\lambda_s - \lambda_i)}{2c_1} \right\} \right\}. \quad (44)$$

Using a similar approach, we obtain the remaining optimal controls:

$$u_2^* = \max \left\{ 0, \min \left\{ 1, \frac{i(t)(\lambda_i - \lambda_\zeta)}{2c_2} \right\} \right\}, \quad (45)$$

$$u_3^* = \max \left\{ 0, \min \left\{ 1, \frac{w(t)\lambda_w}{2c_3} \right\} \right\}. \quad (46)$$

The above results demonstrate the existence of optimal controls ( $u_1^*, u_2^*, u_3^*$ ) that can reduce the spread of waterborne diseases using multiple control measures with minimum cost. The possible magnitudes and trajectories of each of these optimal controls as well as the optimal solutions are investigated further using numerical simulations.

For the numerical simulations, we consider the parameter values presented in Table 1 together with the following values

for the cost factors:  $A_1 = 600.00$ ,  $B_1 = 200.00$ ,  $C_1 = 2$ ,  $C_2 = 6$ , and  $C_3 = 6$  [4]. Numerical solutions of the optimal system are carried out using the forward-backward algorithm as described in [4, 8]. The numerical results of the optimal control functions  $u_1^*$ ,  $u_2^*$ , and  $u_3^*$  that minimize the cost functional subject to the state equations are presented in Figure 2(a). From the results, effective multiple control measures can be achieved with minimum cost by applying controls at the onset of the outbreak. The impact of considering optimal control over no control is investigated by comparing the two cases (Figure 2(b)). The results demonstrate that considering optimal control can prevent about 15% of the total population from getting the disease at minimum cost.

## 5. A Case Study: The Haiti Cholera Outbreak

A realistic case study, a cholera outbreak in Haiti, is considered to validate the control model (11). In particular, this example is used to demonstrate how this model can be used to study, as well as make future predictions of, cholera outbreaks in cholera endemic communities. According to the Haitian Ministry of Public Health and Population (MSPP), a cholera outbreak was confirmed in Haiti on October 21, 2010 [51, 52]. As of August 4, 2013, about 669,396 cases and 8,217 deaths had been reported since the outbreak started [53]. For this study, the number of reported hospitalized cholera cases in Haiti from October 30, 2010 to December 24, 2012, is considered. Haiti is divided into 10 departments (governing regions) and the capital Port-au-Prince. Using the MSPP data, the cumulative number of reported cholera hospitalizations for each department, from October 30, 2010, to December 24, 2012, is given in Figure 3 [52] (note that these are ordered by the size of the regional populations reported in 2009 before

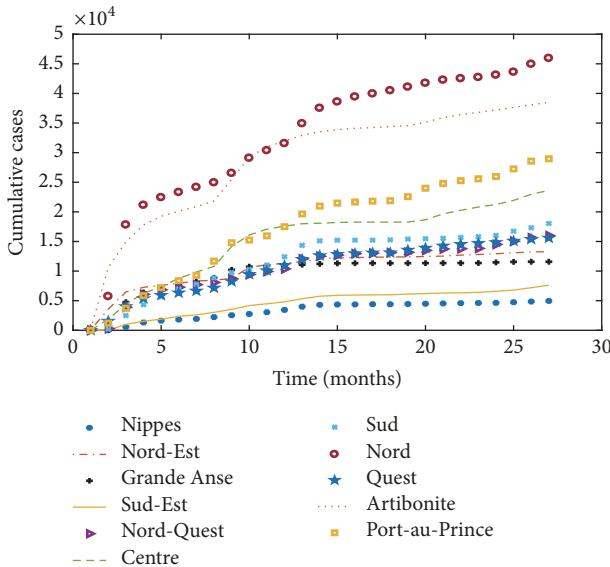


FIGURE 3: A plot showing the cumulative reported hospitalized cholera cases in each department in Haiti from October 30, 2010, to December 24, 2012. The legend is in order of population size (Nippes = 311497, Nord-Est = 358277, Grande Anse = 425878, Sud-Est = 575293, Nord-Quest = 662777, Centre=678626, Sud = 704760, Nord=970495, Quest = 1187833, Artibonite = 1571020, and Port-au-Prince = 2476787).

the outbreak started [54]). From Figure 3 the cases of cholera largely track population size with the Nord having the greatest number of reported cases followed by Artibonite then Port-au-Prince while the department of Nippes has the smallest number of reported hospitalized cases.

The apparent loose correlation between population size and numbers of cases is expected as larger populations would have more cases overall. However, because the model considered here (model (11)) is scaled to the total population  $N$  the data in Figure 3 was also scaled by population, given in Figure 4. This scaling is informative as now some departments with larger populations have less per capita cases of cholera as compared to the others, in particular the capital Port-au-Prince (Figure 4). Alternatively, some departments with smaller populations have higher per capita numbers of cases, in particular Nord-Est (Figure 4). Research globally has shown that cholera is associated with poverty and access to clean water and thus presumably these per capita differences are due to different conditions of access to clean water and treatment in the different locations. For example, these conditions in general would be expected to be comparatively better in the capital of the country, Port-au-Prince, because of better infrastructure and economic conditions. Thus, one might expect the lowest per capita cholera infections as found for Port-au-Prince in Figure 4.

In fitting the model to the data, the parameters  $\gamma, \mu, \sigma, \varepsilon$  (values in Table 1) were fixed because they represent growth and death processes expected to be uniform throughout the country. The other parameters that relate to the various control measures were used as fitting parameters. These model fittings were carried out using the built-in MATLAB

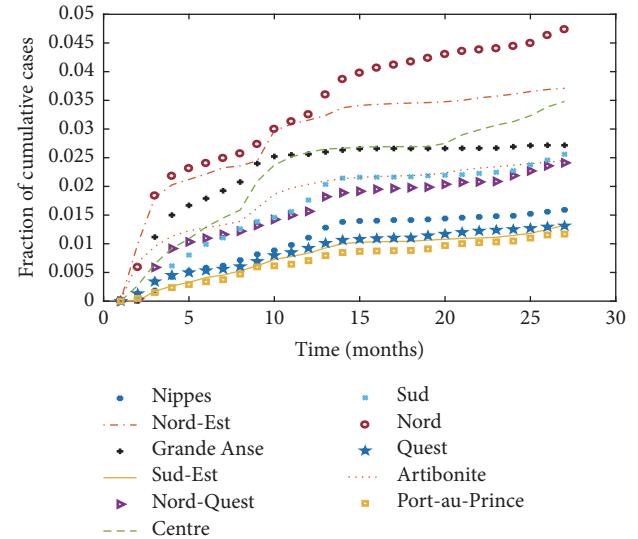


FIGURE 4: A plot showing the cumulative per capita reported hospitalized cholera cases in each department in Haiti from October 30, 2010, to December 24, 2012. Again, the legend is in order of population size.

(Mathworks, Version, R2012b [55]) least-squares fitting routine fmincon in the optimization tool box. The fits using this strategy were good for half of the departments. For the other five, the model overestimated the levels of initial infections. These departments had the four lowest per capita infection rates in Figure 4 and Sud which was also relatively low. For this reason,  $\sigma$  was included as a fitting parameter in that it represents the rate of disease transmission from infected individuals to the water. Presumably this rate is reduced in well-managed areas by providing treated water and so is variable by region. This new fitting resulted in a better fit for all departments (Figure 5). The one poor fit is the capital Port-au-Prince in which the model again overestimates the initial infections, presumably for similar reasons as those given above. However, here the fit in the final months is still close.

These results demonstrate that our model could be used to study and predict cholera outbreaks in Haiti and other communities where cholera is endemic, consistent with other studies of the Haitian cholera outbreak [51, 56–59].

## 6. Discussion

Dynamics and control intervention strategies for waterborne diseases in a homogeneous mixed population have been explored. Our analyses have shown that useful information concerning the dynamics and control of waterborne diseases can be obtained by analysing the appropriate epidemiological models.

In the absence of any control intervention strategy, global stability of the disease-free equilibrium shows it is possible for the waterborne disease to be eradicated from the community irrespective of the initial size of infected population provided the basic reproduction number  $\mathcal{R}_0 < 1$ . This can happen if

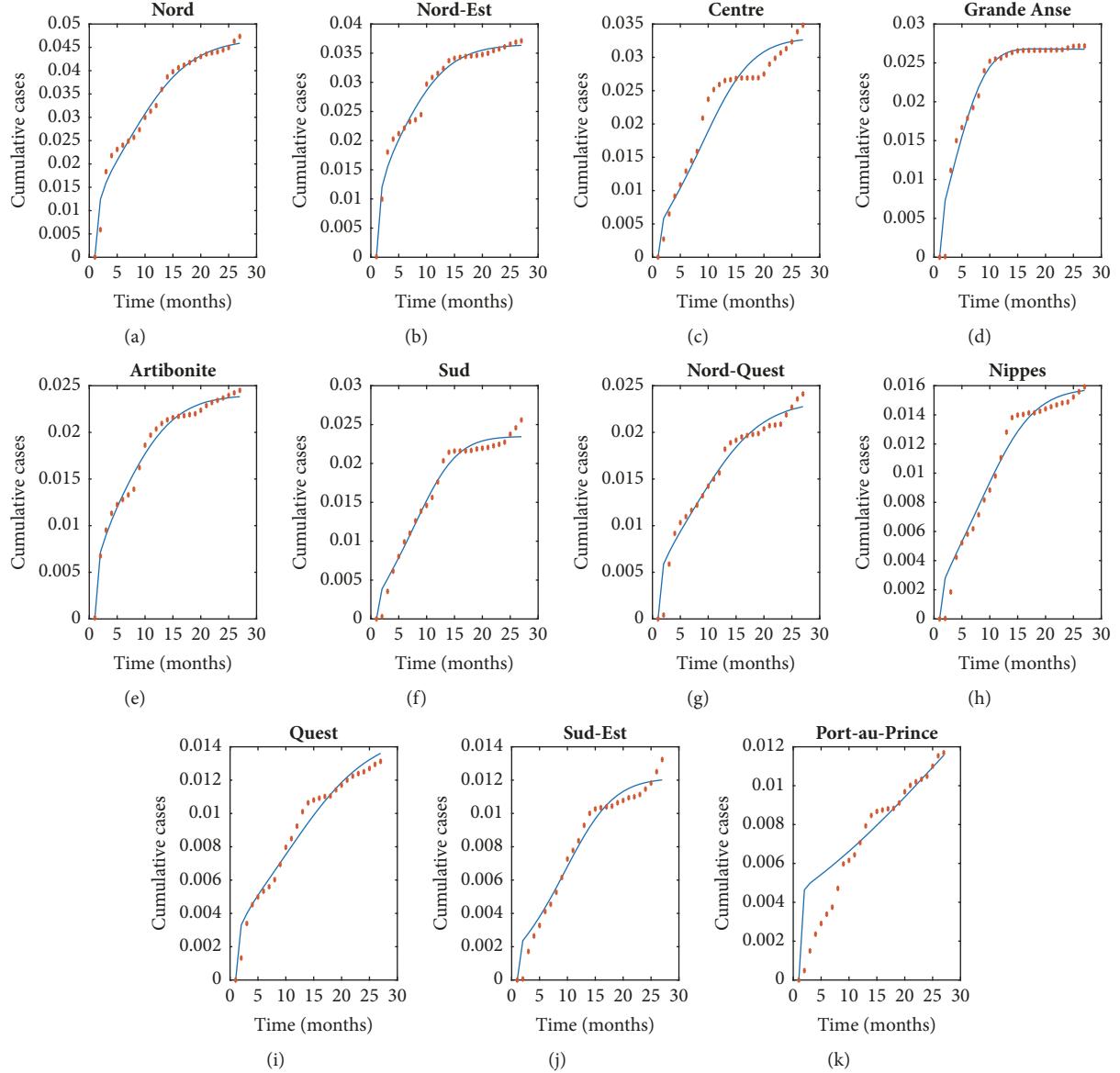


FIGURE 5: Model fitting of the cumulative per capita reported cholera cases for each department in Haiti from October 30, 2010 to December 24, 2012. The bold lines represent the model fit and the stars represent the reported cases in Haiti. These graphs are now ordered according to the per capita overall increases in infections as seen in Figure 4.

the individuals in the community begin to practice healthy living like staying away from contaminated water, boiling water before drinking, proper sewage disposal, etc. On the contrary, if the basic reproduction number is greater than unity the outbreak is likely to persist in the entire population. To determine the likely magnitude of such an outbreak the outbreak growth rate and final outbreak size were computed analytically. In such cases, any outbreak will be difficult to manage without effective control measures.

Next, the model is extended by introducing multiple control intervention strategies: vaccination, treatment, and water purification. Analyses of the multiple control model revealed that introducing multiple control measures can have a significant impact in reducing the spread of disease both at

epidemic and at the endemic stage of an outbreak. Analyses of single and double control strategies showed that considering any control is better than none. However, multiple control measures together have the greatest impact on reducing infections.

Given that waterborne diseases are associated with poverty, we use our model to discuss two methods of reducing the spread of waterborne disease for communities that might not afford multiple control measures. The first method involved finding the most effective control when one or two control measures are introduced. By comparing these different levels of controls, a useful guide can be developed to assist a community choose an affordable alternative. For instance, in the example given above, a single control of

water purification can reduce the number of infections more than a combination of vaccination and treatment. Also, the double control measures of vaccination + water purification has almost the same impact as the using the multiple controls.

Another approach to help communities decide on the most effective control method is to use optimal control analyses which investigate how to reduce the spread of a disease with minimum cost. Results from these analyses showed that it is optimal to introduce effective control measures at the onset of an outbreak. This result agrees with realistic expectations because introducing effective control measures at the onset of the outbreak will reduce the number of initially infected people and thus reduce overall expenditure on controlling the outbreak.

Finally, our model was validated using a cholera outbreak in Haiti. Our model fitted the reported cases of cholera in all the departments in Haiti. Thus, our model could be used to study, as well as make future predictions on, the dynamics of waterborne diseases in Haiti and other communities where there are waterborne disease outbreaks.

Even though this study provides new insights into the dynamics and control intervention strategies for waterborne diseases in a homogeneous population, it has limitations. Firstly, the total population is assumed to be constant. This is not always true in real life especially for an outbreak that lasts for a long period of time. Homogeneity in disease transmission is also assumed, but this is also not always true since heterogeneity is an essential part of epidemiology and has been shown to influence disease dynamics [19, 20]. In reality, individuals in any society belong to different socioeconomic classes and can migrate from one locality to another, thus affecting the spread of a disease. However, as a first step the models presented here enable an overall perspective and can guide disease management. These models also point the way forward to the importance of the approach. Improvements through more elaborate models that remove the limiting assumptions can follow from future work by ourselves and other scientists.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request from Dr. J. Tien, Ohio State University.

## Conflicts of Interest

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

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