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# Mathematical Modeling on the Transmission Dynamics of Diphtheria with Optimal Control Strategies

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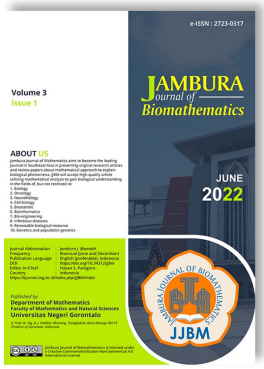


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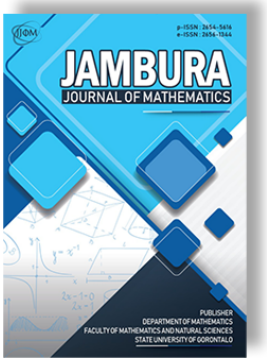


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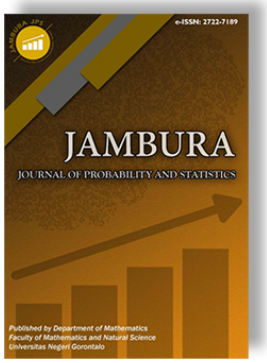


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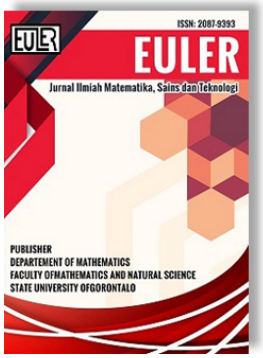


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Research Article

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# Mathematical Modeling on the Transmission Dynamics of Diphtheria with Optimal Control Strategies

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**ABSTRACT.** *Diphtheria is an acute bacterial infection caused by Corynebacterium diphtheriae, characterized by the formation of a pseudo-membrane in the throat, which can lead to airway obstruction and systemic complications. Despite the availability of effective vaccines, diphtheria remains a significant public health concern in many regions, particularly in areas with low immunization coverage. In this study, we formulated and rigorously analyzed a deterministic epidemiological mathematical model to gain insight into the transmission dynamics of Diphtheria infection, incorporating the concentration of Corynebacterium Diphtheriae in the environment. The analysis of the model begins with the computation of the basic reproduction number and the examination of the local stability of the disease-free equilibrium using the Routh-Hurwitz criterion. An in-depth analysis of the model reveals that the model undergoes the phenomenon of backward bifurcation. This characteristic poses significant hurdles in effectively controlling Diphtheria infection within the population. However, under the assumption of no re-infection of Diphtheria infection after recovery, the disease-free equilibrium point is globally asymptotically stable whenever the basic reproduction number is less than one. Furthermore, the sensitivity analysis of the basic reproduction number was carried out in order to determine the impact of each of the model basic parameters that contribute to the transmission of the disease. Utilizing the optimal control theory to effectively curb the spread of Diphtheria, We introduced two time dependent control measures, to mitigate the spread of Diphtheria. These time dependent control measures represent preventive actions, such as public enlightenment campaign to sensitize and educate the general public on the dynamics of Diphtheria and proper personal hygiene which includes regular washing of hands to prevent susceptible individuals from acquiring Diphtheria, and environmental sanitation practices such as cleaning of surfaces and door handle to reduced the concentration of Corynebacterium diphtheriae in the environment. The results from the numerical simulations reveal that Diphtheria infection can successfully be controlled and mitigated within the population if we can increase the vaccination rate and the decay rate of Corynebacterium Diphtheriae in the environment, as well as properly and effectively implementing these optimal control measures simultaneously.*



## 1. Introduction

Diphtheria is a severe bacterial infection caused by species of Corynebacterium. The most prevalent form of diphtheria is the classic respiratory type, which is triggered by toxin-producing *Corynebacterium diphtheriae* [1]. The bacterium primarily leads to a severe respiratory infection, creating a thick, adherent pseudomembrane in the throat, pharynx, and tonsils, which results in a swollen neck, often referred to as a "bull neck" [2]. Less frequently, diphtheria can affect the skin (cutaneous diphtheria) and mucous membranes at other non-respiratory sites, such as the genitalia and conjunctivae [1, 3]. Diphtheria is typically transmitted through the inhalation of airborne droplets, sneezing, coughing, contact with infected skin lesions or contact with contaminated personal items [2, 4, 5]. Diphtheria is a highly contagious and fatal disease that is preventable by vaccination. It can impact the nose and throat, harm the kidneys, nervous system, and heart, and may lead to paralysis, respiratory failure, ulcerating skin lesions, and even death [4]. Diphtheria has a fatality rate of 5-10% in general; however, the case fatality rate (CFR) can rise to 20-40% among children and unvaccinated adults [4]. The largest diphtheria epidemic occurred between 1990 and 1995 in the Russian Federation, where more than 157,000 cases and 5,000 deaths were reported [4]. Currently, diphtheria is extremely rare in developed countries due to high vaccination rates [4]. How-

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**Table 1.** Description of the model variables and parameters

| Variable | Biological interpretation |
|---|---|
| $S$ | Susceptible Individuals. |
| $V$ | Vaccinated Individuals against Diphtheria. |
| $E$ | Exposed Individuals to Diphtheria. |
| $I_A$ | Asymptomatic Infectious Individuals with Diphtheria. |
| $I_S$ | Symptomatic Infectious Individuals with Diphtheria. |
| $T$ | Treated Individuals with Diphtheria. |
| $R$ | Recovered Individuals from Diphtheria. |
| $B$ | Concentration of *Corynebacterium Diphtheriae* in the Environment. |
| **Parameter** | **Description** |
| $\pi$ | Recruitment rate. |
| $\mu$ | Natural death rate. |
| $\beta$ | Effective contact rate between susceptible individuals and infectious individuals. |
| $\beta_d$ | Effective contact rate between susceptible individuals and bacteria in the environment. |
| $\phi$ | Vaccination rate. |
| $\gamma$ | Vaccine-waning rate. |
| $\alpha$ | Progression rate from exposed class to infectious classes. |
| $q$ | Fraction of exposed individuals that progressed to the infectious class that are showing symptoms of Diphtheria. |
| $\sigma$ | Progression rate from asymptomatic to symptomatic. |
| $\eta_1$ | Treatment rate of asymptomatic infectious individuals. |
| $\eta_2$ | Treatment rate of symptomatic infectious individuals. |
| $\delta$ | Disease-induced death rate. |
| $\theta$ | Modification parameter that accounts for reduction in disease-induced death in the treatment class. |
| $\omega$ | Recovery rate of treated individuals. |
| $\psi$ | Vaccination rate of recovered individuals. |
| $\varepsilon$ | Modification parameter that accounts for re-infection after recovery. |
| $\kappa_1$ | Shedding rate of the bacteria in the environment from asymptomatic infectious individuals. |
| $\kappa_2$ | Shedding rate of the bacteria in the environment from symptomatic infectious individuals. |
| $f$ | Fraction of re-infected individuals that are asymptomatic. |
| $\delta_B$ | Decay rate of the bacteria. |
| $K$ | Carrying capacity. |

ever, in low-income countries, particularly in Asia and Africa, low vaccination coverage and poor sanitation conditions have contributed to the re-emergence of diphtheria, with thousands of cases and outbreaks occurring annually [2].

Over the past two decades, mathematical models have played a crucial role in studying the transmission dynamics of infectious diseases (see, for example, [6–14]). Several mathematical models have been developed to explore the dynamics of diphtheria. For instance, Ilahi and Widiana [15] introduced a deterministic SEIR compartmental model to examine the transmission dynamics of diphtheria, incorporating vaccination as a control parameter. Kanchanarat et al. [16] developed a mathematical model for diphtheria that incorporates asymptomatic infection, logistic growth, and vaccination. The model was designed to investigate the effects of asymptomatic infections and imperfect vaccination coverage on the control and prevention of diphtheria. Their numerical simulations revealed that the incubation period of asymptomatic individuals influences the optimal level of vaccination coverage required for the eradication of diphtheria. Gourram et al. [17] developed and thoroughly analyzed a deterministic mathematical model for the transmission dynamics of diphtheria, incorporating optimal control strategies. These strategies include educational and outreach campaigns designed to raise public awareness about diphtheria, encourage individuals to seek hospital care, and promote the uptake of available vaccinations. Madubueze and Tijani [18] designed and qualitatively analyzed a mathematical model for diphtheria to assess the impact of a booster dose of the diphtheria vaccine in a contaminated environment, incorporating optimal control strategies. Their findings indicated that the most effective combination for eradicating diphtheria involves disinfecting the environment, screening and treating asymptomatic infected individuals, and administering booster vaccinations to the community. Izzati et al. [19] formulated an optimal control problem based on a SEIQR model to minimize the spread of diphtheria through quarantine measures and optimize the proportion of vaccinated individuals via an immunization campaign.

In this study, we build upon the work of Kanchanarat et al. [16] and Gourram et al. [17] by introducing a compartment to represent the concentration of Corynebacterium Diphtheriae in the environment, accounting for contaminated objects. Furthermore, we incorporated the possibility of re-infection among recovered individuals and introduced two time-dependent control measures to curb the spread of diphtheria. These control measures represent preventive actions, including public enlightenment campaigns to educate the public on diphtheria dynamics and the importance of proper personal hygiene, such as regular handwashing to protect susceptible individuals. Additionally, we emphasize environmental sanitation practices, such as cleaning surfaces, clothes, materials, and door handles, to reduce the concentration of *Corynebacterium diphtheriae* in the environment. The remainder of the paper is structured as follows: Section 2 presents the model formulation and its fundamental properties, Section 3 provides the model analysis, Section 4 focuses on the optimal control analysis, and Section 5 concludes with the final remarks.

## 2. Model Formulation

At time $t$, we divide the Diphtheria population into two namely, the human population, denoted by $N(t)$, and the con-

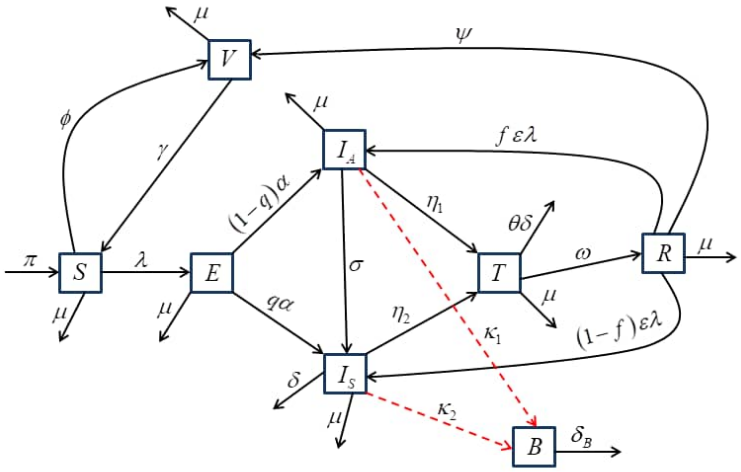



**Figure 1.** Flowchart of the Diphtheria model.

centration of *Corynebacterium Diphtheriae* in the environment, denoted by $B(t)$. The human population $(N(t))$ is further subdivided into seven mutual exclusive compartments of susceptible individuals $S(t)$, vaccinated individuals $V(t)$, exposed individuals $E(t)$, asymptomatic infected individuals with Diphtheria $I_A(t)$, symptomatic infected individuals with Diphtheria $I_S(t)$, treated individuals $T(t)$, and recovered individuals $R(t)$. So that

$$N(t) = S(t) + V(t) + E(t) + I_A(t) + I_S(t) + T(t) + R(t).$$

The population of the susceptible individuals is generated by the recruitment of individuals into the population either by birth or migration at the constant rate $\pi$. Susceptible individuals are vaccinated against Diphtheria at the rate $\phi$. Susceptible individuals acquires Diphtheria infection following an effective contact with either infected individuals with Diphtheria or the concentration of *Corynebacterium Diphtheriae* in the environment at the rate $\lambda$, given by

$$\lambda = \frac{\beta\,(I_A + I_S)}{N} + \frac{\beta_d B}{K + B},$$

where $\beta$ is the transmission probability from infected individuals to susceptible individuals, $\beta_d$ is the transmission probability from the concentration of *Corynebacterium Diphtheriae* in the environment to susceptible individuals, and $K$ is the carrying capacity of *Corynebacterium Diphtheriae*. The rate $\gamma$ is the waning rate of Diphtheria vaccine. Susceptible individuals that come in contact with infected individuals or the concentration of the *Corynebacterium Diphtheriae* in the environment, progressed to the exposed class at the rate $\lambda$, and further progressed to the infected compartments at the rate $\alpha$. A fraction $(1-q)\alpha$ of the exposed individual progressed to the infected asymptomatic compartment, while the remaining fraction exposed individuals progressed to the symptomatic infected compartment at the rate $q\alpha$. Asymptomatic infected individuals with Diphtheria infection progressed to the symptomatic class at the rate $\sigma$. The rate $\mu$ is the human natural death rate, and it is the same in all human compartments. The rate $\eta_1$ is the treatment rates of asymptomatic infected individuals, and $\eta_2$ is the treatment rate of symptomatic infected individuals with Diphtheria infection. The rate $\delta$ is the diseased induced death rate of symptomatic infected individuals with Diphtheria infection. Treated individuals die from the disease at the rate $\theta\delta$, where $\theta$ is the modification parameter that accounts for reduction in Diphtheria death due to treatment. A treated individual recovers from Diphtheria infection at the rate $\omega$. Recovered individuals are re-infected with Diphtheria infection at the rate $\varepsilon\lambda$, where $\varepsilon$ is the modification parameter that accounts for re-infection. The rate $f\varepsilon$ is the fraction of re-infected individuals that are asymptomatic, while $(1-f)\varepsilon$ is the remaining fraction of re-infected that are symptomatic. Recovered individuals are vaccinated at the rate $\psi$.

The concentration of *Corynebacterium Diphtheriae* in the environment is generated by the shedding of the bacteria into the environment by asymptomatic and symptomatic infected individuals with Diphtheria infection at the rate $\kappa_1$ and $\kappa_2$ respectively. The rate $\delta_B$ is the decay rate of *Corynebacterium Diphtheriae* in the environment.

Base on the above formulations and assumptions, the dynamics of the Diphtheria model is governed by a system of nonlinear differential equations given by

$$\begin{aligned}
\frac{dS}{dt} &= \pi - \lambda S - (\phi + \mu)S + \gamma V,\\
\frac{dV}{dt} &= \phi S + \psi R - (\gamma + \mu)V,\\
\frac{dE}{dt} &= \lambda S - (\alpha + \mu)E,\\
\frac{dI_A}{dt} &= (1-q)\alpha E - \sigma I_A - (\eta_1 + \mu)I_A + f\varepsilon\lambda R,\\
\frac{dI_S}{dt} &= q\alpha E + \sigma I_A - (\eta_2 + \delta + \mu)I_S + (1-f)\varepsilon\lambda R,\\
\frac{dT}{dt} &= \eta_1 I_A + \eta_2 I_S - (\omega + \theta\delta + \mu)T,\\
\frac{dR}{dt} &= \omega T - (\varepsilon\lambda + \psi + \mu)R,\\
\frac{dB}{dt} &= \kappa_1 I_A + \kappa_2 I_S - \delta_B B,
\end{aligned} \tag{1}$$

where

$$\lambda = \frac{\beta\left(I_A + I_S\right)}{N} + \frac{\beta_d B}{K + B}$$

### 2.1. Basic Properties of the Model

1. Positivity of solution
For the Diphtheria model in eq. (1) to be biologically meaningful, the solution of the system must remain non-negative for all values of time $t$. Therefore, it is essential to demonstrate that all the state variables of the Diphtheria model in eq. (1) are positive for all $t > 0$ within the feasible region $\mathcal{D}$, defined as follows:

$$\mathcal{D} = \mathcal{D}_H \cup \mathcal{D}_B \subset \mathbb{R}_+^7 \times \mathbb{R}_+^1, \tag{2}$$

where

$$\mathcal{D}_H = \left\{(S, V, E, I_A, I_S, T, R) \in \mathbb{R}_+^7 : N \leq \frac{\pi}{\mu}\right\},$$
$$\mathcal{D}_B = \left\{B \in \mathbb{R}_+^1 : B \leq \frac{\kappa^*}{\delta_B}\left(\frac{\pi}{\mu}\right)\right\}.$$

**Theorem 1.** *Let the initial data for the Diphtheria model in eq. (1) be $S(0) > 0$, $V(0) \geq 0$, $E(0) \geq 0$, $I_A(0) \geq 0$, $I_S(0) \geq 0$, $T(0) \geq 0$, $R(0) \geq 0$, and $B(0) \geq 0$. Then the solution $(S, V, E, I_A, I_S, T, R, B)$ of the Diphtheria model in eq. (1) are non-negative for all time $t > 0$.*

*Proof.* Let $t_f = \sup\{t > 0 : (S > 0, V > 0, E > 0, I_A > 0, I_S > 0, T > 0, R > 0, B > 0 \in [0, t]\}$. Thus, $t_f > 0$.
From the first equation of Diphtheria model system in eq. (1), we have

$$\frac{dS}{dt} = \pi - \lambda S - (\phi + \mu)S + \gamma V.$$

Solving the above equation, we obtained

$$\frac{d}{dt}\left\{S(t)\left[\exp\left(\int_0^t \lambda(r)dr + (\phi+\mu)t\right)\right]\right\} = (\pi + \gamma V)\exp\left(\int_0^t \lambda(r)\,dr + (\phi+\mu)t\right). \tag{3}$$

Integrating the above equation at the range $[0, t_f]$, we obtained

$$\left\{S(t)\exp\left[\int_0^{t_f}\lambda(r)dr + (\phi+\mu)t_f\right]\right\} - S(0) = (\pi+\gamma V)\int_0^{t_f}\exp\left[\int_0^z \lambda(r)dr + (\phi+\mu)z\right]dz. \tag{4}$$

So that

$$S(t) = S(0)\exp\left[-\left(\int_0^{t_f}\lambda(r)dr + (\phi+\mu)t_f\right)\right] + \exp\left[-\left(\int_0^{t_f}\lambda(r)dr + (\phi+\mu)t_f\right)\right] \times (\pi+\gamma V)\int_0^{t_f}\exp\left[\int_0^z \lambda(r)dr + (\phi+\mu)z\right]dz > 0. \tag{5}$$

Similarly, it can be shown that $V > 0$, $E > 0$, $I_A > 0$, $I_S > 0$, $T > 0$, $R > 0$, $B > 0$. □

2. Invariant region

**Lemma 1.** *The region $\mathcal{D} = \mathcal{D}_H \cup \mathcal{D}_B \subset \mathbb{R}_+^7 \times \mathbb{R}_+^1$ is positively invariant and attracts all solution in $\mathbb{R}_+^8$.*

*Proof.* By summing the equations for the human population and the concentration of *Corynebacterium Diphtheriae* in the environmental compartments of the Diphtheria model in eq. (1), the rates of change for the human population and the concentration of *Corynebacterium Diphtheriae* in the environment are expressed as follows:

$$\frac{dN}{dt} = \pi - \mu N - \delta I_S - \theta\delta T,$$
$$\frac{dB}{dt} = \kappa_1 I_A + \kappa_2 I_S - \delta_B B.$$

We have that

$$\frac{dN}{dt} \leq \pi - \mu N,$$
$$\frac{dB}{dt} \leq \kappa^*\left(\frac{\pi}{\mu}\right) - \delta_B B,$$

where $\kappa^* = \max(\kappa_1, \kappa_2)$.
A standard comparison theorem described in [20] can be used to show that

$$N(t) \leq N(0)e^{-\mu t} + \frac{\pi}{\mu}\left(1 - e^{-\mu t}\right),$$
$$B(t) \leq B(0)e^{-\delta_B t} + \frac{\kappa^*}{\delta_B}\left(\frac{\pi}{\mu}\right)\left(1 - e^{-\delta_B t}\right).$$

It follows that if $N(0) \leq \frac{\pi}{\mu}$, and $B(0) \leq \frac{\kappa^*}{\delta_B}\left(\frac{\pi}{\mu}\right)$, then $N(t) \leq \frac{\pi}{\mu}$, and $B(t) \leq \frac{\kappa^*}{\delta_B}\left(\frac{\pi}{\mu}\right)$. Thus, the region $\mathcal{D}$ is positively invariant and attracts all solutions in $\mathbb{R}_+^8$. Therefore, the Diphtheria model eq. (1) is both biologically and mathematically well-posed within the region $\mathcal{D}$. Consequently, it is appropriate to examine the dynamics of the Diphtheria model in eq. (1) in the region $\mathcal{D}$ [21]. □

## 3. Model Analysis

### 3.1. Disease-free Equilibrium

The Disease-free equilibrium (DFE) represents a steady state where Diphtheria is absent from the population. To determine this, the infected variables in the diphtheria model in eq. (1) are set to zero, and the right-hand side of equation in eq. (1) is set to zero as well. Then, the non-infected variables are solved for. The Disease-free equilibrium of the diphtheria model in eq. (1) is given by:

$$\xi_0 = (S^*, V^*, E^*, I_A^*, I_S^*, T^*, R^*, B^*) = \left(\frac{\pi(\gamma+\mu)}{\mu(\gamma+\phi+\mu)}, \frac{\pi\phi}{\mu(\gamma+\phi+\mu)}, 0, 0, 0, 0, 0, 0\right) \tag{6}$$

### 3.2. Basic Reproduction Number

The basic reproduction number, denoted by ($\mathcal{R}_0$), is a crucial threshold parameter that governs the spread of a disease

within a population. It provides insights into the peak and final magnitude of an epidemic and reflects the stability of the disease-free equilibrium (DFE) in a model [22]. The basic reproduction number is defined as the expected number of secondary infections caused by the introduction of a single infectious individual into a fully susceptible population.

The next-generation operator method, as outlined in [22], can be employed to compute the basic reproduction number. Using the methodology described in [22], we obtain the non-negative matrix $\mathcal{F}$ and the non-singular matrix $\mathcal{V}$, which represent the new infection terms and the remaining transition terms, respectively, at the disease-free equilibrium point:

$$\mathcal{F} = \begin{bmatrix} 0 & \frac{\beta S^*}{S^*+V^*} & \frac{\beta S^*}{S^*+V^*} & 0 & \frac{\beta_d S^*}{K} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

$$\mathcal{V} = \begin{bmatrix} (\alpha+\mu) & 0 & 0 & 0 & 0 \\ -(1-q)\alpha & (\sigma+\eta_1+\mu) & 0 & 0 & 0 \\ -q\alpha & -\sigma & (eta_2+\delta+\mu) & 0 & 0 \\ 0 & -\eta_1 & -\eta_2 & (\omega+\theta\delta+\mu) & 0 \\ 0 & -\kappa_1 & -\kappa_2 & 0 & \delta_B \end{bmatrix}.$$

Thus, as stated in [22], it follows that $\mathcal{R}_0 = \rho\left(\mathcal{F}\mathcal{V}^{-1}\right)$, where $\rho$ denotes the spectral radius or the largest eigenvalue of the matrix $\mathcal{F}\mathcal{V}^{-1}$. Therefore,

$$\begin{aligned} \mathcal{R}_0 = & \frac{\beta(\gamma+\mu)\left(A_4A_6+q\alpha A_5+\sigma A_4\right)}{A_3A_5A_6(\gamma+\phi+\mu)} \\ & + \frac{\beta_d\pi(\gamma+\mu)\left(\kappa_1A_4A_6+\kappa_2\left(q\alpha A_5+\sigma A_4\right)\right)}{K\mu\delta_BA_3A_5A_6(\gamma+\phi+\mu)}, \end{aligned} \tag{7}$$

where

$$\begin{aligned} A_1 &= \phi+\mu, \\ A_2 &= \gamma+\mu, \\ A_3 &= \alpha+\mu, \\ A_4 &= (1-q)\alpha, \\ A_5 &= \sigma+\eta_1+\mu, \\ A_6 &= \eta_2+\delta+\mu, \\ A_7 &= \omega+\theta\delta+\mu, \\ A_8 &= \psi+\mu, \\ A_9 &= (1-f)\varepsilon. \end{aligned}$$

### 3.3. Local Stability of the Disease-free Equilibrium

**Theorem 2.** *The disease-free equilibrium ($\xi_0$) of the Diphtheria model in eq. (1) is locally asymptotically stable if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.*

*Proof.* The local stability of the disease-free equilibrium can be analyzed by obtaining the Jacobian matrix of the Diphtheria model in eq. (1), evaluated at the disease-free equilibrium ($\xi_0$), given by

$$\mathcal{J}(\xi_0) = \begin{bmatrix} -A_1 & \gamma & 0 & o_1 & o_2 & 0 & 0 & o_3 \\ \phi & -A_2 & 0 & 0 & 0 & 0 & \psi & 0 \\ 0 & 0 & -A_3 & o_4 & o_5 & 0 & 0 & o_6 \\ 0 & 0 & A_4 & -A_5 & 0 & 0 & 0 & 0 \\ 0 & 0 & q\alpha & \sigma & -A_6 & 0 & 0 & 0 \\ 0 & 0 & 0 & \eta_1 & \eta_2 & -A_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \omega & -A_8 & 0 \\ 0 & 0 & 0 & \kappa_1 & \kappa_2 & 0 & 0 & -\delta_B \end{bmatrix},$$

$$\begin{aligned} o_1 &= -\frac{\beta A_2}{(\gamma+A_1)}, & o_4 &= \frac{\beta A_2}{(\gamma+A_1)}, \\ o_2 &= -\frac{\beta A_2}{(\gamma+A_1)}, & o_5 &= \frac{\beta A_2}{(\gamma+A_1)}, \\ o_3 &= -\frac{\beta_d\pi A_2}{K\mu(\gamma+A_1)}, & o_6 &= -\frac{\beta_d\pi A_2}{K\mu(\gamma+A_1)}, \end{aligned}$$

where

$$\begin{aligned} A_1 &= \phi+\mu, \\ A_2 &= \gamma+\mu, \\ A_3 &= \alpha+\mu, \\ A_4 &= (1-q)\alpha, \\ A_5 &= \sigma+\eta_1+\mu, \\ A_6 &= \eta_2+\delta+\mu, \\ A_7 &= \omega+\theta\delta+\mu, \\ A_8 &= \psi+\mu, \\ A_9 &= (1-f)\varepsilon. \end{aligned}$$

The eigenvalues of the Jacobian matrix $\mathcal{J}(\xi_0)$ is given as the roots of the characteristic polynomial given below

$$\begin{aligned} \mathcal{L}(\lambda) = & \lambda^8+m_1\lambda^7+m_2\lambda^6+m_3\lambda^5+m_4\lambda^4+m_5\lambda^3+m_6\lambda^2 \\ & +m_7\lambda+m_8 = 0. \end{aligned} \tag{8}$$

Where the expression for $m_1, m_2, m_3, m_4, m_5, m_6, m_7$, and $m_8$ are in Appendix A.

Applying the Routh-Hurwitz criterion [23, 24] to the polynomial in eq. (8), which states that all roots of the polynomial in eq. (8) have negative real parts if and only if the coefficient $m_i > 0$, for $i = 1, 2, 3, 4, 5, 6, 7, 8$ . Clearly, for $m_8 > 0$ ; then $\mathcal{R}_0 < 1$ . Therefore, by Routh-Hurwitz criterion, the disease-free equilibrium of the Diphtheria model in eq. (1) is locally asymptotically stable when $\mathcal{R}_0 < 1$.

Epidemiologically, Theorem 2 suggests that a small influx of diphtheria-infected individuals into the population will not lead to an outbreak if $\mathcal{R}_0 < 1$. However, it is important to note that this conclusion depends on the initial number of infected individuals in the population. □

### 3.4. Existence of Diphtheria Endemic Equilibrium Point

In this section, we will examine the existence of the Diphtheria endemic equilibrium point, which occurs when the infected variables are non-zero. To determine the conditions required for the existence of the Diphtheria endemic equilibrium point, the Diphtheria model in eq. (1) is solved in terms of the forces of infection, as defined by:

$$\lambda^{**} = \frac{\beta\left(I_A^{**}+I_S^{**}\right)}{N^{**}} + \frac{\beta_dB^{**}}{K+B^{**}}. \tag{9}$$

Where

$$
\begin{aligned}
N^{**} &= S^{**} + V^{**} + E^{**} + I_A^{**} + I_S^{**} + T^{**} + R^{**},\\
S^{**} &= \frac{\pi A_2A_3A_5A_6A_7\left(\varepsilon\lambda^{**}+A_8\right) - \lambda^{**}\pi\omega A_2A_3Z_2}{\mathcal{O}_1-\mathcal{O}_2},\\
V^{**} &= \frac{\pi\phi A_3A_5A_6\left(\varepsilon\lambda^{**}+A_8\right) - \lambda^{**}\pi\omega\phi A_3Z_2 + \lambda^{**}\pi\omega\psi Z_3}{\mathcal{O}_1-\mathcal{O}_2},\\
E^{**} &= \frac{\lambda^{**}\pi A_2A_5A_6A_7\left(\varepsilon\lambda^{**}+A_8\right) - \lambda^{**2}\pi\omega A_2Z_2}{\mathcal{O}_1-\mathcal{O}_2},\\
I_A^{**} &= \frac{\lambda^{**}\pi A_2A_4A_6A_7\left(\varepsilon\lambda^{**}+A_8\right) + \lambda^{**2}\pi\omega q\alpha f\varepsilon\eta_2A_2}{\mathcal{O}_1-\mathcal{O}_2}\\
&\quad - \frac{\lambda^{**2}\pi\omega\eta_2A_2A_4A_9}{\mathcal{O}_1-\mathcal{O}_2},\\
I_S^{**} &= \frac{\lambda^{**2}\pi\omega\eta_1A_2A_4A_9 - \lambda^{**2}\pi\omega q\alpha f\varepsilon\eta_1A_2}{\mathcal{O}_1-\mathcal{O}_2}\\
&\quad + \frac{\lambda^{**}\pi A_2A_7\left(\varepsilon\lambda^{**}+A_8\right)\left(q\alpha A_5+\sigma A_4\right)}{\mathcal{O}_1-\mathcal{O}_2},\\
T^{**} &= \frac{\lambda^{**}\pi A_2\left(\varepsilon\lambda^{**}+A_8\right)\left(\eta_1A_4A_6+\eta_2(q\alpha A_5+\sigma A_4)\right)}{\mathcal{O}_1-\mathcal{O}_2},\\
R^{**} &= \frac{\lambda^{**}\pi\omega A_2\left(\varepsilon\lambda^{**}+A_8\right)\left(\eta_1A_4A_6+\eta_2(q\alpha A_5+\sigma A_4)\right)}{\mathcal{O}_1-\mathcal{O}_2},\\
B^{**} &= \frac{\lambda^{**}\pi\kappa_1A_2A_4A_6A_7\left(\varepsilon\lambda^{**}+A_8\right) + \lambda^{**2}\pi\omega q\alpha f\varepsilon\kappa_1\eta_2A_2}{\mathcal{O}_1-\mathcal{O}_2}\\
&\quad - \frac{\lambda^{**2}\pi\omega\kappa_1\eta_2A_2A_4A_9}{\mathcal{O}_1-\mathcal{O}_2} - \frac{\lambda^{**2}\pi\omega q\alpha f\varepsilon\kappa_2\eta_1A_2}{\mathcal{O}_3-\mathcal{O}_4}\\
&\quad + \frac{\lambda^{**}\pi\kappa_2A_2A_7\left(\varepsilon\lambda^{**}+A_8\right)\left(q\alpha A_5+\sigma A_4\right)}{\mathcal{O}_3-\mathcal{O}_4}\\
&\quad + \frac{\lambda^{**2}\pi\omega\kappa_2\eta_1A_2A_4A_9}{\mathcal{O}_3-\mathcal{O}_4},\\
\mathcal{O}_1 &= A_3A_5A_6A_7Z_1\left(\varepsilon\lambda^{**}+A_8\right),\\
\mathcal{O}_2 &= \lambda^{**}\omega\left(\psi\gamma\left(\eta_1A_4A_6+\eta_2(q\alpha A_5+\sigma A_4)\right)+A_3Z_1Z_2\right),\\
\mathcal{O}_3 &= \delta_BA_3A_5A_6A_7Z_1\left(\varepsilon\lambda^{**}+A_8\right),\\
\mathcal{O}_4 &= \lambda^{**}\omega\delta_B\left(\psi\gamma\left(\eta_1A_4A_6+\eta_2(q\alpha A_5+\sigma A_4)\right)+A_3Z_1Z_2\right).
\end{aligned}
\tag{10}
$$

with

$$
\begin{aligned}
A_1 &= \phi+\mu,\\
A_2 &= \gamma+\mu,\\
A_3 &= \alpha+\mu,\\
A_4 &= (1-q)\alpha,\\
A_5 &= \sigma+\eta_1+\mu,\\
A_6 &= \eta_2+\delta+\mu,\\
A_7 &= \omega+\theta\delta+\mu,\\
A_8 &= \psi+\mu,\\
A_9 &= (1-f)\varepsilon,\\
Z_1 &= (\lambda^{**}+A_1)A_2-\phi\gamma,\\
Z_2 &= \eta_1f\varepsilon A_6+\eta_2(f\varepsilon\sigma+A_5A_9),\\
Z_3 &= \eta_1A_4A_6+\eta_2(q\alpha A_5+\sigma A_4).
\end{aligned}
$$

Substituting eq. (10) into eq. (9), we obtained

$$
\mathcal{T}(\lambda^{**}) = \Delta_1\lambda^{**4}+\Delta_2\lambda^{**3}+\Delta_3\lambda^{**2}+\Delta_4\lambda^{**}+\Delta_5 = 0, \tag{11}
$$

where

$$
\begin{aligned}
\Delta_1 &= \chi_1\chi_3,\\
\Delta_2 &= \chi_3\chi_9+\chi_4\chi_8-(\chi_1\chi_8+\chi_3\chi_6),\\
\Delta_3 &= \chi_3\chi_{10}+\chi_4\chi_9+\chi_5\chi_8-(\chi_1\chi_9+\chi_2\chi_8+\chi_4\chi_6+\chi_3\chi_7),\\
\Delta_4 &= \chi_4\chi_{10}+\chi_5\chi_9-(\chi_1\chi_{10}+\chi_2\chi_9+\chi_5\chi_6+\chi_4\chi_7),\\
\Delta_5 &= \chi_5\chi_{10}-(\chi_2\chi_{10}+\chi_5\chi_7),\\
&= \pi\mu\delta_BKA_3^2A_5^2A_6^2A_7^2A_8^2(\gamma+\phi+\mu)^2(1-\mathcal{R}_0),
\end{aligned}
$$

with

$$
\begin{aligned}
\chi_1 &= \pi\beta\left(\varepsilon A_2A_7(A_4A_6+q\alpha A_5+\sigma A_4)+\omega q\alpha f\varepsilon A_2(\eta_2-\eta_1)\right.\\
&\quad \left.+\omega A_2A_4A_9(\eta_1-\eta_2)\right),\\
\chi_2 &= \pi\beta A_2A_7A_8(A_4A_6+q\alpha A_5+\sigma A_4),\\
\chi_3 &= \pi\varepsilon A_2(A_6A_7(A_4+A_5)+A_7+\eta_2)(q\alpha A_5+\sigma A_4)\\
&\quad +\eta_1A_4A_6+\pi\omega A_2\left(A_4A_9(\eta_1-\eta_2A_2)\right.\\
&\quad \left.-\eta_2\left(f\varepsilon\sigma+A_5A_9\right)+f\varepsilon\left(\eta_2q\alpha-\eta_1(A_6-q\alpha)\right)\right),\\
\chi_4 &= \pi(\eta_1A_4A_6+\eta_2(q\alpha A_5+\sigma A_4))\left(A_2A_8+\omega(A_2+\psi)\right)\\
&\quad +\pi A_2A_5A_6A_7(\varepsilon A_3+A_8)+\pi A_2A_7A_8(A_4A_6+q\alpha A_5\\
&\quad +\sigma A_4)-\pi\omega A_3\left(\eta_1A_6f\varepsilon+\eta_2(f\varepsilon\sigma+A_5A_9)\right)(A_2+\phi)\\
&\quad +\pi\varepsilon\phi A_3A_5A_6A_7,\\
\chi_5 &= \pi A_3A_5A_6A_7A_8(A_2+\phi),\\
\chi_6 &= \pi\beta_d\left(\varepsilon A_2A_7(\kappa_1A_4A_6+\kappa_2(q\alpha A_5+\sigma A_4))\right.\\
&\quad \left.+\omega A_2\left(\kappa_1q\alpha f\varepsilon\eta_2+\kappa_2\eta_1A_4A_9\right)\right)-\pi\beta_d\omega\left(\kappa_1\eta_2A_4A_9\right.\\
&\quad \left.+\kappa_2q\alpha f\varepsilon\eta_1\right),\\
\chi_7 &= \pi\beta_dA_2A_7A_8\left(\kappa_1A_4A_6+\kappa_2(q\alpha A_5+\sigma A_4)\right),\\
\chi_8 &= \pi\left(\omega A_2\left(\kappa_1q\alpha f\varepsilon\eta_2+\kappa_2\eta_1A_4A_9\right)+\varepsilon A_2A_7(\kappa_1A_4A_6\right.\\
&\quad \left.+\kappa_2(q\alpha A_5+\sigma A_4))\right)+K\left(\varepsilon\delta_BA_2A_3A_5A_6A_7\right.\\
&\quad \left.-\omega\delta_BA_2A_3\left(\eta_1A_6f\varepsilon+\eta_2(f\varepsilon\sigma+A_5A_9)\right)\right)\\
&\quad -\pi\omega A_2\left(\kappa_1\eta_2A_4A_9+\kappa_2q\alpha f\varepsilon\eta_1\right),\\
\chi_9 &= K\left(\varepsilon\delta_BA_3A_5A_6A_7(A_1A_2-\phi\gamma)+\delta_BA_3A_5A_6A_7A_8\right)\\
&\quad -\omega\delta_B\left(\psi\gamma(\eta_1A_4A_6+\eta_2(q\alpha A_5+\sigma A_4))+A_3(A_1A_2\right.\\
&\quad \left.-\phi\gamma)(\eta_1A_6f\varepsilon+\eta_2(f\varepsilon\sigma+A_5A_9))\right)\\
&\quad +\pi A_2A_7A_8(\kappa_1A_4A_6+\kappa_2(q\alpha A_5+\sigma A_4)),\\
\chi_{10} &= \delta_BKA_3A_5A_6A_7A_8(A_1A_2-\phi\gamma).
\end{aligned}
$$

From eq. (11), it is evident that $\Delta_1 > 0$ (since all model parameters are non-negative). Additionally, $\Delta_5 > 0$ whenever $\mathcal{R}_0 < 1$. Therefore, the number of possible positive real roots of the polynomial in eq. (11) is contingent on the signs of $\Delta_2$, $\Delta_3$, and $\Delta_4$. This can be analyzed using Descartes' Rule of Signs applied to the quartic equation $f(x) = \Delta_1x^4+\Delta_2x^3+\Delta_3x^2+\Delta_4x+\Delta_5 = 0$ (with $x = \lambda^{**}$). Consequently, the following results are established.

**Theorem 3.** *The Diphtheria model in eq. (1)*

1. *Has a unique endemic equilibrium if $\mathcal{R}_0 > 1$ and either of the following holds*
   - *(a)* $\Delta_2 > 0, \Delta_3 > 0, \Delta_4 > 0$;
   - *(b)* $\Delta_2 < 0, \Delta_3 < 0, \Delta_4 < 0$;
   - *(c)* $\Delta_2 > 0, \Delta_3 < 0, \Delta_4 < 0$;
   - *(d)* $\Delta_2 > 0, \Delta_3 > 0, \Delta_4 < 0$;

2. *Could have more than one endemic equilibrium if* $\mathcal{R}_0 > 1$ *and either of the following*
   (a) $\Delta_2 < 0, \Delta_3 > 0, \Delta_4 < 0$;
   (b) $\Delta_2 < 0, \Delta_3 < 0, \Delta_4 > 0$;
   (c) $\Delta_2 > 0, \Delta_3 < 0, \Delta_4 > 0$;
   (d) $\Delta_2 < 0, \Delta_3 > 0, \Delta_4 > 0$;
3. *Could have 2 or more endemic equilibria if* $\mathcal{R}_0 < 1$ *and any, or all,* $\Delta_2$, $\Delta_3$, *and* $\Delta_4$ *are negative.*

Item 3 of Theorem 3 suggests the existence of multiple endemic equilibria when $\mathcal{R}_0 < 1$, which typically points to the occurrence of a backward bifurcation [24–30]. Backward bifurcation is a phenomenon where both a stable disease-free equilibrium (DFE) and a stable endemic equilibrium can coexist, even when the reproduction number of the model is less than one. This phenomenon has been observed in various disease transmission models, including those for vector-borne diseases, exogenous re-infection, imperfect vaccination, and multi-group interactions. The presence of this phenomenon in the Diphtheria model will be formally investigated in the following section.

### 3.5. *Possibility of the Existence of Backward Bifurcation*

In this section, we will investigate the potential existence of a backward bifurcation by applying the Center Manifold Theorem, a concept thoroughly explored by Castillo-Chavez and Song in their work [31].

**Theorem 4.** *The model of system in eq. (1) exhibits backward bifurcation at* $\mathcal{R}_0 = 1$.

*Proof.* To apply the Center Manifold Theorem, we will make certain changes to the state variables of the Diphtheria model in eq. (1). We define the variables as follows: $S = x_1$, $V = x_2$, $E = x_3$, $I_A = x_4$, $I_S = x_5$, $T = x_6$, $R = x_7$, and $B = x_8$. Using vector notation, we express the state as $x = (x_1, x_2, x_3, \ldots, x_8)^T$ and the system of equations as $\frac{dx}{dt} = F(x)$, where $F = (f_1, f_2, f_3, \ldots, f_8)^T$. Hence the Diphtheria model in eq. (1) becomes

$$\begin{aligned}
\frac{dx_1}{dt} &\equiv f_1 = \pi - \lambda x_1 - (\phi + \mu)x_1 + \gamma x_2,\\
\frac{dx_2}{dt} &\equiv f_2 = \phi x_1 + \psi x_7 - (\gamma + \mu)x_8,\\
\frac{dx_3}{dt} &\equiv f_3 = \lambda x_1 - (\alpha + \mu)x_3,\\
\frac{dx_4}{dt} &\equiv f_4 = (1-q)\alpha x_3 - (\sigma + \eta_1 + \mu)x_4 + f\varepsilon\lambda x_7,\\
\frac{dx_5}{dt} &\equiv f_5 = q\alpha x_3 + \sigma x_4 - (\eta_2 + \delta + \mu)x_5 + (1-f)\varepsilon\lambda x_7,\\
\frac{dx_6}{dt} &\equiv f_6 = \eta_1 x_4 + \eta_2 x_5 - (\omega + \theta\delta + \mu)x_6,\\
\frac{dx_7}{dt} &\equiv f_7 = \omega x_6 - (\varepsilon\lambda + \psi + \mu)x_7,\\
\frac{dx_8}{dt} &\equiv f_8 = \kappa_1 x_4 + \kappa_2 x_5 - \delta_B x_8,
\end{aligned} \tag{12}$$

where

$$\lambda = \frac{\beta\,(x_4 + x_5)}{x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7} + \frac{\beta_d x_8}{K + x_8}.$$

We Considered $\beta = \beta^*$, as the bifurcation parameter at $\mathcal{R}_0 = 1$. Solving for $\beta = \beta^*$ at $\mathcal{R}_0 = 1$, we obtained

$$\begin{aligned}
\beta^* &= \frac{\mathcal{M}_1 - \mathcal{M}_2}{K\mu\delta_B(\gamma+\mu)\,(A_4A_6 + q\alpha A_5 + \sigma A_4)},\\
\mathcal{M}_1 &= K\mu\delta_B A_3A_5A_6(\gamma + \phi + \mu),\\
\mathcal{M}_2 &= \beta_d\pi(\gamma+\mu)\,(\kappa_1 A_4A_6 + \kappa_2\,(q\alpha A_5 + \sigma A_4))\,,
\end{aligned} \tag{13}$$

where

$$\begin{aligned}
A_1 &= \phi + \mu,\\
A_2 &= \gamma + \mu,\\
A_3 &= \alpha + \mu,\\
A_4 &= (1-q)\alpha,\\
A_5 &= \sigma + \eta_1 + \mu,\\
A_6 &= \eta_2 + \delta + \mu,\\
A_7 &= \omega + \theta\delta + \mu,\\
A_8 &= \psi + \mu,\\
A_9 &= (1-f)\varepsilon.
\end{aligned}$$

Computing the Jacobian of the transformed system in eq. (12) at the disease-free equilibrium (DFE), denoted as $(\xi_0)$ with $\beta = \beta^*$, yields:

$$\mathcal{J}\,(\xi_0)\,|_{\beta=\beta^*} = \begin{bmatrix}
p_1 & \gamma & 0 & p_2 & p_3 & 0 & 0 & p_4\\
\phi & p_5 & 0 & 0 & 0 & 0 & \psi & 0\\
0 & 0 & p_6 & p_7 & p_8 & 0 & 0 & p_9\\
0 & 0 & p_{10} & p_{11} & 0 & 0 & 0 & 0\\
0 & 0 & q\alpha & \sigma & p_{12} & 0 & 0 & 0\\
0 & 0 & 0 & \eta_1 & \eta_2 & p_{13} & 0 & 0\\
0 & 0 & 0 & 0 & 0 & \omega & p_{14} & 0\\
0 & 0 & 0 & \kappa_1 & \kappa_2 & 0 & 0 & p_{15}
\end{bmatrix},$$

$$\begin{aligned}
p_1 &= -A_1, & p_9 &= -\frac{\beta_d\pi A_2}{K\mu(\gamma + A_1)},\\
p_2 &= -\frac{\beta^* A_2}{(\gamma + A_1)}, & p_{10} &= A_4,\\
p_3 &= -\frac{\beta^* A_2}{(\gamma + A_1)}, & p_{11} &= -A_5,\\
p_4 &= -\frac{\beta_d\pi A_2}{K\mu(\gamma + A_1)}, & p_{12} &= -A_6,\\
p_5 &= -A_2, & p_{13} &= -A_7,\\
p_6 &= -A_3, & p_{14} &= -A_8,\\
p_7 &= \frac{\beta^* A_2}{(\gamma + A_1)}, & p_{15} &= -\delta_B.\\
p_8 &= \frac{\beta^* A_2}{(\gamma + A_1)},
\end{aligned}$$

where

$$\begin{aligned}
A_1 &= \phi + \mu,\\
A_2 &= \gamma + \mu,\\
A_3 &= \alpha + \mu,\\
A_4 &= (1-q)\alpha,\\
A_5 &= \sigma + \eta_1 + \mu,
\end{aligned}$$

$$
\begin{aligned}
A_6 &= \eta_2 + \delta + \mu,\\
A_7 &= \omega + \theta\delta + \mu,\\
A_8 &= \psi + \mu,\\
A_9 &= (1-f)\varepsilon.
\end{aligned}
$$

The right eigenvector, denoted as

$$w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8)^T,$$

corresponding to the simple zero eigenvalue, can be derived from $\mathcal{J}(\xi_0)\,|_{\beta=\beta^*} w = 0$, given by

$$
\begin{aligned}
0 &= -A_1 w_1 + \gamma w_2 - \frac{\beta^* A_2 w_4}{(\gamma + A_1)} - \frac{\beta^* A_2 w_5}{(\gamma + A_1)} - \frac{\beta_d \pi A_2 w_8}{K\mu(\gamma + A_1)},\\
0 &= \phi w_1 - A_2 w_2 + \psi w_7,\\
0 &= -A_3 w_3 + \frac{\beta^* A_2 w_4}{(\gamma + A_1)} + \frac{\beta^* A_2 w_5}{(\gamma + A_1)} + \frac{\beta_d \pi A_2 w_8}{K\mu(\gamma + A_1)},\\
0 &= A_4 w_3 - A_5 w_4,\\
0 &= q\alpha w_3 + \sigma w_4 - A_6 w_5,\\
0 &= \eta_1 w_4 + \eta_2 w_5 - A_7 w_6,\\
0 &= \omega w_6 - A_8 w_7,\\
0 &= \kappa_1 w_4 + \kappa_2 w_5 - \delta_B w_8.
\end{aligned}
\tag{14}
$$

Solving the above eq. (14), we obtained

$$
\begin{aligned}
w_1 &= w_1 > 0,\\
w_2 &= \frac{\phi A_5 A_6 A_7 A_8 w_1 + \psi\omega(\eta_1 A_4 A_6 + \eta_2(q\alpha A_5 + \sigma A_4))w_3}{A_2 A_5 A_6 A_7 A_8},\\
w_3 &= w_3 > 0,\\
w_4 &= \frac{A_4 w_3}{A_5},\\
w_5 &= \frac{(q\alpha A_5 + \sigma A_4)w_3}{A_5 A_6},\\
w_6 &= \frac{(\eta_1 A_4 A_6 + \eta_2(q\alpha A_5 + \sigma A_4))w_3}{A_5 A_6 A_7},\\
w_7 &= \frac{\omega(\eta_1 A_4 A_6 + \eta_2(q\alpha A_5 + \sigma A_4))w_3}{A_5 A_6 A_7 A_8},\\
w_8 &= \frac{(\kappa_1 A_4 A_6 + \kappa_2(q\alpha A_5 + \sigma A_4))w_3}{\delta_B A_5 A_6}.
\end{aligned}
\tag{15}
$$

Likewise, the left eigenvector, denoted as

$$v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8),$$

satisfying $v.w = 1$, associated with the simple zero eigenvalue, can be determined from $vJ(\xi_0)\,|_{\beta=\beta^*} = 0$, given by

$$
\begin{aligned}
0 &= -A_1 v_1 + \phi v_2,\\
0 &= \gamma v_1 - A_2 v_2,\\
0 &= -A_3 v_3 + A_4 A_4 + q\alpha v_5,\\
0 &= -\frac{\beta^* A_2 v_1}{(\gamma + A_1)} + \frac{\beta^* A_2 v_3}{(\gamma + A_1)} - A_5 v_4 + \sigma v_5 + \eta_1 v_6 + \kappa_1 v_8,\\
0 &= -\frac{\beta^* A_2 v_1}{(\gamma + A_1)} + \frac{\beta^* A_2 v_3}{(\gamma + A_1)} - A_6 v_5 + \eta_2 v_6 + \kappa_2 v_8,\\
0 &= -A_7 v_6 + \omega v_7,\\
0 &= \psi v_2 - A_8 v_7,\\
0 &= -\frac{\beta_d \pi A_2 v_1}{K\mu(\gamma + A_1)} + \frac{\beta_d \pi A_2 v_3}{K\mu(\gamma + A_1)} - \delta_B v_8.
\end{aligned}
\tag{16}
$$

Solving the above eq. (16), we obtained

$$
\begin{aligned}
v_1 &= v_1 > 0, & v_5 &= \frac{A_3 v_3 - A_4 v_4}{q\alpha},\\
v_2 &= \frac{(A_1 - \gamma)v_1}{\phi - A_2}, & v_6 &= \frac{\psi\omega(A_1 - \gamma)v_1}{(\phi - A_2)A_7 A_8},\\
v_3 &= v_3 > 0, & v_7 &= \frac{\psi(A_1 - \gamma)v_1}{(\phi - A_2)A_8},\\
v_4 &= v_4 > 0, & v_8 &= \frac{\beta_d \pi A_2(v_3 - v_1)}{K\mu\delta_B(\gamma + A_1)}.
\end{aligned}
\tag{17}
$$

The non-zero partial derivatives of $f_1, f_2, f_3, \ldots, f_8$ at the disease-free equilibrium are presented in Appendix B.

The direction of the bifurcation at $\mathcal{R}_0 = 1$ is determined by the sign of the bifurcation coefficients $a$ and $b$, which can be obtained by using the partial derivatives in Appendix B. The bifurcation coefficients $a$ and $b$ are given respectively by

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(\xi_0), \tag{18}$$

$$
\begin{aligned}
a = {} & \frac{2(v_3 - v_1)w_1 w_3 \beta^* \phi\mu\Psi_1}{\pi A_5 A_6(\gamma + A_1)} + \frac{2(v_1 - v_3)w_3^2 \beta^* \mu A_2 \Psi_1}{\pi A_5 A_6(\gamma + A_1)}\\
& + \frac{2(v_1 - v_3)w_3^2 \beta^* \mu A_2 \Psi_1 \Psi_2(A_8 + \omega)}{\pi A_5^2 A_6^2 A_7 A_8(\gamma + A_1)}\\
& + \frac{2(v_1 - v_3)w_3 \beta^* \mu \Psi_1(\phi A_5 A_6 A_7 A_8 w_1 + \psi\omega\Psi_2 w_3)}{\pi A_5^2 A_6^2 A_7 A_8(\gamma + A_1)}\\
& + \frac{2(v_1 - v_3)w_3^2 \beta^* \mu A_2(A_4^2 A_6^2 + (q\alpha A_5 + \sigma A_4)^2)}{\pi A_5^2 A_6^2(\gamma + A_1)}\\
& + \frac{4(v_1 - v_3)w_3^2 \beta^* \mu A_2 A_4(q\alpha A_5 + \sigma A_4)}{\pi A_5^2 A_6(\gamma + A_1)}\\
& + \frac{2(v_3 - v_1)w_1 w_3 \beta_d \Psi_3}{K\delta_B A_5 A_6} + \frac{2(v_1 - v_3)w_3^2 \beta_d \pi A_2 \Psi_3^2}{K^2\mu\delta_B^2 A_5^2 A_6^2(\gamma + A_1)}\\
& - \frac{2v_1 w_3^2 \beta^* \mu\varepsilon\psi\omega\Psi_1\Psi_2(A_1 - \gamma)}{\pi A_5^2 A_6^2 A_7 A_8(\phi - A_2)} + \frac{2v_1 w_3^2 \beta^* \mu f\varepsilon\omega\Psi_1\Psi_2}{\pi A_5^2 A_6^2 A_7 A_8}\\
& - \frac{2v_1 w_3^2 \beta_d \varepsilon\psi\omega\Psi_2\Psi_3(A_1 - \gamma)}{K\delta_B A_5^2 A_6^2 A_7 A_8(\phi - A_2)} + \frac{2v_1 w_3^2 \beta_d f\varepsilon\omega\Psi_2\Psi_3}{K\delta_B A_5^2 A_6^2 A_7 A_8}\\
& + \frac{2(A_3 v_3 - A_4 v_4)w_3^2 \beta^* \mu\omega A_9 \Psi_1 \Psi_2}{\pi q\alpha A_5^2 A_6^2 A_7 A_8}\\
& + \frac{2(A_3 v_3 - A_4 v_4)w_3^2 \beta_d \omega A_9 \Psi_2 \Psi_3}{K q\alpha\delta_B A_5^2 A_6^2 A_7 A_8},
\end{aligned}
\tag{19}
$$

$$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta^*}(\xi_0), \tag{20}$$

$$b = \frac{(v_3 - v_1)w_3 A_2(A_4 A_6 + q\alpha A_5 + \sigma A_4)}{A_5 A_6(\gamma + A_1)} > 0, \tag{21}$$

where

$$\Psi_1 = A_4A_6 + q\alpha A_5 + \sigma A_4,$$
$$\Psi_2 = \eta_1 A_4A_6 + \eta_2(q\alpha A_5 + \sigma A_4),$$
$$\Psi_3 = \kappa_1 A_4A_6 + \kappa_2(q\alpha A_5 + \sigma A_4).$$

Since the bifurcation coefficient $b$ is positive, it follows from theorem 4.1 in [31] that the Diphtheria model in eq. (1) undergoes backward bifurcation at $\mathcal{R}_0 = 1$ whenever $a > 0$. Figure 2 shows the bifurcation diagram of Diphtheria model, where the parameter values used are $\beta = 0.35$ other parameters are as in Table 2. The backward bifurcation shows a locally stable disease-free equilibrium point and a stable endenmic equilibrium point when $\mathcal{R}_0 < 1$, it illustrates the possible number of positive roots of the polynomial in eq. (11). □

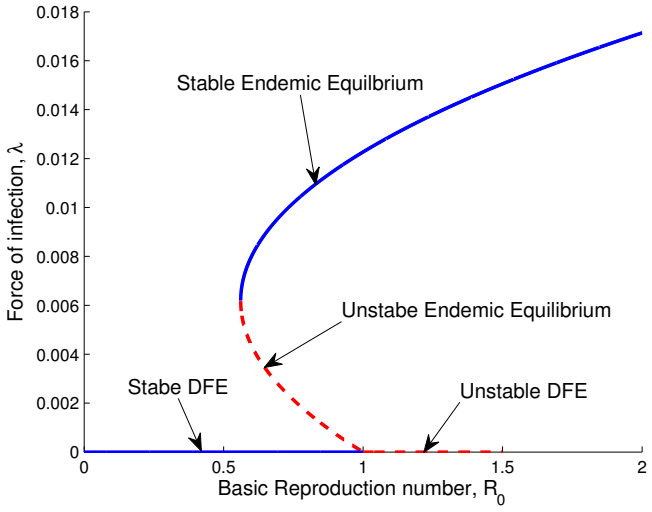



**Figure 2.** Backward bifurcation of the Diphtheria model.

### 3.6. *Global Stability of the Disease-free Equilibrium: Special Case*

Some of the primary causes of backward bifurcation include imperfect vaccination, vector-borne diseases, and re-infection of recovered individuals [24, 29, 31]. Models that incorporate re-infection of recovered individuals are known to lose the backward bifurcation property when the re-infection parameters are set to zero. Therefore, the role of re-infection ($\varepsilon$) in the occurrence of backward bifurcation will be investigated. Thus the Diphtheria model can be re-written as

$$\begin{aligned} \frac{dU}{dt} &= \mathcal{P}(U, W), \\ \frac{dW}{dt} &= \mathcal{G}(U, W), \end{aligned} \tag{22}$$

where $U = (S, V, R)$ and $W = (E, I_A, I_S, T, B)$ with $U \in \mathbb{R}^3_+$ denoting the number of uninfected compartments and $W \in \mathbb{R}^5_+$ denoting the number of infected compartments. Let $\xi_0 = (U^*, 0)$ represents the disease-free equilibrium point of the system. The disease-free equilibrium ($\xi_0$) is globally asymptotically stable for the Diphtheria model if it satisfies condition $\mathcal{S}_1$ and $\mathcal{S}_2$ below.

$$\begin{aligned} &\mathcal{S}_1 : \frac{dU}{dt} = \mathcal{P}(U, 0), U^* \text{ is globally asymptotically stable,} \\ &\mathcal{S}_2 : \frac{dW}{dt} = \mathcal{B}_W\mathcal{G}(U^*, 0) - \hat{\mathcal{G}}(U, W), \hat{\mathcal{G}}(U, W) \geq 0 \; \forall \; (U, W) \in \mathcal{D}, \end{aligned} \tag{23}$$

where $\mathcal{B}_W\mathcal{G}(U^*, 0)$ is the Jacobian of $\mathcal{G}(U, W)$ taking in $(E, I_A, I_S, T, B)$ and evaluated at $(U^*, 0) = \left(\left(\frac{\pi(\gamma+\mu)}{\mu(\gamma+\phi+\mu)}, \frac{\pi\phi}{\mu(\gamma+\phi+\mu)}, 0\right), 0\right)$. If system (22) satisfies the condition, then the following theorem holds.

**Theorem 5.** *The equilibrium point $(U^*, 0)$ of the system in eq. (22) is globally asymptotically stable if $\mathcal{R}_0 \leq 1$, and condition $\mathcal{S}_1$ and $\mathcal{S}_2$ are satisfied.*

*Proof.* From system eq. (1), we obtained $\mathcal{P}(U, W)$ and $\mathcal{G}(U, W)$

$$\mathcal{P}(U, W) = \begin{bmatrix} \pi - \lambda S - (\phi + \mu)S + \gamma V \\ \phi S + \psi R - (\gamma + \mu)V \\ \omega T - (\psi + \mu)R \end{bmatrix},$$

$$\mathcal{G}(U, W) = \begin{bmatrix} \left(\frac{\beta(I_A+I_S)}{N} + \frac{\beta_d B}{K+B}\right) S - (\alpha + \mu)E \\ (1-q)\alpha E - \sigma I_A - (\eta_1 + \mu)I_A \\ q\alpha E + \sigma I_A - (\eta_2 + \delta + \mu)I_S \\ \eta_1 I_A + \eta_2 I_S - (\omega + \theta\delta + \mu)T \\ \kappa_1 I_A + \kappa_2 I_S - \delta_B B \end{bmatrix}.$$

Now, we consider $\frac{dU}{dt} = \mathcal{P}(U^*, 0)$ the reduced system from condition $\mathcal{S}_1$

$$\begin{aligned} \frac{dS}{dt} &= \pi - (\phi + \mu)S + \gamma V, \\ \frac{dV}{dt} &= \phi S - (\gamma + \mu)V, \\ \frac{dR}{dt} &= 0, \end{aligned} \tag{24}$$

$U^* = \left(\frac{\pi(\gamma+\mu)}{\mu(\gamma+\phi+\mu)}, \frac{\pi\phi}{\mu(\gamma+\phi+\mu)}, 0\right)$ is a globally asymptotically stable equilibrium point for the reduced system $\frac{dU}{dt} = \mathcal{P}(U, 0)$ in eq. (24). We note that this asymptotic dynamics is independent of the initial condition in $\mathcal{D}$. Therefore, the convergence of the solution of the reduced system in eq. (24) is global in $\mathcal{D}$. Hence, we compute

$$\mathcal{B}_W\mathcal{G}(U, 0) = \begin{bmatrix} q_1 & q_2 & q_3 & 0 & q_4 \\ q_5 & q_6 & 0 & 0 & 0 \\ q\alpha & \sigma & q_7 & 0 & 0 \\ 0 & \eta_1 & \eta_2 & q_8 & 0 \\ 0 & \kappa_1 & \kappa_2 & 0 & -\delta_B \end{bmatrix},$$

$$\hat{\mathcal{G}}(U, W) = \begin{bmatrix} q_9 + q_{10} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix},$$

$$q_1 = -(\alpha + \mu), \qquad q_5 = (1-q)\alpha,$$
$$q_2 = \frac{\beta(\gamma + \mu)}{(\gamma + \phi + \mu)}, \qquad q_6 = -(\sigma + \eta_1 + \mu),$$

$$
\begin{aligned}
q_3 &= \frac{\beta(\gamma+\mu)}{(\gamma+\phi+\mu)}, \qquad q_7 = -(\eta_2+\delta+\mu),\\
q_4 &= \frac{\beta_d\pi(\gamma+\mu)}{K\mu(\gamma+\phi+mu)}, \; q_8 = -(\omega+\theta\delta+\mu),\\
q_9 &= \beta(I_A+I_S)\left(\frac{\beta(\gamma+\mu)}{(\gamma+\phi+\mu)}-\frac{S}{N}\right),\\
q_{10} &= \beta_d B\left(\frac{\beta_d\pi(\gamma+\mu)}{(\gamma+\phi+\mu)}-\frac{S}{K+B}\right).
\end{aligned}
$$

Here, since $\frac{S}{N} \leq \frac{(\gamma+\mu)}{(\gamma+\phi+\mu)}$ and $\frac{S}{K+B} \leq \frac{\pi(\gamma+\mu)}{K\mu(\gamma+\phi+\mu)}$, it is clear $\hat{\mathcal{G}}(U,W) \geq 0$ that for all $(U,W) \in \mathcal{D}$. Therefore, by Lasalle invariance principle [32], this proves that the disease-free equilibrium is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$. This result indicates that Diphtheria elimination is independent of the initial sizes of the infected individuals in the population. □

### 3.7. Sensitivity Analysis

In this section, we aim to perform a sensitivity analysis on the key parameters that affect the basic reproduction number of the Diphtheria model in eq. (1). The goal is to evaluate how each parameter influences the transmission dynamics of Diphtheria. To do so, we follow the approach described in [10, 24, 33]. In line with the methodology outlined in [10, 24, 33], we utilize the normalized forward sensitivity index of a variable '$u$', which shows differential dependence on the parameter '$v$', as defined by:

$$\mathrm{Q}_v^u = \frac{\partial u}{\partial v} \times \frac{v}{u} \tag{25}$$

Therefore, the sensitivity index of the basic reproduction number for the Diphtheria model in eq. (1) with respect to the parameter '$v$' can be calculated as follows:

$$\mathrm{Q}_v^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial v} \times \frac{v}{\mathcal{R}_0} \tag{26}$$

Therefore, the sensitive indices of the basic reproduction number with respect to the basic parameters is computed as follows;

$$
\begin{aligned}
\mathrm{Q}_\beta^{\mathcal{R}_0} = &\left(\frac{(\gamma+\mu)\left(\alpha q\Phi_1+\sigma(1-q)\alpha+(1-q)\alpha\Phi_2\right)}{\Phi_1\Phi_2\Phi_3(\alpha+\mu)}\right)\beta\\
&\div\left(\frac{\beta(\gamma+\mu)\left(\alpha q\Phi_1+\sigma(1-q)\alpha+(1-q)\alpha\Phi_2\right)}{\Phi_1\Phi_2\Phi_3(\alpha+\mu)}\right.\\
&\left.+\frac{\beta_d\pi(\gamma+\mu)\left(\kappa_1(1-q)\alpha\Phi_2+\kappa_2(\alpha q\Phi_1+\sigma(1-q)\alpha)\right)}{K\delta_B\mu\Phi_1\Phi_2\Phi_3(\alpha+\mu)}\right),\\
\Phi_1 &= \sigma+\eta_1+\mu,\\
\Phi_2 &= \eta_2+\delta+\mu,\\
\Phi_3 &= \gamma+\phi+\mu.
\end{aligned}
\tag{27}
$$

We have that

$$\mathrm{Q}_\beta^{\mathcal{R}_0} = 0.5767. \tag{28}$$

Following a similar approach, we derived the sensitivity indices for the other key parameters that make up the basic reproduction number, which are given by:

$$
\begin{aligned}
&\mathrm{Q}_{\beta_d}^{\mathcal{R}_0} = 0.4233, \quad \mathrm{Q}_q^{\mathcal{R}_0} = -0.0105, \; \mathrm{Q}_{\kappa_1}^{\mathcal{R}_0} = 0.2643,\\
&\mathrm{Q}_{\kappa_2}^{\mathcal{R}_0} = 0.159, \quad \mathrm{Q}_{\delta_B}^{\mathcal{R}_0} = -0.4233, \; \mathrm{Q}_\sigma^{\mathcal{R}_0} = -0.0109,\\
&\mathrm{Q}_{\eta_1}^{\mathcal{R}_0} = -0.5645, \; \mathrm{Q}_{\eta_2}^{\mathcal{R}_0} = -0.3622, \; \mathrm{Q}_\delta^{\mathcal{R}_0} = -0.0084,\\
&\mathrm{Q}_\alpha^{\mathcal{R}_0} = 0.0417, \quad \mathrm{Q}_\gamma^{\mathcal{R}_0} = 0.0114, \quad \mathrm{Q}_\pi^{\mathcal{R}_0} = 0.4233,\\
&\mathrm{Q}_\phi^{\mathcal{R}_0} = -0.0121, \; \mathrm{Q}_K^{\mathcal{R}_0} = -0.4233, \; \mathrm{Q}_\mu^{\mathcal{R}_0} = -0.5181.
\end{aligned}
\tag{29}
$$

### 3.7. Interpretation of the sensitivity indices

The bar chart in Figure 3 shows the sensitivity indices of the basic reproduction number for the Diphtheria model. Parameters with positive indices have a significant impact on accelerating the spread of the disease. Specifically, as the values of these parameters rise, while keeping other parameters constant, there is a marked increase in the basic reproduction number. As a result, higher values of these parameters lead to greater disease transmission. In contrast, parameters with negative indices help reduce the disease burden. When these parameters increase, the basic reproduction number decreases, indicating a reduced spread of the disease.

## 4. Optimal Control Theory

Based on the results from the sensitivity analysis, we introduced two time-dependent control measures to mitigate the spread of diphtheria. These control measures represent preventive actions, such as public enlightenment campaigns to sensitize and educate the general public about the dynamics of diphtheria and the importance of proper personal hygiene, including regular handwashing to prevent susceptible individuals from acquiring diphtheria, denoted by $u_1(t)$, and environmental sanitation practices such as cleaning surfaces, clothes, materials, and door handles to reduce the concentration of Corynebacterium diphtheriae in the environment, denoted by $u_2(t)$. Therefore, the diphtheria model in eq. (1) with the time-dependent control measures becomes:

$$
\begin{aligned}
\frac{dS}{dt} &= \pi-(1-u_1(t))\lambda S-(\phi+\mu)S+\gamma V,\\
\frac{dV}{dt} &= \phi S+\psi R-(\gamma+\mu)V,\\
\frac{dE}{dt} &= (1-u_1(t))\lambda S-(\alpha+\mu)E,\\
\frac{dI_A}{dt} &= (1-q)\alpha E-\sigma I_A-(\eta_1+\mu)I_A+(1-u_1(t))f\varepsilon\lambda R,\\
\frac{dI_S}{dt} &= q\alpha E+\sigma I_A-(\eta_2+\delta+\mu)I_S+(1-u_1(t))(1-f)\varepsilon\lambda R,\\
\frac{dT}{dt} &= \eta_1 I_A+\eta_2 I_S-(\omega+\theta\delta+\mu)T,\\
\frac{dR}{dt} &= \omega T-((1-u_1(t))\varepsilon\lambda+\psi+\mu)R,\\
\frac{dB}{dt} &= \kappa_1 I_A+\kappa_2 I_S-(\delta_B+u_2(t))B,
\end{aligned}
\tag{30}
$$

where

$$\lambda = \frac{\beta\left(I_A+I_S\right)}{N}+\frac{\beta_d B}{K+B}.$$

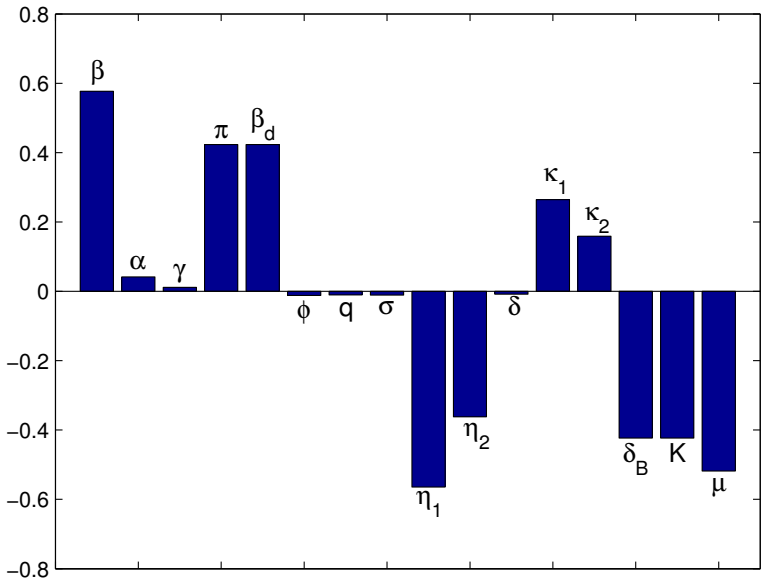



**Figure 3.** Sensitivity index of the basic reproduction number of the Diphtheria model

For this, we considered the objective functional

$$\mathcal{J}[u_1, u_2] = \int_0^{t_f} \left[ b_1 I_A + b_2 I_S + \frac{1}{2}\left(b_3 u_1^2(t) + b_4 u_2^2(t)\right) \right] dt \tag{31}$$

Here, the parameter $b_i$, $(i = 1, 2, 3, 4)$ are the weight factors to help balance each terms in the integrand in eq. (31), so that none of the terms dominate. The terms in the integrand in eq. (31) are explained as follows;

1. The term $b_1 I_A + b_2 I_S$, denotes the expenses in monitoring infected individuals at all stages.
2. The term $b_3 u_1^2(t) + b_4 u_2^2(t)$, represents the cost associated with the public health awareness campaign to educate the public on personal hygiene, sanitation and ways to prevent Diphtheria infection.

The objective is to minimize the total number of infected individuals, while simultaneously minimizing the costs associated with the implemented controls ($u_1(t)$ and $u_2(t)$). The goal is to find an optimal control ($u_1^*(t)$ and $u_2^*(t)$) such that

$$\mathcal{J}[u_1^*, u_2^*] = \min_{u_1, u_2 \in \mathcal{D}^*} \mathcal{J}[u_1, u_2], \tag{32}$$

where

$$\mathcal{D}^* = \left\{ (u_1(t), u_2(t) \in \mathcal{L}^1(0, t_f) | a_1 \leq u_1(t) \geq b_1, a_2 \leq u_2(t) \geq b_2 \right\} \tag{33}$$

is lesbgue measurable.

### 4.1. Analysis of the Optimal Control Model

The necessary conditions that an optimal control must satisfy comes from the Pontryagin's Maximum Principle [34]. This principle converts eq. (30) and eq. (31) into a problem of minimizing pointwise a Hamiltonian $\mathcal{H}$, with respect to the controls $(u_1(t), u_2(t))$. First we formulate the Hamiltonian from the objective functional in eq. (31) and the governing dynamics in eq. (30) to obtain the optimality conditions, given by

$$\begin{aligned}
\mathcal{H} &= b_1 I_A + b_2 I_S + \frac{1}{2}\left(b_3 u_1^2(t) + b_4 u_2^2(t)\right) \\
&+ \Theta_1 \left[ \pi - (1 - u_1(t)) \left( \frac{\beta (I_A + I_S)}{N} + \frac{\beta_d B}{K + B} \right) S \right. \\
&\left. - (\phi + \mu) S + \gamma V \right] + \Theta_2 \left[ \phi S + \psi R - (\gamma + \mu) V \right] \\
&+ \Theta_3 \left[ (1 - u_1(t)) \left( \frac{\beta (I_A + I_S)}{N} + \frac{\beta_d B}{K + B} \right) S \right. \\
&\left. - (\alpha + \mu) E \right] + \Theta_4 \left[ (1 - q)\alpha E - \sigma I_A - (\eta_1 + \mu) I_A \right. \\
&\left. + (1 - u_1(t)) f \varepsilon \left( \frac{\beta (I_A + I_S)}{N} + \frac{\beta_d B}{K + B} \right) R \right] \\
&+ \Theta_5 \left[ q\alpha E + \sigma I_A - (\eta_2 + \delta + \mu) I_S \right. \\
&\left. + (1 - u_1(t))(1 - f) \varepsilon \left( \frac{\beta (I_A + I_S)}{N} + \frac{\beta_d B}{K + B} \right) R \right] \\
&+ \Theta_6 \left[ \eta_1 I_A + \eta_2 I_S - (\omega + \theta\delta + \mu) T \right] + \Theta_7 \left[ \omega T \right. \\
&\left. - \left( (1 - u_1(t)) \varepsilon \left( \frac{\beta (I_A + I_S)}{N} + \frac{\beta_d B}{K + B} \right) + \psi + \mu \right) R \right] \\
&+ \Theta_8 \left[ \kappa_1 I_A + \kappa_2 I_S - (\delta_B + u_2(t)) B \right],
\end{aligned} \tag{34}$$

where $\Theta_1, \Theta_2, \Theta_3, \Theta_4, \Theta_5, \Theta_6, \Theta_7$, and $\Theta_8$ are the adjoint functions associated with the state variables of the model in eq. (30). By applying Pontryagin's Maximum Principle [34] and utilizing the

existence result for the optimal control pair $u_1(t)$ and $u_2(t)$, we have derived the following theorem:

**Theorem 6.** *There exists an optimal control pair $u_1^*(t)$ and $u_2^*(t)$, and corresponding solution ($S^*$, $V^*$, $E^*$, $I_A^*$, $I_S^*$, $T^*$, $R^*$, and $B^*$) that minimize $\mathcal{J}(u_1(t), u_2(t))$ over $\mathcal{D}^*$. Furthermore, there exist adjoint functions, $\Theta_i$, ($i = 1, 2, 3, ..., 8$) such that;*

$$\begin{aligned} &\frac{d\Theta_1}{dt} = \mathcal{B}_1, \frac{d\Theta_2}{dt} = \mathcal{B}_2, \frac{d\Theta_3}{dt} = \mathcal{B}_3, \frac{d\Theta_4}{dt} = \mathcal{B}_4, \\ &\frac{d\Theta_5}{dt} = \mathcal{B}_5, \frac{d\Theta_6}{dt} = \mathcal{B}_6, \frac{d\Theta_7}{dt} = \mathcal{B}_7, \frac{d\Theta_8}{dt} = \mathcal{B}_8, \end{aligned} \tag{35}$$

*where the expression for $\mathcal{B}_1$, $\mathcal{B}_2$, $\mathcal{B}_3$, $\mathcal{B}_4$, $\mathcal{B}_5$, $\mathcal{B}_6$,$\mathcal{B}_7$, and $\mathcal{B}_8$ are in Appendix C. With transerversality conditions*

$$\Theta_i(t_f) = 0, \quad i = 1, 2, 3, ..., 8. \tag{36}$$

*The following characterization holds;*

$$\begin{aligned} u_1^*(t) &= \max\{0, \min(1, \mathcal{M}_1)\}, \\ u_2^*(t) &= \max\left\{0, \min\left(1, \frac{1}{b_4}(\Theta_1 - \Theta_2) S^*\right)\right\}, \end{aligned} \tag{37}$$

*where*

$$\begin{aligned} \mathcal{M}_1 = \frac{1}{b_3}\Bigg((\Theta_3 - \Theta_1)\left(\frac{\beta(I_A^* + I_S^*)}{N^*} + \frac{\beta_d B^*}{K + B^*}\right) S^* + (\Theta_4 f\varepsilon \\ + \Theta_5(1-f)\varepsilon - \Theta_7\varepsilon)\left(\frac{\beta(I_A^* + I_S^*)}{N^*} + \frac{\beta_d B^*}{K + B^*}\right) R^*\Bigg) \end{aligned} \tag{38}$$

*Preposition 1 Corollary 4.2 of (Fleming and Rashel 1975 [35] gives the existence of an optimal control sets($u_1(t)$, and $u_2(t)$) due to the convexity of the integrand of $\mathcal{J}$ with respect of ($u_1(t)$, and $u_2(t)$), a prior boundedness of the state solutions, and the local Lipschitz property of the model in eq. (30) with respect to the variables.*

*Proof.* Using the Pontryagin's Maximum Principles, we obtained

$$\begin{aligned} \frac{d\Theta_1}{dt} &= -\frac{\partial \mathcal{H}}{\partial S}, & \Theta_1(t_f) &= 0, \\ \frac{d\Theta_2}{dt} &= -\frac{\partial \mathcal{H}}{\partial V}, & \Theta_2(t_f) &= 0, \\ \frac{d\Theta_3}{dt} &= -\frac{\partial \mathcal{H}}{\partial E}, & \Theta_3(t_f) &= 0, \\ \frac{d\Theta_4}{dt} &= -\frac{\partial \mathcal{H}}{\partial I_A}, & \Theta_4(t_f) &= 0, \\ \frac{d\Theta_5}{dt} &= -\frac{\partial \mathcal{H}}{\partial I_S}, & \Theta_5(t_f) &= 0, \\ \frac{d\Theta_6}{dt} &= -\frac{\partial \mathcal{H}}{\partial T}, & \Theta_6(t_f) &= 0, \\ \frac{d\Theta_7}{dt} &= -\frac{\partial \mathcal{H}}{\partial R}, & \Theta_7(t_f) &= 0, \\ \frac{d\Theta_8}{dt} &= -\frac{\partial \mathcal{H}}{\partial B}, & \Theta_8(t_f) &= 0, \end{aligned} \tag{39}$$

and considering the optimality condition;

$$\frac{\partial \mathcal{H}}{\partial u_1} = 0, \frac{\partial \mathcal{H}}{\partial u_2} = 0. \tag{40}$$

This optimal control sets($u_1(t)$ and $u_2(t)$) can be solved for subject to the state variables. Taking into account the bounds on the controls, the characterization can be solved as follows;
For the control $u_1(t)$, we have

$$\begin{aligned} \frac{\partial \mathcal{H}}{\partial u_1} = u_1 b_3 - (\Theta_3 - \Theta_1)\left(\frac{\beta(I_A^* + I_S^*)}{N^*} + \frac{\beta_d B^*}{K + B^*}\right) S^* \\ - (\Theta_4 f\varepsilon - \Theta_7\varepsilon)\left(\frac{\beta(I_A^* + I_S^*)}{N^*} + \frac{\beta_d B^*}{K + B^*}\right) R^* \\ - \Theta_5(1-f)\varepsilon\left(\frac{\beta(I_A^* + I_S^*)}{N^*} + \frac{\beta_d B^*}{K + B^*}\right) R^* = 0, \end{aligned}$$

so that

$$\begin{aligned} u_1^*(t) = \frac{1}{b_3}\Bigg((\Theta_3 - \Theta_1)\left(\frac{\beta(I_A^* + I_S^*)}{N^*} + \frac{\beta_d B^*}{K + B^*}\right) S^* + (\Theta_4 f\varepsilon \\ + \Theta_5(1-f)\varepsilon - \Theta_7\varepsilon)\left(\frac{\beta(I_A^* + I_S^*)}{N^*} + \frac{\beta_d B^*}{K + B^*}\right) R^*\Bigg) \end{aligned} \tag{41}$$

For the control $u_2(t)$, we have

$$\frac{\partial \mathcal{H}}{\partial u_2} = u_2 b_4 - \Theta_1 S^* + \Theta_2 S^* = 0$$

we have that

$$u_2^*(t) = \frac{1}{b_4}(\Theta_1 - \Theta_2) S^* \tag{42}$$

Clearly, the optimality conditions obtained by taking the derivatives of the Hamiltonian with respect to the controls on hold in the interior of the control set. This end the proof. □

### 4.2. Numerical Illustration

The computational approach for determining the optimal control solution utilizes the forward-backward sweep method. The algorithm begins with an initial guess for the optimal controls and advances the state variables forward in time using the fourth-order Runge-Kutta method. After this forward simulation, the state variables and the initial control assumption are used to solve the adjoint equation eq. (35) backward in time, starting from a specified final condition. This backward integration is performed using the fourth-order Runge-Kutta method in reverse. The controls, $u_1(t)$ and $u_2(t)$, are then updated and used to resolve the state and adjoint systems once again. This iterative process continues until a satisfactory level of convergence is achieved for the state, adjoint, and control variables, as detailed in previous studies [36–38]. The parameter values utilized for the numerical illustration specifically align with those delineated in Table 2 and the initial conditions used are $S(0) = 360000$, $V(0) = 1000$, $E(0) = 600$, $I_A(0) = 70$, $I_S(0) = 30$, $T(0) = 60$, $R(0) = 0$, and $B(0) = 5000$. Furthermore, numerical simulations with several control strategies are given, such as:

1. Strategy A: control with $u_1$ only (see Figure 5).
2. Strategy B: control with $u_2$ only (see Figure 6).
3. Strategy C: Control with both $u_1(t)$ and $u_2(t)$ (see Figure 7).

**Table 2.** Parameter values for model (1).

| Parameter | Value | Source |
|---|---|---|
| $\pi$ | 0.03661 | [39] |
| $\alpha$ | $\frac{2}{7}$ | [18] |
| $\beta$ | 0.00003 | [16] |
| $\beta_d$ | 0.03 | Assumed |
| $\mu$ | 0.01243 | [40] |
| $\gamma$ | 0.2 | Assumed |
| $\omega$ | $\frac{1}{28}$ | [18] |
| $\sigma$ | 0.08 | [17] |
| $\kappa_1$ | 0.9 | [18] |
| $\kappa_2$ | 0.8 | [18] |
| $f$ | 0.52 | Assumed |
| $\delta_B$ | 0.0345 | [18] |
| $psi$ | 0.1 | [17] |
| $\theta$ | 0.34 | Assumed |
| $\eta_1$ | 0.214 | [17] |
| $\eta_2$ | 0.214 | [17] |
| $\varepsilon$ | 0.42 | Assumed |
| $\phi$ | $\frac{1}{385}$ | [18] |
| $\delta$ | 0.005 | Assumed |
| $q$ | 0.2 | [18] |
| $K$ | 10000 | Assumed |

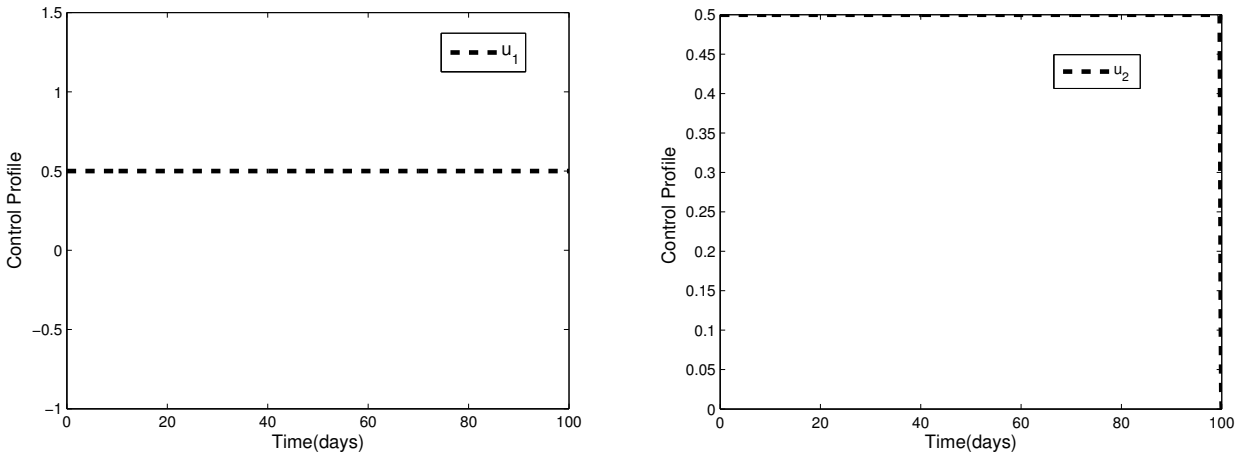


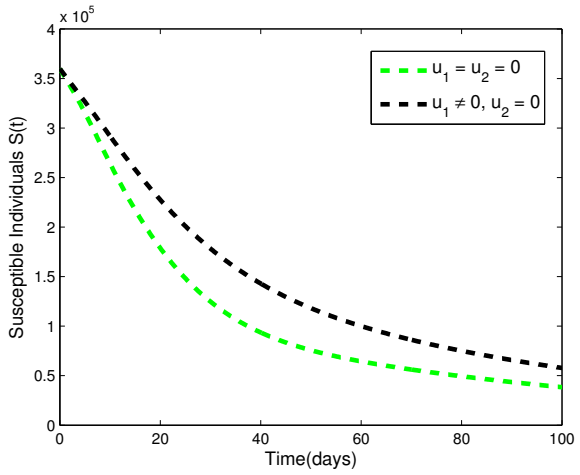

**Figure 4.** Simulation of the (a) Control profile $u_1$ (b) Control profile $u_2$

*Discussion of Results*

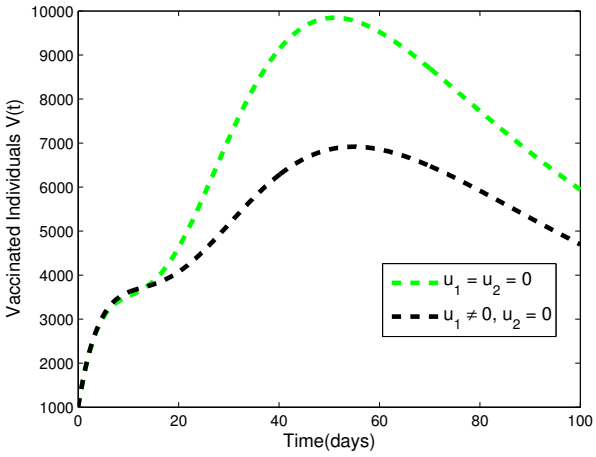
Figure 5 is the simulation of the effect of the control $u_1(t)$ on the human population and the concentration of Corynebacterium Diphtheriae in the environment. In the presence of the control measure $u_1(t)$, the number of the susceptible individuals increases up to 150000 within 40 days, the vaccinated individuals reduces to below 6500 within 60 days, and the exposed individuals reduces below 8000 in 40 days. It is also observed that in the presence of the control measure $u_1(t)$, the number of asymptomatic infected individuals and the number of symptomatic infected individuals decreases to below 4000 and 2500 within 80 days respectively. Furthermore, in the presence of the control measure $u_1(t)$, the number of treated individuals and the number of recovered individuals reduces below 40000 and 12000 within 60 days respectively. It is also observed that in the presence of the control measure $u_1(t)$, the concentration of Corynebacterium Diphtheriae in the environment decreases to below 200000 within 80 days.

Figure 6 depicts the simulation of the effect of the control $u_2(t)$ on the human population and the concentration of Corynebacterium Diphtheriae in the environment. In the presence of the control measure $u_2(t)$, the number of the susceptible individuals increases up to 125000 within 40 days, the vaccinated individuals reduces to below 8000 within 60 days, and the exposed individuals reduces below 10000 in 40 days. It is also observed that in the presence of the control measure $u_2(t)$, the number of asymptomatic infected individuals and the number of symptomatic infected individuals decreases to below 3000 and 2200 within 80 days respectively. Furthermore, in the presence of the control measure $u_2(t)$, the number of treated individuals and the number of recovered individuals reduces below 44000 and 14000 within 60 days respectively. It is also observed that in the presence of the control measure $u_2(t)$, the concentration of Corynebacterium Diphtheriae in the environment decreases to below 10000 within 80 days.

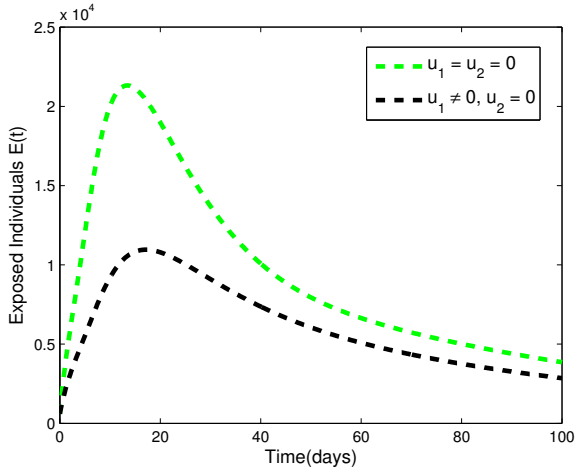
Figure 7 is the simulation of the effect of both the controls


x 10^5
Susceptible Individuals S(t)
Time(days)
u1 = u2 = 0
u1 ≠ 0, u2 = 0

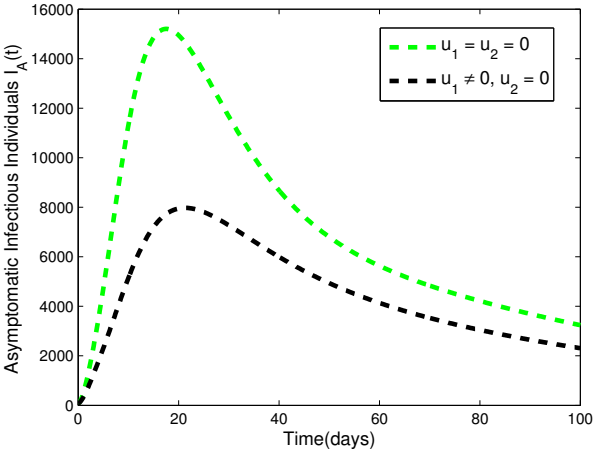
(a)


Vaccinated Individuals V(t)
Time(days)
u1 = u2 = 0
u1 ≠ 0, u2 = 0

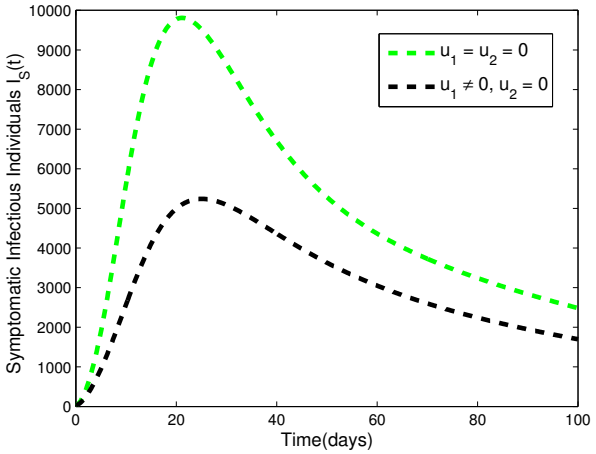
(b)


x 10^4
Exposed Individuals E(t)
Time(days)
u1 = u2 = 0
u1 ≠ 0, u2 = 0

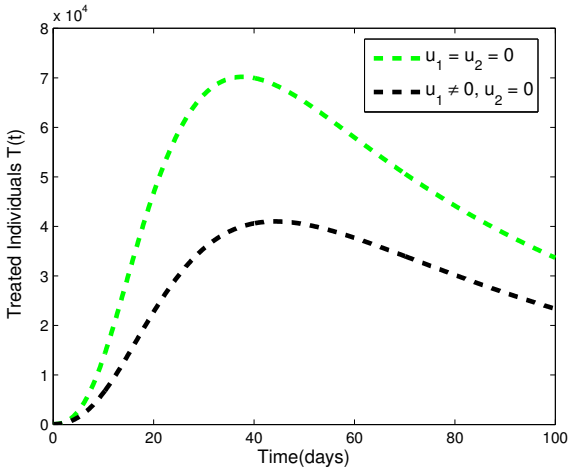
(c)


Asymptomatic Infectious Individuals IA(t)
Time(days)
u1 = u2 = 0
u1 ≠ 0, u2 = 0

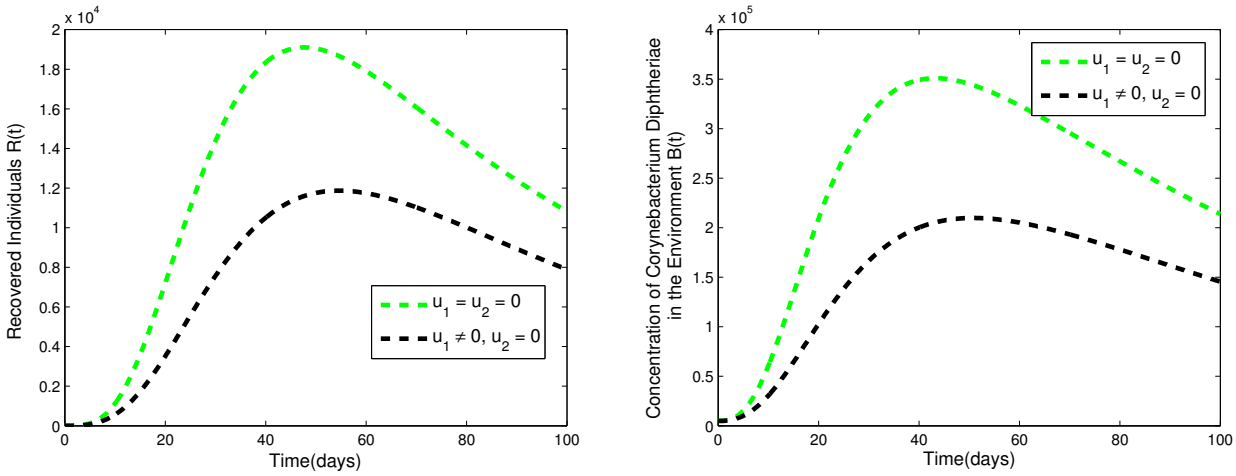
(d)


Symptomatic Infectious Individuals IS(t)
Time(days)
u1 = u2 = 0
u1 ≠ 0, u2 = 0

(e)

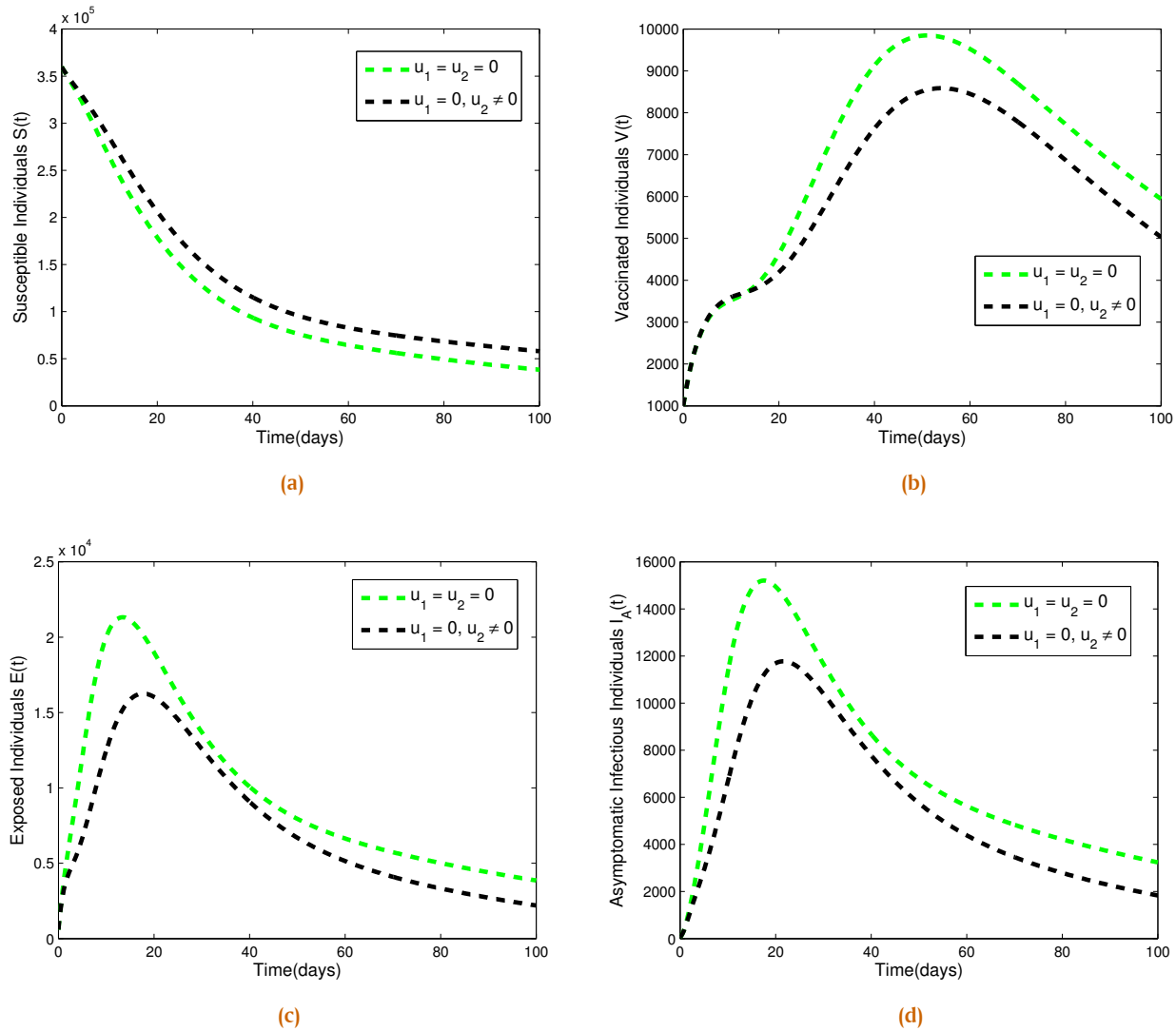

x 10^4
Treated Individuals T(t)
Time(days)
u1 = u2 = 0
u1 ≠ 0, u2 = 0

(f)




(a) (b)

**Figure 5.** Simulation of the (a) effect of $u_1(t)$ on the susceptible individuals (b) effect of $u_1(t)$ on the vaccinated individuals (c) effect of $u_1(t)$ on the exposed individuals (d) effect of $u_1(t)$ on asymptomatic infected individuals with Diphtheria (e) effect of $u_1(t)$ on symptomatic infected individuals with Diphtheria (f) effect of $u_1(t)$ on the treated individuals (g) effect of $u_1(t)$ on the recovered individuals (h) effect of $u_1(t)$ on the Concentration of *Corynebacterium Diphtheriae* in the environment.




(a) (b)

(c) (d)

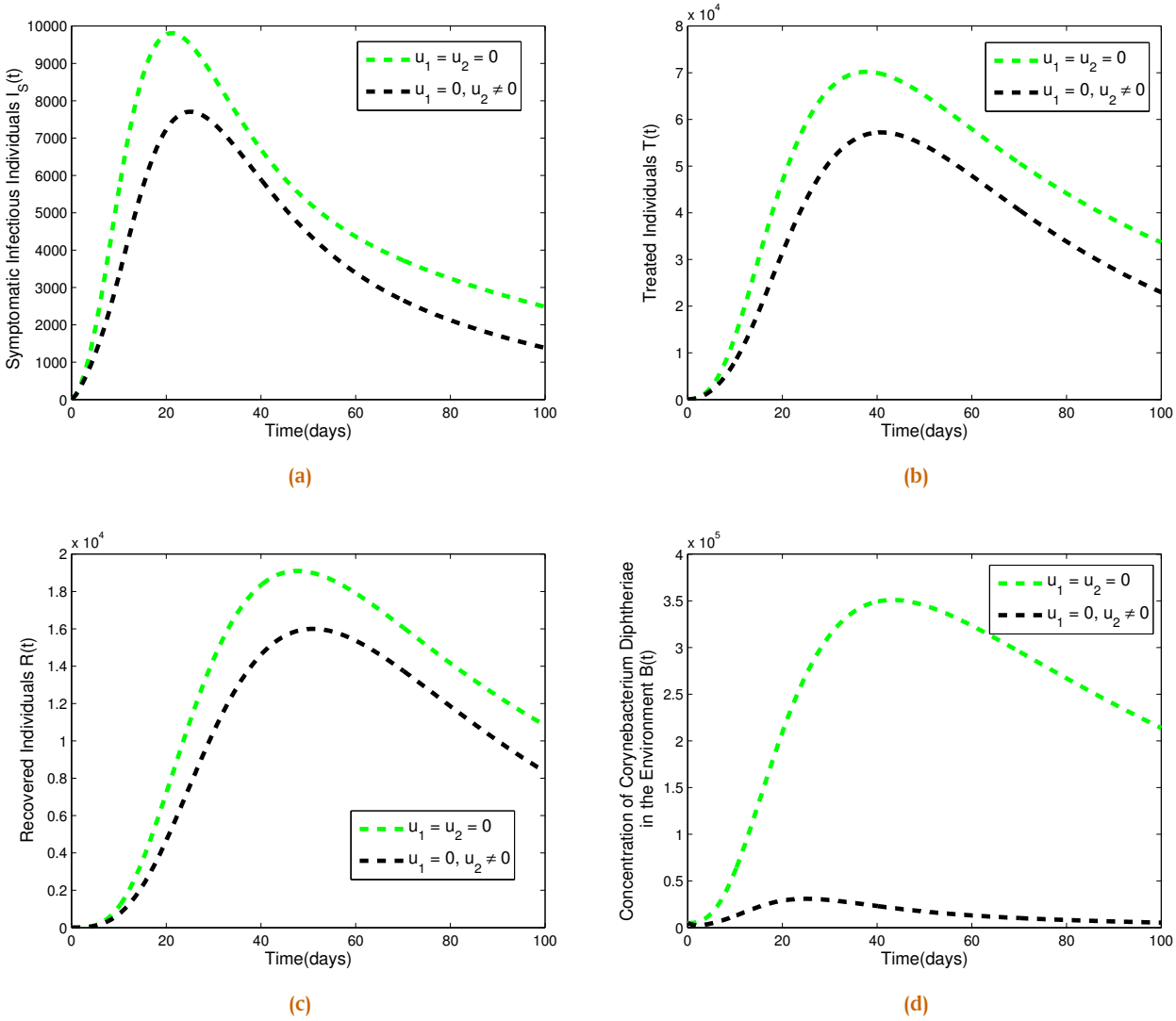
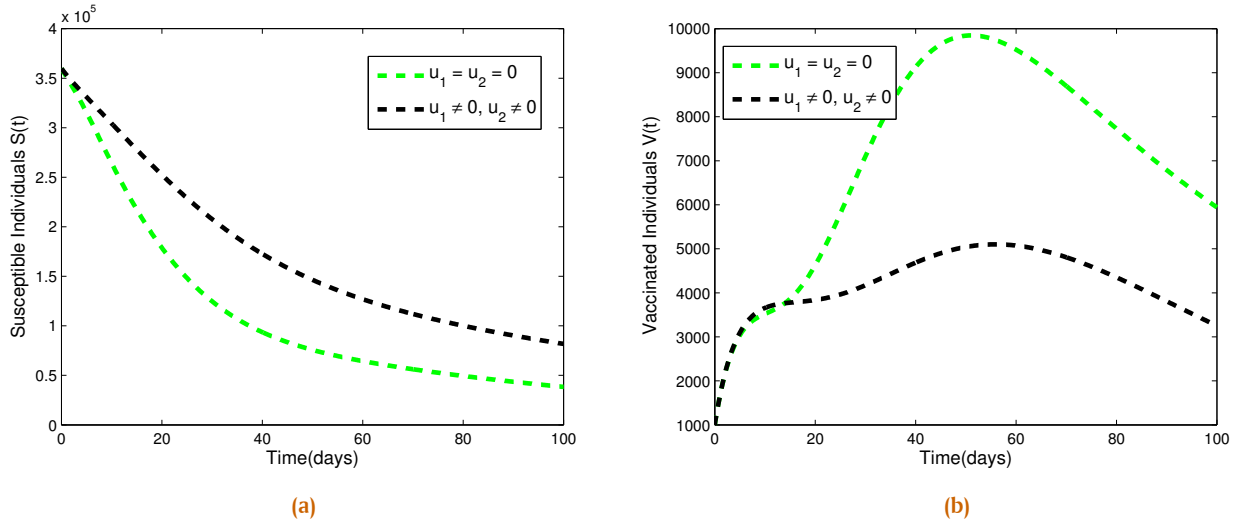



**Figure 6.** Simulation of the (a) effect of $u_2(t)$ on the susceptible individuals (b) effect of $u_2(t)$ on the vaccinated individuals (c) effect of $u_2(t)$ on the exposed individuals (d) effect of $u_2(t)$ on asymptomatic infected individuals with Diphtheria (e) effect of $u_2(t)$ on symptomatic infected individuals with Diphtheria (f) effect of $u_2(t)$ on the treated individuals (g) effect of $u_2(t)$ on the recovered individuals (h) effect of $u_2(t)$ on the Concentration of *Corynebacterium Diphtheriae* in the environment.



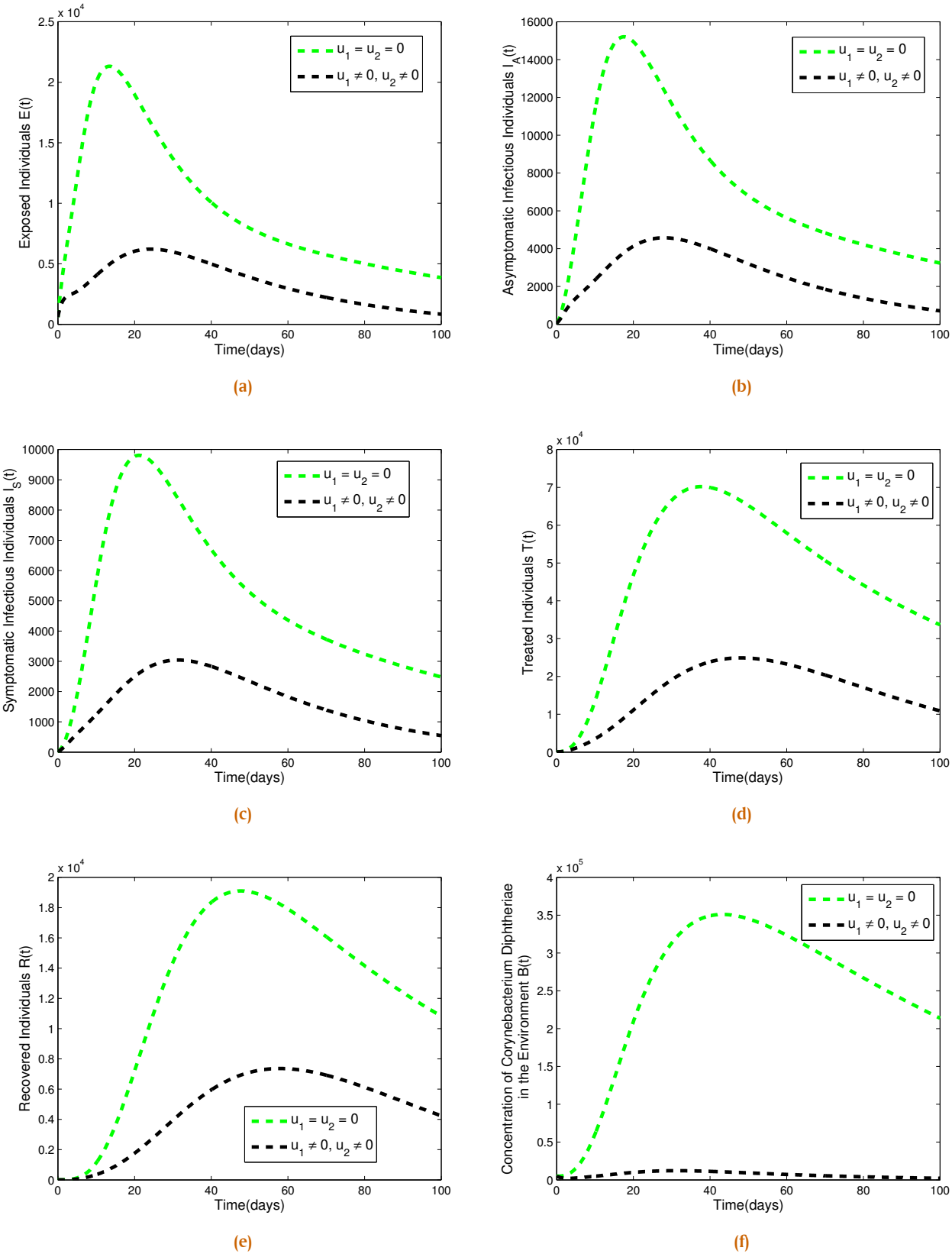



**Figure 7.** Simulation of the (a) effect of $u_1(t)$ and $u_2(t)$ on the susceptible individuals (b) effect of $u_1(t)$ and $u_2(t)$ on the vaccinated individuals (c) effect of $u_1(t)$ and $u_2(t)$ on the exposed individuals (d) effect of $u_1(t)$ and $u_2(t)$ on asymptomatic infected individuals with Diphtheria (e) effect of $u_1(t)$ and $u_2(t)$ on symptomatic infected individuals with Diphtheria (f) effect of $u_1(t)$ and $u_2(t)$ on the treated individuals (g) effect of $u_1(t)$ and $u_2(t)$ on the recovered individuals (h) effect of $u_1(t)$ and $u_2(t)$ on the Concentration of *Corynebacterium Diphtheriae* in the environment.

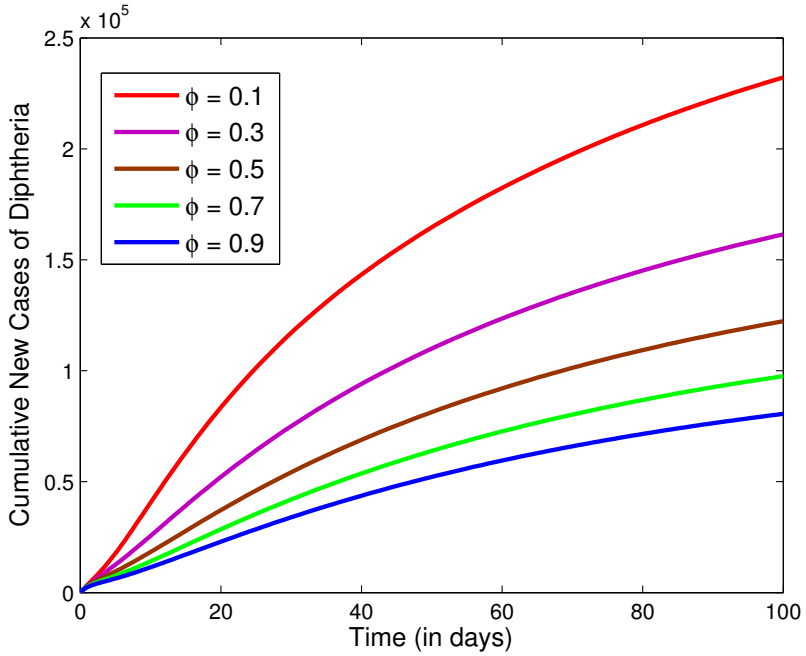



**Figure 8.** The effect of the vaccination rate ($\phi$) on the cumulative new cases of Diphtheria

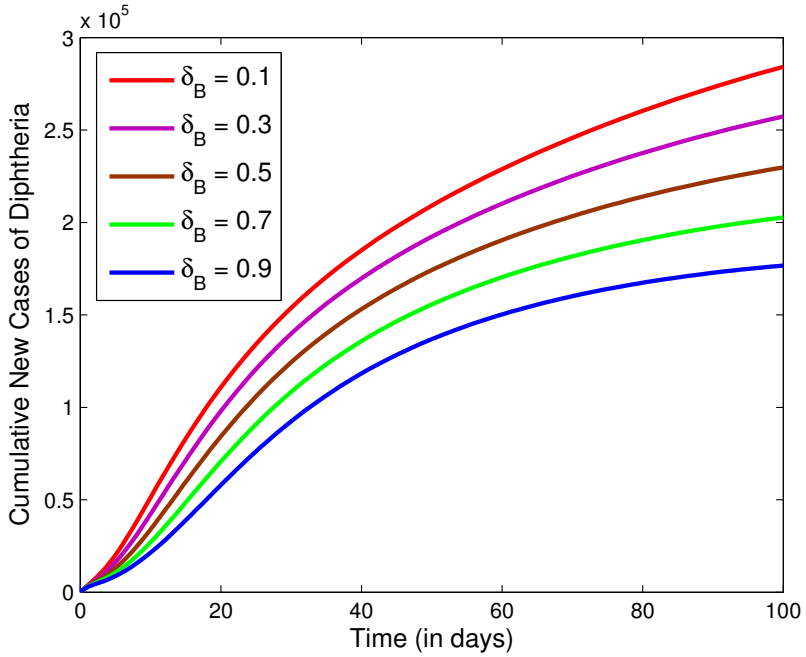



**Figure 9.** The effect of the Corynebacterium Diphtheriae dacay rate in the environment ($\delta_B$) on the cumulative new cases of Diphtheria.

$u_1(t)$ and $u_2(t)$ on the human population and the concentration of Corynebacterium Diphtheriae in the environment. In the presence of the control measures $u_1(t)$ and $u_2(t)$, the number of the susceptible individuals increases up to 170000 within 40 days, the vaccinated individuals reduces to below 4800 within 60 days, and the exposed individuals reduces below 5000 in 40 days. It is also observed that in the presence of the control measures $u_1(t)$ and $u_2(t)$, the number of asymptomatic infected individuals and the number of symptomatic infected individuals decreases to below 1800 and 1000 within 80 days respectively. Furthermore, in the presence of the control measures $u_1(t)$ and $u_2(t)$, the number of treated individuals and the number of recovered individuals reduces below 22000 and 7500 within 60 days respectively. It is also observed that in the presence of the control measures $u_1(t)$ and $u_2(t)$, the concentration of *Corynebacterium Diphtheriae* in the environment decreases to below 9000 within 80 days.

It is important to note that the number of the vaccinated individuals declined when the control measure was implemented, this is due to the fact that in the presence of the control measure the number of infected individuals decreases drastically, which means that the prevalence of Diphtheria decreases. This reduced the necessity for vaccination. Furthermore, the treated individu-

als and recovered individuals reduces also when the control measure was implemented, this is because the number of infected individuals reduced when the control measure was implemented thereby reducing the number of individuals receiving treatment as well as the number of recovered individuals.

Figure 8 and Figure 9 depicts the simulations of the effect of the vaccination rate ($\phi$) and the decay rate ($\delta_B$) of the *Corynebacterium Diphtheriae* in the environment on the cumulative new cases of Diphtheria respectively. It is observed in Figure 8 that as the vaccination rate ($\phi$) increases, the cumulative new cases of Diphtheria decreases. Furthermore, it is observed that if the vaccination rate ($\phi$) can be stepped up to 70%, the cumulative new cases of Diphtheria will be reduced to below 100000 within 80 days. Similarly, in Figure 9, it is observed that as the decay rate ($\delta_B$) increases, the cumulative new cases of Diphtheria reduces, and if the decay rate ($\delta_B$) is increased to 50%, the cumulative cases will be reduced to below 250000 within 80 days.

Conclusively, our results indicates that the best strategy to mitigate and curb the spread of diphtheria is to properly implement the combination of the two control measures as well as increase the vaccination rate and the decay rate of the *Corynebacterium Diphtheriae* in the environment.

## 5. Conclusion

In this study, we formulated and rigorously analyzed a deterministic epidemiological mathematical model to gain insight into the transmission dynamics of Diphtheria infection, incorporating the concentration of *Corynebacterium Diphtheriae* in the environment, dividing the infected compartments into asymptomatic and symptomatic, and also account for re-infection after recovery. The analysis of the model begins with the computation of the basic reproduction number and the examination of the local stability of the disease-free equilibrium using the Routh-Hurwitz criterion. It was observed that whenever the basic reproduction number is less than one ($\mathcal{R}_0 < 1$), the disease-free equilibrium point is locally asymptotically stable and unstable whenever the basic reproduction number is greater than one ($\mathcal{R}_0 < 1$). The existence and stability of the endemic equilibrium point was determined using the Centre Manifold Theorem. It was revealed that the model undergoes the phenomenon of backward bifurcation when the basic reproduction number is less than one. This characteristic makes effective control Diphtheria infection within the population difficulty. However, under the assumption of no re-infection of Diphtheria infection after recovery, the disease-free equilibrium point is globally asymptotically stable whenever the basic reproduction number is less than or equal to one ($\mathcal{R}_0 \leq 1$). Furthermore, the sensitivity analysis of the basic reproduction number was carried out in order to determine the impact of each of the model basic parameters that contribute to the transmission of the disease. We were able to identify the parameters with positive indices, which indicate that they have significant impact on increasing the spread of the disease if their values are increasing. The parameters with negative indices are responsible for mitigating the burden of the disease as their values increases while the others are left constant. We employed the optimal control theory to investigate the optimal intervention strategy for curbing the spread of the disease. We introduced two time dependent control measures to mitigate the spread of Diphtheria. These control measures represent preventive actions, such as public enlightenment campaigns to sensitize and educate the general public about the dynamics of diphtheria and the importance of proper personal hygiene, including regular handwashing to prevent susceptible individuals from acquiring diphtheria, and environmental sanitation practices such as cleaning surfaces, clothes, materials, and door handles to reduce the concentration of *Corynebacterium Diphtheriae* in the environment. The results from the numerical simulations reveal that Diphtheria infection can successfully be controlled and mitigated within the population if we can increase the vaccination rate and the decay rate of *Corynebacterium Diphtheriae* in the environment, as well as properly and effectively implementing these optimal control measures simultaneously.

**Author Contributions.** **Oguntolu, F. A.**: Conceptualization, methodology, software. **Peter, O. J.**: methodology, software, validation, formal analysis. **Omede, B. I.**: project administration, funding acquisition. **Balogun, G. B.**: writing—original draft preparation, writing—review and editing. **Ajiboye, A. O.**: writing—original draft preparation, writing—review and editing. **Panigoro, H. S.**: writing—original draft preparation, writing—review and editing.

**Acknowledgement.** No acknowledgement.

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**Conflict of interest.** There are no conflicts of interest to declare.

**Data availability.** Data used to support the findings of this study are included in the article. The authors used parameter values whose sources are from the literature as shown in Table 2.

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## Appendix

### *A.*

$$
\begin{aligned}
m_1 &= A_1 + A_2 + A_3 + A_5 + A_6 + A_7 + A_8 + \delta_B,\\
m_2 &= A_1\left(A_2 + A_3 + A_5 + A_6 + A_7 + A_8 + \delta_B\right) + A_2(A_3 + A_5 + A_6\\
&\quad + A_7 + A_8 + \delta_B) + A_3\left(A_5 + A_6 + A_7 + A_8 + \delta_B\right) + A_5(A_6\\
&\quad + A_7 + A_8 + \delta_B) + A_6\left(A_7 + A_8 + \delta_B\right) + A_7\left(A_8 + \delta_B\right) + A_8\delta_B\\
&\quad - \phi\gamma - \frac{\beta A_2(q\alpha + A_4)}{(\gamma + A_1)},\\
m_3 &= (A_1A_2 - \phi\gamma)\left(A_3 + A_5 + A_6 + A_7 + A_8 + \delta_B\right) + A_3(A_1\\
&\quad + A_2)\left(A_5 + A_6 + A_7 + A_8 + \delta_B\right) + A_5(A_1 + A_2 + A_3)(A_6\\
&\quad + A_7 + A_8 + \delta_B) + A_6(A_1 + A_2 + A_3 + A_5)\left(A_7 + A_8 + \delta_B\right)\\
&\quad + A_7\left(A_1 + A_2 + A_3 + A_5 + A_6\right)\left(A_8 + \delta_B\right) + A_8\delta_B(A_1 + A_2\\
&\quad + A_3 + A_5 + A_6 + A_7) - \frac{\beta_d\pi A_2(\kappa_1A_4 + \kappa_2q\alpha)}{K\mu(\gamma + A_1)}\\
&\quad - \frac{\beta A_2q\alpha\left(A_1 + A_2 + A_5 + A_7 + A_8 + \delta_B\right)}{(\gamma + A_1)}\\
&\quad - \frac{\beta A_2A_4\left(\sigma + A_1 + A_2 + A_6 + A_7 + A_8 + \delta_B\right)}{(\gamma + A_1)},\\
m_4 &= A_1A_2A_3(A_5 + A_6 + A_7 + A_8 + \delta_B) + A_5(A_1A_2 + A_1A_3\\
&\quad + A_2A_3)(A_6 + A_7 + A_8 + \delta_B) + A_6(A_1(A_2 + A_3 + A_5)\\
&\quad + A_2(A_3 + A_5) + A_3A_5))(A_7 + A_8 + \delta_B) + A_8\delta_B(A_5A_6\\
&\quad + A_5A_7 + A_6A_7) + A_7(A_1(A_2 + A_3 + A_5 + A_6) + A_2(A_3\\
&\quad + A_5 + A_6) + A_3(A_5 + A_6) + A_5A_6)(A_8 + \delta_B) + A_8\delta_B(A_1\\
&\quad + A_2 + A_3)(A_5 + A_6 + A_7) + A_8\delta_B(A_1A_2 + A_1A_3 + A_2A_3)\\
&\quad + \frac{\beta\phi\gamma A_2(q\alpha + A_4)}{(\gamma + A_1)} - \phi\gamma A_3(A_5 + A_6 + A_7 + A_8 + \delta_B)\\
&\quad - \phi\gamma A_5(A_6 + A_7 + A_8 + \delta_B) - \phi\gamma A_6(A_7 + A_8 + \delta_B)\\
&\quad - \phi\gamma(A_7A_8 + A_7\delta_B + A_8\delta_B) - \frac{\beta A_2A_4A_7(A_8 + \delta_B)}{(\gamma + A_1)}\\
&\quad - \frac{\beta A_2A_4A_8\delta_B}{(\gamma + A_1)} - \frac{\beta A_2A_4\sigma(A_1 + A_2 + A_7 + A_8 + \delta_B)}{(\gamma + A_1)}\\
&\quad - \frac{\beta A_2A_4(A_1 + A_2)(A_6 + A_7 + A_8 + \delta_B)}{(\gamma + A_1)}\\
&\quad - \frac{\beta_d\pi\kappa_2A_2\left(q\alpha(A_1 + A_2 + A_5 + A_7 + A_8) + \sigma A_4\right)}{K\mu(\gamma + A_1)}\\
&\quad - \frac{\beta A_2(A_7 + A_8 + \delta_B)(A_4A_6 + q\alpha A_5)}{(\gamma + A_1)} - \frac{\beta A_1A_2^2A_4}{(\gamma + A_1)}\\
&\quad - \frac{\beta q\alpha A_1A_2(A_2 + A_5 + A_7 + A_8 + \delta_B)}{(\gamma + A_1)}\\
&\quad - \frac{\beta q\alpha A_2(A_7A_8 + A_7\delta_B + A_8\delta_B)}{(\gamma + A_1)} - \frac{\beta q\alpha A_2^2(A_5 + A_7 + A_8 + \delta_B)}{(\gamma + A_1)}
\end{aligned}
$$

$$
\begin{aligned}
&- \frac{\beta_d \pi \kappa_1 A_2 A_4 (A_1 + A_2)}{K\mu(\gamma + A_1)} - \frac{\beta_d \pi \kappa_1 A_2 A_4 (A_6 + A_7 + A_8)}{K\mu(\gamma + A_1)},\\
m_5 &= A_1 A_2 A_3 A_5 (A_6 + A_7 + A_8 + \delta_B) + A_6 (A_1 A_2 (A_3 + A_5)\\
&+ A_3 A_5 (A_1 + A_2))(A_7 + A_8 + \delta_B) + A_7 (A_1 A_2 (A_3 + A_5 + A_6)\\
&+ A_1 A_3 (A_5 + A_6) + A_1 A_5 A_6 + A_2 A_3 (A_5 + A_6) + A_5 A_6 (A_2\\
&+ A_3))(A_8 + \delta_B) + A_6 A_7 A_8 \delta_B (A_3 + A_5) + A_5 A_8 \delta_B (A_2\\
&+ A_3)(A_6 + A_7) + A_8 \delta_B (A_1 A_2 + A_1 A_3 + A_2 A_3)(A_5 + A_6 + A_7)\\
&+ A_2 A_8 \delta_B (A_1 A_3 + A_6 A_7) + A_1 A_8 \delta_B (A_5 A_6 + A_5 A_7 + A_6 A_7)\\
&- \frac{\beta q \alpha A_2 A_5 (A_1 + A_2)(A_7 + A_8 + \delta_B)}{(\gamma + A_1)} - \frac{\beta q \alpha A_2 A_7 A_8 \delta_B (A_1 + A_2)}{(\gamma + A_1)}\\
&- \frac{\beta q \alpha A_2 A_7 (A_1 + A_2 + A_5)(A_8 + \delta_B)}{(\gamma + A_1)} - \frac{\beta q \alpha A_2 A_7 A_8 \delta_B (A_5 + A_7)}{(\gamma + A_1)}\\
&- \frac{\beta q \alpha A_2 (A_1 A_2 - \phi\gamma)(A_5 + A_7 + A_8 + \delta_B)}{(\gamma + A_1)} - \frac{\beta_d \pi q \alpha \kappa_2 A_2 A_7 A_8}{K\mu(\gamma + A_1)}\\
&- \frac{\beta \sigma A_1 A_2 A_4 (A_2 + A_7 + A_8 + \delta_B)}{(\gamma + A_1)} + \frac{\beta_d \pi \phi\gamma \kappa_1 A_2 A_4}{K\mu(\gamma + A_1)}\\
&- \frac{\beta A_2 A_4 A_7 (\sigma + A_1 + A_2)(A_8 + \delta_B)}{(\gamma + A_1)} - \frac{\beta_d \pi q \alpha \kappa_2 A_2 A_5 (A_7 + A_8)}{K\mu(\gamma + A_1)}\\
&- \frac{\beta A_2 A_4 (\sigma A_2 + A_1 A_2 + A_1 A_6 + A_2 A_6)(A_7 + A_8 + \delta_B)}{(\gamma + A_1)}\\
&- \frac{\beta A_2 A_4 A_8 \delta_B (\sigma + A_1 + A_2 + A_7)}{(\gamma + A_1)} - \frac{\beta_d \pi q \alpha \kappa_2 A_2^2 (A_5 + A_7 + A_8)}{K\mu(\gamma + A_1)}\\
&- \frac{\beta A_2 A_4 A_6 (A_7 A_8 + A_7 \delta_B + A_8 \delta_B)}{(\gamma + A_1)} + \frac{\beta_d \pi q \alpha \kappa_2 A_2 \phi\gamma}{K\mu(\gamma + A_1)}\\
&- \frac{\beta_d \pi q \alpha \kappa_2 A_1 A_2 (A_2 + A_5 + A_7 + A_8)}{K\mu(\gamma + A_1)} - \frac{\beta_d \pi \kappa_1 A_2 A_4 (A_1 A_2 - \phi\gamma)}{K\mu(\gamma + A_1)}\\
&- \frac{\beta_d \pi \sigma \kappa_2 A_2 A_4 (A_1 + A_2 + A_7 + A_8)}{K\mu(\gamma + A_1)} - \phi\gamma A_6 (A_3 + A_5)(A_7\\
&+ A_8 + \delta_B) - \frac{\beta_d \pi \kappa_1 A_2 A_4 (A_6 A_7 + A_6 A_8 + A_7 A_8)}{K\mu(\gamma + A_1)} - \phi\gamma A_3 A_5 (A_6\\
&+ A_7 + A_8 + \delta_B) + \frac{\beta \phi\gamma A_2 A_4 (\sigma + A_6 + A_7 + A_8 + \delta_B)}{(\gamma + A_1)}\\
&- \phi\gamma A_7 (A_3 + A_5 + A_6)(A_8 + \delta_B) - \phi\gamma A_8 \delta_B (A_3 + A_5 + A_6 + A_7),\\
m_6 &= A_1 A_2 A_3 A_5 A_6 (A_7 + A_8 + \delta_B) + A_7 (A_1 A_2 A_3 (A_5 + A_6)\\
&+ A_5 A_6 (A_1 A_2 + A_1 A_3 + A_2 A_3))(A_8 + \delta_B) + A_5 A_8 \delta_B (A_6\\
&+ A_7)(A_1 A_2 + A_1 A_3 + A_2 A_3) + A_5 A_6 A_7 A_8 \delta_B (A_2 + A_3)\\
&+ A_1 A_6 A_7 A_8 \delta_B (A_2 + A_3 + A_5) + A_1 A_2 A_3 A_8 \delta_B (A_5 + A_6 + A_7)\\
&+ A_2 A_3 A_6 A_7 A_8 \delta_B - \frac{\beta A_1 A_2^2 (q\alpha A_5 + \sigma A_4)(A_7 + A_8 + \delta_B)}{(\gamma + A_1)}\\
&- \frac{\beta q \alpha A_2 A_7 (A_1 (A_2 + A_5) + A_2 A_5)(A_8 + \delta_B)}{(\gamma + A_1)}\\
&+ \frac{\beta q \alpha \phi\gamma A_2 A_5 (A_7 + A_8 + \delta_B)}{(\gamma + A_1)} - \frac{\beta \sigma A_2 A_8 \delta_B (A_2 + A_7)}{(\gamma + A_1)}\\
&- \frac{\beta q \alpha A_2 A_8 \delta_B (A_1 (A_2 + A_5 + A_7) + A_2 (A_5 + A_7) + A_5 A_7)}{(\gamma + A_1)}\\
&- \frac{\beta q \alpha A_2 A_4 A_7 (2\sigma A_4 + A_1 A_2 + 2\sigma A_2)(A_8 + \delta_B)}{(\gamma + A_1)}\\
&+ \frac{\beta q \alpha \phi\gamma A_2 (A_7 A_8 + A_7 \delta_B + A_8 \delta_B)}{(\gamma + A_1)} - \frac{\beta \sigma A_1 A_2 A_4 A_8 \delta_B}{(\gamma + A_1)}\\
&- \frac{\beta \sigma A_1 A_2^2 A_4 (\sigma + A_6)(A_7 + A_8 + \delta_B)}{(\gamma + A_1)} - \frac{\beta_d \pi q \alpha \kappa_2 A_1 A_2 A_7 A_8}{K\mu(\gamma + A_1)}\\
&- \frac{\beta q \alpha A_2 A_4 A_8 \delta_B (\sigma (A_1 + A_2 + A_7) + A_1 A_2)}{(\gamma + A_1)}\\
&- \frac{\beta_d \pi q \alpha \kappa_2 A_2 (A_1 A_2 - \phi\gamma)(A_5 + A_7 + A_8)}{K\mu(\gamma + A_1)}\\
&- \frac{\beta_d \pi \kappa_2 A_2 (\sigma A_2 A_4 + q\alpha A_5 (A_1 + A_2))(A_7 + A_8)}{K\mu(\gamma + A_1)}\\
&- \frac{\beta_d \pi q \alpha \kappa_2 A_2 A_7 A_8 (A_2 + A_5)}{K\mu(\gamma + A_1)} - \frac{\beta_d \pi A_2 A_4 (\kappa_1 A_6 A_7 A_8 - \kappa_2 \phi\gamma\sigma)}{K\mu(\gamma + A_1)}\\
&- \frac{\beta_d \pi \kappa_2 A_2 A_4 (A_7 A_8 + A_1 (A_2 + A_7 + A_8))}{K\mu(\gamma + A_1)}\\
&- \frac{\beta_d \pi \kappa_1 A_2 A_4 (A_1 A_2 - \phi\gamma)(A_6 + A_7 + A_8)}{K\mu(\gamma + A_1)} - \phi\gamma A_3 A_8 \delta_B (A_5 + A_6\\
&+ A_7) - \phi\gamma A_6 A_7 A_8 \delta_B + \frac{\beta \phi\gamma A_2^2 A_4 (\sigma + A_6)(A_7 + A_8 + \delta_B)}{(\gamma + A_1)}\\
&- \frac{\beta_d \pi \kappa_1 A_2 A_4 (A_1 + A_2)(A_6 A_7 + A_6 A_8 + A_7 A_8)}{K\mu(\gamma + A_1)}\\
&- \frac{\beta A_2 A_4 A_6 A_7 (A_1 + A_2)(A_8 + \delta_B)}{(\gamma + A_1)} - \frac{\beta A_1 A_2 A_4 A_8 \delta_B (A_6 + A_7)}{(\gamma + A_1)}\\
&- \frac{\beta A_2 A_4 A_8 \delta_B (A_2 A_6 + A_2 A_7 + A_6 A_7)}{(\gamma + A_1)} - \phi\gamma A_7 (A_3 A_5 + A_3 A_6\\
&+ A_5 A_6)(A_8 + \delta_B) + \frac{\beta \phi\gamma A_2 A_4 (A_7 A_8 + A_7 \delta_B + A_8 \delta_B)}{(\gamma + A_1)}\\
&- \phi\gamma A_5 A_8 \delta_B (A_6 + A_7) - \phi\gamma A_3 A_5 A_6 (A_7 + A_8 + \delta_B),\\
m_7 &= A_1 A_2 A_3 A_5 A_6 A_7 (A_8 + \delta_B) + A_1 A_2 A_3 A_5 A_8 \delta_B (A_6 + A_7)\\
&+ A_1 A_5 A_6 A_7 A_8 \delta_B (A_2 + A_3) + A_2 A_3 A_6 A_7 A_8 \delta_B (A_1 + A_5)\\
&- \frac{\beta A_1 A_2^2 (A_7 A_8 + A_7 \delta_B + A_8 \delta_B)(A_4 A_6 + q\alpha A_5 + \sigma A_4)}{(\gamma + A_1)}\\
&- \frac{\beta_d \pi A_1 A_2^2 A_4 (A_7 + A_8)(\kappa_1 A_6 + \kappa_2 \sigma)}{K\mu(\gamma + A_1)} - \frac{\beta A_1 A_2^2 A_4 A_7 A_8 \delta_B}{(\gamma + A_1)}\\
&- \frac{\beta A_2 A_4 A_7 A_8 \delta_B (A_1 + A_2(\sigma + A_6)}{(\gamma + A_1)} - \frac{\beta_d \pi \kappa_1 A_1 A_2^2 A_4 A_7 A_8}{K\mu(\gamma + A_1)}\\
&- \frac{\beta_d \pi A_2 A_7 A_8 (A_1 + A_2)(\kappa_1 A_4 A_6 + \kappa_2 (q\alpha A_5 + \sigma A_4))}{K\mu(\gamma + A_1)}\\
&- \frac{\beta q \alpha A_2 A_7 A_8 \delta_B (A_1 A_2 + A_1 A_5 + A_2 A_5)}{(\gamma + A_1)}\\
&- \frac{\beta_d \pi q \alpha \kappa_2 A_1 A_2^2 (A_5 A_7 + A_5 A_8 + A_7 A_8)}{K\mu(\gamma + A_1)}\\
&+ \frac{\beta \phi\gamma A_2 (A_7 A_8 + A_7 \delta_B + A_8 \delta_B)(A_4 A_6 + q\alpha A_5 + \sigma A_4)}{(\gamma + A_1)}\\
&+ \frac{\beta \phi\gamma A_2 A_7 A_8 \delta_B (A_4 + q\alpha)}{(\gamma + A_1)} - \phi\gamma A_3 A_5 A_6 (A_7 A_8 + A_7 \delta_B\\
&+ A_8 \delta_B) - \phi\gamma A_7 A_8 \delta_B (A_3 (A_5 + A_6) + A_5 A_6),\\
m_8 &= A_3 A_5 A_6 A_7 A_8 \delta_B (A_1 A_2 - \phi\gamma)(1 - \mathcal{R}_0).
\end{aligned}
$$

## B.

$$
\begin{aligned}
&\frac{\partial^2 f_1}{\partial x_1 \partial x_4} = \frac{\partial^2 f_1}{\partial x_4 \partial x_1} = \frac{\partial^2 f_1}{\partial x_1 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_1} = \frac{\beta^* \mu(\gamma + \mu)}{\pi(\gamma + \phi + \mu)} - \frac{\beta^* \mu}{\pi},\\
&\frac{\partial^2 f_1}{\partial x_2 \partial x_4} = \frac{\partial^2 f_1}{\partial x_4 \partial x_2} = \frac{\partial^2 f_1}{\partial x_3 \partial x_4} = \frac{\partial^2 f_1}{\partial x_4 \partial x_3} = \frac{\partial^2 f_1}{\partial x_4 \partial x_6} = \frac{\partial^2 f_1}{\partial x_6 \partial x_4}\\
&\quad = \frac{\partial^2 f_1}{\partial x_4 \partial x_7} = \frac{\partial^2 f_1}{\partial x_7 \partial x_4} = \frac{\beta^* \mu(\gamma + \mu)}{\pi(\gamma + \phi + \mu)},\\
&\frac{\partial^2 f_1}{\partial x_1 \partial x_8} = \frac{\partial^2 f_1}{\partial x_8 \partial x_1} = -\frac{\beta_d}{K}, \frac{\partial^2 f_1}{\partial x_8^2} = \frac{2\beta_d \pi(\gamma + \mu)}{K^2 \mu(\gamma + \phi + \mu)},\\
&\frac{\partial^2 f_1}{\partial x_2 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_2} = \frac{\partial^2 f_1}{\partial x_3 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_3} = \frac{\partial^2 f_1}{\partial x_5 \partial x_6} = \frac{\partial^2 f_1}{\partial x_6 \partial x_5}\\
&\quad = \frac{\partial^2 f_1}{\partial x_5 \partial x_7} = \frac{\partial^2 f_1}{\partial x_7 \partial x_5} = \frac{\beta^* \mu(\gamma + \mu)}{\pi(\gamma + \phi + \mu)},\\
&\frac{\partial^2 f_1}{\partial x_4 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_4} = \frac{\partial^2 f_1}{\partial x_4^2} = \frac{\partial^2 f_1}{\partial x_5^2} = \frac{2\beta^* \mu(\gamma + \mu)}{\pi(\gamma + \phi + \mu)},\\
&\frac{\partial^2 f_3}{\partial x_1 \partial x_4} = \frac{\partial^2 f_3}{\partial x_4 \partial x_1} = \frac{\partial^2 f_3}{\partial x_1 \partial x_5} = \frac{\partial^2 f_3}{\partial x_5 \partial x_1} = \frac{\beta^* \mu}{\pi} - \frac{\beta^* \mu(\gamma + \mu)}{\pi(\gamma + \phi + \mu)},\\
&\frac{\partial^2 f_3}{\partial x_1 \partial x_8} = \frac{\partial^2 f_3}{\partial x_8 \partial x_1} = \frac{\beta_d}{K}, \frac{\partial^2 f_3}{\partial x_8^2} = -\frac{2\beta_d \pi(\gamma + \mu)}{K^2 \mu(\gamma + \phi + \mu)},\\
&\frac{\partial^2 f_3}{\partial x_2 \partial x_4} = \frac{\partial^2 f_3}{\partial x_4 \partial x_2} = \frac{\partial^2 f_3}{\partial x_3 \partial x_4} = \frac{\partial^2 f_3}{\partial x_4 \partial x_3} = \frac{\partial^2 f_3}{\partial x_4 \partial x_6} = \frac{\partial^2 f_3}{\partial x_6 \partial x_4}\\
&\quad = \frac{\partial^2 f_3}{\partial x_4 \partial x_7} = \frac{\partial^2 f_3}{\partial x_7 \partial x_4} = -\frac{\beta^* \mu(\gamma + \mu)}{\pi(\gamma + \phi + \mu)},\\
&\frac{\partial^2 f_3}{\partial x_2 \partial x_5} = \frac{\partial^2 f_3}{\partial x_5 \partial x_2} = \frac{\partial^2 f_3}{\partial x_3 \partial x_5} = \frac{\partial^2 f_3}{\partial x_5 \partial x_3} = \frac{\partial^2 f_3}{\partial x_5 \partial x_6} = \frac{\partial^2 f_3}{\partial x_6 \partial x_5}\\
&\quad = \frac{\partial^2 f_3}{\partial x_5 \partial x_7} = \frac{\partial^2 f_3}{\partial x_7 \partial x_5} = -\frac{\beta^* \mu(\gamma + \mu)}{\pi(\gamma + \phi + \mu)},
\end{aligned}
$$

$$\frac{\partial^2 f_3}{\partial x_4 \partial x_5} = \frac{\partial^2 f_3}{\partial x_5 \partial x_4} = \frac{\partial^2 f_3}{\partial x_4^2} = \frac{\partial^2 f_3}{\partial x_5^2} = -\frac{2\beta^* \mu(\gamma+\mu)}{\pi(\gamma+\phi+\mu)},$$
$$\frac{\partial^2 f_4}{\partial x_4 \partial x_7} = \frac{\partial^2 f_4}{\partial x_7 \partial x_4} = \frac{\partial^2 f_4}{\partial x_5 \partial x_7} = \frac{\partial^2 f_4}{\partial x_7 \partial x_5} = \frac{\beta^* \mu f \varepsilon}{\pi},$$
$$\frac{\partial^2 f_4}{\partial x_7 \partial x_8} = \frac{\partial^2 f_4}{\partial x_8 \partial x_7} = \frac{\beta_d f \varepsilon}{K}, \frac{\partial^2 f_5}{\partial x_7 \partial x_8} = \frac{\partial^2 f_5}{\partial x_8 \partial x_7} = \frac{\beta_d (1-f)\varepsilon}{K},$$
$$\frac{\partial^2 f_5}{\partial x_4 \partial x_7} = \frac{\partial^2 f_5}{\partial x_7 \partial x_4} = \frac{\partial^2 f_5}{\partial x_5 \partial x_7} = \frac{\partial^2 f_5}{\partial x_7 \partial x_5} = \frac{\beta^* \mu (1-f)\varepsilon}{\pi},$$
$$\frac{\partial^2 f_7}{\partial x_4 \partial x_7} = \frac{\partial^2 f_7}{\partial x_7 \partial x_4} = \frac{\partial^2 f_7}{\partial x_5 \partial x_7} = \frac{\partial^2 f_7}{\partial x_7 \partial x_5} = -\frac{\beta^* \mu \varepsilon}{\pi},$$
$$\frac{\partial^2 f_7}{\partial x_7 \partial x_8} = \frac{\partial^2 f_7}{\partial x_8 \partial x_7} = -\frac{\beta_d \varepsilon}{K}, \frac{\partial^2 f_1}{\partial x_4 \partial \beta^*} = \frac{\partial^2 f_1}{\partial x_5 \partial \beta^*} = -\frac{(\gamma+\mu)}{(\gamma+\omega+\mu)},$$
$$\frac{\partial^2 f_3}{\partial x_4 \partial \beta^*} = \frac{\partial^2 f_3}{\partial x_5 \partial \beta^*} = \frac{(\gamma+\mu)}{(\gamma+\omega+\mu)}.$$

## C.

$$\begin{aligned}
\mathcal{B}_1 = & -\Theta_1\Bigg(\frac{(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} - (1-u_1(t))\Bigg(\frac{\beta(I_A^*+I_S^*)}{N^*} \\
& + \frac{\beta_d B^*}{K+B^*}\Bigg) - \phi - \mu\Bigg) - \Theta_2\phi + \Theta_3\Bigg(\frac{(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} \\
& - (1-u_1(t))\left(\frac{\beta(I_A^*+I_S^*)}{N^*} + \frac{\beta_d B^*}{K+B^*}\right)\Bigg) \\
& + \frac{\Theta_4(1-u_1(t))f\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}} - \frac{\Theta_7(1-u_1(t))\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}} \\
& + \frac{\Theta_5(1-u_1(t))(1-f)\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}, \\
\mathcal{B}_2 = & -\Theta_1\left(\frac{(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} + \gamma\right) + \Theta_2(\gamma+\mu) \\
& + \frac{\Theta_3(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} + \frac{\Theta_4(1-u_1(t))f\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}} \\
& + \frac{\Theta_5(1-u_1(t))(1-f)\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}} \\
& - \frac{\Theta_7(1-u_1(t))\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}, \\
\mathcal{B}_3 = & -\frac{\Theta_1(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} + \Theta_3\Bigg(\frac{(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} \\
& + \alpha + \mu\Bigg) - \Theta_4\left((1-q)\alpha - \frac{(1-u_1(t))f\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}\right) \\
& - \Theta_5\left(q\alpha - \frac{(1-u_1(t))(1-f)\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}\right) \\
& - \frac{\Theta_7(1-u_1(t))\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}, \\
\mathcal{B}_4 = & -b_1 + \Theta_1(1-u_1(t))\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)S^* - \Theta_6\eta_1 - \Theta_8\kappa_1 \\
& - \Theta_3(1-u_1(t))\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)S^* + \Theta_4\Big(\sigma+\eta_1+\mu \\
& - (1-u_1(t))f\varepsilon\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)R^*\Big) - \Theta_5\Big(\sigma + (1 \\
& - u_1(t))(1-f)\varepsilon\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)R^*\Big) + \Theta_7(1 \\
& - u_1(t))\varepsilon\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)R^*, \\
\mathcal{B}_5 = & -b_2 + \Theta_1(1-u_1(t))\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)S^* - \Theta_3(1 \\
& - u_1(t))\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)S^* - \Theta_4(1-u_1(t))f\varepsilon\Big(\frac{\beta}{N^*} \\
& - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\Big)R^* + \Theta_7(1-u_1(t))\varepsilon\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)R^* \\
& + \Theta_5\left(\eta_2 + \delta + \mu - (1-u_1(t))(1-f)\varepsilon\left(\frac{\beta}{N^*} - \frac{\beta(I_A^*+I_S^*)}{N^{*2}}\right)R^*\right) \\
& - \Theta_6\eta_2 - \Theta_8\kappa_2, \\
\mathcal{B}_6 = & -\frac{\Theta_1(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} + \frac{\Theta_3(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} \\
& + \frac{\Theta_4(1-u_1(t))f\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}} + \Theta_6(\omega+\theta\delta+\mu) \\
& + \frac{\Theta_5(1-u_1(t))(1-f)\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}} \\
& - \Theta_7\left(\omega + \frac{(1-u_1(t))\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}\right), \\
\mathcal{B}_7 = & -\frac{\Theta_1(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} - \Theta_2\psi + \frac{\Theta_3(1-u_1(t))\beta(I_A^*+I_S^*)S^*}{N^{*2}} \\
& - \Theta_4\Bigg((1-u_1(t))f\varepsilon\left(\frac{\beta(I_A^*+I_S^*)}{N^*} + \frac{\beta_d B^*}{K+B^*}\right) \\
& \frac{(1-u_1(t))f\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}\Bigg) - \Theta_5\Bigg((1-u_1(t))(1-f)\varepsilon\Big(\frac{\beta(I_A^*+I_S^*)}{N^*} \\
& + \frac{\beta_d B^*}{K+B^*}\Big) - \frac{(1-u_1(t))(1-f)\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}\Bigg) \\
& + \Theta_7\Bigg(\psi + \mu + (1-u_1(t))\varepsilon\left(\frac{\beta(I_A^*+I_S^*)}{N^*} + \frac{\beta_d B^*}{K+B^*}\right) \\
& - \frac{(1-u_1(t))\varepsilon\beta(I_A^*+I_S^*)R^*}{N^{*2}}\Bigg), \\
\mathcal{B}_8 = & \Theta_1(1-u_1(t))\left(\frac{\beta_d}{K+B^*} - \frac{\beta_d B^*}{(K+B^*)^2}\right)S^* - \Theta_3(1-u_1(t))\Big(\frac{\beta_d}{K+B^*} \\
& - \frac{\beta_d B^*}{(K+B^*)^2}\Big)S^* - \Theta_4(1-u_1(t))f\varepsilon\left(\frac{\beta_d}{K+B^*} - \frac{\beta_d B^*}{(K+B^*)^2}\right)R^* \\
& - \Theta_5(1-u_1(t))(1-f)\varepsilon\left(\frac{\beta_d}{K+B^*} - \frac{\beta_d B^*}{(K+B^*)^2}\right)R^* \\
& + \Theta_7(1-u_1(t))\varepsilon\left(\frac{\beta_d}{K+B^*} - \frac{\beta_d B^*}{(K+B^*)^2}\right)R^* + \Theta_8(\delta_B + u_2(t)).
\end{aligned}$$