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Mathematical Modelling of Diphtheria Transmission Dynamics for Effective Strategies of Prevention and Control with Emphasis on Vaccination and Vaccine-Induced Immunity

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Abstract— Diphtheria is a bacterial infection that can cause severe respiratory illnesses leading to death if left untreated. Despite the availability of effective vaccines, diphtheria still poses a significant public health challenge in many parts of the world. Mathematical modelling is a powerful tool that enables researchers to understand the dynamics of diphtheria transmission and evaluate the effectiveness of different control measures. In this study, investigation into transmission dynamics to inform effective strategies for controlling and preventing outbreaks of diphtheria is considered. By developing a mathematical model that accurately represents the dynamics of diphtheria transmission in a population, we can predict how diphtheria will spread under different scenarios and evaluate the effectiveness of different control measures. Effective strategies of controlling and prevention was modelled resulting into blocks of dynamics compartments. Basic properties of the model were also investigated, analyzed and reported. The numerical simulation was carried out to study the effect of the factors responsible for causes, spread as well as control and prevention of the disease. The analysis highlights the importance of vaccination coverage, waning immunity, and susceptibility to the disease in diphtheria transmission. The models also suggest that a combination of vaccination, treatment, and contact tracing can be effective in controlling diphtheria outbreaks. This information can then be used to inform public health policies and strategies for preventing outbreaks and reducing the burden of diphtheria on public health. This research also identifies some gaps in our understanding regarding the role of asymptomatic carriers in diphtheria transmission dynamics. Further research is needed to address these gaps using mathematical modelling approaches.

***Index Terms*— Diphtheria, Mathematical modelling, Strategies, Vaccination, Vaccine-induced immunity.**

1. Introduction

Diphtheria is a highly contagious vaccine-preventable bacterial infection caused by Corynebacterium diphtheriae that primarily infects the throat (pharynx and tonsils) and nose [1]. The bacterium has an estimated basic reproduction number of 1.7–4.3 (median, 2.6). Although diphtheria is treatable if detected early, it can lead to severe complications such as respiratory failure, heart problems and even deaths (case-fatality ratio among untreated, never vaccinated cases 28.8–29.2%) [2]. It remains a health problem in low-resource countries, particularly where vaccination uptake and coverage are low and where sanitation conditions remain poor [3]. On December 1, 2022, the Nigeria Centre for Disease Control (NCDC) was notified of suspected diphtheria outbreaks in two of the largest states in Nigeria, Lagos, and Kano, with a combined population of over 30 million. As of February 3, 2023, 216 confirmed cases and 40 persons have died (case fatality rate of 18.5%) from the infection in the current outbreak in Nigeria [4]. This ongoing outbreak mainly occurred in children aged 2 to 14 (85.2%) and in Kano state (97.7%). It is worth mentioning that only a fraction, 27 (12.5%) of the confirmed cases, were fully vaccinated with diphtheria-tetanus-pertussis (DTP3)—a three-dose vaccine [4]. The Nigerian outbreak has underscored the importance of vaccination and herd immunity and has rekindled the discussion around low vaccination uptake due to COVID-19 in many low-resource countries and consequent opportunistic outbreaks.

Diphtheria vaccination is one of the pentavalent vaccines on the Nigerian childhood immunization schedule. However, vaccination coverage estimates have been on the decline globally [5]. DTP3 vaccination rate dropped from 86% in 2019 to 81% in 2021 [6]. Despite the efforts to reach the diphtheria herd immunity threshold (75–80%) [7], the overall vaccination coverage of 56% in Nigeria remains suboptimal, with significant variations in DPT3 immunization coverage across Nigerian states (<20% to 80%) [6]. Essential vaccination coverage and uptake among Nigeria under-fives are very low [8]. Evidence suggests that maternal education, common misconceptions or beliefs, household decision-making dynamics (influence of male partner and family), misinformation and mistrust in vaccines, adverse events following immunization, unavailability of vaccines, proximity to health facilities and shortage of healthcare workers are associated with low vaccine uptake and differences across states [8], [9]. Furthermore, COVID-19 pandemic impacted

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vaccine uptake by creating barriers to accessing vaccination services and decreasing immunization demand and uptake among caregivers. Movement restrictions and lockdowns also resulted in decreased general healthcare service delivery, increased transportation costs, fewer engagements to promote vaccine uptake, and the discontinuation of mobile vaccination campaigns that targeted hard-to-reach communities [6]. Thus, the decline in the vaccination rate has put vulnerable people, such as children and unvaccinated individuals living in poor sanitary conditions at a greater risk. The World Health Organization (WHO) also noted the components in the recent technical report with proposals to strengthen global emergency preparedness, response, and resilience [10].

A model assessing the impact of booster doses in contaminated environments is developed and reported by [11]. Through numerical simulations and sensitivity analyses, parameters affecting disease dynamics are identified. Results indicate significant reduction in diphtheria with booster doses. In resource-limited settings, prioritizing disinfection, screening/treatment, and booster vaccination is recommended. Overall, the study underscores the importance of booster vaccination in mitigating diphtheria transmission, particularly in contaminated environments. The [12] examined the global stability of two Chikungunya virus (CHIKV) dynamics models incorporating adaptive immune response. The models, one five-dimensional and the other six-dimensional with latency, consider different types of infected cells. A threshold, $\theta 0$, determines CHIKV clearance or persistence. Both models establish CHIKV-free and CHIKV-present steady states. Using Lyapunov function, it's proven that when $\theta 0 \leq 1$, the CHIKV-free state is globally stable, and when $\theta 0 > 1$, the endemic state is stable. Numerical simulations validate these results, contributing to the understanding of CHIKV dynamics and potential control strategies. The diphtheria outbreak serves as a reminder of the ongoing threat of infectious diseases and the importance of vaccination and herd immunity in preventing their spread [13]. Nigeria has recorded diphtheria outbreaks in the past, notably in 2011 and 2022. In 2023, a previous outbreak of diphtheria was recorded between January and April 2023 affecting 21 of the 36 states and the FCT. Details of the outbreak have been published on Disease Outbreak News [14].

UNICEF Nigeria intensified efforts in August 2023 to combat a spreading diphtheria outbreak across 27 states. By July 2023, 3,850 suspected cases were reported, with 1,387 confirmed, resulting in 122 deaths (8.7% fatality rate). The outbreak mainly affected children aged 2 to 14, with Kano, Yobe, Katsina, Lagos, FCT, Sokoto, and Zamfara bearing 98.0% of cases. Only 22% of confirmed cases received routine childhood vaccinations, [15]. UNICEF collaborates closely with Nigeria's Disease Control Center and health agencies, focusing on risk communication, vaccine transportation, health worker training, and urging parents for routine immunizations. Despite challenges, UNICEF remains committed to tackling the outbreak and ensuring a healthier future for Nigerian children. In Indonesia, the 2017 diphtheria outbreak in Jakarta prompted a study to understand transmission dynamics and control strategies [16]. Researchers analyzed surveillance data and used mathematical modeling to estimate susceptibility and transmission parameters [17]. They found that children aged 0 to 4 had the highest susceptibility, with asymptomatic carriers contributing significantly to transmission. Prompt tracing and treatment of cases and contacts were vital for controlling the outbreak, emphasizing the importance of maintaining high vaccination coverage and administering booster doses to prevent future outbreaks. In Kano, Nigeria, a surge in diphtheria cases has overwhelmed Médecins Sans Frontières (MSF) hospitals, with Dr. Hashim Juma Omar treating six afflicted children daily. The outbreak, escalating since May 2022, has caused over 600 deaths, primarily in children, and affected 116 Local Government Areas (LGAs) across 19 states. Contributing factors include population growth, climate-related hygiene declines, and inadequate vaccination coverage [18]. A mathematical model of the disease is proposed, categorizing individuals based on susceptibility, vaccination status, infection, and recovery. Key factors for effective control include monitoring transmission rate, birth rate, and immunity waning rate in imperfectly vaccinated individuals [19]. Their results suggest that periodic booster administration lowers disease proliferation, but treatment of infected individuals and screening of asymptomatic carriers yields maximal disease control.

Despite the effort of previous authors, there is still the need to study diphtheria transmission dynamics for effective prevention and control strategies, with a focus on vaccination and vaccine-induced immunity, so as to develop a comprehensive understanding of how diphtheria spreads within populations and to identify optimal strategies for intervention. Therefore, this study aims to assess the impact of vaccination coverage, vaccine efficacy, and immunity duration on diphtheria transmission dynamics. By simulating various scenarios and interventions, the study seeks to inform public health efforts aimed at reducing diphtheria incidence and mortality through targeted vaccination campaigns and other control measures.

2. Modelling of the Problem

The early model is modified to include Vaccination and Vaccine-induced immunity. The following assumptions were made: Susceptible individuals (S) can become infected (I) at a rate proportional to the transmission rate (β) and the number of susceptible and infected individuals (SI/N). Infected individuals (I) recover (R) at a rate ($\boldsymbol{\gamma}$). Susceptible individuals (S) can become vaccinated (V) at a rate proportional to the vaccine coverage rate ($\boldsymbol{\nu}$) and the reduction in susceptibility due to vaccination (q), and the number of susceptible and vaccinated individuals (SV/N). Vaccinated individuals (V) can also become infected (I) at the same rate (β) as susceptible individuals, but with reduced susceptibility due to vaccination. The compartmental diagram for the mathematical model describing modification of early diphtheria dynamics to include Vaccination and Vaccine-induced immunity as described above is shown in Fig. 1.

Table 1
Biological description of model parameters

Parameters	Biological significance	Values
Λ	Recruitment into susceptible class	0.2 per day
β	Transmission rate	0.2 infections per susceptible per day
ν	Vaccination rate	0.05 vaccinations per susceptible per day
α	Vaccine efficacy	0.8 80% efficacy)
μ	Natural death rate	0.001 births per individual per day
δ	Disease induced death rate	0.008 deaths per individual per day
γ	Recovery rate	0.1 recoveries per day
q	Reduction in susceptibility due to vaccination	0.2 per day

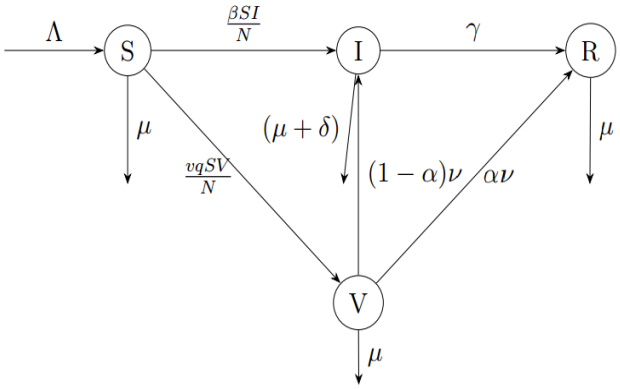

Fig. 1. Compartmental diagram for early diphtheria dynamics with vaccination

Hence, we have the differential equations describing early diphtheria dynamics with vaccination and vaccine-induced immunity are as follows:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\beta SI}{N} - \frac{vqSV}{N} - \mu S \\
\frac{dI}{dt} &= \frac{\beta SI}{N} + (1-\alpha)\nu V - (\mu+\delta)I - \gamma I \\
\frac{dR}{dt} &= \gamma I + \alpha\nu V - \mu R \\
\frac{dV}{dt} &= \frac{vqSV}{N} - (1-\alpha)\nu V - \alpha\nu V - \mu V
\end{aligned} \tag{1}$$

with $S(0) = 0.9, I(0) = 0.1, R(0) = 0, V(0) = 0$

Total population is given by $N(t) = S(t) + I(t) + R(t) + V(t)$ at any time t.

The term $vqSV/N$ represents the rate at which susceptible individuals become vaccinated due to vaccination efforts. This model allows us to explore the impact of vaccination and vaccine-induced immunity on the spread of diphtheria in the population. These equations describe the flow of individuals between the different populations and the effects of vaccination and natural immunity.

3. Analysis of the Model

A. *Positivity and Boundedness*

For the model (1) to be epidemiologically meaningful and mathematically well posed, it is necessary to establish that all solutions of system with positive initial data will remain positive for all times $t > 0$.

Positivity of Solution:
From the last three equations of model (1)

$$\frac{dI}{dt} \geq -(\mu+\delta+\gamma)I \Longrightarrow I(t) \geq I(0)e^{-(\mu+\delta+\gamma)t} \tag{2}$$

$$\frac{dR}{dt} \geq -\mu R \Longrightarrow R(t) \geq R(0)e^{-\mu t} \tag{3}$$

$$\frac{dV}{dt} \geq -(\nu+\mu)V \Longrightarrow V(t) \geq V(0)e^{-(\nu+\mu)t} \tag{4}$$

And by the first equation

$$\frac{dS}{dt} \geq -\left(\frac{\beta I}{N} - \frac{vqV}{N} - \mu\right)S \Longrightarrow \frac{dS}{S} \geq -\left(\frac{\beta I}{N} - \frac{vqV}{N} - \mu\right)dt$$

That is

$$\frac{dS}{S} \geq -\left(\frac{\beta}{N}I(0)e^{-(\mu+\delta+\gamma)t} - \frac{vq}{N}V(0)e^{-(\nu+\mu)t} - \mu\right)dt$$

Thus

$$\begin{aligned}
S(t) \geq{}& \frac{vqV(0)}{N(\nu+\mu)}\left(e^{-(\nu+\mu)t} - 1\right) \\
&+ \frac{\beta I(0)}{N(\mu+\delta+\gamma)}\left(e^{-(\mu+\delta+\gamma)t} - 1\right) - \mu t + S(0)
\end{aligned} \tag{5}$$

It could be observed from equations (2)-(5) that,

(1) $S(t) \geq S(0), I(t) \geq I(0), R(t) \geq R(0), V(t) \geq V(0)$, when $t = 0$

(2) $\max_i \phi(t)_i = \phi(0)_i \; \forall \; i$ at $t \geq 0, where \; i = 1 \cdots 4, \phi = (S, I, R, V)$

It follows that all solutions of the model are non-negative.

Boundedness:
Therefore, adding all the equations of the system together, gives,

$$\frac{dS}{dt}+\frac{dI}{dt}+\frac{dR}{dt}+\frac{dV}{dt}$$
$$= \Lambda - \frac{\beta SI}{N} - \frac{vqSV}{N} - \mu S + \frac{\beta SI}{N}$$
$$+ (1-\alpha)\nu V - (\mu+\delta)I - \gamma I + \gamma I + \alpha\nu V$$
$$- \mu R + \frac{vqSV}{N} - (1-\alpha)\nu V - \alpha\nu V - \mu V$$
$$= \Lambda - \mu S - (\mu+\delta)I - \mu R - \mu V$$

That is

$$\frac{d}{dt}(S+I+R+V) = \Lambda - \mu(S+I+R+V) - (\delta)I$$

If we assume that the rate of recruitment into susceptible class is more that the death due the disease, $\Lambda \gg \delta$ thus

$$\frac{dN}{dt} \geq -\mu N$$

Integrating the above,

$$N(t) \geq N(0)e^{-\mu t}$$

Equation above implies that maximum total population is the population before the outbreak of the disease. It follows that the feasible solution sets of the model remain in the regions: $\Gamma = \{(S,E,I,R) \in R_+^4 : 0 \leq S + I + R + V = N \leq \Lambda/\mu\}$. Observe that if the population is higher than the threshold level, the population reduces to the carrying capacity. If the population is less than the threshold level, then the solutions of the model remain in the invariant region for all $t > 0$.

B. Equilibrium States

Obtaining the equilibrium points of disease mathematical models is crucial. These points play a pivotal role in decision-making regarding disease control and potential elimination strategies. In the realm of mathematical modeling for infectious diseases, two types of equilibrium points are particularly significant: the Disease-Free Equilibrium (DFE) point and the Disease-Endemic Equilibrium (DEE) point. Understanding and analyzing these equilibrium points provide valuable insights into the dynamics and management of infectious diseases

1) The Disease-Free Equilibrium Point (DFEP)

The Disease-Free Equilibrium (DFE) refers to a state in mathematical models of infectious diseases where there are no infected individuals present in the population. It represents a point of stability where the disease is not actively spreading. In the context of disease control and epidemiology, understanding and analyzing the Disease-Free Equilibrium is crucial for assessing the effectiveness of interventions aimed at preventing or eliminating the spread of infectious diseases. In our case, we take $I = 0$, therefore,

$$V = R = 0, S = \frac{\Lambda}{\mu}$$

Hence, at disease free equilibrium,

$$(S,I,R,V) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right) \quad (6)$$

2) The Endemic Equilibrium Point (EEP)

The Endemic Equilibrium Point (EEP) is a concept in mathematical models of infectious diseases representing a stable state where the disease persists within a population at a steady level over time. Unlike the Disease-Free Equilibrium (DFE), which indicates the absence of infected individuals, the EEP reflects a scenario where the disease is actively circulating within the population, but the transmission and recovery rates balance out to maintain a constant level of infection. Understanding the dynamics and characteristics of the Endemic Equilibrium Point is essential for assessing long-term disease control strategies and predicting the impact of interventions on disease prevalence. Thus, we solve the entire system of equations. We have,

$$\begin{bmatrix} S \\ I \\ R \\ V \end{bmatrix} = \left\{ \begin{bmatrix} \frac{\Lambda}{\mu} \\ 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} N\frac{\gamma+\delta+\mu}{\beta} \\ \frac{\Lambda\beta - N\mu(\delta+\gamma+\mu)}{(\gamma+\delta+\mu)\beta} \\ \gamma\frac{\Lambda\beta - N\mu(\delta+\gamma+\mu)}{(\gamma+\delta+\mu)\beta\mu} \\ 0 \end{bmatrix}, \begin{bmatrix} N\left(\frac{\mu+\nu}{\nu q}\right) \\ \nu\frac{(1-\alpha)\left(\Lambda\nu q - \mu N(\mu+\nu)\right)}{\left((\delta+\gamma+\mu)\nu q - (\alpha\nu+\mu)\beta\right)(\mu+\nu)} \\ \frac{\left(\nu q(\gamma+(\delta+\mu)\alpha) - \beta\alpha(\mu+\nu)\right)\left(\Lambda q\nu - \mu N(\mu+\nu)\right)}{q\left((\delta+\gamma+\mu)\nu q - (\alpha\nu+\mu)\beta\right)(\mu+\nu)\mu} \\ \frac{\left((\delta+\gamma+\mu)\nu q - \beta(\mu+\nu)\right)\left(\Lambda\nu q - N\mu(\mu+\nu)\right)}{q\nu\left((\delta+\gamma+\mu)\nu q - (\alpha\nu+\mu)\beta\right)(\mu+\nu)} \end{bmatrix} \right\}$$

C. Stability Analysis

In the context of diphtheria, stability analysis of the SIRV Susceptible-Infectious-Recovered-Vaccinated) model helps predict whether the disease will die out or persist within the population in the long run by examining the equilibrium solutions of the system. In this model, there are three 3 equilibrium points, including the disease-free equilibrium DFE and endemic equilibrium EE. At the DFE, the Jacobian of the system of equation is computed and evaluated at DFE point.

$$J|_{(S^0,I^0,R^0,V^0)} = \begin{bmatrix} -\mu & -\frac{\Lambda\beta}{N\mu} & 0 & -\frac{\nu q\Lambda}{N\mu} \\ 0 & \frac{\Lambda\beta}{N\mu} - (\delta+\gamma+\mu) & 0 & (1-\alpha)\nu \\ 0 & \gamma & -\mu & \alpha\nu \\ 0 & 0 & 0 & \frac{\nu q\Lambda}{N\mu} - \nu - \mu \end{bmatrix}$$

The eigenvalues is,

$$\lambda = \left(\frac{\nu q\Lambda}{N\mu} - \nu - \mu, \frac{\Lambda\beta}{N\mu} - (\delta+\gamma+\mu), -\mu, -\mu\right)$$

With the condition that

$$\lambda < 0\,, \Lambda\nu q < N\mu(\mu+\nu), \text{and } \Lambda\beta < \mathrm{N}\mu\delta+\gamma+\mu)$$

Then all eigenvalues of the Jacobian matrix have negative real parts, this indicates that the disease-free equilibrium point is stable. This means that if the disease is introduced into the population, or if there are small perturbations in the number of infected individuals, the system will eventually return to the disease-free state.

For the EE, there are non-zero populations in all compartments, indicating ongoing transmission of the disease. Thus, we compute the Jacobian Matrix and evaluate at each of the remaining endemic equilibrium points. At the point,

$$(S^1, I^1, R^1, V^1) = \begin{pmatrix} N\frac{\gamma + \delta + \mu}{\beta}, \frac{\Lambda\beta - N\mu(\delta+\gamma+\mu)}{(\gamma+\delta+\mu)\beta}, \\ \gamma\frac{\Lambda\beta - N\mu(\delta+\gamma+\mu)}{(\gamma+\delta+\mu)\beta\mu}, 0 \end{pmatrix}$$

The Jacobian Matrix is,

$$J|_{(S^1,I^1,R^1,V^1)} = \begin{bmatrix} \frac{N\mu(\delta+\gamma+\mu)+\Lambda\beta}{(\delta+\gamma+\mu)N} - \mu & -(\delta+\gamma+\mu) & 0 & -\frac{\nu q(\delta+\gamma+\mu)}{\beta} \\ \frac{\Lambda\beta - N\mu(\delta+\gamma+\mu)}{(\delta+\gamma+\mu)N} & 0 & 0 & (1-\alpha)\nu \\ 0 & \gamma & -\mu & \alpha\nu \\ 0 & 0 & 0 & \frac{\nu q(\delta+\gamma+\mu)}{\beta} - \nu - \mu \end{bmatrix}$$

From where the eigenvalues are obtained as,

$$E_i = \begin{bmatrix} -\mu \\ \frac{a_4\nu q - \beta(\mu+\nu)}{\beta} \\ -\frac{\Lambda\beta - 2\sqrt{N(N\mu(\delta+\gamma+\mu)-\Lambda\beta)(\delta+\gamma+\mu)^2 + \Lambda^2\beta^2}}{2a_4N} \\ -\frac{\Lambda\beta + 2\sqrt{N(N\mu(\delta+\gamma+\mu)-\Lambda\beta)(\delta+\gamma+\mu)^2 + \Lambda^2\beta^2}}{2a_4N} \end{bmatrix}$$

It could be observed that the eigenvalues above are complex with the real part of $E_i \leq 0\ \forall i$ provided $\nu\mathrm{q}(\delta+\gamma+\mu) < \beta(\mu+\nu)$ and $N^2\mu(\delta+\gamma+\mu) + \left(\frac{\Lambda\beta}{(\delta+\gamma+\mu)}\right)^2 < \Lambda N\beta$

D. The Basic Reproduction Number (BRN)

The basic reproduction number is the average number of secondary infections caused by a single infectious individual in an entirely susceptible population during his/her infective period. The next generation matrix approach is used to obtain R_0. Let $X(t) = (S, I)$ and obtain that,

$$X'(t) = \mathcal{F}(t) - \mathcal{V}(t)$$

where:

$$\mathcal{F}(t) = \begin{pmatrix} \frac{\beta SI}{N} & 0 \\ 0 & 0 \end{pmatrix} \text{ and}$$

$$\mathcal{V}(t) = \begin{pmatrix} -\mu-\delta-\gamma & 1-\alpha)\nu \\ 0 & -\frac{N}{N(\mu+\nu)-Sq\nu} \end{pmatrix}$$

Evaluating the derivatives of F and V at the disease-free equilibrium point obtained above, yields $F\mathcal{V}^{-1}$ as seen below:

$$F\mathcal{V}^{-1} = \begin{pmatrix} -\frac{\beta S}{N(\gamma+\delta+\mu)} & -\frac{\beta S1-\alpha)}{(\gamma+\delta+\mu)(N(\mu+\nu)-Sq\nu)} \\ 0 & 0 \end{pmatrix}$$

By solving the dominant eigenvalue of the next generation matrix $F\mathcal{V}^{-1}$, we get the basic reproduction number to be,

$$R_0 = -\frac{\beta S}{N(\gamma+\delta+\mu)}$$

Therefore, the basic reproduction number of the given system of equations denoted by R_0 is:

$$R_0 = -\frac{\beta\Lambda}{\mu N(\gamma+\delta+\mu)}$$

Effective Reproduction Number: The effective reproduction number R_{eff}) is a critical epidemiological measure that offers insights into the transmission dynamics of infectious diseases, guiding public health responses during epidemics and pandemics. It signifies the average number of new infections generated by each infectious individual at a particular time during such outbreaks.

The basic reproduction number is evaluated using the

Table 2
Sensitivity analysis on Basic and Effective Reproduction Number R_0 and R_{eff} respectively

Parameter	Sensitivity Index on R_0 Per 1000	Parameter	Sensitivity Index on R_{eff_1} Per 1000	Parameter	Sensitivity Index on R_{eff_2} Per 1000
Λ	-0.16949	μ	-1	μ	-0.08331
β	-0.08475	β	-1	β	-0.05085
δ	0.143637	ν	-1	ν	0.033898
γ	0.143637	q	-1	q	0.050847
μ	1.838552	δ	-1	δ	0.086182
		γ	-1	γ	0.086182

inequality below,

$$0 < S^* < S$$

Where S is the susceptible when at DFE, S^* is the susceptible when at EE

Thus, we can have

$$0 \leq \frac{S^*}{S} < 1 \tag{7}$$

Multiply 12) by R_0 implies

$$0 \leq R_0 \frac{S^*}{S} < R_0 \tag{8}$$

From equation 13), the relationship between R_{eff}, R_0 S, and S^* can be described using the following equation

$$R_{eff} = R_0 \frac{S^*}{S}$$

Corresponding to the equilibrium points, we have two kinds of effective reproduction numbers depending on $S_i^*, i = 1, 2.$

$$S = \frac{\Lambda}{\mu}, S^* = \left\{ N\frac{\gamma + \delta + \mu}{\beta}, \quad N\frac{\mu + \nu}{\nu\, q} \right\}$$

Thus,

$$R_{eff}^1 = R_0 \frac{S^*}{S}\Big|_{(R_0,S,S_1^*)=\left(-\frac{\beta\Lambda}{\mu N(\gamma+\delta+\mu)}, \frac{\Lambda}{\mu}, N\frac{\gamma+\delta+\mu}{\beta}\right)} = -1$$

And

$$R_{eff}^2 = R_0 \frac{S^*}{S}\Big|_{(R_0,S,S_1^*)=\left(-\frac{\beta\Lambda}{\mu N(\gamma+\delta+\mu)}, \frac{\Lambda}{\mu}, N\frac{\mu+\nu}{\nu\, q}\right)}$$

$$= -\frac{\beta(\mu+\nu)}{\nu\, q(\gamma + \delta + \mu)}$$

E. Parameter Effects on the BRN

Sensitivity analysis is used to obtain the sensitivity index that is a measure of the relative change in a state variable when a parameter changes. We compute the sensitivity indices of R_0 to the model parameters with the approach used by [20]. These indices show the importance of each individual parameter in the disease transmission dynamics and prevalence. The sensitivity of a parameter, say β, of R_0 is defined as,

$$\xi_\beta^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} \tag{9}$$

Therefore, the table 2 present the sensitivity indices of the parameters on Basic Reproduction Number and the Effective Reproduction Numbers (ERN)

4. Discussion of Results

In this study, we utilized a deterministic SIRV model to simulate Diphtheria transmission dynamics under different epidemiological conditions and intervention strategies. The model accounted for key aspects of disease natural history and immunological responses to infection and vaccination**.** Fig. 2 illustrates the dynamics of a disease spread over a 20-day period, with the infection rate peaking around day 20. It appears that the susceptibility rate, which is the proportion of the population that can be infected, also declines around the same time. This could be due to several factors, including the implementation of public health measures such as social distancing and mask-wearing, which reduce the likelihood of transmission. The vaccination rate remains relatively flat throughout this period, which suggests that the vaccination effort has not yet had a significant impact on the spread of the disease. This could be due to a variety of reasons, including limited vaccine supply, vaccine hesitancy, or logistical challenges in distributing the vaccine. The recovery rate shows a steady increase over this period, which suggests that the healthcare system is able to effectively treat infected individuals and that they are recovering at a faster rate synonymous to that at which new infections are occurring.

As expected, increasing the recruitment rate Λ which adds new births/migrations to the susceptible compartment has a direct effect of increasing the size of the susceptible population, at least initially. More individuals entering the susceptible class provides additional fuel for potential infection spread through more available contacts for the disease to transmit to in the early stage as shown in Fig. 3. However, from Fig. 4 the model also shows an interesting consequential effect - the infected population also appreciates with a higher recruitment rate. While recruitment accelerates depletion of the susceptible pool by increasing its size, it also enhances infection transmission by providing renewed opportunities over time as the newly recruited individuals now mix with infectious contacts in the population. This balance of short-term susceptible gain versus long-term infection amplification depends on the interplay between all rates over the full duration. A higher recruitment supports infections not just from initial expansion of S, but from

its continued replenishment of unaware population.

In Fig. 5 and 6, the transmission rate β directly modulates the contact or mixing rate between susceptible and infected individuals. A higher β means each contact is more likely to result in successful transmission. This amplified per-contact infectiousness allows the disease to propagate more efficiently through depletion of available susceptible individuals. We see mathematically in the equation describing the rate of change of susceptible population that β scales the negative term representing the loss of susceptible due to new infections. Consequently, during the initial exponential growth phase, a larger β generates a steeper decline in the S curve. Susceptible are converted to infections at an accelerated pace that outpaces recruitment into the class. Correspondingly, the positive infection-generation term depends on both prevalence of susceptible and infectiousness β. So, a higher β directly fuels more rapid accumulation of new cases, manifesting as appreciation of the I curve. These dynamics unfold until susceptible diminish sufficiently to curb the conditioned growth enabled by abundant contacts. The quantitative differences emerge from β modulating the intensity of interactions between transmission classes.

Basically, it's intuitive that an increase in the recovery rate γ) of an infectious disease would lead to a decline in the infected population, as individuals are recovering from the illness more quickly. However, the relationship between recovery rate, susceptible population, and disease spread is more nuanced than it may initially appear as displayed in Fig. 7, 8 and 9. While a higher recovery rate does facilitate those in the infected category transitioning into the recovered group in shorter order, this does serve to expand the pool of susceptible individuals who are again at risk of contracting the disease. Those who have recovered now possess immunity but rejoin the segment of the population that is not actively infected but can potentially become infected upon contact with the virus or bacteria. What is often overlooked in only considering the direct effect of recovery on infection numbers is the indirect impact on disease transmission dynamics. A larger susceptible population translates to a greater number of potential future hosts for the pathogen. Even as the currently infected cohort decreases due to recovery, the increased reservoir of susceptibility means the conditions are ripe for transmission to accelerate again and push infection levels back up over the long run.

At first glance, it would seem a rise in the natural mortality rate μ) would unambiguously diminish both the susceptible and infected populations of a disease. However, from Fig. 10 and 11 the dynamics at play over different timescales tell a more intricate story. While an increased baseline death rate does immediately cull those in the susceptible class, reducing the pool of potential future infections, this effect is only transitory in nature. Within the first ten months or so, as individuals succumb to other natural causes unrelated to the disease, the size of the susceptible group is contracted. However, after this initial period, the interplay becomes markedly more complex. Not only are births and deaths ongoing, continually reshaping the demographic landscape, but the impact of mortality on transmission must be considered. A higher death rate does remove persons from the infected category in the short-term, as expected. But it also disrupts the forces that drive herd immunity over the long run. With more frequent turnover of the susceptible population due to natural losses, the opportunity for widespread exposure and development of population-level resistance is diminished. This leaves communities more vulnerable to resurgent outbreaks down the line. Moreover, mortality can facilitate transmission under certain conditions. If it preferentially claims the very young, old or immuno-compromised – those less likely to spread disease – it may perversely concentrate the virus among the most active spreaders.

It obviously counterintuitive that increasing disease-induced mortality rate δ could paradoxically serve to enlarge, rather than contract, the pool of individuals susceptible to infection over time. However, pondering the interplay between those who succumb to the illness, recover, and remain at risk of contagion illuminates a more intricate pattern are displayed in Fig. 12 and 13. While a heightened case-fatality ratio removes more people from the recovering category by expedited demise in the short-term, as expected, this also opens space for new susceptible hosts to take their places. As deaths open spaces in the population, births and migration fill these voids with fresh potential victims who lack prior immunity. What's more, a disease with elevated lethality is typically more effective at disrupting progression towards herd protection through natural infection over the long haul. By excessively culling those in recovery, it interrupts the community-wide exposure needed to confer widespread resistance. This resets the initial conditions, placing more persons back into the crosshairs of contagion with each resurgent wave. The combined consequence is ironically an inflation, rather than deflation, of the susceptible class available to fuel ongoing transmission cycles. Of course, disease-caused mortality remains unambiguously tragic for impacted individuals and families. However, zooming out to consider the population-level interplay of contingents over generations reveals counterintuitive phenomenon - how a harsher death toll can broadly undermine, rather than aid, control of spread in an unintended fashion.

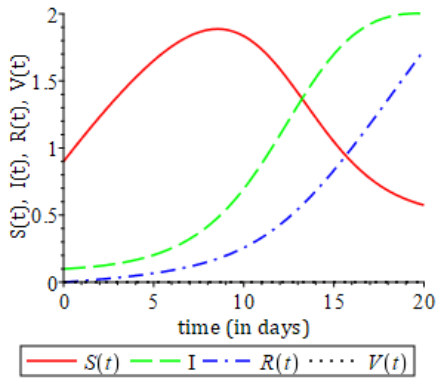

Fig. 2. Growth rate of the different compartment with time days

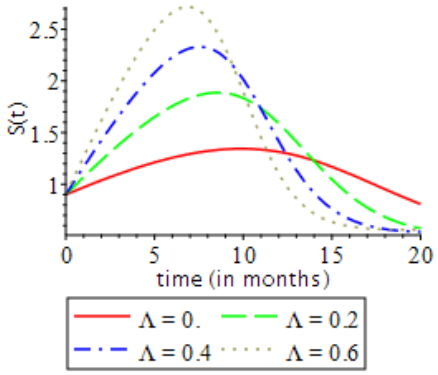

Fig. 3. Effect of the recruitment rate Λ on the susceptible population

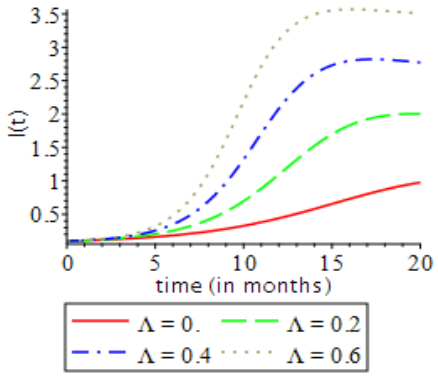

Fig. 4. Effect of the recruitment rate Λ on infected individuals

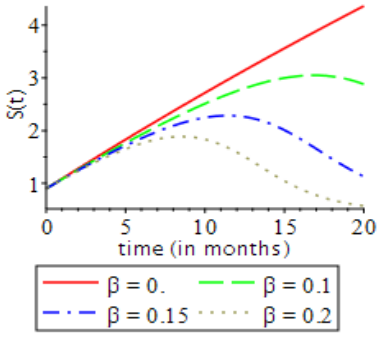

Fig. 5. Effect of the transmission rate β on the susceptible population

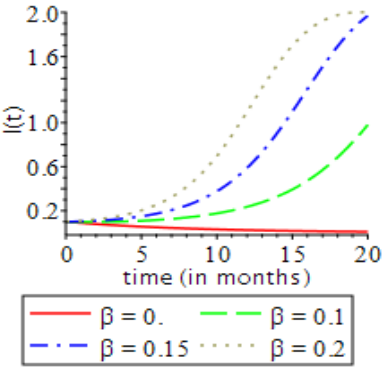

Fig. 6. Effect of the transmission rate β on the infected population

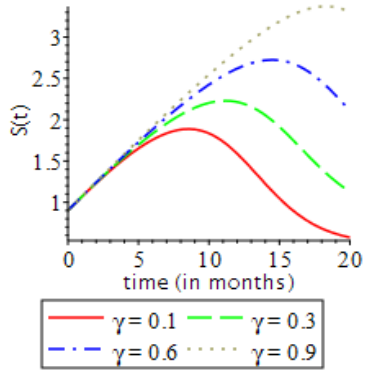

Fig. 7. Effect of the recovery rate γ on the susceptible population

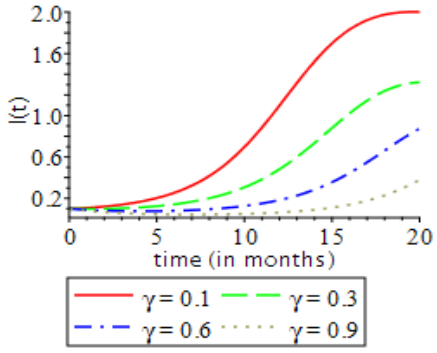

Fig. 8. Effect of the recovery rate γ on the infected population

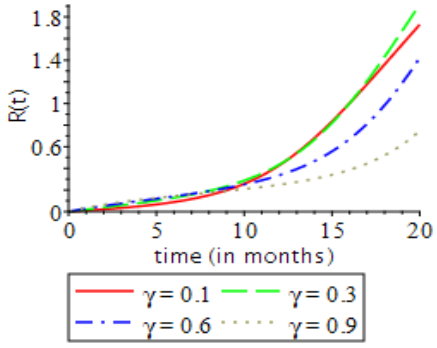

Fig. 9. Effect of the recovery rate γ on the recovered population

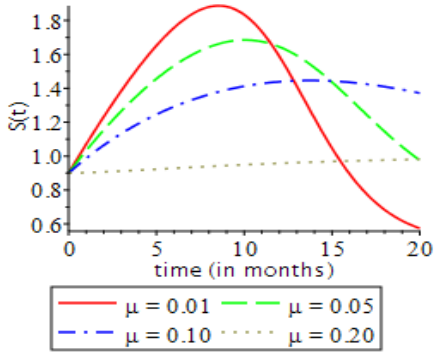

Fig. 10. Effect of the natural mortality rate μ on the susceptible population

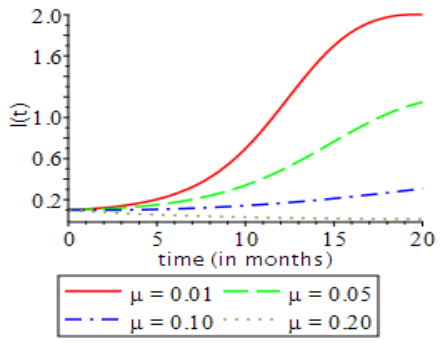

Fig. 11. Effect of the natural mortality rate μ on the infected population

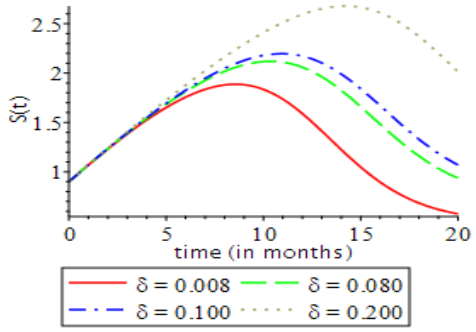

Fig. 12. Effect of the disease induced death rate δ on the susceptible population

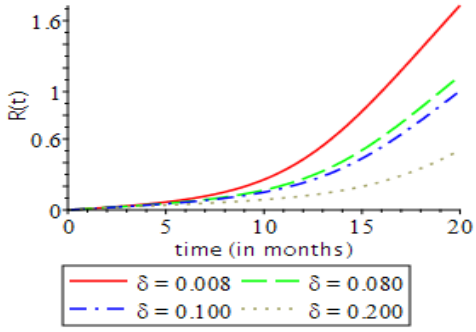

Fig. 13. Effect of the disease induced death rate δ on the recovered population

5. Summary and Conclusion

A. *Summary*

Through analyzing the dynamics of this SIRV model for disease transmission and exploring the impacts of varying key parameters, we have gained valuable insights into the epidemiological drivers of infectious outbreaks. Specifically considering Diphtheria as a case study helps contextualize some of the results. Higher transmissibility represented by increased β was shown to generate a more explosive rise in cases by amplifying each transmission event. However, this early benefit turned into a detriment as epidemics burnt out more quickly by depleting susceptible individuals. For a disease like Diphtheria that can spread rapidly in dense populations with low vaccination, controlling transmission through precautions becomes critically important. Faster recovery γ flattened and contracted the epidemic curve by shortening each infection's duration. This emphasizes the role medical interventions play in containing spread, whether through timely availability of antitoxin treatment or other supportive clinical care for Diphtheria patients. Reducing time spent infectious aids in curtailing onward transmission potential. Larger epidemics correlated with higher recovered populations in the model, reflecting the reality that more cases mean more individuals acquire protective immunity through natural infection. Though severe outbreaks are undesirable, they do confer lasting herd protection if recovery provides lasting resistance as is the case for Diphtheria. Overall, this modeling exercise highlighted key factors influencing the dynamics of an infectious disease like Diphtheria spreading within a population. While simplified, it demonstrates how epidemiological relationships emerge from basic transmission principles incorporated into mathematical frameworks. Continued refinement and integration of additional realistic complexities holds promise for generating insights to guide evidence-based public health.

B. *Conclusion*

This research reinforces how simplifying epidemiological factors into isolated variables misses their interdependence and capacity to produce unanticipated, nonlinear effects at the population level over time. Transmission is a complex, systemic process influenced by myriad shifting dynamics, considering only proximate, short-term impacts of changes like higher recovery or mortality can obscure long-range consequences for disease evolution and spread. Broader time horizons and demographic influencers must be incorporated.

Additionally, while counterintuitive findings do not negate the desirability of certain outcomes - e.g. reduced case fatality - they call for more nuanced strategies accounting for second-order impacts. Goals like herd protection cannot be achieved through reductionism. In conclusion, diseases spread through populations based on relationships that defy simple characterization. Demanding theorists approach transmission as complex, dynamic and sometimes unexpectedly behaving phenomena seems a prudent stance, to avoid misguiding research or policy designs. Further modeling work building on foundations outlined here could generate valuable insight into optimizing control approaches. From the results presented and discussed, the following are deduced from the analysis:

- Public health measures and vaccination efforts impact disease spread.
- Initial increase expands susceptible population, leading to increased infection spread.
- Higher rate leads to more efficient disease propagation.
- Facilitates transition from infected to recovered but expands pool of susceptible individuals.
- Initial decrease in susceptible population, but disrupts herd immunity over the long run.
- Increased disease-induced mortality rate: enlarges susceptible population over time.

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