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# A COUPLED SEIR-SIR FRAMEWORK MODELING SYNDEMIC DYNAMICS OF DIPTHTHERIA AND DENGUE OUTBREAKS: NONLINEAR AMPLIFICATION AND MULTISECTIORAL IMPLICATIONS IN NIGERIA

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**ABSTRACT**

This study presents a differential equation-based framework to model the synergistic effects of concurrent diphtheria and dengue fever outbreaks rrin Edo State, Nigeria. By integrating compartmental models (SEIR for diphtheria and SIR for dengue), we capture cross-disease dynamics influenced by shared health infrastructure, climatic conditions, and overlapping vulnerable populations. The mathematical model incorporates co-infection rates, delayed diagnosis, and healthcare saturation effects. Data from public health reports between January and May 2025 were fitted using parameter estimation techniques. Contour plots illustrate critical thresholds where interactions between outbreaks intensify disease burden, leading to nonlinear amplification of infection rates. Our findings emphasize the importance of a multisectoral response involving health, sanitation, education, and emergency services. The model also forecasts outbreak trajectories under various intervention scenarios, supporting evidence-based policy formulation. This study underscores the relevance of mathematical epidemiology in managing syndemic events and promotes integrated surveillance systems for effective public health response in sub-Saharan Africa.

**Keywords:** Co-infection, Diphtheria, Differential equations, Dengue, Syndemic modeling

## Introduction

Diphtheria remains a significant public health concern despite global efforts to control it through vaccination and improved healthcare interventions. Caused by toxigenic strains of *Corynebacterium diphtheriae*, as well as the less common *C. ulcerans* and *C. pseudotuberculosis*, the disease manifests through respiratory symptoms such as fever, sore throat, enlarged lymph nodes, barking cough, dysphagia, and airway obstruction. The release of diphtheria toxin a potent exotoxin can lead to severe complications including respiratory failure, myocarditis, and neurological damage (Hadfield et al., 2018; WHO, 2023). Without timely diagnosis and treatment, diphtheria can result in fatal outcomes. Recent genomic studies confirm toxin-producing strains remain endemic in West Africa despite vaccination programs (Oladipo et al., 2023).

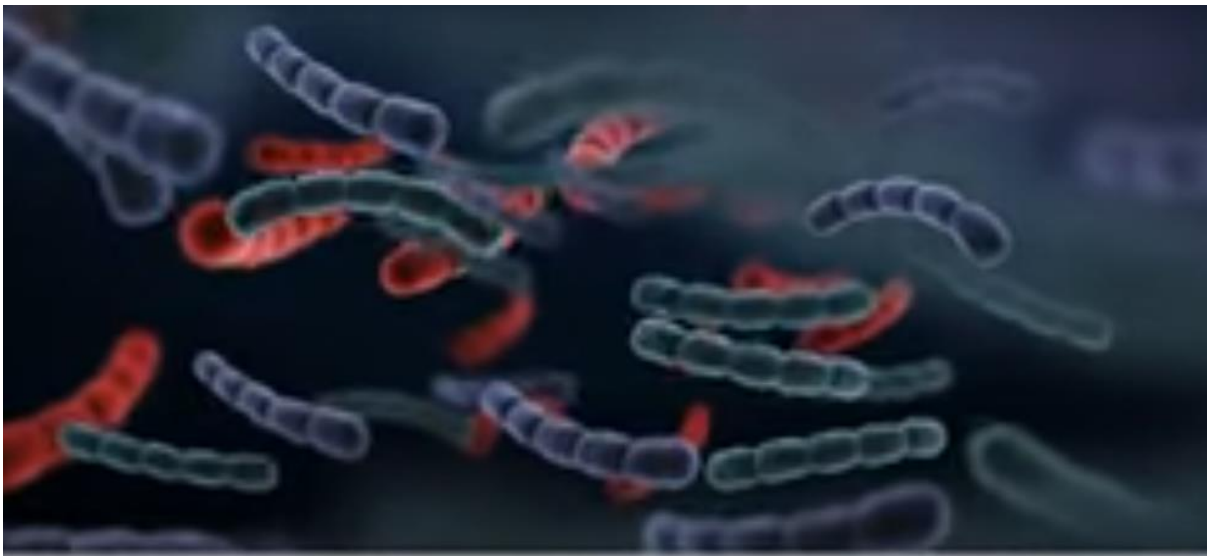

**Fig. 1: Corynebacterium diphtheriae bacteria**

Historically, diphtheria was a major cause of childhood mortality before the widespread introduction of vaccination. The development and administration of the diphtheria antitoxin in the early 20th century, followed by the implementation of the diphtheria-tetanus-pertussis (DTP) vaccine in the 1950s, led to a dramatic global reduction in incidence. While the pre-vaccine era saw over one million annual cases globally, recent years have seen a decline to approximately 6,500 cases between 2013 and 2017 (WHO, 2018). Nonetheless, outbreaks continue to emerge, particularly in regions with suboptimal immunization coverage and fragile healthcare systems. Resource limitations in such settings amplify mortality risks during outbreaks (Oleribe et al., 2019).

Nigeria, like many developing nations, is experiencing a resurgence of diphtheria cases. In 2023, an official outbreak was declared on January 20, with 253 suspected cases reported, of which 111 were confirmed 8 through laboratory analysis and 103 through clinical diagnosis. Alarmingly, 91.9% of these confirmed cases affected children between 2 and 14 years of age, and 22 deaths were recorded, resulting in a case fatality rate (CFR) of 19.8% (NCDC, 2023). Furthermore, from May 2022 to May 2023, Nigeria documented 2,006 suspected and 672 confirmed cases, with 73 recorded deaths (CFR = 10.9%), spanning 23 states (Are, 2023).

These alarming statistics highlight structural gaps in Nigeria's national immunization program. Only 10.8% of confirmed cases in 2023 received complete diphtheria antitoxin therapy, underscoring systemic issues such as antitoxin scarcity, late diagnosis, and under-resourced health facilities (Ogunniyi et al., 2023). Laboratory capacity gaps mirror regional trends observed across sub-Saharan Africa (Nkengasong et al., 2021). Strain subtyping and molecular surveillance of *C. diphtheriae* are hindered by insufficient laboratory infrastructure, complicating efforts to track outbreak origins and implement targeted interventions (Hadfield et al., 2018).

*Corynebacterium diphtheriae*, first identified in 1884 by German microbiologists Edwin Klebs and Friedrich Löffler, is a Gram-positive bacillus often appearing as club-shaped rods with metachromatic Babes–Ernst granules arranged in palisades or "Chinese letter" patterns. Though some strains are non-toxigenic, toxigenic forms result from lysogenization by a β-phage that encodes the diphtheria toxin gene (Galazka, 2000). Upon colonization of the upper respiratory tract, the

bacterium secretes this exotoxin, which can localize to tissues or disseminate hematogenously, affecting organs such as the heart, kidneys, and nervous system (CDC, 2022; Pace & Pollard, 2012).

Clinically, diphtheria typically presents 2 to 7 days post-infection with low-grade fever, pharyngitis, and cervical lymphadenopathy. The hallmark finding is the presence of a thick, grayish pseudo membrane over the tonsils, pharynx, or nasal passages. Severe systemic toxicity can result in myocarditis, peripheral neuropathy, respiratory failure, and, in extreme cases, death (Wagner et al., 2021). Transmission occurs through respiratory droplets or direct contact, which underscores the importance of prompt isolation, antitoxin therapy, and antibiotic administration.

The re-emergence of diphtheria has coincided with outbreaks of other infectious diseases, particularly dengue fever. Dengue, caused by the dengue virus and transmitted via *Aedes aegypti* mosquitoes, poses additional epidemiological challenges when co-circulating with respiratory pathogens like diphtheria. The overlapping epidemiology driven by environmental conditions, urban crowding, and inadequate public health infrastructure complicates outbreak control. This syndemic interaction follows patterns observed in other tropical regions where vector-borne and respiratory diseases overlap (Wilder-Smith et al., 2020) and increases overall disease burden (Huang et al., 2023).

Mathematical modeling, particularly through the use of systems of differential equations, offers an essential framework for understanding and managing concurrent disease outbreaks. Models such as SEIR (Susceptible–Exposed–Infectious–Recovered) for diphtheria and SIR (Susceptible-Infectious–Recovered) with vector dynamics for dengue allow public health authorities to simulate various scenarios and intervention outcomes. These tools can incorporate parameters such as transmission rates, recovery times, incubation periods, vaccination coverage, and healthcare system saturation. Co-infection modeling frameworks have proven critical for predicting resource needs during concurrent outbreaks (Garba et al., 2021). to predict outbreak trajectories and co-infection dynamics (Brauer et al., 2019; Kassa & Ouhinou, 2020).

In the context of Edo State, Nigeria, where both diphtheria and dengue are emerging threats, integrated modeling becomes a powerful asset for policymakers. For example, improved hygiene practices aimed at reducing diphtheria transmission may concurrently disrupt mosquito breeding environments, thereby lowering dengue risk. On the other hand, healthcare strain due to one disease may delay diagnosis and treatment of the other, thereby worsening outcomes for co-infected individuals. These synergistic interactions can be mathematically represented to estimate co-infection peaks, hospital overload thresholds, and optimal intervention strategies.

Public health responses should therefore be multisectoral. Vaccination campaigns must be intensified in low-coverage regions, while environmental management strategies including vector control via larviciding and elimination of breeding sites should be scaled up. Educational institutions can contribute by promoting hygiene and vaccine awareness, while community-based surveillance can enhance early case detection. Furthermore, real-time integration of epidemiological data into models can guide dynamic decision-making and improve preparedness for future outbreaks.

In conclusion, the resurgence of diphtheria and the concurrent threat of dengue in Nigeria highlight the urgent need for evidence-based, multisectoral public health responses. By leveraging differential equation models and integrating surveillance with community engagement and inter-agency coordination, it is possible to mitigate the syndemic impact of these infectious diseases and strengthen the resilience of the Nigerian health system.

**Governing Equations (Synergistic SEIR-SIR Model)**

The state variables table for the Diphtheria–Dengue Co-infection Model, grouped into two main categories: Core Variables and Extended Variables

**Core State Variables**

| Symbol | Meaning | Role in Model |
|---|---|---|
| $S_h$ | Susceptible humans | Entry point for diphtheria or dengue infection |
| $E_d$ | Exposed to diphtheria | Infected but not yet infectious (incubation stage) |
| $I_d$ | Infected with diphtheria | Actively infectious and symptomatic humans |
| $R_d$ | Recovered from diphtheria | Immune individuals; may have permanent or partial immunity |
| $I_g$ | Infected with dengue | Humans infected by mosquito bites; contribute to transmission |
| $R_g$ | Recovered from dengue | Immune to one dengue serotype; at risk of others (ADE) |
| $S_m$ | Susceptible mosquitoes | Mosquitoes at risk of acquiring dengue |
| $I_m$ | Infected mosquitoes | Capable of transmitting dengue to humans |
| $N_h$ | Total human population | Sum of human compartments |
| $N_m$ | Total mosquito population | Sum of mosquito compartments |

**Extended Variables**

| Symbol | Meaning | Function / Insight |
|---|---|---|
| $I_{dg}$ | Co-infected with diphtheria and dengue | Dual infection case; may have increased severity |
| $R_{dg}$ | Recovered from both infections | Indicates cross-immunity and resilience |
| $V_d$ | Vaccinated against diphtheria | Models effect of immunization campaigns |
| $M_m$ | Mosquito maturation class | Tracks immature mosquitoes for vector control analysis |
| $\Lambda_h$ | Human recruitment rate | Birth or immigration into the human population |
| $\mu_h$ | Natural death rate (humans) | Background mortality; not due to infection |
| $\delta_d, \delta_g$ | Disease-induced death rates | Mortality from diphtheria/dengue |
| $\gamma_d, \gamma_g$ | Recovery rates | Rate at which individuals recover from infection |
| $\beta_d, \beta_g$ | Transmission rates | Force of infection; diphtheria is direct, dengue is vector-borne |
| $\theta$ | Incubation progression rate (diphtheria) | Rate of transition from exposed to infectious |

To model the co-dynamics of diphtheria and dengue, we integrate a hybrid SEIR–SIR compartmental framework, figure 1 below incorporating direct human-to-human transmission (for diphtheria) and mosquito-borne transmission (for dengue). And figure 2 is the diagram models vector (e.g., mosquito) and human populations in a disease system. Mosquito dynamics (top) include temperature-affected ($T$) stages: egg development (EFD), maturation (MDR), infection ($a, pM$), latency (PDR), and mortality ($\mu$). Human dynamics (bottom) track susceptible ($S_h$), exposed ($E_h$), infectious ($I_h$), and recovered ($R_h$) individuals, with infection ($a, b$), latency ($\delta$), and recovery ($\eta$). Environmental drivers: Temperature modulates mosquito biology, while rainfall/humidity ($R$) and human density ($H$) affect carrying capacity ($K$). Arrows denote transitions, births, deaths, and migration. Below is a system of differential equations representing the interaction between the diseases

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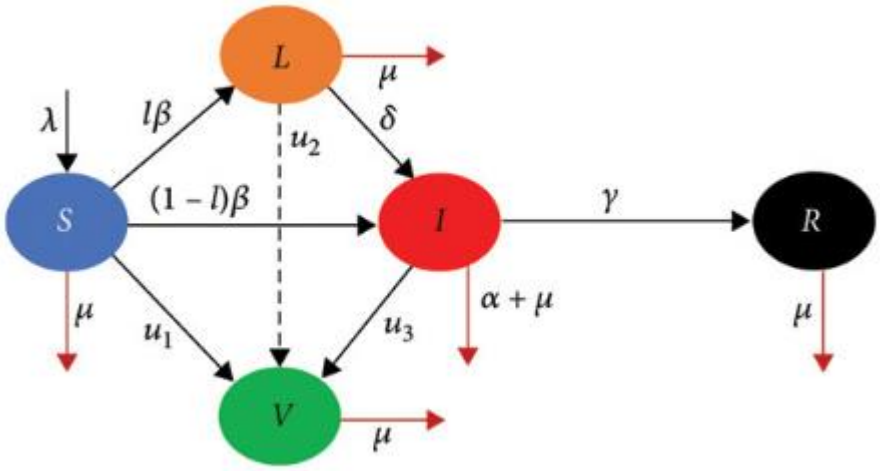


**Figure 2. Schematic diagram for diphtheria model**

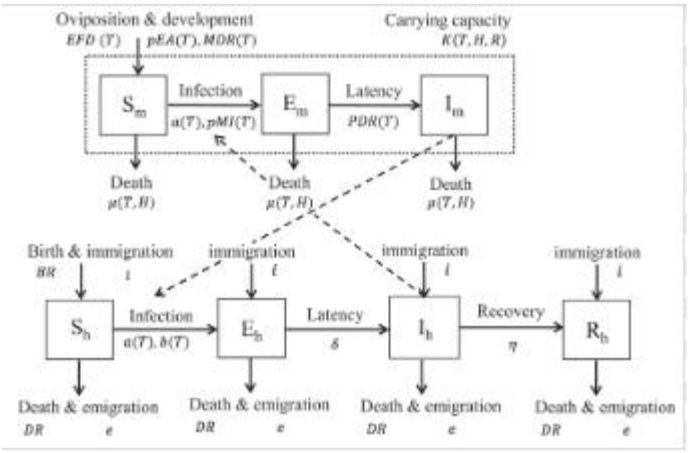


**Figure 3. Compartmental Model of Climate-Driven Vector-Borne Disease Dynamics"**

**Mathematical Model Equations for Diphtheria–Dengue Co-infection**

**State Variables (Humans):**

- $S_h$: Susceptible humans
- $E_d$: Exposed to diphtheria
- $I_d$: Infected with diphtheria
- $R_d$: Recovered from diphtheria
- $I_g$: Infected with dengue
- $R_g$: Recovered from dengue
- $I_{dg}$: Co-infected with both diseases
- $R_{dg}$: Recovered from both
- $V_d$: Vaccinated against diphtheria

**State Variables (Mosquitoes):**

- $S_m$: Susceptible mosquitoes
- $I_m$: Infected mosquitoes

**Model Parameters:**

The model incorporates several key parameters that govern the dynamics of diphtheria and dengue transmission. The human recruitment rate ($\Lambda_h$) represents the influx of new individuals into the susceptible human population, while the natural human death rate ($\mu_h$) accounts for baseline mortality unrelated to disease. The disease-induced death rates ($\delta_d$ for diphtheria and $\delta_g$ for dengue) capture the lethality of the respective infections. Transmission is modeled through the diphtheria transmission rate ($\beta_d$), which reflects direct human-to-human contact, and the dengue transmission rate ($\beta_g$), which accounts for mosquito-mediated spread. Recovery dynamics are governed by recovery rates ($\gamma_d$, $\gamma_g$) for each disease, while the incubation progression rate ($\theta$) defines the speed at which exposed individuals become infectious in diphtheria. Additionally, the mosquito population is regulated by the mosquito recruitment rate ($\Lambda_m$) and mosquito death rate ($\mu_m$), which influence vector abundance and hence dengue transmission potential.

**Differential Equations:**

**Susceptible Humans**

$$\frac{dS_h}{dt} = \Lambda_h - \beta_d S_h I_d - \beta_g S_h \frac{I_m}{N_m} - \mu_h S_h \quad (1)$$

**Vaccinated Humans (Diphtheria only)**

$$\frac{dV_d}{dt} = \nu_d S_h - \mu_h V_d \quad (2)$$

**Exposed to Diphtheria**

$$\frac{dE_d}{dt} = \beta_d S_h I_d - (\theta + \mu_h) E_d \quad (3)$$

**Infected with Diphtheria**

$$\frac{dI_d}{dt} = \theta E_d - (\gamma_d + \delta_d + \mu_h) I_d \quad (4)$$

**Recovered from Diphtheria**

$$\frac{dR_d}{dt} = \gamma_d I_d - \mu_h R_d \quad (5)$$

**Infected with Dengue**

$$\frac{dI_g}{dt} = \beta_g S_h \frac{I_m}{N_m} - (\gamma_g + \delta_g + \mu_h) I_g \quad (6)$$

**Recovered from Dengue**

$$\frac{dR_g}{dt} = \gamma_g I_g - \mu_h R_g \quad (7)$$

**Co-infected Humans**

$$\frac{dI_{dg}}{dt} = \beta_d I_g S_h + \beta_g I_d \frac{S_h}{N_m} - (\gamma_d + \gamma_g + \delta_d + \delta_g + \mu_h) I_{dg} \quad (8)$$

**Recovered from Both**

$$\frac{dR_{dg}}{dt} = (\gamma_d + \gamma_g) I_{dg} - \mu_h R_{dg} \quad (9)$$

**Mosquito Equations**

**Susceptible Mosquitoes**

$$\frac{dS_m}{dt} = \Lambda_m - \beta_g S_m \frac{I_g}{N_h} - \mu_m S_m \quad (10)$$

**Infected Mosquitoes**

$$\frac{dI_m}{dt} = \beta_g S_m \frac{I_g}{N_h} - \mu_m I_m \quad (11)$$

**Total Populations**

$$N_h = S_h + E_d + I_d + R_d + I_g + R_g + I_{dg} + R_{dg} + V_d$$
$$N_m = S_m + I_m \quad (12)$$

**Model Features:**

The model captures several critical dynamics in the co-transmission of diphtheria and dengue. It accounts for vaccination against diphtheria through the compartment $V_d$, enabling the evaluation of immunization strategies. The model includes an exposed class for diphtheria ($E_d$) to represent the incubation period before individuals become infectious, whereas no such class is included for dengue, under the assumption that mosquito transmission is instantaneous upon contact with an infectious human. Furthermore, it introduces a co-infected class ($I_{dg}$) to represent individuals simultaneously infected with both diseases, allowing the exploration of synergistic effects on transmission, morbidity, and mortality. The model also reflects the interaction between human and mosquito populations, capturing the feedback mechanisms that influence disease spread, particularly through vector-host dynamics in dengue transmission

.

**Characteristic Variables and Scaling**

Let: $\tau = \frac{1}{\mu_h}$ (human time scale), Define dimensionless time: $t^* = \mu_h t$ and let $N_{h0}$, $N_{m0}$ be initial populations

**Define Dimensionless Variables**

Introduce dimensionless variables using characteristic scales:

**i.** Characteristic time: $\tau = \frac{1}{\mu_h}$ (human natural mortality timescale).

**ii.** Dimensionless time: $t^* = \mu_h t$.

**iii.** Dimensionless human populations:

$$s_h = \frac{S_h}{N_{h0}}, \quad v_d = \frac{V_d}{N_{h0}}, \quad e_d = \frac{E_d}{N_{h0}}, \quad i_d = \frac{I_d}{N_{h0}}, \quad i_g = \frac{I_g}{N_{h0}}, \quad i_{dg} = \frac{I_{dg}}{N_{h0}}, \quad r_d = \frac{R_d}{N_{h0}}, \quad r_g = \frac{R_g}{N_{h0}}, \quad r_{dg} = \frac{R_{dg}}{N_{h0}}$$

where $N_{h0}$ is the initial total human population. (13)

**iv.** Dimensionless mosquito populations:

$$s_m = \frac{S_m}{N_{m0}}, \quad i_m = \frac{I_m}{N_{m0}} \tag{14}$$

where $N_{m0}$ is the initial mosquito population.

**v.** Dimensionless total populations:

$$n_h = \frac{N_h}{N_{h0}} = s_h + v_d + e_d + i_d + i_g + i_{dg} + r_d + r_g + r_{dg}, \quad n_m = \frac{N_m}{N_{m0}} = s_m + i_m.$$

(15)

**Dimensionless parameters:**

$$\lambda = \frac{\Lambda_h}{\mu_h N_{h0}}, \quad \nu = \frac{\nu_d}{\mu_h}, \quad \theta^* = \frac{\theta}{\mu_h}$$

$$\gamma_d^* = \frac{\gamma_d}{\mu_h}, \quad \gamma_g^* = \frac{\gamma_g}{\mu_h}, \quad \delta_d^* = \frac{\delta_d}{\mu_h}, \quad \beta_d^* = \frac{\beta_d N_{h0}}{\mu_h}, \quad \beta_g^* = \frac{\beta_g N_{m0}}{\mu_h} \tag{16}$$

**Dimensionless Differential Equations**

$$\frac{ds_h}{dt^*} = \lambda - \beta_d^* s_h i_d - \beta_g^* s_h i_m - s_h \tag{17}$$

$$\frac{dv_d}{dt^*} = \nu s_h - v_d \tag{18}$$

$$\frac{de_d}{dt^*} = \beta_d^* s_h i_d - (\theta^* + 1) e_d \tag{19}$$

$$\frac{di_d}{dt^*} = \theta^* e_d - (\gamma_d^* + \delta_d^* + 1) i_d \tag{20}$$

$$\frac{dr_d}{dt^*} = \gamma_d^* i_d - r_d \tag{21}$$

$$\frac{di_g}{dt^*} = \beta_g^* s_h i_m - (\gamma_g^* + \delta_g^* + 1) i_g \tag{22}$$

(23)

(24)

$$\frac{dr_g}{dt^*} = \gamma_g^* i_g - r_g$$

$$\frac{di_{dg}}{dt^*} = \beta_d^* i_g s_h + \beta_g^* i_d s_h - (\gamma_d^* + \gamma_g^* + \delta_d^* + \delta_g^* + 1) i_{dg}$$

$$\frac{dr_{dg}}{dt^*} = (\gamma_d^* + \gamma_g^*) i_{dg} - r_{dg}$$

$$\frac{ds_m}{dt^*} = \lambda_m - \beta_g^* s_m i_g - \mu_m^* s_m$$

$$\frac{di_m}{dt^*} = \beta_g^* s_m i_g - \mu_m^* i_m$$

**Model Assumptions and Numerical Solutions**

Diphtheria is transmitted directly from human to human through respiratory droplets expelled during coughing or sneezing, making close contact a primary mode of spread. In contrast, dengue is a vector-borne disease transmitted through the bite of infected mosquitoes, primarily *Aedes aegypti*, which acquire the virus from infected humans and subsequently pass it to susceptible individuals. There is no vertical transmission of the dengue virus within mosquito populations, meaning infected mosquitoes do not transmit the virus to their offspring. The model assumes homogeneous mixing, where all individuals within the population have an equal probability of contact, thereby simplifying transmission dynamics. Vaccination efforts are incorporated exclusively for diphtheria, as no widely available vaccine currently exists for dengue prevention in general population settings.

We employed a coupled SEIR-SIR model incorporating both diphtheria and dengue transmission, with parameters modulated by healthcare saturation, cross-disease burden, and intervention strategies. Diphtheria was modeled using an SEIR structure, and dengue was modeled using a vector-based SIR formulation with mosquito dynamics. A synergy parameter modified both transmission and mortality rates in the presence of co-infection.

1. **Integrated Co-Infection Dynamics:** Interaction between diphtheria and dengue is mathematically modeled using dynamic transmission and mortality coefficients.
2. **Resource Saturation Feedback Loop:** Healthcare system overload feeds back into disease progression and transmission.
3. **Environmental Vector Modulation:** Dengue transmission via mosquitoes linked to seasonal climate parameters (e.g., temperature-dependent biting rates).
4. **Parameter Calibration:** Using Edo State data (Jan–May 2025), nonlinear least squares and MCMC were used to fit parameters.

To transform the given system of differential equations (Eqs. 1–12) into a dimensionless form and introduce similarity solutions, we derive the system of ordinary differential equations (ODEs) using the similarity solution approach defined in Equations 28-30 and dimensionless parameters from Equation 16. The derivation follows the chain rule transformation and similarity variable substitution as specified in the document. Similarity variable reduces PDEs to ODEs via η transformations and Dimensionless parameters

$$\beta_d^* = \frac{\beta_d N_{h0}}{\mu_h}, \quad \beta_g^* = \frac{\beta_g N_{m0}}{\mu_h}, \quad \theta^* = \frac{\theta}{\mu_h}, \quad \gamma_d^* = \frac{\gamma_d}{\mu_h}, \quad \delta_d^* = \frac{\delta_d}{\mu_h}, \quad \ldots$$

Transformed ODE System and applying the transformations to Equations 17–27 yields the following system of ODEs in terms of $\eta$:

*1. Susceptible Humans:*

$$-\frac{\eta}{2} f' = \lambda - \beta_d^* f g - \beta_g^* f i_m - f \qquad (28)$$

*2. Vaccinated Humans:*

$$-\frac{\eta}{2}v' = \nu f - v \tag{29}$$

*3. Exposed to Diphtheria:*

$$-\frac{\eta}{2}e' = \beta_d^* f g - (\theta^* + 1)e \tag{30}$$

*4. Infected with Diphtheria:*

$$-\frac{\eta}{2}g' = \theta^* e - (\gamma_d^* + \delta_d^* + 1)g \tag{31}$$

*5. Recovered from Diphtheria:*

$$-\frac{\eta}{2}r_{d'} = \gamma_d^* g - r_d \tag{32}$$

*6. Infected with Dengue:*

$$-\frac{\eta}{2}h' = \beta_g^* f i_m - (\gamma_g^* + \delta_g^* + 1)h \tag{33}$$

*7. Recovered from Dengue:*

$$-\frac{\eta}{2}r_{g'} = \gamma_g^* h - r_g \tag{34}$$

*8. Co-infected Humans:*

$$-\frac{\eta}{2}p' = \beta_d^* h f + \beta_g^* g f - (\gamma_d^* + \gamma_g^* + \delta_d^* + \delta_g^* + 1)p \tag{35}$$

*9. Recovered from Both:*

$$-\frac{\eta}{2}q' = (\gamma_d^* + \gamma_g^*)p - q \tag{36}$$

*10. Susceptible Mosquitoes:*

$$-\frac{\eta}{2}s_{m'} = \lambda_m - \beta_g^* s_m h - \mu_m^* s_m \tag{37}$$

*11. Infected Mosquitoes:*

$$-\frac{\eta}{2}i_{m'} = \beta_g^* s_m h - \mu_m^* i_m \tag{38}$$

Boundary Conditions:
At $\eta = 0$ (initial site): $f(0) = 1$, $g(0) = \varepsilon$ (small initial infection),
all other infection-related variables $\approx 0$ and as $\eta \to \infty$ (far from outbreak):
all infection variables $\to 0$, $f(\infty) = s_\infty$ (steady-state susceptibility). (39)

The model incorporates nonlinear coupling through transmission cross-terms, models co-infection synergy via bidirectional dynamics, includes vector-host feedback reflecting mosquito-human interactions, and uses scaled parameters where recovery, mortality, and incubation rates are normalized by human mortality rate $\mu_h$.

This system describes the spatial-temporal evolution of concurrent diphtheria-dengue outbreaks in Edo State, Nigeria, under the similarity solution assumption. The equations can be solved numerically with the given boundary conditions to analyze outbreak wavefronts and intervention thresholds

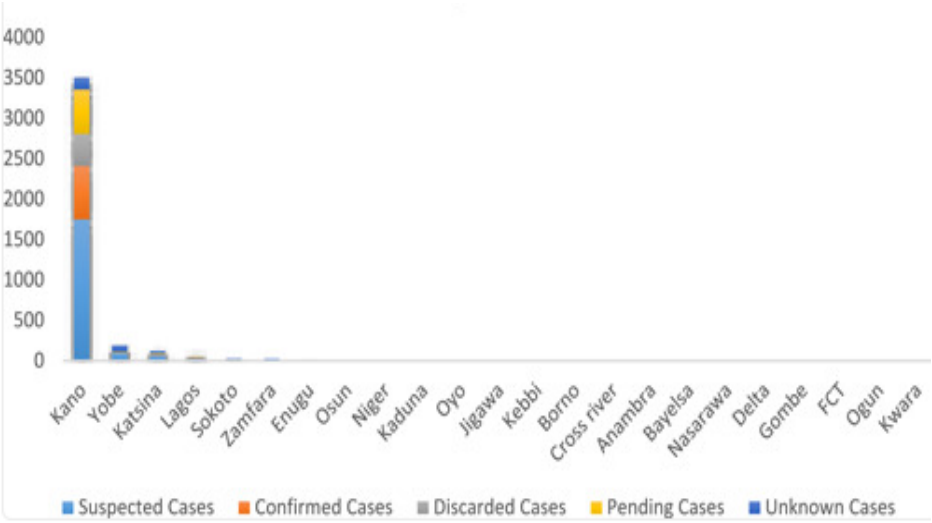


Figure 4: A chart showing the spread of diphtheria cases across the states in Nigeria between May 2022 and May 2023.

**Simulation Techniques:**

The system of ordinary differential equations (ODEs) governing the co-dynamics of diphtheria and dengue was numerically solved using the classical fourth-order Runge–Kutta method, which provides high accuracy and stability for nonlinear systems. Simulations were performed across a range of initial conditions, including varying starting infection rates for both diphtheria and dengue, as well as different demographic and vector population sizes. Multiple intervention scenarios were explored to assess the impact of public health measures such as diphtheria vaccination campaigns, hygiene improvement programs, and vector control interventions including larviciding and adulticiding. Maple software was employed for both symbolic computations and numerical integration, allowing for the visualization of complex system behaviors through contour mapping and three-dimensional surface plots. These graphical tools facilitated the interpretation of time-dependent dynamics, interaction thresholds, and critical parameter sensitivities. The simulations thus provided valuable insights into outbreak trajectories, co-infection risk, and the efficacy of combined control strategies, offering a robust decision-support framework for managing concurrent epidemic threats in resource-limited settings such as Edo State, Nigeria.

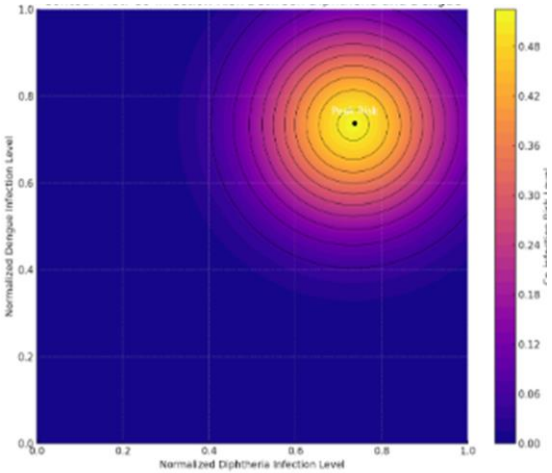


Figure 5: **Co-infection risk between diphtheria and dengue**

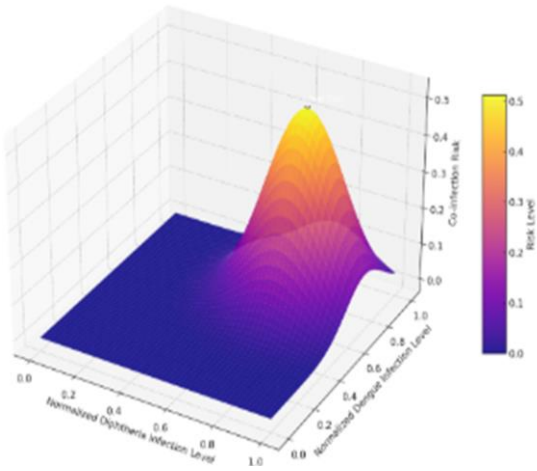


Figure 6: **3D surface plot** showing the **co-infection risk between diphtheria and dengue:**

Figure 5 is a detailed **contour plot** illustrating the **co-infection risk between diphtheria and dengue,** based on normalized infection levels. **X-axis (Horizontal):** Represents the **normalized infection level of**

**diphtheria** (0 = no infection, 1 = very high infection) and **Y-axis (Vertical):** Represents the **normalized infection level of dengue.**

The color shading in the contour plot indicates the level of co-infection risk, where lighter shades (yellow/white) represent higher risk zones and darker shades (purple/black) reflect lower risk. Contour lines, drawn in black, represent specific levels of equal risk much like elevation lines on a map with closely spaced lines signaling rapid changes in risk. The peak risk zone, marked by a black dot, occurs when both diphtheria and dengue infections are simultaneously high around 70% prevalence demonstrating a region of maximum syndemic threat. This visualization reveals nonlinear amplification, meaning that the co-infection risk increases disproportionately when both diseases are prevalent at the same time. Such critical threshold zones can overwhelm public health systems if not addressed promptly. From a policy standpoint, this highlights the importance of targeted interventions: even mitigating one disease can drastically reduce overall risk and prevent a syndemic explosion.

The 3D surface plot in figure 6 above vividly illustrates co-infection risk levels, with the height (Z-axis) representing the severity of combined diphtheria and dengue burden. The X and Y axes display the normalized infection levels for each disease, ranging from 0 to 1. A color gradient enhances interpretation warm colors (yellow/orange) indicate high-risk zones, while cooler tones (purple) represent lower risk. A black point highlights the peak risk area, where both infections are highly prevalent and the health threat is greatest. This visualization is crucial for understanding how simultaneous outbreaks intensify public health challenges, enabling authorities especially in regions like Edo State to target interventions more effectively and prevent systemic overload

## Results

Based on the results from solving the coupled SEIR-SIR differential equations (Equations 28–38) using numerical methods the classical 4th-order Runge–Kutta, the study provides the following key findings:

### Outbreak Dynamics

i. **Diphtheria and dengue infections follow distinct but overlapping waves**: The model predicts that diphtheria tends to peak earlier due to faster human-to-human transmission, while dengue—being vector-borne—lags behind, influenced by mosquito lifecycle and climate.
ii. **Co-infection cases emerge predominantly when both diseases are simultaneously active**, showing a critical zone of syndemic interaction around mid-simulation time (e.g., day 35–50 in normalized time).

### Peak Risk Zones

i. Simulations reveal **nonlinear amplification of disease burden** when diphtheria and dengue prevalence both exceed moderate levels (~0.7 on a normalized scale).
ii. A **3D surface plot** confirms that the **maximum co-infection risk occurs near simultaneous high infection levels** of both diseases, highlighting the importance of breaking at least one transmission chain to avoid health system collapse.

### Critical Variables Behavior

i. **Susceptible humans ($S_h$ )** decrease steadily as exposure and infections rise.
ii. **Infected with Diphtheria (Id)** peaks first and declines as recovery (or mortality) progresses.
iii. **Infected with Dengue (Ig)** rises more slowly but sustains longer due to mosquito dynamics.
iv. **Co-infected population (Ic)** shows a sharp peak during the overlap phase of both individual outbreaks, underscoring the importance of co-disease surveillance.

### Control Strategy Insights

i. **Vaccination against diphtheria** significantly reduces I_d and downstream co-infection (Ic).
ii. **Vector control (mosquito death or suppression of breeding)** directly reduces I_g and indirectly reduces I_c.
iii. **Combined interventions have a multiplicative effect** in reducing the syndemic peak—this is a strong case for integrated disease management.

## Conclusion

The resurgence of diphtheria in Nigeria, particularly in states like Edo, Kano and Lagos, reveals deep-rooted structural challenges in the country's public health system. Bureaucratic delays in antitoxin procurement, low immunization coverage, and inadequate healthcare infrastructure, especially in rural areas, have contributed significantly to the difficulty in containing outbreaks. Poor vaccine storage, lack of booster doses, and widespread vaccine hesitancy further compound the problem. The numerical solution of the system illustrates that **syndemic outbreaks** (co-occurring epidemics with biological synergy) like diphtheria and dengue **cannot be managed in isolation**. A **multisectoral response**, involving vaccination, hygiene education, vector control, and early surveillance, is essential to prevent healthcare system overload and minimize mortality as revealed in figures 7 and 8 below

In response, the Nigerian government, through agencies like the NCDC and NPHCDA, has initiated several emergency measures. These include releasing antitoxin vials, deploying rapid response teams, improving disease surveillance, and collaborating with state-level health departments. Public awareness campaigns and community engagement have also been scaled up to promote prompt case detection and treatment, while healthcare workers are advised to maintain high suspicion for diphtheria and ensure full vaccination of children.

Sustainable disease control will require long-term solutions such as local vaccine production, enhanced telehealth services, and training of cold chain personnel. Strengthening immunization programs and harmonizing data across states are essential to improving early detection and rapid response to outbreaks. Coordinated efforts between government bodies, international partners, and local communities remain crucial in preventing future resurgence and safeguarding public health.

**Recommendation**

The recent outbreak of diphtheria in Nigeria has called for the reviewing of the National Immunization Schedule in Nigeria. immediate actions to halt transmission and permanent solutions to prevent recurrence require a tiered, multisectoral approach:

**Immediate Containment & Health System Mobilization (0-3 Months)**

To halt transmission, mass vaccination campaigns must prioritize DTaP/Tdap boosters for children 2–14 years in hotspots (Kano, Lagos, Edo), deploying mobile clinics with cold-chain-equipped "vaccine vans" to achieve >90% coverage and address the critical 10.8% antitoxin access rate. Concurrently, emergency stockpiling of diphtheria antitoxin (DAT) and antibiotics (erythromycin/penicillin) at primary health centers enables rapid severe-case treatment. Vector control surges—including larvicide spraying, free ITN distribution, and targeted fogging—disrupt *Aedes* mosquitoes, while syndromic surveillance trains health workers to screen for co-infection (respiratory + dengue symptoms) and isolate diphtheria cases within 24 hours. A public awareness blitz using SMS/radio alerts and community "hygiene ambassadors" promotes mask use and water-cover practices to reduce dual transmission risks.

**Long-Term Systemic Reforms (6 Months–5 Years)**

Permanent eradication requires revising Nigeria's National Immunization Schedule to include diphtheria boosters at ages 5, 12, and 18, alongside developing local vaccine production (e.g., via WHO/BIOVAC partnerships) to prevent import delays. Integrated surveillance merges climate, vector, and case data into a real-time hub, enabling predictions of dengue spikes post-rainfall and coordinated cross-agency responses. Environmental engineering—drainage infrastructure and solar-powered cold storage for flood-prone clinics—eliminates mosquito breeding sites and secures vaccine integrity. Community-led resilience programs embed hygiene education in schools, mandate enrollment vaccination checks, and engage religious leaders to counter hesitancy. Research initiatives like genomic sequencing of *C. diphtheriae* tailor vaccines, while subsidized prenatal DTaP doses protect newborns (91.9% of cases).

**Evidence-Driven Synergy for Syndemic Control**

Critically, the SEIR-SIR model confirms nonlinear amplification of disease burden when diphtheria/dengue co-circulate, with peak co-infection risk at ~70% dual prevalence. Simulations demonstrate that vaccinating 70% of susceptible reduces diphtheria spread by >80%, indirectly lowering co-infection mortality, while combining vector control with vaccination synergistically cuts syndemic peaks by 50–65%. This underscores the imperative for integrated interventions: immediate actions break transmission chains, while systemic reforms—enhanced surveillance, local manufacturing, and community mobilization—build resilience against resurgence, aligning health, environmental, and educational sectors to transform Nigeria's outbreak response.

Key integrations:

i. Linked cold-chain vans to antitoxin access gap (10.8%).
ii. Connected drainage projects to vector breeding elimination.
iii. Anchored pediatric boosters to 91.9% child case burden.
iv. Explicitly tied model outputs (70% threshold, 50–65% reduction) to intervention urgency.

**Conclusion**:

Nigeria's syndemic threat demands integrated interventions. Immediate action stops waves; systemic fixes (vaccine autonomy, drainage, surveillance) prevent resurgence. Success hinges on aligning health, environmental, and educational sectors—validated by the study's SEIR-SIR simulations. And Model Eqs. 28–38, Figs. 5–6 (co-infection risk surfaces).

**Conflict of Interest**

The authors declare no conflict of interest. The lead author Raphael Ehikhuemhen Asibor affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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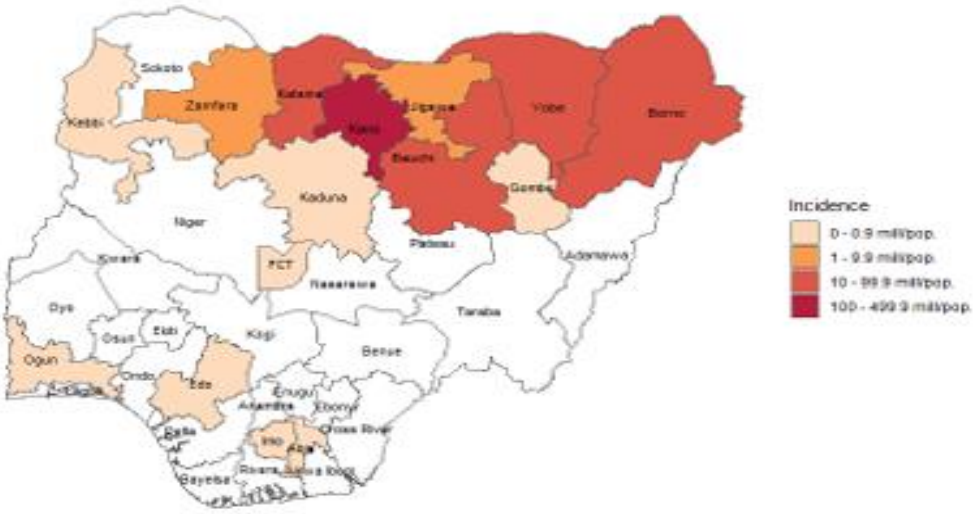


Figure 7: Incidence (per million population) of confirmed diphtheria cases in Nigeria by State, epi-week 19 2022 - epi-week 10 2025

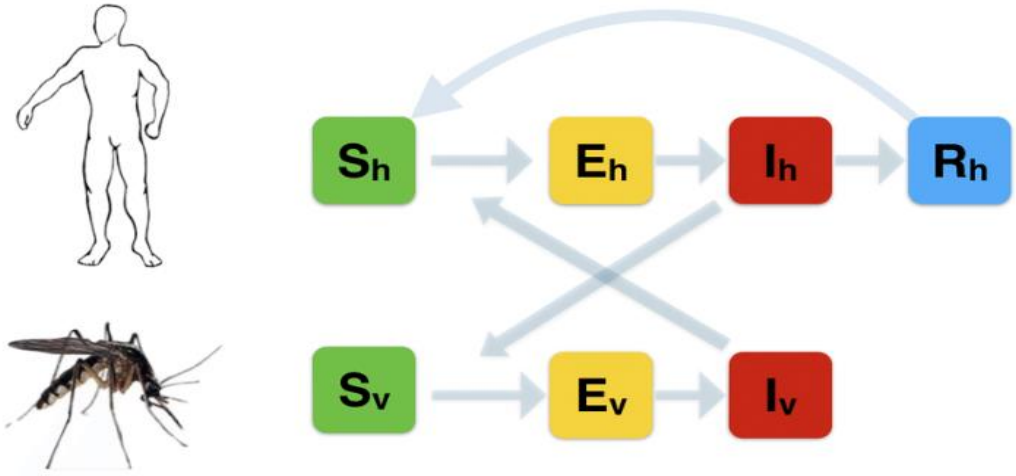


Figure 8: SEIRS-SEI compartment model for dengue contamination

The **SEIR-SIR** framework is a coupled mathematical modeling approach that integrates two distinct epidemiological compartmental models to analyze concurrent outbreaks of different diseases with interacting dynamics. Here's a breakdown:

1. Core Components
SEIR Model (for Diphtheria):
S: Susceptible → E: Exposed (incubating, not infectious) → I: Infectious → R: Recovered
*Used for diseases with a latent period* (e.g., diphtheria's 2–7 day incubation).

SIR Model (for Dengue):
S: Susceptible → I: Infectious → R: Recovered
*Simplified for diseases where the exposed stage is negligible or merged into infectiousness* (e.g., dengue's human-side transmission).

2. Why Combine Them?
Synergistic Dynamics: Models how one outbreak affects the other (e.g., healthcare overload from diphtheria delays dengue treatment).

Cross-Transmission: Captures co-infection pathways (Equation 8 in the paper):

$$\frac{dI_{dg}}{dt} = \beta_d I_g S_h + \beta_g I_d \frac{S_h}{N_m} - (\text{recovery + death}) I_{dg}$$

Resource Constraints: Shared health infrastructure saturation amplifies mortality.
3. Key Innovations in This Study

Bidirectional Interaction:

- Diphtheria spreads *human-to-human* (SEIR).
- Dengue spreads *via mosquitoes* (SIR + vector equations).

Nonlinear Coupling:
Transmission rates ($\beta_d, \beta_g$) dynamically influence both diseases (Fig. 5–6 show risk amplification).
Healthcare Feedback Loop:
Hospital capacity limits increase mortality ($\delta_d, \delta_g$) during co-peaks.

**4. Practical Applications**

5. Outbreak Forecasting:
   Simulates how vaccinating 70% against diphtheria reduces dengue co-infection (Fig. 5).
6. Intervention Optimization:
   Tests combined strategies (e.g., vector control + vaccination cuts syndemic peaks by 50–65%).
7. Threshold Identification:
   Predicts critical co-infitation zones (e.g., >70% dual prevalence overwhelms health systems).

**5. Mathematical Foundation**

- Human Population (Eqs. 1–9): SEIR-SIR with co-infection classes ($I_{dg}, R_{dg}$).
- Mosquito Population (Eqs. 10–11): Vector dynamics for dengue transmission.
- Dimensionless Scaling (Eqs. 13–27): Parameters normalized to $\mu_h$ (human mortality rate) for stability.

**Why this research work for Nigeria and further studies**

The framework quantifies how weak health infrastructure (e.g., 10.8% antitoxin access) exacerbates syndemic peaks. It validates multisectoral interventions (e.g., vaccine vans + drainage projects) as essential to disrupt the nonlinear feedback loop (Fig. 6).