

Research Article

Mathematical Analysis of the Role of Treatment and Vaccination in the Management of the HIV/AIDS and Pneumococcal Pneumonia Co-Infection

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Received 10 August 2024; Accepted 18 December 2024

Academic Editor: Nian-Sheng Tang

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Concomitant infections by two or more pathogens are on upsurge and among these is the interplay between HIV/AIDS and pneumococcal pneumonia infections. A mathematical co-infection model that fronts vaccination and treatment against pneumococcal pneumonia and antiretroviral therapy for HIV/AIDS in the management of the co-infection burden is presented. The model is also extended to include optimal control plans, in line with protection, early detection, and treatment of both HIV/AIDS and pneumococcal pneumonia. Co-infection model analysis manifests that the solutions are positive and bounded, and the disease equilibria stabilities are established in reference to the computed effective reproduction numbers. Sensitivity analysis indicated that infection rate parameters are by far the most influential in the co-infection escalation, whereas treatment and vaccination associated parameters have inhibiting effect towards the co-infection. Numerical simulations reveal that treatment and vaccination interventions are important in co-infection reduction but not sufficient for co-infection elimination. Further analysis indicates that, in addition to treatment and vaccination, adopting all optimal control plans can be a concrete start to co-infection elimination.

Keywords: co-infection; effective reproduction number; HIV/AIDS; optimal control; pneumonia; sensitivity analysis; vaccination

1. Introduction

The co-infection between human immunodeficiency virus (HIV) and pneumococcal pneumonia may present either as a pneumonia pre-existing pathogen which is brought to the fore by introduction of HIV or may appear in the form of new pneumonia infection acquired secondarily due to a compromised immune system by HIV infection.

Bacterial pneumonia, mainly pneumococcal pneumonia, is a persistent cause of fatality and morbidity in individuals suffering from HIV and exacerbates the progression rate from HIV to acquired immunodeficiency syndrome (AIDS) in individuals infected with both HIV and *Streptococcus* [1, 2]. Co-infection with HIV/AIDS and *Streptococcus* is recurrent in sub-Saharan Africa where

HIV/AIDS infection is prevalent, and studies have shown that prevention of *Streptococcus* by vaccination with pneumococcal conjugate vaccines is a promising approach [1]. The possibility of pneumococcal pneumonia is 30 to 100 times higher in individuals with HIV infection in comparison to age-matched controls without pneumococcal pneumonia. Moreover, the case fatality rate with pneumococcal pneumonia is at least 8% higher in HIV-infected individuals [3, 4].

Mathematical models have been decisive in provision of basic frameworks in the understanding of transmission dynamics of communicable diseases. In the development of this paper, a series of literature has been reviewed and conclusively HIV/AIDS-pneumonia co-infection models are very rare compared to their single infection models.

A mathematical model of bacterial pneumonia with inclusion of carriers, temporary immunity, and treatment conducted by the authors of [5] emphasized the role of treatment and isolation where possible in eradication of pneumonia. In [6], a model that incorporated the effects of treatment and the possibility of wrong treatment due to similar symptoms was considered and the study emphasized treatment at critical state and bolstering of natural immunity to completely neutralize pneumonia in children. A mathematical model developed in [7] shows that prevention through health education, treatment, and screening are effective intervention strategies to reduce pneumonia disease.

An HIV model that incorporates prevention strategies, such as use of condoms, ARV therapy, voluntary counseling, and screening, was proposed in [8]. The results revealed that reducing sex partners and increasing condom usage had a huge role in decreasing the transmission of HIV infection. A formulation of an HIV/AIDS model incorporating gradual change of behavior with varying force of HIV infection for the adults was analyzed [9]. Their analysis indicated that the significant decrease in HIV prevalence in Uganda at the start of 1990s would be feasible by reducing the HIV infection force.

In the study [10], it was realized that unaware HIV infected individuals imposed a significant cost on the community. Meanwhile, the research in [11] suggested that the burden of HIV/AIDS could be mitigated by decreasing the effective contact rate with infected individuals, controlling the transition rate of infected individuals to the AIDS class, and most importantly, by isolating susceptible individuals early to reduce the incidence rate.

Regarding the study by the authors of [12], treatment against pneumonia and antiretroviral therapy (ART) for HIV/AIDS would reduce the rate of the interplay between the two diseases. The model developed in [13] showed that merging therapy against HIV/AIDS, vaccination, and treatment against pneumonia were vital in disrupting the HIV/AIDS and pneumonia co-epidemic burden. It is noted that in [13] that pneumonia vaccination is considered at recruitment stage and the pneumonia carrier population is not included in the model development, yet carriers are at the fore of transmission of pneumonia as indicated in [5, 12, 14]. In [15], a compartmental model on the co-infection of pneumonia and HIV/AIDS with optimal control strategies was formulated using the system of ordinary differential equations. The study incorporated pneumonia protection, pneumonia vaccination, HIV/AIDS protection by using condom, pneumonia treatment, and HIV/AIDS treatment measures. The results of the study emphasize simultaneous application of all control strategies in order to decrease the HIV/AIDS and pneumonia co-infection transmission mechanisms. This study however does not extend pneumonia vaccination to HIV/AIDS-infected individuals, and the role played by pneumonia carriers is not investigated. Additionally, the pneumonia submodel is based on mass action principle compared to a nonlinear incidence applied in the current study. The model that incorporates prevention, screening, and treatment efforts for both HIV/AIDS and pneumonia was

developed and analyzed in [14]. The results portray that prevention and treatment of both diseases were instrumental in averting the biggest number of co-infected individuals. Models studied in [12, 14] did not take into account of the role of pneumococcal vaccines in the transmission and control dynamics of HIV/AIDS and pneumonia co-infection.

This study is therefore designed to investigate the influence of HIV/AIDS therapy (ART), pneumococcal pneumonia treatment, and vaccination in the management of HIV/AIDS and pneumococcal pneumonia co-infection. The pneumonia vaccination strategy is intended for the susceptible population, pneumonia-recovered individuals, HIV/AIDS-infected individuals, and individuals under ART. In addition to therapy/treatment and vaccination, optimal control theory is applied to evaluate the role of protection against HIV and pneumococcal pneumonia and early detection and treatment of both infections. The contribution of pneumococcal pneumonia carriers in the transmission dynamics of the co-infection burden is also investigated.

2. Model Formulation

The model is comprised of 12 compartments, namely, susceptible individuals at a threat of getting infected with either HIV or pneumococcal pneumonia ($S(t)$), pneumococcal pneumonia carriers who have no symptoms of the disease and can spread it ($C(t)$), pneumococcal pneumonia-infected individuals, with symptoms of the disease ($P(t)$), pneumococcal pneumonia-recovered individuals who are free of the disease after treatment ($R(t)$), pneumococcal pneumonia-vaccinated individuals but are HIV negative ($V_1(t)$), HIV-infected individuals with no signs and symptoms of AIDS ($H(t)$), HIV-infected individuals with AIDS signs and symptoms ($A(t)$), HIV mono-infected individuals on ART ($T_1(t)$), HIV and pneumococcal pneumonia co-infected individuals ($C_1(t)$), AIDS and pneumococcal pneumonia co-infected individuals ($C_2(t)$), dually infected individuals on treatment for both HIV/AIDS and pneumococcal pneumonia ($T_2(t)$), and pneumococcal pneumonia-vaccinated individuals but on HIV therapy ($V_2(t)$). The sum of all state variables gives the total population as $N(t) = S(t) + P(t) + C(t) + R(t) + V_1(t) + H(t) + A(t) + T_1(t) + C_1(t) + C_2(t) + T_2(t) + V_2(t)$.

2.1. Assumptions of the Model. In the formulation of the co-infection model, it is assumed that

- i. HIV and pneumococcal pneumonia-infected classes are considered susceptible to each other.
- ii. The susceptible compartment consists of the population at a threat of either contracting HIV or pneumococcal pneumonia disease and it is increased by constant recruitment rate Λ .
- iii. Individuals in compartments $T_1(t)$, $T_2(t)$, and $V_2(t)$ are not involved in transmission dynamics because ART decreases the viral load, hence reducing the transmissibility chance. This implies that there is

complete compliancy to medication, and individuals do not default on ART.

- iv. Pneumococcal conjugate vaccines provide long life immunity in presence of booster doses and a negligible class does not respond to the vaccine.

2.2. Parameters of the Co-Infection Model. Parameters used in the co-infection model and their meaning as follows (Table 1):

2.2.1. Compartmental Diagram. A flow diagram for HIV/AIDS and pneumococcal pneumonia co-infection as follows (Figure 1):

2.3. Equations of the Co-Infection Model. Applying the assumptions, parameters given in Table 1, and the flow diagram in Figure 1, the model is derived as a system of 12 first-order nonlinear ordinary differential equations.

$$\begin{aligned}
 \frac{dS(t)}{dt} &= \Lambda + \gamma R(t) - (\alpha_1(t) + \alpha_2(t) + \varphi_1 + \mu)S(t), \\
 \frac{dC(t)}{dt} &= \xi \alpha_1(t)S(t) - (\alpha_2 + \beta + \pi + \mu)C(t), \\
 \frac{dP(t)}{dt} &= (1 - \xi)\alpha_1 S(t) + \beta C(t) - (\alpha_2 + \epsilon + \mu + \nu_1)P(t), \\
 \frac{dR(t)}{dt} &= \epsilon I_P(t) + \pi C(t) - (\alpha_2 + \gamma + \varphi_2 + \mu)R(t), \\
 \frac{dV_1}{dt} &= \varphi_1 S(t) + \varphi_2 R(t) - (\alpha_2 + \mu)V_1(t), \\
 \frac{dH(t)}{dt} &= \alpha_2 S(t) + \alpha_2 R(t) + \alpha_2 V_1(t) - (\alpha_1 + \tau_1 + \lambda_1 + \sigma_1 + \mu)H(t), \\
 \frac{dA(t)}{dt} &= \lambda_1 H(t) - (\alpha_1 + \tau_2 + \sigma_2 + \mu + \nu_2)A(t), \\
 \frac{dT_1(t)}{dt} &= \tau_1 H(t) + \tau_2 A(t) - (\sigma_3 + \mu)T_1(t), \\
 \frac{dC_1(t)}{dt} &= \alpha_2 (C(t) + P(t)) + \alpha_1 H(t) - (\lambda_2 + \tau_3 + \mu + \nu_1)C_1(t), \\
 \frac{dC_2(t)}{dt} &= \alpha_1 A(t) + \lambda_2 C_1(t) - (\tau_4 + \mu + \nu)C_2(t), \\
 \frac{dT_2(t)}{dt} &= \tau_3 C_1(t) + \tau_4 C_2(t) - (\sigma_4 + \mu)T_2(t), \\
 \frac{dV_2(t)}{dt} &= \sigma_1 H(t) + \sigma_2 A(t) + \sigma_3 T_1(t) + \sigma_4 T_2(t) - \mu V_2(t),
 \end{aligned} \tag{1}$$

with initial conditions $S(0) \geq 0, C(0) \geq 0, P(0) \geq 0, R(0) \geq 0, V_1(0) \geq 0, H(0) \geq 0, T_1(0) \geq 0, A(0) > 0, C_1(0) \geq 0, C_2(0) \geq 0, T_2(0) \geq 0$, and $V_2(0) \geq 0$.

The total of all equations in system equation (1) is

$$\frac{dN}{dt} = \Lambda - \mu N - (\nu_1(P + C_1) + \nu_2 A + \nu C_2). \tag{2}$$

The pneumococcal pneumonia force of infection is defined as

$$\alpha_1(t) = \frac{c\rho(P + \omega C + \theta_1 C_1 + \theta_2 C_2)}{N(t)}, \tag{3}$$

where $\theta_2 > \theta_1$ are modification parameters indicating increased infectivity as a result of dual infection. The HIV force of infection is defined as

$$\alpha_2(t) = \frac{k\eta(H + a_1 C_1 + a_2 A + a_3 C_2)}{N(t)}, \tag{4}$$

TABLE 1: Parameters used in the co-infection model and their meaning.

Parameter	Meaning
Λ	Constant recruitment rate into susceptible population
μ	Per capita natural death rate of individuals across all compartments
ν_1	Per capita death rate due to pneumococcal pneumonia
ν_2	Per capita AIDS-related mortality rate
ν	Per capita AIDS and pneumococcal pneumonia co-infection-induced death rate
λ_1	Transfer rate from compartment H to compartment A in absence of therapy
λ_2	Transfer rate from C_1 compartment to C_2 compartment in absence of treatment
τ_1	Treatment rate of HIV-infected individuals
τ_2	Treatment rate of AIDS patients
τ_3	Treatment rate of HIV and pneumococcal pneumonia co-infected individuals
τ_4	Treatment rate of AIDS and pneumococcal pneumonia co-infected individuals
β	Rate at which pneumococcal pneumonia carriers become symptomatic
ξ	Fraction of susceptible population that joins the pneumococcal pneumonia carrier compartment
π	Recovery rate of pneumococcal pneumonia carriers
γ	Rate at which pneumococcal pneumonia-recovered individuals join the susceptible class
ϵ	Recovery rate of pneumococcal pneumonia-infected individuals
ρ	Possibility that a contact is sufficient to cause a pneumococcal pneumonia infection
c	Mean contact rate with individuals infected with <i>Streptococcus</i>
ω	Coefficient of transmission for pneumococcal pneumonia carriers
η	HIV transmission probability upon contact with an HIV-infected individual
k	Mean contact rate with HIV-infected individuals
φ_1	Vaccination rate of pneumococcal pneumonia susceptibles
φ_2	Rate of vaccination of pneumococcal pneumonia-recovered individuals
σ_1	Rate of vaccination against pneumococcal pneumonia in $H(t)$ class
σ_2	Rate of vaccination against pneumococcal pneumonia in $A(t)$ class
σ_3	Rate of vaccination against pneumococcal pneumonia in $T_1(t)$ class
σ_4	Rate of vaccination against pneumococcal pneumonia in $T_2(t)$ class

where $a_3 > a_2 > a_1$ are parameter alterations implying that the infectious rate of HIV of C_2 compartment is higher than that of compartments A and C_1 as a result of increased viral load.

3. Analysis of the Model

3.1. Basic Properties of the Co-Infection Model. In this subsection, the positivity and boundedness of the solutions of model equation (1) which are vital in the proofs of stability are investigated. We show that the state variables of model equation (1) are positive and their corresponding solutions stay positive with positive initial conditions in the feasible region

$$\Omega = \left\{ (S, P, C, R, V_1, H, A, T_1, C_1, C_2, T_2, V_2) \in \mathbb{R}_+^{12}, N \leq \frac{\Lambda}{\mu} \right\}. \quad (5)$$

It is crucial to show that each state variable defined with non-negative initial conditions remains positive for all time $t > 0$ in the feasible region given in equation (5) and model equation (1) is mathematically and epidemiologically meaningful.

Lemma 1. *The state solutions $S(t), P(t), C(t), R(t), V_1(t), H(t), A(t), T_1(t), C_1(t), C_2(t), T_2(t)$, and $V_2(t)$ of system equation (1) are positive for $t \geq 0$.*

Proof 1. Let the initial state solutions of all equations in system equation (1) be positive. The task is to prove that the solution of $S(t)$ is positive. By contradiction, assume that there is a first time t_1 such that $S(t_1) = 0, S'(t_1) < 0$ and $S(t) > 0, C(t) > 0, P(t) > 0, R(t) > 0, V_1(0), H(t) > 0, A(t) > 0, T_1(t) > 0, C_1(t) > 0, C_2(t) > 0, T_2(t) > 0, V_2(0) > 0$ for $0 < t < t_1$. From equation one of system equation (1),

$$\begin{aligned} \frac{dS(t_1)}{dt} &= \Lambda + \gamma R(t_1) - (\alpha_1(t_1) + \alpha_2(t_1) + \varphi_1 + \mu)S(t_1) \\ &= \Lambda + \gamma R(t_1) > 0, \end{aligned} \quad (6)$$

which is a contradicting and consequently, $S(t)$ remains positive. In the same way, it can be proved that the other state variables are positive. Therefore, the solutions of system equation (1) are positive for $t \geq 0$. $\square$

Lemma 2. *All solutions of equation (1) are bounded and eventually enter and remain in the region Ω provided in equation (3).*

Proof 2. By Lemma 1, all the state variables are positive, and hence when there is no death from pneumococcal pneumonia, HIV/AIDS, and their co-infection, equation (2) gives the inequality

$$\frac{dN(t)}{dt} + \mu N(t) \leq \Lambda. \quad (7) \quad \square$$

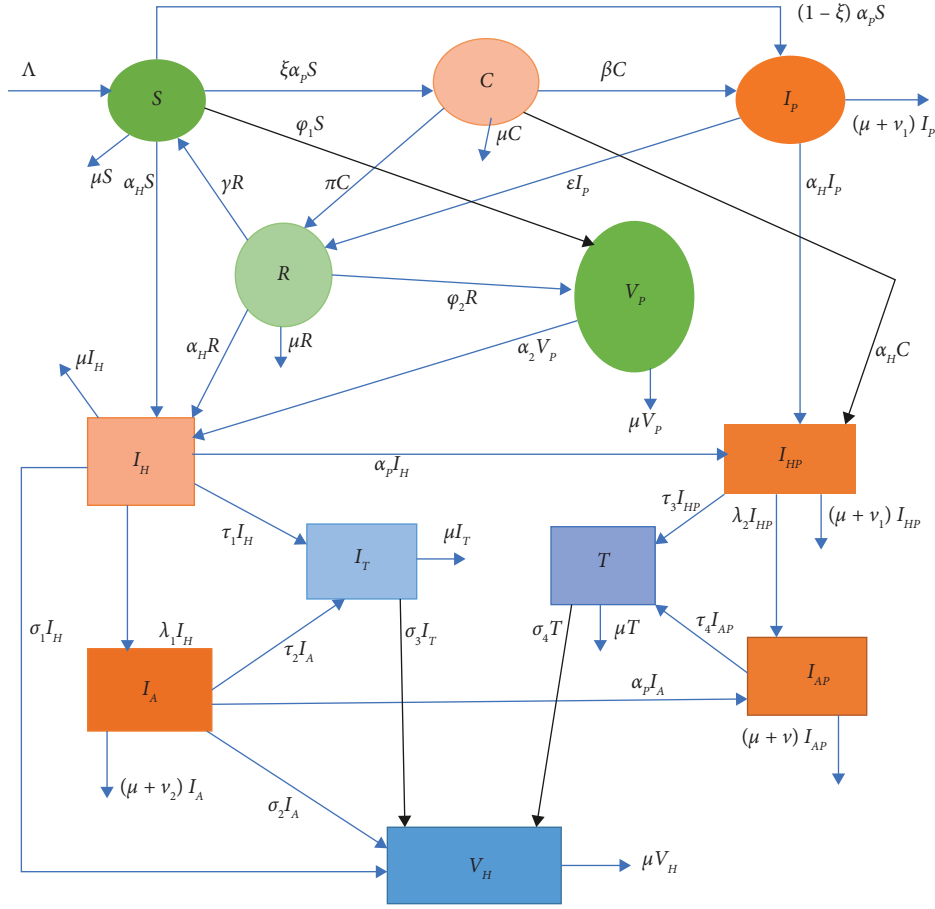


FIGURE 1: A flow diagram for HIV/AIDS and pneumococcal pneumonia co-infection.

Given the initial condition $N(0) = N_0$, integrate equation (7) such that

$$N(t) \leq \frac{\Lambda}{\mu} + \left(N_0 - \frac{\Lambda}{\mu}\right)e^{-\mu t}. \quad (8)$$

From inequality equation (8), it is shown that as $t \rightarrow \infty$

$$N(t) \leq \frac{\Lambda}{\mu}. \quad (9)$$

The inequality equation (9) is the threshold population level and hence, the feasible solution set of system equation (1) enters and is contained in the region equation (5).

Therefore, from Lemmas 1 and 2, it is concluded that the model equation (1) is epidemiologically and mathematically well posed. It is necessary to analyze pneumococcal pneumonia and HIV/AIDS submodels first since the dynamics of the co-infection model is influenced by that of its constituent submodels.

3.2. Analysis of Pneumococcal Pneumonia Submodel. The following pneumococcal pneumonia submodel is obtained when $H(t) = A(t) = T_1(t) = C_1(t) = C_2(t) = T_2(t) = V_2(t) = 0$ such that

$$\frac{dS(t)}{dt} = \Lambda + \gamma R(t) - (\alpha_1 + \varphi_1 + \mu)S(t),$$

$$\frac{dC(t)}{dt} = \xi \alpha_1 S(t) - (\beta + \pi + \mu)C(t),$$

$$\frac{dP(t)}{dt} = (1 - \xi)\alpha_1 S(t) + \beta C(t) - (\epsilon + v_p + \mu)P(t), \quad (10)$$

$$\frac{dR(t)}{dt} = \pi C(t) + \epsilon P(t) - (\gamma + \varphi_2 + \mu)R(t),$$

$$\frac{dV_1(t)}{dt} = \varphi_1 S(t) + \varphi_2 R(t) - \mu V_1(t),$$

where $N(t) = S(t) + P(t) + C(t) + R(t) + V_1(t)$ is the total population and $\alpha_1 = \rho c(\omega C + P/N)$ is the pneumococcal pneumonia force of infection. The feasible region for the pneumococcal pneumonia submodel equation (10) is $\Omega_P = \{(S(t), C(t), P(t), R(t), V_1(t)) \in \mathbb{R}_+^5 : N(t) \leq \Lambda/\mu\}$ which is positively invariant and attracting, that is, the solution starting in Ω_P will remain in Ω_P for all $t \geq 0$.

3.2.1. Pneumococcal Pneumonia-Free Equilibrium Point. The pneumococcal pneumonia-free equilibrium of model equation (10) describes the model in absence of

Streptococcus. Thus, with $C = P = 0$ and $R = 0$, we get $S = \Lambda / \varphi_1 + \mu$ and $V_1 = (\varphi_1 \Lambda) / (\mu(\varphi_1 + \mu))$. Thus, the pneumococcal pneumonia-free equilibrium is $E_{0P} = (S_0, C_0, P_0, R_0, V_{10}) = ((\Lambda / \varphi_1 + \mu), 0, 0, 0, (\varphi_1 \Lambda) / (\mu(\varphi_1 + \mu)))$.

3.2.2. Pneumococcal Pneumonia Effective Reproduction Number. The threshold parameter that directs the transmission of pneumococcal pneumonia, termed as the effective reproduction number, is worked out. It is defined as the number of secondary pneumococcal pneumonia infections due to one carrier/infected individual in presence of control interventions. It is derived by the next generation matrix approach [16, 17], and mathematically, it is the spectral radius of the next generation matrix.

From system equation (10), we use $\mathcal{F}$ for a matrix of new pneumococcal pneumonia infection terms and $\mathcal{V}$ for the matrix of the remaining pneumococcal pneumonia progress terms to get

$$\mathcal{F} = \begin{bmatrix} \xi \alpha_1 S \\ (1 - \xi) \alpha_1 S \end{bmatrix} \text{ and } \mathcal{V} = \begin{bmatrix} k_1 C \\ -\beta C + k_2 P \end{bmatrix}, \quad (11)$$

where $k_1 = (\beta + \pi + \mu)$ and $k_2 = (\epsilon + \nu_1 + \mu)$.

Evaluating the Jacobian matrices of $\mathcal{F}$ and $\mathcal{V}$ at pneumococcal pneumonia-free equilibrium, the matrices F and V are obtained as

$$F = \begin{bmatrix} \xi \rho c \omega \left(\frac{\mu}{\varphi_1 + \mu} \right) & \xi \rho c \left(\frac{\mu}{\varphi_1 + \mu} \right) \\ (1 - \xi) \rho c \omega \left(\frac{\mu}{\varphi_1 + \mu} \right) & (1 - \xi) \rho c \left(\frac{\mu}{\varphi_1 + \mu} \right) \end{bmatrix} \text{ and,} \quad (12)$$

$$V = \begin{bmatrix} k_1 & 0 \\ -\beta & k_2 \end{bmatrix}.$$

Now

$$FV^{-1} = \frac{\rho c \mu}{k_1 k_2 (\varphi_1 + \mu)} \begin{bmatrix} \xi (\omega k_2 + \beta) & \xi k_1 \\ (1 - \xi) (\omega k_2 + \beta) & (1 - \xi) k_1 \end{bmatrix}. \quad (13)$$

The eigenvalues of equation (13) are $\lambda = 0$ and $\lambda = (\rho c \mu) / (k_1 k_2 (\varphi_1 + \mu)) ((1 - \xi) k_1 + \xi (\omega k_2 + \beta))$. Thus, according to [18], the dominant eigenvalue of equation (13) gives the effective reproductive number which is $\mathcal{R}_{ep} = (\rho c \mu) / (k_1 k_2 (\varphi_1 + \mu)) ((1 - \xi) k_1 + \xi (\omega k_2 + \beta))$.

It is noted that in absence of vaccination, that is, when $\varphi_1 = 0$, the basic reproduction number $\mathcal{R}_{0P} = (\rho c / k_1 k_2) ((1 - \xi) k_1 + \xi (\omega k_2 + \beta))$ is obtained. Thus, the effective reproduction number can be given in terms of the basic reproduction number as $\mathcal{R}_{ep} = (\mu \mathcal{R}_{0P}) / (\varphi_1 + \mu)$.

Proposition 1. For any given parameters, $\mathcal{R}_{ep} < \mathcal{R}_{0P}$.

Proof 3. Since $0 < \mu / \varphi_1 + \mu < 1$, it follows that

$$\mathcal{R}_{ep} = \frac{\mu \mathcal{R}_{0P}}{\varphi_1 + \mu} < \mathcal{R}_{0P}, \quad (14)$$

for all values of μ and φ_1 . $\square$

3.2.3. Pneumococcal Pneumonia Endemic Equilibrium Point. The pneumococcal endemic equilibrium denoted by E_{ep} is the solution for system equation (10) that is existent when pneumococcal pneumonia is persistent in the community. Thus, $E_{ep} = (S_e, C_e, P_e, R_e, V_{1e})$ is achieved by solving system equation (10) with right hand side equated to zero.

$$\begin{aligned} \Lambda + \gamma R(t) - \alpha_1 S(t) - k_0 S(t) &= 0, \\ \xi \alpha_1 S(t) - k_1 C(t) &= 0, \\ (1 - \xi) \alpha_1 S(t) + \beta C(t) - k_2 P(t) &= 0, \\ \pi C(t) + \epsilon P(t) - k_3 R(t) &= 0, \\ \varphi_1 S(t) + \varphi_2 R(t) - \mu V_1(t) &= 0, \end{aligned} \quad (15)$$

together with

$$\Lambda - \mu N - \nu_1 P = 0. \quad (16)$$

After several computations, the pneumococcal pneumonia endemic equilibrium point $E_{ep} = (S_e, C_e, P_e, R_e, V_{1e})$ is obtained, where

$$\begin{aligned} S_e &= \frac{k_1 k_2 N}{\rho c ((1 - \xi) k_1 + \xi (\omega k_2 + \beta))}, \\ C_e &= \frac{\xi k_2 k_3 (\Lambda \rho c ((1 - \xi) k_1 + \xi (\omega k_2 + \beta)) - k_0 k_1 k_2 N)}{A}, \\ P_e &= \frac{k_3 (k_1 (1 - \xi) + \xi \beta) (\Lambda \rho c ((1 - \xi) k_1 + \xi (\omega k_2 + \beta)) - k_0 k_1 k_2 N)}{A}, \\ R_e &= \frac{(\Lambda \rho c ((1 - \xi) k_1 + \xi (\omega k_2 + \beta)) - k_0 k_1 k_2 N)}{A} (\pi \xi k_2 - \epsilon (k_1 (1 - \xi) + \xi \beta)), \\ V_{1e} &= \frac{\varphi_1 k_1 k_2 N}{\rho c ((1 - \xi) k_1 + \xi (\omega k_2 + \beta))} + \frac{\varphi_2 (\Lambda \rho c ((1 - \xi) k_1 + \xi (\omega k_2 + \beta)) - k_0 k_1 k_2 N)}{A} (\pi \xi k_2 - \epsilon (k_1 (1 - \xi) + \xi \beta)), \end{aligned} \quad (17)$$

where $A = (\rho c((1 - \xi)k_1 + \xi(\omega k_2 + \beta)))(k_1 k_2 k_3 - \gamma \xi(k_1(1 - \xi) + \xi\beta + k_2\pi))$, $k_0 = (\varphi_1 + \mu)$, $k_1 = (\beta + \pi + \mu)$, $k_2 = (\epsilon + \nu_1 + \mu)$, and $k_3 = (\gamma + \varphi_2 + \mu)$.

Lemma 3. A unique pneumococcal pneumonia endemic equilibrium exists when $\mathcal{R}_{0P} > 1$ and no endemic equilibrium otherwise.

Proof 4. If the disease persists in the community, then $(dC/dt) > 0$ and $(dP/dt) > 0$, that is,

$$\xi\alpha_1 S - k_1 C = \xi\rho c(\omega C + P)\frac{S}{N} - k_1 C > 0, \quad (18)$$

$$(1 - \xi)\alpha_1 S + \beta C - k_2 P = (1 - \xi)\rho c(\omega C + P)\frac{S}{N} + \beta C - k_2 P > 0. \quad (19)$$

□

From inequality equation (18) and applying the fact that $S/N \leq 1$, we have

$$C < \frac{\xi\rho cP}{k_1 - \xi\rho c\omega}. \quad (20)$$

Substituting equations (20) into equation (19) yields

$$\begin{aligned} (1 - \xi)\rho c\omega\left(\frac{\xi\rho cP}{k_1 - \xi\rho c\omega}\right) + (1 - \xi)\rho cP + \beta\left(\frac{\xi\rho cP}{k_1 - \xi\rho c\omega}\right) &> k_2 P, \\ \rho c((1 - \xi)k_1 + \xi(\beta + k_2\omega)) &> k_1 k_2, \\ \mathcal{R}_{0P} = \frac{\rho c}{k_1 k_2}((1 - \xi)k_1 + \xi(\beta + k_2\omega)) &> 1. \end{aligned} \quad (21)$$

Thus, a unique endemic equilibrium point exists when $\mathcal{R}_{0P} > 1$.

Proof 5. Evaluating the Jacobian matrix of submodel system equation (7) at the pneumococcal pneumonia-free equilibrium E_{0P} gives

3.2.4. Local Stability of Pneumococcal Pneumonia-Free Equilibrium Point

Theorem 1. The pneumococcal pneumonia-free equilibrium point E_{0P} of system equation (7) is locally asymptotically stable if $\mathcal{R}_{eP} < 1$ and unstable if $\mathcal{R}_{eP} \geq 1$.

$$J_{(E_{0P})} = \begin{bmatrix} -(\varphi_1 + \mu) & -\rho c\omega \frac{\mu}{\varphi_1 + \mu} & -\rho c \frac{\mu}{\varphi_1 + \mu} & \gamma & 0 \\ 0 & \xi\rho c\omega \frac{\mu}{\varphi_1 + \mu} - k_1 & \xi\rho c \frac{\mu}{\varphi_1 + \mu} & 0 & 0 \\ 0 & (1 - \xi)\rho c\omega \frac{\mu}{\varphi_1 + \mu} + \beta & (1 - \xi)\rho c\omega \frac{\mu}{\varphi_1 + \mu} - k_2 & 0 & 0 \\ 0 & \pi & \epsilon & -k_3 & 0 \\ \varphi_1 & 0 & 0 & \varphi_2 & -\mu \end{bmatrix}. \quad (22)$$

□

The characteristic polynomial of the Jacobian equation (10) is given as

$$P(\lambda) = (\lambda + \varphi_1 + \mu)(\lambda + \mu)(\lambda + k_3)(\lambda^2 + a_1\lambda + a_0), \quad (23)$$

where $a_1 = k_1 + k_2 - (\rho c \mu)/(\varphi_1 + \mu)(\xi \omega + (1 - \xi))$ and $a_0 = k_1 k_2 (1 - (\rho c \mu)/(k_1 k_2 (\varphi_1 + \mu))) ((1 - \xi)k_1 + k_2 \omega + \beta) = k_1 k_2 (1 - \mathcal{R}_{ep})$. The eigenvalues of the characteristic polynomial equation (23), $\lambda = -\varphi_1 - \mu$, $\lambda = -\mu$, $\lambda = -k_3$, are clearly negative. By Routh–Hurwitz criterion, $\lambda^2 + a_1\lambda + a_0 = 0$ has negative eigenvalues if $a_1 > 0$ and $a_0 > 0$ and this is only possible if $k_1 + k_2 > (\rho c \mu)/(\varphi_1 + \mu)(\xi \omega + (1 - \xi))$ and $\mathcal{R}_{ep} < 1$, respectively.

3.2.5. Global Stability of Pneumococcal Pneumonia-Free Equilibrium Point

Lemma 4. [19] Let the pneumococcal pneumonia submodel equation (7) be expressed as

$$\begin{aligned} \frac{dZ_1}{dt} &= F(Z_1, Z_2), \\ \frac{dZ_2}{dt} &= G(Z_1, Z_2), G(Z^*, 0) = 0, \end{aligned} \quad (24)$$

where $Z_1 \in \mathbb{R}^3$ are components of noninfected individuals, $Z_2 \in \mathbb{R}^2$ are components of infected individuals, and $E_{0P} = (Z_1^*, 0)$ defines the pneumococcal pneumonia-free equilibrium corresponding to system equation (24).

Assume

- i. For $(dZ_1/dt) = F(Z_1^*, 0)$, Z^* is globally asymptotically stable.

- ii. $G(Z_1, Z_2) = AZ_2 - \tilde{G}(Z_1, Z_2)$, $G(Z_1, Z_2) \geq 0$ for $(Z_1, Z_2) \in \Omega_P$, where $A = D_{Z_2}G(Z_1^*, 0)$ is an M -matrix (the non-diagonal entries are non-negative) and Ω_P is the invariant region.

Then, the pneumococcal pneumonia-free equilibrium $E_{0P} = (Z_1^*, 0)$ of system equation (24) is globally asymptotically stable when the effective reproduction number is less than one.

Theorem 2. The pneumococcal pneumonia-free equilibrium E_{0P} is globally asymptotically stable if $\mathcal{R}_{ep} < 1$ and the conditions of Lemma 4 are satisfied.

Proof 6. Using the definitions of Lemma 4 on pneumonia submodel equation (7), the following system is obtained:

$$\begin{aligned} F(Z_1, Z_2) &= \begin{bmatrix} \Lambda + \gamma R - (\alpha_1 + \varphi_1 + \mu)S \\ \pi C + \epsilon P - k_3 R \\ \varphi_1 S + \varphi_2 R - \mu V_1 \end{bmatrix}, \\ G(Z_1, Z_2) &= \begin{bmatrix} \xi \alpha_1 S - k_1 C \\ (1 - \xi) \alpha_1 S + \beta C - k_2 P \end{bmatrix}, \\ F(Z_1^*, 0) &= \begin{bmatrix} \Lambda - \mu S_0 \\ 0 \\ \varphi_1 S_0 - \mu V_{10} \end{bmatrix}, \end{aligned} \quad (25)$$

where $Z_1^* = (S_0, V_{10}) = (\Lambda/(\varphi_1 + \mu), (\varphi \Lambda)/(\mu(\varphi_1 + \mu)))$ is globally stable and hence condition (i) of Lemma 4 holds.

$$A = D_{Z_2}G(Z_1^*, 0) = \begin{bmatrix} -k_1 + \xi \rho c \omega \frac{\mu}{\varphi_1 + \mu} & \xi \rho c \frac{\mu}{\varphi_1 + \mu} \\ (1 - \xi) \rho c \omega \frac{\mu}{\varphi_1 + \mu} + \beta & -k_2 + (1 - \xi) \rho c \frac{\mu}{\varphi_1 + \mu} \end{bmatrix}, \quad (26)$$

and

$$\tilde{G}(Z_1, Z_2) = \begin{bmatrix} \tilde{G}_1(Z_1, Z_2) \\ \tilde{G}_2(Z_1, Z_2) \end{bmatrix} = \begin{bmatrix} \xi \rho c \left(\frac{\mu}{\varphi_1 + \mu} - \frac{S}{N} \right) (\omega C + P) \\ (1 - \xi) \rho c \left(\frac{\mu}{\varphi_1 + \mu} - \frac{S}{N} \right) (\omega C + P) \end{bmatrix}. \quad (27)$$

Matrix A is an M -matrix and $\tilde{G}(Z_1, Z_2) \geq 0$ whenever $S/N \leq \mu/(\varphi_1 + \mu)$ which satisfies condition (ii) of Lemma 4. Thus, the pneumococcal pneumonia-free equilibrium is globally asymptotically stable.

3.2.6. Bifurcation Analysis of the Pneumococcal Pneumonia Submodel. Let $S = y_1, C = y_2, P = y_3, R = y_4$, and $V_1 = y_5$ so that $N = y_1 + y_2 + y_3 + y_4 + y_5$. By using the vector notation $y = (y_1, y_2, y_3, y_4, y_5)^T$, the pneumococcal

□

pneumonia submodel equation (10) can be presented as $(dy/dt) = f(y) = (f_1, f_2, f_3, f_4, f_5)$;

$$\frac{dy_1}{dt} = f_1 = \Lambda + \gamma y_4 - (\alpha_1 + \varphi_1 + \mu)y_1,$$

$$\frac{dy_2}{dt} = f_2 = \xi \alpha_1 y_1 - (\beta + \pi + \mu)y_2,$$

$$\frac{dy_3}{dt} = f_3 = (1 - \xi)\alpha_1 y_1 + \beta y_2 - (\epsilon + \nu_1 + \mu)y_3, \quad (28)$$

$$\frac{dy_4}{dt} = f_4 = \pi y_2 + \epsilon y_3 - (\gamma + \varphi_2 + \mu)y_4,$$

$$\frac{dy_5}{dt} = f_5 = \varphi_1 y_1 + \varphi_2 y_4 - \mu y_5,$$

where $\alpha_1 = (\alpha(\omega y_2 + y_3))/(y_1 + y_2 + y_3 + y_4 + y_5)$.

Evaluating the Jacobian matrix of system equation (28) at pneumococcal pneumonia-free equilibrium E_{0P} gives

$$J_{(E_{0P})} = \begin{bmatrix} -(\varphi_1 + \mu) & -\alpha\omega\frac{\mu}{\varphi_1 + \mu} & -\alpha\frac{\mu}{\varphi_1 + \mu} & \gamma & 0 \\ 0 & \xi\alpha\omega\frac{\mu}{\varphi_1 + \mu} - k_1 & \xi\alpha\frac{\mu}{\varphi_1 + \mu} & 0 & 0 \\ 0 & (1 - \xi)\alpha\omega\frac{\mu}{\varphi_1 + \mu} + \beta & (1 - \xi)\alpha\frac{\mu}{\varphi_1 + \mu} - k_2 & 0 & 0 \\ 0 & \pi & \epsilon & -k_3 & 0 \\ \varphi_1 & 0 & 0 & \varphi_2 & -\mu \end{bmatrix}. \quad (29)$$

Taking $\alpha = \alpha^*$ as the bifurcation parameter and studying the situation when $\mathcal{R}_{eP} = 1$ gives $\alpha = \alpha^* = (k_1 k_2 (\varphi_1 + \mu))/(\mu((1 - \xi)k_1 + \xi(k_2\omega + \beta)))$.

Solving the Jacobian matrix equation (29) with $\alpha = \alpha^*$ at $\mathcal{R}_{eP} = 1$, we have the characteristic equation

$$\lambda(\lambda + \varphi_1 + \mu)(\lambda + \mu)(\lambda + k_3)(\lambda + a_1) = 0. \quad (30)$$

By characteristic equation (21), Jacobian equation (29) has a simple zero eigenvalue with all other eigenvalues being negative. Thus, the center manifold theory [20] is now applied to show whether submodel (28) undergoes forward bifurcation at $\mathcal{R}_{eP} = 1$. The right eigenvector $w = (w_1, w_2, w_3, w_4, w_5)^T$ corresponding to the zero eigenvalue is computed from $J_{E_{0P}} w = 0$ which leads to

$$\begin{aligned} w_3 &= -w_2 \left(\omega - \frac{k_1(\mu + \varphi_1)}{\alpha^* \mu \xi} \right), w_2 > 0, w_4 = \frac{w_2}{k_3} \left(\pi - \epsilon \left(\omega - \frac{k_1(\mu + \varphi_1)}{\alpha^* \mu \xi} \right) \right), \\ w_1 &= \frac{w_2}{\alpha^* k_3 \mu \xi (\mu + \varphi_1)} (\epsilon \gamma k_1 (\varphi_1 + \mu) + \alpha^* \mu (\gamma \xi (\pi - \epsilon \omega) - k_1 k_3)), w_5 = \frac{\varphi_1 w_1 + \varphi_2 w_4}{\mu}. \end{aligned} \quad (31)$$

Similarly, the left eigenvector $u = (u_1, u_2, u_3, u_4, u_5)^T$ is computed such that $u J_{E_{0P}} = 0$ which leads to

$$u_1 = u_4 = u_5 = 0, u_2 > 0 \text{ and } u_3 = \left(\frac{k_1(\varphi_1 + \mu) - \xi \alpha^* \omega \mu}{(1 - \xi) \alpha^* \omega \mu + (\mu + \varphi_1) \beta} \right) u_2. \quad (32)$$

The bifurcation constants a and b are derived and obtained as

$$a = \sum_{k,i,j=1}^5 v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j} = \frac{-v_2 w_2^2 (k_1 (1 - \xi) + \beta \xi) (k_1^2 \mathcal{W} + \alpha^* \mu \xi \mathcal{X})}{(\Lambda \alpha^* k_3 \mu \xi^2 (\mu + \varphi_1) (\beta (\mu + \varphi_1) + \alpha^* \mu \omega (1 - \xi)))} < 0,$$

$$b = \sum_{k,i=1}^5 v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \alpha^*} = \frac{w_2 v_2 k_1 (\alpha^* \omega \mu + (\varphi_1 + \mu) (\beta + k_1))}{(1 - \xi) \alpha^{*2} \omega \mu + (\varphi_1 + \mu) \alpha^* \beta} > 0,$$
(33)

where $\mathcal{W} = (2\mu^4 (1 + \epsilon) + 2\mu\varphi_1 (3\mu + \varphi_1) (\epsilon + k_3) (3\mu^2 + \varphi_1) + \epsilon\varphi_1^3 (\varphi_1 + \omega\varphi_2 + (1 - \omega)\gamma) + \epsilon\mu\varphi_2 (\mu^2\omega + 3\varphi_1 (\varphi_1 + \mu)) + \alpha k_3 \mu \varphi_1 (\varphi_1 + \mu))$ and $\mathcal{X} = 2k_1 ((1 + \mu\varphi_1 (\varphi_1 + \mu)) (k_3 + \pi) + \omega (\epsilon + \alpha^*)) + \gamma k_1 \omega \varphi_1 (2\epsilon + \pi) (\varphi_1 + \mu) + \alpha^* \omega (\mu\varphi_1 (k_1 k_3 \omega + \xi\pi (\gamma + \varphi_1)) + \varphi_2 \xi (\pi (1 - \omega) - \omega\epsilon (1 + \omega)))$.

Hence, it follows from [20] that the model equation (28) does not exhibit a backward bifurcation at $\mathcal{R}_{0P} = 1$. Thus, there is only pneumococcal pneumonia-free equilibrium which means that there cannot be a positive pneumococcal pneumonia endemic equilibrium whenever $\mathcal{R}_{eP} < 1$. The above result is summarized as follows.

Theorem 3. *The pneumonia endemic equilibrium point E_{eP} is locally asymptotically stable if $\mathcal{R}_{eP} > 1$ and close to one.*

3.2.7. Global Stability of Pneumococcal Pneumonia Endemic Equilibrium Point

Theorem 4. *If $\mathcal{R}_{eP} > 1$, the pneumococcal pneumonia endemic equilibrium E_{eP} of the system equation (7) is globally asymptotically stable.*

Proof 7. In the proof of global asymptotic stability of the pneumococcal pneumonia endemic equilibrium, the method of Lyapunov functions is applied. Define a Lyapunov function $L(S_e, C_e, P_e, R_e, V_{1e})$ such that

$$L = \left(S - S_e + S_e \ln \frac{S_e}{S} \right) + \left(C - C_e + C_e \ln \frac{C_e}{C} \right) + \left(P - P_e + P_e \ln \frac{P_e}{P} \right) + \left(R - R_e + R_e \ln \frac{R_e}{R} \right) + \left(V_1 - V_{1e} + V_{1e} \ln \frac{V_{1e}}{V_1} \right).$$
(34)

□

Evaluating the time derivative of L in equation (23) together with equations of submodel equation (10) gives

$$\begin{aligned} \frac{dL}{dt} = & \Lambda + \gamma R - (\alpha_1 + \varphi_1 + \mu)S - \lambda \frac{S_e}{S} - \gamma R \frac{S_e}{S} + (\alpha_1 + \varphi_1 + \mu)S_e + \xi \alpha_1 S - k_1 C - \xi \alpha_1 S \frac{C_e}{C} \\ & + k_1 C_e + (1 - \xi) \alpha_1 S + \beta C - k_2 P - (1 - \xi) \alpha_1 S \frac{P_e}{P} - \beta C \frac{P_e}{P} + k_2 P_e + \pi C + \epsilon P - k_3 R \\ & - \pi C \frac{R_e}{R} - \epsilon P \frac{R_e}{R} + k_3 R_e + \varphi_1 S + \varphi_2 R - \mu V_1 - \varphi_1 S \frac{V_{1e}}{V_P} - \varphi_2 R \frac{V_{1e}}{V_1} + \mu V_{1e}, \end{aligned}$$
(35)

$$\frac{dL}{dt} = \mathcal{A}_1 - \mathcal{A}_2,$$

where

$$\begin{aligned}
A_1 &= \Lambda + \gamma R + (\alpha_1 + \varphi_1 + \mu)S_e + \xi\alpha_1 S + k_1 C_e + (1 - \xi)\alpha_1 S \\
&\quad + \beta C + k_2 P_e + \pi C + \epsilon P + k_3 R_e + \varphi_1 S + \varphi_2 R + \mu V_{1e}, \\
\mathcal{A}_2 &= (\Lambda + \gamma R) \frac{S_e}{S} + \alpha_1 S \left(1 + \xi \frac{C_e}{C} + (1 - \xi) \frac{P_e}{P} \right) \\
&\quad + (\varphi_1 S + \varphi_2 R) \left(1 + \frac{V_{1e}}{V_P} \right) + \beta C \left(1 + \frac{P_e}{I_P} \right) + \pi C \left(1 + \frac{R_e}{R} \right), \\
&\quad + \gamma R + \nu_1 P + \mu(S + C + P + R + V_1).
\end{aligned} \tag{36}$$

From equation (24), $(dL/dt) < 0$ if $\mathcal{A}_1 < \mathcal{A}_2$ and $(dL/dt) = 0$ iff $S = S_e, P = P_e, C = C_e, R = R_e$ and $V_1 = V_{1e}$. Therefore, the largest compact invariant set in $\{(S, C, P, R, V_1) \in \Omega_P : (dL/dt) = 0\}$ is the singleton $\{E_{ep}\}$, where E_{ep} is the endemic equilibrium point of submodel equation (7).

Thus, from LaSalle's invariance principle [21], for $\mathcal{R}_{ep} > 1$, it means that E_{ep} is globally asymptotically stable in Ω_P if $\mathcal{A}_1 < \mathcal{A}_2$.

3.3. Analysis of HIV/AIDS Submodel. The HIV/AIDS submodel materializes when $P(t) = C(t) = R(t) = V_1(t) = C_1(t) = C_2(t) = T_2(t) = 0, V_2(t) = 0$ which leads to

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda - (\alpha_2(t) + \mu)S(t), \\
\frac{dH(t)}{dt} &= \alpha_2 S(t) - (\tau_1 + \lambda_1 + \mu)H(t), \\
\frac{dA(t)}{dt} &= \lambda_1 H(t) - (\tau_2 + \nu_2 + \mu)A(t), \\
\frac{dT_1}{dt} &= \tau_1 H(t) + \tau_2 A(t) - \mu T_1(t), \\
\frac{dN(t)}{dt} &= \Lambda - \mu N(t) - \nu_2 A(t),
\end{aligned} \tag{37}$$

where $\alpha_2 = \eta k((H + a_2 A)/N)$ is the HIV infection force. The feasible region for the HIV/AIDS submodel equation (37) is $\Omega_H = \{S(t), H(t), A(t), T_1(t) \in \mathbb{R}_+^4 : N(t) \leq \Lambda/\mu\}$ which is positively invariant and attracting, that is, the solution starting in Ω_H will remain in Ω_H for all $t \geq 0$.

The steady states of HIV/AIDS submodel equation (37) are the HIV/AIDS-free equilibrium $E_{0H} = (\Lambda/\mu, 0, 0, 0)$ and the HIV/AIDS endemic equilibrium $E_{eH} = (S_e, H_e, A_e, T_{1e})$, where

$$\begin{aligned}
S_e &= \frac{Nq_1q_2}{\eta k(q_2 + a_2\lambda_1)}, \\
H_e &= \frac{\mu Nq_1q_2 - \Lambda\eta k(q_2 + a_2\lambda_1)}{q_1\eta k(q_2 + a_2\lambda_1)}, \\
A_e &= \frac{\lambda_1(\mu Nq_1q_2 - \Lambda\eta k(q_2 + a_2\lambda_1))}{q_1q_2\eta k(q_2 + a_2\lambda_1)}, \\
T_{1e} &= \frac{\mu Nq_1q_2 - \Lambda\eta k(q_2 + a_2\lambda_1)}{\mu q_1\eta k(q_2 + a_2\lambda_1)} \left(\tau_1 + \frac{\tau_2\lambda_1}{q_2} \right).
\end{aligned} \tag{38}$$

The HIV/AIDS basic reproduction number corresponding to the submodel equation (37) is

$$\mathcal{R}_{0H} = \frac{\eta k}{q_1q_2} (q_2 + a_2\lambda_1), \tag{39}$$

where $q_1 = \tau_1 + \lambda_1 + \mu$ and $q_2 = \tau_2 + \nu_2 + \mu$.

From equation (26), it is derived that the HIV/AIDS-free equilibrium E_{0H} is both locally and globally asymptotically stable if $\mathcal{R}_{0H} < 1$ and the HIV/AIDS endemic equilibrium point is locally and globally asymptotically stable when $\mathcal{R}_{0H} > 1$. Refer to [12] for detailed analysis of the HIV/AIDS submodel equation (37).

3.4. Analysis of HIV/AIDS and Pneumococcal Pneumonia Co-Infection Model. The model system equation (1) of HIV/AIDS and pneumococcal pneumonia co-infection is considered and analyzed in the bounded region Ω given in equation (5).

3.4.1. HIV/AIDS and Pneumococcal Pneumonia Co-Infection-Free Equilibrium. The HIV/AIDS and pneumococcal pneumonia co-infection-free equilibrium of model equation (1) portrays the model when there is no HIV/AIDS, pneumococcal pneumonia, and their co-infection, that is, $P(t) = C(t) = R(t) = H(t) = A(t) = T_1(t) = C_1(t) = C_2(t) = T_2(t) = V_2(t) = 0$. Thus, solving system equation (1) with the right hand side equated to zero gives $S = \Lambda/\varphi_1 + \mu$ and $V_1 = (\varphi_1\Lambda)/(\mu(\varphi_1 + \mu))$. Therefore, the HIV/AIDS and pneumococcal pneumonia co-infection-free equilibrium is

$$E_0 = \left(\frac{\Lambda}{\varphi_1 + \mu}, 0, 0, 0, \frac{\varphi_1\Lambda}{\mu(\varphi_1 + \mu)}, 0, 0, 0, 0, 0, 0 \right). \tag{40}$$

3.4.2. Effective HIV/AIDS and Pneumococcal Pneumonia Co-Infection Reproduction Number. The effective HIV/AIDS and pneumococcal pneumonia reproduction number $\mathcal{R}_e$

refers to the number of secondary pneumococcal pneumonia (or HIV/AIDS) infections caused by one pneumococcal pneumonia-infective (or single HIV/AIDS infective)

in her or his entire infectious period. Following the procedure in Subsection 3.2.2,

$$FV^{-1} = \begin{bmatrix} \frac{\xi\rho c\mu(\omega k_2 + \beta)}{k_1 k_2(\varphi_1 + \mu)} & \frac{\xi\rho c\mu}{k_2(\varphi_1 + \mu)} & 0 & 0 & \frac{\xi\rho c\mu(d_2\theta_1 + \lambda\theta_2)}{d_1 d_2(\varphi_1 + \mu)} & \frac{\xi\rho c\mu\theta_2}{d_2(\varphi_1 + \mu)} \\ \frac{\xi\rho c\mu(\omega k_2 + \beta)}{k_1 k_2(\varphi_1 + \mu)} & \frac{\xi\rho c\mu}{k_2(\varphi_1 + \mu)} & 0 & 0 & \frac{\xi\rho c\mu(d_2\theta_1 + \lambda\theta_2)}{d_1 d_2(\varphi_1 + \mu)} & \frac{\xi\rho c\mu\theta_2}{d_2(\varphi_1 + \mu)} \\ 0 & 0 & \frac{\eta k(q_2^* + a_2\lambda_1)}{q_1^* q_2^*} & \frac{\eta k a_2}{q_2^*} & \frac{\eta k(d_2 a_1 + a_3\lambda_2)}{d_1 d_2} & \frac{\eta k a_3}{d_2} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}. \quad (41)$$

The eigenvalues of FV^{-1} in equation (41) are $\lambda_1 = (\rho c\mu)/((\varphi_1 + \mu)k_1 k_2) (\xi(\omega k_2 + \beta) + (1 - \xi)k_1) = \mathcal{R}_{eP}$, $\lambda_2 = 0$, $\lambda_3 = (\eta k/q_1^* q_2^*)(q_2^* + a_2\lambda_1) = \mathcal{R}_{eH}$, $\lambda_4 = 0$, $\lambda_5 = 0$,

and $\lambda_6 = 0$. The dominant eigenvalue of equation (41) which is the effective reproduction number of HIV/AIDS and pneumococcal pneumonia co-infection is

$$\mathcal{R}_e = \max \left\{ \frac{\rho c\mu}{(\varphi_1 + \mu)k_1 k_2} (\xi(\omega k_2 + \beta) + (1 - \xi)k_1), \frac{\eta k}{q_1^* q_2^*} (q_2^* + a_2\lambda_1) \right\} = \max \{ \mathcal{R}_{eP}, \mathcal{R}_{eH} \}. \quad (42)$$

It is important to note that when HIV infected individuals and AIDS patients are subjected to pneumococcal vaccination, the expressions for q_1 and q_2 in equation (39) become $q_1^* = (\tau_1 + \sigma_1 + \lambda_1 + \mu)$ and $q_2^* = (\tau_2 + \sigma_2 + \nu_2 + \mu)$, respectively, and thus the effective HIV/AIDS reproduction number is $\mathcal{R}_{eH} = (\eta k/q_1^* q_2^*)(q_2^* + a_2\lambda_1)$.

3.4.3. Local Stability of HIV/AIDS and Pneumococcal Pneumonia Co-Infection-Free Equilibrium

Theorem 5. The HIV/AIDS-pneumococcal pneumonia co-infection-free equilibrium E_0 of system equation (1) is locally asymptotically stable when $\mathcal{R}_e < 1$.

Proof 8. The Jacobian matrix for system equation (1) evaluated at HIV/AIDS-pneumococcal pneumonia co-infection-free equilibrium E_0 is given by

$$J_{(E_0)} = \begin{bmatrix} M & -A\omega & -A & \gamma & 0 & -B & -Ba_2 & 0 & D_1 & D_2 & 0 & 0 \\ 0 & D_3 & \xi A & 0 & 0 & 0 & 0 & 0 & \xi A\theta_1 & \xi A\theta_2 & 0 & 0 \\ 0 & D_4 & D_5 & 0 & 0 & 0 & 0 & 0 & (1 - \xi)A\theta_1 & (1 - \xi)A\theta_2 & 0 & 0 \\ 0 & \pi & \epsilon & -k_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \varphi_1 & 0 & 0 & \varphi_2 & -\mu & C & Ca_2 & 0 & Ca_1 & Ca_3 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & D_6 & \eta k a_2 & 0 & \eta k a_1 & \eta k a_3 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \lambda_1 & -q_2^* & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau_1 & \tau_2 & -q_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -d_1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \lambda_2 & -d_2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_3 & \tau_4 & -d_3 & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma_1 & \sigma_2 & \sigma_3 & 0 & 0 & \sigma_4 & -\mu \end{bmatrix}, \quad (43)$$

where $A = (\rho c \mu) / (\varphi_1 + \mu)$, $B = (\eta k \mu) / (\varphi_1 + \mu)$, $C = (\eta k \varphi_1) / (\varphi_1 + \mu)$, $M = -(\varphi_1 + \mu)$, $D_1 = -(A \theta_1 + B a_1)$, $D_2 = (A \theta_2 + B a_3)$, $D_3 = \xi A \omega - k_1$, $D_4 = (1 - \xi) A \omega + \beta$, $D_5 = (1 - \xi) A k_2$, $D_6 = \eta k - q_1^*$, together with $k_1 = (\beta + \pi + \mu)$, $k_2 = (\epsilon + \nu_1 + \mu)$, $k_3 = (\gamma + \varphi_2 + \mu)$, $q_1^* = (\sigma_1 + \tau_1 + \lambda_1 + \mu)$, $q_2^* = (\sigma_2 + \tau_2$

$+ \nu_2 + \mu)$, $q_3 = (\sigma_3 + \mu)$, $d_1 = (\lambda_2 + \tau_3 + \nu_1 + \mu)$, $d_2 = (\tau_2 + \mu + \mu)$, and $d_3 = (\sigma_4 + \mu)$. $\square$

Referring to Jacobian matrix equation (43), the following characteristic polynomial is established:

$$P(\lambda) = (\lambda + \mu)^2 (\lambda + d_1) (\lambda + d_2) (\lambda + d_3) (\lambda + k_3) (\lambda + q_3) (\lambda + (\varphi_1 + \mu)) (\lambda^2 + m_1 \lambda + m_0) (\lambda^2 + n_1 \lambda + n_0), \quad (44)$$

where

$$\lambda^2 + m_1 \lambda + m_0 = \lambda^2 + \left(k_1 + k_2 - ((1 - \xi) + \xi \omega) \frac{\mu}{\varphi_1 + \mu} \right) \lambda + k_1 k_2 (1 - \mathcal{R}_{ep}), \quad (45)$$

$$\lambda^2 + n_1 \lambda + n_0 = \lambda^2 + (q_1^* + q_2^* - \eta k) \lambda + q_1 q_2 (1 - \mathcal{R}_{eH}). \quad (46)$$

From the characteristic polynomial equation (44), it is seen that the eigenvalues $\lambda = -\mu$ (repeated), $-d_1, -d_2, -d_3, -k_3, -q_3, -(\varphi_1 + \mu)$ are negative and the characteristic polynomial equations (45) and (46) have negative eigenvalues if $\mathcal{R}_{ep} < 1$ and $\mathcal{R}_{eH} < 1$, respectively. Thus, the HIV/AIDS and pneumococcal pneumonia co-infection-free equilibrium is locally asymptotically stable.

Remark 1. The proof of Theorem 5 demonstrates that the local asymptotic stability of the pneumococcal pneumonia and HIV/AIDS-free equilibrium submodels implies the local asymptotic stability of the co-infection-free equilibrium model for HIV/AIDS and pneumococcal pneumonia.

It can be noted that the HIV/AIDS-pneumococcal pneumonia co-infection model dynamics is governed by the dynamics of its constituent submodels. Therefore, since the equilibria of pneumococcal pneumonia and HIV/AIDS submodels are both locally and globally asymptotically stable, then the pneumococcal pneumonia and HIV/AIDS co-infection model cannot display the phenomenon of backward bifurcation [22, 23]. It is therefore valid to conclude that the HIV/AIDS-pneumococcal pneumonia co-infection-free and endemic equilibria of model equation (1) are existent, distinctive, and locally and globally asymptotically stable [22, 24].

4. Optimal Control Analysis of HIV/AIDS and Pneumococcal Pneumonia Co-Infection Model

The ambition of optimal control theory is to determine the control actions that will cause a process to satisfy the physical constraints and at the same time minimize (or maximize) some performance criteria [25]. Optimal control theory has demonstrated to be an efficient tool in understanding ways to restrict the spread of infectious diseases by concocting optimal intervention schemes. The method consists of minimizing the cost of infection or the cost of

implementing the control, or both. Optimal control theory has been put in application in the study of infectious diseases such as those in [10, 14, 15, 22, 26].

The optimal control theory is applied in model equation (1) which was presented in Section 2. The following four controls are fronted in the formulation of the desired optimal control model.

- i. Control $u_1(t)$: Pneumococcal pneumonia protection effort that keeps susceptible individuals safe from acquiring pneumococcal pneumonia. The effort u_1 can be realized through health educational drives directed at increasing community awareness about pneumococcal disease. These may include good hygiene, quitting smoking, and keeping your immune system strong by getting regular physical activity and eating healthy.
- ii. Control $u_2(t)$: Pneumococcal pneumonia early detection and treatment effort, to guide the identification of carrier and infected individuals and treat them. Here, all individuals detected with pneumococcal pneumonia are subjected to treatment.
- iii. Control $u_3(t)$: HIV protection effort that keeps susceptible individuals safe from acquiring HIV. This can be accomplished through health educational drives directed at informing the communities of the existing HIV protection measures like use of condoms and only having partners with the same HIV status, among others.
- iv. Control $u_4(t)$: HIV early detection and treatment effort, to guide the identification of individuals with HIV such that they start on therapy. Here, all individuals found with HIV are subjected to therapy.

This will be instructive in identification of the best intervention plan that will lead to eradication or reduction of the HIV/AIDS and pneumococcal pneumonia co-infection burden.

4.1. Model Formulation. This is a continuation of the model equation (1) by adding control inputs $u_1(t), u_2(t), u_3(t)$, and $u_4(t)$. The state variables of the process at time t are

$S(t), C(t), P(t), R(t), V_1(t), H(t), A(t), T_1(t), C_1(t), C_2(t), T_2(t), V_2(t)$. The resulting system is described by 12 first-order differential equations as shown below:

$$\begin{aligned}
 \frac{dS(t)}{dt} &= \Lambda + \gamma R(t) - ((1 - u_1)\alpha_1 + (1 - u_3)\alpha_2 + \varphi_1 + \mu)S(t), \\
 \frac{dC(t)}{dt} &= (1 - u_1)\xi\alpha_1 S(t) - ((1 - u_3)\alpha_2 + \beta + (\pi + u_2) + \mu)C(t), \\
 \frac{dP(t)}{dt} &= (1 - u_1)(1 - \xi)\alpha_1 S(t) + \beta C(t) - ((1 - u_3)\alpha_2 + (\epsilon + u_2) + \mu + \nu_1)P(t), \\
 \frac{dR(t)}{dt} &= (u_2 + \epsilon)P(t) + (u_2 + \pi)C(t) - ((1 - u_3)\alpha_2 + \gamma + \varphi_2 + \mu)R(t), \\
 \frac{dV_1(t)}{dt} &= \varphi_1 S(t) + \varphi_2 R(t) - ((1 - u_3)\alpha_2 + \mu)V_1(t), \\
 \frac{dH(t)}{dt} &= (1 - u_3)(\alpha_2 S(t) + \alpha_2 R(t) + \alpha_2 V_1(t)) - ((1 - u_1)\alpha_1 + (\tau_1 + u_4) + \lambda_1 + \sigma_1 + \mu)H(t), \\
 \frac{dA(t)}{dt} &= \lambda_1 H(t) - ((1 - u_1)\alpha_1 + (\tau_2 + u_4) + \sigma_2 + \mu + \nu_2)A(t), \\
 \frac{dT_1(t)}{dt} &= (\tau_1 + u_4)H(t) + (\tau_2 + u_4)A(t) - (\sigma_3 + \mu)T_1(t), \\
 \frac{dC_1(t)}{dt} &= (1 - u_3)\alpha_2 (C(t) + P(t)) + (1 - u_1)\alpha_1 H(t) - (\lambda_2 + (\tau_3 + u_2 + u_4) + \mu + \nu_1)C_1(t), \\
 \frac{dC_2(t)}{dt} &= (1 - u_1)\alpha_1 A(t) + \lambda_2 C_1(t) - ((\tau_4 + u_2 + u_4) + \mu + \nu)C_2(t), \\
 \frac{dT_2(t)}{dt} &= (\tau_3 + u_2 + u_4)C_1(t) + (\tau_4 + u_2 + u_4)C_2(t) - (\sigma_4 + \mu)T_2(t), \\
 \frac{dV_2(t)}{dt} &= \sigma_1 H(t) + \sigma_2 A(t) + \sigma_3 T_1(t) + \sigma_4 T_2(t) - \mu V_2(t).
 \end{aligned} \tag{47}$$

The intent is to reduce the number of infectious individuals $C(t), P(t), H(t), A(t), C_1(t)$ and $C_2(t)$ in a community while ensuring that the cost associated with controls u_1, u_2, u_3, u_4 is as low as it can be.

In a mathematical viewpoint, the aim is to achieve a minimum value of the objective function equation (33) for a fixed time t_f .

$$\mathcal{O} = \int_0^{t_f} \left(B_1 C + B_2 P + B_3 H + B_4 A + B_5 T_1 + B_6 C_1 + B_7 C_2 + B_8 T_2 + B_9 V_2 + \frac{1}{2} \sum_{i=1}^4 W_i u_i^2 \right) dt, \tag{48}$$

where $B_n, n = 1, 2, \dots, 8$ and $W_i, i = 1, 2, 3, 4$ are positive constants. The total cost on a bounded time $[0, t_f]$ includes the cost instigated by HIV, AIDS, pneumococcal pneumonia and their co-infection, and the cost due to the control strategies. This implies that $\int_0^{t_f} B_1 C dt$ is the cost instigated by pneumococcal carriers, $\int_0^{t_f} B_2 P dt$ is the cost instigated by

pneumococcal infected individuals, $\int_0^{t_f} B_3 H dt$ is the cost instigated by HIV infected individuals, $\int_0^{t_f} B_4 A dt$ is the cost instigated by individuals with AIDS, $\int_0^{t_f} B_6 C_1 dt$ is the cost instigated by HIV-pneumococcal co-infected individuals, $\int_0^{t_f} B_7 C_2 dt$ is the cost instigated by AIDS-pneumococcal co-

infected individuals, $\int_0^{t_f} B_5 T_1 dt$ is the cost aimed at keeping individuals living with HIV on therapy, $\int_0^{t_f} B_8 T_2 dt$ is the cost instigated by individuals under HIV/AIDS therapy and pneumonia treatment, $\int_0^{t_f} B_9 V_2$ is the cost associated with keeping the individuals in class V_2 under HIV therapy, and $\int_0^{t_f} \sum_1^4 W_i u_i^2 dt$ is the total cost instigated by control strategies $u_i, i = 1, 2, 3, 4$.

The aim is to find optimal controls $u_1^*, u_2^*, u_3^*, u_4^* \in \mathcal{U}$ such that

$$\mathcal{O}(u_1^*, u_2^*, u_3^*, u_4^*) = \min_{u_1, u_2, u_3, u_4 \in \mathcal{U}} \mathcal{O}(u_1, u_2, u_3, u_4), \quad (49)$$

where $\mathcal{U} = \{(u_1, u_2, u_3, u_4); u_1, u_2, u_3, u_4 \text{ is Lebesgue integrable on } 0 \leq u_i < 1, i = 1, 2, 3, 4\}$.

4.2. Characterization of an Optimal Control. Assume there is an optimal control that minimizes the objective function equation (48) subject to system equation (47); then we derive the necessary conditions that an optimal control must satisfy from Pontryagin's maximum principle [14, 26, 27]. By Pontryagin's maximum principle, the following Hamiltonian $\mathcal{H}$ is obtained.

$$\begin{aligned} \mathcal{H} = & B_1 C + B_2 P + B_3 H + B_4 A + B_5 T_1 + B_6 C_1 + B_7 C_2 + B_8 T_2 + B_9 V_2 + \frac{1}{2} \sum_1^4 W_i u_i^2 \\ & + \mathcal{M}_1 \frac{dS}{dt} + \mathcal{M}_2 \frac{dC}{dt} + \mathcal{M}_3 \frac{dP}{dt} + \mathcal{M}_4 \frac{dR}{dt} + \mathcal{M}_5 \frac{dV_1}{dt} + \mathcal{M}_6 \frac{dH}{dt} + \mathcal{M}_7 \frac{dA}{dt} + \mathcal{M}_8 \frac{dT_1}{dt} \\ & + \mathcal{M}_9 \frac{dC_1}{dt} + \mathcal{M}_{10} \frac{dC_2}{dt} + \mathcal{M}_{11} \frac{dT_2}{dt} + \mathcal{M}_{12} \frac{dV_2}{dt}, \\ = & B_1 C + B_2 P + B_3 H + B_4 A + B_5 T_1 + B_6 C_1 + B_7 C_2 + B_8 T_2 + B_9 V_2 + \frac{1}{2} \sum_1^4 W_i u_i^2 \\ & + \mathcal{M}_1 (\lambda + \gamma R - ((1 - u_1)\alpha_1 + (1 - u_3)\alpha_2 + \varphi_1 + \mu)S) + \mathcal{M}_2 (1 - u_1)\xi\alpha_1 S \\ & - ((1 - u_3)\alpha_2 + \beta + (\pi + u_2) + \mu)C + \mathcal{M}_3 (1 - u_1)(1 - \xi)\alpha_1 S + \beta C \\ & - (\alpha_2 + (\epsilon + u_2) + \mu + \nu_1)P + \mathcal{M}_5 (\varphi_1 S + \varphi_2 R - ((1 - u_3)\alpha_2 + \mu)V_1) \\ & + \mathcal{M}_4 ((u_2 + \epsilon)I_1(t) + (u_2 + \pi)C - ((1 - u_3)\alpha_2 + \gamma + \varphi_2 + \mu)R) \\ & + \mathcal{M}_6 ((1 - u_3)(\alpha_2 S + \alpha_2 R + \alpha_2 V_1) - ((1 - u_1)\alpha_1 + (\tau_1 + u_4) + \lambda_1 + \sigma_1 + \mu)H) \\ & + \mathcal{M}_7 (\lambda_1 H - ((1 - u_1)\alpha_1 + (\tau_2 + u_4) + \sigma_2 + \mu + \nu_2)A) + \mathcal{M}_8 (\tau_1 + u_4)H \\ & + (\tau_2 + u_4)A - (\sigma_3 + \mu)T_1 + \mathcal{M}_9 ((1 - u_3)\alpha_2(C + P) + (1 - u_1)\alpha_1 H \\ & - (\lambda_2 + (\tau_3 + u_2 + u_4) + \mu + \nu_1)C_1 + \mathcal{M}_{10} (1 - u_1)\alpha_1 A + \lambda_2 C_1 \\ & - ((\tau_4 + u_2 + u_4) + \mu + \nu)C_2 + \mathcal{M}_{11} (\tau_3 + u_2 + u_4)C_1 + (\tau_4 + u_2 + u_4)C_2 \\ & - (\sigma_4 + \mu)T_2 + \mathcal{M}_{12} (\sigma_1 H + \sigma_2 A + \sigma_3 T_1 + \sigma_4 T_2 - \mu V_2), \end{aligned} \quad (50)$$

where $\mathcal{M}_i, i = 1, 2, 3, \dots, 12$ are adjoint variable functions.

Theorem 6. Let $u_i^*, i = 1, 2, 3, 4$ be the set of optimal controls, and $\mathbf{X} = S^*, C^*, P^*, R^*, V_1^*, H^*, A^*, T_1^*, C_1^*, C_2^*, T_2^*, V_2^*$ be the correspondent set of solution that minimizes $\mathcal{O}$ over $\mathcal{U}$; then there are adjoint variables $\mathcal{M}_X$ such that

$$\frac{d\mathcal{M}_X}{dt} = -\frac{\partial \mathcal{H}}{\partial \mathbf{X}} \text{ adjoint conditions,} \quad (51)$$

$$\mathcal{M}_X(t_f) = 0 \text{ transversality conditions.} \quad (52)$$

Additionally,

$$\frac{\partial \mathcal{H}}{\partial u_i} = 0 \text{ at } u_i^* = 0, \text{ optimality conditions.} \quad (53)$$

Proof 9. We begin by differentiating the Hamiltonian function equation (53) evaluated at optimal control in order to obtain the differential equations with respect to adjoint variables. Then, the adjoint system can be written as follows:

$$\begin{aligned} \frac{d\mathcal{M}_1}{dt} &= -\frac{\partial \mathcal{H}}{\partial S}, \\ \frac{d\mathcal{M}_2}{dt} &= -\frac{\partial \mathcal{H}}{\partial C}, \\ \frac{d\mathcal{M}_3}{dt} &= -\frac{\partial \mathcal{H}}{\partial P}, \\ \frac{d\mathcal{M}_4}{dt} &= -\frac{\partial \mathcal{H}}{\partial R}, \\ \frac{d\mathcal{M}_5}{dt} &= -\frac{\partial \mathcal{H}}{\partial V_1}, \\ \frac{d\mathcal{M}_6}{dt} &= -\frac{\partial \mathcal{H}}{\partial H}, \\ \frac{d\mathcal{M}_7}{dt} &= -\frac{\partial \mathcal{H}}{\partial A}, \\ \frac{d\mathcal{M}_8}{dt} &= -\frac{\partial \mathcal{H}}{\partial T_1}, \\ \frac{d\mathcal{M}_9}{dt} &= -\frac{\partial \mathcal{H}}{\partial C_1}, \\ \frac{d\mathcal{M}_{10}}{dt} &= -\frac{\partial \mathcal{H}}{\partial C_2}, \\ \frac{d\mathcal{M}_{11}}{dt} &= -\frac{\partial \mathcal{H}}{\partial T_2}, \\ \frac{d\mathcal{M}_{12}}{dt} &= -\frac{\partial \mathcal{H}}{\partial V_2}. \end{aligned} \quad (54)$$

□

From equation (38), we differentiate the Hamiltonian function equation (50) with respect to the controls to get

$$\begin{aligned} \frac{\partial \mathcal{H}}{\partial u_1} &= W_1 u_1 + (\mathcal{M}_1 - \xi \mathcal{M}_2 - (1 - \xi) \mathcal{M}_3) \alpha_1 S \\ &\quad + ((\mathcal{M}_6 - \mathcal{M}_9)H + (\mathcal{M}_7 - \mathcal{M}_{10})A) \alpha_1, \\ \frac{\partial \mathcal{H}}{\partial u_2} &= W_2 u_2 + (\mathcal{M}_4 - \mathcal{M}_2)C + (\mathcal{M}_4 - \mathcal{M}_3)P \\ &\quad + (\mathcal{M}_{11} - \mathcal{M}_9)C_1 + (\mathcal{M}_{11} - \mathcal{M}_{10})C_2, \\ \frac{\partial \mathcal{H}}{\partial u_3} &= W_3 u_3 + ((\mathcal{M}_1 - \mathcal{M}_6)S + (\mathcal{M}_2 - \mathcal{M}_9)C \\ &\quad + (\mathcal{M}_3 - \mathcal{M}_9)P + (\mathcal{M}_4 - \mathcal{M}_6)R + (\mathcal{M}_5 - \mathcal{M}_6)) \alpha_2, \\ \frac{\partial \mathcal{H}}{\partial u_4} &= W_4 u_4 + (\mathcal{M}_8 - \mathcal{M}_6)H + (\mathcal{M}_8 - \mathcal{M}_7)A \\ &\quad + (\mathcal{M}_{11} - \mathcal{M}_9)C_1 + (\mathcal{M}_{11} - \mathcal{M}_{10})C_2. \end{aligned} \quad (55)$$

From system equation (55), we have

$$\begin{aligned} u_1^* &= \max\{0, \min\{1, \psi_1\}\}, \\ u_2^* &= \max\{0, \min\{1, \psi_2\}\}, \\ u_3^* &= \max\{0, \min\{1, \psi_3\}\}, \\ u_4^* &= \max\{0, \min\{1, \psi_4\}\}, \end{aligned} \quad (56)$$

where

$$\begin{aligned} \psi_1 &= \frac{((\xi \mathcal{M}_2 + (1 - \xi) \mathcal{M}_3 - \mathcal{M}_1)S + (\mathcal{M}_9 - \mathcal{M}_6)H + (\mathcal{M}_{10} - \mathcal{M}_7)A) \alpha_1}{W_1}, \\ \psi_2 &= \frac{(\mathcal{M}_2 - \mathcal{M}_4)C + (\mathcal{M}_3 - \mathcal{M}_4)P + (\mathcal{M}_9 - \mathcal{M}_{11})C_1 + (\mathcal{M}_{10} - \mathcal{M}_{11})C_2}{W_2}, \\ \psi_3 &= \frac{((\mathcal{M}_6 - \mathcal{M}_1)S + (\mathcal{M}_9 - \mathcal{M}_2)C + (\mathcal{M}_9 - \mathcal{M}_3)P + (\mathcal{M}_6 - \mathcal{M}_4)R + (\mathcal{M}_6 - \mathcal{M}_5)) \alpha_2}{W_3}, \\ \psi_4 &= \frac{(\mathcal{M}_6 - \mathcal{M}_8)H + (\mathcal{M}_7 - \mathcal{M}_8)A + (\mathcal{M}_9 - \mathcal{M}_{11})C_1 + (\mathcal{M}_{10} - \mathcal{M}_{11})C_2}{W_4}. \end{aligned} \quad (57)$$

Equation (54) leads to

$$\begin{aligned}
\frac{d\mathcal{M}_1}{dt} &= (\mathcal{M}_1 - \xi\mathcal{M}_2 - (1 - \xi)\mathcal{M}_3)(1 - u_1)\alpha_1 + (\mathcal{M}_1 - \mathcal{M}_5)\varphi_1 + \mathcal{M}_1\mu + (\mathcal{M}_1 - \mathcal{M}_6)(1 - u_3)\alpha_2, \\
\frac{d\mathcal{M}_2}{dt} &= -B_1 \left(\mathcal{M}_1 - \xi\omega\mathcal{M}_2 - (1 - \xi)\omega\mathcal{M}_3 \frac{S}{N} + (\mathcal{M}_6 - \mathcal{M}_9)\omega \frac{H}{N} + \mathcal{M}_7 - \mathcal{M}_{10}\omega \frac{A}{N} \right) (1 - u_1)\rho c \\
&\quad + (\mathcal{M}_2 - \mathcal{M}_3)\beta + (\mathcal{M}_2 - \mathcal{M}_4)(u_2 + \pi) + \mathcal{M}_2\mu + (\mathcal{M}_2 - \mathcal{M}_9)(1 - u_3)\alpha_2, \\
\frac{d\mathcal{M}_3}{dt} &= -B_2 + \left((\mathcal{M}_1 - \xi\mathcal{M}_2 - (1 - \xi)\mathcal{M}_3) \frac{S}{N} + (\mathcal{M}_6 - \mathcal{M}_9) \frac{H}{N} + (\mathcal{M}_7 - \mathcal{M}_{10} \frac{A}{N}) \right) (1 - u_1)\rho c \\
&\quad + (\mathcal{M}_3 - \mathcal{M}_9)(1 - u_3)\alpha_2 + (\mathcal{M}_3 - \mathcal{M}_4)(\epsilon + u_2) + \mathcal{M}_3(\mu + \nu_1), \\
\frac{d\mathcal{M}_4}{dt} &= (\mathcal{M}_4 - \mathcal{M}_1)\gamma + (\mathcal{M}_4 - \mathcal{M}_6)(1 - u_3)\alpha_2 + (\mathcal{M}_4 - \mathcal{M}_5)\varphi_2 + \mathcal{M}_4\mu, \\
\frac{d\mathcal{M}_5}{dt} &= (\mathcal{M}_5 - \mathcal{M}_6)(1 - u_3)\alpha_2 + \mathcal{M}_5\mu, \\
\frac{d\mathcal{M}_6}{dt} &= -B_3 + (\mathcal{M}_1 - \mathcal{M}_6) \frac{S}{N} + (\mathcal{M}_2 - \mathcal{M}_9) \frac{C}{N} + (\mathcal{M}_3 - \mathcal{M}_9) \frac{P}{N} + (\mathcal{M}_4 - \mathcal{M}_6) \frac{R}{N} \\
&\quad + (\mathcal{M}_5 - \mathcal{M}_6) \frac{V_1}{N} (1 - u_3)\eta k + (\mathcal{M}_6 - \mathcal{M}_9)(1 - u_1)\alpha_1 + (\mathcal{M}_6 - \mathcal{M}_8)\lambda_1 \\
&\quad + (\mathcal{M}_6 - \mathcal{M}_{12})\delta_1 + \mathcal{M}_6\mu, \\
\frac{d\mathcal{M}_7}{dt} &= -B_4 + (\mathcal{M}_1 - \mathcal{M}_6) \frac{S}{N} + (\mathcal{M}_2 - \mathcal{M}_9) \frac{C}{N} + (\mathcal{M}_3 - \mathcal{M}_9) \frac{P}{N} + (\mathcal{M}_4 - \mathcal{M}_6) \frac{R}{N} \\
&\quad + (\mathcal{M}_5 - \mathcal{M}_6) \frac{V_1}{N} (1 - u_3)\eta k a_2 + (\mathcal{M}_7 - \mathcal{M}_{10})(1 - u_1)\alpha_1 + (\mathcal{M}_7 - \mathcal{M}_8)(\tau_2 + u_4) \\
&\quad + (\mathcal{M}_7 - \mathcal{M}_{12})\delta_2 + \mathcal{M}_7(\mu + \nu_2), \\
\frac{d\mathcal{M}_8}{dt} &= -B_5 + (\mathcal{M}_8 - \mathcal{M}_{12})\delta_3 + \mathcal{M}_8\mu, \\
\frac{d\mathcal{M}_9}{dt} &= -B_6 + \left(\mathcal{M}_1 - \xi\mathcal{M}_2 - (1 - \xi)\mathcal{M}_3 \frac{S}{N} + (\mathcal{M}_6 - \mathcal{M}_9) \frac{H}{N} + \mathcal{M}_7 - \mathcal{M}_{10} \frac{A}{N} \right) (1 - u_1)\rho c \theta_1 \\
&\quad + (\mathcal{M}_1 - \mathcal{M}_6) \frac{S}{N} + (\mathcal{M}_2 - \mathcal{M}_9) \frac{C}{N} + (\mathcal{M}_3 - \mathcal{M}_9) \frac{P}{N} + (\mathcal{M}_4 - \mathcal{M}_6) \frac{R}{N} \\
&\quad + (\mathcal{M}_5 - \mathcal{M}_6) \frac{V_1}{N} (1 - u_3)\eta k a_1 + (\mathcal{M}_9 - \mathcal{M}_{10})\lambda_2 + (\mathcal{M}_9 - \mathcal{M}_{11})(\tau_3 + u_2 + u_4) + \mathcal{M}_9(\mu + \nu_1), \\
\frac{d\mathcal{M}_{10}}{dt} &= -B_7 + \left(\mathcal{M}_1 - \xi\mathcal{M}_2 - (1 - \xi)\mathcal{M}_3 \frac{S}{N} + (\mathcal{M}_6 - \mathcal{M}_9) \frac{H}{N} + \mathcal{M}_7 - \mathcal{M}_{10} \frac{A}{N} \right) (1 - u_1)\rho c \theta_2 \\
&\quad + (\mathcal{M}_1 - \mathcal{M}_6) \frac{S}{N} + (\mathcal{M}_2 - \mathcal{M}_9) \frac{C}{N} + (\mathcal{M}_3 - \mathcal{M}_9) \frac{P}{N} + (\mathcal{M}_4 - \mathcal{M}_6) \frac{R}{N} \\
&\quad + (\mathcal{M}_5 - \mathcal{M}_6) \frac{V_1}{N} (1 - u_3)\eta k a_3 + (\mathcal{M}_{10} - \mathcal{M}_{11})(\tau_4 + u_2 + u_4) + \mathcal{M}_{10}(\mu + \nu), \\
\frac{d\mathcal{M}_{11}}{dt} &= -B_8 + (\mathcal{M}_{11} - \mathcal{M}_{12})\delta_4 + \mathcal{M}_{11}\mu, \\
\frac{d\mathcal{M}_{12}}{dt} &= -B_9 + \mathcal{M}_{12}\mu,
\end{aligned} \tag{58}$$

with transversality conditions

$$\mathcal{M}_i(t_f) = 0, \quad \text{for } i = 1, 2, 3, \dots, 12. \quad (59)$$

Thus, the optimality system combines system equations (47) and (58).

5. Sensitivity Analysis and Numerical Simulations

To side with the analytical results in the previous sections, sensitivity analysis and numerical simulations are performed. Different literature has been reviewed and realistic parameter values obtained for the purpose of numerical illustrations.

5.1. Sensitivity Analysis of the Effective Reproduction Number

Definition 1. The normalized forward sensitivity index of a variable, x , that depends differentially on a parameter y is described as $SI(y) = (\partial x / \partial y) \times y / x$ [28, 29].

The sensitivity indices are vital in investigating the comparative influence of different parameters within HIV/AIDS and pneumococcal pneumonia co-infection transmission. The most sensitive parameter is the one that has a larger magnitude of sensitivity index compared to other parameters. Thus, from Definition 1, the sensitivity index of $\mathcal{R}_e$ with respect to parameter y is expressed as

$$\Lambda_y^{\mathcal{R}_e} = \frac{\partial \mathcal{R}_e}{\partial y} * \frac{y}{\mathcal{R}_e}. \quad (60)$$

Applying parameter values in Table 2, the sensitivity indices in Tables 3 and 4 are achieved.

The sensitivity indices in terms of $\mathcal{R}_e = \mathcal{R}_{eH} = (\eta k / q_1^* q_2^*) (q_2^* + a_2 \lambda_1)$ and the sensitivity indices in terms of $\mathcal{R}_e = \mathcal{R}_{eP} = (\rho c \mu) / ((\varphi_1 + \mu) k_1 k_2) (\xi (\omega k_2 + \beta) + (1 - \xi) k_1)$ are given in Tables 3 and 4, respectively, and their graphical representation is displayed in Figure 2.

In reference to Figure 2, parameters η, k, ρ , and c are the most sensitive parameters to $\mathcal{R}_e$ and a reduction in these parameters can have an inhibiting influence on the transmission of both HIV/AIDS and pneumococcal pneumonia. Increasing the values of treatment rates, $\tau_1, \tau_2, \pi, \epsilon$, and vaccination rates, $\sigma_1, \sigma_2, \varphi_1$, can be a decisive step in reducing HIV/AIDS, pneumococcal pneumonia, and hence, their co-infection.

5.2. Numerical Simulations. Here, we conduct numerical solutions of system equation (1) and optimal system equation (47). All numerical computations were performed in MATLAB using ode45 solver. The baseline parameters in Table 2 are used. Additionally, the initial compartmental values $S(0) = 5000, C(0) = 200, I_P(0) = 250, R(0) = 150, V_P(0) = 200, I_H(0) = 400, I_A(0) = 250, I_T(0) = 300, I_{HP}(0) = 2500, I_{AP}(0) = 1500, T(0) = 150$, and $V_H(0) = 10$ are also used. To run the optimal control simulations, the costs $B_1 = 30, B_2 = 35, B_3 = 40, B_4 = 43, B_5 = 50, B_6 = 35, B_7 = 35, B_8 = 55, B_9 = 55$ and weights $W_1 = 25, W_1 = 15, W_3 = 15, W_4 = 20$ are used.

TABLE 2: Parameter values applied the simulation of the model.

Parameter	Value/year ⁻¹	Source
φ_1	0.008	[29]
σ_1	0.2	Assumed
σ_3	0.3	Assumed
μ	0.073	[30]
Λ	2000	Assumed
β	0.01096	[12,31]
ν_2	0.333	[32]
k	1–5	Estimated
τ_3	0.314	Estimated
ξ	0.338	[14]
c	1–50	Assumed
ω	0.41026	[14]
τ_1	0.2	Estimated
a_1, a_2, a_3	1, 1.2, 1.4	Assumed
φ_2	0.6	Assumed
σ_2	0.4	Assumed
σ_4	0.1	Assumed
η	0.075	[33]
γ	0.0621	[12]
ν_1	0.1	[30]
ν	0.42	[32]
ρ	0.89–0.99	[7]
τ_4	0.230	[13]
λ_1, λ_2	0.08, 0.3105	[32]
ϵ	0.2	Assumed
π	0.0115	Estimated
τ_2	0.13	[13]
θ_1, θ_2	1, 1.02	Assumed

TABLE 3: Numerical values of sensitivity indices of $\mathcal{R}_{eH}$

Parameter symbol	Sensitivity index
η	+1.0000
k	+1.0000
a_2	+0.1030
μ	–0.0141
σ_1	–0.3617
τ_1	–0.3617
τ_2	–0.0160
λ_1	–0.0417
ν_2	–0.0410
σ_2	–0.0370

TABLE 4: Numerical values of sensitivity indices of $\mathcal{R}_{eP}$

Parameter symbol	Sensitivity index
ρ	+1.0000
c	+1.0000
ξ	+0.1953
ω	+0.4360
β	–0.0224
μ	–0.3689
ϵ	–0.3024
ν_1	–0.1512
π	–0.0563
φ_1	–0.0988

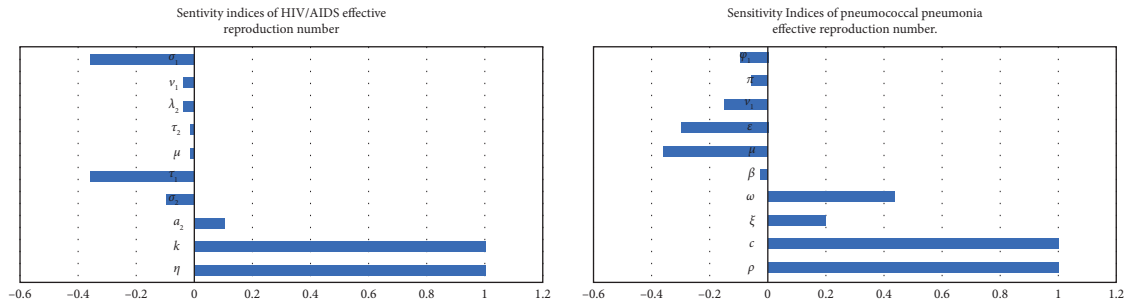


FIGURE 2: Graphical representation of sensitivity indices.

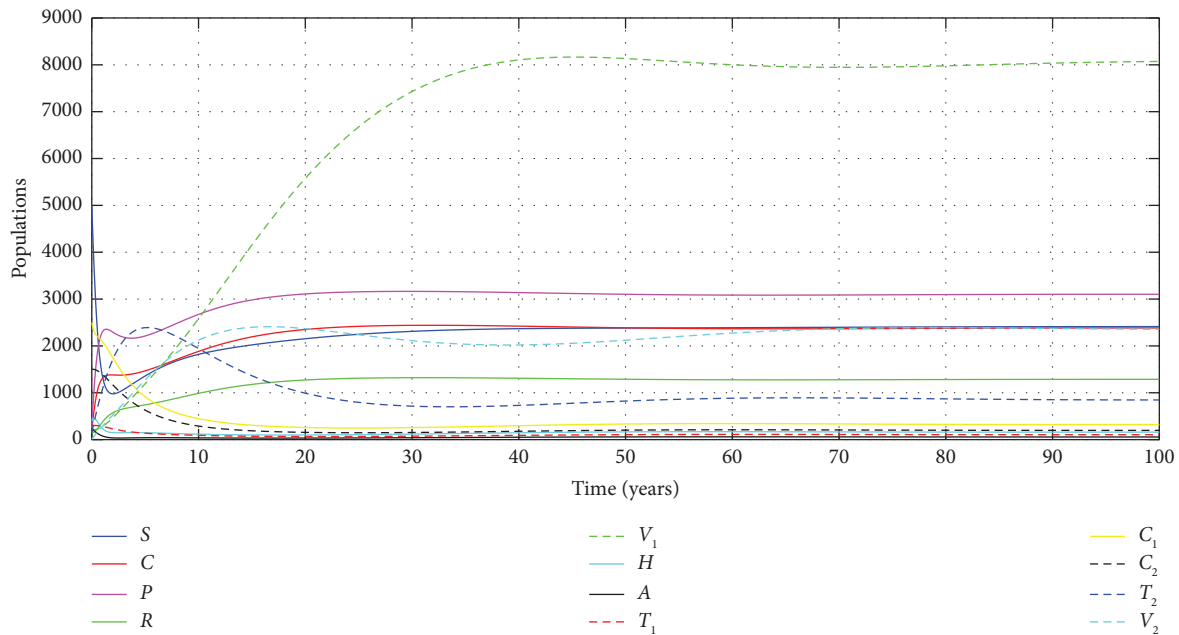


FIGURE 3: Behavior of HIV/AIDS and pneumococcal pneumonia co-infection model.

5.2.1. Simulations of Model System Equation (1). We investigate the nature of state solutions of HIV/AIDS and pneumococcal pneumonia co-infection model equation (1) when $\mathcal{R}_e = \max\{\mathcal{R}_{ep}, \mathcal{R}_{eH}\} = \max\{13.3608, 1.1963\} = 13.3608 > 1$. In Figure 3, all numerical routines show that numerical solution trajectories converge to the endemic stable state of system equation (1).

Figure 4 manifests the effect of combining HIV/AIDS therapy, pneumococcal pneumonia treatment, and vaccination on mono-infected individuals. The results reveal that a combination of treatment and vaccination against pneumonia reduces the carriers and the infected individuals. Furthermore, HIV/AIDS therapy and pneumonia vaccination among HIV/AIDS subpopulations is a better intervention than therapy alone.

The effect of pneumonia treatment, vaccination, and HIV/AIDS therapy on the co-infected individuals is shown in Figure 5. Figure 5 reveals that a combined effort of pneumonia treatment and vaccination and HIV/AIDS therapy has a greater influence in the reduction of co-infected individuals compared to a single intervention or no strategy at all.

Figure 6 shows that increasing the coefficient of transmission of pneumococcal pneumonia carriers implies an increase in the number of HIV/AIDS and pneumococcal pneumonia co-infected individuals.

Figures 7 and 8 show that increasing the rates of pneumonia vaccination in susceptible, recovered, and HIV/AIDS-infected individuals leads to a reduction in the number of co-infected individuals.

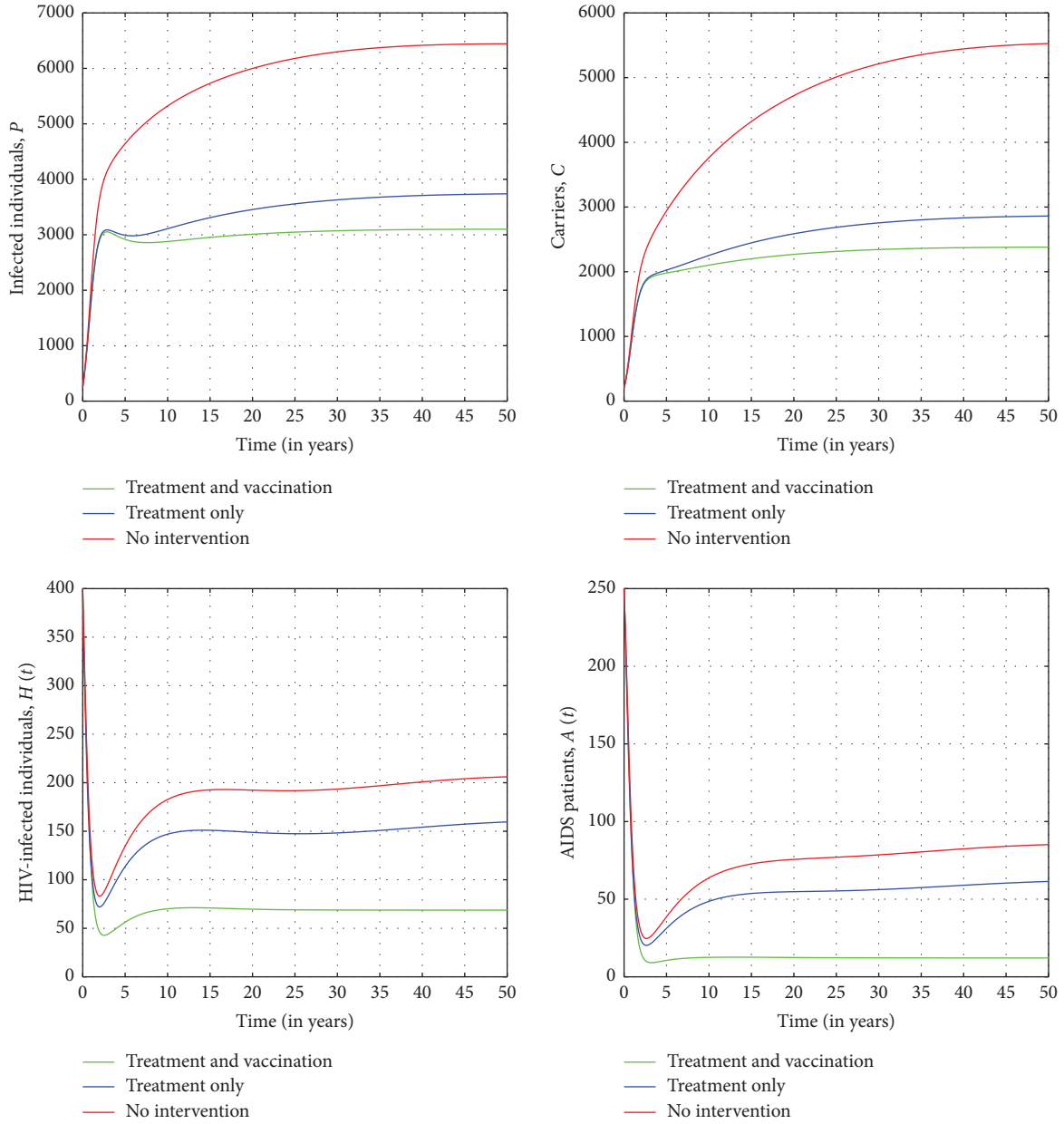


FIGURE 4: Effect of treatment and vaccination on HIV/AIDS and pneumococcal pneumonia mono-infections.

5.2.2. Simulations for the Optimal Control Model. A fourth-order Runge-Kutta algorithm is applied to simulate the optimality system equations (47) and (58) numerically. The following approaches are proposed in the simulation of the optimal system:

Strategy 1: Implementing protection against both HIV and pneumococcal pneumonia only, that is, $u_1 \neq 0, u_2 = 0, u_3 \neq 0, u_4 = 0$.

Strategy 2: Implementing controls fixed on pneumococcal pneumonia alone, that is, $u_1 \neq 0, u_2 \neq 0, u_3 = 0, u_4 = 0$.

Strategy 3: Implementing controls fixed on HIV/AIDS alone, that is $u_1 = 0, u_2 = 0, u_3 \neq 0, u_4 \neq 0$.

Strategy 4: Implementing early detection and treatment for both HIV/AIDS and pneumococcal pneumonia, that is, $u_1 = 0, u_2 \neq 0, u_3 = 0, u_4 \neq 0$.

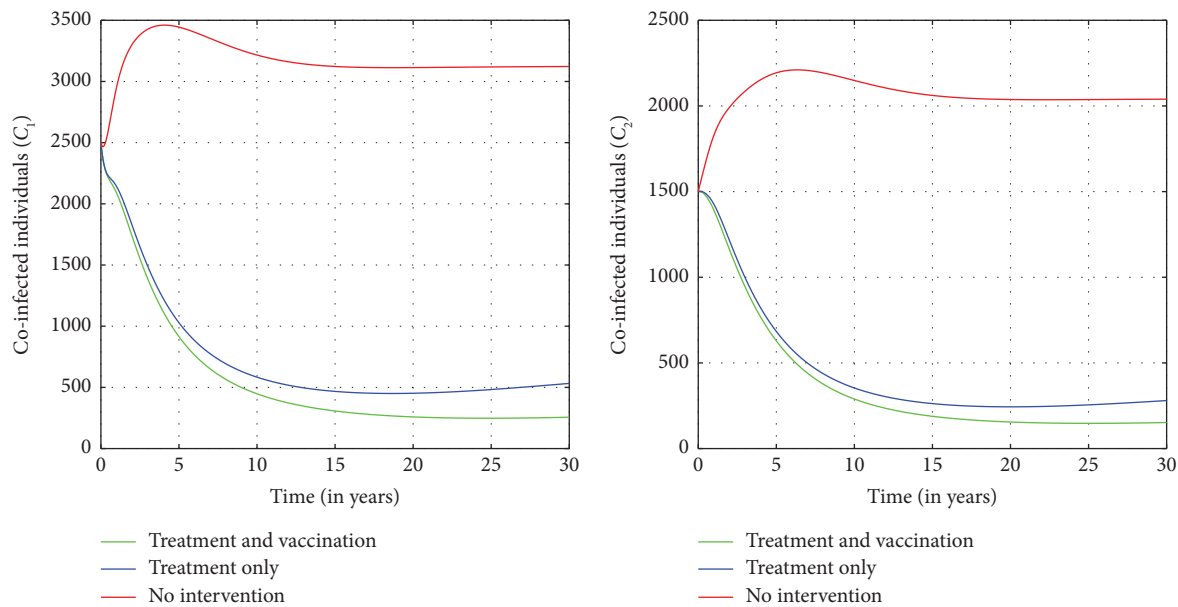


FIGURE 5: Effect of treatment and vaccination on the co-infection.

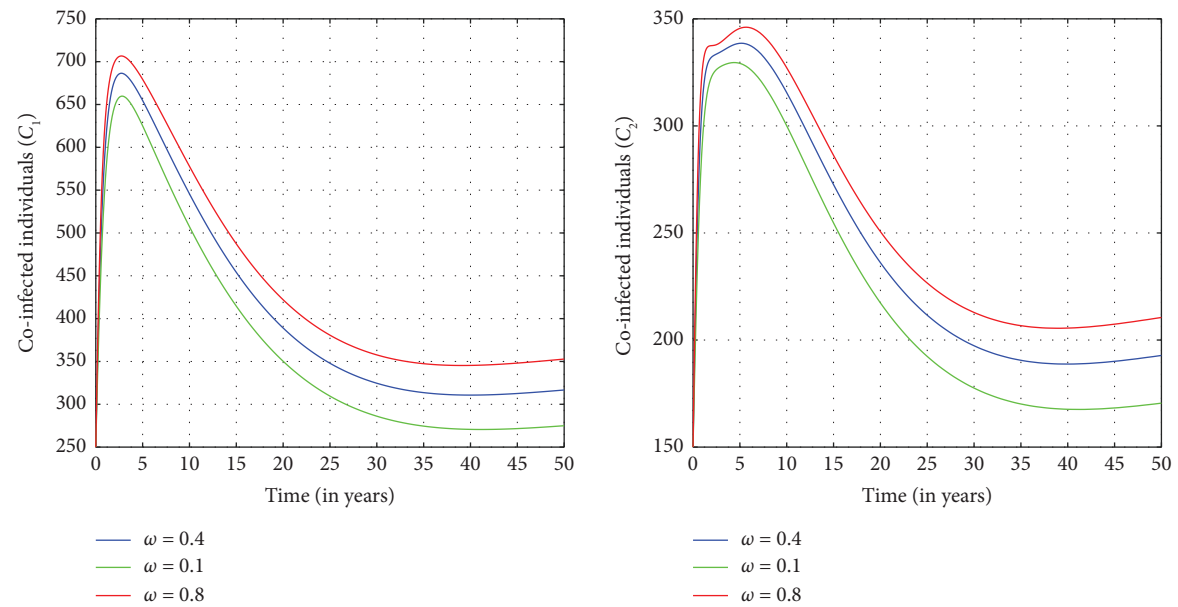


FIGURE 6: Role played by pneumococcal carriers on the dynamics of the co-infection.

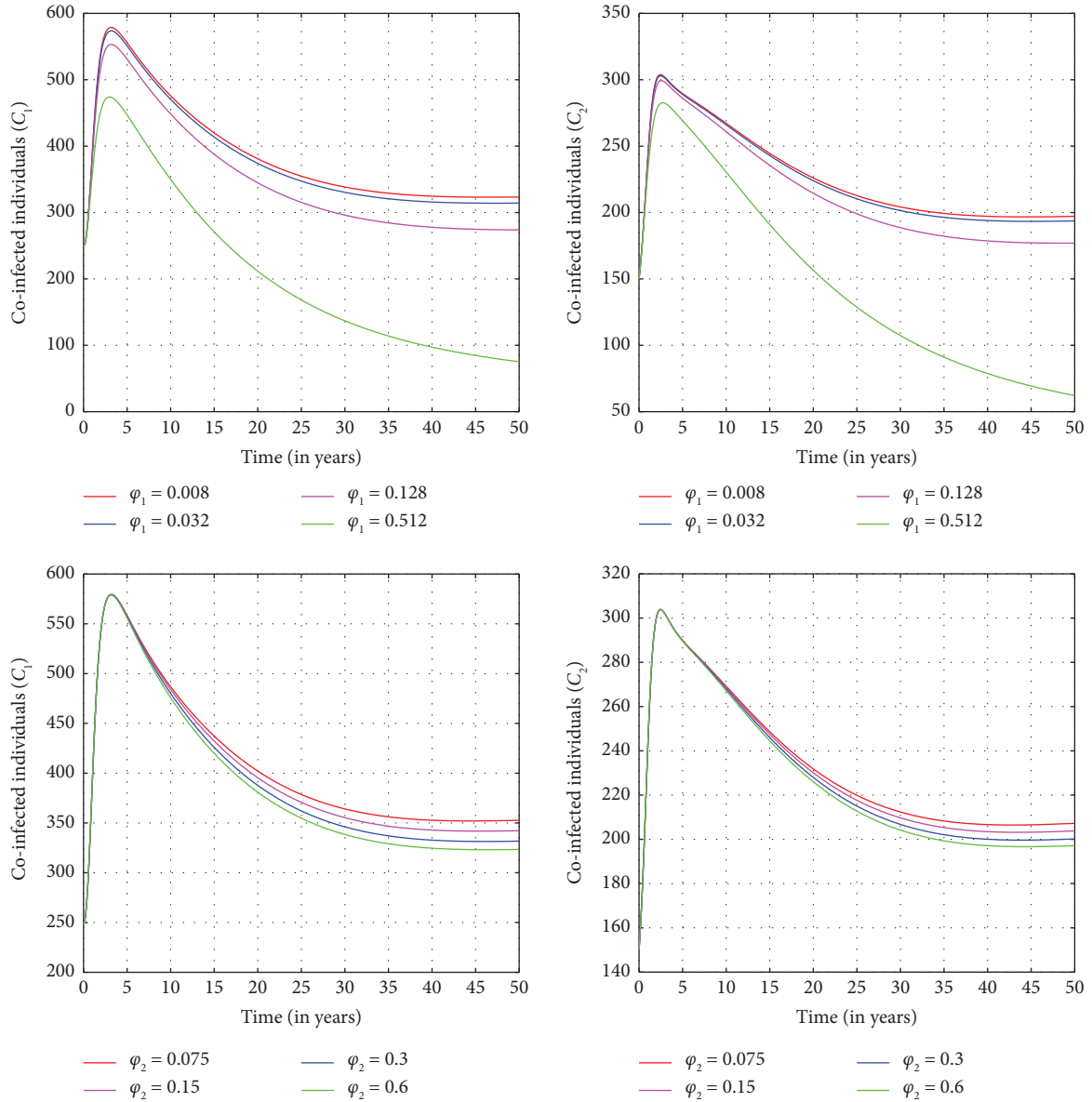


FIGURE 7: Effect of varying vaccination parameters γ_1 and γ_2 on the co-infection.

Strategy 5: Implementing all controls, that is, $u_1 \neq 0, u_2 \neq 0, u_3 \neq 0, u_4 \neq 0$.

HIV and pneumococcal pneumonia protection efforts are implemented in Figure 9. There is a slight decrease in the number of co-infected individuals over time.

In Figure 10, controls u_1 and u_2 are applied to assess their contribution in the control of the co-infection burden. The results in Figure 10 show a decrease in the number of co-infected individuals. The strategy does not demonstrate complete eradication of the co-infection in the short term; however, there is a decrease in the co-infection burden.

Pneumococcal pneumonia is curable and hence if efforts are put in place to identify and treat carriers and infected individuals, then the association between pneumonia and HIV/AIDS can be interrupted.

Controls u_3 and u_4 are taken on in the control dynamics of HIV/AIDS and pneumococcal pneumonia co-infection in Figure 11. Simulations in Figure 11 show a decrease in the number of co-infected individuals.

In Figure 12, efforts u_2 and u_4 are utilized in the dynamics of HIV/AIDS and pneumococcal pneumonia co-infection. Figure 12 manifests a decrease in the number of co-infected individuals.

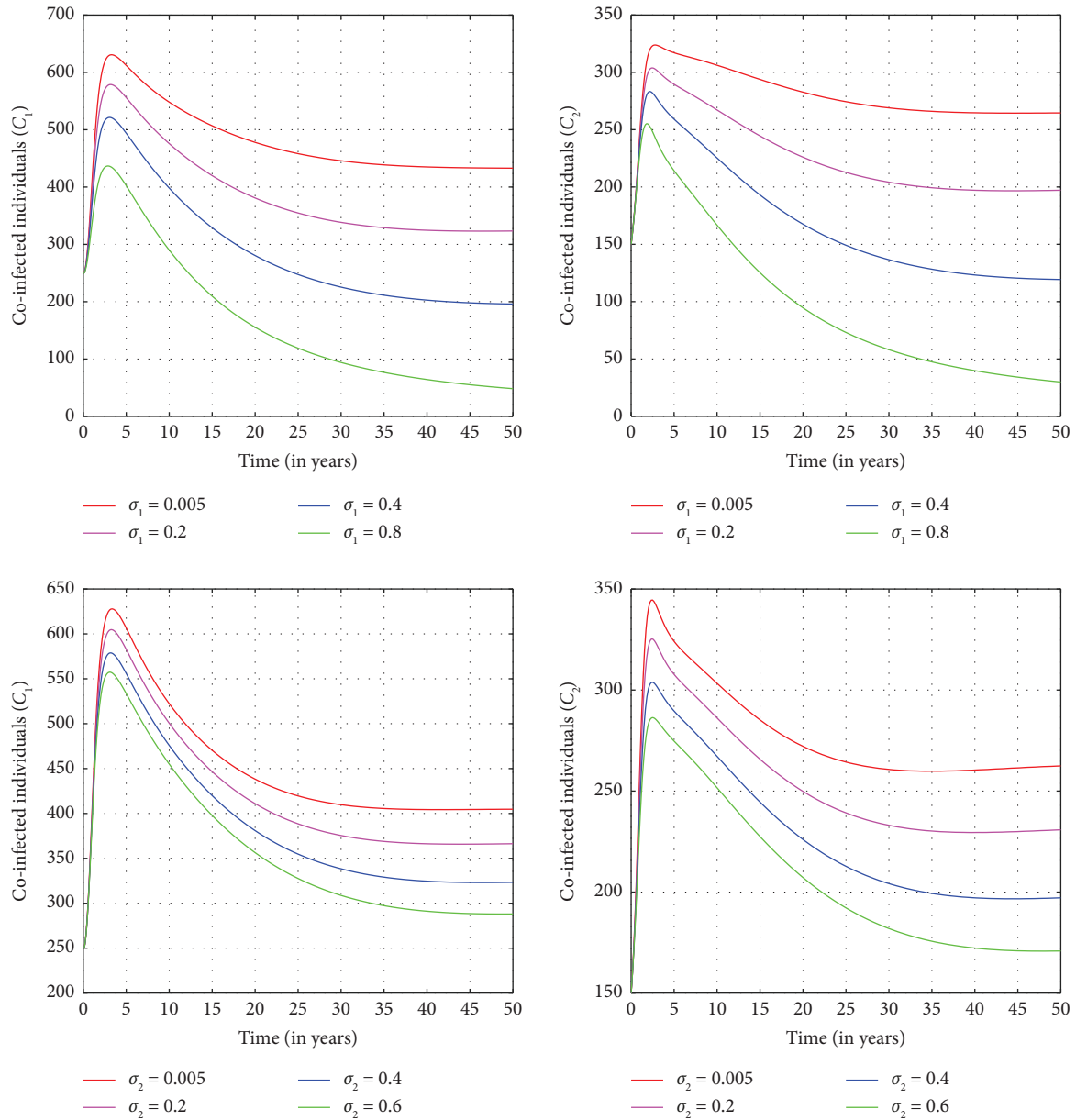
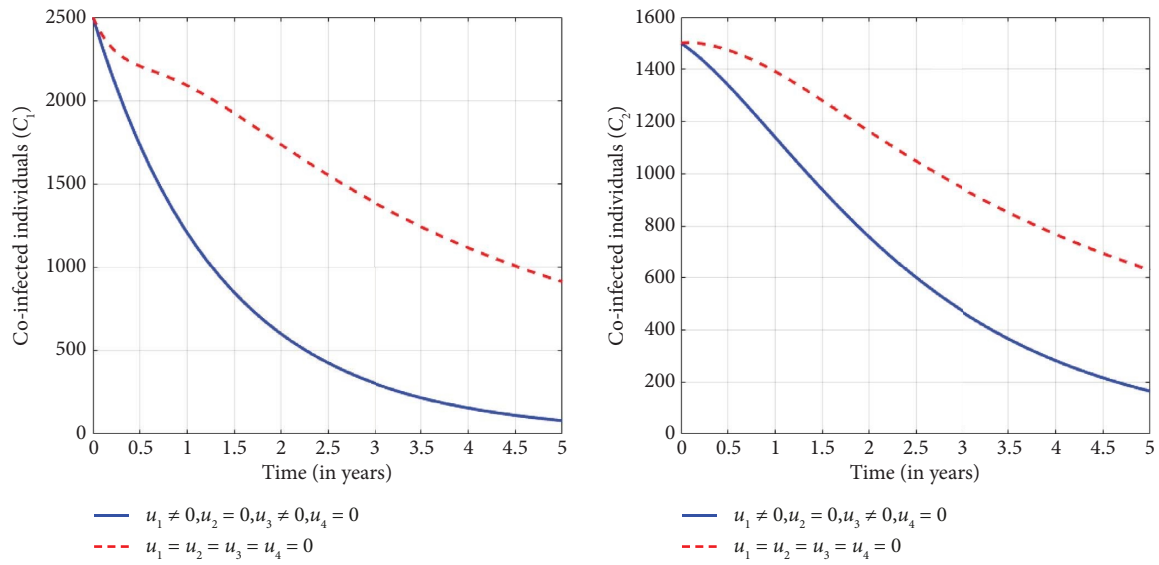
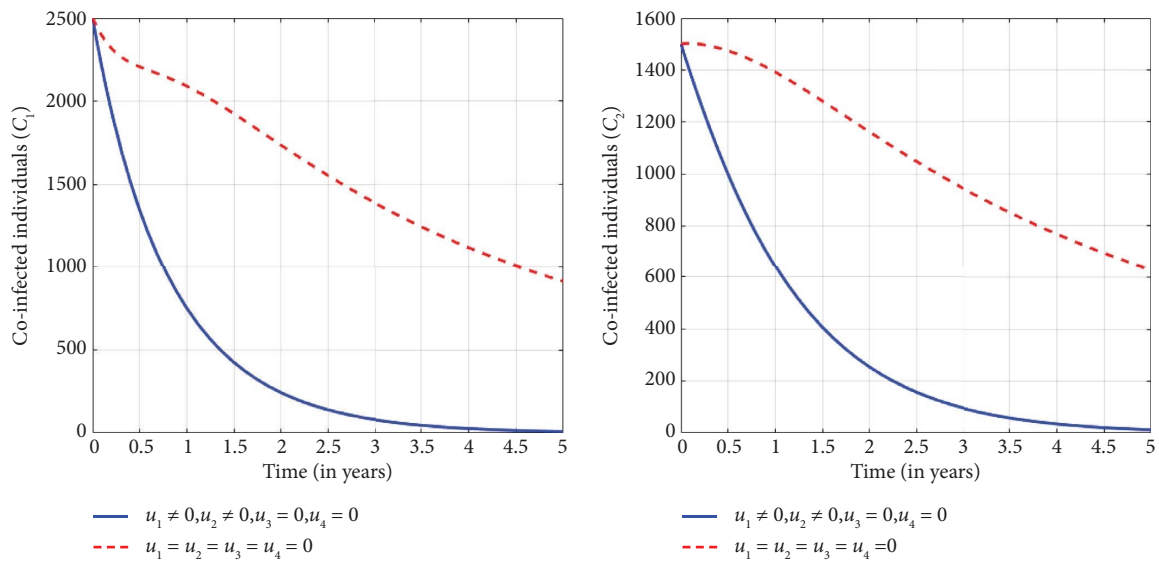
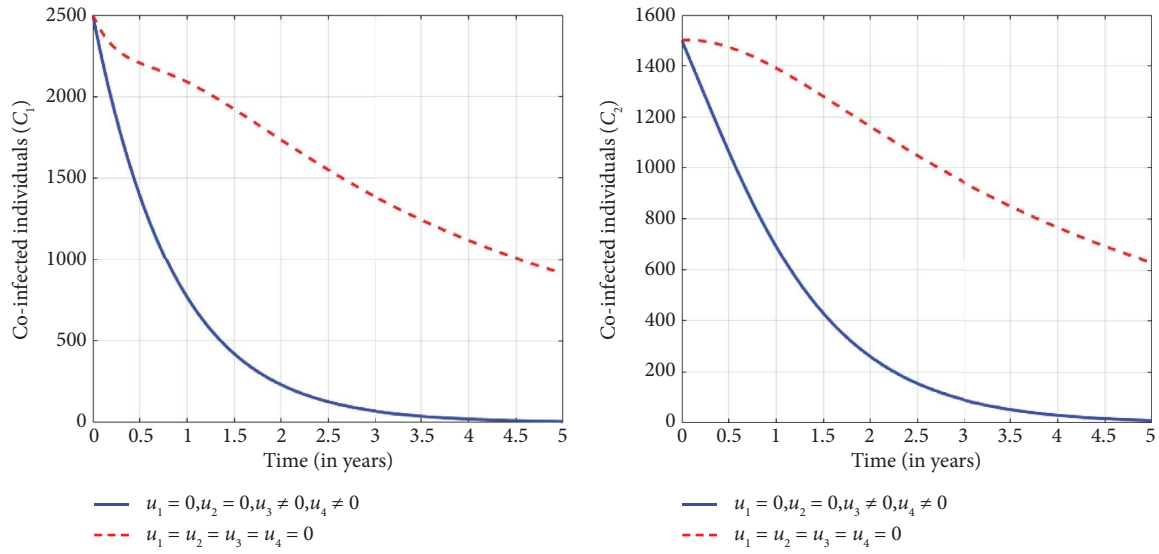
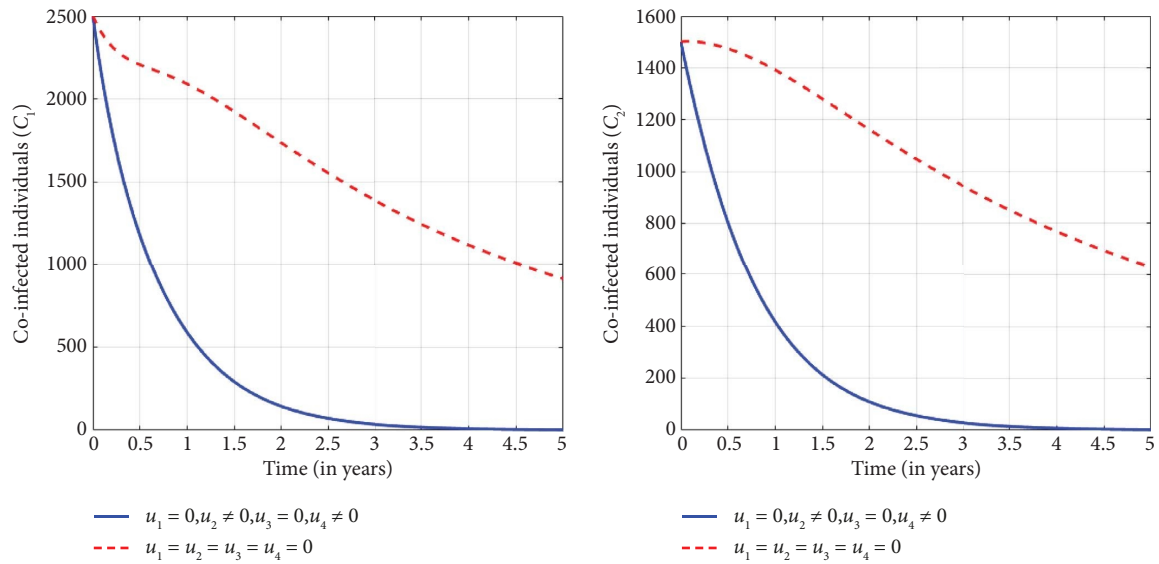


FIGURE 8: Effect of varying vaccination parameters σ_1 and σ_2 on the co-infection.

All the controls u_1 , u_2 , u_3 , and u_4 are put into action to evaluate their effect on the control of HIV/AIDS and pneumonia co-infection in Figure 13. The results in Figure 13 demonstrate a remarkable drop in the number of co-

infected individuals. The results further indicate that the HIV-pneumonia and AIDS-pneumonia co-infected individuals would nearly be wiped out from the community in about two and a half years if all controls are implemented.

FIGURE 9: Effect of prevention interventions (u_1, u_3) on the co-infection.FIGURE 10: Effect of controls u_1 and u_2 on co-infected populations.

FIGURE 11: Effect of controls u_3 and u_4 on co-infected populations.FIGURE 12: Effect of u_2 and u_4 intervention strategies on co-infected populations.

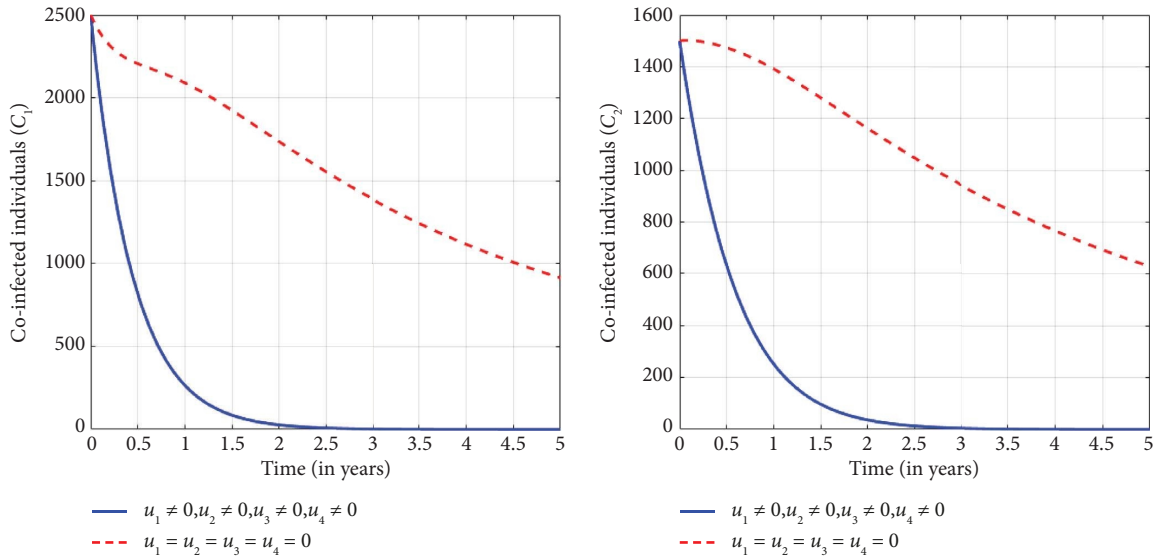


FIGURE 13: Effect of all intervention strategies on the co-infection.

TABLE 5: Percentage reduction in the number of co-infected individuals within 2 years.

Strategy	Co-infected individuals C_1	Co-infected individuals C_2
Treatment only	27	19
Treatment and vaccination	30	22
Strategy 1	77	57
Strategy 2	90	82
Strategy 3	90	83
Strategy 4	94	93
Strategy 5	98	97

5.2.3. Summary of Implementing Each Intervention Strategy.

Table 5 gives a summary of the percentage reductions in the number of co-infected individuals when each strategy is implemented in about 2 years.

6. Discussion and Conclusions

This paper presents the HIV/AIDS and pneumococcal pneumonia co-infection mathematical model designed using ordinary differential equations. The model incorporates interventions that include HIV/AIDS therapy, pneumococcal pneumonia treatment, and vaccination. Careful investigation of the HIV/AIDS and pneumococcal pneumonia co-infection model shows that the solutions are positive and bounded, by the next generation matrix approach, the effective reproduction numbers are computed, and relevant conditions for local and global asymptotic stabilities of both the disease-free and disease endemic equilibria are established. The sensitivity analysis of the co-infection model shows that the important parameters that can be impactful in the effective reproduction numbers of the model are the HIV contact rate and its corresponding probability of infection, pneumococcal pneumonia contact rate and its corresponding probability of infection, and the coefficient of transmission of pneumococcal carriers in acceleration of the co-infection burden. Sensitivity analysis further showed that

HIV/AIDS therapy, pneumococcal treatment, and vaccination rates would decrease the co-infection burden if increased. Moreover, increasing vaccination rates directly leads to reduced co-infected individuals.

To verify analytical results, numerical simulations were executed. It was revealed that the solutions converge to the endemic equilibrium point whenever $\mathcal{R}_e > 1$. Furthermore, numerical simulations indicated that a combination of HIV/AIDS therapy, pneumonia treatment, and vaccination would considerably reduce the co-infection burden compared to a single strategy or no strategy at all. The role played by pneumococcal pneumonia carriers is with no doubt evident and measures should be put in place to detect and treat carriers if the co-infection burden is to be managed.

Having examined the role of treatment/therapy and vaccination, model system equation (1) was extended to include time dependent controls u_1, u_2, u_3 , and u_4 as explained in Section 4. The resulting optimal control system was analyzed by Pontryagin's maximum principle to establish conditions for characterization of the optimality system. Simulations give evidence that each of the combination strategies depicts a reduction in the co-infection burden; however, the level of curtailment is different for each strategy implemented. Simulations support that a combination of all strategies is the most effective with possible eradication of HIV-pneumococcal pneumonia and AIDS-pneumococcal

pneumonia co-infected individuals in about 2 years of implementation as seen in Table 5. In situations where the resources are scanty to enforce all the control strategies, a combination of early detection and treatment for both HIV/AIDS and pneumococcal pneumonia can be taken on in the effort to eradicate or reduce the co-infection burden.

By this result, it is evident that treatment alone is not sufficient in mitigating the HIV/AIDS and pneumonia co-infection burden. Therefore, for extra relief from the co-infection burden, we recommend that a mandatory immunization campaign against pneumonia for all HIV-infected individuals be implemented. Furthermore, implementing a combination of protection against both HIV and pneumococcal pneumonia and early detection and treatment of mono-infected and co-infected individuals are crucial in minimizing the co-infection burden. This result agrees with the work in [15], where a combination of all strategies would lead to co-infection reduction.

The future directions of this study will be including acute and chronic HIV stages of infection, evaluating the role of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) in the dynamics of the co-infection, looking at the effect of pneumococcal vaccine nonreactiveness and individuals who default ART in the co-infection dynamics, and changing the modeling approach to stochastic in order to see how perturbations affect the system.

Data Availability Statement

No new data were created or analyzed in this article.

Conflicts of Interest

The authors declare no conflicts of interest.

Funding

No funding was received for this research.

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