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Computational Modelling of Pneumonia Disease Transmission Dynamics with Optimal Control Analysis

Timothy Kiprono Yano*, Jacob Bitok

Department of Mathematics and Computer Science, University of Eldoret, Eldoret, Kenya

Email address:
yano.timothy@students.jkuat.ac.ke (Timothy Kiprono Yano), jacobbitok@yahoo.com (Jacob Bitok)
*Corresponding author

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Abstract: A normalized pneumonia mathematical model is formulated and analyzed to describe the transmission dynamics of pneumonia disease with a varying population size and in the presence of drug resistance threats. The main aim of the study is to formulate and analyze a pneumonia optimal control model that implements varied control strategies against antibiotic resistance threats and varying population size. The stability theory of differential equations and Pontryagin's Maximum Principle for an optimality system were employed to determine the crucial properties of the mathematical model. The basic reproduction number is determined using the Next generation matrix approach and the stability analysis for the disease-free and as well as for the endemic equilibrium are determined. The sensitivity indices of the effective reproduction number to the crucial parameter values are determined and ranked as per their impact on the transmission of pneumonia disease. We extend the model to an optimal control problem with four control strategies: disease prevention effort, treatment effort that minimize the sensitive and resistant strain and immunity control effort. The optimal control analysis of the adopted control efforts revealed that the combination of prevention and treatment, prevention and immunity control and a combination of all controls are the effective intervention strategies that result in a decrease in infections in the community. Numerical simulations are performed for a combination of other strategies and pertinent results were displayed graphically.

Keywords: Streptococcus Pneumoniae, Effective Reproductive Number, Pontryagin's Maximum Principle, Optimal Control, Sensitivity Indices, Numerical Simulation, Optimal Control Analysis

1. Introduction

The main causative agent of bacterial pneumonia is known as Streptococcus Pneumoniae which is the most rampant community based acquired pneumonia globally [4]. Pneumonia prevalence has witnessed an increased rate in low-income compared to high-income nations with the highest vulnerability seen in minors aged between 0-5 years, the old, and individuals with underlying conditions like terminal illnesses or weak immunity [4, 12].

Pneumonia is widely known to be the greatest contributor to child death globally. Yearly, it is approximated to cause up to 1.2 million deaths especially among children under 5 years of age, which amounts to an estimated 18% occurring in under five-year-old. Pneumonia has a large impact on children and communities globally with the highest and most profound incidences taking place in low-income continents like South Asia and sub-Saharan Africa [12, 7, 4]. Pneumonia bacteria are often sitting in a person's nose, mucus or throat and are mainly transmitted from one person to another through the following ways: Inhaling bacteria through the lungs, transmitted through flying droplets like mucus and saliva emerging due to a cough or sneeze and pneumonia can be transferred through blood with higher cases taking place during and slightly after birth [12, 4].

The features to note in a case of pneumonia infection are: increased episodes of breathing difficulties, constant cough, high fever and feeling chilly and lack of appetite. Severe cases in children lead to lower chest pain when inhaling and exhaling. Extremely severe scenarios lead to inability to eat or drink, loss of consciousness and convulsions see [12, 4]. Bacterial pneumonia can be easily treated in hospitals by administering prescribed antibiotic drugs to the patients. Pneumonia can be

prevented in a number of ways which include: immunization programs given to children between 0-5 years, providing good nutrition to children to help build their immunity and develop a defense mechanism for infectious diseases, addressing environmental contributors such as pollution of air with poisonous gases and dust particles [12].

The WHO 2013 Fact sheet indicates that pneumonia is the world's leader in causing child deaths, estimating 16% of all deaths of children under 5 years old, killing an estimated 2,400 children per day in 2015 [12]. Globally, there exist 120 million cases of pneumonia per year in children under 5, with approximately 10% (14 million) progressing to severe cases. There were approximately 880,000 deaths from pneumonia in children under 5 years old in 2016 [12].

The emergence of antimicrobial resistance to treatment is viewed by many researchers to be one of the concerns, that is, a life threat to human health in the 21st century. Antibiotic resistance is easily enhanced by the misuse and overdose of antibiotic drugs. Poor infection prevention and control strategies also contribute to antibiotic resistance. Intervention strategies can be taken at all levels of society to reduce the impact and limit the spread of resistance [13].

Over the years, pneumonia models have been formulated to describe the transmission dynamics of pneumonia disease. Notably, mathematical modelling has been a significant guide to the development and implementation of policy measures undertaken by health agencies to curb the transmission of infectious diseases, studies done by Assaad et al. [1], Huang et al. [6], Kizito and Tumwiine [8], Mbabazi et al. [9], Otoo et al. [15], Tilahun et al. [18-20] and Swai et al. [17] attempt to describe the transmission dynamics of pneumonia. Some studies have done optimal control analysis of intervention strategies applied to pneumonia transmission dynamics and its impact on disease control. From the reviews of the cited literature, few studies have assessed the dynamics of pneumonia using a varying population size in the presence of drug resistance threats. In addition to a varying population size, this study introduces a drug-resistant strain of pneumonia together with a drug-sensitive strain and we undertake an optimal control analysis of the model.

The paper's main target is to formulate and analyze a pneumonia optimal control model that implements varied control strategies with antibiotic resistance threats and varying population size. The paper is organized as follows: Section 2 was devoted to the formulation of a pneumonia model and indicates the parameters used. In Section 3, we study the model properties qualitatively and identify the key determinants that shape the dynamics. In section 4, we undertake the sensitivity analysis of the model parameters. In this section, we analyze the optimal control problem. Section 5 analyzes the computational findings of the study using tables and graphs. Section 6 was solely used to draw conclusions and areas for further studies.

2. Model Formulation

The model has been designed as follows: Susceptible, S, an infected group which is sensitive to treatment, I_s, an infected group which is anti-biotic resistant, I_r and a recovery, R, represents the vaccinated and recovered from infection who have waning immunity to the disease and progress to the susceptible at the rate ϕ. Individuals are born into the community with the proportion of susceptible that are vaccinated as ε $(0 < \varepsilon < 1)$ and we take the remaining are susceptible. We take that recruitment is by birth approximated by a rate φ with a varying population size. A susceptible individual is infected through contact with an infective drug sensitive individual, approximated by an average contact rate f_1 or through contact with an infective drug resistant individual with an average contact rate $f_2 \cdot \mu$ is the natural death rate for all the groups, α_1 represents death rate due to a drug sensitive disease infection α_2 death rate due to disease infection from drug resistant group. δ is the progression rate from infective but sensitive to treatment group to drug resistant group, σ is the progression rate from drug resistant group to recovered group and ω is the progression rate from infected group to recovered group due to treatment. The controls u_1 represents a prevention effort, that protects susceptible individuals from contacting the disease, u_2 represents a treatment effort, that minimizes infection by treating drug sensitive infectious individuals, u_3 represents a treatment control effort, that minimizes infections by treating drug-resistant individuals and u_4 represents an immunity effort, represents a reduction in the loss of disease immunity due to improved vaccination and treatment efficacy. We obtain the optimal control model problem of pneumonia as:

$$\begin{cases} \frac{dS}{dt} = (1-\varepsilon)\varphi N + (1-u_4)\phi R - (1-u_1)\left(f_1\frac{SI_s}{N} + f_2\frac{SI_r}{N}\right) - \mu S \\ \frac{dI_s}{dt} = (1-u_1)\left(f_1\frac{SI_s}{N} + f_2\frac{SI_r}{N}\right) - u_2\omega I_s - (\delta+\mu+\alpha_1)I_s \\ \frac{dI_r}{dt} = \delta I_s - u_3\sigma I_r - (\mu+\alpha_2)I_r \\ \frac{dR}{dt} = \varepsilon\varphi N + u_2\omega I_s + u_3\sigma I_r - (1-u_4)\phi R - \mu R \end{cases} \quad (1)$$

such that $f_1 = \xi\tau, f_2 = \xi\tau\Upsilon$, where ξ is the number of contacts contact rate, τ is the possibility that a contact is effective to spread the disease and Υ is coefficient for the resistant strain transmission, with initial conditions, $S(0) = S_0, I_s(0) = I_{s(0)}, I_r(0) = I_{r(0)}$ and $R(0) = R_0$ such that $N = S + I_s + I_r + R$ and that $\varphi, \phi, f_1, f_2, \mu, \omega, \delta, \alpha_1, \alpha_2, \sigma$ are all positive constant parameters.

Sum of the equations in the nonlinear system (1) gives

$$\frac{dN}{dt} = \varphi - \mu N - \alpha_1 I_s - \alpha_2 I_r \quad (2)$$

Normalizing the variables, $s = \frac{S}{N}, i_s = \frac{I_s}{N}, i_r = \frac{I_r}{N}$ and

$r = \frac{R}{N}$ which gives the system, we still use $s = S, i_s = I_s, i_r = I_r$ and $r = R$ for convenience.

$$\begin{cases} \frac{dS}{dt} = (1-\varepsilon)\varphi + (1-u_4)\phi R - (1-u_1)(f_1 SI_s + f_2 SI_r) - \varphi S + \alpha_1 SI_s + \alpha_2 SI_r \\ \frac{dI_s}{dt} = (1-u_1)(f_1 SI_s + f_2 SI_r) - u_2\omega I_s - (\delta + \alpha_1)I_s - \varphi I_s + \alpha_1 I_s^2 + \alpha_2 I_s I_r \\ \frac{dI_r}{dt} = \delta I_s - u_3\sigma I_r - \alpha_2 I_r - \varphi I_r + \alpha_1 I_s I_r + \alpha_2 I_r^2 \\ \frac{dR}{dt} = \varepsilon\varphi + u_2\omega I_s + u_3\sigma I_r - (1-u_4)\phi R - \varphi R + \alpha_1 I_s R + \alpha_2 I_r R \end{cases} \tag{3}$$

System (3) can be reduced further by setting $r(t) = 1 - S(t) - I_s(t) - I_r(t)$, giving a sub-system,

$$\begin{cases} \frac{dS}{dt} = (1-\varepsilon)\varphi + (1-u_4)\phi(1 - S(t) - I_s(t) - I_r(t)) - (1-u_1)(f_1 SI_s + f_2 SI_r) - \varphi S + \alpha_1 SI_s + \alpha_2 SI_r \\ \frac{dI_s}{dt} = (1-u_1)(f_1 SI_s + f_2 SI_r) - u_2\omega I_s - (\delta + \alpha_1)I_s - \varphi I_s + \alpha_1 I_s^2 + \alpha_2 I_s I_r \\ \frac{dI_r}{dt} = \delta I_s - u_3\sigma I_r - \alpha_2 I_r - \varphi I_r + \alpha_1 I_s I_r + \alpha_2 I_r^2 \end{cases} \tag{4}$$

3. Model Properties

The zero-infection state, occurs when $I_s = 0, I_r = 0$, with $S = S_0, I_{s(0)} = 0, I_{r(0)} = 0$. Hence, the disease-free state solution becomes, $DFE = \left(\frac{(1-\varepsilon)\varphi+\phi}{\phi+\varphi}, 0, 0\right)$.

Here, we determine the threshold parameter that governs the transmission of a disease, referred to as the effective reproduction number R_{eff}. The Next Generation approach as shown in Van den Driessche and Watmough [21] states that, it is the spectral radius of the next generation matrix. This definition is given for the models that represent the spread of infection in a population. It is obtained by taking the largest (dominant) Eigen value, (spectral radius) of

$$\left[\frac{\partial F_i}{\partial X_j}\right] * \left[\frac{\partial V_i}{\partial X_j}\right]^{-1} \tag{5}$$

Using the Next Generation Matrix, we will consider only the infectious classes in the system of differential equations in (4):

$$\begin{cases} \frac{dI_s}{dt} = (1-u_1)(f_1 SI_s + f_2 SI_r) - u_2\omega I_s - (\delta + \alpha_1)I_s - \varphi I_s + \alpha_1 I_s^2 + \alpha_2 I_s I_r \\ \frac{dI_r}{dt} = \delta I_s - u_3\sigma I_r - \alpha_2 I_r - \varphi I_r + \alpha_1 I_s I_r + \alpha_2 I_r^2 \end{cases} \tag{6}$$

Applying $DFE = \left(\frac{(1-\varepsilon)\varphi+\phi}{\phi+\varphi}, 0, 0\right)$, the disease-free case. The effective reproduction number of the model system (1) yielded,

$$R_{eff} = \frac{\{(\sigma+\varphi+\alpha_2)f_1 + \delta f_2\}\{(1-\varepsilon)\varphi+\phi\}}{(\omega+\delta+\varphi+\alpha_1)(\sigma+\varphi+\alpha_2)(\phi+\varphi)} \tag{7}$$

with $R_0 = \frac{\{(\sigma+\varphi+\alpha_2)f_1+\delta f_2\}}{(\omega+\delta+\varphi+\alpha_1)(\sigma+\varphi+\alpha_2)}$ when ε is zero.

A stability analysis reveals that the disease-free state is locally asymptotically stable if $R_{eff} < 1$ and unstable when $R_{eff} > 1$.

4. Sensitivity Analysis

We determine the sensitivity analysis of the model to compute parameter values that will be helpful in determining their impact on the model transmission dynamics [11, 2].

Definition. The normalized forward sensitivity index of a variable, R_{eff}, that depends differentially on a parameter, ε, is defined as [2]: $Z_\varepsilon^{R_{eff}} = \frac{\partial R_{eff}}{\partial \varepsilon} * \frac{\varepsilon}{R_{eff}}$

We compute the sensitivity indices of R_{eff} using the estimated parameter values in Table 2. Thus, we obtain the following results in table 1: $Z_\varepsilon^{R_{eff}} = \frac{\partial R_{eff}}{\partial \varepsilon} * \frac{\varepsilon}{R_{eff}} = -1.018, Z_{\xi.}^{R_{eff}} = 1.0001$ and $Z_\tau^{R_{eff}} = 1.000$.

Table 1 shows the parameter values arranged from most to least sensitive. The most sensitive parameter is the vaccination coverage, ε, and the least sensitive parameter is the waning rate, ϕ of the disease. These findings reveal that, when the parameters $\Upsilon, \tau, \phi, \delta$ and ξ are increased keeping other parameter values constant they increase the value of R_{eff} hence, they increase the endemicity of the disease in the community as they have positive indices. While the parameters $\varepsilon, \alpha_1, \sigma, \omega, \alpha_2$ and φ decrease the value of R_{eff} when they are increased while the other parameters are kept constant, this means, that they decrease the persistence of the disease as they have negative indices.

Table 1. *Sensitivity indices of* R_{eff}.

Parameter	ε	ξ	τ	α_1	φ	Υ	ω	α_2	δ	σ	ϕ
Sensitivity indices	−1.018	1.0001	1.000	−0.5528	−0.2596	0.1874	−0.1316	−0.1010	0.0559	−0.0360	0.0248

5. Optimal Control of the Meningitis Model

Epidemiologically, the concept of optimal control problem (3) seeks to minimize the transmission or number of new infections and reduce the cost of treatment and preventive measures as control strategies as in Fleming and Rishel [3], Pontryagin [16]. To achieve the optimal control levels, we define a control set U that is Lebesgue measurable as: $= \{(u_1(t); u_2(t); u_3(t); u_4(t)): 0 \leq u_1 < 1; 0 \leq u_2 < 1; 0 \leq u_3 < 1; 0 \leq u_4 < \quad 1; 0 \leq t \leq t_f\}$. The objective functional J that can be used to achieve this is defined as:

$$J = \min_{u_1,u_2,u_3,u_4} \int_0^{t_f} (A_1 I_s + A_2 I_r + B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2 + B_4 u_4^2) \tag{8}$$

subject to the system of differential equations (1) with A_1, A_2, B_1, B_2, B_3 and B_4 representing the positive weight constants to help balance the terms in the integral to avoid the dominance of one over another as in Grassly and Fraser [5]. They serve as the balancing cost factors in the optimal model. The terms $A_1 I_s$ and $A_2 I_r$ are costs incurred with infections in the human population. The quadratic functions: $B_1 u_1^2$ is the cost associated with prevention strategies, $B_2 u_2^2$ is the costs incurred when treating drug senitive infectious individuals, $B_3 u_3^2$ is the costs emanating from in the treatment of infected humans who have developed an antibiotic resistant bacterium and $B_4 u_4^2$ is a reduction in the loss of disease immunity due to improved vaccination and treatment efficacy efforts. The model controls are bi-linear combination of $u_i^2(t), (i = 1,2,3,4)$. The quadratic form is applied since the cost are nonlinear in nature. We target to minimize the number of infectives (drug sensitive and resistant) and the costs of treating the disease.

We seek to determine the optimal functions;

$$(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)): J(u_1^*, u_2^*, u_3^*, u_4^*) = min\left\{\frac{J(u_1,u_2,u_3,u_4)}{u_i} \in U\right\} \tag{9}$$

with $U = \{(u_1, u_2, u_3, u_4): 0 \leq u_i < 1; i = 1,2,3,4; 0 \leq t \leq t_f\}$ being the control set.

Next, we determine the Lagrangian function;

$$L(I_s; I_r; u_1; u_2; u_3; u_4; t) = A_1 I_s + A_2 I_r + B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2 + B_4 u_4^2 \tag{10}$$

We employ the Pontryagin's Maximum Principle which provides the necessary and sufficient conditions to be satisfied by an optimal problem as in Fleming and Rishel [3], Pontryagin [16]. The principle changes the system of differential equations in (3) and equation (8) into a minimization problem point-wise Hamiltonian (H), with respect to $(u_1; u_2; u_3; u_4)$.

$$H(S, I_s, I_r, R, t) = L(I_s; I_r; u_1; u_2; u_3, u_4; t) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dI_s}{dt} + \lambda_3 \frac{dI_r}{dt} + \lambda_4 \frac{dR}{dt} \tag{11}$$

Substituting the equations in system (3), the Hamiltonian becomes:

$$\begin{cases} H = w_1 I_s + w_2 I_r + w_3 u_1^2 + w_4 u_2^2 + w_5 u_3^2 + w_6 u_4^2 \\ +\lambda_1\{(1-\varepsilon)\varphi + (1-u_4)\phi R - (1-u_1)(f_1 S I_s + f_2 S I_r) - \varphi S + \alpha_1 S I_s + \alpha_2 S I_r\} \\ +\lambda_2\{(1-u_1)(f_1 S I_s + f_2 S I_r) - u_2 \omega I_s - (\delta + \alpha_1) I_s - \varphi I_s + \alpha_1 I_s^2 + \alpha_2 I_s I_r\} \\ +\lambda_3\{\delta I_s - u_3 \sigma I_r - \alpha_2 I_r - \varphi I_r + \alpha_1 I_s I_r + \alpha_2 I_r^2\} \\ +\lambda_4\{\varepsilon\varphi + u_2 \omega I_s + u_3 \sigma I_r - (1-u_4)\phi R - \varphi R + \alpha_1 I_s R + \alpha_2 I_r R\} \end{cases} \tag{12}$$

with $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ being the the adjoint variables.

Using the relation;

$$\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial \dot{x}(t)} \tag{13}$$

By differentiation of the function H with respect to (w.r.t) S yields;

$$\begin{aligned} \frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S(t)} &= -\{-\lambda_1(1-u_1)(f_1 I_s + f_2 I_r) - \lambda_1 \varphi + \lambda_1 \alpha_1 I_s + \lambda_1 \alpha_2 I_r + \lambda_2 (1-u_1)(f_1 I_s + f_2 I_r)\} \\ &= \lambda_1(1-u_1)(f_1 I_s + f_2 I_r) + \lambda_1 \varphi - \lambda_1 \alpha_1 I_s - \lambda_1 \alpha_2 I_r - \lambda_2 (1-u_1)(f_1 I_s + f_2 I_r) \\ &= (1-u_1)(f_1 I_s + f_2 I_r)(\lambda_1 - \lambda_2) + \varphi \lambda_1 - \lambda_1 \alpha_1 I_s - \lambda_1 \alpha_2 I_r \end{aligned} \tag{14}$$

Finding $-\frac{\partial H}{\partial \dot{x}(t)}$ of the Hamiltonian function w.r.t (S, E, I_s, I_r, R) and obtain the following adjoint or co-state variables as solutions of adjoint systems;

$$\begin{cases} \frac{d\lambda_1}{dt} = (1-u_1)(f_1I_s + f_2I_r)(\lambda_1 - \lambda_2) + \lambda_1(\varphi - \alpha_1 I_s - \alpha_2 I_r) \\ \frac{d\lambda_2}{dt} = -w_1 + (1-u_1)f_1S(\lambda_1 - \lambda_2) + \lambda_2(u_2\omega + \delta + \alpha_1 + \varphi) - \lambda_1\alpha_1 S - \lambda_2(2\alpha_1 I_s + \alpha_2 I_r) \\ \frac{d\lambda_3}{dt} = -w_2 + (1-u_1)f_2S(\lambda_1 - \lambda_2) + u_3\sigma(\lambda_3 - \lambda_4) + \lambda_3(\varphi + \alpha_2 - \alpha_1 I_s - 2\alpha_2 I_r) - \lambda_2\alpha_2 I_s - \lambda_4\alpha_2 R \\ \frac{d\lambda_4}{dt} = \phi(\lambda_4 - \lambda_1) + \lambda_4(\varphi - \alpha_2 I_r) \end{cases} \tag{15}$$

With transversality conditions $\lambda_i(t_f) = 0;$ for $i = 1,2,3,4.$

We combine the Pontryagin's Maximum Principle and the existence concept of the optimal control as stated by Fleming and Rishel [3], Pontryagin [16]. In addition, we characterize the optimal model by solving;

$$\frac{\partial H}{\partial u_i} = 0, \text{with } u_i = u_i^*, i = 1,2,3, \dots, n. \tag{16}$$

we obtain the control set $(u_1^*; u_2^*; u_3^*, u_4^*)$ by using equation (16) as follows

$$\frac{\partial H}{\partial u_1} = 2B_1u_1 + \lambda_1(f_1I_s + f_2I_r)S - \lambda_2(f_1I_s + f_2I_r)S$$

Thus, $u_1^* = \frac{(\lambda_2 - \lambda_1)(f_1I_s + f_2I_r)S^*}{2B_1}$

We differentiate the Hamiltonian function obtained and apply equation (16), to get the control set $(u_1^*; u_2^*; u_3^*; u_4^*)$ as follows;

$$\begin{cases} u_1^* = \frac{(\lambda_2 - \lambda_1)(f_1I_s + f_2I_r)S^*}{2B_1} \\ u_2^* = \frac{(\lambda_2 - \lambda_4)\omega I_s^*}{2B_2} \\ u_3^* = \frac{(\lambda_2 - \lambda_4)\sigma I_r^*}{2B_3} \\ u_4^* = \frac{(\lambda_1 - \lambda_4)\phi R^*}{2B_4} \end{cases} \tag{17}$$

Theorem 1. The optimal control vector $(u_1^*(t); u_2^*(t); u_3^*(t); u_4^*(t))$ that maximize the objective functional, J over control set U, given by;

$$\begin{cases} u_1^*(t) = \max\left\{0, \min\left(1, \frac{(\lambda_2 - \lambda_1)(f_1I_s + f_2I_r)S^*}{2B_1}\right)\right\} \\ u_2^*(t) = \max\left\{0, \min\left(1, \frac{(\lambda_2 - \lambda_4)\omega I_s^*}{2B_2}\right)\right\} \\ u_3^*(t) = \max\left\{0, \min\left(1, \frac{(\lambda_2 - \lambda_4)\sigma I_r^*}{2B_3}\right)\right\} \\ u_4^*(t) = \max\left\{0, \min\left(1, \frac{(\lambda_1 - \lambda_4)\phi R^*}{2B_4}\right)\right\} \end{cases} \tag{18}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ are the solutions of equation (12) and (15).

Writing using standard control arguments involving bound on the controls, we conclude that;

$$u_1^* = \begin{cases} 0 & \text{if } \emptyset_1 \le 0, \\ \emptyset_1 & \text{if } 0 < \emptyset_1 < 1., \\ 1 & \text{if } \emptyset_1 \ge 1. \end{cases} u_2^* = \begin{cases} 0 & \text{if } \emptyset_2 \le 0, \\ \emptyset_2 & \text{if } 0 < \emptyset_2 < 1., \\ 1 & \text{if } \emptyset_2 \ge 1. \end{cases} u_3^* = \begin{cases} 0 & \text{if } \emptyset_3 \le 0, \\ \emptyset_3 & \text{if } 0 < \emptyset_3 < 1. \\ 1 & \text{if } \emptyset_3 \ge 1. \end{cases} \text{ and } u_4^* = \begin{cases} 0 & \text{if } \emptyset_4 \le 0, \\ \emptyset_4 & \text{if } 0 < \emptyset_4 < 1. \\ 1 & \text{if } \emptyset_4 \ge 1. \end{cases}$$

where, $\emptyset_1 = \frac{(\lambda_2 - \lambda_1)(f_1I_s + f_2I_r)S^*}{2B_1}, \emptyset_2 = \frac{(\lambda_2 - \lambda_4)\omega I_s^*}{2B_2}, \emptyset_3 = \frac{(\lambda_2 - \lambda_4)\sigma I_r^*}{2B_3}$ and $\emptyset_4 = \frac{(\lambda_1 - \lambda_4)\phi R^*}{2B_4}$

Table 2. *Description of variables and parameters of the pneumonia model.*

Parameter	Description	Value	Source
φ	Recruitment rate	0.1	[22]
ε_c	critical vaccination proportion	0.5170	Computed
ϕ	Immunity Wanning rate	0.0025	[19]
ξ	contact rate	$1 - 10$	[14, 8]
τ	probability that a contact is effective to cause infection	$0.89 - 0.99$	[14, 8]
Υ	Transmission coefficient for the carrier	1.2	[18, 19]
μ	Natural death rate	0.00000456621	[8, 19]
ω	progression rate from infected to recovered group	0.0714	[10, 8]
δ	progression rate from drug-sensitive to resistant group	0.0714l	[8]
σ	progression rate from drug-resistant group	0.0714	[17]

Parameter	Description	Value	Source
α_1	death rate due to a drug-sensitive disease infection	0.3	[19, 6]
α_2	death rate due to a drug-resistant disease infection	0.2	Estimated

The optimality system to be analyzed/simulated is obtained from the optimal control system (the state system) and the adjoint variable system by incorporating the characterized control set and initial and transversal conditions.

$$\begin{cases} \frac{dS}{dt} = (1-\varepsilon)\varphi + (1-u_4)\phi R - (1-u_1)(f_1 SI_s + f_2 SI_r) - \varphi S + \alpha_1 SI_s + \alpha_2 SI_r \\ \frac{dI_s}{dt} = (1-u_1)(f_1 SI_s + f_2 SI_r) - u_2\omega I_s - (\delta + \alpha_1)I_s - \varphi I_s + \alpha_1 I_s^2 + \alpha_2 I_s I_r \\ \frac{dI_r}{dt} = \delta I_s - u_3\sigma I_r - \alpha_2 I_r - \varphi I_r + \alpha_1 I_s I_r + \alpha_2 I_r^2 \\ \frac{dR}{dt} = \varepsilon\varphi + u_2\omega I_s + u_3\sigma I_r - (1-u_4)\phi R - \varphi R + \alpha_1 I_s R + \alpha_2 I_r R \\ \frac{d\lambda_1}{dt} = (1-u_1)(f_1 I_s + f_2 I_r)(\lambda_1 - \lambda_2) + \lambda_1(\varphi - \alpha_1 I_s - \alpha_2 I_r) \\ \frac{d\lambda_2}{dt} = -w_1 + (1-u_1)f_1 S(\lambda_1 - \lambda_2) + \lambda_2(u_2\omega + \delta + \alpha_1 + \varphi) - \lambda_1\alpha_1 S - \lambda_2(2\alpha_1 I_s + \alpha_2 I_r) \\ \frac{d\lambda_3}{dt} = -w_2 + (1-u_1)f_2 S(\lambda_1 - \lambda_2) + u_3\sigma(\lambda_3 - \lambda_4) + \lambda_3(\varphi + \alpha_2 - \alpha_1 I_s - 2\alpha_2 I_r) - \lambda_2\alpha_2 I_s - \lambda_4\alpha_2 R \\ \frac{d\lambda_4}{dt} = \phi(\lambda_4 - \lambda_1) + \lambda_4(\varphi - \alpha_2 I_r) \end{cases} \quad (19)$$

6. Computational Results and Discussion

Using a combination of controls such as: one control only with increasing time, two controls against time, and all control strategies against time, then we analyze and compare the numerical results from the simulations. Given that the state system (3) has initial conditions and the adjoint systems (15) have final conditions, we employ the forward 4^{th} order Runge-Kutta method and solve the adjoint system using a backward 4^{th} order Runge-Kutta method. We used $A_1 = 25; A_2 = 25; B_1 = 4; B_2 = 3; B_3 = 5$ and $B_4 = 6$ as weight constants for the pneumonia model with optimal control analysis. In addition, we used $S(0) = 0.5; I_s(0) = 0.25; I_r(0) = 0.15; R(0) = 0.1$ as initial values and $\lambda_i(t_f) = 0, i = 1,2,3,4$.

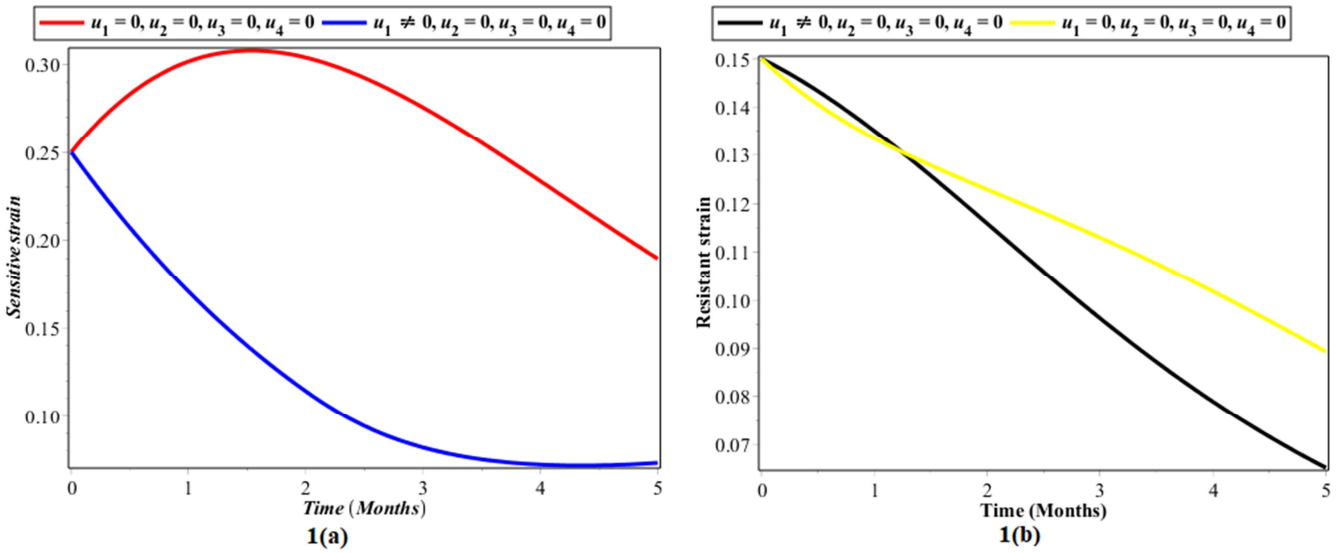

Figure 1. *Graphs displaying pneumonia infection dynamics with and without controls: prevention only.*

We analyze the pneumonia model by applying prevention efforts. In this case, we optimize the prevention ($u_1 \neq 0$) while equating the treatment controls (u_2 and u_3) and immunity efforts (u_4) to zero. From Figure 1(a, b), we see a sharp decrease of sensitive and resistant strain population due to the implementation of prevention interventions. This is due to the fact that prevention reduces the rate of recruitment of persons to the sensitive as well as resistant compartments. This epidemiologically implies that enhanced prevention implementation can wipe out the burden of pneumonia disease within a short time interval compared to a case without controls.

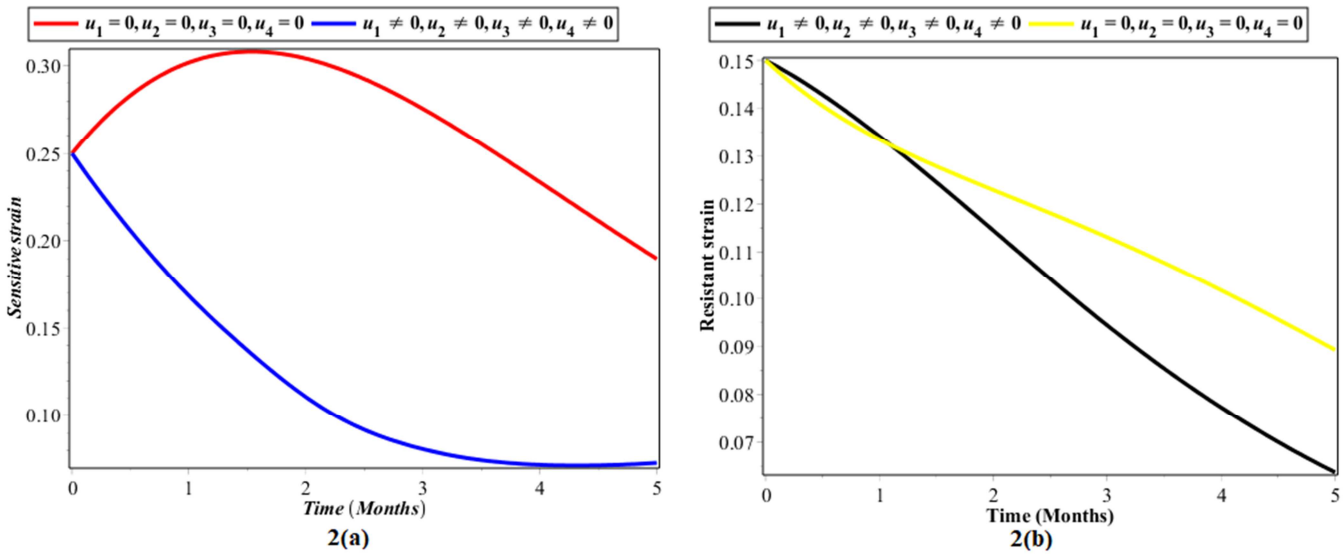

Figure 2. *Graphs displaying pneumonia infection dynamics without and with controls: prevention, treatment and immunity control.*

We employ all the four controls u_1, u_2, u_3 and u_4 to optimise the objective function J. From Figure 2(a, b), we observe that the fractions of the sensitive infectious and resistant infectious populations decrease exponentially as time increases to achieve a zero-infection scenario. This implies that pneumonia disease can be curbed efficiently when all 4 controls are applied as intervention strategies. However, as to whether this strategy is cost effective compared to other strategies requires a cost-effective analysis of the considered model to occur.

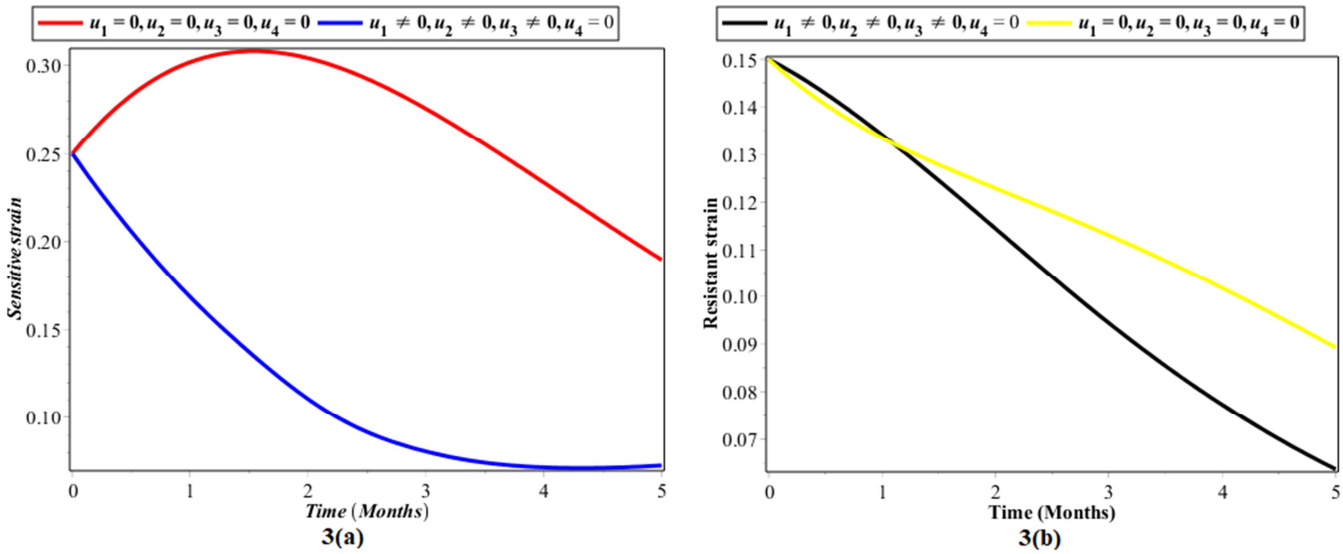

Figure 3. *Graphs displaying pneumonia infection dynamics without and with controls: prevention and treatment.*

The implementation of prevention control u_1 and treatment controls u_2 and u_3 are used to optimize J while we set the immunity control u_4 to zero, and Figure 3 (a, b) displays the output obtained. Clearly, the number of sensitive infectious and resistant infectious populations reduces within a relatively short period of time. Implying that this strategy is capable of efficiently wiping out the disease from the community within known timelines.

Figures 4(a) and 4(b) display an optimal treatment and immunity control case scenario. The task is to optimize J using the prevention control u_1 and immunity control u_4 while the treatment controls u_2, u_3 is equated to zero. Figure 4 demonstrates that due to the control strategies, the population of drug sensitive infective individuals (I_s) and drug resistant infective individuals (I_r) displays a significant impact on decreasing the number of infectives of both strains, with also a notable impact on the timing of wiping out the infection from the community.

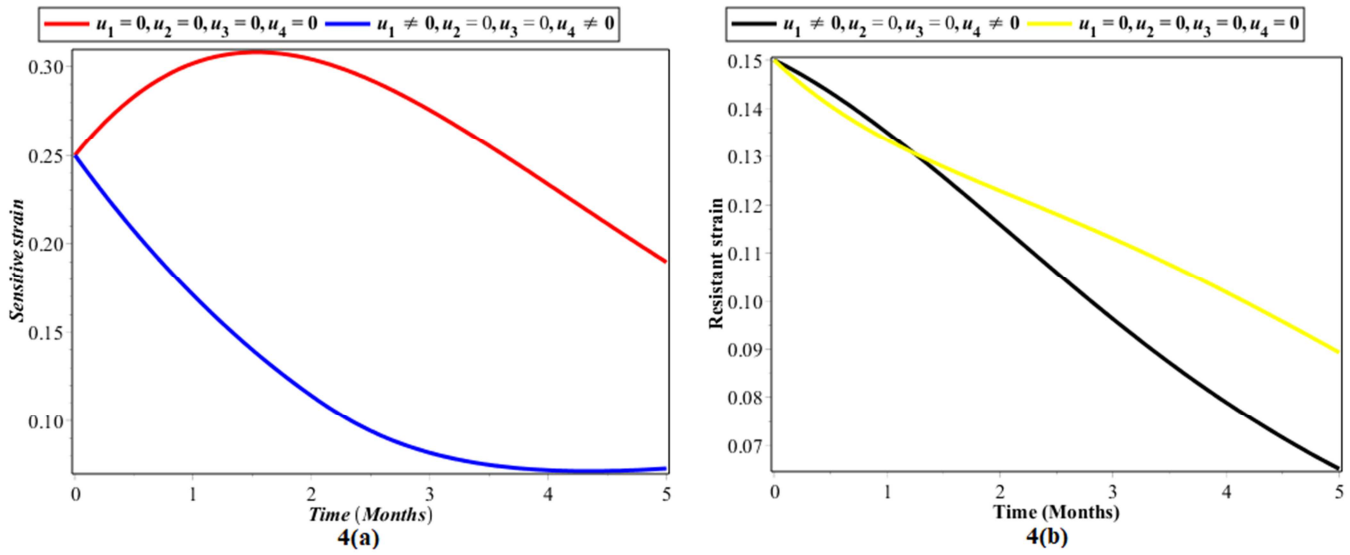

Figure 4. *Graphs displaying pneumonia infection dynamics without and with controls: prevention and immunity control.*

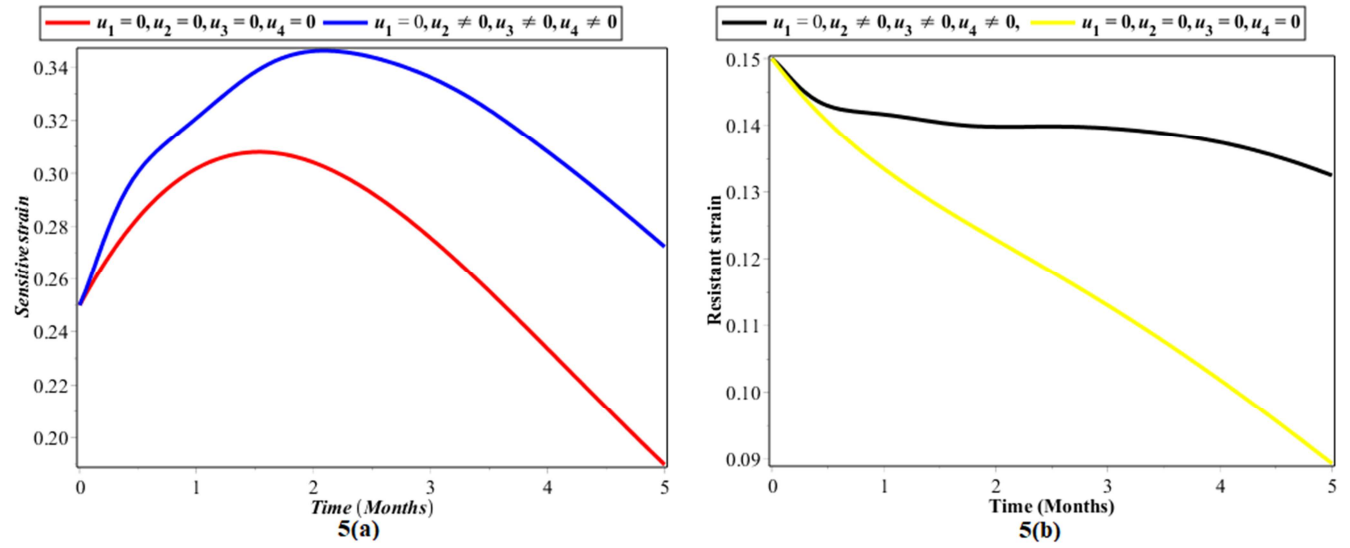

Figure 5. *Graphs displaying pneumonia infection dynamics without and with controls: treatment and immunity control.*

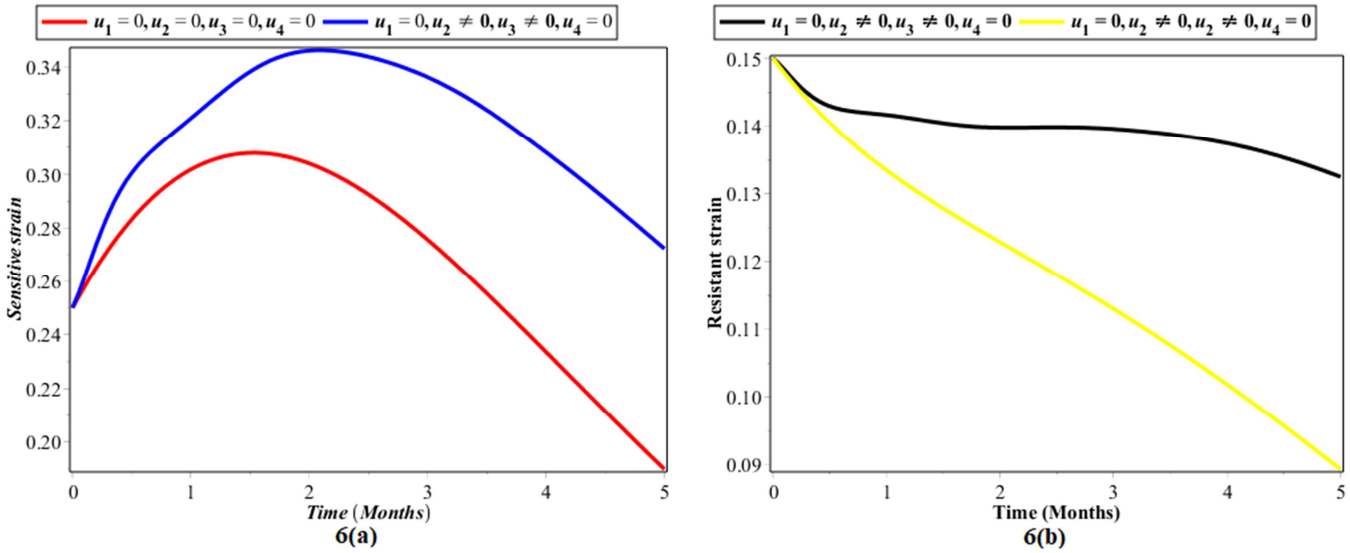

Figure 6. *Graphs displaying pneumonia infection dynamics without and with controls: treatment only.*

Figures 5(a) and 5(b) shows the impact of optimal treatment and immunity control. We optimize the objective function J using the treatment controls u_2, u_3 and immunity control u_4 while the prevention control u_1 is equated to zero. Figure 5(a) displays that the sensitive strain infection will rise to attain a peak with a little notable decrease noted after attaining a peak. The infections display a higher peak compared to the case without controls. Figure 5(a) displays that the control strategy has little notable effect in decreasing the resistant strain infections in the community. This implies that the strategy might not be effective in eradicating a highly infectious disease like pneumonia.

Figures 6(a) and 6(b) shows the impact of treatment. We optimize the objective function J using the treatment controls u_2 and u_3 while immunity control u_4 and the prevention control u_1 are set to zero. From Figure 6, we observe that the controls have little impact reducing the drug-sensitive and drug-resistant strain infections with also little effect on influencing the timing to eradicate the diseases.

7. Conclusions

In this paper, we develop and analyze an optimal control problem for a pneumonia mathematical model to effectively describe the transmission of pneumonia that optimizes control efforts and perform qualitative and quantitative optimal control analysis of the model. The pneumonia model was robustly analyzed to gain insights into its dynamics. The pneumonia model has a locally stable disease-free state when the basic reproduction number $R_{eff} < 1$. The model has a unique endemic equilibrium whenever $R_{eff} > 1$. The study reveals that vaccination proportion value and infection contact rate are the most sensitive parameter values that possess a higher impact in shaping the dynamics of pneumonia disease. Focusing on pneumonia intervention strategies, we observe from Figures 1-4 that the presence of prevention efforts as a control variable has a remarkable significance in decreasing and probably eradicating the infectious infective strains in the population with notable impact on reducing the duration of wiping infection in the community. Administration of both treatment and immunity control or independent implementation has displayed no significant effect in decreasing infections in the community. However, a combination of these efforts with prevention efforts displays a significant reduction of infections in the community. In addition, there is a need for further studies to determine the most cost-effective control strategy as shown in Figures 1-4, considering that the worst hit continents have limited resources and weak challenged economies. The findings of this study can be continued by future research studies to include cost-effective analysis of the control strategies and formulation of delay differential equations to take care of the duration between getting an infection and showing visible symptoms.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability

The data used in the study of the pneumonia model were obtained from published articles and reported studies which have been cited accordingly. Some of the parameter values are estimated.

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