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Research Article

Optimal Control in Two Strain Pneumonia Transmission Dynamics

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A mathematical model for the transmission dynamics of pneumonia disease in the presence of drug resistance is formulated. Intervention strategies, namely, vaccination, public health education, and treatment are implemented. We compute the effective reproduction numbers and establish the local stability of the equilibria of the model. Global stability of the disease-free equilibrium is obtained through the comparison method. On the other hand, we apply the Lyapunov method to show that the drug-resistant equilibrium is globally asymptotically stable under some feasible biological conditions. Furthermore, we apply optimal control theory to the model aiming at minimizing the number of infections from drug-sensitive and drug-resistant strains. The necessary conditions for the optimal solutions of the model were derived by using Pontryagin's Maximum Principle. The optimal controls are characterized in terms of the optimality system, which is solved numerically for several scenarios to investigate the best strategy. The incremental cost-effectiveness analysis technique is used to find the most cost-effective strategy, and it is observed that the vaccination program is the most cost-effective strategy in case of limited resources. However, results show that implementing the three strategies simultaneously provides the best results in controlling the disease.

1. Introduction

Pneumonia is a fatal disease affecting one or both parts of the lungs, mostly the air sacs. It is caused by infectious agents such as bacteria, viruses, and fungi. The common bacteria that cause pneumonia are Streptococcus pneumoniae and Haemophilus influenzae *type b* while the common virus is a respiratory syncytial virus. Pneumonia affects all groups of people, but it affects mostly children under 5 years old, adults over 65 years old, and people with weak immune systems [1, 2]. The transmission of pneumonia occurs through air droplets (e.g., when an infectious individual coughs or sneezes), from bloodborne infection, or by inhaling bacterial pathogen present in the throat or nose into the lungs. The infected individuals show symptoms which include fever, cough, loss of appetite, abnormal lung sound, hypoxia, and tachypnea [2]. According to the data updated in March (2018) from the United Nations Children's Fund, pneumonia is the leading infectious disease that causes deaths to children less than five years, killing about 2,400 children per day in 2015 [3]. Pneumonia kills more children than HIV/AIDS, malaria, and measles [4]. In developing countries, mortality is associated with malnutrition, poverty, and lack of access to health services [5]. For example, according to the WHO data published in 2017, influenza and pneumonia deaths in Tanzania reached 10.46 percent of total death annually [6].

Current strategies for controlling pneumonia include reducing indoor pollution, vaccination, promoting nutrition, and treatment [2]. The available vaccines against Streptococcus pneumoniae (pneumococcus) are the pneumococcal polysaccharide vaccine (PPV), the Hib conjugate vaccine (HibCV), and pneumococcal conjugate vaccine (PCV) [7]. However, the control of pneumonia is facing some challenges, including antibiotic resistance as some bacteria such as Streptococcus pneumoniae can mutate and resist antibiotics hence lead to treatment failures [8]. Misuse and overuse of antibiotics are among the factors that may lead to the rise of antibiotic resistance. As a result of antibiotic resistance,

hospital stay duration increases because of illness and treatment, and this increases costs and the economic burden on societies and families.

Several studies have been carried out to investigate the transmission dynamics of pneumonia. For example, [9] formulated a mathematical model to examine the role of carriers and recovery measures in the pneumonia transmission dynamics among children under five years of age. Also, [10] developed a model for childhood pneumonia dynamics to investigate the role of treatment and natural immunity in pneumonia transmission dynamics. Moreover, [11] developed a deterministic model for a better understanding of pneumonia transmission and assessing the effects of screening and treatment interventions. Furthermore, [12] investigated the efficacy of vaccination drugs and the impact of environment and treatment in reducing pneumonia infection for children under five years in Kenya. The study by [13] determined the impacts of vaccination in the spread of Streptococcus pneumoniae disease. Besides, [14] developed a model for determining optimal strategies (education, screening, and treatment) to reduce infected individuals. On the other hand, the study by [15] examined the effects of treatment and vaccination interventions on pneumonia dynamics.

The spread of pneumonia can be reduced by minimizing the number of infected individuals. This can be achieved by applying optimal control theory. A basic optimal control problem consists of finding piecewise continuous control and the associated state variable to minimize an objective function. The minimizing process is accomplished by adjusting the control variable until the minimum value is achieved. For example, optimal theory can be applied in the model for infectious disease to find the percentage of the individuals to be vaccinated to minimize the number of infections, and the cost of implementing the vaccination strategy [16]. Optimal control theory has been proven to be a useful tool in understanding ways to reduce the spread of infectious diseases by formulating the optimal disease intervention strategies [17]. The optimal control theory has been applied to several studies on epidemiological models such as malaria, HIV, hepatitis B, rabies, HIV-malaria, and TB-HIV coinfection models (e.g., see [18–24]).

Generally, most of the existing studies on pneumonia models did not apply optimal control theory (e.g., see [9–11, 13, 15]). Few studies have applied optimal control theory to the pneumonia model (e.g., see [14, 25]). However, these studies did not consider drug resistance pneumonia strains. Also, optimal control of interventions such as vaccination has not been captured. In this study, we, therefore, modify the model developed by [14] to take into account the drug resistance pneumonia strains. The current study will add up the knowledge to the existing literature and provide a cornerstone for further research on multiple-strain infectious disease modeling such as pneumonia. We assume that drug resistance can emerge by primary infection with resistant bacteria strain or as a consequence of improper dose administration. The model system is formulated as an optimal control problem by implementing public health education, vaccination, and treatment to reduce the number of infectious individuals. Pontryagin's Maximum Principle is applied to find the best control strategy. The rest of the paper is organized as follows: In Section 2, a model is formulated and analyzed to study its equilibrium points and the reproduction number in Section 3. In Section 4, an optimal control problem is formulated and analyzed. In Section 5, numerical simulation is carried out to investigate the effects of control strategies. In Section 6, the economic implications of pneumonia control strategies are evaluated to obtain the best cost-effective strategy. Section 7 contains the concluding remarks.

2. Model Description and Formulation

The human population at any time t, denoted by $N(t)$ is divided into five subpopulations based on the disease status as follows: susceptible individuals who are at risk of acquiring pneumonia infection, $S(t)$, vaccinated individuals, $V(t)$, individuals infected with a drug-sensitive strain who are capable of transmitting the infection to susceptible individuals, $I_{se}(t)$, individuals infected with drug-resistant strain, $I_r(t)$, who can transmit infections to susceptible individuals, and the recovered individuals, $R(t)$. It is assumed that individuals are recruited in the community at a constant rate ν. In this model, it is assumed that ρ is the proportion of recruited individuals who are vaccinated against pneumonia and $(1 - \rho)$ is the proportion of recruited individuals who are susceptible when entering the community. Susceptible individuals are vaccinated at a rate γ in which the acquired immunity to disease wanes out at the rate ω. It is also assumed that an individual can be colonised by either sensitive strain or resistant strain at a given time. A susceptible individual can be infected with pneumonia if he/she comes into effective contact with an infectious individual at an average rate (force of infection) $\alpha_i = \beta_j I_i/N$, where $i = \text{se}, r$ denotes sensitive strain and resistant strain, respectively, and $\beta_j = kP_j$ for $j = 1, 2$ denotes the transmission rates. However, k is the number of contacts, and P_j is the probability for a contact to cause infection. It is assumed that vaccination is not 100% effective; thus, vaccinated individuals in class $V(t)$ have a chance of being infected at a rate $\varepsilon\alpha_i$, where $\varepsilon = (1 - \chi)$ is the stereotype not covered by the vaccine and χ is the efficacy of the vaccine. A newly infected individual can either progress to infectious individuals with sensitive strains or infectious individuals with drug-resistant strains at rates $(1 - k_1)\alpha_{se}$ and $(1 - k_1)\alpha_r$, respectively, where k_1 is the efficacy of public health education. Public health education is offered to individuals to create awareness on how to protect themselves from exposure to risk behaviours. By so doing, the number of infections may significantly be reduced. Also, education may help the individuals on the importance of completing the dose if one gets infected. We assume that the two strains are mutually exclusive in the sense that no susceptible individual can simultaneously be infected with both drug-resistant and drug-sensitive strains. However, the drug-sensitive strain can mutate into a drug-resistant strain at a rate η. Furthermore, it is assumed that individuals infected with drug-sensitive strain in I_{se} compartment receive treatment at a rate ε_{se}. Moreover, it is assumed that individuals infected with bacteria resistant to certain drugs

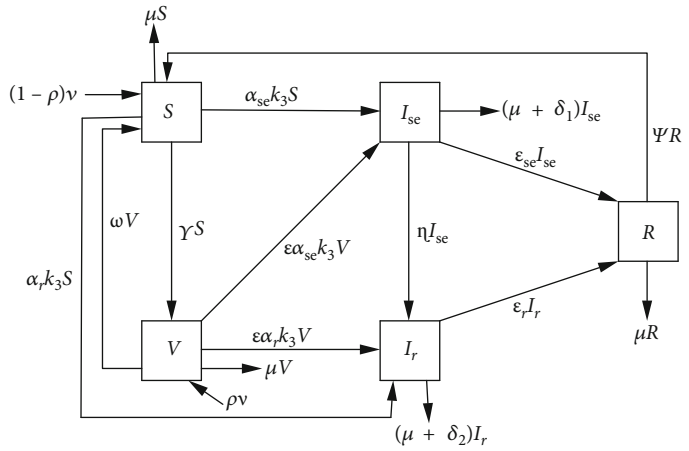

Figure 1: The schematic diagram for the dynamics of pneumonia intervention strategies.

can be treated at a rate ε_r with other drugs and clear the infection. All recovered individuals acquire temporary immunity, which wanes out at the rate ψ and becomes susceptible again. The disease-induced mortality occurs in two compartments, $I_{se}(t)$ and $I_r(t)$ at rates δ_1 and δ_2, respectively. All individuals in different subgroups experience natural death at a rate μ. The model flow diagram is in Figure 1.

Putting together all assumptions and model descriptions, we obtain the following system of nonlinear differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= (1-\rho)\nu - k_3(\alpha_{se}+\alpha_r)S - (\gamma+\mu)S + \psi R + \omega V,\\
\frac{dV}{dt} &= \rho\nu + \gamma S - k_3\varepsilon(\alpha_{se}+\alpha_r)V - \omega V - \mu V,\\
\frac{dI_{se}}{dt} &= \alpha_{se}k_3(S+\varepsilon V) - (\eta+\varepsilon_{se}+\mu+\delta_1)I_{se},\\
\frac{dI_r}{dt} &= \alpha_r k_3(S+\varepsilon V) + \eta I_{se} - (\varepsilon_r+\mu+\delta_2)I_r,\\
\frac{dR}{dt} &= \varepsilon_{se}I_{se} + \varepsilon_r I_r - (\mu+\psi)R,
\end{aligned} \tag{1}$$

where $k_3 = 1 - k_1$.

The initial conditions of the model system (1) are $S(0) \geq 0$, $V(0) \geq 0$, $I_{se}(0) \geq 0$, $I_r(0) \geq 0$, and $R(0) \geq 0$.

3. Model Analysis

3.1. Invariant Region. Since the model system (1) deals with human beings, it is assumed that all parameters and variables in the model are nonnegative for all $t \geq 0$. The discussion on the invariant region involves the description of the region in which the solution of the system makes epidemiological sense. We state and prove the following theorem.

Theorem 1. *The region* $\Omega = \{(S, V, I_{se}, I_r, R) \in \mathfrak{R}^5_+ : N(t) \leq \nu/\mu\}$ *is positively invariant under the flow induced by model system (1).*

Proof. Consider the population size: $N(t) = S(t) + V(t) + I_{se}(t) + I_r(t) + R(t)$ and the rate of change given by

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dV}{dt} + \frac{dI_{se}}{dt} + \frac{dI_r}{dt} + \frac{dR}{dt}, \Rightarrow \frac{dN}{dt} = \nu - N\mu - (\delta_1 I_{se} + \delta_2 I_r). \tag{2}$$

From (2), we have

$$\frac{dN}{dt} \leq \nu - N\mu. \tag{3}$$

Solving (3) for N yields $N \leq (\nu/\mu) + ce^{-ut}$ implying that $N \leq \nu/\mu$ as $t \longrightarrow \infty$, where c is the constant of integration. Therefore, the feasible region solution set of the system enters the region Ω. Thus, the region Ω is a positively invariant set under the flow induced by the model and the model is well-posed and also it is biologically meaningful.

3.2. Positivity of the Solutions. In this section, we describe the positivity of the solution of the model system.

Theorem 2. *The solution set*

$$\Omega = \left\{(S(t), V(t), I_{se}(t), I_r(t), R(t)) \in \mathfrak{R}^5_+ : (S(0), V(0), I_{se}(0), I_r(0), R(0)) > 0\right\} \tag{4}$$

of the model system (1) is positive for all $t \geq 0$.

Proof. Consider the first equation of the model system (1);

$$\frac{dS}{dt} = (1-\rho)\nu - k_3(\alpha_{se}+\alpha_r)S - (\mu+\gamma)S + \omega V + \psi R. \tag{5}$$

It follows that

$$\frac{dS}{dt} \geq -((\alpha_{se}+\alpha_r)k_3 + \mu + \gamma)S. \tag{6}$$

Integrating (6) by separation of variables, we obtain

$$\ln S(t) \geq -((\alpha_{se} + \alpha_r)k_3 + \mu + \gamma)t + K, \tag{7}$$

where K is the constant of integration.

Applying the initial conditions $S(0)$, in (7), gives

$$S(t) \geq S(0)e^{-((\alpha_{se}+\alpha_r)k_3+\mu+\gamma)t} > 0 \text{ provided } ((\alpha_{se} + \alpha_r)k_3 + \mu + \gamma) < \infty. \tag{8}$$

Similarly, the remaining other equations in the model system (1) give the following results:

$$\begin{aligned}
V(t) &\geq V(0)e^{-(\varepsilon k_3(\alpha_{se}+\alpha_r)+\omega+\mu)t} > 0 \text{ provided } (\varepsilon k_3(\alpha_{se} + \alpha_r) + \omega + \mu) < \infty,\\
I_{se} &\geq I_{se}(0)e^{-(\varepsilon_{se}+\eta+\mu+\delta_1)t} > 0 \text{ provided } (\varepsilon_{se} + \eta + \mu + \delta_1) < \infty,\\
I_r(t) &\geq I_r(0)e^{-(\varepsilon_r+\mu+\delta_2)t} > 0 \text{ provided } (\varepsilon_r + \delta_2 + \mu) < \infty,\\
R(t) &\geq R(0)e^{-(\psi+\mu)t} > 0 \text{ provided } (\psi + \mu) < \infty.
\end{aligned} \tag{9}$$

Therefore, the solutions of the model are positive for all values of $t > 0$.

3.3. Disease-Free Equilibrium Point (DFE). The model system (1) has a disease-free equilibrium in which neither drug-sensitive strain nor drug-resistant strain is present (i.e., $I_{se} = I_r = 0$). To find the steady state of the model, the right-hand side of the first two equations of model system (1) is equated to zero to give the disease-free equilibrium point as

$$E_0 = \left(\frac{\nu((1-\rho)\mu + \omega)}{\mu(\omega + \mu + \gamma)}, \frac{\nu(\rho\mu + \gamma)}{\mu(\omega + \mu + \gamma)}, 0, 0, 0\right). \tag{10}$$

3.4. The Effective Reproduction Number. The reproduction number that is used to investigate whether an infection introduced into a population will be eliminated or become endemic is obtained. It is defined as the expected number of secondary cases produced in a completely susceptible population by a typical infectious individual during its period of infectiousness [26]. In contrast to the single-strain model, two strains models have two reproduction numbers, one for each strain.

Following the ideas in [26, 27], we used the next-generation matrix method to obtain the effective reproduction number and we get

$$\begin{aligned}
R_{se} &= \frac{\beta_1 k_3(\omega + \mu(1-\rho) + \varepsilon(\rho\mu + \gamma))}{(\mu + \gamma + \omega)(\eta + \varepsilon_{se} + \mu + \delta_1)},\\
R_r &= \frac{\beta_2 k_3(\omega + \mu(1-\rho) + \varepsilon(\rho\mu + \gamma)}{(\mu + \gamma + \omega)(\varepsilon_r + \mu + \delta_2))}.
\end{aligned} \tag{11}$$

In the model system (1), drug-sensitive strain mutates into the drug-resistant strain. Therefore, the coexistence equilibria such that the possible ultimate outcomes are either coexistence of the two strains or competitive dominance of the drug-resistant strain. Genetic changes alone can give a competitive advantage to drug-resistant strain [28]. The presence of a coexistence equilibrium depends on the invasion reproduction number. The invasion reproduction number of the drug-sensitive (drug-resistant) strain is the number of the secondary infection that one individual infected with drug-sensitive (drug-resistant) strain will generate in a population in which the drug-resistant (drug sensitive) strain is at equilibrium [29]. Using the approach by [28], we present the invasion reproduction number of the drug-sensitive strain as

$$R_{se}^r = \frac{R_{se}}{R_r} = \frac{\beta_1(\varepsilon_r + \mu + \delta_2)}{\beta_2(\eta + \varepsilon_{se} + \mu + \delta_1)}, \tag{12}$$

and the invasion reproduction number of the drug-resistant strain as

$$R_r^{se} = \frac{R_r}{R_{se}} = \frac{\beta_2(\eta + \varepsilon_{se} + \mu + \delta_1)}{\beta_1(\varepsilon_r + \mu + \delta_2)}. \tag{13}$$

3.5. Local Stability of the Disease-Free Equilibrium (DFE). Here, we investigate the local stability of the disease-free equilibrium of the model system (1). For local stability, the spread of infection depends on the initial sizes of the subpopulation. To prove the local stability of the disease-free equilibrium, the eigenvalues of the Jacobian matrix of the system computed at the DFE point are obtained. The Jacobian matrix is obtained from the linearization of the model system (1). The Jacobian matrix J evaluated at DFE point (E_0) is given by

$$J(E_0) = \begin{bmatrix}
-(\mu + \gamma) & \omega & -\dfrac{\beta_1 k_3(\omega + (1-\rho)\mu)}{\omega + \mu + \gamma} & -\dfrac{\beta_2 k_3(\omega + (1-\rho)\mu)}{\omega + \mu + \gamma} & \psi\\
\gamma & -(\omega + \mu) & -\dfrac{\beta_1 k_3 \varepsilon(\rho\mu + \gamma)}{\omega + \mu + \gamma} & -\dfrac{\beta_2 k_3 \varepsilon(\rho\mu + \gamma)}{\omega + \mu + \gamma} & 0\\
0 & 0 & \dfrac{\beta_1 k_3(\omega + (1-\rho)\mu + \varepsilon(\rho\mu + \gamma))}{\omega + \mu + \gamma} - a_2 & 0 & 0\\
0 & 0 & \eta & \dfrac{\beta_2 k_3(\omega + (1-\rho)\mu + \varepsilon(\rho\mu + \gamma))}{\omega + \mu + \gamma} - a_3 & 0\\
0 & 0 & \varepsilon_{se} & \varepsilon_r & -a_5
\end{bmatrix}, \tag{14}$$

where $a_2 = \varepsilon_{se} + \eta + \mu + \delta_1$, $a_3 = \varepsilon_r + \mu + \delta_2$, and $a_5 = \mu + \psi$.

The DFE point is stable if all eigenvalues of the Jacobian matrix at the DFE point are negative. The eigenvalues of the Jacobian matrix (14) are established from the characteristic equation $|J - \lambda I| = 0$. To obtain the eigenvalues of equation (14),

$$\begin{vmatrix} -(\mu+\gamma)-\lambda & 0 & -m_1 & -m_2 & \psi \\ \gamma & -\mu-\lambda & -m_3 & -m_4 & 0 \\ 0 & 0 & m_5 - a_2 - \lambda & 0 & 0 \\ 0 & 0 & \eta & m_6 - a_3 - \lambda & 0 \\ 0 & 0 & \varepsilon_{\mathrm{se}} & \varepsilon_r & -a_5 - \lambda \end{vmatrix} = 0, \tag{15}$$

where $m_1 = \beta_1 k_3(\omega + (1-\rho)\mu)/(\omega + \mu + \gamma)$, $m_2 = \beta_2 k_3(\omega + (1-\rho)\mu)/(\omega + \mu + \gamma)$, $m_3 = \beta_1 k_3 \varepsilon(\rho\mu + \gamma)/(\omega + \mu + \gamma)$, $m_4 = \beta_2 k_3 \varepsilon(\rho\mu + \gamma)/(\omega + \mu + \gamma)$, $m_5 = \beta_1 k_3(\omega + (1-\rho)\mu + \varepsilon(\rho\mu + \gamma))/(\omega + \mu + \gamma)$, and $m_6 = \beta_2 k_3(\omega + (1-\rho)\mu + \varepsilon(\rho\mu + \gamma))/(\omega + \mu + \gamma)$.

Model system (15) has the three eigenvalues

$$\begin{aligned} \lambda_3 &= m_5 - a_2, \\ \lambda_4 &= m_6 - a_3, \\ \lambda_5 &= -a_5, \end{aligned} \tag{16}$$

and the following polynomial equation:

$$P(\lambda) = \lambda^2 + (2\mu + \gamma + \omega)\lambda + \mu(\gamma + \omega + \mu). \tag{17}$$

By Routh-Hurwitz criteria, the polynomial equation (17) has strictly negative root. Furthermore, the two eigenvalues λ_3 and λ_4 in equation (16) can be rewritten as

$$\begin{aligned} \lambda_3 &= a_2\left(\frac{m_5}{a_2} - 1\right) = a_2(R_{\mathrm{se}} - 1), \\ \lambda_4 &= a_3\left(\frac{m_6}{a_3} - 1\right) = a_3(R_r - 1). \end{aligned} \tag{18}$$

From equation (16), the eigenvalue λ_5 is clearly negative. Thus, the disease-free equilibrium is locally asymptotically stable if $\lambda_3 < 0$ and $\lambda_4 < 0$. However, the eigenvalue λ_3 is associated with sensitive strain and hence gives rise to the reproduction number of drug-sensitive strains, R_{se} as shown in equation (18). The eigenvalue λ_4 is associated with resistant strain and hence gives rise to the reproduction number of drug-resistant strains, R_r. Hence, we have the following result:

Theorem 3. *The disease-free equilibrium point is locally asymptotically stable if $R_{se} < 1$ and $R_r < 1$ and unstable if at least one of the inequalities is reversed.*

3.6. Global Stability of Disease-Free Equilibrium. For global stability, the spread of the infection is independent of the initial size of the population. By using the comparison method, we establish the following theorem.

Theorem 4. *The disease-free equilibrium is globally asymptotically stable if $R_{se} < 1$ and $R_r < 1$ and unstable if at least one of the inequalities is reversed.*

Proof. Let F and V be the Jacobian matrices of F_i and V_i defined as $F = [(\partial F_i/\partial x_j)(x_0)]$ and $V = [(\partial V_i/\partial x_j)(x_0)]$; $1 \le i, j \le m$, where x is the number of individuals in each compartment, x_0 is a disease-free equilibrium, F_i is the rate of appearance of new infections in compartment i, $V_i = V_i^- - V_i^+$, in which V_i^+ is the transfer rate of individuals into compartment i, and V_i^- is the rate of transfer of individuals out of compartment i. The rate of change of variables representing the infected components of the model system (1) can be rewritten as

$$\begin{bmatrix} I_{\mathrm{se}}'(t) \\ I_r'(t) \end{bmatrix} = (F - V)\begin{bmatrix} I_{\mathrm{se}} \\ I_r \end{bmatrix} - \begin{bmatrix} \beta_1 k_3 I_{\mathrm{se}}\left(1 - \dfrac{S + \varepsilon V}{N}\right) \\ \beta_2 k_3 I_r\left(1 - \dfrac{S + \varepsilon V}{N}\right) \end{bmatrix}, \tag{19}$$

implying that

$$\begin{bmatrix} I_{\mathrm{se}}'(t) \\ I_r'(t) \end{bmatrix} \le (F - V)\begin{bmatrix} I_{\mathrm{se}} \\ I_r \end{bmatrix}, \tag{20}$$

where the matrices F and V are defined as

$$\begin{aligned} F &= \begin{bmatrix} \dfrac{\beta_1 k_3(\omega + (1-\rho)\mu + \varepsilon(\rho\mu + \gamma))}{\omega + \mu + \gamma} & 0 \\ 0 & \dfrac{\beta_2 k_3(\omega + (1-\rho)\mu + \varepsilon(\rho\mu + \gamma))}{\omega + \mu + \gamma} \end{bmatrix}, \\ V &= \begin{bmatrix} (\varepsilon_{se} + \eta + \mu + \delta_1) & 0 \\ -\eta & (\varepsilon_r + \mu + \delta_2) \end{bmatrix}. \end{aligned} \tag{21}$$

k_3 has the same meaning as it is in the Jacobian matrix (14).

All the eigenvalues of matrix $(F - V)$ have negative real parts if $R_{\mathrm{se}} < 1$ and $R_r < 1$; hence, the inequality (20) is stable for $R_{\mathrm{se}} < 1$ and $R_r < 1$ [27]. Thus, by comparison method, $(I_{\mathrm{se}}, I_r) \longrightarrow (0, 0)$ as $t \longrightarrow \infty$. Furthermore, whenever $I_{\mathrm{se}} = I_r = 0$, model system (1) gives $S(t) \longrightarrow \nu/\mu$, as $t \longrightarrow \infty$. Therefore, $(I_{\mathrm{se}}, I_r) \longrightarrow E_0$ as $t \longrightarrow \infty$ for $R_{\mathrm{se}} < 1$ and $R_r < 1$. Hence, E_0 is globally asymptotically stable. Thus, the system will come to a disease-free equilibrium point from any starting point.

3.7. The Drug-Resistant Dominance and Endemic Equilibria. The drug resistance-strain-dominance equilibrium is a boundary equilibrium in which resistant-strain is present, $I_r \neq 0$, while a sensitive strain is not present $I_{\mathrm{se}} = 0$. To find the drug resistance-strain-dominance equilibrium of the

model, the right-hand side of the model system (1) is equated to zero when $I_{se} = 0$. Thus, we have the following model system:

$$\begin{cases} 0 = (1-\rho)\nu - k_3\alpha_r S - (\mu+\gamma)S + \omega V + \psi R, \\ 0 = \rho\nu + \gamma S - \varepsilon\alpha_r k_3 V - (\omega+\mu)V, \\ 0 = \alpha_r k_3(S+\varepsilon V) - (\varepsilon_r + \mu + \delta_2)I_r, \\ 0 = \varepsilon_r I_r - (\mu+\psi)R. \end{cases} \tag{22}$$

The drug resistance-strain-dominance equilibrium is obtained from model system (22) and given by

$$E_r^* = (S^*, V^*, I_r^*, R^*), \tag{23}$$

where

$$S^* = \frac{a_3a_5(\nu(\rho-1)(a_6+\varepsilon k_3\alpha_r^*) - \rho\nu\omega) - \varepsilon k_3\rho\nu\psi\alpha_r^*\varepsilon_r}{a_3a_5(\gamma\omega - (a_4+k_3\alpha_r^*)(a_6+\varepsilon k_3\alpha_r^*)) + k_3\psi\alpha_r^*\varepsilon_r(a_6+\varepsilon(\gamma+k_3\alpha_r^*))},$$

$$V^* = \frac{a_3a_5(\gamma\nu(\rho-1) - \rho\nu(a_4+k_3\alpha_r^*)) + k_3\rho\nu\psi\alpha_r^*\varepsilon_r}{a_3a_5(\gamma\omega - (a_4+k_3\alpha_r^*)(a_6+\varepsilon k_3\alpha_r^*)) + k_3\psi\alpha_r^*\varepsilon_r(a_6+\varepsilon(\gamma+k_3\alpha_r^*))},$$

$$I_r^* = \frac{a_5k_3\alpha_r^*(a_4\varepsilon\rho\nu + a_6(\nu-\nu\rho) + \gamma(-\varepsilon)\nu(\rho-1) + \varepsilon k_3\alpha_r^*(\nu(-\rho)+\nu+\rho\nu) + \rho\nu\omega)}{a_3a_5((a_4+k_3\alpha_r^*)(a_6+\varepsilon k_3\alpha_r^*) - \gamma\omega) - k_3\psi\alpha_r^*\varepsilon_r(a_6+\varepsilon(\gamma+k_3\alpha_r^*))},$$

$$R^* = \frac{k_3\alpha_r^*\varepsilon_r(-a_4\varepsilon\rho\nu + a_6\nu(\rho-1) + \gamma\varepsilon\nu(\rho-1) - \varepsilon k_3\alpha_r^*(\nu(-\rho)+\nu+\rho\nu) - \rho\nu\omega)}{a_3a_5(\gamma\omega - (a_4+k_3\alpha_r^*)(a_6+\varepsilon k_3\alpha_r^*)) + k_3\psi\alpha_r^*\varepsilon_r(a_6+\varepsilon(\gamma+k_3\alpha_r^*))}. \tag{24}$$

$a_4 = \mu + \gamma$, $a_6 = \mu + \omega$, and a_3, a_5 have the same meaning as in system (14).

Since mutation leads to the coexistence of both sensitive strain and resistant strain, then we established a coexistence equilibrium of our model system. A coexistence equilibrium is an equilibrium for which both sensitive strain and resistant strain are present, that is, $I_{se} \neq 0$ and $I_r \neq 0$. To find the endemic equilibrium (coexistence equilibrium) of the model, the right-hand side of model system (1) is equated to zero hence gives

$$\begin{cases} 0 = (1-\rho)\nu - k_3(\alpha_{se}+\alpha_r)S - (\gamma+\mu)S + \psi R + \omega V, \\ 0 = \rho\nu + \gamma S - k_3\varepsilon(\alpha_{se}+\alpha_r)V - (\omega+\mu)V, \\ 0 = \alpha_{se}k_3(S+\varepsilon V) - (\eta + \varepsilon_{se} + \mu + \delta_1)I_{se}, \\ 0 = \alpha_r k_3(S+\varepsilon V) + \eta I_{se} - (\varepsilon_r + \mu + \delta_2)I_r, \\ 0 = \varepsilon_{se}I_s + \varepsilon_r I_r - (\mu+\psi)R. \end{cases} \tag{25}$$

The coexistence equilibrium is obtained and given by $E^{**} = (S^{**}, V^{**}, I_{se}^{**}, I_r^{**}, R^{**})$ where

$$S^{**} = -\frac{a_2(a_3a_5(\rho\nu\omega - \nu(\rho-1)(a_6+\varepsilon k_3(\alpha_r^{**}+\alpha_{se}^{**}))) + \varepsilon k_3\rho\nu\psi\alpha_r^{**}\varepsilon_r) + b_1}{a_2(b_4b_5 + a_3a_5(\gamma\omega - (a_4+k_3(\alpha_r^{**}+\alpha_{se}^{**}))(a_6+\varepsilon k_3(\alpha_r^{**}+\alpha_{se}^{**})))) + b_2},$$

$$V^{**} = \frac{a_2(a_3a_5(\rho\nu(a_4+k_3(\alpha_r^{**}+\alpha_{se}^{**})) - \gamma\nu(\rho-1)) - k_3\rho\nu\psi\alpha_r^{**}\varepsilon_r) - b_3}{a_2(a_3a_5((a_4+k_3(\alpha_r^{**}+\alpha_{se}^{**}))(a_6+\varepsilon k_3(\alpha_r^{**}+\alpha_{se}^{**})) - \gamma\omega) - b_4b_5) - b_2},$$

$$I_{se}^{**} = \frac{a_3a_5k_3\alpha_{se}^{**}(a_4\varepsilon\rho\nu + a_6(\nu-\nu\rho) + \gamma(-\varepsilon)\nu(\rho-1) + \varepsilon k_3\nu(\alpha_r^{**}+\alpha_{se}^{*}) + \rho\nu\omega)}{a_2(a_3a_5((a_4+k_3(\alpha_r^{**}+\alpha_{se}^{**}))(a_6+\varepsilon k_3(\alpha_r^{**}+\alpha_{se}^{**})) - \gamma\omega) - b_4b_5) - b_2},$$

$$I_r^{**} = -\frac{a_5k_3(a_2\alpha_r^{**} + \eta\alpha_{se}^{**})(-a_4\varepsilon\rho\nu + a_6\nu(\rho-1) + \gamma\varepsilon\nu(\rho-1) - \varepsilon k_3\nu(\alpha_r^{**}+\alpha_{se}^{**}) - \rho\nu\omega)}{a_2(a_3a_5((a_4+k_3(\alpha_r^{**}+\alpha_{se}^{**}))(a_6+\varepsilon k_3(\alpha_r^{**}+\alpha_{se}^{**})) - \gamma\omega) - b_4b_5) - b_2},$$

$$R^{**} = \frac{(\varepsilon_{se}I_{se}^{**} + \varepsilon_r I_r^{**})}{a_5}. \tag{26}$$

For

$$\begin{aligned} b_1 &= \varepsilon k_3\rho\nu\psi\alpha_{se}^{**}(a_3\varepsilon_{se} + \eta\varepsilon_r), \\ b_2 &= k_3\psi\alpha_{se}^{**}(a_3\varepsilon_{se} + \eta\varepsilon_r)b_5, \\ b_3 &= k_3\rho\nu\psi\alpha_{se}^{**}(a_3\varepsilon_{se} + \eta\varepsilon_r), \\ b_4 &= k_3\psi\alpha_r^{**}\varepsilon_r, \\ b_5 &= (a_6 + \varepsilon(\gamma + k_3(\alpha_r^{**}+\alpha_{se}^{**}))), \end{aligned} \tag{27}$$

$a_4 = \mu + \gamma$, $a_6 = \mu + \omega$, and a_2, a_3, a_5 have the same meaning as in system (14).

3.8. Global Stability of Dominance Equilibrium. An important principle in theoretical biology is that of competitive exclusion which states that when n strains compete in a population, the strain with the largest reproduction number out-competes the other strains and drives them to extinction [29]. However, due to mutation, we can only show that the dominant equilibrium (E_r^*) is globally asymptotically stable (GAS) under some feasible biological conditions. The global stability of equilibrium E_r^* has been derived using suitable Lyapunov functions.

Theorem 5. *The mutant-dominant equilibrium E_r^* is globally asymptotically stable if $R_r > 1$, $R_{se} < 1$, and $R_r^{se} > 1$ in the hyperplane $I_{se} = 0$.*

The global stability of equilibrium E_r^* has been derived using the method of Lyapunov functions.

Proof. Define Lyapunov function using the form

$$L = \sum_{i=1}^{n}(x_i - x_i^* - x_i^* \ln x_i) \tag{28}$$

as

$$\begin{aligned} L(S, V, I_r, R) = S - S^* - S^* \ln \frac{S^*}{S} + V - V^* - V^* \ln \frac{V^*}{V} \\ + I_r - I_r^* - I_r^* \ln \frac{I_r^*}{I_r} + R - R^* - R^* \ln \frac{R^*}{R}, \end{aligned}$$

$$\frac{dL}{dt} = \left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + \left(1 - \frac{V^*}{V}\right)\frac{dV}{dt} + \left(1 - \frac{I_r^*}{I_r}\right)\frac{dI_r}{dt} + \left(1 - \frac{R^*}{R}\right)\frac{dR}{dt}, \tag{29}$$

where x_i is a population in compartment i and x_i is the endemic equilibrium point. Substituting the derivative of the model system, we get

$$\frac{dL}{dt} = \left(1 - \frac{S^*}{S}\right)((1-\rho)\nu - k_3\alpha_r S - (\gamma+\mu)S + \omega V + \psi R) + \left(1 - \frac{V^*}{V}\right)(\rho\nu + \gamma S - \varepsilon k_3\alpha_r V - (\omega+\mu)V) + \left(1 - \frac{I_r^*}{I_r}\right)(k_3\alpha_r(S+\varepsilon V) - (\varepsilon_r + \delta_2 + \mu)I_r) + \left(1 - \frac{R^*}{R}\right)(\varepsilon_r I_r - (\mu+\psi)R). \tag{30}$$

At equilibrium, we have

$$\begin{aligned}(1-\rho)\nu &= k_3\alpha_r^* S^* + (\gamma+\mu)S^* - \omega V^* - \psi R^*,\\ \rho\nu &= -\gamma S^* + \varepsilon k_3\alpha_r^* V^* + (\omega+\mu)V^*,\\ (\varepsilon_r + \delta_2 + \mu) &= \frac{k_3\alpha_r^*}{I_r^*}(S^* + \varepsilon V^*),\\ (\mu+\psi) &= \frac{\varepsilon_r I_r^*}{R^*}.\end{aligned} \tag{31}$$

By substituting (31) in equation (30), we obtain

$$\frac{dL}{dt} = \left(1 - \frac{S^*}{S}\right)(k_3\alpha_r^* S^* + \mu S^* + \gamma S^* - \psi R^* - k_3\alpha_r S - (\gamma+\mu)S + \psi R) + \left(1 - \frac{V^*}{V}\right)(\varepsilon k_3\alpha_r^* V^* + (\omega+\mu)V^* - \gamma S^* + \gamma S - \varepsilon k_3\alpha_r V - (\omega+\mu) * V) + \left(1 - \frac{I_r^*}{I_r}\right)\left(k_3\alpha_r(S+\varepsilon V) - \frac{\alpha_r^*}{I_r^*}(S^* + \varepsilon V^*)I_r\right) + \left(1 - \frac{R^*}{R}\right)\left(\varepsilon_r I_r - \frac{\varepsilon_r I_r^*}{R^*}R\right). \tag{32}$$

By simplifying equation (32), we obtain

$$\frac{dL}{dt} = \left(1 - \frac{S^*}{S}\right)(k_3(\alpha_r^* S^* - \alpha_r S) + (\gamma+\mu)(S^* - S) - \omega(V^* - V) - \psi(R^* - R)) + \left(1 - \frac{V^*}{V}\right)(\varepsilon k_3(\alpha_r^* V^* - \alpha_r V) + (\omega+\mu)(V^* - V) - \gamma(S^* - S)) + \left(1 - \frac{I_r^*}{I_r}\right)\left(k_3\alpha_r(S+\varepsilon V) - \frac{k_3\alpha_r^*(S^* + \varepsilon\nu^*)}{I_r^*}I_r\right) + \left(1 - \frac{R^*}{R}\right)\left(\varepsilon_r I_r - \frac{\varepsilon_r I_r^*}{R^*}R\right).$$

$$\frac{dL}{dt} = \left(1 - \frac{S^*}{S}\right)\left(-k_3\alpha_r S\left(1 - \frac{\alpha_r^* S^*}{\alpha_r S}\right) - (\gamma+\mu)S\left(1 - \frac{S^*}{S}\right) + \omega V\left(1 - \frac{V^*}{V}\right) + \psi R\left(1 - \frac{R^*}{R}\right)\right) + \left(1 - \frac{V^*}{V}\right)\left(-\varepsilon k_3\alpha_r V\left(1 - \frac{\alpha_r^* V^*}{\alpha_r V}\right) - (\mu+\omega)V\left(1 - \frac{V^*}{V}\right) + \gamma S\left(1 - \frac{S^*}{S}\right)\right) + \left(1 - \frac{I_r^*}{I_r}\right)\left(k_3\alpha_r(S+\varepsilon V)(1 - \frac{\alpha_r^* I_r(S^* + \varepsilon\nu^*)}{\alpha_r I_r^*(S+\varepsilon V)}\right) + \left(1 - \frac{R^*}{R}\right)\left(\varepsilon_r I_r\left(1 - \frac{I_r^* R}{I_r R^*}\right)\right). \tag{33}$$

Further simplification leads to

$$\frac{dL}{dt} = -(\gamma+\mu)S\left(1 - \frac{S^*}{S}\right)^2 - (\mu+\omega)V\left(1 - \frac{V^*}{V}\right)^2 + g(S, V, I_r, R). \tag{34}$$

where

$$g(S, V, I_r, R) = \left(1 - \frac{S^*}{S}\right)\left(-k_3\alpha_r S\left(1 - \frac{\alpha_r^* S^*}{\alpha_r S}\right) + \omega V\left(1 - \frac{V^*}{V}\right) + \psi R\left(1 - \frac{R^*}{R}\right)\right) + \left(1 - \frac{V^*}{V}\right)\left(\gamma S\left(1 - \frac{S^*}{S}\right) - \varepsilon k_3\alpha_r V\left(1 - \frac{\alpha_r^* V^*}{\alpha_r V}\right)\right) + \left(1 - \frac{I_r^*}{I_r}\right)\left(k_3\alpha_r(S+\varepsilon V)(1 - \frac{\alpha_r^* I_r(S^* + \varepsilon\nu^*)}{\alpha_r I_r^*(S+\varepsilon V)}\right) + \left(1 - \frac{R^*}{R}\right)\left(\varepsilon_r I_r\left(1 - \frac{I_r^* R}{I_r R^*}\right)\right). \tag{35}$$

Following techniques shown in [30, 31], we have $g(S, V, I_r, R) < 0$ for $S, V, I_r, R > 0$ and $dL/dt = 0$ for $S = S^*, V = V^*, I_r = I_r^*, R = R^*$. Furthermore, $dL/dt < 0$ if $S, V, I_r, R > 0$. Thus, whenever $R_r > 1$, $R_{se} < 1$, and $R_r^{se} > 1$, the mutant-dominant equilibrium (E_r^*) is GAS.

3.9. Sensitivity Analysis. Sensitivity indices measure the relative change in a state variable when a parameter change [32]. Through sensitivity analysis we can describe the impact of each parameter to disease transmission. If a variable is differentiable function of the parameter, the sensitivity indices may be alternatively defined using partial derivatives [32]. We intend to know how each parameter affects the effective reproduction number R_e. We use the formula of the normalized sensitivity index of a variable for R_e to achieve our goal.

The normalized forward sensitivity index of a variable, Z, depends differentiability on index of a parameter; ϕ is defined as

$$\gamma_\phi^Z = \left(\frac{\partial Z}{\partial \phi}\right)\left(\frac{\phi}{Z}\right). \tag{36}$$

Applying the formula for R_{se} and R_r, we have

$$\gamma_\phi^{R_{se}} = \left(\frac{\partial R_{se}}{\partial \phi}\right)\left(\frac{\phi}{R_{se}}\right), \tag{37}$$

$$\gamma_\phi^{R_r} = \left(\frac{\partial R_r}{\partial \phi}\right)\left(\frac{\phi}{R_r}\right). \tag{38}$$

Applying the normalized forward sensitivity index defined in (37) and (38) yields to the results in Tables 1 and 2, respectively. The parameter values in Table 3 are used to determine the sensitivity indices.

3.9.1. Interpretation of Sensitivity Indices. The sensitivity indices are presented in Tables 1 and 2. Parameters that have positive sensitivity indices in Tables 1 and 2 indicated that if

Table 1: Values of sensitivity indices of $R_{se.}$

Parameters	Sensitivity index
μ	+0.001416
δ_1	-0.783095
ε_{se}	-0.169433
k	+1
P_1	+1
ρ	-0.000029
k_1	-0.176471
ω	+0.797025
ε	+0.193269
γ	-0.798451
η	-0.047460

Table 2: Values of sensitivity indices of R_r.

Parameters	Sensitivity index
μ	+0.001415
δ_2	-0.822113
ε_r	-0.177875
k	+1
P_2	+1
ρ	-0.000029
k_1	-0.176471
ω	+0.797025
ε	+0.193269
γ	-0.798451

their values are increased while keeping other values constant, R_{se} and R_r increases, respectively. These parameters have a greater influence in spreading the pneumonia infection. But the parameters with negative sensitivity indices in Tables 1 and 2 show that if their values are increased while keeping the rest parameters fixed, R_{se} and R_r decreases, respectively. These parameters play part in reducing the spreading of the disease. Therefore, the important parameters for effective control of the disease are ε_r, ε_{se}, k_1, and γ. The most sensitivity parameters are k and P with positive sensitivity indices. Note that the mortality rates δ_1 and δ_2 have negative sensitivity indices but biologically, it is not recommended to increase these parameters (δ_1 and δ_2) for the purpose of controlling the disease.

4. A Model for the Optimal Control Problem

In this section, we established the time-dependent controls in the model system (1) aiming to determine the best intervention strategies in eradicating pneumonia infections. One of the main side effects of treatment is the development of drug-resistant strains that eventually lead to drug failure to treat the disease. Optimal control has been used to curb the development of drug-resistant strain or drug failure, at the same time reducing the cost of implementing control measures such as vaccination or treatment by imposing a condition that monitors the global effects of the control strategies including vaccination and treatment programs [17]. In addition, public health education has also been proved as an important control in reducing disease infections (e.g., see [14]). We, therefore, establish the time-dependent controls in the model system (1) aiming at obtaining the best control strategy in eradicating pneumonia infections as well as minimizing the cost of implementing the controls. Here are the controls introduced in the model system (1): $u_1(t)$: public health education effort, $u_2(t)$: vaccination effort, $u_3(t)$: control effort on treatment of individuals infected with drug-sensitive strain, and $u_4(t)$: control effort on treatment of individuals infected with drug-resistant strain. Hence, for the optimal control problem, we have the following model system:

$$\begin{aligned}
\frac{dS}{dt} &= (1-\rho)\nu - (1-u_1(t))(\alpha_s+\alpha_r)S - (u_2(t)\gamma+\mu)S + \psi R + \omega V,\\
\frac{dV}{dt} &= \rho\nu + u_2(t)\gamma S - (1-u_1(t))\varepsilon(\alpha_{se}+\alpha_r)V - (\omega+\mu)V,\\
\frac{dI_{se}}{dt} &= \alpha_{se}(1-u_1(t))(S+\varepsilon V) - u_3(t)\varepsilon_{se}I_{se} - (\eta+\mu+\delta_1)I_{se},\\
\frac{dI_r}{dt} &= \alpha_r(1-u_1(t))(S+\varepsilon V) + \eta I_{se} - u_4(t)\varepsilon_r I_r - (\mu+\delta_2)I_r,\\
\frac{dR}{dt} &= u_3(t)\varepsilon_{se}I_{se} + u_4(t)\varepsilon_r I_r - (\mu+\psi)R.
\end{aligned} \tag{39}$$

Control theory that is used to make a decision in a complex biological situation is applied as a mathematical tool. We intend to find the optimal level of the control strategy preferred to minimize the number of infections while keeping low, cost of implementation of the control. We consider the optimal control problem with objective functional J, of the form

$$J(u_1,u_2,u_3,u_4) = \min_{u_1,u_2,u_3,u_4}\int_0^{tf}\left(A_1S + A_2I_{se} + A_3I_r + \frac{1}{2}\sum_{i=1}^{4}B_iu_i^2\right)dt, \tag{40}$$

where A_1, A_2, and A_3 are the weight constants associated with the number of susceptible individuals, the number of individuals infected with drug-sensitive strain, and the number of individuals infected with drug-resistant strain while B_1, B_2, B_3, and B_4 present relative cost weight which is associated with control measures u_1, u_2, u_3, and u_4, respectively. The control variables in the objective functional are in quadratic form because we assume that costs are nonlinear in nature which is a convex function as applied by [17, 33–35]. The aim is to minimize the objective functional such that the optimal control satisfy

$$J(u^*) = \min J(u|u\in U), \tag{41}$$

Table 3: Parameter values.

Parameter	Descriptions	Value	Source
ν	Recruitment rate	100/day	Assumed
μ	Natural death rate	0.00000456621/day	[14]
$P_j, j = 1, 2$	Probability for a contact to cause infection	0.89-0.99	[9, 14, 15]
k	Contact rate	1 to 10 days	[9, 15]
δ_1	Disease induced death rate for individuals infected with the drug-sensitive strain	0.33/day	[9, 10, 15]
δ_2	Disease induced death rate for individuals infected with the drug-resistant strain	0.33/day	Assumed
ε_{se}	Treatment rate for individuals infected with the drug-sensitive strain	0.0714/day	[15]
ε_r	Treatment rate for individuals infected with the drug-resistant strain	0.0714/day	Assumed
η	Mutation rate	0.00046/day	Assumed.
ψ	The rate at which recovered individuals loss their immunity	0.0241/day	[15]
ρ	Proportion of recruited individuals who are vaccinated against pneumonia	0.02	Assumed
γ	Vaccination rate	0.3/day	Assumed
ε	Proportional of the serotype not covered by the vaccine	0.002	[14]
ω	Waning rate	0.0025/day	[14]

where $U = \{(u_1, u_2, u_3, u_4) | u_i$ is Lebesgue measurable with $0 < U \leq 1 \quad t \in [0, t_f], i = 1, 2, 3, 4\}$ is the set of admissible controls.

4.1. Existence of an Optimal Control. For an optimal control problem to exist, the necessary condition that defines the optimal solutions in (41) of the model system (39) derived by Pontryagin's Maximum Principle [36] must be satisfied. We prove the following result:

Theorem 6. *There exists an optimal control* $\left(u_1^*, u_2^*, u_3^*, u_4^*\right)$ *such that*

$$J\left(u_1^*, u_2^*, u_3^*, u_4^*\right) = \min\{J(u_1, u_2, u_3, u_4): (u_1, u_2, u_3, u_4) \in U\}, \tag{42}$$

subject to the control system (39) with initial conditions in model system (1).

Proof. The existence of optimal control can be proved by using the results in [37]. It is clear that, the model system (39) is bounded by a linear system. The boundedness of solutions of the model system (39) for a finite time interval is used to prove the existence of optimal control. To use the theorem in [37], we first check the following conditions:

(1) The set of controls and corresponding state variables are nonempty

(2) The measurable control set is convex and closed

(3) The right-hand side of the state system (39) is bounded by a linear system in the state and control variables

(4) The integrand of the objective functional is convex

(5) There exist constant numbers $d_1, d_2 > 0$ and $q > 1$ such that the integrand of the objective functional satisfies

$$A_1 S + A_2 I_{se} + A_3 I_r + \frac{1}{2}\sum_{i=1}^{4} B_i u_i^2 \geq d_1\left(|u_1|^2 + |u_2|^2 + |u_3|^2 + |u_4|^2\right)^{q/2} - d_2 \tag{43}$$

From model system (39), the set of all state variables and the control variables are nonnegative; thus, the first condition is satisfied. By definition, the control set is convex and closed in U; hence, the second condition is satisfied. The model system (39) is bounded which proves the third condition. The integrand in the objective functional (40) is clearly convex on (u_1, u_2, u_3, u_4) which gives the fourth condition. In addition, since the state variables are bounded, then the integrand is also bounded by $A_1 S + A_2 I_{se} + A_3 I_r + 1/2\sum_{i=1}^{4} B_i u_i^2 \geq d_1\left(|u_1|^2 + |u_2|^2 + |u_3|^2 + |u_4|^2\right)^{q/2} - d_2$ for $d_1, d_2, q > 0$ and $i = 1, 2, 3, 4$ which proves the last condition. All the conditions are satisfied; we conclude that there exists an optimal control $(u_1^*, u_2^*, u_3^*, u_4^*)$ such that

$$J(u_1^*, u_2^*, u_3^*, u_4^*) = \min\{J(u_1, u_2, u_3, u_4)\}. \tag{44}$$

4.2. Characterization of the Optimal Control. Here, we apply Pontryagin's Maximum Principle to derive the necessary conditions that the optimal control solution must satisfy [16]. Pontryagin's Maximum Principle converts the model system (39) and (40) into a problem of minimizing a

Hamiltonian, H, point-wise with respect to u_1, u_2, u_3, and u_4 defined as

$$H(t, x(t), u(t), \lambda(t)) = L(S, I_{se}, I_r, u_1, u_2, u_3, u_4, t) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dV}{dt} + \lambda_3 \frac{dI_{se}}{dt} + \lambda_4 \frac{dI_r}{dt} + \lambda_5 \frac{dR}{dt}, \tag{45}$$

where

$$L(S, I_{se}, I_r, u_1, u_2, u_3, u_4, t) = A_1 S + A_2 I_{se} + A_3 I_r + \frac{1}{2} B_1 u_1^2 + \frac{1}{2} B_2 u_2^2 + \frac{1}{2} B_3 u_3^2 + \frac{1}{2} B_4 u_4^2. \tag{46}$$

The expanded form equation (45) becomes

$$\begin{aligned} H(t, x(t), u(t), \lambda(t)) = {} & L(S, I_{se}, I_r, u_1, u_2, u_3, u_4, t) \\ & + \lambda_1((1-\rho)\nu - (1-u_1)(\alpha_{se} + \alpha_r)S \\ & - (u_2\gamma + \mu)S + \psi R + \omega V) \\ & + \lambda_2(\rho\nu + u_2\gamma S - (1-u_1)\varepsilon(\alpha_{se} + \alpha_r)V \\ & - (\omega + \mu)V) + \lambda_3(\alpha_{se}(1-u_1)(S + \varepsilon V) \\ & - (u_3\varepsilon_{se} + \eta + \mu + \delta_1)I_{se}) + \lambda_4(\alpha_r(1-u_1) \\ & \cdot (S + \varepsilon V) + \eta I_{se} - (u_4\varepsilon_r + \mu + \delta_2)I_r) \\ & + \lambda_5(u_3\varepsilon_{se}I_{se} + u_4\varepsilon_r I_r - (\mu + \psi)R), \end{aligned} \tag{47}$$

where λ_1, λ_2, λ_3, λ_4, and λ_5 are the costate variables or adjoint variables. Pontryagin's Maximum Principle is applied to determine the adjoint variable functions. Thus, we have the following theorem:

Theorem 7. *There exist adjoint variable, λ_1, λ_2, λ_3, λ_4, and λ_5 with transversality conditions $\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = 0$, for an optimal control $(u_1^*, u_2^*, u_3^*, u_4^*)$ that minimizes $J(u_1, u_2, u_3, u_4)$ such that*

$$\begin{aligned} \frac{d\lambda_1}{dt} = {} & -A_1 + \lambda_1((1-u_1)(\alpha_{se} + \alpha_r) + (u_2\gamma + \mu)) - u_2\gamma\lambda_2 \\ & - (1-u_1)\alpha_{se}\lambda_3 - (1-u_1)\alpha_r\lambda_4, \end{aligned}$$

$$\begin{aligned} \frac{d\lambda_2}{dt} = {} & -\omega\lambda_1 + ((1-u_1)\varepsilon(\alpha_{se} + \alpha_r) + \omega + \mu)\lambda_2 \\ & - (1-u_1)\varepsilon\alpha_{se}\lambda_3 - (1-u_1)\varepsilon\alpha_r\lambda_4, \end{aligned}$$

$$\begin{aligned} \frac{d\lambda_3}{dt} = {} & -A_2 + \frac{\beta_1 S(1-u_1)}{N}\lambda_1 + \frac{\beta_1 \varepsilon V(1-u_1)}{N}\lambda_2 \\ & - \left(\frac{\beta_1(1-u_1)(S + \varepsilon V)}{N} - (\eta + u_3\varepsilon_{se} + \mu + \delta_1)\right)\lambda_3 \\ & - \eta\lambda_4 - u_3\varepsilon_{se}\lambda_5, \end{aligned}$$

$$\begin{aligned} \frac{d\lambda_4}{dt} = {} & -A_3 + \frac{\beta_2 S(1-u_1)}{N}\lambda_1 + \frac{\beta_2 \varepsilon V(1-u_1)}{N}\lambda_2 \\ & - \left(\frac{\beta_2(1-u_1)(S + \varepsilon V)}{N} - (u_4\varepsilon_r + \mu + \delta_2)\right)\lambda_4 - u_4\varepsilon_r\lambda_5, \end{aligned}$$

$$\frac{d\lambda_5}{dt} = -\lambda_1\psi + (\mu + \psi)\lambda_5, \tag{48}$$

with transversality conditions at the final time, t_f:

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = 0. \tag{49}$$

Also, we obtain the control set $(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t))$ characterized by

$$\begin{aligned} u_1^* &= \min\{\max\{0, \pi\}, 1\}, \\ u_2^* &= \min\{\max\{0, \pi\}, 1\}, \\ u_3^* &= \min\{\max\{0, \pi\}, 1\}, \\ u_4^* &= \min\{\max\{0, \pi\}, 1\}, \end{aligned} \tag{50}$$

where

$$\begin{aligned} \pi_1 &= \frac{S((\lambda_4 - \lambda_1)\beta_2 I_r + (\lambda_3 - \lambda_1)\beta_1 I_{se}) + \varepsilon V((\lambda_4 - \lambda_2)\beta_2 I_r + (\lambda_3 - \lambda_2)\beta_1 I_{se})}{NB_1}, \\ \pi_2 &= \frac{(\lambda_1 - \lambda_2)\gamma S}{B_2}, \\ \pi_3 &= \frac{(\lambda_3 - \lambda_5)\varepsilon_{se} I_{se}}{B_3}, \\ \pi_4 &= \frac{(\lambda_4 - \lambda_5)\varepsilon_r I_r}{B_4}. \end{aligned} \tag{51}$$

Proof. The form of the adjoint equation and transversality conditions are standard results from Pontryagin's Maximum Principle [36]. We differentiate Hamiltonian (47) with respect to states, S, V, I_{se}, I_r, and R, respectively, and then, the adjoint system can be written as

$$\begin{aligned} \frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S} = {} & -A_1 + \lambda_1((1-u_1)(\alpha_{se} + \alpha_r) + (u_2\gamma + \mu)) \\ & - u_2\gamma\lambda_2 - (1-u_1)\alpha_{se}\lambda_3 - (1-u_1)\alpha_r\lambda_4, \end{aligned}$$

$$\begin{aligned} \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial V} = {} & -\omega\lambda_1 + ((1-u_1)\varepsilon(\alpha_{se} + \alpha_r) + \omega + \mu)\lambda_2 \\ & - (1-u_1)\varepsilon\alpha_{se}\lambda_3 - (1-u_1)\varepsilon\alpha_r\lambda_4, \end{aligned}$$

$$\begin{aligned} \frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial I_{se}} = {} & -A_2 + \frac{\beta_1 S(1-u_1)}{N}\lambda_1 + \frac{\beta_1 \varepsilon V(1-u_1)}{N}\lambda_2 \\ & - \left(\frac{\beta_1(1-u_1)(S + \varepsilon V)}{N} - (\eta + u_3\varepsilon_{se} + \mu + \delta_1)\right)\lambda_3 \\ & - \eta\lambda_4 - u_3\varepsilon_{se}\lambda_5, \end{aligned}$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial I_r} = -A_3 + \frac{\beta_2 S(1-u_1)}{N}\lambda_1 + \frac{\beta_2 \varepsilon V(1-u_1)}{N}\lambda_2 - \left(\frac{\beta_2(1-u_1)(S+\varepsilon V)}{N} - (u_4\varepsilon_r + \mu + \delta_2)\right)\lambda_4 - u_4\varepsilon_r\lambda_5,$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial R} = -\lambda_1\psi + (\mu+\psi)\lambda_5. \tag{52}$$

with transversality conditions at the final time, t_f:

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = 0. \tag{53}$$

By using the approach of Pontryagin et al. [36], we get the controls by solving the equation

$$\frac{\partial H(t, x(t), u(t), \lambda(t))}{\partial u_i} = 0, \tag{54}$$

at u_i^* for $i = 1, 2, 3, 4$ and obtained

$$u_1^* = \frac{S((\lambda_4-\lambda_1)\beta_2 I_r + (\lambda_3-\lambda_1)\beta_1 I_{se}) + \varepsilon V((\lambda_4-\lambda_2)\beta_2 I_r + (\lambda_3-\lambda_2)\beta_1 I_{se})}{NB_1},$$
$$u_2^* = \frac{(\lambda_1-\lambda_2)\gamma S}{B_2},$$
$$u_3^* = \frac{(\lambda_3-\lambda_5)\varepsilon_{se} I_{se}}{B_3},$$
$$u_4^* = \frac{(\lambda_4-\lambda_5)\varepsilon_r I_r}{B_4}. \tag{55}$$

By including the bounds on the controls in (55), we have

$$u_1^* = \begin{cases} 0 & \text{if } \pi_1 \le 0, \\ \pi_1 & \text{if } 0 < \pi_1 < 1, \\ 1 & \text{if } \pi_1 \ge 1, \end{cases}$$
$$u_2^* = \begin{cases} 0 & \text{if } \pi_2 \le 0, \\ \pi_2 & \text{if } 0 < \pi_2 < 1, \\ 1 & \text{if } \pi_2 \ge 1, \end{cases}$$
$$u_3^* = \begin{cases} 0 & \text{if } \pi_3 \le 0, \\ \pi_3 & \text{if } 0 < \pi_3 < 1, \\ 1 & \text{if } \pi_3 \ge 1, \end{cases} \tag{56}$$
$$u_4^* = \begin{cases} 0 & \text{if } \pi_4 \le 0, \\ \pi_4 & \text{if } 0 < \pi_4 < 1, \\ 1 & \text{if } \pi_4 \ge 1. \end{cases}$$

The solution of $u_1^*(t)$, $u_2^*(t)$, $u_3^*(t)$, and $u_4^*(t)$ in (55) are given in compact form as

$$u_1^* = \min\{\max\{0, \pi\}, 1\},$$
$$u_2^* = \min\{\max\{0, \pi\}, 1\},$$
$$u_3^* = \min\{\max\{0, \pi\}, 1\},$$
$$\mathrm{u}_4^* = \min\{\max\{0, \pi\}, 1\}, \tag{57}$$

where

$$\pi_1 = \frac{S((\lambda_4-\lambda_1)\beta_2 I_r + (\lambda_3-\lambda_1)\beta_1 I_{se}) + \varepsilon V((\lambda_4-\lambda_2)\beta_2 I_r + (\lambda_3-\lambda_2)\beta_1 I_{se})}{NB_1},$$
$$\pi_2 = \frac{(\lambda_1-\lambda_2)\gamma S}{B_2},$$
$$\pi_3 = \frac{(\lambda_3-\lambda_5)\varepsilon_{se} I_{se}}{B_3},$$
$$\pi_4 = \frac{(\lambda_4-\lambda_5)\varepsilon_r I_r}{B_4}. \tag{58}$$

The state system (39) with its initial conditions together with the adjoint variable system in Theorem 7 with its transversality conditions (49) form the optimality system.

$$\frac{dS}{dt} = (1-\rho)\nu - (1-u_1(t))(\alpha_{se}+\alpha_r)S - (u_2(t)\gamma+\mu)S + \psi R + \omega V,$$
$$\frac{dV}{dt} = \rho\nu + u_2(t)\gamma S - (1-u_1(t))\varepsilon(\alpha_{se}+\alpha_r)V - (\omega+\mu)V,$$
$$\frac{dI_{se}}{dt} = \alpha_{se}(1-u_1(t))(S+\varepsilon V) - u_3(t)\varepsilon_{se} I_{se} - (\eta+\mu+\delta_1)I_{se},$$
$$\frac{dI_r}{dt} = \alpha_r(1-u_1(t))(S+\varepsilon V) + \eta I_{se} - u_4(t)\varepsilon_r I_r - (\mu+\delta_2)I_r,$$
$$\frac{dR}{dt} = u_3(t)\varepsilon_{se} I_{se} + u_4(t)\varepsilon_r I_r - (\mu+\psi)R,$$
$$\frac{d\lambda_1}{dt} = -A_1 + \lambda_1((1-u_1)(\alpha_{se}+\alpha_r) + (u_2\gamma+\mu)) - u_2\gamma\lambda_2 - (1-u_1)\alpha_{se}\lambda_3 - (1-u_1)\alpha_r\lambda_4,$$
$$\frac{d\lambda_2}{dt} = -\omega\lambda_1 + ((1-u_1)\varepsilon(\alpha_{se}+\alpha_r) + \omega + \mu)\lambda_2 - (1-u_1)\varepsilon\alpha_{se}\lambda_3 - (1-u_1)\varepsilon\alpha_r\lambda_4,$$
$$\frac{d\lambda_3}{dt} = -A_2 + \frac{\beta_1 S(1-u_1)}{N}\lambda_1 + \frac{\beta_1(1-u_1)\varepsilon V}{N}\lambda_2 - \left(\frac{\beta_1(1-u_1)(S+\varepsilon V)}{N} - (\eta + u_3\varepsilon_{se} + \mu + \delta_1)\right)\lambda_3 - \eta\lambda_4 - u_3\varepsilon_{se}\lambda_5,$$
$$\frac{d\lambda_4}{dt} = -A_3 + \frac{\beta_2 S(1-u_1)}{N}\lambda_1 + \frac{\beta_2\varepsilon V(1-u_1)}{N}\lambda_2 - \left(\frac{\beta_2(1-u_1)(S+\varepsilon V)}{N} - (u_4\varepsilon_r + \mu + \delta_2)\right)\lambda_4 - u_4\varepsilon_r\lambda_5,$$
$$\frac{d\lambda_5}{dt} = -\lambda_1\psi + (\mu+\psi)\lambda_5,$$

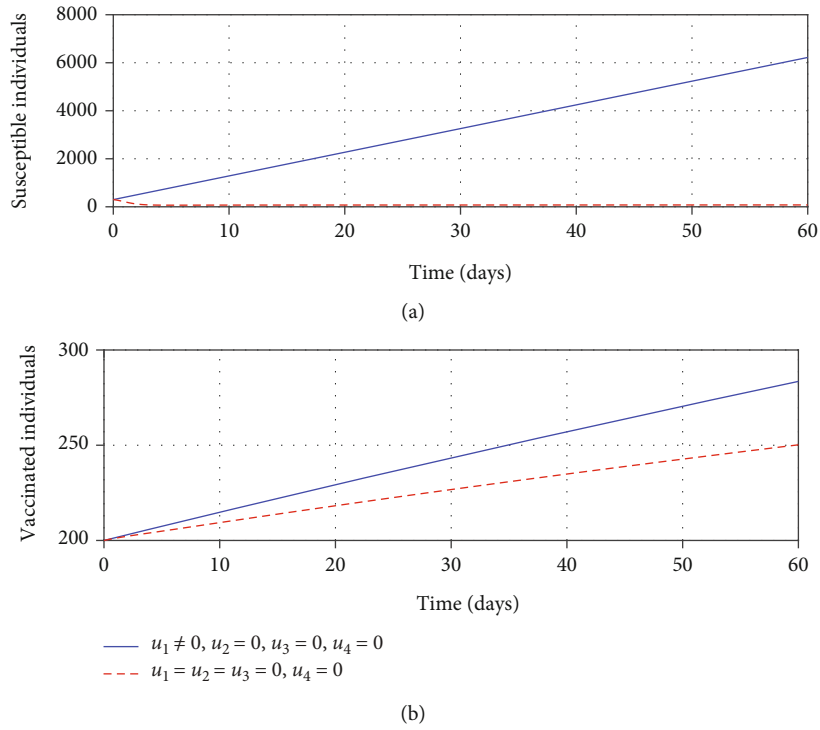

Figure 2: Simulation of the optimal model showing the effect of education on (a) susceptible individuals and (b) vaccinated individuals.

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = 0, \quad (59)$$

$S(0) \geq 0$, $V(0) \geq 0$, $I_{se}(0) \geq 0$, $I_r(0) \geq 0$, and $R(0) \geq 0$.

5. Numerical Results

In this section, we study the optimal control strategies of the model system (39) and its effects on the spread of pneumonia disease numerically. The optimal control strategies are obtained by solving the optimality system from the state equation (39) and the adjoint system. For a model with terminal conditions $\lambda(t_f) = 0$, the system is solved through the backward fourth-order Runge-Kutta method coded in Matlab programming language. For a model with initial conditions $X(0)$ and initial value of controls $u_i(0)$, the system is solved using the forward fourth-order Runge-Kutta method coded in Matlab programming language. Therefore, we solve the state system by using the forward in time Runge-Kutta scheme and the adjoint system by using the backward in time Runge-Kutta scheme. The solution iterative scheme involves making an initial guess of the control variables, $u_i(0)$, and then solves the state system by using that guess. The adjoint system is solved by using the initial guess of the control variables $u_i(0)$ and the solution of the state system. The control is updated after each iteration through the convex combination of the previous system, and the current values obtained using the characterizations (to obtain the new solution for X and λ_i). The iterative process continues until the current iteration values are close enough to the values of the previous iteration [16]. Various parameters from different literature, as presented in Table 3, have been used in the simulation. Additionally, we used $S(0) = 300$, $V(0) = 200$, $I_{se}(0) = 105$, $I_{r(0)}$, $R(0) = 10$, $B_1 = 6$, $B_2 = 2$, $B_3 = 2$, $B_4 = 4$, $A_1 = 0.2$, $A_2 = 4$, and $A_3 = 4$. These parameters have been chosen arbitrarily to illustrate the control strategies given.

5.1. Control Scenarios. To assess the impact of each control on the battle against the spread of pneumonia, we examine the following seven strategies:

(1) Strategy A: control with education only, $(u_1 \neq 0, u_2 = 0, u_3 = 0, u_4 = 0)$

(2) Strategy B: control with vaccination only, $(u_1 = 0, u_2 \neq 0, u_3 = 0, u_4 = 0)$

(3) Strategy C: control with treatment only, $(u_1 = 0, u_2 = 0, u_3 \neq 0, u_4 \neq 0)$

(4) Strategy D: control with education and vaccination, $(u_1 \neq 0, u_2 \neq 0, u_3 = 0, u_4 = 0)$

(5) Strategy E: control with education and treatments, $(u_1 \neq 0, u_2 = 0, u_3 \neq 0, u_4 \neq 0)$

(6) Strategy F: control with vaccination and treatment, $(u_1 = 0, u_2 \neq 0, u_3 \neq 0, u_4 \neq 0)$

(7) Strategy G: control with education, vaccination, and treatments, $(u_1 \neq 0, u_2 \neq 0, u_3 \neq 0, u_4 \neq 0)$

5.1.1. Strategy A: Control with Education Only. With strategy A, only one control measure (education, u_1) is applied while the rest controls are set to zero. It is seen from Figure 2(a) that, with the application of education control, susceptible individuals increase compared to the case without control.

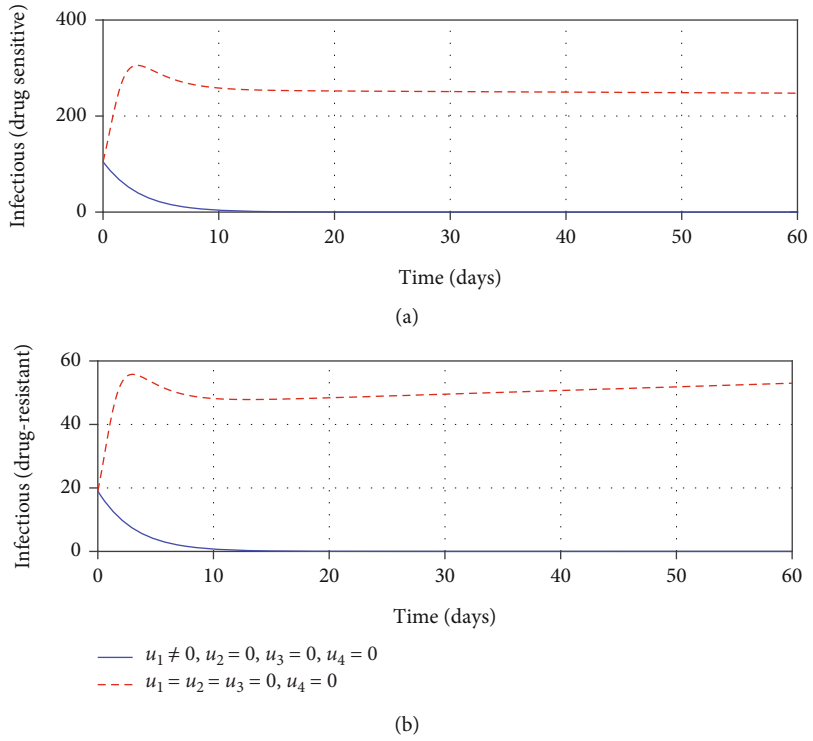

Figure 3: Simulation of the optimal model showing the effect of education on (a) individuals infected with drug-sensitive strain and (b) individuals infected with a drug-resistant strain.

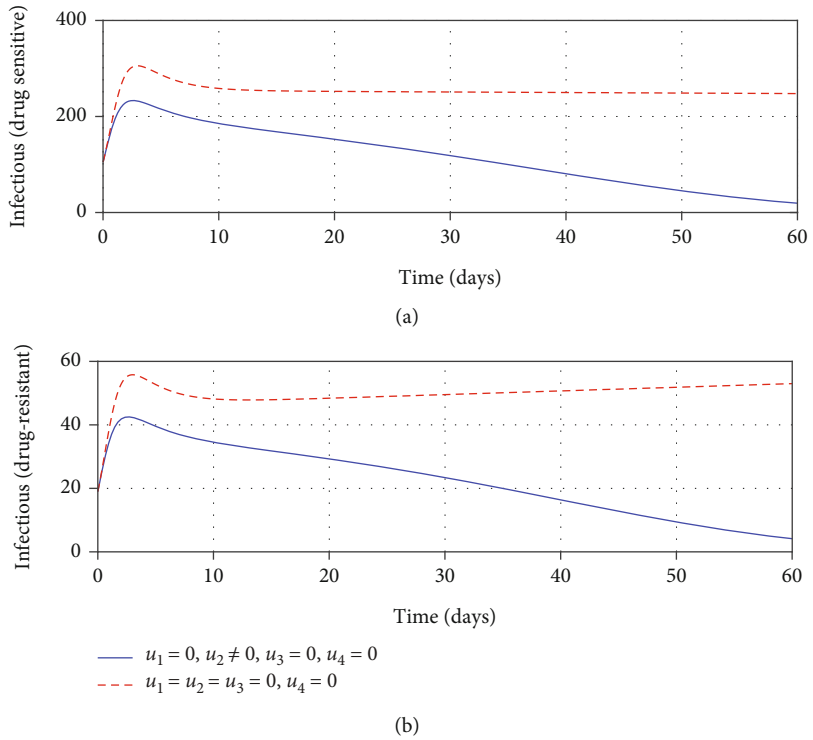

Figure 4: Simulation of the optimal model showing the effect of vaccination on (a) individuals infected with drug-sensitive strain and (b) individuals infected with a drug-resistant strain.

Figure 2(b) shows that with the application of education control, the number of vaccinated individuals is large compared to the case without control. Also, it can be observed from Figures 3(a) and 3(b) that, with the application of education control, individuals infected with drug-sensitive and drug-resistant strains are decreasing, respectively, compared to

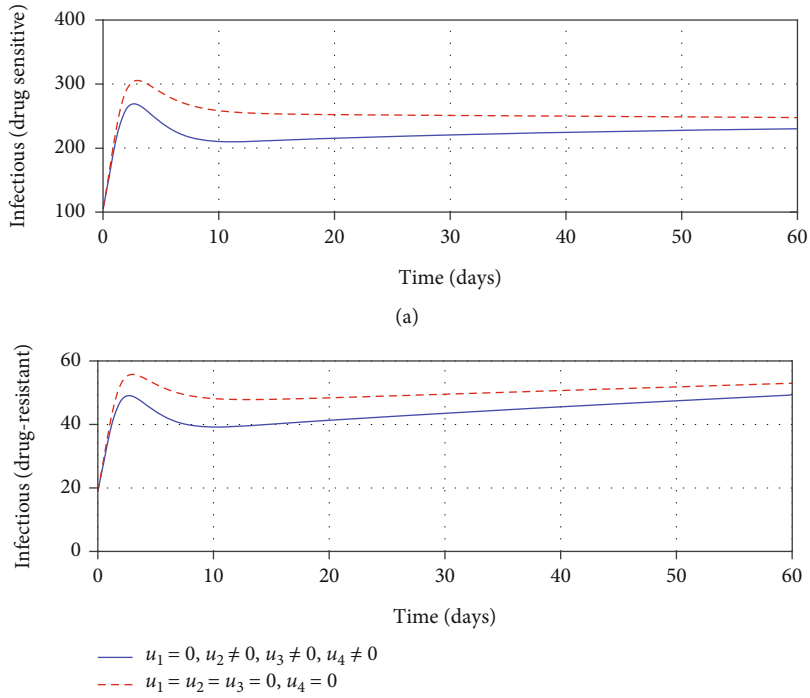

FIGURE 5: Simulation of the optimal model showing the effect of treatment, (u_3), and u_4 on (a) individuals infected with drug-sensitive strain and (b) individuals infected with a drug-resistant strain.

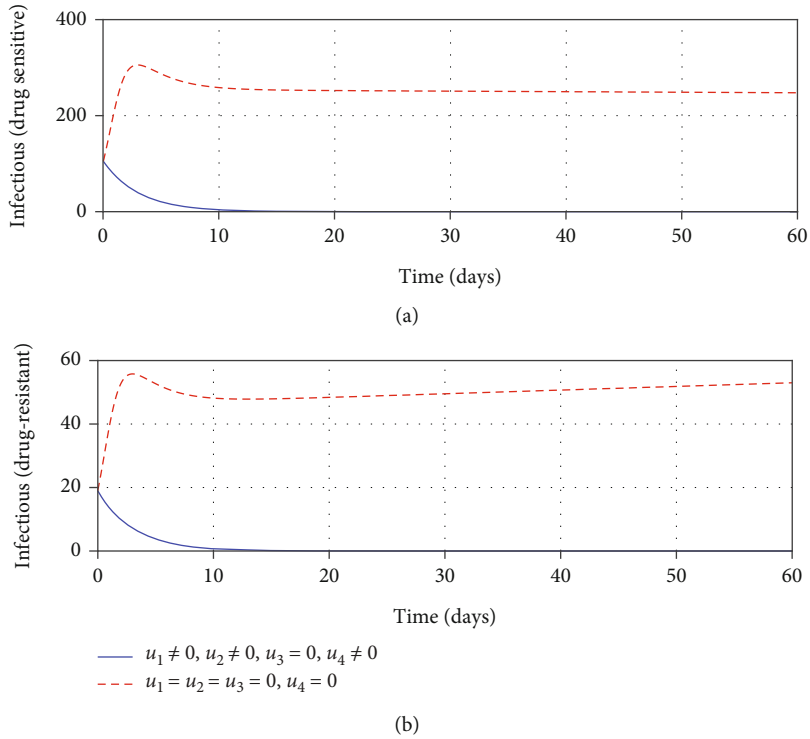

FIGURE 6: Simulation of the optimal model showing effect of education and vaccination on (a) individuals infected with drug-sensitive strain and (b) individuals infected with a drug-resistant strain.

the case without control. Specifically, using this strategy, the number of infections starts to decrease from the beginning of the intervention and can clear the epidemic within ten days. Therefore, these results indicate that public health education can play a big role in reducing pneumonia infections.

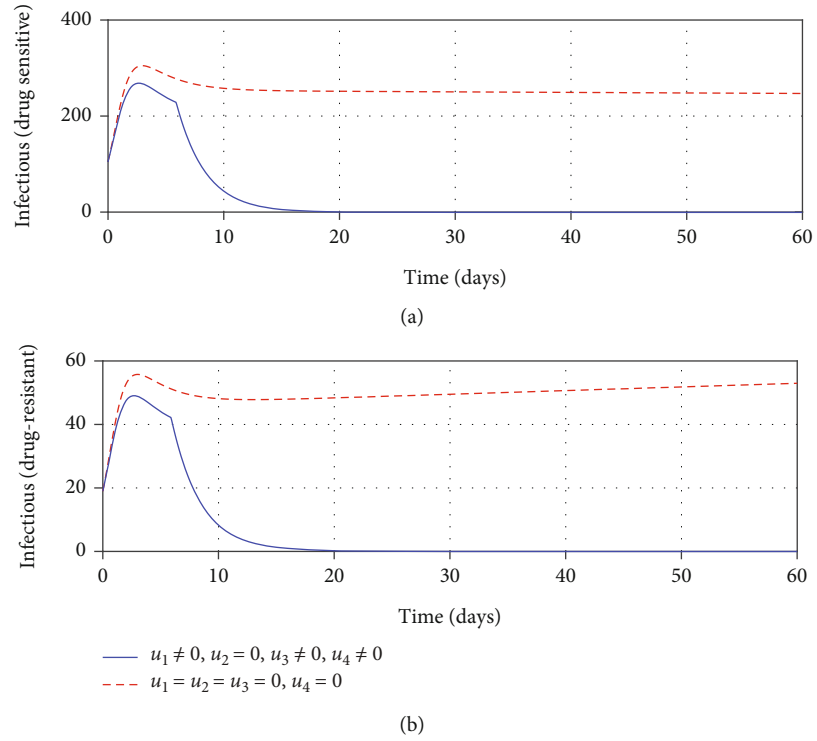

FIGURE 7: Simulation of the optimal model showing the effect of education and treatment on (a) individuals infected with drug-sensitive strain and (b) individuals infected with a drug-resistant strain.

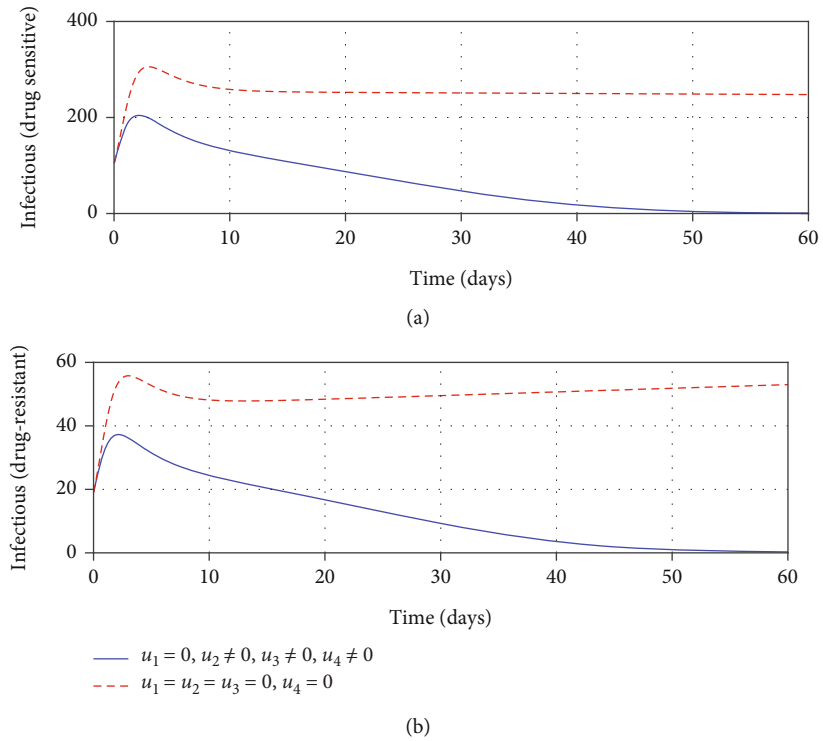

FIGURE 8: Simulation of the optimal model showing the effect of vaccination and treatment on (a) individuals infected with drug-sensitive strain and (b) individuals infected with a drug-resistant strain.

5.1.2. Strategy B: Control with Vaccination Only. With strategy B, one control measure (vaccination, u_2) is applied while the rest controls are set to zero. Figure 4(a) shows that the number of individuals infected with drug-sensitive strain is decreasing in the presence of a control strategy. It can also be observed in Figure 4(b) that the number of individuals

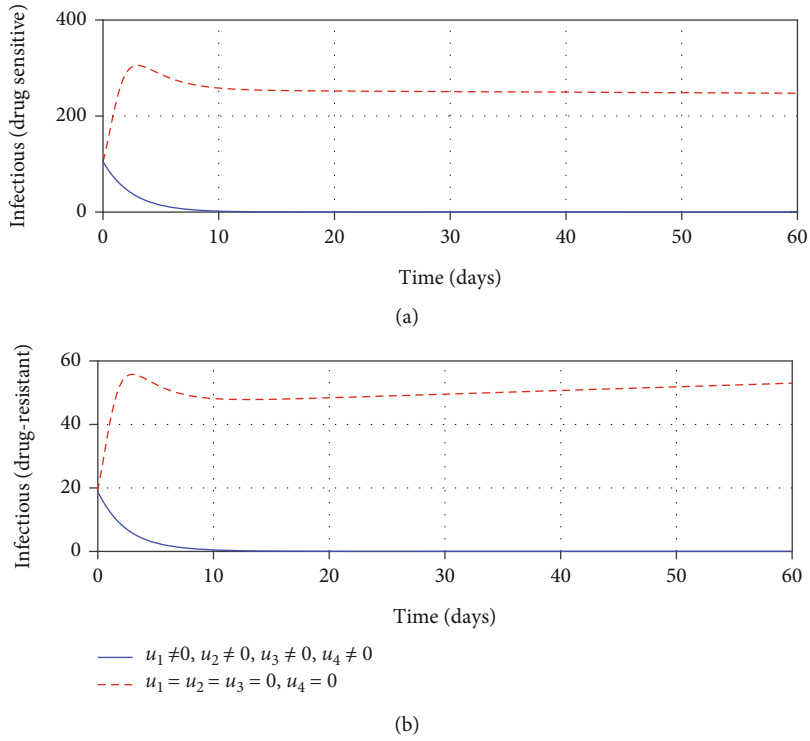

FIGURE 9: Simulation of the optimal model showing the effect of vaccination, education, and treatment on (a) individuals infected with drug-sensitive strain and (b) individuals infected with a drug-resistant strain.

infected with a drug-resistant strain decreases in the presence of control. However, these results show that vaccination alone is not sufficient to eradicate the disease. Hence, to eliminate the disease, other interventions are also needed.

5.1.3. Strategy C: Control with Treatment Only. In strategy C, only treatment is applied. Figures 5(a) and 5(b) show that treatment has a positive impact in reducing the number of individuals infected with drug-sensitive and drug-resistant strains, respectively. It can be noted that the number of infected individuals decreases little; hence, more interventions are needed to eliminate the disease from the community.

5.1.4. Strategy D: Control with Education and Vaccination. With strategy D, two control measures (vaccination, u_2, and public health education, u_1) are applied while the rest controls are set to zero. From Figure 6(a), it can be seen that in the presence of a control strategy, the number of individuals infected with drug-sensitive strain is decreasing. Similar results can be observed in Figure 6(b) where there is a decrease in the number of individuals infected with drug-resistant strain. These indicate that the combination of vaccination and education can play an important role in reducing the number of pneumonia infections than vaccination alone.

5.1.5. Strategy E: Control with Education and Treatment. Control measures (u_1, u_3, and u_4) are applied while control u_2 is set to zero. The individuals infected with drug-sensitive and drug-resistant strains decrease as shown in Figures 7(a) and 7(b), respectively. From these results, we observed that the combination of education and treatment helps to minimize pneumonia infections earlier than the usage of treatment alone.

5.1.6. Strategy F: Control with Vaccination and Treatment. The control measures (u_2, u_3, and u_4) are applied while control measure (u_1) is set to zero. It can be noted from Figure 8(a) that the number of individuals infected with drug-sensitive strain decreases. Figure 8(b) shows that the number of individuals infected with drug-resistant strain decreases. This strategy minimizes the number of pneumonia infections to a lower value than applying either vaccination alone or treatment alone. Furthermore, the application of vaccination and treatment seems to be useful and increasing efficiency as time passes.

5.1.7. Strategy G: Control with Education, Vaccination, and Treatment. In this strategy, all controls (u_1, u_2, u_3, and u_4) are applied together to reduce the number of pneumonia infections. From Figures 9(a) and 9(b), it can be observed that the number of individuals infected with drug-sensitive and drug-resistant strains greatly decreased, respectively. These indicate that the combination of education, vaccination, and treatment is the best strategy to clear pneumonia infections.

5.1.8. Control Profile. The control profile in Figure 10 suggests that the education control u_1 should maintain the maximum effort for about 58.68 days before dropping to the lower bound. It can also be noted that the vaccination control u_2 should be at maximum for the entire period of

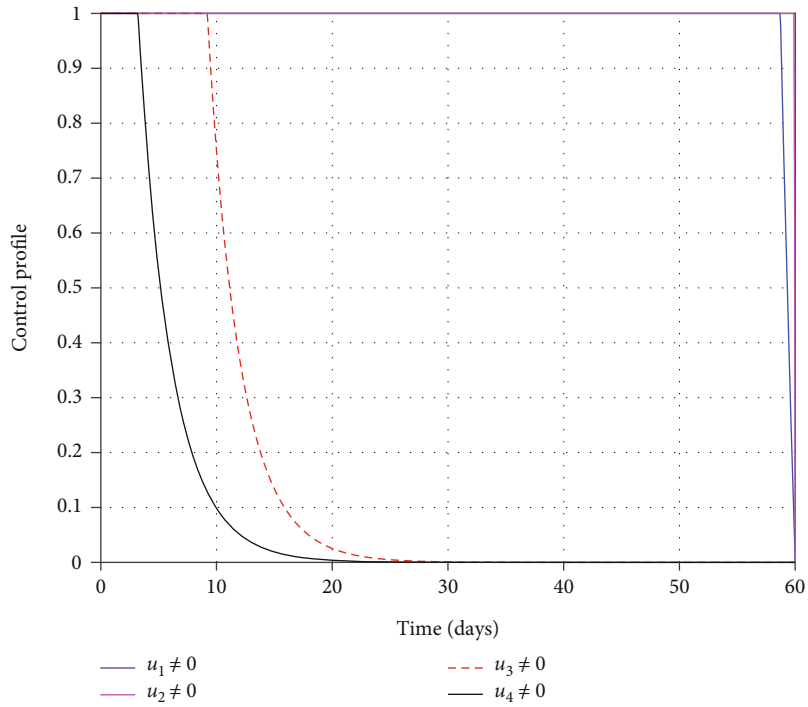

Figure 10: Optimal control trajectories.

intervention. Furthermore, it can be seen that treatment controls (u_3 and u_4) should maintain the maximum effort for about 9.18 days and 3.18 days before dropping to a lower bound. Therefore, these results suggest that education, vaccination, and treatment need to be applied in the community in order to minimize the number of pneumonia infections. However, it can be seen that treatment minimizes the number of infections earlier than other controls. This is an appealing result because long-term usage of treatment has side effect implications.

From the numerical results, we observed how each strategy plays a role in controlling the disease's transmission rate. Figure 3 reveals that strategy A is the most effective among the strategies that contained single control. While a combination of two controls in a single strategy shows that strategy E is the best in averting more infections. On the other hand, strategy G (education, vaccination, and treatment) is proved to be more effective in reducing the number of pneumonia infections. However, it is not easy to conclude the best strategy for implementation with limited resources. Therefore, we need to analyze the costs and benefits of each strategy. However, this can be achieved through cost-effectiveness analysis.

6. Cost-Effectiveness Analysis

The cost-effective analysis is a type of economic evaluation that measures the incremental costs and outcomes that result from choosing one option over another, providing the comparative advantage of each strategy. It deals with analyzing the costs and benefits of competing strategies. The term costs here refers to the actual resources utilized to provide health care than what is charged or paid [38]. Thus, in this section, we use cost-effectiveness analysis to rank the implemented strategies in terms of their cost. It allows us to decide on which intervention to choose. The cost-effectiveness analysis helps us to determine and propose the most cost-effective strategy to implement in case of limited resources. We used incremental cost-effectiveness (ratio) to evaluate the costs. We compare the difference between the costs and the health outcomes of the two competing intervention strategies whereby each intervention is compared to the next less effective alternative [35]. The incremental cost-effectiveness (ratio) is calculated by

$$\text{ICER} = \frac{\text{Difference in costs between strategies}}{\text{Difference in health effects between strategies}} = \frac{\Delta C_T}{\Delta E}, \tag{60}$$

where C_T is the total cost for implementing a particular strategy and E is the total infections averted. For example, let U and V be the two strategies being compared, then

$$\text{ICER}(V) = \frac{\text{Cost}(V) - \text{Cost}(U)}{\text{Effectiveness}(V) - \text{Effectivness}(U)}. \tag{61}$$

The total cost associated with each strategy is obtained by using the formula

$$C_T = \int_0^{tf} [C_1 u_1 (S(t) + V(t) + I_{se}(t) + I_r(t)) + C_2 u_2 S(t) + C_3 u_3 I_{se}(t) + C_4 u_4 I_r(t)]dt, \tag{62}$$

Table 4: Number of infections averted and total cost of each strategy.

Strategies	Infections	Infections averted (E)	Costs \$ (C_T)
No control	303400	—	0
A	6481.4	296918.6	1261600
B	139520	163880	6907.2
C	266560	36840	2655.6
D	6401.4	296998.6	1263500
E	38596	264804	1000800
F	76003	227397	10028
G	5294.9	298105.1	1252900

where C_1 presents per person unit cost for education intervention, C_2 presents per person unit cost of the vaccine, C_3 is the per person unit cost of treatment of individuals infected with drug-sensitive strains, and C_4 is the per person unit cost of treatment of individuals infected with drug-resistant strains. We have chosen arbitrarily the following parameter values for illustration: $C_1 = 6$, $C_2 = 2$, $C_3 = 2$, and $C_4 = 4$.

The total infections averted (effectiveness) are determined by taking the difference between the total number of infectious individuals without control and the total number of infectious individuals with control. Thus, the total infections averted (E) is given by

$$E = \int_0^{tf} (I_{se}(0) + I_r(0))dt - \int_0^{tf} (I_{se}^*(t) + I_r^*(t))dt, \quad (63)$$

where $I_{se}(0)$ and $I_r(0)$ present the initial condition that is obtained as the equilibrium of the model system (39) when $u_1 = u_2 = u_3 = u_4 = 0$, while each $I_{se}^*(t)$, $I_r^*(t)$ presents the optimal solution associated with the optimal controls $(u_1^*, u_2^*, u_3^*, u_4^*)$.

The infections averted (effectiveness) and the costs associated with the infections averted by the control strategies are obtained through numerical simulations. The total control costs are calculated and estimated in terms of USD (\$) for one year, respectively. The total number of infections averted are ranked in ascending order so that we can apply ICER to determine the cost-effectiveness. The number of infections averted and the total cost for the implemented strategies are presented in Table 4.

From Table 5, the ICER for strategies B and C is calculated as follows:

$$\text{ICER(C)} = \frac{2655.6}{36840} = 0.072085,$$
$$\text{ICER(B)} = \frac{6907.2 - 2655.6}{163880 - 36840} = \frac{4251.6}{127040} = 0.033467. \quad (64)$$

The comparison between strategies B and C has been done. The ICER of strategy C indicates that C is dominated. Thus, we exclude C from the set of alternatives and compare strategy B and strategy F.

Table 5: Incremental cost-effectiveness ratios of different optimal control strategies.

Strategies	E	ΔE	C_T	ΔC_T	ICER ($\Delta C_T/\Delta E$)
C	36840	36840	2655.6	2655.6	0.072085
B	163880	127040	6907.2	4251.6	0.033467
F	227397	63517	10028	3120.8	0.049133
E	264804	37407	1000800	990772	26.486273
A	296918.6	32114.6	1261600	260800	8.120917
D	296998.6	80	1263500	1900	23.75
G	298105.1	1106.5	1252900	-10600	-9.579756

Table 6: Incremental cost-effectiveness ratios for optimal control strategies B and F.

Strategies	E	ΔE	C_T	ΔC_T	ICER ($\Delta C_T/\Delta E$)
B	163880	163880	6907.2	6907.2	0.042148
F	227397	63517	10028	3120.8	0.049133

From Table 6, the ICER for strategies B and F is calculated as follows:

$$\text{ICER(B)} = \frac{6907.2}{163880} = 0.042148,$$
$$\text{ICER(F)} = \frac{10028 - 6907.2}{227397 - 163880} = \frac{3120.8}{63517} = 0.049133. \quad (65)$$

The comparison between strategies B and F has been done. It can be noted that the ICER of strategy F is greater than the ICER of strategy B. This implies strategy F is more expensive and less effective than strategy B. Thus, we exclude strategy F from the set of alternatives and compare strategy B and strategy E.

From Table 7, the ICER for strategies B and E is calculated as follows:

$$\text{ICER(B)} = \frac{6907.2}{163880} = 0.042148,$$
$$\text{ICER(E)} = \frac{1000800 - 6907.2}{264804 - 163880} = \frac{993892.8}{100924} = 9.847933. \quad (66)$$

It can be observed that ICER(B) < ICER(E). Thus, strategy E is more costly than strategy B. Therefore, we exclude strategy E from the set of alternative; hence, we compare strategy B and strategy A, as follows:

$$\text{ICER(B)} = \frac{6907.2}{163880} = 0.042148,$$
$$\text{ICER(A)} = \frac{1261600 - 6907.2}{296918.6 - 163880} = \frac{1254692.8}{133038.6} = 9.431043. \quad (67)$$

Table 7: Incremental cost-effectiveness ratios for optimal control strategies B and E.

Strategies	E	ΔE	C_T	ΔC_T	ICER ($\Delta C_T/\Delta E$)
B	163880	163880	6907.2	6907.2	0.042148
E	264804	100924	1000800	993892.8	9.847933

Table 8: Incremental cost-effectiveness ratios for optimal control strategies B and A.

Strategies	E	ΔE	C_T	ΔC_T	ICER ($\Delta C_T/\Delta E$)
B	163880	163880	6907.2	6907.2	0.042148
A	296918.6	133038.6	1261600	1254692.8	9.431043

Table 9: Incremental cost-effectiveness ratios for optimal control strategies B and D.

Strategies	E	ΔE	C_T	ΔC_T	ICER ($\Delta C_T/\Delta E$)
B	163880	163880	6907.2	6907.2	0.042148
D	296998.6	133118.6	1263500	1256592.8	9.439649

Table 10: Incremental cost-effectiveness ratios for optimal control strategies B and G.

Strategies	E	ΔE	C_T	ΔC_T	ICER ($\Delta C_T/\Delta E$)
B	163880	163880	6907.2	6907.2	0.042148
G	298105.1	134225.1	1252900	1245992.8	9.282860

It is seen from Table 8 that ICER(A) > ICER(B). This result implies that strategy A is more expensive than strategy B. Therefore, we exclude strategy A from the set of alternatives; hence, we compare strategy B and strategy D.

From Table 9, the ICER for strategies B and D is calculated as follows:

$$\begin{aligned}\mathrm{ICER(B)} &= \frac{6907.2}{163880} = 0.042148,\\ \mathrm{ICER(D)} &= \frac{1263500 - 6907.2}{296998.6 - 163880} = \frac{1256592.8}{133118.6} = 9.439649.\end{aligned} \tag{68}$$

It is observed from ICER(B) and ICER(D) that strategy D is dominated. That is, strategy D is more expensive than strategy B. Therefore, we exclude strategy D from the set of alternatives and compare strategy B and strategy G.

$$\begin{aligned}\mathrm{ICER(B)} &= \frac{6907.2}{163880} = 0.042148,\\ \mathrm{ICER(G)} &= \frac{1252900 - 6907.2}{298105.1 - 163880} = \frac{1245992.8}{134225.1} = 9.282860.\end{aligned} \tag{69}$$

The comparison between strategy B and strategy G indicates that strategy G is a bit expensive than strategy B as shown in Table 10 whereby ICER(G) > ICER(B). Therefore, these results show that strategy B (vaccination) is the most cost-effective of all strategies for pneumonia disease in case of limited resources.

7. Conclusion

A deterministic model with the optimal control for pneumonia disease is derived and analyzed to investigate the best strategy for controlling this disease by considering the lowest possible cost. This model considered two classes of infectious individuals (individuals infected with a drug-sensitive strain and individuals infected with drug-resistant strains). The qualitative properties of the model are obtained. The necessary conditions for the optimal control strategies (education, vaccination, and treatment) are derived by using Pontryagin's Maximum Principle to minimize the spread of pneumonia and reducing the number of infectious individuals. Also, the optimal control is aimed at reducing the number of individuals developing resistant pneumonia strains. Numerical analysis of the optimal model system (39) is carried out to illustrate the effectiveness of the control strategies. The results show that strategy G (education, vaccination, and treatment) can reduce the number of infectious individuals more than other control strategies. The cost-effectiveness results suggest strategy B (vaccination) is the most cost-effective of all strategies for pneumonia disease in case of limited resources.

Through this study, based on the results in Figure 9, we recommend the combination of interventions such as vaccination, public health education to the population, and treatment to be applied to infectious individuals to reduce new infection cases and the number of deaths due to pneumonia in our community. Moreover, as per the findings in Figure 5, we also advise patients to adhere to a doctor's instructions to minimize the number of infections and the development of drug resistance.

In future studies, one can extend similar work to include the age-structure model, which would give more appealing results.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

No potential conflict of interest was reported by the authors.

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