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On Optimal Control Analysis of Pneumonia

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Abstract The optimal control of pneumonia disease is very important in the management of the disease within a given population. Pneumonia is one of the leading causes of death worldwide, especially among children below 5 years old, the elderly above 65 years old and people with a weaker immune system. In this research work, the basic mathematical properties of a deterministic SEIR model for pneumonia disease were first presented. These properties include the invariant region, disease free equilibrium, basic reproduction number and the disease endemic equilibrium. The optimal control problem, which is the main focus of this work, was ushered in and thoroughly dealt with using the Pontryagin's Maximum Principle. The control measures include the prevention effort of the susceptible class, the vaccination intervention strategy and the treatment intervention strategy. The Hamiltonian of the control problem was defined and used together with the adjoint equations to obtain the optimality system and the optimal values of the controls. Numerical simulations were carried out using various combinations of these control measures (prevention, vaccination and treatment). The results were presented and compared to determine the best strategy that should be taken in order to eliminate the disease from a given population within a desired period of time. It is observed that the combination with all three controls gives the best intervention strategy for the elimination of the disease.

Keywords Pneumonia, Optimal, Pontryagin, Simulations, Optimal Control

1. Introduction

In epidemiology, the general subject matter of mathematical modelling is to build models that will help in the decision-making process [4]. Identifying the optimal strategy that will minimize the unwanted features of a disease at the minimum cost is a very fascinating aspect in the study of epidemic models [2]. Optimal control problems have made their place in many classical books like Sethi and Thompson [40]. The utility theory which was systematically introduced in Von-Neumann and Morgenstem [42] gives rise to the approach of modelling cost by a function as perceived by the one making the decision. Typically, suppose x is the cost of applying a procedure and y is the number of individuals receiving the procedure, then the cost of administering the procedure is simply xy. Of all the diseases affecting humans, pneumonia is one of the leading causes of death [14]. In fact, pneumonia was referred to as the "captain of the men of death" because of the great toll it exacted on humanity [15]. Pneumonia has also been referred to as "the old man's friend" because it shortens the suffering of those already close to death [11]. George [11] also revealed that the introduction of vaccines and antibiotics in the 20th century improved the chance of survival of pneumonia patients. Several authors have proposed mathematical models for the pneumonia dynamics, which are used for making quantitative predictions of different intervention strategies and their effectiveness [21]. Amongst the models are [16, 21, 29, 30]. Getachew [16] modeled the co-dynamics of pneumonia and meningitis diseases via SIR system, while in 2017, he developed a SVCIR model for the pneumonia disease, studied the optimal control of the disease with cost-effective strategies and obtained that the combination of prevention and treatment is the best cost-effective strategy with health benefits. Getachew, Oluwole and Malonza [45] formulated a control problem of a mathematical model for the pneumonia disease using the

Pontryagin's maximum principle and they employed education, treatment and screening as their control measures. It was revealed in their cost-effectiveness analysis that the combination of treatment and prevention is the most cost-effective intervention strategy to combat the pneumonia pandemic. Kanyiri, Luboobi and Kimathi [22] applied optimal control to investigate optimal strategies for controlling the co-infection of pneumonia and antiviral resistance using prevalence reduction and treatment as the system control variables. [22] stated via their simulation results that implementing prevention measures can sufficiently eradicate the co-infection of pneumonia and influenza from a given population. A mathematical modelling and analysis of pneumonia infection dynamics was done by Ossaiugbo and Okposo [35]. The research work established that the disease-free equilibrium is locally asymptotically stable if the basic reproduction number is less than 1, and the disease-endemic equilibrium is globally asymptotically stable if the basic reproduction number is greater than 1. Ossaiugbo and Okposo [35] also employed the centre manifold theory to study the bifurcation analysis, and it was shown that the model exhibits forward bifurcation. They showed that the rate of transmission and the rate at which exposed individuals become infectious are the most sensitive parameters. The optimal control problem was not considered in [35]. This is therefore our motivation to undertake this study in order to fill the gap.

2. Model Preliminaries

As presented in Ossaiugbo and Okposo [35], the model, its flow diagram, parameters descriptions, invariant region, disease free equilibrium, basic reproduction number and disease endemic equilibrium are presented in equ. 1, fig. 1, table 1 and equ. 3, 4, 5, 6, respectively.

$$\begin{cases} \frac{dS(t)}{dt} = \Lambda + \delta R - (\mu + \varpi)S \\ \frac{dE(t)}{dt} = \varpi S - (\mu + \gamma + \psi)E \\ \frac{dI(t)}{dt} = \gamma E - (\mu + \beta + \eta)I \\ \frac{dR(t)}{dt} = \psi E + \beta I - (\mu + \delta)R \end{cases} \quad (1)$$

initial conditions:

$$S(0) = S_0 \geq 0, \quad E(0) = E_0 \geq 0,$$
$$I(0) = I_0 \geq 0, \; R(0) = R_0 \geq 0. \quad (2)$$

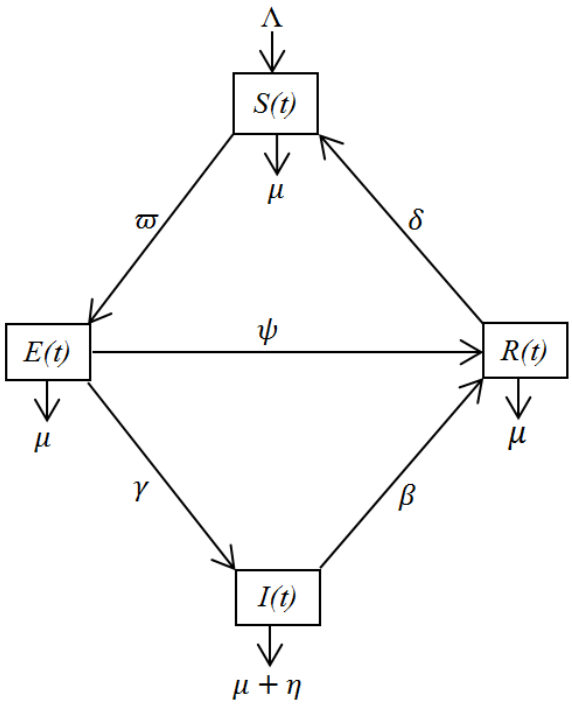

Figure 1. Model Flow Diagram

Table 1. Description of the model variables and parameters

Variables/ Parameters	Description
$S(t)$	Individuals who are at risk of acquiring the pneumonia disease at time t.
$E(t)$	Individuals who have caught the disease but are not infectious at time t.
$I(t)$	Infectious individuals who have caught the disease and are capable of transmitting the infection to individuals at risk at time t.
$R(t)$	Individuals who have been treated for the pneumonia disease at time t.
Λ	Recruitment rate of susceptible humans.
ϖ	Force of infection of the susceptible class.
χ	Rate of transmission.
k	Per capita contact rate of susceptible individuals with the infectious individuals.
τ	The probability that a contact is effective to cause infection.
β	Per capita recovery rate of the infectious.
ψ	Per capita recovery rate of the exposed.
η	Per capita disease induced mortality rate.
γ	Rate at which exposed becomes infectious.
μ	Per capita natural mortality rate of individuals.
δ	Rate at which treated individuals become susceptible.

$$\Gamma = \left\{(S,E,I,R) \in \mathbb{R}_+^4 : 0 \le S+E+I+R = N \le \frac{\Lambda}{\mu}\right\} \quad (3)$$

$$E_0 = (S^0, E^0, I^0, R^0) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right) \quad (4)$$

$$R_0 = \frac{\chi\gamma}{(\mu+\gamma+\psi)(\mu+\beta+\eta)} \quad (5)$$

$$\begin{cases} I^* = \dfrac{\gamma\Lambda(\mathrm{R}_0-1)(\delta+\mu)}{\mathrm{R}_0\left((\beta+\eta+\mu)(\mu\gamma+\mu(\delta+\mu+\psi))+\delta\gamma(\eta+\mu)\right)-\gamma\eta\mu-\gamma\delta\eta}, \\ S^* = \dfrac{(\gamma(\delta+\mu)+(\eta+\mu)(\delta+\mu+\psi)+\beta(\gamma+\delta+\mu+\psi))}{(\mathrm{R}_0-1)\gamma(\delta+\mu)} I^*, \\ E^* = \dfrac{(\beta+\eta+\mu)}{\gamma} I^*, \\ R^* = \dfrac{((\eta+\mu)\psi+\beta(\gamma+\psi))}{\gamma(\delta+\mu)} I^*. \end{cases} \quad (6)$$

3. Optimal Control Analysis

In this section, we extend the basic model given in system (1) to the optimal control model by adding three control parameters. The effect of these measures in controlling the pneumonia disease is noteworthy. The intervention strategies are:

(1) the prevention effort (v_1) of the susceptible class
(2) the vaccination intervention (v_2) strategy, and
(3) the treatment intervention strategy (v_3).

The control model is given below:

$$\begin{cases} \frac{dS(t)}{dt} = \Lambda - (1-v_1)(1-v_2)\frac{\chi I}{N}S - \mu S \\ \frac{dE(t)}{dt} = (1-v_1)(1-v_2)\frac{\chi I}{N}S - (v_3+\mu+\gamma+\psi)E \\ \frac{dI(t)}{dt} = \gamma E - (v_3+\mu+\beta+\eta)I \\ \frac{dR(t)}{dt} = (v_3+\psi)E + (v_3+\beta)I - \mu R \\ S(0) = S_0, E(0) = E_0, I(0) = I_0, \\ R(0) = R_0,\ V(0) = V_0 \end{cases} \quad (7)$$

The control parameters are lebesgue measurable and bounded in the interval $[0,1]$. Thus, we have the Lebesgue measurable control set

$$U = \left\{(v_1(t), v_2(t), v_2(t)) : 0 \le v_1(t) \le 1,\ 0 \le v_2(t) \le 1, 0 \le v_3(t) \le 1\right\}.$$

Our goal is to obtain an optimal value (v_1^*, v_2^*, v_3^*) of the control parameters (v_1, v_2, v_3), which minimizes the objective functional

$$J(v_1,v_2,v_3) = \\ = \int_0^T \left(K_1E + K_2I + K_3\frac{{v_1}^2}{2} + K_4\frac{{v_2}^2}{2} + K_5\frac{{v_3}^2}{2}\right)dt \quad (8)$$

where K_1, K_2, K_3, K_4, K_4 are positive. K_1E and K_2I represent the total number of exposed individuals and infective individuals respectively, while $K_3\frac{{v_1}^2}{2}$, $K_4\frac{{v_2}^2}{2}$ and $K_5\frac{{v_3}^2}{2}$ represent the cost of the awareness and educational campaign programmes, the vaccination exercise and the treatment intervention, respectively. Hence, we seek an optimal control (v_1^*, v_2^*, v_3^*) such that

$$J(v_1^*, v_2^*, v_3^*) = min\{J(v_1,v_2,v_3) : v_1, v_2, v_3 \in U\} \quad (9)$$

3.1. The Hamiltonian and Optimality System

In this subsection, we applied the Pontryagin's Maximum Principle [37]. From the maximum principle, we defined the Hamiltonian of the control problem as:

$$\begin{cases} H = K_1E + K_2I + K_3\frac{{v_1}^2}{2} + K_4\frac{{v_2}^2}{2} + K_5\frac{{v_3}^2}{2} \\ +\lambda_S\left(\Lambda - (1-v_1)(1-v_2)\frac{\chi I}{N}S - \mu S\right) + \lambda_E \\ \left((1-v_1)(1-v_2)\frac{\chi I}{N}S - (v_3+\mu+\gamma+\psi)E\right) \\ +\lambda_I(\gamma E - (v_3+\mu+\beta+\eta)I) \\ +\lambda_R\left((v_3+\psi)E + (v_3+\beta)I - \mu R\right) \end{cases} \quad (10)$$

Given the adjoint equations:

$$\frac{\partial\lambda_S}{\partial t} = -\frac{\partial H}{\partial S}, \quad \frac{\partial\lambda_E}{\partial t} = -\frac{\partial H}{\partial E}, \\ \frac{\partial\lambda_I}{\partial t} = -\frac{\partial H}{\partial I}, \quad \frac{\partial\lambda_R}{\partial t} = -\frac{\partial H}{\partial R},$$

we obtained the optimality system below

$$\begin{cases} \frac{dS(t)}{dt} = \Lambda - (1-v_1)(1-v_2)\frac{\chi I}{N}S - \mu S \\ \frac{dE(t)}{dt} = (1-v_1)(1-v_2)\frac{\chi I}{N}S - (v_3+\mu+\gamma+\psi)E \\ \frac{dI(t)}{dt} = \gamma E - (v_3+\mu+\beta+\eta)I \\ \frac{dR(t)}{dt} = (v_3+\psi)E + (v_3+\beta)I - \mu R \\ \frac{\partial\lambda_S}{\partial t} = -\frac{1}{N^2}\left(I(E+I+R)\chi(v_1-1)(v_2-1)\lambda_E - \left(\mu\mathrm{N}^2 + I(E+I+R)\chi + I(E+I+R)\chi(v_1(v_2-1)-v_2)\right)\lambda_S\right) \\ \frac{\partial\lambda_E}{\partial t} = -\left(K_1 + \gamma\lambda_I + \left(-\gamma-\mu-\psi - \frac{SI\chi(v_1-1)(v_2-1)}{\mathrm{N}^2} - v_3\right)\lambda_E + \frac{SI\chi(v_1-1)(v_2-1)\lambda_S}{\mathrm{N}^2} + (\psi+v_3)\lambda_R\right) \\ \frac{\partial\lambda_I}{\partial t} = -\left(K_2 + \frac{-(\beta+\eta+\mu+v_3)\lambda_I\mathrm{N}^2 + (\beta+v_3)\lambda_R\mathrm{N}^2 + S(S+E+R)\chi(v_1-1)(v_2-1)(\lambda_E-\lambda_S)}{\mathrm{N}^2}\right) \\ \frac{\partial\lambda_R}{\partial t} = -\left(\frac{SI\chi(v_1-1)(v_2-1)(\lambda_S-\lambda_E)}{\mathrm{N}^2} - \mu\lambda_R\right) \end{cases} \quad (11)$$

Now, from the optimality conditions given below:

$$\frac{dH}{dv_1} = \frac{dH}{dv_2} = \frac{dH}{dv_3} = 0,$$

we obtained:

$$\begin{cases} \frac{dH}{dv_1} = \frac{\mathrm{N}K_3v_1 + SI\chi(v_2-1)(\lambda_E-\lambda_S)}{N} = 0 \\ \frac{dH}{dv_2} = \frac{\mathrm{N}K_4v_2 + SI\chi(v_1-1)(\lambda_E-\lambda_S)}{N} = 0 \\ \frac{dH}{dv_3} = K_5v_3 - I\lambda_I - E\lambda_E + (E+I)\lambda_R = 0 \end{cases} \quad (12)$$

Solving for v_1, v_2 and v_2 in system (12), we obtained:

$$\begin{cases} v_1 = -\frac{SI\chi(\lambda_E-\lambda_S)(\mathrm{N}K_4 + SI\chi(\lambda_S-\lambda_E))}{S^2I^2\chi^2(\lambda_E-\lambda_S)^2 - \mathrm{N}^2K_3K_4} \\ v_2 = -\frac{SI\chi(SI\chi(\lambda_E-\lambda_S) - \mathrm{N}K_3)(\lambda_E-\lambda_S)}{\mathrm{N}^2\left(K_3K_4 - \frac{S^2I^2\chi^2(\lambda_E-\lambda_S)^2}{\mathrm{N}^2}\right)} \\ v_3 = \frac{E\lambda_E + I\lambda_I - (E+I)\lambda_R}{K_5} \end{cases} \quad (13)$$

Therefore, the optimal values (v_1^*, v_2^*, v_3^*) of the control parameters (v_1, v_2, v_3) must satisfy

$$\begin{cases} {v_1}^* = max\left\{0, min\left(1, -\frac{SI\chi(\lambda_E-\lambda_S)(\mathrm{N}K_4 + SI\chi(\lambda_S-\lambda_E))}{S^2I^2\chi^2(\lambda_E-\lambda_S)^2 - \mathrm{N}^2K_3K_4}\right)\right\} \\ {v_2}^* = max\left\{0, min\left(1, -\frac{SI\chi(SI\chi(\lambda_E-\lambda_S) - \mathrm{N}K_3)(\lambda_E-\lambda_S)}{\mathrm{N}^2\left(K_3K_4 - \frac{S^2I^2\chi^2(\lambda_E-\lambda_S)^2}{\mathrm{N}^2}\right)}\right)\right\} \\ {v_3}^* = max\left\{0, min\left(1, \frac{E\lambda_E + I\lambda_I - (E+I)\lambda_R}{K_5}\right)\right\} \end{cases} \quad (14)$$

3.2. Numerical Simulation

In this section, we performed numerical simulations of the optimality system. We applied an iterative scheme to obtain the optimal solution of the optimality system (11). In this iterative scheme, an initial guess of the controls v_1, v_2, v_3 is made and used to solve the state system.We obtained an approximate solution of the state system using the 'NDSolve' and 'Simplify' numerical functions in the Mathematica programming language. Since the state variables appear in the adjoint system, we also employ the 'NDSolve' and 'Simplify' functions to solve the adjoint system using the initial guess of the controls together with the solution of the state system. The solutions of the state system and the adjoint system are then substituted into (14) to obtain new values of the controls v_1, v_2, v_3. A convex combination of these new values and the previous values of the controls are then used to repeat the iteration process until the values of v_1, v_2, v_3 in the current iteration are close enough to the previous iteration values.

We proposed the following five combination strategies for the numerical simulation and used the parameter values listed in table 1 for the simulation:

Using none of the three intervention strategies.

Using prevention effort only.

Using vaccination only.

Using treatment intervention only.

Using all three intervention strategies ($v_1 \neq 0$, $v_2 \neq 0$, $v_3 \neq 0$).

Table 2. Parameter values for simulation

Parameter	Value	Source
χ	0.376	Estimated
γ	0.001 to 0.01095 per day	Assumed
μ	0.0012	Estimated
β	0.2	[16]
ψ	0.02	Assumed
p	0.8	Assumed
η	0.057	[16]
Λ	0.001	Assumed
δ	0.1	[16]

We also used $k_1 = 15$, $k_2 = 10$, $k_3 = 2$, $k_4 = 6$, $k_5 = 2$, $T = 7$, $S_0 = 700$, $E_0 = 20$, $I_0 = 30$, $R_0 = 50$ as initial values.

3.2.1. Simulation without any of the Control Strategies

In simulating the model without any of the three control measures (prevention, vaccination and treatment), we observe from fig.2 that the number of exposed individuals has increased by over twice its initial value, while the infectious class has dropped by 77% only, within the period of time. Thus, without any of the control measures, the exposed and infectious compartments cannot be emptied within the period of 7 months.

3.2.2. Control with Prevention Effort only

With only the prevention effort of the susceptible individuals, the exposed class dropped by 17% only. This is shown in fig.3. This improvement is simply due to the preventive effort of the susceptible individuals. But again, this is not a victory because individuals are still exposed. Here, the infectious class has dropped by 78%. Therefore, fig.3 shows that prevention effort only, does not guarantee a total reduction of the disease from the population within the desired period.

3.2.3. Control with Vaccination only

We simulate the model using the vaccination intervention strategy only. In simulating the model with vaccination only, from fig.4, we observe a 17.5% drop in the exposed class within the period of time. Fig. 4 also shows that the infectious class dropped by 78% only. Thus, vaccination alone does not guarantee a total reduction of the disease from the population within the desired period of time.

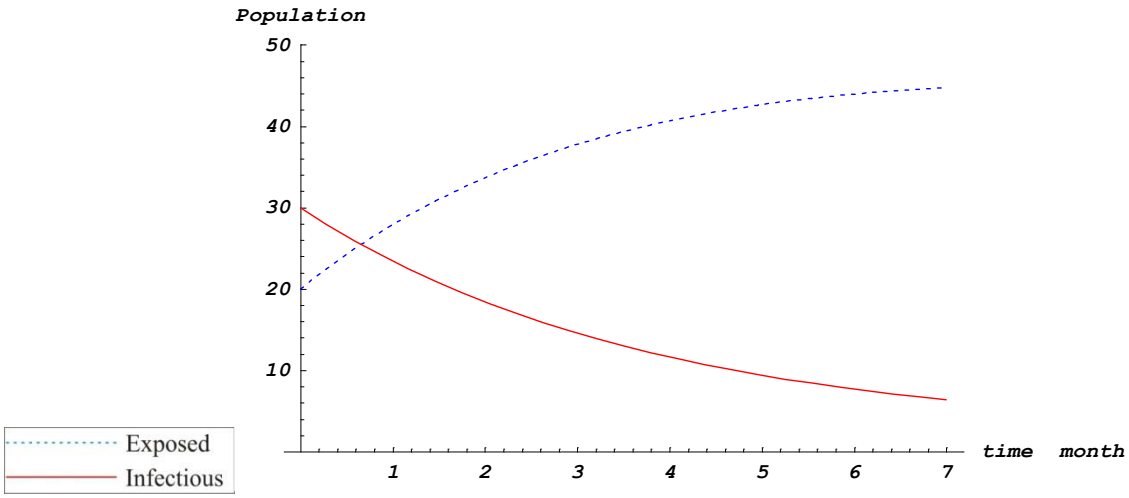

Figure 2. Exposed and infectious individuals without any control strategy

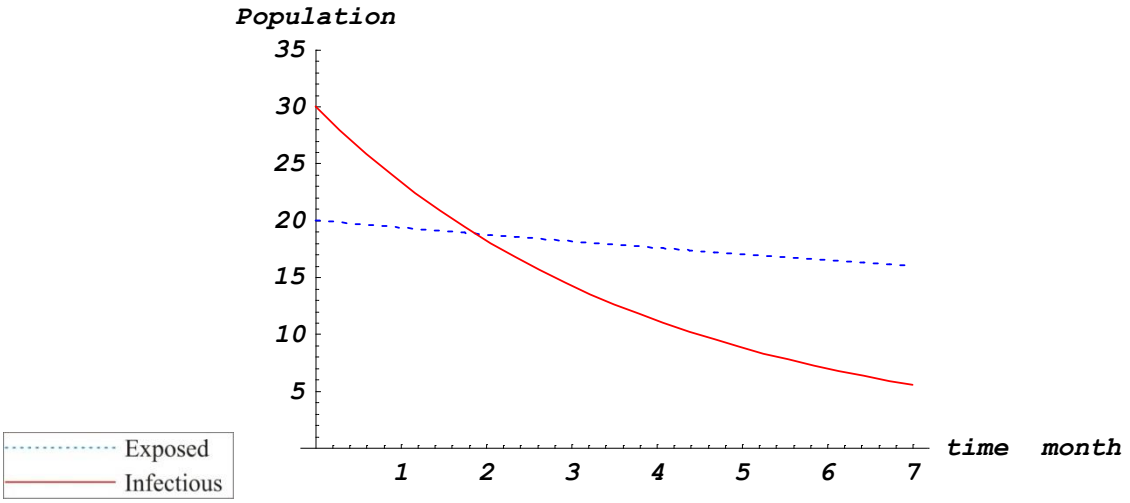

Figure 3. Exposed and Infectious individuals with prevention effort only

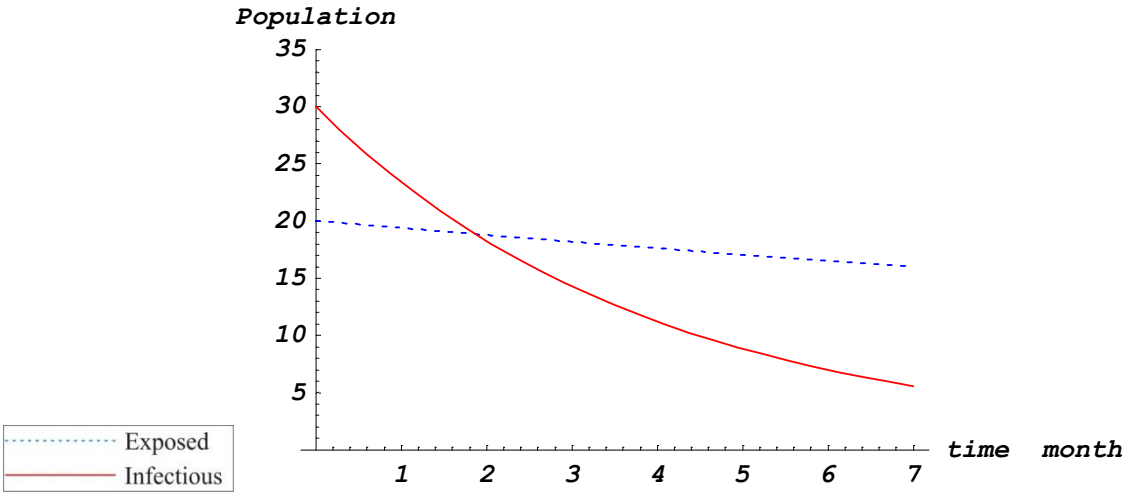

Figure 4. Exposed and Infectious individuals with vaccination only

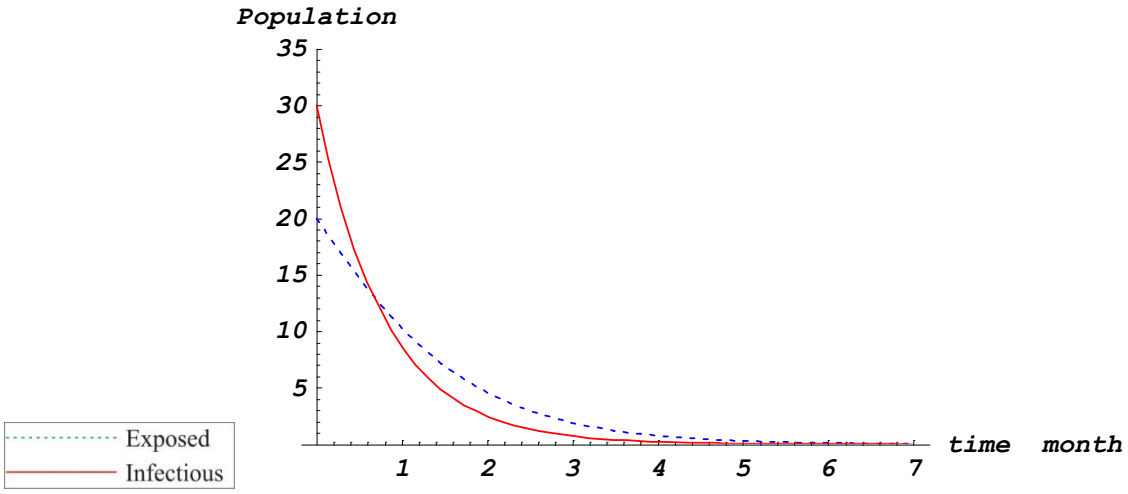

Figure 5. Exposed and Infectious individuals with treatment only

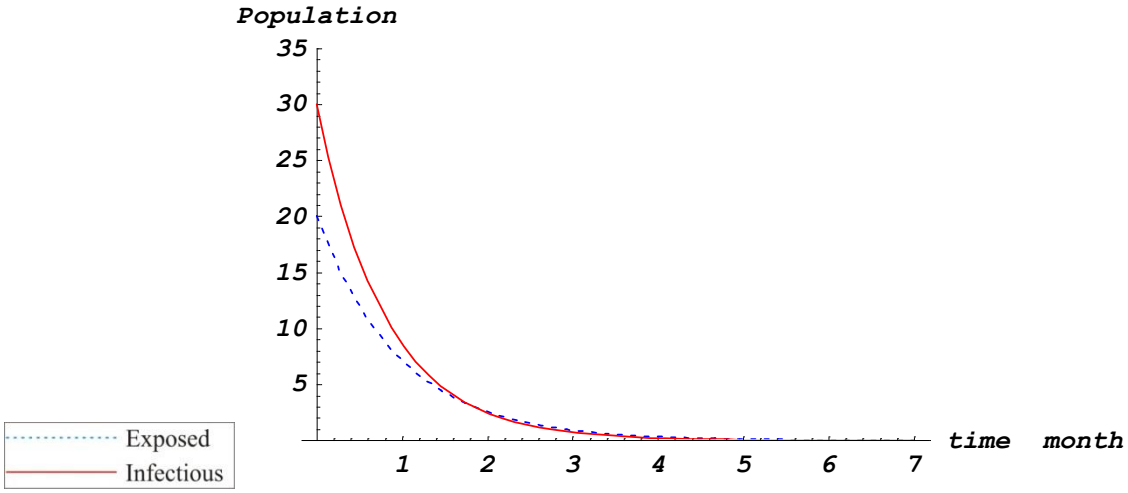

Figure 6. Effect of all three controls on the exposed and infectious population

3.2.4. Control with Treatment only

From fig.5, we observe that the exposed class and the infectious compartment have respectively dropped by 80% and 87% only, and by the end of the 7 months period, a remarkable result is already obtained.

This simulation also shows that the infectious class has dropped by 90% within the first 2 months, and the number of infectious individuals continues to drop remarkably. Although commendable, treatment alone does not guarantee a total reduction of the disease from the population within the said period of time.

3.2.5. Control with all three Intervention Strategies

In simulating the model with all three controls, fig. 6 shows that the exposed and infectious compartments are eliminated from the population within the specified period of time. It can be seen from fig. 6 that a plausible result is also obtained within the first 2 months for both compartments, most especially the exposed class. Therefore, applying this control strategy helps to eradicate the pneumonia disease from a population within a specified period of time.

4. Discussion and Conclusions

This study has considered an optimal control analysis of the pneumonia disease. The basic mathematical model is a deterministic system of non-linear ordinary differential equations which represent the dynamics of the pneumonia disease in four mutually-exclusive time-dependent human population compartments. In section 2, the basic mathematical properties and results arising from the model formulation were presented. Some of these results include the boundedness of solution, the pneumonia-free equilibrium, the basic reproduction number and the pneumonia-endemic equilibrium.

The optimal control problem was studied in section 3. Here, the prevention effort of the susceptible class, the vaccination intervention strategy and the treatment intervention strategy were incorporated into the basic

model to form the control model, and the Lebesgue measurable controls are given on a closed interval. The goal was to obtain an optimal value of the three control parameters, which minimizes the stated objective functional. The Pontryagin's Maximum Principle was employed in order to obtain the optimal values of the control parameters. This principle led to the construction of the Hamiltonian of the control problem and hence, the optimality system. From the optimality condition, the expressions for the control parameters were obtained.

We applied an iterative scheme to obtain the optimal solution of the optimality system. In this iterative scheme, an initial guess of the controls was made and used to solve the state system. We obtained an approximate solution of the state system using the 'NDSolve' and 'Simplify' numerical functions in the Version 12 Mathematica programming software. Since the state variables appear in the adjoint system, we also employ the 'NDSolve' and 'Simplify' functions to solve the adjoint system using the initial guess of the controls together with the solution of the state system. The solutions of the state system and the adjoint system are then substituted into the characterizations of the controls to obtain new values of the controls. Then, a convex combination of these new values of the controls and the previous values of the controls are used to update the controls. The updated controls are then used to repeat the iteration process until the values of the controls in the current iteration are close enough to the previous iteration values, and consequently, we obtained the optimal values of the control parameters.

We considered numerical simulations of the control model with different combinations of the controls. The version 12 MATHEMATICA programming software was used for the numerical simulations. The five combination strategies used in the numerical simulations include using prevention effort only, using vaccination only, using treatment intervention only, using none of the three intervention strategies and using all three intervention strategies. The simulations clearly revealed that without any of the control measures, the class of exposed individuals and the class of infectious individuals cannot be emptied within the stated period of time. We obtained that each of the control measures is significant in the pneumonia disease management and control, but the treatment intervention strategy has a greater effect on the reduction of the disease.

The combination of all three control measures in the control process gives the best result, as the combination helps to eradicate the pneumonia disease from the population within the shortest period of time. Therefore, we highly recommend this combination strategy in order to completely eradicate the pneumonia disease from a given population.

Data Availability

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

Conflicts of Interest

The author declares that there are no conflicts of interest.

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