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OPTIMAL CONTROL OF INFLUENZA A DYNAMICS IN THE EMERGENCE OF A TWO STRAIN

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Abstract. *This paper examines the influenza spread model by considering subpopulation, vaccination, and resistance to analgesic/antipyretic drugs + nasal decongestants Based on the studied model, the non-endemic, endemic stability points and the basic reproduction number are determined. In the model studied, control is given in an effort to prevent contact between individuals infected with influenza and susceptible (u_1), and control treatment for infected individuals in an effort to accelerate the recovery of infected individuals (u_2). In the numerical simulation, using the control u_1 the number of infected individuals in the subpopulation decreased compared to that without control. The number of individual recovered subpopulations using the u_2 control increased more than that without the control.*

Keywords: *optimal control, influenza, resistance, prevention, treatment.*

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1. INTRODUCTION

Flu or influenza sufferers will experience a fever, headache, runny nose, stuffy nose, and cough. A person can catch the flu if he accidentally inhales the droplets of saliva in the air, which are released by the sufferer when he sneezes or coughs. In addition, touching the mouth or nose after handling objects that have been splashed by the patient's saliva can also be a means of transmitting the flu virus [1].

Mathematics can play a role in controlling, analyzing, evaluating, and optimizing control of the spread of influenza. Mathematical models can be used to analyze the dynamics of flu transmission by including aspects of drug resistance [2]. Post-coinfection mathematical system with flu and a Gram-positive, used a Gram-positive, and COPD risk appraisal [3]. Study of a good system of avian flu with fifty percent-impregnated prevalence, developed a formula of avian flu for both raspberry and mortal poeples. The factor of half-impregnated prevalence on the transmission dynamics of the complaint is delved into [4]. The study of the epidemiological consequences of viral interferences: a mathematical model of two interacting viruses investigates the spread of two contagions that come into contact with repression of a single contagious if the two contagions do in these hosts [5]. The formulation system studied flu and other spreadable diseases of the respiratory tract. Influenza and infectious disease transmission in vivo, regardless of the effect of prolixity and advection on disease kinetics and sites [6].Recent timing and estimation of initial conditions of Zika transmission were also studied [7].

Modeling studies of drug-resistant antimicrobials in patients who have not recovered for a long time also discuss resistance to new pathogens [8]. E-commerce analysis between the ingrain and the adaptive susceptibility response to COVID-19 and the aftermath of growing pathogenesis [9]. Influenza infection models in the host or cell culture need to be investigated for the future [6]. Multiscale studies for different spatial scales of flu spread in individuals ranging from small to large to population scale.[10]. The study aimed to develop a model for calculating the transmissibility of the infection [11].

Influenza vaccine is a vaccine to prevent flu. Influenza vaccination is recommended to be carried out regularly every year to maintain optimal vaccine protection. Research has also been done to control flu, by giving vaccinations, paying attention to priority groups, and individuals who are resistant to flu drugs [12]. Control of treatment and prevention is given in an effort to optimize the prevention of the transmission of flu [13], [14]. This paper will examine the optimal control of overcoming the spread of influenza by amount consideration to vaccination and drug resistance. The controls given are: prevention control and treatment control.

2. RESEARCH METHODS

This research method is a literature review on the influenza spread model. The population in this paper is divided into five subpopulations. The susceptible subpopulation, that is, individuals who are still healthy but susceptible to infection with influenza, is denoted by S. Vaccination subpopulations are individuals who are vaccinated, denoted by V. Subpopulation infected with type A-strain, that is individuals who are still sensitive to analgesic/antipyretic drugs + nasal decongestants and are denoted by I_A. Subpopulation infected with type B-strain, that is individuals infected with influenza virus who are already resistant to analgesic/antipyretic drugs + nasal decongestants and are denoted by I_B. The recovered subpopulation is individuals who have recovered from influenza or are immune from vaccination and are denoted by R.

The assumption of the model studied in this paper is that recruitment individuals enter the S subpopulation at a rate of η. S subpopulation enter to V subpopulation at a rate of φ. Individuals of the S subpopulation in contact with the I_A individuals enter to the I_A subpopulation at a rate of β_1. Individuals of the S subpopulation in contact with I_B individuals entered to the I_B subpopulation at a rate of β_2. Individuals in I_A subpopulation treated with analgesics/antipyretics + nasal decongestants and recovered into the R subpopulation at a rate of t_1, Individuals who are resistant to analgesics/antipyretics + nasal decongestants enter the I_B subpopulation, with the rate of γ. Individuals in the I_B subpopulation were treated with analgesics/antipyretics + nasal decongestants + antihistamines + antitussives/expectorants and recovered into subpopulation R, with a cure rate of t_2. Infected individuals with influenza do not cause death. Individuals who have recovered or who are temporarily immune from vaccination may be susceptible to influenza re-

infection with the rate of δ. Individuals in each population can die naturally with the rate of μ. The schematic diagram of the mathematical model of the spread of influenza can be expressed as Figure 1 below.

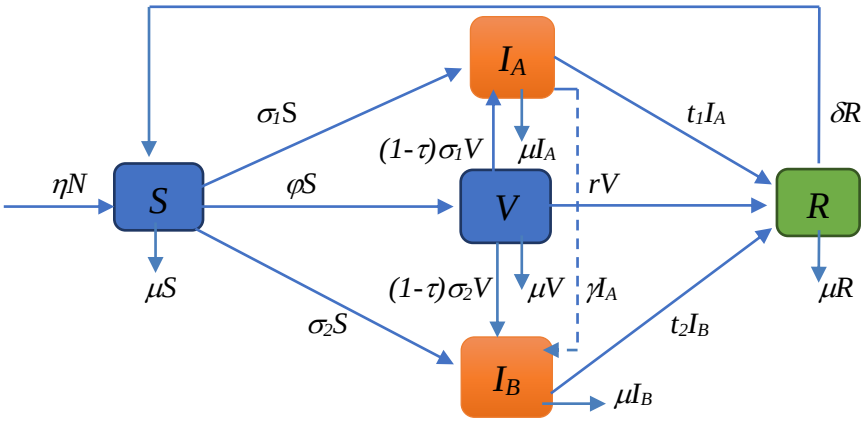

Figure 1. Influenza spread models and control

Based on the model assumptions, the study model in this paper can be expressed as of differential equations system:

$$\frac{dS}{dt} = \eta N + \delta R - \sigma_1 S - \sigma_2 S - (\varphi + \mu)S \quad (1)$$

$$\frac{dV}{dt} = \varphi S - (1-\tau)\sigma_1 V - (1-\tau)\sigma_2 V - (r+\mu)V \quad (2)$$

$$\frac{dI_A}{dt} = \sigma_1 S + (1-\tau)\sigma_1 V - (t_1 + \gamma + \mu)I_A \quad (3)$$

$$\frac{dI_B}{dt} = \sigma_2 S + (1-\tau)\sigma_2 V + \gamma I_A - (t_2 + \mu)I_B \quad (4)$$

$$\frac{dR}{dt} = rV + t_1 I_A + t_2 I_B - (\delta + \mu)R \quad (5)$$

with $\sigma_1 = \frac{\beta_1 I_A}{N}$, $\sigma_2 = \frac{\beta_2 I_B}{N}$, $N(t) = S(t) + V(t) + I_A(t) + I_B(t) + R(t)$ (6)

Based on equation (1)-(6), we get

$$\frac{dN}{dt} = \eta N - \mu N \quad (7)$$

We assume that all parameters in model are positive and the initial conditions of system (1)-(6) are given:

$$S(0) > 0, V(0) \geq 0, I_A(0) \geq 0, I_B(0) \geq 0, R(0) \geq 0.$$

Parameters, parameter explanations and source of parameter values are stated in Table 1 below:

Table 1. Parameters and descriptions used in the model

Parameter	Description	Value	Reference
η	Recruitment rate	0.0381	[2]
δ	The rate of return of the R subpopulation	0.08	assumed
β_1	Individual contact rates of S or V subpopulations with I_A	0.00102 day^{-1}	[2]
β_2	Individual contact rates of S or V subpopulations with I_B	0.00026 day $^{-1}$	[2]
φ	Vaccination rates from subpopulation S to V	0.002	assumed
$\frac{1}{\mu}$	Average human lifespan	70 × 365 days	[2]
τ	Vaccine efficacy	0,77	assumed
r	The rate of individual immunity from subpopulation V to R	0,8	assumed
t_1	Individual cure rates from I_A to R subpopulations	0.05 per day	[4]
γ	Individual transfer rate from compartment I_A to I_B	0.05	assumed
t_2	Individual cure rates from subpopulation I_B to R	0.01 per day	[4]

2.1 Equilibrium point of System

Disease-free equilibrium point, based on Eq. (1)-(6), equilibrium point of influenza disease-free provided that each subpopulation change per unit time is equal to zero and the number of infected individuals is equal to zero, in other words $\frac{dS}{dt} = \frac{dV}{dt} = \frac{dI_A}{dt} = \frac{dI_B}{dt} = \frac{dR}{dt} = 0$, and $I_A = I_B = 0$ [15], obtained

$$E_0 = (S^*, V^*, I_A^*, I_B^*, R^*) = \left(\frac{\eta k_1 k_3 N}{k_1 k_2 k_3 - \delta r \varphi}, \frac{\eta \varphi k_3 N}{k_2(k_1\delta + \mu) - \delta r \varphi}, 0, 0, \frac{r \eta \varphi N}{k_2(k_1\delta + \mu) - \delta r \varphi}\right), \quad (8)$$

with $k_1 = r + \mu, k_2 = \varphi + \mu$, dan $k_3 = \delta + \mu$.

Endemic equilibrium point, based on Eq. (1)-(6), equilibrium point of influenza disease-free provided that each subpopulation change per unit time is equal to zero and the number of infected individuals is not equal to zero, in other words $\frac{dS}{dt} = \frac{dV}{dt} = \frac{dI_A}{dt} = \frac{dI_B}{dt} = \frac{dR}{dt} = 0$, $I_A \neq 0$ dan $I_B \neq 0$, obtained

$$E_1 = (S^{**}, V^{**}, I_A^{**}, I_B^{**}, R^{**}), \quad (9)$$

with

$V^{**} = \frac{k_5 N - \beta 1 S^{**}}{\beta 1(1-\tau)}$, $I_A^{**} = \frac{\beta_1 k_4 - \beta_2 k_5}{\beta_1 \gamma} = k_6$, $I_B^{**} = \frac{\varphi \beta 1(1-\tau) SN - k1N(k_5 N - \beta 1 S^{**}) - (1-\tau)\beta_1 k6(k_5 N - \beta 1 S^{**})}{(1-\tau)\beta_2(k_5 N - \beta 1 S^{**})}$,

$R^{**} = \frac{r(k_5 N - \beta_1 S^{**})}{\beta_1(1-\tau)k_3} + \frac{t_1 k_6}{k_3} + \frac{t_2(\varphi\beta_1(1-\tau)S^{**}N - k_1 N(k_5 N - \beta_1 S^{**}) - (1-\tau)\beta_1 k_6(k_5 N - \beta_1 S^{**})}{(1-\tau)\beta_2 k_3(k_5 N - \beta_1 S^{**})}$,

$k_4 = t_2 + \mu$, $k_5 = t_1 + \gamma + \mu$.

From Eq. (1) by substituting $S^{**}, I_A^{**}, I_B^{**}, R^{**}$ to $\frac{dS}{dt} = 0$, then obtained S^{**}.

2.2 Reproduction number ($\mathcal{R}_0$)

Reproduction number is a parameter to determine whether the number of spread of the disease is increasing or decreasing. If $\mathcal{R}_0 < 1$, then the disease has decreased or disappeared in the population. If $\mathcal{R}_0 = 1$, then the number of infected people in the population is monotonous. If $\mathcal{R}_0 > 1$, then the number of infected in the population increases. reproduction number obtained by using the next generation matrix method [16]. To determine $\mathcal{R}_0$ can be determined by involving Eq. (3)-(5). The first step is to determine the Jacobian matrix by substituting the non-endemic equilibrium point of Eq. (3)-(5) in the subpopulation whose contacts are between susceptible and infected, the matrix F is obtained.

$$F = \begin{bmatrix} \frac{\beta_1 \eta k_1 k_3}{k_1 k_2 k_3 - \delta r \varphi} + \frac{p \beta_1 \eta \varphi k_3}{k_1 k_2 k_3 - \delta r \varphi} - k_3 & 0 & 0 \\ 0 & \frac{\beta_2 \eta k_1 k_3}{k_1 k_2 k_3 - \delta r \varphi} + \frac{p \beta_2 \eta \varphi k_3}{k_1 k_2 k_3 - \delta r \varphi} - k_4 & 0 \\ t_1 & t_2 & -k_5 \end{bmatrix}$$

Furthermore, the individual Jacobian matrices are determined by substituting the non-endemic equilibrium point in the Eq. (3)-(5) in the subpopulations that leave each compartment, the matrix G is obtained.

$$G = \begin{bmatrix} k_5 & 0 & 0 \\ -\gamma & k_4 & 0 \\ -t_1 & -t_2 & k_3 \end{bmatrix}.$$

So that we get the matrix FG^{-1}, reproduction number is obtained the maximum eigenvalue from the characteristic equation of $\det(\lambda I_3 - FG^{-1}) = 0$. The maximum eigenvalue corresponding to the spectral radius $\rho(FV^{-1},)$ of the matrix FG^{-1}, is production number, which is given by

$$\mathcal{R}_0 = max\{\mathcal{R}_a, \mathcal{R}_B\},$$

where

$$\mathcal{R}_a = \frac{\beta_1 \eta p \varphi k_3 + \beta_1 \eta k_1 k_3 - \delta k_1 k_2 k_5 + \delta k_5 r \varphi - k_1 k_2 k_5 \mu}{k_4(\delta k_1 k_2 - \delta r \varphi + k_1 \mu k_2)},$$

$$\mathcal{R}_{\mathcal{B}} = \frac{\beta_2\eta p\varphi k_3 + \beta_2\eta k_1 k_3 - \delta k_1 k_2 k_4 + \delta k_4 r\varphi - k_1 k_2 k_4 \mu}{k_4(\delta k_1 k_2 - \delta r\varphi + k_1 \mu k_2)}.$$

$\mathcal{R}_{\mathcal{A}}$ is the expectation of individuals infected with influenza caused by one individual subpopulation I_A entering a susceptible subpopulation. $\mathcal{R}_{\mathcal{B}}$ is the expectation of individuals infected with influenza caused by one individual I_B subpopulation entering a susceptible subpopulation.

2.3 Optimal Control of Influenza

Optimal control of countermeasures to combat the spread of influenza, given control of prevention by providing campaigns in the form of counseling to susceptible subpopulation individuals which is denoted by u_1. Treatment control is given to individuals in the I_A and I_B subpopulation in an effort to accelerate healing by providing vitamins which are denoted by u_2.

Based on Eq. (1)-(5), given the control u_1 and u_2, the system of differential equations is obtained as follows:

$$\frac{dS}{dt} = \eta N + \delta R - \sigma_1(1-u_1)S - \sigma_2(1-u_1)S - (\varphi+\mu)S \quad (10)$$

$$\frac{dV}{dt} = \varphi S - (1-\tau)\sigma_1 V - (1-\tau)\sigma_2 V - (r+\mu)V \quad (11)$$

$$\frac{dI_A}{dt} = \sigma_1(1-u_1)S + (1-\tau)\sigma_1 V - (t_1(1+u_2)+\gamma+\mu)I_A \quad (12)$$

$$\frac{dI_B}{dt} = \sigma_2(1-u_1)S + (1-\tau)\sigma_2 V + \gamma I_A - (t_2(1+u_2)+\mu)I_B \quad (13)$$

$$\frac{dR}{dt} = rV + t_1(1+u_2)I_A + t_2(1+u_2)I_B - (\delta+\mu)R \quad (14)$$

Control function $u_1(t)$ dan $u_2(t)$ are bounded, Lebesgue integrable functions. Control (1- u_1) given in an effort to reduce contact between infected individuals with susceptible individuals and between infected individuals with vaccination individuals. Control (1 + u_2) given in an effort to accelerate the healing of infected subpopulation individuals. The objective function is defined as follows:

$$J = min_{u_1,u_2} \int_0^{t_f} (AI_A(t) + BI_B(t) + C_1u_1^2(t) + C_2u_2^2(t))dt, \quad (15)$$

with t_f is the end time of influenza control, A and B, is the balance weight of influenza treatment costs, C_1 and C_2 is the balancing weight cost of influenza control.

The optimal control will be determined such that $U = \{(u_1(t), u_2(t)) \,|(u_1(t), u_2(t))\}$ measurable, $0 \le (u_1(t), u_2(t)) \le 1$, $t \in [0, t_f]$. Necessary conditions for optimal control must satisfy with the Pontryagin Maximum Principle [17]. To optimize control $u_1(t), u_2(t)$ of the system (10)-(14), used Hamiltonian equation. The Hamiltonian function is obtained by using the objective functional equation of the equation (15) and system (10)-(14) obtained:

$$\begin{aligned} H = {} & AI_A(t) + BI_B(t) + C_1u_1^2 + C_2u_2^2 + \\ & \lambda_1(\eta N + \delta R - \sigma_1(1-u_1)S - \sigma_2(1-u_1)S - (\varphi+\mu)S) + \\ & \lambda_2(\varphi S - (1-\tau)\sigma_1 V - (1-\tau)\sigma_2 V - (r+\mu)V) + \\ & \lambda_3(\sigma_1(1-u_1)S + (1-\tau)\sigma_1 V - (t_1(1+u_2)+\gamma+\mu)I_A) + \\ & \lambda_4(\sigma_2(1-u_1)S + (1-\tau)\sigma_2 V + \gamma I_A - (t_2(1+u_2)+\mu)I_B) + \\ & \lambda_5(rV + t_1(1+u_2)I_A + t_2(1+u_2)I_B - (\delta+\mu)R). \end{aligned} \quad (16)$$

where the $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ are the match costate for the state S, V, I_A, I_B, R. The system of Eq. (10)-(14) is found by taking the suitable halfway subsidiaries of the Hamiltonian (16) with respect to the associated state variable.

Theorem 1

Let $S^*(t), V^*(t), I_A^*(t), I_B^*(t)$ and $R^*(t)$ be optimal state solutions with related optimal control variable $u_1^*(t)$, $u_2^*(t)$ for the optimal control problem (10)-(15). Then, there exist costate variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ that satisfy:

$$\lambda_1'(t) = \lambda_1(\sigma_1(1-u_1) + \sigma_2(1-u_1) + \varphi + \mu) + \lambda_2\,\varphi - \lambda_3\sigma_1(1-u_1) - \lambda_4\sigma_2(1-u_1) \quad (17)$$

$$\lambda_2'(t) = \lambda_2\big((1-\tau)\sigma_1 + (1-\tau)\sigma_2 + (r+\mu)\big) - \lambda_3(1-\tau)\sigma_1 - \lambda_4(1-)\sigma_2 \quad (18)$$

$$\lambda_3'(t) = -A + (\lambda_1-\lambda_3)\beta_1(1-u_1)\frac{S}{N} + (\lambda_2-\lambda_3)\beta_1(1-\tau)\frac{V}{N} + (\lambda_3-\lambda_5)t_1(1+u_2) + (\lambda_3-\lambda_4)\gamma + \lambda_3\mu \quad (19)$$

$$\lambda_4'(t) = -B + (\lambda_1-\lambda_4)\beta_2(1-u_1)\tfrac{S}{N} + (\lambda_2-\lambda_4)\beta_2(1-\tau)\tfrac{V}{N} + (\lambda_4-\lambda_5)t_2(1+u_2) + \lambda_4\mu \quad (20)$$

$$\lambda_5'(t) = (\lambda_5-\lambda_1)\delta + \lambda_5\mu, \quad (21)$$

and with transversality conditions $\lambda_i(t_f) = 0$, $i = 1, 2, 3, 4, 5$, $u_1^*(t), u_2^*(t)$ is given

$$u_1^*(t) = \min\left\{1, max\left(0, \frac{-\lambda_1(\sigma_1+\sigma_2)S+\lambda_3\sigma_1 S+\lambda_4\sigma_2 S}{2C_1}\right)\right\}, \quad (22)$$

$$u_2^*(t) = \min\left\{1, max\left(0, \frac{\lambda_3 t_1 I_A+\lambda_4 t_2 I_B-\lambda_5(t_1 I_A+t_2 I_B)}{2C_2}\right)\right\}, \quad (23)$$

Proof.

The costate functions obtained with use the Hamiltonian (16), with associated to S, V, I_A, I_B and R, we obtain

$$\lambda_1'(t) = -\frac{\partial H}{\partial S} = \lambda_1(\sigma_1(1-u_1) + \sigma_2(1-u_1) + \varphi + \mu) + \lambda_2\,\varphi - \lambda_3\sigma_1(1-u_1) - \lambda_4\sigma_2(1-u_1)$$

$$\lambda_2'(t) = -\frac{\partial H}{\partial V} = \lambda_2\big((1-\tau)\sigma_1 + (1-\tau)\sigma_2 + (r+\mu)\big) - \lambda_3(1-\tau)\sigma_1 - \lambda_4(1-)\sigma_2$$

$$\lambda_3'(t) = -\frac{\partial H}{\partial I_A} = -A + (\lambda_1-\lambda_3)\beta_1(1-u_1)\frac{S}{N} + (\lambda_2-\lambda_3)\beta_1(1-\tau)\frac{V}{N} + (\lambda_3-\lambda_5)t_1(1+u_2) + (\lambda_3-\lambda_4)\gamma + \lambda_3\mu$$

$$\lambda_4'(t) = -\frac{\partial H}{\partial I_B} = -B + (\lambda_1-\lambda_4)\beta_2(1-u_1)\frac{S}{N} + (\lambda_2-\lambda_4)\beta_2(1-\tau)\frac{V}{N} + (\lambda_4-\lambda_5)t_2(1+u_2) + \lambda_4\mu$$

$$\lambda_5'(t) = -\frac{\partial H}{\partial R} = (\lambda_5-\lambda_1)\delta + \lambda_5\mu.$$

Solving for u_1^*, u_1^* subject to the constraints, from Eq. (16) can be derived to u_1, u_2 and we obtain

$$\frac{\partial H}{\partial u_1} = 0$$

$$2C_1u_1 + \lambda_1(\sigma_1+\sigma_2)S - \lambda_3\sigma_1 S + \lambda_4\sigma_2 S = 0$$

$$u_1^* = \frac{-\lambda_1(\sigma_1+\sigma_2)S+\lambda_3\sigma_1 S+\lambda_4\sigma_2 S}{2C_1}.$$

Using three control standard intervals, we obtain:

$$u_1^*(t) = \begin{cases} 0, & if\ \frac{-\lambda_1(\sigma_1+\sigma_2)S+\lambda_3\sigma_1 S+\lambda_4\sigma_2 S}{2C_1} \le 0 \\ \frac{-\lambda_1(\sigma_1+\sigma_2)S+\lambda_3\sigma_1 S+\lambda_4\sigma_2 S}{2C_1}, & if\ 0 < \frac{-\lambda_1(\sigma_1+\sigma_2)S+\lambda_3\sigma_1 S+\lambda_4\sigma_2 S}{2C_1} < 1 \\ 1, & if\ \frac{-\lambda_1(\sigma_1+\sigma_2)S+\lambda_3\sigma_1 S+\lambda_4\sigma_2 S}{2C_1} \ge 1. \end{cases}$$

Can be rewritten in compact form

$$u_1^*(t) = \min\left\{1, max\left(0, \frac{-\lambda_1(\sigma_1+\sigma_2)S+\lambda_3\sigma_1 S+\lambda_4\sigma_2 S}{2C_1}\right)\right\},$$

Similarly, for u_2^* obtained

$$u_2^*(t) = \min\left\{1, max\left(0, \frac{\lambda_3 t_1 I_A+\lambda_4 t_2 I_B-\lambda_5(t_1 I_A+t_2 I_B)}{2C_2}\right)\right\}.$$ □

3. RESULTS AND DISCUSSION

Solution of a dynamic model with control intervention using an iterative method with a Runge–Kutta fourth orders. Solution dynamic model with control intervention with an initial guess forward in time next we solve the costate models backward in time. Starting with an initial guess for the costate variables, obtained solution the state equation a forward Runge-Kutta fourth order method in time [17]. In the numerical simulation, we will compare the spread of influenza for susceptible subpopulations, vaccination, infected and recovered with control and without control. Suppose the initial number of each subpopulation $S(0) = 1000000$, $V(0) = 100000$, $I_A(0) = 50000$, $I_B(0) = 20000$, dan $R(0) = 0$, parameter value used on Table 1. Numerical simulation for suspected subpopulation with control and without control can be seen as Figure 2.

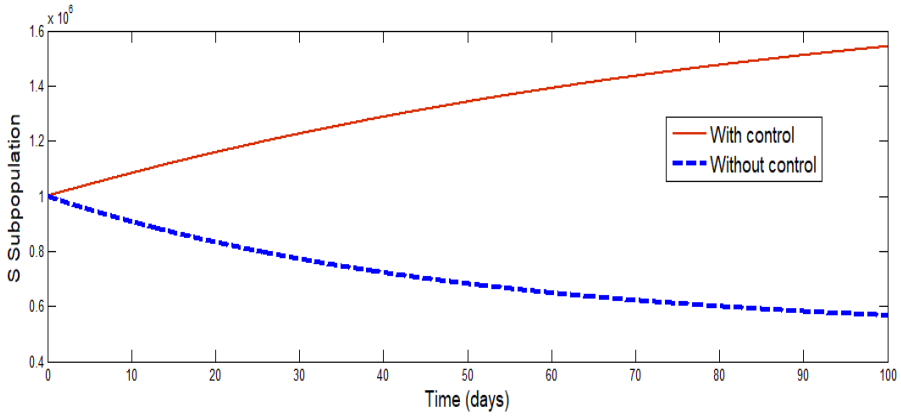

Figure 2. Spread of susceptible subpopulation with u_1 and without u_1

Based on Figure 2, the number of individual susceptible subpopulations decreases with no control and increases with u_1 control.

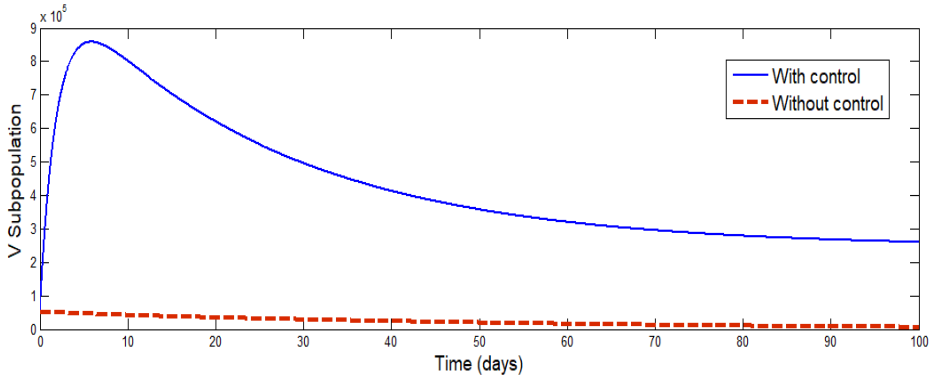

Figure 3. Spread of vaccination subpopulation with u_1 and without u_1

Based on Figure 3, the number of individuals in the vaccinated subpopulation with control increases from time $t = 0$ to $t = 5$ days, and decreases from time $t = 5$ days to $t = 100$ days. Whereas, with u_1 control, it decreased from the time $t = 0$ to $t = 100$ days.

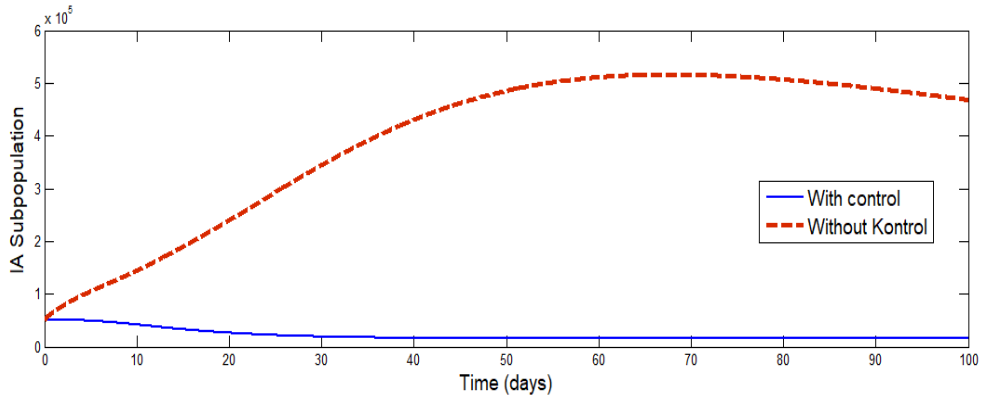

Figure 4. Spread of I_A subpopulation with u_1 and u_2 and without u_1 and u_2

Based on Figure 4, the number of individuals in the I_A subpopulation with no control increased from time $t = 0$ to $t = 65$ days, and after time $t = 65$ days it decreases slowly until time $t = 100$ days. Whereas, with control, the number of individuals in the I_A subpopulation decreased slowly from the time $t = 0$ to $t = 100$ days.

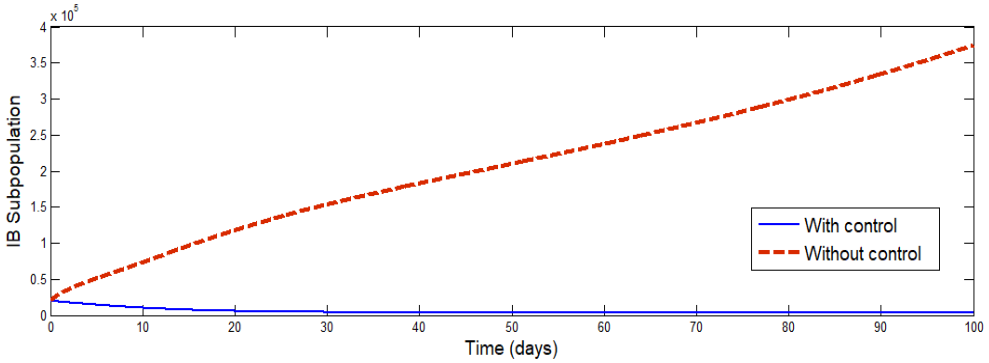

Figure 4. Spread of I_B subpopulation with u_1 and u_2 and without u_1 and u_2

Based on Figure 4, the number of individual I_B subpopulations without u_1 and u_2 increased from time $t = 0$ to $t = 100$ days. Whereas, with u_1 and u_2, the number of individuals in the I_A subpopulation decreased slowly from time $t = 0$ to $t = 100$ days.

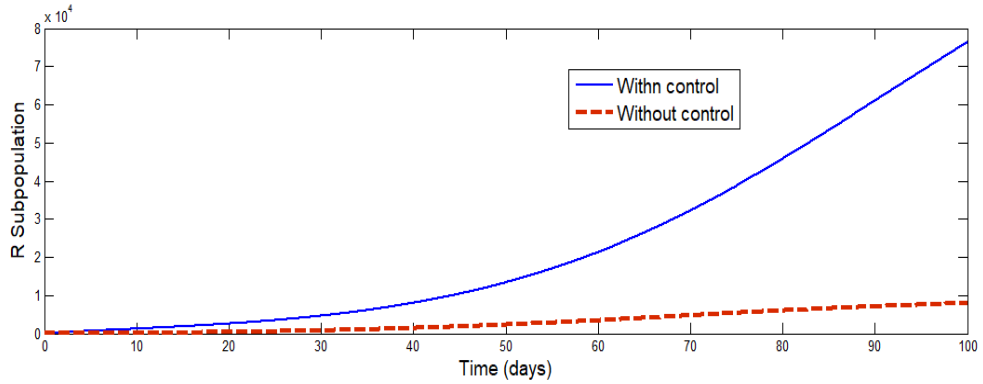

Figure 5. Spread of recovered subpopulation with u_2 and without u_2

Based on Figure 5, the number of individuals subpopulation R with u_2 increased quickly from time $t = 0$ to $t = 100$ days. Whereas, without control, the number of individuals in the R subpopulation continued to increase but very slowly from time $t = 0$ to $t = 100$ days.

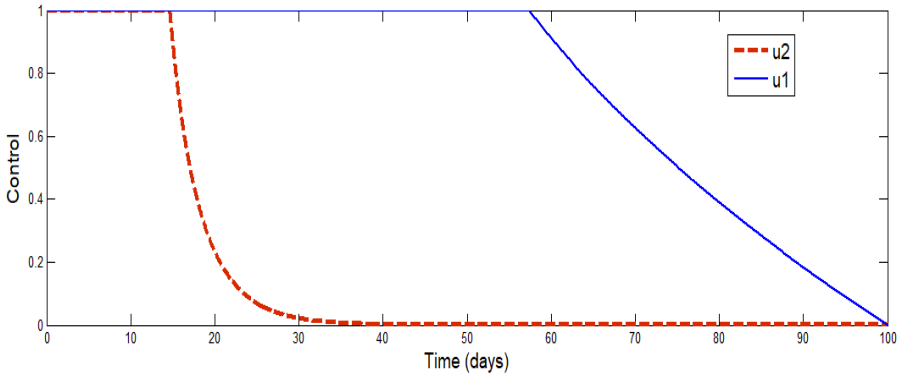

Figure 6. Dynamics of u_1 and u_2 on influenza spread

Based on Figure 6, optimal u_1 from time $t = 0$ to $t = 57$ days, while from time $t = 57$, u_1 decreased until $t = 100$ days. Optimal u_2 from time $t = 0$ to $t = 15$ days after $t = 15$ days u_2 decreased until time $t = 40$ days, after $t = 40$ days treatment control was no longer needed, as all individuals of the influenza-treated subpopulation had recovered.

4. CONCLUSIONS

Based on the results of the study and control measures in the model of the spread of influenza, the following conclusions were obtained: (1) Analysis of the influenza disease-free equilibrium point, the endemic equilibrium point, and the basic reproduction number. (2) In the model given control of influenza prevention (u_1) and control of influenza disease treatment (u_2). In the model of the spread of influenza that is given control, we obtain the theorem for the existence of adjoint variables from the state variables in the system. (3) The results of numerical simulations show that the individual subpopulations I_A and I_B with controls u_1 and u_2 decreased from time $t = 0$ to $t = 100$ days. Whereas, individuals in the I_A subpopulation with no control increased from time $t = 0$ to $t = 65$ days, and after time $t = 65$ days it decreases slowly until time $t = 100$ days and individuals in the I_A subpopulation with no control increased from time $t = 0$ to $t = 65$ days, and after time $t = 65$ days it decreases slowly until time $t = 100$ days. The number of individual recovered subpopulations increased more with the u_2 control than without the control.

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