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The 5th Seminar Nasional Matematika dan Pendidikan Matematika (SENATIK) 2020

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Preface

The fifth Seminar Nasional Matematika dan Pendidikan Matematika (SENATIK) was held by Mathematics Education Study Program, Universitas PGRI Semarang, Indonesia, in 2020. This seminar has objectives to improve mathematics teaching, to solve the mathematics problem, and to expand mathematics contribution to society.

Freedom learning is a new policy of the Ministry of Education and Culture of the Republic of Indonesia to improve the national education system that seems monotonous. Through freedom learning, it is expected that it can create happiness and a joyful learning atmosphere for both students and teachers. Learning activities will be effective if the learning atmosphere is enjoyable. By having a joyful learning environment and adequate learning facilities, students are expected to be able to construct knowledge and support in generating motivation to learn actively. Also, by giving freedom in carrying out learning through their learning will train and instill a democratic attitude for students and also shape students' creativity to explore their potential. As technology develops, teachers are expected to use technology for joyful learning. Through the integration of technology in the freedom of learning, it is expected that effective and efficient learning will be created. Therefore, teachers are required to be able to do innovative learning. In view of that, the Mathematics Education Study Program of Universitas PGRI Semarang invites researchers, practitioners, and educators to participate in and contribute to the fifth SENATIK 2020 under the theme "Freedom of Learning: Integration Technology in Mathematics Learning."

The keynote presentations are provided to show the contribution of mathematics educators in mathematics education towards research and knowledge sharing. We have three keynote speakers, that's are Prof. Dr. Ratu Ilma Indra Putri, M.Si. (Universitas Sriwijaya, Indonesia). Dr. Irwan Endrayanto Aluiciues, S.Si., M.Sc. (Universitas Gajah Mada, Indonesia), and Dr. Achmad Buchori, M.Pd. (Universitas PGRI Semarang, Indonesia). We also have two speakers in the workshop session that are Dr. Rully Charitas Indra Prahmana (Universitas Ahmad Dahlan, Indonesia) and Dr. Muhtarom (Universitas PGRI Semarang).

On this seminar implementation, from one hundred and thirty-one full paper registers, there are sixty-nine presenters declared to be qualified. Our wish all the participants would enjoy the seminar, so they involve valuable and rewarding, and improve the knowledge and experiences.

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Optimal control of diphtheria epidemic model with prevention and treatment

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Abstract. Diphtheria is an infectious and deadly disease that spread through droplet transmission. Nevertheless, diphtheria can be prevented by immunization. One of many ways to gain immunity against the disease is by getting a vaccine. Diphtheria vaccine should be given at least three times in one's lifetime and will be effective if given every ten years. However, the immunization program in developing countries, such as Indonesia, is not optimal yet, and that is one of the causes of the outbreak. Therefore, it is necessary to optimize the immunization program. In this study, we propose a mathematical model to describe the spreading of diphtheria disease. We formulate an optimal control problem on the SEIQR model to minimize the spreading through quarantine and optimize the proportion of vaccinated people through the immunization campaign. Here, we apply Pontryagin Minimum Principle to find the characteristics of the solution of optimal control problems analytically, and DOTcvpSB is used to solve the problem numerically. Based on the analytical and numerical solutions, the optimal control problem constructed could minimize the spread of the outbreak and its cost function.

1. Introduction

Diphtheria is an acute infectious disease caused by a bacteria called *Corynebacterium Diphtheriae*. This disease is transferred through droplets (a very small drop of a liquid) from an infected individual. The droplet transmission occurs when the infected one coughs, sneezes, or even talks. The droplets land on hands, or other surfaces, that come in close contact with the susceptible ones. The transmission also happens when sharing food or kitchen utensils with the infected ones.

According to the US Centers for Disease Control and Prevention, diphtheria was one of the biggest killers for children in the pre-vaccine era. The diphtheria vaccine was developed in 1923, and the rates of diphtheria diseases declined significantly [1]. Ideally, the vaccine is given as 3 series since age 2 years and continue every ten years. Nonetheless, the immunization program in some developing countries is still suboptimal, and it causes the outbreak happen again.

At the end of 2017, the diphtheria outbreak occurred in Indonesia, at least 20 provinces are affected by the disease. According to data from the Ministry of Health of Republic Indonesia, up to November 2017, diphtheria cases were found in 95 regencies and cities in 20 provinces. These provinces are Sumatera Barat, Jawa Tengah, Aceh, Sumatera Selatan, Sulawesi Selatan, Kalimantan Timur, Riau, Banten, DKI Jakarta, Jawa Barat, and Jawa Timur. Overall, there were 954 cases and 44 deaths. In 2018, the number of diphtheria cases reached 1.386 cases, and the number of the deaths was 29 cases [2]. The number of the cases in 2018 increased dramatically compared to the previous year. While on 2019, there

were 530 cases, and 23 deaths were reported [3]. As a precaution against the outbreaks in the future, it is necessary to study the disease and the optimization of the immunization program.

The dynamics and controls of diseases have been studied in the field of mathematical modeling. The first mathematical model for the epidemic spread is *SIR* model, in which *S*, *I*, *R* denote the number of susceptible, infected, and recovered individuals [4]. *SIR* model have been elaborated to generate different types of epidemic spread model, such as *SEI*, *SEIQR*, *SEIS*, *SIRS*, *SEIT*, *SIQR*, *SEIRS*, et cetera [5][6][7][8][9][10][11]. Variables *S*, *E*, *I*, *R*, *T*, and *Q* refers to susceptible, exposed, infected, recovered, treatment, and quarantine individuals. Dynamical analysis of the mathematical model is used to determine behavior of the system over time. The existence of the controls on *SEIT* model is proved, and the optimal control obtained by applying Pontryagin Minimum Principle [9].

Motivated by the fact of suboptimal immunization in Indonesia and those preceding researches, this study discusses formulating an optimal control problem on the diphtheria epidemic model with vaccination as prevention and quarantine as a treatment. The optimal control problem formulation involves the objective function to minimize the number of infected people and the cost of the immunization campaigns and quarantine. The optimal control problem is solved analytically and numerically to obtain optimal control and state variables. The solutions are then interpreted and verified with medical validity. Finally, the optimal control variables obtained and be applied to minimize the spread of diphtheria.

2. Methods

The mathematical model we propose in this study, is a modification of the former model, that given by system (1) [10]. Where variabel *N* represents total population, parameters *p* is proportion of vaccinated individual within population, μ is birth rate, α is probability of interaction between the susceptible and infected, γ is rate of individual get quarantined each time unit, and ε is the rate of recovery.

$$\begin{aligned}
\frac{dS}{dt} &= (1-p)\mu N - \mu S - \alpha \frac{S}{N} I \\
\frac{dI}{dt} &= \alpha S \frac{I}{N} - \mu I - \gamma I \\
\frac{dQ}{dt} &= \gamma I - \mu Q - \varepsilon Q \\
\frac{dR}{dt} &= p\mu N + \varepsilon Q - \mu R \\
N &= S + I + Q + R
\end{aligned} \tag{1}$$

The first thing we carry out is modifying the mathematical model to give more relevant characteristics of the spread of diphtheria disease by considering other variables and parameters in the system. After model modification, we formulate the optimal control problem and solve it by Pontryagin Minimum Principle and DOTcvpSB [12][13]. Based on the analytical and numerical solution, the optimal control of the problem is obtained, and the result of this study is concluded.

3. Result and discussion

This section discusses the modification process, formulation and solution of the optimal control problem, and numerical simulation.

3.1. Mathematical model

In this study, we consider some characteristics of diphtheria disease and set some assumptions and boundaries: 1) Ones that are living in crowded and unclean conditions, who aren't well-nourished, children under 5 and adults over 60 years old, especially who don't get up-to-date vaccinations, are at high risk of diphtheria infection; 2) People who interact with the infected one can be exposed to the

disease. We assume that all the exposed ones, at a certain rate, will be infected by the bacteria. During some period, the exposed ones will not show any signs or symptoms. This period is called by an incubation period. The incubation period of diphtheria is 2-5 days. After that period, early signs and symptoms start to appear. The infected ones can infect others for up to 4 weeks; 3) The infected people will get some treatments. We assume all the treatments and medications are included in the quarantine state; 4) People in the quarantine period will recover at a certain rate, 5) People who got up-to-date vaccinations, and people who already recovered from the infection are assumed to have immunity to diphtheria; 6) The number of population is affected by the population growth rate and natural mortality rate, 7) To simplify the model, we assume the death rate due to diphtheria is equal to the natural mortality rate.

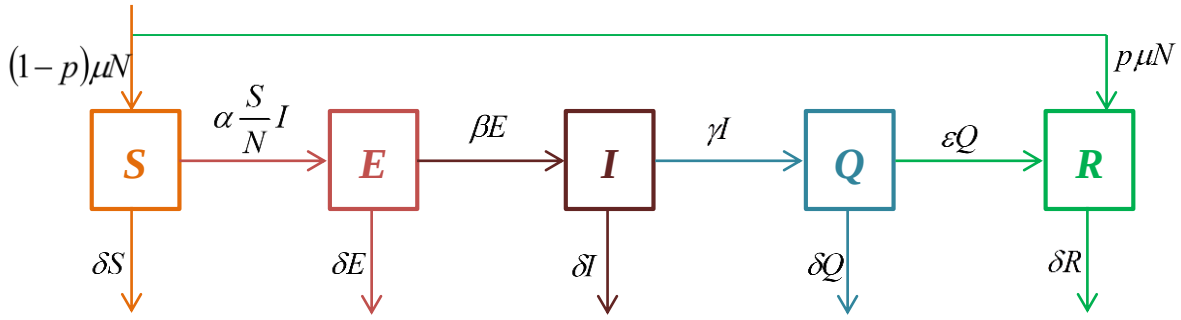

Figure 1. Compartment diagram of the model.

Considering those preceding assumptions and boundaries in figure 1, we classify the total number of population (N) into five subpopulations, i.e., Susceptible (S), Exposed (E), Infected (I), Quarantine (Q), and Recovered (R), and obtain a mathematical model given by system (2).

$$\begin{aligned}
\frac{dS}{dt} &= (1-p)\mu N - \alpha \frac{S}{N} I - \delta S \\
\frac{dE}{dt} &= \alpha \frac{S}{N} I - \beta E - \delta E \\
\frac{dI}{dt} &= \beta E - \gamma I - \delta I \\
\frac{dQ}{dt} &= \gamma I - \varepsilon Q - \delta Q \\
\frac{dR}{dt} &= p\mu N + \varepsilon Q - \delta R \\
N &= S + E + I + Q + R
\end{aligned} \tag{2}$$

Where parameter μ represents the natural increase rate, δ represents natural mortality rate, α is the probability of interaction between the susceptible and infected, β is the infection rate, γ is the handling or treatment rate (the rate of individual get quarantined each time unit), and ε is the rate of recovery.

Furthermore, non-dimensional analysis on the system (2) allows us to rewrite the model by the system (3). Let $s = \frac{S}{N}$, $e = \frac{E}{N}$, $i = \frac{I}{N}$, $q = \frac{Q}{N}$, and $r = \frac{R}{N}$ are non-dimensional variables, then system (2) could be written as the system (3). Where *s*, *e*, *i*, *q*, and *r* represent the proportion of the number of individual in each subpopulation.

$$\begin{aligned}
\frac{ds}{dt} &= (1-p)\mu - \alpha si - \delta s \\
\frac{de}{dt} &= \alpha si - \beta e - \delta e \\
\frac{di}{dt} &= \beta e - \gamma i - \delta i \\
\frac{dq}{dt} &= \gamma i - \varepsilon q - \delta q \\
\frac{dr}{dt} &= p\mu + \varepsilon q - \delta r \\
s + e + i + q + r &= 1
\end{aligned} \tag{3}$$

3.2. Formulation of optimal control problem

In this subsection, we formulate an optimal control problem to minimize the spread of diphtheria disease. One factor that could suppress the rate of the spread is by optimizing the treatment rate of infected people. Besides the treatment rate, another factor that causes the spread of infectious disease is the suboptimal immunization. Thus, the proportion of the people who got an up-to-date vaccine must be improved. We assume that the number of proportion could be increased by the immunization campaign. When people understand the importance of immunization, it will encourage them to get a vaccine.

Let the effort of the immunization campaign be considered as a control variable u_1 and the rate of treatment as a control variable u_2. Then, considering those two control variables, u_1 and u_2, into the system (3), we obtain the system to be controlled, that is

$$\begin{aligned}
\frac{ds}{dt} &= (1-(p+u_1))\mu - \alpha si - \delta s \\
\frac{de}{dt} &= \alpha si - \beta e - \delta e \\
\frac{di}{dt} &= \beta e - u_2 i - \delta i \\
\frac{dq}{dt} &= u_2 i - \varepsilon q - \delta q \\
\frac{dr}{dt} &= p\mu + \varepsilon q - \delta r
\end{aligned} \tag{4}$$

Therefore, the main components of this optimal control problem are:

1. The mathematical description of the process to be controlled is the system (4).
2. The objective function of the optimal control problem, which aim to minimize the number of infected subpopulation, the cost of treatment, and immunization campaign. The cost of treatment and immunization campaigns are assumed to be related to the total expended energy in the system. Thus, the objective function is mathematically expressed as equation (5).

$$\min \quad J = \int_{t_0}^{t_f} I(t) + \frac{C_1}{2} {u_1}^2(t) + \frac{C_2}{2} {u_2}^2(t)\, dt \tag{5}$$

where C_1 and C_2 are their weighting factors.

3. The constraints of the state and control variables are $S, E, I, Q, R \geq 0$, $0 < u_1 \leq 1-p$, and $0 < u_2 \leq 1$. Which means, immunization campaign could increase the percentage of vaccine recipient

coverage, up to (100-*p*)%, where *p* depends on the initial vaccine recipient coverage. At the same time, the treatment rate could handle up to 100% of the infected people.

3.3. Pontryagin minimum principle

Using Pontryagin Minimum Principle [12] on the optimal control problem formulated in subsection 3.2, we obtain equations and system (6), (7), (8), (9), and (10).

1. Pontryagin H function.

$$\begin{aligned} H = I + \frac{C_1}{2}{u_1}^2 + \frac{C_2}{2}{u_2}^2 + \lambda_1\left[\left(1-\left(p+u_1\right)\right)\mu - \alpha si - \delta s\right] + \lambda_2\left[\alpha si - \beta e - \delta e\right] \\ + \lambda_3\left[\beta e - \gamma i - \delta i\right] + \lambda_4\left[u_2 i - \varepsilon q - \delta q\right] + \lambda_5\left[\left(p+u_1\right)\mu + \varepsilon q - \delta r\right] \end{aligned} \tag{6}$$

2. Optimal controls ${u_1}^*$ and ${u_2}^*$.

$$\frac{\partial H}{\partial {u_1}^*} = 0 \Leftrightarrow {u_1}^* = \frac{\left(\lambda_1 - \lambda_5\right)\mu}{C_1} \tag{7}$$

$$\frac{\partial H}{\partial {u_2}^*} = 0 \Leftrightarrow {u_2}^* = \frac{\left(\lambda_3 - \lambda_4\right)i}{C_2} \tag{8}$$

3. State equations:

$$\begin{aligned} \dot{s} &= \frac{\partial H}{\partial \lambda_1} = \left(1-\left(p+u_1\right)\right)\mu - \alpha si - \delta s \\ \dot{e} &= \frac{\partial H}{\partial \lambda_2} = \alpha si - \beta e - \delta e \\ \dot{i} &= \frac{\partial H}{\partial \lambda_3} = \beta e - \gamma i - \delta i \\ \dot{q} &= \frac{\partial H}{\partial \lambda_4} = u_2 i - \varepsilon q - \delta q \\ \dot{r} &= \frac{\partial H}{\partial \lambda_5} = \left(p+u_1\right)\mu + \varepsilon q - \delta r \end{aligned} \tag{9}$$

4. Costate equations:

$$\begin{aligned} \dot{\lambda}_1 &= -\frac{\partial H}{\partial s} = \alpha\lambda_1 i + \delta\lambda_1 - \alpha\lambda_2 i \\ \dot{\lambda}_2 &= -\frac{\partial H}{\partial e} = \beta\lambda_2 + \delta\lambda_2 - \lambda_3\beta \\ \dot{\lambda}_3 &= -\frac{\partial H}{\partial i} = -1 + \alpha\lambda_1 s - \lambda_2\alpha s + \lambda_3 u_2 + \lambda_3\delta - \lambda_4 u_2 \\ \dot{\lambda}_4 &= -\frac{\partial H}{\partial q} = \varepsilon\lambda_4 + \lambda_4\delta - \varepsilon\lambda_5 \\ \dot{\lambda}_5 &= -\frac{\partial H}{\partial r} = \lambda_5\delta \end{aligned} \tag{10}$$

With initial conditions, $S(0) = S_0$, $E(0) = E_0$, $I(0) = I_0$, $Q(0) = Q_0$, $R(0) = R_0$, $u_1(0) = 0$, $u_2(0) = 0$, and $\lambda_1(0) = \lambda_2(0) = \lambda_3(0) = \lambda_4(0) = \lambda_5(0) = 0$.

Solving equations (6)-(10) will obtain the optimal controls and leads to the optimal system (4) with objective to function (5). Equation (7) implies that the value of optimal control u_1 (immunization campaign) is affected by μ (population growth rate), and optimal control u_2 (treatment rate) is affected by the number of infected people (i). Nevertheless, equations (6), (7), (8), (9), and (10) are nonlinear system, and it is tricky to find the solution analytically. Thus, we compute it numerically to find the solutions of the problem. The results of numerical computations are discussed in subsection 3.4.

3.4. Numerical simulation

This section displays the results of numerical simulation by using DOTcvpSB [13]. The simulations are run using the main components of the optimal control problem. The simulations are executed by setting $S_0 = 0.95$, $E_0 = 0$, $I_0 = 0.05$, $Q_0 = 0$, $R_0 = 0$, an initial condition of each subpopulation. In other words, in the beginning, the number of an infected subpopulation is 5% of the total population, and the remaining 95% are susceptible. The value of each parameter is shown in table 1. Some of the parameters used are taken from the former researches, and some are processed from various data sources.

Table 1. Parameters of the system.

Parameter	Value	Source
μ	0.019	[14]
δ	0.006	[14]
α	0.570	[10]
β	0.230	[9]
ε	0.500	[10]

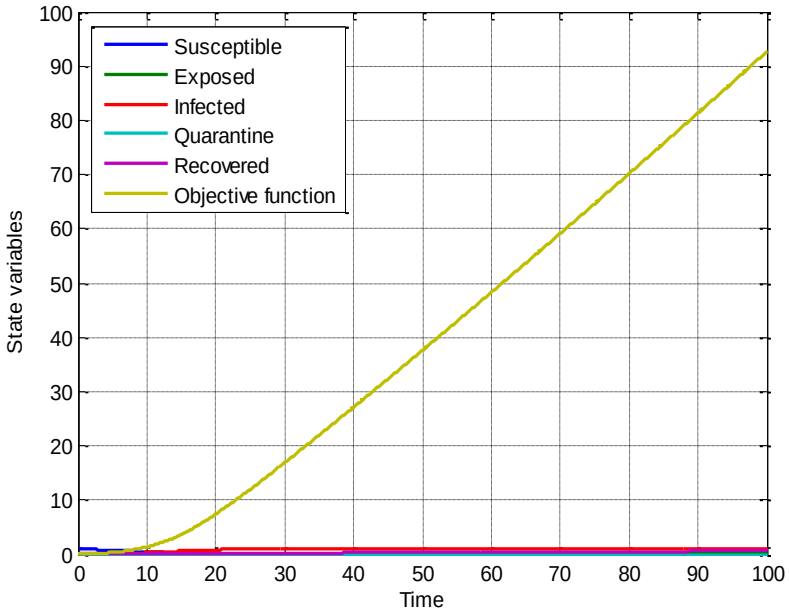

Figure 2. The trajectory of state variables when the proportion of vaccinated individual within population is 50% (before optimization).

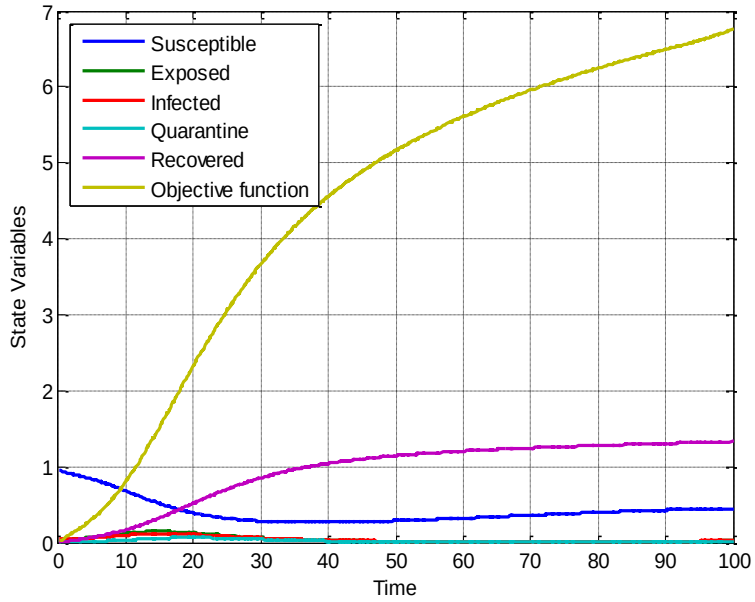

Figure 3. The trajectory of state variables when the proportion of vaccinated individuals within the population is 50% (after optimization).

We consider two cases of the problem. Case 1, occurs when the proportion of vaccinated individuals within the population, before the immunization campaign, is far from the strategic plan target 2020, which is 95% ($p < 0.95$) [2]. In Case 1, we consider the coverage of complete basic immunization in areas that covers 50% of the infants ($p = 0.5$). While in Case 2, we consider a condition when the coverage is 90% ($p = 0.9$). These scenarios are meant to show the difference in optimal control obtained in each situation. For Case 1, the simulations are shown in figures 2, 3, and 4. And for Case 2, the results are portrayed in figures 5, 6, and 7.

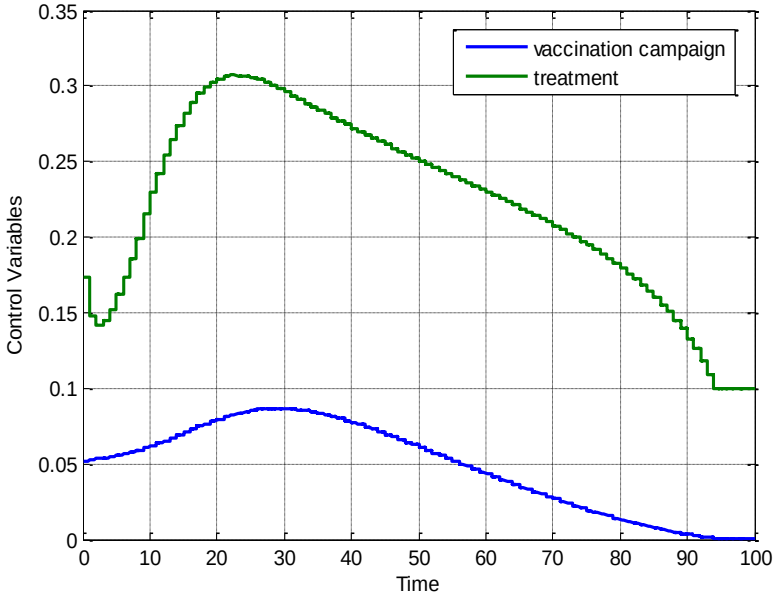

Figure 4. The profile of optimal control variables when the proportion of vaccinated individuals within the population is 50%.

In figure 2, it is known that $S_f = 0.013$, $E_f = 0.036$, $I_f = 1.139$, $Q_f = 0$, and $R_f = 0.064$. In other words, when the immunization coverage is 50%, and there is no campaign to develop the coverage nor quarantine over the infected, the number of infected one's increases from 5% to 114% compared to the initial condition, the exposed increases from 0% to 3.6%, the recovered reaches 6.4%. After optimization through campaign and quarantine, it is known from Figure 3, that $S_f = 0.436$, $E_f = 0.024$, $I_f = 0.030$, $Q_f = 0.005$, and $R_f = 1.332$. This means by immunization campaign and quarantine, the number of the infected decreases from 5% to 3%, the exposure is 1.2% less than before optimization, and the recovered reaches 133%. Figure 4 shows the optimal value of vaccination campaigns and treatment over time. In the beginning of time, the treatment $u_2 = 0.173$, went downhill to $u_2 = 0.14$, then bounced back to $u_2 = 0.31$, and finally stabilized at its lowest level, $u_2 = 0.1$, that should handle the treatment of 10% of the total population over time. While the campaign slowly increases from $u_1 = 0.052$ to $u_1 = 0.08$, with the increasing of the infected number, then decreases when the number slowly goes down, and finally stabilized at 0%.

Similar to the first case, the scenario of the second case are displayed in figures 5, 6, and 7. Before the optimization, the value of each state variables in the final time is, $S_f = 0.004$, $E_f = 0.007$, $I_f = 0.665$, $Q_f = 0$, and $R_f = 1.151$. From the result, it is known that the number of infected ones increases from 5% to 66.5%, and the recovered reached 115%. And after the optimization, the value yielded are, $S_f = 0.173$, $E_f = 0.002$, $I_f = 0.005$, $Q_f = 0.001$, and $R_f = 1.646$. The profile of optimal control variables in Case 2, which is shown in figure 7 is slightly different to figure 4. At the earlier time shown in figure 7, the campaign, slowly rises from $u_1 = 0.061$ to $u_1 = 0.07$, then continue to decrease until it is close zero. While the treatment $u_2 = 0.188$, decreased to $u_2 = 0.16$, then climbed up to $u_2 = 0.32$, and finally stabilized at its lowest level, $u_2 = 0.1$. A stark difference lies in the time it takes for the curve to rise and fall, then finally stable in its lowest point. The other difference is seen in the decrease in the curves. These differences imply that the higher coverage of complete basic immunization in an area, the sooner an outbreak could be handled. Furthermore, a comparison between the profile of optimal control variables in both cases, it is shown that the coverage of vaccine recipient increased by doing the campaign, from 50% to 55% in Case 1 and from 90% to 96% in Case 2. And the treatment rate could handle 10-31% in Case 1 and 10-32% in Case 2. These percentages may seem low, but the values are the optimal value needed to optimize the system with the objective of minimizing the costs.

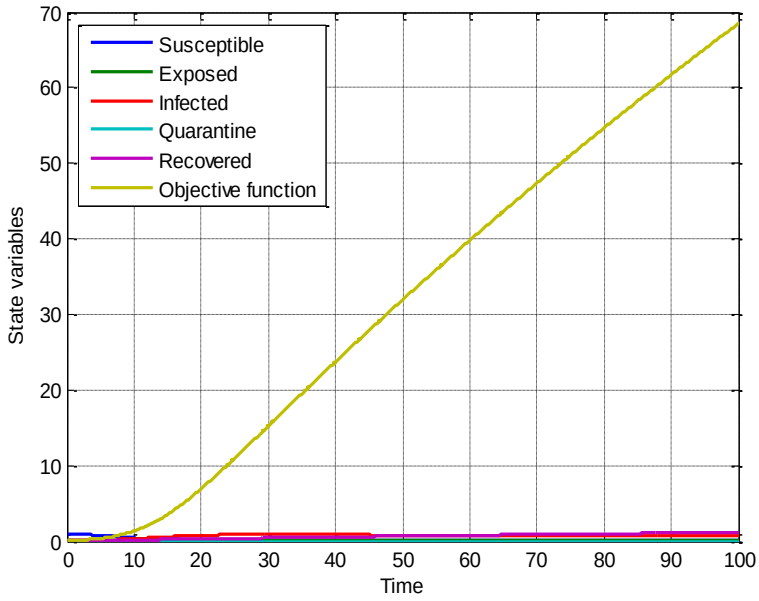

Figure 5. The trajectory of state variables when the proportion of vaccinated individuals within the population is 90% (before optimization).

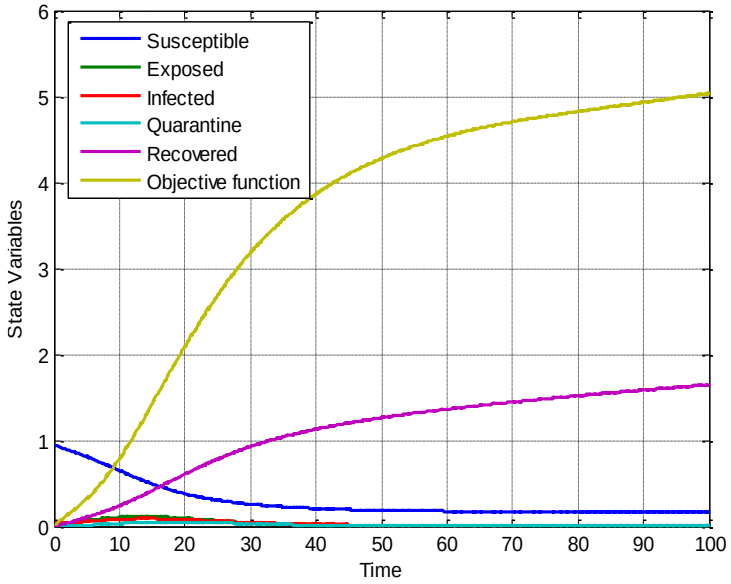

Figure 6. The trajectory of state variables when the proportion of vaccinated individuals within the population is 90% (after optimization).

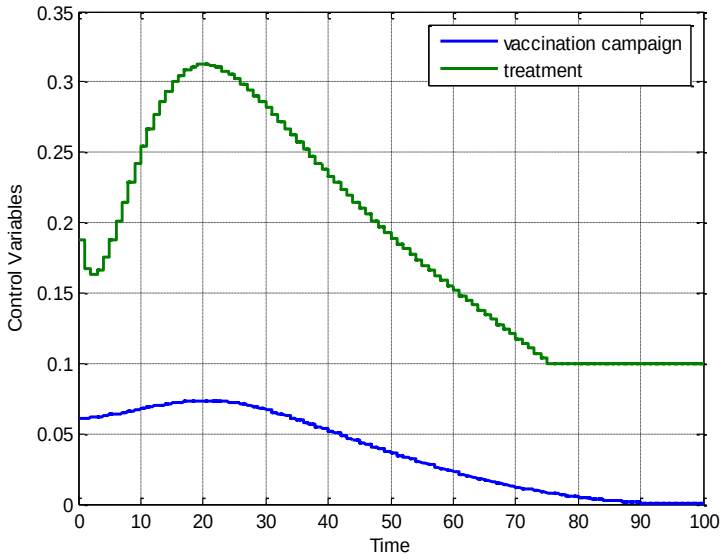

Figure 7. The profile of optimal control variables when the proportion of vaccinated individuals within the population is 90%.

A comparison between the results of the cases is presented in table 2. Comparing the values of before and after optimization in table 2, we know that the optimal control problem applied in the system is able to increase the number of a recovered subpopulation and reduce the number of the infected, the exposed, and its objective function (from 92.6 to 6.8 in Case 1, and 68.4 to 5,1 in Case 2). Whilst comparing the values of both cases, it is shown that the number of a recovered subpopulation in Case 2 is relatively high, even before the optimization. This implies that even without the immunization campaign, the coverage of basic immunization (p) is already high so that the number of recovered subpopulations before the optimization could become quite high. The value of p affects the effort to maximize the coverage of vaccine recipients. The higher p does, the less effort it takes to maximize the coverage by doing a campaign, and vice versa.

Table 2. Comparison of the state variables on final time, before and after optimal controlling.

	Case 1		Case 2	
	Before	After	Before	After
Susceptible	0.01299	0.43623	0.00437	0.17264
Exposed	0.03575	0.02388	0.00703	0.00221
Infected	1.13900	0.02992	0.66520	0.00515
Quarantine	0.00000	0.00516	0.00000	0.00103
Recovered	0.63920	1.33199	1.15100	1.64613
Objective function	92.6000	6.76148	68.4400	5.03610

4. Conclusion

From the result and discussion, we conclude that the optimal control problem formulated in this study succeeds in minimizing the number of infected people, the cost of the campaign, and the treatment. Comparing the cases, it is known that the higher proportion of vaccinated individuals in the initial time, i.e., before the campaign, the less cost needed to prevent the outbreak, and vice versa. The value of optimal control variables varies over time. The effort of the immunization campaign is affected by the population growth rate, while the treatment rate is affected by the number of infected people. With the objective to minimize the number of infected people and the cost incurred, the optimal effort of immunization campaign should develop 5-6% of the coverage of complete basic immunization in an area, and the optimal number of infected people that should be quarantined is 10-32%.

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