Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2022, 2022:19
https://doi.org/10.28919/cmbn/7124
ISSN: 2052-2541

OPTIMAL CONTROL AND SENSITIVITY ANALYSIS OF COVID-19 TRANSMISSION MODEL WITH THE PRESENCE OF WANING IMMUNITY IN WEST JAVA, INDONESIA

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Abstract: In this paper, we developed optimal control and sensitivity analysis on the model of SEIQR COVID-19 transmission in the presence of waning immunity by adding the combination of Partical Rank Correlation Coefficient (PRCC) and Latin Hypercube Sampling (LHS). The most influental parameters to the model are the isolation rate, the infection rate and the recovery rate. We used daily cases of COVID-19 data in West Java, Indonesia to parameterize the infection rate and the recovery rate of the model. Optimal control is applied to the most sensitive parameter i.e. treatments. Treatment is effective to reduce the infected population.

Keywords: COVID-19; LHS; PRCC; waning immunity; isolation; optimal control; sensitivity analysis.

2010 AMS Subject Classification: 92D25, 92D30.

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Received December 30, 2021

1. INTRODUCTION

COVID-19 began in December 2019 in Wuhan city, Hubei province, China. This disease was caused by the virus named SARS-CoV which spread rapidly throughout the world and caused an epidemic [1]. The beginning symptoms of COVID-19 are not nonspecific syndromes, i.e. dry cough, fatigue and fever. These symptoms could involve multiple systems that caused comorbidity, i.e. musculoskeletal (muscleache), gastrointestinal (vomiting, nausea, and diarrhea), neurologic (confusion and headache), and respiratory (sore throat, cough, rhinorrhea, short of breath, chest pain, and hemoptysis) [2]. The origin of COVID-19 is believed to be a zoonotic virus because of sequence identity to the bat-CoV, it is likely that bats are the primary vector for this virus [3,4]. COVID-19 first appeared in Indonesia on March 2, 2020. This was discovered after a citizen was declared infected with the coronavirus after arriving in West Java, Indonesia. As the cases of Covid-19 continue to grow, it is hard to sync between eliminating Covid-19, balancing the economy, and applying the social restriction that will affect many sector [5]. To minimize the spreading of the disease and stop the pandemic, It is widely assumed that to reach ~67% herd immunity, 175 million Indonesian citizens need to be vaccinated. It means 350 million vaccines are necessary to be supplied nationwide [6]. As the province with the largest population, West Java contributes a large percentage of the total positive cases of COVID-19 in Indonesia.

COVID-19 Researchers are competing to find a solution for COVID-19, whether it is a vaccine or a cure. Mathematician contribute through modelling the dynamics of COVID-19. Mathematical model of COVID-19 transmission with vaccination and treatment [7-9]. Some other models of COVID-19 considering isolation or quarantined compartment [10,11]. Also, a model with waning immunity that caused reinfection of this disease [12]. In our previous research [13], We developed a mathematical model of COVID-19 disease with vaccination and isolation in the presence of waning immunity. We analized the endemic and non-endemic equilibrium with its stability. The Basic Reproduction number $(\mathfrak{R}_0)$ showed the threshold of the model. The non-endemic equilibrium (disease free equilibrium) is locally asymtotically stable when $\mathfrak{R}_0 < 1$. The endemic equilibrium is locally asymtotically stable with a certain condition when $\mathfrak{R}_0 > 1$. We concluded that vaccination and isolation are an effective way to reduce the spreading of the disease.

2. Material and Methods

The data used for this research were obtained from pikobar.jabarprov.go.id, the data covers a period of three (2) months, starting from 19th of June, 2021 to the 16th of August, 2021. We continued our research on the Mathematical model of COVID-19 transmission in the presence of waning immunity [13], by adding the combination of Partical Rank Correlation Coefficient (PRCC) and Latin Hypercube Sampling (LHS) to determine the most important parameter of the model. Then, we also added optimal control to the most sensitive parameter i.e. treatments. The population is divided into five compartments, namely Susceptible population (S), Exposed population (E), Infected population (I), Isolated population (Q), and Recovered population (R). We used daily cases of COVID-19 data in West Java, Indonesia to parameterize the infection rate and the recovery rate of the model. The transition and transmission diagram of the COVID-19 model from (Inayaturohmat, 2021) is given in FIGURE 1. below.

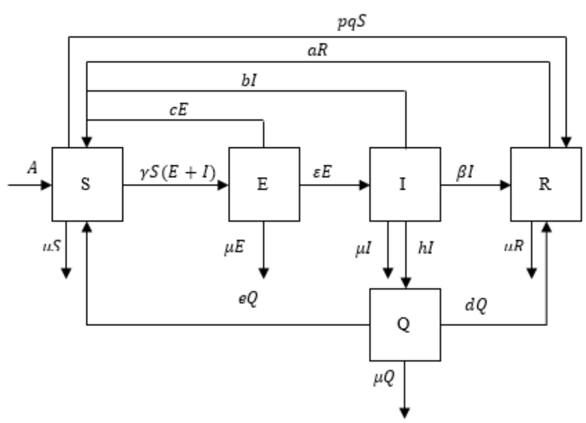

FIGURE 1. Transmission and Transition Diagram of COVID-19 Model

From (Inayaturohmat, 2021), The differential equation system with $A = \mu$ as follow :

$$\frac{dS}{dt} = \mu - \gamma S(t)\big(E(t) + I(t)\big) + cE(t) + bI(t) + \alpha R(t) + eQ - \mu S(t) - pqS(\mathrm{t})$$

$$\frac{dE}{dt} = \gamma S(t)\big(E(t) + I(t)\big) - (c + \varepsilon + \mu)E(t)$$

$$(1)\quad \frac{dI}{dt} = \varepsilon E(t) - (\beta + b + \mu + h)I(t)$$

$$\frac{dQ}{dt} = hI(t) - (\mu + d + e)Q(t)$$

$$\frac{dR}{dt} = \beta I(t) - (\alpha + \mu)\, R(t) + pq\, S(t) + dQ(t)$$

Table 1 provides the list of the parameters of the model and its values according to previous research and the data from pikobar.jabarprov.go.id.

Table 1. Parameter Description

Parameter	Description	Value	Source
α	The Rate at which the recovered become susceptible again	0.35	[13]
β	The Rate of recovery	0.0147	Estimated
γ	The Rate of infection	0.0001075	Estimated
ε	$\frac{1}{\text{The incubation period}}$	0.15	[13]
μ	The Rate of natural death	0.015	[13]
b	The Rate at which the infected become susceptible again	0.025	[13]
c	The Rate at which the exposed become susceptible again	0.35	[13]
h	The Rate at which the infected human to be isolated	0.35	Assumed
p	The Efficacy of vaccination	0.2	[13]
q	The Proportion of vaccination	0.2	[13]
d	The Rate of recovery from isolated	0.5	[13]
e	The Rate at which the isolated become susceptible again	0.35	[13]

3. Main Results

3.1 Partial Rank Corellation Coefficient (PRCC)

We analyzed the global sensitivity analysis of the model. We used the Latin Hypercube Sampling (LHS) to take samples from each partition evenly and Partial Rank Correlation Coefficient (PRCC) to determine the most significant and sensitive parameters of the model [14-16]. This method shows the correlation between parameters and compartments, it could be a positive or a negative correlation. $(-1,1)$. A positive correlation indicates that each parameter increases, the compartment will also increase, otherwise for a negative correlation The result of sensitivity analysis for all parameters to the infected population is given in FIGURE 2 below.

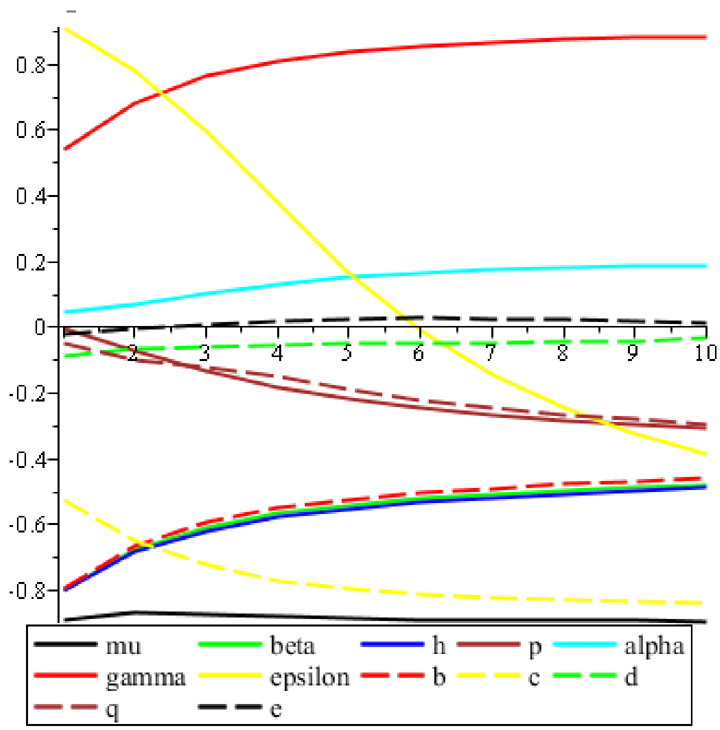

FIGURE 2. Partial Rank Corellation Coefficient

The most sensitve parameters are rate of isolation (h), rate of recovery (β), and rate of infection(γ). We can conclude that isolation is an effective intervention to reduce COVID-19 transmission. Recovery rate (β) is also one of the most sensitive parameter, optimal control i.e. treatment can be applied to this parameter to minimize the infected population. Whereas, we used model (1) to analyze the spreading of COVID-19 in West Java by using daily cases of COVID-19 data from pikobar.jabarprov.go.id which is processed into infection rate(γ) with poisson process.

3.2 Daily Cases of COVID-19 in West Java

Daily Positive confirmation data for COVID-19 in West Java from 19th of June 2021 to 16th of August 2021 can be seen in FIGURE 3 below.

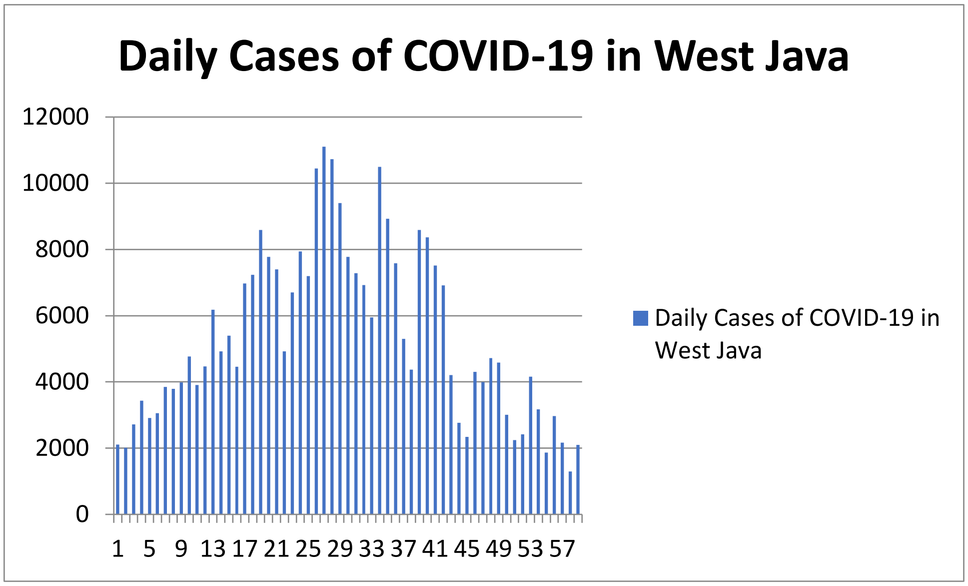

FIGURE 3. Daily Cases of COVID-19 in West Java from 19th of June 2021 to 16th of August 2021

The Indonesian government imposed social restrictions to minimize the daily cases of COVID-19 in Indonesia in several stages, two of the latest are *"PPKM Darurat"* and *"PPKM 4 level"*. The effect of social restriction to daily cases of COVID-19 can be seen in the Table 2 below:

Table 2. Effect of social restriction to daily cases of COVID-19

Enforcement of Social Restriction	West Java		
	2 Weeks Before Enforcement	Time of Enforcement	2 Weeks After Enforcement
PPKM Darurat (3rd – 25th July 2021)	Increasing Cases	Increasing Cases then Decreasing Cases	Decreasing Cases
PPKM 4 Level (26th July – 2nd August 2021)	Increasing then Decreasing Cases	Decreasing Cases	Decreasing Cases

From Table 2. We know that the enforcement of social restriction by The Indonesian Government is effective to reduce daily cases of COVID-19 in West Java. When the cases increase, the policy is PPKM Darurat which is the highest level. Then, the cases started to decrease, the regulations can be relaxed to a lower level so it changed to PPKM 4 level. PRCC shows that the isolation rate (h) is a very influental parameter to the model. We can conclude that the enforcement of social restriction is on point considering the data and PRCC of the model.

The number of COVID-19 cases based on data of Daily cases of COVID-19 in West Java from 19th June 2021 to 16th August 2021. Therefore, It can be analyzed by using poisson process with rate (λ) which is time dependant [17-19]. Assume $t = (0{,}59]$, We can estimated the infection rate (β) and the recovery rate (γ). Daily cases of COVID-19 can be seen as the Poisson process with the rate $(\lambda_1) = 5{,}367$ people per day [18]. By dividing λ_1 with the total population of West Java, we have the infection rate $(\gamma = 0.0001075)$. Daily recovery cases of COVID-19 can be seen as the Poisson process with the rate $(\lambda_2) = 4{,}652$ people per day [20]. By dividing λ_2 with the total population of the infected (assume including the exposed and the isolated population) in West Java, we have the recovery rate $(\beta = 0.0147)$.

3.3 Optimal Control of COVID-19 Model with Waning Immunity

The optimal control of the covid-19 transmission model is to obtain a policy which is a treatment to the infected population and isolated population. The constant treatment parameter value u and v are assumed to be the control $u(t)$ and $v(t)$ that will be determined optimally. The purpose is to minimize the infeced population $I(t)$ and isolated population $Q(t)$ by adding control variable $u(t)$ and $v(t)$. Performance index function as follow :

(2) $$J(u,v) = \int_0^{t_f} (TI + Uv^2 + BQ + Au^2)dt$$

with $0 \le t \le t_f, 0 \le u \le 1$ and $0 \le v \le 1$.

$s.t$

(3) $$\frac{dS}{dt} = \mu - \gamma S(t)\big(E(t) + I(t)\big) + cE(t) + bI(t) + \alpha R(t) + eQ - \mu S(t) - pqS(\mathrm{t})$$

(4) $$\frac{dE}{dt} = \gamma S(t)\big(E(t) + I(t)\big) - (c + \varepsilon + \mu)E(t)$$

(5) $$\frac{dI}{dt} = \varepsilon E(t) - (v(t)\beta + b + \mu + h)I(t)$$

(6) $$\frac{dQ}{dt} = hI(t) - (\mu + u(t)d + e)Q(t)$$

(7) $$\frac{dR}{dt} = v(t)\beta I(t) - (\alpha + \mu)R(t) + pqS(t) + u(t)dQ(t)$$

where $S(t) \ge 0, E(t) \ge 0, I(t) \ge 0, Q(t) \ge 0, R(t) \ge 0,\ 0 \le t \le t_f, 0 \le u \le 1$ and $0 \le v \le 1$.

T and B are the weight of the infected and the isolated population, respectively. U and A are he cost of treatments on the performance index function.

The Hamiltonian function for optimal control model as follow :

$$(8)\quad H = TI + Uv^2 + BQ + Au^2$$
$$+\lambda_1\big(\mu - \gamma S(t)\big(E(t) + I(t)\big) + cE(t) + bI(t) + \alpha R(t) + eQ - \mu S(t) - pqS(\mathrm{t})\big)$$
$$+\lambda_2\left(\gamma S(t)\big(E(t) + I(t)\big) - (c + \varepsilon + \mu)E(t)\right)$$
$$+\lambda_3\big(E(t) - (v(t)\beta + b + \mu + h)I(t)\big)$$
$$+\lambda_4(hI(t) - (\mu + u(t)d + e)Q(t))$$
$$+\lambda_5(v(t)\beta I(t) - (\alpha + \mu)R(t) + pqS(t) + u(t)dQ(t)\,)$$

where λ_i for $i = 1,2,\dots,5$ is adjoint variable for S, Q, E, I, R

The Co State equation of the control optimal model as follow :

$$(9)\quad \frac{d\lambda_1}{dt} = -\lambda_1(t)\big(-\gamma\big(E(t) + I(t)\big) - \mu - pq\big) - \lambda_2(t)\left(\gamma\big(E(t) + I(t)\big)\right) - \lambda_5(t)pq$$

$$(10)\frac{d\lambda_2}{dt} = -\lambda_1(t)(-\gamma S(t) - c) - \lambda_2(t)\big(\gamma S(t) - (c + \varepsilon + \mu)\big) - \lambda_3(t)\varepsilon$$

$$(11)\frac{d\lambda_3}{dt} = -T - \lambda_1(t)(-\gamma S(t) + b) - \lambda_2(t)\gamma S(t) - \lambda_3\big(-(v(t)\beta + b + \mu + h)\big)$$
$$-\lambda_4(t)h - \lambda_5(t)v(t)\beta$$

$$(12)\frac{d\lambda_4}{dt} = -B - \lambda_1(t)e - \lambda_4(t)(-(\mu + u(t)d + e) - \lambda_5(t)u(t)d$$

$$(13)\frac{d\lambda_5}{dt} = -\lambda_1(t)\alpha - \lambda_5(t)(-(\alpha + \mu))$$

by solving the optimal control model with $0 \le (u, v) \le 1$, we get u^* and v^* as shown below :

$$u^* = min\left\{1, max\left\{0, \frac{\lambda_4 dQ - \lambda_5 dQ}{2A}\right\}\right\}$$

$$v^* = min\left\{1, max\left\{0, \frac{\lambda_3 \beta I - \lambda_5 d\beta I}{2U}\right\}\right\}$$

3.3 Numerical Simulation

The purpose of this numerical simulation is to display the dynamics of the population which is divided into two cases. Case [i] is the dynamics of the population without control by setting $u^* =$

0 and $v^* = 0$. Case [ii] is the dynamics of the population with control where $0 < (u^*, v^*) \leq 1$ based on the value of the given parameters in Table 1 and initial values $S(0) = 0.6, E(0) = 0.1, I(0) = 0.05, Q(0) = 0.05$ and $R(0) = 0.2$. The result can be seen in Figure 5 below. Figure 6 show the treatment (u and v) that needs to be applied to the population will decrease over time.

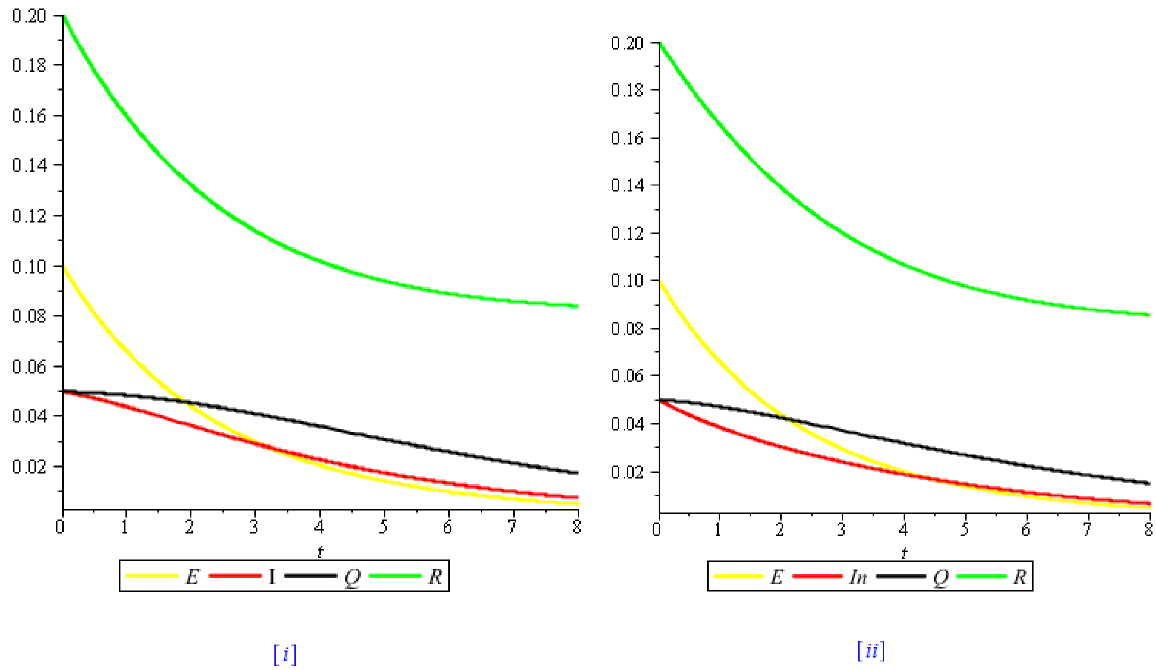

FIGURE 5. Population Dynamics without control [i] and with control [ii]

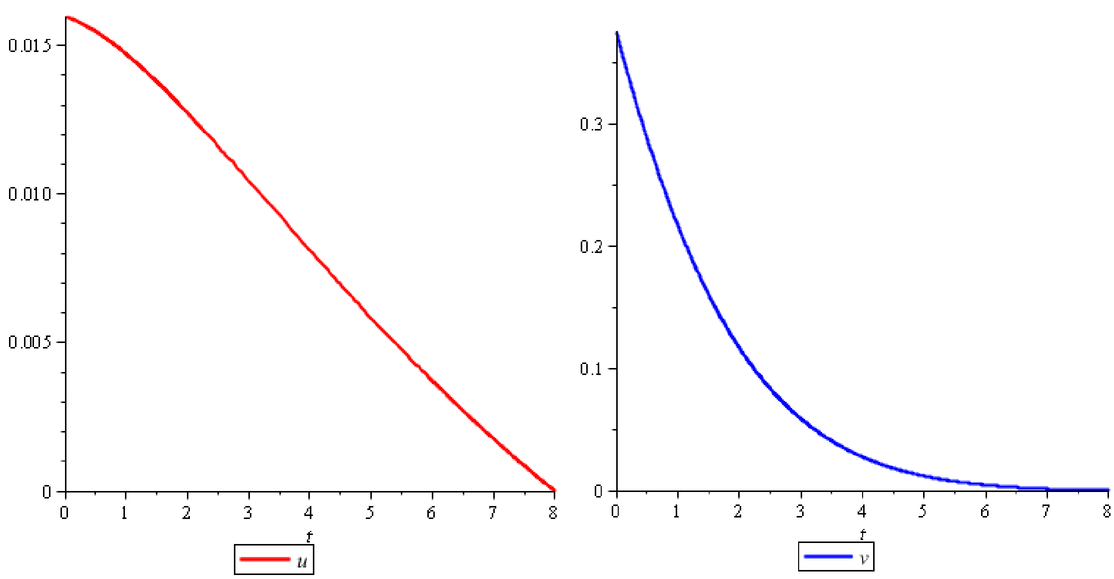

FIGURE 6. Optimal Control u^* and v^*

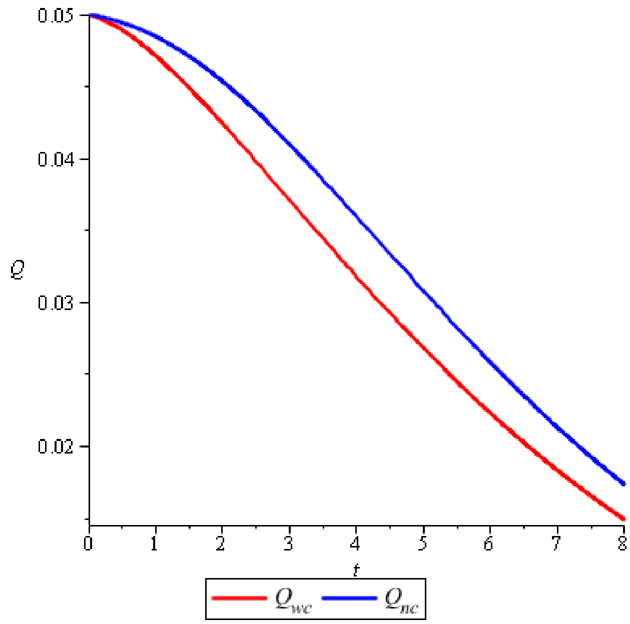

FIGURE 7. Isolated Population with without control (Q_{nc}) and control (Q_{wc})

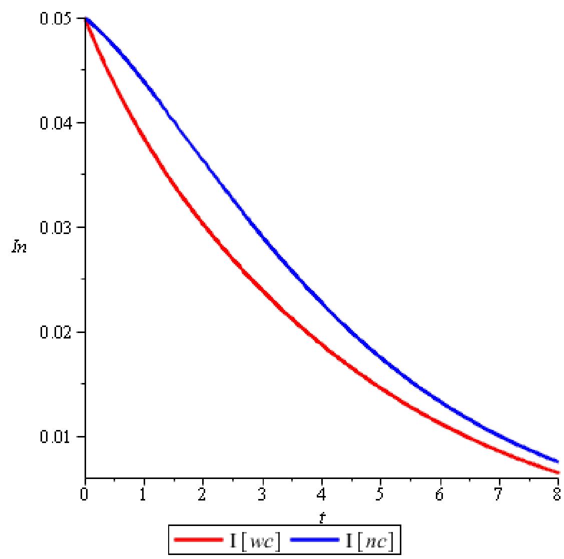

FIGURE 8. Infected Population without control (I_{nc}) and with control (I_{wc})

From Figure 7. and Figure 8. we can see that the isolated and the infected population is decreasing faster with optimal control u^* and v^*. It means, for these populations, treatment (control) is the recommended solution compared to waiting for human immunity to cure itself (without control) [21]. Even there is no certain cure for COVID-19, treatments for patient is a must especially patient with comorbidity i.e. Tuberculosis, Pneumonia, etc.

4. CONCLUSION

In this paper, we presented an SEIQR model of COVID-19 in the presence of waning immunity. Sensitivity analysis was done using Partial Rank Correlation Coefficient (PRCC) and optimal control in the form of treatment to the isolated and the infected populations is added accordingly. We used daily cases of COVID-19 data from pikobar.jabarprov.go.id to do the numerical simulation. From the data, we showed that the Indonesian government policy of social restriction is on point, this is supported by the result of the PRCC. The PRCC shows that the isolation rate (h), the infection rate (γ), and the recovery rate (β) are the most influental parameters (most sensitive) to the model. It can be concluded that optimal control in the form of treatment is effective and faster to decrease the spreading of COVID-19 than without any control.

ACKNOWLEDGMENTS

This research is supported and funded by Universitas Padjadjaran through Beasiswa Unggulan Pascasarjana Padjadjaran (BUPP) with contract number 1595/UN6.3.1/PT.00/2021. Also, the authors thank the reviewers for the valuable review of this paper.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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