5

Available online at http://scik.org Commun. Math. Biol. Neurosci. 2023, 2023:94 https://doi.org/10.28919/cmbn/8157 ISSN: 2052-2541

A PONTRYAGIN PRINCIPLE AND OPTIMAL CONTROL OF SPREADING COVID-19 WITH VACCINATION AND QUARANTINE SUBTYPE

LUKMAN HAKIM*

Department of Computer Science, Faculty of Technology and Design, Institute of Technology and Business Asia,

Malang, East Java, Indonesia

Copyright © 2023 the author(s). This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract: A mathematical model is a beautiful and powerful way to depict the condition of epidemiological disease transmission. In this work, we used a nonlinear differential equation to construct a mathematical model of COVID-19. Nonlinear differential equation illustrates the spread of COVID-19 disease incorporating the vaccinated and quarantined subpopulations. A compartment of a model of COVID-19 disease was carried out involving several control variables and several biological assumptions. Applying the control variables to a mathematical model is the prevention of direct contact between infected and susceptible subpopulations, a vaccination control process, and an intensive handling of infected and quarantined populations. In the next section, an investigation of the positivity and boundedness of the solution COVID-19 disease, and an analysis of the existence and uniqueness of the solution was carried out. Then, the existence of the control variables involved in the mathematical model that has been designed is demonstrated. Furthermore, by applying the Pontryagin Principle to determine the optimal conditions and best values for each control variable that holds on. On the other hand, in addition to the mathematical analysis result, provides numerical simulations using MATLAB software as one of the steps in describing the behavior of the dynamical solution or the phase portrait. Finally, the last section shows that the optimal control

^{*}Corresponding author

E-mail address: bledeklukman@gmail.com

Received July 30, 2023

condition carried out is able to reduce the density of infected and quarantined subpopulations, respectively. Hence, it is in line with the functional objective that has been constructed.

Keywords: epidemiological model; COVID-19; vaccination; quarantined; optimal control; pontryagin principle.2020 AMS Subject Classification: 34A12, 49J30, 92D25, 93A30.

1. INTRODUCTION

A specific destructive disease has been shocked humans around the world near the end of 2019 i.e. COVID-19 disease, and it is an illness caused by the SARS-CoV-2 virus that primarily touches the human pulmonary chronic infection [1], [2]. In general, the cases are spread by droplets on an object or individual between one and two meters away, as well as through coughing and sneezing [3]. In most incidences, the virus induces relatively minor to serious respiratory transmittal, such as influenza, and clears up on its own. On the other hand, the virus causes serious respiratory disorders such as lung disease (pneumonia) and potentially death [4]. In addition, this illness affects the public health care mechanism, and human mobilizations, and slows the growth of developing country economies [5].

The Biggest Health Organization in the world reports that the Coronavirus or COVID-19 disease was found in China (Wuhan) on 31 December 2019. Furthermore, on March 11, 2020, the Health Organization revealed that COVID-19 had infected around 118,000 people worldwide, spanning across 114 countries [6]. Then, on October 5, 2021, the total number of confirmed positive cases was seriously around 4.221.610 people, including 142.338 deaths. The mortality rate for COVID-19 is around 3.37% [7]. On the other side, on March 2, 2020, the Indonesian government recognized the first incidence of COVID-19, involving two Indonesians who tested positive for Coronavirus [6]. Unfortunately, the illness will continue to spread over the whole world, as in influenza, cancer, and hepatitis, etc. Further, WHO has categorized COVID-19 as a global disease.

COVID-19 has placed a tremendous strain on nations all around the world, and many countries are looking for ways to manage and safeguard their humans while maintaining the economic

SPREADING COVID-19 WITH VACCINATION AND QUARANTINE SUBTYPE

stability. Various western ways, traditional ways, and home treatments may ease or diminish COVID-19 symptoms, and especially result from research no particular drug or medicine has been suggested to prevent COVID-19 [7]. Despite the fact, by recalling Indonesian government, several strategies for managing the transmission of COVID-19 in Indonesia are being implemented, such as wearing masks, washing hands periodically, staying away from crowds, keeping a distance, and limiting contact and mobility [6], [8]. With respect to Wuhan, the government has proposed an isolation strategy or quarantine for infected persons, perhaps to reduce interaction between the infected subtype and the people public [9]. Many countries all across the world, adopt quarantine regulations [10], [11]. Several clinical studies on both Western and traditional techniques are now underway. Health organizations in the world maintain to coordinate several vaccine developments works for COVID-19 and to offer the goal. Several COVID-19 vaccines have been produced and tested by some companies, such as Sinovac, Moderna, AstraZeneca, Pfizer, and Janssen [12], [13].

The other point of view, scientists and epidemiologists support to find a strategy by using a mathematical model approach. Several researchers have developed some models to examine the dynamic behavior and COVID-19 transmission, which could be useful in predicting to next disease or disease prevention. In fact, 1927, Kermack and McKendrick proposed the first epidemic model, the SIR compartment model [14]. This model is the basic conceptual model to establish of COVID-19 mathematical model, as deep research by Li et al [15], Awasthi [16], Mandal et al [17], Yang et al [18]. Additionally, some mathematical models have been established by Haq et al [5], Musafir et al [11], Ega et al [19], Ali et al [20], Khan et al [21] depend on isolation and quarantine strategies. To reduce the COVID-19 outbreak, the mathematical dynamic was specifically redesigned by including the usage of masks. The farther a systematical behavior model of COVID-19 with a vaccine effort in a compartment provides as a further resource[3], [5], [22]–[24].

As far as we can see from previously mentioned, the optimal control problem needs to be pursued to conduct some control. Utilizing optimal control principles to control the Ebola disease [25], [26], Malaria disease [27], Diabetes Meletus [28], Tuberculosis and HIV [29]–[31], and

Cervical Cancer Model [32]. Furthermore, optimal control was implemented in the control of Measles illness [33], [34], Type B of Hepatitis [35], Cholera disease [36], SARS-Cov-2 (COVID-19) [6], [37]–[39]. Based on earlier research, the optimal control theorem was used as an infection control tool. The objective of this study is to construct a modified model for predicting the dynamics of the COVID-19 epidemic with a control variable in a previous model [5], taking into consideration a variety of intervention scenarios that may offer insight into the best way to proceed to reduce the threat spread. This work's sections have been laid out as follows: The background and research introduction declared in Section 1, and Section 2 deal with some biological assumptions and construction models involving the control variable. The properties of the model are discussed in section 3, with part 3.1 about the nonnegativity and boundedness, then existence and uniqueness in part 3.2, respectively. Section 4 covers the characterization of the optimal control condition. This part is broken into two sub-chapters i.e. objective function, and the Hamiltonian function. Section 5, on the other hand, examines a numerical and its interpretation of the model. Finally, the last Section 6 we offer about final remarks and conclusion.

2. ASSUMPTIONS AND CONSTRUCTION OF THE EPIDEMIC MODEL WITH CONTROL

According to the biological assumptions, we formulated a compartment model of COVID-19 by recalling the model of COVID-19 given by Haq et al [5]. Then, for controlling the COVID-19 disease, we reconstruction the model that developed by Haq et al [5] with several control variables, namely:

- 1. Control variable $u_1(t)$ is the education and effort of direct control between susceptible populations with infected and exposed subpopulations.
- 2. Control variable $u_2(t)$ is a vaccination effort into susceptible subpopulations S(t).
- 3. Control variable $u_3(t)$ is a treatment for exposed subpopulations E(t) by giving extra medicine, vitamins, and food to prevent exposed subpopulations from becoming infected subpopulations.

4. Control variable $u_4(t)$ is a treatment effort into infected subpopulations I(t) by using extra medicine, vitamins, and food to speed up healing an infection process.

Based on the descriptions and assumptions of the control variable above, we have the deterministic system model with some controls given by

$$\frac{dS(t)}{dt} = (1 - \delta)\tau - (\mu + \theta)S(t) - (1 - u_1(t))\beta S(t)(E(t) + I(t)) - u_2(t)S(t)
\frac{dV(t)}{dt} = \delta\tau + \theta S(t) - (\gamma + \mu)V(t) + u_2(t)S(t)
\frac{dE(t)}{dt} = (1 - u_1(t))\beta S(t)(E(t) + I(t)) + \gamma V(t) - (\mu + \alpha + \pi)E(t) - u_3(t)E(t)
\frac{dI(t)}{dt} = \pi E(t) - (\omega + \mu)I(t) - u_4(t)I(t)
\frac{dQ(t)}{dt} = \alpha E(t) + \omega I(t) - (\eta + \mu)Q(t)
\frac{dR(t)}{dt} = \eta Q(t) - \mu R(t) + u_3(t)E(t) + u_4(t)I(t),$$
(1)

the total populations N(t) = S(t) + V(t) + E(t) + I(t) + Q(t) + R(t), and the control variables in domain $\mathcal{U} = \{u_i: 0 \le u_i \le 1, i = 1,2,3,4\}$. The variable S(t) describes the density of the susceptible subpopulation in time and this class who are at risk of infection. Variable E(t) interpret the density of the vaccinated subpopulation. E(t) is a subpopulation that has been infected by the COVID-19 virus but does not seem a hazardous infection and is well-known by exposed populations. I(t) figure the density of the infected subpopulation, i.e. humans who have the hazardous infection and symptoms of the disease. Variable Q(t) and R(t) represent the size of the quarantine subpopulation, and the last variable is declared as a subpopulation that is fully healthy and recovered from COVID-19 infection respectively. The positive parameters of systems (1) are explained in the Table 1.

Parameter	Description	Value	Source
τ	A recruitment rate of susceptible subpopulation	1,5	Assumed
δ	Proportions of recruitment rate	1/40	[40]
μ	The natural mortality rate	0,0991	[40]
θ	The vaccination rate	0,4	[5]
β	The contact rate of susceptible with infected or exposed subpopulation	0,25	Assumed
γ	A vaccination subpopulation rate becomes exposed	0,3002	[40]
α	The quarantine rate of exposed subpopulation	0,2	[40]
π	An infected rate	0,1	Assumed
ω	The quarantine rate of infected subpopulation	0,05	Assumed
η	Recovery rate	1/14	[41]

Table 1. Parameters Interpretation

3. PROPERTIES OF THE MATHEMATICAL MODEL WITH CONTROL VARIABLE

3.1 Positivity and Boundedness Condition Of Solution

In this passage, we will indicate the non-negativity and boundedness of the solutions toward the model (1), and for declaring that the model is most impactfully.

Theorem 1. *The set* W *is the invariant manifold of model (1), and is ultimately bounded.*

Proof. The total populations N(t) = S(t) + V(t) + E(t) + I(t) + Q(t) + R(t), and it is satisfying

$$\frac{dN(t)}{dt} = \frac{dS(t)}{dt} + \frac{dV(t)}{dt} + \frac{dE(t)}{dt} + \frac{dI(t)}{dt} + \frac{dQ(t)}{dt} + \frac{dR(t)}{dt}.$$
(2)

Then, by substituting equations (1) in equation (2) gives

$$\frac{dN(t)}{dt} = (1 - \delta)\tau - (\mu + \theta)S(t) - (1 - u_1(t))\beta S(t)(E(t) + I(t)) - u_2(t)S(t)
+ \delta\tau + \theta S(t) - (\gamma + \mu)V(t) + u_2(t)S(t)
+ (1 - u_1(t))\beta S(t)(E(t) + I(t)) + \gamma V(t) - (\mu + \alpha + \pi)E(t)
- u_3(t)E(t) + \pi E(t) - (\omega + \mu)I(t) - u_4(t)I(t) + \alpha E(t) + \omega I(t)
- (\eta + \mu)Q(t) + \eta Q(t) - \mu R(t) + u_3(t)E(t) + u_4(t)I(t).$$
(3)

By operating simple algebra, we have

$$\frac{dN(t)}{dt} = \tau - \mu \big(S(t) + V(t) + E(t) + I(t) + Q(t) + R(t) \big). \tag{4}$$

Since S(t) + V(t) + E(t) + I(t) + Q(t) + R(t) = N(t), we obtain

$$\frac{dN(t)}{dt} = \tau - \mu N(t).$$
(5)

After rearranging equation (5), we get the first-order linear ordinary differential equation i.e.

$$\frac{dN(t)}{dt} + \mu N(t) = \tau.$$
(6)

It is obvious to solve equation (6), through integrating factors we have the solution form as

$$N(t) = \frac{\tau}{\mu} + K e^{-\mu t},\tag{7}$$

where K is constant, and by taking t = 0, we have $N(0) = \frac{\tau}{\mu} + K$. Therefore,

$$K = N(0) - \frac{\tau}{\mu}.$$
(8)

Applying the value of *K* into equation (7), the solutions of equation (6) with the initial condition is

$$N(t) = \frac{\tau}{\mu} + \left(N(0) - \frac{\tau}{\mu}\right)e^{-\mu t}.$$
(9)

It is clear that $\lim_{t\to\infty} N(t) = \frac{\tau}{\mu}$, and thus N(t) is bounded with value $\frac{\tau}{\mu}$. Then we can conclude that all solutions in equation (1) are in line with the field

$$\mathcal{W} = \left\{ (S, V, E, I, Q, R) \in \mathbb{R}_+^6 : 0 \le N \le \frac{\tau}{\mu} \right\},\$$

with
$$S(0), V(0), E(0), I(0), R(0) \in \mathcal{W}$$

Theorem 2. If the initial conditions $S(0), V(0), E(0), I(0), R(0) \ge 0 \in W$, the general solutions of the equation (1) are positive values.

Proof. It is obvious to represent that all solutions of the equation (1) are non-negative values

$$\begin{split} \left. \frac{dS(t)}{dt} \right|_{S=0} &= (1-\delta)\tau > 0, \quad \left. \frac{dV(t)}{dt} \right|_{V=0} = \delta\tau + \left(\theta + u_2(t)\right)S(t) > 0\\ \left. \frac{dE(t)}{dt} \right|_{E=0} &= \left(1 - u_1(t)\right)\beta I(t) + \gamma V(t) \ge 0, \quad \left. \frac{dI(t)}{dt} \right|_{I=0} = \pi E(t) \ge 0\\ \left. \frac{dQ(t)}{dt} \right|_{Q=0} &= \alpha E(t) + \omega I(t) \ge 0, \quad \left. \frac{dR(t)}{dt} \right|_{R=0} = \eta Q(t) + u_3(t)E(t) + u_4(t)I(t) \ge 0, \end{split}$$

which summarizes all of the results as positive values.

3.2 Uniqueness and Existence Of Solution

In this passage, we present about the existence properties and uniqueness properties of the equation system (1). By recalling the equation (1) in the form other as

$$f_{S}(t,\psi) = (1-\delta)\tau - (\mu + \theta + (1-u_{1})\beta(E+I) + u_{2})S$$

$$f_{V}(t,\psi) = \delta\tau - (\gamma + \mu)V + (\theta + u_{2})S$$

$$f_{E}(t,\psi) = (1-u_{1})\beta SI + \gamma V + ((1-u_{1})\beta S - \mu - \alpha - \pi - u_{3})E$$

$$f_{I}(t,\psi) = \pi E - (\omega + \mu + u_{4})I$$

$$f_{Q}(t,\psi) = \alpha E + \omega I - (\eta + \mu)Q$$

$$f_{R}(t,\psi) = \eta Q - \mu R + u_{3}E + u_{4}I,$$
where $\psi = (S, V, E, I, Q, R).$
(10)

Theorem 3. Suppose that $f(t, \psi)$ holds the Lipschitz condition

$$|f(t,\psi_1) - f(t,\psi_2)| \le K |\psi_1 - \psi_2|,$$

with the pair (t, ψ_1) and (t, ψ_2) belong to the feasible region W, where K is a positive constant, such that exactly one solution (uniqueness).

 \cdot

·

Proof. Now, we provided the Lipschitz condition in system (1). Let, we start with the susceptible subpopulation of the system (10), and continue to other population classes.

$$\begin{aligned} \left| f(t,\psi_{S_1}) - f(t,\psi_{S_2}) \right| &= \left| (\mu + \theta + (1-u_1)\beta(E+I) + u_2)(S_2 - S_1) \right| \\ &= \left| \mu + \theta + (1-u_1)\beta(E+I) + u_2 \right| \left| S_2 - S_1 \right| \\ &\leq (\left| \mu \right| + \left| \theta \right| + \left| (1-u_1)\beta E + (1-u_1)\beta I \right| + \left| u_2 \right| \right) \left| S_1 - S_2 \right| \\ &\leq \left(\mu + \theta + (1-u_1)\beta \sup_{t \in D_S} \left| E \right| + (1-u_1)\beta \sup_{t \in D_S} \left| I \right| + u_2 \right) \left| S_1 - S_2 \right| \\ &\leq (\mu + \theta + (1-u_1)\beta M_E + (1-u_1)\beta M_I + u_2) \left| S_1 - S_2 \right| \\ &\leq K_S |S_1 - S_2|, \end{aligned}$$

where $K_S = (\mu + \theta + (1 - u_1)\beta M_E + (1 - u_1)\beta M_I + u_2)$. Furthermore, analogous to the same way in the susceptible subtype, we describe the Lipchitz condition to other subpopulations, as below:

$$|f(t, \psi_{V_1}) - f(t, \psi_{V_2})| = |(\gamma + \mu)(V_2 - V_1)|$$

= $|\gamma + \mu||V_2 - V_1|$
 $\leq (\gamma + \mu)|V_1 - V_2|$
 $\leq K_V|V_1 - V_2|$

where $K_V = (\gamma + \mu)$.

$$\begin{aligned} \left| f(t,\psi_{E_1}) - f(t,\psi_{E_2}) \right| &= \left| \left((1-u_1)\beta S - \mu - \alpha - \pi - u_3 \right) (E_1 - E_2) \right| \\ &= \left| (1-u_1)\beta S - \mu - \alpha - \pi - u_3 \right| |E_1 - E_2| \\ &\leq \left(\left| (1-u_1)\beta S \right| + |\mu| + |\alpha| + |\pi| + |u_3| \right) |E_1 - E_2| \\ &\leq \left((1-u_1)\beta \sup_{t \in D_E} |S| + \mu + \alpha + \pi + u_3 \right) |E_1 - E_2| \\ &\leq \left((1-u_1)\beta M_S + \mu + \alpha + \pi + u_3 \right) |E_1 - E_2| \\ &\leq K_E |E_1 - E_2|, \end{aligned}$$

where $K_E = ((1 - u_1)\beta M_S + \mu + \alpha + \pi + u_3).$

$$\begin{aligned} \left| f(t, \psi_{I_1}) - f(t, \psi_{I_2}) \right| &= \left| (\omega + \mu + u_4) (I_2 - I_1) \right| \\ &= \left| \omega + \mu + u_4 \right| |I_2 - I_1| \\ &\leq (\omega + \mu + u_4) |I_1 - I_2| \\ &\leq K_I |S_1 - S_2|, \end{aligned}$$

where $K_I = (\omega + \mu + u_4)$.

$$\begin{aligned} \left| f(t,\psi_{Q_1}) - f(t,\psi_{Q_2}) \right| &= \left| (\eta + \mu)(Q_2 - Q_1) \right| \\ &= \left| (\eta + \mu) \right| |Q_2 - Q_1| \\ &\leq (\eta + \mu) |Q_1 - Q_2| \\ &\leq K_Q |Q_1 - Q_2|, \end{aligned}$$

where $K_Q = (\eta + \mu)$.

$$|f(t, \psi_{R_1}) - f(t, \psi_{R_2})| = |\mu(R_2 - R_1)|$$

$$\leq \mu |R_1 - R_2|$$

$$\leq K_R |R_1 - R_2|,$$

where $K_R = \mu$. Therefore, system (1) holds on to the Lipchitz conditions, and thus model admits a unique solution.

Theorem 4. Suppose that $f(t, \psi)$ has a continuous partial derivative and satisfies a Lipschitz condition such that there exists a solution of the system that is bounded.

Proof. By taking the right side of the system (10), then obvious that $\frac{\partial f_i}{\partial \psi_j}$ is continuous and $\left|\frac{\partial f_i}{\partial \psi_j}\right| < \infty$, with the set i, j = S, V, E, I, Q, R. From the susceptible class equation, we have the partial derivate as follows,

$$\frac{\partial f_S}{\partial S} = -(\mu + \theta) - (1 - u_1)\beta(E + I) - u_2, \text{ then}$$
$$\left|\frac{\partial f_S}{\partial S}\right| = \left|-(\mu + \theta) - (1 - u_1)\beta(E + I) - u_2\right| < \infty.$$

$$\begin{split} \frac{\partial f_V}{\partial V} &= -(\gamma + \mu), \text{then} \quad \left| \frac{\partial f_V}{\partial V} \right| = \left| -(\gamma + \mu) \right| < \infty. \\ \frac{\partial f_E}{\partial E} &= (1 - u_1)\beta I - (\mu + \alpha + \pi) - u_3, \text{then} \\ \left| \frac{\partial f_E}{\partial E} \right| &= \left| (1 - u_1)\beta I - (\mu + \alpha + \pi) - u_3 \right| < \infty. \\ \frac{\partial f_I}{\partial I} &= -(\omega + \mu + u_4), \text{then} \quad \left| \frac{\partial f_I}{\partial I} \right| = \left| -(\omega + \mu + u_4) \right| < \infty. \\ \frac{\partial f_Q}{\partial Q} &= -(\eta + \mu), \text{then} \quad \left| \frac{\partial f_Q}{\partial Q} \right| = \left| -(\eta + \mu) \right| < \infty. \quad \frac{\partial f_R}{\partial R} = -\mu, \text{then} \left| \frac{\partial f_R}{\partial R} \right| = \left| -\mu \right| < \infty. \end{split}$$

Then, analogous to the above in susceptible subpopulations, we obtain that all systems (10) are continuous and bounded.

4. CHARACTERIZATION OF OPTIMAL CONTROL PROBLEMS

4.1 The Functional Objective

The goal of control characteristic is to be carried out with the best value criteria of the model (1). Then the following section, we elaborate on an optimum control condition to figure out by using the minimum functional objective, such that

$$J(u_{1}(t), u_{2}(t), u_{3}(t), u_{4}(t)) = \int_{t_{0}}^{t_{f}} (E(t) + I(t) + C_{1}u_{1}^{2}(t) + C_{2}u_{2}^{2}(t) + C_{3}u_{3}^{2}(t) + C_{4}u_{4}^{2}(t))dt.$$
(11)

Thus, functional objective equations were created to minimize the exposed and infected subpopulation. While the parameters C_1 , C_2 , C_3 , and C_4 represent the weight of the effort required to implement the control process. By recalling all nonnegative parameters in a functional objective, we derive the best control $u_1^*(t)$, $u_2^*(t)$, $u_3^*(t)$, and $u_4^*(t)$ such that:

$$J(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)) = \min\{J(u_1(t), u_2(t), u_3(t), (t), u_4(t))\},$$
(12)

where the $u_i(t) \in U$, $i = 1, 2, 3, 4, t = [t_0, t_f]$ and the regard domain is

$$\mathcal{U} = \{ (u_i(t)) | 0 \le u_i(t) \le 1, i = 1, 2, 3, 4 \}.$$

Therefore, we have an existence condition of control problem (3) in the system (1), provided by the succeeding theorem.

Theorem 5. Suppose any control variable $\mathcal{U} = (u_1(t), u_2(t), u_3(t), (t), u_4(t))$ exists in the system (1), such that the following term is hold

$$\min_{u \in \mathcal{U}} J(u_1(t), u_2(t), u_3(t), (t), u_4(t)) = J(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t))$$

Proof. Based on the analysis in [42], [43], we determine that the optimal control will exist in the system (1), if several conditions below are satisfied.

1. The control \mathcal{U} is not an empty set.

It is obvious, that giving control can realize the objective function. By using the contradiction proof, suppose we set the functional objective below

$$\max J(\vec{u}) = \int_{t_0}^{t_f} \left(E(t) + I(t) + C_1 u_1^2(t) + C_2 u_2^2(t) + C_3 u_3^2(t) + C_4 u_4^2(t) \right) dt.$$

It means that the goal of the objective function is to maximize the exposed and infected subpopulation. On the other side, we have that the range $t = [t_0, t_f]$ is bounded i.e. there is a process to restrain disease. Then, the control variable must be a minimum form

$$\min J(\vec{u}) = \int_{t_0}^{t_f} \left(E(t) + I(t) + C_1 u_1^2(t) + C_2 u_2^2(t) + C_3 u_3^2(t) + C_4 u_4^2(t) \right) dt,$$

and proved that control is not an empty set.

- 2. The set of control \mathcal{U} is convex and closed.
 - a. Let $u \in \mathcal{U}$, and $u' \in \mathcal{U}$, will be shown that $z = \theta u + (1 \theta)u' \in \mathcal{U}$, $\forall \theta \in [0,1]$. It is clear, if $\theta u \leq \theta$ and $(1 \theta)u' \leq (1 \theta)$, then we obtain $\theta u + (1 \theta)u' \leq \theta + (1 \theta) = 1$. Finally, obtained $0 \leq \theta u + (1 \theta)u' \leq 1$, $\forall u \in \mathcal{U}$, and $\forall \theta \in [0,1]$. Then, the set of control \mathcal{U} is a convex set.
 - b. Suppose the anything of control $u \notin [a, b]$, it means u < a or u > b. Now, if u < a, then exist $\epsilon_u = |u a| > 0$, such that we have the intersection of the set and the neighborhood

of control is an empty set, $[a, b] \cap V_{\epsilon}(u) = \emptyset$. If u > ba, then exist $\epsilon_u = |u - b| > 0$, such that we get the intersection of the set and the neighborhood of control is an empty set, $[a, b] \cap V_{\epsilon}(u) = \emptyset$. So, the control u is a closed set, where $u \in \mathcal{U}$.

3. The right-hand equation of the systems (1) is bounded by some control design and linear function.

Based on the system (1), we manipulate to matrix form, namely

$$\begin{bmatrix} \frac{dS(t)}{dt} \\ \frac{dV(t)}{dt} \\ \frac{dE(t)}{dt} \\ \frac{dI(t)}{dt} \\ \frac{dQ(t)}{dt} \\ \frac{dQ(t)}{dt} \\ \frac{dQ(t)}{dt} \\ \frac{dR(t)}{dt} \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix} \begin{bmatrix} (\mu + \theta)S - \beta S(E + I) \\ \theta S - (\gamma + \mu)V \\ \beta S(E + I) + \gamma V - (\mu + \alpha + \pi)E \\ \pi E - (\omega + \mu)I \\ \alpha E + \omega I - (\eta + \mu)Q \\ \eta Q - \mu R \end{bmatrix} + \begin{bmatrix} u_1\beta S(E + I) - u_2S \\ u_2S \\ -u_1\beta S(E + I) - u_3E \\ u_4I \\ 0 \\ u_3E + u_4I \end{bmatrix} + \begin{bmatrix} (1 - \delta)\tau \\ \delta\tau \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

$$= \begin{bmatrix} \sigma & \sigma & \sigma \\ \theta & \sigma & \sigma \\ \beta & S(E+I) + \gamma & V \\ \pi & E & \sigma \\ \alpha & E + \omega & I \\ \eta & Q \end{bmatrix} - \begin{bmatrix} \alpha & \gamma & \gamma & \gamma & \gamma \\ (\gamma + \mu)V & \sigma \\ (\mu + \alpha + \pi)E & \sigma \\ (\omega + \mu)I & \sigma \\ (\eta + \mu)Q & \sigma \\ \mu & R \end{bmatrix} + \begin{bmatrix} \alpha_{1}\rho\sigma(E+I) & \sigma \\ u_{2}S & \sigma \\ 0 & \sigma \\ u_{4}I & \sigma \\ 0 & \sigma \\ u_{3}E + u_{4}I & \sigma \\ u_{3}E + u_{4}I & \sigma \\ 0 & \sigma \\ u_{3}E + u_{4}I & \sigma \\ 0 &$$

	Γ	μR		Ţ	L
	$\begin{bmatrix} u_2 \end{bmatrix}$	S]		$(1-\delta)\tau$	1
_	$u_2 S u_1 \beta S(E+I) + u_3 E$			$\delta \tau \\ 0$	
	C)	т	0	
	C)		0	
	LC) _		L 0 .]

$$< \begin{bmatrix} 0 \\ \theta S \\ \beta S(E+I) + \gamma V \\ \pi E \\ \alpha E + \omega I \\ \eta Q \end{bmatrix} + \begin{bmatrix} u_1 \beta S(E+I) \\ u_2 S \\ 0 \\ u_4 I \\ 0 \\ u_3 E + u_4 I \end{bmatrix} + \begin{bmatrix} (1-\delta)\tau \\ \delta\tau \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

$$\leq \begin{bmatrix} 0 \\ \theta S \\ \beta S(E+I) + \gamma V \\ \pi E \\ \alpha E + \omega I \\ \eta Q \end{bmatrix} + \begin{bmatrix} u_1 \beta S(E+I) \\ u_2 S \\ 0 \\ u_4 I \\ 0 \\ u_3 E + u_4 I \end{bmatrix} + \begin{bmatrix} (1-\delta)\tau \\ \delta \tau \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \leq \vec{M} = \begin{bmatrix} M_1 \\ M_2 \\ M_3 \\ M_4 \\ M_5 \\ M_6 \end{bmatrix}$$

Obvious that the right-part side of the system (1) is bounded by some control design and linear function.

4. The integrand of the functional objective is convex in region \mathcal{U}

Take any variable $u_i, v_j \in U$, with i, j = 1, 2, 3, 4, and interval of $0 \le \theta \le 1$. In this part, will be shown that

$$J((1-\theta)\vec{u}(t) + \theta\vec{v}(t)) \le (1-\theta)J(\vec{u}(t)) + \theta J(\vec{v}(t)),$$
(13)

with $\vec{u} = (u_1(t), u_2(t), u_3(t), u_4(t))^T$, and $\vec{v} = (v_1(t), v(t), v_3(t), v_4(t))^T$. Then, by implementing the objective function (11) into equation (13), such that

$$E(t) + I(t) + C_1 ((1 - \theta)u_1(t) + \theta v_1(t))^2 + C_2 ((1 - \theta)u_2(t) + \theta v_2(t))^2 + C_3 ((1 - \theta)u_3(t) + \theta v_3(t))^2 + C_4 ((1 - \theta)u_4(t) + \theta v_4(t))^2 \leq (1 - \theta) (E(t) + I(t) + C_1 u_1^2(t) + C_2 u_2^2(t) + C_3 u_3^2(t) + C_4 u_4^2(t)) + \theta (E(t) + I(t) + C_1 u_1^2(t) + C_2 u_2^2(t) + C_3 u_3^2(t) + C_4 u_4^2(t)).$$
(14)

Next, by operating and arranging the equation (14) that we have the detail and equivalent representation term

$$\begin{split} (1-\theta)C_1u_1^2(t) &+ \theta C_1v_1^2(t) - C_1(1-\theta)^2u_1^2(t) - 2C_1(1-\theta)\theta u_1(t)v_1(t) - C_1\theta^2v_1^2 \\ &+ (1-\theta)C_2u_2^2(t) + \theta C_2v_2^2(t) - C_2(1-\theta)^2u_2^2(t) \\ &- 2C_2(1-\theta)\theta u_2(t)v_2(t) - C_2\theta^2v_2^2 + (1-\theta)C_3u_3^2(t) + \theta C_3v_3^2(t) \\ &- C_3(1-\theta)^2u_3^2(t) - 2C_3(1-\theta)\theta u_3(t)v_3(t) - C_3\theta^2v_1^2 + (1-\theta)C_4u_4^2(t) \\ &+ \theta C_4v_4^2(t) - C_4(1-\theta)^2u_4^2(t) - 2C_4(1-\theta)\theta u_4(t)v_4(t) - C_4\theta^2v_4^2 \ge 0, \end{split}$$

$$\begin{aligned} \text{SPREADING COVID-19 WITH VACCINATION AND QUARANTINE SUBTYPE} \\ C_1 u_1^2(t) \Big((1-\theta) - (1-\theta)^2 \Big) + C_1 \theta v_1^2(t) (1-\theta) - 2C_1 (1-\theta) \theta u_1(t) v_1(t) \\ &+ C_2 u_2^2(t) \Big((1-\theta) - (1-\theta)^2 \Big) + C_2 \theta v_2^2(t) (1-\theta) \\ &- 2C_2 (1-\theta) \theta u_2(t) v_2(t) + C_3 u_3^2(t) \Big((1-\theta) - (1-\theta)^2 \Big) \\ &+ C_3 \theta v_3^2(t) (1-\theta) - 2C_3 (1-\theta) \theta u_3(t) v_3(t) \\ &+ C_4 u_4^2(t) \Big((1-\theta) - (1-\theta)^2 \Big) + C_4 \theta v_4^2(t) (1-\theta) \\ &- 2C_4 (1-\theta) \theta u_4(t) v_4(t) \ge 0, \\ C_1 \theta \Big((1-\theta) u_1^2(t) - 2(1-\theta) u_1(t) v_1(t) + (1-\theta) v_1^2(t) \Big) \\ &+ C_2 \theta \Big((1-\theta) u_2^2(t) - 2(1-\theta) u_2(t) v_2(t) + (1-\theta) v_2^2(t) \Big) \\ &+ C_3 \theta \Big((1-\theta) u_3^2(t) - 2(1-\theta) u_3(t) v_3(t) + (1-\theta) v_3^2(t) \Big) \\ &+ C_4 \theta \Big((1-\theta) u_4^2(t) - 2(1-\theta) u_4(t) v_4(t) + (1-\theta) v_4^2(t) \Big) \ge 0, \\ C_1 \theta \Big(\sqrt{(1-\theta)} u_1(t) - \sqrt{(1-\theta)} v_1(t) \Big)^2 + C_2 \theta \Big(\sqrt{(1-\theta)} u_2(t) - \sqrt{(1-\theta)} v_2(t) \Big)^2 \\ &+ C_3 \theta \Big(\sqrt{(1-\theta)} u_3(t) - \sqrt{(1-\theta)} v_3(t) \Big)^2 \\ &+ C_4 \theta \Big(\sqrt{(1-\theta)} u_4(t) - \sqrt{(1-\theta)} v_4(t) \Big)^2 \ge 0. \end{aligned}$$

Therefore, the integrand value of the functional objective is convexity.

5. The integrand of functional objectives is bounded

If there are parameters $\xi_1 > C_1$, $\xi_2 > C_2$, $\xi_3 > C_3$, $\xi_4 > C_4$, and variable E(t), I(t) bounded by the interval $[t_0, t_f]$, such that we have the size of exposed population $E(t) \le E(t_f)$, and $I(t) \le I(t_f)$. Hence, the objective function (11),

$$\begin{split} &E(t) + I(t) + C_1 u_1^2(t) + C_2 u_2^2(t) + C_3 u_3^2(t) + C_4 u_4^2(t) \\ &\leq E(t_f) + I(t_f) + \xi_1 u_1^2(t) + \xi_2 u_2^2(t) + \xi_3 u_3^2(t) + \xi_4 u_4^2(t) \\ &\leq E(t_f) + I(t_f) + \xi_1 |u_1^2|(t) + \xi_2 |u_2^2|(t) + \xi_3 |u_3^2|(t) + \xi_4 |u_4^2|(t) = \mathcal{M}. \end{split}$$

Then, obvious that the objective function bounded by the $\mathcal{M} = E(t_f) + I(t_f) + \xi_1 |u_1^2|(t) + \xi_2 |u_2^2|(t) + \xi_3 |u_3^2|(t) + \xi_4 |u_4^2|(t).$

4.2 The Hamiltonian Function

Pontryagin Minimum Principle leads to an optimal control condition, that the minimum principle brings out the system (1), (11), and (12), into a Hamiltonian model, as shown below:

$$H = E(t) + I(t) + C_{1}u_{1}^{2}(t) + C_{2}u_{2}^{2}(t) + C_{3}u_{3}^{2}(t) + C_{4}u_{4}^{2}(t) + \lambda_{S} \left((1 - \delta)\tau - (\mu + \theta)S(t) - (1 - u_{1}(t))\beta S(t)(E(t) + I(t)) - u_{2}(t)S(t) \right) + \lambda_{V} \left(\delta\tau + \theta S(t) - (\gamma + \mu)V(t) + u_{2}(t)S(t) \right) + \lambda_{E} \left((1 - u_{1}(t))\beta S(t)(E(t) + I(t)) + \gamma V(t) - (\mu + \alpha + \pi)E(t) \right)$$
(15)
$$- u_{3}(t)E(t) + \lambda_{I} \left(\pi E(t) - (\omega + \mu)I(t) - u_{4}(t)I(t) \right) + \lambda_{Q} \left(\alpha E(t) + \omega I(t) - (\eta + \mu)Q(t) \right) + \lambda_{R} \left(\eta Q(t) - \mu R(t) + u_{3}(t)E(t) + u_{4}(t)I(t) \right),$$

and some costate (adjoint) variables denoted by λ_S , λ_V , λ_E , λ_I , λ_Q , λ_R . Hence, the optimal control theorem is figured by using Pontryagin's Minimum Principle, which is denoted by the following theorem.

Theorem 6. If any control $u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t), u_5^*(t)$ exist, and the well solution of $S^*(t), V^*(t), E^*(t), I^*(t), Q^*(t), R^*(t)$ holds on the autonomous system (1), that reduces $J(u_1(t), u_2(t), u_3(t), u_4(t))$ in U. Therefore, the adjoint (costate) variables $\lambda_S, \lambda_V, \lambda_E, \lambda_I, \lambda_Q, \lambda_R$ exist and all the variables satisfy the equations system,

$$\frac{d\lambda_S}{dt} = \lambda_S \left(\mu + \theta + (1 - u_1(t))\beta(E(t) + I(t)) + u_2(t)) - \lambda_V (\theta + u_2(t)) - \lambda_E \left((1 - u_1(t))\beta(E(t) + I(t)) \right) \right)$$

$$\frac{d\lambda_V}{dt} = \lambda_V (\gamma + \mu) - \lambda_E \gamma$$

$$\frac{d\lambda_E}{dt} = -1 + \lambda_S (1 - u_1(t))\beta S(t) - \lambda_E \left((1 - u_1(t))\beta S(t) - (\mu + \alpha + \pi) - u_3(t) \right) - \lambda_I \pi - \lambda_Q \alpha - \lambda_R u_3(t)$$
(16)

$$\begin{aligned} \frac{d\lambda_I}{dt} &= -1 + \lambda_S \big(1 - u_1(t) \big) \beta S(t) - \lambda_E \big(1 - u_1(t) \big) \beta S(t) + \lambda_I \big(\omega + \mu + u_4(t) \big) - \lambda_Q \omega \\ &- \lambda_R u_4(t) \end{aligned}$$
$$\begin{aligned} \frac{d\lambda_Q}{dt} &= \lambda_Q (\eta + \mu) - \lambda_R \eta \\ \frac{d\lambda_R}{dt} &= \lambda_R \mu. \end{aligned}$$

Incorporate the transversality condition $\lambda_S(t_f) = \lambda_V(t_f) = \lambda_E(t_f) = \lambda_I(t_f) = \lambda_Q(t_f) = \lambda_R(t_f) = 0$, such that the best value of control sets $u_1^*(t), u_2^*(t), u_3^*(t)$ and $u_4^*(t)$ are provided by

$$u_{1}^{*}(t) = \min\left\{\max\left(0, \frac{(\lambda_{E} - \lambda_{S})\beta S(t)(E(t) + I(t))}{2C_{1}}\right), 1\right\}$$

$$u_{2}^{*}(t) = \min\left\{\max\left(0, \frac{(\lambda_{S} - \lambda_{V})S(t)}{2C_{2}}\right), 1\right\}$$

$$u_{3}^{*}(t) = \min\left\{\max\left(0, \frac{(\lambda_{E} - \lambda_{R})E(t)}{2C_{3}}\right), 1\right\}$$

$$u_{3}^{*}(t) = \min\left\{\max\left(0, \frac{(\lambda_{I} - \lambda_{R})I(t)}{2C_{4}}\right), 1\right\}$$
(17)

Proof: According to the convexity theorem of functional objective $J(u_1(t), u_2(t), u_3(t), u_4(t))$ and involved into Lipschitz criteria of the state autonomous system. Working through Pontryagin's Minimum Principle, we can examine for the existence condition of an optimum control. The costate variables are achieved by differentiating the Hamiltonian function toward the state variable, and the autonomous system is directly identified below.

$$\begin{aligned} \frac{d\lambda_S}{dt} &= \lambda_S \big(\mu + \theta + \big(1 - u_1(t) \big) \beta \big(E(t) + I(t) \big) + u_2(t) \big) - \lambda_V \big(\theta + u_2(t) \big) \\ &- \lambda_E \left(\big(1 - u_1(t) \big) \beta \big(E(t) + I(t) \big) \big) \right) \\ \frac{d\lambda_V}{dt} &= \lambda_V (\gamma + \mu) - \lambda_E \gamma \\ \frac{d\lambda_E}{dt} &= -1 + \lambda_S \big(1 - u_1(t) \big) \beta S(t) - \lambda_E \left(\big(1 - u_1(t) \big) \beta S(t) - (\mu + \alpha + \pi) - u_3(t) \big) - \lambda_I \pi \end{aligned}$$

 $-\lambda_0 \alpha - \lambda_R u_3(t)$

$$\frac{d\lambda_I}{dt} = -1 + \lambda_S (1 - u_1(t)) \beta S(t) - \lambda_E (1 - u_1(t)) \beta S(t) + \lambda_I (\omega + \mu + u_4(t)) - \lambda_Q \omega$$
$$-\lambda_R u_4(t)$$
$$\frac{d\lambda_Q}{dt} = \lambda_Q (\eta + \mu) - \lambda_R \eta$$
$$\frac{d\lambda_R}{dt} = \lambda_R \mu.$$
with the condition transfer $\lambda_S (t_f) = \lambda_V (t_f) = \lambda_E (t_f) = \lambda_I (t_f) = \lambda_Q (t_f) = \lambda_R (t_f)$

with the condition transfer $\lambda_S(t_f) = \lambda_V(t_f) = \lambda_E(t_f) = \lambda_I(t_f) = \lambda_Q(t_f) = \lambda_R(t_f) = 0$. Further step is an optimal control can be shown by differentiating of Hamiltonian toward the control variables, and calculating the outcome to be zero, such that

$$\begin{aligned} \frac{\partial H}{\partial u_1(t)} &= 2C_1 u_1(t) + \lambda_S \beta S(t) \big(E(t) + I(t) \big) - \lambda_E \beta S(t) \big(E(t) + I(t) \big) = 0 \\ \frac{\partial H}{\partial u_2(t)} &= 2C_2 u_2(t) - \lambda_S S(t) + \lambda_V S(t) = 0 \\ \frac{\partial H}{\partial u_3(t)} &= 2C_3 u_3(t) - \lambda_E E(t) + \lambda_R E(t) = 0 \\ \frac{\partial H}{\partial u_4(t)} &= 2C_4 u_4(t) - \lambda_I I(t) + \lambda_R I(t) = 0. \end{aligned}$$

Consequently, it is clear that an optimization problem gives

$$\begin{split} u_1^*(t) &= \min\left\{\max\left(0, \frac{(\lambda_E - \lambda_S)\beta S(t) \left(E(t) + I(t)\right)}{2C_1}\right), 1\right\}\\ u_2^*(t) &= \min\left\{\max\left(0, \frac{(\lambda_S - \lambda_V)S(t)}{2C_2}\right), 1\right\}\\ u_3^*(t) &= \min\left\{\max\left(0, \frac{(\lambda_E - \lambda_R)E(t)}{2C_3}\right), 1\right\}\\ u_4^*(t) &= \min\left\{\max\left(0, \frac{(\lambda_I - \lambda_R)I(t)}{2C_4}\right), 1\right\}. \end{split}$$

5. NUMERICAL SIMULATIONS

To back up and confirm the analytical works of the optimum control theorem previously. Using the MATLAB program, we show a numerical of a system (2). In this passage, we perform the weight value for the functional objective are $C_1 = C_2 = C_3 = C_4 = 0,75$ and some initial condition values are S(0) = 10, V(0) = 2, E(0) = 2, I(0) = Q(0) = R(0) = 1. According to the parameter value in Table 1, we get the number of reproductions $R_0 = 653,81 > 1$, which indicates the spreading of COVID-19 will persist in a population. Hence, implementing an optimal control to reduce COVID-19 disease must be carried out to minimize the disease, and will be shown in some figures below by using the Runge Kutha method.



Figure 1. Dynamical solution of susceptible subpopulation (S) without control and with control



Figure 2. Dynamical solution of vaccination subpopulation (V) without control and with control

Figure 1 demonstrates the dynamical solutions of susceptible subpopulations without control and with some controls. We have seen in Figure 1 that the dynamical solution of susceptible without control has decreased from the beginning. Hence, the part of the susceptible subpopulation has changed into the exposed or infected population. On the other hand, applying the control $u_1(t)$, $u_2(t)$, $u_3(t)$, $u_4(t)$ and their combination can prevent the size of susceptible subpopulations. From the simulation, we know that the best control to prevent the susceptible is control $u_1(t)$ rates, namely the effort to handle the direct interaction between susceptible with the exposed and infected subpopulation is impactfully. Figure 2 illustrates the size transformation of the vaccinated subpopulation, according to the simulation, all of the controls can keep the density of the vaccinated subpopulation without applying control, and the best strategy was combining the all of control variables.



Figure 3. Dynamical solution of exposed subpopulation (E) without control and with control



Figure 4. Dynamical solution of infected subpopulation (1) without control and with control

In this part and based on Figure 3, we describe that the control variable seems good to reduce the size number of the exposed population from the start in implementing all controls. In fact, a control $u_2(t)$ is not enough good to manage the exposed subpopulation, since it works slowly, and additionally, the control $u_1(t)$, $u_3(t)$ works better than other controls. Further, the best strategy is to apply the combination of all of the controls to reduce the density of the exposed subpopulation. Building upon Figure 4, it is shown that the control $u_1(t)$, $u_2(t)$, $u_3(t)$, and $u_4(t)$ are working together to reduce the infected subpopulation. This simulation brings out that the control variable is used suitably with the functional objective constructed.



Figure 5. Dynamical solution of quarantined subpopulation (Q) without control and with control



Figure 6. Dynamical solution of recovered subpopulation (R) without control and with control



Figure 7. Dynamical profile of control variable $u_1(t), u_2(t), u_3(t), u_4(t)$

The simulation results in Figure 5 provide an understanding that the application of control variables has been able to reduce the density of quarantined. All of the controls have been used through an intensive handling process intended for quarantined subpopulations. As a result, it will mitigate the size of the quarantined subpopulation by recovering from Covid-19 infection. Figure 6 shows that the recovered population has increased very sharply due to several controls. This gives a conclusion that the combination of all controls can increase the total of recovered populations. Figure 7 illustrates the dynamics of the solution for each control assignment in system (1). Based on the simulation, it can be seen that the weight that correlates with the effort to give and apply control $u_3(t)$ is greater than the other control variables, then the largest weight lies in the control $u_4(t)$ and $u_1(t)$. The application of control $u_1(t)$ looks so significant because, for the 5th time, it can control the system (1). However, based on all the simulations that have been carried out, in order to realize an optimal objective function (11), the control variables must be carried out together.

6. CONCLUSION

This work, we develop a mathematical system of COVID-19 by adding control variables to diminish the spread of COVID-19 disease. Several biological assumptions are used as controls, namely efforts to provide education and understanding that COVID-19 transmission can be through direct interaction. Other control variables used include vaccine strategy, as well as intensive prevention and management of infected and quarantined subpopulations. In addition, the constructed optimal control problem is examined about non-negativity properties, boundedness, existence condition, and uniqueness criteria of the behavior's solution. Then, by applying the Pontryagin Principle, the characteristics of optimal control problem are obtained, i.e. the existence of control variable, and the existence of adjoint equations that hold on the autonomous system. Finally, the confirmation is carried out with numerical simulations to support the results of the previous investigation. Simulation results suggest that implementing the optimal control problem

can decrease the infected and quarantine subpopulations. On the other hand, it follows and does not conflict with the functional objective previously that has been formulated.

CONFLICT OF INTEREST

The author declares that there is no conflict of interests.

References

- R.I. Gweryina, C.E. Madubueze, M.A. Nwaokolo, Mathematical modelling and control of COVID-19 transmission in the presence of exposed immigrants, Commun. Biomath. Sci. 4 (2021), 93-105. https://doi.org/10.5614/cbms.2021.4.2.2.
- Q. Lin, S. Zhao, D. Gao, et al. A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action, Int. J. Infect. Dis. 93 (2020), 211-216. https://doi.org/10.1016/j.ijid.2020.02.058.
- [3] O.J. Peter, H.S. Panigoro, A. Abidemi, et al. Mathematical model of COVID-19 pandemic with double dose vaccination, Acta Biotheor. 71 (2023), 9. https://doi.org/10.1007/s10441-023-09460-y.
- [4] F. Isbaniah, A.D. Susanto, Pneumonia corona virus infection disease-19 (COVID-19), J. Indones. Med. Assoc. 70 (2020), 87-94. https://doi.org/10.47830/jinma-vol.70.4-2020-235.
- [5] I.U. Haq, N. Ullah, N. Ali, et al. A new mathematical model of COVID-19 with quarantine and vaccination, Mathematics. 11 (2022), 142. https://doi.org/10.3390/math11010142.
- [6] L. Hakim, Multiple strategies as optimal control of a COVID-19 disease with quarantine and using health masks,
 BAREKENG: J. Mat. Terapan. 16 (2022), 1059-1068. https://doi.org/10.30598/barekengvol16iss3pp1059-1068.
- [7] Fatmawati, C.W. Chukwu, R.T. Alqahtani, et al. A Pontryagin's maximum principle and optimal control model with cost-effectiveness analysis of the COVID-19 epidemic, Decision Anal. J. 8 (2023), 100273. https://doi.org/10.1016/j.dajour.2023.100273.
- [8] M.Z. Ndii, P. Hadisoemarto, D. Agustian, et al. An analysis of Covid-19 transmission in Indonesia and Saudi Arabia, Commun. Biomath. Sci. 3 (2020), 19-27. https://doi.org/10.5614/cbms.2020.3.1.3.
- B. Batista, D. Dickenson, K. Gurski, et al. Minimizing disease spread on a quarantined cruise ship: A model of COVID-19 with asymptomatic infections, Math. Biosci. 329 (2020), 108442. https://doi.org/10.1016/j.mbs.2020.108442.
- [10] F.S. Alshammari, F.T. Akyildiz, M.A. Khan, et al. A stochastic mathematical model for understanding the

COVID-19 infection using real data, Symmetry. 14 (2022), 2521. https://doi.org/10.3390/sym14122521.

- [11] R.R. Musafir, A. Suryanto, I. Darti, Dynamics of COVID-19 epidemic model with asymptomatic infection, quarantine, protection and vaccination, Commun. Biomath. Sci. 4 (2021), 106–124. https://doi.org/10.5614/cbms.2021.4.2.3.
- [12] A.A. Thirthar, H. Abboubakar, A. Khan, et al. Mathematical modeling of the COVID-19 epidemic with fear impact, AIMS Math. 8 (2023), 6447-6465. https://doi.org/10.3934/math.2023326.
- [13] P.A. Naik, M. Yavuz, S. Qureshi, et al. Modeling and analysis of COVID-19 epidemics with treatment in fractional derivatives using real data from Pakistan, Eur. Phys. J. Plus. 135 (2020), 795. https://doi.org/10.1140/epjp/s13360-020-00819-5.
- [14] W.O. Kermack, A.G. McKendrick, A contribution to the mathematical theory of epidemics, Proc. R. Soc. Lond.
 A. 115 (1927), 700-721. https://doi.org/10.1098/rspa.1927.0118.
- [15] X.P. Li, Y. Wang, M.A. Khan, et al. A dynamical study of SARS-COV-2: A study of third wave, Results Phys. 29 (2021), 104705. https://doi.org/10.1016/j.rinp.2021.104705.
- [16] A. Awasthi, A mathematical model for transmission dynamics of COVID-19 infection, Eur. Phys. J. Plus. 138 (2023), 285. https://doi.org/10.1140/epjp/s13360-023-03866-w.
- [17] M. Mandal, S. Jana, S.K. Nandi, et al. A model based study on the dynamics of COVID-19: Prediction and control, Chaos Solitons Fractals. 136 (2020), 109889. https://doi.org/10.1016/j.chaos.2020.109889.
- [18] H.M. Yang, L.P. Lombardi Junior, F.F.M. Castro, et al. Mathematical modeling of the transmission of SARS-CoV-2—Evaluating the impact of isolation in São Paulo State (Brazil) and lockdown in Spain associated with protective measures on the epidemic of CoViD-19, PLoS ONE. 16 (2021), e0252271. https://doi.org/10.1371/journal.pone.0252271.
- [19] T.T. Ega, R.C. Ngeleja, Mathematical model formulation and analysis for COVID-19 transmission with virus transfer media and quarantine on arrival, Comput. Math. Methods. 2022 (2022), 2955885. https://doi.org/10.1155/2022/2955885.
- [20] M. Ali, S.T.H. Shah, M. Imran, et al. The role of asymptomatic class, quarantine and isolation in the transmission of COVID-19, J. Biol. Dyn. 14 (2020), 389-408. https://doi.org/10.1080/17513758.2020.1773000.
- [21] M.A. Khan, A. Atangana, E. Alzahrani, et al. The dynamics of COVID-19 with quarantined and isolation, Adv. Differ. Equ. 2020 (2020), 425. https://doi.org/10.1186/s13662-020-02882-9.
- [22] V.R. Saiprasad, R. Gopal, V.K. Chandrasekar, et al. Analysis of COVID-19 in India using a vaccine epidemic model incorporating vaccine effectiveness and herd immunity, Eur. Phys. J. Plus. 137 (2022), 1003. https://doi.org/10.1140/epjp/s13360-022-03216-2.

- [23] M.A. Acuña-Zegarra, S. Díaz-Infante, D. Baca-Carrasco, et al. COVID-19 optimal vaccination policies: A modeling study on efficacy, natural and vaccine-induced immunity responses, Math. Biosci. 337 (2021), 108614. https://doi.org/10.1016/j.mbs.2021.108614.
- [24] H. HUkmah, M.R. Nisardi, S. Sulma, et al. Mathematical model of COVID-19 with quarantine and vaccination,
 J. Mat. Stat. Komput. 19 (2023), 266-285. https://doi.org/10.20956/j.v19i2.22301.
- [25] M.D. Ahmad, M. Usman, A. Khan, et al. Optimal control analysis of Ebola disease with control strategies of quarantine and vaccination, Infect. Dis. Poverty. 5 (2016), 72. https://doi.org/10.1186/s40249-016-0161-6.
- [26] R. Seck, D. Ngom, B. Ivorra, et al. An optimal control model to design strategies for reducing the spread of the Ebola virus disease, Math. Biosci. Eng. 19 (2021), 1746-1774. https://doi.org/10.3934/mbe.2022082.
- [27] Fatmawati, F.F. Herdicho, Windarto, et al. An optimal control of malaria transmission model with mosquito seasonal factor, Results Phys. 25 (2021), 104238. https://doi.org/10.1016/j.rinp.2021.104238.
- [28] A. El Mansouri, I. Smouni, B. Khajji, et al. Optimal control in a mathematical model of a spread of the obesity epidemic and its impact on diabetes, Commun. Math. Biol. Neurosci. 2023 (2023), 74. https://doi.org/10.28919/cmbn/8041.
- [29] M. Marsudi, N. Hidayat, R. Bagus, et al. Application of optimal control strategies for the spread of HIV in a population, Res. J. Life Sci. 4 (2017), 1-9. https://doi.org/10.21776/ub.rjls.2017.004.01.1.
- [30] N. Shofianah, S. Fitri, Trisilowati, et al. Optimal control of HIV/AIDS epidemic model with two latent stages, vertical transmission and treatment, J. Phys.: Conf. Ser. 1562 (2020), 012017. https://doi.org/10.1088/1742-6596/1562/1/012017.
- [31] Fatmawati, H. Tasman, An optimal treatment control of TB-HIV coinfection, Int. J. Math. Math. Sci. 2016 (2016), 8261208. https://doi.org/10.1155/2016/8261208.
- [32] K.T. Kristanti, T. Trisilowati, A. Widodo, Optimal control of cervical cancer model with vaccination and screening, J. Exp. Life Sci. 10 (2020), 72-78. https://doi.org/10.21776/ub.jels.2020.010.02.01.
- [33] R. Viriyapong, W. Ridbamroong, Global stability analysis and optimal control of measles model with vaccination and treatment, J. Appl. Math. Comput. 62 (2019), 207-237. https://doi.org/10.1007/s12190-019-01282-x.
- [34] L. Hakim, Strategi kontrol optimal model SIQR pada penyebaran penyakit campak, Leibniz. 2 (2022), 65-76. https://doi.org/10.59632/leibniz.v2i2.177.
- [35] P. Yosyingyong, R. Viriyapong, Stability analysis and optimal control of a Hepatitis B virus transmission model in the presence of vaccination and treatment strategy, Naresuan Univ. J.: Sci. Technol. 30 (2022), 66-86. https://doi.org/10.14456/NUJST.2022.17.
- [36] L. Hakim, T. Trisilowati, I. Darti, Optimal control of a cholera desease model with vaccination, Int. J. Appl.

Math. Stat. 53 (2015), 65-72.

- [37] A.R. Nuha, N. Achmad, G.A. Rahman, et al. Analysis of optimum control on the implementation of vaccination and quarantine on the spread of COVID-19, BAREKENG: J. Mat. Terapan. 16 (2022), 1139–1146. https://doi.org/10.30598/barekengvol16iss4pp1139-1146.
- [38] M.A. Rois, T. wati, U. Habibah, Optimal Control of Mathematical Model for COVID-19 with Quarantine and Isolation, Int. J. Eng. Trends Technol. 69 (2021), 154-160. https://doi.org/10.14445/22315381/ijett-v69i6p223.
- [39] Md.A.B. Masud, M. Ahmed, Md.H. Rahman, Optimal control for COVID-19 pandemic with quarantine and antiviral therapy, Sensors Int. 2 (2021), 100131. https://doi.org/10.1016/j.sintl.2021.100131.
- [40] M. Yavuz, F.Ö. Coşar, F. Günay, et al. A new mathematical modeling of the COVID-19 pandemic including the vaccination campaign, Open J. Model. Simul. 09 (2021), 299-321. https://doi.org/10.4236/ojmsi.2021.93020.
- [41] M.L. Diagne, H. Rwezaura, S.Y. Tchoumi, et al. A mathematical model of COVID-19 with vaccination and treatment, Comput. Math. Methods Med. 2021 (2021), 1250129. https://doi.org/10.1155/2021/1250129.
- [42] A.V. Dmitruk, N.V. Kuz'kina, Existence theorem in the optimal control problem on an infinite time interval, Math. Notes. 78 (2005), 466-480. https://doi.org/10.1007/s11006-005-0147-3.
- [43] M.I.A. Fathoni, M. Mardlijah, H. Hariyanto, Eksistensi kontrol dan ketunggalan sistem optimal pada model epidemi SEIT, Pros. Semin. Nas. Mat. Pendidik. Mat. 2015, no. 978, pp. 229–238, 2015.