J.Natn.Sci.Foundation Sri Lanka 2023 51 (1): 159- 174
DOI: http://dx.doi.org/10.4038/jnsfsr.v51i1.10698

RESEARCH ARTICLE

Mathematical Modelling

Analyzing the effects of quarantine, isolation, and vaccination on the spread of COVID-19 via a mathematical model

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Submitted: 09 September 2021; Revised: 25 July 2022; Accepted: 26 August 2022

Abstract: The main COVID-19 control strategies presently practiced are maintaining social distancing, quarantining suspected exposures, and isolating infectious people. In this paper, a deterministic compartmental mathematical model is proposed considering these three control strategies. Based on the proposed model the effect of vaccination on the suppression of the disease is discussed. Critical vaccination rate and vaccinated population size relevant to disease suppression are determined based on the proposed mathematical model. Different forms of the most used key term in infectious disease modelling, reproduction number, are determined relevant to the proposed model. Sensitivity analysis of the reproduction numbers is done to identify model parameters mostly affecting the spread of the disease. Based on the reproduction number of the model disease controlling parameter regions are determined and graphical representations of those parameter regions are presented. Based on the results of the proposed mathematical model, it is observed that earlier implementation of the vaccination process is helpful to better control the disease. However, it takes considerable time to invent successful vaccinations for newly out-breaking diseases like COVID-19. Therefore, it took considerable time to start the vaccination process for COVID-19. It is observed that after starting a vaccination process at a particular rate it should continue until the vaccinated population reaches a critical size.

Keywords: COVID-19, compartmental models, critical vaccination rate, disease control strategies, disease modelling, sensitivity Index.

INTRODUCTION

COVID-19 is a disease due to a virus named severe acute respiratory syndrome coronavirus 2 (SARS-COV-2 virus). It originated in Wuhan city China in late 2019, and spread throughout the world very rapidly. According to the World Health Organization (WHO) COVID-19 was reported to WHO on December 31, 2019. WHO declared the COVID-19 outbreak to be a global health emergency on January 30, 2020. Also, it declared COVID-19 a global pandemic on March 11, 2020. Maintaining social distancing, quarantining exposures, and isolating infectious people were the main control strategies until successful vaccinations were invented for the disease. The role of a vaccine is to prevent susceptible people from being infected for a time period or for their lifetime. However, according to WHO (2021a), the presently available vaccines for COVID-19 do not have fully immunizing ability but prevent people from getting seriously ill or dying from COVID-19. According to WHO, there is no confirmation about the full effectiveness of the vaccines in controlling COVID-19. Therefore, though vaccinated, people

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need to take preventive measures (WHO, 2021c). The WHO updates the COVID-19 vaccine database regularly twice a week. According to updates on 17 June 2021, there are 287 total candidate vaccines and among these 102 are in the clinical phase and 185 are in the pre-clinical phase (WHO, 2021b). Recently, several kinds of vaccines were being developed by several countries. The WHO evaluated vaccines for COVID-19 by 3rd June 2021 are AstraZeneca/Oxford vaccine, Johnson and Johnson, Moderna, Pfizer/BionTech, Sinopharm, and Sinovac. Presently vaccines play an important role in avoiding serious illnesses due to COVID-19 and reducing the death toll.

Mathematical models are helpful in analyzing and forecasting the spread of infectious diseases and those results are useful for disease management policymakers and healthcare sectors to make their decisions on disease management processes. This paper proposes a mathematical model for the control process of COVID-19 by considering the control strategies quarantine, isolation, and vaccination. For this model seven population sub classes susceptible (S), exposed (E), quarantined (Q), infectious (I), isolated (J), removed (R) and vaccinated (V) are taken into account (SEQIJRV models). Several studies on mathematical models for infectious diseases considering vaccination factors are reported. SIR models with vaccinations (SIRV models) for infectious diseases are reported by Ledzewicz & Schättler (2011), and Chanprasopchai *et al.* (2018). Chanprasopchai *et al.* (2018) proposed an SIR mathematical model for dengue fever and the effect of the dengue vaccine was discussed. Optimal control analysis of an SIR model with vaccination and treatment was done by Ledzewicz & Schättler (2011). In that paper, an optimal strategy in terms of combined efforts of vaccination and treatment, such that the disease-specific death and the cost of vaccination and treatments are minimized, is described. An SIQR-type mathematical model for the spread of diseases considering vaccination, elimination, and quarantine strategies was proposed by Ma *et al.* (2018) and the model analyzed theoretically and numerically.

A mathematical model for the Ebola virus was proposed by Ahmad *et al.* (2016) considering quarantine, hospitalization, and vaccination components. The effect of the pulse vaccine strategy on the control of infectious disease was discussed by Shulgin *et al.* (1998). SEIR models with vaccinations (SEIRV models) were reported by Sun & Hsieh (2010), Biswas *et al.* (2014), d'Onofrio (2002), and Ghostine *et al.* (2021). An SEIR model with vaccination strategy was investigated by Biswas *et al.* (2014). The stability properties of the pulse vaccination strategy were discussed by d'Onofrio (2002) based on an SEIR epidemic model. The effects of the introduction of constraints for state variables on optimal control problem was studied by Ghostine *et al.* (2021) based on an SEIR model with vaccination. A mathematical model for Ebola virus disease was discussed by Ahmad *et al.* (2016) considering quarantine, hospitalization, and vaccination components. An SEQIJR mathematical model for the severe acute respiratory syndrome (SARS) was reported by Gumel *et al.* (2004). In that paper, the authors have examined the impact of isolation and quarantine on the control of SARS outbreaks. An extension of that model considering the imperfect vaccine effect was reported by Safi & Gumel (2011) and numerical and analytical studies of the model have been done by the authors. An SIQR type mathematical model for the spread of diseases considering vaccination, elimination, and quarantine strategies was proposed by Ma *et al.* (2018) who analyzed the model theoretically and numerically. A mathematical model considering quarantine, hospitalization, and vaccination components was proposed by Ahmad *et al.* (2016) for the Ebola virus. In that paper, their proposed model is used to predict resource utilization for disease control and the effectiveness of vaccination on infected populations, and the most sensitive parameters which effectively contribute to changing the disease dynamics are identified. Different types of deterministic compartmental mathematical models for COVID-19 for different purposes, such as parameter estimations Tang *et al.* (2020) & Anastassopoulou *et al.* (2020), studying the effects of control strategies Mishra *et al.* (2020), and predictions Agarwal & Jhajharia (2021).

MATERIAL AND METHODS

This section proposes a deterministic compartmental mathematical model for COVID-19 considering control strategies social distancing, quarantining, isolation, and vaccination.

Proposed mathematical model

A sketch for the transfer behaviour between compartments of the proposed model are shown in the Figure 1. In this figure S, E, Q, I, J, R, V and M represent susceptible, exposed, quarantined, infectious, isolated, recovered, vaccination and total population sizes respectively.

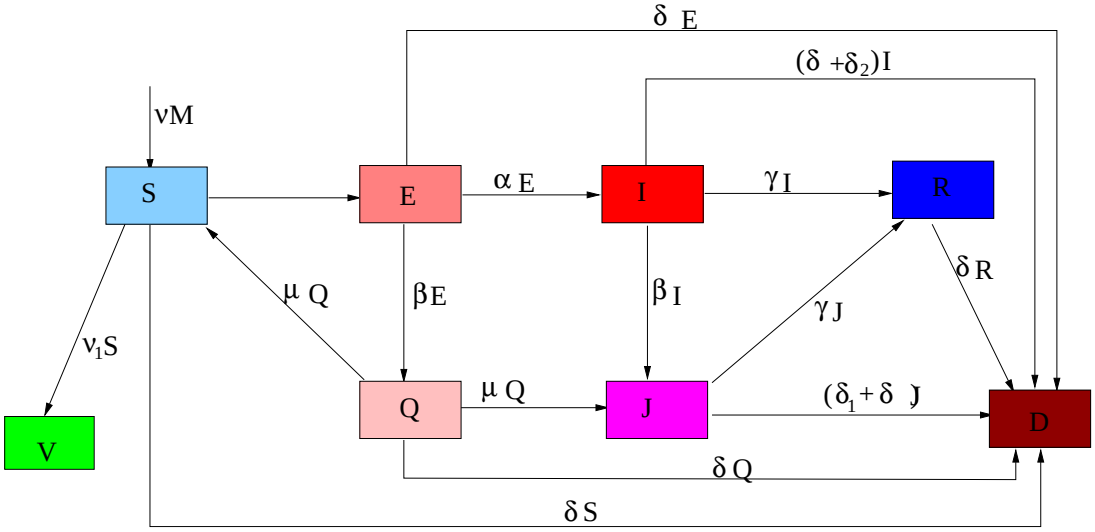

Figure 1: Schematic flow diagram for the SEQIJRV model.

Considering the schematic flow diagram in Figure 1, an SEQIJRV type mathematical model can be formulated as follows:

$$\begin{aligned}
\frac{dS}{dt} &= \nu M - \sigma\nu_1 S - \alpha_1 \frac{(I+\varepsilon_e E+\varepsilon_q Q+\varepsilon_j J)}{M} S - (\nu_1+\delta_2)S + \mu_2 Q,\\
\frac{dE}{dt} &= \alpha_1 \frac{(I+\varepsilon_e E+\varepsilon_q Q+\varepsilon_j J)}{M} S - (\alpha_2+\beta_1+\delta_2)E,\\
\frac{dQ}{dt} &= \beta_1 E - (\delta_2+\mu_1+\mu_2)Q,\\
\frac{dI}{dt} &= \alpha_2 E - (\gamma_1+\beta_2+\delta_1+\delta_2)I,\\
\frac{dJ}{dt} &= \beta_2 I + \mu_1 Q - (\gamma_2+\delta_1+\delta_2)J,\\
\frac{dR}{dt} &= \gamma_1 I + \gamma_2 J - \delta_2 R,\\
\frac{dV}{dt} &= \sigma\nu_1 S - \delta_2 V.
\end{aligned} \tag{1}$$

The initial conditions for the model are of the form

$$S(0) > 0,\ E(0) \geq 0,\ Q(0) \geq 0,\ I(0) \geq 0,\ J(0) \geq 0,\ R(0) \geq 0,\ V(0) \geq 0. \tag{2}$$

Table 1: Parameters interpretation of the proposed mathematical model

Parameter	Description
ν	Natural birth rate.
ν_1	Vaccination rate.
σ	Efficiency of the vaccination.
α_1	The transmission coefficient from the susceptible class to the exposed class.
α_2	The transfer rate from the exposed class to the infectious class.
β_1	The transfer rate from the exposed class to the quarantined class.
β_2	The transfer rate from the infected class to the isolated class.
μ_1	The transfer rate from the quarantined class to the isolated class.
μ_2	The transfer rate from the quarantined class to the susceptible class.
γ_1	The transfer rate from the infected class to the recovered class.
γ_2	The transfer rate from the quarantined class to the recovered class.
$\varepsilon_e, \varepsilon_q, \varepsilon_j$ δ	Exposing weights for the disease due to the classes E, Q and J respectively.Disease-specifi
$_1, \delta_2$	c and natural death rates respectively.

Equilibrium points of the system

There are two equilibrium points of the system:

$$\mathscr{E}_1^* \equiv (S_1^*, E_1^*, Q_1^*, I_1^*, J_1^*, R_1^*, V_1^*) \equiv \left(\frac{M\nu}{\delta_2+\nu_1}, 0, 0, 0, 0, 0, \frac{M\nu\nu_1}{\delta_2(\delta_2+\nu_1)}\right) \text{ and } \mathscr{E}_2^* \equiv (S_2^*, E_2^*, Q_2^*, I_2^*, J_2^*, R_2^*, V_2^*).$$

Here,

$$I_2^* = \frac{\alpha_2 A_2 M\left(A_2\left(A_4\left(\alpha_1\nu\left(\alpha_2+A_3\varepsilon_e\right)-A_1A_3\left(\delta_2+\nu_1\sigma\right)\right)+\alpha_1\alpha_2\beta_2\nu\varepsilon_j\right)+\alpha_1A_3\beta_1\nu\left(A_4\varepsilon_q+\mu_1\varepsilon_j\right)\right)}{\alpha_1A_3\left(A_1A_2-\beta_1\mu_2\right)\left(A_2\left(A_4\left(\alpha_2+A_3\varepsilon_e\right)+\alpha_2\beta_2\varepsilon_j\right)+A_3\beta_1\left(A_4\varepsilon_q+\mu_1\varepsilon_j\right)\right)},$$

$S_2^* = \frac{\alpha_2A_2\nu M+A_3\beta_1\mu_2I_2^*+A_1A_2A_3(-I_2^*)}{\alpha_2A_2\left(\delta_2+\nu_1\sigma\right)}$, $E_2^* = \frac{A_3I_2^*}{\alpha_2}$, $Q_2^* = \frac{A_3\beta_1I_2^*}{\alpha_2A_2}$, $J_2^* = \frac{I_2^*\left(\alpha_2A_2\beta_2+A_3\beta_1\mu_1\right)}{\alpha_2A_2A_4}$,

$R_2^* = \frac{\gamma_1I_2^*+\gamma_2J_2^*}{\delta_2}$, and $V_2^* = \frac{\sigma\nu_1S_2^*}{\delta_2}$. Here, $A_1 = \alpha_2+\beta_1+\delta_2$, $A_2 = \delta_2+\mu_1+\mu_2$, $A_3 = \beta_2+\gamma_1+\delta_1+\delta_2$, and

$A_4 = \gamma_2+\delta_1+\delta_2$. Since $A_1A_2 > \beta_1\mu_2$, I_2^* is positive if and only if

$$\frac{\nu\alpha_1\left(A_2\left(A_4\left(\alpha_2+A_3\varepsilon_e\right)+\alpha_2\beta_2\varepsilon_j\right)+A_3\beta_1\left(A_4\varepsilon_q+\mu_1\varepsilon_j\right)\right)}{A_1A_2A_3A_4(\delta_2+\nu_1\sigma)} > 1 \Longrightarrow \frac{\nu}{(\delta_2+\nu_1\sigma)}\mathscr{R}_0 > 1.$$

Here,

$$\begin{aligned}\mathscr{R}_0 =& \frac{\alpha_1\left(A_2\left(A_4\left(\alpha_2+A_3\varepsilon_e\right)+\alpha_2\beta_2\varepsilon_j\right)+A_3\beta_1\left(A_4\varepsilon_q+\mu_1\varepsilon_j\right)\right)}{A_1A_2A_3A_4}\\ =& \frac{\alpha_1}{A_1}\left(\varepsilon_e\delta_2+\frac{\alpha_2}{A_3}+\frac{\beta_1\varepsilon_q}{A_2}+\frac{\varepsilon_j\beta_1\mu_1}{A_2A_4}+\frac{\varepsilon_j\alpha_2\beta_2}{A_3A_4}\right)\end{aligned}$$

This implies that, the positive endemic equilibrium $\mathscr{E}_2^*$ exists if and only if $\frac{\nu}{(\delta_2+\nu_1\sigma)}\mathscr{R}_0 > 1$. Also, if $\mathscr{R}_0 < 1$ then the disease free equilibrium state $\mathscr{E}_1^*$ is stable. If $\mathscr{R}_0 > 1$ then the endemic equilibrium point is stable and the disease free equilibrium point becomes unstable.

Non-negativity of the solutions of the system

Let $M(t) = S(t)+E(t)+Q(t)+I(t)+J(t)+R(t)+V(t)$ be the total population size at time t. Summing up all the equations of the system (1) result in

$$\frac{dM}{dt} = M(\nu - \delta_2) - (u+v)\delta_1 \geq M(\nu - \delta_2 - \delta_1).$$

$M(t) \geq M(0)e^{(\nu-\delta_1-\delta_2)t}$, where $M(0)$ is the initial total population size.

Also $\frac{dM}{dt} \leq M(\nu - \delta_2) \Longrightarrow M(t) \leq M(0)e^{(\nu-\delta_2)t}$.

$M(0)e^{(\nu-\delta_1-\delta_2)t} \leq M(t) \leq M(0)e^{(\nu-\delta_2)t}$.

Therefore at any finite time the total population size is bounded. From the second equation of the system (1) we have the inequality

$$\frac{dE}{dt} \geq -(\alpha_2+\beta_1+\delta_2)E.$$

$\Longrightarrow E(t) \geq E(0)e^{-(\alpha_2+\beta_2+\delta_2)t}$.

This implies that $E(t)$ is non-negative. Similarly it can be shown that $Q(t)$, $I(t)$, $J(t)$, $R(t)$ and $V(t)$ are non-negative. Since the total population size is non-negative $S(t)$ should also be non-negative.

Basic reproduction number and the effective reproduction number

The basic reproduction number ($\mathscr{R}_0$): The basic reproduction number of an infectious disease is a measure of the transmissibility of the disease. $\mathscr{R}_0$ defines as the average number of new cases produced by an infected individual during the individual's infectious period in the absence of any prevention strategies. A measure for the average number of new cases produced by an infected individual when control strategies are implemented can be derived based on mathematical models formulated for the disease transmission process. Expressions for this reproduction number depend on the parameters of the mathematical model. One measure of the efficiency of a control strategy is its ability to reduce $\mathscr{R}_0$. In order to control the spread of a disease, it is very important to take action to implement control strategies to gain the condition $\mathscr{R}_0 < 1$.

The effective reproduction number ($\mathscr{R}_e$): . In general the whole population would not be susceptible to an infectious disease. For some infectious diseases, infectious individuals become immunized for life to that disease. Also, individuals become partially or fully immunized by vaccinations. Therefore, not all contacts will become infected in such populations and an average number of secondary cases per infectious case will be lower than the basic reproduction number. The effective reproductive number ($\mathscr{R}_e$) is the average number of secondary cases per infectious individual in a population made up of both susceptible and non-susceptible hosts (Arenas *et al.*, 2020). If $\mathscr{R}_e > 1$, then the disease persists(secondary cases will increase) while disease dies out (secondary cases decrease) if $\mathscr{R}_e < 1$. When $\mathscr{R}_e = 1$, secondary cases remains unchanged. The effective reproduction number can be defined as the product of the basic reproductive number and the fraction of the host population that is susceptible (r). That is

$$r = \frac{\text{Susceptible population size}}{\text{Total population size}} \text{ and } \mathscr{R}_e = r\mathscr{R}_0.$$

If it is assumed that all the vaccinated people are immunized then $r = \frac{M-V}{M}$ and if the efficiency of the vac-

cination is σ then $r = \dfrac{M-\sigma V}{M}$, where V is the total vaccinated population size. For some infectious diseases recovered individuals become fully immunized for their lifetime. In such cases

$$r = \frac{\text{Total population size} - \text{Total recovered population size}}{\text{Total population size}} = \frac{(M-R)}{M}.$$

Time-dependent effective reproduction number ($R_e(t)$): The time-dependent effective reproduction number can be defined as

$$\mathscr{R}_e(t) = \mathscr{R}_0 \frac{(\text{Susceptible population size at time } t)}{\text{Total population size}} = \mathscr{R}_0 \frac{S(t)}{M}$$

Basic reproduction number of the model

The basic reproduction number of the proposed model is calculated using the *next-generation matrix* (NGM) method (Diekmann *et al.*, 2010, Gumel *et al.*, 2004, Yang, 2014). The infected subsystem (see Diekmann *et al.* (2010)) of the model system (1) is:

$$\begin{aligned}
\frac{dE}{dt} &= \alpha_1 \frac{(I + \varepsilon_E E + \varepsilon_Q Q + \varepsilon_J J)}{M} S - (\alpha_2 + \beta_1 + \delta_2) E \\
\frac{dQ}{dt} &= \beta_1 E - (\delta_2 + \mu_1 + \mu_2) Q \\
\frac{dI}{dt} &= \alpha_2 E - (\gamma_1 + \beta_2 + \delta_1 + \delta_2) I \\
\frac{dJ}{dt} &= \beta_2 I + \mu_1 Q - (\gamma_2 + \delta_1 + \delta_2) J
\end{aligned} \tag{3}$$

In the process of calculating $\mathscr{R}_0$ using the next-generation method, the first step is to linearize the infected subsystem about the disease-free equilibrium point $\mathscr{E}_1^*$. The Jacobian matrix of the linearized infectious subsystem for disease-free equilibrium is

$$J = \begin{pmatrix}
-A_1 + \frac{\alpha_1 \nu \varepsilon_e}{\delta_2 + \nu_1 \sigma} & \frac{\alpha_1 \nu \varepsilon_q}{\delta_2 + \nu_1 \sigma} & \frac{\alpha_1 \nu}{\delta_2 + \nu_1 \sigma} & \frac{\alpha_1 \nu \varepsilon_j}{\delta_2 + \nu_1 \sigma} \\
\beta_1 & -A_2 & 0 & 0 \\
\alpha_2 & 0 & -A_3 & 0 \\
0 & \mu_1 & \beta_2 & -A_4
\end{pmatrix}.$$

Now decompose the Jacobian matrix into two sub-matrices called the transmission matrix (see Diekmann *et al.* (2010)), J_T (*the production of new infections*) and transition matrix (see Diekmann *et al.* (2010)), J_M (*the changes in the state*). Then

$$J_T = \begin{pmatrix}
\frac{\alpha_1 \nu \varepsilon_e}{\delta_2 + \nu_1 \sigma} & \frac{\alpha_1 \nu \varepsilon_q}{\delta_2 + \nu_1 \sigma} & \frac{\alpha_1 \nu}{\delta_2 + \nu_1 \sigma} & \frac{\alpha_1 \nu \varepsilon_j}{\delta_2 + \nu_1 \sigma} \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0
\end{pmatrix} \text{ and } J_M = \begin{pmatrix}
-A_1 & 0 & 0 & 0 \\
\beta_1 & -A_2 & 0 & 0 \\
\alpha_2 & 0 & -A_3 & 0 \\
0 & \mu_1 & \beta_2 & -A_4
\end{pmatrix}.$$

The reproduction number for the disease-free equilibrium point, $\mathscr{R}_{df}$, is the maximum eigenvalue of the matrix $-J_T J_M^{-1}$. $\mathscr{R}_{df}$ can be derived in the form:

$$\mathscr{R}_{df} = \frac{\nu\alpha_1}{A1(\delta_2+\nu_1\sigma)}\left(\varepsilon_e\delta_2 + \frac{\alpha_2}{A_3} + \frac{\beta_1\varepsilon_q}{A_2} + \frac{\varepsilon_j\beta_1\mu_1}{A_2A_4} + \frac{\varepsilon_j\alpha_2\beta_2}{A_3A_4}\right).$$

The basic reproduction number of the model can be obtained by considering the fact that the susceptible population size is equal to the total population size. In order to keep the susceptible population size unchanged, the death rate and birth rate should be equal in the case of no vaccinations. That is $\mathscr{R}_0$ is the value of $\mathscr{R}_{df}$ when $\nu = \delta_2$ and $\nu_1 = 0$. Then

$$\mathscr{R}_0 = \frac{\alpha_1}{A1}\left(\varepsilon_e\delta_2 + \frac{\alpha_2}{A_3} + \frac{\beta_1\varepsilon_q}{A_2} + \frac{\varepsilon_j\beta_1\mu_1}{A_2A_4} + \frac{\varepsilon_j\alpha_2\beta_2}{A_3A_4}\right).$$

In other words $\mathscr{R}_{df} = \dfrac{\nu}{(\delta_2+\nu_1\sigma)}\mathscr{R}_0$. The time-dependent effective reproduction number of the model, subject to the assumption that recovered people are not immunized and the effectively vaccinated population is fully immunized is $\mathscr{R}_e(t) = \mathscr{R}_0 \times \dfrac{(M-\sigma V(t))}{M}$.

If the recovered people are also immunized then the corresponding effective reproduction number is

$$\mathscr{R}_e(t) = \mathscr{R}_0 \times \frac{(M-\sigma V(t)-R(t))}{M}.$$

Sensitivity analysis

The sensitivity index provides information about the importance of each model parameter to a state variable that depends on the model parameters. The sensitivity index of a state variable (say $\mathscr{V}$) which depends on the model parameters is a measure of the relative change in $\mathscr{V}$ when a parameter (say p) changes and it is defined as $\mathscr{S}_p^{\mathscr{V}} = \left(\dfrac{\partial\mathscr{V}}{\partial p}\right)\dfrac{p}{\mathscr{V}}$ (Siriprapaiwan *et al.*, 2018, Bajiya *et al.*, 2020). Sensitivity analysis is useful in determining parameters that have high impacts on $\mathscr{V}$. If a given change in a model parameter will cause a large change in the $\mathscr{V}$ then it is said that the parameter is highly sensitive. The sensitivity index determines whether each parameter is sensitive (quite responsive), unit sensitive, or insensitive (not very responsive). The sensitivity index may be negative or positive. If the sensitivity index is positive (or negative) then the increases of the parameter increases (or decreases) the $\mathscr{V}$. The unitary sensitivity index implies that a change in the parameter leads to an equal change of the state variable $\mathscr{V}$.

Sensitivity index of the basic reproduction number $\mathscr{R}_0$

The initial disease transmission strength is related to the basic reproduction number. Therefore, sensitivity analysis of the basic reproduction number is helpful to identify model parameters which have a greater effect on the initial disease transmission. Identifying those parameters is helpful to take necessary actions to suppress the disease transmission. The sensitivity index of the basic reproduction number, $\mathscr{R}_0$, relative to a model parameter, θ, is:

$\mathscr{S}_\theta^{\mathscr{R}_0} = \dfrac{\partial\mathscr{R}_0}{\partial\theta}\dfrac{\theta}{\mathscr{R}_0}$. Accordingly $\mathscr{S}_{\alpha_1}^{\mathscr{R}_0} = 1$, $\mathscr{S}_{\alpha_2}^{\mathscr{R}_0} = \dfrac{\alpha_1\alpha_2}{A_1\mathscr{R}_0}\left(\dfrac{1}{A_3} + \dfrac{\varepsilon_j\beta_2}{A_3A_4}\right) - \dfrac{\alpha_2}{A_1}$, $\mathscr{S}_{\varepsilon_j}^{\mathscr{R}_0} = \dfrac{\alpha_1\varepsilon_j}{A_1\mathscr{R}_0}\left(\dfrac{\beta_1\mu_1}{A_2A_4} + \dfrac{\beta_2\alpha_2}{A_3A_2}\right)$,

$\mathscr{S}_{\beta_1}^{\mathscr{R}_0} = \dfrac{\alpha_1\beta_1}{A_1\mathscr{R}_0}\left(\dfrac{\varepsilon_q}{A_2} + \dfrac{\varepsilon_j\mu_1}{A_2A_4}\right) - \dfrac{\beta_1}{A_1}$, $\mathscr{S}_{\beta_2}^{\mathscr{R}_0} = \dfrac{\alpha_1\beta_2\alpha_2}{A_1A_3\mathscr{R}_0}\left(\dfrac{\varepsilon_j}{A_4} - \dfrac{\varepsilon_j\beta_2}{A_3A_4} - \dfrac{1}{A_3}\right)$, $\mathscr{S}_{\mu_1}^{\mathscr{R}_0} = \dfrac{\alpha_1\mu_1\beta_1}{A_1A_2\mathscr{R}_0}\left(\dfrac{\varepsilon_j}{A_4} - \dfrac{\varepsilon_j\mu_1}{A_2A_4} - \dfrac{\varepsilon_q}{A_2}\right)$,

$\mathscr{S}_{\mu_2}^{\mathscr{R}_0} = -\dfrac{\alpha_1\mu_1\beta_1}{A_1{A_2}^2\mathscr{R}_0}\left(\varepsilon_q + \dfrac{\varepsilon_j\mu_1}{A_4}\right)$, $\mathscr{S}_{\varepsilon_e}^{\mathscr{R}_0} = \dfrac{\alpha_1\varepsilon_e}{A_1\mathscr{R}_0}$, $\mathscr{S}_{\varepsilon_q}^{\mathscr{R}_0} = \dfrac{\alpha_1\beta_1\varepsilon_q}{A_1A_2\mathscr{R}_0}$, $\mathscr{S}_{\gamma_1}^{\mathscr{R}_0} = -\dfrac{\alpha_1\gamma_1}{A_1A_3^2\mathscr{R}_0}\left(\alpha_2 + \dfrac{\beta_2\alpha_2\varepsilon_j}{A_4}\right)$, and

$\mathscr{S}_{\gamma_2}^{\mathscr{R}_0} = -\dfrac{\alpha_1\gamma_2\varepsilon_j}{A_4^2\mathscr{R}_0}\left(\dfrac{\beta_1\mu_1}{A_2} + \dfrac{\beta_2\alpha_2}{A_3}\right)$.

Since $\mathscr{R}_{df} = \dfrac{\nu}{(\delta_2 + \nu_1\sigma)}\mathscr{R}_0$, the sensitivity indices of $\mathscr{R}_{df}$ against all the parameters except ν_1 are same as that of $\mathscr{R}_0$. Also, $\mathscr{S}_{\nu_1}^{\mathscr{R}_{df}} = \dfrac{-\sigma\nu_1}{\delta_2 + \nu_1\sigma}$. In the numerical simulations of the paper, parameters are chosen based on some assumptions. Those assumptions and relevant parameter values are tabulated in Table 2.

Table 2: Parameter values relevant to the assumptions/facts

Assumptions/facts	Parameter value relevant to the assumption (unit: per day)
The natural death rate and birth rate in Sri Lanka are 6.818 and 15.135 per thousand per year respectively	$\delta_2 = 6.818/(365 \times 1000)$, $\nu = 15.135/(365 \times 1000)$
Expose rate of COVID-19 is 0.19.	$\alpha_1 = 0.19$.
10% of the exposed people are quarantined and their average staying time in the exposed class is 2 days.	$\beta_1 = 0.1/2 = 0.05$.
90% of the exposed people may infect and the average staying time in the exposed class is 5 days (it is assumed incubation period of COVID-19 is 5 days).	$\alpha_2 = 0.90/5 = 0.18$.
5% of the quarantined people are infected and transferred to the isolated class and their average staying time in the quarantined class is 4 days.	$\mu_1 = 0.05/4$
During the 14 days quarantined period 95% of the quarantined class remain uninfected and they are transferred to the susceptible class	$\mu_2 = 0.95/14$
90% of the infectious people and 94% of isolated people recover and their average staying time in the infectious and isolated classes is 10 days.	$\gamma_1 = 0.9/10 = 0.09$ and $\gamma_2 = 0.94/10 = 0.094$.
3% of each infectious and isolated class died due to Covid-19 and their staying period in the respective class is 14 days.	$\delta_1 = 0.03/14$.
Infection transmission weights from classes E, Q, and J to the class S are 10%, 5% and 1% respectively.	$\varepsilon_e = 0.1$, $\varepsilon_q = 0.05$ and $\varepsilon_j = 0.01$.
10% of the exposed people are quarantined and their average staying period in the exposed classes is 2 days.	$\beta_1 = 0.1/2 = 0.05$.
9% of the identified infectious people are hospitalized(isolated) and their average staying time in the infectious class is 3 days.	$\beta_3 = 0.09/3 = 0.03$.
The effective contact rate is 0.18.	$\alpha_1 = 0.18$.
The vaccination rate is 0.00002.	$\nu_1 = 0.00002$.

RESULTS AND DISCUSSION

This section discusses the effect of the control strategies, social distancing, quarantining, isolation and vaccination on the spread of COVID-19, based on the results obtained by the proposed mathematical model.

Sensitivity Analysis

This section explains the sensitivity of model parameters on the model's state variables $\mathscr{R}_{df}$ and endemic infectious population sizes I_2^* and J_2^*.

Table 3: Sensitivity indices of $\mathscr{R}_{df}$ relevant to the model parameters

Parameter	Sensitivity indices of $\mathscr{R}_{df}$	Parameter	Sensitivity indices of $\mathscr{R}_{df}$	Parameter	Sensitivity indices of $\mathscr{R}_{df}$
α_1	1	β_1	-0.19755	μ_2	-0.016734
γ_1	-0.676366	α_2	0.135520	ε_j	0.0033575
ν_1	-0.461368	ε_e	0.0621130	γ_2	-0.003282
β_2	-0.22260	ε_q	0.0193196	μ_1	-0.00258

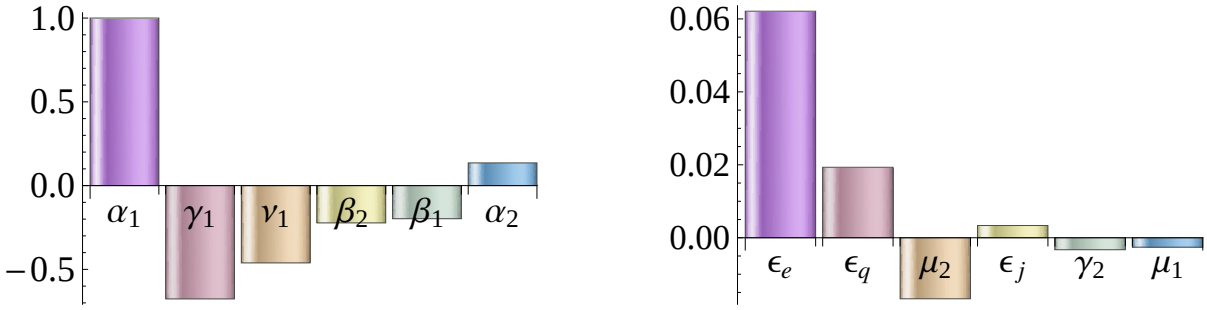

Figure 2: Graphical interpretation of sensitivity indices of $\mathscr{R}_{df}$.

Sensitivity of $\mathscr{R}_{df}$

Sensitivity analysis of $\mathscr{R}_{df}$ is helpful to identify the model parameters which have a greater effect on the disease transmission when vaccination is started. For the above set of parameters $\mathscr{R}_{df} = 1.61314$. The sensitivity indices of $\mathscr{R}_{df}$ is shown in Table 3. Graphical interpretation of the sensitivity indices of $\mathscr{R}_{df}$ is shown in Figure 2.

Since the sensitivity indices of $\mathscr{R}_{df}$ against α_1, α_2, ε_e, ε_q, and ε_j are positive, R_{df} increases as these parameters increase. $\mathscr{R}_{df}$ decreases as the rest of the parameters increase since the corresponding sensitivity indices are negative. Also, the most sensitive parameter for $\mathscr{R}_{df}$ is α_1, and the least sensitive parameter is μ_1 for both $\mathscr{R}_0$ and $\mathscr{R}_{df}$. That is, the transmission rate from the susceptible class to the exposed class is the most dominant and the transmission rate from the quarantine class to the isolated class is the least effective parameter for the spread of the disease. In other words, maintaining social distancing and proper hygiene strategies are the most effective control strategy for controlling the spread of COVID-19. The next sensitive parameter for the $\mathscr{R}_{df}$ is vaccination rate ν_1 for the considered set of parameters. Sensitivity indices of $\mathscr{R}_{df}$ shown in Table 3 are arranged in decreasing order of their effectiveness. Since $S_{\alpha_1}^{\mathscr{R}_{df}} = 1$, a 10% increase (or decrease) in α_1 from the current value results in a 10% increase (or decrease) of $\mathscr{R}_{df}$. Also, since $S_{\nu_1}^{\mathscr{R}_{df}} = -0.461368$ a 10% increase of ν_1 ($0.00002 \times 10/100 = 0.000002$), results in a 4.6% decrease of R_{df}. Similar interpretations can be given to other parameters.

Sensitivity of I_2^* and J_2^*

In the endemic equilibrium $\mathscr{E}_2^*$, especially I_2^*, and J_2^* are measures of the prevalence of the disease. Therefore, sensitivity analysis of I_2^* and J_2^* are helpful to identify more sensitive parameters on the disease prevalence. Sensitivity indices of I_2^* and J_2^* corresponding to parameter values are shown in the Table 4. Three consecutive more sensitive parameters of I_2^* and J_2^* are α_1, μ_2, ν_1 and α_1, γ_2, β_2 respectively of the chosen set of parameters. Also, the third sensitive parameter for the total infectious population, $I_2^* + J_2^*$, is ν_1. That is vaccination plays an important role in controlling the disease.

Table 4: Sensitivity indexes of I_2^* and J_2^*.

Parameter	Sensitivity index of		
	I_2^*	J_2^*	$(I_2^*+J_2^*)$
α_1	-1.4322	-1.4322	-1.4321
α_2	-0.0784	-0.4393	-0.3780
β_1	0.2389	0.5998	0.5385
β_2	-0.2069	0.7083	0.5527
μ_1	-0.1879	0.1168	0.0651
μ_2	0.6873	0.3826	0.4344

Parameter	Sensitivity index of		
	I_2^*	J_2^*	$(I_2^*+J_2^*)$
γ_1	-0.0552	0.0276	0.0136
γ_2	0.0351	-0.9424	-0.7762
ε_e	-0.1605	-0.1605	-0.1605
ε_q	-0.4991	-0.4991	-0.4991
ε_j	-0.0359	-0.0359	-0.0359
ν_1	0.6608	0.6608	0.6608

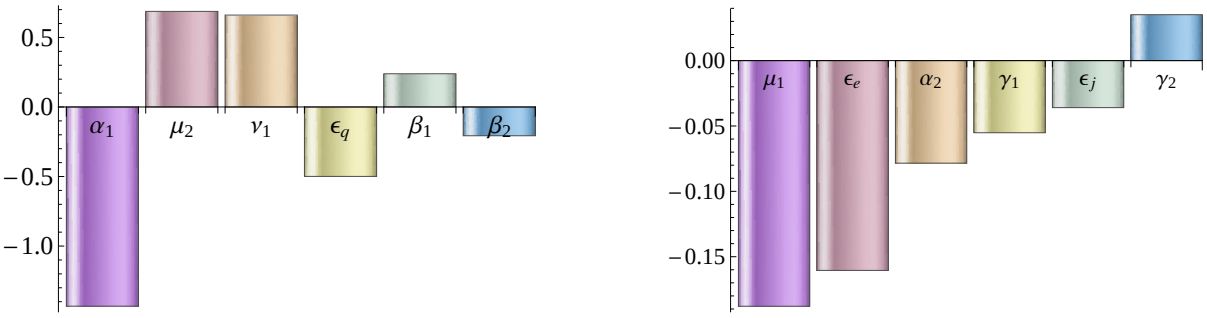

Figure 3: Graphical interpretation of sensitivity indices of I_2^*.

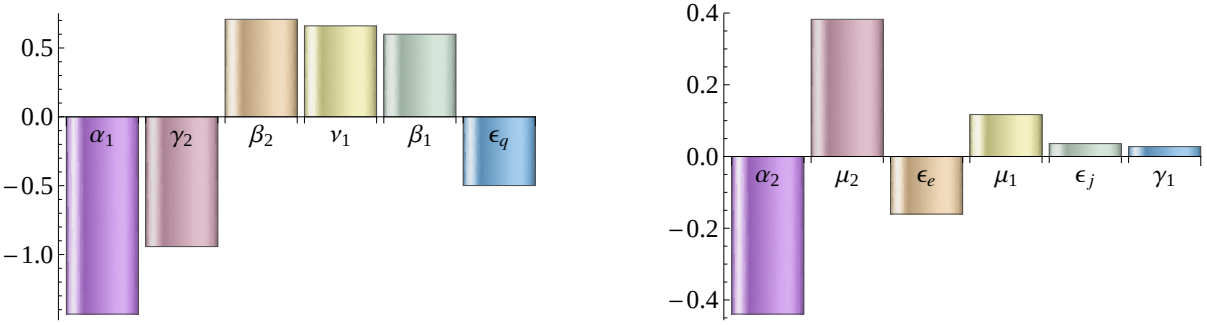

Figure 4: Graphical interpretation of sensitivity indices of J_2^*.

Identifying sufficient levels of control strategies in controlling the spread of a disease

Critical immunization population size

In order to prevent the disease, it is necessary to take actions to gain $\mathscr{R}_{ef} < 1$. Let V_c be the critical vaccinated population size. Then, $1 = \mathscr{R}_{ef} = \mathscr{R}_0 \frac{(M - V_c)}{M}$. That is $V_c = M\left(1 - \frac{1}{\mathscr{R}_0}\right)$. Suppose that the vaccination process is planned to complete within T_v days. Then it is needed to vaccinate a number of people $\lceil V_c/T_v \rceil$ per day to reach the disease dies-out level. If the health care sector's maximum vaccination capacity is V_0 per day then the vaccination campaign should continue $\lceil V_c/V_0 \rceil$ days to reach the disease dies-out level. Here, $\lceil x \rceil$ denotes the smallest integer greater than the real number x.

The effect of vaccination level and starting time

This section discusses the effect of vaccination level and vaccination starting time on the spread of the disease.

Critical immunization rate

Since $\mathscr{R}_{df} = \frac{\nu}{(\delta_2 + \nu_1 \sigma)} \mathscr{R}_0$, the critical vaccination rate, ν_{1c} satisfies
$\frac{\nu}{(\delta_2 + \nu_{1c}\sigma)} \mathscr{R}_0 = 1$. That is $\nu_{1c} = \frac{\nu \mathscr{R}_0 - \delta_1}{\sigma}$.

Figures 5(a) and 5(b) shows the variation of percentage infectious and death population sizes when the vaccination strategy is started at different time levels, and 5 (c), and 5(d) shows the same for different strengths of vaccinations. For these simulations it is assumed that $\beta_1 = 0$, and $\beta_2 = 0$ and for Figures 5(a), 5(b), the vaccination rate, $\nu_1 = 0.001$. Also, the critical vaccination level for the considered set of parameters is $\nu_{1c} = 0.0000161147$.

According to Figures 5(a) and 5(b), the earlier vaccination process starts, the more helpful it is for the better control of the disease. According to Figures 5(c), and 5(d) we can conclude that there is no benefit in implementing a lesser vaccination strategy than ν_{1c} in controlling the diseases since there is no significant decrease of death and infectious population sizes for implementing such control strategies (since infectious curves and death curves for $\nu < \nu_{1c}$ are almost overlapping). Vaccination strategies higher than ν_{1c} help to control the disease and higher vaccination rates suppress the disease better. Figure 6 shows the variation of $\mathscr{R}_e(t)$ when vaccinations are applied at different time levels and when vaccination is started in different strengths. It is assumed that time is measured from the date of the first patient identified. Now we assume that the effective vaccinated population is fully immunized against the disease and any recovered people are not immunized. Then $\mathscr{R}_e(t) = \mathscr{R}_0 \frac{(M - V(t))}{M}$. Figure 6(a) and 6(b) shows the variation of $\mathscr{R}_e(t)$ against time for different levels of starting time of vaccination and different levels of vaccination rates respectively. The vaccination level for the results in Figure 6(a) is $\nu = 0.001$. The vaccination starting time for the results in Figure 6(b) is day 200. According to Figure 6(b) one can observe that $\mathscr{R}_e(t)$ reaches to one at a particular time, t_c, when $\nu_1 > \nu_{1c}$. Table 5 shows the t_c values for considered levels of ν_1. Approximately $(1 - \frac{1}{\mathscr{R}_0})100\% = 42\%$ people are vaccinated when $t = t_c$ at each vaccination level. The effect of vaccination on the reproduction number for the set of parameters shown in Table 2 is shown in Figure 7. According to this Figure, when the vaccination rate increases the reproduction number at the disease-free equilibrium point decreases and it reaches the critical value $\mathscr{R}_{df} = 1$ at $\nu_{1c} = 0.0000482191$. That is, for the chosen set of parameters, the vaccination rate should be increased up to ν_{1c} to suppress the disease.

Figure 8 shows the $\mathscr{R}_{df} = 1$ surface against β_1, β_2 and ν_1, that is the variation of ν_{1c} against β_1 and β_2. It can be observed that as β_1 and β_2 increase ν_{1c} decreases. That is when quarantine and isolation rates increase the critical vaccination level decreases.

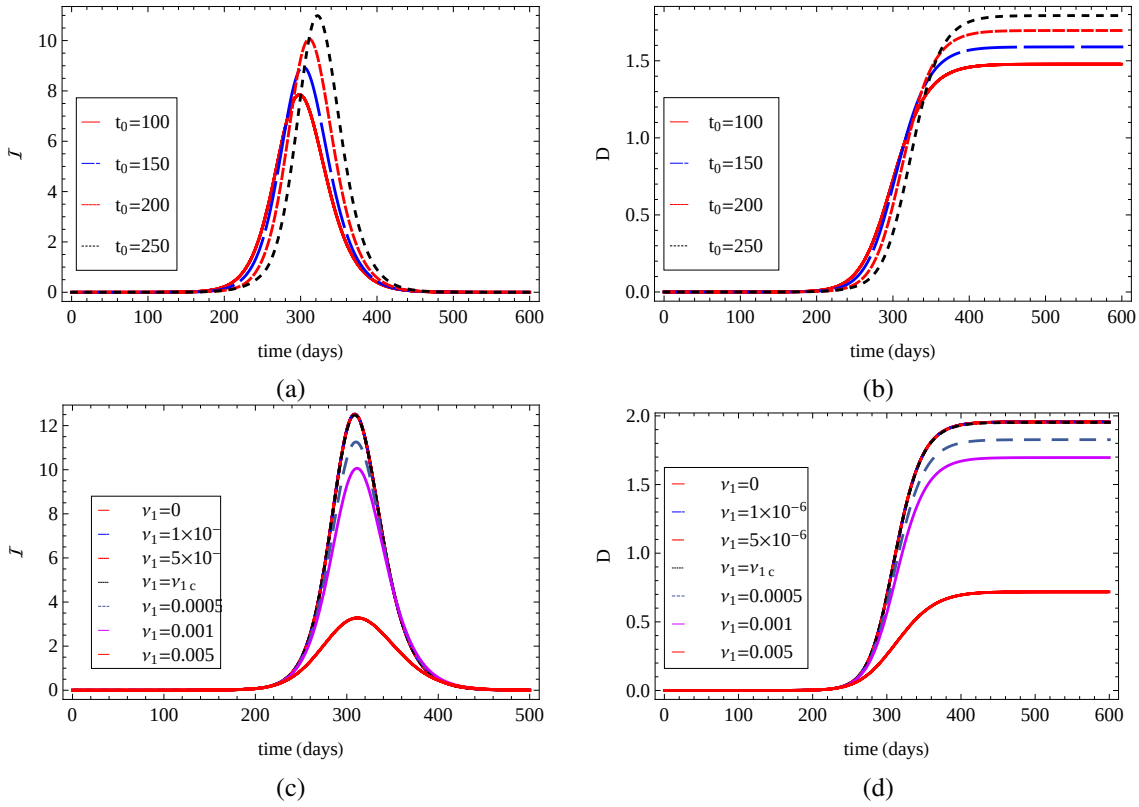

Figure 5: Variation of percentage infectious population size and death population size (a), (b): when vaccination starts at different time levels (t_0) and (c), (d): for different vaccination levels (ν_1).

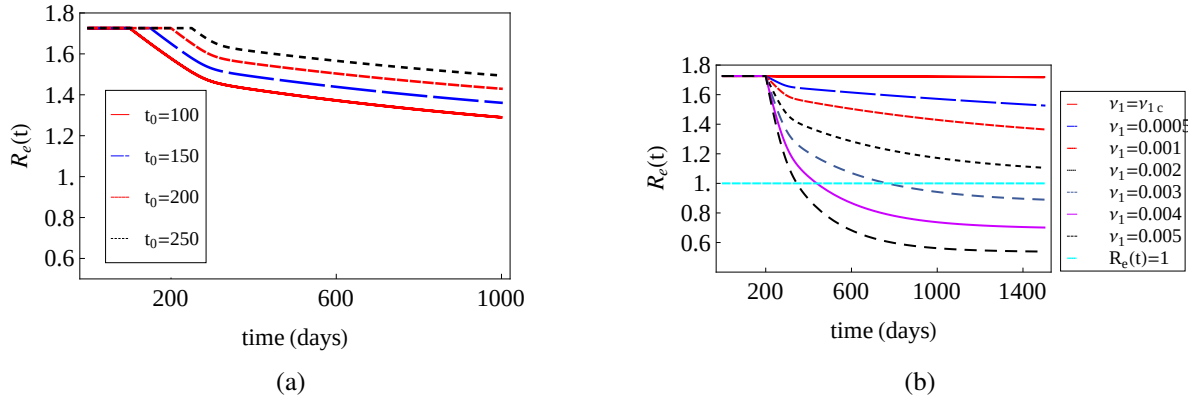

Figure 6: Variation of $\mathscr{R}_e(t)$ against time (a): when vaccination starts at different time and (b): for different vaccination levels.

Table 5: t_c correspond to ν_1.

ν_1	0.002	0.003	0.004	0.005
t_c	≈6561	≈768	≈438	≈346

Table 6: Critical vaccination rates when both quarantine and isolation are applied, only one control strategy is applied and non of these control strategies is applied.

β_1	β_2	ν_{1c}
0.05	0.03	0.0000482191
0	0.03	0.0000684917

β_1	β_2	ν_{1c}
0.05	0	0.0000707346
0	0	0.0000980088

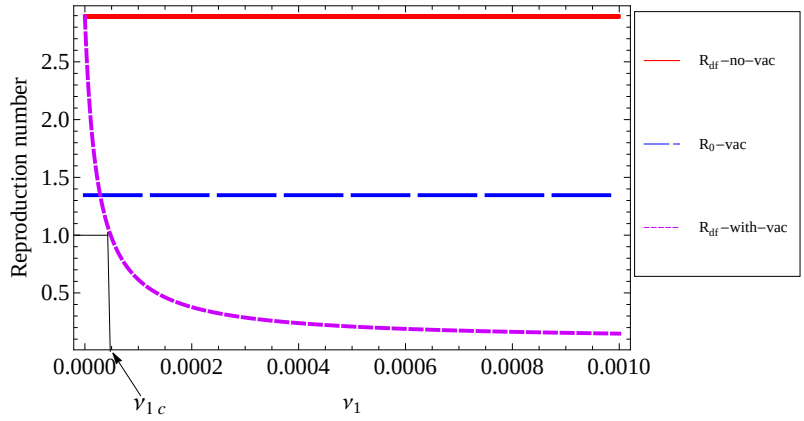

Figure 7: Variation of $\mathscr{R}_{df}$ against ν_1. $\mathscr{R}_0$-vac: Basic reproduction number considering vaccination. $\mathscr{R}_{df}$-no-vac: Disease-free reproduction number without vaccination. $\mathscr{R}_{df}$-with-vac: Disease-free reproduction number with vaccination.

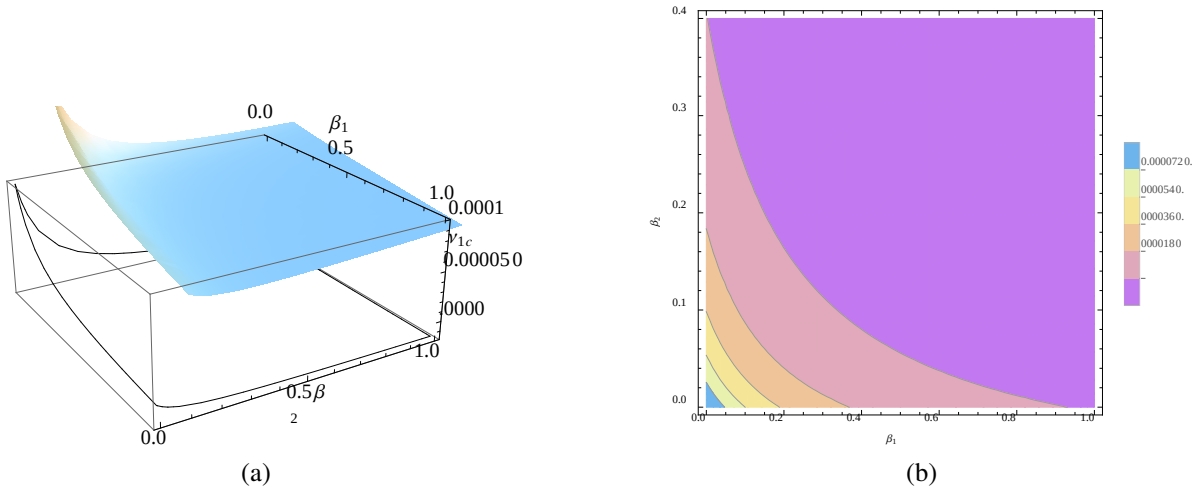

Figure 8: (a): ν_{1c} surface against β_1 and β_2, (b): contour plot of ν_{1c} against β_1 and β_2.

Table 6 shows the critical vaccination levels when both quarantine and isolation strategies are implemented, one of these is implemented, and none of these is applied. Based on the results shown in Figure 8 and Table 6, one can conclude that critical vaccination levels decrease when quarantine and isolation control strategies increase. This implies that even though vaccination started, maintaining the quarantining and isolation strategies is helpful for the suppression of the disease. Also, it is possible to suppress the disease only by a vaccination strategy if it is possible to maintain the vaccination rate greater than the critical value 0.0000980088.

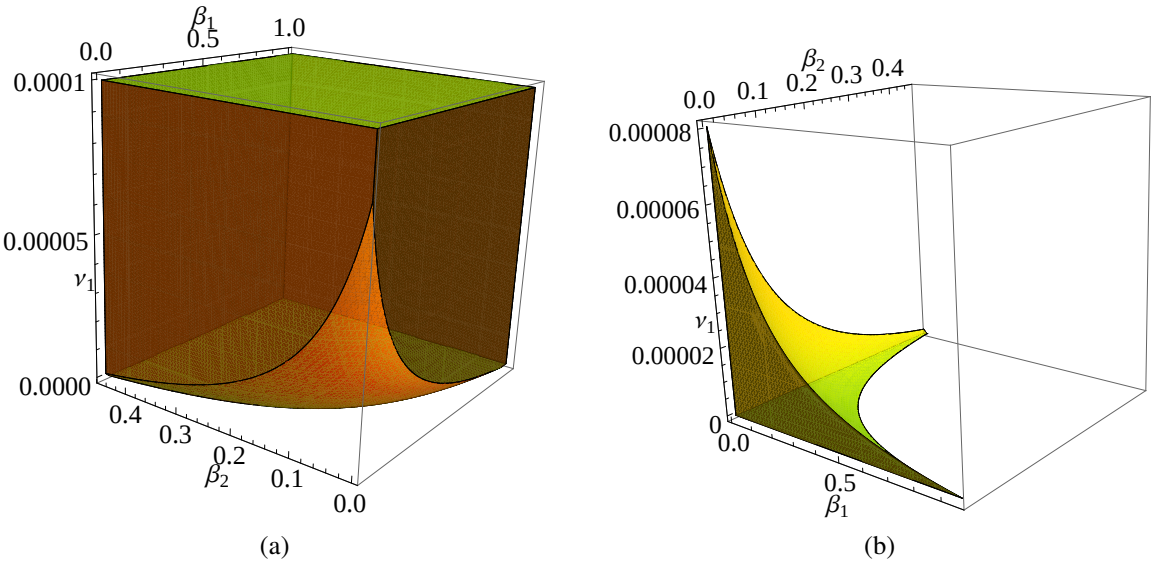

Figure 9: (a): $\mathscr{R}_{df} < 1$ parameter region (b): $\mathscr{R}_{df} > 1$ parameter region

Figure 9 shows the $\mathscr{R}_{df} < 1$ and $\mathscr{R}_{df} > 1$ parameter regions. In order to suppress the disease, it is needed to take actions to maintain control strategies such that control rates remain within the $\mathscr{R}_{df} < 1$ parameter region.

CONCLUSION

A deterministic mathematical model for COVID-19 is proposed considering the main control strategies of quarantine, isolation, and vaccination. Mostly using model-specific key terms in infectious disease modelling, the basic reproduction number, disease-free reproduction number, and effective reproduction number of the model are derived. Based on the sensitivity analysis of the reproduction number, it is observed that three most sensitive parameters of the model are transmission rates from the susceptible class to the exposed class, the recovery rate of infectious people, and the vaccination rate respectively for the chosen set of parameters. Since the sensitivity index of $\mathscr{R}_{df}$ provides information about the importance of each model parameter on the spread of the disease, vaccination plays the third important role in the disease control process. Critical vaccination rate and critical percentage vaccination population size for the chosen set of parameters are $\nu_{1c} = 0.0000161147$ and $V_c = 42\%$ respectively. That is, to get full control of the disease, the vaccination process should be continued until 42% of the total population is vaccinated. For vaccination processes such that $\nu_1 > \nu_{1c}$, the minimum vaccination period to suppress the disease is determined. Disease die-out control parameter regions of the model are determined and a graphical interpretation of the region is presented. In order to suppress the disease, it is needed to strengthen the control strategies such that relevant parameters lie in the disease die-out parameter region. Based on the results of the proposed model it is found that earlier implementation of an effective vaccination process is helpful in properly controlling the disease. In the formulation of the model, it is assumed that all the vaccinated people are fully immunized to the diseases. But, the vaccinations investigated so far for COVID-19 do not fully immunize people to the disease. Therefore, the critical values derived here may beyond the actual situation of COVID-19. Therefore, in future research, the author expects to modify the model by taking into account the immunization failure of the COVID-19 vaccinations.

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