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RESEARCH ARTICLE

An Optimal Control of SIRS Model with Limited Medical Resources and Reinfection Problems

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Abstract COVID-19 is a global public health problem that causes severe acute respiratory syndrome (SARS). It is also extremely contagious with rapidly increasing death rates. In this paper, we propose an optimal control model with SIRS (Susceptible–Infected–Recovered- Susceptible) kinetics to examine the effects of several intervention measures (e.g., vaccination and treatment) under the limited medical resources scenarios. This model is also employed to investigate the possibility of reinfection because of the fading of immunity problem. As a case study, the modeling framework is parametrised using COVID-19 daily confirmed and recovered cases in Malaysia. The parameters have been approximated by relying on the model's best fit to actual data published by the Malaysian Ministry of Health (MOH). Our numerical simulation results show that the inclusion of optimal control components with vaccination and treatment strategies would dramatically reduce the number of active cases even in the presence of reinfection forces. Regardless of the relative weightage (or costs) of vaccination and treatment, as well as the possibility of reinfection, it is critical to plan effective COVID-19 control measures by vaccinating as many people as possible (and as early as possible). Overall, these insights help explore the importance of intervention measures and the allocation of medical resources to control the severity of this pandemic.

Keywords: SIRS, optimal control, vaccination, limited medical resources, reinfection.

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Introduction

The new coronavirus called SARS-CoV-2 (or previously known as 2019-nCov) and the disease associated with this virus, COVID-19, have been discovered in December 2019 [1]. This coronavirus has caused severe pandemic and massive global health problems across the globe. As of May 21, 2021, the number of the confirmed cases worldwide was 166,000,000, with a total death of 3,430,000 people [2]. For Malaysia, 518,694 confirmed cases have been recorded with 2,438 deaths occurred as of May 21, 2021. Furthermore, over 213 countries and territories have confirmed the existence of COVID-19 diagnosed cases, indicating that the coronavirus has quickly spread across continents. [3,4].

To control the spread of COVID-19 in Malaysia, the relevant agencies such as Malaysian National Security Council and Ministry of Health (MOH) have put in place rigorous intervention policies, including movement control order (MCO) and lockdown [5,6]. Besides MCO, the government also employs different non-pharmaceutical intervention (NPI) measures, such as social distancing, tracing close contacts, wearing face masks in public and quarantine [7–9]. These preventive measures effectively worked from the public health perspectives, and during the first and second waves of outbreak, Malaysia was able to flatten the curve of COVID-19 infections up until September 2020 [10].

This observation illustrates the importance of NPI strategies and adaptation of individuals to reduce infection risks of COVID-19 until large stocks of vaccines are available to immunize the whole populations of Malaysia.

However, starting from October 2020 [11,12], the number of daily active cases has risen up considerably, and this country has faced the third and fourth waves of the pandemic. During these phases, the infection trend is experiencing exponential growth across the population, with irregular peaks in the number of active cases [13]. Although some people believe that the rebound effect in the COVID-19 infection dynamics occurs due to previously imposed preventive measures being relaxed in Malaysia, emergence variants of concern, scarcity of medical resources and reinfection problems, may influence COVID-19 pandemic outbreaks [9,14,15]. Some countries have also reported significant number of reinfection cases such as in the United States [16], Hong Kong [17], Brazil [18] and the United Kingdom [19, 20]. Given this pandemic is an emerging infectious disease, much remains unknown about this viral infection and the effectiveness of some intervention measures to control COVID-19, given that Malaysia may have tacked the scarcity of medical resources and the potential reinfection problems.

Malaysia and most countries worldwide have employed different pharmaceutical intervention measures to tame this raging pandemic, including treatment and vaccination programs [21–24]. Numerous mathematical models have been formulated incorporating an optimal control approach to examine the effects of such preventive measures in controlling this pandemic [25–29]. Optimal control is a valuable technique for assessing the interplay between different intervention measures, which can help government to make an informed decision with the aim to significantly reduce COVID-19 incidence and prevalence in the population [23]. This technique is based on the calculus of variations, and often it can help reveal intriguing insights on the most effective intervention measures. Motivated by this observation, we develop an optimal control model with $SIRS$ (Susceptible-Infected-Recovered-Susceptible) kinetics to examine the effects of several intervention measures (e.g., vaccination and treatment) under the scenarios of a shortage in medical resources and the possibility of reinfection.

The article is organized as follows. After outlining the $SIRS$ model with a limited medical resources component, we derive the optimal control system using Pontryagin's maximum principle. Then, we investigate the effects of pharmaceutical intervention measures on the long-term dynamics of COVID-19 in Malaysia. Finally, we also discuss further epidemiological implications of our results.

Model Formulation

We employ a basic SIR system and extensions thereof to investigate the combined effects of lack of medical resources and the reinfection problems on COVID-19 dynamics in Malaysia. The prediction model that has been established is in the form of a $SIRS$-type ordinary differential equations (ODE) system [9,30-33]:

$$\begin{cases} \dfrac{ds}{dt} = \beta N - \dfrac{vSI}{N} + \varepsilon R - \delta S. \\ \dfrac{dI}{dt} = \dfrac{vSI}{N} - (\psi + v)I - \dfrac{\rho I}{\varphi + I} \\ \dfrac{dR}{dt} = \psi I + \dfrac{\rho I}{\varphi + I} - (\varepsilon + \delta)R \\ N = S + I + R \end{cases} \tag{1}$$

Figure 1 illustrates the schematic diagram of flow diagram representing Covid-19 SIRS model (1). The concept of this model is to divide the entire population into three different compartments (Susceptible-Infected-Recovered), and the individuals are transferred among these compartments according to certain parameters.

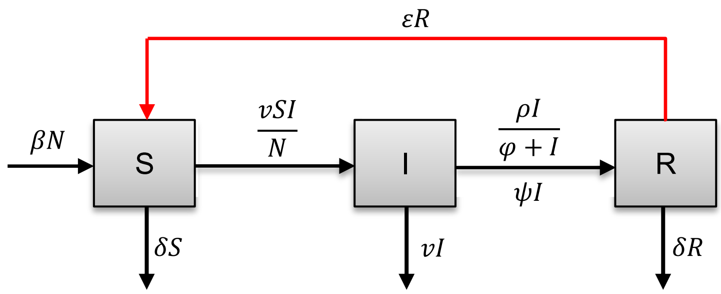

Figure 1. Flow diagram of COVID-19 model (1)

where N denotes the total number of populations, which are divided into three groups: (i) the susceptible compartment is denoted by the variable $S(t)$; (ii) the infected compartment is represented by the variable $I(t)$; and (iii) the removal compartment is modeled using the variable $R(t)$, which includes both recovered and death cases. The terms β is the birth rate, v is the death rate, δ is the transmission rate, and ψ is the population recovery rate in the modelling framework (1). To investigate the impact of reinfection on COVID-19 outbreak, a proportion of recovered individuals from the removal group is allowed to re-enter the susceptible compartment with a rate ε; hence, ε yields the reinfection force. The term $\frac{\rho I}{\varphi+I}$ is often used to assess the effects of a shortage in healthcare supplies on the COVID-19 outbreak dynamics; it is first introduced by Zhou and Fan [15]. The parameter ρ denotes the healthcare supplies per unit time, and φ is the half-saturation value, which represents the effectiveness of a supply of medical resources. In general, the effectiveness of medical supplies would depend on distinct epidemiological factors and control strategies e.g., quarantine, movement control order, drugs, and vaccines [14, 15]. In the absence of the reinfection factor and medical resource issues (i.e., $\varepsilon = \rho = 0$), the model is represented by a basic SIR-type model and we will also present some of the analysis of this fundamental system in the following section.

To examine the biologically significant aspects of COVID-19 trajectories, it is assumed that all of the parameters of the model are non-negative. For further details on some theoretical analysis such as estimation of equilibria, local stability analysis and the derivation of basic reproduction number of the model (1), interested reader are referred to Salman et al. [9], Mohd and Sulayman [14] & Jamiluddin et al. 2021 [34].

Optimal Control Strategies

In this section, we now include the pharmaceutical control measures i.e., vaccination and treatment strategies using an optimal control approach. We modify the system (1) by the incorporation of some controls components in the form of treatment and vaccination [31, 32, 35], which vary with time. The control function $\vartheta(t)$ represents the vaccination effort by government and the control function $\tau(t)$ indicates the treatment effort provided to the infected population. So, the model (1), which has been extended with the control functions, ϑ and τ, becomes:

$$\begin{cases} \frac{dS}{dt} = \beta N - \frac{vSI}{N} + \varepsilon R - (\delta + \vartheta)S. \\ \frac{dI}{dt} = \frac{vSI}{N} - (\psi + v + \tau)I - \frac{\rho I}{\varphi + I} \\ \frac{dR}{dt} = (\psi + \tau)I + \frac{\rho I}{\varphi + I} - (\varepsilon + \vartheta + \delta)R \\ \qquad N = S + I + R \end{cases} \tag{2}$$

Using Equation (2), we seek to minimize the objective functional defined by:

$$U = \{J(\vartheta,\tau) \in L^1(0,T) \big| (\vartheta(t),\tau(t)) \in [0,\vartheta_{max}] \times [0,\tau_{max}] \forall t \in [0,T]\} \tag{3}$$

Given that we have two controls $\vartheta(t)$ and $\tau(t)$, we want to find the optimal controls $\vartheta^*(t)$ and $\tau^*(t)$ such that:

$$J(\vartheta^*,\tau^*) = min\{J(\vartheta,\tau),\vartheta,\tau \in U\} \tag{4}$$

Using Pontryagin's maximal principal, we determine the necessary conditions of this optimal control system. In particular, we convert the optimization problem described in (3)-(4) to the problem of finding the point-wise minimum relative to ϑ and τ of the Hamiltonian:

$$H = C_1 I + C_2 R\vartheta^2 + C_3\tau^2 + \lambda_1 \frac{dS(t)}{dt} + \lambda_s \frac{dI(t)}{dt} + \lambda_3 \frac{dR(t)}{d(t)} \tag{5}$$

where $\lambda_i, i = 1,2,3$ are the associated adjoints for the states S, I, and R. The parameters C_1, C_2 and C_3 in the objective function (5) are positive constants representing weightage (or relative costs) of applying respective control strategies. The term C_1 represents the weightage for the number infected, C_2 represents weightage for vaccination effort and C_3 represents the weightage for treatment strategy. This kind of objective function is rather popular, and it is inspired by some optimal control studies [23,26,36,37]. We choose the objective function given by equation (5) simply because this formulation could satisfy the convexity property of the cost function (Agusto [38], Jung et al. [39], Kim et al. [40]).

We obtain the system of adjoint equations by using the partial derivatives of the Hamiltonian (5) with respect to each state variable:

$$\begin{cases} \dfrac{d\lambda_1}{dt} = (\lambda_1 - \lambda_2)\dfrac{vI}{N} + (\lambda_1 - \lambda_3)\vartheta + \lambda_1\delta \\ \dfrac{d\lambda_2}{dt} = -C_1 + (\lambda_1 - \lambda_2)\dfrac{vS}{N} + (\lambda_2 - \lambda_3)\dfrac{\rho\varphi(\psi+\tau)}{(\psi+I)^2} + \lambda_2\delta \\ \dfrac{d\lambda_3}{dt} = -C_2\varphi^2 + (\lambda_3 - \lambda_1)\varepsilon + \lambda_3(\delta+\vartheta) \end{cases} \tag{6}$$

with transversality conditions $\lambda_1(t) = \lambda_2(t) = \lambda_3(t) = 0$. Furthermore, as long as the optimal removed class R^* is nonzero, we may characterize the optimal pair by the continuous functions:

$$\begin{cases} \vartheta^*(t) = min\left(max\left(0, \dfrac{(\lambda_1 - \lambda_3)S^* + \lambda_3 R^*}{2C_2 R^*}\right), \vartheta_{max}\right), \\ \tau^*(t) = min\left(max\left(0, \dfrac{(\lambda_2 - \lambda_3)I^*}{2C_3}\right), \tau_{max}\right), \end{cases} \tag{7}$$

In general, the restriction on R^* can be imposed by assuming a nonzero initial value of the removed population for mathematical convenience. From a biological perspective, this condition is not necessary.

Parameter Estimation and Numerical Simulation

Some parameter estimation and numerical simulation techniques of the $SIRS$-type model with optimal control components is also employed in this work. In particular, MATLAB software has been used to perform parameter estimation analysis of the system (1) when $\epsilon = 0$ and $\rho = 0$ (for basic transmission dynamics scenario using SIR epidemiological system). The parameters are estimated based on actual COVID-19 cases in Malaysia in the interval between December 1, 2020, and December 31, 2020. To fit the data to the models, we employed the nonlinear least-squares fitting routine. The sum of squared errors (SSE) is defined as:

$$SSE(\theta) = \sum_{i=1}^{n} \left(y_i - f(x_i, \theta)\right)^2 \tag{8}$$

where y_i represents the actual data or observation at time t, and f indicates the model solution. The epidemiological model is numerically solved to obtain a value for $SSE(\theta)$ given an initial guess (θ) of the unknown parameters. Then "fminsearch" algorithm is employed for direct searching process to discover the smallest value of least squares error function $SSE(\theta)$ and an initial estimation of the parameter value. To guarantee that the minimum value produced by "fminsearch" is not merely a local minimum, the process is repeated with many initial guesses. Figure 2 demonstrates the data fitting procedure using the minimisation of SSE and Matlab 'fminsearch' function with the minimum sum squared errors, $MSSE = 1.0137 \times 10^{-5}$. The blue dots denote the actual infected cases, and the yellow dashed curve indicates the fitted daily active cases. Similarly, the red dots denote the real removed cases, and the purple dashed curve indicates the fitted daily removed cases. Overall, it can be observed that the actual infected (I) and removed (R) cases are in agreement with the fitted trajectories from the modeling framework, and the essential epidemiological parameters such as transmission and recovery rates can be estimated using this data fitting procedure. Figure 2B shows an example of SIR long term trajectories using fitted parameter values. Unless otherwise stated, the parameters used in the numerical simulation are shown in Table 1. In all cases, we employed numerical simulation using MATLAB ode15s solver for sufficient time until a steady state is reached.

Table 1. Parameter values

Symbol	Description	Value
β	The birth rate	0.000006 [9]
δ	The death rate	0.00002 [9]
υ	The transmission rate	0.11747 (Estimated)
ψ	The recovery rate	0.076403 (Estimated)
ε	The reinfection force	Vary (Hypothetical Values)
ρ	The medical resources supplied per unit time	0.0584 [15]
φ	Half-saturation constant	3.0173 [15]
C_1	Weight for number infected	100000
C_2	Weight for vaccination	$100000 - 500000$
C_3	Weight for treatment	$1000 - 5000$
ϑ_{max}	Max vaccination rate	0.15/day
τ_{max}	Max treatment rate	0.1/day
$S(0)$	Initial susceptible population	500000 (Fitted)
$I(0)$	Initial infected population	10495 (Observed)
$R(0)$	Initial removal class population	56674 (Observed)

Results and Discussion

In the absence of optimal control strategies, an epidemiological model (1) is analyzed. The daily active cases trajectories are studied for numerous reinfection scenarios (dotted curves), as shown in Figure 3(A-B). In comparison, the associated real active cases (black dots) in Malaysia are also plotted started from December 1, 2020. The modelling framework analysis matches with the number of active cases in Malaysia, and the system (1) can mimic the trend of infection trajectories of the COVID-19 in this country. Next, we examine several hypothetical scenarios (dotted red, cyan and green curves) under varying reinfection forces to illustrate distinct possibilities of COVID-19 transmission dynamics in Malaysia. First, we investigate an outcome of a simple SIR (dotted red) in Figure 3(A) where the scarcity of medical resources is not present ($\rho = 0$), and the reinfection force is relaxed ($\varepsilon = 0$) in this system. It can be seen that the infection trajectory is increasing daily and that the active cases will peak in a few months. The infection frequency then begins to decrease under this simplified scenario analysis (i.e., the SIR system assumes that enough medical resources are being allocated to combat this pandemic, in addition to the use of the best screening and isolation measures). As a result, the SIR model predicts that flattening the infection curve and reducing the number of infected people to a low level of active cases will take around a year.

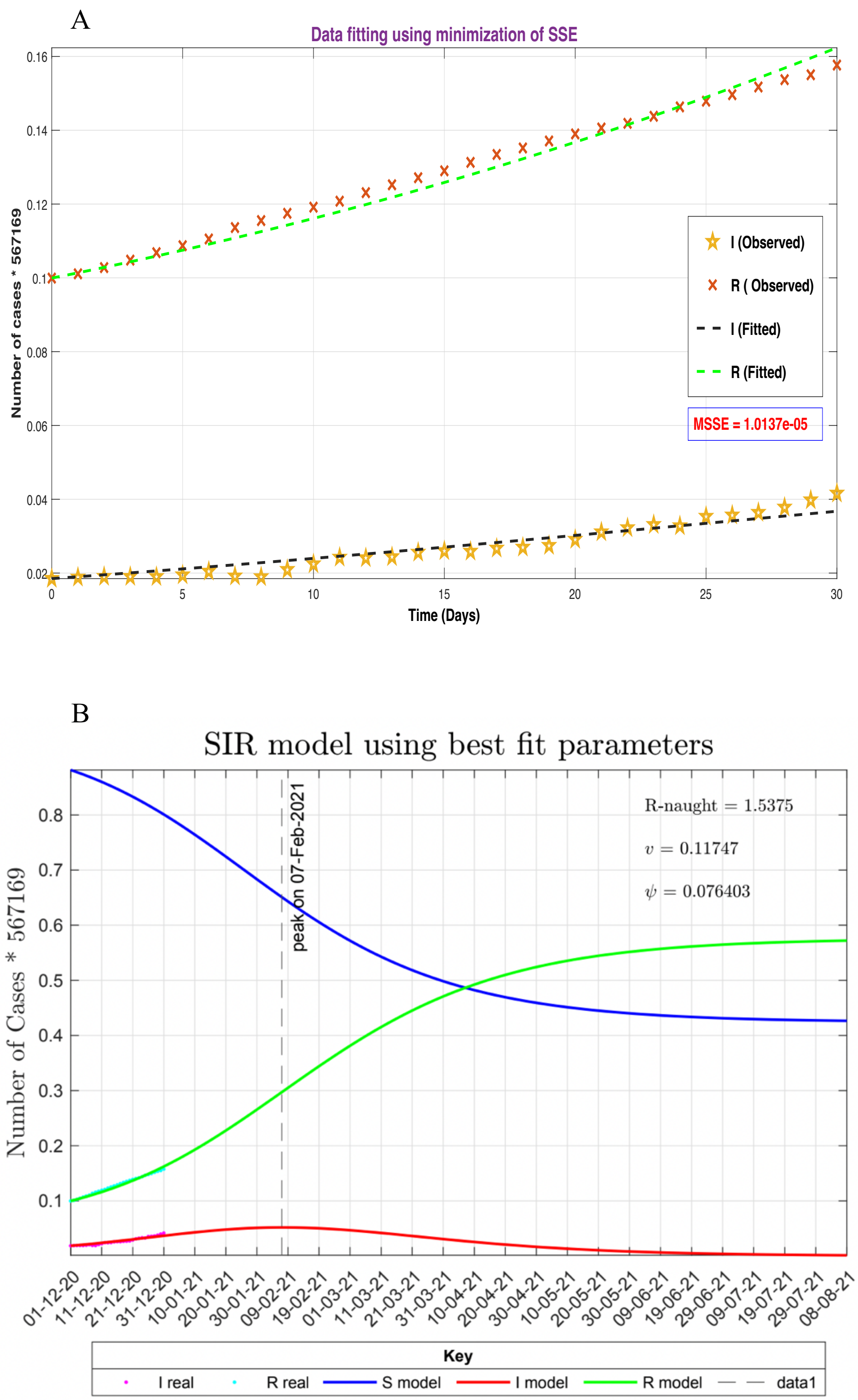

Figure 2. (A) illustrates the data fitting using minimization of SSE. Figure 1. (B) shows SIR model estimation for the period from 1 Dec. 2020 to 31 Dec. 2020 and projection for the next 220 days.

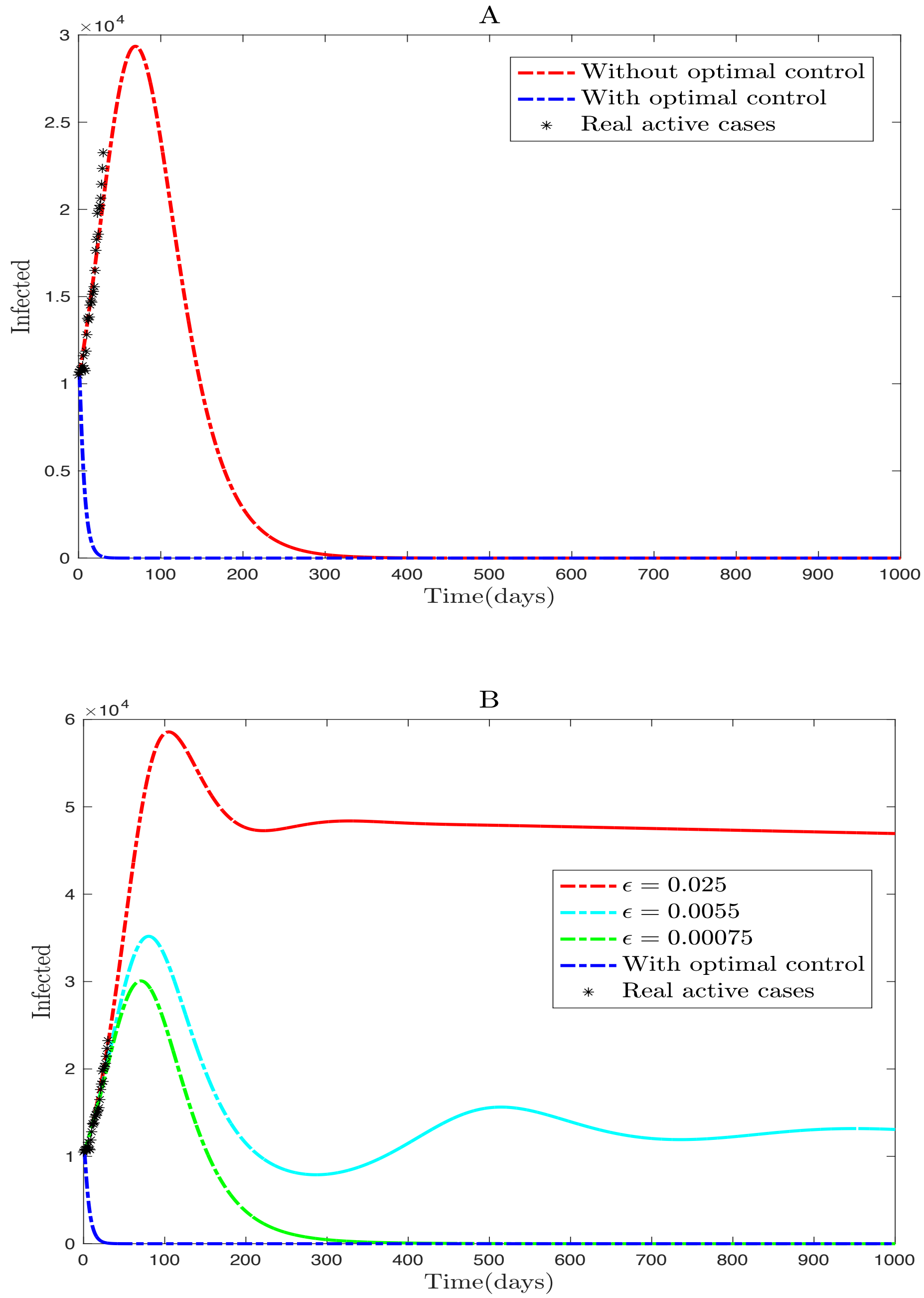

Figure 3. The plot illustrates the dynamic of infected population using SIRS-type epidemiological model after incorporating the pharmaceutical control measures i.e., vaccination and treatment strategies using an optimal control approach (blue line) and without control (red dashed line). (A) The reinfection parameter is relaxed $\varepsilon = 0$ and transmission rate $v = 0.11747$. (B) The reinfection force varies (we take more than one case) for $\varepsilon > 0$ and comparison with the number of active cases in Malaysia (black stars). The parameters used to generate the plot are given in Table 1. The initial values are $S(0) = 500000, I(0) = 10495$ and $R(0) = 56674$.

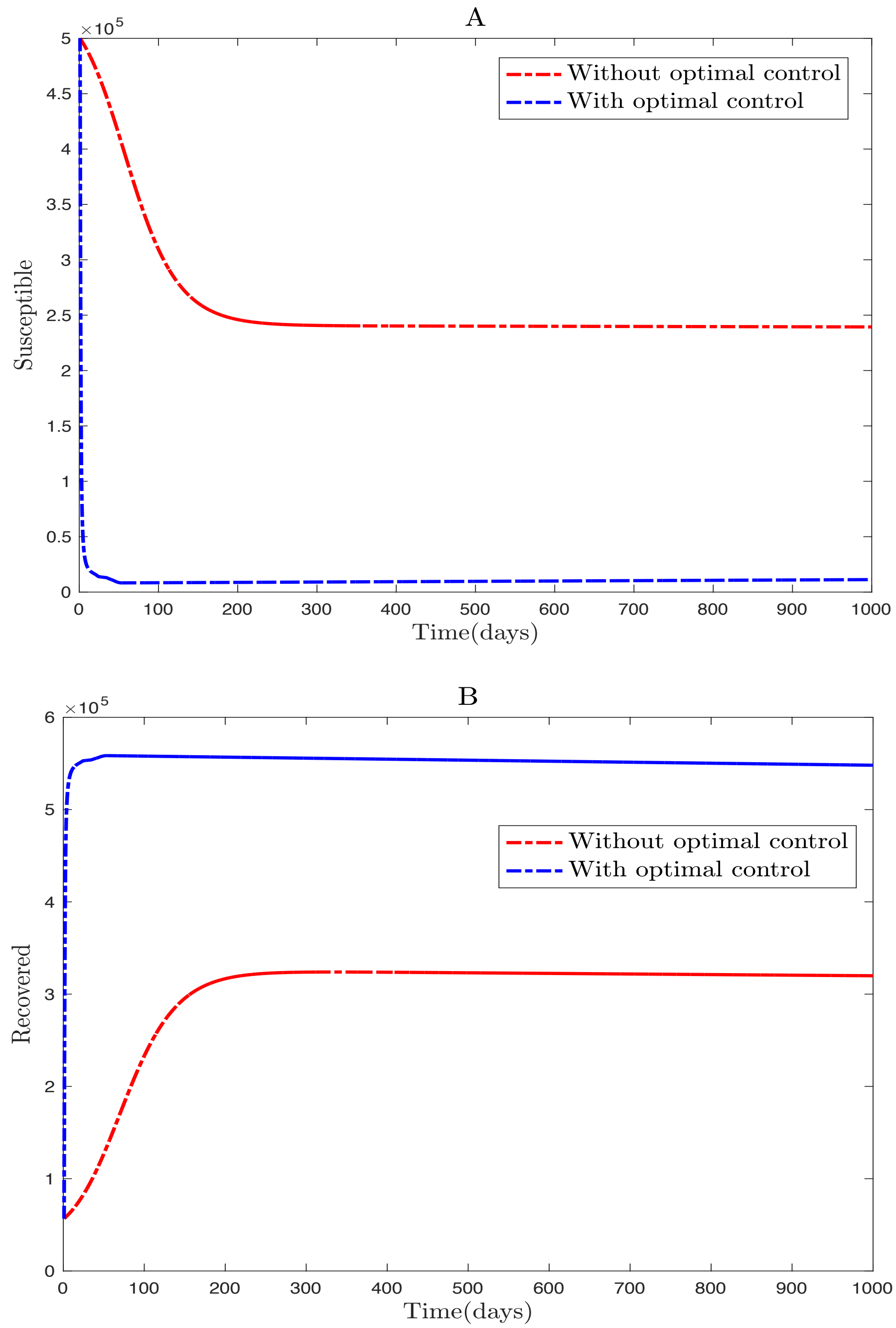

Figure 4. The plot illustrates the dynamic of susceptible (A) and recovered (B) populations using $SIRS$-type epidemiological model after incorporating the pharmaceutical control measures i.e., vaccination and treatment strategies using an optimal control approach (blue line) and without control (red dashed line). The parameters used to generate the plot are given in Table 1. The initial values are $S(0) = 500000, I(0) = 10495$ and $R(0) = 56674$.

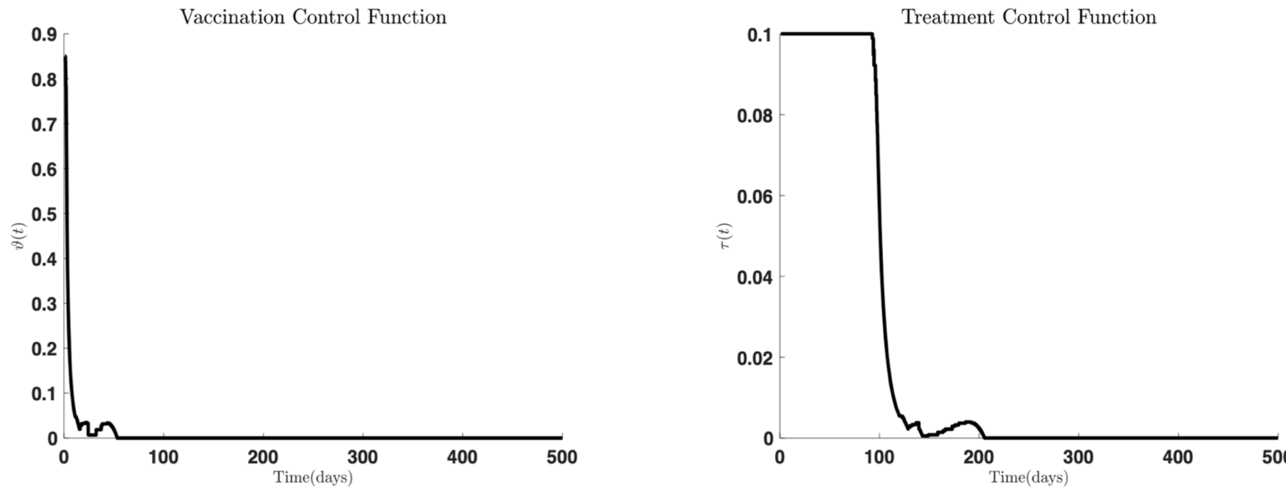

Figure 5. Optimal-control values for vaccination control $\vartheta(t)$ and treatment control $\tau(t)$ over 500 days. The plot generated using equation (7).

We then extend this scenario analysis by evaluating the severity of COVID-19 outbreaks in Malaysia and their combined effects with different epidemiological forces. This analysis aims to examine the transmission trajectories and other dynamical behaviors of the model (1). It also displays some of the most likely epidemiological predictions mediated by the interaction of reinfection force (ε) and limited medical resource (ρ) problems. Increasing the intensity of ε and with limited medical capacity $(\rho > 0)$ could lead to a more potent infection force influencing COVID-19 transmission dynamics, as shown by Figure 3(B). For example, as the reinfection force is relatively weak (e.g., $\varepsilon = 0.000755$; dotted green), a flattening phenomenon is observed similar to the outcome of the basic SIR model. However, after several years, a rebound effect in transmission can be seen if reinfection force is moderate (e.g., $\varepsilon = 0.0055$; dotted cyan), and the severity of rebounds in the transmission are dependent on the magnitude of ε. Further increasing the intensity of ε would lead to the number of individuals infected with COVID-19 reaching a plateau (e.g., $\varepsilon = 0.025$; dotted red). The number of infected cases would remain constant for an extended length of time. This plateauing phenomenon has been noticed in the actual world COVID-19 data from several nations, including the US [16] and United Kingdom [19, 20].

Inspired by our observations without the optimal control strategies above, one of the critical questions that remain to be answered is that: if reinfections are going to happen for COVID-19 and there is a possibility of limited medical resources problem, what are the main effects of pharmaceutical intervention measures (e.g., vaccination and treatment)? To investigate these scenarios, we employ the optimal control system (6) and assess the combined impacts of pharmaceutical intervention measures, reinfection problem and shortage of medical supplies on the long-term behavior of COVID-19 outbreaks in Malaysia. Our numerical simulation results in Figure 3(A-B) demonstrate that the inclusion of optimal control approaches (blue curves) would dramatically reduce the number of active cases even in the presence of reinfection forces. Therefore, regardless of the relative weightage (or costs) of vaccination and treatment, as well as the possibility of reinfection, it is critical for effective COVID-19 control measures to vaccinate as many people as possible (and as early as possible). This recommended strategy can reduce the number of infected people and the effort required to control this pandemic. Furthermore, as shown by Figure 4(B) (respectively, Figure 4(A)), the step mentioned above would enhance (respectively, reduce) the number of recovered (respectively, susceptible) people due to the treatment and vaccination strategies. Additionally, Figure 5 illustrates another view of the pharmaceutical mitigation strategies provided by the optimal control simulations using equation (7). We should emphasise on the effective plans for vaccinating at the highest rate possible; if this results in fewer susceptible individuals remaining and being vaccinated, more healthcare resources and funding may be spent on treatment while maintaining the recommended vaccination rate.

Conclusions

This work employs the SIRS epidemic model with reinfection force and limited medical resources components to examine the combined effects of vaccination and treatment strategies on COVID- 19 transmission dynamics in Malaysia. Our findings demonstrate that the optimal vaccination and treatment strategies are required to control this raging pandemic effectively. Overall, the insights from our modeling framework help explore the relative importance of intervention measures and the allocation of medical resources to control the severity of this pandemic.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper. Some of the information you choose to provide here may constitute your “sensitive personal data”.

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