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Optimal control-based vaccination and testing strategies for COVID-19

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Abstract

Background and Objective: Assuming the availability of a limited amount of effective COVID-19 rapid tests, the effects of various vaccination strategies on SARS-CoV-2 virus transmission are compared for different vaccination scenarios characterized by distinct limitations associated with vaccine supply and administration. Methods: The vaccination strategies are defined by solving optimal control problems of a compartmental epidemic model in which the daily vaccination rate and the daily testing rate for the identification and isolation of asymptomatic subjects are the control variables. Different kinds of algebraic constraints are considered, representing different vaccination scenarios in which the total amount of vaccines available during the time period under consideration is limited or the number of daily available vaccines is limited. These optimal control problems are numerically solved by means of a direct transcription technique, which allows both equality and inequality constraints to be straightforwardly included in the formulation of the optimal control problems. Results: Several numerical experiments are conducted, in which the objective functional to be minimized is a combination of the number of symptomatic and asymptomatic infectious subjects with the cost of vaccination of susceptible subjects and testing of asymptomatic infectious subjects. The results confirm the hypothesis that the implementation of early control measures significantly reduces the number of symptomatic infected subjects, which is a key aspect for the resilience of the healthcare system. The sensitivity analysis of the solutions to the weighting parameters of the objective functional reveals that it is possible to obtain a vaccination strategy that allows vaccination supplies to be saved while keeping the same number of symptomatic infected subjects. Furthermore, it indicates that if the vaccination plan is not supported by a sufficient rate of testing, the number of symptomatic infected subjects could increase. Finally, the sensitivity analysis shows that a significant reduction in the efficacy of the vaccines could also lead to a relevant increase in the number of symptomatic infected subjects. Conclusions: The numerical experiments show that the proposed approach, which is based on optimal control of compartmental epidemic models, provides healthcare systems with a suitable method for scheduling vaccination plans and testing policies to control the spread of the SARS-CoV-2 virus.

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1. Introduction

The problem of determining the most effective strategy for controlling the spread of an epidemic disease like COVID-19 can be formulated as an Optimal Control Problem (OCP), in which the goal is to minimize, over a time period, an objective functional typically associated with the cost of the control measures or the number of infectious subjects, in the presence of dynamic constraints, which represent the dynamic system that models the disease transmission, and algebraic constraints, such as limitations on the vaccination and testing supplies.

This paper considers an objective functional that combines the number of symptomatic and asymptomatic infected subjects with the cost of vaccination of susceptible subjects and testing of asymptomatic infectious subjects. Moreover, different scenarios are studied, which are represented by different algebraic constraints in the OCP, in which the total amount of vaccines available during the time period under consideration is limited or the number of daily available vaccines is limited. The disease transmission and its interaction with these control measures are modeled using a compartmental epidemic model.

Optimal control is a research field with many applications in biology [1] and biomedicine [2]. More specifically, it has been widely used to investigate compartmental models in epidemiology. The following relevant related research works are highlighted. In [3], a time-optimal control problem is formulated, in which different
control policies such as vaccination, isolation, culling, and reduction of transmission, have been considered. In [4], a spatiotemporal epidemic model is formulated as a system of parabolic partial differential equations with no-flux boundary conditions, where immunity is forced through vaccine distribution, which is considered the control variable. A Bernstein-Bézier parametrization and an echo state networks-based algorithm are proposed in [5] to solve an OCP with two control variables of the epidemic model. In [6], an optimal impulse control approach is used to solve an isolation problem for an epidemic model describing the transmission of HIV. In [7], optimal coverage strategies are derived for an epidemic model consisting of two groups of hosts under the assumption of a resource-constrained environment. A vaccination strategy for influenza outbreaks is obtained in [8] using a reaction-diffusion model. In [9], five different control strategies are presented for curtailing dengue fever spread. Non-pharmaceutical measures like public health education, isolation, and quarantine are investigated in [10] as time-dependent interventions to determine their contributions to COVID-19 transmission dynamics. In [11], real data from China are used to formulate an optimal control strategy for vaccine administration in COVID-19 pandemic treatment. A COVID-19 disease spread model with free terminal optimal time is described in [12], in which the aim is to reduce the size of susceptible, infected, exposed, and asymptomatic groups to eliminate the infection through quarantine and treatment of infected subjects.

As mentioned above, this paper considers the problem of determining and comparing optimal vaccination and testing strategies for a compartmental model of the COVID-19 transmission dynamics derived from the epidemic model introduced in [13]. More specifically, it analyzes and compares the effects of different vaccination and testing strategies on the disease transmission based on the definition of different scenarios that are modeled as OCPs with different kinds of algebraic constraints. These OCPs are numerically solved by means of a direct transcription technique, which allows both equality and inequality constraints to be included in their formulation in a straightforward manner. In particular, the Hermite-Simpson collocation method [14] is used. The NLP solver IPOPT [15] is employed to solve the Non Linear Programming (NLP) problems derived from the transcription of these OCPs. The numerical experiments show that the proposed approach provides healthcare systems with a suitable method for scheduling vaccination plans and testing policies to control the spread of the SARS-CoV-2 virus.

2. Methods

2.1. Mathematical model of COVID-19 transmission dynamics

A modified SEIR compartmental model, introduced in [13] and denoted as SEISlaQR, is used in this paper to represent the COVID-19 transmission dynamics, in which, following [16], a vaccination term is added to the model as shown in Fig. 1.

The state space representation of the SEISlaQR model is given by the following system of Ordinary Differential Equations (ODE):

\[ \dot{S}(t) = \frac{-\theta L(t) + \alpha L(t)}{N(t)} S(t) - \nu(t)S(t), \]  

\[ \dot{E}(t) = \frac{\theta L(t) + \alpha L(t)}{N(t)} S(t) - \frac{E(t)}{\tau_{lat}}, \]  

\[ \dot{I}_s(t) = \left(1 - \beta\right) \frac{E(t)}{\tau_{lat}} - \left(\kappa_s + \frac{1}{\tau_{inf}}\right) I_s(t), \]  

\[ \dot{I}_a(t) = \beta \frac{E(t)}{\tau_{lat}} - \left(\kappa_a(t) + \frac{1}{\tau_{inf}}\right) I_a(t), \]

\[ Q(t) = \frac{\kappa I_s(t) + \kappa_a I_a(t)}{\tau_{ter}} - \frac{Q(t)}{\tau_{ter}}, \]  

\[ R(t) = \frac{I_s(t) + I_a(t)}{\tau_{inf}} + \frac{Q(t)}{\tau_{ter}} + v(t) S(t), \]

in which \( N(t) \) and the variables with time derivative are the state variables of the system. More specifically, \( S(t) \) denotes the number of subjects susceptible to infection, \( E(t) \) denotes the number of exposed subjects, \( I_s(t) \) denotes the number of symptomatic subjects, \( I_a(t) \) denotes the number of asymptomatic subjects, \( Q(t) \) denotes the number of isolated subjects, \( R(t) \) denotes the number of recovered and deceased subjects, and \( N(t) \) denotes the total population, which satisfies the condition

\[ N(t) = S(t) + E(t) + I_s(t) + I_a(t) + Q(t) + R(t), \]

for all \( t \in [0, t_f] \), where \( [0, t_f] \) is the time period under consideration.

The control variables of the system (1) are \( \nu(t) \) and \( \kappa_s(t) \). The control variable \( \nu(t) \) represents the daily vaccination rate, which ranges from 0 to \( \nu_u \), where \( \nu_u \) is an upper bound that the designers of the OCP must specify. Thus, \( \nu(t)S(t) \) represents the vaccination strategy in system (1). The control variable \( \kappa_s(t) \) represents the daily testing rate for the identification and isolation of asymptomatic subjects, which ranges from 0 to \( \kappa_u \), where \( \kappa_u \) is an upper bound that the designers of the OCP must also specify.

The parameters \( \theta \) and \( \kappa_s \) of the system (1) are associated with the use of non-pharmaceutical containment strategies, where \( \theta \) denotes the replication factor and \( \kappa_s \) denotes the daily testing rate for the identification and isolation of symptomatic subjects. The parameters \( \tau_{ter}, \tau_{ins}, \tau_{inf}, \alpha, \beta \) and \( \kappa_s \) of the system (1) do not depend on containment or mitigation strategies, where \( \tau_{ter} \) is the mean serial time interval, \( \tau_{lat} \) is the incubation period, \( \tau_{inf} = \tau_{ter} - \tau_{lat} \) is the infectious period, \( \alpha \) is the ratio between the infectiousness of asymptomatic and symptomatic subjects, and \( \beta \) is the population ratio that remains asymptomatic or mild symptomatic. The values for all these parameters used in the numerical experiments are the same as in [16].

In this paper, following [16], a vaccination term is included in the model proposed in [13] and several OCPs are formulated considering different kinds of algebraic constraints, in which both the daily vaccination rate \( \nu(t) \) and the daily testing rate for the identification and isolation of asymptomatic subjects \( \kappa_s(t) \) are assumed to be the control variables.

2.2. Vaccination scenarios for COVID-19

Depending on the scenario and the objective functional considered, it is possible to determine different vaccination and testing strategies for controlling the spread of COVID-19 represented by the model (1). In this paper, three different scenarios have been considered, in which vaccination supplies are limited:

- Scenario 1, in which the number of vaccines administered during the time period \([t_1, t_f]\) is fixed.
- Scenario 2, in which there is an upper bound on the number of vaccines administered during the time period \([t_1, t_f]\).
- Scenario 3, in which there is an upper bound on the number of vaccines administered each day.

They correspond to three different kinds of constraints, namely an isoperimetric constraint, a state constraint, and a mixed state-control constraint, respectively.

In all three cases, the objective functional to be minimized has been assumed to be a combination of the number of symptomatic and asymptomatic infectious subjects with the overall cost of the
vaccination of susceptible subjects and the testing of asymptomatic infectious subjects during a fixed time period, that is, 
\[ J(I_v(t), I_s(t), v(t), \kappa(t)) = \int_{t_1}^{t_f} (A_1 I_v(t) + A_2 I_a(t) + A_3 v(t) + A_4 \kappa_0(t)) dt, \]  
(2)

where \( A_i \in [0, 1], i = 1, 2, 3, 4, \) are weighting parameters that the designers of the OCP must specify according to their preferences. For instance, larger values of \( A_3 \) give more importance to the vaccination cost.

### 2.2.1. Scenario 1

In this scenario, it is assumed that the number of vaccines available during the time period \([t_1, t_f]\) is known and that they are all administered. Thus, the number of vaccines administered during the time period \([t_1, t_f]\) is fixed and, according to Neilan and Lenhart [17], this condition can be modeled by the following isoperimetric constraint 
\[ \int_{t_1}^{t_f} v(t)S(t) = V_f, \]  
(3)

where \( V_f \) denotes the total number of susceptible people that are vaccinated over the time period \([t_1, t_f]\). The integral constraint (3) can be tackled by defining a new state variable \( W(t) \) and a new differential equation together with its corresponding boundary conditions, as follows:
\[ W(t) = v(t)S(t), \]
\[ W(t_1) = 0, \]
\[ W(t_f) = V_f. \]

### 2.2.2. Scenario 2

In this scenario, unlike Scenario 1, in which it is assumed that the number of vaccines available in the time period \([t_1, t_f]\) is known and they are used completely, it is assumed that they can either be administered completely or not. While the isoperimetric constraint (3) assumes that all the vaccines available are used, according to [18], this condition can be easily relaxed by considering the inequality constraint 
\[ W(t_f) \leq V_f, \]  
(4)

instead of \( W(t_f) = V_f \), which represents an overall upper bound on the supply of vaccines over the time period \([t_1, t_f]\). Notice that the inequality constraint \( W(t_f) \leq V_f \) is a state constraint.

### 2.2.3. Scenario 3

In this scenario, it is assumed that the daily number of vaccines available during the time period \([t_1, t_f]\) is known and that they can either be used completely or not. This condition, according to Biswas et al. [18], can be modeled replacing the state constraint (4) with the constraint 
\[ v(t)S(t) \leq V_0, \text{ with } t \in [t_1, t_f], \]  
(5)

where the parameter \( V_0 \) denotes an upper bound on the number of daily vaccinated susceptible people. Notice that the expression (5) is a mixed state-control constraint.

Thus, the OCP of the SEIsaQR compartmental model (1) with mixed state-control constraint can be stated as follows:
\[ \min_{\theta, \alpha, \kappa} J(I_v(t), I_s(t), v(t), \kappa(t)) \]  
subject to:
\[ \dot{S}(t) = -\frac{\theta}{T_{inf}} I_v(t) + \frac{\alpha I_s(t)}{N(t)} S(t) - v(t)S(t), \]  
(6b)

\[ \dot{E}(t) = \frac{\theta}{T_{inf}} I_v(t) + \frac{\alpha I_s(t)}{N(t)} S(t) - \frac{E(t)}{T_{lat}}. \]  
(6c)
\[
\dot{\xi}(t) = (1 - \beta) \frac{E(t)}{T_{\text{lat}}} - \left( \kappa_s + \frac{1}{T_{\text{inf}}} \right) \xi(t), \tag{6d}
\]

\[
\hat{\xi}(t) = \beta \frac{E(t)}{T_{\text{lat}}} \left( \kappa_s + \frac{1}{T_{\text{inf}}} \right) \nu(t), \tag{6e}
\]

\[
\dot{Q}(t) = \kappa_s \dot{I}_s(t) + \kappa_a \dot{I}_a(t) - \frac{Q(t)}{T_{\text{ser}}}, \tag{6f}
\]

\[
\dot{R}(t) = \frac{I_s(t) + I_a(t)}{T_{\text{inf}}} + \frac{Q(t)}{T_{\text{ser}}} + \nu(t) S(t). \tag{6g}
\]

\[
\dot{R}(t) = \frac{I_s(t) + I_a(t)}{T_{\text{inf}}} + \frac{Q(t)}{T_{\text{ser}}} = 0, \tag{6h}
\]

\[
S(t_f) = S_0, \quad I(t_f) = I_0, \quad I_s(t_f) = I_s_0, \tag{6j}
\]

where \(I_s(t), I_a(t), S(t), \) and \( \kappa_s(t) \) is defined as in (2), \( \kappa_a(t) \in [0, \kappa_f] \). Notice that similar OCPs can be formulated using isoperimetric and state constraints.

2.3. Numerical resolution of the optimal control problem

The OCP formulated in (6) is a particular case of a more general OCP of the form:

\[
\min_{u(t)} J(x(t), u(t)) = M(x(t_f)) + \int_{t_i}^{t_f} L(x(t), u(t)) \, dt, \tag{7a}
\]

subject to:

\[
\dot{x}(t) = f(x(t), u(t)), \tag{7b}
\]

\[
g(x(t), u(t)) \leq 0, \tag{7c}
\]

in which \( t \) represents time, with \( t_i \) and \( t_f \) denoting the initial and final times, respectively, \( u(t) \) represents the vector of control variables, and \( x(t) \) represents the vector of state variables, where \( x_i \) and \( x_f \) are the vector of initial and final states, respectively. The objective functional \( J(\cdot) \) in (7a) is formulated in Bolza form. It is a combination of two terms, namely a Mayer term \( M(\cdot) \), representing a terminal cost, and a Lagrange term \( L(\cdot) \), representing a running cost. Equation (7b) represents the set of differential equations that describes the dynamical system, Eq. (7c) represents the set of algebraic constraints, and Eq. (7d) represents the boundary conditions.

Notice that the Lagrange term in the objective functional (7a) can be converted to a Mayer term by adding a new state variable, \( x_M(t) \), and a new differential equation together with the corresponding initial condition, namely:

\[
\dot{x}_M(t) = L(x(t), u(t)),
\]

\[
x_M(t_i) = 0. \tag{7d}
\]

Then, the expression \( x_M(t_f) \) can be used in place of the Lagrange term.

The Hermite-Simpson direct collocation method [19] is used in this paper to transform the OCP formulated in (7) a NLP problem. This method is a particular case of a family of direct transcription methods known as Hermite-Legendre-Gauss-Lobatto methods [20]. Following [14], the time period \([t_i, t_f]\) is subdivided into \( N \) subintervals of equal length \( \Delta t \), the endpoints of which are \([t_0, t_1, \ldots, t_N]\).

with \( t_0 = t_i \) and \( t_N = t_f \). In each subinterval \([t_i, t_{i+1}], i = 0, \ldots, N-1\), the Hermite-Simpson numerical integration scheme is employed. The obtained NLP problem, which is solved using the open source IPOPT solver [15], consists of the Hermite-Simpson system constraints associated with the differential constraint (7b) and the discretized form of the algebraic constraints (7c) and the boundary conditions (7d).

3. Results

In order to illustrate the application of the proposed approach to determine the optimal vaccination and testing strategies to control SARS-CoV-2 virus transmission using the SEIslaQR compartmental model (1), various numerical experiments are conducted which take into account the vaccination scenarios defined in Section 2.2. According to Olivares and Staffetti [16], a nondimensionalized form of the model (1) with \( N(t) = 1 \) is used, in which the following initial conditions are set:

\[
(S_0 = 0.84908, E_0 = 0.00102, I_{00} = 0.00002, I_{m0} = 0.00008, Q_0 = 0, R_0 = 0.1489). \tag{7d}
\]

Additionally, 95% vaccine efficacy is assumed with an upper bound \( V = 0.0035 \) on the daily vaccination rate. It is also assumed that two doses of vaccine are required to develop immunity and an upper bound \( \kappa_f = 0.25 \) on the daily identification and isolation rate of asymptomatic subjects is considered. Moreover, these numerical experiments are solved assuming mild containment measures and the identification and isolation of the majority of infected symptomatic subjects. In particular, according to Manchein et al. [13], the replication factor is set to \( \beta = 3 \) and the daily testing rate for identification and isolation of symptomatic subjects is set to \( \kappa_s = 0.95 \).

3.1. Optimal vaccination strategies for the different vaccination scenarios

This section, the optimal vaccination and testing strategies obtained by solving the OCP for the SEIslaQR compartmental model defined in (1) for scenarios 1, 2, and 3 defined in Section 2.2 with different values of the weighting parameters will be examined. In all these OCPs, 95% vaccine efficacy has been assumed and the weighting parameters have been set to \( A_1 = 1, A_2 = 0.1, A_3 = 0.5, \) and \( A_4 = 0.0025 \).

For the sake of comparison, the optimal vaccination and testing strategies for Scenario 3 have been determined first, assuming an upper bound \( V = 0.0015 \) on the proportion of daily vaccinated susceptible people. Then, the overall number of vaccines corresponding to this solution has been calculated and the optimal vaccination and testing strategies for scenarios 1 and 2 have been computed considering the same upper bound, which has been set to \( V_f = 0.22 \).

The control variables obtained in these solutions, which represent the daily vaccination rate and the daily testing rate for the identification and isolation of asymptomatic subjects, are represented in Fig. 2, whereas the corresponding state variables that describe each compartment of the model are depicted in Fig. 3. Notice that the solutions obtained for scenarios 1 and 2 are the same, since the state constraint in Scenario 2 is saturated. More
Fig. 2. Optimal daily vaccination rate \( v(t) \) and optimal daily testing rate \( \kappa_a(t) \) obtained for scenarios 1 and 2 (blue) and for Scenario 3 (green). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 3. Proportions of subjects in each compartment obtained for scenarios 1 and 2 (blue) and for Scenario 3 (green). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Specifically, the optimal solution indicates that the whole amount of available vaccines in both cases should be used 80 days before the end of the considered time period.

Figure 2a shows that the optimal vaccination strategy obtained for Scenario 3 differs significantly from the optimal vaccination strategies obtained for the other scenarios.

In the optimal vaccination strategy obtained for Scenario 3, the scheduled daily vaccination rate grows progressively during the first 100 days, until it reaches its upper bound. After maintaining the maximum value for 40 days, it decreases at a high rate until it reaches zero at the end of the considered time period. In the optimal vaccination strategy for scenarios 1 and 2, a bang-bang control is obtained, in which the maximum daily vaccination rate is scheduled during the first 100 days until the vaccination supplies run out.

Figure 2b shows that similar optimal testing strategies for the identification and isolation of asymptomatic subjects are obtained in the solutions of the OCPs for scenarios 1 and 2 and Scenario 3. The maximum daily testing rate is scheduled during the first 105 days and then it decreases progressively until it reaches zero at the end of the considered time period. In the case of Scenario 3, the decrease is slightly steeper.

These different optimal vaccination strategies yield significant differences in the state variables as shown in Fig. 3. The optimal vaccination strategy for Scenario 3 results in higher peaks for the proportions of subjects in compartments \( E, I_s, I_a \), and \( Q \). For in-
stance, in the worst case, the percentage of symptomatic subjects in a single day is 0.0406% in scenarios 1 and 2, whereas this percentage rises to 0.0626% in Scenario 3. While the percentage in the first case could be handled by a sufficiently resilient healthcare system, it could place considerable stress on the healthcare system in the second case. Moreover, the percentage of immunized subjects at the end of this time period would be 58.57% in scenarios 1 and 2 and 67.15% in Scenario 3. This last percentage would be close to the estimated threshold for achieving herd immunity [21]. Notice that, as mentioned above, in all three scenarios, 22% of the susceptible subjects would become immune through vaccination in six months.

3.2. Sensitivity of the optimal vaccination and testing strategies to the weighting parameters of the objective functional

In this section, the optimal vaccination strategies obtained by solving the OCP for the SEIIsaQR compartmental model defined in (1) for Scenario 3 defined in Section 2.2 with different values of the weighting parameters will be examined to analyze the sensitivity of the optimal vaccination and testing strategies to the weighting parameters of the objective functional (2). In all these OCPs, 95% vaccine efficacy has been assumed and different values for the weighting parameters have been considered.

Figure 4 shows the optimal daily vaccination rate $v(t)$, the optimal daily testing rate for the identification and isolation of asymptomatic subjects $\kappa_a$, and the corresponding proportions of symptomatic subjects $I_s$, and recovered subjects $R$ obtained in three solutions of the OCP computed assuming three different values of the parameters $A_1 = 0.01$ (orange), $A_1 = 0.1$ (blue), and $A_1 = 1$ (green), and $A_2 = 0.1$, $A_3 = 0.5$, and $A_4 = 0.0025$ fixed. For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.

Figure 4. Optimal daily vaccination rate $v(t)$, optimal daily testing rate $\kappa_a(t)$, proportion of symptomatic subjects $I_s(t)$, and proportion of recovered subjects $R(t)$ obtained assuming that $A_1 = 0.01$ (orange), $A_1 = 0.1$ (blue), and $A_1 = 1$ (green), keeping parameters $A_2 = 0.1$, $A_3 = 0.5$, and $A_4 = 0.0025$ fixed. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
considered. Therefore, it can be deduced that there is a threshold for the weighting parameter $A_4$ above which the optimal daily vaccination and testing rates change significantly, and the corresponding proportion of symptomatic subjects increases dramatically.

3.3. Sensitivity of the optimal vaccination and testing strategies to the vaccine efficacy

In this section, the optimal vaccination strategies obtained by solving the OCP for the SEIslaQR compartmental model defined in (1) for Scenario 3 defined in Section 2.2 with different levels of vaccine efficacy will be examined to analyze the sensitivity of the optimal vaccination and testing strategies to the vaccine efficacy. In these OCPs, three different levels of vaccine efficacy have been considered, namely 50%, 75%, and 95%.

Figure 6 shows the optimal daily vaccination rate $v(t)$, the optimal daily testing rate $k_e(t)$, proportion of symptomatic subjects $I_s(t)$, and proportion of recovered subjects $R(t)$ obtained assuming that $A_3 = 0.5$ (green), $A_3 = 1$ (blue), $A_3 = 10$ (orange), keeping parameters $A_1 = 1, A_2 = 0.1$, and $A_4 = 0.0025$ fixed. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

![Figure 5](image1.png)  
**Fig. 5.** Optimal daily vaccination rate $v(t)$, optimal daily testing rate $k_e(t)$, proportion of symptomatic subjects $I_s(t)$, and proportion of recovered subjects $R(t)$ obtained assuming that $A_3 = 0.001$ (orange), $A_3 = 0.1$ (blue), $A_3 = 1$ (green), keeping parameters $A_1 = 1, A_2 = 0.5$, and $A_4 = 0.0025$ fixed. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

![Figure 6](image2.png)  
**Fig. 6.** Optimal daily vaccination rate $v(t)$, optimal daily testing rate $k_e(t)$, proportion of symptomatic subjects $I_s(t)$, and proportion of recovered subjects $R(t)$ obtained assuming that $A_3 = 0.5$ (green), $A_3 = 1$ (blue), $A_3 = 10$ (orange), keeping parameters $A_1 = 1, A_2 = 0.1$, and $A_4 = 0.0025$ fixed. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
proportion of symptomatic subjects changes significantly. Therefore, since the optimal vaccination strategy barely changes, a decrease in the level of vaccine efficacy implies an increase in the proportion of symptomatic subjects that could imply an overwhelmed healthcare system.

4. Discussion

In this paper, several vaccination and testing strategies for the control of the SARS-CoV-2 virus transmission for three different vaccination scenarios characterized by different constraints associated with vaccine availability and administration have been proposed and their effects on the disease transmission have been compared. The results of the numerical experiments show that identical vaccination strategies are obtained for Scenario 1, in which the total number of vaccines used is fixed at a certain value, and Scenario 2, in which the total number of vaccines used is upper-bounded at the same value. Moreover, the optimal vaccination strategies for scenarios 1 and 2 confirm the hypothesis that the implementation of early control measures significantly reduces the number of symptomatic infected subjects, which is a key aspect for the resilience of the healthcare system. The optimal vaccination strategy obtained in Scenario 3 differs significantly from the optimal vaccination strategies obtained for the other scenar-
ios, whereas the optimal testing strategies for identification and isolation of asymptomatic subjects obtained for the three scenarios are similar. Scenario 3 would be compatible with a vaccination program in which the availability of vaccines would gradually increase. The sensitivity analysis of the solutions to the weighting parameters of the objective functional reveals that it is possible to obtain a vaccination strategy that allows almost 6% of vaccination supplies to be saved while keeping the same number of symptomatic infected subjects. Furthermore, it indicates that if the vaccination plan is not supported by a sufficient rate of testing, the number of symptomatic infected subjects could increase considerably. Similarly, the sensitivity analysis of the solutions to vaccine efficacy shows that a significant reduction in the efficacy of the vaccines could also lead to a relevant increase in the number of symptomatic infected subjects.

**Declaration of Ethical Approval**

The authors state that ethical approval is not required for this type of study in the country where the study was conducted.

**Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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