Article

Not peer-reviewed version

Epidemic Control: Social Distancing or Antiviral Medications?

Alexandra Smirnova *, Mona Baroonian, Xiaojing Ye

Posted Date: 28 August 2024

doi: 10.20944/preprints202408.2036.v1

Keywords: Epidemiology; compartmental model; transmission dynamic; optimal control

 doi:10.20944/preprints202408.2036.v1

Article

Epidemic Control: Social Distancing or Antiviral Medications?

Alexandra Smirnova *, Mona Baroonian and Xiaojing Ye

Department of Mathematics & Statistics, Georgia State University, Atlanta, USA; mbaroonian1@student.gsu.edu; xye@gsu.edu
* Correspondence: asmirnova@gsu.edu

Abstract: In this study, we investigate different control scenarios through theoretical analysis and numerical simulations. To account for two important types of control for an early ascending stage of an outbreak, social distancing and treatment with antiviral medications, a compartmental model is considered with one control, $u_1(t)$, aimed to lower the disease transmission rate and the other control, $u_2(t)$, aimed to lower the period of infectiousness. In all experiments, the implementation of control strategies reduces the daily cumulative number of cases, $N - \mathcal{S}(t)$, and successfully "flattens the curve", $\mathcal{I}(t)$. The reduction in the cumulative cases is achieved by eliminating or delaying new cases. This delay is incredibly valuable as it provides public health organizations with more time to advance antiviral treatments and devise alternative preventive measures. The main theoretical result of the paper, Theorem 3.1, concludes that the optimal control functions, $u_i(t)$, $i = 1, 2$, may be increasing until some moment $\tau \in [0, T)$. However, for all $t \in [\tau, T]$, both controls, $u_i(t)$, decline as t approaches T (possibly causing the number of newly infected people to grow). Numerical simulations presented in Section 4 confirm theoretical findings, which indicates that, ideally, around the time $t = \tau$, the control strategy has to be upgraded and a vaccination campaign needs to start to ensure the epidemic wave does not rebound.

Keywords: Epidemiology; compartmental model; transmission dynamic; optimal control

1. Introduction

Advanced modeling and parameter estimation algorithms form a solid background for the design of optimal strategies to control infectious diseases, which reduces illness and mortality rates. Vaccination, isolation, and public health education are examples of important control techniques that protect people at risk and make effective use of healthcare resources [1–3].

Timely control measures can mitigate the impact of outbreaks, prevent widespread transmission, and save lives. For instance, vaccination programs have been instrumental in controlling diseases such as measles, polio, and influenza [4,5]. Quarantine and isolation protocols were key in managing the spread of diseases like Ebola and COVID-19 [6]. Public health campaigns promoting handwashing and sanitation have significantly reduced the transmission of diseases such as cholera and dysentery. The eradication of smallpox is a prime example of how global vaccination campaigns can lead to complete elimination of a disease [7]. Similarly, the rapid response to the H1N1 influenza pandemic in 2009, including the development and distribution of vaccines, helped to control the spread of the virus and reduce its impact [8].

By analyzing data that use different models and algorithms, epidemiologists can forecast future incidence cases and evaluate various control strategies. Systematic preventive measures can help in reducing the spread of diseases. At first glance, choosing healthcare policies seems obvious, but in reality it is a very complicated task. One needs to put forward control strategies that are practical and, at the same time, have manageable consequences. At the onset of COVID-19, lockdowns were helpful, but they were not sustainable long term [9–11]. Thus, choosing the best intervention at the right time is critical [12,13].

The study in [14] introduced a two-stage epidemic model for the spread of COVID-19 and proposed optimal control strategies based on actual data and cost considerations. The research underscores the importance of contact tracing and isolation in minimizing the costs and effectively curbing the

 doi:10.20944/preprints202408.2036.v1

spread of a disease. Numerical simulations and model analysis provide actionable recommendations for public health authorities, highlighting the critical role of controlling the transmission rate in epidemic management.

The research in [15] modeled the spread of COVID-19 and assessed the impact of social intervention measures during the early outbreak phase, focusing on optimal control strategies and the identifiability of model parameters. It found that optimal control strategies, especially social distancing and self-isolation, significantly reduced transmission rates when implemented early. The study emphasized the importance of structural identifiability for accurate parameter estimation in COVID-19 models. It shows that implementing control measures effectively "flattens the curve" and lowers the burden on healthcare systems.

Another study, [16], focused on an SIR model with saturated incidence and treatment rates, analyzing equilibrium points, bifurcation, and optimal control strategies that utilize vaccination and treatment with antiviral medication in order to contain the outbreak. The authors' findings, derived from numerical simulations and efficiency analysis, demonstrated that vaccination control stands to reduce the cumulative number of infections more rapidly than control by antiviral treatment. This research underscored the value of mathematical modeling in epidemiology and the strategic implementation of vaccination to prevent disease transmission.

2. Control of an Emerging Disease

In the study of epidemic control, effective management of a disease spread is crucial, particularly at the onset of an outbreak. While the importance of vaccination in fighting infectious diseases is undeniable, it takes time to develop a vaccine for an emerging strain. Various parameters including environmental factors, immunity patterns, and behavioral changes impact the circulation of a virus. Social distancing and personal hygiene measures (non-medical interventions) play an important role in containing the disease at an early ascending stage. By optimizing the implementation of non-medical interventions over time the effectiveness of these interventions can be increased.

Another essential component of control and prevention is treatment with antiviral medications, which allows to reduce the period of infectiousness and/or reduce the disease fatality rate. To account for these two important types of control, we consider the following SIR (Susceptible-Infectious-Removed) model [17] for early disease transmission:

$$\begin{aligned} \frac{d\mathcal{S}}{dt} &= -\beta\frac{\mathcal{S}(t)\mathcal{I}(t)}{N} \\ \frac{d\mathcal{I}}{dt} &= \beta\frac{\mathcal{S}(t)\mathcal{I}(t)}{N} - \gamma\mathcal{I}(t) \\ \frac{d\mathcal{R}}{dt} &= \gamma\mathcal{I}(t) \end{aligned} \tag{1}$$

In system (1), we assume that individuals who have recovered from the disease gain immunity for the duration of the study and do not return to the susceptible class, $\mathcal{S}$. Additionally, we assume that natural birth and death rates balance one another and the removed class, $\mathcal{R}$, contains individuals who recovered from the disease and those who died. The two disease parameters, $\beta > 0$ and $\gamma > 0$ are transmission and recovery rates, respectively.

The focus of this research is on introducing optimal controls during initial weeks of a pandemic in order to delay and reduce the daily number of infections. This approach enables health centers and decision-making organizations to implement more effective operations. In what follows, we

 doi:10.20944/preprints202408.2036.v1

incorporate two different kinds of control in SIR model [18] resulting in the system $\frac{d\mathbf{x}}{dt} = f(\mathbf{x}, \mathbf{u})$, where

$$\begin{aligned} f_1(\mathbf{x}, \mathbf{u}) &:= -\beta(1 - u_1(t))S(t)I(t) \\ f_2(\mathbf{x}, \mathbf{u}) &:= \beta(1 - u_1(t))S(t)I(t) - (\gamma + \varepsilon u_2(t))I(t) \\ f_3(\mathbf{x}, \mathbf{u}) &:= (\gamma + \varepsilon u_2(t))I(t). \end{aligned} \tag{2}$$

Here $S(t) := \frac{\mathcal{S}(t)}{N}$, $I(t) := \frac{\mathcal{I}(t)}{N}$, and $R(t) := \frac{\mathcal{R}(t)}{N}$ are normalized susceptible, infected and removed compartments, respectively, and N is the population of the region at the beginning of the study period. The function $u_1(t)$ represents nonmedical controls (social distancing, remote work, online education, restriction on travel, lockdowns, etc.), while $u_2(t)$ stands for treatment with antiviral medications and other medical interventions. A positive parameter, ε, is the efficacy of antiviral treatments [19]. In the above, $\mathbf{x} := [S, I, R]^\top$, $\mathbf{u} := [u_1, u_2]^\top$, and the admissible set for each control function is

$$\mathcal{U} = \Big\{ u_i \in \mathcal{L}^1[0, T], \quad 0 \le u_i(t) < 1, \quad i = 1, 2 \Big\}. \tag{3}$$

In (2), the first control, $u_1(t)$, aims to change the disease transmission rate from β to $\beta(1 - u_1(t))$ while the second control, $u_2(t)$, is expected to reduce the period of infectiousness, which is $\frac{1}{\gamma}$ in the initial system (1). In combination, the two controls, $u_1(t)$ and $u_2(t)$, are meant to minimize the force of infection, $\beta(1 - u_1(t))S(t)I(t)$, while keeping the costs at bay. The costs are considered in a general sense, which includes a negative impact on mental health, education, economy and on overall quality of life.

In Lemma 2.1 below we show that following the introduction of a time-dependent transmission rate, $\beta(t) := \beta(1 - u_1(t))$, and a time-dependent recovery rate, $\gamma(t) := \gamma + \varepsilon u_2(t)$, the model $\frac{d\mathbf{x}}{dt} = f(\mathbf{x}, u)$ in (2) remains well-defined in the sense that the state variables, $S(t), I(t), R(t)$, originating in a positive octant do not leave the octant for all values of $t > 0$. The proof of this lemma is similar to the argument in [20], where system (2) was considered with nonmedical controls only (that is, $u_2(t) = 0$).

Lemma 2.1 [20]. *Let $u_i(t)$, $i = 1, 2$, be admissible control trajectories with $\mathbf{x}(t)$ satisfying $\frac{d\mathbf{x}}{dt} = f(\mathbf{x}, \mathbf{u})$ given by (2) and*

$$(S(0), I(0), R(0)) \in \Delta^2 := \{(z_1, z_2, z_3) \in \mathbb{R}^3 : z_1 + z_2 + z_3 = 1,\ z_1, z_2, z_3 \ge 0\},$$

the probability simplex in $\mathbb{R}^3$. Then $(S(t), I(t), R(t)) \in \Delta^2$ for all $t \ge 0$.

Note that the argument in [20] implies that the conclusion of Lemma 2.1 is not limited to $\beta(t) := \beta(1 - u_1(t))$ and $\gamma(t) := \gamma + \varepsilon u_2(t)$. It is valid for any integrable nonnegative functions $\beta(t)$ and $\gamma(t)$. To optimize the implementation of both controls, $u_1(t)$ and $u_2(t)$, we consider the following objective functional

$$J(\mathbf{x}, \mathbf{u}) := \int_0^T \Big\{ (\beta(1 - u_1(t))S(t)I(t) + \lambda^\top C(\mathbf{u}(t)) \Big\}\, dt.$$

According to system (2), one can integrate the first term to obtain

$$J(\mathbf{x}, \mathbf{u}) = S(0) - S(T) + \int_0^T \lambda^\top C(\mathbf{u}(t))\, dt := h(\mathbf{x}(T)) + \int_0^T L(\mathbf{x}(t), \mathbf{u}(t))\, dt, \tag{4}$$

where $C(\mathbf{u}) := [C_1(u_1), C_2(u_2)]^\top$ is the assumed cost of control and $\lambda := [\lambda_1, \lambda_2]^\top$, $\lambda_1, \lambda_2 > 0$, is the regularization parameter (weight). As our numerical experiments show, the choice of the cost function, $C(\mathbf{u})$, significantly influences the resulting control strategy. From practical standpoint, neither $u_1(t)$ nor $u_2(t)$ should take negative values. At the same time, the cost, $C_i(u_i)$, must increase dramatically as $u_i(t)$ approaches 1, the upper bound of the feasible set (3), since it is impossible to entirely eliminate the

 doi:10.20944/preprints202408.2036.v1

disease transmission ($u_1(t) = 1$). It is equally impossible to reach full capacity of antiviral treatment ($u_2(t) = 1$) due to limitations of testing and other factors. Therefore, in our approach we impose the following assumptions on the cost functions, $C_1(u_1)$ and $C_2(u_2)$ [20]:

$$\begin{aligned} C_i''(u) > 0, \qquad C_i(0) = 0, \qquad C_i'(u) > 0 \ \text{ for } \ u > 0, \\ C_i'(u) < 0 \quad \text{for} \ \ u < 0 \ \ \text{and} \quad \lim_{u \to 1^-} C_i(u) = \infty, \quad i = 1, 2. \end{aligned} \tag{5}$$

These assumptions on the cost of control were first proposed in [20] for a special case when $u_2(t) = 0$. The authors of [20] employed the techniques of machine learning to show that under assumptions (5), the global minimum of the Hamiltonian gives rise to the optimal control strategy, $u_1(t)$, which stays within the feasible set (3) for all values of $t \in [0, T]$. Assumptions (5) are the alternative to a more traditional cost function, $C(u) = u^2$, that is often used in control literature. However, $C(u) = u^2$ does not, generally, prevent the global minimum from becoming greater than 1 for some values of t, even for large weights, λ.

3. Theoretical Study and Discussion

In this section we state and prove our main theoretical result.

Theorem 3.1. *Let $u \in \mathcal{U}$ be an optimal control strategy with respect to the objective functional $J(\mathbf{x}, \mathbf{u})$ defined in (4) and biological model $\dot{\mathbf{x}} = f(\mathbf{x}, \mathbf{u})$, $\mathbf{x}(0) = \mathbf{x_0}$, introduced in (2), with $C(\mathbf{u}) := [C_1(u_1), C_2(u_2)]^\top$ satisfying (5) and $\lambda := [\lambda_1, \lambda_2]^\top$, $\lambda_1, \lambda_2 > 0$. Then there is $\tau \in [0, T)$ such that for any $t \in (\tau, T)$, the derivative, $\dfrac{du_i}{dt}$, $i = 1, 2$, exists and $\dfrac{du_i}{dt} < 0$. In other words, there is $\tau \in [0, T)$ such that for any $t \in (\tau, T)$, both optimal controls, $u_1(t)$ and $u_2(t)$, are decreasing.*

Proof. According to the Pontryagin's Minimum Principle [21,22], if $u \in \mathcal{U}$ is an optimal control with respect to the objective functional $J(\mathbf{x}, \mathbf{u}) = h(\mathbf{x}(T)) + \int_0^T L(\mathbf{x}(t), \mathbf{u}(t))\, dt$ and the system $\dot{\mathbf{x}} = f(\mathbf{x}, \mathbf{u})$, $\mathbf{x}(0) = \mathbf{x_0}$, then there is a trajectory $\mathbf{p}(t)$ such that

$$\dot{\mathbf{p}}(t) = -\partial_{\mathbf{x}} H(\mathbf{x}, \mathbf{u}, \mathbf{p})^\top \Big|_{\mathbf{x}(t), \mathbf{u}(t), \mathbf{p}(t)}, \quad \mathbf{p}(T) = \partial_{\mathbf{x}} h(\mathbf{x})^\top \Big|_{\mathbf{x}(T)}, \tag{6}$$

$$\mathbf{u}(t) = \arg\min_{\mathbf{v} \in \mathcal{U}} H(\mathbf{x}(t), \mathbf{v}(t), \mathbf{p}(t)), \quad H(\mathbf{x}, \mathbf{v}, \mathbf{p}) := L(\mathbf{x}, \mathbf{v}) + \mathbf{p}^\top f(\mathbf{x}, \mathbf{v}). \tag{7}$$

By the properties (5) of the cost, $C(\mathbf{u})$, one has $C_i'(u) > 0$ for $u > 0$ and $\lim_{u \to 1^-} C_i(u) = \infty$, which prevents any $\mathbf{u} = [u_1, u_2]^\top$, $u_i \geq 1$, $i = 1, 2$, from being the optimal of $H(\mathbf{x}, \mathbf{u}, \mathbf{p})$ with respect to $\mathbf{u}$ at any time $t \in [0, T]$. Therefore, the Karush–Kuhn–Tucker (KKT) conditions for the optimal control problem (2), (3), (4) take the form

$$(K1) \quad \partial_{\mathbf{u}} H(\mathbf{x}, \mathbf{u}, \mathbf{p}) - q(t) = \mathbf{0}, \quad q(t) := [q_1(t), q_2(t)]^\top \tag{8}$$

$$(K2) \quad \dot{\mathbf{p}}(t) = -\partial_{\mathbf{x}} H(\mathbf{x}, \mathbf{u}, \mathbf{p})^\top \Big|_{\mathbf{x}(t), \mathbf{u}(t), \mathbf{p}(t)}, \ \mathbf{p}(T) = \partial_{\mathbf{x}} h(\mathbf{x})^\top \Big|_{\mathbf{x}(T)} \tag{9}$$

$$(K3) \quad \dot{\mathbf{x}}(t) = f(\mathbf{x}, \mathbf{u}), \quad \mathbf{x}(0) = \mathbf{x}_0 \tag{10}$$

$$(K4) \quad q_i(t) \geq 0, \ u_i(t) \geq 0, \ i = 1, 2, \quad q(t)^\top \mathbf{u}(t) = 0 \quad \forall t \in [0, T]. \tag{11}$$

 doi:10.20944/preprints202408.2036.v1

As it follows from (2), (4), and (7),

$$\begin{aligned}\partial_{\mathbf{u}} H(\mathbf{x},\mathbf{u},\mathbf{p}) &= \partial_{\mathbf{u}} L(\mathbf{x},\mathbf{u}) + \mathbf{p}^{\top}\partial_{\mathbf{u}} f(\mathbf{x},\mathbf{u}) \\ &= \begin{bmatrix} \dfrac{\partial L}{\partial u_1} & \dfrac{\partial L}{\partial u_2} \end{bmatrix} + [p_1,p_2,p_3] \begin{bmatrix} \dfrac{\partial f_1}{\partial u_1} & \dfrac{\partial f_1}{\partial u_2} \\ \dfrac{\partial f_2}{\partial u_1} & \dfrac{\partial f_2}{\partial u_2} \\ \dfrac{\partial f_3}{\partial u_1} & \dfrac{\partial f_3}{\partial u_2} \end{bmatrix} \\ &= \begin{bmatrix} \lambda_1 \dfrac{dc_1}{du_1} & \lambda_2 \dfrac{dc_2}{du_2} \end{bmatrix} + [p_1,p_2,p_3] \begin{bmatrix} \beta SI & 0 \\ -\beta SI & -\varepsilon I \\ 0 & \varepsilon I \end{bmatrix}, \end{aligned} \tag{12}$$

which yields

$$\lambda_1 \frac{dc_1}{du_1} - q_1(t) = -\beta(p_1 - p_2)SI \tag{13}$$

$$\lambda_2 \frac{dc_2}{du_2} - q_2(t) = -\varepsilon(p_3 - p_2)I. \tag{14}$$

To show that on some (τ, T) the derivative, $\dfrac{du_1}{dt}$, exists and $\dfrac{du_1}{dt} < 0$, we follow [20]. Conditions (K2) and (K3) imply that $(p_1 - p_2)SI$ is differentiable and therefore continuous for any $t \in [0,T]$. From Lemma 2.1, one concludes that $S(t), I(t) > 0$ as long as $S(0)$ and $I(0)$ are positive. On the other hand, since $p_1(T) = -1 < 0 = p_2(T)$, there is $\tau_1 \in [0,T)$ such that $p_1(t) - p_2(t) < 0$ for all $t \in [\tau_1, T)$. Suppose at some point $t \in [\tau_1, T]$, the Lagrange multiplier, $q_1(t)$, is greater than zero. Then from (K4) it follows that $u_1(t) = 0$. By (5), this implies $\dfrac{dc_1}{du_1}(t) = 0$, which means that in (13) $\dfrac{dc_1}{du_1}(t) - q_1(t) < 0$, while $-\beta(p_1 - p_2)SI > 0$. Hence, we arrive at the contradiction. Therefore, for any $t \in [\tau_1, T]$, one has $q_1(t) = 0$ and $\lambda_1 \dfrac{dc_1}{du_1} = -\beta(p_1 - p_2)SI$. By implicit function theorem, for $t \in (\tau_1, T)$ the derivative, $\dfrac{du_1}{dt}$, exists and

$$\frac{du_1}{dt} = -\frac{\beta[S(t)I(t)(p_1(t) - p_2(t))]'}{\lambda_1 c_1''(u_1)} \quad \text{for all} \quad t \in (\tau_1, T). \tag{15}$$

Taking into consideration (2), (4), and (7), one obtains

$$\begin{aligned}\partial_{\mathbf{x}} H(\mathbf{x},\mathbf{u},\mathbf{p}) &= \partial_{\mathbf{x}} L(\mathbf{x},\mathbf{u}) + \mathbf{p}^{\top}\partial_{\mathbf{x}} f(\mathbf{x},\mathbf{u}) \\ &= \begin{bmatrix} \dfrac{\partial L}{\partial S} & \dfrac{\partial L}{\partial I} & \dfrac{\partial L}{\partial R} \end{bmatrix} + [p_1,p_2,p_3] \begin{bmatrix} \dfrac{\partial f_1}{\partial S} & \dfrac{\partial f_1}{\partial I} & \dfrac{\partial f_1}{\partial R} \\ \dfrac{\partial f_2}{\partial S} & \dfrac{\partial f_2}{\partial I} & \dfrac{\partial f_2}{\partial R} \\ \dfrac{\partial f_3}{\partial S} & \dfrac{\partial f_3}{\partial I} & \dfrac{\partial f_3}{\partial R} \end{bmatrix} \\ &= \begin{bmatrix} 0 & 0 & 0 \end{bmatrix} + [p_1,p_2,p_3] \begin{bmatrix} -\beta(1-u_1)I & -\beta(1-u_1)S & 0 \\ \beta(1-u_1)I & \beta(1-u_1)S - (\gamma + \varepsilon u_2) & 0 \\ 0 & (\gamma + \varepsilon u_2) & 0 \end{bmatrix}. \end{aligned} \tag{16}$$

 doi:10.20944/preprints202408.2036.v1

Furthermore, from (4) one gets $\partial_x h(\mathbf{x}) = [-1, 0, 0]^\top$. This together with (16) implies that $p_3(t) = 0$ and the costate equations for $p_1(t)$ and $p_2(t)$ take the form:

$$\begin{aligned} \dot{p}_1 &= \beta(1-u_1(t))(p_1(t)-p_2(t))I(t) \\ \dot{p}_2 &= \beta(1-u_1(t))(p_1(t)-p_2(t))S(t) + p_2(t)(\gamma+\varepsilon u_2(t)) \\ p_1(T) &= -1, \quad p_2(T) = 0. \end{aligned} \tag{17}$$

Combining (2) and (17), one can rewrite $[S(t)I(t)(p_1(t)-p_2(t))]'$ as follows

$$\begin{aligned} [S(t)I(t)(p_1(t)-p_2(t))]' &= (S'I+SI')(p_1-p_2) + (p_1'-p_2')S(t)I(t) \\ &= \{-\beta(1-u_1)SI^2 + \beta(1-u_1)S^2I - (\gamma+\varepsilon u_2)SI\}(p_1-p_2) \\ &+ \{\beta(p_1-p_2)(1-u_1)(I-S) - p_2(\gamma+\varepsilon u_2)\}SI \\ &= -p_1(\gamma+\varepsilon u_2)SI. \end{aligned} \tag{18}$$

From (24) and (15), one concludes

$$\frac{du_1}{dt} = \frac{\beta p_1(\gamma+\varepsilon u_2)SI}{\lambda_1 c_1''(u_1)} \quad \text{for all} \quad t \in (\tau_1, T). \tag{19}$$

Since $p_1(T) = -1 < 0$ and $S(t), I(t) > 0$, $\gamma + \varepsilon u_2 > 0$, $\lambda_1 c_1''(u_1) > 0$ for $t \in [0, T]$, there exists $\tau_2 \in [0, T)$ such that $p_1(t) < 0$ and $\dfrac{\beta p_1(\gamma+\varepsilon u_2)SI}{\lambda_1 c_1''(u_1)} < 0$ for all $t \in [\tau_2, T]$. Let $\tau = \max(\tau_1, \tau_2)$, then $\dfrac{du_1}{dt}$ is negative in (τ, T). As noted above, $p_3(t) = 0$, therefore identity (14) yields

$$\lambda_2 \frac{dc_2}{du_2} - q_2(t) = \varepsilon p_2 I. \tag{20}$$

Taking into account (17), one arrives at

$$\frac{d}{dt}\left(p_2(t)\mathrm{e}^{\int_t^T(\gamma+\varepsilon u_2(\mu))d\mu}\right) = \beta(1-u_1(t))(p_1(t)-p_2(t))S(t)\mathrm{e}^{\int_t^T(\gamma+\varepsilon u_2(\mu))d\mu}. \tag{21}$$

Integrating (21) from t to T and substituting $p(T) = 0$, one gets

$$p_2(t) = -\beta \mathrm{e}^{-\int_t^T(\gamma+\varepsilon u_2(\mu))d\mu} \int_t^T (1-u_1(\nu))(p_1(\nu)-p_2(\nu))S(\nu)\mathrm{e}^{\int_\nu^T(\gamma+\varepsilon u_2(\mu))d\mu} d\nu. \tag{22}$$

As shown above, $p_1(t) - p_2(t)$ is negative on $[\tau, T]$. Thus (3) and (22) imply that $p_2(t) > 0$ for all $t \in [\tau, T)$. Using the same argument as in the case of $u_1(t)$, one can now conclude that $q_2(t)$ in (20) is equal to zero on $[\tau, T]$, that is, the constraint $u_2(t) \geq 0$ is not active for $t \in [\tau, T)$ and $\lambda_2 \dfrac{dc_2}{du_2} = \varepsilon p_2 I$. By implicit function theorem, for $t \in (\tau, T)$ the derivative, $\dfrac{du_2}{dt}$, exists and

$$\frac{du_2}{dt} = \frac{\varepsilon[p_2 I]'}{\lambda_2 c_2''(u_2)} \quad \text{for all} \quad t \in (\tau, T). \tag{23}$$

From (2) and (17) one has

$$[p_2 I]' = \{\beta(1-u_1)(p_1-p_2)S + p_2(\gamma+\varepsilon u_2)\}I + p_2\{\beta(1-u_1)SI - (\gamma+\varepsilon u_2)I\}. \tag{24}$$

$$= \beta p_1(1-u_1)SI < 0 \quad \text{on} \quad [\tau, T], \tag{25}$$

 doi:10.20944/preprints202408.2036.v1

since $p_1(t) < 0$ for all $t \in [\tau_2, T]$ and $\tau \geq \tau_2$. This implies $\frac{du_2}{dt} < 0$ in (τ, T), which completes the proof. □

Remark 3.2 By (5) and (7), $\partial^2_{\mathbf{u}} H(\mathbf{x}, \mathbf{u}, \mathbf{p}) = \begin{bmatrix} \lambda_1 c_1''(u_1) & 0 \\ 0 & \lambda_2 c_2''(u_2) \end{bmatrix}$. Therefore, $\partial^2_{\mathbf{u}} H(\mathbf{x}, \mathbf{u}, \mathbf{p})$ is positive definite and $H(\mathbf{x}, \mathbf{u}, \mathbf{p})$ has a unique global minimum with respect to $\mathbf{u}$. From the proof of Theorem 3.1, it follows that both coordinates of the global minimum, $u_1(t)$ and $u_2(t)$, are guaranteed to be less than 1, pointwisely, but they are not guaranteed to be greater than 0 necessarily, which means the solution to our optimal control problem can be a local minimum rather than global. The reason the coordinates of the global minimum, $u_i(t)$, $i = 1, 2$, can potentially be less than zero for some values of t is that, counterintuitively, a smaller effective reproduction number, $r(t)$, in the SIR model does not always imply a smaller cumulative number of infected people, $S(0) - S(t)$. Hence, even though for system (2), the effective reproduction number, $r(t) = \beta(1 - u_1(t))/(\gamma + \varepsilon u_2(t))$, goes down with more control, it does not guarantee that $r(t) \geq \bar{r}(t)$ yields $S(t) \leq \bar{S}(t)$ for every value of t. One can, however, show that if $r(t) \geq \bar{r}(t)$ and $r(t)$ is non-increasing, then $S(t) \leq \bar{S}(t)$. This result is important in its own right. Its proof is given in Appendix.

Remark 3.3 Despite the fact that, theoretically, the solution to our optimal control problem can be a local minimum rather than global, in all numerical experiments presented in the next section, the optimal strategy is a unique global minimum. In other words, in all our experiments, the optimal control has been computed from the first-order necessary condition for unconstrained minimization, and nonnegativity constraints held without being enforced. For all cost functions, $C(\mathbf{u}(t))$, satisfying (5), the global minimum of $H(\mathbf{x}, \mathbf{u}, \mathbf{p})$ with respect to $\mathbf{u}$ has nonnegative coordinates, $u_i(t)$, $i = 1, 2$. That is, $\mathbf{u}(t) = \arg\min_{\mathbf{v} \in \mathcal{U}} H(\mathbf{x}(t), \mathbf{v}(t), \mathbf{p}(t))$ is equivalent to $\mathbf{u}(t) = \arg\min_{\mathbf{v} \in \mathcal{L}^1[0,T]} H(\mathbf{x}(t), \mathbf{v}(t), \mathbf{p}(t))$ for all $t \in [0, T]$. This illustrates that conditions (5) lead to a practically justified mitigation scenario. Numerical simulations have also confirmed, as proven in Theorem 3.1, that both controls, $u_1(t)$ and $u_2(t)$, are decreasing toward the end of the study period.

4. Numerical Experiments

In our numerical study, we use a second-order trust-region algorithm for nonlinear optimization 'lsqnonlin' combined with ode15s built-in function to approximate the solution to optimal control problem (4) subject to compartmental model (2) and costate system (17). For every value of $\mathbf{u}_k$, we solve system (2) forward in time (starting with $\mathbf{x}(0) = \mathbf{x_0}$), to get $\mathbf{x}_k$ using ode15s. Then system (17) is solved back in time by ode15s to obtain $\mathbf{p}_k$. Given $(\mathbf{x}_k, \mathbf{u}_k, \mathbf{p}_k)$, we find $\mathbf{u}_{k+1}$ by applying a second-order trust-region 'lsqnonlin' algorithm.

Following [20], we consider three different cost functions, $C_{i,1}$, $C_{i,2}$, and $C_{i,3}$, satisfying conditions (5):

$$\begin{aligned} C_{i,1}(u) &= -0.830071\, \ln(1 - u^2), \quad C_{i,2}(u) = -0.672850\, u \ln(1 - u) \\ C_{i,3}(u) &= -u - \ln(1 - u), \quad C_{i,4}(u) = 1.424546\, u^2 \quad i = 1, 2. \end{aligned} \tag{26}$$

In (26), the coefficients are chosen to minimize the weighted distance [20]

$$\int_0^1 w(z) |C_{i,j}(z) - C_{i,3}(z)|^2 \, dz, \quad w(z) = \sqrt{1 - z^2}, \quad j = 1, 2, 4. \tag{27}$$

The cost of control, $C_{i,1}(u)$, $C_{i,2}(u)$, and $C_{i,3}(u)$, is infinite as u approaches its ultimate value, 1. For comparison, we also use the cost function $C_{i,4}(u) = u^2$, for which (5) does not hold. The cost function $C_{i,4}(u) = u^2$ is popular in applications of control theory in epidemiology and other fields, since for this function the first order optimality condition is linear with respect to u. This is a useful property that simplifies numerical algorithms. However, the cost of control, $C_{i,4}(u)$, is finite at $u = 1$, which is not realistic in real-world scenarios. Figures 4 and 7 show that the global minimum, $\mathbf{u}(t)$, of the

 doi:10.20944/preprints202408.2036.v1

Hamiltonian, $H(\mathbf{x}(t), \mathbf{u}(t), \mathbf{p}(t))$, does not stay in the range of $[0,1]$ if the cost is given by $C_{i,4}(u) = u^2$, especially for small values of λ_i, $i = 1,2$. Thus, an explicit constraint $u_i(t) \leq 1$ must be imposed in the case of $C_{i,4}(u)$. Even with the constraint $u_i(t) \leq 1$, the optimal control function, $\mathbf{u}(t)$, often reaches the ultimate level [15], $u_i(t) = 1$, which is not practical.

In all numerical experiments presented in this section, $C_{1,j}(u) = C_{2,j}(u)$, $j = 1,2,3,4$. Therefore, moving forward, we omit the first index and set $C_{i,j}(u) := C_j(u)$. Comparison of the four cost functions in the interval $[-1,1]$ is illustrated in Figure 1.

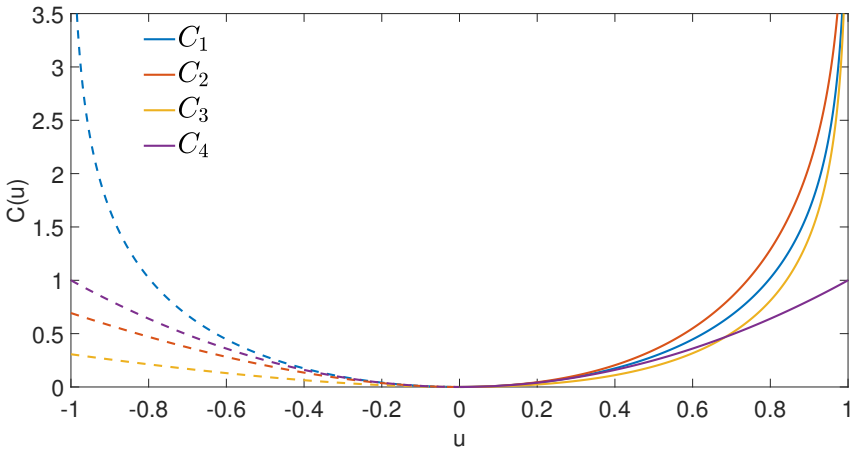

Figure 1. Comparison of the four control cost functions used in numerical experiments below: $C_1(u) = -0.830071\ \ln(1-u^2)$, $C_2(u) = -0.672850\,u\ln(1-u)$, $C_3(u) = -z - \ln(1-u)$, $C_4(u) = 1.424546\,u^2$.

In this study, numerical simulations are conducted for λ_1 and λ_2 equal to 0.1, 0.05, 0.01, 0.001 and 10^{-7}. Three different scenarios are explored. First, there is only non-medical control, $u_1(t)$, (social distancing, behavioral changes, hand washing, etc.) in the system and treatment with antiviral medications, $u_2(t)$, is not available. Second, only control $u_2(t)$, treatment with antiviral medications, is applied; no social distancing. And third, controls $u_1(t)$ and $u_2(t)$, medical and non-medical, are used in combination. In our experiments, the population of the region, N, is assumed to be 10^7. The initial number of infected individuals on day 1 is 200, and the duration of the study period is 120 days. Transmission rate, β, and recovery rate, γ, are assumed to be 0.3, and 0.1, respectively, leading to the basic reproduction number $r = 3$. The efficacy of antiviral medication, ε, is assumed to be 0.5 when applicable.

4.1. Scenario 1: Social Distancing Control Only

In the first scenario, only one (non-medical) control, $u_1(t)$, is applied (Figures 2, 3, and 4). As one can see in the figures, when the weight of control, λ_1, increases, the effectiveness of control goes down; see also Table 1 that illustrates how $\mathcal{I}(t)$ changes over time for the cost $C_1(u)$ with different values of λ_1 (find similar Tables for C_2, C_3, and C_4 in the Appendix). One can conclude from Figure 2 that control $u_1(t)$ works by eliminating some cases but also by delaying some of them. Therefore, even though the cumulative number of infections in the controlled environment is significantly less than in the environment with no control, towards the end of the study period the daily number of infected individuals in the controlled environment may be higher.

 doi:10.20944/preprints202408.2036.v1

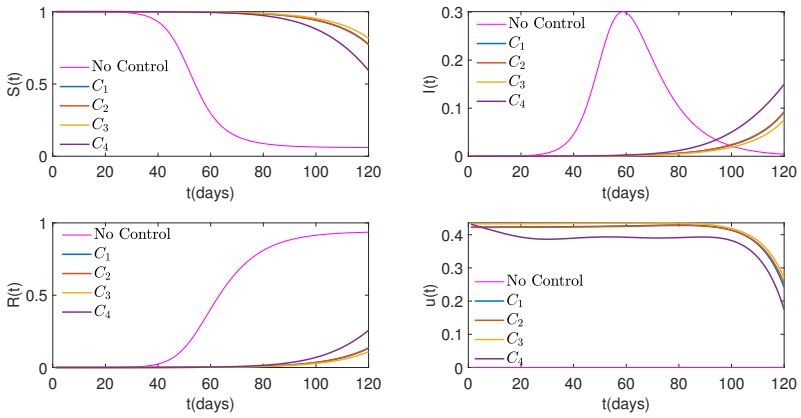

Figure 2. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and control $u_1(t)$ (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight is $\lambda_1 = 0.05$.

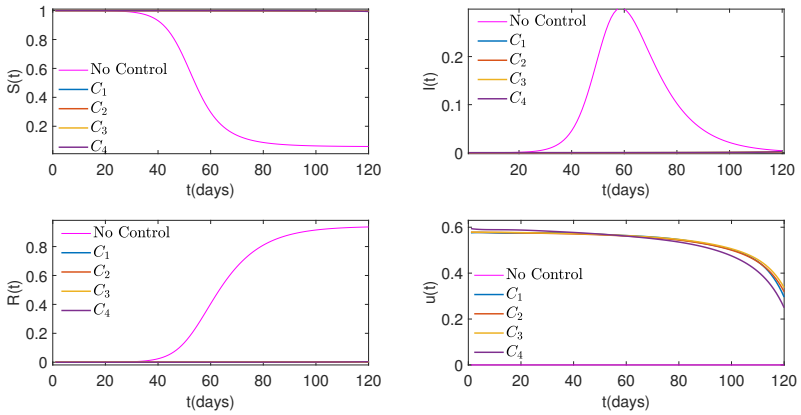

Figure 3. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and control $u_1(t)$ (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight is $\lambda_1 = 0.001$.

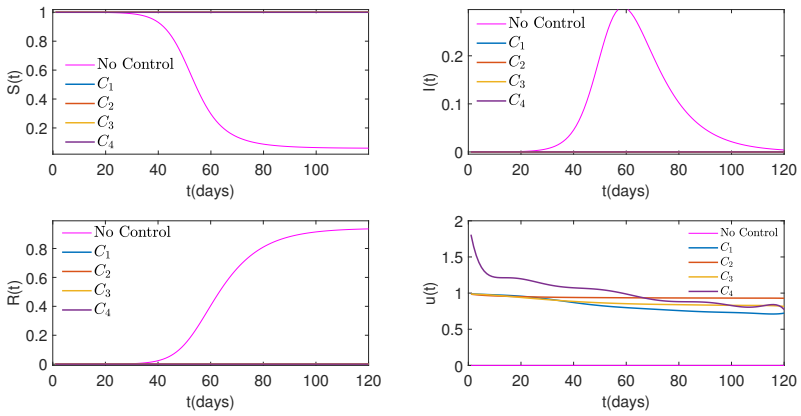

Figure 4. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and control $u_1(t)$ (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight is $\lambda_1 = 10^{-7}$. For the cost function C_4, $u_1(t)$ stays above the ultimate value, $u_1(t) = 1$, for more than half of the study period, which is not practical.

 doi:10.20944/preprints202408.2036.v1

Table 1. Comparison of $\mathcal{I}(t)$ for cost function C_1 in case when only control u_1 is applied and λ_1 varies. As λ_1 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_1 = 10^{-7}$ **No** 2^{nd} **Control**	$\lambda_1 = 0.001$ **No** 2^{nd} **Control**	$\lambda_1 = 0.01$ **No** 2^{nd} **Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No Control**
1	200	200	200	200	200
10	85	253	315	387	1,237
20	34	329	527	812	9,228
30	15	432	880	1,691	67,606
40	7	571	1,466	3,514	456,639
50	4	761	2,447	7,267	1,985,292
60	3	1,028	4,089	14,927	2,987,989
70	2	1,416	6,873	30,388	2,015,872
80	1	2,003	11,678	61,024	1,023,788
90	1	2,953	20,264	120,429	474,813
100	1	4,643	36,661	233,756	213,085
110	1	8,190	72,008	453,110	94,393
120	1	18,714	174,758	922,708	41,578

Figures 2, 3, and 4 with λ_1 equal to 0.05, 0.001, and 10^{-7}, respectively, show the pattern of $I(t)$ decreasing as the values of λ_1 go down. Based on these figures and Table 1, the "flattening of the curve" is evident.

4.2. Scenario 2: Control with Antiviral Medication Only

For the next set of experiments, it was assumed that there is only control $u_2(t)$ in the system. In Figures 5, 6, 7, one can see the effect of the weight, λ_2, on different cost functions and, as the result, on state variables $S(t)$, $I(t)$, and $R(t)$ over time. Again, as the weight, λ_2, decreases the control plays a more effective role in reducing the number of infected people (See Tables 2, A16, A17, and A18 for more details).

Table 2. Comparison of $\mathcal{I}(t)$ for cost function C_1 in case when only control u_2 is applied and λ_2 varies. As λ_2 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_2 = 10^{-7}$ **No** 1^{st} **Control**	$\lambda_2 = 0.001$ **No** 1^{st} **Control**	$\lambda_2 = 0.01$ **No** 1^{st} **Control**	$\lambda_2 = 0.05$ **No** 1^{st} **Control**	$\lambda_2 = 0.1$ **No** 1^{st} **Control**	**No Control**
1	200	200	200	200	200	200
10	18	181	254	318	377	1,237
20	1	168	332	530	756	9,228
30	0	164	437	880	1,503	67,606
40	0	166	581	1,456	2,949	456,639
50	0	177	782	2,395	5,693	1,985,292
60	0	198	1,073	3,938	10,735	2,987,989
70	0	234	1,515	6,481	19,547	2,015,872
80	0	299	2,226	10,735	34,005	1,023,788
90	0	420	3,485	18,210	56,943	474,813
100	0	676	6,092	33,048	95,559	213,085
110	0	1,391	13,102	70,339	177,085	94,393
120	0	5,265	49,724	244,998	499,616	41,578

 doi:10.20944/preprints202408.2036.v1

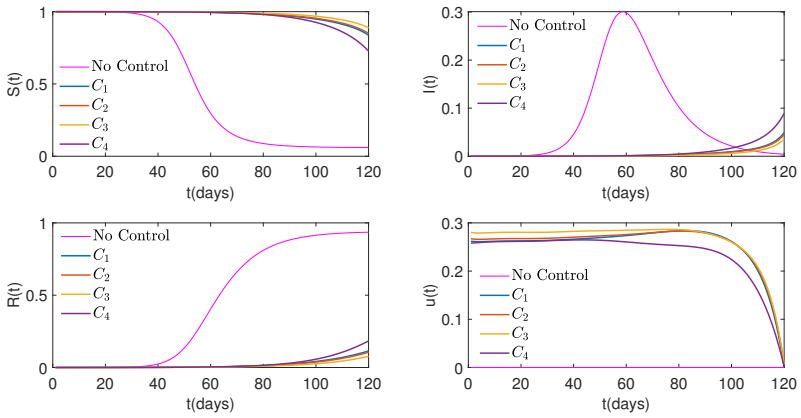

Figure 5. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and control $u_2(t)$ (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight is $\lambda = 0.1$.

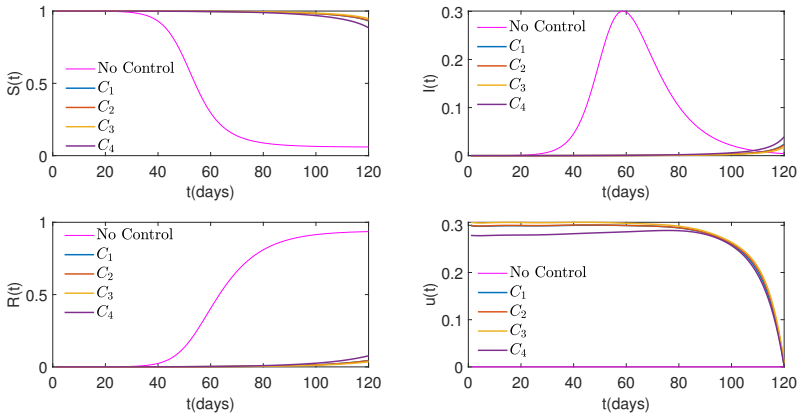

Figure 6. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and control $u_2(t)$ (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight is $\lambda_2 = 0.05$.

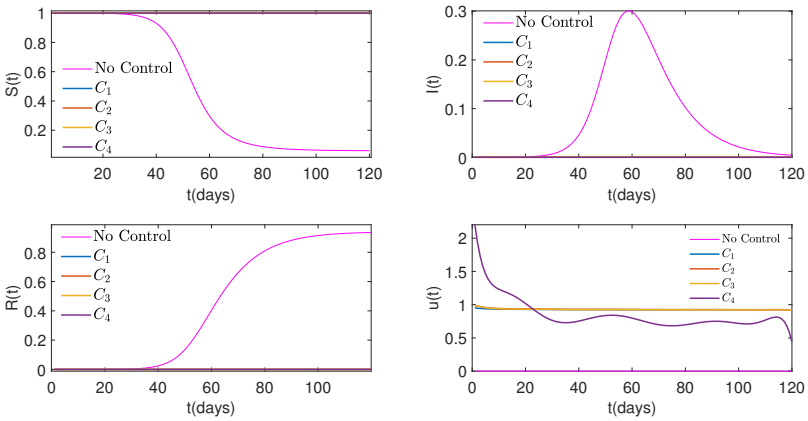

Figure 7. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and control $u_2(t)$ (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight is $\lambda_2 = 10^{-7}$.

 doi:10.20944/preprints202408.2036.v1

Overall, the effects of controls $u_1(t)$ and $u_2(t)$ on the system, when only one control is applied, are similar. However, as one can clearly see from Table 3, for the same cost and over the same time interval, control $u_2(t)$ suppresses infections more aggressively than $u_1(t)$. Also, there is a significant difference between the results for cost function $C_4(u)$ and the rest of the cost functions. While for $C_1(u)$, $C_2(u)$, and $C_3(u)$ the maximum number of infected people on any given day in the case of "first control only" is 923, 332, this number is 1, 511, 537 for $C_4(u)$. Additionally, in the case of "second control only", the maximum daily number of infected individuals for $C_4(u)$ exceeds the maximum daily number for other cost functions by 154, 151 cases. The best performance among all cost functions can be attributed to $C_3(u)$ in both cases where only control $u_1(t)$ or only control $u_2(t)$ is applied. For details, one can see Table 3 and Figure 8.

Table 3. Comparison of $\mathcal{I}(t)$ for all cost functions in the case when only control u_1 is applied ($\lambda_1 = 0.05$) or only control u_2 is applied ($\lambda_2 = 0.05$) over time.

Day	$\lambda_1 =$ 0.05 **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 =$ 0.05	$\lambda_1 =$ 0.05 **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 =$ 0.05	$\lambda_1 =$ 0.05 **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 =$ 0.05	$\lambda_1 =$ 0.05 **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 =$ 0.05
	C_1		C_2		C_3		C_4	
1	200	200	200	200	200	200	200	200
10	387	318	388	317	377	308	401	349
20	812	530	816	527	766	495	918	644
30	1,691	880	1,706	872	1,552	795	2,133	1,178
40	3,514	1,456	3,557	1,439	3,134	1,273	4,939	2,133
50	7,267	2,395	7,379	2,362	6,302	2,034	11,366	3,816
60	14,927	3,938	15,209	3,879	12,618	3,258	25,851	6,733
70	30,388	6,481	31,076	6,381	25,120	5,256	57,953	11,672
80	61,024	10,735	6,2623	10,561	49,586	8,558	127,302	19,877
90	120,429	18,210	123,913	17,880	96,926	14,338	266,304	33,825
100	233,756	33,048	240,619	32,336	188,180	25,768	509,874	60,100
110	453,110	70,339	463,527	67,697	367,745	53,756	899,275	123,379
120	922,708	244,998	923,332	229,683	760,101	183,048	1,511,537	399,149

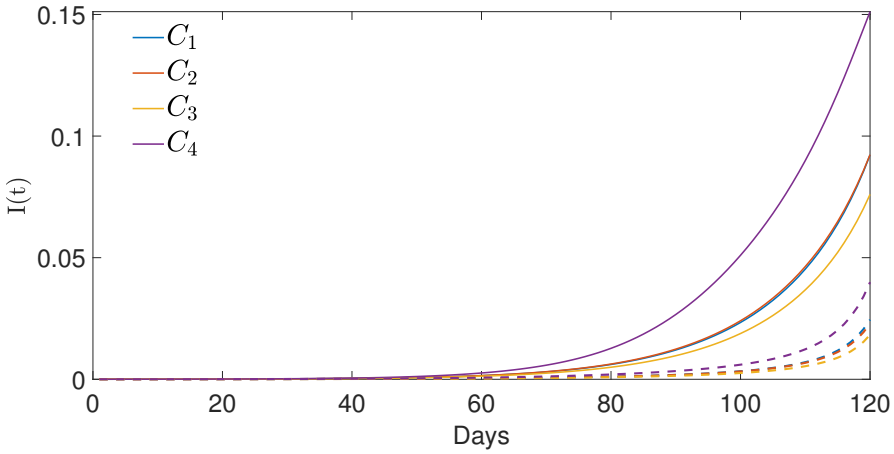

Figure 8. Graphs of $I(t)$ for different cost functions C_1, C_2, C_3, C_4 when only u_1 is applied and $\lambda_1 = 0.05$ (shown with solid lines), and when only u_2 is applied and $\lambda_2 = 0.05$ (shown with dashed line).

4.3. Scenario 3: Non-Medical and Medical Controls in Combination

For the next step, we apply two controls to the *SIR* system, $u_1(t)$ and $u_2(t)$, together with the same weights, $\lambda_1 = \lambda_2 = \lambda$, in order to evaluate their effect on the outbreak (See Figures 9, 10, and

 doi:10.20944/preprints202408.2036.v1

11). As expected, in terms of its dependence on λ, the combination of two controls, $u_1(t)$ and $u_2(t)$, behaves pretty similar to the case of one control in a sense that when the weight, λ, decreases, the controls become more effective, and the daily number of infected humans goes down.

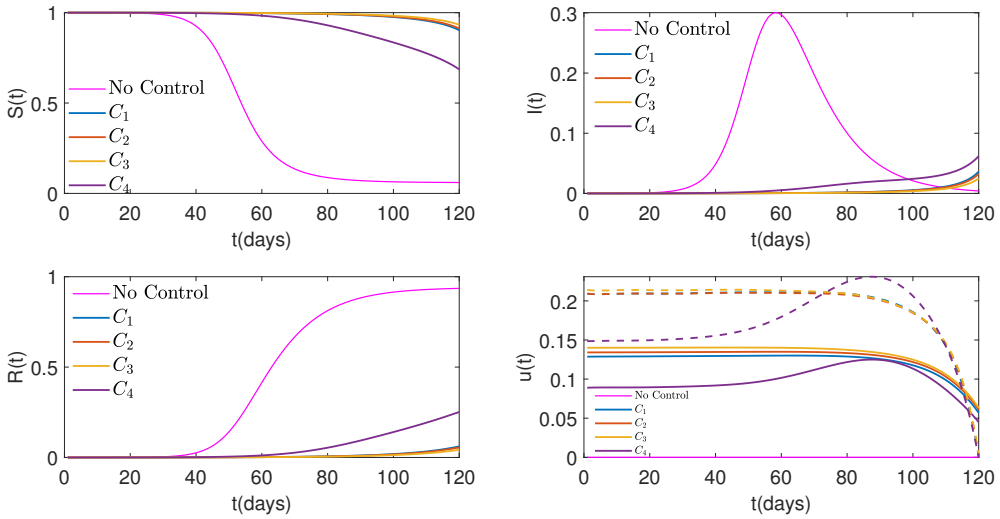

Figure 9. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and controls $u_1(t)$ shown with solid lines, and $u_2(t)$ with dashed lines (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weights, λ_1, and λ_2, for both controls are 0.1.

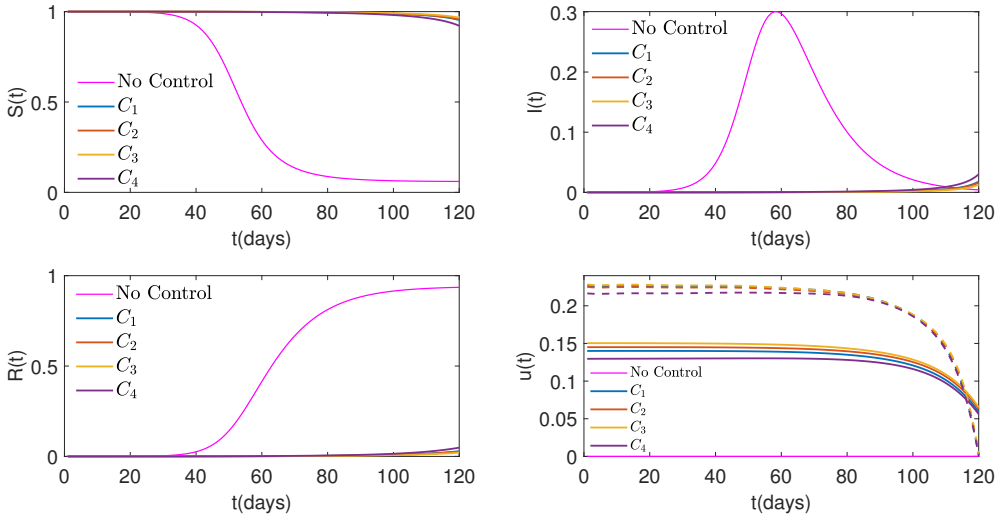

Figure 10. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and control u_1 shown with solid lines, and u_2 with dashed lines (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight, λ, for both controls is $\lambda_1 = \lambda_2 = \lambda = 0.05$.

Tables 4 and 5 show the daily number of infected individuals, $\mathcal{I}(t)$, and the cumulative number of infected individuals up to day t, $N - \mathcal{S}(t)$, for different control scenarios. This gives an insight into how the two controls, $u_1(t)$ and $u_2(t)$, compare individually and in combination subject to the same cost, $C_1(u)$, and the same weight, $\lambda_1 = \lambda_2 = \lambda = 0.05$.

 doi:10.20944/preprints202408.2036.v1

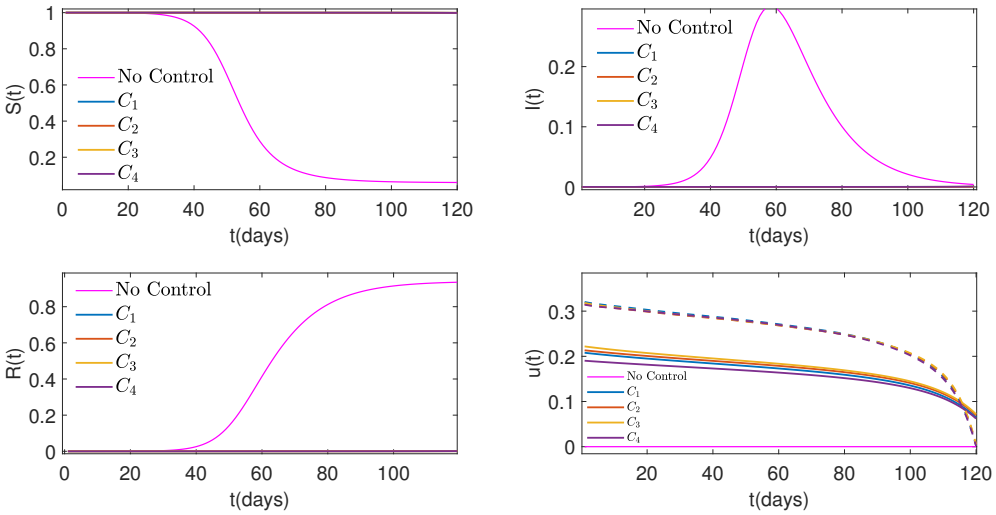

Figure 11. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and controls $u_1(t)$ shown with solid lines, and $u_2(t)$ with dashed lines (bottom on the right) over time for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight, λ, for both controls is $\lambda_1 = \lambda_2 = \lambda = 0.001$.

Table 5 illustrates that the cumulative number of infections after applying both controls for 120 days is 454, 205, while the "no control" counterpart is 9, 397, 865. And in the case of control with antiviral medication, $u_2(t)$, after 120 days there are more than 3 times fewer cases as compared to the case of social distancing control, $u_1(t)$ (692, 160 vs. 2, 256, 854). Similar tables related to the cost functions $C_2(u)$, $C_3(u)$, and $C_4(u)$ can be found in Appendix (Tables A1 - A6).

Table 4. Comparison of $\mathcal{I}(t)$ for cost function C_1 when there is only u_1, only u_2, and both u_1, u_2 applied versus No Control case over time when $\lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,237	387	318	300
20	9,228	812	530	472
30	67,606	1,691	880	743
40	456,639	3,514	1,456	1,167
50	1,985,292	7,267	2,395	1,834
60	2,987,989	14,927	3,938	2,897
70	2,015,872	30,388	6,481	4,625
80	1,023,788	61,024	10,735	7,522
90	474,813	120,429	18,210	12,727
100	213,085	233,756	33,048	23,355
110	94,393	453,110	70,339	50,792
120	41,578	922,708	244,998	173,543

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 August 2024 doi:10.20944/preprints202408.2036.v1

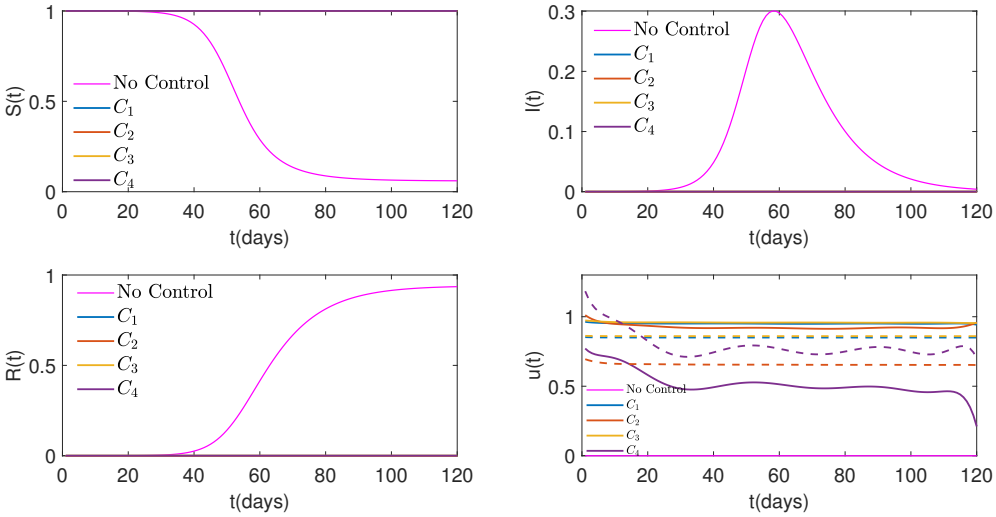

Figure 12. Graphs of Susceptible $S(t)$ (top on the left), Infected $I(t)$ (top on the right), Recovered $R(t)$ (bottom on the left) people, and controls $u_1(t)$ shown with solid lines and $u_2(t)$ with dashed lines (bottom on the right) for four different cost functions C_1, C_2, C_3, C_4 versus No Control when weight, λ, for both controls is $\lambda_1 = \lambda_2 = \lambda = 10^{-8}$. Control u_2 for cost function C_4 takes unrealistic values above 1 at the early period of the study.

Table 5. Cumulative number of infections up to day t, $N - \mathcal{S}(t)$ for cost function C_1 when there is only u_1, only u_2, and both u_1, u_2 versus No Control case over time when weight $\lambda_1 = \lambda_2 = \lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,756	643	898	772
20	13,747	1,649	2,156	1,761
30	101,568	3,735	4,239	3,312
40	697,572	8,067	7,686	5,748
50	3,338,392	17,006	13,356	9,562
60	7,032,920	35,334	22,686	15,568
70	8,627,485	72,609	37,993	25,108
80	9,121,747	147,335	63,222	40,496
90	9,292,217	294,458	105,246	66,067
100	9,358,556	579,209	178,417	111,270
110	9,386,082	1,130,270	320,258	202,389
120	9,397,865	2,256,854	692,160	454,205

In the next series of experiments, controls $u_1(t)$ and $u_2(t)$ have different weights, λ_1 and λ_2, applied to their respective cost functions. We consider two cases. First, for the cost function $C_1(u)$, the weight of control $u_1(t)$ is less than the weight of control $u_2(t)$ ($\lambda_1 < \lambda_2$). Table 6 shows changes in daily numbers of infected people, $\mathcal{I}(t)$, for the cost function $C_1(u)$, in the case of fixed weight ($\lambda_1 = 0.05$) for control $u_1(t)$ and different weights for control $u_2(t)$ (Tables A7 - A9 for cost functions $C_2(u), C_3(u)$, and $C_4(u)$ can be found in Appendix). As it follows from Table 6, adding the second control, $u_2(t)$, with any weight, λ_2, helps to better contain the outbreak and to decrease the daily number of infected people and the cumulative number of cases. Even for high effort case of $\lambda_2 = 0.1$, the number of daily infections is 624,040 cases less than the daily number of infected individuals in case when there is no control $u_2(t)$. However, when the weight of the second control, λ_2, increases, the effort required to implement that measure also rises, making it increasingly challenging to execute.

 doi:10.20944/preprints202408.2036.v1

If the roles are reversed, that is, for the cost function $C_1(u)$, the weight, $\lambda_2 = 0.05$, of the second control, $u_2(t)$, is fixed and the sensitivity of the system to the first control, $u_1(t)$, is observed, the pattern is similar. Namely, adding a non-medical control, $u_1(t)$, reduces the daily number of infected people. Even though it is not as consequential as in the case when control $u_2(t)$ is added, still there are fewer infected people in all cases with two controls as opposed to the case of $u_2(t)$ only. At the same time, it is evident that the second control, $u_2(t)$, is more efficient. Indeed, for the high effort case of $\lambda_1 = 0.1$, the number of daily infections is only 44,983 cases less than the daily number of infected individuals in case when there is no control $u_1(t)$ (as opposed to 624,040 reduction when $u_2(t)$ was added with the same effort, 0.1). The difference in the daily number of infected individuals between the case of no $u_1(t)$ (i.e., $u_2(t)$ only with weight $\lambda_1 = 0.05$) and the case of $u_2(t)$ with $\lambda_1 = 0.05$ and $u_1(t)$ with varying weights ranges from 244,998 to 16,608. See Tables 7, A10, A11, and A12 for more details.

Table 6. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_1 with the weight $\lambda_1 = 0.05$ for $u_1(t)$. The weights for the control $u_2(t)$ are $\lambda_2 = 0.001$, 0.01, 0.05, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_2(t)$ over time.

Day	$\lambda_1 = 0.05$ $\lambda_2 = 0.001$	$\lambda_1 = 0.05$ $\lambda_2 = 0.01$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.1$	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**
1	200	200	200	200	200
10	180	251	300	321	387
20	167	323	472	545	812
30	163	421	743	925	1,691
40	165	554	1,167	1,561	3,514
50	175	737	1,834	2,629	7,267
60	195	1,002	2,897	4,428	14,927
70	231	1,404	4,625	7,481	30,388
80	291	2,049	7,522	12,748	61,024
90	403	3,188	12,727	22,274	120,429
100	646	5,554	23,355	41,465	233,756
110	1,306	11,909	50,792	89,010	453,110
120	4,879	44,363	173,543	280,668	922,708

Figures 13 and 14 show the behavior of controls and their effect on the graphs of $I(t)$ for different cost functions and different weights. As it is evident from the graphs, when $\lambda_1 = 0.05$ and $\lambda_2 = 0.01$, the second control, $u_2(t)$, is dominant and very efficient. At the same time, when $\lambda_1 = 0.05$ and $\lambda_2 = 0.1$, the two controls, $u_1(t)$ and $u_2(t)$, are about the same, and there are more infected people towards the end of the study period, that is, the control strategy in Figure 14 is less efficient as compared to the case of Figure 13. The two figures, once again, underline the significance of the second control, $u_2(t)$.

 doi:10.20944/preprints202408.2036.v1

Table 7. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_1 with the weight $\lambda_2 = 0.05$ for $u_2(t)$. The weights for the control $u_1(t)$ are $\lambda_1 = 0.001, 0.01, 0.05$, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_1(t)$ over time.

Day	$\lambda_1 = 0.001$ $\lambda_2 = 0.05$	$\lambda_1 = 0.01$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.1$ $\lambda_2 = 0.05$	**No 1^{st} Control** $\lambda_2 = 0.05$
1	200	200	200	200	200
10	245	281	300	306	318
20	308	411	472	492	530
30	390	604	743	791	880
40	500	890	1,167	1,268	1,456
50	649	1,318	1,834	2,028	2,395
60	857	1,976	2,897	3,253	3,938
70	1,159	3,016	4,625	5,258	6,481
80	1,621	4,732	7,522	8,613	10,735
90	2,383	7,788	12,727	14,602	18,210
100	3,777	13,962	23,355	26,759	33,048
110	6,844	29,381	50,792	57,816	70,339
120	16,608	90,271	173,543	200,015	244,998

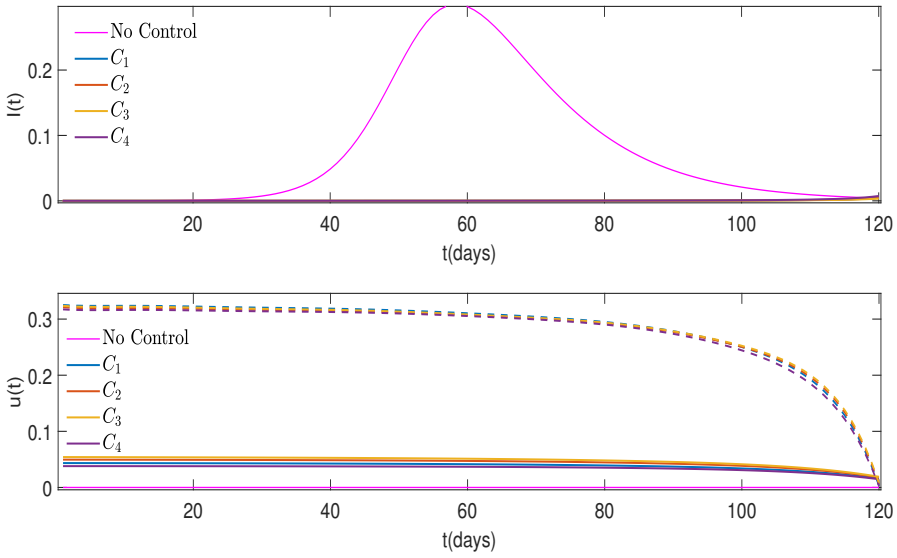

Figure 13. The proportion of Infected people, $I(t)$, for different cost functions and No Control case when $\lambda_1 = 0.05, \lambda_2 = 0.01$ (on the top) and controls $u_1(t)$ shown with solid lines, and $u_2(t)$ with dashed lines (on the bottom).

 doi:10.20944/preprints202408.2036.v1

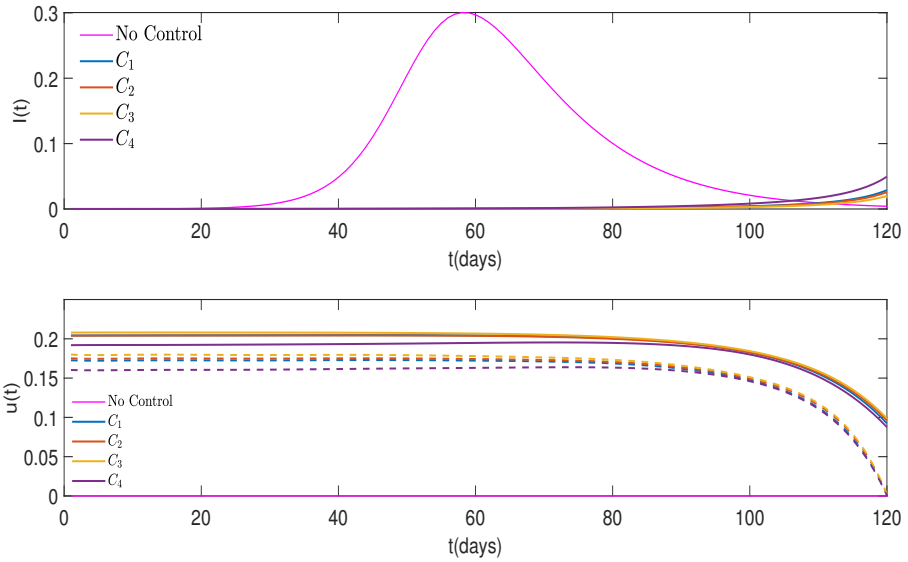

Figure 14. The proportion of Infected people, $I(t)$, for different cost functions and No Control case when $\lambda_1 = 0.05, \lambda_2 = 0.1$ (on the top) and controls $u_1(t)$ shown with solid lines, and $u_2(t)$ with dashed lines (on the bottom).

5. Conclusion

To summarize, in this study, we investigated different control scenarios through theoretical analysis and numerical simulations. To account for two important types of control, social distancing and treatment with antiviral medications, the SIR (Susceptible-Infectious-Removed) model [17] for an early ascending stage of an outbreak has been considered with the first control, $u_1(t)$, aimed to lower the disease transmission rate and the second control, $u_2(t)$, aimed to lower the period of infectiousness. In all experiments, the implementation of control strategies reduced the daily cumulative number of cases, $N - \mathcal{S}(t)$, and successfully "flattened the curve", $\mathcal{I}(t)$. The reduction in the cumulative cases was achieved by eliminating or delaying new cases. This delay is incredibly valuable as it provides public health organizations and researchers with more time to advance antiviral treatments and devise alternative preventive measures.

The main theoretical result of this paper, Theorem 3.1, concludes that the optimal control functions, $u_i(t)$, $i = 1, 2$, may be increasing until some moment $\tau \in [0, T)$. However, for all $t \in [\tau, T]$, the derivatives, $\dfrac{du_i}{dt}$, become negative and $u_i(t)$ decline as t approaches T (possibly causing the number of newly infected people to grow). Numerical simulations presented in Section 4 confirm our theoretical findings. So, ideally, around the time $t = \tau$, the control strategy has to be upgraded and a vaccination campaign needs to start to ensure the epidemic wave does not rebound.

Appendix A. Appendix

Appendix A.1. Properties of SIR Model with Time-Dependent Coefficients

In Section 3, it has been pointed out that even though for system (2), the effective reproduction number, $r(t) = \beta(1 - u_1(t))/(\gamma + \varepsilon u_2(t))$, goes down with more control, it does not guarantee that $r(t) \geq \bar{r}(t)$ yields $S(t) \leq \bar{S}(t)$ for every value of t. One can, however, show that if $r(t) \geq \bar{r}(t)$ and $r(t)$ is non-increasing, then $S(t) \leq \bar{S}(t)$. The proof of this result is given below.

 doi:10.20944/preprints202408.2036.v1

Theorem A.1 Assume that $\frac{d\mathbf{x}}{dt} = f(\mathbf{x}, \beta, \gamma)$, $\mathbf{x}(0) = \mathbf{x}_0$, where $\mathbf{x}(t) = [S(t), I(t), R(t)]^\top$,

$$\begin{aligned} f_1(\mathbf{x}, \beta, \gamma) &:= -\beta(t)S(t)I(t) \\ f_2(\mathbf{x}, \beta, \gamma) &:= \beta(t)S(t)I(t) - \gamma(t)I(t) \\ f_3(\mathbf{x}, \beta, \gamma) &:= \gamma(t)I(t), \end{aligned} \tag{A1}$$

$$\text{and} \quad \mathbf{x}_0 \in \Delta^2 := \{(z_1, z_2, z_3) \in \mathbb{R}^3 : z_1 + z_2 + z_3 = 1,\ z_1, z_2, z_3 \geq 0\}. \tag{A2}$$

Let $\mathbf{x}(t)$ and $\hat{\mathbf{x}}(t)$ satisfy $\frac{d\mathbf{x}}{dt} = f(\mathbf{x}, \beta, \gamma)$ and $\frac{d\hat{\mathbf{x}}}{dt} = f(\hat{\mathbf{x}}, \hat{\beta}, \hat{\gamma})$, respectively, with the same initial condition $\mathbf{x}_0 = \hat{\mathbf{x}}_0 = [S_0, I_0, R_0]^\top$, $R_0 \geq 0$, $S_0, I_0 > 0$, $\beta(t), \gamma(t), \hat{\beta}(t), \hat{\gamma}(t) > 0$ for any $t \in [0, T]$, and $\beta(0) > \hat{\beta}(0) > 0$. Suppose $r(t) := \beta(t)/\gamma(t)$, $\hat{r}(t) := \hat{\beta}(t)/\hat{\gamma}(t)$, and $r(t) \geq \hat{r}(t)$ for all $t \in [0, T]$. If $r(t) \in \mathcal{L}^1[0, T]$ and $r(t)$ is non-increasing, then $S(t) \leq \hat{S}(t)$ for any $t \in [0, T]$.

Proof. Since $\mathbf{x}_0 = \hat{\mathbf{x}}_0$, $S_0, I_0 > 0$ and $\beta(0) > \hat{\beta}(0)$, one concludes that $S_0 = \hat{S}_0 > 0$, $I_0 = \hat{I}_0 > 0$, and $\beta(0)S_0I_0 > \hat{\beta}(0)\hat{S}_0\hat{I}_0$. Therefore by (A1), $S'(0) < \hat{S}'(0)$ and there exists $\epsilon > 0$ such that $S(t) < \hat{S}(t)$ for any $t \in (0, \epsilon]$. If the claim does not hold, then there is $\mu > \epsilon$ such that $S(\mu) > \hat{S}(\mu)$. By intermediate value theorem, there exists $\tau \in (\epsilon, \mu)$ such that

$$\begin{aligned} S(t) &< \hat{S}(t) \quad \text{for any} \quad t \in (0, \tau) \\ S(\tau) &= \hat{S}(\tau) \quad \text{and} \quad S'(\tau) \geq \hat{S}'(\tau). \end{aligned} \tag{A3}$$

From (A3), one obtains

$$S'(\tau) = -\beta(\tau)S(\tau)I(\tau) > -\hat{\beta}(\tau)\hat{S}(\tau)\hat{I}(\tau) = S'(\tau), \tag{A4}$$

that is,

$$I(\tau) \leq \hat{I}(\tau). \tag{A5}$$

On the other hand, according to (A2)

$$I(\tau) - \hat{I}(\tau) = 1 - S(\tau) - R(\tau) - (1 - \hat{S}(\tau) - \hat{R}(\tau)) = \hat{R}(\tau) - R(\tau). \tag{A6}$$

As it follows from (A1),

$$(\ln S(t))' = -\beta(t)I(t) = -\frac{\beta(t)}{\gamma(t)}R'(t) = -r(t)R'(t). \tag{A7}$$

This yields,

$$R(\tau) = R_0 + \int_0^\tau R'(t)dt = R_0 - \int_0^\tau \frac{(\ln S(t))'}{r(t)}dt. \tag{A8}$$

Identities (A7) and (A8) imply,

$$\begin{aligned} I(\tau) - \hat{I}(\tau) &= \int_0^\tau \left\{ \frac{(\ln S(t))'}{r(t)} - \frac{(\ln \hat{S}(t))'}{\hat{r}(t)} \right\} dt = \int_0^\tau \frac{(\ln S(t))' - (\ln \hat{S}(t))'}{r(t)} dt \\ &= \int_0^\tau \left\{ \frac{1}{r(t)} - \frac{1}{\hat{r}(t)} \right\} (\ln \hat{S}(t))' dt := \mathcal{T}_1 + \mathcal{T}_2. \end{aligned} \tag{A9}$$

 doi:10.20944/preprints202408.2036.v1

Since $r(t) \in \mathcal{L}^1[0,T]$ is non-increasing, $S(t) < \hat{S}(t)$ for any $t \in (0,\tau)$, $S(0) = \hat{S}(0)$, and $S(\tau) = \hat{S}(\tau)$, by intermediate value theorem for the first term in (A9), one has

$$\begin{aligned}\mathcal{T}_1 &= \int_0^\tau \frac{(\ln S(t))' - (\ln \hat{S}(t))'}{r(t)} dt = \frac{\ln S(t) - \ln \hat{S}(t)}{r(t)} \Big|_0^\tau + \int_0^\tau \{\ln S(t) - \ln \hat{S}(t)\} \frac{r'(t)}{r^2(t)} dt \\ &= -\frac{r'(\nu)}{r^2(\nu)} \int_0^\tau \{\ln \hat{S}(t) - \ln S(t)\} dt \geq 0, \end{aligned} \tag{A10}$$

where $\nu \in [0,\tau]$. Furthermore, by Lemma 2.1, $S(t), I(t) > 0$ and $(\ln S(t))' < 0$ for any $t \in [0,T]$. Hence from $r(t) \geq \hat{r}(t)$ it follows that

$$\begin{aligned}\mathcal{T}_2 &= \int_0^\tau \left\{\frac{1}{r(t)} - \frac{1}{\hat{r}(t)}\right\} (\ln \hat{S}(t))' dt = \left\{\frac{1}{r(\sigma)} - \frac{1}{\hat{r}(\sigma)}\right\} \int_0^\tau (\ln \hat{S}(t))' dt \\ &= \left\{\frac{1}{\hat{r}(\sigma)} - \frac{1}{r(\sigma)}\right\} \frac{\hat{S}(0)}{\hat{S}(\tau)} > 0. \end{aligned} \tag{A11}$$

Combining (A10) and (A11), one concludes that $I(\tau) > \hat{I}(\tau)$, which contradicts (A5). This completes the proof. □

Appendix A.2. Additional Tables

Table A1. Comparison of $\mathcal{I}(t)$ for cost function C_2 when there is only u_1, only u_2, and both u_1, u_2 applied versus No Control case over time when $\lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,237	388	317	298
20	9,228	816	527	464
30	67,606	1,706	872	725
40	456,639	3,557	1,439	1,132
50	1,985,292	7,379	2,362	1,765
60	2,987,989	15,209	3,879	2,772
70	2,015,872	31,076	6,381	4,403
80	1,023,788	62,623	10,561	7,122
90	474,813	123,913	17,880	11,975
100	213,085	240,619	32,336	21,814
110	94,393	463,527	67,697	46,675
120	41,578	923,332	229,683	156,190

 doi:10.20944/preprints202408.2036.v1

Table A2. Comparison of $\mathcal{I}(t)$ for cost function C_3 when there is only u_1, only u_2, and both u_1, u_2 applied versus No Control case over time when $\lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,237	377	308	289
20	9,228	766	495	437
30	67,606	1,552	795	662
40	456,639	3,134	1,273	1,003
50	1,985,292	6,302	2,034	1,524
60	2,987,989	12,618	3,258	2,333
70	2,015,872	25,120	5,256	3,624
80	1,023,788	49,586	8,558	5,751
90	474,813	96,926	14,338	9,523
100	213,085	188,180	25,768	17,140
110	94,393	367,745	53,756	36,352
120	41,578	760,101	183,048	121,390

Table A3. Comparison of $\mathcal{I}(t)$ for cost function C_4 when there is only u_1, only u_2, and both u_1, u_2 applied versus No Control case over time when $\lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,237	417	349	323
20	9,228	942	644	550
30	67,606	2,150	1,178	935
40	456,639	4,890	2,133	1,581
50	1,985,292	11,061	3,816	2,663
60	2,987,989	24,982	6,733	4,478
70	2,015,872	55,154	11,672	7,537
80	1,023,788	113,747	19,877	12,760
90	474,813	214,937	33,825	22,145
100	213,085	393,864	60,100	41,039
110	94,393	765,135	123,379	88,776
120	41,578	1,493,486	399,149	292,220

 doi:10.20944/preprints202408.2036.v1

Table A4. Cumulative number of infections up to day t, $N - \mathcal{S}(t)$ for cost function C_2 when there is only u_1, only u_2, and both u_1, u_2 versus No Control case over time when weight $\lambda_1 = \lambda_2 = \lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,756	644	897	767
20	13,747	1,657	2,149	1,738
30	101,568	3,762	4,215	3,249
40	697,572	8,148	7,626	5,604
50	3,338,392	17,229	13,223	9,267
60	7,032,920	35,913	22,418	15,000
70	8,627,485	74,051	37,492	24,055
80	9,121,747	150,774	62,328	38,584
90	9,292,217	302,212	103,637	62,591
100	9,358,556	595,429	175,436	104,787
110	9,386,082	1,158,900	313,167	188,825
120	9,397,865	2,283,654	665,799	416,713

Table A5. Cumulative number of infections up to day t, $N - \mathcal{S}(t)$ for cost function C_3 when there is only u_1, only u_2, and both u_1, u_2 versus No Control case over time when weight $\lambda_1 = \lambda_2 = \lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,756	629	885	754
20	13,747	1,575	2,078	1,677
30	101,568	3,482	3,988	3,067
40	697,572	7,331	7,047	5,170
50	3,338,392	15,051	11,930	8,358
60	7,032,920	30,487	19,736	13,210
70	8,627,485	61,195	32,284	20,701
80	9,121,747	121,742	52,562	32,483
90	9,292,217	239,921	85,884	51,635
100	9,358,556	469,095	143,369	84,866
110	9,386,082	916,823	253,443	150,547
120	9,397,865	1,846,297	536,094	328,156

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 August 2024 doi:10.20944/preprints202408.2036.v1

Table A6. Cumulative number of infections up to day t, $N - \mathcal{S}(t)$ for cost function C_4 when there is only u_1, only u_2, and both u_1, u_2 versus No Control case over time when weight $\lambda_1 = \lambda_2 = \lambda = 0.05$.

Day	**No Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No** 1^{st} **Control** $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$
1	200	200	200	200
10	1,756	685	937	803
20	13,747	1,863	2,398	1,927
30	101,568	4,545	5,068	3,835
40	697,572	10,636	9,909	7,055
50	3,338,392	24,388	18,614	12,483
60	7,032,920	55,445	34,055	21,602
70	8,627,485	123,916	60,931	36,924
80	9,121,747	264,191	106,859	62,740
90	9,292,217	525,613	184,436	106,949
100	9,358,556	1,000,085	317,429	186,138
110	9,386,082	1,928,590	565,198	344,961
120	9,397,865	3,757,435	1,169,728	768,757

Table A7. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_2 with the weight $\lambda_1 = 0.05$ for $u_1(t)$. The weights for the control $u_2(t)$ are $\lambda_2 = 0.001, 0.01, 0.05$, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_2(t)$ over time.

Day	$\lambda_1 = 0.05$ $\lambda_2 = 0.001$	$\lambda_1 = 0.05$ $\lambda_2 = 0.01$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.1$	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**
1	200	200	200	200	200
10	183	251	298	317	388
20	171	324	464	532	816
30	168	422	725	892	1,706
40	171	556	1,132	1,490	3,557
50	182	740	1,765	2,483	7,379
60	203	1,006	2,772	4,143	15,209
70	240	1,408	4,403	6,949	31,076
80	302	2,046	7,122	11,770	62,623
90	415	3,162	11,975	20,464	123,913
100	656	5,454	21,814	37,902	240,619
110	1,290	11,440	46,675	80,593	463,527
120	4,634	41,179	156,190	251,157	923,332

 doi:10.20944/preprints202408.2036.v1

Table A8. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_3 with the weight $\lambda_1 = 0.05$ for $u_1(t)$. The weights for the control $u_2(t)$ are $\lambda_2 = 0.001, 0.01, 0.05$, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_2(t)$ over time.

Day	$\lambda_1 = 0.05$ $\lambda_2 = 0.001$	$\lambda_1 = 0.05$ $\lambda_2 = 0.01$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.1$	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**
1	200	200	200	200	200
10	179	245	289	308	377
20	165	309	437	498	766
30	160	394	662	807	1,552
40	161	508	1,003	1,305	3,134
50	168	662	1,524	2,107	6,302
60	185	884	2,333	3,416	12,618
70	216	1,217	3,624	5,586	25,120
80	267	1,739	5,751	9,264	49,586
90	361	2,647	9,523	15,856	96,926
100	560	4,497	17,140	29,108	188,180
110	1,074	9,247	36,352	61,700	367,745
120	3,747	32,698	121,390	194,169	760,101

Table A9. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_4 with the weight $\lambda_1 = 0.05$ for $u_1(t)$. The weights for the control $u_2(t)$ are $\lambda_2 = 0.001, 0.01, 0.05$, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_2(t)$ over time.

Day	$\lambda_1 = 0.05$ $\lambda_2 = 0.001$	$\lambda_1 = 0.05$ $\lambda_2 = 0.01$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.1$	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**
1	200	200	200	200	200
10	185	263	323	351	401
20	177	357	550	658	918
30	177	490	935	1,227	2,133
40	185	675	1,581	2,274	4,939
50	202	937	2,663	4,178	11,366
60	232	1,326	4,478	7,610	25,851
70	284	1,929	7,537	13,717	57,953
80	373	2,911	12,760	24,464	127,302
90	540	4,681	22,145	43,673	266,304
100	907	8,432	41,039	80,621	509,874
110	1,955	18,778	88,776	166,824	899,275
120	7,639	71,495	292,220	482,565	1,511,537

 doi:10.20944/preprints202408.2036.v1

Table A10. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_2 with the weight $\lambda_2 = 0.05$ for $u_2(t)$. The weights for the control $u_1(t)$ are $\lambda_1 = 0.001, 0.01, 0.05$, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_1(t)$ over time.

Day	$\lambda_1 = 0.001$ $\lambda_2 = 0.05$	$\lambda_1 = 0.01$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.1$ $\lambda_2 = 0.05$	**No** 1^{st} **Control** $\lambda_2 = 0.05$
1	200	200	200	200	200
10	244	279	298	304	317
20	308	406	464	485	527
30	391	593	725	773	872
40	501	869	1,132	1,232	1,439
50	650	1,280	1,765	1,957	2,362
60	859	1,908	2,772	3,124	3,879
70	1,163	2,896	4,403	5,028	6,381
80	1,628	4,517	7,122	8,203	10,561
90	2,393	7,382	11,975	13,833	17,880
100	3,793	13,124	21,814	25,193	32,336
110	6,858	27,281	46,675	53,697	67,697
120	16,447	82,599	156,190	181,647	229,683

Table A11. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_3 with the weight $\lambda_2 = 0.05$ for $u_2(t)$. The weights for the control $u_1(t)$ are $\lambda_1 = 0.001, 0.01, 0.05$, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_1(t)$ over time.

Day	$\lambda_1 = 0.001$ $\lambda_2 = 0.05$	$\lambda_1 = 0.01$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.1$ $\lambda_2 = 0.05$	**No** 1^{st} **Control** $\lambda_2 = 0.05$
1	200	200	200	200	200
10	241	274	289	295	308
20	299	388	437	456	495
30	375	546	662	705	795
40	475	772	1,003	1,090	1,273
50	609	1,116	1,524	1,682	2,034
60	795	1,636	2,333	2,617	3,258
70	1,065	2,421	3,624	4,119	5,256
80	1,473	3,676	5,751	6,596	8,558
90	2,138	5,900	9,523	10,976	14,338
100	3,349	10,387	17,140	19,806	25,768
110	5,944	21,561	36,352	41,897	53,756
120	13,985	65,461	121,390	141,870	183,048

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 August 2024 doi:10.20944/preprints202408.2036.v1

Table A12. Comparison of the daily number of infected people, $\mathcal{I}(t)$, for the cost function C_4 with the weight $\lambda_2 = 0.05$ for $u_2(t)$. The weights for the control $u_1(t)$ are $\lambda_1 = 0.001, 0.01, 0.05$, and 0.1 for the second, third, and fourth columns, respectively, and the fifth column shows the case of No Control $u_1(t)$ over time.

Day	$\lambda_1 = 0.001$ $\lambda_2 = 0.05$	$\lambda_1 = 0.01$ $\lambda_2 = 0.05$	$\lambda_1 = 0.05$ $\lambda_2 = 0.05$	$\lambda_1 = 0.1$ $\lambda_2 = 0.05$	**No** 1^{st} **Control** $\lambda_2 = 0.05$
1	200	200	200	200	200
10	243	295	323	331	349
20	305	458	550	581	644
30	386	711	935	1,016	1,178
40	493	1,105	1,581	1,765	2,133
50	642	1,723	2,663	3,040	3,816
60	857	2,705	4,478	5,206	6,733
70	1,181	4,303	7,537	8,876	11,672
80	1,688	7,008	12,760	15,100	19,877
90	2,559	11,918	22,145	26,079	33,825
100	4,271	21,947	41,039	47,785	60,100
110	8,353	47,241	88,776	101,665	123,379
120	22,600	146,614	292,220	334,465	399,149

Table A13. Comparison of $\mathcal{I}(t)$ for cost function C_2 in case when only control u_1 is applied and λ_1 varies. As λ_1 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_1 = 10^{-7}$ **No** 2^{nd} **Control**	$\lambda_1 = 0.001$ **No** 2^{nd} **Control**	$\lambda_1 = 0.01$ **No** 2^{nd} **Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No Control**
1	200	200	200	200	200
10	88	255	317	388	1,237
20	36	334	533	816	9,228
30	15	441	894	1,706	67,606
40	6	586	1,498	3,557	456,639
50	3	786	2,512	7,379	1,985,292
60	1	1,068	4,219	15,209	2,987,989
70	0	1,479	7,126	31,076	2,015,872
80	0	2,101	12,151	62,623	1,023,788
90	0	3,105	21,130	123,913	474,813
100	0	4,883	38,221	240,619	213,085
110	0	8,576	74,708	463,527	94,393
120	0	19,158	177,113	923,332	41,578

 doi:10.20944/preprints202408.2036.v1

Table A14. Comparison of $\mathcal{I}(t)$ for cost function C_3 in case when only control u_1 is applied and λ_1 varies. As λ_1 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_1 = 10^{-7}$ **No** 2^{nd} **Control**	$\lambda_1 = 0.001$ **No** 2^{nd} **Control**	$\lambda_1 = 0.01$ **No** 2^{nd} **Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No Control**
1	200	200	200	200	200
10	86	254	314	377	1,237
20	35	332	522	766	9,228
30	15	437	867	1,552	67,606
40	8	579	1,438	3,134	456,639
50	4	773	2,388	6,302	1,985,292
60	2	1,044	3,972	12,618	2,987,989
70	1	1,437	6,644	25,120	2,015,872
80	1	2,025	11,220	49,586	1,023,788
90	0	2,963	19,303	96,926	474,813
100	0	4,592	34,478	188,180	213,085
110	0	7,879	66,265	367,745	94,393
120	0	16,955	153,051	760,101	41,578

Table A15. Comparison of $\mathcal{I}(t)$ for cost function C_4 in case when only control u_1 is applied and λ_1 varies. As λ_1 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_1 = 10^{-7}$ **No** 2^{nd} **Control**	$\lambda_1 = 0.001$ **No** 2^{nd} **Control**	$\lambda_1 = 0.01$ **No** 2^{nd} **Control**	$\lambda_1 = 0.05$ **No** 2^{nd} **Control**	**No Control**
1	200	200	200	200	200
10	28	248	319	401	1,237
20	4	315	542	918	9,228
30	1	405	917	2,133	67,606
40	0	527	1,550	4,939	456,639
50	0	696	2,623	11,366	1,985,292
60	0	936	4,447	25,851	2,987,989
70	0	1,296	7,593	57,953	2,015,872
80	0	1,865	13,135	127,302	1,023,788
90	0	2,840	23,348	266,304	474,813
100	0	4,726	43,733	509,874	213,085
110	0	9,137	91,108	899,275	94,393
120	0	24,025	240,585	1,511,537	41,578

 doi:10.20944/preprints202408.2036.v1

Table A16. Comparison of $\mathcal{I}(t)$ for cost function C_2 in case when only control u_2 is applied and λ_2 varies. As λ_2 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_2 = 10^{-7}$ **No** 1^{st} **Control**	$\lambda_2 = 0.001$ **No** 1^{st} **Control**	$\lambda_2 = 0.01$ **No** 1^{st} **Control**	$\lambda_2 = 0.05$ **No** 1^{st} **Control**	$\lambda_2 = 0.1$ **No** 1^{st} **Control**	**No Control**
1	200	200	200	200	200	200
10	17	183	255	317	369	1,237
20	1	172	335	527	722	9,228
30	0	169	444	872	1,404	67,606
40	0	173	592	1,439	2,701	456,639
50	0	185	797	2,362	5,115	1,985,292
60	0	207	1,095	3,879	9,510	2,987,989
70	0	245	1,546	6,381	17,215	2,015,872
80	0	311	2,267	10,561	30,078	1,023,788
90	0	437	3,527	17,880	51,136	474,813
100	0	695	6,103	32,336	87,648	213,085
110	0	1,398	12,821	67,697	164,273	94,393
120	0	5,103	46,967	229,683	464,307	41,578

Table A17. Comparison of $\mathcal{I}(t)$ for cost function C_3 in case when only control u_2 is applied and λ_2 varies. As λ_2 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_2 = 10^{-7}$ **No** 1^{st} **Control**	$\lambda_2 = 0.001$ **No** 1^{st} **Control**	$\lambda_2 = 0.01$ **No** 1^{st} **Control**	$\lambda_2 = 0.05$ **No** 1^{st} **Control**	$\lambda_2 = 0.1$ **No** 1^{st} **Control**	**No Control**
1	200	200	200	200	200	200
10	17	180	250	308	347	1,237
20	1	166	321	495	636	9,228
30	0	161	417	795	1,159	67,606
40	0	163	546	1,273	2,096	456,639
50	0	171	723	2,034	3,752	1,985,292
60	0	189	978	3,258	6,656	2,987,989
70	0	219	1,359	5,256	11,661	2,015,872
80	0	274	1,962	8,558	20,100	1,023,788
90	0	377	3,014	14,338	34,531	474,813
100	0	587	5,134	25,768	61,227	213,085
110	0	1,147	10,559	53,756	120,600	94,393
120	0	4,067	37,929	183,048	365,469	41,578

 doi:10.20944/preprints202408.2036.v1

Table A18. Comparison of $\mathcal{I}(t)$ for cost function C_4 in case when only control u_2 is applied and λ_2 varies. As λ_2 increases, the number of infected individuals, $\mathcal{I}(t)$, gets higher on most days.

Day	$\lambda_2 = 10^{-7}$ **No** 1^{st} **Control**	$\lambda_2 = 0.001$ **No** 1^{st} **Control**	$\lambda_2 = 0.01$ **No** 1^{st} **Control**	$\lambda_2 = 0.05$ **No** 1^{st} **Control**	$\lambda_2 = 0.1$ **No** 1^{st} **Control**	**No Control**
1	200	200	200	200	200	200
10	2	185	265	349	381	1,237
20	0	177	364	644	767	9,228
30	0	177	501	1,178	1,531	67,606
40	0	186	695	2,133	3,019	456,639
50	0	204	972	3,816	5,908	1,985,292
60	0	235	1,384	6,733	11,591	2,987,989
70	0	288	2,021	11,672	22,889	2,015,872
80	0	382	3,067	19,877	45,018	1,023,788
90	1	559	4,960	33,825	86,814	474,813
100	1	949	8,995	60,100	165,937	213,085
110	0	2,069	20,200	123,379	338,415	94,393
120	0	8,174	78,701	399,149	878,072	41,578

References

1. Cai, L.; Li, X.; Tuncer, N.; Martcheva, M.; Lashari, A.A. Optimal control of a malaria model with asymptomatic class and superinfection. *Mathematical Biosciences* **2017**, *288*, 94–108. https://doi.org/10.1016/j.mbs.2017.03.003.
2. Panovska-Griffiths, J.; Kerr, C.C.; Stuart, R.M.; Mistry, D.; Klein, D.J.; Viner, R.M.; Bonell, C. Determining the optimal strategy for reopening schools, the impact of test and trace interventions, and the risk of occurrence of a second COVID-19 epidemic wave in the UK: a modelling study. *The Lancet Child & Adolescent Health* **2020**, *4*, 817–827.
3. Paltiel, A.D.; Zheng, A.; Walensky, R.P. Assessment of SARS-CoV-2 screening strategies to permit the safe reopening of college campuses in the United States. *JAMA network open* **2020**, *3*, e2016818–e2016818.
4. Aaby, P.; Samb, B.; Simondon, F.; Seck, A.M.C.; Knudsen, K.; Whittle, H. Non-specific beneficial effect of measles immunisation: analysis of mortality studies from developing countries. *Bmj* **1995**, *311*, 481–485.
5. Ahmed, F.; Lindley, M.C.; Allred, N.; Weinbaum, C.M.; Grohskopf, L. Effect of influenza vaccination of healthcare personnel on morbidity and mortality among patients: systematic review and grading of evidence. *Clinical infectious diseases* **2014**, *58*, 50–57.
6. Sivaraman, K.; Dhawan, S.; Chopra, A.; Bhat, S.G. How Effective Were Isolation and Quarantine Strategies during the COVID-19 Pandemic: Challenges and Lessons Learned So Far? *Preprints.org* **2024**.
7. Strassburg, M.A. The global eradication of smallpox. *American journal of infection control* **1982**, *10*, 53–59.
8. D'Ortenzio, E.; Do, C.; Renault, P.; Weber, F.; Filleul, L. Enhanced influenza surveillance on Réunion Island (southern hemisphere) in the context of the emergence of influenza A(H1N1)v. *Eurosurveillance* **2009**, *14*, 19239.
9. Barlow M., M.N.; R., T. Optimal shutdown strategies for COVID-19 with economic and mortality costs: British Columbia as a case study. *Royal Society Open Science* **2021**, *8*, 1 – 18.
10. Saha, S.; Samanta, G. Modelling the role of optimal social distancing on disease prevalence of COVID-19 epidemic. *International Journal of Dynamics and Control* **2021**, *9*, 1053–1077.
11. Saha, S.; Samanta, G.; Nieto, J. Impact of optimal vaccination and social distancing on COVID-19 pandemic. *Mathematics and Computers in Simulation* **2022**, *200*, 285–314.
12. Firth, J.A.; Hellewell, J.; Klepac, P.; Kissler, S.; Kucharski, A.J.; Spurgin, L.G. Using a real-world network to model localized COVID-19 control strategies. *Nature medicine* **2020**, *26*, 1616–1622.
13. Köhler, J.; Schwenkel, L.; Koch, A.; Berberich, J.; Pauli, P.; Allgöwer, F. Robust and optimal predictive control of the COVID-19 outbreak. *Annual Reviews in Control* **2021**, *51*, 525–539.
14. Lü, X.; Hui, H.w.; Liu, F.f.; Bai, Y.l. Stability and optimal control strategies for a novel epidemic model of COVID-19. *Nonlinear Dynamics* **2021**, *106*, 1491–1507.

 doi:10.20944/preprints202408.2036.v1

15. Tuncer, N.; Timsina, A.; Nuno, M.; Chowell, G.; Martcheva, M. Parameter identifiability and optimal control of an SARS-CoV-2 model early in the pandemic. *Journal of Biological Dynamics* **2022**, *16*, 412–438.
16. Ghosh, J.K.; Ghosh, U.; Biswas, M.; Sarkar, S. Qualitative analysis and optimal control strategy of an SIR model with saturated incidence and treatment. *Differential Equations and Dynamical Systems* **2019**, pp. 1–15.
17. Kermack, W.O.; McKendrick, A.G. A contribution to the mathematical theory of epidemics. *Proceedings of the royal society of london. Series A, Containing papers of a mathematical and physical character* **1927**, *115*, 700–721.
18. Hethcote, H.W.; Yorke, J.A. *Gonorrhea transmission dynamics and control*; Vol. 56, Springer, 2014.
19. Lee, S.; Chowell, G.; Castillo-Chávez, C. Optimal control for pandemic influenza: The role of limited antiviral treatment and isolation. *Journal of Theoretical Biology* **2010**, *265*, 136–150. https://doi.org/10.1016/j.jtbi.2010.04.003.
20. Smirnova, A.; Ye, X. On Optimal Control at the Onset of a New Viral Outbreak. *Infectious Disease Modelling* **2024**.
21. Lenhart, S.; J.T.Workman. Optimal control applied to biological models. *Chapman and Hall/CRC* **2007**. doi:https://doi.org/10.1201/9781420011418.
22. Pontryagin, L.S. *Mathematical Theory of Optimal Processes*; Routledge, 2018.