Optimal control strategies to prevent the hospital beds collapse during Covid-19 outbreak

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Leonardo Pio Lo Porto
Simone Rotondi

Abstract: In 2020 the world has faced a serious challenge since the breakout of corona-virus started in Wuhan, China. The deathly disease has killed about 1.770.000 and infected more than 80 millions humans around the globe since December 2019 to 27 of December 2020.

The paper presents a new mathematical model for the SARS-CoV-2 virus propagation, designed to include all the possible actions to prevent the spread and to help in the healing of infected people, including the new inoculation to the SARS-CoV-2. The objective of this project is to propose the possibility of optimal controls over the susceptible and the infected subjects considering different cost functions in order to see the effects of different optimised control actions on the evolution of the epidemic spread and in particular how these controls should be tuned in order to avoid the hospital beds collapse. The optimal control analysis was carried out using the Pontryagin's maximum principle to figure out the optimal strategy necessary to curtail the disease.and the existence of the optimal solution is assessed. Numerical evaluations are developed for a more intuitive and immediate presentation, showing the consequences on the classes of interest.

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1 1. Introduction

Coronavirus disease 2019 (COVID-19) is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2).

Italy has been severely affected[5]. After the first indigenous case on 21 February 2020 in Lodi province, several suspect cases (initially epidemiologically linked) began to emerge in the south and southwest territory of Lombardy[6]. A 'red zone', encompassing 11 municipalities where SARS-CoV-2 infection was endemic, was instituted on 22 February 2020, and put on lockdown to contain the emerging threat. A campaign to identify and screen all close contacts with confirmed cases of COVID-19 resulted in taking 691,461 nasal swabs as of 5 April 2020. Of the 128,948 detected cases, 91,246 were currently infected (28,949 hospitalized, 3,977 admitted

to intensive care units (ICUs) and 58,320 quarantined at home), 21,815 had been discharged due to recovery and 15,887 had died7. In the early days of the epidemic in Italy, both symptomatic and asymptomatic people underwent screening. A government regulation dated 26 February 2020 limited screening to symptomatic subjects only[8]. On 8 March 2020, to further contain the spread of SARS-CoV-2, the red zone was extended to the entire area of Lombardy and 14 more northern Italian provinces. On 9 March 2020, lockdown was declared for the

entire country[9] and progressively stricter restrictions were adopted. COVID-19 displays peculiar epidemiological traits when compared with previous coronavirus outbreaks of SARS-CoV and MERS-CoV. According to Chinese data[10], a large number of transmissions, both in nosocomial and community settings, occurred through human-to-human contact with individuals showing no or mild symptoms. The estimated basic reproduction number ($R0$) for

SARS-CoV-2 ranges from 2.0 to 3.5[11–13], which seems comparable, or possibly higher, than for SARS-CoV and MERS-CoV. High viral loads of SARS-CoV-2 were found in upper respiratory specimens of patients showing little or no symptoms, with a viral shedding pattern akin to that of influenza viruses[14]. Hence, inapparent transmission may play a major and underestimated role in sustaining the outbreak.

Until the end of December the disease had neither approved medicine nor vaccine and has made governments and scholars search for drastic measures in combating the pandemic. The 26th of **December the first 10.000 doses of vaccine have been delivered in Italy but the effectiveness of it is not yet guaranteed and the first side effects have been occured in different countries.**

Predictive mathematical models for epidemics [15–18] are fundamental to understand the course of the epidemic and to plan effective control strategies. One commonly used model is the SIR model[19] for human-to-human transmission, which describes the flow of individuals through three mutually exclusive stages of infection: susceptible, infected and recovered. More complex models can accurately portray the dynamic spread of specific epidemics. For the COVID-19 pandemic, several models have been developed for specific classes of infections, to better describe their propagation and to particularize the specific control actions against its spread.

In this paper a quite rich model is proposed, composed by 8 different classes and the model parameters are identified on the basis of the available data. To have a more detailed model all the known preventive and active actions that can be put in place are considered, at an organizational and decisional level as well as from a medical point of view, to contain the virus spread. For the aim of our work, the model explains in a better way the compartments of infected people drawing a distinction between different type of infectious and paying attention to those that are in the hospitals.

Regrettably, the spread of the virus and mortality due to COVID-19 has continued to increase daily. **Hence, it is imperative to control the spread of the disease particularly using nonpharmacological strategies (and in a second case pharmacological one) such as quarantine, isolation, and public health education.**

This work studied the effect of these different control strategies using mathematical modeling and optimal control approach to ascertain their contributions in the dynamic transmission of COVID-19.

In the following paragraph the model is presented and described.

2 2. Methods

2.1 2.1 Mathematical Model

The mathematical model here adopted is an enrichment of a classical SEQIR one, usually adopted to describe the dynamic of epidemic spreads in presence of a virus incubation phase (E) in which the quarantine compartment (Q) is considered. To the standard SEQIR model more classes are added, the possible ways of intervention are modelled in order to make available some numerical evaluations about the potential epidemic diffusion depending on the different strategies. We have considered the $SEI_aQI_1I_2RV$ epidemic model for Covid-19 transmission, where each class is defined as follow:

- Susceptible (S): people who are not yet infected but they are potentially plagued by the virus.
- Expose (E): people who have been infected but they still can not spread the virus because of the incubation period.
- Infected undetected (I_a): fraction of population that can infect the susceptible class because they are not yet detected and so they could have contacts with susceptible people.
- Quarantined (Q): fraction of population detected with or without symptoms quarantined and due to this fact they can not have contact with susceptible.

- Hospitalized infected non-ICu (I_1): fraction of population detected, with symptoms and hospitalized not in Intensive Care (IC).
- Hospitalized infected in ICu (I_2): fraction of population detected that due to the heavy symptoms has been hospitalized in Intensive Care (IC).
- Recovered (R): fraction of population healed from the virus and temporarily immune.
- Vaccinated (V): fraction of population vaccinated and immune.

The mathematical model proposed is the following one[1]:

$$\dot{S} = b - dS - \beta S I_a (1 - u_p) + \eta R - u_{va} S$$
$$\dot{E} = -dE + \beta S I_a (1 - u_p) - kE$$
$$\dot{I}_a = -dI + kE - \lambda\tau I_a \quad -\gamma_1 I_a$$
$$\dot{Q} = -dQ + p\lambda\tau I_a - \gamma_2 Q - \quad \sigma_1 Q \qquad (1)$$
$$\dot{I}_1 = -dI_1 + \sigma_1 Q - \gamma_3 I_1 - \rho_1 u_1 I_1 - \sigma_2 (1 - u_1) I_1 + (1 - p)\lambda\tau I_a$$
$$\dot{I}_2 = -dI_2 - mI_2 + \sigma_2 (1 - u_1) I_1 - \rho_2 I_2 u_2$$
$$\dot{R} = -dR - \eta R + \gamma_1 I_a + \gamma_2 Q + \gamma_3 I_1 + \rho_1 u_1 I_1 + \rho_2 u_2 I_2$$
$$\dot{V} = -dV + u_{va} S$$

With initial conditions:

$S(0) = S_0, E(0) = E_0, I_a(0) = I_a^0, Q(0) = Q_0, I_1(0) = I_1^0, I_2(0) = I_2^0, R(0) = R_0, V(0) = V_0$ *(2)*

And with the control bounds:

$u_{min}^p \leq u^p(t) \leq u_{max}^p$, *(3a)*
$u_{min}^1 \leq u^1(t) \leq u_{max}^1$, *(3b)*
$u_{min}^2 \leq u^2(t) \leq u_{max}^2$, *(3c)*
$u_{min}^{va} \leq u^{va}(t) \leq u_{max}^{va}$ *(3d)*

Where $u_{min} = 0, u_{max} = 0.9$ (depending on the type of the control we are considering the upper bound changes).

The model in Equation (1) subdivides human population into eight mutually exclusive compartments defined previously. The uppercase letters are the state variables and they represent the fraction of population in each stage; the considered parameters, denoted by lowercase Greek and Latin letters, are positive numbers. The interactions among different stages of infection are visually represented in the block diagram in Fig.1. Now we will describe the variation of each compartment to understand how the different terms flow through the system and how the different compartments interact among them:

1. *Modelling of susceptible population ($\dot{S}(t)$):* By the number of births per day in Italy b and by the fraction of population that was recovered but no longer immune by the virus (ηR), the susceptible population is augmented. The susceptible population decreases through natural death (dS), the interaction between a susceptible individual and infected but not detected by testing individual ($\beta S I_a$); the latter term is mitigated by a preventive control): it means that if the control effort in prevention, such as correctly using the mask in a public place or during interaction with people, washing hands accurately, is strongly applied the fraction of population infected during a contact is quite lower. Thanks to the vaccine campaign that in the last few months are carried on by the government this compartment could decrease also thanks the vaccine control (u_{va}).

2. *Modelling of Infected but not contagious due to the incubation period ($\dot{E}(t)$):* the fraction of population in this compartment increases due to the contact between a susceptible and an infected but not yet detected induvial influenced by the preventive control ($\beta S I_a (1 - u_p)$). In this compartment, people cannot infect a susceptible individual because of the incubation period k (period in which people are infected but not ye infectious). After this period, exposed individuals flow out (kE) and they are led in the next compartment I_a.

[1] Note that for a better view of the system we have omitted the time dependences of the state variables and parameters in the system that are intrinsically in.

3. *Modelling of Infected but not detected by testing population ($\dot{I}_a(t)$):* The income population comes from the previous compartment (E) at the end of the incubation period (kE. Now, those individuals are infected and infectious but not detected; they can decrease either through the natural death or due to detection at a rate λ after a time τ that represents the inverse of the mean time to swab ($\lambda\tau I_a$) or, moreover, thanks to a spontaneous recovery rate γ_1.

4. *Modelling of quarantine population ($\dot{Q}(t)$):* on one hand the growth of quarantine population depends on the detected individuals that are subjected by a parameter p that represents the percentage of detected people solitary confinement ($p\lambda\tau I_a$). On the other hand, its decreasing is affected by the natural death (dQ), an healing factor that is the spontaneous recovery rate ($\gamma_2 Q$)and the complication of the disease that brings those people in hospital ($\sigma_1 Q$).

5. *Modelling of symptomatic hospitalized Infected but not in Intensive Care population ($\dot{I}_1(t)$):* in this compartment two different terms converge: one from the quarantine compartment due to disease complications, the other comes from the remaining part of detected people ($(1-p)\lambda\tau I_a$). The reasons that are the causes of a decreasing evolution are pointed out by the following reasons: natural death (dI_1), disease complication that bring the individuals from this compartment to the infected in intensive care class ($\sigma_2(1-u_1)I_1$) affected by the hospital treatments (the more is the effort the lower is the fraction of hospitalized population that flows in intensive care), spontaneous recovery ($\gamma_3 I_1$) and "controlled" recovery thanks to the drugs and the medical staff looks after the patients ($\rho_1 u_1 I_1$) depending on the effectiveness of the control ρ_1.

6. *Modelling of symptomatic hospitalized Infected in Intensive Care population ($\dot{I}_2(t)$):* this compartment is nurtured by those people that because of a complication of the diseases are obliged to go in IC ($\sigma_2(1-u_1)I_1$). In this compartment the only way to be recovered ($\rho_2 I_2 u_2$) is using ventilator, oxygen, specific equipment and machineries that are translated in a control parameter u_2 and it is affected by its effectiveness ρ_2. Otherwise, natural death (dI_2) and death due to the disease (mI_2) are the causes of the decreasing.

7. *Modelling of recovered population ($\dot{R}(t)$):* infected not yet detected, quarantined individuals, hospitalized infected not in IC recover spontaneously from the disease ($\gamma_1 I_a+\gamma_2 Q+\gamma_3 I_1$ at rates $\gamma_1, \gamma_2, \gamma_3$ respectively. For hospitalized infected not in IC and in IC it is possible to recover through a control action u_1, u_2 respectively and they are represented by the terms $\rho_1 u_1 I_1, \rho_2 u_2 I_2$ (with effectiveness of the two controls ρ_1, ρ_2).

8. *Modelling of vaccinated population ($\dot{V}(t)$):* the inflow and outflow of this compartment depend on the vaccinated fraction of susceptible population ($u_{va}S$) through a control action u_{va} representing the investment cost on vaccine and the natural death respectively (dV).

Figure 1: The model. Graphical scheme representing the interactions among different stages of infection in the mathematical model *$SEI_aQI_1I_2RV$.* Each stage has a natural death rate(d) output

[Warning: Draw object ignored]

The parameters of the considered model are presented in **Table 1.**

Discussion on modelling choices: In the model, we omit the control referring to the swabs considering just the percentage of the positive people. This choice is given by the fact that we are interested in the study of the infected people, so we assume that all the people that are infected not yet detected are positive with a precise percentage given by estimations on real data.

In the model, we have decided to consider a parameter ρ that has the purpose to mitigate the effectiveness of the control in the case in which the control effort is maximum. In a matter of fact, we have supposed that, even if the effort on hospitalised control with respect to non IC units and IC units, is maximum, it is not certain that the outcome of this choice has its maximum effectiveness. About the recoveries we have assumed that it is possible to heal even without drugs only if the infected people are not yet detected and without symptoms (it means in I_a), quarantined (in Q) or hospitalized but not in IC. In the latter case we have considered those infected people that go to the hospital just for a check or would have recovered also without any treatments. On the other side, to be more realistic, the infected people in IC can be healed just through treatments and the usage of ventilator and oxygen, so in this class the only way to be recovered is with a control effort.

Table 1: parameters of the considered model

Symbol	Interpretation
u_p	**Prior control (social distancing, masks, information campaigns)**
u_1	**Hospital treatments control over non-IC patients (availability of beds, medical staff, use of drugs)**
u_2	**Hospital treatments control over IC patients (availability of beds in IC units, ventilator, oxygen, medial staff)**
u_{va}	**Control over vaccine inoculation and production.**
b	**Number of births.**
d	**Death rate in Italy**
β	**Contact rate**
k	**Incubation period**
λ	**Percentage of positive**
p	**Percentage of quarantined people.** ***(1-p):*** **percentage of hospitalized patients not in IC**
σ_1	**Percentage of people that from quarantine move to Covid units after complications.**
σ_2	**Percentage of people that from Covid units move to IC units after complications.**
γ_i	**Recovery rate without use of drugs in I_a(i=*1*), Q (i=2), I_1 (i=3)**
m	**Death rate**
ρ_j	**Control effectiveness (ρ_1 *with respect to* u_1 *and* ρ_2 *with respect to* u_2*)**
τ	**Inverse of the mean time to swab (both referring to the onset of symptoms and the time spent to know about the contact with a positive person)**
η	**Inverse of the mean time to be again susceptible**

2.2 2.2 Model Fitting

2.2.1 Motivations

In this subsection we briefly discuss the main reasons on why before the optimal control we have decided to fit some parameters of the model.

Before we could get to the optimization of the model the fitting problem was considered. The aim of this additional step before optimization is to check that the proposed model should follow the real data. To accomplish this task, we have had to find the parameters that would reproduce the real behaviour. Some of those parameters was inferred based on the official data and statistics (source: Protezione Civile, Ministero della Salute, Istat) like death rate (d, m), number of births (b), the delays τ, η; the remaining ones ($p, \gamma_i, \lambda, \sigma_i, \rho_i$plus the base control applied by the government u_{va}, u_1, u_2, u_p) has been estimated due to the lack of information and the uncertainties on the data. (**All these parameters are bounded between 0 and 1. DA INSERIRE IN RESULTS AND DISCUSSIONS (Risposta: sono bounded by construction)**)

The fitting has been performed to start the control optimization from a more solid and realistic base so that the data source could be more easily visualized and compared. **(una stima di alcuni parametri, secondo noi, avrebbe permesso una successiva ottimizzazione partendo da guess quanto più reali possibili e ottimizzando i parametri in direzioni accettabili e coerenti con l'andamento)**

2.2.1 Fitting strategy and objective function definition

We have decided to fit the parameters based on data given by italian "Protezione Civile"[6] on the Hospedalized non IC, Hospedalized IC, and Quarantined people because we are mostly interested to follow in as accurate as possible way the behaviour of those individuals that are hospitalized in Intensive Care and not due to our initial optimal control purpose.

To achieve this objective the fitting strategy was to reduce the error between the real behaviour and the estimated one by minimizing the difference between real Q, I_1, I_2 and our model. This objective can be translated in a mathematical way as a cost function of this type:

$$J(r,x) = \int_{t_i}^{t_f} (r(t) - x(t))^T M (r(t) - x(t))\, dt$$

$$\int_{t_i}^{t_f} \left((Q_r - Q_e)^T\right)^2 M_{11} (Q_r - Q_e)^2 + \left((I_{1_r} - I_{1_e})^T\right)^2 M_{22} (I_{1_r} - I_{1_e})^2 + \left((I_{2_r} - I_{2_e})^T\right)^2 M_{33} (I_{2_r} - I_{2_e})^2$$

Where the subscript r represents the reference data and e the estimated state variables. M is a matrix non-singular, symmetric, and semi definite positive that weights the different components of the cost function.

2.3 2.3 Optimal Control strategy

2.3.1 Motivations on the use of optimal control strategies

In the past few months Italy has been affected by the second wave of the Covid-19. During this period, a lot of infected people are carried to the hospital because of complications. This situation has caused on the whole Italian territory hospitals overcrowding and a collapse of the IC beds' hospital with very hard consequences in the number of deaths. Due to this the government has taken very heavy decisions at the expense of the economy but most of all the life of many people. The growth of infected in IC has led to the requirement of new IC units that it is translated in economic terms in an outlay by the government.

So, the purpose is to find an optimal control strategy through the optimal control theory and the use of different objective function to avoid as much as possible the overcrowding of the hospital minimising the number of infected people and simultaneously minimising also the economic costs due to the control applied on infected people and on susceptible population, in such a way that there are mild consequences on the daily life of the Italian people.

2.3.2 Optimal control strategies and objective function definitions

In this paper we have considered different strategies using different objective function in order to achieve our goal: minimise the number of infected hospitalized patient in IC and not in IC in order to avoid death and simultaneously minimise the control effort that the government has to face. Most precisely we have selected four different strategies to study:

1. Maximize susceptible class (S);
2. Minimize hospitalized patients in IC (I_2) and hospitalized with symptoms not in IC (I_1);
3. Maximize susceptible (S) and minimize hospitalized individuals in IC (I_2) and hospitalized with symptoms not in IC (I_1);
4. Maximize the number of vaccinated individuals (V);

These four strategies result in the following four cost functions:

1) $J_1(x_1,u) = \int_{t_i}^{t_f} L_1(x_1,u) = \int_{t_i}^{t_f} -\alpha_1 S + \frac{1}{2}u^T\beta u$ *(5a)*
2) $J_2(x_2u) = \int_{t_i}^{t_f} L_2(x_2,u) = \int_{t_i}^{t_f} \gamma_1 I_1 + \gamma_2 I_2 + \frac{1}{2}u^T\beta u$ *(5b)*
3) $J_3(x_3,u) = \int_{t_i}^{t_f} L_3(x_3,u) = \int_{t_i}^{t_f} -\alpha_2 S + \gamma_3 I_1 + \gamma_4 I_2 + \frac{1}{2}u^T\beta u$ *(5c)*
4) $J_4(x_4,u) = \int_{t_i}^{t_f} L_4(x_4,u) = \int_{t_i}^{t_f} \zeta V + \frac{1}{2}u^T\beta u$ *(5d)*

Where $\alpha_i, \beta, \gamma_j, \zeta > 0 i = 1,2; j = 1,2,3,4$ representing the weights in the cost index, $t_i \geq 0$ is the fixed initial time and $t_f \geq 0$ is the fixed final time of the control interval, $x_i \geq 0 i = 1,2,3,4$ the corresponding state variables considered for each cost function and $u = \{(u_p, u_1, u_2, u_{va})\}$. All control efforts *u(t)* are assumed to be bounded. The control effort set is possible to be defined as

$U = \{(u_p, u_1, u_2, u_{va}) : 0 \leq u_p \leq 1, 0 \leq u_1 \leq 1, 0 \leq u_2 \leq 1, 0 \leq u_{va} \leq 1, \}$ *(6)*

Based on the literature for the optimal control of epidemics, the cost of the controls is assumed to be nonlinear and quadratic. **[inserire riferimento ad uno degli articoli che sis ta seguendo].**

If $u_p(t) = u_1(t) = u_2(t) = u_{va}(t) = 1$, then 100% effort is applied in prevention, treatments for hospitalized non-IC patients, treatments for hospitalized IC patients and vaccines. Conversely, if $u_p(t) = u_1(t) = u_2(t) = u_{va}(t) = 0$, then no effort in prevention, treatments for hospitalized non-IC patients, treatments for hospitalized IC patients and vaccines is applied.

In the following subsection we will describe with the use of the optimal control theory the optimal control problem and its solutions.

2.3.3 Optimal control problem and solutions (Pontryagin)

The optimal control problem is stated below.

Problem: Given the model *(1)* with initial condition *(2),* determine the state x° and the controls u° satisfying the system *(1),* the conditions *(3)* and that minimize the considered cost index among the four different ones.

The aim is to determine the best strategy that minimizes the infected hospitalized non in IC and in IC and the control resources in the fixed control interval.

From the optimal control theory **[INSERIRE LIBRO DA CUI PRENDERE QUESTA INFO]**, the necessary conditions that an optimal solution must satisfy are obtained by applying the Pontryagin's Maximum Principle to the COVID-19 model of equation *(1)*. This principòe converts system *(1)* and the selected cost function in *(5)* into a proble of minimizing poinwise the Hamiltoninan, H, given as:

$H(x(t), U, \lambda_0, \lambda(t)) = \lambda_0 L_i(x(t), U) + \lambda^T(t) f(x(t), U)\, i = 1,2,3,4$ *(7)*

Where λ_0, λ are the Lagrange multipliers and $L_i(x(t), U)$ the Lagrange function depending on which cost function we are considering.

The general optimal solution is given by the following theorem.

Theorem: Let consider an admissible solution *(x*, U*)* satisfies the dynamic control systems *(1)*, the initial condition *(2)* and the constraint *(6)*. It is an optimal solution (global minimum) if there exist a λ_0 constant, functions $\lambda^T(t) \in \overline{C}^1[t_i, t_f]$ not simultaneous equal to zero such that:

$$\dot{\lambda}^\square = -\left.\frac{\partial H}{\partial x}\right|^T$$

$$H\left(x^\square(t), \omega, \lambda_0^\square, \lambda^\square(t)\right) \geq H\left(x^\square(t), U^\square(t), \lambda_0^\square, \lambda^\square(t)\right) \forall admissible\, control \omega \qquad (8)$$

$$H|^\square = 0$$

$$\lambda(t_f) = 0$$

(8) are necessary and sufficient condition for optimality of the solution *(x*, U*)*.

The notation $\overline{C}^1[t_i, t_f]$ denotes all the function piecewise continuously differentiable. Note that the singular case $\lambda_0 = 0$ is not possible; in fact, in this case, taking into account the last condition in *(8),* the existence and

uniqueness theorem for differential equations implies $\lambda_i = 0 i = 1, 2, \ldots, 8$ which is impossible because as stated by the theorem, the Lagrange multipliers cannot be simultaneously equal to zero.

Let particularize the necessary condition of optimality assuming $\lambda_0 = 1$ and consider the four different case:

Case 1 (first strategy). In the first strategy we recall we want to maximize susceptible. Using *(5a)*, the Hamiltonian becomes

$$H_1\left(x\left(t\right), U, \lambda_0, \lambda\left(t\right)\right) = \lambda_0\left[-\alpha_1 S + \tfrac{1}{2}u^T \beta u\right] + \lambda_1\left(t\right)\left[b - dS - \beta S I_a\left(1 - u_p\right) + \eta R - u_{va} S\right] \tag{9}$$

$$+\lambda_2\left(t\right)\left[-dE + \beta S I_a\left(1 - u_p\right) - kE\right]$$
$$+\lambda_3\left(t\right)\left[-dI + kE - \lambda\tau I_a - \gamma_1 I_a\right]$$
$$+\lambda_4\left(t\right)\left[-dQ + p\lambda\tau I_a - \gamma_2 Q - \sigma_1 Q\right]$$
$$+\lambda_5\left(t\right)\left[-dI_1 + \sigma_1 Q - \gamma_3 I_1 - \rho_1 u_1 I_1 - \sigma_2\left(1 - u_1\right) I_1 + \left(1 - p\right)\lambda\tau I_a\right]$$
$$+\lambda_6\left(t\right)\left[-dI_2 - mI_2 + \sigma_2\left(1 - u_1\right) I_1 - \rho_2 I_2 u_2\right]$$
$$+\lambda_7\left(t\right)\left[-dR - \eta R + \gamma_1 I_a + \gamma_2 Q + \gamma_3 I_1 + \rho_1 u_1 I_1 + \rho_2 u_2 I_2\right]$$
$$+\lambda_8\left(t\right)\left[-dV + u_{va} S\right]$$

Then there exist $\lambda \in R^8$ such that the first order necessary conditions for the existence of optimal control are given by the equations:

$$\frac{\partial \lambda_1}{\partial t} = \frac{-\partial H_1}{\partial S} = ? - \left(\alpha_1 + \lambda_8 u_{va} - \lambda_1\left(d_1 + u_{va} - I_a\beta\left(u_p - 1\right)\right) - I_a\beta\lambda_2\left(u_p - 1\right)\right)$$

$$\frac{\partial \lambda_2}{\partial t} = \frac{-\partial H_1}{\partial E} = k{*}\lambda_3 - \lambda_2{*}\left(d2 + k\right)$$

$$\frac{\partial \lambda_3}{\partial t} = \frac{-\partial H_1}{\partial I_a} = \gamma_1{*}\lambda_7 - \lambda_3{*}\left(d3 + \gamma_1 + \lambda{*}\tau\right) + \lambda{*}\lambda_4{*}p{*}\tau + S{*}\beta{*}\lambda_1{*}\left(u_p - 1\right) - S{*}\beta{*}\lambda_2{*}\left(u_p - 1\right) - \lambda{*}\lambda_5{*}tau{*}\left(p - 1\right)$$

$$\frac{\partial \lambda_4}{\partial t} = \frac{-\partial H_1}{\partial Q} = \gamma_2{*}\lambda_7 + \lambda_5{*}\sigma_1 - \lambda_4{*}\left(d4 + \gamma_2 + \sigma_1\right)$$

$$\frac{\partial \lambda_5}{\partial t} = \frac{-\partial H_1}{\partial I_1} = \lambda_7{*}\left(\gamma_3 + \rho_1{*}u_1\right) - \lambda_5{*}\left(d5 + \gamma_3 + \rho_1{*}u_1 - \sigma_2{*}\left(u_1 - 1\right)\right) - \lambda_6{*}\sigma_2{*}\left(u_1 - 1\right)$$

$$\frac{\partial \lambda_6}{\partial t} = \frac{-\partial H_1}{\partial I_2} = \lambda_7{*}\rho_2{*}u_2 - \lambda_6{*}\left(d6 + m + \rho_2{*}u_2\right)$$

$$\frac{\partial \lambda_7}{\partial t} = \frac{-\partial H_1}{\partial R} = \lambda_7{*}\rho_2{*}u_2 - \lambda_6{*}\left(d6 + m + \rho_2{*}u_2\right)$$

$$\frac{\partial \lambda_8}{\partial t} = \frac{-\partial H_1}{\partial V} = -d8{*}\lambda_8$$

Case 2 (second strategy). In the second strategy we recall we want to minimize hospitalized patients in IC and hospitalized with symptoms not in IC. Using *(5b)*, the Hamiltonian becomes

$$H_1\left(x\left(t\right), U, \lambda_0, \lambda\left(t\right)\right) = \lambda_0\left[\gamma_1 I_1 + \gamma_2 I_2 + \frac{1}{2}u^T \beta u\right] + \lambda_1\left(t\right)\left[b - dS - \beta S I_a\left(1 - u_p\right) + \eta R - u_{va} S\right]$$

$$+\lambda_2\left(t\right)\left[-dE + \beta S I_a\left(1 - u_p\right) - kE\right]$$
$$+\lambda_3\left(t\right)\left[-dI + kE - \lambda\tau I_a - \gamma_1 I_a\right]$$
$$+\lambda_4\left(t\right)\left[-dQ + p\lambda\tau I_a - \gamma_2 Q - \sigma_1 Q\right]$$
$$+\lambda_5\left(t\right)\left[-dI_1 + \sigma_1 Q - \gamma_3 I_1 - \rho_1 u_1 I_1 - \sigma_2\left(1 - u_1\right) I_1 + \left(1 - p\right)\lambda\tau I_a\right]$$
$$+\lambda_6\left(t\right)\left[-dI_2 - mI_2 + \sigma_2\left(1 - u_1\right) I_1 - \rho_2 I_2 u_2\right]$$
$$+\lambda_7\left(t\right)\left[-dR - \eta R + \gamma_1 I_a + \gamma_2 Q + \gamma_3 I_1 + \rho_1 u_1 I_1 + \rho_2 u_2 I_2\right]$$
$$+\lambda_8\left(t\right)\left[-dV + u_{va} S\right]$$

Performing computations as before:

$$\frac{\partial \lambda_1}{\partial t} = \frac{-\partial H_2}{\partial S} =?$$
$$\frac{\partial \lambda_2}{\partial t} = \frac{-\partial H_2}{\partial E} =?$$
$$\frac{\partial \lambda_3}{\partial t} = \frac{-\partial H_2}{\partial I_a} =?$$
$$\frac{\partial \lambda_4}{\partial t} = \frac{-\partial H_2}{\partial Q} =?$$
$$\frac{\partial \lambda_5}{\partial t} = \frac{-\partial H_2}{\partial I_1} =?$$
$$\frac{\partial \lambda_6}{\partial t} = \frac{-\partial H_2}{\partial I_2} =?$$
$$\frac{\partial \lambda_7}{\partial t} = \frac{-\partial H_2}{\partial R} =?$$
$$\frac{\partial \lambda_8}{\partial t} = \frac{-\partial H_2}{\partial V} =?$$

Case 3 (third strategy). In the third strategy we recall we want to maximize susceptible class and minimize hospitalized individuals in IC and hospitalized with symptoms not in IC. Using *(5c)*, the Hamiltonian becomes

$$H_1\left(x\left(t\right), U, \lambda_0, \lambda\left(t\right)\right) =?$$
$$\lambda_0\left[-\alpha_2 S + \gamma_3 I_1 + \gamma_4 I_2 + \frac{1}{2}u^T \beta u\right] + \lambda_1\left(t\right)\left[b - dS - \beta S I_a\left(1-u_p\right) + \eta R - u_{va} S\right]$$
$$+\lambda_2\left(t\right)\left[-dE + \beta S I_a\left(1-u_p\right) - kE\right]$$
$$+\lambda_3\left(t\right)\left[-dI + kE - \lambda\tau I_a - \gamma_1 I_a\right]$$
$$+\lambda_4\left(t\right)\left[-dQ + p\lambda\tau I_a - \gamma_2 Q - \sigma_1 Q\right]$$
$$+\lambda_5\left(t\right)\left[-dI_1 + \sigma_1 Q - \gamma_3 I_1 - \rho_1 u_1 I_1 - \sigma_2\left(1-u_1\right) I_1 + \left(1-p\right)\lambda\tau I_a\right]$$
$$+\lambda_6\left(t\right)\left[-dI_2 - mI_2 + \sigma_2\left(1-u_1\right) I_1 - \rho_2 I_2 u_2\right]$$
$$+\lambda_7\left(t\right)\left[-dR - \eta R + \gamma_1 I_a + \gamma_2 Q + \gamma_3 I_1 + \rho_1 u_1 I_1 + \rho_2 u_2 I_2\right]$$
$$+\lambda_8\left(t\right)\left[-dV + u_{va} S\right]$$

Computing the necessary condition of optimality:

$$\frac{\partial \lambda_1}{\partial t} = \frac{-\partial H_3}{\partial S} =?$$
$$\frac{\partial \lambda_2}{\partial t} = \frac{-\partial H_3}{\partial E} =?$$
$$\frac{\partial \lambda_3}{\partial t} = \frac{-\partial H_3}{\partial I_a} =?$$
$$\frac{\partial \lambda_4}{\partial t} = \frac{-\partial H_3}{\partial Q} =?$$
$$\frac{\partial \lambda_5}{\partial t} = \frac{-\partial H_3}{\partial I_1} =?$$
$$\frac{\partial \lambda_6}{\partial t} = \frac{-\partial H_3}{\partial I_2} =?$$
$$\frac{\partial \lambda_7}{\partial t} = \frac{-\partial H_3}{\partial R} =?$$
$$\frac{\partial \lambda_8}{\partial t} = \frac{-\partial H_3}{\partial V} =?$$

Case 4 (fourth strategy). In the fourth strategy we recall we want to maximize the number of vaccinated individuals. Using *(5d)*, the Hamiltonian becomes

$$H_1\left(x\left(t\right),U,\lambda_0,\lambda\left(t\right)\right)=\lambda_0\left[\zeta V+\frac{1}{2}u^T\beta u\right]+\lambda_1\left(t\right)\left[b-dS-\beta SI_a\left(1-u_p\right)+\eta R-u_{va}S\right]$$
$$+\lambda_2\left(t\right)\left[-dE+\beta SI_a\left(1-u_p\right)-kE\right]$$
$$+\lambda_3\left(t\right)\left[-dI+kE-\lambda\tau I_a-\gamma_1 I_a\right]$$
$$+\lambda_4\left(t\right)\left[-dQ+p\lambda\tau I_a-\gamma_2 Q-\sigma_1 Q\right]$$
$$+\lambda_5\left(t\right)\left[-dI_1+\sigma_1 Q-\gamma_3 I_1-\rho_1 u_1 I_1-\sigma_2\left(1-u_1\right)I_1+\left(1-p\right)\lambda\tau I_a\right]$$
$$+\lambda_6\left(t\right)\left[-dI_2-mI_2+\sigma_2\left(1-u_1\right)I_1-\rho_2 I_2 u_2\right]$$
$$+\lambda_7\left(t\right)\left[-dR-\eta R+\gamma_1 I_a+\gamma_2 Q+\gamma_3 I_1+\rho_1 u_1 I_1+\rho_2 u_2 I_2\right]$$
$$+\lambda_8\left(t\right)\left[-dV+u_{va}S\right]$$

The necessary condition of optimality is particularized for this last case in this following way:

$$\frac{\partial\lambda_1}{\partial t}=\frac{-\partial H_4}{\partial S}=?$$
$$\frac{\partial\lambda_2}{\partial t}=\frac{-\partial H_4}{\partial E}=?$$
$$\frac{\partial\lambda_3}{\partial t}=\frac{-\partial H_4}{\partial I_a}=?$$
$$\frac{\partial\lambda_4}{\partial t}=\frac{-\partial H_4}{\partial Q}=?$$
$$\frac{\partial\lambda_5}{\partial t}=\frac{-\partial H_4}{\partial I_1}=?$$
$$\frac{\partial\lambda_6}{\partial t}=\frac{-\partial H_4}{\partial I_2}=?$$
$$\frac{\partial\lambda_7}{\partial t}=\frac{-\partial H_4}{\partial R}=?$$
$$\frac{\partial\lambda_8}{\partial t}=\frac{-\partial H_4}{\partial V}=?$$

2.4 Optimal Control

Let us define initial conditions:

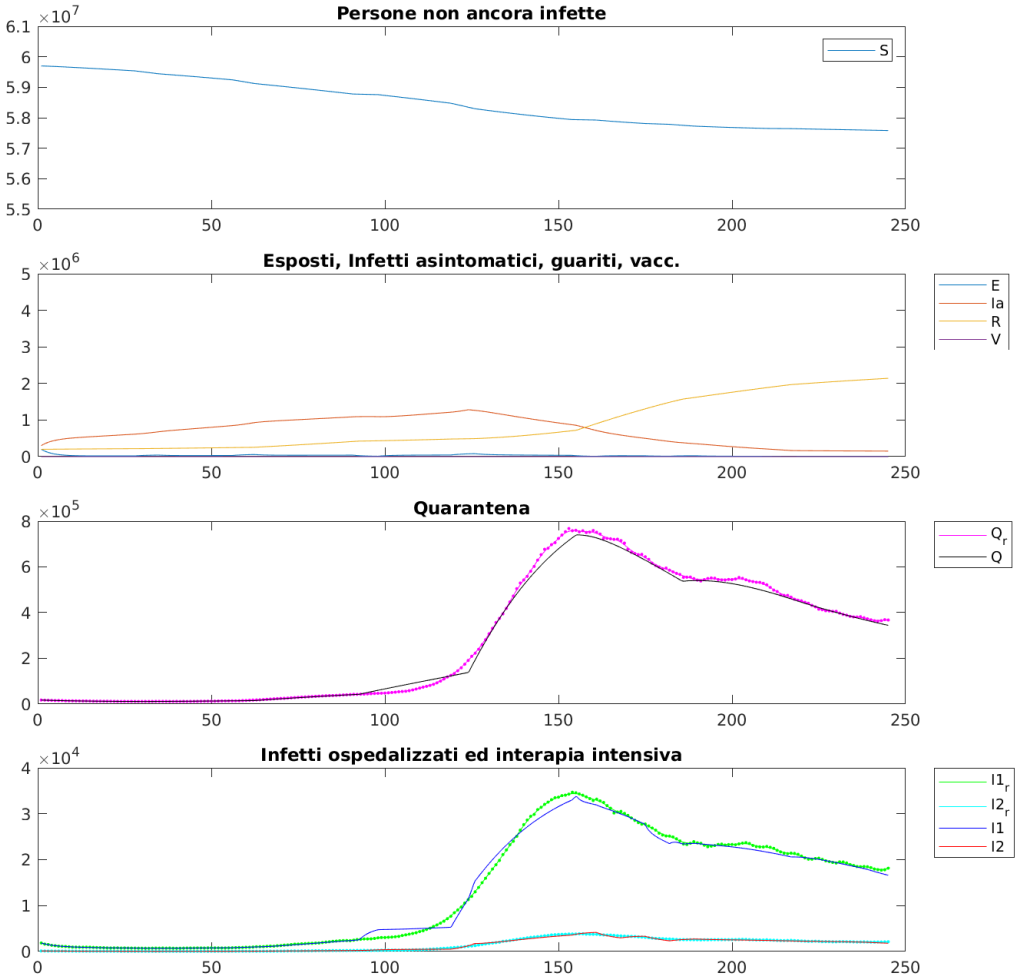
$$S\left(0\right)=59699728 E\left(0\right)=200000 I_a\left(0\right)=300000$$
$$Q\left(0\right)=17605 I_1\left(0\right)=1853 I_2\left(0\right)=115$$
$$R\left(0\right)=200000 V\left(0\right)=0$$

Q, I_1, I_2 data has been taken from measured data and the other initial conditions were estimated.

2.4.1 Existance of the solution

2.4.2 Optimal control strategy

We have defined 4 different control strategies


Persone non ancora infette
×10^7
6.1
6
5.9
5.8
5.7
5.6
5.5
0
50
100
150
200
250
S
Esposti, Infetti asintomatici, guariti, vacc.
×10^6
5
4
3
2
1
0
E
Ia
R
V
Quarantena
×10^5
8
6
4
2
0
Q_r
Q
Infetti ospedalizzati ed interapia intensiva
×10^4
4
3
2
1
0
I1_r
I2_r
I1
I2

3 3. Results

Necessario controllo ottimo per minimizzare il carico del controllo usato minimizzando allo stesso tempo il numero di persone infette. Infatti, un problema che tuttora è presente è la difficoltà di gestire i pazienti ospedalizzati (fare un controllo ottimo su infetti in terapia intensiva e non, quindi I1 e I2 e allo stesso tempo minimizzare il controllo sulle cure)

- Chiedere alla professoressa il significato dei pesi imposti sul controllo delle cure (teoricamente il peso aumenta se aumenta la conoscenza della malattia, ossia si sa come trattarla

4. Conclusions

4 Bibliografia

[6] https://github.com/pcm-dpc/COVID-19/blob/master/dati-andamento-nazionale/dpc-covid19-ita-andamento-nazionale.csv