Optimal intervention and vaccination strategies for the COVID-19 pandemic under limited immunity

Analysis of optimal government intervention and vaccination strategies

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Abstract

The COVID-19 pandemic had a tremendous socio-economic effect throughout the world. Governments around the world aimed to mitigate its rapid spread and limit the number of diseases by implementing intervention policies, such as social distancing, closing schools, encouraging working from home and imposing lock-downs. Such strict government measures, although limiting the disease spread, cause significant socio-economic costs. The development of vaccines during the pandemic offered an additional tool to mitigate its impact by offering immunity to the population. However, it was seen that the immunity for vaccinated and recovered population was temporal and had a declining effect with time.

Considering the above, this thesis aims to study the progression of the pandemic and propose suitable intervention and vaccination strategies. In addition, it aims to study the impact of the declining immunity in the population. In particular, we consider a compartment LI-SIDAREV model, with Susceptible (S), Infected Undetected (I), Infected Detected (D), Acutely symptomatic (A), Recovered (R), Extinct (E), and vaccinated (V) states. The LI-SIDAREV model is modified to enable the transition of the population from the vaccinated and recovered states towards the susceptible state, in order to model the declining effect of immunity.

An optimal control problem is formulated that aims to obtain the government intervention and vaccination strategies that optimize the trade-off between the socio-economic costs from imposing such policies and the number of deceases. The optimal strategies were obtained by applying Pontryagin's minimum principal in the considered problem.

A large number of case studies has been considered to investigate the effect of the costs associated with the deceased and acutely symptomatic population on the optimal government strategies. Moreover, the effect of the declining immunity for the vaccinated and the recovered population is studied over different time periods (one and three years respectively). Our results demonstrate that the effect of the declining immunity is significant in terms of the number of diseases and required intervention strategies. In addition, when a larger time duration was considered, the optimal intervention strategies demonstrated a fluctuating behaviour similar to what observed in practice. Furthermore, the increased time duration resulted in increased deceases and cost associated with intervention measures but a decreased optimal vaccination rate.

We envision that our results will find practical applications in designing effective and efficient intervention strategies and motivate further research on the topic.

Acknowledgement

The development of this research is taking place during COVID-19 pandemic, which is the reason this dissertation was written. This research describes the way in which optimal government intervention and vaccination strategies can be taken in the case of a disease outbreak.

This research project was carried out as part of my Master's Degree in Computer Engineering at the University of Cyprus. It extends the research of Andreas Kasis, Stelios Timotheou, Nima Monshizadeh and Marios Polycarpou, *"Optimal intervention strategies to mitigate the COVID-19 pandemic effects"*[1].

Regarding the end of my academic route and the completion of current thesis, I would like to thank the unwavering support of my supervisor Dr. Stelios Timotheou. His trust has been significantly important for me, since he gave me the opportunity to study the current project, which interests the whole world community and has been particularly appealing to me.

Moreover, I would like to thank Dr. Andreas Kasis for encouraging me and giving me the opportunity to work on such an important and interesting study. Without him and his valuable support, the completion of this dissertation would have been impossible. His help, knowledge and advices have been catalytic for the completion of this research.

Finally, I feel the need to express a special thanks to my family and friends. Their support and encouragement throughout my whole academic path were priceless and played a major role on my success and journey.

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Chapter 1

Introduction

1.1 Motivation

The COVID 19 pandemic is an ongoing global concern which Was first reported in Wuhan, China, at the beginning of December 2019 [2]. On March 11 2020, the World Health Organization (WHO) declared the state of the disease as a pandemic resulting from SARS-COV2 infection [3]. The outbreak of COVID 19 has resulted in multiple infections and deaths along with socio-economic devastating consequences. At the time of writing (27/05/2022), there have been more than 6 million deaths, and more than 500 million confirmed cases, worldwide[4]. To restrict the spread of such diseases, there are several mitigating measures that can be implemented. Indeed, governments across the world have implemented numerous non-pharmaceutical interventions such as lock-downs, self-isolation, banning of public events, and social distancing. While such interventions may limit the spread of a globally affecting disease, they lead to numerous significant economic effects.

To overcome the pandemic and its effects, vaccines were created by pharmaceutical companies. The first authorized vaccines were approved from authorization bodies in early December 2020. After the first vaccinations took place, the research community further examined the immunity period of the vaccines, which is an important parameter for the evolution of the pandemic.

Governments have implemented strategies in order to mitigate the effects of the pandemic and reduce the spread of the virus itself. The implementation of such strategies has been found to be costly and to have a negative impact on the economy. Therefore, it would be beneficial for governments and the wider economic environment to implement optimal control strategies in order to achieve the highest possible efficiency with the lowest associated cost.

1.2 Objectives

The problem identified and which needs to be addressed is the way of reducing the total cost resulting from the pandemic. The total cost consists of four (4) costs, as explained below. The first one is the socio-economic cost resulting from government measures, such as the financial cost created by the imposition of lock-downs since people are not able to go to work, stores are closing, and companies go bankrupt.

There is also a social cost since people cannot move around in public spaces and have limited options for entertainment and socialization. Another part of the total cost is the cost associated with the acutely symptomatic. This occurs due to the cost of hospitalisation and health care that these people need. Additionally, part of the total cost is the cost of vaccination which consists of the cost associated with the supply, preservation and storage of the vaccines, and the cost of vaccinating the population. Finally, part of the total cost is the cost associated with the extinct population, which includes the reduction of the government's tax income as the deceased population will not contribute the expected taxes.

For minimising the total cost, a trade-off between the aforementioned costs, socioeconomic cost, cost associated with the threatened and deceased population and vaccination cost, needs to be implemented. More specifically, Pontryagin's minimum principle is used, and the Hamiltonian function is derived. Multiple simulations have been generated, using combinations of the costs mentioned above, to examine the effect of each cost on the optimal control solution in order to minimize the total cost.

1.3 Contribution

The objective is to find the optimal strategy among the measures implemented by the government in combination with the vaccination strategy with the lowest possible total cost. This is why the Limited Immunity-SIDAREV model is implemented. This model considers the availability of vaccines as well as the fact that the immunity offered by the vaccine is limited. In addition, the immunity acquired from contracting a given disease is also temporary. Furthermore, the limited immunity offered by the vaccinations and the contraction of a decease is not a factor considered with the other models that were investigated. Additionally, using tools from optimal control theory, the government interventions and vaccination policy can be controlled. This is achieved by using two (2) control inputs, the strictness of the measures and the vaccination rate. By exporting the optimal control solution for both vaccination policies and restrictive measures, the objective of this research is achieved.

1.4 Research report outline

Chapter 2 includes the literature review on modelling, optimal control, and the parameters used for this research. After that, the methodology used in this research is presented in chapter 3. Afterwards, Chapter 4 describes an analysis of the model LI-SIDAREV. Subsequently, Chapter 5 includes the formulation of the optimal control problem. The experiments performed and their respective results are presented in Chapter 6. Chapter 7 provides the conclusions of the research and how it can be further expanded. Finally, Chapter 8 includes the MATLAB code.

Chapter 2

Literature review

In this chapter, a literature review of the mathematical modelling and optimal control is presented. Alongside, published studies are examined in order to export the parameters used while modelling a disease outbreak.

2.1 Modeling

Through mathematical models, researchers can study the dynamics of the transmission of infectious diseases. Understanding these dynamics can help develop effective strategies to control the spread of these infections. Mathematical models based on dynamic equations can be found effective for analyzing the dynamics of epidemics, however, they are less considered compared to standard statistical methods.

Various theories have been presented in order to predict the spread of the COVID-19 virus in the population. The spread of the disease and its various stages can be predicted by dividing the population into several sub-populations, so called compartments[5]. Some of the compartments of an infectious disease commonly used by other studies are 'susceptible', 'infected', and 'recovered'[6]. For instance, the former refers to an individual who is not immune to the disease but can still be infected with it. Infected describes the individuals that are infected with the decease and are able to transmit it to others. Recovered describes the individual who has become immune to the disease and cannot be re-contaminated. Existing models are further expanded by adding compartments such as Exposed' (E), 'Diagnosed' (D), 'Ailing' (A), 'Recognized' (R), 'Threatened' (T), 'Extinct' (E) and 'Vaccinated' (V)[7].

The models are based on flow patterns between different compartments and are used to represent the dynamics of an infectious disease. A set of differential equations known as the disease dynamics is used to determine the transfer rate between these compartments.

2.2 Optimal control theory

The concept of optimal control theory has been successfully used in developing effective strategies to control the spread of infectious diseases. It involves the consid-

eration of various factors, such as intervention strategies that affect the transmission of the disease. In the past, extensive research has been conducted on the various factors that affect the spread of the COVID-19 pandemic. One of the main findings of [1] was the development of an optimal control strategy that involves optimizing the trade-off between the number of deceased population and socio-economic costs. However Kasis et. al. has not captured Vaccinated compartment in his model since authorised vaccines were not available at the time.

Furthermore, Kasis et. al. used a control input u to minimize the infection rate β. The study reached to conclusions on what policies could be implemented to control the spread of the disease and the time that a certain policy needs to be implemented or ceased.

A later study [8] based on Kasis et. al. proposed three control inputs u_1, u_2, u_3 to reduce the infection rate β, testing rate ν, and vaccination rate ψ. The results of the study revealed that the strategies could help minimize the socioeconomic cost and the cost associated with the threatened and diseased population.

In addition, the results of the study [9] indicate that the use of preventive measures such as vaccinations and public health education could reduce the number of deaths caused by the COVID-19 pandemic.

2.3 Parameters

The various factors that affect the spread of the disease are also taken into account when developing effective control strategies. These include the healthcare capacity of the population, social distancing, lock-downs, and testing rates. For example, if

the hospital capacity is exceeded, an acutely sick individual will not have the chance to be hospitalised, resulting in death. This is deduced from the study of [10] who compared the fatality rate of two regions in Italy (Lombardy and Veneto). They concluded that the fatality rate in Lombardy would be about five-fold due to the presence of more than 80% healthcare capacity compared to up to 40% healthcare capacity in Veneto. Moreover, the low testing rate could also contribute to the spread of the disease since undetected infected asymptomatic individuals will still contribute to the spread of the pandemic. This could affect the overall decease rate of the pandemic [8]. Furthermore, the basic reproduction number is defined as the average number of secondary cases that one primary case will generate in a given population, where nobody is either immune or vaccinated. It depends on the probability of infecting a susceptible individual during one contact, the duration of the infectious period and the number of new susceptible individuals contacted per unit of time. The basic reproduction is assumed to be 3.27 [11] [12].

The duration of immunity for vaccinated and recovered individuals are factors affecting the pandemic. Various researches [13], [14] have shown that the effectiveness of the vaccines after a period of 20 weeks has dropped to 40% of its initial effects. In addition, the COVID-19 immunity period for the recovered population lasts for up to 13 months [15].

Chapter 3

Methodology

Description of the background of mathematical modelling, of the optimal control and epidemics is presented in this chapter.

3.1 Epidemiological models

Mathematical models are used for the simulation of a disease outbreak of an epidemic. By categorizing a population into smaller groups (compartments), the representation of several disease outbreak stages can be achieved. The most common compartments used to categorize the population are Susceptible, Exposed, Infected and Recovered. Susceptible (S) are the individuals that are vulnerable to the disease due to the absence of immunization, despite the fact that they are not currently infected. Exposed (E) are the individuals that are currently infected, although they are not yet able to transfer the disease to one another. The third compartment, Infected (I), as the name recalls, are the individuals who are currently infected and able to spread the disease. The last category mentioned above, Recovered (R), are the individuals who got infected and are now cured, developing immunization against the disease and therefore cannot infect or get infected by others. Rate of transmission between different compartments and the connection among them establishes the dynamics of the disease.

After the research conducted for the purpose of this project, it was identified that SIR model has been widely used as the base model for the development of more complex epidemiological models. The SIR stands for the three compartments Susceptible (S), Infected (I) and Recovered (R) described above. Figure 3.1 shows a schematic representation of the SIR. Progress of the pandemic can be analysed by the following disease dynamics representation:

$$\begin{aligned} \dot{s} &= -\beta i s, \\ \dot{i} &= \beta i s - \gamma i, \\ \dot{r} &= -\gamma i. \end{aligned} \tag{3.1a}$$

where $s(t), i(t)$, and $r(t)$ are the number of individuals in the compartments and $s(t) + i(t) + r(t) = N$, with the total population N constant.

Figure 3.1: Schematic representation of the SIR compartment model.

Figure 3.2 presents the behavior of the compartments of the model [16]. It can be observed that at time zero of the pandemic, the vast majority of the population are susceptible to the disease and only a small portion of the population are infectious. As time passes, more individuals are infected and can transmit the disease resulting in an increasing trend of the Recovered population and the sudden decrease of the Susceptible population. When the infected population reaches its maximum, the slopes of the other two compartments are also at maximum. After about 150 days the value of Infected individuals tents to zero. Despite the fact that a small fraction of susceptible population remains, a balance has been reached since there are only a few individuals who can transfer the disease to susceptible individuals, causing the disease to die out.

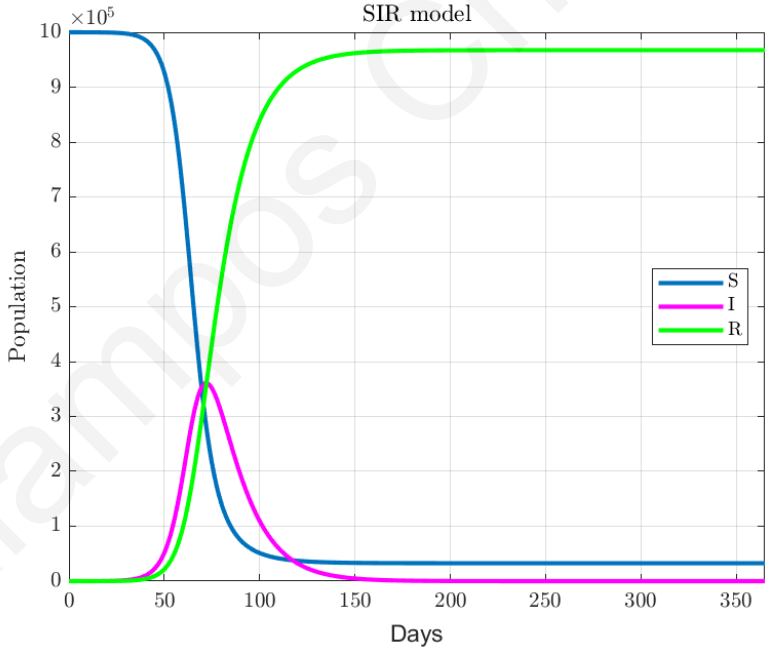


Figure 3.2: SIR model dynamics.

Adding one more compartment to the SIR model, Exposed (E), the SEIR model is created. The population now consists of the sub-population groups Susceptible (S), Exposed (E), Infected (I) and Recovered (R).A schematic representation of the SEIR is shown in the figure 3.3. The disease dynamics explaining the progress of the pandemic are:

$$\dot{s} = -\beta i s \tag{3.2a}$$

$$\dot{e} = \beta i s - \sigma e \tag{3.2b}$$

$$\dot{i} = \sigma e - \gamma i \tag{3.2c}$$

$$\dot{r} = \gamma i \tag{3.2d}$$

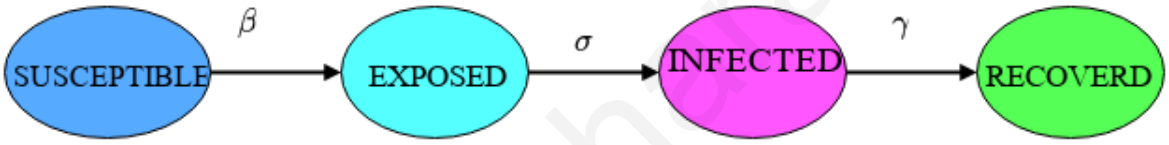


Figure 3.3: Schematic representation of the SEIR compartment model.

The behavior of the variables of SEIR model is shown in figure 3.4. Exposed (E) state follows similar pattern as the infected state and therefore similar results are extracted from the two models.

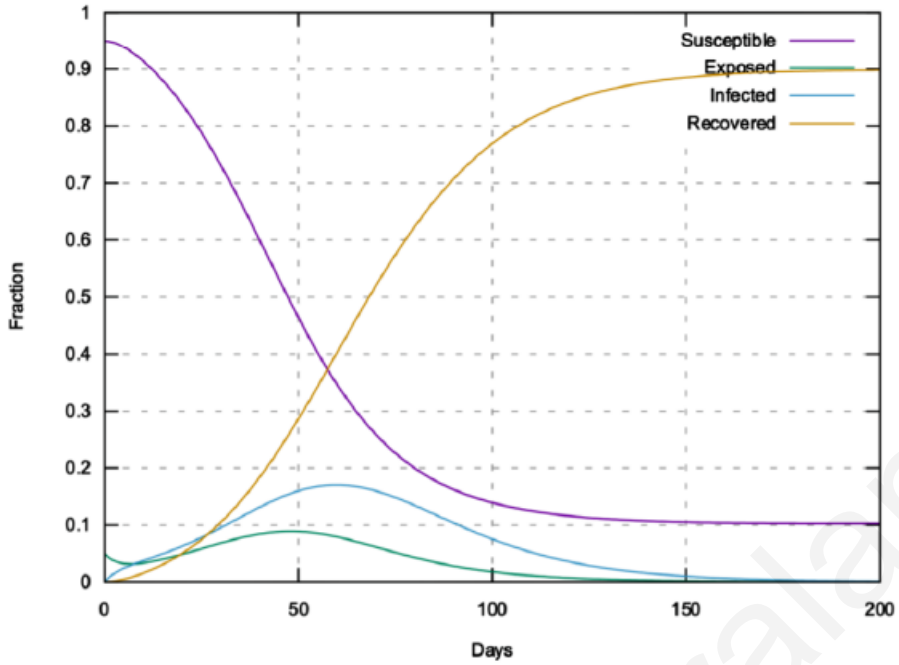


Figure 3.4: SEIR model dynamics.

The last compartment model that will be discussed is the SIDARE model. This consists of six categories which are: 'Susceptible' (S), 'Infected' (I), 'Detected' (D), 'Acutely Symptomatic' (A), 'Recovered' (R) and 'Extinct' (E). This model's dynamics, consists of seven differential equations, describing the evolution of the population in each stage over time. These are the following:

$$\dot{s} = -\beta si, \tag{3.3a}$$

$$\dot{i} = \beta si - \gamma_i i - \nu i - \xi_i i, \tag{3.3b}$$

$$\dot{d} = \nu i - \gamma_d d - \xi_d d, \tag{3.3c}$$

$$\dot{a} = \xi_i i + \xi_d d - \gamma_a a - \mu a, \tag{3.3d}$$

$$\dot{r} = \gamma_i i + \gamma_d d + \gamma_a a, \tag{3.3e}$$

$$\dot{e} = \mu a. \tag{3.3f}$$

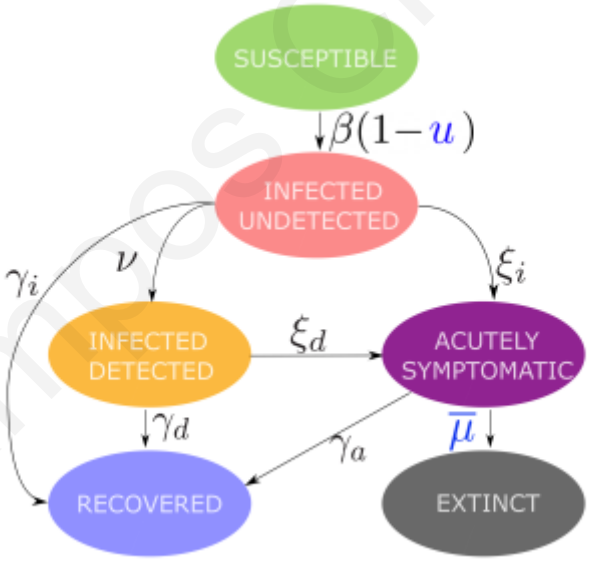


Figure 3.5: SIDARE model dynamics.

3.2 Optimal control in epidemiology

3.2.1 Formulating the optimal control problem

The formulation of an optimal control problem is vital for the creation of an optimal control strategy. For the creation of the optimal control problem, it is essential for

the objective function to be optimised. The objective function is to reduce the sum of the costs of the state variables $x(t)$ (e.g. deceased and infected population) and the costs resulting from the control variables $u(t)$ and therefore it needs to be minimum. It can be described as:

$$J(u) = \int_0^T x^T Q x \, dt + \int_0^T u^T R u \, dt + E(x(T)). \tag{3.4}$$

Moreover, the matrices Q is the cost associated with control inputs and R are the costs associated with the states. A term $E(x(T))$ must be added to the objective function, because the evaluation of the costs must consider the ending time of the pandemic. A common time interval $[0, T]$ is from the beginning of the pandemic until the vaccination deployment.This is due to the fact that it is believed that when vaccinations are available, the population builds immunity against the disease, and it is assumed that control strategies are no longer needed. Quadratic terms are often present in the objective function since usually the costs are non-linear or the differential equations obtained from this optimal control problem have a known solution.

$$J(\hat{u}) = min_{u \in U} J(u), \tag{3.5}$$

on the set $\mathcal{U} = u \in L^\infty(0, \infty) : 0 \leq u(\cdot) \leq u_{max}$, where $u_{max} \leq 1$ and L^∞ , is the vector space of essentially bounded measurable functions [17].The solution of equation (3.5) can be found by formulating the optimal control problem that consists of the objective function subject to the model dynamics and initial conditions.

3.2.2 Solving the optimal control problem

The optimal control $u(t)$ can be derived by using Pontryagin's maximum principle. Pontryagin's maximum principle is a tool that creates a system of ODE's in terms of state and adjoint variables (with initial and boundary conditions, respectively) which are satisfied at the optimum. The optimal control can be denoted as $u^*(t)$ and state and adjoint variables evaluated at the optimum can be denoted as $x^*(t)$ and $\lambda^*(t)$, respectively.

It should be mentioned that the names and symbols vary in the literature when describing Pontryagin's maximum principle. For instance, both $c(t)$ and $u(t)$ describe optimal control. Moreover, co-state variable is the same as the adjoint system. In addition, by multiplying the objective function by -1 the Pontryagin's maximum principle becomes Pontryagin's minimum principle.

Moreover, the Hamiltonian function should be exported. The Hamiltonian function connects the objective function to the state equations using Lagrange multipliers $\lambda(t)$. Hamiltonian function H, in the general form, is described as:

$$H(t, x, \lambda, u) = f(t, x, u) + \lambda g(t, x, u), \tag{3.6}$$

where the adjoint variable is expressed as λ, the optimal control as u and the state variable as x[18]. The term $f(t, x, u)$ represents the integrand of the objective function, and the term $\lambda g(t, x, u)$ represent the adjoint variable times the right-hand side of the differential equations of the state variable.

In order to solve the optimal control problem, the first-order optimality condition must be used. This can be derived by applying Pontryagin's maximum principle, which is as follows [8]:

Theorem 1. *For the optimality of control $u^*(t)$ and corresponding state trajectory $x^*(t)$ with $t \in [0, T]$, it is necessary that there exist a piecewise differentiable adjoint function $\lambda(t)$, such that*

$$\dot{x}(t) = \frac{\partial H}{\partial \lambda}(x(t), u(t), \lambda(t)), \tag{3.7}$$

$$\dot{\lambda} = \frac{\partial H}{\partial x}(x(t), u(t), \lambda(t)), \tag{3.8}$$

so that

$$H(x^*(t), u^*(t), \lambda^*(t)) \leq H(x^*(t), u^*(t), \lambda^*(t)), u \in U, \tag{3.9}$$

and the corresponding boundary conditions hold

$$x(0) = x_0, \tag{3.10}$$

$$\lambda(T) = E(x(T)). \tag{3.11}$$

Equation (3.8) is called the adjoint equation and equation (3.11) is called the transversallity condition. From equation (3.9) the optimality equation can be derived, i.e.

$$\frac{\partial H}{\partial u}(x(t), u(t), \lambda(t)) = 0, \tag{3.12}$$

$$\tag{3.13}$$

where $u_{min} \leq u(t) \leq u_{max}$. The proof can be found in the [19]. Furthermore, for the minimization of the control problem the following equation at u^* must hold:

$$\frac{\partial^2 H}{\partial u^2} \geq 0. \tag{3.14}$$

3.2.3 Forward-backward sweep method

The forward-backward sweep method is a procedure that explains how Pontryagin's principle is applied in order to solve an optimal control problem. Figure 3.6 reveals the steps involved in implementing this method.

In 2007, Workman and Lenhart [19]explained how the forward-backward sweep method can be used to solve a control problem. The first step involves entering the model parameters. After that, an initial guess is made based on the control input $u(u_{old})$. Usually, the initial guess of $u_{old} = 0$ is enough to solve the problem. The state equations must be solved forward in time and the adjoint equations $\dot{\lambda}$ must

be solved backward in time. After that, the optimally equation for the variables x and λ is calculated and gives a new optimal control u_{new}. The primary guess u_{old} and the computed u_{new} must be updated with an updated policy to obtain control input u_{update}. A frequently used policy is to determine the average value of the two $u's$. An additional update policy is to add a certain weight to one of the $u's$.

$$u_{new} * (1 - c^i) + u_{old} * c^i, \tag{3.15}$$

where $0 < c < 1$ and i is the present iteration. When the variables of the current iteration compared to the previous iteration are inside a fixed tolerance, the convergence must be achieved, i.e.

$$\frac{||u_{update} - u_{old}||}{||u_{update}||} \leq \delta, \tag{3.16}$$

$$\tag{3.17}$$

where δ is the accepted tolerance. In the case where the outcome is not within the accepted limit, the updated $u(u_{update})$ must replace the old $u(u_{old})$, and the forward-backward sweep method must be used again. In the case where the outcome is within the accepted limit, the method stops. These are the final values and the optimal control has been determined. Moreover, when variables x and λ converge, the method stops as well.

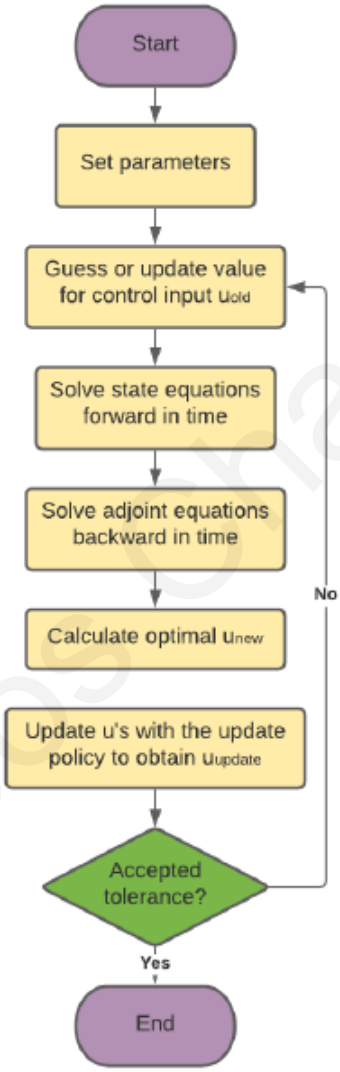


Figure 3.6: Block diagram Forward-Backward sweep method.

Chapter 4

The LI-SIDAREV Model

This chapter describes the epidemiological compartment model that is used for this research. The Limited Immunity SIDAREV model is a variation of SIDARE model used in the research of Kasis et al.[1]. In the proposed model an extra state for the vaccinated population, a feedback rate from recovered state to susceptible and vaccinated to susceptible are added. Therefore this model is called LI-SIDAREV.

4.1 Compartment model description

The LI-SIDAREV model consists of seven compartments to categorize the population: 'Susceptible' (S), 'Infected Undetected' (I), 'Infected Detected' (D), 'Acutely symptomatic' (A), 'Recovered' (R), 'Extinct' (E) and 'Vaccinated' (V). A schematic representation of the LI-SIDAREV model is shown.

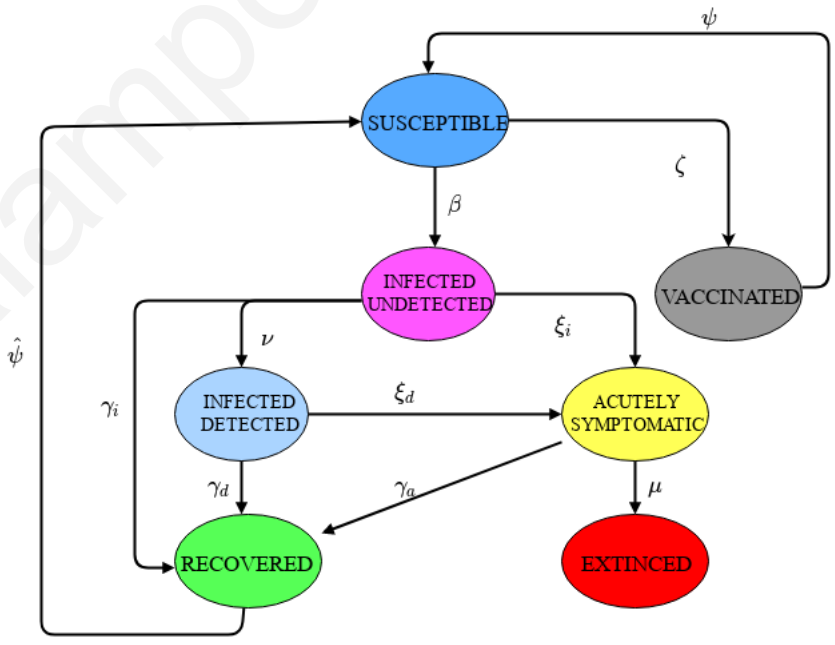


Figure 4.1: Schematic representation of the LI-SIDAREV compartment model

As shown in the schematic, there are parameters between different states. A certain value can be given to the parameters that indicate the transfer rate between the states. Setting values for certain parameters to zero, we exclude states. For example, by setting $\zeta = 0$ no transfer will occur to the Vaccinated state. Furthermore, by setting the parameter $\psi = 0$ and $\hat{\psi} = 0$ the vaccinated and recovered population will never be susceptible again and remained vaccinated and recovered. Implementing the above modification will result to the SIDARE model.

4.2 System dynamics

The dynamical behavior of a disease outbreak can be mathematically described with a set of differential equations which can be described as follows:

$$\dot{s} = -\beta si + \psi v + \hat{\psi} r - \zeta s, \tag{4.1a}$$

$$\dot{i} = \beta si - \gamma_i i - \nu i - \xi_i i, \tag{4.1b}$$

$$\dot{d} = \nu i - \gamma_d d - \xi_d d, \tag{4.1c}$$

$$\dot{a} = \xi_i i + \xi_d d - \gamma_a a - \bar{\mu} a, \tag{4.1d}$$

$$\dot{r} = \gamma_i i + \gamma_d d + \gamma_a a - \hat{\psi} r, \tag{4.1e}$$

$$\dot{e} = \bar{\mu} a, \tag{4.1f}$$

$$\dot{v} = \zeta s - \psi v, \tag{4.1g}$$

$$s(0) = s_0, i(0) = i_0, d(0) = d_0, a(0) = a_0, r(0) = r_0, e(0) = e_0, v(0) = v_0. \tag{4.1h}$$

where $s, i, d, a, r, e, v \in [0, 1]$ are the states of the system describing the portions of susceptible, infected - undetected, infected - detected, threatened, recovered and deceased population respectively. Moreover, $s_0, i_0, d_0, a_0, r_0, e_0, v_0 \in [0, 1]$ denote the initial values for s, i, d, a, r, e respectively. The model parameters are briefly summarized below:

- β : infection rate for susceptible individuals.
- $\gamma_i, \gamma_d, \gamma_a$: recovery rates for infected undetected, infected detected and threatened individuals.
- ν : rate of detection of infected individuals, associated with the adopted level of testing.
- ξ_i, ξ_d : rates at which infected undetected and infected detected individuals become acutely symptomatic.

- μ : rate at which acutely symptomatic individuals decease.
- ζ : rate of vaccination of susceptible individuals.
- ψ : rate at which vaccinated individuals become susceptible.
- $\hat{\psi}$: rate at which recovered individuals become susceptible.

Note that all model parameters are assumed non-negative and constant.The LI-SIDAREV uses the same assumptions as the SIDARE model as described in the research of Kasis et al. [1]. Also, there is an additional assumption regarding the vaccinated individuals. For clarity, the assumptions are listed below.

- Actively recovered individuals are immune to the disease for limited period.
- Actively vaccinated individuals are immune to the disease for limited period.
- The considered population is constant. Meaning that births and deaths not attributed to the particular disease outbreak are not considered.
- The concerned population (or area) is isolated, and imported cases are not included.
- Infected individuals that are detected are assumed to be quarantined, i.e. they do not contribute to new infections.
- Infected individuals become acutely symptomatic before they decease.
- Acutely symptomatic individuals require hospitalization since they are considered threatened for decease.
- Only susceptible individuals are vaccinated.
- The population is willing to vaccinate.

Chapter 5

Optimal control design for LI-SIDAREV model

This chapter describes the optimal control design for the LI-SIDAREV model. First, it is explained which control actions are applied to the current model and how the dynamic system should be adapted. Then the optimal control problem for the model is explained, after which, Pontryagin's maximum principle is applied.

5.1 Control design

The control inputs u and ζ have been added to the LI-SIDAREV model, and their functions are explained in the following sections. A schematic representation of LI-SIDAREV is shown in figure 5.1 with the controllers incorporated.

5.1.1 Intensity of measures for controlling the rate of infection

The first controller applied to the model is control input u. Control input u indicates the strength of government interventions. Since the government applied measures to contain the spread of the disease, the term (1-u) will become smaller than 1, affecting the infection rate β to be reduced. If control input u = 0 (no government intervention) the infection rate β will not be affected.

$u \in U = [0, \bar{u}]$ and $\bar{u} \leq 1$ is a positive constant that denotes the maximum value that the intervention policy u can take. The purpose of government interventions is to decrease the spread rate of the disease so the control input u can only take positive values. Higher values of u indicate stricter intervention policies.

5.1.2 Vaccination strategy for controlling the vaccination rate

The second controller applied to the model is control input ζ. Control input ζ indicates the strength of vaccination policy. $\zeta \in Z = [0, \bar{\zeta}]$ and $\bar{\zeta} \leq 1$ is also a positive constant that denotes the maximum number of vaccinations that a government can afford per day. Control input ζ shows us the vaccination rate. Higher values of ζ

means that more individuals are getting vaccinated per day, and lower values of ζ means less individuals are getting vaccinated per day.

The dynamics of the LI-SIDAREV model, including the controllers, can be described as follows:

$$\dot{s} = -\beta s(1-u)i + \psi v + \hat{\psi} r - \zeta s, \tag{5.1.a}$$

$$\dot{i} = \beta s(1-u)i - \gamma_i i - \nu i - \xi_i i, \tag{5.1.b}$$

$$\dot{d} = \nu i - \gamma_d d - \xi_d d, \tag{5.1.c}$$

$$\dot{a} = \xi_i i + \xi_d d - \gamma_a a - \bar{\mu} a, \tag{5.1.d}$$

$$\dot{r} = \gamma_i i + \gamma_d d + \gamma_a a - \hat{\psi} r, \tag{5.1.e}$$

$$\dot{e} = \mu a, \tag{5.1.f}$$

$$\dot{v} = \zeta s - \psi v, \tag{5.1.g}$$

$$s(0) = s_0, i(0) = i_0, d(0) = d_0, a(0) = a_0, r(0) = r_0, e(0) = e_0, v(0) = v_0, \tag{5.1.h}$$

$$s + i + d + a + r + e + v = 1. \tag{5.1.i}$$

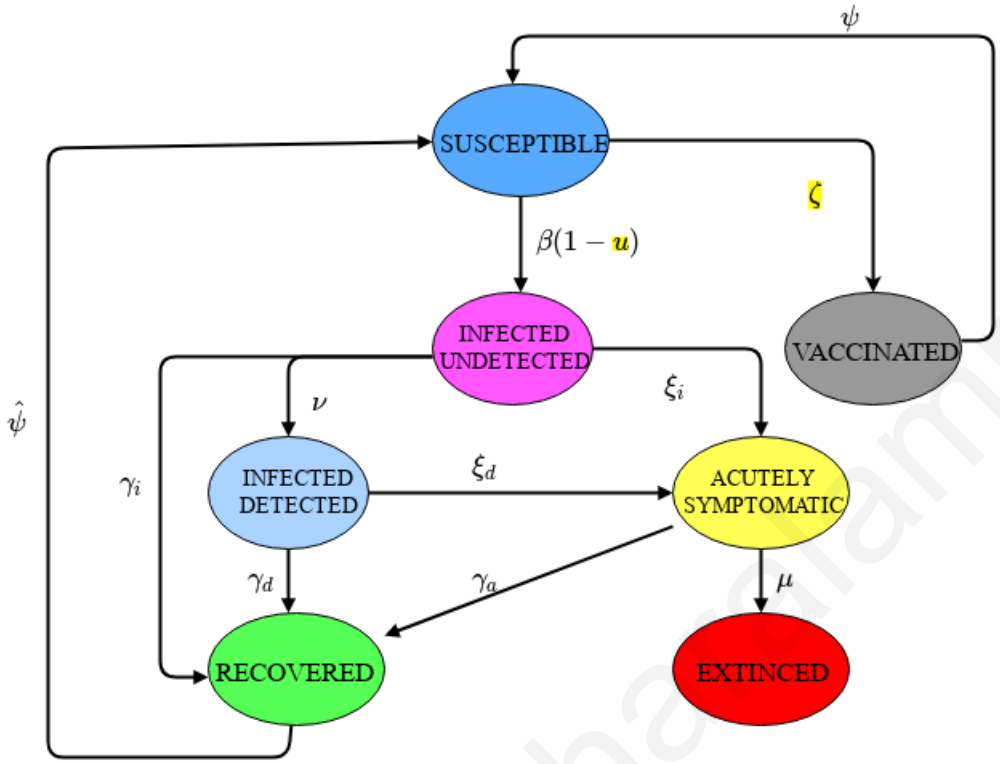


Figure 5.1: Schematic representation of the SIDAREV model with controllers

5.1.3 Dynamics of controlled LI-SIDAREV model

5.2 Optimal control problem

A well-designed government strategy should minimize the number of fatalities while at the same time, ensuring that the costs associated with implementing the intervention and vaccination policies are minimized. The optimal control problem is a function that aims to minimize the cost associated with extinct population, cost of acutely symptomatic individuals, cost of vaccinations and the socio-economic cost resulting from intervention strategies. The function is defined over a time period of [0, T] and is the summation of four terms:

$$C = \int_0^T \frac{1}{2}u(t)^2\,dt + \Theta_a \int_0^T \frac{1}{2}a(t)^2\,dt + \Theta_e e(T) + \Theta_\zeta \int \frac{1}{2}\zeta(t)^2\,dt. \tag{5.2}$$

Control input u, which states the strictness of the government policy that will be applied, is the first term of the function above and is associated with the cost of the side effects on the economy and the society in general.

When an individual needs to be hospitalised there is a socio-economic cost to the government. This cost is described by the second term of the optimization function which refers to acutely symptomatic individuals. Furthermore the positive weight factor Θ_a indicates the weight that is given on the cost associated with the

threatened population. Higher values of the parameter Θ_a means that people who are acutely symptomatic are important to be saved.

Fatalities are shown in the optimization function through the third term. This term is ensuring that the deceased individuals can be reduced to a minimum at time T. Weight factor Θ_e in the term describes the importance of the cost of total fatalities. Θ_e acts like Θ_a above. By increasing Θ_e the government policy aims to minimize the number of fatalities and acutely symptomatic individuals, which means that the value of u will approach $\hat{u}$ at all times. On the other hand, by decreasing the value of Θ_e close to zero, the economic and social cost of the intervention strategy will be minimized which subsequently results to u approaching 0 for all values of T.

Control input ζ, which indicates the amount of vaccinations that will be performed, is the last term of the cost function and is associated with the cost of vaccinations Θ_ζ. Θ_ζ parameter varies the importance of vaccination cost as Θ_a, Θ_e.

The three cost-weight factors Θ_a, Θ_e, Θ_ζ are unknown. The aim of this project is to identify the effect that those parameters will have on the optimal solution of the problem. Further explanation and values for these factors are provided in Chapter 6. A quadratic cost is considered, therefore, the Optimal Control Problem is the minimization of the cost function explained as:

$$\min_{(u\in U,\zeta\in Z)} J(a,e,u,\zeta) = \int_0^T \frac{1}{2}u^2(t)\,dt + \Theta_a \int_0^T \frac{1}{2}a^2(t)\,dt + \Theta_e(T) + \Theta_\zeta \int \frac{1}{2}\zeta^2(t)\,dt \tag{5.3}$$

subject to (5.1).

5.3 Applying Pontryagin's minimum principle

Pontryagin's maximum principle is presented in this section. Initially, the Hamiltonian function is derived. After that, the adjoint system is created. At last, the solution to the optimal control problem is provided.

The Hamiltonian function can be described as follows:

$$H(x,u,\zeta,\lambda) = \frac{1}{2}u^2 + \frac{1}{2}\Theta_\alpha a^2 + \frac{1}{2}\Theta_\zeta \zeta^2 + \lambda^T(f_0(x) + f_1(x)u + f_2(x)\zeta) \tag{5.4}$$

where $\lambda \in R^7$ is called the co-state of the system and $f_0(x)$, $f_1(x)$, $f_2(x)$ follow from equation 5.1, are given by:

$$f_0(x) = \begin{bmatrix} -\beta si + \psi v + \hat{\psi} r \\ +\beta si - \gamma_i i - \nu i - \xi_i i \\ \nu i - \gamma_d d - \xi_d d \\ \xi_i i + \xi_d d - \gamma_a a - \bar{\mu} a \\ \gamma_i i + \gamma_d d + \gamma_a a - \hat{\psi} r \\ \bar{\mu} a \\ -\psi v \end{bmatrix}, f_1(x) = \begin{bmatrix} \beta si \\ -\beta si \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, f_2(x) = \begin{bmatrix} -s \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ s \end{bmatrix}, \tag{5.5}$$

To create the adjoint system,

$$\dot{\lambda}^T = -\frac{\partial H}{\partial x}(x(t), u(t), \zeta(t), \lambda(t)) \tag{5.6}$$

the Hamiltonian function must be differentiated with respect to the adjoint variables λ_j , $j \in 1, 2, ..., 7$.

$$\dot{\lambda}^T = -[\Theta_a a + \lambda^T[\nabla f_0(x) + u\nabla f_1(x) + \zeta\nabla f_2(x)]]. \tag{5.7}$$

This results in:

$$\dot{\lambda}_1 = \lambda_1(\zeta + \beta i - \beta i u) - \lambda_2(\beta i - \beta i u) - \lambda_7\zeta, \tag{5.8a}$$

$$\dot{\lambda}_2 = \lambda_1(\beta s - \beta s u) + \lambda_2(\gamma_i + \xi_i + \nu - \beta s + \beta s u) - \lambda_3\nu - \lambda_4\xi_i - \lambda_5\gamma_i, \tag{5.8b}$$

$$\dot{\lambda}_3 = \lambda_3(\gamma_d + \xi_d) - \lambda_4\xi_d - \lambda_5\gamma_d, \tag{5.8c}$$

$$\dot{\lambda}_4 = \lambda_4(\gamma_a + \bar{\mu}) - \lambda_5\gamma_a - \lambda_6\bar{\mu} - \alpha\Theta_a, \tag{5.8d}$$

$$\dot{\lambda}_5 = -\lambda_1\hat{\psi} + \lambda_5\hat{\psi}, \tag{5.8e}$$

$$\dot{\lambda}_6 = 0, \tag{5.8f}$$

$$\dot{\lambda}_7 = -\lambda_1\psi + \lambda_7\psi. \tag{5.8g}$$

By taking the multiplication of adjoint variables λ_j , $j \in 1, 2, ..., 7$. with the relative co-state of the system, $f_1(x)$ or $f_2(x)$ optimal controls can be determined:

$$\hat{u} = [-\lambda^T f_1(x)]_U = min[max(\beta i s(\lambda_2 - \lambda_1), 0), \bar{u}], \tag{5.9}$$

$$\hat{\zeta} = [-\lambda^T f_1(x)]_\zeta = min[max(s(\lambda_1 - \lambda_7)/\Theta_\zeta, 0), \bar{\zeta}]. \tag{5.10}$$

Chapter 6

Results and discussion

6.1 Parametrization of the model

The various models that have been used to study the evolution of COVID-19 include the LI-SIDAREV model. This section discusses the various assumptions that have been made regarding the model's parameters.

The initial conditions of the model are presented in Table 6.1. The LI-SIDAREV model indicates that during the early stages of the pandemic, a small number of people are infected and to be more specific 0.001% of the population. Thus the susceptible population is 1 - 0.00001. It also assumes that there are no cases of people who have been infected but have recovered, and no vaccinated people. Moreover, it is assumed that there are no cases of acutely symptomatic, infected-detected and dead.

The basic reproduction number is an important factor that is used in studies on the progression of the pandemic. It is calculated by taking into account the number of people who were infected by the average person when the following conditions are applied. There is no immunization from either vaccination or recovered individuals and also there are no intervention policies against the spread of the disease. Infection rate can be calculated by using the formula $\bar{R}_0 = \beta s_0/(\gamma_i + \xi_i + \nu)$. The basic reproduction value is assumed to be 3.27. Assuming that at the beginning of the pandemic $t = 0$, the detection rate is zero, the rate of infection is 0.251.

The recovery rate for mild cases is typically two weeks. Based on the WHO's

State variable	Symbol	Initial value
s_0	$\bar{s}$	1-0.00001
i_0	$\bar{i}$	0.00001
d_0	$\bar{d}$	0
a_0	$\bar{a}$	0
r_0	$\bar{r}$	0
e_0	$\bar{e}$	0
v_0	$\bar{v}$	0

Table 6.1: Initial conditions LI-SIDAREV model

Symbol	Value	Justification
β	2/3	[11]
γ_i, γ_d	1/14	[4]
γ_a	1/12.4	[21]
ξ_d, ξ_i	0.0053	[12]
μ	0.0085	[12]
ψ_r	1/140	[14], [13]
$\hat{\psi}_r$	1/395	[15]

Table 6.2: Overview parameters for LI-SIDAREV model

2020 guidance, it is assumed that the recovery rate for mild COVID-19-detected individuals is typically two weeks. Therefore, infected-detected (γ_d) and infected-undetected(γ_i) value are 1/14, which means that an individual needs 14 days to recover from the infection [20]. The recovery rate for individuals infected with acutely symptoms from COVID-19 is calculated by taking into account the length of time they spent in the hospital. According to Wang et al., an average hospitalization usually takes around 12.4 days. Thus the recovery rate for acutely symptomatic (γ_a) is assumed to be 1/12.4[21].

Studies [12] have shown that the rates at which COVID-19-detected individuals and those who were not vaccinated develop symptoms that require hospitalization are similar. These studies were performed on the severity of the disease and on the hospitalization rates in different age groups. Hence, the value of infected undetected (ξ_i) and infected detected (ξ_d) requires hospitalization is 0.0053.

The mortality rate of COVID-19 has been estimated to be around 1% [22]. In a study conducted in 2022 [1], researchers used mortality rate of 0.0085 and for convenience this study has chosen the same mortality rate (μ).

Various studies show that the vaccine effectiveness against COVID - 19 is waning after 20 weeks and the protection after recovery lasts up to 13 months. Therefore, the value of a vaccinated individual becoming susceptible (ψ) is selected to be 1/140 (after 140 days of the vaccination) and for a recovered individual becoming susceptible ($\hat{\psi}$) is chosen to be 1/395 (after 13 months of recovered).

The value of $\bar{u}$ is used to determine the maximum allowed value for the input u and was selected to be 0.8. While the value $\bar{\zeta}$ is used to determine the maximum allowed value for the input u and was selected to be 0.005. The testing rate, on the other hand, is used to be 0.05 which reflects the slow testing rate. This was found by taking the average used for fast and no testing. The simulation of the COVID-19 pandemic is carried out using the following parameters and with time frame $[0, T]$. The value of T is chosen to be 365 and 1095 that indicates 1 and 3 years respectively. The parameters are summarized in Table 6.3.

6.2 Experiments design

The goal of this thesis is to analyze the effects of the immunity period on the optimal control solution. In order to reach a solution that is both feasible and cost-effective, various scenarios have been created.

The cost-coefficient parameters are Θ_a, Θ_ζ and Θ_e. The values used in this function are selected to investigate the various cases related to each of the parameters.

Cost of death (Θ_e):
The cost coefficients of the deceased population have been considered in order to arrive at a range of values that are appropriate for each case.
$\Theta_e \in [0, 3000, 6000, 9000, 12 \times 10^3, 15 \times 10^3, 20 \times 10^3]$

Costs for acutely symptomatic (Θ_a):
For Θ_a parameter, 2 values were selected which are associated with no and medium emphasis on acutely symptomatic individuals and are 0 and 50×10^3 respectively.

Costs for vaccinations (Θ_ζ):
As with cost of vaccinations, a medium cost emphasis is selected which is $\Theta_\zeta = 5 \times 10^3]$.

Experiment	Immunity period	Considered period	Cost of acutely symptomatic
1.1	Infinite	1 year	50×10^3
1.2	Regular	1 year	50×10^3
1.3	Low	1 year	50×10^3
2.1	Regular	3 years	50×10^3
2.2	Regular	3 years	0

Table 6.3: Experiments and the associate variables

6.3 Results from experiments

This section shows the results from the experiments that implemented. Each one of the four subsections that are following is for different values of ψ and $\hat{\psi}$ and 2 different values of T. The aforesaid values are for endless immune period ($\psi = 0$ and $\hat{\psi} = 0$) with $T = 365$, medium immune period ($\psi = 1/140$ and $\hat{\psi} = 1/395$) with $T = 365$, low immune period ($\psi = 1/140$ and $\hat{\psi} = 1/395$) with $T = 365$ and medium immune period ($\psi = 1/140$ and $\hat{\psi} = 1/395$) with $T = 1095$.

6.3.1 Experiment 1 - Impact of immunity period

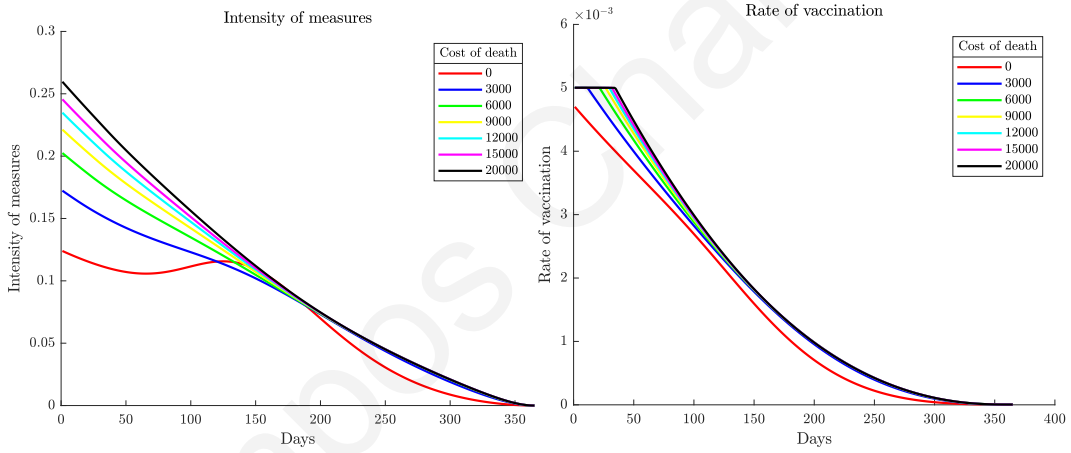
In this section the impact of immunity period will be observed. Different values of immunity period such as infinite period, regular period and low period.

Experiment 1.1 - Infinite immunity period

For this experiment the cost-coefficient values are: $\Theta_a = 5000$ and $Theta_\zeta = 5000$. The immune period of vaccinations and recovered equals to zero.

The figures below shown the following. The least strict measures are observed when $\Theta_e = 0$. The initial density of measures value is between 0.1-0.15 and is following a decreasing trend during the first 70 days. It then starts increasing up until day 150 reaching a maximum to a value close to the initial. Then the intensity of measures start to fall again up until they reach 0 at the end of an annual period. For any other values of Θ_e the trend is always decreasing reaching zero at the end of the 365 days period.

For all the possible values of Θ_e, except zero, it is observed that the maximum rate of vaccination is followed during the first days of the pandemic following a decreasing trend, reaching zero rate of vaccination at the final stage. in case of Θ_e=0 the initial rate of vaccination is lower than the maximum although it follows the same pattern as in the case of the others.



(a) Intensity of measures (b) Rate of vaccination

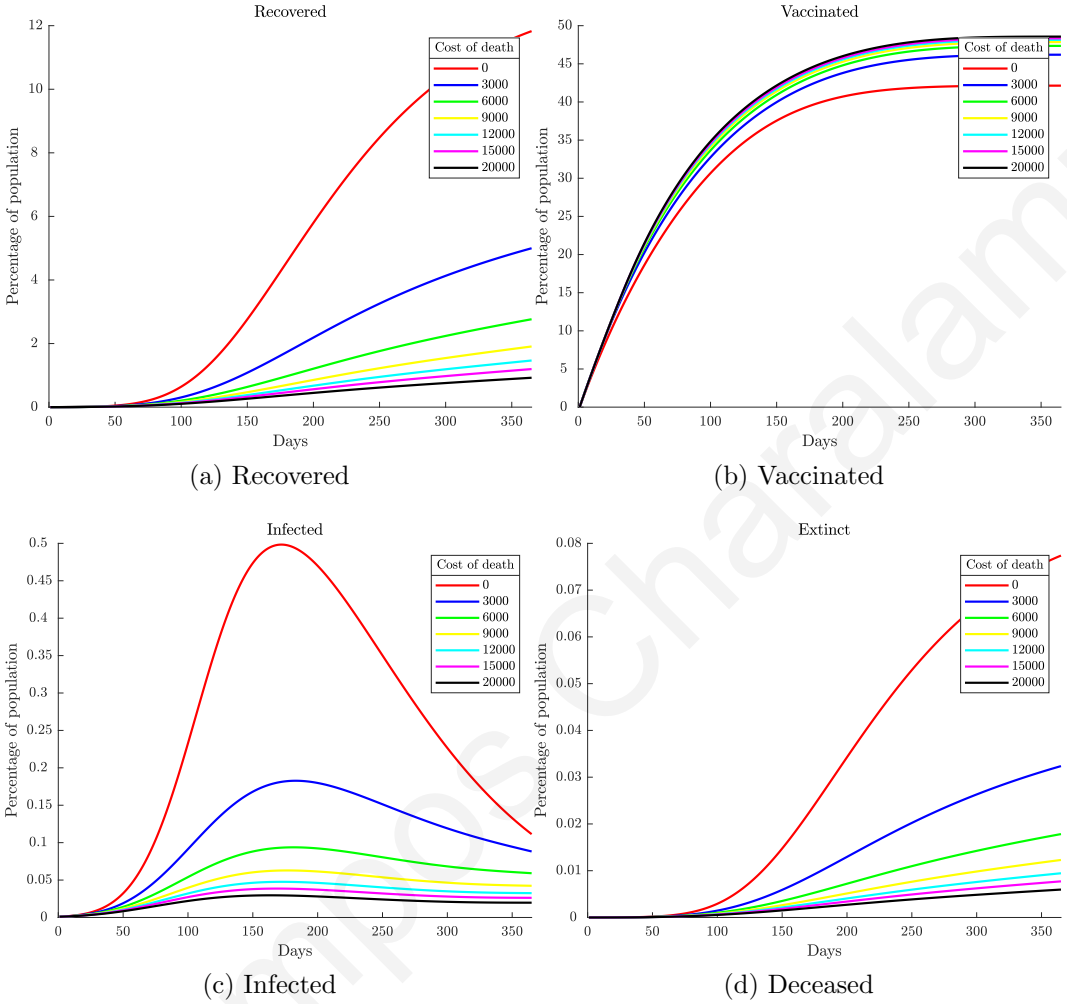
Figure 6.1: Experiment 1.1 - Intervention and vaccination strategies for infinite immunity period, 1 year considered period, medium vaccination and acutely symptomatic cost

When Θ_e= 0 the percentage of population infected reaches maximum at around day 150, which is also the maximum value of infected people shown in the graph. After that it starts decreasing although it is not reaching zero. The same trend is followed by the other values of Θ_e, although as Θ_e is increasing, the maximum value reached and the final value of infected people is decreasing.

An increasing trend is observed regarding the fatalities and recovered individuals having 0 figures for the first 50 days. As Θ_e is increasing, the maximum Percentage of extinct and recovered population is decreasing.

Similar trend is observed regarding vaccinated population when different Θ_e are

applied. The maximum percentage of vaccinated individuals increases with Θ_e. What is shown in the first experiment is that a high number of vaccinations is implemented with vaccinated population percentage peak at 50%. That resulting to low number of infected population and intensity of measures. In addition the fatalities and recovered is also low.



(a) Recovered (b) Vaccinated

(c) Infected (d) Deceased

Figure 6.2: Experiment 1.1 - States for infinite immunity period, 1 year considered period, medium vaccination and acutely symptomatic cost

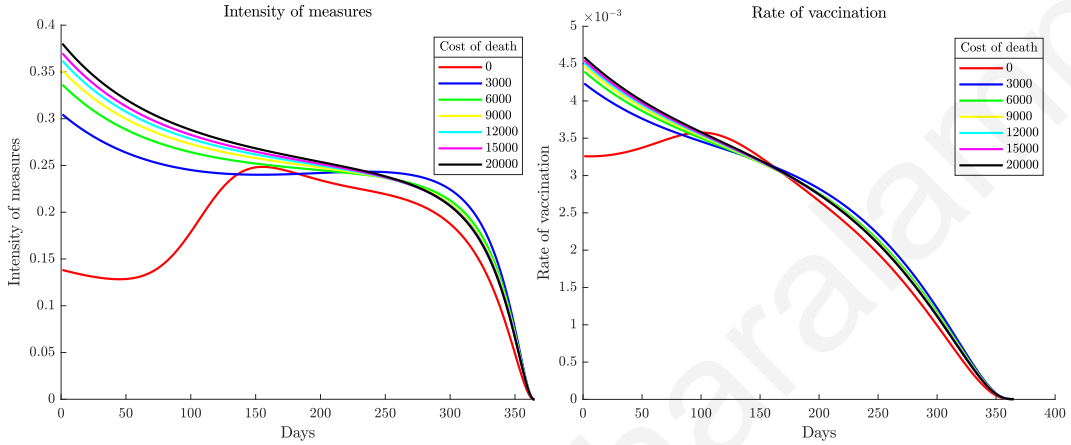
Experiment 1.2 - Regular immunity period

For this experiment the cost-coefficient values are: $\Theta_a = 5000$ and $\Theta_\zeta = 5000$. The immune period of vaccinations and recovered are $\psi = 1/140$ and $\hat{\psi} = 1/395$.

From the following figure is observed that with $\psi = 1/140$ the values of intensity of measures are increasing as well. When Θ_e =0 the initial value of intensity of measures is closer to 1.5. The value is decreasing for the first 70 days and then start increasing to 0.25 as maximum until around day 150. For the next 150 days it follows a falling trend although a rapid fall is observed after day 300 reaching 0 at the end of the annual period. For Θ_e= 3000 the curve has a negative gradient during the initial 150 days, then having a zero to positive gradient up until day

270,starting to fall for the next 50 days, following a rapid fall until day 365. The other values of Θ_e show similar trends with an increasing negative gradients and a rapid fall after day 300.

For all the possible values of Θ_e, except zero, it is observed a decreasing trend, reaching zero rate of vaccination at the final stage. In case of Θ_e=0 the initial rate of vaccination is lower than the maximum and is initially increasing until 100 days. From that point Θ_e=0 it follows the same pattern as in the case of the others.



(a) Intensity of measures (b) Rate of vaccination

Figure 6.3: Experiment 1.2 - Intervention and vaccination strategies for regular immunity period, 1 year considered period, medium vaccination and acutely symptomatic cost

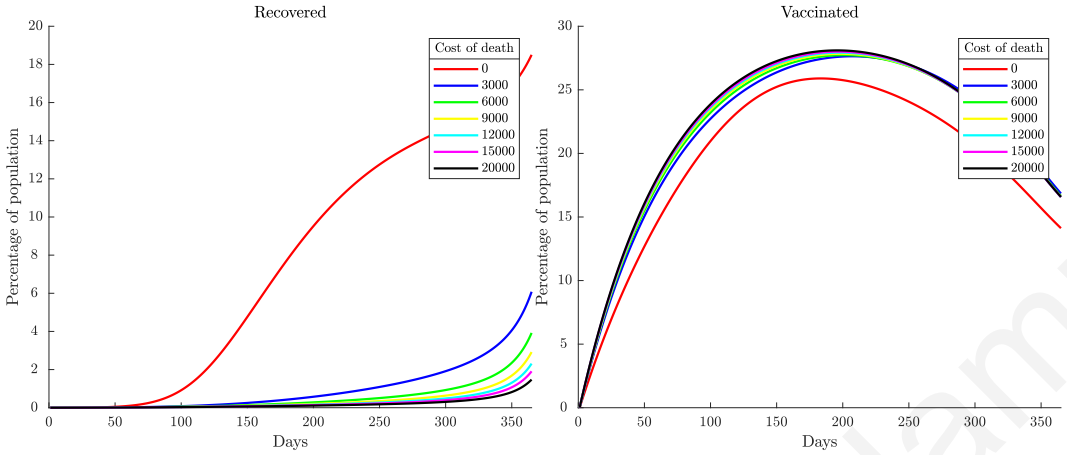
As it is with $\psi = 0$ in case of Θ_e= 0 the percentage of population infected reaches maximum at around day 150, which is also the maximum value of infected people shown in the graph. After that it starts decreasing until reaching 300 days. Afterwords it is starting increasing once more until at the end of time.The trend for the rest of Θ_e values it increasing until 320 days followed by a rabbit increasing until the end of time as in the case of $\Theta_e = 0$.

Regarding the fatalities and recovered individuals it is observed the same trend as in case of $\psi = 0$. The maximum for this case is about two times higher for both extinct and recovered population for $\Theta_e = 0$.

Similar trend is observed regarding vaccinated population when different Θ_e are applied. The maximum percentage of vaccinated individuals increases with Θ_e. At approximately 160 days it reaching maximum and is followed by a falling trend in contrast of case $\psi = 0$ which is stable.

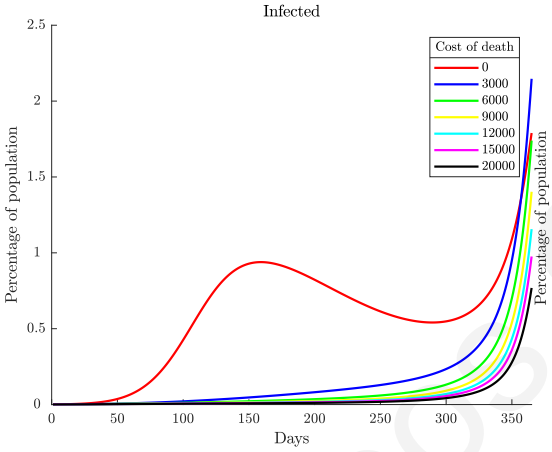
What is concluded in this experiment is that with the existence of ψ and $\hat{\psi}$, with value 1/140 and 1/395 respectively, the vaccination rate is lowered compare to experiment 1.1 resulting to lower actively vaccinated population. The highest actively vaccinated population is 27%. Furthermore, the infected population is increased compared to experiment 1.1 resulting to the increase of recovered population. The

insensitive of measures is shown a significant rise. Also the extinct population is twice higher.

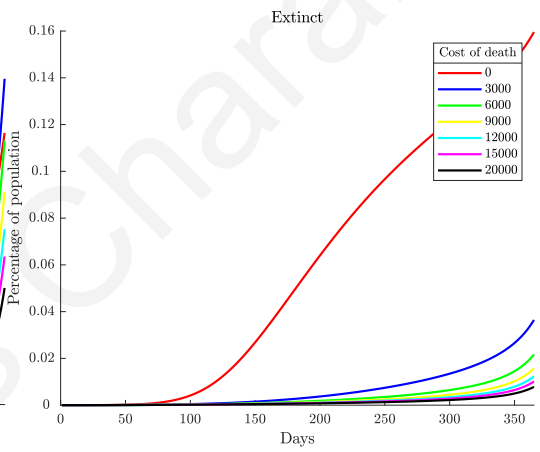


(a) Recovered

(b) Vaccinated



(c) Infected



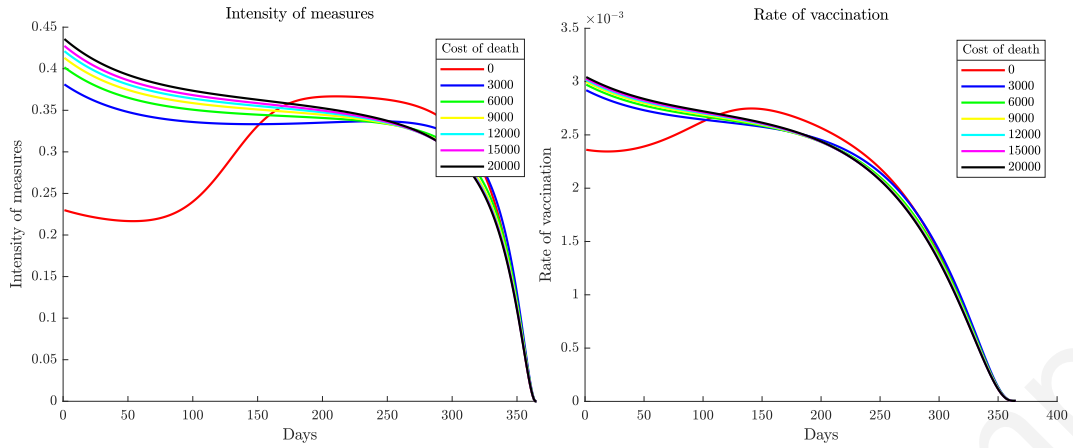
(d) Deceased

Figure 6.4: Experiment 1.2 - States for regular immunity period, 1 year considered period, medium vaccination and acutely symptomatic cost

6.3.2 Experiment 1.3 - Low immunity period

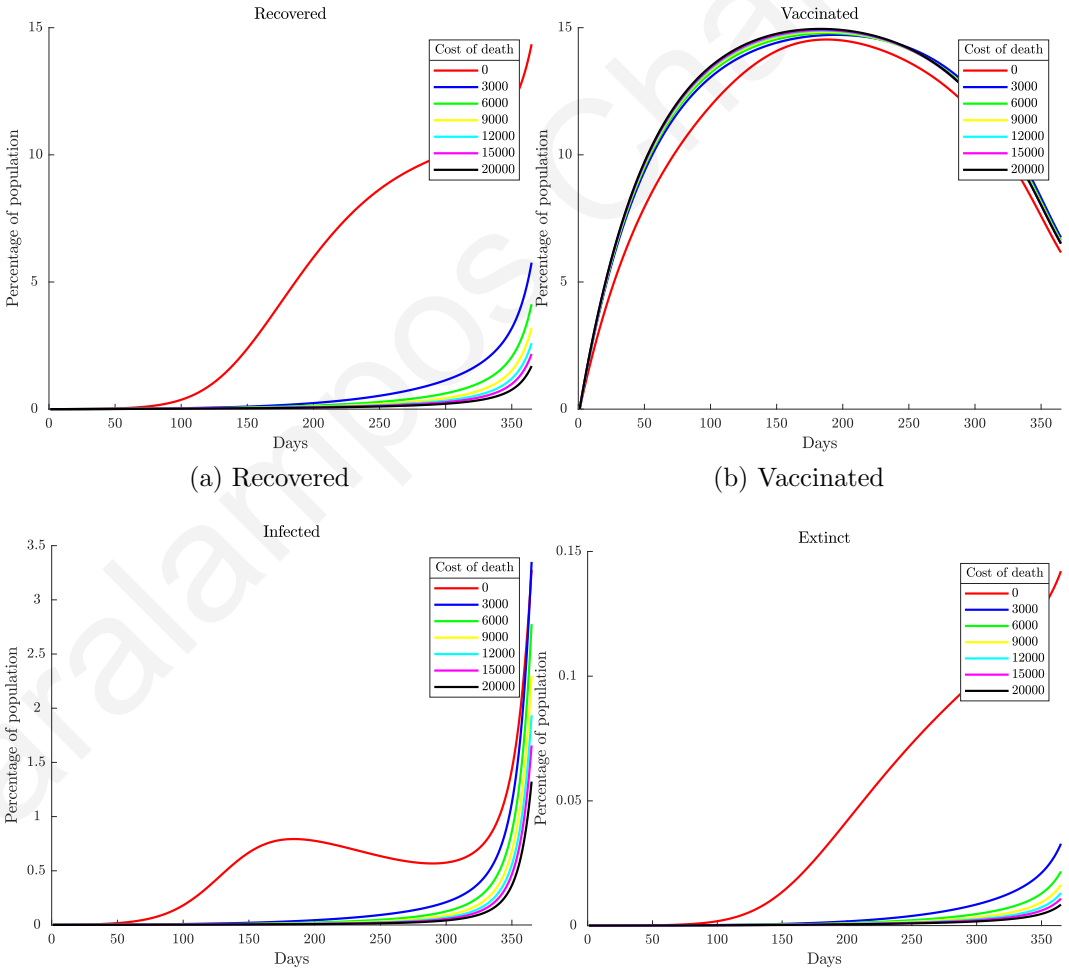
For this experiment the cost-coefficient values are: $\Theta_a = 5000$ and $\Theta_\zeta = 5000$. The immune period of vaccinations and recovered are $\psi = 2/140$ and $\hat{\psi} = 2/395$

For this experiment the trends are all similar to the trends of the previews experiment. The difference is at the maximums. In this experiment the intensity of measures is stricter. Vaccination rate, actively vaccinated and recovered are lower. Regarding the infected populations is higher compared to experiment 1.2. Moreover, the extincted population percentage is similar to the experiment above.



(a) Intensity of measures (b) Rate of vaccination

Figure 6.5: Experiment 1.3 - Intervention and vaccination strategies for low immunity period, 1 year considered period, medium vaccination and acutely symptomatic cost



(a) Recovered (b) Vaccinated

(c) Infected (d) Deceased

Figure 6.6: Experiment 1.3 - States for low immunity period, 1 year considered period, medium vaccination and acutely symptomatic cost

6.3.3 Experiment 2

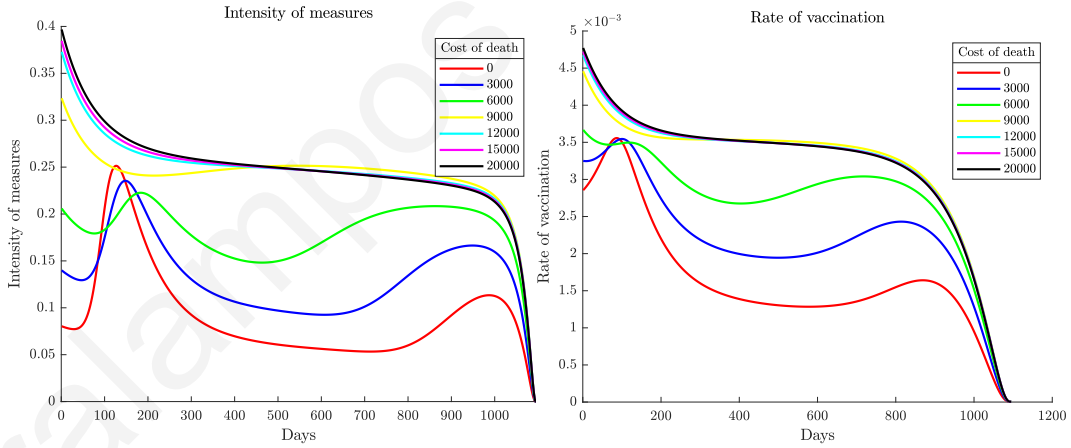
The consider period is examined in this section. The period values are 1 and 3 years.

Experiment 2.1

In this experiment $\Theta_a = 50000$. What we can observed from the below figures is the following.

Increasing time T to 1095 days, which means 3 years, the intensity of measures for higher values of Θ_e it is not observed any significant difference regarding the strictness of measures. On the other hand for values of $\Theta_e = 0, 3000, 6000$ it can be observed a fluctuation of intensity of measures. The same trend is shown for the three values with different maximum for each Θ_e. For the first 200 days $\Theta_e = 0$ has the highest maximum between the three lowest Θ_e and about 1000 days $\Theta_e = 6000$ is reaching the highest maximum.

For values of $\Theta_e \geq 9000$ it is observed that the maximum rate of vaccination is followed during the first days of the pandemic following a decreasing trend until 250 days.Afterword a stability is shown for the next 600 days and is followed by a negative gradient reaching zero rate of vaccination at the final stage. In case of $\Theta_e \leq 6000$ the initial rate of vaccination is lower than the maximum. A fluctuation is also noticeable and a maximum is reached at day 100. It is then followed by a decreasing pattern reaching day 400. Moreover a positive gradient is noticed until day 900 and start to fall again up until they reach 0 at the end of the 3 years period.



(a) Intensity of measures (b) Rate of vaccination

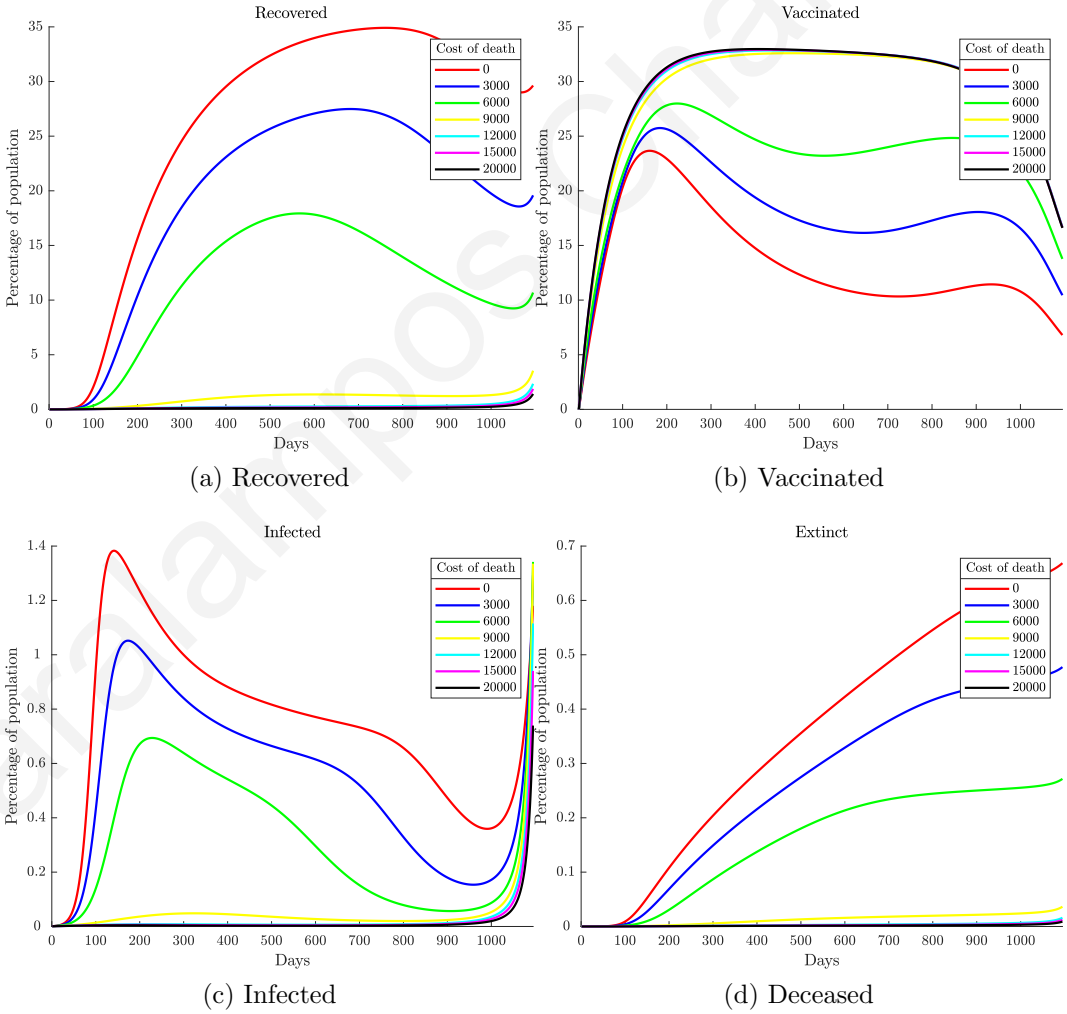
Figure 6.7: Experiment 2.1 - Intervention and vaccination strategies for regular immunity period, 3 year considered period, medium vaccination and acutely symptomatic cost

When $\Theta_e \geq 9000$ the percentage of population infected is almost zero until the final stage which a rabbit increase is observed. In case of the rest values of Θ_e a maximum at 200 days is noticed with the highest infected population percentage for $\Theta_e = 0$ which is 1.4%. A negative gradient pattern is shown after 200 days and it last for 700 days. At the final stage a skyrocket increasing trend is observed similar to all values of Θ_e.

An increasing trend is observed regarding the fatalities and recovered individuals having 0 figures for the first 50 days. As Θ_e is increasing, the maximum Percentage of extinct and recovered population is decreasing. The percentage of recovered population is shown a decreasing between 600, 700 and 800 days for $\Theta_e = 6000, 3000 and 0$ respectively.

Regarding vaccinated population different pattern is noticed between $\Theta_e \geq 9000$ and $\Theta_e \leq 6000$. In case of $\Theta_e \geq 9000$ the trend is similar to vaccinated population of $\psi = 1$ for 1 year period with a relative constant trend between 200 and 800 days. For the rest of Θ_e values a fluctuation is observed with maximum turning points at 200 and 950 days.

What is observed in this experiment is that there is a fluctuating trend for the vaccination rate, actively vaccinated population, intensity of measures and the recovered in case of $\Theta_e \leq 6000$. This is the effect of the 3 years period combined with ψ and $\hat{\psi}$ values. The intensity of measures has lower average value compared to 1 year period. At the period of 200 days the percentage of extinct population is higher in that case.



(a) Recovered (b) Vaccinated

(c) Infected (d) Deceased

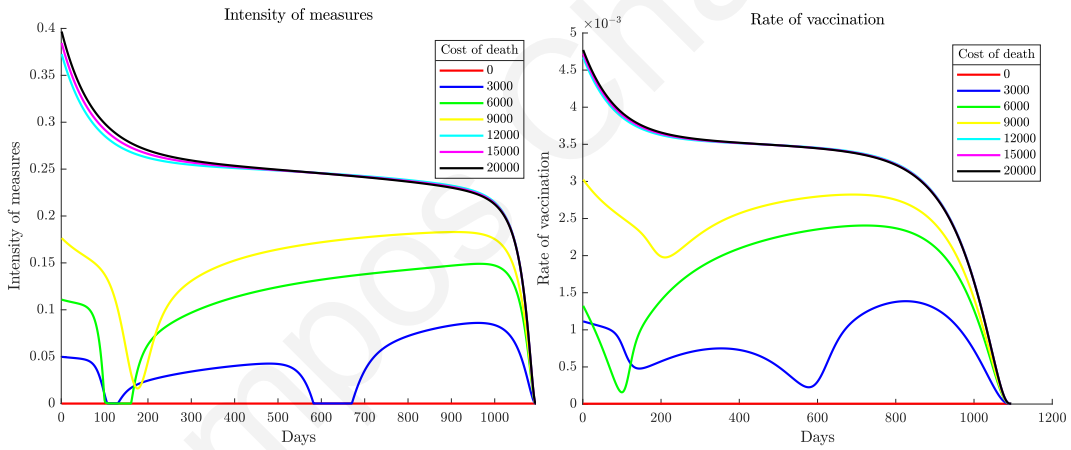
Figure 6.8: Experiment 2.1 - States for regular immunity period, 3 year considered period, medium vaccination and acutely symptomatic cost

Experiment 2.2

In these experiment $\Theta_a = 0$. What we can observed from the below figures is the following.

With Θ_e= 0 the intensity of measures stays to zero.Increasing Θ_e to 3000 an initial value of intensity of measures of 0.05 is observed. for the first 100 days the measures stay almost constant, following a rapid fall to 0 for around 20 days. An increase of the measures with a decreasing positive gradient follows up until day 570 leading to a fall to 0 little before day 600. 0 measures are applied until day 670 which then there is another increase with decreasing negative gradient until around day 1000 reaching the highest value of intensity of measures with Θ_e=3000 . Then a fall to 0 is observed until the end of the three years period.

For values of $\Theta_e \geq 12000$ it is observed identical trend to above experiment. In case of $0 < \Theta_e \leq 9000$ the initial rate of vaccination is lower than the maximum. A fluctuation is also noticeable and $\Theta_e = 3000$ has 2 minimum turning points, at 150 and 550 days, in contrast to other 2 Θ_e with 1 minimum turning point. At the final stage the trend for $\Theta_e > 0$ start to fall up until they reach 0 at the end of the 3 years period. For the case of $\Theta_e = 0$ it is constant at zero.



(a) Intensity of measures (b) Rate of vaccination

Figure 6.9: Experiment 2.2 - Intervention strategies and vaccination strategies for regular immunity period, 3 year considered period, medium vaccination cost and none cost associated with acutely symptomatic population

When $\Theta_e \geq 12000$ there is a constant trend with minimal value percentage of infected population. On the other side when $\Theta_e \leq 9000$ a fluctuating pattern is observed. For $\Theta_e = 0$ 3 maximum turning points are showing at 100, 580 and 950 days with the global maximum at day 100 with 16% infected population. In case of $\Theta_e = 3000$ 2 maximum turning points are showing at 100 and 650 days with the maximum at day 100 with 12% infected population. For the rest values of Θ_e 1 maximum turning point is noticed at around day 150 and 200.

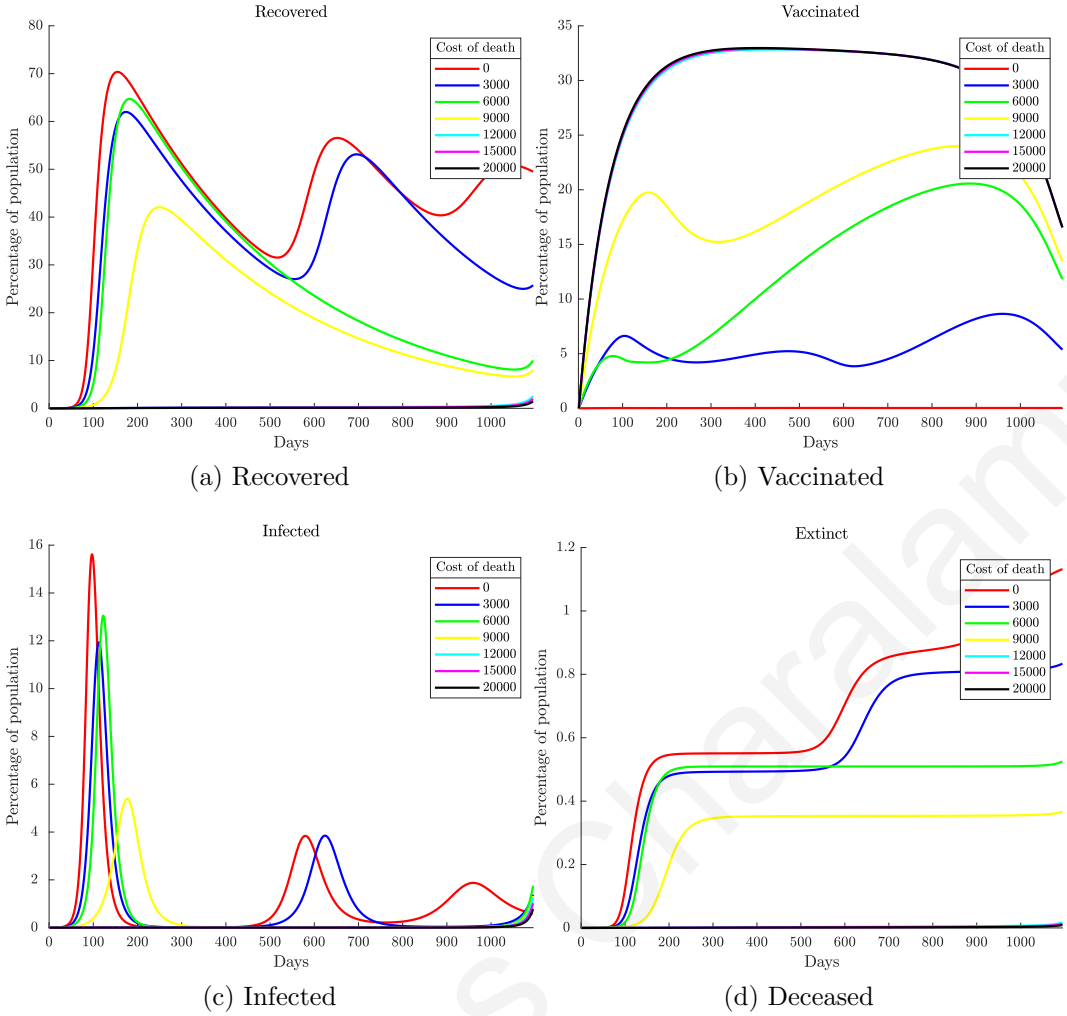
A step trend is observed when $\Theta_e \leq 9000$ regarding the fatalities. 1 step is shown

in case of $\Theta_e \in [6000, 9000]$ and 2 steps in case of $\Theta_e \in [0, 3000]$. highest percentage of deceased population is noticed at $\Theta_e = 0$ and is 1.2%. For $\Theta_e \geq 12000$ is constant at minimal value.

Recovered population is starting increasing at the first 50 days. For $\Theta_e = 0$ reaching maximum of 70% at about 170 days. Then for $\Theta_e \leq 9000$ a negative gradient is shown and for $\Theta_e \in [6000, 9000]$ last to the final stage. In case of $\Theta_e \in [0, 3000]$ the negative gradient last until about 300 days. Afterword a second maximum turning point is observed at 650 days and the case of $\Theta_e = 3000$ staring to falling. $\Theta_e = 0$ case is reached to a third and final maximum turning point at 1050 days.

Regarding the vaccinated population the pattern for $\Theta_e \geq 12000$ is identical to the experiment 2.1. In case of $\Theta_e \in [6000, 9000]$ is following a similar trend to experiment 2.1 also but with lower values. The case of $\Theta_e = 3000$ is the only case that is observed 3 maximum turning points. A constant zero is noticed for $\Theta_e = 0$.

In this experiment can noticed that by not assigned a cost to acutely symptomatic individuals has significant impact on the intensity of measures and vaccinations again for the case of $\Theta_e \leq 9000$. The intensity of measures and vaccinations means are lower compared to experiment 2.1. Infections is also greater resulting to more recovered population.



(a) Recovered (b) Vaccinated

(c) Infected (d) Deceased

Figure 6.10: Experiment 2.2 States for regular immunity period, 3 year considered period, medium vaccination cost and none cost associated with acutely symptomatic population

6.4 Implications

For the first experiment, the impact of the immunity period of vaccinated and recovered population for different costs of death is examined. It is proven that with the increasing immunity period the deceased population is decreasing and vice versa. In table 6.4, when the cost of death is zero, it is observed that with a regular immunity period the deceased population is doubled compared to infinite immunity period. Even a slight interest by the government, which is reflected on the cost of death value, will result in a dramatic decrease in the deceased population for all the values of immunity period. In the case of a high immunity period, a slight reduction of deceased population is noticed compared to regular immunity period.

The table above demonstrates how cost of death Θ_e and immunity period ψ and $\hat{\psi}$ affect extinct population when the three different cases are examined. Increasing the cost of death causes a decrease in extinct population percentages. There is a large decrease of percentage of extinctions comparing when Θ_e=0 and Θ_e =3000 in

	Percentage of extinct population		
Cost of death	Experiment 1.1	Experiment 1.2	Experiment 1.3
0	0.08%	0.16%	0.14%
3×10^3	0.03%	0.04%	0.03%
6×10^3	0.02%	0.02%	0.02%
9×10^3	0.01%	0.02%	0.02%
12×10^3	0.01%	0.01%	0.01%
15×10^3	0.01%	0.01%	0.01%
20×10^3	0.01%	0.01%	0.01%

Table 6.4: Impact of cost of death Θ_e and immunity period ψ, $\hat{\psi}$ on extinct population when Infinite Immunity (Experiment 1.1), Regular Immunity (1.2) and Lower Immunity (1.3) cases are considered.

contrast to when Θ_e goes from the value of 3000 to the value of 6000, or generally any other increment.

	Average rate of vaccinations		
Cost of death	Experiment 1.1	Experiment 1.2	Experiment 1.3
0	0.15%	0.24%	0.21%
3×10^3	0.17%	0.26%	0.21%
6×10^3	0.18%	0.26%	0.21%
9×10^3	0.18%	0.26%	0.21%
12×10^3	0.18%	0.26%	0.21%
15×10^3	0.18%	0.26%	0.21%
20×10^3	0.18%	0.26%	0.21%

Table 6.5: Impact of cost of death Θ_e and immunity period ψ, $\hat{\psi}$ on average vaccinations rate when Infinite Immunity (Experiment 1.1), Regular Immunity (1.2) and Lower Immunity (1.3) cases are considered.

	Total cost of government's interventions		
Cost of death	Experiment 1.1	Experiment 1.2	Experiment 1.3
0	1.22	6.53	15.85
3×10^3	1.68	10.17	19.09
6×10^3	2.07	10.93	19.80
9×10^3	2.34	11.39	20.30
12×10^3	2.55	11.73	20.70
15×10^3	2.72	12.00	21.03
20×10^3	2.94	12.36	21.47

Table 6.6: Impact of cost of death Θ_e and immunity period ψ, $\hat{\psi}$ on total cost of government's intervention strategies when Infinite Immunity (Experiment 1.1), Regular Immunity (1.2) and Lower Immunity (1.3) cases are considered.

The total cost of intervention strategies is increasing as the cost of death is increasing. Also an increase in the total cost of intervention strategies is observed

as the period of immunity is falling. Furthermore, the rate of increase of the cost of intervention strategies is falling as the cost of death is increasing.

	Percentage of extinct population	
Cost of death	Experiment 2.1	Experiment 1.2
0	0.67%	0.16%
3×10^3	0.48%	0.04%
6×10^3	0.27%	0.02%
9×10^3	0.04%	0.02%
12×10^3	0.02%	0.01%
15×10^3	0.01	% 0.01%
20×10^3	0.01	% 0.01%

Table 6.7: Impact of cost of death Θ_e and considered period T on extinct population

On the above table, the comparison of different considered period T against the cost of death on the percentage of extinct population is examined. On experiment 2.1 T=3 and on experiment 1.2 T=1. As expected, it is observed that the percentage of extinct population is significantly larger when the time period of the pandemic is larger although the numbers are not proportional. For example, with cost of death 0, the extinct population numbers are increased by a number of four between the two experiments. When the cost of death is 3000, the increase is twelve times bigger.

	Average rate of vaccinations	
Cost of death	Experiment 2.1	Experiment 1.2
0	0.17%	0.24%
3×10^3	0.22%	0.26%
6×10^3	0.27%	0.26%
9×10^3	0.32%	0.26%
12×10^3	0.32%	0.26%
15×10^3	0.32%	0.26%
20×10^3	0.32%	0.26%

Table 6.8: Impact of cost of death Θ_e and considered period T on average vaccinations rate

A comparison of the two different Ts mentioned above was performed. With cost of death values up to 3000, it is observed that there is a decrease of the average vaccination rates from T=1 to T=3. However, when the value of cost of death increases, the average vaccination rate becomes larger for T=3 compared to T=1. Also, there is a greater increase of the average vaccination rates as cost of death is increasing for T= 3 compared to T= 1 values and thus the above statement is proven correct.

Cost of death	Total cost of government's interventions Experiment 2.1	Experiment 1.2
0	5.93	6.53
3×10^3	10.51	10.17
6×10^3	18.51	10.93
9×10^3	32.24	11.39
12×10^3	34.00	11.73
15×10^3	34.45	12.00
20×10^3	34.95	12.36

Table 6.9: Impact of cost of death Θ_e and considered period T on total cost of government's intervention strategies

The above table describes how the cost of death and the considered period impact the total cost of the government's intervention strategies. The general trend for the above relationship is an increase of the cost of government's intervention strategies when the considered time period is increased. The only exemption to the trend is for the first case, Θ_e=0 where there is a reduction of the cost of the government's intervention strategies when the considered period is increased.

Chapter 7

Conclusions and future work

7.1 Summary

For the past two and a half years, humanity has faced an unprecedented and extremely difficult situation. COVID-19 has rapidly spread inter alia, due to globalization, from a huge number of individuals travelling around the globe and due to the lack of knowledge and information about the new virus. The above have turned the situation into a pandemic. Governments had to make rapid and critical decisions, with no background knowledge, regarding the economy, health and social status of their country. Many different strategies were applied all over the globe, with no certain estimation of their outcomes. Decisions ranged from shutting down the economy in order to save people from the disease while letting the economy and social life collapse, to taking minimal measures while letting the number of infected and deceased people to increase rapidly.

The epidemiological models which are able to present the dynamic evolution of the pandemic is an important tool which assists governments in taking the best decision possible. The minimization of the impact of the disease can be achieved by applying the most effective policies. Current epidemic models do not take into account that recovered and vaccinated people can become susceptible after a period of time. This has motivated the development of the LI-SIDAREV model (Susceptible, Infected undetected, infected Detected, Acutely symptomatic, Recovered, Extinct, Vaccinated). The LI-SIDAREV model has then been adapted by adding two control parameters to control the cost of governments intervention to mitigate the spread and the rate of vaccination. The issue that this thesis aimed to address, keeping in mind the minimization of the costs, was to select the optimal strategy regarding vaccination and intervention policies that must be followed. Inspired from previous studies, the formulation of an optimization problem was performed in order to investigate the minimization of costs for implementing governmental measures and vaccination policies. We aimed to optimize the trade off between the economic impact of measures and the number of fatalities by implementing the best possible strategy. The considered cost to be minimized comprised of the cost associated with socio-economic cost, the cost of vaccination and acutely symptomatic and extinct population costs. Tools from optimal control theory were used to solve this highly challenging problem. In particular, Pontryagin's minimum principle was applied to obtain the optimal intervention and vaccination strategies.

Once the optimal control strategies were derived, multiple scenarios were created, using a wide range of weight factors associated with the above mentioned costs. Various simulations have been performed based on the different costs for acutely symptomatic, and deceased individuals. In addition, different values for the immunity of the vaccinated and recovered population were also considered.

The main results of this thesis demonstrate that as the immunity period increases, the deceased population decreases, as well as the average rate of vaccination and the cost associated with government intervention strategies. For a medium cost of death, the cost of government intervention strategies when infinite and low immunity are considered increases by almost ten times. The average vaccination rate, when a medium cost of death is considered, increases from 0.18% to 0.26% when infinite and regular immunity rates are considered. However, when regular to lower immunity are compared, the amount of decrease is reduced from 0.26% to 0.24%. When the cost of death is zero and infinite to regular immunity cases are considered, the amount of deceased population increases from 0.08% to 0.16%.

When the considered period increases from one to three years, the deceased population and the average rate of vaccinations increase. Furthermore, on average rate of vaccination,for cost of death lower than 6000 is decreasing and for higher cost of death it is increasing and the cost associated with government intervention strategies follows the same pattern as with the average rate of vaccinations.

By finishing this thesis, we hope to aid government decision making in order to implement improved intervention and vaccination strategies.

7.2 Future work

With the constant detection of new COVID-19 variants and other information regarding already detected variants, data gathering and the associated studies need to address this potential new information. One fact that can be added to the model is the infection of vaccinated individuals and the effectiveness of vaccines[23]. Vaccinated individuals also contribute to the spread of the disease and this is an interesting topic for future work.

One of the assumptions made for this thesis is the maximum vaccination rate per day. The maximum percentage of vaccinations is assumed to be equal to 0.5% in one day. The study of the impact of different maximum vaccination rates per day is also an interesting topic to be examined.

Furthermore, the willingness of individuals to be vaccinated is another assumption that is sustained in this thesis. It is assumed that all individuals are willing to be vaccinated. Due to the fact that a fraction of the population is not willing to be vaccinated and therefore choose not to, different vaccination strategies might be taken by governments.

Moreover, this thesis considers all individuals equally and does not take into consideration the differences between gender and age groups in the population. This

can impact the mortality rate as the older population has a greater possibility to die compared to younger population[24]. Furthermore, mortality rate for men seems to be greater than women [25]. Additionally, the immunity period between age groups may differ. [26].

In addition, the weather conditions is another factor that can be interesting to study. The disease infection rate can be higher in winter were the weather conditions are ideal for a virus to spread rather than in summer period[27].

These are a few examples of differently considered values for the models parameters that can be taken into account for future work. COVID-19 is still evolving and new data is collected on a daily basis, making it extremely difficult to identify and assess all the possible scenarios. For the above reason, assumptions had to be made, and possible future work was considered and proposed in order to enhance these findings. We hope that, as a result, the findings of this thesis will be used in order to assist in future studies.

Chapter 8

MATLAB code

Script to simulate a number of cases on the controlled LI-SIDAREV model.

```
clear all;
clc;

v_val = 0.05; %Testing rate values - values of v
Q_val = [0;50000]; %Costs associated with acutely symptomatic ...
    population
thetaz_val = [50;5000]; %Costs associated with vaccines
%Costs associated with diseased population
C_dth = [0; 3000; 6000; 9000; 12000; 15000; 20000];
N = length(C_dth); %number of iterations

%Data (Italy)
Rho = 3.27; %based on 'Monitoring transmissibility and mortality'
gamma_i = 1/14; % Recovery rate from infected undetected
gamma_d = 1/14; % Recovery rate from infected detected
gamma_a = 1/12.39; %Recovery rate from hospitalized
H_in = 0.06925; %percentage of hospitalized - range between 5% ...
    and 12%
a_d = 0.0066/H_in; %so the infection mortality rate is 0.66%
mu = a_d/(1-a_d)*gamma_a; %Transition rate from acutely ...
    symptomatic to deceased
psi = 1/140; %Susceptible rate from vaccinated
psi_hat = 1/395; %Susceptible rate from recovered
zmaxn = 0.005;
psin = 1;
dt = 1; %time increments

for q = 1:2 %associated with three different cost weights for ...
    the acutely symptomatic population
     for f=1:1 %Different testing rate policies
         for j = 1:2 %Different cost weights for vaccination

             ksi_i = H_in/(1-H_in)*gamma_i; %Transition rate from ...
                 infected undetected to acutely symptomatic
             ksi_d = H_in/(1-H_in)*gamma_d; %Transition rate from ...
                 infected detected to acutely symptomatic
             beta = Rho*(gamma_i + ksi_i); %Definition of R0 in ...
                 SIDARE, proven in our paper

             Q = diag([0;0;0;Q_val(q,1);0;0;0]); %Cost associated ...
```

```
                with states
34
35              v_set = v_val(1,1); %Adopted testing rate
36
37              %***theta_z = 1 or 500 or 5000 or 500000***
38              theta_z = thetaz_val(j,1);
39
40              %Different cases of cost weights associated with ...
                   deceased
41              %population-----------------------------------------------
42              parfor i=1 + (j-1)*N:N + (j-1)*N
43                  [x{i}, u(i,:), zeta(i,:),C(:,i), C1(:,i), ...
                       C2(:,i), C3(:,i), C4(:,i)] = ...
                       Sim_simple(dt,beta, gamma_i, gamma_d, ...
                       gamma_a, ksi_i, ksi_d, mu,  C_dth(i - ...
                       (j-1)*N,1), Q, v_set, psi, psi_hat, theta_z);
44              end
45          end
46
47          %Workspace is saved in a local folder
48          FileName    = ['Q_' num2str(Q(4,4)) '_ThZ_' ...
                num2str(theta_z) '_Zmax_' num2str(zmaxn) '_Psi_' ...
                num2str(psin) '.mat'];
49          save(FileName)
50
51      end
52  end
```

Function that takes as inputs a set of model parameters associated with the controlled LI-SIDAREV model and gives the optimal continuous strategy u, optimal vaccination strategy zeta, the resulting state trajectories x, and cost C. Costs C1 is associated with interventions strategies cost, C2 is associated the acutely symptomatic population, C3 is associated the number of deaths,and C4 with vaccinations.

```
1  %Function that takes as inputs a set of model paramters ...
       associated with the
2  %controlled SIDARE model and gives the optimal continuous ...
       strategy u,
3  %the resulting state trajectories x, and cost C. Costs C1, C2 ...
       and C3 are
4  %associated with the strategy, the acutely symptomatic ...
       population and the
5  %number of deaths ...
       respectively.-------------------------------------------
6  function [x, u, zeta, C, C1, C2, C3, C4] = Sim_simple(dt, beta,  ...
       gamma_i, gamma_d, gamma_a, ksi_i, ksi_d, mu, C_dth, Q, ...
       v_set, psi, psi_hat, theta_z)
7
8  T_days = 365 * 3; %Number of days
9
10 R = 1; %Cost associated with government strategy (used as basis)
11 z_max = 0.005;
12
13 %Initial conditions
14 r = 0.00001;
15 x(1,1) = 1 - r; %S
16 x(2,1) = r; %I
```

```
x(3,1) = 0; %D
x(4,1) = 0; %A
x(5,1) = 0; %R
x(6,1) = 0; %E
x(7,1) = 0; %V

%Data (Italy)
T = T_days/dt;
l(1:length(x(:,1)),T) = 0; %Lambda boundary conditions
l((length(x(:,1)) - 1),T) = C_dth; %Cost attributed to number of ...
    deaths
mu_h = 5*mu; %infection decease rate when hospital capacity is ...
    exceeded
u_max = 0.8; %maximum value for u

u(1:T,1) = 0.4; %Initialisation of u
v(1:T,1) = v_set; %Constant value of testing rate,
zeta(1:T,1) = 0.1;          %Initialisation of z

%Initialization of states and costs
for k=2:T
x(:,k) = epidem(dt, x(:,k-1), beta(1,1), u(k-1,1), v(k-1,1), ...
    zeta(k-1,1), gamma_i, gamma_d, gamma_a, ksi_i, ksi_d, mu, ...
    psi, psi_hat);
end

for k=T-1:-1:1
[l(:,k), dl(:,k)] = pontr(dt, l(:,k+1), x(:,k+1), u(k+1,1), ...
    v(k+1,1), zeta(k+1,1), beta(1,1), gamma_i, gamma_d, gamma_a, ...
    ksi_i, ksi_d, mu, Q, psi, psi_hat);
end


%Cost function - aggregate and ...
    components---------------------------------
C1(1,1) = 0.5*dt*(R(1,1)*u.'*u); %cost associated with ...
    government strategy u
C2(1,1) = 0.5*dt*(Q(4,4)*(x(4,:)*x(4,:).')); %cost associated ...
    with the acutely symptomatic population
C3(1,1) = x((length(x(:,1)) - 1),T)*C_dth; %cost associated with ...
    number of deaths
C4(1,1) = 0.5*dt*(zeta.'*zeta)*theta_z;                          ...
    %cost associated with vaccination
C(1,1) = C1(1,1)+C2(1,1)+C3(1,1)+C4(1,1);                        ...
    %Total Cost

N_iter = 100000 / 5; %number of iterations for the convergence ...
    of the algorithm

for j=1:N_iter

    %Calculation of the new value for u
    u0 = u;
    zeta0 = zeta;
    for k=1:T
        u1(k,1) = ...
            min(max(inv(R(1,1))*beta(1,1)*x(1,k)*x(2,k)*(l(2,k) ...
            - l(1,k)),0),u_max);
```

```
60          zeta1(k,1) = min(max((x(1,k) * (l(1,k) - l(7,k)))/ ...
                theta_z, 0),z_max);
61      end
62
63      a = 0.9995; %coefficient used to update the current u
64      u = a*u0 + (1-a)*u1; %new strategy u
65      zeta = a*zeta0 + (1-a)*zeta1; %new strategy z
66
67      %Update the SIDARE model trajectory based on current u
68      for k=2:T
69          %Controlled SIDARE epidemic model
70          x(:,k) = epidem(dt, x(:,k-1), beta(1,1), u(k-1,1), ...
                v(k-1,1), zeta(k-1,1), gamma_i, gamma_d, gamma_a, ...
                ksi_i, ksi_d, mu, psi, psi_hat);
71      end
72
73      %Update the costate variables
74      for k=T-1:-1:1
75          %Pontryagin equations
76          [l(:,k), dl(:,k)] = pontr(dt, l(:,k+1), x(:,k+1), ...
                u(k+1,1), v(k+1,1), zeta(k+1,1), beta(1,1), gamma_i, ...
                gamma_d, gamma_a, ksi_i, ksi_d,mu, Q, psi, psi_hat);
77      end
78
79      %C(j,1) = 0.5*dt*(R(1,1)*u.'*u +  Q(4,4)*(x(4,:)*x(4,:).')) ...
            + x((length(x(:,1)) -1),T)*C_dth; %total cost
80      C1(j,1) = 0.5*dt*(R(1,1)*u.'*u);  %cost associated with ...
            government strategy u
81      C2(j,1) = 0.5*dt*(Q(4,4)*(x(4,:)*x(4,:).'));  %cost ...
            associated with the acutely symptomatic population
82      C3(j,1) = x((length(x(:,1)) -1),T)*C_dth; %cost associated ...
            with number of deaths
83      C4(j,1) = 0.5*dt*(zeta.'*zeta)*theta_z; ...
                                        %cost associated with ...
            vaccination
84      C (j,1) = C1(j,1) + C2(j,1) + C3(j,1) + C4(j,1); ...
                                    %Total Cost
85  end
```

The function describing the dynamics of the controlled LI-SIDAREV model.

```
1   %function describing the dynamics of the controlled SIDARE model
2   function [y,dy] = epidem(dt, x, beta, u, v, zeta, gamma_i, ...
        gamma_d, gamma_a, ksi_i, ksi_d, mu, psi, psi_hat)
3
4       %Controlled SIDARE model
5       dy(1,1) = -beta*(1 - u)*x(1,1)*x(2,1) + psi*x(7,1) + ...
            psi_hat*x(5,1) - zeta*x(1,1); %Susceptible State
6       dy(2,1) = beta*(1 - u)*x(1,1)*x(2,1) - gamma_i*x(2,1) - ...
            ksi_i*x(2,1) - v*x(2,1); %Infected undetected State
7       dy(3,1) = v*x(2,1) - gamma_d*x(3,1) - ksi_d*x(3,1); ...
            %Detected infected State
8       dy(4,1) = ksi_i*x(2,1) +  ksi_d*x(3,1) - gamma_a*x(4,1) - ...
            mu*x(4,1); %Acutely symptomatic State
9       dy(5,1) = gamma_i*x(2,1) +  gamma_d*x(3,1) + gamma_a*x(4,1) ...
            - psi_hat*x(5,1); %Recovered State
10      dy(6,1) = mu*x(4,1); %Extinct (Deceased) State
```

```
11      dy(7,1) = zeta*x(1,1) - psi*x(7,1); %Vaccinated State
12      y = x + dt*dy; %State update
```

The function of costate variables update based on Pontryagin's minimum principle.

```
1  %function of co-state variables update based on Pontryagin's ...
       minimum principle
2
3  function [y,dy] = pontr(dt, l, x, u, v, zeta, beta, gamma_i, ...
       gamma_d, gamma_a, ksi_i, ksi_d,mu, Q, psi, psi_hat)
4
5      %Equations based on Pontryagin's minimum principle
6
7      dy = -[beta*x(2,1)*(l(2,1) - l(1,1))*(1-u) + zeta*(l(7,1) - ...
           l(1,1));
8      beta*x(1,1)*(l(2,1) - l(1,1))*(1-u) + v*(l(3,1)-l(2,1)) + ...
           gamma_i*(l(5,1) - l(2,1)) + ksi_i*(l(4,1) - l(2,1));
9      gamma_d*(l(5,1) - l(3,1))  + ksi_d*(l(4,1) - l(3,1));
10     Q(4,4)*x(4,1) + gamma_a*(l(5,1) - l(4,1)) + mu*(l(6,1) - ...
           l(4,1));
11     psi_hat*(l(1,1) - l(5,1));
12     0;
13     psi*(l(1,1) - l(7,1))];
14     y = l - dy*dt; %backwards in time, since boundary condition ...
           for costate variables is at t = T
```

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