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Master's Research Project

WMIE901-30

OPTIMAL CONTROL OF EPIDEMICS

Analysis of optimal government intervention-, testing-, and vaccination strategies

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Abstract

Keywords— SIDAREV model, optimal control, Pontryagin's maximum principle, COVID-19

This study seeks for optimal control strategies for the implementation of measures during a disease outbreak. The existing SIDARE model, which stands for Susceptible (S), Infected Undetected (I), Infected Detected (D), Acutely symptomatic or Threatened (A), Recovered (R), and Extinct (E), is modified by adding a compartment for vaccination (V), creating the SIDAREV model. An optimal control problem is formulated to minimize the threatened and deceased population and the overall costs. Model parameters for simulating the COVID-19 pandemic have been used. The control inputs u_1, u_2 and u_3 for affecting the infection rate (β), testing rate (ν) and vaccination rate (ψ), respectively, are proposed. Pontryagin's maximum principle is applied to determine the optimal controls. Consequently, the optimal strategies for the control inputs have been determined. By applying optimal control strategies the socio-economic costs and the costs associated with the threatened and deceased population are minimized. Moreover, it appears that the peak of threatened individuals can be flattened and pushed further into the future and that the deceased individuals at the end of a disease outbreak will be reduced.

Preface

This report was written in response to the COVID-19 pandemic that is taking place during the conduct of this research project. The report describes how optimal measures can be taken in the event of a disease outbreak.

This research project was carried out as part of my Master's in Industrial Engineering and Management at the University of Groningen. This research project builds on the (to be published) research of Kasis et al. (2021).

I would like to thank everyone who contributed to this research. Specifically, I am profoundly grateful to my first supervisor Dr N. Monshizadeh Naini, for the weekly guidance and feedback on my work. Although only digital communication was possible due to the COVID-19 pandemic, the collaboration helped me a lot, and I have experienced a lot of pleasure in it. Besides, I would like to thank my second supervisor, Prof. Dr Ir. M. Cao, for his feedback on the report and final presentation. I also express my gratitude to Dr A. Kasis for his help with the numerical simulations and my fellow student T. Venema for the brainstorming sessions and feedback on my work. Finally, I would like to thank my other fellow students, friends and family for mental and motivational support.

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Chapter 1: Introduction to Optimal Control of Epidemics

This chapter provides an introduction to this research and describes the problem and objective. The research questions are mentioned, and a report outline is given.

1.1 Research motivation

At the beginning of December 2019, an outbreak of COVID-19 was reported in Wuhan, China. The virus was spreading fast to other countries, and consequently, on March 11 2020, the World Health Organization (WHO) declared COVID-19 a pandemic (Organization et al., 2020). When there is no immunity in a population, and no vaccines are available yet, it becomes hard to prevent a new disease from spreading. Therefore, measures can be taken to counteract the spreading of the disease. For instance, non-pharmaceutical interventions (NPIs) such as intensive hand hygiene, home quarantine, and social distancing measures. COVID-19 measures should be taken so that the available number of intensive care unit (ICU) beds are not exceeded (Kantner and Koprucki, 2020).

Epidemiological models can help understand the spread of a disease. It is also possible to assess the efficacy of different NPIs and estimate the corresponding demands of a health care system. Various variables can be added to models, such as the amount of susceptible, infected, recovered, etc. As a result of the new COVID-19 virus, several new models have been developed quickly. Models differ from each other because different variables and parameters are used. Models can be controlled by adding a controller to the system. A controller ensures that one or more variables are steered to a specific desired direction.

It is necessary to pursue an optimal policy so that effective measures can be taken to obtain the desired outcome with minimal costs. In the outbreak of the COVID-19 pandemic, it is desirable that hospital capacities are not exceeded and that the deceased population remains minimal. Measures that can be taken are government intervention, which includes measures such as social distancing, closing of public buildings and schools, curfews, and lockdowns. Another measure is a testing policy so that infections can be diagnosed and people can be quarantined to prevent further spread. Moreover, vaccinations can be administered so that immunity against the disease is obtained.

1.2 Problem and goal statement

The problem is that the total costs of a disease outbreak should be minimized. These costs consist of socio-economic costs and the costs associated with the threatened and deceased population. Socio-economic costs are the costs associated with the implementation of measures. For example, a lockdown policy has economic costs because shops are closed, companies go bankrupt, and people cannot go to work. But also, social costs due to the prohibition of people's freedom of movement. Costs associated with the threatened and deceased population are costs for hospitalization and extra care that people need. The problem statement is therefore: *Both the socio-economic costs and the costs associated with the threatened and deceased population must be minimized.*

To minimize the costs, a trade-off must be made between the socio-economic costs and the costs associated with the threatened and deceased population. This study therefore looks for the most optimal strategy to achieve this. The goal statement is: *Seek for optimal control strategies for the*

implementation of government intervention-, testing-, and vaccination policies during a disease outbreak.

1.3 Research questions

Research questions have been devised for this study. The main question of this research is: *'What are the optimal control strategies for implementing government intervention-, testing-, and vaccination policies if the costs associated with the threatened and deceased population and socio-economic costs must be minimized?'* To answer the main question, sub-questions have been devised, and they are as follows.

1. Which epidemiology models are available that include government intervention-, testing-, and vaccination policy, or how can such a model be made?
2. How can the epidemiological model be adapted such that government intervention-, testing-, and vaccination policies can be controlled?
3. How can an optimization problem be formulated such that the costs of the implementation of measures, the socio-economic costs and the costs associated with the threatened and deceased population are minimized?
4. How can the aforementioned optimization problem be solved, such that the optimal strategy for the implementation of measures can be found?
5. What is the influence of optimal measures compared to non-optimal measures for the above optimization problem?

1.4 Research report outline

In chapter 2, the background of epidemiological models and optimal control is described, and preliminaries of optimal control theory are explained. Chapter 3 describes the model analysis for the SIDAREV model used in this study. Chapter 4 describes the optimal control analysis, whereas the control design is explained, and the optimal control problem is formulated. Chapter 5 describes which experiments were performed. In chapter 6, the results of the experiments are analyzed. Chapter 7 describes the discussion and the future research. Chapter 8 draws the conclusions of the study. Lastly, in chapter 9 the MATLAB codes that are used for the simulations are provided.

Chapter 2: Background in Optimal Control and Preliminaries

This chapter describes the background in mathematical modelling of epidemics and optimal control. It also examines how an optimal control problem can be formulated and be solved.

2.1 Mathematical modelling of epidemics

The evolution of an epidemic of a disease outbreak can be simulated using mathematical models. By dividing a population into several subpopulations, which are called compartments, different stages of a disease outbreak can be represented (Eubank et al., 2020) (Sharomi and Malik, 2017). The compartments are, for example, 'Susceptible' (S), which means that an individual does not carry the disease at the present moment, but can get the disease because no immunity has been built up (the individual is not vaccinated), or 'Exposed' (E) where an individual is infected with the disease but cannot yet transmit it to other individuals. Other compartments can be 'Infected' (I), in which logically the individual has contracted the disease but is also infectious to other individuals or 'Recovered' (R), where the individual has been cured of the disease and has become immune so that it cannot be re-infected. A compartment model can be expanded with different compartments such as 'Diagnosed' (D), 'Ailing' (A), 'Recognized' (R), 'Threatened' (T), 'Extinct' (E) and 'Vaccinated' (V) (Giordano et al., 2020). The disease dynamics can be represented by connecting the different compartments and the flow from one compartment to another.

The Susceptible-Infected (SI) model, the Susceptible-Infected-removed (SIR) model and the Susceptible-Exposed-Infectious-Removed (SEIR) model, are common in literature and often form the basis of more complex compartment models. In the SI model the entire population consists of just two groups, namely susceptible and infected individuals, and in the SIR model the population consists of three groups, namely susceptible, infected and recovered individuals. Lastly, in the SEIR model, the population is divided into four groups that consist of susceptible, exposed, infected and recovered individuals. A schematic example of an SI and SIR compartment model is shown in figure 2.1.

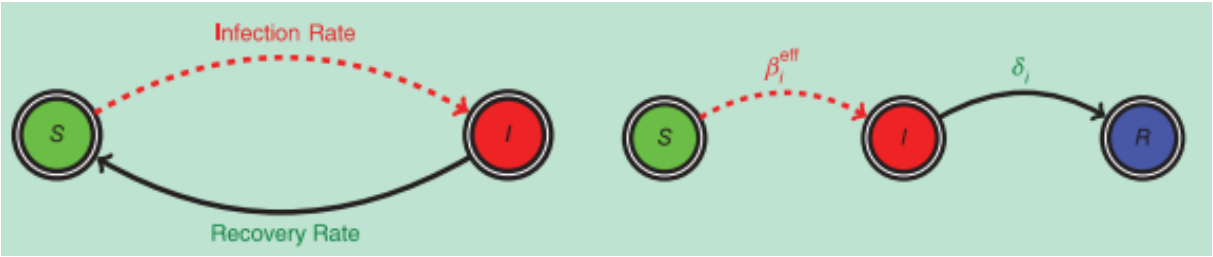


Figure 2.1: SI model (left) and SIR model (right) (Nowzari et al., 2016). In the SI model, susceptible individuals can transition to infected individuals with infection rate β and can return to become susceptible with recovery rate δ. Note that individuals cannot become immune to the disease. In the SIR model, the 'Removed' (R) compartment is added. Once an individual reaches the recovered state, it is not able to go back to the susceptible nor infected state, and thus has become immune

The dynamics of a compartment model can be described based on ordinary differential equations (ODEs). As an example, the SIR model dynamics are described below (Kermack and McKendrick, 1927), (Hethcote, 2000).

$$\left.\begin{array}{ll} \dot{S} = -\beta IS/N, & S(0) = S_0 \geq 0, \\ \dot{I} = \beta IS/N - \gamma I, & I(0) = I_0 \geq 0, \\ \dot{R} = \gamma I, & R(0) = R_0 \geq 0, \end{array}\right\} \tag{2.1}$$

where $S(t)$, $I(t)$, and $R(t)$ are the number of individuals in the compartments and $S(t) + I(t) + R(t) = N$.

The system dynamics are programmed in MATLAB, and a plot is made to show the behaviour of the variables (figure 2.2). The MATLAB script that was created can be found in section 9.1. What can be seen in the figure is that at the start of a disease outbreak, almost everyone is susceptible, and only a few individuals are contagious. As soon as more people are contagious, the total infected individuals quickly reach their peak. After that, the number of infected also decreases rapidly. The number of recovered individuals increases as long as people recover from an infection. In this specific example, it can be seen that no more infections take place after about 150 days. However, a small number of individuals is still susceptible, and so not everyone is recovered. This is because a balance has been reached in which there are too few individuals who can transfer the disease to susceptible individuals, causing the disease to die out.

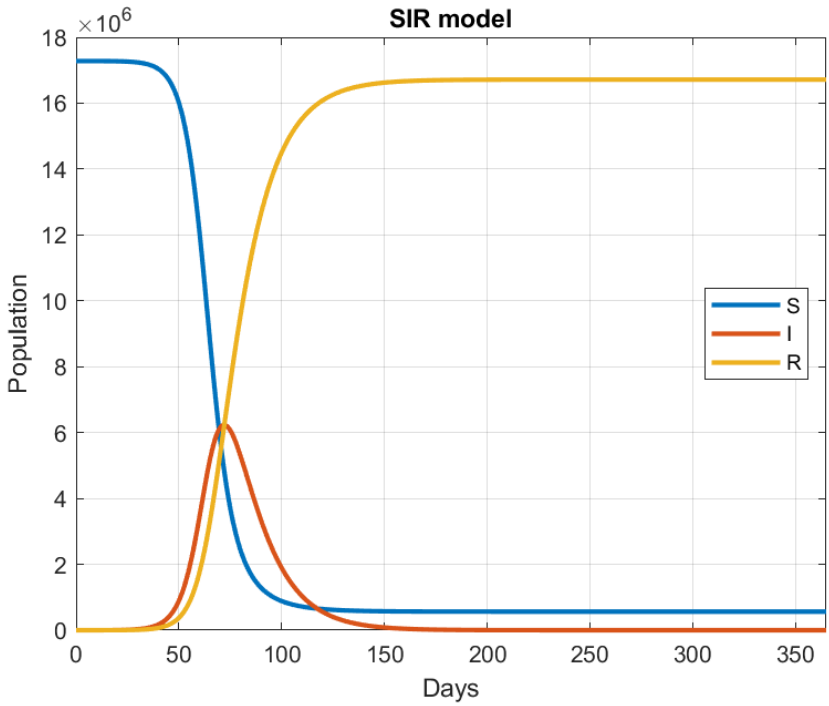


Figure 2.2: SIR model dynammics

2.2 Optimal control in epidemiology

A model can be controlled by adding controllers to the model. Controllers are added to direct the model variables in a specific desired direction. According to Nowzari et al. (2016), a distinction can be made between two sorts of control in epidemiology, namely spectral control and optimal control. Spectral control focuses on static resource allocation to make a disease-free state stable at minimum costs, i.e. optimally invest resources to diminish the spread of disease when having a fixed budget. Optimal control focuses on dynamic feedback strategies in which both the costs of a control strategy to be applied and the economic and healthcare costs are minimized. So optimal control looks at the ideal situation for minimizing the total costs and maximizing the

desired outcome. In this report, only optimal control is used and discussed, and thus spectral control is not taken into account.

Research has already been conducted into optimal control in epidemics (particularly due to the COVID-19 pandemic). In the study of Djidjou-Demasse et al. (2020), an optimal control strategy was investigated in which the number of deaths and the costs related to the implementation of the control strategy is minimized. An important assumption was made that no vaccine is available during the control period. It turns out that optimal control strategies outperform other strategies. In the study of Deressa and Duressa (2021), an optimal control analysis was performed, which showed that optimal preventive strategies such as public health education, personal protective measures and treatment of hospitalized cases effectively reduce the number of COVID-19 deaths. Furthermore, in the research of Köhler et al. (2020), two optimal control policies are analyzed. The first is the open-loop optimal control policy, in which it appears that the number of fatalities can be decreased significantly under the assumption of exact model knowledge. However, they state that this is not a realistic scenario in the real world since there should be dealt with uncertain data and model mismatch. Therefore they designed a feedback strategy that updates the policy weekly using model predictive control (MPC). They found this feedback control is robust and also necessary for reliably handling an outbreak. Other studies where optimal control is applied can be found in (Kantner and Koprucki, 2020), (Hansen and Day, 2011).

2.3 Formulating the optimal control problem

An optimal control problem must be formulated to create an optimal control strategy for a disease outbreak. An important part of the optimal control problem is the function to be optimized, also called the objective function. This is a cost function that must be minimized. The general form of the objective function consists of the sum of the cost of the state variable(s) $x(t)$ to be minimized (e.g. infected and/or deceased population) and the cost of implementing the control variable $u(t)$ and can be described as:

$$J(u) = \int_0^T x(t)\,dt + b\int_0^T u^2(t)\,dt. \tag{2.2}$$

Coefficient b is to weight the cost associated with the control input $u(t)$ to the relative importance of the state variable $x(t)$. It is also possible that the costs are evaluated at the final time so that a term $S(x(T))$ must be added to the objective function. A common time interval $[0, T]$ is from the pandemic start to vaccination deployment, as it is believed that when vaccinations are available, the population becomes immune, and control strategies are no longer needed. It often happens that there are quadratic terms in the objective function because either it is assumed that the costs are non-linear or that the differential equations obtained from this optimal control problem have a known solution. Moreover, functions without quadratic terms appear difficult to solve) (Lenhart and Workman, 2007). Ultimately, the goal is to find a function u^* that satisfies the function:

$$J\left(u^*\right) = \min_{u\in\mathcal{U}} J(u), \tag{2.3}$$

on the set $\mathcal{U} = \{u \in L^\infty(0,\infty) : 0 \le u(\cdot) \le u_{\max}\}$, where $u_{\max} \le 1$, and L^∞ is the vector space of essentially bounded measurable functions (Djidjou-Demasse et al., 2020). The solution of equation (2.3) can be found by formulating the optimal control problem that consists of the objective function subject to the model dynamics and initial conditions.

2.4 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 created system can then be solved numerically. 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 noted that in most literature, different names and symbols are used when describing Pontryagin's maximum principle. For example, the optimal control is often described as $u(t)$, but sometimes also as $c(t)$. Likewise, in the literature, different terms for the same mathematical theory are used, so does the adjoint variable mean the same as the co-sate variable. In addition, the symbols for these variables can be expressed as p, ψ or λ. Furthermore, Pontryagin's maximum principle explained as Pontryagin's minimum principle, but this can be changed by multiplying the objective function by -1.

According to Pontryagin's maximum principle, it is necessary to derive the Hamiltonian function. The Hamiltonian function connects the objective function to the state equations using Lagrange multipliers $\lambda(t)$. The general form of the Hamiltonian function H can be described as:

$$H(t, x, \lambda, u) = f(t, x, u) + \lambda g(t, x, u), \tag{2.4}$$

where the adjoint variable is expressed as λ, the optimal control as u and the state variable as x (Kirk, 2004). 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 (RHS) of the differential equations of the state variable (RHS of model dynamics).

The first-order necessary optimality condition for solving the optimal control problem can be derived by applying Pontryagin's maximum principle, which is as follows.

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*

$$\dot{x}(t) = \frac{\partial H}{\partial \lambda}(x(t), u(t), \lambda(t)), \tag{2.5}$$

$$\dot{\lambda}(t) = -\frac{\partial H}{\partial x}(x(t), u(t), \lambda(t)), \tag{2.6}$$

so that

$$H\left(x^*(t), u^*(t), \lambda^*(t)\right) \leq H\left(x^*(t), u(t), \lambda^*(t)\right), u \in \mathcal{U}, \tag{2.7}$$

and the corresponding boundary conditions hold

$$x(0) = x_0, \tag{2.8}$$

$$\lambda(T) = S(x(T)). \tag{2.9}$$

Equation (2.6) is called the adjoint equation and equation (2.9) is called the transversallity condition. From equation (2.7) the optimality equation can be derived, i.e.

$$\frac{\partial H}{\partial u}(x(t), u(t), \lambda(t)) = 0, \tag{2.10}$$

where $u_{min} \leq u(t) \leq u_{max}$. The proof can be found in (Lenhart and Workman, 2007). Furthermore, for the minimization of the control problem the following equation at u^* must hold:

$$\frac{\partial^2 H}{\partial u^2} \geq 0. \tag{2.11}$$

2.5 Forward-backward sweep method

The forward-backward sweep method is an indirect method to solve the optimal control problem. In this method, the created ODEs of Pontryagin's maximum principle are solved numerically (McAsey et al., 2012). The block diagram in figure 2.3 shows which steps must be performed to implement the method.

According to Lenhart and Workman (2007), the steps to perform the forward-backward sweep method are as follows. First, the model parameters must be entered to obtain the desired simulation for the disease outbreak. After that, an initial guess has to be made for the control input u ($= u_{old}$), where the initial guess $u_{old} = 0$ almost always suffices. The state equations ($\dot{x}$) must now be solved forward in time. After that, the adjoint equations ($\dot{\lambda}$) must be solved backwards in time. Now that the variables x and λ are solved, a new optimal control u_{new} can be calculated based on the optimality equation. The calculated u_{new} and the initial guess u_{old} must be updated with a update policy to obtain control input u_{update}. Various update policies are possible. A common update policy is to calculate the average value of the two $u's$. However, it is possible that this update policy does not always work. Another update policy is where a certain weight is added to the old or new $u's$, namely

$$u_{new} * \left(1 - \mathrm{c}^{\mathrm{i}}\right) + \mathrm{u_{old}} * \mathrm{c}^{\mathrm{i}}, \tag{2.12}$$

where $0 < c < 1$ and i is the current iteration. Ultimately, it must be examined whether convergence can be achieved. Convergence is achieved when the variables of the current iteration compared to the previous iteration are within a certain tolerance, i.e.

$$\frac{\|u_{update} - u_{old}\|}{\|u_{update}\|} \leq \delta, \tag{2.13}$$

where δ is the accepted tolerance. If the outcome is not within the accepted tolerance, the updated u (u_{update}) must replace the old u (u_{old}), and the forward-backward sweep method must be performed again. The method stops when u_{update} is within the accepted tolerance. If the latter is the case, then these are the final values, and the optimal control has been determined. It should be noted that convergence can also occur with the variables x and λ, meaning that once these variables achieve convergence, the method stops as well.

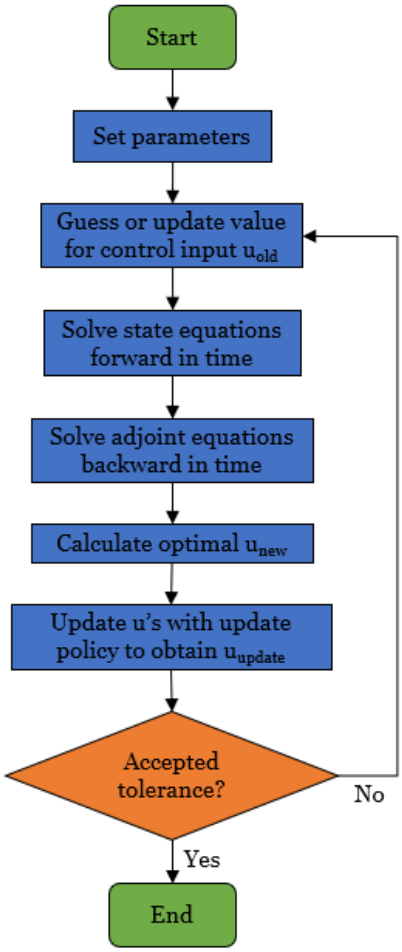


Figure 2.3: Block diagram forward backward sweep method

Chapter 3: SIDAREV Model Analysis

This chapter describes the epidemiological compartment model that is used for this research. The model used is a modified version of the existing SIDARE model used in the research of Kasis et al. (2021). In the proposed model, a vaccination compartment is added to the model, and therefore this model is called SIDAREV.

3.1 Compartment model description

The compartment model consists of seven compartments, namely Susceptible (S), Infected Undetected (I), Infected Detected (D), Acutely symptomatic - Threatened (A), Recovered (R), Extinct (E) and Vaccinated (V). A schematic representation of the SIDAREV model is shown in figure 3.1.

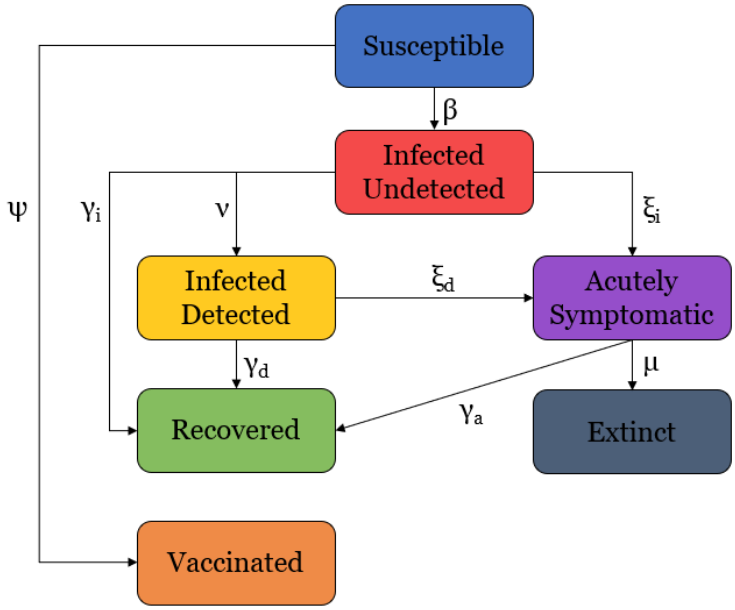


Figure 3.1: Schematic representation of the SIDAREV compartment model.

It can be seen that there are parameters between the different compartments. A certain value can be given to the parameters that indicate the transfer rate between the different compartments. By not assigning values to certain parameters, it is possible to exclude compartments. For example, by not giving a value to the parameter ψ, that is, when $\psi = 0$, no transfer will occur to the 'Vaccinated' compartment, and as a result, the model functions similar to the SIDARE model. It is also possible to omit the vaccination compartment and link the vaccination parameter ψ directly to the recovered compartment (Couras et al., 2020). However, it was decided not to do this because it is considered less clear.

3.2 System dynamics

The dynamical behavior of a disease outbreak can be mathematically described with a set of differential equations (i.e. the dynamic system), and can be described as follows:

$$\dot{x_1} = -\beta x_1 x_2 - \psi x_1 \tag{3.1}$$

$$\dot{x_2} = \beta x_1 x_2 - \gamma_i x_2 - \xi_i x_2 - \nu x_2 \tag{3.2}$$

$$\dot{x_3} = \nu x_2 - \gamma_d x_3 - \xi_d x_3 \tag{3.3}$$

$$\dot{x_4} = \xi_i x_2 + \xi_d x_3 - \gamma_a x_4 - \mu x_4 \tag{3.4}$$

$$\dot{x_5} = \gamma_i x_2 + \gamma_d x_3 + \gamma_a x_4; \tag{3.5}$$

$$\dot{x_6} = \mu x_4 \tag{3.6}$$

$$\dot{x_7} = \psi x_1 \tag{3.7}$$

$$x_1(0) = x_{1_0}, x_2(0) = x_{2_0}, x_3(0) = x_{3_0}, x_4(0) = x_{4_0}, x_5(0) = x_{5_0}, x_6(0) = x_{6_0}, x_7(0) = x_{7_0} \tag{3.8}$$

Note that for computational reasons the variables (S, I, D, A, R, E, V) have been changed to x-values $\in [0, 1]$ and for clarity this means the following:

- $x_1(t)$ portion of susceptible population at time t
- $x_2(t)$ portion of infected - undetected population at time t
- $x_3(t)$ portion of infected - detected population at time t
- $x_4(t)$ portion of threatened population at time t
- $x_5(t)$ portion of recovered population at time t
- $x_6(t)$ portion of deceased population at time t
- $x_7(t)$ portion of vaccinated population at time t

Furthermore the values x_{1_0}, x_{2_0}, x_{3_0}, x_{4_0}, x_{5_0}, x_{6_0}, x_{7_0} are the initial values of x_1, x_2, x_3, x_4, x_5, x_6, $x_7 \in [0, 1]$. The parameters that are used are constant and non-negative and their functions are described below.

- β describes the infection rate for susceptible individuals.
- ν describes the rate of detection of infected individuals based on the level of testing.
- γ_i, γ_d, γ_a describe the recovery rate for infected undetected, infected detected, and acutely symptomatic (threatened) individuals.
- ξ_i, ξ_d describe the rate at which infected individuals become acutely symptomatic (threatened).
- ν describes the rate at which acutely symptomatic individuals decease.
- ψ describes the rate at which susceptible individuals got vaccinated.

Assumptions
The SIDAREV uses the same assumptions as the SIDARE model as described in the research of Kasis et al. (2021). Also, there is an additional assumption regarding the vaccinated individuals. For clarity, the assumptions are listed below.

- Recovered individuals are immune to the disease and thus cannot become susceptible anymore.
- The considered population is constant; this means 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 detected individuals (thus positively tested individuals) are assumed to be isolated immediately so that they do not contribute to new infections.
- Infected individuals become first acutely symptomatic before they decease.
- Acutely symptomatic individuals should be hospitalized as they are considered threatened for decease.
- Only susceptible individuals are vaccinated.
- Vaccinated individuals are immune to the disease and thus cannot become susceptible anymore.

Chapter 4: Optimal Control Design for SIDAREV Model

This chapter describes the optimal control design for the 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. Subsequently, it is explained and substantiated which parameters are used. Finally, the proposed control design is validated based on simulations.

4.1 Control design

The control inputs u_1, u_2 and u_3 have been added to the SIDAREV model, and their functions are explained in the following sections. For the sake of clarity, the schematic SIDAREV is shown in figure 4.1 with the controllers incorporated.

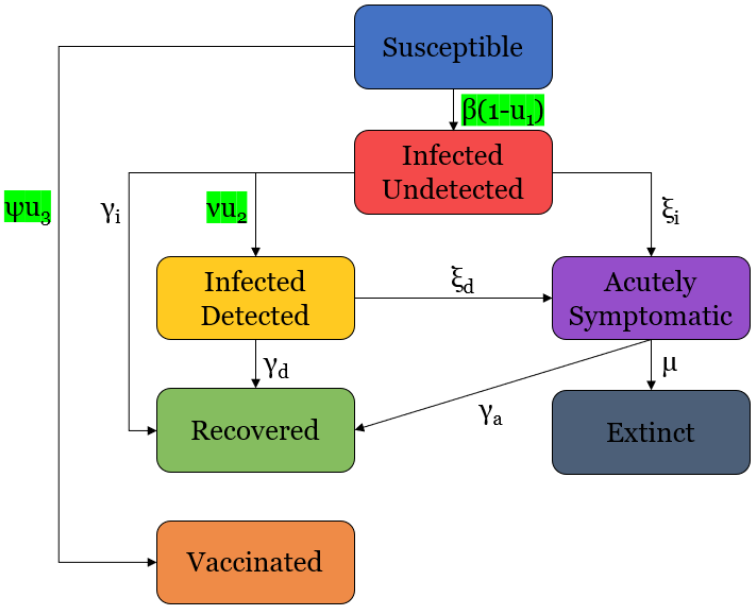


Figure 4.1: Schematic SIDAREV model with controllers

4.1.1 Control input u_1 for controlling the rate of infection

The first controller applied to the model is control input u_1. Control input u_1 indicates the strength of the government interventions. The function of this control input is to optimize the infection rate β. To realise this, the current β is replaced by $\beta(1 - u_1)$. If no control input is applied, the control input will remain 0, and the infection rate will not be affected. However, once u_1 gets a value, the term $(1 - u_1)$ will become smaller than 1, affecting the β parameter.

4.1.2 Control input u_2 for controlling the rate of testing

The second controller applied to the model is control input u_2. Control input u_2 indicates the strength of the testing policy. The function of this control input is to optimize the testing parameter ν. By replacing the parameter ν in the model with νu_2, the ν parameter can be controlled. Since ν is multiplied with control input u_2, the value of ν changes linearly with the control input. If there is no control input, so where $u_2 = 0$, the value of ν will also be 0. However, if the value of $u_2 \geq 0$, the value of ν would increase.

For this study, it is assumed that the minimum testing rate is 0, meaning that no tests are being done, and the maximum testing rate is 0.1, which means that 1 in 10 infected individuals got tested positively, and must go into quarantine. In addition, a distinction is made between no, slow and fast testing, with the testing rates being $\nu = 0$, $\nu = 0.05$ and $\nu = 0.1$, respectively. The assumptions made for the testing rates are described in section 4.4.

4.1.3 Control input u_3 for controlling the rate of vaccination

The third controller applied to the model is control input u_3. Control input u_3 indicates the strength of the vaccination policy. The function of this control input is to optimize the vaccination rate ψ. By replacing the parameter ψ in the model with ψu_3, the ψ parameter can be controlled. Since ψ is multiplied with control input u_3, the value of ψ changes linearly with the control input. If there is no control input, where $u_3 = 0$, the value of ψ will also be 0. However, if the value of $u_3 \geq 0$, the value of ψ would increase.

For this study, it is assumed that the minimum vaccination rate is 0, meaning no vaccinations are administered, and the maximum vaccination rate is 0.01, meaning 1 in 100 people is vaccinated daily. In addition, a distinction is made between no, slow, medium and fast vaccination, with the vaccination rates being $\psi = 0$, $\psi = 0.001$, $\psi = 0.0025$ and $\psi = 0.01$, respectively. The assumptions made for the vaccination rates are described in section 4.4.

4.1.4 Mortality rate when healthcare capacity is exceeded

As with the research of Kasis et al. (2021), the impact of healthcare capacity on mortality rate is included. It is assumed that once the healthcare capacity is exceeded, the mortality rate will increase. This is because regular care can no longer take place at this time, and as a result, many more individuals decease. This change in the mortality rate can be modelled as follows:

$$\bar{\mu}(x_4) = \begin{cases} \mu x_4, \text{ if } x_4 \leq \bar{h}, \\ \mu\bar{h} + \hat{\mu}(x_4 - \bar{h}), \text{ if } x_4 > \bar{h}, \end{cases} \tag{4.1}$$

where the function $\bar{\mu} : \mathbb{R} \to \mathbb{R}$ describes the mortality of the acutely symptomatic population. Furthermore, $\bar{h}$ indicates the hospital capacity and $\hat{\mu}$ a five times higher than the current morality rate, i.e. $\hat{\mu} = 5\mu$. The formula states that the more the healthcare capacity is exceeded, the higher the mortality rate becomes.

4.1.5 Dynamics of controlled model

The dynamics of the SIDAREV model including the controllers and the change of the mortality rate can be described as follows:

$$\left.\begin{aligned} \dot{x_1} &= -\beta x_1 x_2 (1 - u_1) - \psi x_1 u_3 \\ \dot{x_2} &= \beta x_1 x_2 (1 - u_1) - \gamma_i x_2 - \xi_i x_2 - \nu x_2 u_2 \\ \dot{x_3} &= \nu x_2 u_2 - \gamma_d x_3 - \xi_d x_3 \\ \dot{x_4} &= \xi_i x_2 + \xi_d x_3 - \gamma_a x_4 - \bar{\mu}(x_4) \\ \dot{x_5} &= \gamma_i x_2 + \gamma_d x_3 + \gamma_a x_4 \\ \dot{x_6} &= \bar{\mu}(x_4) \\ \dot{x_7} &= \psi x_1 u_3 \end{aligned}\right\} \tag{4.2}$$

4.2 Optimal control problem

The optimal control problem consists of a function that minimizes the threatened and deceased individuals. Besides, the costs associated with the implementation of an optimal control strategy have also been added. The function is defined over a time period of $[0, T]$.

The first term of the optimization function refers to the integral of the portion of threatened individuals (x_4) and can be described as

$$\int_0^T \frac{c_1}{2} x_4(t)^2 dt. \tag{4.3}$$

This term enumerates the portion of threatened individuals to minimize them in the optimization function. The term c_1 is a positive weight factor to get balance in the optimization function. Specifically, the factor describes how much weight is given to the portion of threatened individuals compared with the costs of intervention policies. When the weight factor c_1 is high, the focus is to save people who become acutely symptomatic or threatened. On the other hand, when the weight factor c_1 is low, the focus is on minimizing the cost of intervention policies, resulting in a low optimal control. As can be seen, the term is quadratic because of the ease of the solution.

The second, third and fourth terms of the optimization function refer to the optimal control inputs u_1, u_2 and u_3. For the same reason as before, an integral and a quadratic function are used. The functions are as follows:

$$\int_0^T (\frac{b_1}{2} u_1^2 + \frac{b_2}{2} u_2^2 + \frac{b_3}{2} u_3^2) dt. \tag{4.4}$$

The factors b_1, b_2 and b_3 measures the relative cost of optimal control input and can be adjusted as desired.

The last term of the optimization function ensures that the total portion of deceased individuals at the final time T can be minimized. This term can be described as follows:

$$c_2 x_6(T). \tag{4.5}$$

As with the first term, the factor c_2 provides a positive weight factor to balance the optimization function. Compared to the first term, the difference with this function is that with a high weight factor of c_2, the focus is to save people who might decease. Also, when weight factor c_2 is small, the focus is on minimizing the cost of intervention policies, resulting in a low optimal control.

The total optimization function is the sum of all the terms mentioned and can be described as

$$J_c(x_4, x_6, u_1, u_2, u_3) = \int_0^T (\frac{c_1}{2} x_4(t)^2 + \frac{b_1}{2} u_1^2 + \frac{b_2}{2} u_2^2 + \frac{b_3}{2} u_3^2) dt + c_2 x_6(T). \tag{4.6}$$

The optimal control problem is the minimization of the cost function where the cost function is subjected to the constraints given by dynamics or the epidemiological model. The optimal

control problem can be described as follows:

$$
\begin{aligned}
&\min J(x_4, x_6, u_1, u_2, u_3) = \int_0^T (\tfrac{c_1}{2} x_4(t)^2 + \tfrac{b_1}{2} u_1^2 + \tfrac{b_2}{2} u_2^2 + \tfrac{b_3}{2} u_3^2) dt + c_2 x_6(T) \\
&\text{subject to} \\
&\quad \dot{x_1} = -\beta x_1 x_2 (1 - u_1) - \psi x_1 u_3 \\
&\quad \dot{x_2} = \beta x_1 x_2 (1 - u_1) - \gamma_i x_2 - \xi_i x_2 - \nu x_2 u_2 \\
&\quad \dot{x_3} = \nu x_2 u_2 - \gamma_d x_3 - \xi_d x_3 \\
&\quad \dot{x_4} = \xi_i x_2 + \xi_d x_3 - \gamma_a x_4 - \bar{\mu}(x_4) \\
&\quad \dot{x_5} = \gamma_i x_2 + \gamma_d x_3 + \gamma_a x_4; \\
&\quad \dot{x_6} = \bar{\mu}(x_4) \\
&\quad \dot{x_7} = \psi x_1 u_3 \\
&\quad 0 \leqslant u_1 \leqslant 0.8 \\
&\quad 0 \leqslant u_2 \leqslant 1 \\
&\quad 0 \leqslant u_3 \leqslant 1 \\
&\quad x_1(0) = x_{1_0}, \quad x_2(0) = x_{2_0}, \quad x_3(0) = x_{3_0}, \quad x_4(0) = x_{4_0}, \\
&\quad x_5(0) = x_{5_0}, \quad x_6(0) = x_{6_0}, \quad x_7(0) = x_{7_0}.
\end{aligned}
\tag{4.7}
$$

4.3 Applying the Pontryagin's maximum principle

In this section, Pontryagin's maximum principle is applied. First, the Hamiltonian function is derived. Thereafter, the adjoint system is created. Finally, the solution to the optimal control problem is given.

The Hamiltonian function can be described as follows:

$$
\begin{aligned}
H(x, u, \lambda, t) = \frac{c_1}{2} x_4(t)^2 + \frac{b_1}{2} u_1(t)^2 + \frac{b_2}{2} u_2(t)^2 + \frac{b_3}{2} u_3(t)^2 + \lambda_1 k_1(t) + \lambda_2 k_2(t) \\
+ \lambda_3 k_3(t) + \lambda_4 k_4(t) + \lambda_5 k_5(t) + \lambda_6 k_6(t) + \lambda_7 k_7(t)
\end{aligned}
$$

where,

$$
\begin{aligned}
&k_1 = -\beta x_1 x_2 (1 - u_1) \\
&k_2 = \beta x_1 x_2 (1 - u_1) - \gamma_i x_2 - \xi_i x_2 - \nu x_2 u_2 \\
&k_3 = \nu x_2 u_2 - \gamma_d x_3 - \xi_d x_3 \\
&k_4 = \xi_i x_2 + \xi_d x_3 - \gamma_a x_4 - \bar{\mu}(x_4) \\
&k_5 = \gamma_i x_2 + \gamma_d x_3 + \gamma_a x_4 \\
&k_6 = \bar{\mu}(x_4) \\
&k_7 = \psi x_1 u_3
\end{aligned}
\tag{4.8}
$$

To create the adjoint system, the Hamiltonian function must be differentiated with respect to the adjoint variables $\lambda_j, j \in 1, 2, ..., 7$. This results in the following adjoint system:

$$
\begin{aligned}
&\dot{\lambda_1} = \tfrac{d\lambda_1}{dt} = -\tfrac{\partial \mathrm{H}}{\partial x_1} = -\{\lambda_1(-\beta x_2(1 - u_1) + \lambda_2(\beta x_2(1 - u_1)) + \lambda_7 \psi u_3\} \\
&\dot{\lambda_2} = \tfrac{d\lambda_2}{dt} = -\tfrac{\partial \mathrm{H}}{\partial x_2} = -\{\lambda_1(-\beta x_1(1 - u_1)) + \lambda_2(\beta x_1(1 - u_1) - \gamma_i - \xi_i - \nu u_2) + \lambda_3 \nu u_2 + \lambda_4 \xi_i\} \\
&\dot{\lambda_3} = \tfrac{d\lambda_3}{dt} = -\tfrac{\partial \mathrm{H}}{\partial x_3} = -\{\lambda_3(-\gamma_d - \xi_d) + \lambda_4 \xi_d\} \\
&\dot{\lambda_4} = \tfrac{d\lambda_4}{dt} = -\tfrac{\partial \mathrm{H}}{\partial x_4} = -\{\lambda_4(-\gamma_a - \bar{\mu}(x_4)) + \lambda_6 \bar{\mu}(x_4) + c_1 x_4\} \\
&\dot{\lambda_5} = \tfrac{d\lambda_5}{dt} = -\tfrac{\partial \mathrm{H}}{\partial x_5} = 0 \\
&\dot{\lambda_6} = \tfrac{d\lambda_6}{dt} = -\tfrac{\partial \mathrm{H}}{\partial x_6} = 0 \\
&\dot{\lambda_7} = \tfrac{d\lambda_7}{dt} = -\tfrac{\partial \mathrm{H}}{\partial x_7} = 0
\end{aligned}
$$

Simplifying gives:

$$\left.\begin{aligned}
\dot{\lambda_1} &= (\lambda_1 - \lambda_2)\beta x_2(1-u_1) + \lambda_7\psi u_3 \\
\dot{\lambda_2} &= (\lambda_1 - \lambda_2)\beta x_1(1-u_1) + \lambda_2(\gamma_i + \xi_i + \nu u_2) - \lambda_3\nu u_2 - \lambda_4\xi_i \\
\dot{\lambda_3} &= \lambda_3(\gamma_d + \xi_d) - \lambda_4\xi_d \\
\dot{\lambda_4} &= \lambda_4(\gamma_a + \bar{\mu}(x_4)) - \lambda_6\bar{\mu}(x_4) - c_1x_4 \\
\dot{\lambda_5} &= 0 \\
\dot{\lambda_6} &= 0 \\
\dot{\lambda_7} &= 0
\end{aligned}\right\} \tag{4.9}$$

Furthermore, the transversality conditions can be described as:

$$\lambda(T) = \frac{\partial S}{\partial x}(x(T) = \frac{\partial}{\partial x}c_2x_6(T) = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ c_2 \\ 0 \end{pmatrix} \tag{4.10}$$

The optimal controls can be determined by taking the derivative of the Hamiltonian function with respect to the optimal control input u. For the optimal control inputs u_1, u_2 and u_3 this means the following.

$$\begin{aligned}
&\frac{\partial H}{\partial u_1} = b_1u_1 - \lambda_1\beta x_1x_2 + \lambda_2\beta x_1x_2 = 0 \\
&u_1 = \begin{cases} 0 & \text{if} \quad \frac{\partial H}{\partial u_1} < 0 \\ \frac{(\lambda_2-\lambda_1)\beta x_1x_2}{b_1} & \text{if} \quad \frac{\partial H}{\partial u_1} = 0 \\ 0.8 & \text{if} \quad \frac{\partial H}{\partial u_1} > 0 \end{cases}
\end{aligned} \tag{4.11}$$

$$\begin{aligned}
&\frac{\partial H}{\partial u_2} = b_2u_2 - \lambda_2\nu x_2 + \lambda_3\nu x_2 = 0 \\
&u_2 = \begin{cases} 0 & \text{if} \quad \frac{\partial H}{\partial u_2} < 0 \\ \frac{(\lambda_2-\lambda_3)\nu x_2}{b_2} & \text{if} \quad \frac{\partial H}{\partial u_2} = 0 \\ 1 & \text{if} \quad \frac{\partial H}{\partial u_2} > 0 \end{cases}
\end{aligned} \tag{4.12}$$

$$\begin{aligned}
&\frac{\partial H}{\partial u_3} = b_3u_3 - \lambda_1\psi x_1 + \lambda_7\psi x_1 = 0 \\
&u_3 = \begin{cases} 0 & \text{if} \quad \frac{\partial H}{\partial u_3} < 0 \\ \frac{(\lambda_1-\lambda_7)\psi x_1}{b_3} & \text{if} \quad \frac{\partial H}{\partial u_3} = 0 \\ 1 & \text{if} \quad \frac{\partial H}{\partial u_3} > 0 \end{cases}
\end{aligned} \tag{4.13}$$

The optimality conditions can then be described as:

$$\begin{aligned}
u_1^*(t) &= \min[0.8, \max(0, \tfrac{(\lambda_2-\lambda_1)\beta x_1x_2}{b_1})] \\
u_2^*(t) &= \min[1, \max(0, \tfrac{(\lambda_2-\lambda_3)\nu x_2}{b_2})] \\
u_3^*(t) &= \min[1, \max(0, \tfrac{(\lambda_1-\lambda_7)\psi x_1}{b_3})]
\end{aligned} \tag{4.14}$$

4.4 Parametrization of the model

Assumptions have been made for the model based on the COVID-19 disease outbreak. This section describes the assumptions made for the various parameters. The parameters with corresponding description and values are summarized in table 4.1.

The infection rate β is calculated based on a reproduction number. A reproduction number indicates how many second cases one case will give in a disease outbreak. The basic reproduction number (R_0) is the reproduction number when there is no immunity to previous exposures of the disease and when no vaccinations have been made to immunize a disease, or deliberate interventions have been made against the spread of disease. From the latter, the infection rate can be calculated with the formula $\bar{R}_0 = \beta s_0 / (\gamma_i + \xi_i + \nu)$. The basic reproduction is assumed to be 3.27 (Yuan et al., 2020). Assuming that at the beginning of a disease outbreak, i.e. when $t = 0$, the rate of detection is 0, the infection rate is 0.251.

According to WHO (2020) the recovery rate for mild cases is approximately two weeks. Therefore, it has been assumed that both the recovery rate for detected (γ_d) and undetected (γ_i) individuals are 1/14, which means that an individual has recovered 14 days after infection. The recovery rate of an acutely symptomatic (or threatened) individual is the length of time that an individual is hospitalized. According to Wang et al. (2020), an average hospitalization takes 12.4 days. For this reason, the recovery rate for threatened individuals (γ_a) is assumed to be 1/12.4.

The testing rates are taken from the research of Kasis et al. (2021), where the minimum and maximum testing rates are between 0 and 0.1. A distinction is made by applying different testing policies, namely 'no testing', 'slow testing' and 'fast testing'. In slow testing, 5% of the infected population is tested positive, and in fast testing, 10% is tested positive on the disease. The associated testing rates (ν) are 0, 0.05 and 0.1, respectively.

The rate that infected individuals become threatened and therefore also have to be admitted to hospital has also been taken over from the research of Kasis et al. (2021). The rate is based on findings from the study of Verity et al. (2020), where estimates are made of the severity of COVID-19 and where the hospitalization rate per age group are examined. The rate at which both infected individuals become threatened (ξ_i) and infected detected individuals become threatened (ξ_d) is assumed to be 0.0053.

The healthcare capacity indicates how many care beds are available. The healthcare capacity is assumed to be 333 per 100,000 individuals (Rhodes et al., 2012). The corresponding healthcare capacity parameter ($\hat{h}$) is therefore $333/100,000 = 0.00333$.

Several studies have shown that the disease mortality rate of COVID-19 is just below 1% Mallapaty (2020). In the research of Kasis et al. (2021), a disease mortality rate of 0.0085 and for convenience, it has been chosen to use the same mortality rate (μ). Also, the article of Catena and Holweg (2020) reads that when the healthcare capacity is exceeded up to about 5 times more people decease, thus the mortality rate when healthcare capacity is exceeded is assumed to be 5μ.

The vaccination rates are assumed based on current vaccination rates achieved by countries worldwide (in the period December 2020 to February 2021). An overview of the data on vaccination rates is shown in chapter B. According to OurWorldData (2021), Israel is currently the fastest country that vaccinates, achieving vaccination rates of over 2 in 100 people per day. Since two vaccinations are currently required for immunity, the rate at which immunity is achieved is $1/100 = 0.01$. This rate is therefore used in the controlled model and characterized as 'fast vaccination'. Furthermore, it can be seen that the United Kingdom can vaccinate 0.5 in 100

people per day, resulting in a rate that can be used in the model of $2.5/1000 = 0.00025$. This rate is characterized as 'medium vaccination'. Finally, European countries such as The Netherlands, Germany, Italy and Belgium are currently a lot slower with vaccinations. The vaccination rate used for the model is $1/1000 = 0.0001$ and is characterized as 'slow vaccination'.

Table 4.1: Overview parameters for SIDAREV model

Symbol	Description	Value
β	Infection rate susceptible individuals	2/3
γ_i	Recovery rate undetected individual	1/14
γ_d	Recovery rate detected individual	1/14
γ_a	Recovery rate threatened individual	1/12.4
ν	Rate of detection of infected individuals (level of testing)	0 - 0.10
ξ_i	Rate infected individual threatened	0.0053
ξ_d	Rate infected detected individual threatened	0.0053
$\hat{h}$	Healthcare capacity	0.00333
μ	Mortality rate of disease	0.0085
$\bar{\mu}$	Mortality rate of disease when healthcare capacity is exceeded	5μ
ψ	Vaccination rate of susceptible individuals	0 - 0.01

The initial conditions for the SIDAREV model are as follows. It is assumed that 0.0001% of the population is infected with the virus at the start of the pandemic. The susceptible population is thus $1 - 0.0001\%$. Furthermore, it is assumed that there are no detected, acutely symptomatic, deceased or recovered individuals at the start of the pandemic. Also, it is assumed that there are no vaccinated individuals at the start of the pandemic. The pandemic is simulated with the above parameters on a time frame of $[0, T]$. The final time T is set equal to 365 days.

Table 4.2: Initial conditions SIDAREV model

State variable	Symbol	Initial value
S_0	x_{1_0}	$1 - 0.00001$
I_0	x_{2_0}	0.00001
D_0	x_{3_0}	0
A_0	x_{4_0}	0
R_0	x_{5_0}	0
E_0	x_{6_0}	0
V_0	x_{7_0}	0

4.5 Validation of the control design

In the research of Kasis et al. (2021), different government intervention strategies are compared to a certain percentage of the deceased population while different testing policies are applied. The different testing policies are no testing at all ($\nu = 0$), slow testing ($\nu = 0.05$) and fast testing ($\nu = 0.1$). To validate the model and approach described in this chapter, it was decided to perform the same experiments. The results of the experiments can be seen in the figures below. The results are compared with the results of the experiment conducted by Kasis et al. (2021) (chapter C). It appears that the results are the same, and therefore it is assumed that the control design described in this chapter is valid.

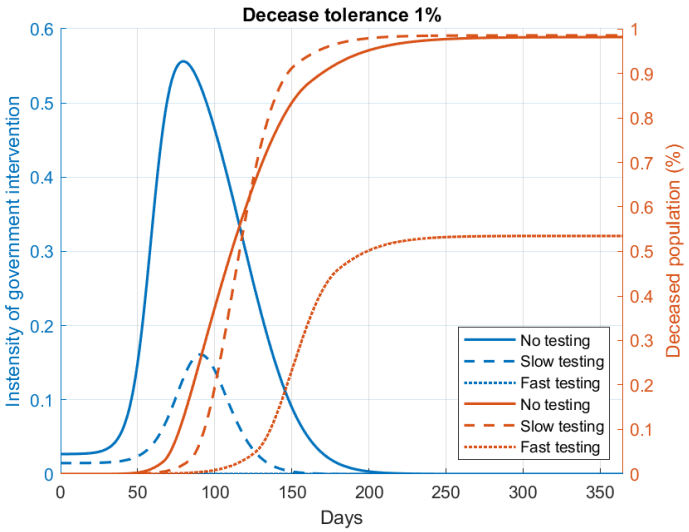


Figure 4.2: Optimal intervention with varying testing policies - decease tolerance is 1%

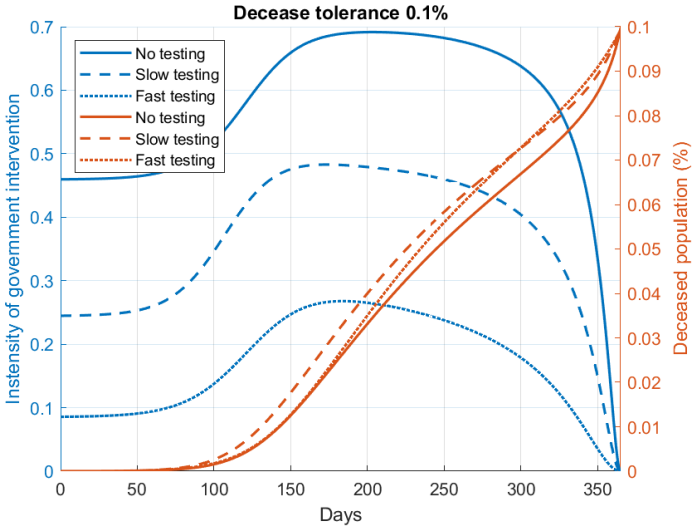


Figure 4.3: Optimal intervention with varying testing policies - decease tolerance is 0.1%

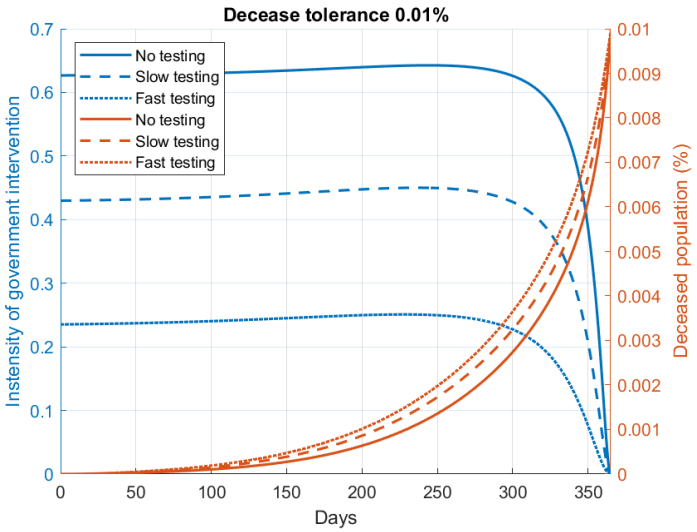


Figure 4.4: Optimal intervention with varying testing policies - decease tolerance is 0.01%

Chapter 5: Experiments Design

Section 5.1 describes the experiments related to optimizing control inputs u_1, u_2 and u_3. In these experiments, one or more control inputs are switched off or fixed to a value to analyze the influence of specific control input. Section 5.2 explains the experiments for the optimization of an optimal government intervention strategy when a vaccine is available and when a decease tolerance is maintained. Section 5.3 describes the experiment comparing optimal control with non-optimal controls. For clarity, the created optimization function from section 4.2 is stated again:

$$J_c(x_4, x_6, u_1, u_2, u_3) = \int_0^T (\frac{c_1}{2}x_4(t)^2 + \frac{b_1}{2}u_1^2 + \frac{b_2}{2}u_2^2 + \frac{b_3}{2}u_3^2)dt + c_2x_6(T). \tag{5.1}$$

5.1 Experiment 1-5: Optimizing control inputs u_1, u_2 and u_3

The purpose is to optimize the control inputs both independently and simultaneously. Experiment 1 concerns the case where no control inputs are optimized. In experiments 2, 3, and 4, the control inputs u_1, u_2 and u_3, respectively, are optimized separately from each other. In experiment 5 control inputs u_1 and u_3 are optimized simultaneously. In experiment 6 control inputs u_1, u_2 and u_3 are optimized simultaneously.

Experiment 1: No optimization of control inputs

No control inputs are optimized in this experiment. This experiment is performed to show the course of the different variables of the SIDAREV model. In this experiment, all control inputs are set to 0. This means that no government interventions are carried out, no tests are taken, and no vaccinations are given. In other words, this experiment shows what the effects of a disease outbreak are when a disease can run its free course.

Experiment 2: Optimization of control input u_1

This experiment concerns the case where only control u_1 is optimized. Control input u_1 affects the infection rate (β) of susceptible individuals. The maximum value that u_1 can take is 0.8. This means that the number of infection can be decreased at its max by 80%. In this experiment, multiple scenarios are created in which weight factor c_1 changes continuously such that different effects on the optimal control can be analyzed. The c_1 values indicate costs related to the threatened population, thus the higher c_1 the more costs are given to the threatened population. The scenarios start with weight factor $c_1 = 0$ and are continuously increased with either a step size of 1,000 (section 6.1.2) or 10,000 (section 6.1.2). The following assumptions are made:

- No vaccinations are available, i.e. control input $u_3 = 0$
- A constant testing rate is applied, whereas u_2 is fixed to 1 and the testing policies are:
  - fast testing: $\nu = 0.1$ (results in section 6.1.2)
  - slow testing: $\nu = 0.05$ (results in section D.1)
  - no testing: $\nu = 0$ (results in section D.1)

Experiment 3: Optimization of control input u_2

This experiment concerns the case where only control u_2 is optimized. Control input u_2 affects the rate of detection (ν) of infected individuals. The maximum value that u_2 can take is 1. When the control input equals 0, the rate of detection of infected individuals is 0%. When the control input equals 1, the rate of detection of infected individuals is 100%. In this experiment, multiple scenarios are created in which weight factor c_1 changes continuously such that different effects on the optimal control can be analyzed. The scenarios start with weight factor $c_1 = 0$ and are

continuously increased with either a step size of 1,000 (section 6.1.3) or 10,000 (section 6.1.3). The following assumptions are made:

- No government intervention is done, i.e. control $u_1 = 0$
- No vaccinations are available, i.e. control input $u_3 = 0$
- The (maximum) testing rate ν is set to 0.1

Experiment 4: Optimization of control input u_3
This experiment concerns the case where only control u_3 is optimized. Control input u_3 affects the rate of vaccination (ψ) of susceptible individuals. The maximum value that u_3 can take is 1. When no control input is applied, the rate of vaccination of susceptible individuals is 0%. When the maximal control input is applied, the rate of vaccination of susceptible individuals is 100%. In this experiment, multiple scenarios are created in which weight factor c_1 changes continuously such that different effects on the optimal control can be analyzed. The scenarios start with weight factor $c_1 = 0$ and are continuously increased with either a step size of 1,000 (section 6.1.4) or 10,000 (section 6.1.4). The following assumptions are made:

- No government intervention is done, i.e. control $u_1 = 0$
- A constant (fast) testing rate is applied, i.e. $u_1 = 1$ and $\nu = 0.1$
- The (maximum) vaccination rate ψ is set to 2.5/1000

Experiment 5: Optimizing control inputs u_1, u_2 and u_3 simultaneously
This experiment concerns the case where the control inputs u_1, u_2 and u_3 are optimized simultaneously. The influence of the control inputs will be analyzed based on a changing weight factor c_1. Scenarios are created in which weight factor c_1 changes continuously. The scenarios start with weight factor $c_1 = 0$ and are continuously increased with either a step size of 1,000 (section 6.1.5) or 10,000 (section 6.1.5). The following assumptions are made:

- The (maximum) testing rate ν is set to 0.1
- The (maximum) vaccination rate ψ is set to 2.5/1000
- The costs of applying control input u_1 are the most expensive, followed by control input u_2 and the cheapest is applying control input u_1
- The weight factors for b are assumed to be $b_1 = 3$, $b_2 = 2$ and $b_3 = 1$

5.2 Experiment 6: Optimal exit strategies

This experiment examines optimal exit strategies for a disease outbreak. As soon as a vaccine is available, the goal is to optimally eradicate a disease or build up group immunity so that no new infections occur. This experiment explores how optimal government interventions (u_1) can be performed when different vaccination policies are applied. Instead of continuously adjusting the weight factor c_1, a decease tolerance of 0.01% is maintained in this experiment. This means that the weight factors are adjusted so that the maximum percentage of the deceased population at the final time does not exceed 0.01% of the total population. The vaccination policies used in this experiment are, no vaccination ($\psi = 0$), slow vaccination ($\psi = 1/1000$), medium vaccination ($\psi = 2.5/1000$) and fast vaccination ($\psi = 1/100$). It is assumed that there is a test policy at all times where fast testing is applied, i.e. $\nu = 0.1$.

The experiment is run three times using different initial conditions. Different initial conditions represent different stages of the progress of the disease outbreak.

- Experiment 6A uses initial conditions representing a disease outbreak where 0.0001% of the population is infected with the disease.

- Experiment 6B uses initial conditions that represent a disease outbreak where 0.001% of the population is infected with the disease.
- Experiment 6C uses initial conditions representing a disease outbreak where 0.06% of the population is infected with the disease.

5.3 Experiment 7: Different (non-optimal) control strategies

In this experiment, different control strategies will be applied to analyse to what extent a non-optimal control strategy differs from an optimal control strategy. First of all, the most extreme control possibilities will be applied, namely the minimum and maximum control. The minimum control inputs for all control inputs u_1, u_2 and u_3 are equal to zero. The maximum control strategy for control input u_1 is 0.8 and the maximum control inputs for both u_2 and u_3 is 1. Also the optimal control strategy whereby weight factor c_1 is set to $50,000$ will be applied for all control inputs u_1, u_2 and u_3. Finally, the average of the optimal control strategy will be calculated and then will be set as a continuous control input. By plotting these four different control strategies in one figure, it is possible to compare the optimal government intervention strategies and their influences on the threatened and deceased population. Experiments 7A, 7B and 7C analyze the control inputs u_1, u_2 and u_3, respectively.

Chapter 6: Results from Experiments

In this chapter, the results of the simulation experiments are described.

6.1 Results experiment 1-5: Optimizing control inputs u_1, u_2 and u_3

The results are discussed in which optimal control inputs u_1, u_2 and u_3 are optimized separately and simultaneously.

6.1.1 Results from experiment 1: No optimization of control inputs

Figure 6.1 shows the graph from the simulation where no optimization of control inputs are done and where all control inputs are fixed to 0. Thus, no government intervention is done, no tests are taken, and no vaccinations are given. At the start of the disease outbreak, almost the entire population is in the susceptible state. The initial condition of the susceptible individuals (x_1) is 1-0.00001, which equals 99.99%. The susceptible population decreases as infections occur. There is a clear peak in the infected undetected individuals (x_2). The peak reaches its top on day 59, and by that time, about 34% of the population is infected undetected. No infected detected individuals (x_3) can be seen in the graph because testing is not taking place. A smaller peak can be seen in the threatened individuals (x_4). This peak reaches its top on day 68, and by that time, about 1.6% of the population is in a threatening situation. Moreover, these people must be hospitalized. Since it is assumed that hospitals have a capacity of 0.33% of the population, it can be noted that this capacity is far exceeded. Also, it can be noted that the peak of the threatened individuals is 9 days later than the peak of the infected undetected individuals. It can also be seen that the recovered individuals (x_5) increase as more people have become infected with the disease. At the end of the disease outbreak, the majority of the population, about 95%, is recovered from the disease. There are two reasons why not everyone is recovered from the disease outbreak. The first is that a part of the population is deceased (x_6) at the end of the disease outbreak, namely around 2.1%. The second reason is that the disease has been eradicated because there were too few infected individuals, and too many recovered individuals to create new infections. Finally, it can be seen that no vaccinations have been taken because the vaccinated population (x_7) is 0 during the entire disease outbreak.

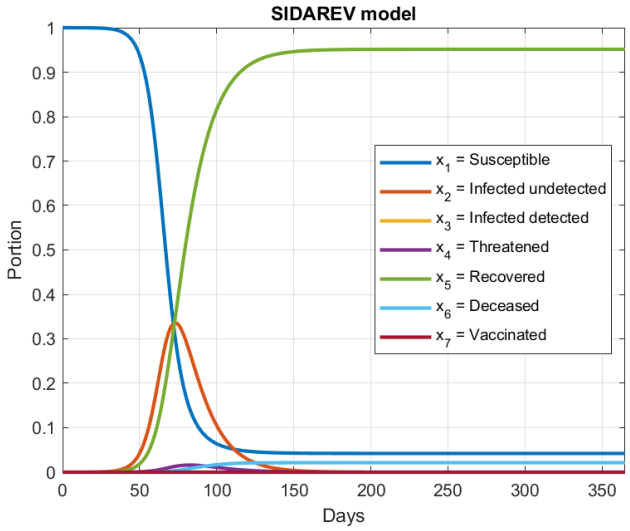


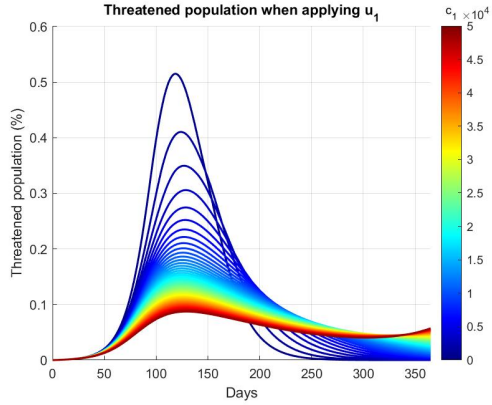
Figure 6.1: System dynamics SIDAREV model without optimizing the control inputs

6.1.2 Results from experiment 2: Optimizing control input u_1

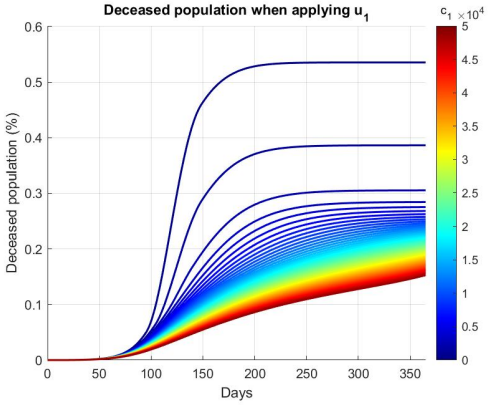
The influence of control input u_1 with different weights for c_1 is analyzed. Two simulations have been performed where the first simulation uses a step size for c_1 of 1,000 (figure 6.2) and the second simulation uses a step size for c_1 of 10,000 (figure 6.3).

Results experiment 2A where step size is 1,000

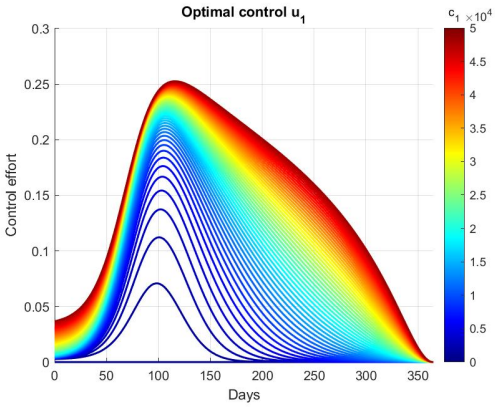
Figure 6.2 shows that the control effort must be built up quickly and then reduced very slowly until the end of the time horizon. The maximum control effort required is 0.25. An increasing weight factor c_1 results in a reduction in the peak of the threatened population from 0.51% to 0.09%. Moreover, the peak of the threatened population is spread over a longer period. Furthermore, an increasing weight factor decreases the deceased population from 0.39% to 0.15%. Also, the amount of the deceased population is more gradual than with a low weight factor.



(a) Threatened population



(b) Deceased population

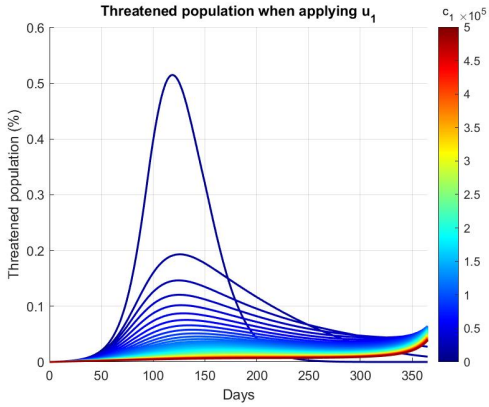


(c) Control effort u_1

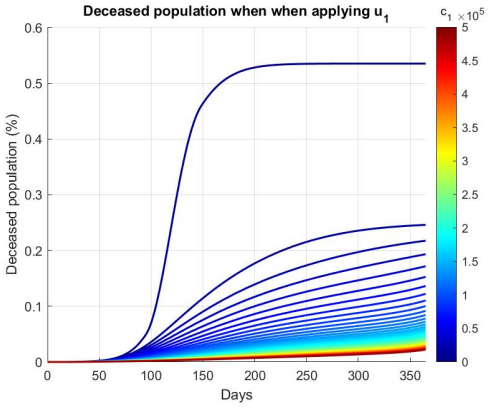
Figure 6.2: Optimization control input u_1 - step size 1,000

Results experiment 2B where step size is 10,000

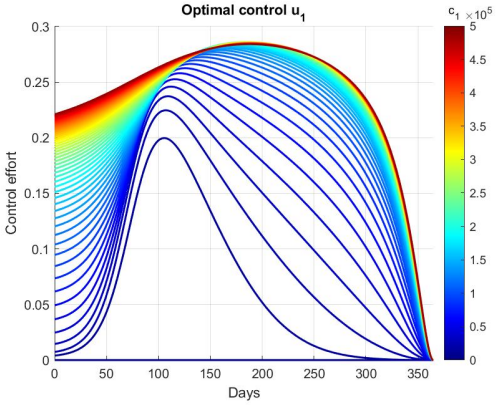
Figure 6.3 shows that a more continuous control effort is required for higher weight factors, i.e. directly start controlling and hold it for a long period. Accordingly, the peak of the threatened population flattens completely. It should be noted that at the end of the horizon, the threatened population is rising again. An increase of up to 0.04% in the threatened population can be seen at the end of the horizon. This is a consequence of a finite horizon problem and is also called 'turnpike behaviour', meaning that the consequences of decision making become visible after the time horizon has passed Köhler et al. (2020). In other words, by stopping the control effort early, the threatened and deceased population increases, but because this mainly falls outside the time horizon, the associated costs are not included in the cost function. Furthermore, an increasing weight factor results in a decrease of the deceased population to 0.02%.



(a) Threatened population



(b) Deceased population



(c) Control effort u_1

Figure 6.3: Optimization control input u_1 - step size 10,000

Conclusion experiment 2

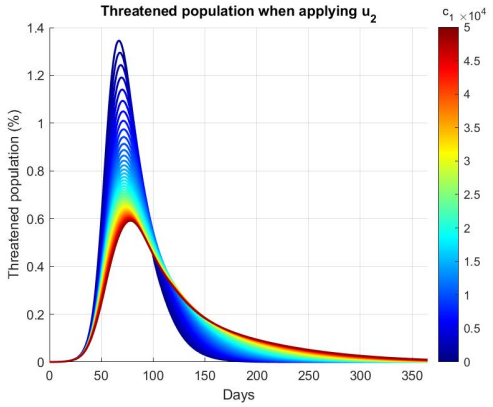
The optimal control strategy is to build up and slowly reduce the control effort quickly. The higher the value for c_1, thus the more costs are given to the threatened population, the longer the control effort must be held. Due to the highest proposed control effort the peak of the threatened population can be reduced by 92% and the deceased population can be reduced by 95% compared to when no control effort is applied.

6.1.3 Results from experiment 3: Optimizing control input u_2

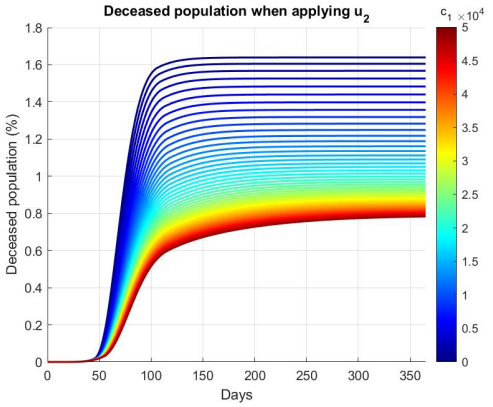
The influence of control input u_2 with different weights for c_1 is analyzed. Two simulations have been performed where the first simulation uses a step size for c_1 of 1,000 (figure 6.4) and the second simulation uses a step size for c_1 of 10,000 (figure 6.5).

Results experiment 3A where step size is 1,000

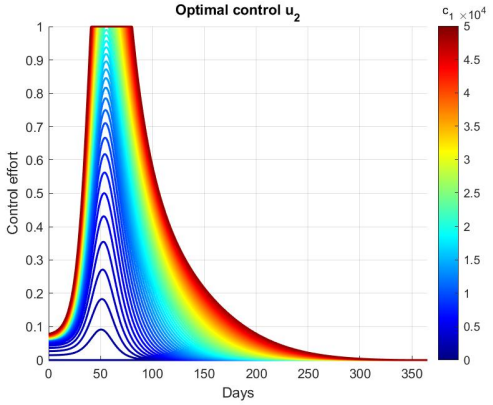
Figure 6.4 shows that the control effort must be built up quickly to the maximum and must remain at maximum for a while and then be reduced again until the end of the time horizon. The maximum control effort is reached, which may indicate that more control effort is required than is possible. In other words, the used testing rate ($\nu = 0.1$) should be increased if possible. An increasing weight factor c_1 results in a reduction in the peak of the threatened population from 1.35% to 0.59%. Furthermore, an increasing weight factor results in a decrease of the deceased population from 1.64% to 0.78%.



(a) Threatened population



(b) Deceased population

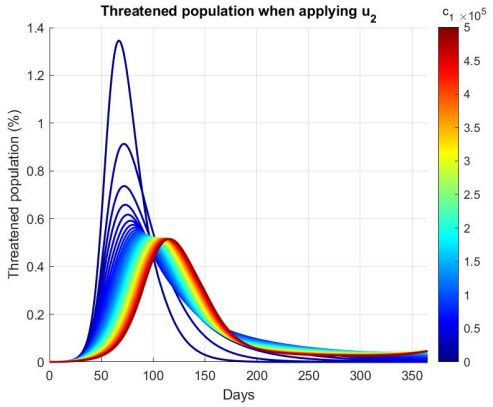


(c) Control effort u_2

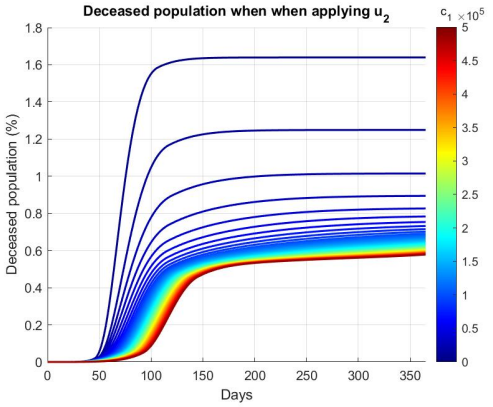
Figure 6.4: Optimization control input u_2 - step size 1,000

Results experiment 3B where step size is 10,000

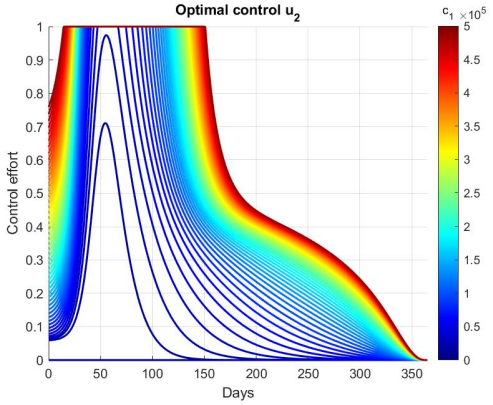
Figure 6.5 shows that higher weight factors show fairly similar behaviour as in the previous simulation. However, this time, faster and more control effort must be delivered in the beginning and the control effort must be kept maximum for a longer period of time. A rapid decrease in control effort can be seen after 150 days, this is the moment when the peak of the threatened population is almost over. If the rapid decrease has been, a slow decline follows until the end of the time horizon. Again the maximum control effort is reached, which implies higher testing rate may be desirable. Due to higher weight factors, the threatened population falls to 0.52%. In addition, the peak has been moved further into the future, where the peak used to be on day 67, it is now on day 115. It is noticeable that the peak first decreases in size, after which it hardly decreases but is moved further into the future. Furthermore, an increasing weight factor results in a decrease of the deceased population to 0.58%. Lastly, it is also clearly visible that the curves are getting closer to each other. This indicates that a higher weight factor contributes relatively less to the optimization problem.



(a) Threatened population



(b) Deceased population



(c) Control effort u_2

Figure 6.5: Optimization control input u_2 - step size 10,000

Conclusion experiment 3

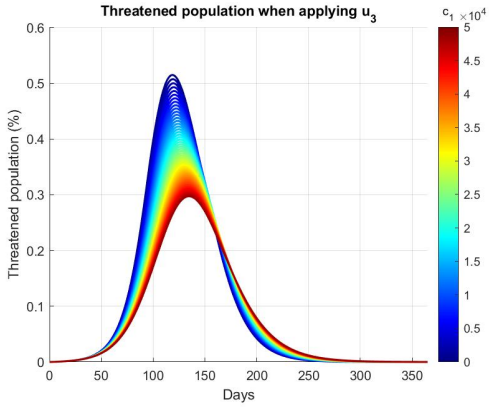
The optimal control strategy is to quickly build up and slowly reduce the control effort. In most cases, the control effort reaches its maximum, which indicates that a higher testing rate may be desirable. The higher the value for c_1, the longer the control effort must be held at its maximum. Due to the highest proposed control effort, the peak of the threatened population can be reduced by 61% and the deceased population can be reduced by 65% compared to when no control effort is applied. Besides, the peak of threatened population will be moved further into the future by 48 days. Finally, it can be noted that a higher weight factor contributes relatively less to the optimization because the curves are getting closer to each other.

6.1.4 Results from experiment 4: Optimizing control input u_3

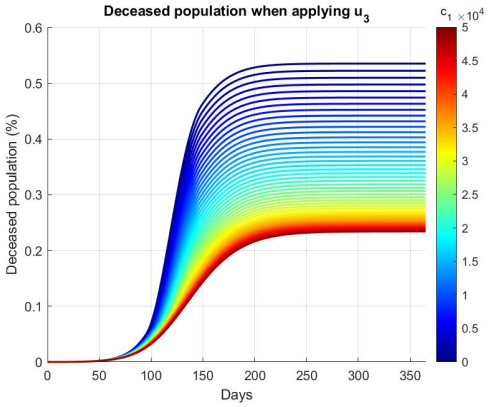
The influence of control input u_3 with different weights for c_1 is analyzed. Two simulations have been performed where the first simulation uses a step size for c_1 of 1,000 (figure 6.6) and the second simulation uses a step size for c_1 of 10,000 (figure 6.7).

Results experiment 4A where step size is 1,000

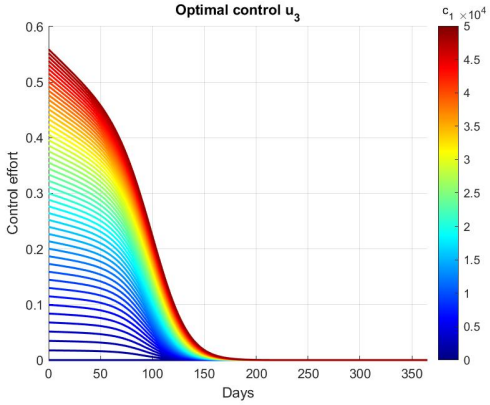
Figure 6.6 shows that the control effort must be made immediately and can then be reduced. The maximum control effort required is 0.56. An increasing weight factor c_1 results in a reduction in the peak of the threatened population from 0.51% to 0.30%. Also, the peak is moved slightly further into the future, where the peak used to be on day 118, it is now on day 135. Furthermore, an increasing weight factor results in a decrease of the deceased population from 0.54% to 0.23%.



(a) Threatened population



(b) Deceased population

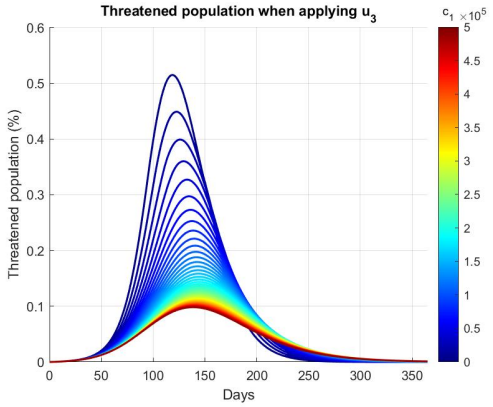


(c) Control effort u_3

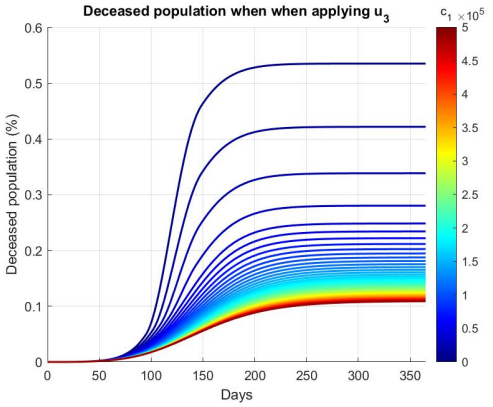
Figure 6.6: Optimization control input u_3 - step size 1,000

Results experiment 4B where step size is 10,000

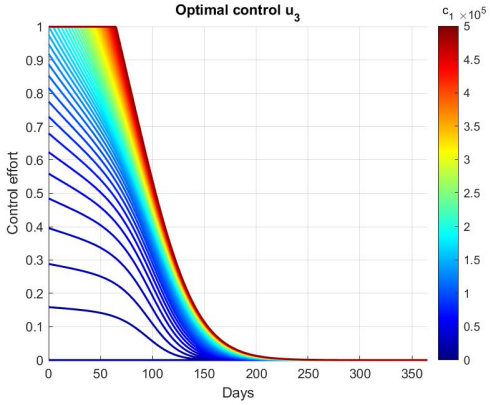
Figure 6.6 shows that a much higher weighting factor c_1 show fairly similar behaviour as in the previous simulation. However, this time the maximum control effort is reached, which indicates that a higher vaccination rate may be desirable. In other words, the used vaccination rate ($\psi = 2.5/1000$) should be increased if possible. Due to higher weight factors, the threatened population falls to 0.10%. Besides, the peak has been moved further into the future, where the peak used to be on day 119, it is now on day 139. Furthermore, an increasing weight factor results in a decrease of the deceased population to 0.11%. Lastly, it is also clearly visible that the curves are getting closer to each other. This indicates that a higher weight factor contributes relatively less to the optimization problem



(a) Threatened population



(b) Deceased population



(c) Control effort u_3

Figure 6.7: Optimization control input u_3 - step size 10,000

Conclusion experiment 4

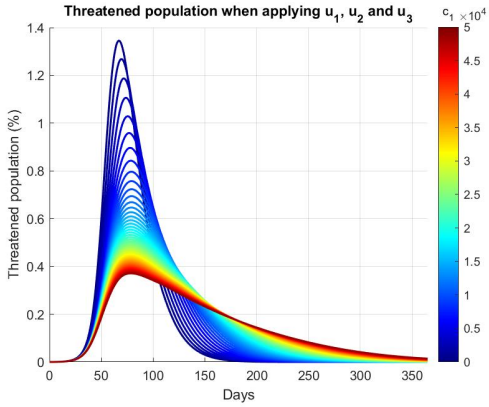
The optimal control strategy is to make an immediate control effort, that in some cases mush be held for some time, after which it can be reduced. In some cases the control effort reaches its maximum, which indicates that a higher vaccination rate may be desirable. The higher the value for c_1, the longer the control effort must be held at its maximum. Due to the highest proposed control effort, both the peak of the threatened population and the deceased population can be reduced by 80% compared to when no control effort is applied. Besides, the peak of threatened population will be moved further into the future by 20 days. Finally, it can be noted that a higher weight factor contributes relatively less to the optimization because the curves are getting closer to each other.

6.1.5 Results from experiment 5: Optimizing control inputs u_1, u_2 and u_3

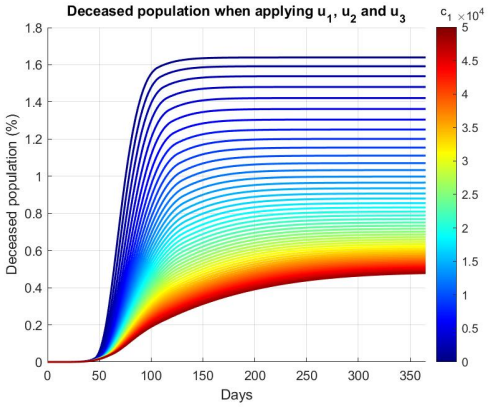
The influence of control inputs u_1, u_2 and u_3 with different weights for c_1 is analyzed. Two simulations have been performed where the first simulation uses a step size for c_1 of 1,000 (figure 6.8) and the second simulation uses a step size for c_1 of 10,000 (figure 6.9).

Results experiment 5A where step size is 1,000

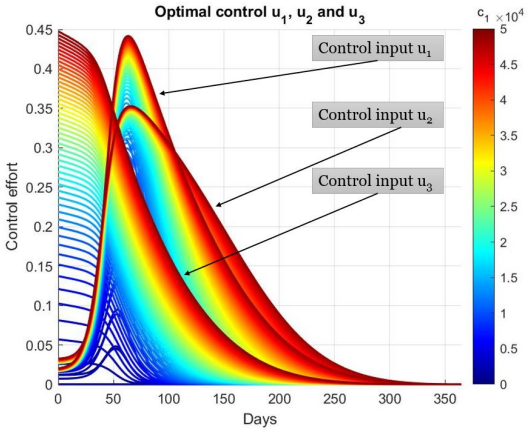
Figure 6.8 shows that the control effort for u_1 must be made immediately and can then be reduced. The control efforts for u_2 and u_3 must be built up quickly and reduced slowly. Due to the control effort of all the three control inputs, the peak of the threatened population decreases from 1.34% to 0.37% and is spread over a longer period of time. Moreover, the deceased population decreases from 1.64% to 0.48%.



(a) Threatened population



(b) Deceased population

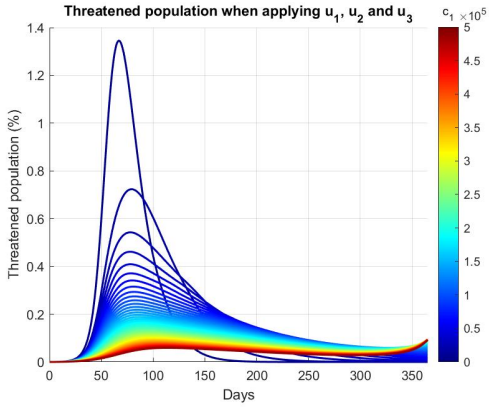


(c) Control effort u_1, u_2 and u_3

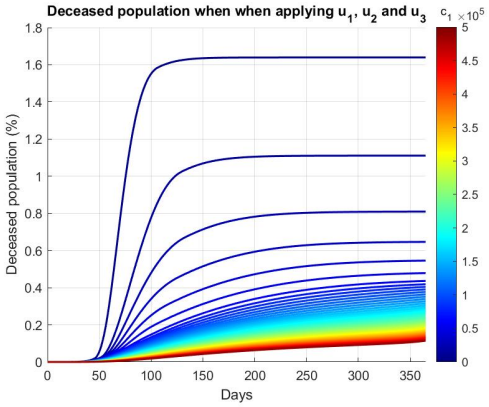
Figure 6.8: Optimization control input u_1, u_2 and u_3 - step size 1,000

Results experiment 5B where step size is 10,000

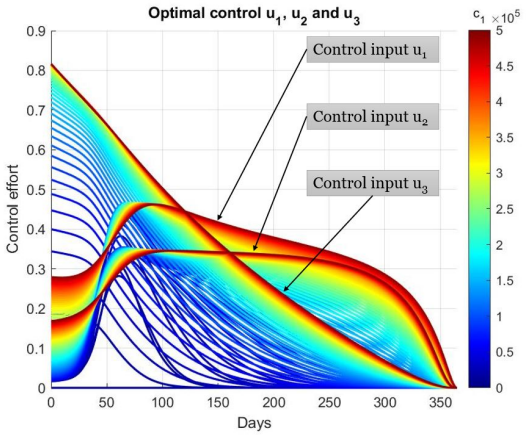
Figure 6.9 shows that a much higher weighting factor c_1 show fairly similar behaviour as in the previous simulation. However, this time, the control efforts must be held for a longer period of time. Accordingly, the threatened population decreases to 0.06% and the deceased population decreases to 0.11%. At the end of the time horizon in the threatened population, an increase can be seen, which again indicates turnpike behavior, just as mentioned in experiment 2B.



(a) Threatened population



(b) Deceased population



(c) Control effort u_1, u_2 and u_3

Figure 6.9: Optimization control input u_1, u_2 and u_3 - step size 10,000

Conclusion experiment 5

When the control inputs u_1, u_2 and u_3 are applied simultaneously, similar control effort must be applied as when applied separately. The higher the value for c_1, the longer the control effort must be held. Due to the highest proposed control effort, the peak of the threatened population can be reduced by 96% and the deceased population can be reduced by 93% compared to when no control effort is applied. Furthermore, a higher weight factor contributes relatively less to the optimization because the curves are getting closer to each other.

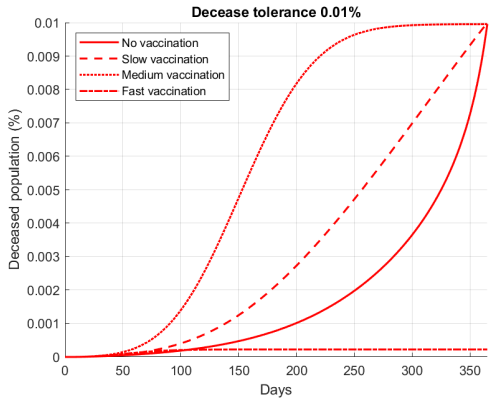
6.2 Results experiment 6: optimal exit strategy

This section shows the results of the optimal exit strategies. The subsections describe optimal exit strategies with low initial conditions, medium initial conditions and high initial conditions.

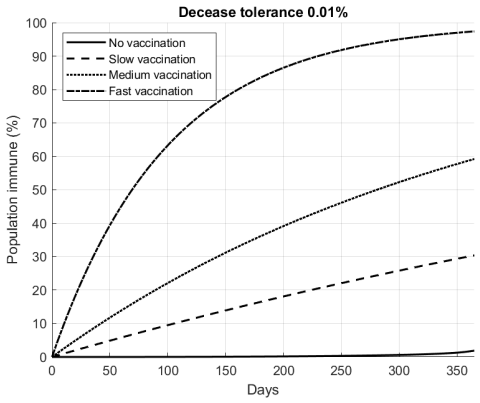
6.2.1 Results experiment 6A: Optimal exit strategy - low initial conditions

The course of the optimal government intervention strategy, disease and immune population is shown in the figures below. Figure 6.10c shows that a low vaccination rate leads to relatively high government intervention intensity, and a faster vaccination rate leads to a relatively low intensity of government intervention. Moreover, the fast vaccination policy no longer requires government intervention at all. Figure 6.10a shows that with a higher vaccination rate, the deceased population will increase less quickly. The deceased population remains very low when a fast vaccination policy is applied. Figure 6.10b shows the amount of immunity built up. The immune population consists of susceptible individuals who have been vaccinated and recovered individuals. As the vaccination rate increases, more asymptotic growth can be seen. This can be

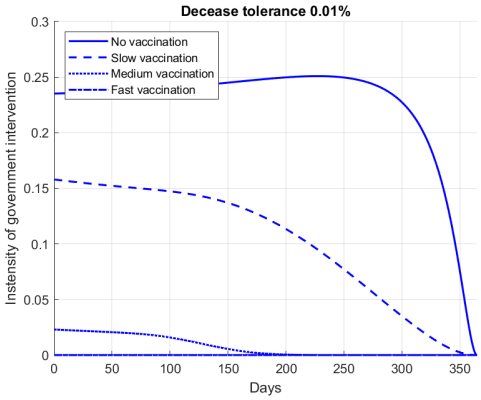
explained by the fact that the susceptible population continues to decrease, but the vaccination rate remains the same.



(a) Deceased population



(b) Immune population

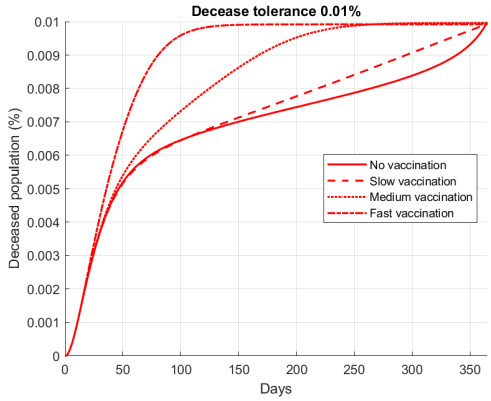


(c) Intensity government intervention

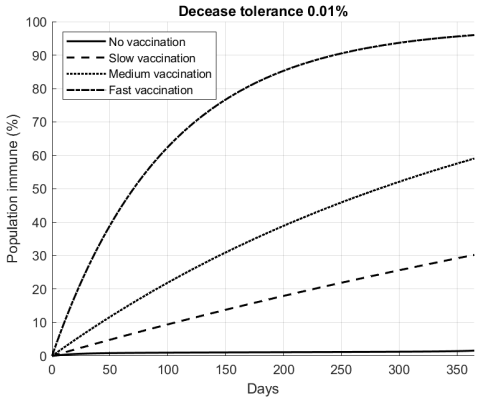
Figure 6.10: Optimal exit strategy - low initial conditions

6.2.2 Results experiment 6B: Optimal exit strategy - medium initial conditions

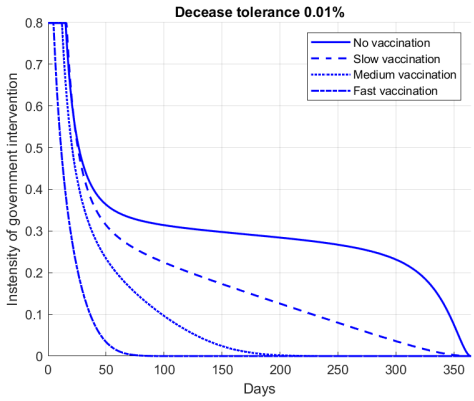
The course of the optimal government intervention strategy, disease and immune population is shown in the figures below. The same findings can be made as with the case when low initial conditions are applied. However, differences can be seen in the course of the intensity of government intervention and the course of the deceased population. It can be seen that during the first days, a maximum intensity of government interventions is required, while this was not necessary in the case with low initial conditions. It can also be seen that the deceased population increases sharply in the beginning instead of gradually, as in the case with low initial conditions.



(a) Deceased population



(b) Immune population

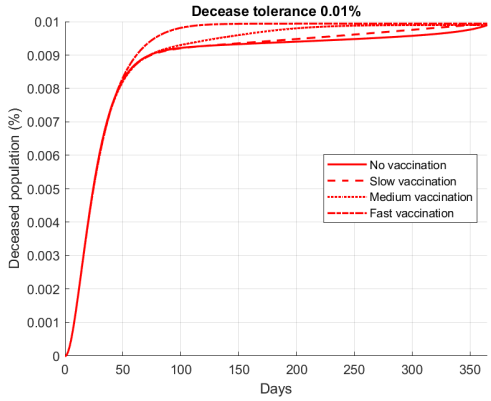


(c) Intensity government intervention

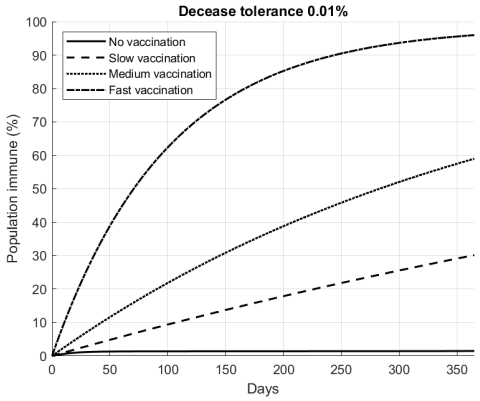
Figure 6.11: Optimal exit strategy - medium initial conditions

6.2.3 Results experiment 6C: Optimal exit strategy - high initial conditions

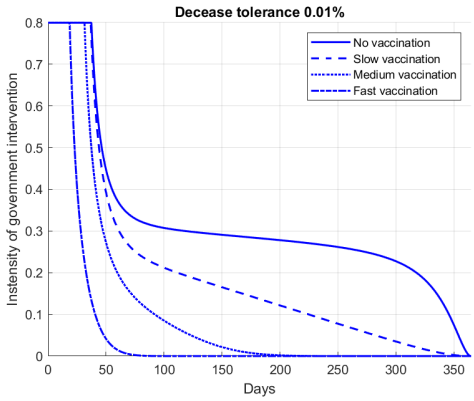
The course of the optimal government intervention strategy, disease and immune population is shown in the figures below. Again, the same findings can be made as in the cases above. The difference compared to the case where medium initial conditions are applied is that at the beginning, the intensity of government interventions has to be maintained for an even longer time. Also, the deceased population continues to rise steeply for a longer period of time.



(a) Deceased population



(b) Immune population



(c) Intensity government intervention

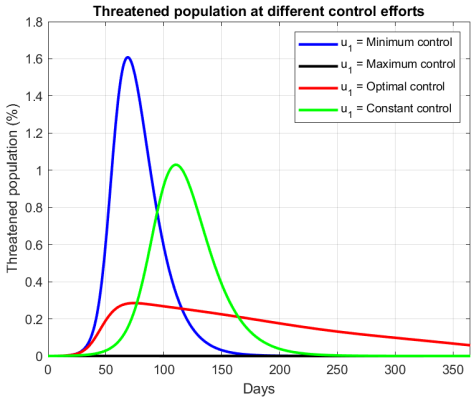
Figure 6.12: Optimal exit strategy - high initial conditions

6.3 Results experiment 7: Different (non-optimal) control strategies

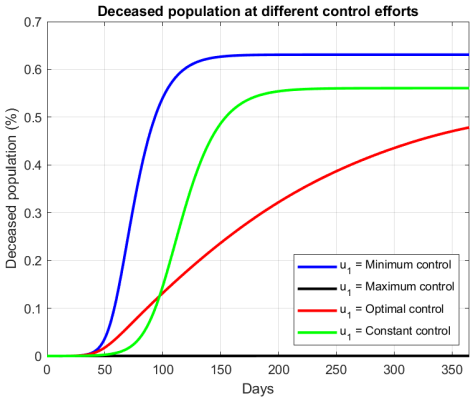
The different strategies that have been applied are maximum control, minimum control, optimal control and average control of the optimal control effort. The different control strategies for control inputs u_1, u_2 and u_3 are described in the subsections.

6.3.1 Results experiment 7A: different control strategies for u_1

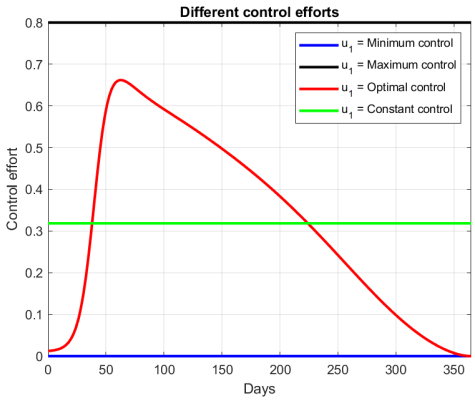
Different control strategies for u_1 show different behaviour in the effects of the threatened and deceased population. It can be seen that when maximum and average control is applied that a clear peak is visible in the threatened population. The peak decreases as the constant control effort increases, and besides, the peak moves further into the future. At maximum control effort, there is no peak at all, and the number of head threatened population remains zero. The effects of optimal control are that the peak is flattened and distributed over the entire time horizon. It can also be seen that when maximum and average control is applied, the deceased population increases rapidly and then remains constant. With maximum control, the amount of the deceased is zero. With the optimal control input, there is an almost constant increase in the amount of deceased.



(a) Threatened population



(b) Deceased population

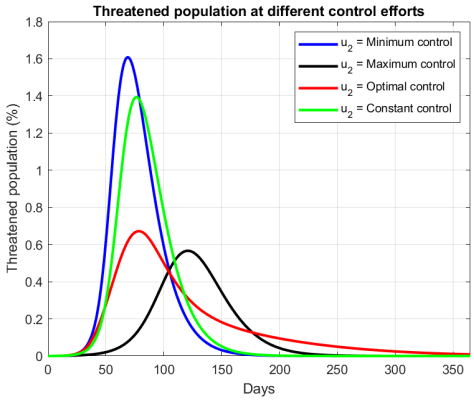


(c) Control strategies for u_1

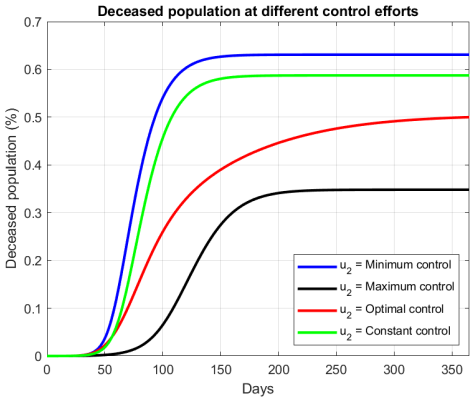
Figure 6.13: Non-optimal control strategies for u_1

6.3.2 Results experiment 7B: Different control strategies for u_2

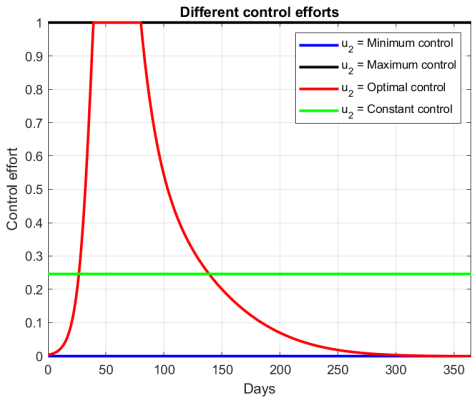
Different control strategies of u_2 show different behaviour in the effects of the threatened and deceased population. A peak in the threatened population remains visible in all forms of control strategies. The peak decreases significantly with both optimal and maximum control. Also, the optimal control strategy spreads the threatened population over a longer period. With the maximum control strategy, the peak moves further into the future. It can also be seen that the effects of minimum control, maximum control and average control strategy show the same behaviour in the deceased population, namely the shape of the curve remains the same. The optimal control strategy ensures a constant increase in the deceased population; namely, the corresponding curve is much more gradual.



(a) Threatened population



(b) Deceased population

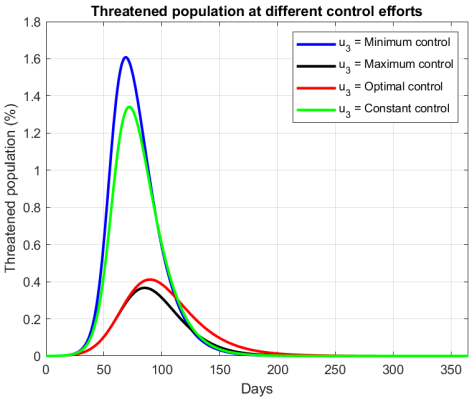


(c) Control strategies for u_2

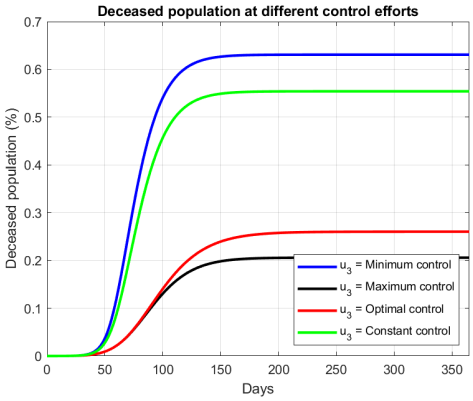
Figure 6.14: Non-optimal control strategies for u_2

6.3.3 Results experiment 7C: Different control strategies for u_3

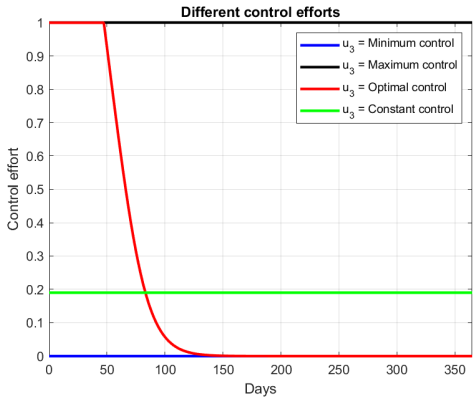
Different control strategies of u_3 show different behaviour in the effects of the threatened and deceased population. It can be seen that with a minimal and average control strategy, a high peak in the threatened population remains. This peak decreases sharply if a maximum or optimal control strategy is applied. The peak will then also be moved slightly further into the future. Also, it can be seen that with a minimal and average control strategy, the deceased population remains high. With a maximum or optimal control strategy, the deceased population will be much lower. It is striking that despite the short control effort with the optimal control strategy compared to the long control effort with maximum control strategy, the effects on the threatened and deceased population are almost the same.



(a) Threatened population



(b) Deceased population



(c) Control strategies for u_3

Figure 6.15: Non-optimal control strategies for u_3

Chapter 7: Discussion and future research

By using a wide range of weight factors for the threatened population, it was possible to create multiple scenarios in which different optimal control effort are compared with the dynamics of the threatened and deceased population. This makes it possible to make the right trade-off for the implementation of the measures and the consequences of a disease outbreak, such as the expectation in the threatened and deceased population. The experiment in which no control inputs are used can be addressed as the reference scenario. The other experiments in which control inputs were used can be compared with this. This makes it possible to express the effectiveness of the controls inputs in percentages.

The results where the control input is optimized both separately and at the same time indicate what the control effort should be. The results show a continuous control effort trajectory. This is very useful so that it can be seen at what times and how much control effort must be applied. However, it is unlikely to provide a continuous control effort in the real world. In practice, this will mean that the measures will have to be continuously adjusted during the day. A discrete control strategy is more applicable to use in the real world. This means that the control strategies should be divided into portions, whereas each portion contains a specific package of measures. In contrast to this research, it has been included in the research of Kasis et al. (2021) where various policy changes indicate this. Accordingly, in future research a translation to a discrete control policy could be done.

The usefulness of optimal control results in testing policy (experiment 3 and 5) can be questioned. This experiment looks at variable test rates depending on the degree of infected individuals. Since testing is essential to find out to what extent the population is infected, it is not logical to implement a changing testing policy. It makes more sense that once a certain testing capacity is available and it is possible that people can have themselves tested for symptoms of the disease, this capacity is fully used to estimate the level of infections in the population. Hence, it is logical to consider how government interventions should be adapted to a constant testing policy, as was done in the other experiments in this study.

For experiment 5, where all three control inputs are applied simultaneously, it was assumed that the costs for the implementation of government intervention policy are the most expensive, followed by the testing policy and finally the vaccination policy. It was therefore assumed that the weight factor for government intervention policy is three times as high as vaccination policy and that the testing policy is twice as high. However, these assumptions can be strongly questioned as it is very difficult to estimate the actual implementation costs of the control inputs.

Furthermore, the research leans towards a socio-technical problem. Human behaviour plays an important role in the effectiveness of the solution to the problem. In particular, the effectiveness of government intervention strongly depends on this. It strongly depends on the extent to which people adhere to the imposed measures. Where people adhere to the measures, in the beginning, it may be that after some time, this no longer applies (RIVM, 2021). Changing human behaviour has not been included in the assumptions of this study. The optimal control theory that has been used is based on an open-loop circuit where the optimal strategy is determined with the initial conditions and parameters. Hence, strategies are not adjusted during their implementation. In the research of Köhler et al. (2020), a feedback strategy that updates the policies using model predictive control was analyzed, and it was concluded that this contributes to the reliable handling of a disease outbreak. For future research the use of such a feedback algorithm can be considered.

Lastly, it was assumed that the individuals are equal to each other and that all assumptions are the same for every individual. In the real world this is not the case. For example, there is a difference between the mortality rate of individuals. The mortality rate in old people is much higher than in young people (O'Driscoll et al., 2021). Moreover, the research of Costa et al. (2020) shows that the degree of infections also depends on the geographic location. A metapopulation can be used to include such differences in the model. Thus, future research can focus on how optimal control theory can be applied in a metapopulation model to get more accurate results.

Chapter 8: Conclusion

In this report, the epidemiological SIDAREV model is proposed, and the optimal control strategies for a disease outbreak have been analyzed. Three controls have been added to the model that can influence the infection-, testing-, and vaccination rate. Optimal control theory was used to optimize the control strategies for government intervention-, testing-, and vaccination policies. Pontryagin's maximum principle was applied to find the necessary conditions for the optimal control problem and the forward backward sweep method was used to find the optimal controls.

The research question that was formulated in the introduction of the report was: *'What are the optimal control strategies for implementing government intervention-, testing-, and vaccination policies if the costs associated with the threatened and deceased population and socio-economic costs must be minimized?'* The report answered this question by proposing different optimal control strategies. Since each measure requires its own trajectory of optimal control effort, the findings are summed up below:

- The optimal control strategy for government intervention policy is to quickly build up and slowly reduce the control effort until the end of the time horizon. It appeared that by only applying optimal government interventions, the peak of the threatened population could be reduced by 92% and the deceased population by 95% compared to when no control effort was applied.
- The optimal control strategy for the testing policy is to quickly build up and slowly reduce the control effort until the time horizon. It appeared that by only applying optimal testing policy, the peak of the threatened population could be reduced by 61% and the deceased population by 65% compared to when no control effort was applied.
- The optimal control strategy for vaccination policy is to immediately start with control effort, after which it can be reduced. It appeared that by only applying optimal vaccination policy, both the peak of the threatened population and the deceased population could be reduced by 80% compared to when no control effort was applied.
- When all three optimal control measures are applied simultaneously, it appears that the peak of the threatened population could be reduced by 96% and the deceased population by 93% when no control effort was applied.

Furthermore, it was investigated what the optimal exit strategy is for a disease outbreak, i.e. analyzing the optimal government interventions using different vaccination rates and a constant testing rate. It was found that higher vaccination rates require less government intervention than lower vaccination rates. The strength of government intervention depends on the amount of infected individuals during disease outbreak. It has been found that, when a relatively large number of individuals are infected with the disease, the optimal control strategy is to provide maximum control effort to bring the infections down, after which the control effort can be slowly reduced.

Finally, non-optimal control strategies were compared with the optimal control strategies. The different control strategies were maximum control, minimum control, optimal control and average control of the optimal control effort. The results of average control came close to the results of minimum control, and the results of optimal control were close to maximum control. This means that a high effectiveness can be achieved with optimal control. In addition, the advantage of optimal control compared to maximum control is that it leads much lower costs. This motivates to apply optimal control strategies in a disease outbreak for the best trade-off between socio-economic costs and costs related to the threatened and deceased population.

Chapter 9: MATLAB codes

9.1 MATLAB code for SIR model example

```
clc; close all; clear all;  % Clear command, close figures, clear workspace

t0 = 0;                     % Initial time
tf = 365;                   % Final time
M = 999;                    % Number of nodes
t = linspace(t0,tf,M+1);    % Time variable
h = tf/M;                   % Spacing between nodes

% PARAMETERS
N = 17280000;               % Population of The Netherlands
gamma = 1/14;               % Recovery rate undetected: 14 days
beta = 0.25;                % Infection rate

% INITIAL CONDITIONS MODEL
S = zeros(1,M+1);           % Susceptible
I = zeros(1,M+1);           % Infected
R = zeros(1,M+1);           % Recovered
S(1) = (1-0.00001).*N;
I(1) = 0.00001.*N;
R(1) = 0;

% SYSTEM DYNAMICCS
    for i = 1:M
        m11 = - beta*S(i)*I(i)./N;
        m12 = beta*S(i)*I(i)./N - gamma*I(i);
        m13 = gamma*I(i);
        S(i+1) = S(i) + h*m11;
        I(i+1) = I(i) + h*m12;
        R(i+1) = R(i) + h*m13;
    end

figure(1)
plot(t,S, t,I, t,R, 'LineWidth',2); grid on;
title('SIR model');
xlabel('Days'); xlim([0 365]);
ylabel('Population');
legend('S', 'I', 'R', 'Location', 'east');
saveas(1,'SIR_model_example.png');
```

9.2 MATLAB script controlled SIDAREV model

```
clc; close all; clear all;  % Clear command window, close tabs/figures, clear ...
    workspace

% SETUP FOR FORWARD-BACKWARD SWEEP METHOD
test = -1;                  % Test variable; as long as variable is negative ...
    the while loops keeps repeating
t0 = 0;                     % Initial time
tf = 365;                   % Final time
Δ = 0.00001;            % Accepted tollerance
M = 999;                    % Number of nodes
t = linspace(t0,tf,M+1);    % Time variable where linspace creates M+1 ...
    equally spaced nodes between t0 and tf, including t0 and tf.
h = tf/M;                   % Spacing between nodes
h2 = h/2;                   % Spacing equal to 2 for Runge-Kutta method

% MODEL PARAMETERS
gamma_i = 1/14;     % Recovery rate undetected: 14 days
gamma_d = 1/14;     % Recovery rate detected: 14 days
gamma_a = 1/12.4;   % Recovery rate threatend: 12.4 days
beta = 0.251;       % Infection rate
xi_i = 0.0053;      % Rate infected undetected to acutely symtomatic
xi_d = 0.0053;      % Rate infected detected to acutely symtomatic
mu = 0.0085;        % Mortality rate
mu_hat = 5*mu;      % Mortality rate when hospital capacity is exceeded
nu = 0.1;           % Testing rate (no, slow, fast testing = 0, 0.05, 0.10)
h_bar = 0.00333;    % Hospital capacity rate (0.00222, 0.00333, 0.00444)
psi = 0;            % Rate of vaccination

% WEIGHT FACTORS
c1 = 0;     % Weight on threatened population
c2 = 0;     % Weigth on deceased population
c3 = 0;
b1 = 1;
b2 = 1;
b3 = 1;

% INITIAL CONDITIONS MODEL
x1=zeros(1,M+1);    % Susceptible
x2=zeros(1,M+1);    % Infected - undetected
x3=zeros(1,M+1);    % Infected - detected
x4=zeros(1,M+1);    % Acutely symptomatic - Threatened
x5=zeros(1,M+1);    % Recovered
x6=zeros(1,M+1);    % Deceased
x7=zeros(1,M+1);    % Vaccinated

x1(1) = 1-0.00001;
x2(1) = 0.00001;
x3(1) = 0;
x4(1) = 0;
x5(1) = 0;
x6(1) = 0;
x7(1) = 0;

% INITIAL GUESS FOR OPTIMAL CONTROL INPUT
u1 = zeros(1,M+1);  % Control input for government intervention
u2 = zeros(1,M+1);  % Control input for testing
u3 = zeros(1,M+1);  % Control input for vaccinating

% INITIAL CONDITIONS ADOINT SYSTEM
```

```
L1 = zeros(1,M+1);
L2 = zeros(1,M+1);
L3 = zeros(1,M+1);
L4 = zeros(1,M+1);
L5 = zeros(1,M+1);
L6 = zeros(1,M+1);
L7 = zeros(1,M+1);

L1(M+1) = 0;
L2(M+1) = 0;
L3(M+1) = 0;
L4(M+1) = 0;
L5(M+1) = 0;
L6(M+1) = c2;
L7(M+1) = 0;

% FORWARD-BACKWARD SWEEP METHOD
loopcnt = 0;    % Count number of loops
while(test < 0)
    loopcnt = loopcnt + 1;

    oldu1 = u1;
    oldu2 = u2;
    oldu3 = u3;

    oldx1 = x1;
    oldx2 = x2;
    oldx3 = x3;
    oldx4 = x4;
    oldx5 = x5;
    oldx6 = x6;
    oldx7 = x7;

    oldL1 = L1;
    oldL2 = L2;
    oldL3 = L3;
    oldL4 = L4;
    oldL5 = L5;
    oldL6 = L6;
    oldL7 = L7;

    % SYSTEM DYNAMICCS
    for i = 1:M

        % IMPACT HEALTHCARE CAPACITY ON MORTALITY RATE
        if x4(i) ≤ h_bar
           mu_bar = mu*x4(i);
           else
           mu_bar = mu*h_bar + mu_hat*(x4(i) - h_bar);
        end

        m11 = -beta*x1(i)*x2(i)*(1-u1(i)) - psi*u3(i)*x1(i);
        m12 = beta*x1(i)*x2(i)*(1-u1(i)) - gamma_i*x2(i) - xi_i*x2(i) - ...
            nu*x2(i)*(u2(i));
        m13 = nu*x2(i)*(u2(i))-gamma_d*x3(i)-xi_d*x3(i);
        m14 = xi_i*x2(i)+xi_d*x3(i)-gamma_a*x4(i)-mu_bar;
        m15 = gamma_i*x2(i) + gamma_d*x3(i) + gamma_a*x4(i);
        m16 = mu_bar;
        m17 = psi*u3(i)*x1(i);

        x1(i+1) = x1(i) + h*m11;
```

```
117         x2(i+1) = x2(i) + h*m12;
118         x3(i+1) = x3(i) + h*m13;
119         x4(i+1) = x4(i) + h*m14;
120         x5(i+1) = x5(i) + h*m15;
121         x6(i+1) = x6(i) + h*m16;
122         x7(i+1) = x7(i) + h*m17;
123
124     end
125
126     % ADJOINT SYSTEM
127     for i = 1:M         % From initial to final value
128         j = M + 2 - i;  % From final value to initial value
129
130         n11 = (L1(j)-L2(j))*beta*x2(j)*(1-u1(j)) + L7(j)*psi*u3(j);
131         n12 = (L1(j)-L2(j))*beta*x1(j)*(1-u1(j)) + L2(j)*(gamma_i + xi_i) + ...
                L2(j)*(nu*(u2(j))) - L3(j)*(nu*(u2(j))) - L4(j)*xi_i;
132         n13 = L3(j)*(gamma_d + xi_d) - L4(j)*xi_d;
133         n14 = L4(j)*(gamma_a + mu_bar) - L5(j)*mu_bar - L6(j)*mu_bar - c1*x4(j);
134         n15 = 0;
135         n16 = 0;
136         n17 = 0;
137
138         L1(j-1) = L1(j) - h*n11;
139         L2(j-1) = L2(j) - h*n12;
140         L3(j-1) = L3(j) - h*n13;
141         L4(j-1) = L4(j) - h*n14;
142         L5(j-1) = L5(j) - h*n15;
143         L6(j-1) = L6(j) - h*n16;
144         L7(j-1) = L7(j) - h*n17;
145     end
146
147     % OPTIMALITY CONDITIONS
148     U1 = min(0.8,max(0,(L2-L1).*beta.*x1.*x2./(b1)));
149     u1 = 0.01.*U1 +0.99.*oldu1;
150
151     U2 = min(1, max(0, (((L2-L3).*nu.*x2)./(b2))));
152     u2 = 0.01.*U2 +0.99.*oldu2;
153
154     U3 = min(1, max(0, (((L1-L7).*psi.*x1)./(b3))));
155     u3 = 0.01.*U3 +0.99.*oldu3;
156
157     % COST FUNCTION
158     J = c1./2*sum(x4.^2)*h + b1./2*sum(u1.^2)*h + b2./2*sum(u2.^2)*h + ...
            b3./2*sum(u3.^2)*h+ c2*max(x6);
159
160     Cost1 = c1./2.*cumsum(x4.^2)*h;      % Total cost of threatened population
161     Cost2 = b1./2.*cumsum(u1.^2)*h;      % Total cost of control input u1
162     Cost3 = b2./2.*cumsum(u2.^2)*h;      % Total cost of control input u2
163     Cost4 = b2./2.*cumsum(u3.^2)*h;      % Total cost of control input u3
164     Cost5 = c2.*x6;                      % Total cost of deceased population
165     J2 = Cost1 + Cost2 + Cost3 + Cost4 + Cost5; % Cost at each time for ...
            plotting graphs
166
167     % CHECK CONVERGENCE TO STOP SWEEP METHOD
168     temp1 = ∆*sum(abs(u1)) - sum(abs(oldu1 - u1));
169     temp2 = ∆*sum(abs(u2)) - sum(abs(oldu2 - u2));
170     temp3 = ∆*sum(abs(u3)) - sum(abs(oldu3 - u3));
171
172     temp4 = ∆*sum(abs(x1)) - sum(abs(oldx1 - x1));
173     temp5 = ∆*sum(abs(x2)) - sum(abs(oldx2 - x2));
174     temp6 = ∆*sum(abs(x3)) - sum(abs(oldx3 - x3));
```

```
175       temp7 = Δ*sum(abs(x4)) - sum(abs(oldx4 - x4));
176       temp8 = Δ*sum(abs(x5)) - sum(abs(oldx5 - x5));
177       temp9 = Δ*sum(abs(x6)) - sum(abs(oldx6 - x6));
178       temp10 = Δ*sum(abs(x7)) - sum(abs(oldx7 - x7));
179
180       temp11 = Δ*sum(abs(L1)) - sum(abs(oldL1 - L1));
181       temp12 = Δ*sum(abs(L2)) - sum(abs(oldL2 - L2));
182       temp13 = Δ*sum(abs(L3)) - sum(abs(oldL3 - L3));
183       temp14 = Δ*sum(abs(L4)) - sum(abs(oldL4 - L4));
184       temp15 = Δ*sum(abs(L5)) - sum(abs(oldL5 - L5));
185       temp16 = Δ*sum(abs(L6)) - sum(abs(oldL6 - L6));
186       temp17 = Δ*sum(abs(L7)) - sum(abs(oldL7 - L7));
187
188       test = min([temp1 temp2 temp3 temp4 temp5 temp6 temp7 temp8 temp9 temp10 ...
              temp11 temp12 temp13 temp14 temp15 temp16 temp17]);
189   end
190
191   disp(['number of loops: ' num2str(loopcnt)]);
192   disp(['Cost function: ' num2str(J)]);
193   disp(['Portion deceased: ' num2str(max(x6))]);
194
195   y(1,:) = t;
196   y(2,:) = x1;
197   y(3,:) = x2;
198   y(4,:) = x3;
199   y(5,:) = x4;
200   y(6,:) = x5;
201   y(7,:) = x6;
202   y(8,:) = x7;
203   y(9,:) = L1;
204   y(10,:) = L2;
205   y(11,:) = L3;
206   y(12,:) = L4;
207   y(13,:) = L5;
208   y(14,:) = L6;
209   y(15,:) = L7;
210   y(16,:) = u1;
211   y(17,:) = u2;
212   y(18,:) = u3;
213   y(19,:) = J;
214
215   % IMMUNITY REACHED
216   imm = x5+x7.*100; % Percentage immune
217
218       x4_per = x4*100; % percentage threatened
219       x6_per = x6*100; % percentage deceased
```

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Appendix A: Deriving the optimality equation

Theorem 2. *Suppose that $f(t,x,u)$ and $g(t,x,u)$ are both continuously differentiable functions in their three arguments and concave in u. Suppose u^* is an optimal control for the optimal control problem, with associated state x^*, and λ a piecewise differentiable function with $\lambda(t) \geq 0$ for all t. Suppose for all $t_0 \leq t \leq T$*

$$0 = H_u\left(t, x^*(t), u^*(t), \lambda(t)\right) \tag{A.1}$$

Then for all controls u and each $t_0 \leq t \leq T$, we have

$$H\left(t, x^*(t), u(t), \lambda(t)\right) \leq H\left(t, x^*(t), u^*(t), \lambda(t)\right) \tag{A.2}$$

Proof.

Fix a control u and a point in time $t_0 \leq t \leq T$. Then,

$$\begin{aligned}
&H\left(t, x^*(t), u^*(t), \lambda(t)\right) - H\left(t, x^*(t), u(t), \lambda(t)\right) \\
&= \left[f\left(t, x^*(t), u^*(t)\right) + \lambda(t) g\left(t, x^*(t), u^*(t)\right)\right] \\
&\quad - \left[f\left(t, x^*(t), u(t)\right) + \lambda(t) g\left(t, x^*(t), u(t)\right)\right] \\
&= \left[f\left(t, x^*(t), u^*(t)\right) - f\left(t, x^*(t), u(t)\right)\right] \\
&\quad + \lambda(t)\left[g\left(t, x^*(t), u^*(t)\right) - g\left(t, x^*(t), u(t)\right)\right] \\
&\geq \left(u^*(t) - u(t)\right) f_u\left(t, x^*(t), u^*(t)\right) \\
&+ \lambda(t)\left(u^*(t) - u(t)\right) g_u\left(t, x^*(t), u^*(t)\right) \\
&= \left(u^*(t) - u(t)\right) H_u\left(t, x^*(t), u^*(t), \lambda(t)\right) = 0 \\
&= H_u\left(t, x^*(t), u^*(t), \lambda(t)\right) = 0 \\
&\text{hence, } \tfrac{\partial H}{\partial u}\left(t, x^*(t), u^*(t), \lambda(t)\right) = 0
\end{aligned} \tag{A.3}$$

□

Appendix B: Data vaccination program

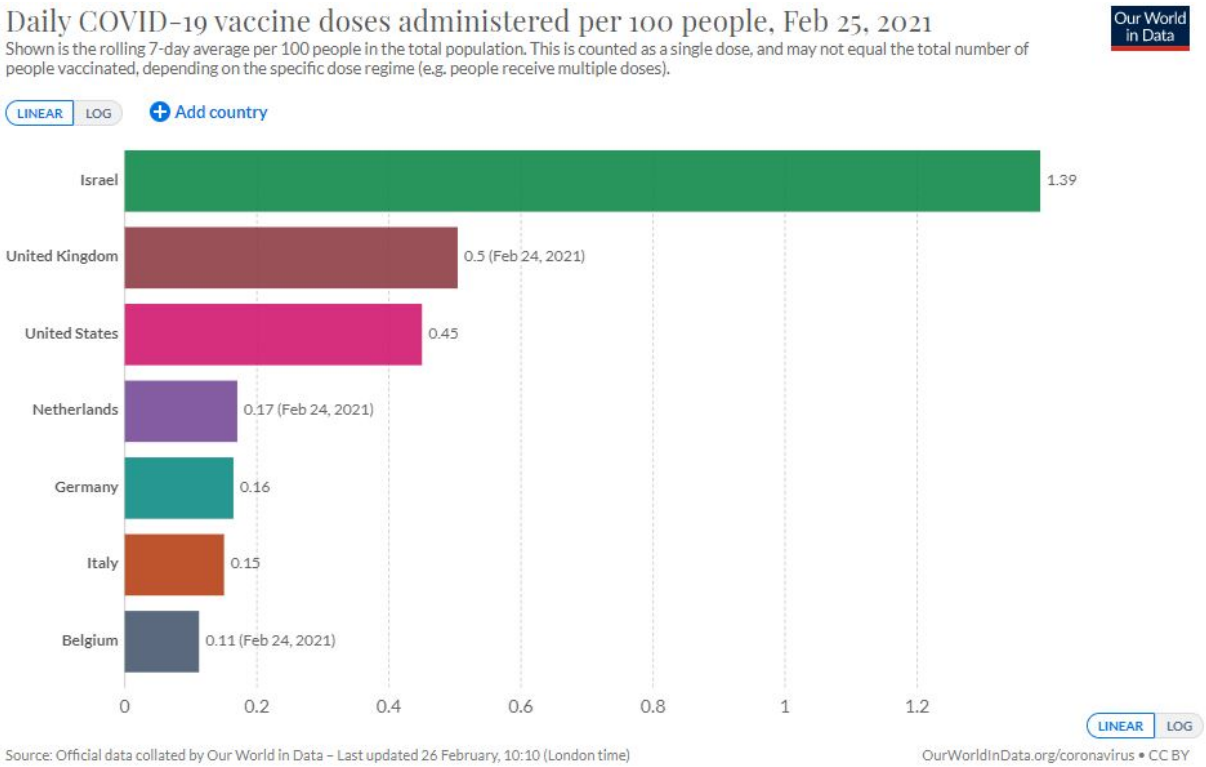


Figure B.1: Vaccination doses per 100 people on daily basis (OurWorldData, 2021)

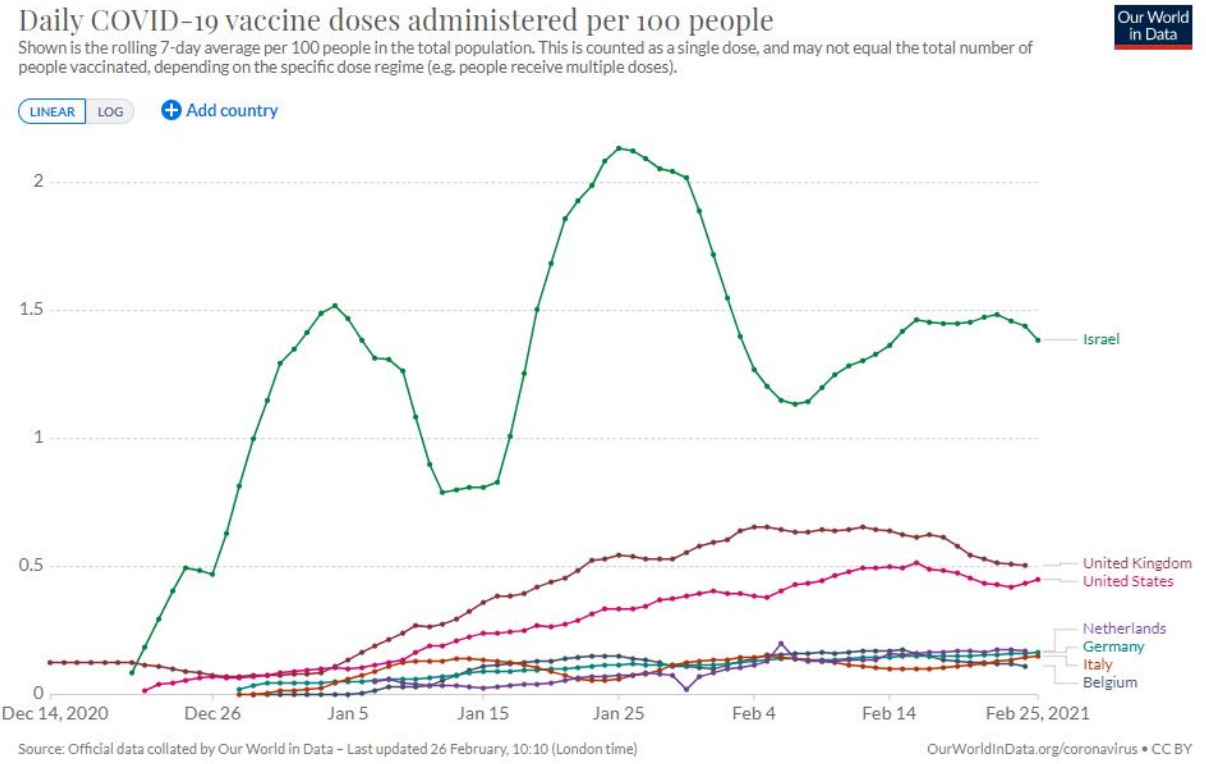


Figure B.2: Vaccination doses per 100 people on daily basis (OurWorldData, 2021)

Appendix C: Comparison research results

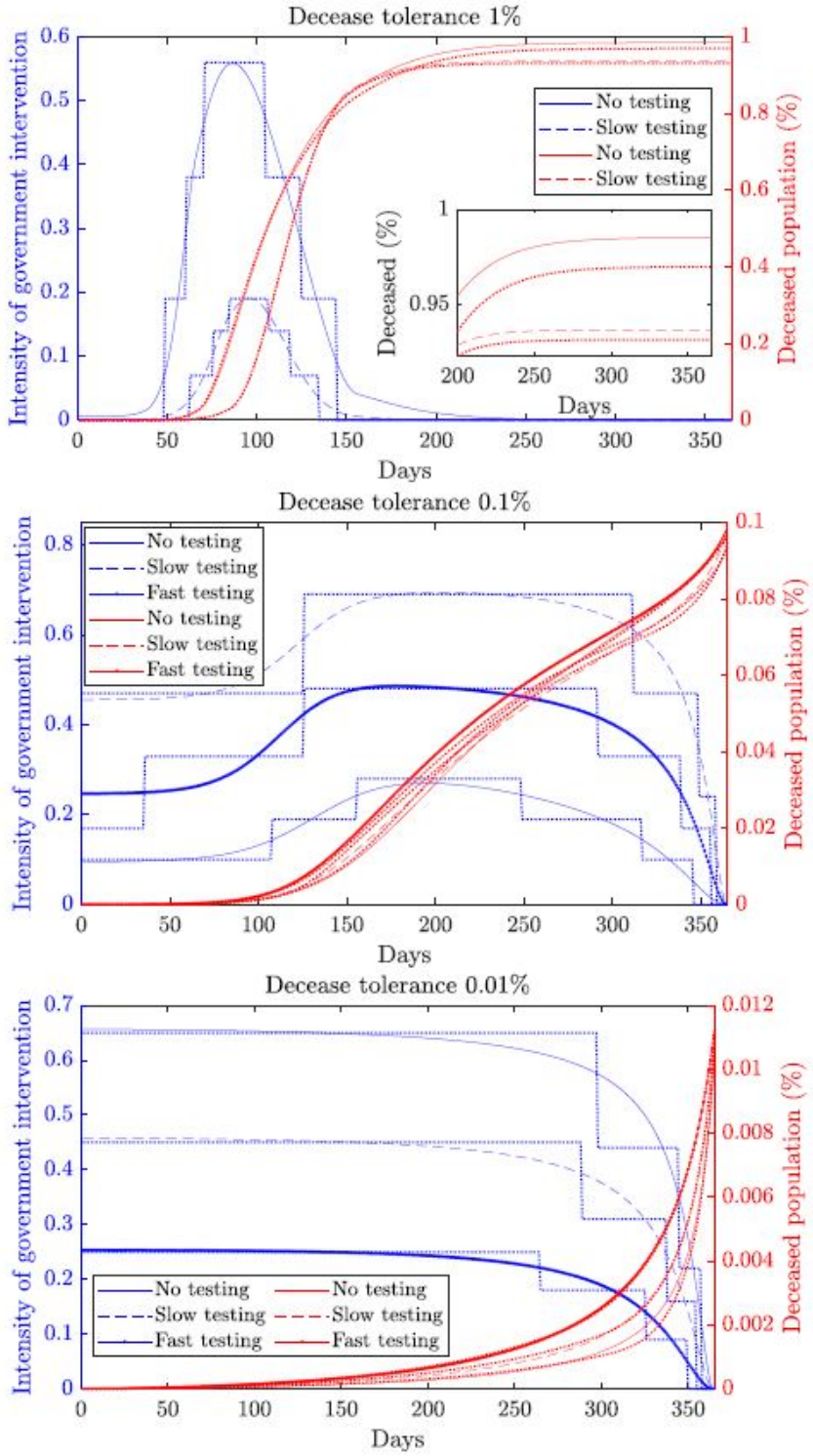
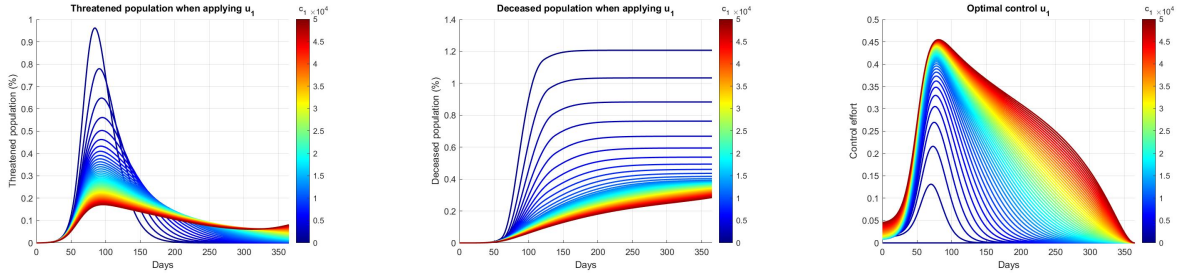


Figure C.1: Research results from Kasis et al. (2021)

Appendix D: Additional results from experiments

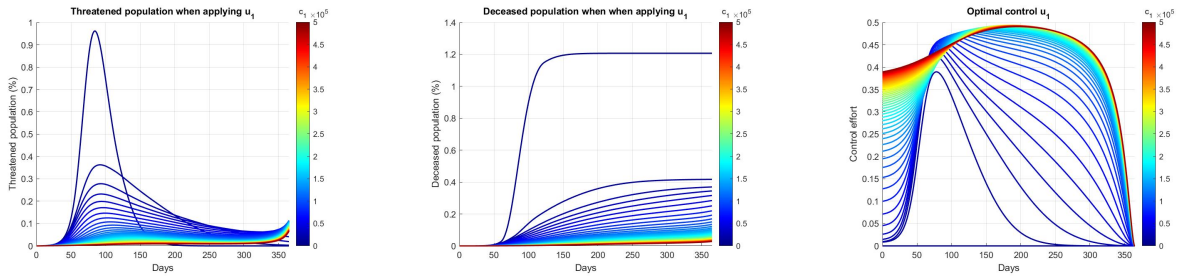
D.1 Additional results from experiment 2

Result experiment 2 - slow testing



(a) Threatened population *(b) Deceased population* *(c) Control effort u_1*

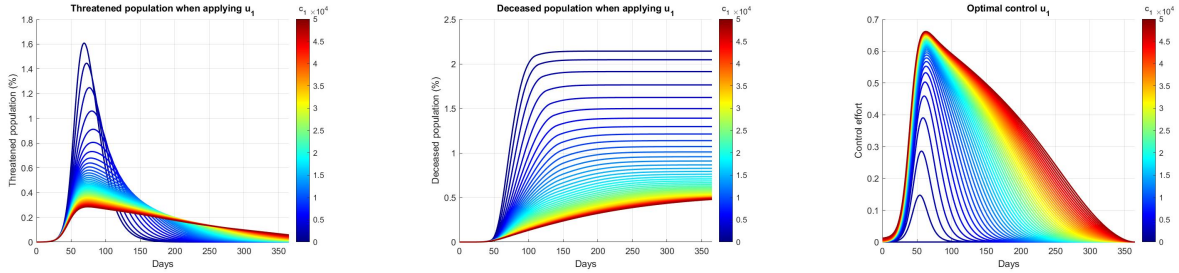
Figure D.1: Optimization control input u_1 - step size 1,000 - slow testing



(a) Threatened population *(b) Deceased population* *(c) Control effort u_1*

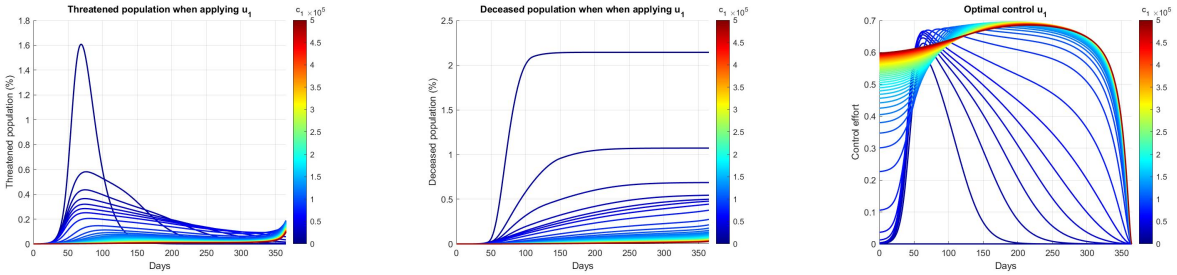
Figure D.2: Optimization control input u_1 - step size 10,000 - slow testing

Result experiment 2 - no testing



(a) Threatened population *(b) Deceased population* *(c) Control effort u_1*

Figure D.3: Optimization control input u_1 - step size 1,000 - no testing



(a) Threatened population *(b) Deceased population* *(c) Control effort u_1*

Figure D.4: Optimization control input u_1 - step size 10,000 - no testing