

École polytechnique de Louvain

Model predictive and optimal control for epidemic management

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Abstract

Given the serious consequences that an epidemic may have, it is essential to control its spread through several interventions such as social distancing, lockdown or vaccination. However, these interventions have a cost and they have to be implemented properly to be effective. The challenge of managing epidemics is therefore to limit their spread as much as possible while minimizing the cost of the interventions implemented.

This master thesis addresses several questions of epidemic management in the context of the COVID-19 outbreak in Belgium. The main questions considered in this work are: For each week of a one-year horizon, what is the optimal transmission rate of the disease to minimize its spread and the cost of the health measures implemented to achieve such a rate? Should health measures be different for the vulnerable and the non-vulnerable population? Who should be vaccinated first between the vulnerable population, the non-vulnerable population and the health care workers? To answer these questions, we use a control approach. Indeed, we design optimal control problems and model predictive control problems to find the optimal intervention strategies in order to curtail the spread of the disease while minimizing the cost of the interventions.

Keywords: Epidemic management, Optimal control, Model predictive control, Epidemic compartmental models.

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Chapter 1

Introduction

When an epidemic spreads, it can have far-reaching consequences, including human suffering and loss of life. The most recent and telling example is the spread of the COVID-19 epidemic. COVID-19 emerged in Wuhan in late 2019 before spreading around the world. By the end of March 2022, the World Health Organisation (WHO) reported that the disease had caused over 6.1 million deaths worldwide [1]. Moreover, the COVID-19 epidemic is far from being the only one to have caused serious consequences worldwide. Other major epidemics have also occurred in the 21st century, such as the Ebola epidemic and the H1N1 pandemic.

Given the serious consequences that an epidemic can have, it is therefore essential to implement countermeasures to limit its spread. For this, there are different types of interventions. Some of these reduce the risk of transmission within the population with actions like lockdown, closing schools or quarantine. Others, such as vaccination, allow decreasing the number of individuals susceptible to be infected. It is also possible to decrease the duration of infectiousness thanks to treatments. For these interventions to be effective, they need to be implemented at the right time and in the right way.

However, these actions have a social and an economic cost. For example, lockdown greatly reduces the economic activity of the country in which it is imposed. In addition, lockdown has a social cost as it greatly reduces social contact. The trade-off between the desire to minimize the spread of an epidemic as much as possible thanks to very strict measures and the cost of these interventions is what makes epidemic management complex and challenging.

When talking about the management of epidemics, many questions arise. The non-exhaustive list of questions that this master thesis seeks to answer, in the context of the COVID-19 epidemic in Belgium, is as follows:

- For each week of a one-year horizon, what is the optimal transmission rate of the disease in order to minimize its spread and the cost of the health measures implemented to achieve such a rate?
- Should health measures be different for the vulnerable and the non-vulnerable population?
- Who should be vaccinated first between the vulnerable population, the non-vulnerable population and the health care workers?
- How can health measures be optimally implemented when the measures imposed on each individual depend on their epidemic status?

¹To answer these questions, a number of assumptions had to be made for modelling purposes. The results obtained therefore depend on the assumptions made and the conclusions should not be taken literally.

In this master thesis, the dynamics of the COVID-19 epidemic is modelled using dynamical systems, called compartmental models in epidemiology. These models divide the population into several epidemic classes such as the susceptible, infectious and removed classes and represent the evolution of this population between the epidemic classes. They also allow to model the interventions put in place to curtail the spread of the disease. Indeed, in an epidemic model, each state variable represents the number of individuals present in a specific compartment and the input or control variables represent the interventions implemented. Several epidemic models are designed in this work to model different types of interventions but also different ways of modelling interactions in the Belgian population.

To answer the questions listed above, we use a control approach. Whatever the question of interest, the general aim is to determine the optimal intervention strategy leading to the best trade-off between minimizing the loss of life caused by the disease and minimizing the cost of the interventions. To achieve this goal, we design control problems. We want to find the optimal control and state trajectories for the epidemic model, representing the dynamics of the COVID-19 epidemic, in order to minimize a certain cost function. This cost function is composed of the number of deaths caused by the disease and the cost of the interventions implemented. Thanks to this control approach, the trade-off between minimizing the loss of life due to the disease and the cost of the interventions is therefore explicitly taken into account. Moreover, minimizing this cost function will lead to the best trade-off.

Concerning the cost of the interventions implemented to curb the epidemic, we have no a priori information. We therefore consider different costs and make assumptions about them. However, once we have set the cost of the interventions, our control approach allows us to find the optimal intervention strategy. This is the strength of this approach compared to an approach that tests several intervention strategies to see which is the best option.

In this master thesis, the control problems are solved using two different control approaches: the optimal control approach and the model predictive control (MPC) approach. The principle of these two control techniques is detailed in Chapter 2. In particular, the first question in the above list is first answered using optimal control. In the literature, the majority of the optimal control problems are solved thanks to the Pontryagin's Minimum Principle or a nonlinear programming solvers like Ipopt 2 or Knitro 3. In this master thesis, optimal control problems are solved by explicitly using the gradient descent and the Newton's method. This is the first contribution of this work. The first question of the above list is also answered using model predictive control. This will allow to highlight the similarities and differences between the two control approaches.

To answer the other questions of the above list, the model predictive control (MPC) approach is used. Several papers have already been published on the modelling and control of COVID-19 via MPC. However, to the best of my knowledge, very few or no articles answer these questions. This is the second principal contribution of this master thesis.

Finally, this master thesis is structured as follows. In Chapter 2, the state-of-the-art presents the modelling technique allowing to describe disease transmission thanks to compartmental models. The principle of the optimal control and the model predictive control is also detailed.

Chapter 3 is devoted to optimal control. First, the optimal control problem is defined properly. This problem aims to find the optimal transmission rate of the COVID-19 disease in order to minimize the number of deaths caused by the disease while minimizing the cost of the health measures implemented to achieve such a rate. Several methods are used to solve this optimal

control problem: gradient descent, Newton's method and quasi-Newton's method. The results and performances of each method are compared in this chapter. Finally, the results obtained for the optimal transmission rate are discussed based on the cost function used to model the cost of the health measures.

In Chapter 4, a model predictive control problem is designed. The aim of this problem is the same as in the previous chapter: find the optimal transmission rate to minimize the number of deaths and the cost of the sanitary measures. However, the way to proceed will be different compared to the optimal control. The results obtained via MPC for the optimal transmission rate are presented and discussed. Then, the results are compared to the ones obtained via optimal control. This allows to highlight the similarities and differences between the two control approaches.

Chapter 5 presents an epidemic model that takes into account the non-uniform mortality rate of the COVID-19 disease in the population. The model is stratified into a non-vulnerable population with a low infection fatality ratio (IFR) and a vulnerable population with a higher IFR. The aim of this chapter is then to look at the optimal health measures to be imposed within and between each population. This will help to determine whether it makes sense or not to impose different measures on the vulnerable and non-vulnerable people.

Chapter 6 is devoted to the vaccination strategies. This intervention is modelled in a population stratified into three groups: a vulnerable sub-population, a non-vulnerable sub-population and the health care workers. A model predictive control problem is then designed to find the optimal way to vaccinate these three groups and to study how the optimal health measures are affected by the vaccination. The optimal vaccination is then discussed according to the contacts of the health professionals.

In Chapter 7, the health measures imposed on each individual will depend on their epidemic status (susceptible, infectious,...). A distinction must then be made between infectious people who are aware of their infectiousness and those who are not. The former will be able to take measures accordingly, while the latter will not be able to do so because they do not know that they are infectious. Testing people can therefore be a useful intervention to increase the number of people who know they are infectious and this will be discussed in this chapter.

Chapter 2

State-of-the-art

As said in the introduction, in this master thesis we use a control approach to answer different questions of epidemic management. In this chapter, we first present how an epidemic can be represented thanks to a compartmental model. Then, we present two ways to control epidemic models: the optimal control and the model predictive control.

2.1 Compartmental models in epidemiology

Compartmental models are a modelling technique used to describe disease transmission. The principle is to divide the population into different compartments corresponding to epidemic classes and to represent the passage of people from one compartment to another using rates. The basic compartmental models describing disease transmission were developed by Kermack and McKendrick in 1927 [4]. The SIR model of Kermack and McKendrick is composed of three compartments: S , I and R . $S(t)$ denotes the number of individuals at time t who are susceptible to the disease and are therefore not yet infected. $I(t)$ denotes the number of individuals who are infectious and can therefore transmit the disease to the susceptible persons. $R(t)$ denotes the number of recovered (and immune) or dead individuals after being infected by the disease. This class can also be called the "removed" class.

In a SIR model, the infection process is represented thanks to the force of infection, λ . The force of infection is the risk for a susceptible individual to become infected [5]. It is defined as $\lambda = \beta \frac{I}{N}$. It is thus the transmission rate of the disease, β , multiplied by the proportion of infectious individuals in the population. The susceptible persons thus arrive at a rate $\beta \frac{I}{N} S$ per unit time in the infectious class (I). Then, they leave the infectious class at a rate γI per unit time to go in the removed class (R). γ is the removed or recovery rate and $1/\gamma$ is the mean duration of the infectious period.

The continuous-time SIR model is given by

$$\begin{aligned}\frac{dS(t)}{dt} &= -\beta S(t) \frac{I(t)}{N} \\ \frac{dI(t)}{dt} &= \beta S(t) \frac{I(t)}{N} - \gamma I(t) \\ \frac{dR(t)}{dt} &= \gamma I(t)\end{aligned}$$

Its discrete-time version is given by

$$\begin{aligned} S_{t+1} &= S_t - \beta S_t \frac{I_t}{N} \\ I_{t+1} &= I_t + \beta S_t \frac{I_t}{N} - \gamma I_t \\ R_{t+1} &= R_t + \gamma I_t \end{aligned} \tag{2.1}$$

where S_t, I_t and R_t denote the number of susceptible, infectious and removed individuals at time t .

The most common compartmental models are the SIS, SIR, SEIR and SIRD models. The name of the models shows the flow pattern of the individuals between the compartments. In addition to the 3 compartments already discussed for the SIR model, the compartment E corresponds to the exposed individuals, i.e. the ones who are infected but not yet infectious and the compartment D refers to people who died from the disease. In this master thesis, the SIRD model will be extended to take into account different phenomena: the distinction between the vulnerable and the non-vulnerable population, the vaccination and the different types of infectious people (pre-symptomatic, symptomatic and asymptomatic). All these models will be detailed later.

A very important concept in epidemiology is the basic reproduction number, R_0 . The basic reproduction number is the average number of secondary cases produced by one infectious individual introduced into a population only composed of susceptible individuals [6]. R_0 thus indicates how the number of infectious people will evolve if infectious individuals are introduced in a fully susceptible population. Indeed, if $R_0 < 1$, the number of infectious people present in the population decreases monotonically to zero. On the other hand, if $R_0 > 1$, the number of infectious people increases.

The basic reproduction number R_0 can be calculated for any compartmental model. R_0 is computed either intuitively or using the next generation matrix method. Let us first compute intuitively R_0 for the simple SIR model given in (2.1). When a population is fully susceptible, the SIR model is at the disease free equilibrium (DFE) with $(S_{0-}, I_{0-}, R_{0-}) = (N, 0, 0)$ and N the number of individuals in the population. When infectious people are introduced into the population, the initial behavior of the SIR model is governed by the sign of $\frac{\beta S_{0-}}{N} - \gamma$, or equivalently $\frac{\beta S_{0-}}{\gamma N} - 1$. If $\frac{\beta S_{0-}}{\gamma N} > 1$, the number of infectious people increases while if $\frac{\beta S_{0-}}{\gamma N} < 1$, the number of infectious people decreases. This corresponds to the definition of R_0 , with $R_0 = \frac{\beta S_{0-}}{\gamma N} = \frac{\beta}{\gamma}$.

Let us now present the next generation matrix method coming from [7]. This method allows to compute R_0 for any compartmental model. Since we will work with discrete-time epidemic models in this master thesis, we will present the discrete-time method. Let

$$x_t = (x_t^1, \dots, x_t^n)^T \in \mathbb{R}_+^n$$

be the number of individuals in the compartments containing infectious people and

$$y_t = (y_t^1, \dots, y_t^m)^T \in \mathbb{R}_+^m$$

be the number of individuals in the other compartments. The equations of the model for the compartments with infectious people can be written in the following way:

$$x_{t+1}^i = \mathcal{F}_i(x_t, y_t) + \mathcal{V}_i(x_t, y_t) \quad \text{for } i = 1, \dots, n$$

with $\mathcal{F}_i(x_t, y_t)$ the rate of appearance of new infections in compartment i and $\mathcal{V}_i(x_t, y_t)$ the rate of other transitions between the compartment i and the other compartments.

Then, let us define the two $n \times n$ matrices

$$F = \left[\frac{\partial \mathcal{F}_i(x_{0-}, y_{0-})}{\partial x^j} \right] \text{ and } V = \left[\frac{\partial \mathcal{V}_i(x_{0-}, y_{0-})}{\partial x^j} \right] \text{ for } 1 \leq i, j \leq n$$

with (x_{0-}, y_{0-}) the disease free equilibrium of the epidemic model. If $\phi(0)$ is the initial number of infectious individuals, then the matrix $F(I_d - V)^{-1} \phi(0)$ gives the expected number of new infections caused by these individuals, with I_d is the identity matrix. Moreover, the entry (i, j) of $F(I_d - V)^{-1}$ gives the expected number of secondary infections in compartment i produced by an infected individual introduced in compartment j . Finally,

$$R_0 = \rho(Q)$$

where $Q = F(I_d - V)^{-1}$ and ρ denotes the spectral radius.

As an illustration, we can derive the expression of R_0 for a SIR model thanks to the next generation matrix method. In the SIR model, the only compartment containing infectious people is the compartment I . Therefore, $x_t = I_t$ and $y_t = (S_t, R_t)$. Moreover, as said before, the disease free equilibrium of the SIR model is $(x_{0-}, y_{0-}) = (I_{0-}, S_{0-}, R_{0-}) = (0, N, 0)$. The equation of the SIR model for the compartment I is given by

$$I_{t+1} = \underbrace{\mathcal{V}_1(x_t, y_t)}_{I_t - \gamma I_t} + \underbrace{\mathcal{F}_1(x_t, y_t)}_{\beta S_t \frac{I_t}{N}}.$$

Therefore, F and V are equal to

$$F = \left[\frac{\partial \mathcal{F}_1(x_{0-}, y_{0-})}{\partial I} \right] = \beta \frac{S_{0-}}{N} \quad \text{and} \quad V = \left[\frac{\partial \mathcal{V}_1(x_{0-}, y_{0-})}{\partial I} \right] = 1 - \gamma.$$

Finally,

$$Q = F(I_d - V)^{-1} = \frac{\beta S_{0-}}{\gamma N} \quad \text{and} \quad R_0 = \rho(Q) = \frac{\beta S_{0-}}{\gamma N} = \frac{\beta}{\gamma}.$$

The expression for R_0 is well the same as that one found previously.

Once an epidemic has started to spread, the population is no longer fully susceptible. To take this into account, another quantity, close to R_0 , is the effective reproduction number, R_t . The effective reproductive number is defined as the average number of secondary cases per infectious case in a population composed of susceptible and non-susceptible hosts. It can be computed at each time t of an epidemic. To compute R_t thanks to the next generation matrix method, F and V are evaluated at (x_t, y_t) instead of (x_{0-}, y_{0-}) . The effective reproduction number of a SIR model is therefore $R_t = \frac{\beta S_t}{\gamma N}$.

2.2 Optimal control in epidemiology

In epidemiology, the compartmental models can be controlled using optimal control. Optimal control theory is the process of determining the control and state trajectories of a dynamical system over a period of time such that an objective function is optimized [8]. In the context of epidemics, the dynamical system is a compartmental epidemic model as described in Section

2.1. The objective function to be optimized represents the cost of infection of the disease, the cost of the control strategy or both. The cost of infection may include one or several of the following elements: the number of dead, infected or hospitalised people caused by the disease. The control strategy can be a non-pharmaceutical intervention such as quarantine, isolation, wearing the mask, etc. Some studies also research ways to curtail the spread of the epidemic through vaccination, medical treatment or testing.

One of the methods of the optimal control theory is the Pontryagin's Minimum Principle. It provides necessary conditions for finding the solution of an optimal control problem. These conditions are determined through the introduction of adjoint variables and the minimization of the Hamiltonian. The Pontryagin's Minimum Principle is the following [9, 10].

Theorem 1 (Pontryagin's Minimum Principle) *Let $x_k \in \mathcal{X} \subset \mathbb{R}^n$ be the state variables of the system and $u_k \in \mathcal{U} \subset \mathbb{R}^m$ be the control variables at time k . If u_k^* and x_k^* are optimal for the problem*

$$\begin{aligned} \min_{\mathbf{u}} J[\mathbf{x}, \mathbf{u}], \quad \text{where } J[\mathbf{x}, \mathbf{u}] &= l(x_{t_f}) + \sum_{k=0}^{t_f-1} g(x_k, u_k) \\ \text{subject to } x_{k+1} &= f(x_k, u_k) \quad \text{for } k = 0, \dots, t_f - 1 \end{aligned} \quad (2.2)$$

then, there exists an adjoint trajectory λ_k such that

$$H_k(x_k^*, u_k^*, \lambda_{k+1}) \leq H_k(x_k^*, u_k, \lambda_{k+1})$$

for all controls u_k at each time step k , where the Hamiltonian H_k is given by

$$H_k(x_k, u_k, \lambda_{k+1}) = g(x_k, u_k) + f(x_k, u_k)^T \lambda_{k+1}$$

and

$$\begin{aligned} \lambda_k &= \frac{\partial}{\partial x_k} H_k(x_k^*, u_k^*, \lambda_{k+1}) \\ \lambda_{t_f} &= \frac{\partial}{\partial x_{t_f}} l(x_{t_f}). \end{aligned}$$

There is also a continuous time version of the Pontryagin's Minimum Principle, but it will not be detailed here.

To illustrate the Pontryagin's Minimum Principle in the context of epidemic management, let us take an example coming from [9]. In this example, the intervention considered to curtail the spread of a disease is the vaccination. More precisely, the goal of this example is to find the optimal vaccination strategy in order to minimize the number of individuals infected by the disease while minimizing the cost of vaccination.

This example therefore considers a discrete-time SIR model with vaccination. A new compartment is therefore added to the SIR model: the compartment V regrouping the individuals who get vaccinated when susceptible. These individuals move from the compartment S to the compartment V at rate $u_k S_k$ per unit time. The control variable u_k , with $0 \leq u_k \leq 1$, represents the fraction of susceptible individuals who get vaccinated at time k . The control u_k therefore represents the vaccination strategy. Since the vaccine is not 100% efficient, the vaccinated individuals can be infected through contact with individuals in the infected class I but at a lower transmission rate $\beta\epsilon$ ($0 \leq \epsilon < 1$). Finally, births are represented by adding Π individuals in the compartment S at each time step k . Natural death occurs in all classes with μ being the death rate. The SVIR model is the following:

$$\begin{aligned}
S_{k+1} &= \Pi - (\mu - 1)S_k - \beta S_k I_k - u_k S_k \\
V_{k+1} &= u_k S_k - (\mu - 1)V_k - \beta \epsilon V_k I_k \\
I_{k+1} &= \beta (S_k + \epsilon V_k) I_k - (\mu - 1)I_k - \gamma I_k \\
R_{k+1} &= \gamma I_k - (\mu - 1)R_k
\end{aligned} \tag{2.3}$$

To minimize the cost of infection of the disease and the cost of vaccination, the optimal vaccination strategy, represented by the optimal control $\mathbf{u}^*$, must be such that the following cost function is minimized:

$$J[\mathbf{x}, \mathbf{u}] = A_{t_f} I_{t_f} + \sum_{k=0}^{t_f-1} \left(A_k I_k + \frac{B_k}{2} u_k^2 \right)$$

with $A_k > 0$ and $B_k > 0$ for $k = 1, \dots, t_f$. The term $A_k I_k$ represents the cost of infection, while the term $\frac{B_k}{2} u_k^2$ represents the cost of vaccination at time step k . However, the cost of vaccination defined in this example is questionable. When the Pontryagin's Minimum principle is used in the literature, the cost of administering the control u_k is generally assumed to be quadratic and of the form $\frac{B_k}{2} u_k^2$ for simplicity. This implies in this case that the vaccination cost only depends on the fraction of people u_k which are vaccinated at time k . A vaccination cost depending on $u_k S_k$, i.e. the number of people vaccinated at time k , would have been more appropriate.

To sum up, the goal of the control problem is to find the optimal control $\mathbf{u}^*$ such that:

$$J[\mathbf{x}^*, \mathbf{u}^*] = \min_{\Omega} J[\mathbf{x}, \mathbf{u}] \tag{2.4}$$

where

$$\Omega = \{\mathbf{u} \mid 0 \leq \mathbf{u} \leq 1\}.$$

Let us now apply the Pontryagin's Minimum Principle. Given the optimal control u_k^* and the corresponding solution $(S_k^*, V_k^*, I_k^*, R_k^*)$ of the system (2.3), minimizing $J[\mathbf{x}, \mathbf{u}]$ over Ω , there exists adjoint variables λ_k such that:

$$H_k(x_k^*, u_k^*, \lambda_{k+1}) \leq H_k(x_k^*, u_k, \lambda_{k+1})$$

for all controls u_k . The Hamiltonian H_k is given by

$$H_k(x_k, u_k, \lambda_{k+1}) = A_k I_k + \frac{B_k}{2} u_k^2 + \sum_{i=1}^4 \lambda_{i,k+1} f_i$$

where f_i are the right-hand sides of the system (2.3). Moreover, the adjoint variables, $\lambda_{1,k}, \dots, \lambda_{4,k}$ must satisfy the following equations:

$$\begin{aligned}
\lambda_{1,k} &= \frac{\partial H_k}{\partial S_k} = \lambda_{1,k+1} [-(\mu - 1) - \beta I_k^* - u_k^*] + \lambda_{2,k+1} u_k^* + \lambda_{3,k+1} \beta I_k^* \\
\lambda_{2,k} &= \frac{\partial H_k}{\partial V_k} = \lambda_{2,k+1} [-(\mu - 1) - \beta \epsilon I_k^*] + \lambda_{3,k+1} \beta \epsilon I_k^* \\
\lambda_{3,k} &= \frac{\partial H_k}{\partial I_k} = A_k - \lambda_{1,k+1} \beta S_k^* - \lambda_{2,k+1} \beta \epsilon V_k^* + \lambda_{3,k+1} [\beta (S_k^* + \epsilon V_k^*) \\
&\quad - (\mu - 1) - \gamma] + \lambda_{4,k+1} \gamma \\
\lambda_{4,k} &= \frac{\partial H_k}{\partial R_k} = -\lambda_{4,k+1} (\mu - 1)
\end{aligned} \tag{2.5}$$

with the conditions:

$$\begin{aligned}\lambda_{i,t_f} &= 0, \quad i = 1, 2, 4 \\ \lambda_{3,t_f} &= A_{t_f}\end{aligned}$$

Finally, the optimality condition for the control $\mathbf{u}^*$ is given by:

$$u_k^* = \min \left(\max \left(0, \frac{S_k^* (\lambda_{1,k+1} - \lambda_{2,k+1})}{B_k} \right), 1 \right) \quad \text{for } k = 0, \dots, t_f - 1 \quad (2.6)$$

where the expression for u_k^* is obtained by minimizing the Hamiltonian H_k with respect to u_k .

Thanks to the equations (2.3) and (2.5), the control problem (2.4) can be solved using an iterative forward-backward method [11]. The steps of this iterative method are the following. First, the SVIR system is solved forward in time from the time step $k = 0$ to $k = t_f$ with an initial condition for the control and state variables. Then, the adjoint variables are computed in a backward way using the current solution of the SVIR system. The control variables u_k^* are finally updated for the time steps $k = 0, \dots, t_f - 1$ thanks to (2.6). This scheme is then iterated until a certain convergence criterion is achieved.

In the literature, the Pontryagin's Minimum Principle has been applied in different epidemiological contexts. The authors in [12] apply optimal control theory in the context of influenza. The aim is to minimize the expected person-days lost due to deaths from influenza and due to the implementation of non-pharmaceutical interventions (NPI) to limit the spread of this disease. An optimal policy is derived for the control model using a linear NPI implementation cost. This leads to an optimal policy in which NPIs are applied at maximum strength when certain state criteria are met. In [9], several epidemiological models are designed to take into account different interventions in order to curtail the spread of an infectious disease: vaccination, treatment, quarantine and isolation. The Pontryagin's Minimum Principle is applied on each of these models to deduce the optimal strategy of each intervention.

In the COVID-19 context, optimal control theory is used in [13] to control a SEQIJR epidemic model. This model considers the evolution of the number of susceptible (S), Exposed (E), Quarantined (Q), Infectious (I), Isolated (J), and Recovered (R) individuals in the population. In this paper, three interventions are implemented to limit the spread of the disease: quarantine, isolation, and public health education. The Pontryagin's Minimum Principle determines the optimal control allowing to reduce the number of infectious individuals present in the population while minimizing the cost of the three interventions. It is shown that these interventions, when optimally used, will reduce the number of infectious people drastically within a short time but not to zero. Other interventions, such as vaccination, are thus needed to stop the spread of COVID-19.

In contrast with the Pontryagin's Minimum Principle, an optimal control problem can also be solved thanks to a direct method which does not require explicit derivation of necessary conditions. Indeed, the optimal control problem (2.2) can also be treated as a nonlinear constrained optimization problem. In this case, the problem is solved using a nonlinear programming solver like Ipopt as in [14, 15] or like Knitro as in [16]. The direct method allows to solve more complex control problems than the Pontryagin's Minimum Principle. Indeed, the applicability of the latter is restricted due to its theoretical approach. However, the Pontryagin's Minimum Principle provides an analytical expression for the optimal control variables, which is not the case of the direct method.

In this master thesis, optimal control is used to answer the following question in the COVID-19 context: For each week of a one-year horizon, what is the optimal transmission rate of the

disease to minimize its spread and the cost of the health measures implemented to achieve such a rate?

To answer this question, we design an optimal control problem that controls a SIRD model. All the details about this control problem are presented in Chapter 3. Compared to the literature, this optimal control problem will be solved by explicitly using the gradient descent and the Newton's method. This is the first contribution of this master thesis.

2.3 Model predictive control in epidemiology

An epidemic model can also be controlled using model predictive control [17]. The principle of the model predictive control is to determine the optimal behaviour of a system over a time horizon that we will call the *whole horizon* T . To find the input (or control) trajectory and the state trajectory of the system, an iterative algorithm is applied in the following way. At each time step, the control trajectory is computed by solving an optimization problem over a finite *prediction horizon* P that can be different from the *whole horizon* T . This optimization problem thus corresponds to an optimal control problem as describes in Section 2.2. Once this problem is solved at the time step t , only the first step of the control trajectory is applied to get the state of the system at the time step $t + 1$. Then, another optimal control problem is solved based on the new state of the system and with a shifted prediction horizon. This iterative procedure is repeated until the last time step of the *whole horizon* T .

More formally, the optimal control problem (OCP) solved at each time step t of the MPC algorithm is the following:

$$\min_{\mathbf{x}, \mathbf{u}} \quad l(x_P) + \sum_{k=0}^{P-1} g(x_k, u_k) \quad (2.7a)$$

$$\text{subject to} \quad x_0 = \hat{x}_0 \quad (2.7b)$$

$$x_{k+1} = f(x_k, u_k) \quad \text{for } k = 0, \dots, P-1 \quad (2.7c)$$

$$h(x_k, u_k) \leq 0 \quad \text{for } k = 0, \dots, P-1 \quad (2.7d)$$

$\mathbf{x}$ is the vector that gathers all the state variables of the system from time $k = 0$ to $k = P$ and $\mathbf{u}$ the one with all the control variables from time $k = 0$ to $k = P - 1$. In model predictive control, the control variables are also called manipulated variables and this terminology will be used in the rest of the master thesis. $g(x_k, u_k)$ is the cost at each time k and $l(x_P)$ is the terminal cost. The meaning of each constraint of the OCP (2.7) is the following:

- the constraint (2.7b) enforces the current state of the system, $\hat{x}_0$, to be the initial state x_0 of the system for the optimal control problem.
- the constraint (2.7c) makes sure that the state variables satisfy the dynamics of the system.
- the constraint (2.7d) represents the set of constraints imposed on the state variables and the manipulated variables at each time k .

The MPC algorithm is the following:

MPC Algorithm

For $t = 0, \dots, T - 1$:

- (1) Set $\hat{x}_0 = x_t$, where x_t is the current state of the system.
- (2) Solve the optimal control problem (2.7) for $\hat{x}_0 = x_t$ to obtain the optimal control sequence $\mathbf{u}^*$.
- (3) Define the MPC control law value $\mu_P(x_t) := \mathbf{u}^*(0)$.
- (4) Apply the control value $\mu_P(x_t)$ to the system, $t := t + 1$ and go to (1).

Several articles have already answered some questions about the management of the COVID-19 epidemic using model predictive control. In [18], MPC is used to optimally determine the deployment of the two-dose vaccination for the COVID-19 pandemic in Italy. In the MPC problem, the health care needs and socio-economic costs associated with the epidemic are taken into account. The optimal deployment of the vaccination found tends to distribute the first and second dose evenly with an alternation between the two doses. The authors in [19] investigate optimal strategies to control the COVID-19 pandemic thanks to social distancing measures. They minimize the number of fatalities over the course of two years without inducing excessive social costs. Although the number of deaths is significantly reduced by social distancing measures, they conclude that eradication of the virus is not possible without the availability of a vaccine.

In this master thesis, we answer further questions about the management of the COVID-19 epidemic using model predictive control. The main questions addressed are:

- Should health measures be different for the vulnerable and the non-vulnerable population?
- Who should be vaccinated first between the vulnerable population, the non-vulnerable population and the health care workers?
- How can health measures be optimally implemented when the measures imposed on each individual depend on their epidemic status?

To the best of my knowledge, very few or no articles answer these questions. This is therefore the second principal contribution of this master thesis. To answer these questions, we design three model predictive control problems in Chapters 5, 6 and 7 respectively.

Chapter 3

Optimal control of the COVID-19 transmission rate

The aim of this chapter is to control the COVID-19 transmission rate in order to minimize the number of deaths caused by the disease while minimizing the cost of health measures imposed on the population to achieve such a transmission rate. What makes this problem complex and very interesting is that these two elements to be minimized are opposed to each other. Indeed, the desire to limit the number of deaths as much as possible will lead to strict and costly sanitary measures. Conversely, reducing the cost and thus the severity of the measures will lead to an increase in the number of people infected with COVID-19 and therefore ultimately to more deaths. A trade-off must therefore be found between these two opposing elements to be minimized.

In this chapter, we want therefore to find the optimal transmission rate β_t for each week t of a one-year horizon such that it minimizes a certain cost. To achieve this goal, we use an optimal control approach and β_t is the control variable. The cost function of the optimal control problem (OCP) is composed of two elements: the cumulative number of deaths caused by the disease at the end of a one-year horizon and the cost of the sanitary measures.

Firstly, the cumulative number of deaths is given by an epidemic model representing the dynamics of the COVID-19 epidemic. In this chapter, a SIRD model is used and is defined in Section [3.1](#). Secondly, we have no a priori information on the cost of health measures. Since the aim of the health measures is to reduce the transmission rate β_t of the disease, we assume that their cost depends on β_t . In this master thesis, different cost functions for the health measures are studied. All these cost functions are scaled so that they are in the same range of value when evaluated between β_{min} and β_{max} . β_{max} is the transmission rate of the disease when there is no health measures and is therefore the maximum value that β_t can have. On the other hand, β_{min} is assumed to be the minimum value that β_t can reach when the health measures are as strict as possible. All the assumptions made about the cost of the health measures are presented and justified in Section [3.2](#).

To sum up, the aim of this chapter is to answer the following question: For each week t of a one-year horizon, what is the optimal transmission rate β_t of the disease, with $\beta_t \in [\beta_{min}, \beta_{max}]$, in order to minimize the number of death caused by the disease and the cost of the health measures?

3.1 The SIRD epidemic model

The dynamics of the COVID-19 epidemic is modelled thanks to a compartmental system. This system will allow, among other things, to compute the cumulative number of deaths caused by the disease and involved in the objective function of the optimal control problem. This first model is intended to be simple and general. It is an epidemic model with four compartments: S , I , R and D . S_t denotes the number of susceptible individuals at time t who can be infected by the disease. I_t denotes the number of infectious people who can infect the susceptible individuals. R_t is the number of people who have recovered from the disease after being infected and D_t the number who died from the disease. The SIRD model is given by:

$$\begin{aligned} S_{t+1} &= S_t - \beta_t S_t \frac{I_t}{N} \\ I_{t+1} &= I_t + \beta_t S_t \frac{I_t}{N} - \gamma I_t \\ R_{t+1} &= R_t + \gamma(1 - \delta) I_t \\ D_{t+1} &= D_t + \gamma \delta I_t \end{aligned} \tag{3.1}$$

N is the number of individuals in the population. β_t is the transmission rate of the disease in week t . Since the time step of the system is equal to one week, β_t is expressed in [1/week]. More precisely, the transmission rate is defined as:

β_t = the transmission rate between a susceptible individual and the infectious people in week t
= the number of contacts of a susceptible person with the general population in week t
× the probability of a successful transmission in case of contact between a susceptible and an infectious individual

γ is the rate at which the infectious people leave the compartment I . This rate, expressed in [1/week], is equal to the inverse of the infectious period, i.e. the average time period during which an infectious individual may transmit the disease. Finally, when leaving the compartment I , a fraction $(1 - \delta)$ of the infectious individuals recover while a fraction δ of them die. δ is the infection fatality ratio (IFR). It is the proportion of infected people who die from the disease.

3.1.1 Parameter estimation

The value of all the parameters of the SIRD model is chosen to best represent the COVID-19 epidemic in Belgium. Firstly, the Belgian population is around $N = 11.52$ million [20]. The infection fatality ratio for COVID-19 in Belgium is estimated to be $\delta = 0.015$ [21]. Moreover, the infectious period for COVID-19 is estimated to be about one week [22]. Therefore, $\gamma = 1$ [1/week]. This value for γ implies that all people who are infectious in week t will no longer be infectious in week $t + 1$. One may then ask whether a time step of one week is not a too large time step. This question will be answered in Section 3.6 where we will solve the optimal control problem with a daily time step instead of a weekly time step. We will see that the results are very similar in both cases and therefore that a weekly time step is acceptable for the SIRD model.

Let us then estimate the value of β_{max} and β_{min} . As a remainder, β_{max} is the transmission rate of the disease when there is no health measure. β_{max} is computed thanks to the basic reproduction number, R_0 . At the beginning of the COVID-19 epidemic, on 1st March 2020, the estimated value for R_0 was 2.33 in Belgium [23]. This means that one infected person was infecting an average of 2.33 people. It is supposed to be the maximum value for R_0 since no

health measures were implemented to limit the spread of the disease at this time of the epidemic. In order to deduce β_{max} from R_0 , let us compute the basic reproduction number of the SIRD model (3.1) by using the next generation matrix method. As the compartment D does not influence the expression of R_0 , this latter is the same for a SIR and a SIRD model. Therefore, as already computed in Section 2.1, the basic reproduction number of a SIRD model is $R_0 = \frac{\beta}{\gamma}$. Since $\gamma = 1$ [1/week], $\beta = 2.33$ [1/week]. Moreover, since $R_0 = 2.33$ is assumed to be the maximum value for the basic reproduction number, $\beta = 2.33$ [1/week] is the maximum value for the transmission rate and $\beta_{max} = 2.33$ [1/week].

As no accurate value for the minimum transmission rate was found in the literature, let us take $\beta_{min} = 0.01$ [1/day] = 0.07 [1/week]. β_{min} is chosen different from zero since it is impossible to impose health measures such that the transmission rate is zero. For example, people have to go shopping for basic necessities and even if everything was delivered to them, some people have to work to make this possible. The transmission rate can therefore never be reduced to zero.

3.2 Cost of health measures

One way to limit the spread of a disease is to decrease its transmission rate. This transmission rate can be reduced through the application of health measures imposed by the government. However, these measures obviously have a social and economic cost for the population. To ensure that all elements of the objective function to be minimized in the OCP have the same units, the cost of the measures is expressed in number of deaths per day. It is thus a daily cost.

As we have no a priori information on the cost of health measures, the cost functions used in this master thesis are arbitrary and we have to make assumptions. We assume that the cost of the governmental measures is a decreasing function of β_t : the higher the desired transmission rate, the lighter the measures to achieve it and therefore the lower the cost of these measures. Moreover, the cost is assumed to be convex. The hypothesis about the convexity represents the fact that the stricter the measures, the more expensive it is to add an additional measure to further reduce the transmission rate. Some examples of convex cost functions are:

$$L_1(\beta_t) = \frac{1}{\beta_t} \quad L_2(\beta_t) = \frac{1}{\beta_t^2} \quad L_3(\beta_t) = \frac{1}{\beta_t^3}$$

These 3 cost functions can have very different values for the same transmission rate. For example,

$$L_1(0.1) = 10 \quad L_2(0.1) = 100 \quad L_3(0.1) = 1000$$

We therefore scale these cost functions so that they are all in the range $[0, \lambda]$ when evaluated between β_{min} and β_{max} :

$$\lambda L_{s,i}(\beta_t) = \lambda \frac{L_i(\beta_t) - L_i(\beta_{max})}{L_i(\beta_{min}) - L_i(\beta_{max})}$$

with $L_i(\beta_t) = \frac{1}{\beta_t^i}$ and $\beta_t \in [\beta_{min}, \beta_{max}]$.

Thanks to this scaling, the cost functions are all equal to 0 when evaluated at β_{max} and to λ at β_{min} . Between β_{min} and β_{max} , the value of the scaled functions differs according to their convexity. Having a zero cost at β_{max} is very relevant in this context. Indeed, the maximum transmission rate, β_{max} , is the one when no governmental measures are imposed. It therefore makes sense that the cost to impose the maximum transmission rate is zero. Finally, the parameter λ represents the daily cost of the sanitary measures to set the minimum transmission

rate β_{min} and is expressed in terms of number of deaths per day. For example, if we assume that the daily cost of the measures needed to enforce a transmission rate of β_{min} is 1000 deaths per day, then $\lambda = 1000$. The value of λ is arbitrary and different values of λ are studied in this master thesis. In conclusion, the daily cost of the sanitary measures allowing to impose the transmission rate β_t to the population is given by $\lambda L_{s,i}(\beta_t)$.

3.3 Problem statement

The previous two sections have defined the two elements to be minimized in the cost function of the optimal control problem. Let us put them together to state the OCP. The aim is to determine the optimal weekly transmission rate, β_t^* , so that the number of deaths caused by the disease and the cost of the health measures are minimized. The cost function of the OCP is first composed of D_T , the cumulative number of deaths caused by the disease at the end of the T weeks of the time-horizon. The time horizon of the OCP will be of one year and T will therefore be equal to 52 weeks. Then, $\lambda L_{s,i}(\beta_t)$ is the daily cost of the government measures allowing to impose the transmission rate β_t . Since it is a daily cost and that each transmission rate is imposed during one week, the weekly cost of the measures is $7\lambda L_{s,i}(\beta_t)$. The optimal control problem (OCP) is therefore:

$$\begin{aligned} \min_{\mathbf{x}, \mathbf{u}} f(\mathbf{x}, \mathbf{u}) &= D_T + \sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t) \\ \text{subject to } & \text{(3.1)} \quad \text{for } t = 0, \dots, T-1 \\ & \beta_{min} \leq \beta_t \leq \beta_{max} \quad \text{for } t = 0, \dots, T-1 \end{aligned} \quad (3.2)$$

$\mathbf{x}$ is the vector that gathers all the state variables of the SIRD system (3.1) from $t = 0$ to $t = T$. $\mathbf{u} = [\beta_0, \dots, \beta_{T-1}]$ is the vector containing all the weekly transmission rates. All these transmission rates must be between β_{min} and β_{max} .

For the initial condition of the optimal control problem, we take the situation observed in Belgium for COVID-19 on 25th April 2020. On that date, there were approximately 30 000 infectious persons [24]. Therefore, we set $I_0 = 30\,000$. In addition, about 50 000 people were infected and had already recovered or died before that date. With the infection fatality ratio δ defined above, we therefore fix the number of recoveries and deaths at $R_0 = 50\,000 \cdot (1 - \delta)$ and $D_0 = 50\,000 \cdot \delta$ respectively. Finally, we set $S_0 = N - I_0 - R_0 - D_0$. The initial condition of the epidemic model (3.1) involved in the OCP is therefore

$$x_0 = [S_0, I_0, R_0, D_0] = [11\,440\,000, 30\,000, 49\,250, 750].$$

3.4 Methods to solve the optimal control problem (3.2)

This section will present the different methods used to solve the control problem (3.2). As explained in the state-of-the-art, optimal control is used to determine the optimal control and state trajectories of a dynamical system so that an objective function is minimized. In our case, the SIRD system (3.1) is controlled by the weekly transmissions rate, β_t , and the objective function is defined in (3.2). Moreover, the optimal transmission rates β_t is determined for the whole time horizon of T weeks, based solely on the initial condition of the system. In the model predictive control problem designed in Chapter 4, this will no longer be the case.

The optimal control problem (3.2) is solved using three different methods: the gradient descent method, the Newton's method and the L-BFGS-B algorithm. All these methods are explained in the following three sections.

3.4.1 Gradient descent according to $\mathbf{u}$

The gradient descent is a first-order iterative algorithm for finding a local minimum of a differentiable function. At each step, to obtain the current solution, a shift is made in the opposite direction to the gradient so that the function decreases. In our case, the gradient descent algorithm is used to solve the optimal control problem (3.2). Moreover, a projected version of the gradient descent is used to satisfy the second constraint of the problem, i.e.

$$\mathbf{u} \in C = \{\mathbf{u} : \beta_{min} \leq \beta_t \leq \beta_{max} \text{ for } t = 0, \dots, T-1\}.$$

At each step, the current solution is therefore projected onto the constraint set C . The iterative algorithm is thus the following:

Given $\mathbf{x}_0, \mathbf{u}_0, f(\mathbf{x}, \mathbf{u}), \nabla f(\mathbf{x}, \mathbf{u}), j = 0$
While $\|\nabla f(\mathbf{x}_j, \mathbf{u}_j)\| > \epsilon$
 $\mathbf{u}_{j+1} = \mathbb{P}_C [\mathbf{u}_j - \alpha \nabla f(\mathbf{x}_j, \mathbf{u}_j)]$
 $\mathbf{x}_{j+1}$ computed by the SIRD model (3.1) with $\mathbf{u}_{j+1}$
 $j \leftarrow j + 1$

$\mathbf{x}_j$ and $\mathbf{u}_j$ are the vectors $\mathbf{x}$ and $\mathbf{u}$, as defined in Section 3.3, at the iteration j of the gradient descent. $\mathbb{P}_C$ is the projection operator onto the set C . The stopping criteria of the gradient descent algorithm is chosen to be $\epsilon = 10^{-3}$. The learning rate is $\alpha = 10^{-5}$. This is the highest rate allowing to converge to the solution. The optimal state and control variables, $\mathbf{x}^*$ and $\mathbf{u}^*$, are the ones obtained at the last iteration of the gradient descent, before the method stops.

Now that the algorithm is defined, let us look at the computation of $\nabla f(\mathbf{x}, \mathbf{u})$. As a reminder, the objective function to be minimized in (3.2), $f(\mathbf{x}, \mathbf{u})$ is

$$f(\mathbf{x}, \mathbf{u}) = D_T + \sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t).$$

The gradient of $f(\mathbf{x}, \mathbf{u})$ is defined as

$$\nabla f(\mathbf{x}, \mathbf{u}) = \left[\frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial \beta_0}, \dots, \frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial \beta_{T-1}} \right]$$

with

$$\frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial \beta_k} = \frac{\partial D_T}{\partial \beta_k} + 7\lambda \frac{\partial L_{s,i}(\beta_k)}{\partial \beta_k} \quad \text{for } k = 0, \dots, T-1.$$

Then, $\frac{\partial D_T}{\partial \beta_k}$ is computed in an iterative way. Indeed, D_T depends on D_{T-1} which itself depends on D_{T-2} and so on, as shown by the SIRD system (3.1). Therefore, $\frac{\partial D_{T-1}}{\partial \beta_k}$ is needed to compute $\frac{\partial D_T}{\partial \beta_k}$ and so on. Moreover, D_T depends on I_{T-1} which itself depends on S_{T-2} . In conclusion, to compute $\frac{\partial D_T}{\partial \beta_k}$, all the following quantities are needed:

$$\frac{\partial D_t}{\partial \beta_k}, \quad \frac{\partial I_t}{\partial \beta_k}, \quad \frac{\partial S_t}{\partial \beta_k} \quad \forall t \in \{0, \dots, T-1\}.$$

The computation of these partial derivatives is divided into 3 cases:

- $\forall k, t \in \{0, \dots, T-1\}$ such that $k = t$,

$$\begin{aligned}\frac{\partial S_{t+1}}{\partial \beta_k} &= \frac{\partial S_t}{\partial \beta_k} - \frac{S_t I_t}{N} - \frac{\beta_t I_t}{N} \frac{\partial S_t}{\partial \beta_k} - \frac{\beta_t S_t}{N} \frac{\partial I_t}{\partial \beta_k} \\ \frac{\partial I_{t+1}}{\partial \beta_k} &= (1 - \gamma) \frac{\partial I_t}{\partial \beta_k} + \frac{S_t I_t}{N} + \frac{\beta_t I_t}{N} \frac{\partial S_t}{\partial \beta_k} + \frac{\beta_t S_t}{N} \frac{\partial I_t}{\partial \beta_k} \\ \frac{\partial D_{t+1}}{\partial \beta_k} &= \frac{\partial D_t}{\partial \beta_k} + \delta \gamma \frac{\partial I_t}{\partial \beta_k}\end{aligned}$$

- $\forall k, t \in \{0, \dots, T-1\}$ such that $k > t$,

$$\frac{\partial S_{t+1}}{\partial \beta_k} = 0$$

$$\frac{\partial I_{t+1}}{\partial \beta_k} = 0$$

$$\frac{\partial D_{t+1}}{\partial \beta_k} = 0$$

- $\forall k, t \in \{0, \dots, T-1\}$ such that $k < t$,

$$\begin{aligned}\frac{\partial S_{t+1}}{\partial \beta_k} &= \frac{\partial S_t}{\partial \beta_k} - \frac{\beta_t I_t}{N} \frac{\partial S_t}{\partial \beta_k} - \frac{\beta_t S_t}{N} \frac{\partial I_t}{\partial \beta_k} \\ \frac{\partial I_{t+1}}{\partial \beta_k} &= (1 - \gamma) \frac{\partial I_t}{\partial \beta_k} + \frac{\beta_t I_t}{N} \frac{\partial S_t}{\partial \beta_k} + \frac{\beta_t S_t}{N} \frac{\partial I_t}{\partial \beta_k} \\ \frac{\partial D_{t+1}}{\partial \beta_k} &= \frac{\partial D_t}{\partial \beta_k} + \delta \gamma \frac{\partial I_t}{\partial \beta_k}\end{aligned}$$

Moreover, since the initial condition of the SIRD system does not depend on any transmission rate β_k

$$\frac{\partial D_0}{\partial \beta_k} = 0, \quad \frac{\partial I_0}{\partial \beta_k} = 0, \quad \frac{\partial S_0}{\partial \beta_k} = 0 \quad \forall k \in \{0, \dots, T-1\}.$$

Thanks to the iterative computation of these partial derivatives, we have now all we need to compute $\nabla f(\mathbf{x}, \mathbf{u})$ and to apply the gradient descent algorithm. The results obtained with this method can be found in Section [3.5.2](#)

Gradient descent according to $\mathbf{w} = \ln(\mathbf{u})$

The gradient descent can also be done according to $\mathbf{w} = \ln(\mathbf{u})$, where $\mathbf{w} = [w_0, \dots, w_{T-1}] = [\ln(\beta_0), \dots, \ln(\beta_{T-1})]$. The purpose of this change of variable is to accelerate the speed of convergence of the algorithm and we will see in Section [3.5.2](#) that it effectively decreases the number of iterations required to reach the solution. With this change of variable, the projected gradient method becomes

Given $\mathbf{x}_0, \mathbf{w}_0, \mathbf{u}_0 = e^{\mathbf{w}_0}, f(\mathbf{x}, \mathbf{u}), \nabla_w f(\mathbf{x}, \mathbf{u}), j = 0$
 While $\|\nabla_w f(\mathbf{x}_j, \mathbf{u}_j)\| > \epsilon$
 $\mathbf{w}_{j+1} = \mathbb{P}_S [\mathbf{w}_j - \alpha \nabla_w f(\mathbf{x}_j, \mathbf{u}_j)]$
 $\mathbf{u}_{j+1} = e^{\mathbf{w}_{j+1}}$
 $\mathbf{x}_{j+1}$ computed by the SIRD model (3.1) with $\mathbf{u}_{j+1}$
 $j \leftarrow j + 1$

$\mathbb{P}_S$ is the projection operator onto the constraint set S defined as

$$S = \{\mathbf{w} : \ln(\beta_{min}) \leq w_t \leq \ln(\beta_{max}) \text{ for } t = 0, \dots, T-1\}.$$

The stopping criteria of the gradient descent algorithm is chosen to be $\epsilon = 10^{-3}$. The learning rate is $\alpha = 10^{-4}$.

Moreover, $\nabla_w f(\mathbf{x}, \mathbf{u})$ is defined as

$$\nabla_w f(\mathbf{x}, \mathbf{u}) = \left[\frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial w_0}, \dots, \frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial w_{T-1}} \right]$$

with

$$\frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial w_k} = \frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial \beta_k} \frac{\partial \beta_k}{\partial w_k} = \frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial \beta_k} \beta_k \quad \text{for } k = 0, \dots, T-1$$

where $\frac{\partial f(\mathbf{x}, \mathbf{u})}{\partial \beta_k}$ has already been calculated above for the gradient method according to $\mathbf{u}$. The results obtained with this method can be found in Section 3.5.2

3.4.2 Newton's method

The Newton's method is a second-order iterative algorithm for finding a local minimum of a differentiable function. This method is investigated because the convergence of the second-order methods may be much faster than the one of the first-order methods. The objective is thus to decrease the number of iterations needed to solve the optimal control problem compared to the one needed with the gradient descent algorithm. The Newton's method used to solve the OCP (3.2) is:

Given $\mathbf{x}_0, \mathbf{u}_0, f(\mathbf{x}, \mathbf{u}), \nabla f(\mathbf{x}, \mathbf{u}), \nabla^2 f(\mathbf{x}, \mathbf{u}), j = 0$
 While $\lambda_j^2/2 > \epsilon$
 $\mathbf{u}_{j+1} = \mathbb{P}_C [\mathbf{u}_j - \nabla^2 f(\mathbf{x}_j, \mathbf{u}_j)^{-1} \nabla f(\mathbf{x}_j, \mathbf{u}_j)]$
 $\mathbf{x}_{j+1}$ computed by the SIRD model (3.1) with $\mathbf{u}_{j+1}$
 $j \leftarrow j + 1$

where $\lambda_j^2 = \nabla f(\mathbf{x}_j, \mathbf{u}_j)^T \nabla^2 f(\mathbf{x}_j, \mathbf{u}_j)^{-1} \nabla f(\mathbf{x}_j, \mathbf{u}_j)$. The stopping criteria is $\lambda_j^2/2 > \epsilon$ with $\epsilon = 10^{-3}$. $\mathbb{P}_C$ is the projection operator onto the set C .

The computation of $\nabla f(\mathbf{x}, \mathbf{u})$ has already been discussed in the section about the gradient descent method. The Hessian of $f(\mathbf{x}, \mathbf{u})$ is defined as

$$\nabla^2 f(\mathbf{x}, \mathbf{u}) = \begin{bmatrix} \frac{\partial^2 f(\mathbf{x}, \mathbf{u})}{\partial \beta_0^2} & \dots & \frac{\partial^2 f(\mathbf{x}, \mathbf{u})}{\partial \beta_0 \partial \beta_{M-1}} \\ \vdots & \ddots & \vdots \\ \frac{\partial^2 f(\mathbf{x}, \mathbf{u})}{\partial \beta_{T-1} \partial \beta_0} & \dots & \frac{\partial^2 f(\mathbf{x}, \mathbf{u})}{\partial \beta_{T-1}^2} \end{bmatrix}$$

with

$$\frac{\partial^2 f(\mathbf{x}, \mathbf{u})}{\partial \beta_l \partial \beta_k} = \frac{\partial^2 D_T}{\partial \beta_l \partial \beta_k} + 7\lambda \frac{\partial^2 L_{s,i}(\beta_k)}{\partial \beta_l \partial \beta_k} \quad \text{for } k, l = 0, \dots, T-1.$$

For the same reason as for the computation of the first-order partial derivatives of D_T , $\frac{\partial^2 D_T}{\partial \beta_l \partial \beta_k}$ is computed iteratively and to compute this second-order partial derivative, all the following quantities are needed:

$$\frac{\partial^2 D_t}{\partial \beta_l \partial \beta_k}, \quad \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}, \quad \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} \quad \forall t \in \{0, \dots, T-1\}.$$

For the sake of brevity, the computation of these partial derivatives is given in appendix [3.A](#). After these tedious calculations, we can apply the Newton's method. The results obtained with this method can be found in Section [3.5.2](#).

3.4.3 L-BFGS-B algorithm

The optimal control problem [\(3.2\)](#) can also be solved thanks to the L-BFGS-B algorithm. This algorithm is implemented in the Python package `scipy.optimize` [\[25\]](#). The L-BFGS-B algorithm belongs to the family of quasi-Newton methods. In the quasi-Newton methods, the Hessian of the objective function $f(\mathbf{x}, \mathbf{u})$ to be minimized is approximated at each iteration, whereas in the Newton's method the Hessian is fully computed as in the previous section. Moreover, the L-BFGS-B algorithm approximates the Broyden–Fletcher–Goldfarb–Shanno (BFGS) algorithm. Like the original BFGS, L-BFGS-B uses an estimate of the inverse Hessian matrix to steer its search through variable space, but where BFGS stores a dense matrix to approximate the inverse Hessian, L-BFGS-B stores only a few vectors that represent the approximation implicitly [\[26\]](#). This is why it is called the Limited-memory BFGS-B algorithm. Finally, the letter B stands for bounds because the L-BFGS-B algorithm allows to handle bound constraints. This algorithm is the third method used to solve the optimal control problem [\(3.2\)](#). The results obtained with this method can be found in Section [3.5.2](#).

3.5 Results

This section presents the results obtained for the optimal weekly transmission rate β_t^* by solving the optimal control problem [\(3.2\)](#). As a reminder, this problem aims to find the optimal transmission rate β_t^* in order to minimize the cumulative number of deaths caused by the disease at the end of a one-year horizon while minimizing the cost of the health measures implemented to achieve such a rate. The control problem is first solved using the L-BFGS-B algorithm and with three different cost functions, $\lambda L_{s,i}$, for the health measures. Then, the temporal evolution of the optimal transmission rate β_t^* , obtained with the four methods detailed in Section [3.4](#) are compared. The performances of each method, i.e. the number of iterations required to converge to the solution and the execution time, are also discussed. Finally, we analyse the temporal evolution of the optimal transmission rate to be imposed on the population for high cost functions $\lambda L_{s,i}$.

3.5.1 Results obtained with the L-BFGS-B algorithm

The optimal control problem (3.2) is first solved with the three following daily cost functions for the sanitary measures:

$$\begin{aligned}\lambda_1 L_{s,1/2}(\beta_t) &= 1000 \frac{1/\beta_t^{1/2} - 1/\beta_{max}^{1/2}}{1/\beta_{min}^{1/2} - 1/\beta_{max}^{1/2}} & \lambda_1 L_{s,1}(\beta_t) &= 1000 \frac{1/\beta_t - 1/\beta_{max}}{1/\beta_{min} - 1/\beta_{max}} \\ \lambda_1 L_{s,2}(\beta_t) &= 1000 \frac{1/\beta_t^2 - 1/\beta_{max}^2}{1/\beta_{min}^2 - 1/\beta_{max}^2}\end{aligned}\tag{3.3}$$

These cost functions are represented in Figure 3.1. When there are no sanitary measures to reduce the transmission rate, i.e. $\beta_t = \beta_{max}$ and thus $\beta_t/\beta_{max} = 1$, the cost is zero. The daily cost of the measures to be imposed to achieve the minimum transmission rate, i.e. $\beta_t/\beta_{max} = \beta_{min}/\beta_{max} = 0.03$, is assumed to be $\lambda_1 = 1000$ deaths. This value is chosen for the parameter λ to represent the fact that the measures to be imposed to achieve the minimum transmission rate are very costly. As desired in Section 3.2, the cost is a decreasing function of β_t and is convex. While the three cost functions shown in Figure 3.1 have the same value when evaluated at β_{min} and β_{max} , their behaviour differs between these two rates. We will see if it has an impact on the results of the optimal control problem.

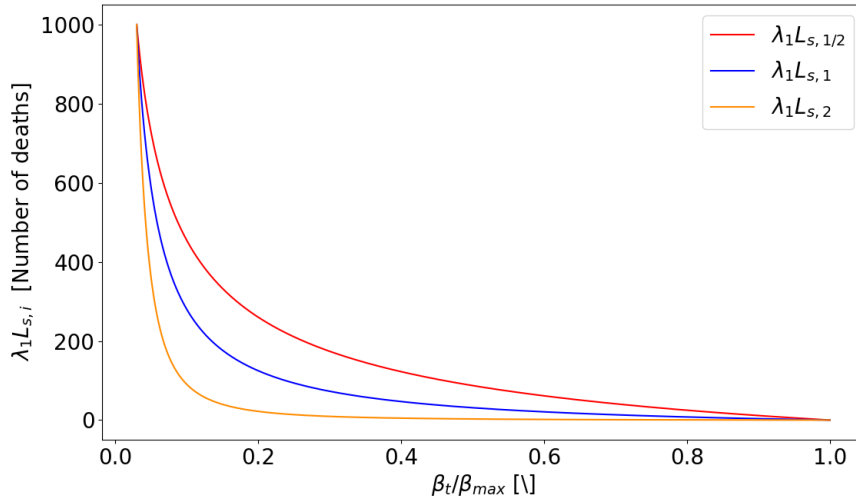


Figure 3.1: Daily cost functions $\lambda_1 L_{s,i}$, as defined in (3.3), for the health measures imposed to reduce the transmission rate β_t .

Let us then look at the results. First, we analyze the evolution of the optimal weekly transmission rate β_t^* over the one-year horizon for the cost function $\lambda_1 L_{s,1}$. The optimal transmission rate is the one which minimizes the number of deaths caused by the disease and the cost of the health measures, i.e. the rate minimizing the objective function in (3.2). Figure 3.2a shows that the optimal transmission rate is increasing over time. At the beginning of the one-year horizon, the transmission rate is very low. Indeed, $\beta_0^* \approx 0.2\beta_{max}$. This means that the health measures imposed to achieve this transmission rate must be strict. Thanks to this low rate, the spread of the disease is limited and the number of infectious people present in the population decreases as shown in Figure 3.2b. Consequently, the number of deaths caused by the disease, which is the first part of the objective function to be minimized, also decreases.

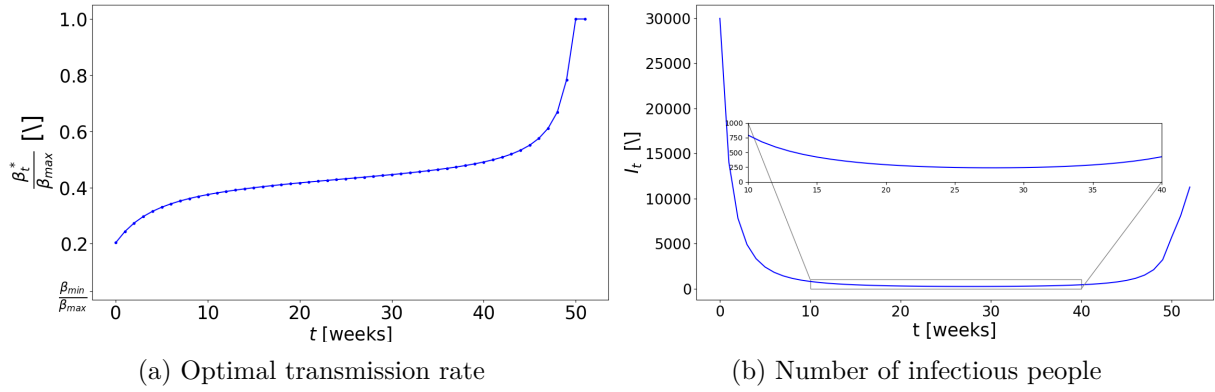


Figure 3.2: Results obtained by solving the optimal control problem (3.2) with the daily cost function $\lambda_1 L_{s,1}$ for the health measures. In (a), the temporal evolution of the optimal weekly transmission rate β_t^* . In (b), the temporal evolution of the number of infectious people I_t present in the population the week t .

Then, during the first 10 weeks, we observe that β_t^* increases. However, the number of infectious people in the population still decreases since β_t^* is still low. Thanks to this low β_t^* imposed during the first 10 weeks, the number of infectious people present in the population becomes more reasonable: they are less than 1000 in week 10 instead of 30 000 initially. Between the weeks 10 and 40, β_t^* increases but only slightly. We also observe in Figure 3.2b that during this period the number of infectious people in the population is almost constant and is low (between 250 and 1000 people). Since this number is almost constant with the β_t^* imposed, if β_t^* had increased much more between the 10th and 40th week, the number of infectious people in the population would not have been almost constant but would have increased significantly. Therefore, we can say that between the weeks 10 and 40, after reducing the number of infectious people to a more reasonable number, β_t^* increases only slightly and the number of infectious people remains almost constant.

Finally, at the end of the year, the transmission rate increases significantly. This implies an increase in the number of infectious people. However, the optimal control problem does not take into account the influence of this increase on the weeks after the end of the time horizon. Indeed, the increase in infectious persons during the weeks before the end of the horizon will cause deaths during the weeks after the end of the horizon and these deaths are not accounted for by the problem. This is why the transmission rate increases significantly and is equal to β_{max} at the end of the year. This is a drawback of this optimal control problem. Indeed, in reality, the number of deaths caused by an epidemic does not stop at the end of the year if the epidemic is not eradicated and in our case, it is clearly not eradicated. Indeed, the number of infectious people increases again at the end of the time horizon. This drawback will be improved later thanks to the model predictive control approach as we will see in Chapter 4.

Figure 3.3 compares the evolution of the optimal weekly transmission rate, β_t^* , over the one-year horizon for each cost function $\lambda_1 L_{s,i}$ shown in Figure 3.1. For each cost function $\lambda_1 L_{s,i}$, the optimal transmission rate is increasing and its evolution is very similar for the three costs. However, we will see in Section 3.5.3 that it is not the case for all the cost functions. β_t^* is slightly higher for the cost function $\lambda_1 L_{s,1}$ than for $\lambda_1 L_{s,2}$ since the cost function $\lambda_1 L_{s,1}$ is higher than $\lambda_1 L_{s,2}$. Indeed, in the case of a slightly higher cost for the health measures, it is preferable to impose a slightly higher transmission rate in order to reduce the cost of the sanitary measures, even if it slightly increases the number of deaths caused by the disease. By the same reasoning,

β_t^* is slightly higher for the cost function $\lambda_1 L_{s,1/2}$ than for $\lambda_1 L_{s,1}$.

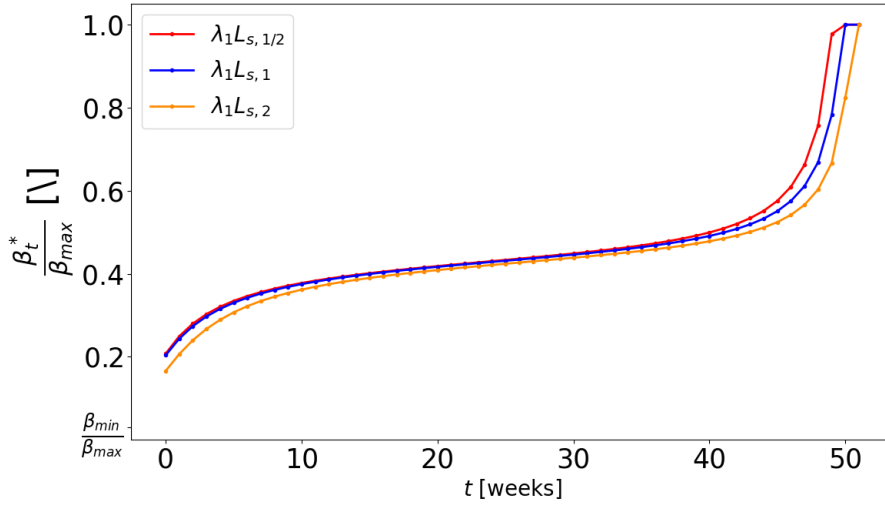


Figure 3.3: Temporal evolution of the optimal weekly transmission rate β_t^* obtained by solving the optimal control problem (3.2) with the three daily cost functions $\lambda_1 L_{s,i}$ for the health measures.

Table 3.1 compares, for the three cost functions $\lambda_1 L_{s,i}$, the cumulative number of deaths caused by the disease at the end of a one-year horizon (D_T) and the yearly cost of the measures to impose β_t^* ($\sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t^*)$). This table also includes the total cost, i.e. the sum of the two preceding quantities. D_T is relatively similar for the three cost functions compared to the yearly cost of the measures. It makes sense since the temporal evolution of the optimal weekly transmission rate β_t^* is similar for the three cost functions. However, since β_t^* is similar for the three cost functions but since these cost functions are not the same, the yearly cost of the health measures is higher when the cost function is higher. As a result, the total cost is also higher.

	D_T [# deaths]	$\sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t^*)$ [# deaths]	$f(\mathbf{x}, \mathbf{u}) = D_T + \sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t^*)$
$\lambda_1 L_{s,1/2}$	3034	39 370	42 404
$\lambda_1 L_{s,1}$	2358	15 624	17 982
$\lambda_1 L_{s,2}$	1666	1976	3642

Table 3.1: Comparison, for the three cost functions $\lambda_1 L_{s,i}$, of the cumulative number of deaths caused by the disease at the end of a one-year horizon (D_T), the yearly cost of the measures to impose β_t^* ($\sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t^*)$) and the total cost being the sum of the previous two quantities.

3.5.2 Comparison of the different methods

In this section, the optimal control problem (3.2) is solved for the cost functions $\lambda_1 L_{s,2}$ with the four methods described in Section 3.4: the gradient descent according to $\mathbf{u}$ and $\ln \mathbf{u}$, the Newton's method and the L-BFGS-B algorithm. Figure 3.4 shows the temporal evolution of β_t^* obtained with each of the 4 methods. As expected, this evolution is the same in the 4 cases since the same problem is solved several times but with different methods. This allows to confirm the results obtained with each method.

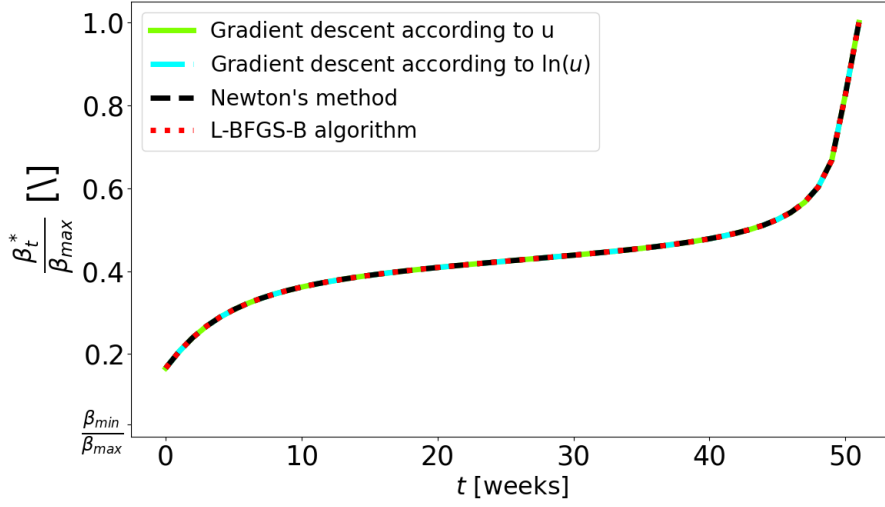


Figure 3.4: Temporal evolution of the optimal weekly transmission rate β_t^* obtained by solving the optimal control problem (3.2) with each method of Section 3.4 and with the daily cost function $\lambda_1 L_{s,2}$.

Then, let us compare the performances of each method. Table 3.2 presents the number of iterations required to converge to the solution and the execution time of each method. Firstly, the gradient descent according to $\mathbf{u}$ is the method which requires the highest number of iterations and the highest execution time. Secondly, as expected, the descent gradient according to $\ln(\mathbf{u})$ allows to greatly reduce the number of iterations. Indeed, it is reduced by a factor of 30 compared to the gradient descent according to $\mathbf{u}$. The execution time therefore also decreases by a factor of 30.

Then, the number of iterations is again significantly reduced thanks to the Newton's method which requires only 11 iterations to converge. The number of iterations is reduced by a factor of 191 compared to the gradient descent according to $\ln(\mathbf{u})$. However, the execution time is only reduced by a factor 2. This kind of results is quite often observed when comparing the performances of a first-order method, like the gradient descent, to the ones of a second-order method, like the Newton's method. Indeed, while the convergence of second-order methods may be faster, the computation at each iteration may be more expensive. This is because second-order methods exploit second-order information (computation of the Hessian of the objective function to be minimized) while first-order methods do not. This is exactly what happens in our case since computing the Hessian of the objective function is very costly as shown in appendix 3.A.

Finally, let us compare the performance of the L-BFGS-B algorithm implemented by the Python package `scipy.optimize`. With this method, the number of iterations required is more numerous than with the Newton's method. However, the execution time is only 1.83 seconds instead of 8.76 seconds for the Newton's method. One explanation for this performance could be that the Hessian of the objective function is approximated in the L-BFGS-B algorithm while it is fully computed in the Newton's method. This will increase the number of iterations required to converge for the L-BFGS-B algorithm but decrease the execution time and it is well what it is observed in our case.

	Number of iterations	Execution time (in seconds)
Gradient descent in $\mathbf{u}$	63971	614.16
Gradient descent in $\ln(\mathbf{u})$	2102	20.33
Newton's method	11	8.76
L-BFGS-B algorithm	68	1.83

Table 3.2: Comparison of the execution time and number of iterations required by each method to solve the problem (3.2)

3.5.3 High cost functions $\lambda L_{s,i}$

Looking at Figure 3.3, one could think that the temporal evolution of the optimal transmission rate will always be increasing whatever the cost function $\lambda L_{s,i}$. However, we will see in this section that it is no longer the case for high cost functions. Let us compare the evolution of the optimal weekly transmission rate β_t^* for the two following cost functions:

$$\lambda_1 L_{s,1}(\beta_t) = 1000 \frac{1/\beta_t - 1/\beta_{max}}{1/\beta_{min} - 1/\beta_{max}} \quad \lambda_2 L_{s,1}(\beta_t) = 10\lambda_1 L_{s,1}(\beta_t) = 10000 \frac{1/\beta_t - 1/\beta_{max}}{1/\beta_{min} - 1/\beta_{max}}$$

The temporal evolution of β_t^* for $\lambda_1 L_{s,1}$ has already been shown in Figure 3.3. This evolution is compared in Figure 3.5 with the one for a cost functions 10 times higher, i.e. $\lambda_2 L_{s,1} = 10\lambda_1 L_{s,1}$. While β_t^* is always increasing for $\lambda_1 L_{s,1}$, it is no longer the case for $\lambda_2 L_{s,1}$. For the latter, at the beginning of the year, $\beta_t^* = \beta_{max}$. Then, β_t^* decreases to reach $\beta_t^* = 0.43\beta_{max}$ in week 7. Finally, β_t^* increases progressively to reach β_{max} in week 22 and remains at the maximum rate until the end of the year.

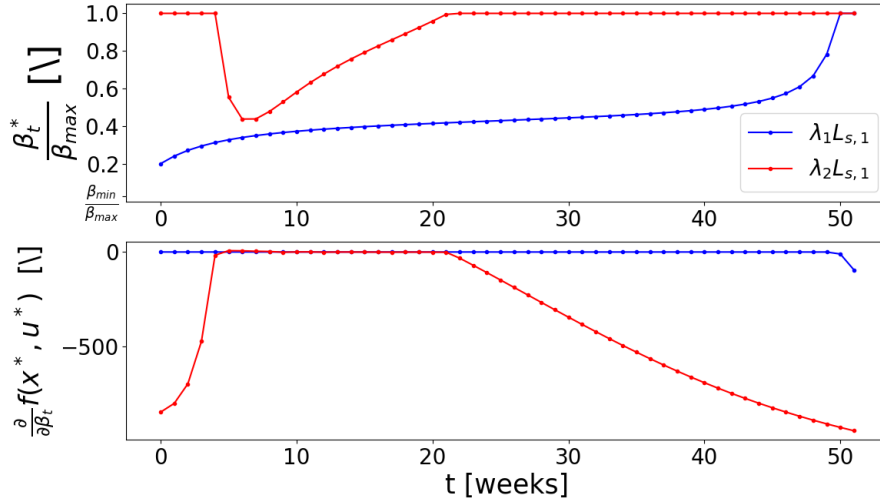


Figure 3.5: Comparison of the results obtained by solving the OCP (3.2) with the two cost functions $\lambda_1 L_{s,1}$ and $\lambda_2 L_{s,1}$. In the upper figure, the temporal evolution of the optimal weekly transmission rate β_t^* . In the lower figure, the value of the derivative of the objective function $f(\mathbf{x}^*, \mathbf{u}^*)$ at the optimum with respect to β_t .

To verify that the temporal evolution of β_t^* in Figure 3.5 is optimal for the two cost functions, we can compute

$$\frac{\partial}{\partial \beta_t} f(\mathbf{x}^*, \mathbf{u}^*) \quad \forall t \in \{0, \dots, T-1\} \quad (3.4)$$

where $f(\mathbf{x}, \mathbf{u})$ is the objective function of the OCP (3.2). $\mathbf{u}^* = [\beta_0^*, \dots, \beta_{T-1}^*]$ contains all the optimal weekly transmission rates and $\mathbf{x}^*$ contains all the state variables of the epidemic model computed with $\mathbf{u}^*$. If β_t^* is optimal $\forall t \in \{0, \dots, T-1\}$, the derivative (3.4) must be equal to 0 when the constraint $\beta_{min} \leq \beta_t \leq \beta_{max}$ of the problem is not tight. As shown in Figure 3.5, it is well the case for the two cost functions $\lambda_1 L_{s,1}$ and $\lambda_2 L_{s,1}$. The evolution of β_t^* is thus well optimal in each case.

Then, let us try to understand why the non-increasing evolution of β_t^* for the cost function $\lambda_2 L_{s,1}$ is optimal. The explanation will be divided into two parts. First, we will explain why it is optimal to have $\beta_t^* = \beta_{max}$ for the majority of the year when we are facing high cost functions such as $\lambda_2 L_{s,1}$. Then, we will show that it is not always optimal to have an increasing evolution for β_t^* .

The fact that $\beta_t^* = \beta_{max}$ for the majority of the year with the cost function $\lambda_2 L_{s,1}$ can be explained in the following way. Firstly, let us consider the case where no measures are imposed on the population, i.e. $\beta_t^* = \beta_{max}$ during the whole year. In this case, the cost of the measures is zero and the number of deaths caused by the disease is 162 279. The total cost (number of deaths + cost of the measures) at the end of the year is therefore 162 279 deaths. Secondly, let us take the optimal transmission rate β_t^* obtained with the cost function $\lambda_1 L_{s,1}$ and compute the cost of the measures allowing to impose this β_t^* if the cost function was now $\lambda_2 L_{s,1}$. With the cost function $\lambda_2 L_{s,1}$, the cost of the measures allowing to impose the optimal transmission rate β_t^* obtained with the cost function $\lambda_1 L_{s,1}$ is 165 248 deaths. In conclusion, in the case of the cost function $\lambda_2 L_{s,1}$, it is therefore more optimal to set $\beta_t^* = \beta_{max}$ for the whole year than to impose the optimal transmission rate obtained with the cost function $\lambda_1 L_{s,1}$ (the blue curve in Figure 3.5). This gives the strong hint that in the case of a high cost function such as $\lambda_2 L_{s,1}$, it is optimal to let the epidemic spread and to impose health measures only at certain times of the year when the spread is much too great. This allows to limit the cost of measures even if it increases the number of deaths.

Another reason why it may be optimal to impose no measures for most of the year is that the optimal control problem applies to a limited population, that of Belgium. Due to this limited population, the number of infectious people in the population will stop growing at some point, even if no measures are imposed, because the majority of the population will have been infected. This is also due to the assumption that people can only contract the disease once. The consequence is that the disease cannot grow exponentially and indefinitely. Since the number of infected people, and therefore the number of deaths, cannot increase indefinitely, when the cost functions for the measures are too high, it is more optimal to impose no measures for most of the year. Indeed, for high cost functions $\lambda L_{s,i}$, the total cost (number of deaths + cost of the health measures) with nearly no measure will be lower than the total cost with strict measures.

Let us now explain why in case of high cost functions like $\lambda_2 L_{s,1}$, for which $\beta_t^* = \beta_{max}$ most of the year, the evolution of β_t^* is not increasing. The advantage to have a non-increasing evolution of β_t^* in this case is the following. When it is only possible to impose sanitary measures at certain times because the cost of such measures is too high, imposing the most stringent measures later in the year helps to stop the spread of the disease once it has become much too great. Furthermore, after the number of infectious persons in the population has been reduced to a lower level by these measures, when the measures are relaxed again, the number of infectious persons in the population no longer increases. This is due to the effective reproduction number of the disease, R_t , which is now below 1. Indeed, for a SIRD model, $R_t = \frac{\beta_t S_t}{\gamma N}$ and the number of people susceptible at time t , S_t , has decreased sharply due to the first "wave of infections" caused by the absence of measures at the beginning of the year. For example, for the

cost function $\lambda_2 L_{s,1}$, 55% of the population was infected after the first wave. So, only 45% of the population is still susceptible after this wave. Thanks to this, R_t is then always smaller than 1 for the rest of the one-year horizon and the number of infectious people in the population no longer increases even with $\beta_t^* = \beta_{max}$.

On the other hand, if the most stringent measures are imposed at the beginning of the one-year horizon, then the number of infectious people in the population is reduced when the epidemic has not yet spread too far. However, in this case, when the measures are relaxed, R_t is not smaller than 1 because S_t has not decreased and almost the entire population is still susceptible since the spread of the epidemic was constrained from the beginning of the year. The number of infectious people will therefore increase exponentially since $R_t > 1$ and we will not be able to impose any more measures because we have already "exhausted" all the measures to which we were entitled.

To reinforce this argument, we consider the following problem. We put ourselves in a very simple case where we are allowed to impose measures such that $\beta_t = \beta_{min}$ during one week and the rest of the year we must set $\beta_t = \beta_{max}$. We then look for the optimal week to impose $\beta_t = \beta_{min}$ in order to minimize the cumulative number of deaths caused by the disease at the end of a one-year horizon: this is the 6th week. This therefore confirms that it is not optimal to put the strictest measures at the beginning of the one-year horizon when the measures that we can impose are limited.

Finally, the evolution of β_t^* is compared in Figure 3.6 for the following cost functions:

$$a\lambda_1 L_{s,1} \quad \text{with} \quad a = 1, 4, 6, 7, 8, 10, 50, 100.$$

For $a = 4, 6, 7$, the evolution of β_t^* is similar to the one obtained with the cost function $\lambda_1 L_{s,1}$ (i.e. with $a = 1$) already analysed above. For these cost functions, we can impose sanitary measures during the whole year since the cost functions of the measures are not too high. In this case, as explained before, β_t^* is low at the beginning of the year to decrease the number of infectious people. Then, β_t^* increases progressively but not too much so that the number of infectious people present in the population does not increase. Finally, β_t^* increases rapidly to β_{max} at the end of the year.

For $a = 8, 50, 100$, the evolution of β_t^* is similar to the one for the cost function $10\lambda_1 L_{s,1}$ (i.e. with $a = 10$) already analysed in Figure 3.5. We therefore observe that there is a cost function from which the cost of imposing measures all year round becomes too high. Among the functions tested, the first for which it is the case is $a\lambda_1 L_{s,1}$ with $a = 8$. For these high cost functions, sanitary measures are only imposed at certain times of the year to slow down the spread of the epidemic when it becomes much too great. We also observe that when the cost function is higher, the sanitary measures are lighter and imposed for a shorter period of time, which makes sense. However, these cost functions seem to be too high as they lead to very extreme situations. Indeed, these cost functions imply that no measures are taken during the first weeks, allowing the epidemic to spread significantly. This implies the infection of 60% of the population by the end of the one-year horizon. By comparison, there were about 950 000 infections after 1 year in Belgium, which represents about 8.5% of the population [24].

In the rest of this master thesis, we will therefore focus on cost functions such as $\lambda_1 L_{s,i}$ with $i \in \{1/2, 1, 2\}$ as defined in (3.3), for which the observed optimal measures are closer to those imposed in Belgium, i.e. strict measures at the beginning.

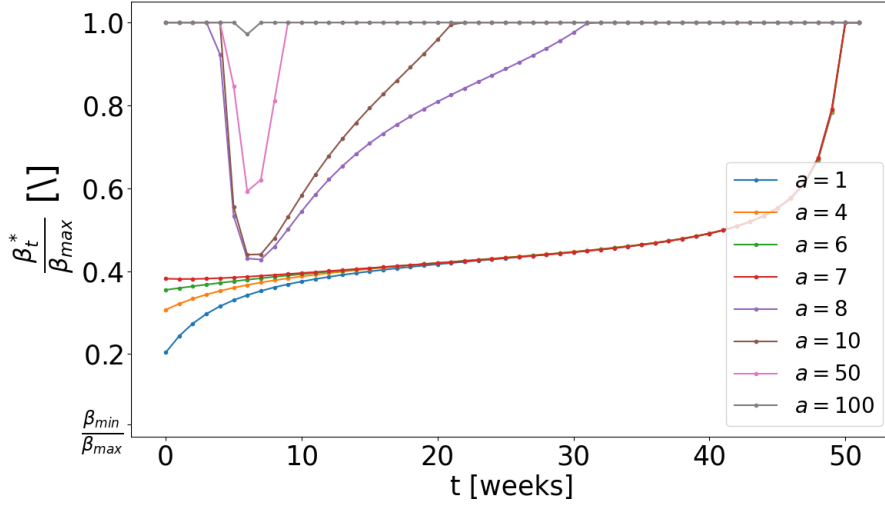


Figure 3.6: Temporal evolution of the optimal weekly transmission rate β_t^* for the cost functions $a\lambda_1 L_{s,1}$ with $a = 1, 4, 6, 7, 8, 10, 50, 100$.

3.6 Discussion about the time step of the optimal control problem (3.2)

In this section, we will discuss the time step of the OCP (3.2). Until now, we have looked at the optimal weekly transmission rate and the time step of the SIRD system involved in the OCP was the week. In that case, the rates of the SIRD system were expressed in [1/week] and the removed rate was $\gamma = 1$ [1/week]. This value for γ implies that all people who are infectious in week t will no longer be infectious in week $t + 1$. One may then ask whether a time step of one week is not a too large time step. This is why, in this section, we will look at the optimal daily transmission rate of the disease. The time step of the SIRD system will then be the day instead of the week. To find the optimal daily transmission rate, we solve the following optimal control problem:

$$\begin{aligned}
 \min_{\mathbf{x}, \mathbf{u}} f(\mathbf{x}, \mathbf{u}) &= D_J + \sum_{j=0}^{J-1} \lambda L_{s,i}(\beta_j) \\
 \text{subject to } & \text{(3.1)} & \text{for } j = 0, \dots, J-1 \\
 & \beta_{min} \leq \beta_j \leq \beta_{max} & \text{for } j = 0, \dots, J-1
 \end{aligned} \tag{3.5}$$

As said before, the difference with the previous OCP (3.2) is that the time step of the SIRD system (3.1) is now the day instead of the week. The rates of the system are therefore expressed in [1/day] and the removed rate is $\gamma = 1/7$ [1/day] instead of $\gamma = 1$ [1/week]. The deterministic effect with which all infectious people recover or die in one week is therefore no longer present. In this problem, $\mathbf{x}$ is the vector that gathers all the state variables of the SIRD system (3.1) from $j = 0$ to $j = J$, with $J = 365$ days, i.e. the number of days in the one-year horizon. $\mathbf{u} = [\beta_0, \dots, \beta_{J-1}]$ is the vector containing all the daily transmission rates. All these transmission rates must be between $\beta_{min} = 0.01$ [1/day] and $\beta_{max} = 0.33$ [1/day]. The daily cost of the government measures allowing to impose the transmission rate β_j is still $\lambda L_{s,i}(\beta_j)$. However, this cost is no longer multiplied by 7 since β_j changes each day and not each week.

The OCP (3.5) is solved with the three following cost functions for the health measures:

$$\lambda_1 L_{s,1/2}(\beta_j) = 1000 \frac{1/\beta_j^{1/2} - 1/\beta_{max}^{1/2}}{1/\beta_{min}^{1/2} - 1/\beta_{max}^{1/2}} \quad \lambda_1 L_{s,1}(\beta_j) = 1000 \frac{1/\beta_j - 1/\beta_{max}}{1/\beta_{min} - 1/\beta_{max}}$$

$$\lambda_1 L_{s,2}(\beta_j) = 1000 \frac{1/\beta_j^2 - 1/\beta_{max}^2}{1/\beta_{min}^2 - 1/\beta_{max}^2}$$

These cost functions have already been presented in Figure 3.1. For these three cost functions, the evolution of the optimal daily transmission rate β_j^* is shown in Figure 3.7. We observe that the evolution of the optimal daily transmission rate is very similar to the evolution of the optimal weekly transmission rate computed in Section 3.5.1 (Figure 3.3). The daily time step does not seem to change the results and we will therefore continue to work with a weekly time step in this master thesis.

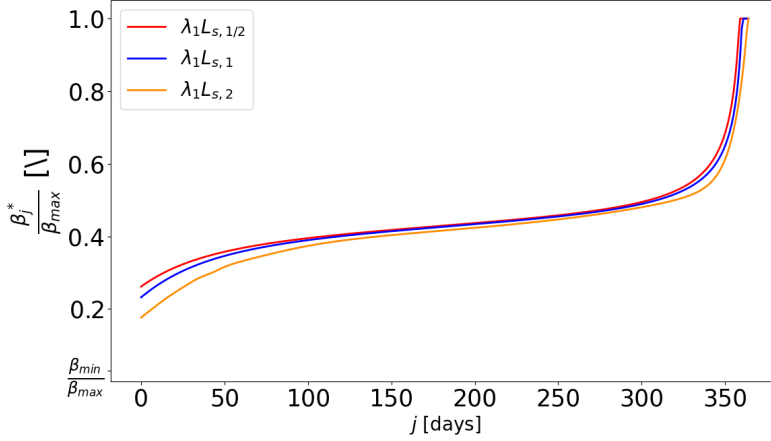


Figure 3.7: Temporal evolution of the optimal daily transmission rate β_j^* obtained by solving the optimal control problem (3.5) with the three cost function $\lambda_1 L_{s,i}$ for the health measures.

3.7 Conclusion

In this chapter, an optimal control problem was designed in order to find the optimal weekly transmission rate allowing to minimize the cumulative number of deaths caused by the disease at the end of a one-year horizon and the cost of the sanitary measures. It has been shown that the temporal evolution of the optimal transmission rate depends on the cost function of the health measures. For the cost functions $\lambda_1 L_{s,i}$ with $i \in \{1/2, 1, 2\}$, defined in (3.3), the evolution of the optimal weekly transmission rate β_t^* is increasing. This evolution corresponds to strict measures at the beginning of the one-year horizon. This allows to reduce the number of infectious people to a more reasonable one. Indeed, after the 10th week, there are less than 1000 infectious people in the population instead of 30 000 initially. Between the 10th and the 40th week, the measures are only slightly relaxed so that the number of infectious people, now more reasonable, remains relatively constant. At the end of the year, there is a strong relaxation of the measures because the optimal control problem does not take into account the consequences of this decision on the weeks after the end of the one-year horizon.

However, in case of high cost functions for the health measures, such as $a\lambda_1 L_{s,1}$ with $a = 10, 50, 100$, the evolution of the optimal weekly transmission rate β_t^* is no longer increasing.

Since the cost of imposing sanitary measures is high, it is optimal to impose measures only at certain times. There is therefore no health measure at the beginning of the one-year horizon. Then, some measures are imposed for a few weeks to stop the spread of the epidemic when it becomes much too great, before being completely relaxed again. However, these cost functions seem to be too high as they lead to very extreme situations. In the rest of this master thesis, we will therefore focus on cost functions such as $\lambda_1 L_{s,i}$ with $i \in \{1/2, 1, 2\}$, as defined in (3.3).

3.A Computation of the second order partial derivatives of S_t , I_t and D_t

This appendix aims to compute

$$\frac{\partial^2 D_t}{\partial \beta_l \partial \beta_k}, \quad \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}, \quad \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} \quad \forall t, l, k \in \{0, \dots, T-1\}.$$

The computation of these partial derivatives is divided into 5 cases:

- $\forall k, l, t \in \{0, \dots, T-1\}$ such that $k = l = t$,

$$\frac{\partial^2 S_{t+1}}{\partial \beta_l \partial \beta_k} = \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - 2 \frac{\partial S_t}{\partial \beta_l} \frac{I_t}{N} - 2 \frac{\partial I_t}{\partial \beta_l} \frac{S_t}{N} - 2 \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} - \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

$$\frac{\partial^2 I_{t+1}}{\partial \beta_l \partial \beta_k} = (1 - \gamma) \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k} + 2 \frac{\partial S_t}{\partial \beta_l} \frac{I_t}{N} + 2 \frac{\partial I_t}{\partial \beta_l} \frac{S_t}{N} + 2 \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} + \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} + \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

$$\frac{\partial^2 D_{t+1}}{\partial \beta_l \partial \beta_k} = \frac{\partial^2 D_t}{\partial \beta_l \partial \beta_k} + \delta \gamma \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

- $\forall k, l, t \in \{0, \dots, T-1\}$ such that $k > t$ or $l > t$,

$$\frac{\partial^2 S_{t+1}}{\partial \beta_l \partial \beta_k} = 0$$

$$\frac{\partial^2 I_{t+1}}{\partial \beta_l \partial \beta_k} = 0$$

$$\frac{\partial^2 D_{t+1}}{\partial \beta_l \partial \beta_k} = 0$$

- $\forall k, l, t \in \{0, \dots, T-1\}$ such that $k = t$ and $l < t$,

$$\frac{\partial^2 S_{t+1}}{\partial \beta_l \partial \beta_k} = \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - \frac{\partial S_t}{\partial \beta_l} \frac{I_t}{N} - \frac{\partial I_t}{\partial \beta_l} \frac{S_t}{N} - \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} - \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_k} \frac{\partial I_t}{\partial \beta_l} - \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

$$\frac{\partial^2 I_{t+1}}{\partial \beta_l \partial \beta_k} = (1 - \gamma) \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k} + \frac{\partial S_t}{\partial \beta_l} \frac{I_t}{N} + \frac{\partial I_t}{\partial \beta_l} \frac{S_t}{N} + \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} + \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_k} \frac{\partial I_t}{\partial \beta_l} + \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} + \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

$$\frac{\partial^2 D_{t+1}}{\partial \beta_l \partial \beta_k} = \frac{\partial^2 D_t}{\partial \beta_l \partial \beta_k} + \delta \gamma \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

- $\forall k, l, t \in \{0, \dots, T-1\}$ such that $k < t$ and $l = t$,

$$\frac{\partial^2 S_{t+1}}{\partial \beta_l \partial \beta_k} = \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - \frac{\partial S_t}{\partial \beta_k} \frac{I_t}{N} - \frac{\partial I_t}{\partial \beta_k} \frac{S_t}{N} - \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} - \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_k} \frac{\partial I_t}{\partial \beta_l} - \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

$$\frac{\partial^2 I_{t+1}}{\partial \beta_l \partial \beta_k} = (1 - \gamma) \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k} + \frac{\partial S_t}{\partial \beta_k} \frac{I_t}{N} + \frac{\partial I_t}{\partial \beta_k} \frac{S_t}{N} + \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} + \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_k} \frac{\partial I_t}{\partial \beta_l} + \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} + \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

$$\frac{\partial^2 D_{t+1}}{\partial \beta_l \partial \beta_k} = \frac{\partial^2 D_t}{\partial \beta_l \partial \beta_k} + \delta \gamma \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}$$

- $\forall k, l, t \in \{0, \dots, T-1\}$ such that $k < t$ and $l < t$,

$$\begin{aligned}\frac{\partial^2 S_{t+1}}{\partial \beta_l \partial \beta_k} &= \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} - \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_k} \frac{\partial I_t}{\partial \beta_l} - \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} - \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k} \\ \frac{\partial^2 I_{t+1}}{\partial \beta_l \partial \beta_k} &= (1 - \gamma) \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k} + \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_l} \frac{\partial I_t}{\partial \beta_k} + \frac{\beta_t}{N} \frac{\partial S_t}{\partial \beta_k} \frac{\partial I_t}{\partial \beta_l} + \frac{\beta_t I_t}{N} \frac{\partial^2 S_t}{\partial \beta_l \partial \beta_k} + \frac{\beta_t S_t}{N} \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k} \\ \frac{\partial^2 D_{t+1}}{\partial \beta_l \partial \beta_k} &= \frac{\partial^2 D_t}{\partial \beta_l \partial \beta_k} + \delta \gamma \frac{\partial^2 I_t}{\partial \beta_l \partial \beta_k}\end{aligned}$$

Moreover, since the initial condition of the SIRD system does not depend on any transmission rate,

$$\frac{\partial^2 D_0}{\partial \beta_l \partial \beta_k} = 0, \quad \frac{\partial^2 I_0}{\partial \beta_l \partial \beta_k} = 0, \quad \frac{\partial^2 S_0}{\partial \beta_l \partial \beta_k} = 0 \quad \forall k, l \in \{0, \dots, T-1\}.$$

Chapter 4

Model predictive control of the COVID-19 transmission rate

This chapter still aims to find the optimal weekly transmission rate of the COVID-19 disease in order to minimize the number of deaths caused by the disease and the cost of the health measures imposed to achieve such a transmission rate. However, the way we proceed to find this optimal rate differs from the previous chapter. In this chapter, a model predictive control (MPC) problem is implemented. In model predictive control, at each time step, an optimal control problem is solved over a *prediction horizon* which can be different from the *whole horizon* of the MPC problem. Only the first step of the control input obtained is executed to get the new state of the system and, at the next sampling time, a new optimal control problem is solved based on this new state. The difference between the model predictive control and the optimal control is that the former is a closed-loop control while the latter is an open-loop control.

This chapter first defines in detail the MPC problem allowing to find the optimal transmission rate of the disease. Then, the results obtained by solving this MPC problem are presented. They are finally compared to the ones obtained previously in Chapter 3 when the optimal rate was found by using an optimal control approach in which only one optimal control problem is solved.

4.1 Problem statement

In model predictive control, as described above, there are two time horizons: the *whole horizon* and the *prediction horizon*. As in Chapter 3, we look at the weekly transmission rate β_t over one year allowing to minimize the number of deaths caused by the disease and the cost of the health measures. The *whole horizon* is therefore 1 year. However, at each time step of the *whole horizon*, an optimal control problem is solved over a *prediction horizon* of $P = 15$ weeks. As in the literature [27] [18], the *prediction horizon* is smaller than the *whole horizon* to keep a reasonable computational complexity. The optimal control problem (OCP) solved at each time step of the *whole horizon* is the following:

$$\min_{\mathbf{x}_P, \mathbf{u}_P} \quad D_P + \sum_{k=0}^{P-1} 7\lambda L_{s,i}(\beta_k) \quad (4.1a)$$

$$\text{subject to} \quad x_0 = \hat{x}_0 \quad (4.1b)$$

$$\text{\textcolor{red}{(3.1)}} \quad \text{for } k = 0, \dots, P-1 \quad (4.1c)$$

$$\beta_{min} \leq \beta_k \leq \beta_{max} \quad \text{for } k = 0, \dots, P-1 \quad (4.1d)$$

$\mathbf{x}_P$ is the vector that gathers all the state variables of the SIRD system \text{\textcolor{red}{(3.1)}} from time $k = 0$ to $k = P$. $\mathbf{u}_P$ is the vector containing the control variables, called manipulated variables

in MPC. $\mathbf{u}_P = [\beta_0, \dots, \beta_{P-1}]$ therefore contains the weekly transmission rate. D_P denotes the cumulative number of deaths caused by the disease at the end of the P weeks of the *prediction horizon*. The daily cost of the health measures allowing to impose the transmission rate β_k is $\lambda L_{s,i}(\beta_k)$, which is multiplied by 7 to obtain the weekly cost.

The meaning of each constraint of the OCP (4.1) is the following:

- the constraint (4.1b) enforces the current state of the SIRD system, $\hat{x}_0$, to be the initial state x_0 of the system for the optimal control problem.
- the constraint (4.1c) makes sure that the state variables satisfy the dynamics of the SIRD system (3.1).
- the constraint (4.1d) imposes to the transmission rate to be between β_{min} and β_{max} .

Now that the optimal control problem is defined, let us look at the MPC algorithm allowing to compute the optimal transmission rates over the *whole horizon* $T = 52$ weeks. Based on the MPC algorithm of the state-of-the-art, the algorithm for our MPC problem is the following.

MPC Algorithm

For $t = 0, \dots, T - 1$:

- (1) Set $\hat{x}_0 = x_t$, where $x_t = [S_t, I_t, R_t, D_t]$ is the current state of the SIRD model (3.1).
- (2) Solve the optimal control problem (4.1) for $\hat{x}_0 = x_t$ to obtain the optimal control sequence $\mathbf{u}_P^*$.
- (3) Define the MPC control law value $\mu_P(x_t) := \mathbf{u}_P^*(0) = \beta_{k=0}^*$.
- (4) Apply the control value $\mu_P(x_t)$ to the system (3.1), $t := t + 1$ and go to (1).

Thanks to the MPC algorithm implemented using the Python package `do-mpc` [28], we obtain the optimal weekly transmission rate, β_t^* , for each week t of the one-year horizon. Indeed,

$$\beta_t^* = \mu_P(x_t) \quad \text{for } t = 0, \dots, T - 1.$$

The initial condition of the MPC algorithm again corresponds to the situation observed in Belgium for COVID-19 on 25th April 2020 as in Chapter 3. The initial condition of the epidemic model (3.1) involved in the MPC algorithm is therefore

$$x_0 = [S_0, I_0, R_0, D_0] = [11\,440\,000, 30\,000, 49\,250, 750].$$

4.2 Results

As for the optimal control approach in Chapter 3, the MPC algorithm is used to find the optimal weekly transmission rate, β_t^* , with the three following cost functions for the health measures:

$$\begin{aligned} \lambda_1 L_{s,1/2}(\beta_t) &= 1000 \frac{1/\beta_t^{1/2} - 1/\beta_{max}^{1/2}}{1/\beta_{min}^{1/2} - 1/\beta_{max}^{1/2}} & \lambda_1 L_{s,1}(\beta_t) &= 1000 \frac{1/\beta_t - 1/\beta_{max}}{1/\beta_{min} - 1/\beta_{max}} \\ \lambda_1 L_{s,2}(\beta_t) &= 1000 \frac{1/\beta_t^2 - 1/\beta_{max}^2}{1/\beta_{min}^2 - 1/\beta_{max}^2} \end{aligned}$$

These functions have already been discussed and presented in Figure 3.1. For each of these cost functions, the evolution of β_t^* is increasing as shown in Figure 4.1. As for the optimal control problem in Chapter 3, at the beginning of the one-year horizon, β_t^* is low in order to limit the spread of the disease. This will decrease the number of infectious people present in the population. As a result, this will also decrease the number of deaths caused by the disease, which is the first part of the objective function to be minimized. Then, β_t^* increases over the year. However, β_t^* increases less and less as the year goes on and reaches approximately $0.44\beta_{max}$ at the end of the year for each of the three cost functions $\lambda_1 L_{s,i}$. This behaviour can be justified a posteriori thanks to the effective reproduction number.

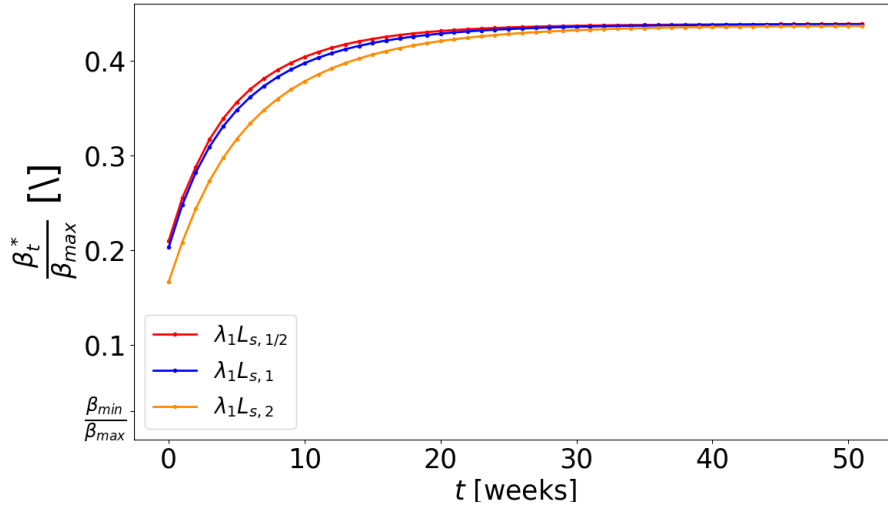


Figure 4.1: Temporal evolution of the optimal transmission rate, β_t^* , obtained thanks to the MPC algorithm with the three daily cost functions $\lambda_1 L_{s,i}$ for the health measures

As a remainder, the effective reproduction number, R_t , is the average number of secondary cases caused by one infectious individual in a population composed of both susceptible and non-susceptible hosts at any time t of an epidemic. Moreover, as explained in the state-of-the-art section, R_t can be computed thanks to the next generation matrix method. As already computed, for a SIRD model,

$$R_t = \frac{\beta_t S_t}{\gamma N}.$$

R_t is then computed for β_t^* and S_t^* , i.e. with the optimal transmission rate and the optimal state variables obtained by solving the MPC problem. The evolution of R_t over the year is shown in Figure 4.2. At the beginning, R_t is between 0.4 and 0.5 for each of the cost functions. Since $R_t < 1$, the number of infectious people present in the population decreases. Then, we observe that R_t increases over the year since β_t^* increases. Indeed, in the expression of R_t , γ is fixed and S_t^*/N , the proportion of susceptible people in the population at time t , decreases very slowly since the transmission rate β_t^* is low at the beginning of the year. Thus, by increasing β_t^* , R_t increases. However, β_t^* increases in a limited way so that R_t is always lower than 1. If R_t had been greater than 1, the number of infectious people present in the population would have increased. Increasing β_t^* so that R_t tends towards 1 but never exceeds 1 therefore allows to have the highest possible transmission rate, thus the least severe sanitary measures, without increasing the number of infectious people present in the population. Moreover, since $R_t \approx 1$, for the last weeks of the one-year horizon, the number of infectious people in the population is nearly constant.

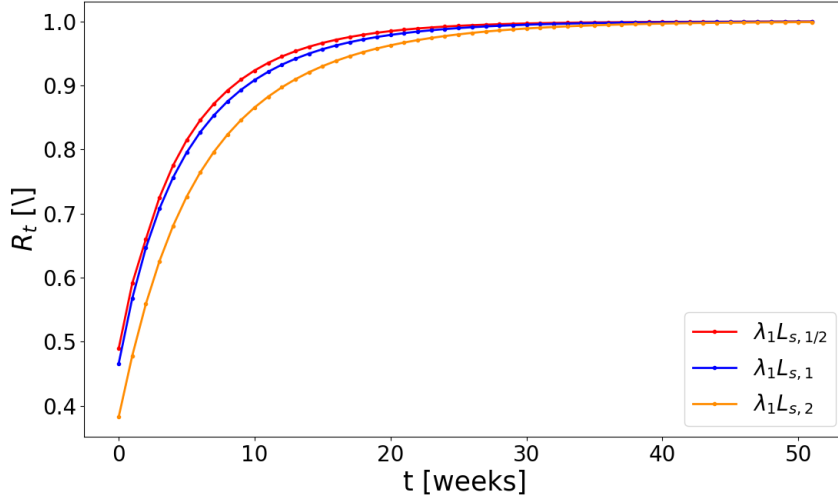


Figure 4.2: Temporal evolution of the effective reproduction number, R_t , with the three daily cost functions $\lambda_1 L_{s,i}$ for the health measures

In conclusion, the general evolution of the optimal transmission rate, β_t^* , for the three cost functions $\lambda_1 L_{s,i}$ is the following. Firstly, at the beginning of the one-year horizon, β_t^* is low so that the number of infectious people, initially 30 000, decreases to a more reasonable number. After the 5th week, there are less than 5000 infectious people in the population no matter the cost function $\lambda_1 L_{s,i}$ and this number will always decrease over the year. Secondly, β_t^* increases progressively to the highest possible rate so that R_t tends towards 1 but never exceeds 1 at the end of the one-year horizon. The number of infectious people, which is lower than 1000 during the last weeks of the year, therefore becomes almost constant in the population.

Looking at β_t^* over the whole year, we observe that β_t^* is relatively low even at the end of the one-year horizon. Indeed, $\beta_t^* \approx 0.44\beta_{max}$ at that time for each of the cost functions $\lambda_1 L_{s,i}$. This implies relatively strict health measures to be imposed in order to achieve such a rate. One of the reason is that, at the end of the year, 97% of the population is still susceptible to be infected. One way to reduce the number of susceptible people is to vaccinate them. This is why Chapter 6 is devoted to the vaccination.

Finally, let us compare the evolution of β_t^* for the three cost functions $\lambda_1 L_{s,i}$. As shown in Figure 4.1, β_t^* is the lowest when the cost to impose this β_t^* is the lowest, which makes sense. Indeed,

$$\lambda_1 L_{s,2}(\beta_t) < \lambda_1 L_{s,1}(\beta_t) < \lambda_1 L_{s,1/2}(\beta_t) \quad \forall \beta_t \in]\beta_{min}, \beta_{max}[$$

and the optimal evolution of β_t^* is the smallest for $\lambda_1 L_{s,2}$. Table 4.1 compares, for the three cost functions $\lambda_1 L_{s,i}$, the cumulative number of deaths caused by the disease at the end of the one-year horizon, the yearly cost of the measures and the total cost, i.e. the sum of the two preceding quantities. As already observed in Chapter 3, D_T is relatively similar for the three cost functions compared to the yearly cost of the measures. It makes sense since the temporal evolution of β_t^* is similar for the three cost functions. Since β_t^* is similar for the three cost functions but since these cost functions are not the same, the yearly cost of the health measures is higher when the cost function is higher. As a result, the total cost is also higher.

	D_T [# deaths]	$\sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t^*)$ [# deaths]	$f(\mathbf{x}, \mathbf{u}) = D_T + \sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t^*)$
$\lambda_1 L_{s,1/2}$	2363	43 617	45 980
$\lambda_1 L_{s,1}$	2213	17 004	19217
$\lambda_1 L_{s,2}$	1648	2082	3730

Table 4.1: Comparison, for the three cost functions $\lambda_1 L_{s,i}$, of the cumulative number of deaths caused by the disease at the end of the one-year horizon (D_T), the yearly cost of the measures to impose β_t^* ($\sum_{t=0}^{T-1} 7\lambda L_{s,i}(\beta_t^*)$) and the total cost, i.e. the sum of the previous two quantities.

4.2.1 Comparison of the results with the optimal control approach

Let us now compare the optimal transmission rate obtained in the case of the optimal control approach (Chapter 3) with the one in the case of the model predictive control approach (Chapter 4).

As a reminder, in Chapter 3, the optimal weekly transmission rate β_t^* is obtained using optimal control. In this case, the OCP (3.2) is solved only once with the initial condition x_0 for the SIRD system. In this section, this OCP will be called OCP_1 to insist on the fact that this OCP is solved only once to obtain the weekly transmission rates for the entire one-year horizon.

In Chapter 4, the optimal transmission rate is computed using model predictive control (MPC). In this case, the OCP (4.1) is solved iteratively at each time step t of the MPC algorithm with the initial condition x_t . x_t is the current state of the SIRD system at time t . The OCP of the MPC algorithm will be called OCP_{MPC} to insist on the fact that this OCP is solved at each iteration of the MPC algorithm. Only in this section, the *prediction horizon* of the OCP_{MPC} is equal to 52 weeks instead of 15 weeks. With this change, the OCP_1 is the same as the OCP_{MPC} : the only difference is that the initial condition of the OCP_{MPC} is x_t , the current state of the SIRD system at time step t of the MPC algorithm, and not x_0 .

Figure 4.3 compares the temporal evolution of the optimal transmission rate β_t^* obtained by solving the OCP_1 of Chapter 3 (optimal control approach) with the evolution of β_t^* obtained with the MPC algorithm (model predictive control approach).

First, the transmission rate β_0^* obtained with the OCP_1 and the MPC algorithm is the same. It was expected since at the time step 0 of the MPC algorithm, the initial condition for the OCP_{MPC} is $x_t = x_0$. Thus, at the time step 0 of the MPC algorithm, the OCP_{MPC} is exactly the same than the OCP_1 .

Then, as we progress through the year, the evolution of β_t^* obtained with the OCP_1 and the one obtained with the MPC algorithm differ more and more. This is because the OCP_{MPC} solved at each iteration of the MPC algorithm is no longer the same as the OCP_1 . Moreover, at the end of the year, while β_t^* increases more and more in the case of the OCP_1 , β_t^* seems to be almost constant in the case of the MPC algorithm. This difference can be explained in the following way. At time t of the MPC algorithm, the OCP_{MPC} allowing to compute β_t^* takes into account the influence of this β_t^* on the SIRD system during one year after the time t . Indeed, to find β_t^* , the initial condition is the current state of the SIRD system at time t and the *prediction horizon* of the OCP_{MPC} is 52 weeks. On the other hand, to compute β_t^* , the OCP_1 only takes into account the influence of β_t^* on the SIRD system until the end of the one-year horizon. For example, to compute β_{T-1}^* , the OCP_1 takes only into account the influence of β_{T-1}^* on the last week of the one-year horizon and not on the weeks after the end of the year. This is why β_t^* reaches $\beta_{\max}$ at the end of the year in the case of the optimal control approach. On contrary,

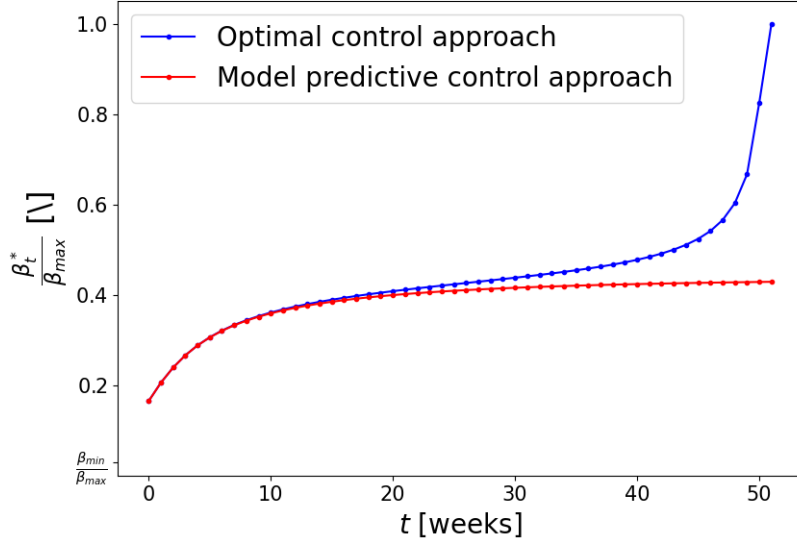


Figure 4.3: Comparison of the temporal evolution of the optimal transmission rate β_t^* obtained by solving the OCP₁ of Chapter 3 (optimal control approach) with the evolution of β_t^* obtained with the MPC algorithm (model predictive control approach).

since the MPC algorithm takes always into account the influence that has β_t^* on the next 52 weeks no matter the time t , β_t^* does not increase at the end of the one-year horizon. The way the optimal transmission rate is computed in the MPC algorithm is more rigorous and better reflects reality. This is why in the rest of this master thesis, we will focus on model predictive control to answer several questions about epidemic management.

4.3 An alternative modelling of the MPC problem

The rest of this master thesis still aims to find the optimal transmission rate of disease in order to minimize the number of deaths and the cost of the health measures. However, the population will now be divided into several sub-populations. There will therefore be more than one transmission rate to be optimized. For example, if there are 2 sub-populations, there will be 4 transmission rates defined as $\beta^{kl} \forall k, l \in \{1, 2\}$. These transmission rates may be different since the contacts within and between each sub-population may be different. Moreover, the health measures imposed on the contacts within and between each group may be different. This is why we will see in the next chapter that it is more convenient to introduce a new manipulated variable. This new manipulated variable is u_t^{kl} and will represent the effect of the sanitary measures on the transmission rate β_t^{kl} . This new manipulated variable u_t^{kl} will be studied in more detail in the next chapter.

In this section, we will see that the MPC problem solved previously for a single general population can also be solved with the new manipulated variable u_t instead of β_t . Moreover, we will see that the results will be exactly the same. u_t represents the effect of the weekly health measures on the weekly transmission rate β_t . The effective transmission rate at time t is thus now defined as

$$\beta_t = u_t \beta_{max}$$

where β_{max} is the maximum transmission rate when there is no health measures. This means that when there is no measures, $u_t = u_{max} = 1$ and $\beta_t = \beta_{max}$. Moreover, in order to set

$\beta_t = \beta_{min}$, the health measures must be such that $u_t = u_{min} = \frac{\beta_{min}}{\beta_{max}}$. Therefore,

$$u_t \in [u_{min}, u_{max}] = \left[\frac{\beta_{min}}{\beta_{max}}, 1 \right] \quad \forall t.$$

In this alternative MPC problem, the aim is therefore to find the weekly optimal variable u_t^* such that the number of deaths and the cost of the health measures are minimized. Now that the manipulated variable is u_t , the cost of the sanitary measures will be expressed in terms of this manipulated variable. The idea is to keep the same cost as the one defined in Section 3.2 when it was expressed in terms of β_t . Therefore, it is only a "rescaling" of the cost function. The daily cost of the health measures which was

$$\lambda L_{s,i}(\beta_t) = \lambda \frac{L_i(\beta_t) - L_i(\beta_{max})}{L_i(\beta_{min}) - L_i(\beta_{max})} \quad \text{with} \quad \beta_t \in [\beta_{min}, \beta_{max}]$$

becomes

$$\lambda L'_{s,i}(u_t) = \lambda \frac{L_i(u_t) - L_i(u_{max})}{L_i(u_{min}) - L_i(u_{max})} \quad \text{with} \quad u_t \in \left[\frac{\beta_{min}}{\beta_{max}}, 1 \right] \quad (4.3)$$

where $L_i(u_t) = \frac{1}{u_t}$. As for the previous cost function, the range of $\lambda L'_{s,i}(u_t)$ is $[0, \lambda]$: it is equal to λ when evaluated at u_{min} and to 0 when u_{max} . $\lambda L'_{s,i}(u_{min}) = \lambda$ is therefore the assumption we make about the cost of imposing the most stringent measures possible. The cost of setting $u = u_{max}$ is 0 and it is relevant since u_{max} represents the case in which there is no sanitary measures.

To find the optimal manipulated variable u_t^* for each week t thanks to model predictive control, the following optimal control problem is solved at each time step t of the MPC algorithm.

$$\min_{\mathbf{x}_P, \mathbf{u}_P} \quad D_P + \sum_{k=0}^{P-1} 7\lambda L'_{s,i}(u_k) \quad (4.4a)$$

$$\text{subject to} \quad x_0 = \hat{x}_0 \quad (4.4b)$$

$$(3.1) \quad \text{for } k = 0, \dots, P-1 \quad (4.4c)$$

$$u_{min} \leq u_k \leq u_{max} \quad \text{for } k = 0, \dots, P-1 \quad (4.4d)$$

This OCP is the same as the one when the manipulated variable was β_k , except that now the OCP is expressed in terms of the new manipulated variable u_k . The MPC algorithm is the same as the one in (4.2). However, the MPC algorithm is now applied with the OCP (4.4) and the MPC control law is now defined as $\mu_P(x_t) := \mathbf{u}_P^*(0) = u_{k=0}^*$.

Figure 4.4 shows the temporal evolution of the optimal manipulated variable u_t^* representing the effect of the measures at time t on the transmission rate β_t . The evolution of u_t^* obtained by solving the OCP (4.4) with the cost function $\lambda_1 L'_{s,2}$ is exactly the same as the evolution of β_t^*/β_{max} obtained by solving the OCP (4.1) with the same cost. It makes sense since $u_t^* = \beta_t^*/\beta_{max}$ and the only difference between the two OCP is that one is expressed in terms of u_t^* while the other in terms of β_t^* . All the results obtained previously in this master thesis could therefore have been obtained by looking at the optimal manipulated variable u_t^* with $\beta_t^* = u_t^* \beta_{max}$ instead of looking at the optimal manipulated variable β_t^* .

4.4 Conclusion

In this chapter, the optimal weekly transmission rate β_t^* minimizing the number of deaths and the cost of the health measures was found using model predictive control. For the three

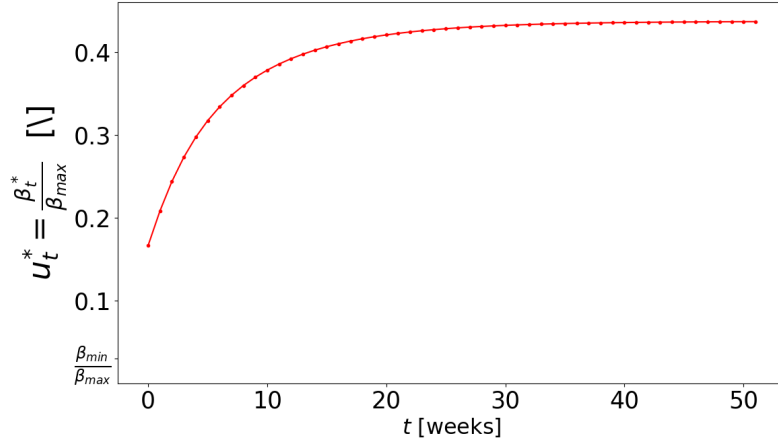


Figure 4.4: Temporal evolution of the optimal manipulated variable u_t^* , representing the effect of the measures at time t on the transmission rate β_t , with the cost function $\lambda_1 L'_{s,2}$.

cost functions $\lambda_1 L_{s,i}$ with $i \in \{1/2, 1, 2\}$, the evolution of β_t^* is the following. At the beginning of the one-year horizon, β_t^* is low in order to decrease the number of infectious people present in the population. Moreover, we observed a posteriori that β_t^* increases progressively over the year but in a limited way so that the reproduction number R_t tends towards 1 but never exceeds 1. Thanks to this optimal transmission rate, the number of infectious people only decreased throughout the year to become almost constant at the end of the year. At that time, there are less than 1000 infectious people in the population instead of 30 000 initially. As in [13, 19], we have therefore observed that the sanitary measures allowing to reduce the transmission rate of the disease reduce significantly the number of infectious people but not to zero. This is why we will look at the vaccination of the population in Chapter 6 to see if this intervention can stop the spread of COVID-19.

This chapter has also shown that the MPC problem allows to take into account the influence of β_t^* on the weeks that follow the end of the one-year horizon. This was not the case in Chapter 3 when β_t^* was found by solving only one optimal control problem. In the rest of this master thesis, we will therefore focus on model predictive control problems because it better reflects the reality. Several MPC problems will be designed in order to answer different questions about epidemic management. For the sake of brevity, the results will be presented with the cost function $\lambda_1 L'_{s,1}$ for the sanitary measures. However, the results were also checked for $\lambda_1 L'_{s,1/2}$ and $\lambda_1 L'_{s,2}$ and are very similar.

Chapter 5

Consideration of the vulnerable population

The severity of a disease may depend on the population category to which a person belongs. Indeed, as an illustration, an important feature of COVID-19 is its highly non-uniform attack of the different age groups in the population. COVID-19 has shown a low infection fatality ratio in young, healthy individuals. In contrast, the severity of the disease in the elderly as well as in individuals with underlying health problems has resulted in a more significant mortality rate worldwide.

This chapter aims to model this non-uniform infection fatality ratio in the population. First, the SIRD model is extended to stratify the population into two groups with different mortality rates. Then, we will look at the optimal transmission rates of the disease to be imposed within and between each population group. This will allow us to answer the following question: Should health measures be different for the vulnerable and the non-vulnerable population?

5.1 Problem specifications

In this chapter, the population is divided into two groups: a non-vulnerable population with a low infection fatality ratio and a vulnerable population with a higher one. The vulnerable population includes the individuals over 65 years of age and younger people with health problems. The estimated number of vulnerable individuals in Belgium is about 2.5 million, or approximately 20% of the population [29]. The non-vulnerable population includes the rest of the population, i.e. 80%. The infection fatality ratio (IFR) for COVID-19 in Belgium, being the proportion of infected people who die from the disease, is estimated to be 0.071 in the vulnerable population. The IFR in the non-vulnerable population is about 7.6×10^{-4} [21]. By taking a weighted average of these two IFR, we obtain that the IFR for the general population is 0.015. It is actually in this way that the IFR for the general population in Chapter 3 was computed.

The SIRD model designed in Section 3.1 is now extended to take into account the differentiation between the vulnerable and the non-vulnerable populations. The non-vulnerable group is labelled with the letter A and the vulnerable one with the letter B .

Now that there are two population groups, there are four transmissions rates. Indeed, the transmission rate between a susceptible individual of group k and the infectious people of group l is denoted as $\beta^{kl} \forall k, l \in \{A, B\}$.

When there is no sanitary measures imposed by the government, these four rates are at their maximum value. The maximum transmission rate between a susceptible individual of group k

and the infectious people of group l is defined as:

$$\beta_{max}^{kl} = p^{kl} \beta_{max} \quad \forall k, l \in \{A, B\}$$

where p^{kl} is the proportion of contacts that a person of group k has with people of group l . As a remainder, β_{max} is the maximum transmission rate between a susceptible individual and the infectious people in the case of a general population, when there is no stratification. More precisely, β_{max} is defined as:

β_{max} = the number of contacts a susceptible person has per week with the general population when there is no health measures $\times$ the probability of a successful transmission in case of contact between a susceptible and an infectious individual when no health measures.

Let us define the value of these parameters. As already mentioned, the non-vulnerable population (group A) is composed of 80% of the total population and the vulnerable population (group B) is composed of 20% of the total population. By assuming that the contacts are uniform in the population, a person from group A has 80% of his contacts with group A and 20% of his contacts with group B. Therefore,

$$p^{AA} = 0.8, \quad \beta_{max}^{AA} = 0.8\beta_{max}, \quad p^{AB} = 0.2, \quad \beta_{max}^{AB} = 0.2\beta_{max}. \quad (5.1)$$

Moreover, a person from group B has 80% of his contacts with group A and 20% of his contacts with group B. Therefore,

$$p^{BA} = 0.8, \quad \beta_{max}^{BA} = 0.8\beta_{max}, \quad p^{BB} = 0.2, \quad \beta_{max}^{BB} = 0.2\beta_{max}. \quad (5.2)$$

By the same reasoning, $\beta_{min}^{kl} = p^{kl} \beta_{min}$. Therefore,

$$\beta_{min}^{AA} = 0.8\beta_{min}, \quad \beta_{min}^{AB} = 0.2\beta_{min}, \quad \beta_{min}^{BA} = 0.8\beta_{min}, \quad \beta_{min}^{BB} = 0.2\beta_{min}.$$

This chapter still aims to find the optimal transmission rate of the disease in order to minimize the number of deaths caused by the disease and the cost of the health measures. However, there is now more than one transmission rate to be optimized. Indeed, as an example, β_t^{kk} can be different from β_t^{ll} if the health measures within groups k and l are different. As previously introduced in Section 4.3, it is now more convenient for the design of the problem to control a new manipulated variable. This new manipulated variable is u_t^{kl} and will represent the effect of the sanitary measures on the transmission rate β_t^{kl} . The effective transmission rate at time t is therefore:

$$\beta_t^{kl} = u_t^{kl} \beta_{max}^{kl} = u_t^{kl} p^{kl} \beta_{max}$$

where u_t^{kl} is now the manipulated variable of the problem while p^{kl} and β_{max} are fixed.

When there is no health measures to decrease the transmission rate β_t^{kl} , $\beta_t^{kl} = \beta_{max}^{kl}$ and $u_t^{kl} = 1 = u_{max}$. Moreover, in order to set $\beta_t^{kl} = \beta_{min}^{kl}$, the health measures must be such that:

$$u_t^{kl} = \frac{\beta_{min}^{kl}}{\beta_{max}^{kl}} = \frac{p^{kl} \beta_{min}}{p^{kl} \beta_{max}} = \frac{\beta_{min}}{\beta_{max}} = u_{min}.$$

Therefore,

$$u_t^{kl} \in [u_{min}, u_{max}] = \left[\frac{\beta_{min}}{\beta_{max}}, 1 \right] \quad \forall t \text{ and } \forall k, l.$$

In this chapter, the population is divided into two groups (A and B). There are therefore 3 types of contacts: the "AA", "BB" and "AB" contact type. Consequently, there are 3 types of

sanitary measures and 3 different manipulated variables:

u^{AA} represents the effect of the sanitary measures imposed within group A on β^{AA} .
 u^{BB} represents the effect of the sanitary measures imposed within group B on β^{BB} .
 $u^{AB} = u^{BA}$ represents the effect of the sanitary measures imposed between group A and group B on β^{AB} and β^{BA} .

Indeed, the sanitary measures decreasing the contacts of a person in group A with group B must be the same that the sanitary measures decreasing the contacts of a person in group B with group A. Otherwise, there would be a mismatch in the contacts.

The SIRD model stratifying the whole population into a non-vulnerable group (A) and a vulnerable group (B) is the following:

$$\begin{aligned}
S_{t+1}^A &= S_t^A - S_t^A \left(u_t^{AA} \beta_{max}^{AA} \frac{I_t^A}{N_A} + u_t^{AB} \beta_{max}^{AB} \frac{I_t^B}{N_B} \right) \\
I_{t+1}^A &= I_t^A + S_t^A \left(u_t^{AA} \beta_{max}^{AA} \frac{I_t^A}{N_A} + u_t^{AB} \beta_{max}^{AB} \frac{I_t^B}{N_B} \right) - \gamma I_t^A \\
R_{t+1}^A &= R_t^A + \gamma(1 - \delta_A) I_t^A \\
D_{t+1}^A &= D_t^A + \gamma \delta_A I_t^A \\
S_{t+1}^B &= S_t^B - S_t^B \left(u_t^{AB} \beta_{max}^{BA} \frac{I_t^A}{N_A} + u_t^{BB} \beta_{max}^{BB} \frac{I_t^B}{N_B} \right) \\
I_{t+1}^B &= I_t^B + S_t^B \left(u_t^{AB} \beta_{max}^{BA} \frac{I_t^A}{N_A} + u_t^{BB} \beta_{max}^{BB} \frac{I_t^B}{N_B} \right) - \gamma I_t^B \\
R_{t+1}^B &= R_t^B + \gamma(1 - \delta_B) I_t^B \\
D_{t+1}^B &= D_t^B + \gamma \delta_B I_t^B
\end{aligned} \tag{5.3}$$

N_A and N_B are the number of individuals in the non-vulnerable and the vulnerable population respectively. For each of the two groups, there are 4 compartments: the susceptible (S), infectious (I), recovered (R) and dead (D) compartment. A non-vulnerable or vulnerable individual who is susceptible can be infected by an infectious non-vulnerable or vulnerable person. Once they are infected, the individuals move in the infectious compartment, I^A or I^B , depending on their status in the population. Then, their removed rate is γ regardless of whether they are vulnerable or not. Concerning the non-vulnerable individuals, they recover at a rate $\gamma(1 - \delta_A)$ and they die at a rate $\gamma \delta_A$, where δ_A is the infection fatality ratio of the non-vulnerable population. The vulnerable persons recover at a rate $\gamma(1 - \delta_B)$ and they die at a rate $\gamma \delta_B$, where δ_B is the infection fatality ratio of the vulnerable population.

The parameters of the epidemic model (5.3) are summarised in Table 5.1. The value of these parameters is chosen to represent at best the COVID-19 epidemic in Belgium.

$N = 11.52 \times 10^6$	$N_A = 0.8N = 9.216 \times 10^6$	$N_B = 0.2N = 2.304 \times 10^6$
$\gamma = 1$ [1/week]	$\delta_A = 7.6 \times 10^{-4}$	$\delta_B = 0.071$

Table 5.1: Parameter values of the epidemic model (5.3)

5.1.1 Cost of health measures

Now that there are 3 types of health measures and therefore 3 manipulated variables u_t^{AA} , u_t^{BB} and u_t^{AB} , the cost of the sanitary measures will be expressed in terms of these manipulated variables. The daily total cost of the sanitary measures will be the sum of these three following costs:

$$\lambda L'_{s,i}(u_t^{AA}), \quad \lambda L'_{s,i}(u_t^{BB}) \quad \text{and} \quad \lambda L'_{s,i}(u_t^{AB})$$

where the cost function $\lambda L'_{s,i}(u_t)$ was already defined in Section 4.3. $\lambda L'_{s,i}(u_t^{AA})$ represents the cost of the sanitary measures imposed within group A, $\lambda L'_{s,i}(u_t^{BB})$ the one within group B and $\lambda L'_{s,i}(u_t^{AB})$ the one between groups A and B. However, the sum of these 3 cost functions is weighted because each sanitary measure does not affect the same proportion of contacts.

Concretely, the proportion of contacts affected by the sanitary measures imposed within group A is

$$p_A \cdot p^{AA} = 0.8 \cdot 0.8 = 0.64.$$

$p_A = 0.8$ is the proportion of people who belong to group A and p^{AA} is the proportion of contacts that a person of group A has with people of group A. p^{AA} was already computed in (5.1) and is equal to 0.8.

The proportion of contacts affected by the sanitary measures imposed within group B is

$$p_B \cdot p^{BB} = 0.2 \cdot 0.2 = 0.04$$

where p_B and p^{BB} are defined in the same way as above but for group B.

Finally, the proportion of contacts affected by the sanitary measures imposed between groups A and B is

$$p_A \cdot p^{AB} + p_B \cdot p^{BA} = 0.8 \cdot 0.2 + 0.2 \cdot 0.8 = 0.32.$$

p^{AB} is the proportion of contacts that a person of group A has with people of group B and p^{BA} is the one that a person of group B has with people of group A.

The daily total cost of the sanitary measures is therefore

$$\begin{aligned} & p_A \cdot p^{AA} \lambda L'_{s,i}(u_t^{AA}) + p_B \cdot p^{BB} \lambda L'_{s,i}(u_t^{BB}) + (p_A \cdot p^{AB} + p_B \cdot p^{BA}) \lambda L'_{s,i}(u_t^{AB}) \\ \Leftrightarrow & 0.64 \lambda L'_{s,i}(u_t^{AA}) + 0.04 \lambda L'_{s,i}(u_t^{BB}) + 0.32 \lambda L'_{s,i}(u_t^{AB}). \end{aligned}$$

5.1.2 Problem statement

The MPC problem designed in this chapter aims to find the three optimal manipulated variables u_t^{*AA} , u_t^{*BB} and u_t^{*AB} for each week t of a one-year horizon. These variables represent the effect of the sanitary measures on their respective transmission rate. The lower u_t^{kl} is, the more severe are the health measures between groups k and l and the lower is the transmission

β_t^{kl} . In this control problem, we want to find the optimal value of these variables in order to minimize the cumulative number of deaths caused by the disease at the end of a one-year horizon while minimizing the cost of the health measures. The manipulated variables u_t^{*AA} , u_t^{*BB} and u_t^{*AB} for each week t are found using model predictive control (MPC). The optimal control problem solved at each time step t of the MPC algorithm is:

$$\min_{\mathbf{x}_P, \mathbf{u}_P} D_P^A + D_P^B + 7\lambda \left(\sum_{k=0}^{P-1} 0.64 L'_{s,i}(u_k^{AA}) + 0.04 L'_{s,i}(u_k^{BB}) + 0.32 L'_{s,i}(u_k^{AB}) \right) \quad (5.4a)$$

$$\text{subject to } x_0 = \hat{x}_0 \quad (5.4b)$$

$$\boxed{5.3} \quad \text{for } k = 0, \dots, P-1 \quad (5.4c)$$

$$u_{min} \leq u_k^{AA}, u_k^{BB}, u_k^{AB} \leq u_{max} \quad \text{for } k = 0, \dots, P-1 \quad (5.4d)$$

$\mathbf{x}_P$ is the vector that gathers all the state variables of the epidemic model $\boxed{5.3}$ from time $k = 0$ to $k = P$. $\mathbf{u}_P$ is the vector containing the weekly manipulated variables u_k^{AA} , u_k^{BB} and $u_k^{AB} \forall k \in \{0, \dots, P-1\}$. D_P^A denotes the cumulative number of deaths caused by the disease in the non-vulnerable population, at the end of the $P = 15$ weeks of the *prediction horizon*. D_P^B is the one in the vulnerable population.

The meaning of each constraint of the OCP $\boxed{5.4}$ is the following:

- the constraint $\boxed{5.4b}$ enforces the current state of the epidemic model $\boxed{5.3}$, $\hat{x}_0$, to be the initial state x_0 of the model for the optimal control problem.
- the constraint $\boxed{5.4c}$ makes sure that the state variables satisfy the dynamics of the epidemic model $\boxed{5.3}$.
- the constraint $\boxed{5.4d}$ imposes to the manipulated variables to be between u_{min} and u_{max} .

The MPC algorithm is the same as the one in $\boxed{4.2}$. However, the MPC algorithm is now applied with the OCP $\boxed{5.4}$ and the epidemic model $\boxed{5.3}$. Moreover, the MPC control law is now defined as

$$\mu_P(x_t) := \mathbf{u}_P^*(0) = [u_{k=0}^{*AA}, u_{k=0}^{*BB}, u_{k=0}^{*AB}].$$

Thanks to the MPC algorithm, we obtain the weekly optimal manipulated variables u_t^{*AA} , u_t^{*BB} and u_t^{*AB} for each week t of the one-year horizon. Indeed,

$$[u_t^{*AA}, u_t^{*BB}, u_t^{*AB}] = \mu_P(x_t) \quad \text{for } t = 0, \dots, T-1$$

with $T = 52$ weeks.

For the initial condition of the MPC algorithm, we take the situation observed in Belgium for COVID-19 on 25th April 2020. On that date, there were approximately 30 000 infectious persons $\boxed{24}$. In addition, about 50 000 people were infected and had already recovered or died before that date. Since we assumed that the infectious people are evenly distributed in the population, we have:

$$\begin{aligned} I_0^A &= 30\,000 \cdot p_A & R_0^A &= 50\,000 \cdot p_A \cdot (1 - \delta_A) & D_0^A &= 50\,000 \cdot p_A \cdot \delta_A \\ I_0^B &= 30\,000 \cdot p_B & R_0^B &= 50\,000 \cdot p_B \cdot (1 - \delta_B) & D_0^B &= 50\,000 \cdot p_B \cdot \delta_B \end{aligned}$$

where p_j is the proportion of people in group j and δ_j is the infection fatality ratio in group j

with $j \in \{A, B\}$. Finally, we set $S_0^A = N_A - I_0^A - R_0^A - D_0^A$ and $S_0^B = N_B - I_0^B - R_0^B - D_0^B$. The initial condition of the epidemic model (5.3) involved in the MPC algorithm is therefore

$$x_0 = [S_0^A, I_0^A, R_0^A, D_0^A, S_0^B, I_0^B, R_0^B, D_0^B]$$

with

$$\begin{array}{llll} S_0^A = 9\,152\,000 & I_0^A = 24\,000 & R_0^A = 39\,969 & D_0^A = 31 \\ S_0^B = 2\,288\,000 & I_0^B = 6\,000 & R_0^B = 9286 & D_0^B = 714. \end{array}$$

5.2 Results and discussion

In this section, we present the results obtained for u_t^{AA} , u_t^{BB} and u_t^{AB} using model predictive control with the following cost functions for the sanitary measures:

$$\lambda_1 L'_{s,1}(u_t) = 1000 \frac{1/u_t - 1/u_{max}}{1/u_{min} - 1/u_{max}}. \quad (5.5)$$

As already mentioned, the results were also checked for $\lambda_1 L'_{s,1/2}$ and $\lambda_1 L'_{s,2}$ and are very similar. Therefore, for the sake of brevity, the results are only presented for the cost function $\lambda_1 L'_{s,1}$.

Figure 5.1 shows the temporal evolution of u_t^{AA} , u_t^{BB} and u_t^{AB} . This evolution is compared to the one of u_t^* , i.e. the effect of the sanitary measures on the transmission rate β_t when there was no distinction between the vulnerable and non-vulnerable population (as computed in Chapter 4). As a remainder, the lower u_t^* is, the more severe the health measures are and the lower the transmission rate β_t^* is.

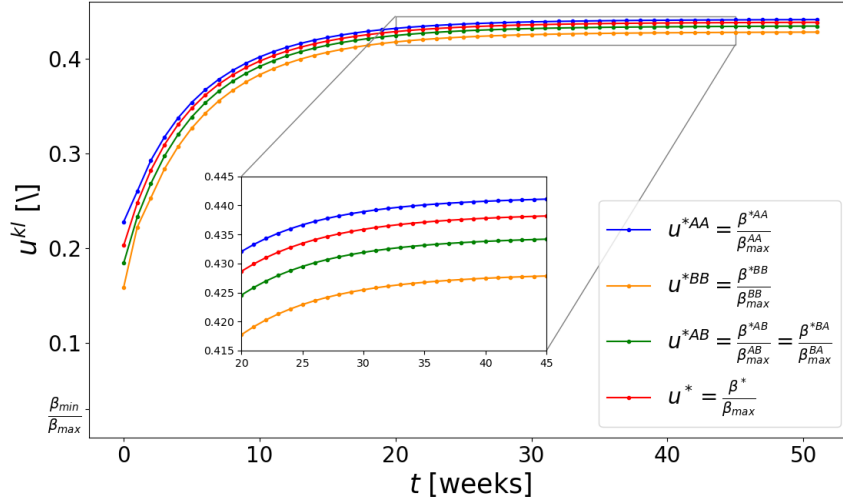


Figure 5.1: Temporal evolution of the optimal variables u_t^{AA} , u_t^{BB} and u_t^{AB} . They represent the effect of the health measures of each contact type on their respective transmission rate.

In Figure 5.1, it is observed that

$$u_t^{BB} < u_t^{AB} < u_t^* < u_t^{AA} \quad \forall t = 0, \dots, T-1.$$

However, the measure are not significantly different since at each time t , u_t^{AA} , u_t^{BB} and u_t^{AB} are closed. This means that the health measures imposed within the vulnerable population

(group B) and between the non-vulnerable (group A) and the vulnerable population are only slightly stricter than the ones imposed in the case of a general population. On the other hand, the health measures within the non-vulnerable population are only slightly less strict. This means that the difference in the infection fatality ratio between the two populations does not imply a major difference in health measures. This can be explained in the following way.

The non-vulnerable population cannot have less strict measures for two reasons. Firstly, even if their infection fatality ratio is lower, if their sanitary measures are too light, this can lead to an exponential increase in the number of infectious people in this population. Since the number of deaths is a fraction of the infections, it would also increase exponentially. Indeed, let us take the simple case of a population only composed of non-vulnerable people (A). At the beginning of the one-year horizon, i.e. when $S_t^A = 0.99N_A \approx N_A$, the number of infectious people is given by

$$\begin{aligned} I_{t+1}^A &= I_t^A + u_t^{AA} \beta_{max}^{AA} I_t^A \frac{S_t^A}{N_A} - \gamma I_t^A \\ &\approx (1 + u_t^{AA} \beta_{max}^{AA} - \gamma) I_t^A. \end{aligned}$$

By supposing that u_t^{AA} is constant,

$$I_t^A \approx I_0^A (1 + u^{AA} \beta_{max}^{AA} - \gamma)^t$$

evolves exponentially. Moreover, since the number of deaths is a fraction of the infections, the number of deaths caused by the infections at time t is given by

$$d_t^A \approx \delta_A I_0^A (1 + u^{AA} \beta_{max}^{AA} - \gamma)^t.$$

Therefore, even if the IFR δ_A is low, the number of deaths can increase exponentially if the health measures are too light, i.e. if u^{AA} is too high. Moreover, in the case of a population composed solely of vulnerable persons, the number of deaths caused by the infection at time t is given by

$$d_t^B \approx \delta_B I_0^B (1 + u^{BB} \beta_{max}^{BB} - \gamma)^t.$$

Therefore, the parameters u^{AA} and u^{BB} have more influence than δ_A and δ_B on the number of deaths. This is the first reason why the parameters u_t^{*AA} and u_t^{*BB} are closed even if the IFR are $\delta_A = 7.6 \times 10^{-4}$ and $\delta_B = 7.1 \times 10^{-2}$. Moreover, this argument is valid for the entire one-year horizon since $S_t^A \approx N_A$ and $S_t^B \approx N_B$ throughout the year. Indeed, due to the relatively strict health measures imposed, only 3% of the population was infected during the year. At the end of the year, $S_t^A \approx 0.97N_A$ and $S_t^B \approx 0.97N_B$.

Secondly, an increase of the infectious people in the non-vulnerable group (A) would also lead to an increase of the infections in the vulnerable group (B). Indeed, if the number of infections in group A increases, the proportion of infectious people in group A increases and a susceptible person in group B is more likely to be infected when in contact with group A. This is the second reason why measures cannot be too light, even in the non-vulnerable population.

However, it makes sense that the sanitary measures are slightly stricter in the vulnerable group than in the general population since the IFR is higher in the vulnerable group than in the general population. On the other hand, it is coherent that the sanitary measures are a little lighter in the non-vulnerable group than in the general population since the IFR is smaller in this group. Finally, the intensity of the measures imposed for the contacts between individuals of groups A and B falls between the two previous ones since these contacts involve one person with a low IFR and one person with a higher IFR.

Concerning the temporal evolution of the sanitary measures, as in the case of a general population, the intensity of the measures within and between each group are increasing over time. Moreover, their intensity increases less and less over the year. This behaviour can be justified once again a posteriori thanks to the effective reproduction number.

The effective reproduction number R_t of the disease is the average number of cases caused by one infectious people at time t of the epidemic. It therefore depends on the health measures u_t^{AA} , u_t^{BB} and u_t^{AB} imposed on their respective transmission rates. The reproduction number R_t can be computed by applying the next generation matrix method on the epidemic model (5.3) and the computation is detailed in appendix 5.A. R_t is then evaluated at the optimal manipulated variables u_t^{*AA} , u_t^{*BB} and u_t^{*AB} .

The evolution of R_t over the one-year horizon is shown in Figure 5.2. At the beginning of the year, $R_t = 0.49$. An infectious individual will therefore cause on average only 0.49 secondary case. Since $R_t < 1$, the number of infectious people present in the population decreases. During the year, R_t is always increasing but in a limited way such that R_t is always lower than 1. Thanks to that, the number of infectious people present in the population will never increase. For the last weeks of the one-year horizon, since $R_t \approx 1$, the number of infectious people is nearly constant. The conclusion concerning the evolution of the sanitary measures, and therefore the transmission rates, over the year is the following. The optimal transmission rate of each type of contact, depending on u_t^{*AA} , u_t^{*BB} and u_t^{*AB} , is such that R_t is first low in order to decrease the number of infectious people. Then, the transmission rate of each type of contact increases progressively so that R_t tends towards 1 at the end of the year but never exceeds 1. Thanks to these transmission rates, the number of infectious people, much lower during the last weeks (approximately 650 instead of 30 000 initially), remains almost constant at this time of the year. This evolution for the transmission rates is optimal in the sense that it minimizes the number of deaths caused by the disease and the cost of the sanitary measures allowing to impose these transmission rates. At the end of the one-year horizon, the total cost, i.e. the cumulative number of deaths at the end of the year and the cost of the health measures imposed throughout the year, is 19 176 deaths. In comparison with Chapter 4, when there was no distinction between the vulnerable and the non-vulnerable population, the total costs was 19 217 deaths. The small difference in health measures for the vulnerable and the non-vulnerable population therefore did not significantly reduce the total cost.

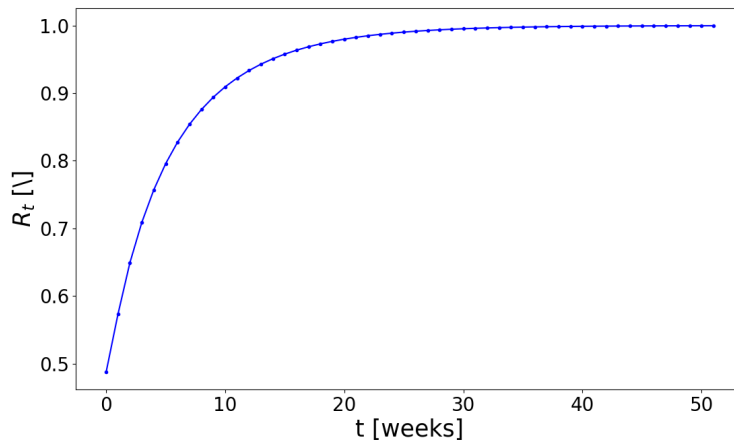


Figure 5.2: Temporal evolution of the effective reproduction number R_t .

Over the entire one-year horizon, the optimal variables u_t^{*AA} , u_t^{*BB} and u_t^{*AB} imply relatively severe health measures for each type of contact. Indeed, the measures must be such that each transmission rate is at least halved from its maximum value, no matter the time of the year (u_t^{*AA} , u_t^{*BB} and u_t^{*AB} are lower than 0.5 $\forall t$). Even at the end of the year, each transmission rate is between 40% and 45% of its maximum value as shown in Figure 5.1. One of the reason of these severe measures is that 97% of the whole population is still susceptible to be infected at that time. One way to reduce the number of susceptible people in the population is to vaccinate them. This is why the next chapter will be devoted to the vaccination.

5.3 Conclusion

In this chapter, we have taken into account the difference between the IFR in the non-vulnerable population and the one in the vulnerable population. The aim was then to see whether the health measures would be different within and between each population. This chapter showed that although the measures in the non-vulnerable group are a little lighter than in the vulnerable group, the measures within these two groups are very close. As a result, the measures imposed on the contacts between the two groups are also close to the ones within the two groups.

Concerning the temporal evolution of the measures, as in the case where the measures are chosen for a general population, the measures are strict at the beginning of the one-year horizon. They are relaxed slowly and progressively during the year so that the effective reproduction number R_t tends towards 1 but does not exceed 1. The number of infectious people in the population only decreases throughout the year as R_t is always smaller than 1. However, this still implies quite strict measures at the end of the year and this is why we are going to look at vaccination in the next chapter to see if it can lead to lighter measures.

5.A Computation of the reproduction number for the epidemic model (5.3)

The aim of this appendix is to compute the effective reproduction number R_t of the epidemic model (5.3) thanks to the next generation matrix method detailed in Section 2.1. In the epidemic model (5.3), there are two compartments containing infectious people: I^A and I^B . Therefore, $x_t = (I_t^A, I_t^B)$ and $y_t = (S_t^A, R_t^A, D_t^A, S_t^B, R_t^B, D_t^B)$. The equations of the model for the compartments I^A and I^B are

$$\begin{aligned} I_{t+1}^A &= \underbrace{I_t^A - \gamma I_t^A}_{\mathcal{V}_1(x_t, y_t)} + \overbrace{S_t^A \left(u_t^{AA} \beta_{max}^{AA} \frac{I_t^A}{N_A} + u_t^{AB} \beta_{max}^{AB} \frac{I_t^B}{N_B} \right)}^{\mathcal{F}_1(x_t, y_t)} \\ I_{t+1}^B &= \underbrace{I_t^B - \gamma I_t^B}_{\mathcal{V}_2(x_t, y_t)} + \underbrace{S_t^B \left(u_t^{AB} \beta_{max}^{BA} \frac{I_t^A}{N_A} - u_t^{BB} \beta_{max}^{BB} \frac{I_t^B}{N_B} \right)}_{\mathcal{F}_2(x_t, y_t)}. \end{aligned}$$

Therefore, the two matrices F and V are equal to

$$\begin{aligned} F &= \left[\frac{\partial \mathcal{F}_i(x_t, y_t)}{\partial x^j} \right] = \begin{bmatrix} u_t^{AA} \beta_{max}^{AA} \frac{S_t^A}{N_A} & u_t^{AB} \beta_{max}^{AB} \frac{S_t^A}{N_B} \\ u_t^{AB} \beta_{max}^{BA} \frac{S_t^B}{N_A} & u_t^{BB} \beta_{max}^{BB} \frac{S_t^B}{N_B} \end{bmatrix} \\ V &= \left[\frac{\partial \mathcal{V}_i(x_t, y_t)}{\partial x^j} \right] = \begin{bmatrix} 1 - \gamma & 0 \\ 0 & 1 - \gamma \end{bmatrix}. \end{aligned}$$

Finally, the effective reproduction number is given by

$$R_t = \rho(Q) \quad \text{with} \quad Q = F(I_d - V)^{-1}$$

where I_d is the identity matrix and ρ denotes the spectral radius.

Chapter 6

Optimal vaccination

One type of intervention to control an infectious disease is to decrease the number of individuals susceptible to be infected. To achieve this goal, the most commonly used intervention is the vaccination. The question then becomes: Who to vaccinate first or how to administer the vaccine doses optimally? To answer this question, the epidemic model stratifying the population into a non-vulnerable and a vulnerable group is first extended to take into account the vaccination. Secondly, a stratification in three population groups is modelled in order to distinguish the health care workers from the two other populations. This third population differs from the other two as it has a lot of contacts with the vulnerable population. As an example, this third population includes the health personnel working in hospitals or in retirement homes. Moreover, these contacts are vital to take care of the vulnerable population and they cannot be removed. The aim of this chapter is thus to look at the optimal way to vaccinate the population thanks to these two epidemic models.

6.1 Vaccination of the non-vulnerable and vulnerable groups

This chapter first aims to look at the optimal vaccination for a population stratified into two groups: the non-vulnerable and the vulnerable population. We therefore begin by presenting a new epidemic model that takes the vaccination into account. Then, we defined the MPC problem allowing to find the optimal vaccination and the results obtained are analysed.

6.1.1 Epidemic model

In this section, the epidemic model (5.3) stratifying the population into a non-vulnerable and a vulnerable group is extended to take into account the vaccination of these two groups. Therefore, the type of epidemic model used is no longer a SIRD model but a SVIRD model. This means that both populations will have a fifth compartment labelled by the letter "V" to represent the people who have been vaccinated.

In the model, initially no one is vaccinated. Then, each week, a weekly number of vaccine doses for the entire population can be administered. The number of vaccine doses administered to the non-vulnerable group in week t is denoted by the manipulated variable d_t^A . The one administered to the vulnerable group is denoted by d_t^B .

Although vaccination is added in this chapter, we still look at the optimal transmission rates of the disease for each type of contact. Indeed, since the number of susceptible people present in each population will decrease thanks to the vaccination, the optimal sanitary measures allowing to decrease the transmission rate of each type of contact will change. Therefore, there are now 5 manipulated variables : $u_t^{AA}, u_t^{BB}, u_t^{AB}, d_t^A$ and d_t^B . We will look at the optimal value of

these manipulated variables in order to minimize the number of deaths caused by the disease while minimizing the cost of the sanitary measures imposed to decrease the different transmission rates. We assume that the administration of the vaccine doses is free but that there is a maximum number of vaccines that can be administered each week. Based on the data about the weekly number of doses administered in Belgium for COVID-19 [30], we assume that the maximum number of vaccine doses that can be administered each week is $D = 7 \times 10^5$ doses.

The model taking into account the vaccination is the following:

$$\begin{aligned}
S_{t+1}^A &= S_t^A - S_t^A \left(u_t^{AA} \beta_{max}^{AA} \frac{I_t^A}{N_A} + u_t^{AB} \beta_{max}^{AB} \frac{I_t^B}{N_B} \right) - d_t^A \\
V_{t+1}^A &= V_t^A + d_t^A - \epsilon V_t^A \left(u_t^{AA} \beta_{max}^{AA} \frac{I_t^A}{N_A} + u_t^{AB} \beta_{max}^{AB} \frac{I_t^B}{N_B} \right) \\
I_{t+1}^A &= I_t^A + \left(S_t^A + \epsilon V_t^A \right) u_t^{AA} \beta_{max}^{AA} \frac{I_t^A}{N_A} + \left(S_t^A + \epsilon V_t^A \right) u_t^{AB} \beta_{max}^{AB} \frac{I_t^B}{N_B} - \gamma I_t^A \\
R_{t+1}^A &= R_t^A + \gamma(1 - \delta_A) I_t^A \\
D_{t+1}^A &= D_t^A + \gamma \delta_A I_t^A \\
S_{t+1}^B &= S_t^B - S_t^B \left(u_t^{AB} \beta_{max}^{BA} \frac{I_t^A}{N_A} + u_t^{BB} \beta_{max}^{BB} \frac{I_t^B}{N_B} \right) - d_t^B \\
V_{t+1}^B &= V_t^B + d_t^B - \epsilon V_t^B \left(u_t^{AB} \beta_{max}^{BA} \frac{I_t^A}{N_A} + u_t^{BB} \beta_{max}^{BB} \frac{I_t^B}{N_B} \right) \\
I_{t+1}^B &= I_t^B + \left(S_t^B + \epsilon V_t^B \right) u_t^{AB} \beta_{max}^{BA} \frac{I_t^A}{N_A} + \left(S_t^B + \epsilon V_t^B \right) u_t^{BB} \beta_{max}^{BB} \frac{I_t^B}{N_B} - \gamma I_t^B \\
R_{t+1}^B &= R_t^B + \gamma(1 - \delta_B) I_t^B \\
D_{t+1}^B &= D_t^B + \gamma \delta_B I_t^B
\end{aligned} \tag{6.1}$$

For each of the two populations, there are 5 compartments: the susceptible (S), vaccinated (V), infectious (I), recovered (R) and dead (D) compartment. A non-vulnerable or vulnerable individual who is susceptible can be infected by an infectious non-vulnerable or vulnerable person. To decrease the risk of infection, a susceptible person can be vaccinated. Each week, there are d_t^A non-vulnerable and d_t^B vulnerable people who receive a dose of vaccine. For simplicity, we model a vaccination procedure in which each individual can only receive one dose. When an individual is vaccinated, he moves from the susceptible compartment S to the vaccinated compartment V . Moreover, once he is vaccinated, its risk to be infected decreases. This is why each transmission rate in the vaccinated compartments is multiplied by ϵ , where $1 - \epsilon$ is the efficacy of one dose of vaccine and $0 \leq \epsilon \leq 1$.

Once they are infected, the individuals move in the infectious compartment, I_A or I_B depending on their status in the population. Then, their removed rate is γ regardless of whether they are vulnerable or not. Concerning the non-vulnerable individuals, they recover at a rate $\gamma(1 - \delta_A)$ and they die at a rate $\gamma \delta_A$, where δ_A is the infection fatality ratio of the non-vulnerable individuals. The vulnerable persons recover at a rate $\gamma(1 - \delta_B)$ and they die at a rate $\gamma \delta_B$, where δ_B is the infection fatality ratio of the vulnerable individuals.

All the parameters of this epidemic model are chosen to represent at best the COVID-19 epidemic in Belgium. Their value was already defined in Table 5.1 in Chapter 5, except for ϵ . As said before, $1 - \epsilon$ denotes the efficacy of one dose of vaccine. In this case, vaccine efficacy refers to the percentage of reduction in the risk of infection. For COVID-19 in Belgium, the efficacy of one dose of vaccine is about 75% [31]. This implies that $\epsilon = 0.25$.

6.1.2 Problem statement

The optimal way to vaccinate the vulnerable and the non-vulnerable population and the optimal health measures for each type of contact are determined using model predictive control (MPC). As a remainder, we want to find the optimal manipulated variables u_t^{*AA} , u_t^{*BB} , u_t^{*AB} , d_t^{*A} and d_t^{*B} for each week t of a one-year horizon in order to minimize the number of deaths caused by the disease and the cost of the health measures. The objective function to be minimized is therefore the same as in Chapter 5 since there is no cost for the administration of the vaccine. The optimal control problem solved at each time step t of the MPC algorithm is the following:

$$\min_{\mathbf{x}_P, \mathbf{u}_P} \quad D_P^A + D_P^B + 7\lambda \left(\sum_{k=0}^{P-1} 0.64 L'_{s,i}(u_k^{AA}) + 0.04 L'_{s,i}(u_k^{BB}) + 0.32 L'_{s,i}(u_k^{AB}) \right) \quad (6.2a)$$

$$\text{subject to} \quad x_0 = \hat{x}_0 \quad (6.2b)$$

$$(6.1) \quad \text{for } k = 0, \dots, P-1 \quad (6.2c)$$

$$u_{min} \leq u_k^{AA}, u_k^{BB}, u_k^{AB} \leq u_{max} \quad \text{for } k = 0, \dots, P-1 \quad (6.2d)$$

$$d_k^A, d_k^B \geq 0 \quad \text{for } k = 0, \dots, P-1 \quad (6.2e)$$

$$d_k^A + d_k^B \leq 7 \times 10^5 \quad \text{for } k = 0, \dots, P-1 \quad (6.2f)$$

$$S_k^A, S_k^B \geq 0 \quad \text{for } k = 0, \dots, P \quad (6.2g)$$

$\mathbf{x}_P$ is the vector that gathers all the state variables of the epidemic model (6.1) from time $k = 0$ to $k = P$. $\mathbf{u}_P$ is the vector containing the weekly manipulated variables u_k^{AA} , u_k^{BB} , u_k^{AB} , d_k^A and $d_k^B \forall k \in \{0, \dots, P-1\}$. The prediction horizon of the OCP is still $P = 15$ weeks.

The meaning of each constraint of the OCP (6.2) is the following:

- the constraint (6.2b) enforces the current state of the epidemic model (6.1), $\hat{x}_0$, to be the initial state x_0 of the model for the optimal control problem.
- the constraint (6.2c) makes sure that the state variables satisfy the dynamics of the epidemic model (6.1).
- the constraint (6.2d) imposes to the manipulated variables to be between u_{min} and u_{max} .
- the constraints (6.2e) and (6.2f) make sure that the number of vaccine doses administered each week is positive and does not exceed $D = 7 \times 10^5$, the maximum number of doses that is possible to administer each week.
- the constraint (6.2g) ensures that the number of administered doses in the non-vulnerable and vulnerable population is not higher than the number of susceptible individuals in these two populations.

The MPC algorithm allowing to find u_t^{*AA} , u_t^{*BB} , u_t^{*AB} , d_t^{*A} and d_t^{*B} for each week t of the one-year horizon is the same as the one in (4.2). However, the MPC algorithm is now applied

with the OCP (6.2) and the epidemic model (6.1). Moreover, the MPC control law is now defined as

$$\mu_P(x_t) := \mathbf{u}_P^*(0) = [u_{k=0}^{*AA}, u_{k=0}^{*BB}, u_{k=0}^{*AB}, d_{k=0}^{*A}, d_{k=0}^{*B}].$$

The initial condition of the MPC problem is the same as the one for the MPC problem without vaccination in Chapter 5 and no one is vaccinated initially. Therefore,

$$\begin{aligned} S_0^A &= 9\,152\,000 & V_0^A &= 0 & I_0^A &= 24\,000 & R_0^A &= 39\,969 & D_0^A &= 31 \\ S_0^B &= 2\,288\,000 & V_0^B &= 0 & I_0^B &= 6\,000 & R_0^B &= 9286 & D_0^B &= 714. \end{aligned}$$

6.1.3 Results

Figure 6.1 shows the optimal vaccination of the population obtained by solving the MPC problem. During the first 3 weeks, only the vulnerable population is vaccinated. All the D doses that can be given each week are therefore intended for the vulnerable group during these first 3 weeks. During the fourth week, the rest of the vulnerable population is vaccinated and the remaining doses from that week are used to start vaccinating the non-vulnerable population. Then, until the week $t = 17$, the non-vulnerable group is vaccinated with the possible D doses each week. At the end of that week, the entire population is vaccinated. It makes sense to vaccinate the vulnerable population first as they have the highest infection fatality ratio. Indeed, by vaccinating someone, its risk of infection is reduced by 75%. Reducing the risk of infection of the vulnerable population is therefore the optimal way to decrease the number of deaths caused by the disease since this population has the highest infection fatality ratio.

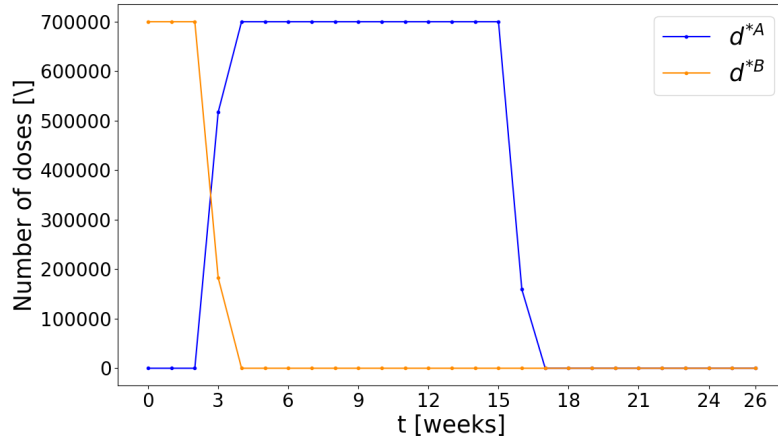


Figure 6.1: Optimal vaccination of the non-vulnerable and the vulnerable population obtained using model predictive control. d_t^{*A} and d_t^{*B} are the optimal number of vaccine doses administered in week t in the non-vulnerable and the vulnerable population respectively.

Let us then look at the optimal health measures when the vaccination is introduced in the population. Figure 6.2 shows the effects of the sanitary measures on the transmission rate of each type of contact. For the first week of the year, when no one is vaccinated, the optimal health measures are such that

$$u_0^{*BB} < u_0^{*AB} < u_0^{*AA}.$$

This means that the optimal health measures are slightly stricter among the vulnerable population (group B), followed by those concerning the contacts between the non-vulnerable and vulnerable groups and finally those among the non-vulnerable population (group A) which are

the lightest (they are however also strict). This is the same conclusion as in the control problem in Chapter 5 where vaccination was not taken into account. This was expected since at the beginning of the one-year horizon nobody is vaccinated.

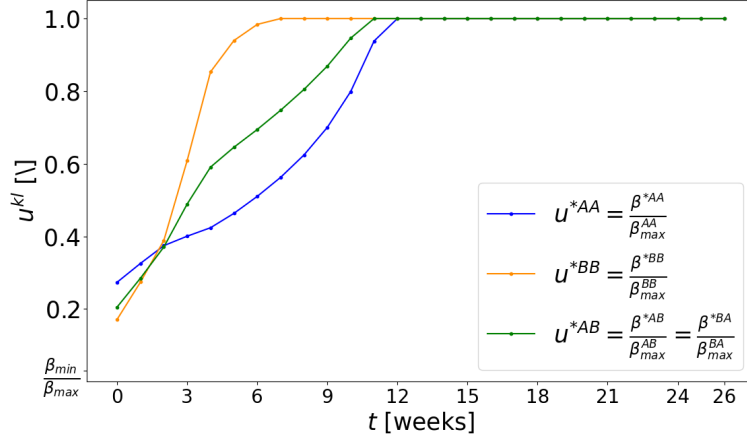


Figure 6.2: Temporal evolution of the optimal variables u_t^{AA} , u_t^{BB} and u_t^{AB} when the population is being vaccinated. They represent the effect of the health measures of each contact type on their respective transmission rates.

However, while the vulnerable population is being vaccinated, the optimal health measures within this population are becoming less and less stringent compared to the measures for the other types of contacts. Indeed, after 3 weeks, the measures are the lightest in the vulnerable population as shown in Figure 6.2. This is consistent since, at this time of the year, 60% of the vulnerable group is vaccinated while no one is vaccinated in the non-vulnerable group. From the week $t = 3$ to the week $t = 11$,

$$u_t^{AA} < u_t^{AB} < u_t^{BB}.$$

The measures are stricter in the non-vulnerable group than in the vulnerable group since the proportion of people vaccinated is lower in the former than in the latter. The intensity of the measures for the contacts between the non-vulnerable and vulnerable groups is between the two others because these are contacts between a highly vaccinated population (group B) and a less vaccinated one (group A).

After 12 weeks, the transmission rate for each type of contact is maximal since u_t^{AA} , u_t^{AB} and u_t^{BB} are equal to 1 from this moment. There are therefore no more health measures. Moreover, after 12 weeks, the entire vulnerable population is vaccinated but only 74% of the non-vulnerable population is vaccinated. This means that it is not necessary for the population to be fully vaccinated in order to have no more health measures. Moreover, after 26 weeks, while there are no more measures, the number of infectious people in the whole population falls below 5. The disease is then considered eradicated. The vaccination therefore made it possible to eradicate the COVID-19 epidemic in 26 weeks, whereas in the case with no vaccination (Chapter 5), the disease is not eradicated at the end of the year and the sanitary measures are still strict. The eradication of the disease was however possible thanks to the vaccination of the entire population in 17 weeks.

6.2 Consideration of the health care workers

In this section, in addition to the vulnerable and the non-vulnerable population, a third sub-population is added: the health care workers. The specificity of this third sub-population is that it has a lot of contacts with the vulnerable population. The purpose of this section is then to answer the following question: When is it optimal to vaccinate the health workers compared to the vulnerable and the non-vulnerable population? To answer this question, a number of assumptions had to be made for modelling purposes. These assumptions can clearly be discussed and changed.

6.2.1 Epidemic model

The epidemic model (6.1) is now extended to take into account the health care workers. There are thus the non-vulnerable (A), the vulnerable (B) and the health workforce (H) population. In addition, in this section, the contacts are no longer uniform. This means that the proportion of a certain type of contact is no longer given by the size of the populations that this contact involves. For example, the health care workers have a lot of contact with the vulnerable population, although this population represents only 20% of the total population.

Let us first determine the proportion of each population. In Belgium, there were 416 038 health care professionals in 2020 [32]. The proportion of the health care workers population is therefore $p_H = 3.6\%$. We consider this population to be part of the non-vulnerable population. Therefore, the proportion of the non-vulnerable population (without the health care staff) is now $p_A = 0.8 - p_H = 76.4\%$. The proportion of the vulnerable population is still $p_B = 20\%$.

Let us then choose the proportion of contacts that a person of group k has with people of group l , i.e. $p^{kl} \forall k, l \in \{A, B, H\}$. These proportions are subject to certain constraints. First,

$$\sum_l p^{kl} = 1 \quad \forall k \in \{A, B, H\}$$

means that the sum of all the proportions of contacts that a person of group k has is equal to 1.

Then, the second constraint makes sure that the number of contacts made each week between two groups matches well. As an example, this means that if group A has a total of 300 contacts with group B each week, group B must have a total of 300 contacts with group A each week. Otherwise, there is a mismatch in the contacts. This example translates into the following equation

$$\underbrace{N_A}_{p_A N} p^{AB} n_A = \underbrace{N_B}_{p_B N} p^{BA} n_B$$

where N_A and N_B are the number of people in groups A and B. n_A and n_B is the total number of contacts that a person of group A and B respectively has each week. The proportions p_A , p_B , p^{AB} and p^{BA} were already defined above. Assuming that each person has the same number of contacts each week regardless of the group to which he belongs, i.e. $n_A = n_B = n_H$, the constraint becomes

$$p_A p^{AB} = p_B p^{BA}.$$

The general constraint is therefore

$$p_k p^{kl} = p_l p^{lk} \quad \forall l, k \in \{A, B, H\}.$$

To choose the proportions, assumptions are made about three of them and the others are derived from the constraints. We make the hypothesis that 40% of health workers' contacts are with the vulnerable population, i.e. $p^{HB} = 0.4$. The rest of their contacts are equally

divided between the non-vulnerable population and the health worker population itself, i.e. $p^{HA} = p^{HH} = 0.3$. Moreover, we assumed that 15% of the contacts of the non-vulnerable population are with the vulnerable population, i.e. $p^{AB} = 0.15$. All the other proportions are derived from the constraints and are summarised below:

$$\begin{aligned} p^{HB} &= 0.4 & p^{HA} &= \frac{1 - p^{HB}}{2} = 0.3 & p^{HH} &= 1 - p^{HB} - p^{HA} = 0.3 \\ p^{AH} &= \frac{p_H p^{HA}}{p_A} = 0.014 & p^{AB} &= 0.15 & p^{AA} &= 1 - p^{AH} - p^{AB} = 0.836 \\ p^{BH} &= \frac{p_H p^{HB}}{p_B} = 0.07 & p^{BA} &= \frac{p_A p^{AB}}{p_B} = 0.57 & p^{BB} &= 1 - p^{BH} - p^{BA} = 0.36 \end{aligned} \quad (6.3)$$

Since there are now 3 population groups, there are thus 9 transmission rates. The transmission rate between a susceptible individual of group k and the infectious people of group l is denoted as $\beta^{kl} \forall k, l \in \{A, B, H\}$. As in the previous chapter, the maximum transmission rate is defined as:

$$\beta_{max}^{kl} = p^{kl} \beta_{max} \quad \forall k, l \in \{A, B, H\}.$$

Moreover, since there are 3 populations, there are 6 types of contacts: "AA", "AB", "AH", "BB", "HH", "BH". There are therefore 6 types of sanitary measures, where their effect on their respective transmission rate is denoted by

$$u^{AA}, u^{AB}, u^{AH}, u^{BB}, u^{HH}, u^{BH}.$$

However, we assumed that the contacts between the health care workers and the vulnerable population are vital because the latter must receive care from health professionals. Therefore, these contacts can not be reduced and there is no sanitary measures for this type of contact. Consequently, u^{BH} is always equal to 1 and this manipulated variable is not included in the model.

As in the previous chapter, the cost of the health measures for each type of contact is weighted by the proportion of that type of contact in the population. These proportions are given below:

$$\begin{aligned} w^{AA} &= p_A p^{AA} \\ w^{AB} &= p_A p^{AB} + p_B p^{BA} \\ w^{AH} &= p_A p^{AH} + p_H p^{HA} \\ w^{BB} &= p_B p^{BB} \\ w^{HH} &= p_H p^{HH}. \end{aligned}$$

The daily total cost of the sanitary measures is therefore given by

$$\lambda \left(w^{AA} L'_{s,i}(u^{AA}) + w^{BB} L'_{s,i}(u^{BB}) + w^{AB} L'_{s,i}(u^{AB}) + w^{AH} L'_{s,i}(u^{AH}) + w^{HH} L'_{s,i}(u^{HH}) \right)$$

where the cost $L'_{s,i}(u)$ is given in (4.3). λ is the daily cost of the measures (in number of deaths) allowing to impose $u = u_{min}$, i.e. the strictest possible health measures.

The following epidemic model stratifies the population into three sub-populations (A, B and H) and takes into account the vaccination. This model is the same as the model (6.1) except that the health care workers population (H) is added.

$$\begin{aligned}
S_{t+1}^A &= S_t^A - S_t^A \left(\beta_t^{AA} \frac{I_t^A}{N_A} + \beta_t^{AB} \frac{I_t^B}{N_B} + \beta_t^{AH} \frac{I_t^H}{N_H} \right) - d_t^A \\
V_{t+1}^A &= V_t^A + d_t^A - \epsilon V_t^A \left(\beta_t^{AA} \frac{I_t^A}{N_A} + \beta_t^{AB} \frac{I_t^B}{N_B} + \beta_t^{AH} \frac{I_t^H}{N_H} \right) \\
I_{t+1}^A &= I_t^A + (S_t^A + \epsilon V_t^A) \left(\beta_t^{AA} \frac{I_t^A}{N_A} + \beta_t^{AB} \frac{I_t^B}{N_B} + \beta_t^{AH} \frac{I_t^H}{N_H} \right) - \gamma I_t^A \\
R_{t+1}^A &= R_t^A + \gamma(1 - \delta_A) I_t^A \\
D_{t+1}^A &= D_t^A + \gamma \delta_A I_t^A \\
\\
S_{t+1}^B &= S_t^B - S_t^B \left(\beta_t^{BA} \frac{I_t^A}{N_A} + \beta_t^{BB} \frac{I_t^B}{N_B} + \beta_{\max}^{BH} \frac{I_t^H}{N_H} \right) - d_t^B \\
V_{t+1}^B &= V_t^B + d_t^B - \epsilon V_t^B \left(\beta_t^{BA} \frac{I_t^A}{N_A} + \beta_t^{BB} \frac{I_t^B}{N_B} + \beta_{\max}^{BH} \frac{I_t^H}{N_H} \right) \\
I_{t+1}^B &= I_t^B + (S_t^B + \epsilon V_t^B) \left(\beta_t^{BA} \frac{I_t^A}{N_A} + \beta_t^{BB} \frac{I_t^B}{N_B} + \beta_{\max}^{BH} \frac{I_t^H}{N_H} \right) - \gamma I_t^B \\
R_{t+1}^B &= R_t^B + \gamma(1 - \delta_B) I_t^B \\
D_{t+1}^B &= D_t^B + \gamma \delta_B I_t^B \\
\\
S_{t+1}^H &= S_t^H - S_t^H \left(\beta_t^{HA} \frac{I_t^A}{N_A} + \beta_{\max}^{HB} \frac{I_t^B}{N_B} + \beta_t^{HH} \frac{I_t^H}{N_H} \right) - d_t^H \\
V_{t+1}^H &= V_t^H + d_t^H - \epsilon V_t^H \left(\beta_t^{HA} \frac{I_t^A}{N_A} + \beta_{\max}^{HB} \frac{I_t^B}{N_B} + \beta_t^{HH} \frac{I_t^H}{N_H} \right) \\
I_{t+1}^H &= I_t^H + (S_t^H + \epsilon V_t^H) \left(\beta_t^{HA} \frac{I_t^A}{N_A} + \beta_{\max}^{HB} \frac{I_t^B}{N_B} + \beta_t^{HH} \frac{I_t^H}{N_H} \right) - \gamma I_t^H \\
R_{t+1}^H &= R_t^H + \gamma(1 - \delta_H) I_t^H \\
D_{t+1}^H &= D_t^H + \gamma \delta_H I_t^H
\end{aligned} \tag{6.4}$$

The notation $\beta_t^{kl} = u_t^{kl} \beta_{\max}^{kl}$ is used to simplify the notations. $\beta_{\max}^{HB}$ and $\beta_{\max}^{BH}$ are in blue to remember that these transmission rates cannot be reduced. All the parameters involved in this model were already summarised in Table 5.1, except N_H and δ_H . As already mentioned, they were $N_H = 416\,038$ health care professionals in Belgium in 2020. Since health care workers are considered to be non-vulnerable, their infection fatality ratio is $\delta_H = \delta_A = 7.6 \times 10^{-4}$.

6.2.2 Problem statement

The aim of this control problem is to determine the optimal way to vaccinate the three population groups (A, B and H) and the optimal health measures for each type of contact in order to minimize the number of death caused by the disease and the cost of the health measures. This problem is solved using model predictive control (MPC). The optimal control problem solved at each time step t of the MPC algorithm is the same OCP as the one in (6.2) except that the health care workers population (H) is added.

$$\begin{aligned}
& \min_{\mathbf{x}_P, \mathbf{u}_P} \quad D_P^A + D_P^B + D_P^H + 7\lambda \left[\sum_{k=0}^{P-1} w^{AA} L'_{s,i}(u_k^{AA}) + w^{BB} L'_{s,i}(u_k^{BB}) \right. \\
& \quad \left. + w^{AB} L'_{s,i}(u_k^{AB}) + w^{AH} L'_{s,i}(u_k^{AH}) + w^{HH} L'_{s,i}(u_k^{HH}) \right] \\
& \text{subject to} \quad x_0 = \hat{x}_0 \\
& \quad (6.4) \quad \quad \quad \text{for } k = 0, \dots, P-1 \quad (6.5) \\
& \quad u_{min} \leq u_k^{AA}, u_k^{BB}, u_k^{AB}, u_k^{AH}, u_k^{HH} \leq u_{max} \quad \text{for } k = 0, \dots, P-1 \\
& \quad d_k^A, d_k^B, d_k^H \geq 0 \quad \text{for } k = 0, \dots, P-1 \\
& \quad d_k^A + d_k^B + d_k^H \leq 7 \times 10^5 \quad \text{for } k = 0, \dots, P-1 \\
& \quad S_k^A, S_k^B, S_k^H \geq 0 \quad \text{for } k = 0, \dots, P
\end{aligned}$$

The MPC algorithm is the same as the one in (4.2). However, the MPC algorithm is now applied with the OCP (6.5) and the epidemic model (6.4). Moreover, the MPC control law is now defined as

$$\mu_P(x_t) := \mathbf{u}_P^*(0) = \left[u_{k=0}^{AA}, u_{k=0}^{BB}, u_{k=0}^{AB}, u_{k=0}^{AH}, u_{k=0}^{HH}, d_{k=0}^A, d_{k=0}^B, d_{k=0}^H \right].$$

For the initial condition of the MPC algorithm, we take the situation observed in Belgium for COVID-19 on 25th April 2020. On that date, there were approximately 30 000 infectious persons [24]. Moreover, about 50 000 people were infected and had already recovered or died before that date. We assumed that the infectious persons are evenly distributed in the population and that no one is vaccinated initially. Therefore, $\forall j \in \{A, B, H\}$,

$$I_0^j = 30\,000 \cdot p_j \quad V_0^j = 0 \quad R_0^j = 50\,000 \cdot p_j \cdot (1 - \delta_j) \quad D_0^j = 50\,000 \cdot p_j \cdot \delta_j$$

where p_j is the proportion of people who belong to the population j and δ_j is the infection fatality ratio in group j . Finally, we set $S_0^j = N_j - I_0^j - R_0^j - D_0^j$. The initial condition of the epidemic model (6.1) involved in the MPC algorithm is therefore

$$\begin{array}{lllll}
S_0^A = 8\,740\,281 & V_0^A = 0 & I_0^A = 22\,920 & R_0^A = 38\,171 & D_0^A = 29 \\
S_0^B = 2\,288\,000 & V_0^B = 0 & I_0^B = 6000 & R_0^B = 9286 & D_0^B = 714 \\
S_0^H = 411\,719 & V_0^H = 0 & I_0^H = 1080 & R_0^H = 1798 & D_0^H = 2.
\end{array}$$

6.2.3 Results

First, we look at the optimal vaccination for the proportions of contacts given in (6.3) and with the following cost functions for the health measures

$$\lambda_1 L'_{s,1}(u_t) = 1000 \frac{1/u_t - 1/u_{max}}{1/u_{min} - 1/u_{max}}.$$

In this case, the optimal vaccination is shown in Figure 6.3. During the first 3 weeks, only the vulnerable population is vaccinated with the D possible weekly doses. During the fourth week, the rest of the vulnerable population and the health worker population is vaccinated. Moreover, the remaining doses of that week allows to start vaccinating the non-vulnerable population. Then, all the weekly doses D are administered to the non-vulnerable population until the week $t = 17$. After that week, the entire population is vaccinated.

The order of vaccination of the 3 populations makes sense. Indeed, the vulnerable population is first vaccinated since they have the highest infection fatality ratio. Moreover, the vulnerable

population has $p^{BH} = 7\%$ of its contacts with the health worker population and these contacts cannot be reduced because they are vital for the vulnerable population. The only way to reduce the risk of infection for this type of contact is thus to vaccinate these two populations. This second reason also allows to explain why the health worker population is vaccinated before the non-vulnerable population. Indeed, the health worker population has $p^{HB} = 40\%$ of its contacts with the vulnerable population and these contacts cannot be reduced. On the other hand, all contacts of the non-vulnerable population can be reduced as none are considered vital¹. This is why the health care workers are vaccinated before the non-vulnerable population.

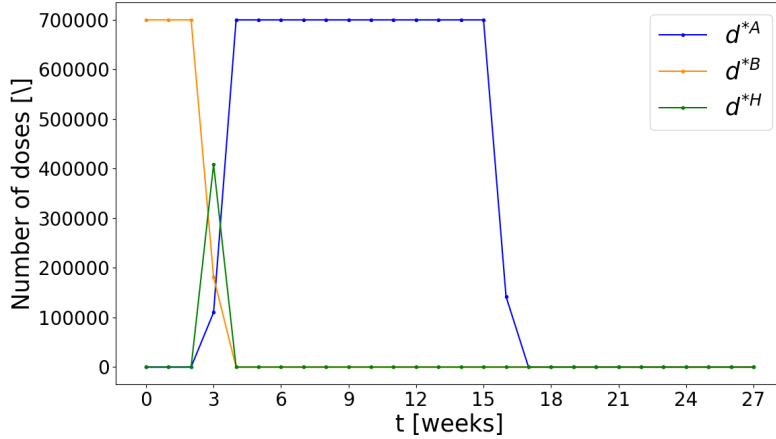


Figure 6.3: Optimal vaccination of the health care workers, the non-vulnerable and the vulnerable population with the proportions given in (6.3) for the contacts. d_t^{*A} , d_t^{*B} and d_t^{*H} are the optimal number of vaccine doses administered in week t in the non-vulnerable, the vulnerable and the health worker population respectively.

However, conclusions about the order of vaccination may change if assumptions about the proportions of contacts for each population are different. We now hypothesise that health care workers have even more contacts with vulnerable people. 60% of their contacts is now with vulnerable people instead of 40% previously. The proportions of all the contacts therefore become

$$\begin{aligned}
 p^{HB} &= 0.6 & p^{HA} &= \frac{1 - p^{HB}}{2} = 0.2 & p^{HH} &= 1 - p^{HB} - p^{HA} = 0.2 \\
 p^{AH} &= \frac{p_H p^{HA}}{p_A} = 0.009 & p^{AB} &= 0.15 & p^{AA} &= 1 - p^{AH} - p^{AB} = 0.841 \\
 p^{BH} &= \frac{p_H p^{HB}}{p_B} = 0.11 & p^{BA} &= \frac{p_A p^{AB}}{p_B} = 0.57 & p^{BB} &= 1 - p^{BH} - p^{BA} = 0.32
 \end{aligned} \tag{6.6}$$

With these new proportions for the contacts, the optimal vaccination is different as shown in Figure 6.4. The health care workers are vaccinated first, followed by the vulnerable and then the non-vulnerable population. One of the reasons why the health care workers are now vaccinated before the vulnerable population is the following. 60% of the healthcare workers' contacts are with vulnerable people. Since it is assumed that these contacts cannot be reduced, 60% of the caregivers' contacts cannot be reduced and therefore they have a very high risk of infection. This risk becomes so great that it is optimal to vaccinate them before the vulnerable people even if the latter have a higher infection fatality ratio. Moreover, if the proportion of infectious people increases in the health worker population, the risk of infection for the vulnerable population

¹It is clearly a modelling hypothesis, some contacts of the non-vulnerable population could be vital.

will increase when they are in contacts with the health care workers. This is also why it is important to vaccinate the health care workers so that the proportion of infectious people in this population remains low.

There is therefore a proportion p^{HB} of the healthcare workers' contacts, between 40% and 60%, at which it becomes optimal to vaccinate first the health worker population and then the vulnerable population. By assuming that $p^{HB} = x$ and $p^{HA} = p^{HH} = \frac{1-x}{2}$, this proportion is $p^{HB} = 0.42$. Therefore, under the assumptions made in this chapter, if the healthcare workers have more than 42% of their contacts with the vulnerable population, they have to be vaccinated before this population.

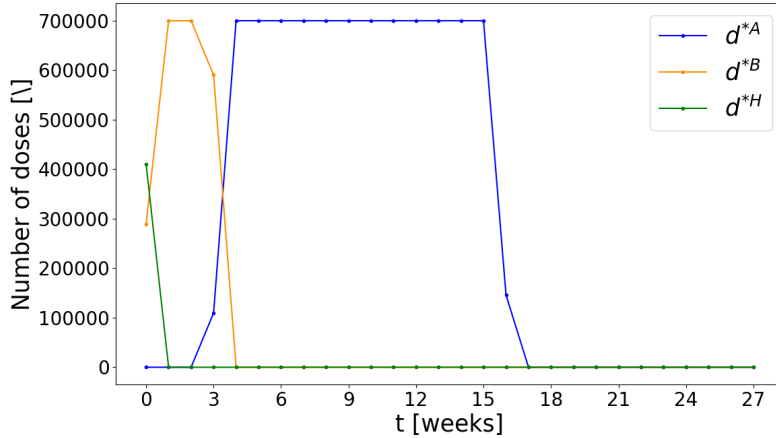


Figure 6.4: Optimal vaccination of the health care workers, the non-vulnerable and the vulnerable population with the proportions given in (6.6) for the contacts. d_t^{*A} , d_t^{*B} and d_t^{*H} are the optimal number of vaccine doses administered in week t in the non-vulnerable, the vulnerable and the health worker population respectively.

6.3 Conclusion

Firstly, this chapter looked at the optimal vaccination of the vulnerable and non-vulnerable people. It was shown that for a population where the contacts are homogeneous, the optimal way to vaccinate the population was to start with the vulnerable people. Regarding the sanitary measures, these are lighter thanks to the vaccination since people are less likely to be infected when they are vaccinated. Moreover, thanks to the vaccination, after 12 weeks, there are no more measures and after 26 weeks the disease is eradicated. However, this has involved the vaccination of the entire population in 17 weeks.

Secondly, the health care workers were added to the MPC problem. We have observed that the optimal order to vaccinate the 3 sub-populations may change if the contacts of the health professionals change. At first, it was assumed that the health care workers have 40% of their contacts with the vulnerable population, 30% with the non-vulnerable one and 30% with other carers. In this case, the vulnerable people are vaccinated first, followed by the health professionals and finally the non-vulnerable people. However, if the health care workers have even more contacts with the vulnerable population, the order of the optimal vaccination changes. Indeed, under the assumptions made in this chapter, if the healthcare workers have more than 42% of their contacts with the vulnerable population, they have to be vaccinated before this population.

Chapter 7

Differentiation of health measures according to the epidemic status

In the previous chapters, the health measures have always been imposed for the whole population or a whole sub-population. People in the same population therefore had the same health measures regardless of their epidemic status. A susceptible person therefore had the same restrictions as an infectious person. To improve the effectiveness of the health measures, it may be appropriate to impose different measures depending on the epidemic status of each person and, more specifically, to differentiate between those intended for infectious persons and those intended for the rest of the population.

However, knowing that someone is infectious can be challenging. For example, an infectious person may be asymptomatic and therefore may not know that he is infectious. Testing people to see if they are infectious can therefore be a useful intervention in the management of an epidemic. This will also be discussed in this chapter.

7.1 Problem specifications

The objective of this chapter is to distinguish the infectious people from the rest of the population to see if the optimal sanitary measures will be different for the infectious population. The idea behind this distinction is of course to impose very strict measures, such as isolation, on infectious people in order to limit the spread of the disease as much as possible. However, it can be difficult for a person to know if he is infectious or not. Indeed, an infectious person may be asymptomatic. The only way for them to be aware of their infectiousness is to be tested.

In this chapter, the population will be divided into two sub-populations:

- The first sub-population (group 1) is composed of the whole population, except the aware infectious people. This group therefore includes the susceptible (S), recovered (R) and dead (D) individuals but also the infectious people who are unaware that they are infectious. These unaware infectious people are either pre-symptomatic individuals (I^{Pre}) who do not yet have symptoms or unaware asymptomatic individuals (I^U).
- The second sub-population (group 2) is composed of the aware infectious people (I^{Aw}). This group includes symptomatic infectious people who are aware due to their symptoms and asymptomatic people who are aware that they are infectious because they have been tested. These infectious people can be distinguished from the rest of the population because they know they are infectious.

In the epidemic model of this chapter, there are therefore 6 compartments: $S, I^{Pre}, I^U, I^{Aw}, R$ and D . The scheme in Figure 7.1 illustrates the flows of individuals in the compartmental model. For this model, we choose to take a daily time step and not a weekly time step for the following reason. In the context of COVID-19, it is estimated that an individual remains pre-symptomatic for 2 days [33]. The pre-symptomatic people must therefore stay in average 2 days in the compartment I^{Pre} . Since people stay less than a week in some compartments, the time step of the model must be smaller than a week and we therefore take a daily time step. All the details about this epidemic model are presented below.

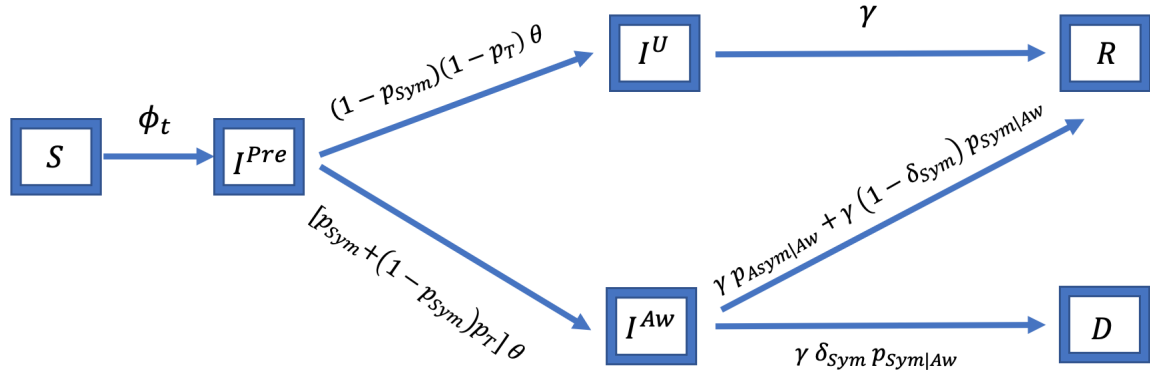


Figure 7.1: Schematic representation of the flows of individuals in the compartmental model.

Since all the people susceptible to be infected are in group 1, new infections will only occur in group 1. A susceptible individual can become infected in two ways: he can be infected by an infectious person of group 1 or an infectious person of group 2. There are therefore two transmission rates. The transmission rate β^{11} is the one between a susceptible individual of group 1 and the (unaware) infectious people of group 1, i.e. I^{Pre} and I^U . The transmission rate β^{12} is the one between a susceptible individual of group 1 and the (aware) infectious people of group 2, i.e. I^{Aw} . The force of infection for one susceptible individual on day t , i.e. its risk to be infected, is therefore defined as

$$\phi_t = \beta_t^{11} \frac{(I_t^{Pre} + I_t^U)}{N} + \beta_t^{12} \frac{I_t^{Aw}}{N}$$

where β_t^{11} and β_t^{12} are more precisely defined as

β_t^{11} = the number of contacts a susceptible person has the day t with the general population
 × the probability of a successful transmission in case of contact between a susceptible and
 an infectious individual of group 1 at time t

β_t^{12} = the number of contacts a susceptible person has the day t with the general population
 × the probability of a successful transmission in case of contact between a susceptible and
 an infectious individual of group 2 at time t

As in the previous chapters, each transmission rate will depend on the health measures imposed on it. The transmission rates are therefore given by

$$\beta_t^{11} = u_t^{11} \beta_{max} \quad \text{and} \quad \beta_t^{12} = u_t^{12} \beta_{max}$$

where u_t^{11} and u_t^{12} are the two manipulated variables representing the effects of the measures on each transmission rate at time t .

The epidemic model allowing to differentiate the unaware and aware infectious people is the following:

$$\begin{aligned}
S_{t+1} &= S_t - \frac{S_t}{N} \left(\beta_t^{11}(I_t^U + I_t^{Pre}) + \beta_t^{12}I_t^{Aw} \right) \\
I_{t+1}^{Pre} &= I_t^{Pre} + \frac{S_t}{N} \left(\beta_t^{11}(I_t^U + I_t^{Pre}) + \beta_t^{12}I_t^{Aw} \right) - \theta I_t^{Pre} \\
I_{t+1}^U &= I_t^U + (1 - p_{Sym})(1 - p_T)\theta I_t^{Pre} - \gamma I_t^U \\
I_{t+1}^{Aw} &= I_t^{Aw} + [p_{Sym} + (1 - p_{Sym})p_T]\theta I_t^{Pre} - \gamma I_t^{Aw} \\
R_{t+1} &= R_t + \gamma \left(I_t^U + p_{Asym|Aw} I_t^{Aw} \right) + \gamma(1 - \delta_{Sym}) p_{Sym|Aw} I_t^{Aw} \\
D_{t+1} &= D_t + \gamma \delta_{Sym} p_{Sym|Aw} I_t^{Aw}
\end{aligned} \tag{7.1}$$

A susceptible individual (S) can be infected by an unaware infectious individual (I^{Pre} or I^U) or an aware infectious people (I^{Aw}). This susceptible individual thus becomes pre-symptomatic infectious: he has no symptoms yet but is already infectious (I^{Pre}). Then, the pre-symptomatic individual can become an aware infectious individual (I^{Aw}) at a rate

$$[p_{Sym} + (1 - p_{Sym})p_T] \theta$$

where p_{Sym} is the probability of becoming symptomatic for a pre-symptomatic infectious person. For COVID-19 in Belgium, the estimated probability of being symptomatic is $p_{Sym} = 0.36$ [34]. $(1 - p_{Sym})p_T$ is the probability for an individual to be asymptomatic but to be tested (with a probability p_T). This individual is therefore also aware that he is infectious even if he is asymptomatic and therefore also goes into the I^{Aw} compartment. The probability p_T will be discussed in Section 7.2. Finally, θ is the rate at which an individual leaves the pre-symptomatic compartment. It is estimated that an individual remains pre-symptomatic for 2 days. Therefore, $\theta = 1/2$ [1/day].

A pre-symptomatic individual (I^{Pre}) can also become an unaware asymptomatic person (I^U) at a rate

$$(1 - p_{Sym}) (1 - p_T) \theta$$

where $(1 - p_{Sym}) (1 - p_T)$ is the probability of being asymptomatic and not being tested.

Then, the asymptomatic people "recover" at a rate γ , i.e. they are no longer infectious. As in the previous chapters, the infectious period for COVID-19 is estimated to be about one week. Therefore, $\gamma = 1$ [1/week] = $1/7$ [1/day]. In compartment I^U , containing the unaware asymptomatic people, everyone is asymptomatic. In this compartment, everyone therefore "recovers" at a rate γ . In compartment I^{Aw} , there are symptomatic and aware asymptomatic people. The asymptomatic people of compartment I^{Aw} "recover" at a rate $\gamma p_{Asym|Aw}$ where

$$p_{Asym|Aw} = \frac{(1 - p_{Sym})p_T}{p_{Sym} + (1 - p_{Sym})p_T}$$

is the probability that a person is asymptomatic, knowing that he is aware of its infectiousness.

A symptomatic infectious individual will recover at a rate $\gamma(1 - \delta_{Sym})$ and die at a rate $\gamma\delta_{Sym}$, where δ_{Sym} is the infection fatality ratio (IFR) of the symptomatic people. δ_{Sym} is defined as

$$\delta_{Sym} = \frac{\delta}{p_{Sym}}$$

where $\delta = 0.015$ was the IFR in the general population when there was no distinction between symptomatic and asymptomatic people. The symptomatic people of compartment I^{Aw} therefore recover at a rate

$$\gamma (1 - \delta_{Sym}) p_{Sym|Aw}$$

and die at a rate

$$\gamma \delta_{Sym} p_{Sym|Aw}$$

where

$$p_{Sym|Aw} = \frac{p_{Sym}}{p_{Sym} + (1 - p_{Sym})p_T}$$

is the probability that a person is symptomatic, knowing that he is aware of its infectiousness.

7.1.1 Cost of health measures

In this chapter, the sanitary measures are imposed on two types of contacts. Indeed, the health measures will reduce the contacts within group 1 (contact type "11") with the manipulated variable u^{11} and reduce the contacts between groups 1 and 2 (contact type "12") with u^{12} . As in the previous chapters, the cost of the measures for each type of contact will be weighted and the total daily cost of the health measure at time t is therefore

$$w_t^{11} \lambda L'_{s,i}(u_t^{11}) + w_t^{12} \lambda L'_{s,i}(u_t^{12}).$$

However, as indicated by the notation, the weight w_t^{11} and w_t^{12} are now time-dependent for the following reason. These weights represent the proportion of each type of contact in the population. Moreover, the number of people in each group (1 and 2) is now changing over time. Therefore, the proportion of each type of contact in the population changes over time. We suppose that the contacts are uniform in the population. Therefore, the proportion of the contact type "11" is

$$w_t^{11} = p_t^1 \cdot p_t^1$$

where $p_t^1 = \frac{N - I_t^{Aw}}{N}$ is the proportion of the population that is in group 1 at time t . The proportion of the contact type "12" is

$$w_t^{12} = 2 p_t^1 \cdot p_t^2$$

where $p_t^2 = \frac{I_t^{Aw}}{N}$ is the proportion of the population that is in group 2 at time t .

7.1.2 Problem statement

The goal of the control problem is to look at the optimal health measures to be imposed within group 1 and between groups 1 and 2 such that the number of deaths and the cost of the health measures are minimized. This problem is solved using model predictive control (MPC). The optimal control problem solved at each time step t of the MPC algorithm is the following:

$$\min_{\mathbf{x}_P, \mathbf{u}_P} \quad D_P + \lambda \left(\sum_{k=0}^{P-1} w_k^{11} L'_{s,i}(u_k^{11}) + w_k^{12} L'_{s,i}(u_k^{12}) \right) \quad (7.2a)$$

$$\text{subject to} \quad x_0 = \hat{x}_0 \quad (7.2b)$$

$$\text{\textcolor{red}{(7.1)}} \quad \text{for } k = 0, \dots, P-1 \quad (7.2c)$$

$$u_{min} \leq u_k^{11}, u_k^{12} \leq u_{max} \quad \text{for } k = 0, \dots, P-1 \quad (7.2d)$$

Since the time step of the epidemic system is now equal to one day, the *prediction horizon* of the problem is no longer 15 weeks but $P = 105$ days. $\mathbf{x}_P$ is the vector that gathers all the state variables of the epidemic model [\(7.1\)](#) from time $k = 0$ to $k = P$. $\mathbf{u}_P$ is the vector containing the

weekly manipulated variables u_k^{11} and $u_k^{12} \forall k \in \{0, \dots, P-1\}$.

The MPC algorithm allowing to find the optimal manipulated variables u_t^{*11} and u_t^{*12} is the same as the one in (4.2). However, the MPC algorithm is now applied with the OCP (7.2) and the epidemic model (7.1). Moreover, the MPC control law is now defined as $\mu_P(x_t) := \mathbf{u}_P^*(0) = [u_{k=0}^{*11}, u_{k=0}^{*12}]$.

For the initial condition of the MPC algorithm, we take the situation observed in Belgium for COVID-19 on 25th April 2020. On that date, there were approximately 30 000 infectious persons [24]. We choose to distribute these infectious people as follows:

$$I_0^{pre} = 10\,000, \quad I_0^U = 20\,000(1 - p_{Sym})(1 - p_T), \quad I_0^{Aw} = 20\,000[(1 - p_{Sym})p_T + p_{Sym}].$$

Moreover, about 50 000 people were infected and had already recovered or died before that date. Therefore,

$$R_0 = 50\,000 \cdot (1 - \delta) = 49250 \quad D_0 = 50\,000 \cdot \delta = 750.$$

Finally, we set $S_0 = N - I_0^{pre} - I_0^U - I_0^A - R_0 - D_0$.

7.2 Results and discussion

In this section, we will discuss the results obtained for the health optimal measures by taking different values for the probability p_T that an infectious asymptomatic individual is tested. Moreover, the optimal health measures within group 1, u^{*11} , and between groups 1 and 2, u^{*12} , will be compared to the ones imposed on the general population when the aware infectious people were not distinguished from the rest of the population. u^{*11} and u^{*12} will therefore be compared to u^* which was computed in Chapter 4. The results are shown for the cost function $\lambda_1 L'_{s,1}$, as defined in (5.5), but the same behaviour for the optimal health measures were obtained with $\lambda_1 L'_{s,1/2}$ and $\lambda_1 L'_{s,2}$.

Let us first analyse the results for $p_T = 0.5$. In this case, an asymptomatic infectious individual has a 50% chance of being tested and therefore of knowing that he is infectious. For $p_T = 0.5$, the optimal sanitary measures u^{*11} and u^{*12} are shown in Figure 7.2. Firstly, the optimal health measures between groups 1 and 2 are as strict as possible throughout the year. Indeed,

$$u_t^{*12} = u_{min} = \frac{\beta_{min}}{\beta_{max}} = 0.03 \quad \text{for } t = 0, 1, \dots, 365 \text{ days.}$$

This means that when someone is aware that he is infectious, i.e. a person in group 2, he should isolate himself from group 1 to have as little contact as possible with this group. Indeed, all susceptible individuals are in group 1, so isolating the aware infectious persons from group 1 will minimize as much as possible the new infections caused by these aware infectious persons. Moreover, it is optimal to isolate as much as possible the aware infectious people because it is a small group (group 2) only composed of infectious people and it is not too expensive to isolate this group since it is small. Indeed, the proportion of aware infectious people in the population, $\frac{I^{Aw}}{N}$, is less than 0.2% at the beginning of the one-year horizon and will always decrease thanks to the health measures.

Secondly, the optimal health measures imposed within group 1, containing the whole population except the aware infectious people, are strict at the beginning of the one-year horizon and become lighter and lighter thereafter. Indeed, u_t^{*11} is increasing. We also observe that these measures are lighter than the measures which were imposed on the whole population when

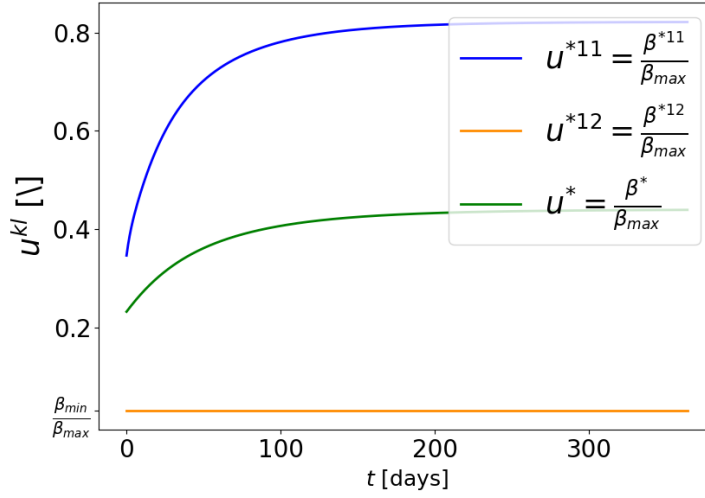


Figure 7.2: Temporal evolution of the manipulated variables u_t^{*11} , u_t^{*12} and u_t^* for $p_T = 0.5$. They represent the effect of the health measures on the transmission rates β_t^{11} , β_t^{12} and β_t respectively.

the aware infectious people were not isolated. Indeed, $u_t^{*11} > u_t^*$ throughout the year. This is because the aware infectious individuals have been isolated from group 1. As a result, there are fewer infectious individuals in contact with susceptible individuals. This means that a susceptible person is less likely to be infected and health measures can therefore be lighter. However, there must still be measures in group 1 because there are still infectious people who do not isolate themselves because they are not aware that they are infectious. This is why $u_t^{*11} \neq u_{max} = 1$.

Let us then discuss the optimal health measures obtained for the limit case where $p_T = 1$. In this case, an asymptomatic infectious individual has a 100% chance of being tested and therefore of knowing that it is infectious. As shown in Figure 7.3, the optimal health measures between groups 1 and 2 are once again as strict as possible throughout the year since $u_t^{*12} = u_{min} \forall t$. Indeed, for the same reason as before it is optimal to isolate the aware infectious people (group 2) from group 1. However, the optimal health measures within the group 1 are lighter when $p_T = 1$ than when $p_T = 0.5$. This makes sense since more asymptomatic infectious people are isolated from group 1 with a higher probability of testing p_T . There is thus less infectious people remaining in group 1 with $p_T = 1$. Actually, with $p_T = 1$, only pre-symptomatic infectious people remain in group 1 during two days. As a result, the susceptible people are less likely to be infected and the health measures can be lighter. Moreover, we observe that there are no more measures within group 1 after 8 days. After 71 days, the disease is supposed to be eradicated since there are less than 5 infectious people left in the population. However, $p_T = 1$ is a limit case since it implies that an asymptomatic infectious individual has a 100% chance of being tested. Since we do not know in advance who is asymptomatic in the population, we should test everyone every day, which is not possible.

Finally, we look at the smallest value for p_T such that the disease is eradicated before the end of the one-year horizon. By trial and error, we found that it is for $p_T = 0.77$ and the disease is eradicated after 349 days as shown in Figure 7.4. This means that testing 77% of asymptomatic infectious people and imposing the strictest possible measures on all aware infectious people can eradicate the disease before the end of the year. This percentage of testing is again very difficult to achieve and the model assumed that everyone respects the health measures imposed on them, which is not always the case in reality. However, it also means that we do not have to

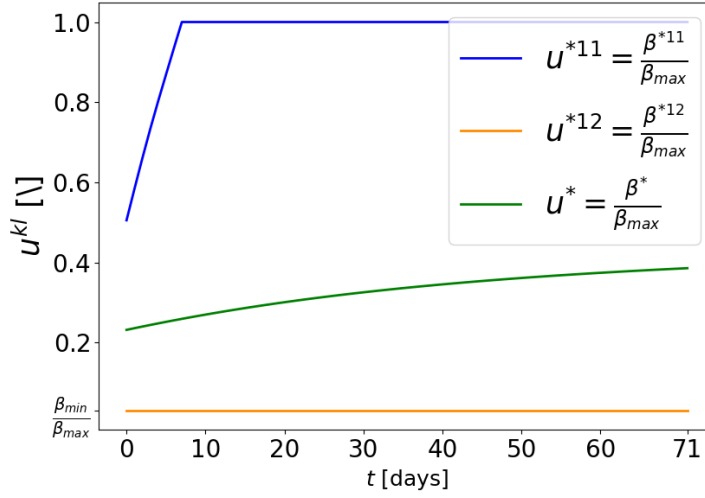


Figure 7.3: Temporal evolution of the manipulated variables u_t^{*11} , u_t^{*12} and u_t^* for $p_T = 1$. They represent the effect of the health measures on the transmission rates β_t^{11} , β_t^{12} and β_t respectively.

identify all the asymptomatic infectious people and to isolate them from the susceptible people to eradicate the disease.

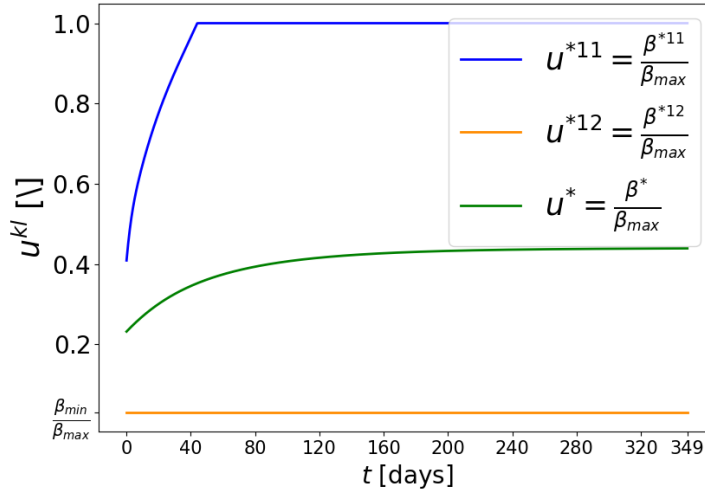


Figure 7.4: Temporal evolution of the manipulated variables u_t^{*11} , u_t^{*12} and u_t^* for $p_T = 0.77$. They represent the effect of the health measures on the transmission rates β_t^{11} , β_t^{12} and β_t respectively.

7.3 Conclusion

This chapter has shown that by imposing very strict sanitary measures on the aware infectious people to isolate them from the susceptible individuals, less strict measures can be imposed on the rest of the population. Moreover, we have seen that the greater the number of people aware of their infectiousness, the greater the number of infectious people isolated from susceptible people and the lighter the measures imposed within group 1, containing the entire population except the aware infectious people.

In order to increase the number of infectious people aware of their infectiousness, it may therefore be important to test the population. It has been shown in this chapter that if 77% of the asymptomatic infectious people can be identified by testing and if they follow the measures imposed on the aware infectious people, then the disease could be eradicated in less than one year. However, this depends very much on the assumptions of the model. Indeed, in this model, it is assumed that all the aware infectious people comply with the very strict measures imposed on them, which is not always the case in reality. Moreover, identifying 77% of the asymptomatic infectious people through testing them is very difficult since we do not know in advance who is asymptomatic. Vaccination therefore seems to be a better intervention to eradicate the COVID-19 disease.

Chapter 8

Conclusion

In the recent context of the COVID-19 pandemic, the management of epidemics is a topic of interest worldwide. More generally, whatever the epidemic concerned, it is essential to limit its spread in order to avoid the serious consequences that this latter can cause. Several interventions can be implemented to control an epidemic. However, these interventions have a cost and they have to be implemented properly to be effective. The challenge of epidemic management is therefore to limit as much as possible the spread of an epidemic while minimizing the cost of the interventions implemented.

In this master thesis, two control approaches have been used to control the spread of the COVID-19 epidemic in Belgium: the optimal control and the model predictive control approach. In Chapter 3, an optimal control problem was implemented to find the optimal weekly transmission rate of the disease. This rate is optimal in the sense that it minimizes the cumulative number of deaths at the end of a one-year horizon and the cost of the health measures implemented to achieve such a rate. It was observed that the temporal evolution of the optimal weekly transmission rate depends on the cost function representing the cost of the health measures.

Firstly, for the cost functions for which it is possible to limit the spread of the epidemic by imposing health measures during the majority of the one-year horizon, the optimal transmission rate is increasing. At the beginning of the year, this rate must be low. Thanks to this low rate, after the 10th week, there are about 1000 infectious people in the population instead of 30 000 initially. Between the 10th and the 40th week, the optimal transmission rate increases only slightly so that the number of infectious people remains almost constant. Finally, at the end of the year, the transmission rate increases significantly because the consequences of this decision on the weeks after the end of the one-year horizon are not taken into account by the optimal control problem.

However, for the cost functions which are so high that it is only optimal to impose measures at certain times of the epidemic, the optimal transmission rate is no longer increasing. For these cost functions, it is optimal to let the epidemic spread during the first weeks of the year. During this period, there is no health measure and the transmission rate is therefore at its maximum value. Then, some measures are imposed for a few weeks to stop the spread of the epidemic when it becomes much too great, before being completely relaxed again. These cost functions therefore lead to extreme situations where we let the epidemic spread, causing the infection of 60% of the population in one year. In the rest of this master thesis, we have therefore preferred to focus on the first type of cost functions for which the observed optimal measures are closer to those imposed in Belgium, i.e. strict measures at the beginning.

In Chapter 4, the weekly optimal transmission rate β_t^* minimizing the number of deaths

and the cost of the health measures was found using model predictive control. In MPC, β_t^* is obtained by solving iteratively an optimal control problem at each time step t of the MPC algorithm. For the cost functions $\lambda_1 L_{s,i}$, as defined in (3.3), the optimal transmission rate β_t^* is increasing. As in optimal control, β_t^* is low at the beginning of the one-year horizon to decrease the number of infectious people present in the population. Moreover, it was observed a posteriori that β_t^* increases in a limited way such that the effective reproduction number R_t tends towards 1 at the end of the one-year horizon but never exceeds 1. As a result, the number of infectious people only decreased throughout the year to become almost constant at the end of the year. Since the MPC algorithm allows to take into account the influence of β_t^* on the weeks that follow the end of the horizon, the optimal transmission rate no longer increases at the end of the year. The health measures are therefore quite strict throughout the year and this is why we have looked at the vaccination in Chapter 6 to see if this intervention may help to alleviate the sanitary measures.

The aim of this master thesis was then to provide elements of response to several questions of epidemic management thanks to the model predictive control approach. In Chapter 5, the population was divided into a non-vulnerable sub-population with a low infection fatality ratio and a vulnerable sub-population with a higher one. The question was then to know whether the health measures allowing to decrease the transmission rate of the disease should be different for the two sub-populations. Due to the exponential behaviour of the spread of an epidemic, it was shown that the transmission rate of the disease has a higher influence on the number of deaths caused than the infection fatality ratio (IFR). As a result, the health measures for the non-vulnerable and the vulnerable population are very closed even if the IFR of the non-vulnerable group is lower. Another reason why the measures are so closed for the two groups is that too light measures within the non-vulnerable population will also have negative consequences for the vulnerable one. Indeed, if the proportion of infectious people increases in the non-vulnerable group, the risk of infection for a vulnerable person will increase when he is in contact with the non-vulnerable population.

Chapter 6 was devoted to the optimal vaccination in order to minimize the number of deaths caused by the disease and the cost of the health measures. Firstly, the question was: Who should be vaccinated first between the vulnerable population and the non-vulnerable population? It was shown that if the contacts are homogeneous between these two groups, the optimal way to vaccinate the population is to start with the vulnerable people and then vaccinate the non-vulnerable ones. Moreover, thanks to the vaccination, the health measures are lighter and the disease can be eradicated in 26 weeks if everyone is vaccinated. Secondly, the health care workers were added to the problem and we have observed that the optimal order to vaccinate the 3 sub-populations may change if the contacts of the health professionals change. Indeed, under the assumptions made in this chapter, when the health care workers have less than 42% of their contacts with the vulnerable group, the optimal order is to vaccinate the vulnerable people first, followed by the health care professionals and then the non-vulnerable people. However, when the health care workers have more than 42% of their contacts with the vulnerable group, it is optimal to vaccinate first the caregivers.

Chapter 7 aimed to look at the optimal health measures when they can be different for the aware infectious people compared to the rest of the population. It was observed that isolating the aware infectious people from the rest of the population allows for less strict measures to be imposed on this latter. However, all the infectious people are not aware of their infectiousness because they can be asymptomatic. It is therefore important to test the population in order to increase the number of people who are aware of their infectiousness. Under the assumptions of this chapter, if 77% of the asymptomatic infectious people can be identified by testing and

if they follow the measures imposed on the aware infectious people, the disease can be eradicated before the end of the one-year horizon. This means that we do not have to identify all the asymptomatic infectious people to eradicate the disease. However, identifying 77% of the asymptomatic infectious people through testing is very difficult since we do not know in advance who is asymptomatic. Vaccination therefore seems to be a better intervention to eradicate the COVID-19 disease.

This master thesis has answered several questions of epidemic management but further work can be made. First, in this work, it was assumed that the cost functions of the health measures are convex. It might however be interesting to look at linear or concave cost functions. A further improvement would be to make these cost functions time-dependent. This would make it possible to model a cost that increases if the health measures are imposed for a too long time period. The epidemic models representing the spread of COVID-19 could also be improved. A first improvement would be to take into account the fact that a person who has recovered from the disease may be infected again after some time, as observed during the COVID-19 epidemic. This could be modelled thanks to a SIRDS instead of a SIRD model. In this SIRDS model, the individuals in the recovered compartment will move back to the susceptible compartment at a certain rate.

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