A SEIR-model of the Covid-19 Pandemic; Developed, Optimized and Explained.

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A Master's Thesis
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June 1, 2022

Acknowledgements

I would like to thank Guttorm Alendal, for supervision and guidance through the process of writing this master's thesis.

I would like to thank Eirik V. Stokke for excellent teamwork this semester.

Then I would like to thank Kim A. Haugland and Pandemisenteret in Bergen for allwing us to hold a presentation of our work and providing helpful feedback.

Thank you to Preben Aavitsland and FHI for assisting in providing reports and parameters needed for simulations of the model developed in this thesis.

Finally I would like to thank friends and classmates throughout my time at UiB for laughs and conversation, collaboration and assistance, and meaningful friendships.

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Bergen, June 2022

Abstract

In this thesis I seek to develop a compartmental model that describes the Covid-19 pandemic. This will be a SEIR model that includes parameters of vaccine rate and vaccine efficacy. The model is developed and analyzed using classic epidemiological modelling techniques as well as standard exploration of non-linear differential equations. The finalized model, parameters used, analysis of the equilibrium points and simulations are presented.
I then use the model in an optimization problem where the goal is to explore how to minimize the resulting total cost of the pandemic given various values of vaccination rate. The optimization problem was attempted solved in numerous ways using the programming language Python. I eventually found that in most cases, despite various cost-relationships between infected, vaccinated and deceased individuals, a high vaccination rate is cost-beneficial.
As I through my studies obtain both a master's degree in applied mathematics as well as a teacher's degree an ulterior motive of the model initially developed is to be able to utilize it for educational purposes in the general population. When reflecting on how to accomplish this, experiences from practical training as a teacher and feedback from audience were crucial. Exploring how to make the material in this thesis explainable led to a complete manuscript for a hypothetical presentation. This is presented later in Appendix C.

Contents

Chapter 1

Introduction

1.1 Background

1.1.1 History of the Pandemic this far

On the 31st of December 2019 the World Health Organization (WHO) was notified by China about an outbreak of cases of pneumonia of unknown cause in the city of Wuhan [1]. The initial cases had been linked to a local seafood market, and on January 1st 2020 the market was closed. Some days later the cause was identified as a coronavirus - that would later be called SARS-CoV-2 - that had originated from said market [1]. Cases started to spread rapidly and on January 23rd the city of Wuhan was placed under lockdown. Infection spread to other countries through individuals with no connection to Wuhan, indicating that the virus was spreading between humans. On the 5th of March 2020 96,000 cases in 87 different countries worldwide had been reported and on March 11th 2020 WHO declared the outbreak a global pandemic as it had spread worldwide [1] [2] [3].
On the 26th of February 2020 the first case was confirmed in Norway. A woman had arrived from China and tested positive. She was quarantined and it was believed no one else had been infected. This was reported by news channels in Norway [4].
After some time people that had traveled to the Austrian Alps for winter-break arrived back in Norway and brought more of the virus with them. Gradually new cases occurred as the virus continued spreading. On March 12th Norway was placed under lockdown [5]. This lockdown was accompanied by what the prime minister called "the most intrusive control measures the population of Norway had seen in time of peace" [5].

1.1.2 Mitigation

The measures initiated on March 12th was meant to slow down the spread and keep the peak of infection as low as possible such that the epidemic would last longer but less people would be infected at the same time, a strategy known as "flattening the curve" [5] [6]. These measures included practicing good personal hygiene, like e.g. washing hands and using hand sanitizer, testing and isolating exposed individuals, tracking infection, limiting people travelling into Norway and reducing contact rate. It also meant

keeping a greater distance on public transportation and in grocery stores, as well as closing down schools, kindergartens, restaurants, pubs, gyms, salons, etc. In the days more measures and shutdowns were put in place as the virus kept spreading [5].

1.1.3 The Basic Reproduction Number

As the virus persisted in Norway the "R-number" became frequently mentioned in media as a means to indicate the severity of the situation (as e.g seen in [7]).
The basic reproduction number, R_0, is defined as the number of new cases an infected individual will cause in a population of susceptible individuals and is used as one indication of severity in epidemiology [8]. The value of the basic reproduction number will often vary among different populations and different diseases as it depends on several factors, like the duration of the infectious period and the probability of infecting others [9]. Often R_0 represents a threshold-value of the outbreak, where $R_0 > 1$ will mean that one infected individual will transmit the disease to more than one other individual and an epidemic breaks out, whereas $R_0 < 1$ means the opposite [8]. There are several ways of calculating R_0, and while there is no universal method the method of calculating the spectral radius of the Next Generation Matrix will be used later in this paper [10].

1.2 Motivation

The beginning of the pandemic was scary for everyone. The uncertainty and speculation of what might happen when - not *if* - the virus spread to our home country was overwhelming. Then the virus came, lockdown was issued, society closed down, infection spread fast, the healthcare system was trembling, people were dying and it was even worse than a lot of us had imagined. As time went on things started to partly open back up and we all settled in to a new normal, with a sense of understanding of how the disease had to be handled. Then new variants emerged, which caused new waves of infection and more restrictions.
Stuck in pandemic-life and with Covid starting to feel gradually more familiar, some restrictions started to feel exaggerated and unnecessary. In addition to fear, a feeling of frustration became apparent as the severity of the control measures didn't feel like it matched the actual situation we witnessed in our society.

As I study to become a teacher of mathematics and natural sciences I personally have a mostly unwavering faith in scientists and experts but that might be because I have knowledge of how the scientific method works. I am able to accept decisions made by experts because I trust that they make decisions based on what the data and science tell them. This might not be the case for the general population that do not have a deep understanding of mathematics and the scientific method. Therefore I want to propose a way to present the basics of epidemiological mathematics, models, and applications as this is often what is behind decisions made regarding control measures. Hopefully this will provide some peace and acceptance among those who - understandably - struggle.

1.3 Problem Statement

While restrictions and control measures have been introduced to contain the spread of the Covid-19 virus, they have occasionally been met with opposition and resistance. This thesis presents a simplified model of the pandemic, which potentially could be understandable to the general population. The hope is that knowledge and understanding of the mathematics behind restrictions will help motivate change in behavior and a widespread acceptance of control measures.
This thesis also presents a different use for the simple epidemiological model that also engage the public: economic costs.

1.4 Objectives

The objective is to develop and analyze a SEIR-model of the Covid-19-pandemic simple enough that it can be used to educate non-mathematicians in the general population about the mathematics behind the spread of infection, while still maintaining a level of relevance and accuracy so that it - acknowledging its limitations to a specific scenario - somewhat resembles the current situation.
A program used to determine the optimal vaccination rate in order to minimize the economic costs of the pandemic will also be proposed.

1.5 Contribution

While keeping the developed model simple it will still provide insight into how vaccines and vaccine efficacy affect spread of disease as well as how vaccines contribute to minimizing the economic cost of a pandemic.
At the end of the thesis important reflections concerning how data and models should be presented together in a way that supports understanding and consequently leniency in a population is also presented.

1.6 Thesis Outline

The work done in chapter 2, 3 and 5 and corresponding appendices is done in coorporation with Eirik V. Stokke [1]. These chapters and appendices are mostly identical. We will develop and analyze a SEIR-model that illustrates the development of the Covid-19 pandemic, given certain limitations and parameters. The model will include a vaccine rate and vaccine efficacy and a simulations with various parameters will be run.
This model will later be used as a tool as I explore optimization of cost. Assuming that infection and vaccination are the main contributors of economic expenditure, a connection between various cost-relationships between these and the total cost generated from various vaccination rates will be sought out. Given the SEIR-model and parameters, programming and minimization tools will be used to seek an optimal vaccination rate

[1] See Eirik V. Stokke's master's thesis titled: *A Delayed SEIR-model of the Covid-19 Pandemic.*, University of Bergen, June 2022.

so as to generate the lowest total cost of the pandemic.
While the SEIR-model itself will be limited as to how representative it is of the actual situation, the final goal is to use the model as a tool to explain epidemic mathematics and models to a population of non-mathematicians. Experiences after having held a presentation in front of other academics at Pandemisenteret (the Pandemic Centre [2]) about the work done will be presented. Finally a complete manuscript of how one could present the same material to the general non-academic population will be suggested.

[2] Pandemic Centre Webpage: https://www.uib.no/en/pandemic

Chapter 2

Modelling

2.1 SIR- and SEIR-models

2.1.1 SIR

A popular mathematical model in epidemiology is the SIR-model. It is a model made up of differential equations that each denote changes within different groups in a population as time goes on. It is used for simulating, analyzing, and predicting how a pandemic or epidemic will develop, and can be used as a tool for e.g. governments to handle outbreaks.
While developing a SIR-model one first identifies the initial set of dependent variables, and denote the size of the different groups of people in the population, divided into number of susceptible, $S(t)$, infected $I(t)$, and recovered, $R(t)$ individuals as time, t, progresses [11]. It is assumed that a recovered individual has immunity and can not go back to being susceptible. Recovered can also mean removed, in that people who die from the disease being studied also falls into this category [12].
Visually these transitions can be presented in a flowchart as in figure 2.1, where S, I and R denotes the susceptible, infected and recovered individuals in a population, respectively.

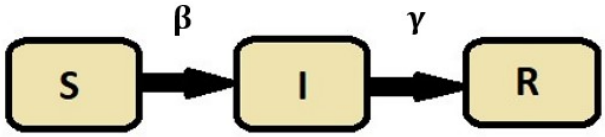


Figure 2.1: Flowchart of a SIR-model, where S, I and R denotes the susceptible, infected and recovered individuals in a population, respectively.

Certain parameter-values are needed to describe the rate of which individuals transition from S to I and from I to R. For this purpose β is used as the parameter describing the effective transmission rate that transfer individuals from S to I, and γ is the recovery-rate, describing the rate of which individuals go from being infected to being recovered. See figure 2.1.

A set of dependent variables denote the *change* in variables S, I and R in that they describe how quickly the sizes of the compartments increase or decrease as individuals move from one box to the next. These changes are described by differential equations and these are the equations that make up the model itself. A basic SIR-model could look like this:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dT} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I \end{aligned} \tag{2.1}$$

The first equation describes how many susceptible individuals are in contact with infected individuals and consequently get infected and then leaves the susceptible-compartment. The second equation correspondingly increase by the susceptible individuals that get infected, and also decrease as those who are infected recover (or die). The final equation describes the amount of individuals who have recovered (or died) from the disease being studied [12].
One of several properties of model 2.1 is that the total population, N, is conserved. Since the equations $\frac{dS}{dt}$ and $\frac{dI}{dt}$ does not depend on R, one can write

$$R = N - S - I. \tag{2.2}$$

This helps make the later analysis of the model easier, as it is sufficient to consider the equations not depending on R while constructing e.g. the Jacobian matrix [13].

2.1.2 SEIR

The SIR-model can be expanded in numerous ways, where one of the most common is to add a compartment, E, which denotes those individuals that have been exposed to the disease but have not yet reached an infectious state. One can also add rates of natural births and deaths in a population, here denoted by μ, see fig. 2.2.

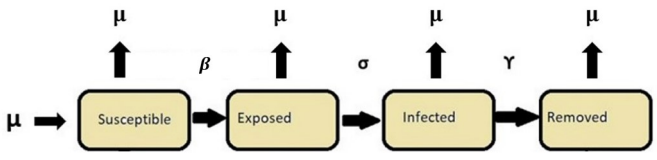


Figure 2.2: Flowchart of a SIR-model, where S, E, I and R denotes the susceptible, exposed, infected and recovered individuals in a population, respectively.

Inspired by how Osman and Adu constructed a similar model for their work on Malaria transmission, we propose an example of what a general SEIR-model can look

like [14]:

$$\begin{aligned} \frac{dS}{dt} &= \mu - \beta SI - \mu S \\ \frac{dE}{dT} &= \beta SI - \sigma E - \mu E \\ \frac{dI}{dt} &= \sigma E - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I - \mu R \end{aligned} \tag{2.3}$$

Where μ, β, σ and γ represent the natural birth-/death rate, transmission rate, incubation rate and recovery rate, respectively.
To find the basic reproduction number, R_0, for this model we use the Next Generation Method [10]. To use this method, we first need to find the disease-free equilibrium point of the system, then find the corresponding *next generation matrix* and finish by calculating the *spectral radius* of that matrix. The next generation matrix is denoted by FV^{-1}, so we first need to find both F and V. F is the infection ratio. In other words it is the ratio in which new infection enters different compartments. In the model in eq. 2.3 new infection can originate from $\frac{dS}{dt}$ and $\frac{dR}{dt}$ as these are what is called *non infection categories*. From $\frac{dS}{dt}$ infection is only generated by the term βSI, so we have $F_1 = \beta SI$. From $\frac{dR}{dt}$ no new infection is generated, so $F_2 = 0$. As compartments $\frac{dE}{dt}$ and $\frac{dI}{dt}$ are the ones that pass infection through the population, we consider these dimensions when constructing the F-matrix containing partial derivatives. F will then be

$$F = \begin{bmatrix} \frac{\delta F_1}{\delta E} & \frac{\delta F_1}{\delta I} \\ \\ \frac{\delta F_2}{\delta E} & \frac{\delta F_2}{\delta I} \end{bmatrix}$$

with respect to the disease-free equilibrium point. This point exists prior to infection entering the system, thus when $(S,E,I) = (1,0,0)$.
This makes:

$$F = \begin{bmatrix} 0 & \beta \\ \\ 0 & 0 \end{bmatrix}.$$

V is the ratio of which the infectious part of the population transfers from one compartment to another. For V we have $V_1 = (\mu + \sigma)E$, the transfer rate in E and $V_2 = -\sigma E + (\mu + \gamma)I$ which is the transfer rate in I. We can now calculate

$$V = \begin{bmatrix} \frac{\delta V_1}{\delta E} & \frac{\delta V_1}{\delta I} \\ \\ \frac{\delta V_2}{\delta E} & \frac{\delta V_2}{\delta I} \end{bmatrix} = \begin{bmatrix} \mu + \sigma & 0 \\ -\sigma & \mu + \gamma \end{bmatrix}.$$

Now we can get V^{-1} and from this, finally FV^{-1}:

$$V^{-1} = \frac{1}{(\mu + \sigma)(\mu + \gamma)} \begin{bmatrix} \mu + \gamma & 0 \\ \sigma & \mu + \sigma \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} \frac{\beta\sigma}{(\mu+\sigma)(\mu+\gamma)} & \frac{\beta(\mu+\sigma)}{(\mu+\sigma)(\mu+\gamma)} \\ 0 & 0 \end{bmatrix}$$

The spectral radius of a square matrix is the eigenvalue with largest absolute real value, which in this case gives us the following basic reproduction number:

$$R_0 = \frac{\beta\sigma}{(\mu+\sigma)(\mu+\gamma)} \tag{2.4}$$

[10], [15], [8].

SEIR-model including vaccines

In this thesis we developed a SEIR-model to be used on the Covid-19-pandemic. Several expansions and versions of the SIR-model were visited before we concluded on the model below:

$$\begin{aligned} \frac{dS}{dt} &= \mu - \beta SI(x(1-\varepsilon)+(1-x)) - x\varepsilon S - \mu S \\ \frac{dE}{dT} &= \beta SI(x(1-\varepsilon)+(1-x)) - \sigma E - \mu E \\ \frac{dI}{dt} &= \sigma E - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I + xeS - \mu R \end{aligned} \tag{2.5}$$

Where μ, β, σ, γ, x, and ε are the birth-/death-rate, transmission rate, incubation rate, recovery rate, vaccination rate and vaccine efficiency, respectively. The various stages of the development of this model are explained in Appendix B.

Using the next generation method on this model we get the following R_0:

$$R_0 = \frac{\beta\mu\sigma(1-x\varepsilon)}{(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu)}.$$

To verify that this represents an appropriate R_0, we can set the vaccination rate to zero. We then get the same expression of R_0 as for the general SEIR-model, found in eq. 2.3, confirming potential legitimacy of our model.

2.1.3 Limitations and Assumptions

A model of any phenomena is just that; a model. It is an attempt of representing natural occurrences as well as possible, but a model will never be completely accurate or predictive. As the purpose of this paper is partly to represent a model of the Covid-19 pandemic in a relatively understandable way a lot of assumptions and simplifications have been applied, making the model less accurate and predictive. The model is still useful as an illustrative and descriptive tool, but a lot of other factors that apply to the actual situation have not been considered. The final results will hence most likely not

reflect the actual current situation.
Below follows a short summary of several factors that have not been taken into considerations when developing the model of this paper:

- Quarantine and isolation: Quarantine and isolation are measures put in place to limit spread of infection. Quarantining restricts movement of exposed individuals as they wait to see if they are in fact infected, and isolation separates infected people from individuals who are not sick [16]. Both measures have been largely used all over the world during the Covid-19 pandemic, but are not included in our model. The result of this is that the spread of infection simulated by the model spreads much faster than it would in the real world. According to our model infected people would interact with susceptible people at the same rate as in usual everyday life, which largely is not the case. If so desired quarantine and isolation could be included by changing parameters, but we decided to not take it into consideration.

- Reinfection: Already prior to any notable variants of the Coronavirus, the topic of reinfection was discussed. Mainly immunity was assumed post undergone infection, but a handful of cases of reinfections had been reported as of December 2020 [17]. One specific case presented a middle-aged man with asymptomatic infection who after a period of testing negative got infected a second time which suggests a strong possibility of reinfection [17]. This paper's model does assume complete immunity after undergone infection. This leads to a simulation where the pandemic ends faster than it would in real life as the recovered-compartment would actually grow slower than it does in the model. This could be included in our model by adding a link from the recovered-compartment back to the susceptible-compartment, but we decided to leave it out for simplicity.

- Early vaccinations: As mentioned earlier, Norway was put under lockdown on March 12th 2020. From data provided by the Norwegian Institute of Public Health (FHI) and Pandemisenteret one can see that the first doses of the vaccine however were not administered until week 50 of 2020 when 8 doses were given. It was not before well into 2021 that mass-vaccination was underway. In our model vaccinations are administered from day 1, simulating earlier higher levels of immunity than were actually the case. This results in a simulation where more individuals count as recovered or immune earlier than in reality.

- Constant vaccination rate and efficacy: Our model assumes a constant vaccination rate. After prolonged periods of vaccination the unvaccinated part of the population would eventually get smaller and consequently the vaccination rate would decrease. Another aspect of vaccination rate is vaccine hesitancy which also potentially limits the vaccination rate [18]. This leads to the recovered-compartment growing faster in the model than it would in real life as we assume a prolonged, high daily vaccine rate.
  The vaccine efficacy is also held constant in the model. In reality some studies have identified waning effectiveness within a time period following vaccination [19]. In the model it is assumed that a portion of vaccinated individuals gains complete lasting immunity, when in reality vaccinated individuals would go back to being susceptible after the duration of the vaccines' effectiveness has passed.

- Several doses: In addition to assuming vaccines were already distributed at the beginning of the pandemic, the model also only takes one dose and the corresponding efficacy into consideration. In the real world several doses provide increased immunity. In addition to this vaccines do not necessarily prevent infection, but protect against severe illness, hospitalization and death.

- Multiple strains: As the pandemic has progressed several variants of the Covid-19-virus have developed. These have among other things led to increased probability of reinfections by different variants, varying effectiveness of the vaccines and varying transmission rate [20]. The consequence of this is a pandemic that lasts for a longer time than what the model in this thesis simulates. Because of all assumptions and simplifications made the model only goes through one wave of infection before it settles at an endemic equilibrium point, when in reality it will develop differently and several waves of infection occur.

- Parameters: The beta, β, used in this thesis assumes that every individual in the population interact with each other at the same rate. This is not the case, as people's living situation differs, geographical differences play a big role, people change their behaviour during difficult times, different occupations sometimes require people to interact with many/few people, etc. All of this play a role on the average transmission rate of the virus in society, but it is hard to include every sociocultural difference into one parameter. A similar characteristic goes for the other parameters as well, as individuals of e.g. varying age and health status might exhibit different rates of both incubation and recovery.

- Compartments: For simplicity reasons our model only contains four compartments; susceptible, exposed, infected, and recovered. It is possible however to include a multitude of various compartments describing the different states individuals can be in, depending on how complex and accurate of a model one seeks to work with. Reference number [10] and [21] provide examples of more complex compartmental models developed for the Covid-19 pandemic.

2.2 A Comment on R_0

At this point, the only thing that has been mentioned about the R_0-number is a short introduction to the concept. However, while it may seem simple and practical to calculate a number that can act as an indicator of severity, R_0 is flawed [22] [23]. Initially the concept was introduced in demography to count offspring, but has since been adopted and adapted by epidemiology [22]. Numerous variations have been proposed. However these are not identical which makes the applicability of the concept challenging. Simply interpreting a given value of R_0 requires sublime understanding of the structures, inputs and interactions of the model used for generating the number [22]. Many researchers, let alone the general population, have no training when it comes to such complicated mathematical techniques, which inevitably increases the risk that R_0 is misinterpreted, misapplied and misrepresented [22].
There are several ways to calculate the R_0-number, such as e.g. *The Survival Function*, *The Jacobian*, *Constant term of the Characteristic Polynomial*, *The Next-Generation*

Method, *The Graph-Theoretic Method* and *Existence of the Endemic Equilibrium*, and mostly these do not agree with each other [23]. See Li et.al for a brief explanation of each [23].
Consequently the method one chooses to use when calculating R_0 of a given disease will provide a different number than a different method would. Only intricate knowledge of the method used would let oneself understand what the R_0-number really means.

2.2.1 Factors Used in Calculation

R_0 is often estimated based on three main factors: the duration of contagiousness, likelihood of infection per contact, and contact rate, along other parameters [22]. The general situation related to a disease may also inspire a various range of parameters to include in the calculation of R_0. Because of this, the applicability of a disease is often strictly limited to the region it was calculated [22]. In addition to factors related to the disease itself, population density, social integration, and even weather will affect the contact rate, meaning that R_0 is not only a function of the biological characteristics of a pathogen but also of human behaviors [22]. This largely varies as e.g. studies have shown that more than 20 different values of R_0 was reported for measles across different time periods and places [22].

2.2.2 Vaccines and the Basic Reproduction Number

Vaccines have proven to be efficient when it comes to mitigating outbreaks by reducing the amount of people that is susceptible to a disease, but does not directly affect the basic reproduction number [22]. This might seem contradictory but R_0 is an indication of contagiousness in a completely susceptible population, meaning that the R_0-number would not apply in an immune population. Vaccines reduces the value of the *effective reproductive number* that does not assume complete susceptibility in a population. If vaccines are used to mitigate outbreaks, the R_0-number is not a good metric to include [22].

2.2.3 Problems with R_0

The three main properties of the basic reproduction number are [23]:

- An endemic infection persists only if $R_0 > 1$.
- R_0 is a measure of the control efforts required to eliminate infection.
- Pathogens evolve to maximize their value of R_0.

However, as proved by Roberts [24], all of these properties can be false.
The first statement can fail if there is a backwards bifurcation. This occurs when there exist multiple stable equilibrium points even when $R_0 < 1$ [23].
The second property can fail because control measures differ between different groups of hosts in the population. R_0 is determined by averaging across all hosts of the

pathogen, and as different control efforts are required among groups at different levels of risk R_0 does not describe a universal indicator of required efforts [23].
The third property can be false if there are two pathogens that coexist in a stable steady state, but their separate steady states are unstable. The order of which the pathogens establish in a population matters, but the pathogen with the largest R_0-number will not necessarily exclude the other [23].

Why R_0 then?

R_0 has a big role in disease modelling but is indeed complicated [23]. As we have seen it almost never calculates consistently and does not even always satisfy its most fundamental properties. Different diseases can't be compared unless the same method has been used. Even still, it is what we've got. The concept itself can be understood across several different modelling specialized fields, and terms regarding the calculation of the basic reproduction number has intuitive appeal [23]. What is needed is a simple, accurate measure that non-mathematicians can understand [23].

Interpretation of R_0

As mentioned earlier we used the Next Generation Method when calculating the basic reproduction number that characterize the pandemic simulated by our model. This number was calculated to be:

$$R_0 = \frac{\beta\mu\sigma(1-x\varepsilon)}{(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu)}.$$

In this case R_0 includes vaccination rate and efficacy which goes against the definition of R_0 as it includes a control measure that makes part of the population immune to the disease. As R_0 describes how infectious a disease or virus is in a completely susceptible population, it will by definition no longer be applicable in this situation. We did however not ignore this fact when working on this thesis and started calculating the basic reproduction number. During our research we discovered several articles that implement the Next Generation Method and claim an R_0-number, see [10] and [25]. Confidently leaning on work already done we decided to move forward with the method.
At a later point, with a desire to keep true to the definition of R_0, which we have already seen is such a complicated metric, we do admit it is not directly relevant in this situation. However, R_0 and the Next Generation Method can aid in expressing R_{eff} and R_v which are other important epidemiological metrics.
R_{eff} is called the effective reproductive number and allows for including immunity in a population. This can be expressed as

$$R_{eff} = R_0 S,$$

where S is the susceptible portion of the population [25]. R_{eff} aids in categorizing the spread of disease in a partial susceptible population [25].
Using the Next Generation Method to calculate R_0 on a system including vaccines does not truly find R_0, but rather what is called the *vaccination reproduction number*, R_v

[15]. This number can in certain cases provide insight into how large portion of a population must be vaccinated in order to obtain herd immunity [15].
As we include vaccines in our model in eq. 2.5 we assume we obtain R_v through the Next Generation Method, and not the true R_0.

By abuse of notation we will continue to use the notation R_0 when referring to this reproduction number.

2.3 Analyzing Equilibrium Points and Stability

The equilibrium points of the model in eq. 2.5 is found by setting $\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$. As neither $\frac{dS}{dt}$, $\frac{dE}{dt}$ nor $\frac{dI}{dt}$ depend on R we can expand on equation 2.2 to get:

$$R = 1 - S - E - I,$$

where 1 is the normalized N and hence S, E, I and R represent proportions of the population belonging to the respective compartments. This allows us, without loss of generality, to only consider (S^*, E^*, I^*) when stating the equilibrium points. Our system has two equilibrium points:

$$(S_1^*, E_1^*, I_1^*) = \left(\frac{\mu}{x\varepsilon + \mu}, 0, 0\right)$$

and

$$(S_2^*, E_2^*, I_2^*) = \left(\frac{\mu}{R_0(x\varepsilon+\mu)}, \frac{(\gamma+\mu)(R_0-1)(x\varepsilon+\mu)}{\sigma\beta(1-x\varepsilon)}, \frac{(R_0-1)(x\varepsilon+\mu)}{\beta(1-x\varepsilon)}\right),$$

where

$$R_0 = \frac{\beta\mu\sigma(1-x\varepsilon)}{(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu)}.$$

(S_1^*, E_1^*, I_1^*) represents a disease free environment of 2.5 as both $I_1^* = 0$ and $E_1^* = 0$, indicating that infection has not yet entered the system. As S_1^* includes vaccination parameters the model represents a situation where vaccination occurs in a disease free environment, which can be interpreted as a precautionary measure. R_1^* in this case is $\frac{x\varepsilon}{x\varepsilon+\mu}$.
As we consider a normalized population, $(0,0,0) \leq (S,E,I) \leq (1,1,1)$ must be true. As we study (S_2^*, E_2^*, I_2^*) we see that for this to hold R_0 must be > 1 and infection persists. Then, by definition (S_2^*, E_2^*, I_2^*) is an endemic equilibrium point.

Categorizing equilibrium points

In order to classify the disease free equilibrium point, (S_1^*, E_1^*, I_1^*), we do a linear analysis by constructing a Jacobian matrix:

$$\mathcal{J}(S_1^*, E_1^*, I_1^*) = \begin{bmatrix} -\mu - x\varepsilon & 0 & -\frac{\beta\mu}{x\varepsilon+\mu}(x(1-\varepsilon)+(1-x)) \\ 0 & -\sigma-\mu & \frac{\beta\mu}{x\varepsilon+\mu}(x(1-\varepsilon)+(1-x)) \\ 0 & \sigma & -\gamma-\mu \end{bmatrix}.$$

From this we get the characteristic polynomial:

$$p(\lambda) = det(J - \lambda I) = -(\mu + x\varepsilon + \lambda)\left((\mu + \sigma + \lambda)(\gamma + \mu + \lambda) - \frac{\beta\sigma\mu(1-x\varepsilon)}{\mu + x\varepsilon}\right).$$

From which we get three roots, $\lambda_1, \lambda_2, \lambda_3$:

$$\lambda_1 = -\mu - x\varepsilon.$$

λ_2 and λ_3 are the roots of $(\mu + \sigma + \lambda)(\gamma + \mu + \lambda) - \frac{\beta\sigma\mu(1-x\varepsilon)}{\mu + x\varepsilon}$,
which can be written as:

$$\lambda^2 + \lambda(\sigma + \gamma + 2\mu) + \sigma\mu + \sigma\gamma + \mu^2 + \mu\gamma - \frac{\sigma\beta\mu(1-x\varepsilon)}{x\varepsilon + \mu}.$$

Using Zabczyk's theorem [26] (see Appendix B, section B.1.2, theorem iv.) we get the constants:

$$a = \sigma + \gamma + 2\mu > 0$$

and

$$b = \sigma\mu + \sigma\gamma + \mu^2 + \mu\gamma - \frac{\sigma\beta\mu(1-x\varepsilon)}{x\varepsilon + \mu}.$$

Using that $R_0 = \frac{\beta\mu\sigma(1-x\varepsilon)}{(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu)}$, we can rewrite b as:

$$b = (\gamma + \mu)(\sigma + \mu) - R_0(\gamma + \mu)(\sigma + \mu) = (1 - R_0)(\gamma + \mu)(\sigma + \mu),$$

from which we get that R_0 must be < 1 for the polynomial to be stable.

The endemic equilibrium point S_2^*, E_2^*, I_2^* is:

$$\left(\frac{\mu}{R_0(x\varepsilon + \mu)}, \frac{(\gamma + \mu)(R_0 - 1)(x\varepsilon + \mu)}{\sigma\beta(1 - x\varepsilon)}, \frac{(R_0 - 1)(x\varepsilon + \mu)}{\beta(1 - x\varepsilon)}\right).$$

Which gives us the following Jacobi matrix:

$$\mathcal{J}(S_2^*, E_2^*, I_2^*) = \begin{bmatrix} -\mu - x\varepsilon - (R_0 - 1)(x\varepsilon + \mu) & 0 & -\frac{\beta\mu(1-x\varepsilon)}{R_0(x\varepsilon+\mu)} \\ (R_0 - 1)(x\varepsilon + \mu) & -\sigma - \mu & \frac{\beta\mu(1-x\varepsilon)}{R_0(x\varepsilon+\mu)} \\ 0 & \sigma & -\gamma - \mu \end{bmatrix}$$

With the characteristic equation

$$det(J - \lambda I) = [(1 - R_0)(x\varepsilon + \mu) - x\varepsilon - \mu - \lambda][(-\sigma - \mu - \lambda)(-\gamma - \mu - \lambda) - \frac{\sigma\beta\mu(1 - x\varepsilon)}{R_0(x\varepsilon + \mu)}]$$

$$+(1 - R_0)(x\varepsilon + \mu)\frac{\sigma\beta\mu(1 - x\varepsilon)}{R_0(x\varepsilon + \mu)} = 0.$$

We need the equation on the following form to be able to use Zabczyk's theorem (see Appendix B, section B.1.2, theorem iv.):

$$\lambda^3 + a\lambda^2 + b\lambda + c.$$

To get there, we need to do some substantial calculations. These are presented in more detail in Appendix D. Following these calculations we are able to express $det(J-\lambda I)$ as such:

$$\lambda^3+\lambda^2(2\mu+\gamma+\sigma+R_0(x\varepsilon+\mu))$$
$$+\lambda(R_0(xe+\mu)(2\mu+\gamma+\sigma))+(R_0-1)(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu)=0.$$

The following conditions must fulfilled:

$$a=2\mu+\gamma+\sigma+R_0(x\varepsilon+\mu)>0,$$

$$b=R_0(x\varepsilon+\mu)(2\mu+\gamma+\sigma)>0,$$
$$c=(R_0-1)(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu)>0.$$

We see that a, b and c are all positive for $R_0>1$, but theorem iv. also require ab $>$ c. We get:

$$ab-c=(2\mu+\gamma+\sigma)(R_0(x\varepsilon+\mu)(2\mu+\gamma+\sigma))+R_0^2(x\varepsilon+\mu)^2(2\mu+\gamma+\sigma)$$
$$-(R_0-1)(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu),$$

which can be rewritten as

$$R_0^2(x\varepsilon+\mu)(2\mu+\gamma+\sigma)+R_0(3\mu^2+3\mu\sigma+3\mu\gamma+\sigma^2+\sigma\gamma+\gamma^2)+\gamma\sigma+\gamma\mu+\mu\sigma+\mu^2$$

from which we see that $ab>c$. All conditions are fulfilled and we conclude that the endemic equilibrium point is stable for $R_0>1$.

Chapter 3

Numerical Results

In this chapter we explain how we obtained the desired parameter values. We also provide simulations run on the model in eq. 2.5 with parameters from different countries and compare the results.

For directions to the code used to run simulations in this section, see Appendix A.

Reaching out to FHI

Ultimately we wanted to run simulations using Norwegian parameter values. In order to do this we reached out to FHI [1] and Pandemisenteret [2] at UiB in Bergen to get as accurate estimates of the parameters included in the model as possible. The following was requested:

- β: the product of contact rate and transmissibility. We realize these values have varied throughout the pandemic, but we would like an estimate from early on in the pandemic before intrusive measures were put in place.
- σ: describes the incubation period. We would like the average incubation period of the virus.
- γ: describes how long an individual is infectious for.
- x: describes the rate of vaccination. What proportion of the population gets vaccinated daily (estimated from the time of mass vaccination)?
- ε: describes the efficacy of the vaccine. We treat efficacy as the percentage of the vaccinated individuals that is considered immune to the virus (estimate from early on in the vaccination process).

Using numbers provided by reports done by FHI [3] we get $\sigma = 0.25$ and $\gamma = 0.157$. Using raw data provided by FHI of how many have received their first vaccination dose

[1] FHI Webpage: https://www.fhi.no/en/

[2] Pandemic Center Webpage: https://www.uib.no/en/pandemic

[3] 2020.05.04 Corona Report used for parameters σ and γ: https://www.fhi.no/en/id/infectious-diseases/coronavirus/coronavirus-modelling-at-the-niph-fhi/

each week since the beginning of vaccination, we calculate x to be 0.002. We arrived at this by averaging the number of weekly vaccinated individuals through the entire vaccination period, but excluding the earlier weeks as a negligible number of vaccines were distributed at that time. From Polack's research on vaccine safety and efficacy, we get $\varepsilon = 0.52$ [27]. Birth- and death rate, μ, was determined by first dividing the number of births in Norway in 2021 by 365 days [4]. The resulting number was again divided by Norway's total population as of January 1st 2022 [5]. All of this is listed in table 3.1:

Table 3.1: Norwegian parameter values gathered from various sources.

σ: 0.25 per day
γ: 0.157 per day
x: 0.002 per day
ε: 0.52
μ: 2.829 $\times 10^{-5}$ per day

Still, a few parameters were lacking for us to run a simulation. While working to obtain these we continued to explore data found from other parts of the world.

3.1 USA

We study parameter values from Wintachai & Prathom's paper on stability analysis done in USA and India [28]. As that paper uses different parameter values to describe birth- and death rate and our model assumes they are the same we will only be using their estimate of birth rate. In that paper $E(0)$ and $I(0)$ are combined into one number when identifying initial values. In our simulation we divide this number by 2 to obtain separate initial values. The paper does not include values of vaccination rate and vaccine efficacy, x and ε, so we use the values listed in table 3.1.
Combining this we get the parameter values for USA collected in table 3.2.

Table 3.2: Parameter Values from USA.

Transmission rate	β	0.462
Recovery rate	γ	0.0696 per day
Incubation rate	σ	0.0870 per day
Birth-/ death rate	μ	3.178×10^{-5} per day
Vaccine rate	x	0.002 per day
Vaccine efficacy	ε	0.52
Initial values	S0, E0+I0, R0	0.97286, 0.00905, 0.01809

[4]Number of births in Norway in 2021 found at: https://www.ssb.no/befolkning/fodte-og-dode/statistikk/fodte

[5]Norwegian population as of January 1st 2022 found at: https://snl.no/befolkning

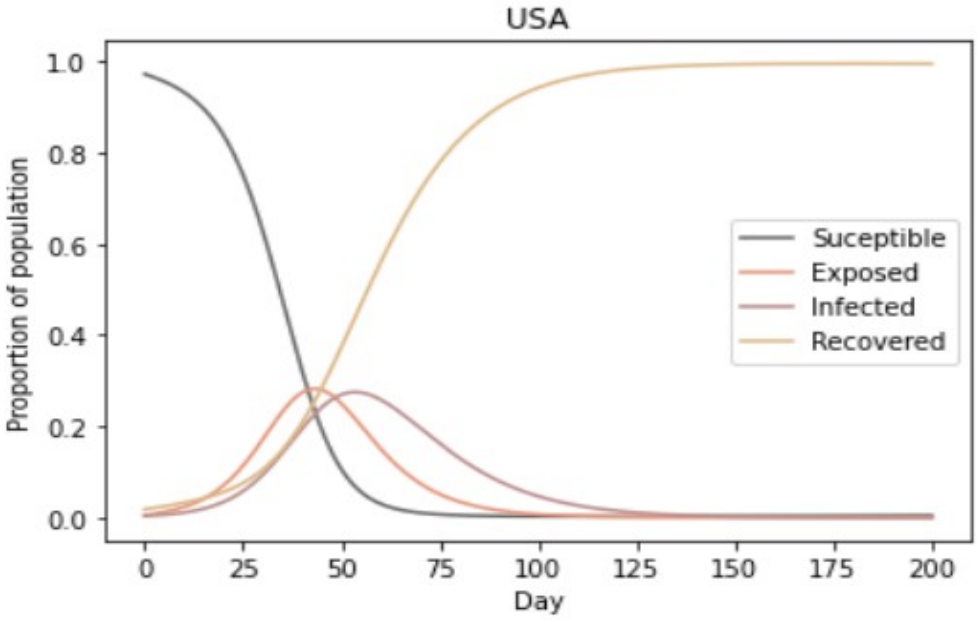


Figure 3.1: Simulation using data from USA, table 3.2.

Running a simulation of the model with the values from USA in table 3.2 we get the graphs in figure 3.1. Peak of infection occurs on day 53 with 27.5% of the population being infected at the same time.

3.2 India

We still look to Wintachai's paper and its parameter values identified for the situation in India [28]. Using these as well as x and ε from table 3.1 we get the values presented in table 3.3.

Table 3.3: Parameter Values from India.

Transmission rate	β	0.32
Recovery rate	γ	0.0686 per day
Incubation rate	σ	0.0870 per day
Birth-/ death rate	μ	4.893×10^{-5} per day
Vaccine rate	x	0.002 per day
Vaccine efficacy	ε	0.52
Initial values	S0, E0+I0, R0	0.994, 3.813×10^{-4}, 5.569×10^{-3}

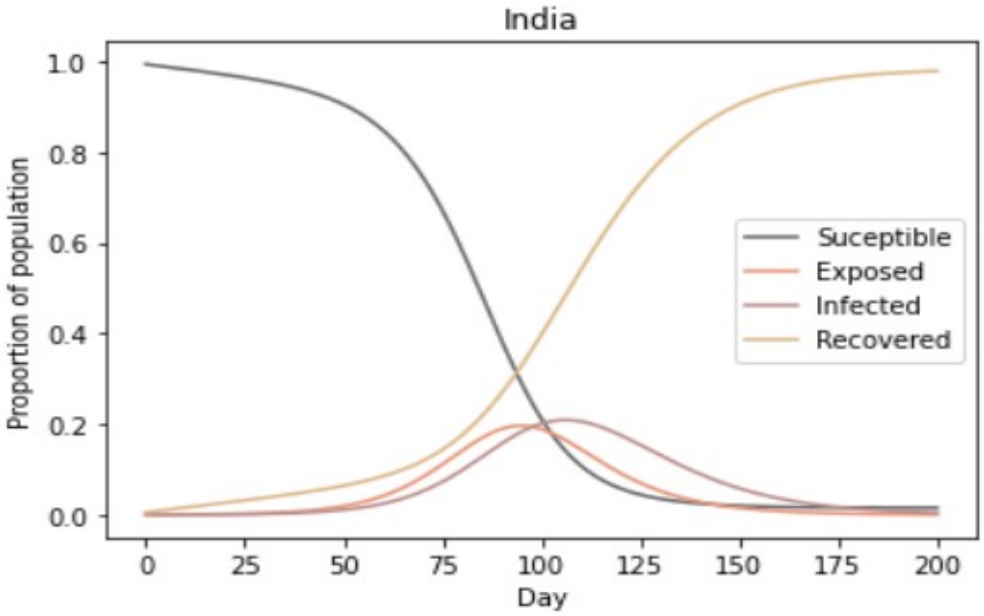


Figure 3.2: Simulation using data from India, table tab 3.3.

Running a simulation of the model with the values from India in table 3.3 we get figure 3.2. Here the peak of infection occurs on day 106 with 20.9% of the population being infected at the same time. Comparing the graphs from figure 3.1 and 3.2, we clearly see a difference in when the peak of infection occurs and how extensive it is.

The main difference between the data from USA and India are the respective values of the parameter β and the initial values. Running test-simulations where only the initial values are exchanged we can conclude that the results are sensitive to both β and the initial values as this leads to changes in both height and time of the peak of infection, see figure 3.3.

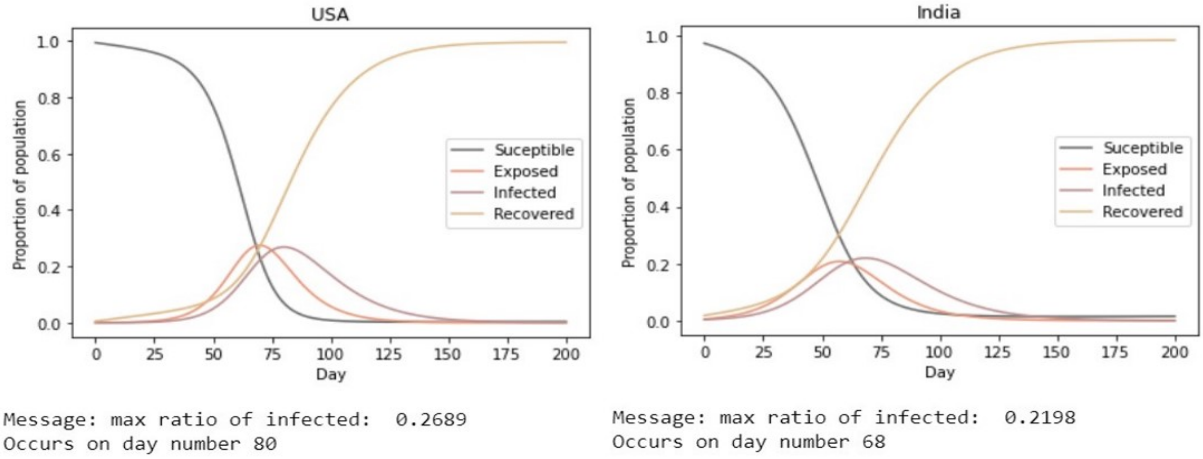


Figure 3.3: Initial conditions in table 3.2 and 3.3 exchanged.

3.3 Norway

Now we want to run a simulation using the parameters from Norway. As we were unable to obtain specifically Norwegian values for every parameter, we use the same β and initial values as in table 3.3. All parameters used when running a simulation from Norway are presented in the table below.

Table 3.4: Norwegian parameter values gathered from various sources

Transmission rate	β	0.32
Recovery rate	γ	0.157 per day
Incubation rate	σ	0.25 per day
Birth-/ death rate	μ	2.829×10^{-5} per day
Vaccine rate	x	0.002 per day
Vaccine efficacy	ε	0.52
Initial values	S0, E0+I0, R0	0.994, 3.813×10^{-4}, 5.569×10^{-3}

This lets us run the following simulation:

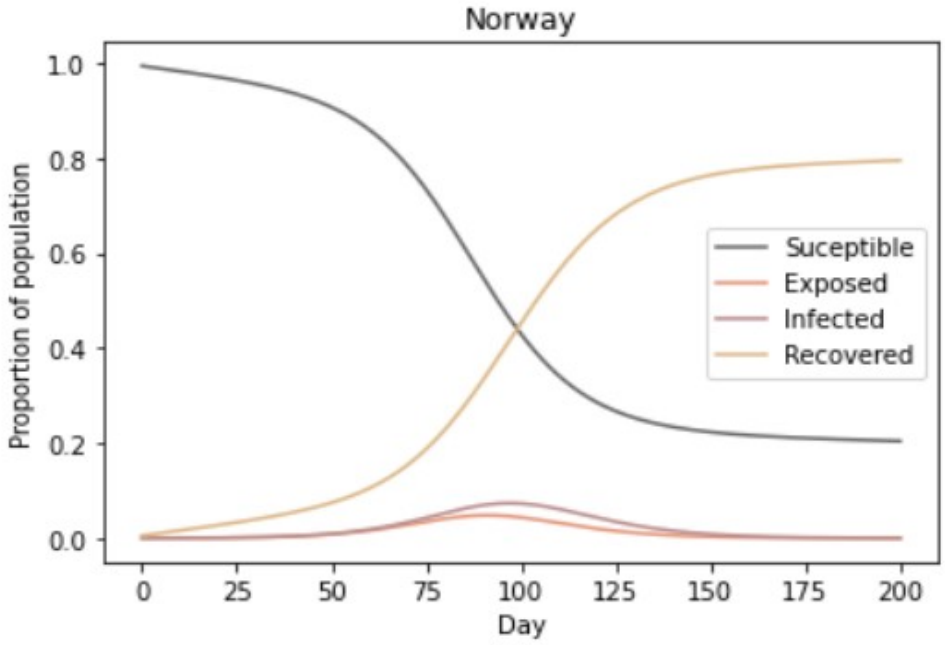


Figure 3.4: Simulation using data from Norway, table 3.4.

In this simulation the peak of infection occurs on day 97 with 7.39% of the population being infected. This is much lower than what we saw in simulations using parameters from USA and India. We see significant differences between the parameters γ and σ as the Norwegian values for these are much higher. With large values of γ and σ individuals would move from exposed to infected and from infected to removed rather quickly. This can lead to a situation where exposed individuals get infected and then recover before they have had much time to spread the disease. As we see in the simulation in figure 3.4 a large portion of the population end up in the recovered-compartment, either through infection or vaccination, without the peak of infection ever getting as high

as the simulations done for USA and India.
This is not how reality looked in Norway where peak of infection occurred around 2 years after the first case of Covid was confirmed and as of May 24th 2022 more than 1.4 million cases of Covid have been reported in Norway [6].
This substantial inaccuracy is due to the many limitations of this model, some of which are presented in section 2.1.3.

[6]Number of confirmed cases of Covid in Norway as of May 24th 2022 found at: https://www.fhi.no/en/id/infectious-diseases/coronavirus/daily-reports/daily-reports-COVID19/

Chapter 4

Minimizing the cost of Covid

In this chapter the vaccination rate, previously denoted by x, will be denoted by v. I will include parameter values found in table 3.3.

4.1 The Diet Problem

In 1945, Stigler posed a problem he called "the Diet problem." He wondered how much, among 77 different foods of varying nutritional value, would a moderately active man need each day to cover dietary needs while keeping the cost of the diet minimal [29]. He formulated the problem as *minimize* cX, *subject to* $AX \geq b$, $X \geq 0$, where X is a vector of different foods, c is a vector of corresponding prices of foods, the matrix A contains nutritional values of the foods, and vector b describes the minimum requirements for the different nutrients [29]. While the problem and it's solution have received critique, e.g. for using large averages of data and hence loosing the day-to-day applicability, it was a starting point for a wide range of linear programming problems with many applications [29].
In this chapter I will humbly try and use linear programming to examine the possibility of optimizing the cost of the Covid-19 pandemic. Cost can be measured in many more ways than economic and the pandemic has already cost many people more than words can say, but for the sake of this problem I will focus only on economic cost. The cost of hospitalized Covid-19-patients are high, and it costs society a lot of resources when infected individuals have to stay home from work, but there are also a lot of resources being spent on developing and distributing vaccinations. Using an indicator of the average cost of infected and vaccinated individuals I hope to identify a balance between infection and vaccination that generates as low a total cost as possible despite the pandemic being on the rise.

4.2 The "Minimizing the Cost of Covid"-Problem

In a linear programming problem (LPP) there will be variables to be optimized in some fashion, called *decision variables* [30]. In this case, number of infected and vaccinated, here denoted by I and V respectively, are the variables to be optimized.
In an LPP one seeks to maximize or minimize what is called an objective function which is a combination of these decision variables. In this case, if there is a number,

I, that describes the total number of infected individuals and an estimate of cost, $cost_i$, that describes what one infected individual costs on average, the total cost of infection can be expressed as $cost_i \cdot I$. Similarly, if there is a number, V, that describes the total number of vaccinated individuals and a corresponding cost-estimate, $cost_v$, that describe the average cost of vaccination per individual, the total cost of vaccination can be expressed as $cost_v \cdot V$. Assuming that infection and vaccination are what generate costs during a pandemic, the total cost of these is what I will seek to minimize. The objective function to be minimized, that describes the total cost of the pandemic, will then be the combined cost of infection and vaccination:

$$\textit{minimize} \ \text{cost}_i I + \text{cost}_v V.$$

While minimizing the value of the objective function one also has to take certain constraints into consideration. Such constraints are some form of limiting inequality- or equality equations regarding the relationship between the decision variables. These equations must be true at all times for the problem to be feasible [30].
The only description I have available of how the numbers of infected and vaccinated individuals develop is the SEIR-model previously developed. Therefore I let the SEIR-model provide the equations that will serve as the limiting constraints for this problem as these describe how quickly individuals transfer from one compartment to the next.
I let model 2.5 provide these constraints and can formulate thee problem as such:

$$\textit{minimize} \ \text{cost}_i I + \text{cost}_v V \ \text{ subject to:}$$
$$\begin{bmatrix} \mu - \beta SI(1-v+v(1-e)) - evS - \mu S \\ \beta SI(1-v+v(1-e)) - \sigma E - \mu E \\ \sigma E - \gamma I - \mu I \\ \gamma I - \mu R + evS \end{bmatrix}$$

However, to have meaning the SEIR-equations used as constraints must be inequality- or equality-equations limited by specific values. The equations are the differential equations describing the change in each compartment of the SEIR-model. This means that should e.g. the top expression, which describes the change in the susceptible compartment of the model, $\mu - \beta SI(1-v+v(1-e)) - evS - \mu S$, be negative, the total number of susceptible individuals in a given population would be decreasing.
The aim of this problem is to minimize the cost of infection and vaccination while a pandemic is still on the rise. In such a situation the number of susceptible would decrease, while the number of exposed and consequently infected and recovered would increase. This leads to the first equation being limited to ≤ 0, while the remaining three equations must be ≥ 0.

The problem will finally be formulated as follows:

$$\textit{minimize } \text{cost}_i I + \text{cost}_v V \text{ subject to}$$

$$\begin{bmatrix} \mu - \beta SI(1-ve) - veS - \mu S \\ \beta SI(1-ve) - \sigma E - \mu E \\ \sigma E - \gamma I - \mu I \\ \gamma I - \mu R + veS \end{bmatrix} \begin{matrix} \leq \\ \geq \\ \geq \\ \geq \end{matrix} \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \tag{4.1}$$

However, a *linear* programming problem must consist of *linear* equations, but not all of the constraints in the current problem are. A potential solution to this: linear approximation.

4.2.1 Linear Approximation

Most functions describing phenomena in the world are nonlinear. However, by zooming in on a specific point, a non-linear function will start to resemble a linear function and one can find a linear approximation of the function in that point. This can be achieved by Taylor expansion of the first order [31].
The linear approximation of a function, f, in a point, x_0, is given by ([31]):

$$L_f = f(\mathbf{x}_0) + \nabla f(\mathbf{x}_0) \cdot (\mathbf{x} - \mathbf{x}_0) \tag{4.2}$$

Which will allow me to find a linear expression of the non-linear constraints in 4.1 in a specific point.

Changing base model

The goal of this chapter is to to determine the lowest cost generated by an ideal number of infected and vaccinated individuals while the constraints hold. However, in order to do this, "number of vaccinated" will preferably be a decision variable but as of now it is simply determined by a parameter. Therefore I will change the model by adding a compartment to include vaccinated individuals as well as the number of susceptible, exposed, infected, and recovered/removed:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI - \alpha S \\ \frac{dE}{dt} &= \beta SI - \sigma E + \mu VI \\ \frac{dI}{dt} &= \sigma E - \gamma I \\ \frac{dR}{dt} &= \gamma I \\ \frac{dV}{dt} &= \alpha S - \mu VI \end{aligned} \tag{4.3}$$

Where β, α, σ, μ and γ are the transmission rate, rate of vaccination, incubation rate, rate of which vaccinated individuals get exposed and then infected, and recovery rate, respectively. Constraints $\frac{dS}{dt}$, $\frac{dE}{dt}$ and $\frac{dV}{dt}$ are non-linear and must be locally linearized.
I call $f(S,E,I,R,V) = \frac{dS}{dt}$ and linearize in a point (S_0,E_0,I_0,R_0,V_0) using equation 4.2 as follows:

$$L_f = f(S_0,E_0,I_0,R_0,V_0) + a(S-S_0) + b(E-E_0) + c(I-I_0) + d(R-R_0) + e(V-V_0)$$

Where a, b, c, d and e denote the partial derivatives of f in the point (S_0,E_0,I_0,R_0,V_0):

$$\frac{\partial f}{\partial S} = -\beta I_0 - \alpha$$
$$\frac{\partial f}{\partial E} = \frac{\partial f}{\partial R} = \frac{\partial f}{\partial V} = 0$$
$$\frac{\partial f}{\partial I} = -\beta S_0$$

Using this and setting $f(S_0,E_0,I_0,R_0,V_0) = K$, I get:

$$L_f = K - (\beta I_0 + \alpha)(S-S_0) - \beta S_0(I-I_0)$$

The linearization of $g(S,E,I,R,V) = \frac{dE}{dt}$ and $h(S,E,I,R,V) = \frac{dV}{dt}$ is done in the same way. $\frac{dI}{dt}$ and $\frac{dR}{dt}$ are already linear and no further action is necessary. Replacing the non-linear constraints with the now locally linearized equations L_f, L_g and L_h I get the following set of constraints:

$$\begin{aligned} K - (\beta I_0 + \alpha)(S-S_0) - \beta S_0(I-I_0) &\leq 0 \\ L + \beta I_0(S-S_0) - \sigma(E-E_0) + \mu V_0(I-I_0) + \mu(V-V_0) &\geq 0 \\ \sigma E - \gamma I &\geq 0 \\ \gamma I &\geq 0 \\ P + \alpha(S-S_0) - \mu V_0(I-I_0) - \mu I_0(V-V_0) &\geq 0 \end{aligned} \tag{4.4}$$

$$0 \leq S,E,I,R,V \leq 1$$

Where K, L and P denote the value of $f(S_0,E_0,I_0,R_0,V_0)$, $g(S_0,E_0,I_0,R_0,V_0)$ and $h(S_0,E_0,I_0,R_0,V_0)$, respectively.

Choosing point of linearization

A local linearization will only be applicable in an interval surrounding the point of which one in linearizing. I choose to use one of the simulations done on the SEIR-model developed earlier as a starting point (see 3.2). From the simulation it can be seen that I_{max} occurs near day 100. As the purpose of this optimization is to limit the number of infected and vaccinated individuals, some time prior to this point is a candidate.
I will therefore use the data generated by the SEIR-model to extract the point around which I will apply problem 4.4. This point is:

$$Day\ 25 : (S_0,E_0,I_0,R_0,V_0) = (0.75,\ 0.11,\ 0.058,\ 0.076,\ 0.038)$$

When linear approximation doesn't work

Combining 4.4 with the objective function:

$$minimize \quad cost_i I + cost_v V$$

in a Python program provides no solution. This means there is no point where the distributed amount of susceptible, exposed, infected, recovered and vaccinated individuals satisfy all constraints. As mentioned above, a solution must contain values of the decision variables that satisfy each constraint simultaneously. It seems I am unable to identify such a point and therefore not find an optimal solution to problem 4.4.

4.2.2 Nonlinear Programming and Optimization

There are also ways to program and optimize *non*-linear systems. One of the packages in Python that can aid with this is the scipy.optimize-package [1].
Scipy.optimize contains several methods for solving nonlinear problems, both unconstrained and constrained. The method that will be used in this chapter is the 'Sequential Least Squares Programming'-, or the 'SLSQP'-method [2].

Now I make the decision to simplify the problem and use a slightly altered variation of the model in eq. 2.5. I consider a population divided into groups of susceptible, infected and recovered individuals and assume a closed population (I exclude any parameter of birth- and death rate). I will also include parameters of rate of vaccination and vaccine efficacy, v and ε respectively. Assuming only susceptible individuals get vaccinated, the amount of vaccinated individuals is denoted by vS.
Now I use the 'SLSQP'-method and write a Python-program that allows me to use SIR-equations as well as boundaries for the decision variables to identify the vaccination rate that will generate a minimal total cost of the pandemic given values for both the cost of infection and of vaccination: cost_i and cost_v.
I'm currently working with the following SIR-equations:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI(v(1-\varepsilon)+(1-v)) - v\varepsilon S \\ \frac{dI}{dt} &= \beta SI(v(1-\varepsilon)+(1-v)) - \gamma I \\ \frac{dR}{dt} &= \gamma I + v\varepsilon S \end{aligned} \tag{4.5}$$

As the minimization-problem takes place at the beginning of the pandemic I assume that the number of susceptible individuals will decrease and the number of infected and recovered will increase. The goal is to find the optimal situation despite this. As I consider a normalized population the decision variables, S, I, and R must all be between 0 and 1. Hence, the current objective function and constraints are:

[1] See overview at: https://docs.scipy.org/doc/scipy/reference/optimize.html
[2] See overview at: https://docs.scipy.org/doc/scipy/reference/optimize.minimize-slsqp.html

$$
\begin{aligned}
&\textit{minimize} \quad cost_i I + cost_v vS \quad s.t. \\
&\begin{array}{rcl}
-\beta SI(v(1-\varepsilon)+(1-v)) - v\varepsilon S & \leq & 0 \\
\beta SI(v(1-\varepsilon)+(1-v)) - \gamma I & \geq & 0 \\
\gamma I + v\varepsilon S & \geq & 0
\end{array} \\
&0 \leq S, I, R \leq 1
\end{aligned}
\tag{4.6}
$$

At this point the constraints only consider how infection spreads in a population. No limitations to how many could potentially be vaccinated are implemented yet.

Running the program provides no solution. Output message reads:
`Positive directional derivative for linesearch .`

Error: Positive directional derivative for linesearch

Algorithms for optimization and nonlinear programming are iterative. This means that an initial guess at a solution will be a starting point and then a sequence of improved suggestions for a solution are generated. Iterations will terminate when an optimal solution is reached [32].
One of the methods of moving from one iterate to the next is called *line search*. Simply put, this method chooses a direction and searches along it from the previous solution for a new solution with a lower - more optimal - function value [33]. To find such a direction, called p_k, a possible method is the *steepest descent method*, in which the line search moves along $-\nabla f_k$ of the function one seeks to minimize [33]. Intuitively enough, the ideal direction would be the one where the function value decreases the most.
The step direction can also be determined in other ways, as long as the direction is one where the function value decreases and it makes an angle of less than $\frac{\pi}{2}$ radians with $-\nabla f_k$. This will guarantee a more optimal solution for a function f provided that the step size is small enough [33].

As I attempt to interpret the error-message provided by the Python program it seems that the program seeks to find a step direction along $-\nabla f_k$. However positive derivatives prevents this. As a result the program does not know in which direction to go next and the iteration terminates without necessarily having found an optimal solution.
Different algorithms use different ways of determining the value of the next iterate. A lot of complicated calculations are behind this, but I will not go into further detail regarding this.
I will now try and take a step back from the SIR-equations and consider a different way of formulating constraints.

New formulation of constraints

In order to prevent the program from simply setting any decision variables to zero in order to minimize resulting cost I let the point identified in section 4.2.1 provide some

limiting values in addition to how the normalized population means that the minimum or maximum value of any decision variable can be 0 or 1, respectively. I still assume that the number of susceptible individuals will decrease and that the number of exposed, infected and recovered individuals will increase. Constrained by this, in addition to my own equations describing the number of infected and recovered, I will hopefully find an optimal solution to my objective function.
My constraints this far are:

- S + E + I + R = 1
- S < S0, E > E0, I > I0, R > R0
- $0 \leq$ S,E,I,R ≤ 1

I then define the number of infected individuals as the portion of susceptible individuals who are vaccinated but still get infected plus the remaining, unvaccinated portion of the susceptible population who get infected:

- I = $(\sigma \cdot v \cdot$ S) + $(\beta \cdot (1 - v) \cdot$ S)

Then I define the number of recovered individuals as the portion of infected individuals that have recovered plus the portion of vaccinated individuals that don't get infected:

- R = $(\gamma \cdot$ I) + $(v \cdot (1 - \sigma) \cdot S)$

Where in this case σ, v, β, and γ are the probability of getting infected despite vaccination, vaccination rate, transmission rate and recovery rate, respectively.

Failure

Investigating the self-generated constraints closer leads to the realization that they do not work. The optimization problem requires knowledge of the total number of infected and susceptible individuals in the time period being studied. As the constraints above apply to a certain point in time, the current state of the problem would not apply to the whole picture.

4.2.3 Using a SEIR-model to Generate Values

Returning to the initial problem, the goal is still to minimize the total cost of infected and vaccinated individuals, now formulated as:

$$minimize \quad cost_i \cdot I + cost_v \cdot Sv.$$

This while taking how the pandemic evolves into consideration.

What has been missing so far is a way of determining the total number of infected and vaccinated individuals in the entire given time period, as the SEIR-equations only describe the change in each compartment at a given *point* in time.
One idea for solving this is to use the SEIR-model and integration.
By integrating over the graphs generated by the program developed to run simulations of the model, an estimate of the total amount of individuals in the various compartments can be obtained. The area under the graphs are easily found with the help of a python command called `scipy.integrate.simps` which utilizes the composite Simpson's rule to determine the integral [3]. Now that an estimate of a total I and vS can be obtained from the SEIR-model, the model and the optimization problem can be merged in a way that hopefully will let the problem finally be solved.
Certain parameters cannot be changed, like the recovery rate and incubation period as they are specific characteristics of the disease. However the vaccination rate and to a certain degree the transmission rate can potentially be changed to fit what would be the optimal way to move forward.

Vaccination rate as a decision variable

Using parameter values from table 3.3 and only focusing on finding the optimal value for the vaccination rate, v, I write a Python program that only has one decision variable; the vaccination rate. The SEIR-model is introduced, using already determined values for most parameters as well as the decision variable, v, as arguments. The program solves the differential equations and returns the indication of the total number of infected and vaccinated as the area below the graphs.
As fixed values for $cost_i$ and $cost_v$ are extremely hard to determine, I will seek to establish a relationship between the optimal vaccination rate and rather the relationship between $cost_i$ and $cost_v$. I will establish vectors that indicate the cost of infection relative to the cost of vaccination and then run the optimization code for every cost-relationship in these vectors. For each of these cost-relationships the optimization problem returns the total cost of the pandemic as well as the optimal value of v.

Raw data provided by FHI and Pandemisenteret includes an overview of weekly vaccination statistics from late 2020 to early 2022. During this time period the second week of 2022 was the week when most people got vaccinated. This week 384 708 individuals got their first dose. This gives an average of approximately 54 958 vaccinations daily during this week. With a population of 5.43 million people, this corresponds to a daily vaccination rate of 0.010121% of the population, which will be used as an upper bound for v in the program.

4.2.4 Failure Again

While using the SEIR-model to generate values describing the total number of infected and susceptible individuals is definitely part of the solution, I am starting to doubt whether the Python package scipy.optimize will in fact be able to help me determine a

[3] See overview at: https://docs.scipy.org/doc/scipy-0.14.0/reference/generated/scipy.integrate.simps.html

true solution.
During the process of solving the "minimize the cost of Covid"-problem, scipy.optimize has been used together with the iterative "SLSQP"-method. Seemingly the program I have created is unable to find an unambigous solution. When running the code for different cost-relationships, scipy.optimize alternates between solutions, presumably due to the iterative nature of the method. With each small-scale increase in $cost_i$ relative to $cost_v$ the method pivots in a completely different direction instead of giving a clear picture of the relationship between total cost and an optimal vaccination rate.
The scipy.optimize package undoubtedly has a wide range of applications, provided that is is applied appropriately. However, the solutions provided in this case raises more questions than answers which quite possibly is because I have been unable to do so.
For the sake of time this package is now abandoned.
Still committed to finding a relationship between the cost of Covid and the vaccination rate I will try yet another time to accomplish this. This time by moving away from scipy.optimize and rather explore the development directly.

4.3 One Final Attempt

With scipy.optimize discarded for this purpose, I decided to take matters into my own hands. The goal has slightly changed, from seeking to find one optimal general vaccine rate to rather explore the *relationship* between various vaccine rates as the cost of infection increase relative to the cost of vaccination.
I decide to examine seven different cost-relationships:

- $cost_i$ is 10% of $cost_v$
- $cost_i$ is 50% of $cost_v$
- $cost_i$ is the same as $cost_v$
- $cost_i$ is 1.5 times as high as $cost_v$
- $cost_i$ is 15 times as high as $cost_v$
- $cost_i$ is 50 times as high as $cost_v$
- $cost_i$ is 100 times as high as $cost_v$

Keeping with a maximum possible daily vaccination rate of 0.010121, a Python-program will use the SEIR-model in eq.2.5 to determine the total cost generated by every possible vaccination rate from 0.0 to 0.010121 for each of the cost-relationships. For each cost-relationship the relationship between total cost and vaccination rate will be determined and illustrated.

Using the SEIR-model as a tool to determine the total amount of infected and vaccinated susceptible individuals combined with fundamental Python commands will allow for this to be done. Seemingly simple this looks to be the best way to finally solve the "minimize the cost of Covid"-problem. For directions to the code developed for this purpose, see Appendix A.

Including deaths in the model

Adding a compartment to the model that describes the part of the population that pass away from the disease turns the model into an SEIRD-model. Death also brings a large cost and will be examined in a new version of the program. Including a death-rate, δ, the rate of which individuals go from being infected to diseased can be described as:

$$\frac{dD}{dt} = \delta I(1 - v + v(1 - \varepsilon_2)),$$

where ε_2 denotes the vaccine efficacy when it comes to protecting from death.
The SEIRD-model used in this stage is the following:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI(v(1-\varepsilon) + (1-v)) - v\varepsilon S \\ \frac{dE}{dT} &= \beta SI(v(1-\varepsilon) + (1-v)) - \sigma E \\ \frac{dI}{dt} &= \sigma E - \gamma I - \delta I(1 - v + v(1-\varepsilon_2)) \\ \frac{dR}{dt} &= \gamma I + v\varepsilon S \\ \frac{dD}{dt} &= \delta I(1 - v + v(1-\varepsilon_2)) \end{aligned} \tag{4.7}$$

Where β, σ, γ, v, ε, δ, and ε_2 are transmission rate, incubation rate, recovery rate, vaccination rate, vaccine efficiency regarding getting infected, death rate, and vaccine efficacy regarding death, respectively.
One article found that a single dose of one Covid-19 vaccine was 85% effective at preventing death [34]. Hence $\varepsilon_2 = 0.85$ will be used.
Several factors will affect the death rate of Covid-19, e.g. age and underlying conditions [35]. A review from 2020 found that the mortality rate varys from 0.40% in those below 50 years, to 14.8% among those over 80 years old [36]. One study analysing more than 3600 cases in China found that the overall death rate was 0.66% which will be used here [37].

The same process described in 4.3 will be repeated with the SEIRD-model proposed in the previous section. In this case it is assumed that vaccination, infection and deaths are the causes of economic costs, and the function to be minimized is:

$$minimize \quad cost_v Sv + cost_i I + cost_d D$$

Here the following cost-relationships will be examined:

- $cost_d$ is 1.5 times as high as $cost_v$
- $cost_d$ is 10 times as high as $cost_v$
- $cost_d$ is 100 times as high as $cost_v$
- $cost_d$ is 1000 times as high as $cost_v$
- $cost_d$ is 10000 times as high as $cost_v$

Each of these relationships will be applied to the various costs of infection.

Parameters

The tables below contain parameters implemented when running the code on the SEIR-model and SEIRD-model.

Table 4.1: Parameter values used in SEIR optimization code.

Transmission rate	β	0.32
Recovery rate	γ	0.157 per day
Incubation rate	σ	0.25 per day
Vaccine efficacy	ε	0.52
Initial values	S0, E0+I0, R0	0.994, 9.065×10^{-4}, 5.569×10^{-3}

Table 4.2: Parameter values used in SEIRD optimization code.

Transmission rate	β	0.32
Recovery rate	γ	0.157 per day
Incubation rate	σ	0.25 per day
Vaccine efficacy (infection)	ε	0.52
Vaccine efficacy (Death)	ε_2	0.85
Death rate	δ	0.0066
Initial values	S0, E0+I0, R0, D0	0.994, 9.065×10^{-4}, 5.569×10^{-3}, 0

4.3.1 Results; SEIR

The relationship between the total cost and the daily vaccination rate obtained from the SEIR-model for various cost relationships are presented in the following figures. Some commentary on each of the figures is also presented. The vertical axis indicates a total cost, but will not have numerical values. This is because I explore how the total cost *develops* as the vaccination rate increases, not what the total cost is. I do not have accurate descriptions of the actual cost of infection and vaccination, I only provide an illustration of how the total cost change as the relationship between these evolve.

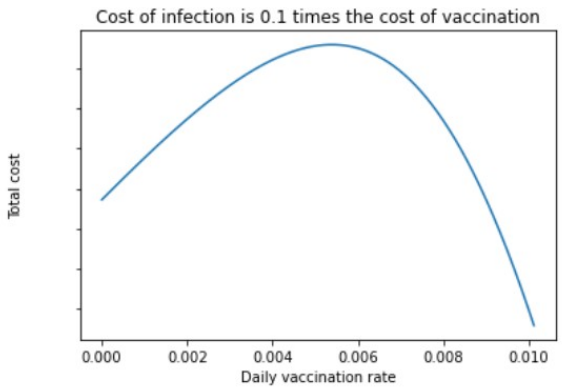


Figure 4.1: Cost of infection is 10% of cost of vaccination

In figure 4.1 I see that with low vaccination rates, vaccination doesn't seem to contribute to anything but increasing the total cost. As vaccination rates increase so does the total cost until the daily rate reaches ≈ 0.00539. When this vaccination rate is surpassed a relatively steep drop in total cost can be seen.
The total cost is a result of the vaccination rate as well as the total number of infected and vaccinated susceptible individuals and high vaccination rates would make both of these groups as small as possible as quick as possible. Low vaccination rates does not seem to drastically affect this.

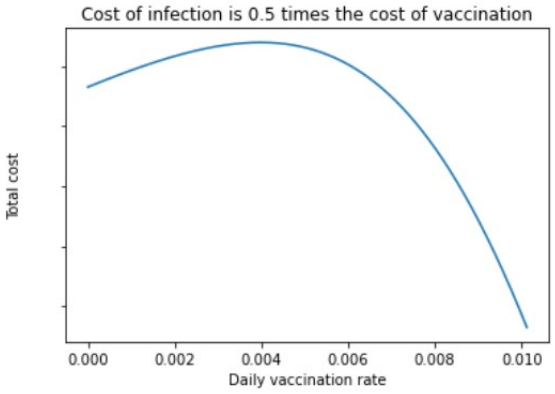


Figure 4.2: Cost of infection is 50% of cost of vaccination

The similar pattern as in figure 4.1 can be seen in figure 4.2 although the "turning point" follows a lower vaccination rate, in this case when the vaccination rate reaches ≈ 0.00398. As infection is more expensive than in the previous scenario in figure 4.1 it makes sense that the relief from infection the vaccines provide comes into play at lower vaccination rates.

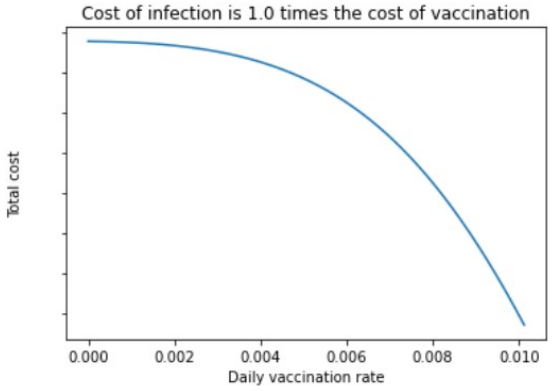


Figure 4.3: Cost of infection is the same as cost of vaccination

In figure 4.3 infection and vaccination cost the same. While the graph might look slightly similar to those in figure 4.1 and 4.2, the maximum total cost occurs when vaccination rate is $= 0$ after which it decreases as the vaccination rate gets higher.

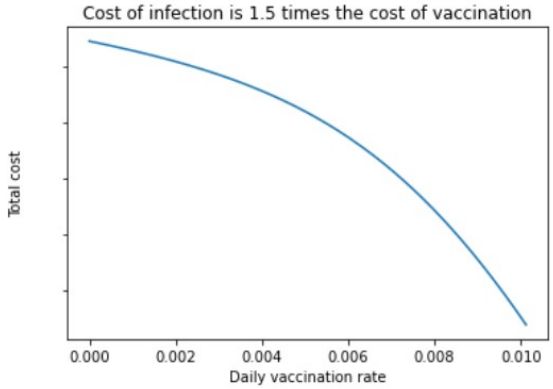


Figure 4.4: Cost of infection is 1.5 times as high cost of vaccination

I see in figure 4.4 that as infection gets more expensive than vaccination, the trend of lower costs when vaccination rates get higher is clear from the beginning. As infection here costs more than vaccination, high vaccination rates will be optimal as it aids in reducing the number of infected individuals.

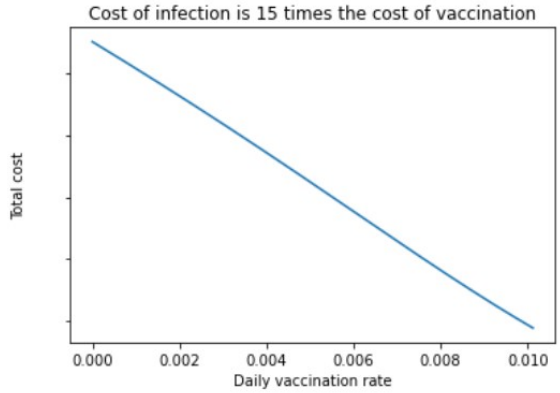


Figure 4.5: Cost of infection is 15 times as high as cost of vaccination

The same trend as in figure 4.4 is even more striking in figure 4.5. It becomes clear that when the cost of infection is much higher than the cost of vaccination, there occurs a linear relationship between decreasing costs and increasing vaccine rates.

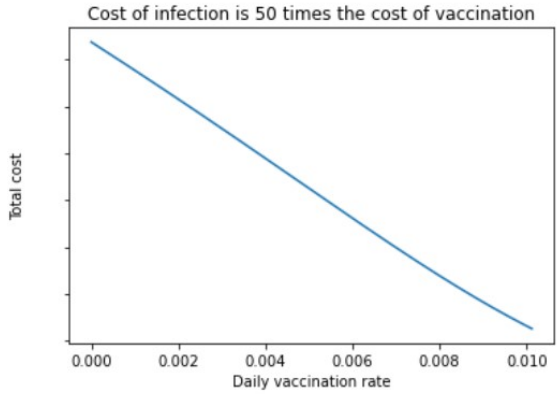


Figure 4.6: Cost of infection is 50 times as high as cost of vaccination

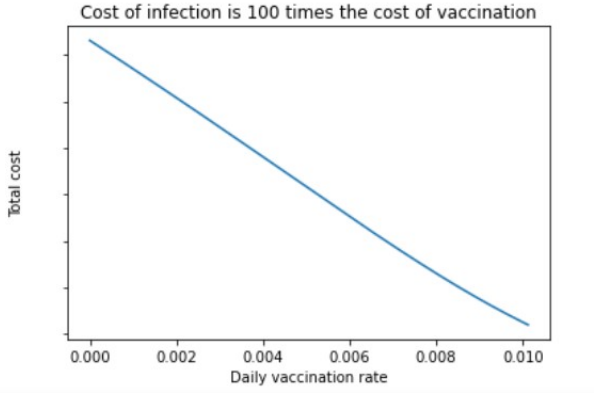


Figure 4.7: Cost of infection is 100 times as high as cost of vaccination

I see similar trends in figures 4.5-4.7. I assume that a similar relationship will be seen as infection keeps getting more expensive compared to vaccination.

Even though I have set the maximum value of v to be 0.010121, I am curious to what happens if I allow for a higher vaccination rate. In test-simulations with the same cost-relationships as in figures 4.1 and 4.6 but where I let the maximum vaccination rate go as unrealistically high as $v = 0.1$, meaning that 10% of the population would get vaccinated daily, I get the following results:

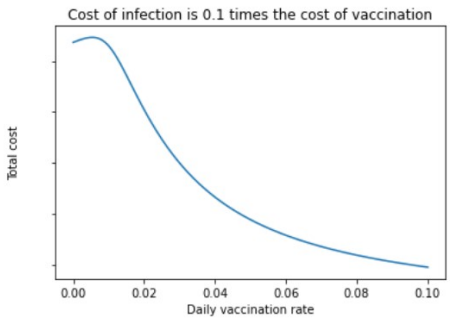


Figure 4.8: Cost of infection is 10% of cost of vaccination.
Maximum total cost at $v = 0.00539$, minimum total cost at $v = 0.1$

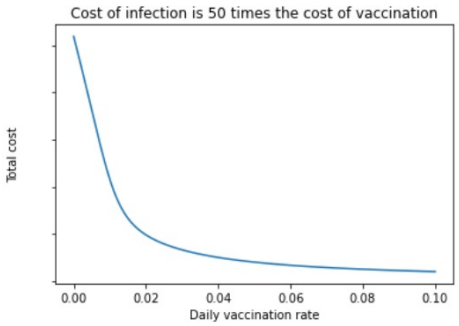


Figure 4.9: Cost of infection is 50 times as high as cost of vaccination.
Maximum total cost at $v = 0.0$, minimum total cost at $v = 0.1$

Simulations indicate that increasing the vaccination rate will keep contributing to lowering the total cost. Even though the drop in total cost evens out as v gets large, it does keep slowly reducing. We recognize the slight increase in total cost as v goes from 0.0 to 0.00539 followed by a drastic drop in total cost as seen in figure 4.1. The decrease in total cost as seen in figure 4.6 appeared linear, but when allowing v to get much higher we see that the reduction in cost in only steep as v goes toward ≈ 0.02, after which the decrease is much slighter.

4.3.2 Results; SEIRD

A selection of figures illustrating the relationship between the total cost and the daily vaccination rate obtained from the SEIRD-model for various cost relationships are presented below.

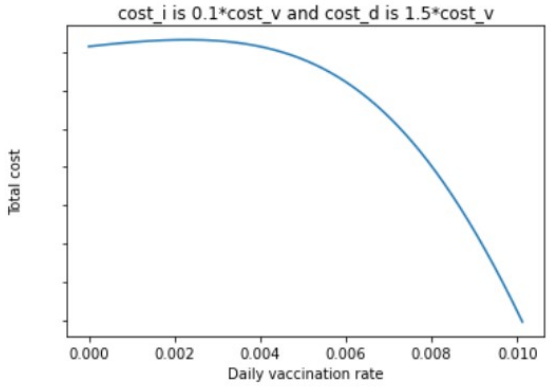


Figure 4.10: Cost of infection is 10% times as high as cost of vaccination, cost of death is 1.5 times as high as cost of vaccination.

I see in figure 4.10 that when infection is only 10% as costly as vaccination, if deaths are 1.5 times more costly than vaccination, there initially is an increase in the total cost as vaccination rates increase. The maximum total cost is generated when the vaccination rate is at ≈ 0.00229. When v gets higher than this the total cost decrease.

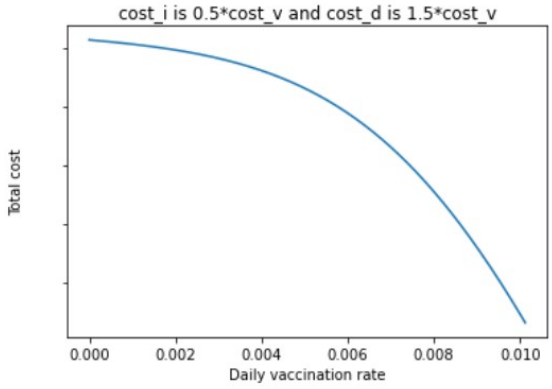


Figure 4.11: Cost of infection is 50% of the cost of vaccination, cost of death is 1.5 times as high as cost of vaccination.

For the SEIR-model, when cost of infection was only 50% of the cost of vaccination (see figure 4.2), an initial increase in total cost could be seen as v went towards ≈ 0.00398. When including the death-compartment as in figure 4.11 there is no initial increase even though cost of infection is still 50% of cost of vaccination. Vaccinations immediately contribute to lowering the total cost, indicating that the cost of death outweigh the cost of infection.

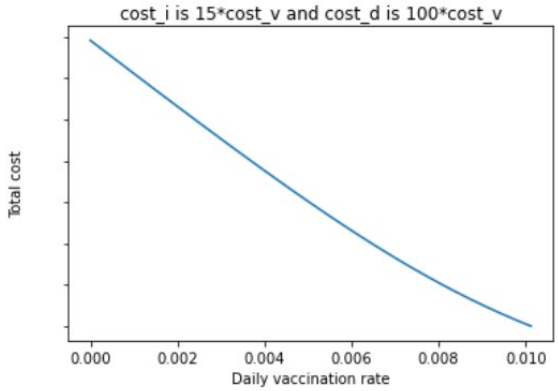


Figure 4.12: Cost of infection is 15 times as high as the cost of vaccination, cost of death is 100 times as high as cost of vaccination.

Although not strictly linear, when the cost of infection 15 times as high as the cost of vaccination and the cost of death is 100 times higher, as seen in figure 4.12, the largest total cost is when there is no vaccination. The total cost decreases as v increases.

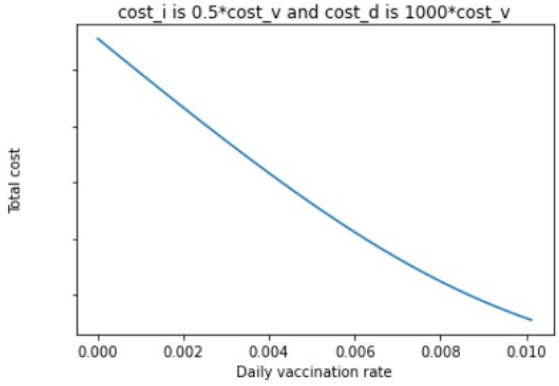


Figure 4.13: Cost of infection is 50% of the cost of vaccination, cost of death is 1000 times as high as cost of vaccination.

I see a similar trend in figure 4.13 as in figure 4.12. The total cost decreases as the vaccination rate increases. Both when the cost of infection is smaller and greater than the cost of vaccination, when cost of death is higher as large a vaccination rate as possible seems to be optimal.

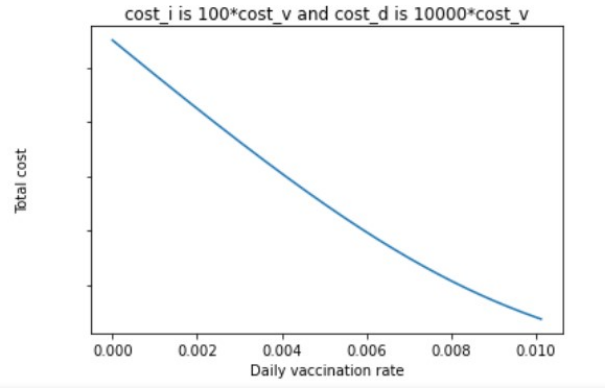


Figure 4.14: Cost of infection is 100 times as high as cost of vaccination, cost of death is 10 000 times as high as cost of vaccination.

In figure 4.14 when cost of infection is 100 times as large as the cost of vaccination and the cost of death is 10 000 times as high at the cost of vaccination the total costs decrease as v increase. The graph turns slightly convex as the effect of vaccinations is especially prominent initially. When the cost of death gets noticeable higher than the cost of vaccination it almost looks like the total cost nears a minimum.

Again I am curious to what happens if I allow for higher a vaccination rate. In a new test-simulation where I again let the maximum vaccination rate go as unrealistically high as $v = 0.1$, while keeping the same cost relationships as in fig. 4.10 and 4.14, I get the following results:

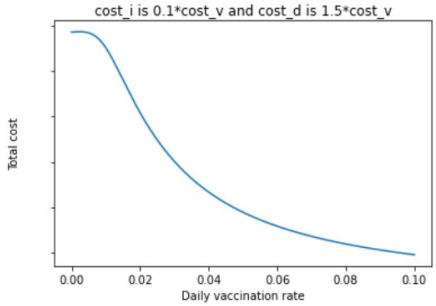


Figure 4.15: Cost of infection is 10% of cost of vaccination, cost of death is 1.5 times as high as cost of vaccination.
Maximum total cost at $v = 0.00229$, minimum total cost at $v = 0.1$.

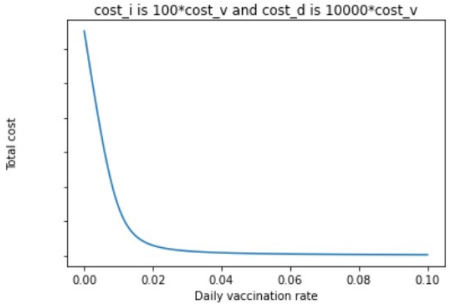


Figure 4.16: Cost of infection is 100 times as high as cost of vaccination, cost of death is 10 000 times as high as cost of vaccination.
Maximum total cost at , minimum total cost at $v = 0.1$.

The same trends is seen as when doing the similar simulations for the SEIR-model. Again we recognize the slight increase in total cost as v goes to 0.00229 as in figure 4.10, as well as the initial steep drop in total cost as seen in figure 4.14, after which the reduction in cost slows down. However it still seems like the total cost still continues to get slightly smaller as the vaccination rate gets higher.

4.4 Discussion

SEIR: Optimal vaccination rates

It can be clearly seen that in a scenario that the current SEIR-model of this thesis describes higher vaccination rates will lead to lower costs. When cost of infection is high compared to cost of vaccination one should aim to maintain as high vaccination rates as possible in order to optimize economic cost.
However, should the case be that the cost of infection is in fact *lower* than the cost of vaccination one must examine how high vaccination rates one can maintain. If one is able to vaccinate at as high rates as this model has taken into account one should do that. If not, cost will only continue to increase as the vaccination rates increases to a certain point. This is relevant in two of the scenarios explored above:

- If cost of infection is 10% of the cost of vaccination the total cost will increase until the vaccination rate reaches ≈ 0.00539. If one will not be able to exceed this, it will be economically beneficial to not distribute vaccinations at all (see figure 4.1).

- If cost of infection is 50% of the cost of vaccination the total cost will increase until the vaccination rate reaches ≈ 0.00398. If one will not be able to exceed this, it will be economically beneficial to not distribute vaccinations at all (see figure 4.2).

SEIRD: Optimal vaccination rates

It is apparent that when including deaths in the model vaccines prove even more beneficial as they clearly aid in reducing the cost of the pandemic. This trend of decreasing costs as v increases is obvious in every scenario examined except for when the cost of infection is 10% of the cost of vaccination and cost of death is 1.5 times as high as the cost of vaccination. In this case total cost keeps increasing until the vaccination rate reaches ≈ 0.00229 after which the total cost drops significantly (see figure 4.10).
In a scenario where it is impossible to exceed a daily vaccination rate of 0.00229 it would be economically beneficial to not distribute vaccinations at all, although preferably the vaccination rate should be as close to 0.010121 as possible to minimize the total cost.
As I deem is unlikely that the cost of infection will ever be as small as 10% of the cost of vaccinations, this scenario is rather improbable. It is more likely that one of the other scenarios explored are closer to reality, in which case a daily vaccination rate of 0.010121 will generate the lowest total cost.

My solution to "The minimizing the cost of Covid"-problem is that for various relationships between costs of infection, vaccination and death, most often the cost of Covid will be minimal when the daily vaccination rate is as high as possible.

4.4.1 Changing β

For the simulations run in this section, $\beta = 0.32$ has been used, among other parameters, as it is the β estimated in India by Wintachai [28]. The same paper estimated $\beta = 0.462$ in USA.
When experimenting with running simulations on both the SEIR-model and SEIRD-model with this transmission rate and the cost relationships listed below, there are some interesting results.

- $cost_i$ is 10% of $cost_v$
- $cost_i$ is 20% of $cost_v$
- $cost_i$ is 30% of $cost_v$
- $cost_i$ is 40% of $cost_v$
- $cost_i$ is 50% of $cost_v$
- $cost_i$ is 10% of $cost_v$, $cost_d$ is 1.5 times as high as $cost_v$

The resulting graphs and the corresponding vaccination rate for maximum total costs are presented below.

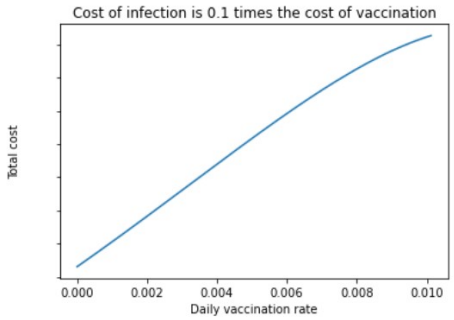


Figure 4.17: Cost of infection is 10% of cost of vaccination.
Maximum total cost at $v = 0.010121$.

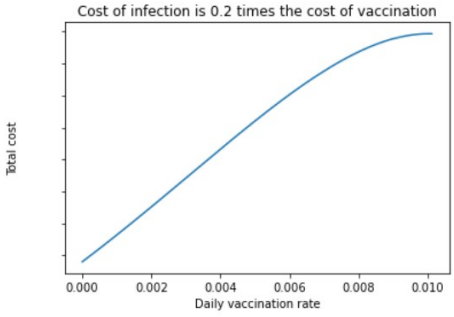


Figure 4.18: Cost of infection is 20% of cost of vaccination.
Maximum total cost at $v = 0.010034$.

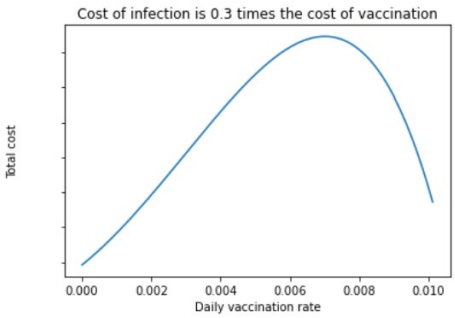


Figure 4.19: Cost of infection is 30% of cost of vaccination.
Maximum total cost at $v = 0.007005$.

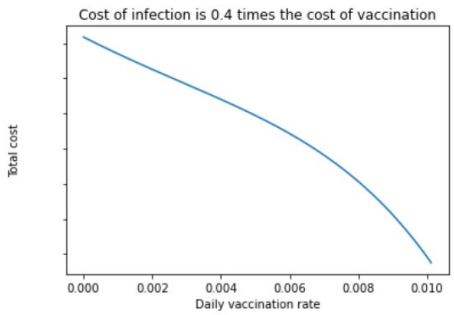


Figure 4.20: Cost of infection is 40% of cost of vaccination.
Maximum total cost at $v = 0.0$.

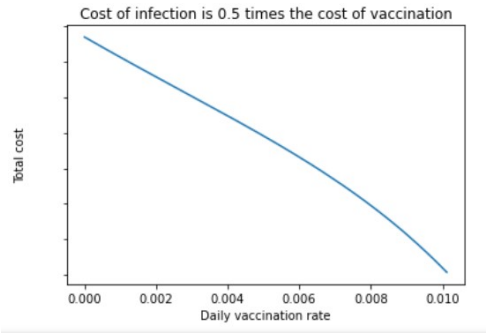


Figure 4.21: Cost of infection is 50% of cost of vaccination.
Maximum total cost at $v = 0.0$.

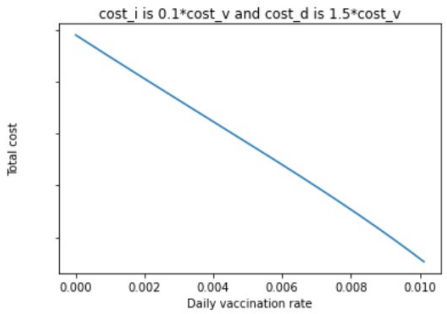


Figure 4.22: Cost of infection is 10% of cost of vaccination. Cost of death is 1.5 times as high as cost of vaccination. Maximum total cost at $v = 0.0$.

Discussion

In figure 4.22 a similar trend to the other simulations from the SEIRD-model can be seen. When including the cost of death vaccination will still be beneficial as the total cost appears to be decreasing nearly linearly as the daily vaccination rate increases.

When running simulations with the SEIR-model, one initially sees the opposite. When cost of infection is one tenth of the cost of vaccination, see figure 4.17, the total cost is actually increasing when v increases, and is at its highest when vaccination is at its maximum, $v = 0.010121$.
As cost of infection slightly increase relative to the cost of vaccination, the vaccination rate causing the maximum cost starts moving to the left. It can be seen that the maximum total cost increases as v gets higher, but decreases when surpassing the peak. However, when cost of infection reaches 40% of the cost of vaccination the relationship has reversed and the maximum total cost is yet again at $v = 0.0$, as can be seen in figure 4.20. There seems to be a specific relationship between cost of infection being 30% and it being 40% of the cost of vaccination where vaccines go from initially raising costs to only lowering costs.

If $\beta = 0.462$, should the factual cost relationship be that the cost of infection is closer to 30% of the cost of vaccination, or less, the most inexpensive alternative is to keep the vaccination rate at zero. On the other hand, should the situation be that the cost of infection is closer to 40% of the cost of vaccination or more, vaccinating as many individuals as possible will contribute to lowering costs.

Chapter 5

Presenting Mathematical Models

By: Maria M. Jacobsen & Eirik V. Stokke

5.1 Explaining Mathematical Models to Non-mathematicians

To model a real life problem, one often have to make some difficult decisions about what to include and exclude in the model. As a result the mathematical model will only be uniquely determined by the situation in the most simple cases [38].
The main task of a mathematical model, if not the only task, is to describe or represent a real situation. Sometimes models are even used in an attempt to predict the future. It's important to note that a mathematical model is based on a hypothetical situation and will therefore never be an exact reflection of what it tries to represent. One of the challenges with mathematical models is to figure out to which degree they match reality [39]. Even though there is uncertainty around models, a famous quote by George E. P. Box: *All model are wrong, but some are useful*, should be taken into account. Many models are close enough to reality that they can provide valuable information. Therefore many decisions are based on the information given from models. One example is when airline companies use an "overbooking model" to figure out how they can most likely in the long run profit from overbooking their planes [39]. The conclusion of the example is one of the core properties of a mathematical model: that we can gain valuable insight into different hypothetical situations, but also that "most likely" and "guaranteed" are not the same thing [39]. During the Covid-19 pandemic FHI have used mathematical models to look at other hypothetical situations.

For anyone other than an expert modeller, the transition between the real world and mathematical models can be difficult to grasp [40]. Mathematical modelling involves several challenging processes, like deciding how to mathematise real-world problems, decide which aspects of the real world are relevant or not, and also using techniques to test the model against reality [40]. Studies have shown that the context is relevant to how well young students understand the link between reality and models. This understanding could also impact student's experiences with models in university [40].
In a commentary form 1989, John Durant, Geoffrey Evans and Geoffrey Thomas explore the public interest in and knowledge of science [41]. Through surveys in both the US and the UK they discovered that the public reports high levels of interest for scien-

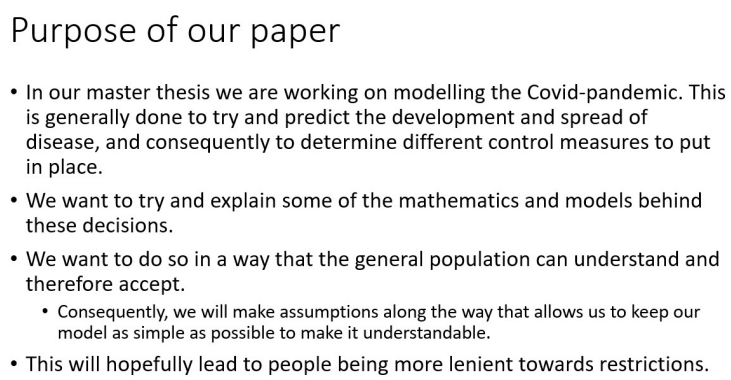
tific topic, but that the scientific knowledge was not necessarily corresponding. They identified relationships between education, gender, age, etc. and knowledge of science, as well as a strong association between interest and understanding [41].

5.2 Preparing for the Presentation

During the work on this thesis an opportunity arose to present our model and findings to an interdisciplinary audience from both social and natural sciences at Pandemisenteret [1]. In this context there would be master students, PhD students, professors and other academic staff from various specialties. We were invited to hold a presentation about what we have been working on with this thesis. As one aspect of this thesis is to be able to present the SEIR-model and its implications to the public in an understandable way, this was a great opportunity to test just that.
As chapter 2, 3 and 5 are joint work as mentioned, we cooperated on presenting these, after which we presented our separate projects. My separate work is done on optimizing.
Remembering how difficult mathematical modelling is to non-mathematicians and the public's difficulties with scientific understanding, we had to prepare a well thought-out explanation and some accompanying presentation slides that summarizes what we wanted to convey.

5.2.1 Presentation Slides and Reflections Done Prior to Presentation

Here we present the slides that would be part of the presentation and corresponding reflections done and plans made during our preparations prior to the presentation.



When getting new and difficult stuff presented it can occasionally be hard to find motivation to be invested in learning. Knowing why one has to learn the material might help with this. As the pandemic and its consequent restrictions are something that affects almost everyone, it will hopefully be easy to understand why it can be useful to gain some knowledge into this.

[1] Pandemisenteret Webpage: https://www.uib.no/en/pandemic

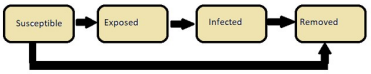
Therefore the presentation will start with a transparent statement about how we want to promote understanding of the reasoning behind the restrictions in order to provide some motivation for following them.

Mathematical models

- "All models are wrong, but some are useful." (George E.P. Box)
- A model is just that; a model. It is an attempt to illustrate and/or predict a phenomenon.
- It is not an exact representation of reality. Still, it can be very helpful.
  - A model can never take every factor into account, it can still give somewhat of a picture of a situation and its development. This makes it our best shot at making the best possible decisions.
- In our work we have tried to model a very specific scenario; the spread of the COVID-19-virus with vaccines as the only control measure.
- SEIR-model

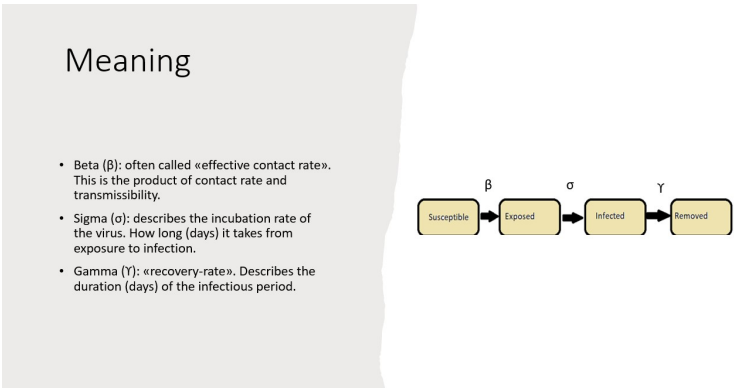
At first it is important that we introduce the concept of a model and challenges regarding accuracy. When large sets of data are available a model can get potentially more accurate, but during the pandemic every day have brought new discoveries. Models have been made, but only based on what little knowledge was available. With no way of knowing how infectious the virus was, how it spread, etc., a lot of assumptions had to be made and one had to rely on the models we had developed for other epidemics. We must explain this.

SEIR-model

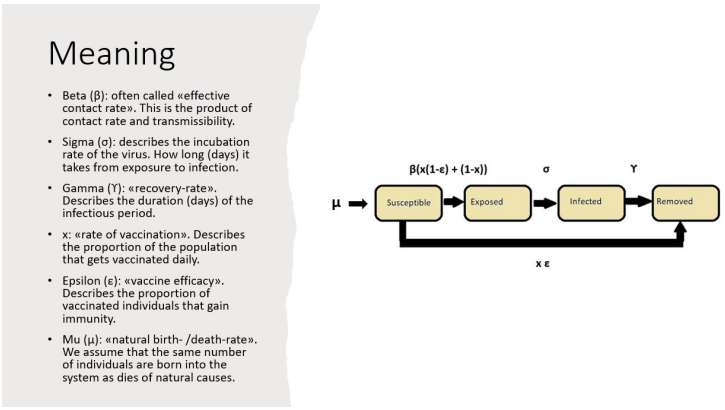


- We divide the population into four groups: susceptible, exposed, infectious and recovered/removed (immune).
  - Susceptible: Healthy individuals that might get infected.
  - Exposed: Individuals that have been exposed to the virus but are not yet infected/infectious.
  - Infected: individuals that are infected and might infect others.
  - Removed: Individuals that have been through infection and have gained immunity through recovery. Vaccines can also provide immunity and allow susceptible individuals to move directly to the "removed-box."
- Mathematical equations describe at which rates people move from one box to the next.
- The model illustrates how large proportion of the population belong to the different boxes at any given time.

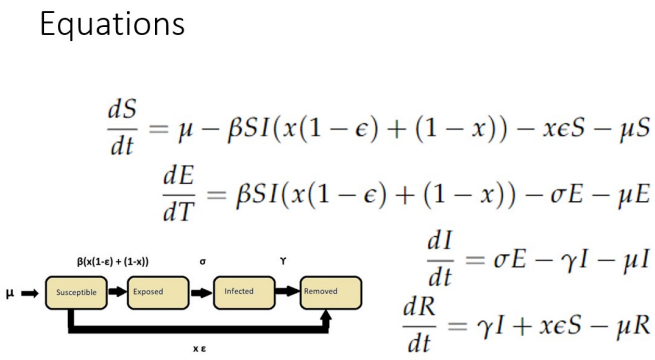
Then the SEIR-model will be introduced. It will be important to use visual components like the box-diagram, as it can help illustrate how the model works. The audience will with high probability have personal experiences with the virus which will be helpful, as context is important for understanding models. An extremely large proportion of the worlds population is now familiar with how the virus spreads. This will set a clear context for the models relevance and hence the audiences understanding. As the pandemic has greatly affected the everyday life of the population, one can also assume that interest will be high.



To make it easier for the audience and avoid too much new information at once, we will present the most general parameters first (β, σ, γ). We will first describe what each parameter means and what they represent. The flowchart will be presented to make it easier to follow where the parameters come into play in the model.

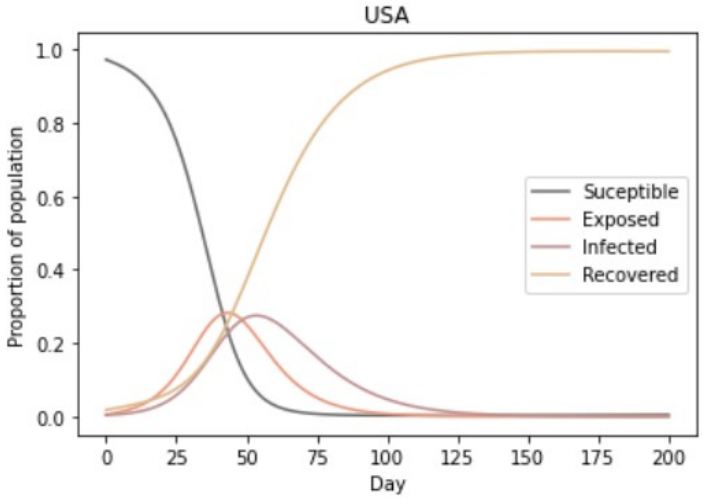


Then we add the remaining three parameters (x, ε, and μ) so the complete flow between the boxes can be visualized before the equations are presented. We will first explain the vaccination-term, as it will make the resulting expansion of the beta-term more understandable. We will avoid the term "normalized" as it is not necessarily a word everyone know the meaning of. Instead we will say that we look at a "proportion" of the population.

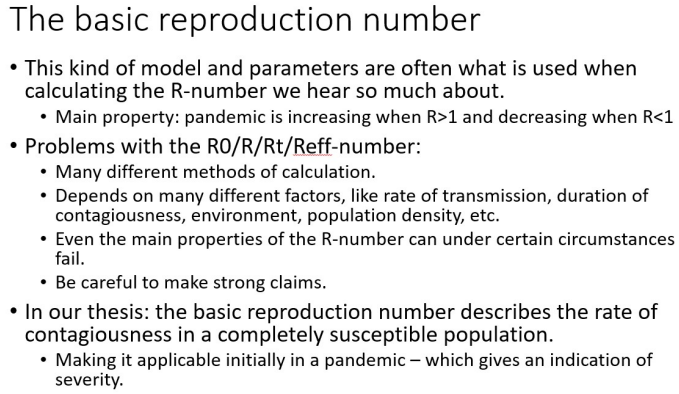


The slide with the four equations might initially seem intimidating, but we will try to explain one equation at a time and show how a term that is subtracted from one

equation is added to the next. Then we must explain that these terms denote individuals that "change groups." We will also use the flowchart from the previous slide to show where each term comes from. By teaching the audience the thought-process behind the system of equations, they will hopefully have a stronger foundation for understanding more complex models. A possibility to make this easier to follow could be to show the equations in a standard SEIR-model first and then show where the extra parameters come in.



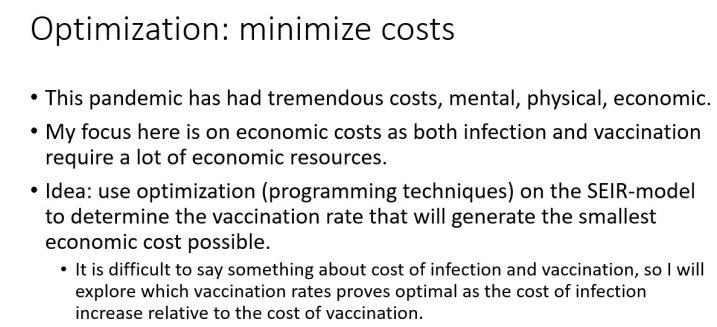
Here we will show the audience an example of a simulation that uses the model combined with parameters from USA. We will start with explaining the x-axis and y-axis, since a graph without axis does not make sense, and again mention that 1 means the whole population. With this simulation the audience will be able see that as the susceptible portion of the population decreases, the recovered portion increases, and that the infected-curve follows the exposed-curve with a little delay.



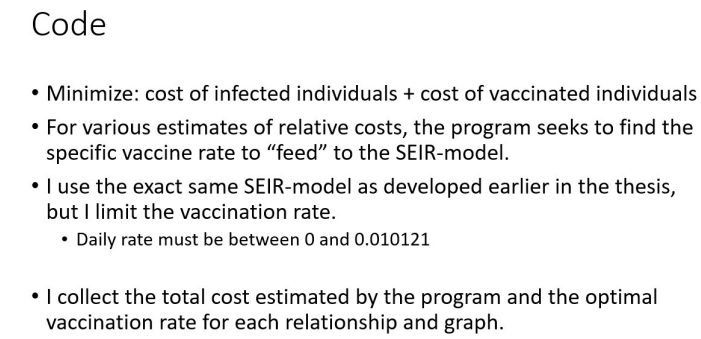
The reproduction number might be the hardest thing to explain in a simple way, if one goes further than the easiest property. We decide it will be sufficient to explain *why* it is such a difficult topic and complicated entity. Then we will explain how it has been used for this specific thesis, which is always important when talking about the R-number. The R-number can be calculated in many different ways and contain a

lot of different factors. It will be important to explain this fact to the audience, but we will not demonstrate the mathematics behind it as that is hard to comprehend for even experienced mathematicians.

5.2.2 My Specific Project



The concept of optimization and minimizing might be new to a lot of the people attending the presentation. I will avoid going into detail about the methods and processes I have gone through, but rather explain the idea behind the problem and purpose of what I have been doing.



I will not go into detail about the code itself as that will only contribute to confusion and disarray, but rather explain with words what it’s doing. It is not important that the audience knows how the program works. Instead I will talk more generally about my thought process when developing the final product.

5.3 Feedback After Presenting to Non-mathematicians

The following feedback was requested:

- We would like to know how understandable the presentation is as one of the main ideas behind our thesis is to be able to convey this information to people without a mathematical background.

- What is easy to understand?
- Are there any terms that should have been explained more in depth?
- Do we loose you? Where?

The responses, although not completely compatible with what was requested, can be summarized as follows:

What is worth doing? Do we just avoid the inevitable? Vaccines change the game.
The participant reflected on how at the start of a pandemic there is a discussion of what measures are worth implementing. This because if you flatten the initial curve the next wave will become bigger as a result. The vaccines change the game by making a part of the population immune or protected against serious illness given enough time. Then we move from discussing how much of the curve is worth flattening, to how we can give the vaccines enough time to work.

Will the unfairness be part of the modelling?
The context for the question was that the less fortunate part of the population lives in smaller homes and often with more people together. As a result the contact rate would generally be higher for this part of the population. However, in the simplified model in our thesis we have used the same β for the whole population. To take into account scenarios like economical situations we would need to split the model into several variants that looks at small areas at the time. We would also need a large amount of data to figure out the specific β in the each area. In an ideal situation this is something that the model should include as it matters for accuracy, but with our limited amount of time and resources, this has not been considered.

Making models understandable is good. Modelling is a tool to ***either*** *make people change behavior* ***or*** *as an explanation of reality. To my understanding you guys are aiming for the first one. There is a fine line between simplifying the model so that its understandable, and making it so simple that it loses all relevance because it is too far away from reality.*

The model does not consider the change in human behavior as a result of large infection numbers. With a higher risk of getting infected, many people will naturally avoid large crowds and stay more at home, and as a result the contact rate will go down. While this is true it would require greater access to data than what we've had.

How is your model suppose to help? Many of those who are sceptical to vaccines and control measures already do not listen to the experts, so why would they listen to you? Is the lack of trust the problem? It is indeed difficult for us to say if the problem is trust or something else entirely. From our math-teacher-perspective the hope is that an explanation of models and the process around epidemiological modelling will give some understanding that causes some changes in attitude towards the measures implemented. The goal is not to argue with conspiracy theorists, but rather provide some knowledge and insight for those who want to do what they can but are getting tired of following restrictions they do not understand the reasoning behind.

Other comments were largely concerned about details regarding vaccines and the consequences of simplifying the model as much as we have. A discussion on what could and should be included or not in an epidemiological model and how this would affect its relevance is something that serves as a great teaching tool and should be encouraged. This is simply a sign that the listeners are engaged in what is being presented and understands aspects of both the relevance and limitations of the model, which is the essence of what we seek to teach.

It generally seemed like the audience understood the mathematics and models that was presented. Rather than questioning what had been said, they even had questions and input regarding aspects of the thesis itself. Some of the feedback received have already been addressed in the section concerning limitations of the model, see 2.1.3.

5.3.1 What Should be Done Differently?

Given the feedback on the different aspects of reality that is not included in our model, it would possibly be beneficial to dedicate more time to reflect on the consequences of this. Perhaps after presenting our simple model and explaining thoroughly the mathematical modelling concepts behind it we can assume the audience understands the material well enough that it is safe to discuss how, potentially, one could expand the model further. As a lot of feedback addressed the sociocultural differences and social aspects of reality, it seems including reflections on this will help engage the listeners. Some specific examples of this might also be helpful as long as we take the time to explain all additional pieces of information.
Based on this one could argue that our model is perhaps too simple for an engaged audience. Still, we have to remember that the purpose of the model is to illustrate a simplified, very specific scenario for teaching-purposes, not necessarily to develop a replication of the reality at hand. We wish to provide some knowledge of what models are, how they work, and what they are used for. Because our model is so simple, explaining and teaching is more easily achieved. Again taking the time to go through the assumptions made during the development of the model and what scenario this model specifically illustrates seems important if we want the audience to accept the current model and understand how is can be expanded on to closer resemble what health-care executives use when making decisions about control measures.

Potential sources of error regarding the feedback we received is presented below.

Sources of error

Even though most of the audience were non-mathematicians, they are highly educated individuals. This opens the possibility that their understanding was higher than it would be among the general population as this group of people are all very well trained in critical and analytical thinking.

We have to trust that the feedback was genuine. However there is a possibility that some people might not be comfortable admitting that something is difficult to understand, and hence saying that the presentation was understandable regardless of what their personal perception was.

Interest is important for understanding. This presentation was held in an interdisciplinary space started with the purpose of learning from the Covid-19 pandemic from each other, so it's safe to assume that interest was high. Understanding might have been higher in this space than it would be elsewhere where attendees do not actively seek to learn from the pandemic.

Considering our experience with this presentation, the feedback from the audience and potential sources of error, we utilized the slides used for the presentation, and developed a manuscript of how a presentation of the same material ideally could be held for the general, non-mathematical, non-academic population. This manuscript is presented in its entirety in Appendix C.

Chapter 6

Conclusions and Future Work

After several iterations of a SIR-model, one including both an exposed-compartment and rates of vaccination and vaccine efficacy was finalized. With this followed an analysis of its equilibrium points and the basic reproduction number, R_0.
Several limitations and simplifications was made to make the model understandable and possible to present to non-mathematicians. These were listed and examined as the final model represents a very specific scenario that does not align with how the Covid-19 pandemic has evolved. However, we notice that it is not too different from the model used by FHI, as the main difference is that that model includes separate compartments for presymptomatic and asymptomatic exposed individuals and symptomatic and asymptomatic infected individuals [1].

The journey to solving the "minimize the cost of Covid"-problem was long and hard. I visited the possibility of linear approximation and linear programming, nonlinear optimization with the use of the *scipy.optimize-package* in the programming language Python, before a "hands-on"-strategy as the final attempt was the method that would finally work. Several different relationships between cost of infection, cost of vaccination, and cost of death was examined, with the conclusion that high vaccination levels will most often contribute to minimizing the total cost of the pandemic. Depending on the cost-relationships however, one should be certain that a sufficiently high vaccination rate is maintainable. As this is purely a hypothetical and somewhat cynical aspect of the situation, it is currently nothing more than an interesting perspective to explore. Potentially, even though the hope is that is it would not need to come to it, this could be a strategy developing countries would be forced to follow in order to save money and distribute vaccine doses. Obviously the model would have to be vastly more complex for it to have actual applications, but the idea is there.
Another important aspect to reflect on is how one would decide who gets vaccinated first when vaccination resources are limited. One could argue that young individuals should be prioritized for vaccination as they have many years ahead of them where they'll work, pay taxes and contribute to society while elderly individuals who are already well into retirement will only require resources for years to come. Therefore young individuals should be protected. On the other hand young individuals have a higher probability of recovering from the virus even without being vaccinated whereas

[1] De Blasio, B. F. (2022) *Coronavirus modelling at the NIPH* . https://www.fhi.no/en/id/infectious-diseases/coronavirus/coronavirus-modelling-at-the-niph-fhi/

elderly individuals will more likely fall very ill, get hospitalized, and therefore require large amounts of help, or worse. Therefore elderly individuals should be prioritized as their health and lives will be more at stake without the vaccine and we should protect those who are most vulnerable. In Norway the last perspective prevailed and the oldest citizens were offered the vaccines first and over time vaccines were offered to gradually younger age groups [2]. The code developed for the "Minimizing the cost of Covid"-problem already has the potential to assess the total cost if I include the different age-groups of the population as well as probability of risk of death, hospitalization and recovery for each of these groups given a vaccine or not.

The model itself and its implications, as well as the idea behind the optimization problem, was presented in an interdisciplinary space as part of a project to learn from the pandemic from people from different specialties. Using this as a way to gain insight into how the work done in this thesis can be presented in an understandable way as well as getting actual feedback on the presentation, a manuscript of how the same material ideally should be presented to the general population of non-mathematicians was developed.
It is my hope that some insight into how decisions to limit spread of infection are made will help motivate acceptance, understanding and compassion in the face of restrictions and hardships during the Covid-19 pandemic.

Future work might include developing a model that takes several other factors into consideration. The listed overview of simplifications done on the model represents adjustments that could be made in order to make the model even more realistic. This concerns both the SEIR-model and the code developed for minimizing.

[2] FHI's Vaccination Calender: https://www.fhi.no/en/publ/posters/vaksineringsscenario/.

Appendix A

Code

The code used in section 3 when running the final SEIR-model is found at https://github.com/mariajac/Master-thesis-SEIR-model

The finalized code used in section 4.3 for "The Minimizing the Cost of Covid"-problem is found at: https://github.com/mariajac/Minimizing-the-cost-of-covid

Appendix B

Stages of Development of our Covid Model

B.1 Developing the Vaccination Model

B.1.1 SIRV

We wanted our model to show how individuals move between belonging to the susceptible, exposed, infectious or removed (recovered or dead) groups of the population, as well as how vaccination affects this development. Our starting point was a general SIR-model, like system 2.1, to which we added a vaccination-compartment. Birth- and death-rates were left out for simplicity. We constructed this model inspired by Ghostine, Gharamti, Hassrouny, and Hoteits ([42]) work with modelling the Covid-19 pandemic in Saudi-Arabia. Their model contains several compartments we decided to leave out of our model for simplicity, but we were inspired when it came to describing how individuals move to and from the vaccinated-compartment. As the vaccines are not completely efficient, we also added the vaccine-inefficacy-parameter which moved individuals from the vaccinated-compartment to the infectious-compartment. The flow with corresponding parameters is illustrated in the flowchart in figure B.1.

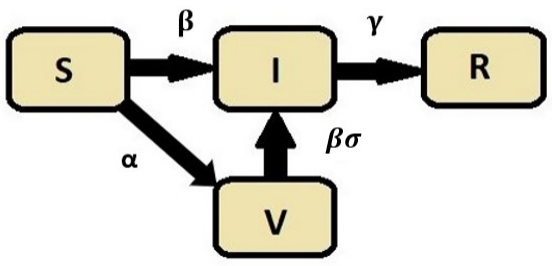


Figure B.1: Flowchart of the SIRV-model.

This results in the SIRV-model as presented in system B.1.

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI - \alpha S \\ \frac{dI}{dT} &= \beta SI - \gamma I + \sigma\beta VI \\ \frac{dR}{dt} &= \gamma I \\ \frac{dV}{dt} &= \alpha S - \sigma\beta VI \end{aligned} \tag{B.1}$$

Where the parameters $\beta, \alpha, \gamma, \sigma$ symbolize the transmission rate, vaccination rate, the recovery rate, and the vaccine inefficacy, respectively.

Since natural birth- and death rate are ignored, we consider the size of the population as a fixed number N, so that $S+I+R+V=N$. Viewing the variables S, I, R and V as respective proportions of the population we get that $\frac{S}{N}+\frac{I}{N}+\frac{R}{N}+\frac{V}{N}=1$. Occasionally it will make sense to change the numbers of the variables when normalizing so that $\frac{S}{N}=s,\ +\frac{I}{N}=i,\ \frac{R}{N}=r,\ \frac{V}{N}=v$ and $s+i+r+v=1$, but we will keep using upper case letters and keep in mind that we consider a normalized population. Noting that change in susceptibles, infectious and vaccinated is not dependent on the "removed" group we see that it is adequate to consider the change in S, I and V when finding critical points as we can simply put R as $R=1-S-I-V$.

This model has a critical point in $(0,0,\frac{\gamma}{\sigma\beta})$. Intuitively, this point represents what is called the endemic equilibrium point where there is no susceptible or infected individuals left in a population because everyone has gained immunity either through vaccination or recovery. The Jacobian matrix corresponding to this point is:

$$\mathcal{J}(0,0,\frac{\gamma}{\sigma\beta}) = \begin{bmatrix} -\alpha & 0 & 0 \\ 0 & 0 & 0 \\ \alpha & -\gamma & 0 \end{bmatrix}$$

Now, our goal is to classify the critical point by first computing and analyzing the characteristic polynomial $p(\lambda)=\det(\mathcal{J}(0,0,\frac{\gamma}{\sigma\beta})-\lambda I)$ [31]. From $p(\lambda)=0$ we find the eigenvalues, λ, of the matrix. As the entire right row is made up of zeroes, one of the eigenvalues will be $\lambda=0$. When we venture on to finding eigenvectors from $p(\lambda)-\lambda I=0$ this eigenvalue will leave us with the original Jacobian matrix. This matrix is singular, as $\Delta=0$ [43]. Consequently there is no unique solution to $p(\lambda)-\lambda I=0$. Therefore, we cannot find the corresponding eigenvector and our analysis comes to a halt.

We also notice that our model has only one equilibrium point which is an endemic point. The fact that the model is lacking a disease-free equilibrium point is a large red flag. However, we will try to manipulate our equations to work out these issues.

In order to find a solution to our problems, we started by searching for a different way to express the vaccination rate α. One approach was to view the vaccination-rate as a function of the number of infected and vaccinated, like such: $\alpha = f(I,V)$, changing the term describing the vaccinated individuals from αS to $f(I,V)S$. The new system now looked like this:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI - f(I,V)S \\ \frac{dI}{dT} &= \beta SI - \gamma I + \sigma\beta VI \\ \frac{dR}{dt} &= \gamma I \\ \frac{dV}{dt} &= f(I,V)S - \sigma\beta VI \end{aligned} \tag{B.2}$$

In order to calculate the disease-free equilibrium point of this model, we put $I = 0$. However, we quickly notice that regardless of what $f(I,V)$ is, in this case the model doesn't tell us anything about either S or V. The endemic equilibrium point is the same, and brings the same problems, as for the model in eq. B.1.
After several variations of the SIRV-model we concluded that including a vaccination-compartment was incompatible with the way we wanted to analyze our model, as when e.g. calculating the basic reproduction number of this model using the Next Generation Method proved impractical.

B.1.2 SEIR

We decided to pivot to a standard SEIR-model, like system 2.3, that we could expand on to represent what we needed to model. This model has a disease-free equilibrium point when both I and E is zero. We get the Jacobian matrix:

$$\mathcal{J}(1,0,0) = \begin{bmatrix} -\mu & 0 & -\beta \\ 0 & -\sigma-\mu & \beta \\ 0 & \sigma & -\gamma-\mu \end{bmatrix}$$

When categorizing the stability of equilibrium points we will use a variation of the Routh-Hurwitz Stability Criterion presented as a theorem by Zabczyk in his book *Mathematical Control Theory: An Introduction* [44] [26]. This is presented as follows:

Polynomials with real coefficients:

i. $\lambda + a$,

ii. $\lambda^2 + a\lambda + b$,

iii. $\lambda^3 + a\lambda^2 + b\lambda + c$,

iv. $\lambda^4 + a\lambda^3 + b\lambda^2 + c\lambda + d$

are stable if and only if, respectively:

i. $a > 0$,

ii. $a > 0, b > 0$,

iii. $a > 0, b > 0, c > 0$ and $ab > c$,

iv. $a > 0, b > 0, c > 0, d > 0$ and $abc > c^2 + a^2 d$ [26] .

For system 2.3, the characteristic polynomial can be written as:

$$p(\lambda) = -(\mu + \lambda)\left((\sigma + \mu + \lambda)(\gamma + \mu + \lambda) - \sigma\beta\right),$$

making $\lambda_1 = -\mu$, and we can use Zabczyk's theorem on the remaining part:

$$(\sigma + \mu + \lambda)(\gamma + \mu + \lambda) - \sigma\beta.$$

This can be rewritten as:

$$\lambda^2 + \lambda(2\mu + \sigma + \gamma) + \sigma\mu + \sigma\gamma + \mu\gamma + \mu^2 - \sigma\beta.$$

From this we get that

$$a = 2\mu + \sigma + \gamma > 0.$$

Using $R_0 = \frac{\beta\sigma}{(\mu+\sigma)(\mu+\gamma)}$ we get

$$b = (\mu + \sigma)(\mu + \gamma) - R_0(\mu + \sigma)(\mu + \gamma) = (1 - R_0)(\mu + \sigma)(\mu + \gamma),$$

from which we get that R_0 must be < 1 for the polynomial to be stable, which is consistent with traditional properties of R_0 [22].

B.1.3 Further Expansion

In order to expand on the SEIR-model we used Meng, Cai, Si, and Duan as our inspiration [10]. In their work with their model, instead of adding vaccination as a compartment, they establish coefficients representing rates of vaccination and vaccine efficacy and use these as a means to move individuals from susceptibles to exposed and removed. They also introduce a coefficient that denotes the natural birth- and death rate. First we tried including vaccination rates, but not natural birth- and death rates as our system is closed. We made it so that some vaccinated individuals gain immunity and move from the susceptible-compartment to recovered. We also wanted to take vaccine-efficacy into consideration, and adding a parameter denoting this allowed us to do that. This is illustrated in figure B.2.

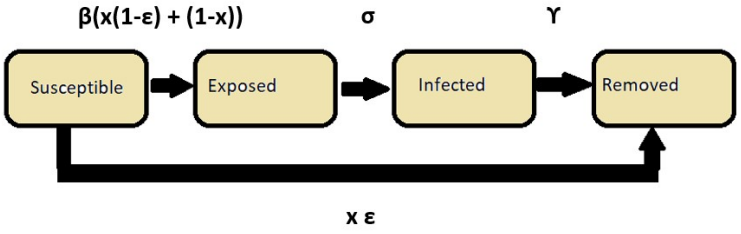


Figure B.2: Flowchart of a SEIR-model with vaccine-parameter.

The new system of equations now looks like this:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI(x(1-\varepsilon)) + (1-x) - x\varepsilon S \\ \frac{dE}{dT} &= \beta SI(x(1-\varepsilon)) + (1-x) - \sigma E \\ \frac{dI}{dt} &= \sigma E - \gamma I \\ \frac{dR}{dt} &= \gamma I + x\varepsilon S \end{aligned} \tag{B.3}$$

Where β, σ, γ, x, and ε are the transmission rate, incubation rate, recovery rate, vaccination rate and vaccine efficiency, respectively. This model has a disease-free equilibrium point when S, E, and I are zero. $S = 0$ is found from $-\beta SI(x(1-\varepsilon)+(1-x)) - x\varepsilon S = 0$ which becomes $-x\varepsilon S = 0$ when $I = 0$. This implies that $S = 0$ but if we think about it intuitively we could say that in a disease-free environment there would be no vaccination, so we can put $x = 0$ instead. This still leaves us with the Jacobian:

$$\mathcal{J}(S,0,0) = \begin{bmatrix} 0 & 0 & -\beta S \\ 0 & -\sigma & \beta S \\ 0 & \sigma & -\gamma \end{bmatrix}$$

And we end with the same problem as for the model in eq. B.1.

We then chose to add a parameter of birth- and death rate to this system. Assuming that birth- and death rate is the same, we get the flowchart in figure B.3:

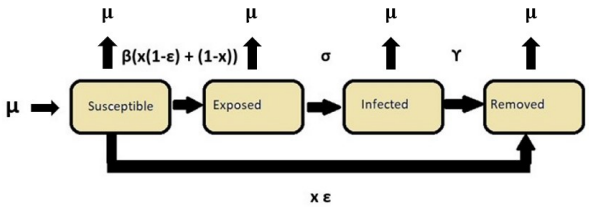


Figure B.3: Flowchart of the final SEIR-model with vaccine-parameter.

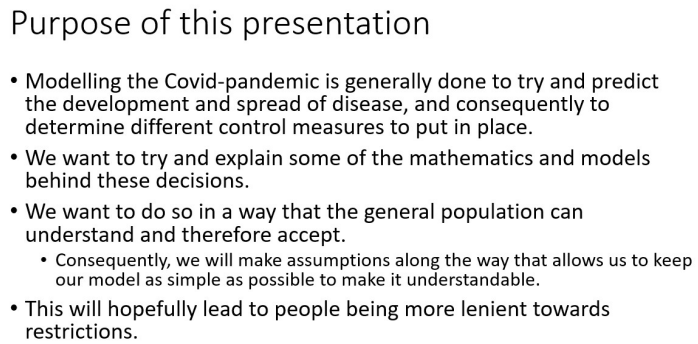
And the final system of equations:

$$\begin{aligned} \frac{dS}{dt} &= \mu - \beta SI(x(1-\varepsilon)+(1-x)) - x\varepsilon S - \mu S \\ \frac{dE}{dT} &= \beta SI(x(1-\varepsilon)+(1-x)) - \sigma E - \mu E \\ \frac{dI}{dt} &= \sigma E - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I + xeS - \mu R \end{aligned} \tag{B.4}$$

Where μ, β, σ, γ, x, and ε are the birth-/death-rate, transmission rate, incubation rate, recovery rate, vaccination rate and vaccine efficiency, respectively.

Appendix C

Manuscript



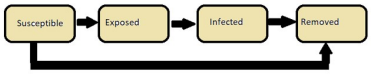
The purpose of this presentation is to try and make the mathematics behind the pandemic a little more understandable. Restrictions and frustration are just some of the many things we've all had to deal with through the past couple of years. Especially during a lockdown or during times with varying levels of infection when health-executives and governments announce more and more strict control measures, one can feel helpless and hopeless if what is being done doesn't make any sense.
Our hope is that knowledge and understanding can help ease some of the hopelessness and frustration and aid in motivation for keeping with the restrictions.
We will demonstrate how mathematical models used in epidemiology work, and develop our own model for a specific scenario. Our model will be much simpler than what the actual situation is like, but the goal is to show how models help us predict possible outcomes and consequently to make decisions about control measures.

Mathematical models

- "All models are wrong, but some are useful." (George E.P. Box)
- A model is just that; a model. It is an attempt to illustrate and/or predict a phenomenon.
- It is not an exact representation of reality. Still, it can be very helpful.
  - A model can never take every factor into account, it can still give somewhat of a picture of a situation and its development. This makes it our best shot at making the best possible decisions.
- In our work we have tried to model a very specific scenario; the spread of the COVID-19-virus with vaccines as the only control measure.
- SEIR-model

The quote by George E.P. Box encompasses very well what a model can be, as it is just that: a model. It is an attempt at illustrating a phenomenon, but it will never be able to replicate reality exactly. The world is unpredictable and there are countless factors coming into play in different situations, which makes it impossible to make a completely accurate prediction.
Some models CAN get close enough to reality and those models can be very helpful. A somewhat realistic prediction can help us prepare for what will happen. SEIR-models are a class of mathematical models used in epidemiology. This is the kind of model we have been developing and working with on our master project.

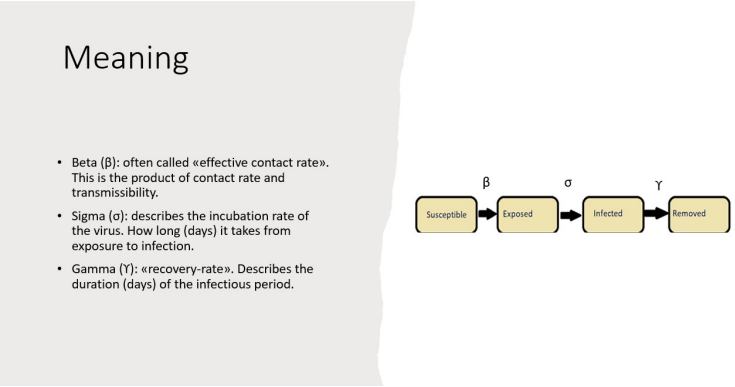
SEIR-model



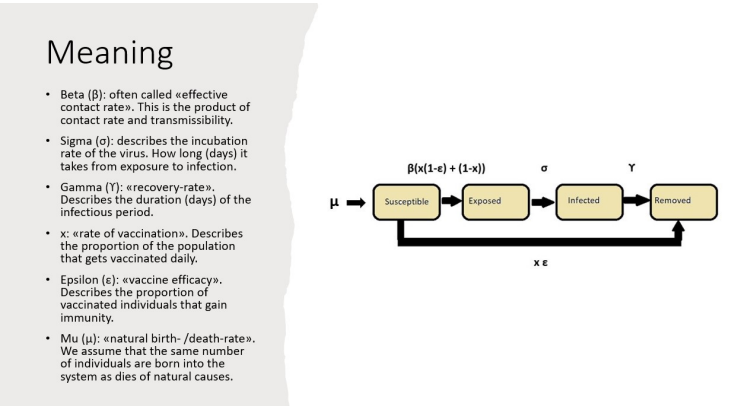
- We divide the population into four groups: susceptible, exposed, infectious and recovered/removed (immune).
  - Susceptible: Healthy individuals that might get infected.
  - Exposed: Individuals that have been exposed to the virus but are not yet infected/infectious.
  - Infected: individuals that are infected and might infect others.
  - Removed: Individuals that have been through infection and have gained immunity through recovery. Vaccines can also provide immunity and allow susceptible individuals to move directly to the "removed-box."
- Mathematical equations describe at which rates people move from one box to the next.
- The model illustrates how large proportion of the population belong to the different boxes at any given time.

These boxes illustrate how the coronavirus travels through the population. First we have to imagine that we divide the population into four categories; susceptible, exposed, infected, and recovered (or removed).
At the beginning of the pandemic, we are all in the susceptible category as the virus has not started spreading and none of us have been exposed yet. Then as time progresses, the virus starts moving. When a person gets exposed to an infected individual it moves to the exposed category. Then after the incubation period this person tests positive and moves to the infected box. Finally, when the person has recovered it moves to the recovered category. We all know that with the different variants one can get reinfected, but for simplicity in our work we have assumed that one gains complete immunity after having had Covid.

In our thesis we have also included vaccines. The arrow at the bottom illustrates those who get vaccinated and then gains immunity and can then count as recovered without having gone through the disease. In reality there are several doses, varying vaccine efficacy from variant to variant and the fact that the (current) vaccine protects mainly against severe disease and not from infection itself. Again, for simplicity, we assume that some portion of the vaccinated individuals gain immunity, and the rest are unlucky enough to still be susceptible to getting the virus.
In the model itself there are mathematical equations that describe at which rates people move from one box to the next.
We can then illustrate how large proportion of the population belong to the different boxes at any given time.



To describe the change between the boxes, we need some parameters. We start by looking at the three most used. For someone to move from susceptible to exposed they need to come into contact with someone that is infectious. To measure this scenario we use beta, often called effective contact rate. This is the product of contact rate and transmissibility. Then those who are exposed move to the infected-box after an incubation period. We use sigma for the incubation rate. Lastly after being sick, you move to the removed box. We use gamma as the recovery rate, which is an average of how many days people are infectious.



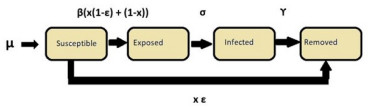
Here we have added three more parameters as we take birth/death and vaccination into account. Mu is the rate of birth and natural death, which we assume is the same for

simplicity. The only way the susceptible-box gets more members is through birth, and we might lose someone in any of the boxes if they die. Here we only look at death from natural causes. If someone dies from the disease they are still moved to the removed-box. Then for vaccination we have two parameters; x for the rate of which people are vaccinated daily, and epsilon for the vaccine efficacy. Since the vaccine is not 100% effective, we have chosen to look at a scenario were you either gain immunity or the vaccine has no effect on you. The arrow that moves from susceptible directly to removed symbolizes those who are successfully vaccinated, denoted by the rate x times epsilon. Where we on the last slide only had beta, we now see some more terms. We look at proportions of the population and therefore use 1 if we speak of whole population. This means that 1-x describes the portion of the population who are not yet vaccinated. Then similarly those who are vaccinated but did not gain immunity is described by x(1-epsilon).

Equations

$$\frac{dS}{dt} = \mu - \beta SI(x(1-\epsilon) + (1-x)) - x\epsilon S - \mu S$$

$$\frac{dE}{dT} = \beta SI(x(1-\epsilon) + (1-x)) - \sigma E - \mu E$$

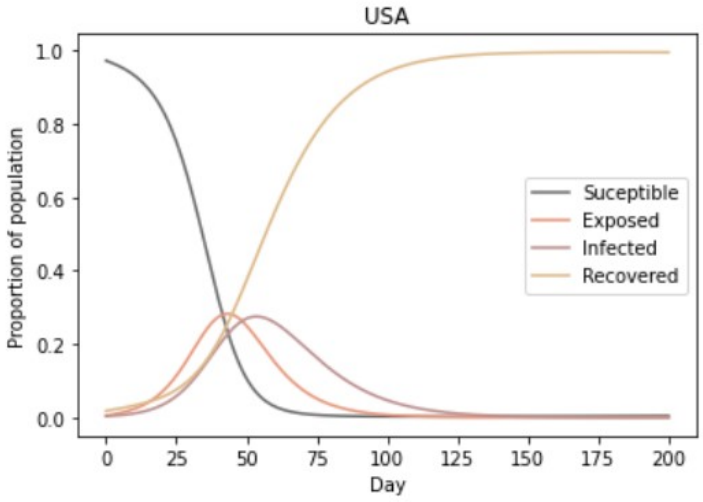


$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

$$\frac{dR}{dt} = \gamma I + x\epsilon S - \mu R$$

Now to make use if these parameters and describe the movement in and out of each box, we have four equations, where dS/dt means the change in the susceptible population per time, which is per day on this case. If the terms are positive it describes movement into the box, while negative terms describe movement out of the box. We can start with the first equation. As we saw in the last slide, mu is for newborns entering the susceptible population. Then we have the big, "scary" term that describes those who get exposed to the virus. We see this term between the susceptible- and exposed-box. In the term we also see S and I because it matters how many people are moving around and how many infectious individuals are out there that they can come into contact with. Then we have x epsilon S denoted those who get successfully vaccinated. The S is added because we need to take into account how many people can get the vaccine. Then at the end we have mu S for those who dies of natural causes. In the second equation we recognize the first term as those who have become exposed to the virus and have moved from the susceptible-box. Sigma E is for those who are finished with the incubation period and finally mu E denote those who dies of natural causes. Then again in the third equation we see the sigma E term again, as it describes those who moves from exposed to infected. Then we have gamma I for those who have recovered and are no longer infectious. Then as always, we have the term describing natural death. In the final equation that describes the movement in and out of the removed category, we again see the gamma I term. We also have those who got vaccinated and moved from susceptible directly to removed, and finally those who dies of natural causes while in

the removed category.



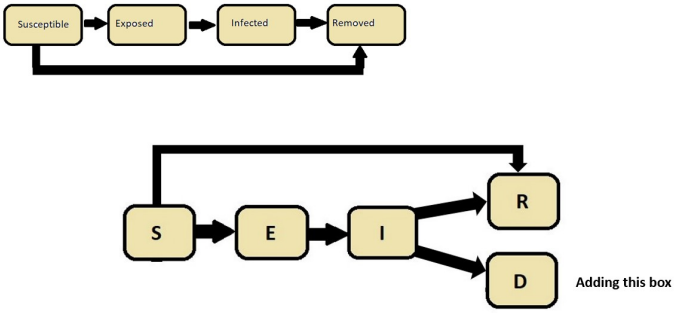
To see the model in action, we here have a simulation with data from 2020 in USA. As mentioned earlier, this simulation has vaccination as the only control measure, so there is no quarantine, no social distancing, people dont stay at home when they are sick, but moves freely around and infect others. On the x-axis we have number of days into the pandemic and on the y-axis, we have the proportion of the population in each of the categories. In this specific scenario we get an infection peak at over 25% of the population, which is extremely high.

The basic reproduction number

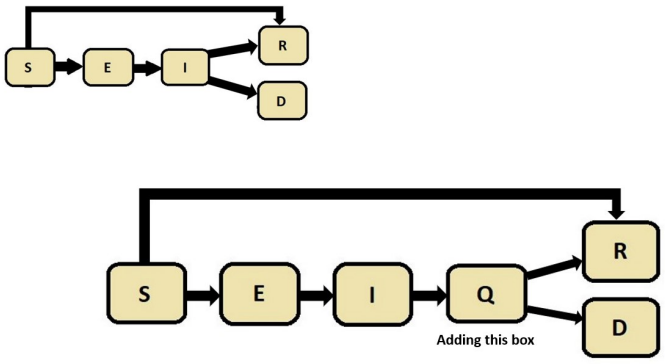
- This kind of model and parameters are often what is used when calculating the R-number we hear so much about.
  - Main property: pandemic is increasing when R>1 and decreasing when R<1
- Problems with the R0/R/Rt/Reff-number:
  - Many different methods of calculation.
  - Depends on many different factors, like rate of transmission, duration of contagiousness, environment, population density, etc.
  - Even the main properties of the R-number can under certain circumstances fail.
  - Be careful to make strong claims.
- In our thesis: the basic reproduction number describes the rate of contagiousness in a completely susceptible population.
  - Making it applicable initially in a pandemic – which gives an indication of severity.

I will now talk a little bit about the R-number that we have heard so much about in the news. Quickly explained the basic reproduction number is defined as the number of new cases an infected individual will cause in a population of completely susceptible individuals.
We can quickly identify one problem; it is confusing. In the media we hear about one R (at least that was my impression), but when reading articles for our thesis we have discovered that there are several different variations of R-numbers. All of these deal with roughly the same thing, but there are differences to each of them.
In our thesis we have been using the basic reproduction number, R0, and have seen

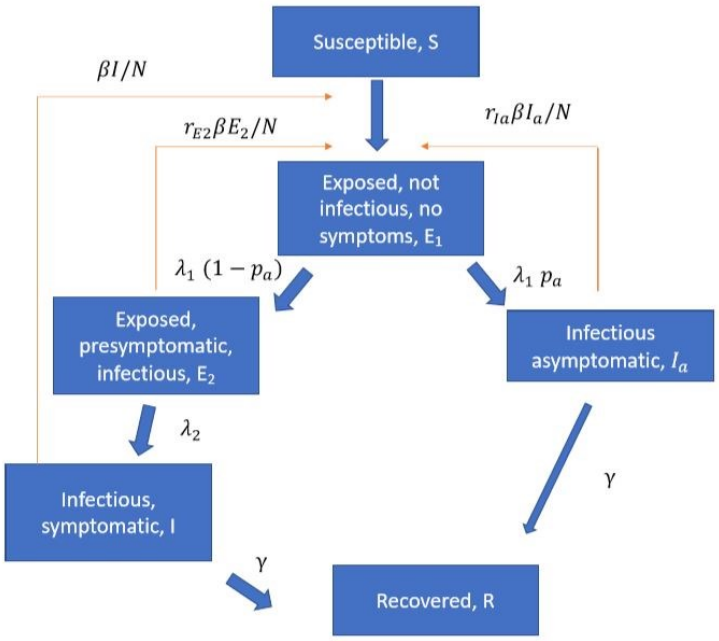
that there are many different methods of calculating this and that the number can vary depending on the disease and population it describes. A lot of different factors are considered when calculating R0, like factors regarding the disease, for example the infectiousness and duration of contagiousness, as well as factors regarding the community, for example the environment and population density.
The R0 used in this paper is supposed to describe the infectiousness in a general population where there is no immunity. As we include vaccines and assume that they do provide immunity, our R0 will not be applicable. Generally it can be used as an indication of expected spread initially in the pandemic.



Before we move on I would just like to present a couple examples of ways to expand on this model. If we seek to make the model more realistic we have to include more aspects of reality. In our model we have a removed-box that includes both those who have gained immunity through recovering from the virus as well as those who die from it. In reality one would absolutely not put these individuals in the same category. Here you see an example of a flowchart where we separate these individuals into two different compartments by adding a box that will include those who sadly dies from the disease, which we will call a SEIRD-model. In this case everyone is a susceptible individual initially, before they eventually gain immunity through vaccination or get exposed to the virus. Following exposure comes infection, as we have already seen. But in this example we rightfully differentiate between what happens next; one either recovers and gains immunity or one passes away.

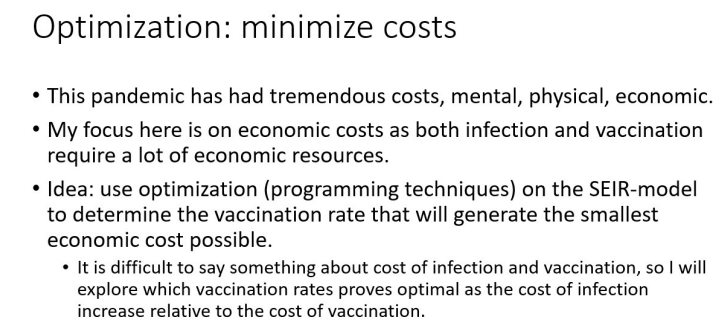


To complicate things even further we can add another box to the model that includes infected individuals that are in quarantine. In this scenario we assume that shortly after an individual gets infected it is placed in quarantine, where he or she cannot infect any more individuals. The flowchart follows the same order as in the SEIRD-model, only following infection we add a "quarantine"-compartment. Now infected individuals are "safely" isolated while they wait to either recover or die. We can call this version a SEIQRD-model. Both in this and the SEIRD-model different parameters and equations will describe how quickly individuals move from one compartment to the next, as we have already seen for the SEIR-model. As we add compartments to the model it gets more and more complicated, but we also see that it includes various aspects of the Covid-reality we actually recognize.

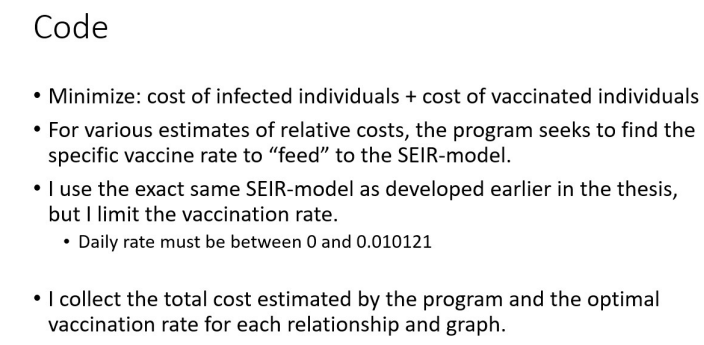


Different goals and uses require different models. Now we have learned so much that we can take a quick look at the actual model used by FHI in Norway [1]*. Instead of adding compartments describing individuals who pass away or are in quarantine, FHIs needs require them to rather include compartments that differentiate between symptomatic and asymptomatic exposed and infected individuals.*

[1] Picture taken from FHI/NIPH article (May 26th 2022): De Blasio, B. F. et.al. *Coronavirus modelling at the NIPH*. From https://www.fhi.no/en/id/infectious-diseases/coronavirus/coronavirus-modelling-at-the-niph-fhi/.



Now over to something else. Briefly summarized: for this part of the thesis, I will use programming and optimization methods to calculate the vaccination rate given the vaccine efficacy, transmission rate, and the other parameters we've talked about that generates the lowest total cost of the pandemic.
In the coding language I am using, Python, there are several tools I can use to determine ideal values of different parameters based on what I'm looking for.
This pandemic has taken a lot from us. It has cost lives, physical health, mental health, money, time, and resources, and it will take a long time for many people to recover completely. In hindsight it's easy to wonder what could have been done differently for things to have gone differently. I will not try to find a perfect answer, but I will explore the economic perspective and how economic costs can be minimized with the help of vaccines. Vaccine development and distribution cost a lot of money, and infection leads to having to stay at home from work and potentially being hospitalized which also demands a lot of resources.
In our work with this paper we have only looked at the vaccine efficacy after one dose. While keeping this at 52% I will seek to find the ideal vaccination rate which creates a balance between infected and vaccinated individuals that minimizes the total cost of the pandemic.



I will not go into detail about the code itself, but I will try to explain the process. At least what I am trying to do.
First, what I want to minimize, or make as small as possible, is this: the total economic cost of all those individuals who get infected plus the cost of all of those who get vaccinated.

Then I have a section in my code that explores the ideal vaccination rate given a specific relationship between the cost of infection and the cost of vaccination. For many different increasing "suggestions" of the vaccination rate the SEIR-model we have developed generates the resulting amount of infected and vaccinated individuals and hence the consequent total cost of this. I will repeat this process for various cost-relationships between infection and vaccination. Ultimately, the code identifies one optimal vaccination rate for each cost-relationship.
I also need to limit the possible values of the vaccination rate or else I might risk that the program wants to vaccinate the entire population every day. It is important to keep what I can as realistic as possible, which is why I have decided to limit the vaccination rate so that is must be between 0 and 0.010121. This is based on actual vaccination data provided by FHI. I identified one week last year that had the highest vaccination numbers, and use this as the maximum possible vaccination rate.
Finally I will illustrate the relationship between an increasing vaccination rate and the total cost generated.
Of course, it is important to note that there are a wide range of ethical aspects to consider, but I think this is an interesting idea to explore.

Appendix D

Calculations

In order to get

$$det(J-\lambda I) = [(1-R_0)(x\varepsilon+\mu)-x\varepsilon-\mu-\lambda][(-\sigma-\mu-\lambda)(-\gamma-\mu-\lambda)-\frac{\sigma\beta\mu(1-x\varepsilon)}{R_0(x\varepsilon+\mu)}]$$

$$+(1-R_0)(x\varepsilon+\mu)\frac{\sigma\beta\mu(1-x\varepsilon)}{R_0(x\varepsilon+\mu)} = 0$$

on the form of: $\lambda^3 + a\lambda^2 + b\lambda + c$, the following calculations were made:

$$(1-R_0)(x\varepsilon+\mu)(-\sigma-\mu-\lambda)(-\gamma-\mu-\lambda) - (1-R_0)(x\varepsilon+\mu)\frac{\sigma\beta\mu(1-x\varepsilon)}{R_0(x\varepsilon+\mu)}$$

$$-(x\varepsilon+\mu+\lambda)(-\sigma-\mu-\lambda)(-\gamma-\mu-\lambda)+$$

$$(x\varepsilon+\mu+\lambda)\frac{\sigma\beta\mu(1-x\varepsilon)}{R_0(x\varepsilon+\mu)} + \frac{\sigma\beta\mu(1-x\varepsilon)(1-R_0)}{R_0} = 0$$

This is rewritten as:

$$-\lambda^3 - \lambda^2(2\mu+\sigma\gamma-(1-R_0)(x\varepsilon+\mu)+x\varepsilon+\mu)$$

$$-\lambda[\mu^2+\sigma\gamma+\sigma\mu+\mu\gamma-(1-R_0)(x\varepsilon+\mu)(\sigma+2\mu+\gamma)+$$

$$(x\varepsilon+\mu)(\sigma+\gamma+2\mu) - \frac{\sigma\beta\mu(1-x\varepsilon)(1-R_0)}{R_0(x\varepsilon+\mu)}]$$

$$+(1-R_0)(x\varepsilon+\mu)(\gamma+\mu)(\sigma+\mu) - (x\varepsilon+\mu)(\gamma+\mu)(\sigma+\mu)+$$

$$\frac{\sigma\beta\mu(1-x\varepsilon)(1-R_0)}{R_0} = 0$$

Since $R_0 = \frac{\beta\mu\sigma(1-x\varepsilon)}{(\gamma+\mu)(\sigma+\mu)(xe+\mu)}$ we can write $\frac{\beta\mu\sigma(1-x\varepsilon)}{R_0(xe+\mu)} = (\gamma+\mu)(\sigma+\mu)$ Using that and multiplying by -1 we get

$$\lambda^3 + \lambda^2(2\mu+\gamma+\sigma+R_0(x\varepsilon+\mu))$$

$$+\lambda(R_0(xe+\mu)(2\mu+\gamma+\sigma)) + (R_0-1)(\gamma+\mu)(\sigma+\mu)(x\varepsilon+\mu) = 0$$

and we can identify the constants a, b and c.

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