Erasmus
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ERASMUS UNIVERSITY ROTTERDAM
Erasmus School of Economics
Master Thesis [MSc Health Economics]

Health benefits under different Covid-19 mitigation strategies in The Netherlands

Name student: Pranaav Ganesh
Student ID number: 473528

Supervisor: Prof. Pieter van Baal
Second assessor: Prof. Pilar Garcia Gomez

Word count: 12370 | Date final version: 11-08-2022

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Abstract

The second wave of Covid-19 in The Netherlands lasted from September 2020 to June 2021, leading to 11,000 excess deaths in the population. This thesis aims to estimate the true health burden of the pandemic, through calculating the Years of Life Lost and Quality Adjusted Life years Lost in the population due to Covid-19. It also aims to estimate and compare the effect of mitigation strategies on health outcomes using a Susceptible-Exposed-Infected-Recovered model. The health outcomes of these scenarios, measured in deaths, are then converted to Years of Life Lost and QALYs Lost using the average estimates derived from the original scenario. The main findings from the research were that in total there were 77,000 Life years Lost and 50,000 QALYs Lost in the population during the second wave. The health burden was mainly concentrated amongst the elderly population aged 70 and above, while the health burden amongst the younger population was relatively higher in the second wave compared to the first wave. The forecasted scenarios showed that the implementation of a lockdown by the Dutch government in the second wave resulted in 60,000 QALYs being gained compared to no lockdown. It also showed that an earlier lockdown, if implemented would have resulted in 22,000 QALYs being gained.

Acknowledgement

I would like to thank those who have supported and guided me over these last few months. Firstly, I would to thank my thesis supervisor Prof. Pieter van Baal. Pieter promptly guided me though the thesis process and gave me a lot of freedom to explore my own research ideas around the topic of Covid-19 and population health. I would like to thank all my professors during my master and have inspired me to write this paper. This Thesis is a unique reflection of the concepts and theories I have learnt in their courses. I would like to thank friends and family for supporting me through this process. Lastly, since this thesis is an investigative research into the mortality burden that occurred during the Covid-19 pandemic I want to pay tribute to the lives that were lost around the world due to Covid-19.

1 Introduction

“With Covid-19, we’ve made it to the life raft. Dry land is far away, and science is our only exit strategy” – Marc Lipsitch

The COVID-19 Pandemic has been ongoing for more than 2 years since its inception in January 2020. As the disease has progressed and new variants have emerged, countries have shifted their approach of intensive lock downs towards targeted vaccination efforts to combat the disease. At the time of writing this paper, countries are beginning to adopt leniency in measures to combat the pandemic. Yet, we are still seeing waves of Covid-19, with an unprecedented loss of life still occurring in parts of the world.

Improving Public health has always been elemental to the goals of government health policy. With COVID-19, this became ever-significant as governments all over the world were at the forefront of containment of the disease within their sub-populations. This level of involvement also resulted in backlash from the public, who perceived these public health measures as restriction of their freedoms, leading to public protests that were seen worldwide. A pandemic can play out in different ways depending on how people, governments, and other institutions respond to it. Governments have been criticised for not doing enough or even doing too much in this pandemic.

Throughout this pandemic, countries have adopted measures ranging from different levels of stringency. On one spectrum, China’s stringent Zero-COVID policy which was declared as a "Top objective of the country", emphasized complete zero tolerance of Covid-19. The actions of the policy resulted in regular city lock downs, mass testing of populations in infected provinces/cities and strict quarantine periods for infected people. On the other side of the spectrum, we had countries such as Sweden that did not enforce any strict lockdowns or many measures in their populations (Normile, 2021).

The Oxford stringency index measures government responses since the beginning of the pandemic, helping policymakers to understand the effect of policies on disease spread. Responses are measured using a containment and health index (CHI) which groups 19 indicators in the themes of closure, health and economic support. A paper by Hale et al. (2021) which analysed these measures showed that there was a high degree of congruity in the responses of governments during the first months of the pandemic. These responses however, diverged after the first wave, as there was more variability in the timing and stringency of the policies that governments sought to re-impose.

These strict measures were either supported or denounced by scientists. Kulldorff et al. (2020) took a stance against restrictive measures such as lockdowns to control community spread. It instead advocated for a "Focused Protection" of older demographics who were more likely to die from COVID-19 or suffer long term complications.Their declaration suggested that countries should head towards the herd immunity of their population instead of lock downs and measures. This was opposed by another group of scientists through Alwan et al. (2020), who argued that herd immunity lacked evidence to support that natural infection from the virus would provide lasting immunity. They suggested that implementing these restrictive measures would lead to a reduction in short term COVID-19 induced mortality and compromise the treatment of several acute and chronic conditions, with long-lasting-negative repercussions.

It is thus important to realise, what are the resulting actions of these public health measures and how can we evaluate their success? Quantifying the health impact of policies can help in measuring the positive or negative impact these policies have on population health. It also helps is assessing whether the entire health of the population or certain sections are affected. Approaches to quantify health impacts include estimating number of lives lost, number of life years lost, expected increase/decrease in number of incidents, and Quality adjusted Life Years (QALYS) lost. Calculating QALYs lost is preferable as it combines the impact on the loss of life years and the impact on quality of life into a single measure. it also enables comparisons ac cross different disease areas (Whithead and Ali, 2010).

This thesis thus aims to evaluate the related Quality-adjusted life years (QALYs) lost for the actual scenario and the Covid-19 outcomes under different mitigation strategies. The following research question(s) are proposed to address this issue.

(a) What is the number of QALYs lost in the actual COVID-19 measures adopted in the Netherlands during the second wave of Covid-19?

(b) What are the health outcomes due to COVID-19 from imposing different mitigation strategies?

There has existed misinformation and mistrust of policies implemented by the Dutch government to combat Covid-19, namely a law that obligated to use of face masks and a lockdown imposed by the government during the second wave.The most controversial policy that was to be implemented perhaps in the Netherlands was the '3G system' which required citizens of The Netherlands to have either proof of vaccination, recovery from Covid-19, or a negative test result. With repercussions surrounding these measures, and several other steps taken by governments around the world, it is important to assess and analyse 'What-if scenarios' if governments had acted/ not acted on implementing such strategies.

This research thus expels falsifications surrounding the need for such measures in society to combat infectious diseases. Evidence from this paper can be used to inform governments and health authorities about the effects of public health policies in combating infectious diseases. This research also supports an inquiry into the health mortality burden during the second wave of Covid-19 in the Netherlands. A recent article by CBS (2022) discusses the excess mortality in this period, indicating that there were nearly 11,000 deaths during this period. This thesis expatiates on these excess deaths by measuring crude estimates of mortality in the form of YLL and QALYs Lost, and then standardizes these estimates for the underlying health of the population.

A brief description of the structure of the thesis is as follows. First, the Theoretical Framework provides background about various themes this Thesis addresses. Information related to Covid-19 and epidemiological modelling is first presented, followed by the application of these models in previous research published. This section then delves into the theory and previous research around using YLL and QALYs Lost to evaluate mortality. The next section, Methodology and Strategy section also explains how these QALYs lost is calculated using a standardised life table approach. This section also provides the tools estimate the effect of mitigation strategies in using a SEIR model. The Results section first provides a detailed analysis of the health burden during the second wave in The Netherlands. it then compares the outcomes of these scenarios with the actual scenario using QALYs Lost as the main criterion. The Discussion and Conclusion section aims to then answer the important research question in this section, and providing policy implications and further recommendations for research.

2 Theoretical framework

2.1 Taxonomy and Pathology

Covid-19 is an infectious disease caused by the SARS-CoV-2 Virus. The virus spreads person-to-person through respiratory droplets and aerosols. Infection from the virus can lead to anything ranging from a mild respiratory illness to becoming seriously ill and deceased. The virus first appeared in a large cluster in Wuhan, China in December 2019 and rapidly spread around the world, leading to an estimated death toll as noted by Wang et al. (2022) of 18.2 million people.

SARS-CoV-2 or COVID-19 is more transmissible than epidemics that have been eradicated in the past, such as the severe acute respiratory syndrome (SARS) and the Middle East respiratory disease (MERS). The added difficulty with COVID-19 is its protracted incubation period, which can be as long as 1 to 14 days. During the time of incubation, infected people while having no symptoms, are contagious. As a result, those who are vulnerable might not be are infected, making it difficult to quickly identify them and track down their contacts. The unpredictability, transmission, and mutation are some of the major aspects that define COVID-19 as a persistent, uncharted, and changing pandemic. The mutation of the virus resulted in multiple variants, that have been documented worldwide. During the second wave, the Alpha variant (B.1.1.7) and the Delta variant (B.1.617.2) were most dominant in The Netherlands.

2.2 Infectious Disease Modelling

Mathematical models are often used in epidemiology to represent a way to investigate factors that affect disease spread and to predict the magnitude of an epidemic within a population. Such models offer public health planners to make predictions about the impact of emerging disease, as well as the effects of interventions. As noted by Jit and Brisson (2011),infectious disease models are also of interest for economists as they can estimate the effects of an intervention and the associated costs and outcomes of that intervention.

The effect of interventions such as vaccination and social distancing can be modelled in these infectious disease models, and the related costs associated with the interventions can used to make economic decisions. The merging of health economic modelling and infectious disease modelling therefore proves useful for resource allocation decisions and brings a 'responsible' analytical approach as noted by Anonychuk and Krahn (2011). Governments and other public institutions play a big role in defining the public health policies or more specifically the mitigation strategies used to combat an infectious disease.

Specifically, to slow the pandemic and bring infections under control, most governments have implemented many non-pharmaceutical interventions (NPIs) such as social distancing, school and university closures, infective isolation or quarantine, banning public events and travel, etc. The type of policy and timing of the policy is essential in decreasing the number of infections and deaths (Cao et al., 2021). Since the start of the pandemic, there has been important research assessing the effect of these policies using epidemiological models.

These models can either be stochastic or deterministic models. Deterministic models predict a unique outcome with certainty, determined by the parameters in the model. Stochastic models allow for random variation in the outcomes, predicting them with uncertainty. The outcomes generally tested in these models are the number of infectious persons, number of deaths or in some cases the growth rate of the virus. An example of such a model is a Susceptible-Exposed-infected-Recovered (SEIR) model, which provides the most practical way of estimating how an epidemic behaves in a closed system, where the population can be compartmentalised into different disease states.

To represent the initial COVID-19 epidemic in China,Tang et al. (2020) used a generalized SEIR model which additionally included compartments of Asymptomatic infections and Hospitalisations. They found that Intensive contact tracking, followed by quarantine and isolation, can successfully lower the reproduction number and transmission risk. A paper by Berger et al. (2020) published in Review of Economic Dynamics, uses a SEIR model to study how virological and serological testing can affect the number of deaths and economic output. Their results find that weekly testing leads to more lives being saved, lower output losses and lower costs.

Hsiang et al. (2020) estimate the effect of anti-contagion policies on the growth rate of COVID-19 infections. They used reduced econometric techniques to study the effect of changes in policy on the average daily growth rate in infections. In absence of policy actions, The authors initially use a simple SIR model to generate infections before and after. They then use a first difference approach to estimate the causal effect of the policy on the change in infections. Their results find that early infections of COVID-19 exhibited growth rates of nearly 38 percent per day.

A paper by Ferguson et al. (2020) examined the efficacy of non-pharmaceutical interventions (NPIs) targeted at lowering population contact rates and minimizing virus transmission. They use a individual based simulation model to study two countries: the United Kingdom and the United States. The research indicates that the use of numerous treatments in combination is more likely to have a significant impact on transmission. An optimal mitigation policy involving home isolation of suspected cases and the social distancing of populations at high-risk may reduce the number of deaths by half.

Other research in this area is focused on evaluating the impact of policies using statistical methods instead of epidemiological models. A paper by Flaxman et al. (2020) uses a Bayesian mechanistic model that links the cycle of infection to reported mortality. The paper aims to determine if interventions were effective in bringing the reproductive number(R_t) to values below 1. They find in their results that Lockdowns had an identifiable large effect on transmission, reducing the R_t by 81 percent. They also find that across 11 countries, 3.1 million deaths were averted due to NPIs during the first wave of the pandemic.

A paper by Liu et al. (2021) studies the impact of NPIs on COVID-19 transmission across 130 countries, regressing the time varying reproduction number against the different NPIs. They find that there is strong evidence for an association with school closures and movement restrictions and a reduced reproduction number. Similar research by **?** finds that a combination of physical distancing measures, if implemented early, can be effective in containing COVID-19—Other restrictions such as working from home, and a full lockdown in the case of a probable uncontrolled outbreak also significantly decrease the reproductive number.

2.3 Health impact of COVID-19

While the burden of an epidemic is estimated by the number of deaths, this may be underestimated in the case of Covid-19. Official death tolls do not account for those individuals who did not test positive before dying and there are often lags in the data due to delays in processing deaths certificates. Accounting for the problem involves estimating the excess mortality, which compares excess deaths in a given period to the historical baseline deaths from recent years during that period. In an article by the Economist (2021) using a similar methodology to calculate excess mortality, it was found that there have been greater than 7 million deaths worldwide during 2020 alone.

Calculating excess deaths is a crude measure of estimating the health impact as it only includes mortality but not the morbidity. Years of Life lost (YLL) Quality adjusted life years (QALYs) lost provide a truer estimate as it looks at the number of years that the deceased would have lived but for the cause of death. As Ugarte et al. (2022) note in their paper, the case fatality rate of COVID increases with age and mainly affects individuals over 80 years old. COVID-19 not only affects the elderly but also is a cause of premature mortality in the elderly.

Briggs et al.(2020) provided the initial calculation to estimate QALYs lost from COVID-19 mortality data using Life expectancy tables for 5 countries. Life tables models a probability of developing a given disease at different ages and the respective mortality rates once a disease is acquired. The increased risk of COVID-19 mortality amongst those with comorbidities such as diabetes, COPD and heart disease is captured along with factors such as age and sex. In their paper, the authors find that a substantial QALYs and life Years are lost even for older persons with high levels of comorbidities.

A report on the expected outcome of vaccination strategies by Ainslie et al. (2021) looks at the disease burden due to Covid-19 and calculates the expected impact of vaccination on health outcomes. To calculate the impact, the authors use an age-structured SEIR model which included compartments for vaccinated individuals, hospitalisations, intensive care admissions, and deaths. The results of the simulation model suggests that regardless of vaccination strategy, implementing a COVID-19 vaccination program leads to fewer infections, deaths, life years lost and Disability Adjusted Life years (DALYs) lost. The strategy with the best outcomes was to vaccinate from old to young which would result in 5,307 deaths and a total of 82,557 Life Years being lost. Similar research was done by Ferranna et al. (2021) for the U.s, using identical the methods as Ainslie et al. (2021). According to their findings, prioritizing essential workers is an effective way to decrease the number of cases and years of life lost. However in most scenarios, prioritizing older people will result in the biggest drop in fatalities.

Calculation of YLLs and QALYs lost were also done for The Netherlands by Wouterse et al. (2020) and Wouterse et al. (2022) respectively using Life Expectancy Tables. The methods used in the papers focused on estimating YLLs and QALYs lost for The Netherlands by adjusting for the underlying health of the population and additionally accounted for those living in nursing home facilities, as many COVID-19 related deaths occurred in this setting. Only looking at comorbidities in the nursing home population does not capture their poor health and low survival. Their results showed that an average of 8.76 and 8.69 Life Years were lost for men and women respectively. The number of average QALYs lost for men and women were 7.35 and 6.85 respectively.

A paper by Quast et al. (2022) done for the US measuring YLLs using multi-state life tables found that on average 9.2 YLLs per death. A study byReif et al. (2021) also done for the US further incorporates ethnicity and a multitude of comorbidity factors prevalent amongst Covid patients to measure YLLs and QALYs lost. Instead of using life tables, the authors use a microsimulation model which predicts the health outcomes at an individual level. Using this approach helps to fully assess the mortality burden and look into sections of the population losing the most life years. On average 12.2 YLLs and 9.84 QALYs lost per person in the US in 2020, with the greatest toll amongst black and Hispanic men over 65 years old. Compared to Life tables, Micro simulation models are flexible in modelling interaction between diseases and can be used for various scenario analysis. The drawbacks of this method include the increased intensity of computation (Briggs et al.,2016). Research in this area can also extend to papers such as Basu and Gandhay (2021) which use a more individualistic approach, by looking at the QALYs gained by averting a single COVID-19 infection. The authors account for losses in QALYs experienced by a patient through a COVID-infection and losses experienced by family members. They find that 0.061 QALYs can be averted for a single infection.

3 Methodology and Strategy

This section explains the methodology used to derive the YLLs and QALYs lost during the second wave of the pandemic and for the different mitigation scenarios. Calculating the health outcomes under the different scenarios first requires predicting the number of infectious persons using a deterministic SEIR model. These infections are then translated to deaths using an infection fatality ratio (IFR). The final step involves estimating the total YLL and QALYs Lost for these scenarios. This will be derived from an estimate of YLL and QALYs Lost for the actual scenario, using a standard life table approach.

Data used for this research was derived from different sources. Epidemiological data related to spread of COVID-19 in The Netherlands was derived from The National Institute for Public Health and the Environment (RIVM). Public Data sets available from RIVM included the number of infectious persons per day, the daily effective reproduction number (R_t) and vaccine coverage. These data sources were used to determine parameters in the SEIR Model. To calculate the YLLs and QALYs lost, multiple data sources were used. Excess mortality data derived from CBS (Statistics Netherlands) was used to calculate the mortality burden during the second wave. Data related to life expectancy for the Dutch population was also derived from CBS for the year 2020, and then adjusted for comorbidities using estimates from scientific papers. Data related to Quality of Life, proportion of commodities were derived from academic papers and are discussed further in detail later in this chapter.

3.1 Estimation of SEIR Model

A basic SEIR(Susceptible- Exposed-Infected-Recovered) model can be used to predict the number of people in each of the compartmental states. Differential equations appearing as derivatives are used to describe movements between these states. The SEIR model structure is assumed with individuals transitioning between compartmental states once each day. The *epimodels* package from STATA® created by Radyakin and Verme (2020) is designed for specifying the exogenous parameters of the epidemic. Initial conditions based on transition between these compartmental states will be used to generate the number of infections. A diagrammatic representation of a SEIR Model is shown below in Figure 1.

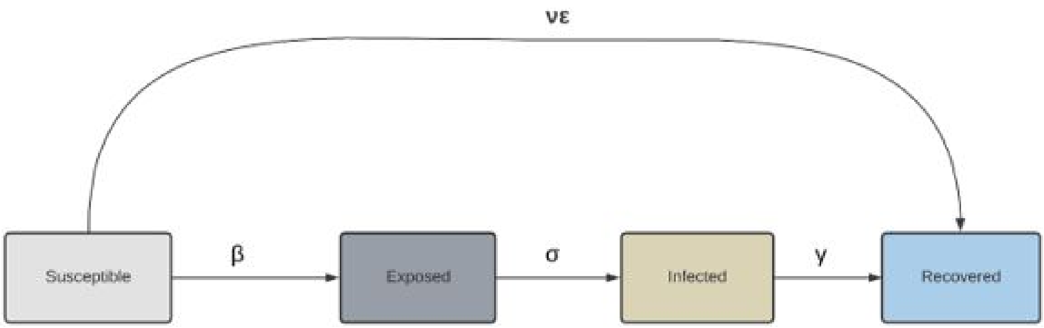


Figure 1: SEIR Model

N represents the total population. At the beginning of an epidemic, the total population(N) is equal to the Susceptible population S(t). During an epidemic, the total population size is divided into different compartmental states, where:(N)= S + E + I + R.

S(t) is the Susceptible population i.e. the number of people not yet infected by the virus but can potentially become infected by the virus. At the start of the pandemic, the entire population was susceptible to the virus. E(t) is the Exposed population who are exposed to the virus but are not yet contagious. This is during the incubation period of the virus. I(t) is the Infected population i.e. people confirmed to have been infected and can potentially transmit the virus to others. R(t) is the Recovered population i.e., affected by COVID-19 anymore. This model assumes that once recovered, a person cannot be infected again.

In order to understand how individuals move between these compartmental states, transition probabilities between each state are assumed. β is the transmission rate from a Susceptible population to an Infected population, which has not been detected. It is measured as 1/ average period an infectious person makes an infectious contact (days). σ is the Transmission rate of confirmed infected people from the exposed population. This is estimated as 1/ average incubation period of the virus. ν is the Vaccination rate (proportion of the susceptible population undergoing complete vaccination each day). ε is the vaccine efficacy (relative risk reduction of infection achieved through vaccination). To measure S, E, I, R over time, a system of differential equations are used to differentiate these four variables.

$$\frac{dS}{dt} = N - \frac{\beta S(t)I(t))}{N} - \nu\varepsilon S(t)) \tag{1}$$

$$\frac{dE}{dt} = \frac{\beta S(t)I(t))}{N} - \sigma E(t)) \tag{2}$$

$$\frac{dI}{dt} = \sigma E(t)) - \gamma I(t)) \tag{3}$$

$$\frac{dR}{dt} = \gamma I(t)) + \nu\varepsilon S(t) \tag{4}$$

In eq.1, the change in the Susceptible population is derived as the number of the persons moving from the susceptible population S(t) to the exposed population E(t) and the number of persons moving from the susceptible population to the recovered population R(t), subtracted from the overall population (N). In eq.2, The change in the exposed population comprises of individuals moving to the infected population I(t), subtracted from the persons currently in the Exposed population. In eq.3, The change in the infected population comprises of individuals moving to the recovered population R(t), subtracted from the persons currently in the Infected population. In eq.4, The change in the Recovered population comprises of individuals moving to the recovered population from the susceptible population and individuals moving from the infected population to the recovered population.

R_0 is the basic reproduction number or the expected number of cases directly generated by one case in the population. It represents the number of secondary infections generated at the beginning of an epidemic when there are no measures present. Locatelli et al. (2021) estimated the R_0 for Covid-19 at the start of the pandemic in Europe to be 2.2. $\beta 0$ is the initial contact rate at the beginning of an outbreak and can be expressed as function of the basic reproduction number and the infectious period (1/γ), represented in eq.5

$$Ro = \beta o * (1/\gamma) \tag{5}$$

Similarly, Rt is the reproduction number that changes at any time during an epidemic. It is important to define the *Rt* which changes dynamically in response to mitigation strategies and public health interventions. The value of R_t must fall below 1 for case numbers to decline. βt is the contact rate at time (t) during the outbreak and can be expressed as function of the effective reproduction number (R_t) and the infectious period (1/γ), represented in eq.6.

$$Rt = \beta t * (1/\gamma) \tag{6}$$

The basic reproductive number (R_0) also provides information on the level of herd immunity that has to be achieved in order for the reproduction number to fall below 1. As an approximation, the proportion of population that should be immune is based on the Ro estimate we obtained from Locatelli et al. (2021). The proportion of population for transmission to be halted is 55 percent. This number gives us a target for vaccination programs, which is another parameter included in the SEIR model. It is assumed that susceptible individuals can move to a recovered state through vaccination, without being infected by the virus. ν is the rate of complete vaccination of individuals per day. ε is the efficacy of the vaccine. These values can be obtained from a recent report published by RIVM, which uses an SEIR model to determine the incidence of infections and hospital admissions specifically under different vaccination strategies between 1st February 2021 and 1st September 2021. The main findings of this report found that initiating a vaccination program, regardless of the vaccination strategy, resulted in fewer new infections, new cases, hospital admissions, IC admissions, and new deaths (Ainslie et al., 2021).

3.2 Derivation of transition probabilities

Once, we have defined the various parameters of a SEIR model, the next step involves providing estimates to these parameters.

The βt is the transmission rate of the virus, which is largely influenced by the number of contacts an infectious individual makes. It is also impacted by the mitigation policies put into place by governments, as discussed in detail later in this chapter. The transmission rate βt is also closely related to the effective reproductive number (R_t) estimates. Using published RIVM Covid-19 data, the average R_t ranged from 0.74 to 1.45 during 2020-21. This would mean that the βt ranges from 0.078 to 0.152 in the course of the pandemic, as βt is estimated as a function of Rt and γ.

The average time an infectious individual remains infectious can be assumed to be 9.5 days. The value for γ assumed in this model is therefore 1/9.5 or 0.105. The infectious period of Covid-19 is assumed as 10 days for this study. An early estimate from RIVM about the incubation period suggested on average 5-6 days, which can be used to model . Thus, the assumed is 1/5 or 0.2.

Since The Netherlands started vaccinating individuals at the start of 2021, we can assume an average vaccination rate(ν) observed per day, based on the total archived RIVM second vaccination dose figures between January and July 2021. It is calculated that around 56,000 people were (fully) vaccinated each day, which is around 0.0032 percent of the population each day. A vaccine with an efficacy(ε) of 90 percent is assumed. Thus, 0.027 percentage of the Susceptible population moves to a recovered state each day after vaccination. *Table 1* below shows the parameters we assume as inputs to estimate a SEIR Model, using the *db episeir* command on STATA.

Another important factor to consider is the size of the Susceptible and Infected populations at the start of the second wave. On 01/09/2020, there were close to 19145 infected individuals in the population, derived from a RIVM dataset estimating the number of infectious persons in the population every day. It was estimated that 2.8 percent of the Dutch population was infected during the first wave based on Vos et al. (2021). The size of the Susceptible population is thus reduced to 15.6 million people at the start of the second wave.

Table 1: Transition probabilities assumed in the SEIR Model

Parameter	Value	Source
β(beta)	0.078-0.152	–
γ(gamma)	0.105	Byrne et al. (2020)
σ(sigma)	0.2	RIVM (2022)
ν(nu)	0.003	Own Assumption
ε(epsilon)	0.92	RIVM (2022)
Susceptible Population	15.6 million	Vos et al. (2021)
Infected Population	19145	RIVM (2022)

3.3 Impact of Mitigation strategies

In 2020-21, The Netherlands used a combination of mitigation strategies that included social distancing, school closures, partial travel restrictions, mask-wearing in all public spaces, and vaccination. In order to estimate the impact of measures on the number of infections, it is first important to assume a counterfactual situation in which these measures do not take place. Thus, the main method of estimating impact is through the number of contacts a person makes at time *t*. This is also the β_t we assume in the SEIR model, which is the beta parameter derived at time *t*. Thus when estimating the mitigation scenarios, we make assumptions about the value of β_t. To derive the impact of these policies, the following methods are used.

To forecast an unmitigated pandemic, without any measures, the baseline value of R_0 is used at the start of the pandemic, before any measures were introduced. The value of the baseline, derived from Locatelli et al. (2021) is 2.2. Estimating β as a function of R_o, the value of β is 0.232.

To forecast a scenario without any lockdown, we look at the value of Rt at the start of the second wave which was 1.35. At the start of the second wave, there were only measures in place to restrict movement of individuals. Assuming that no further measures were put in place, we can estimate the effect of not having a lockdown as the value of β of 0.142 at the start of the second wave. This scenario will include an additional sub-scenario where vaccination is introduced at the start of 2021. In the actual situation, completer vaccination of began only around early February, as the vaccination program started in early January. For the purpose of this scenario however, we assume that persons in the Susceptible population begin complete vaccination from the 1st of January onwards.

The final scenario tested is the implementation of an early lockdown. For this scenario, an estimate that the (R_t) is reduced by 0.296 is assumed from Levelu and Sandkamp (2022). In this working paper, the authors estimate the marginal effects of NPIs on the reproduction rate (R_t)) using a fixed-effects regression. For example, school closures alone can lead to a decrease in the R_t by 0.079, ceteris paribus. Assuming that a complete lockdown includes School closures, Work closures, Restriction on gatherings, Stay at home requirements, ban on international and domestic travel, the effect of a lockdown on the R_t is 0.296, ceteris paribus. This estimate is also close to the what **?** derive in their paper (-0.3186) for the impact of a lockdown on the R_t. Estimating β as a function of R_t, the value of β is assumed as 0.11 in the model. The intervention is made 45 days after the start of the second wave on 15/10/20. It is also assumed in this scenario that the vaccination program begins on 1st of January.

Table 2: Assumptions for each mitigation policy

Policy	β	Source
Unmitigated Scenario	0.232	Locatelli et al. (2021)
No Lockdown Scenario	0.135	Assumption made from value of R_t on 01/09/20
Early lockdown Scenario	0.110	Levelu and Sandkamp (2022)

3.4 Estimating number of deaths due to COVID-19

3.4.1 Estimating deaths from the SEIR Model

While the SEIR Model gives us the estimate of infections, translating infections into deaths involves using an Infection-Fatality Ratio(IFR). The IFR is the percentage of infections that result in deaths in the population, as represented in eq.7. The IFR may only enable us to arrive at a crude estimate of deaths as it is based on historical deaths due to COVID-19. Nevertheless it enables us to effectively compare mortality estimates across different scenarios we estimate.

$$infection\ fatality\ ratio = \frac{Number\ of\ deaths\ from\ a\ disease}{Number\ of infected\ individuals} * 100 \tag{7}$$

Since the IFR varies due to geographical location and the population age structure, for simplification, we can use the age-standardised IFR for The Netherlands derived from cov (2022). The age-standardized IFR during the second wave of Covid-19 was estimated to be 0.482 percent during the wave. To remove the impact of vaccination on IFR during this period, the authors exclude age-specific observations of sero-prevalence and deaths that occurred after vaccines were introduced. These estimates of IFR can therefore be applied to the infections derived from the SEIR model for the various scenarios, to estimate the deaths from those respective scenarios.

3.4.2 Estimating excess deaths from actual COVID data

For the scenarios derived from the SEIR model, the total deaths are estimated after applying the IFR to the total infections. For the actual Covid-19 situation in The Netherlands however, excess mortality data from CBS (2022) during the second Covid-19 wave will be used. The data was extracted from early September till the end of June as COVID-19, generating a two-week lag from the start of the second wave to account for the 2 week time lag between COVID-19 case and deaths (Testa et al., 2020). A total of 10898 excess deaths were estimated during this in the time period.

The data available for excess mortality is distributed across 3 age groups i.e. 0-64; 65-79; 80 years and above. The excess deaths obtained from CBS will be further split across 5-year groups based on the age patterns of COVID-19 deaths observed by the National Institute for Public Health and the Environment (RIVM). The excess mortality data is then estimated by gender based on the proportion of actual deaths by gender due to COVID-19 for the same respective week. These age proportions are also available by gender, enabling us to differentiate COVID-19 mortality at different ages by gender.

As shown in the Figure 2 below, excess mortality increases in the first two phases of the second wave (Sep 2020-Jan 2021) when Covid-19 infections were at the highest in the population. As described in an earlier section, the excess mortality increases due to a higher death rate amongst 80 years or older who are higher. Only for this age group can it be observed that more women die than men. This can attributed to the fact that women have a longer life expectancy than men, thus more women live above 80 years old. In the second phase of the second wave (Jan 2021- June 2021), the death rate amongst 80 years or older decreases leading to negative excess mortality. After this point however, the excess mortality amongst men remains higher than women until the end of the wave. It can also be noticed the deaths in the 0-64 age group remain high even in the last two phases of the second wave.

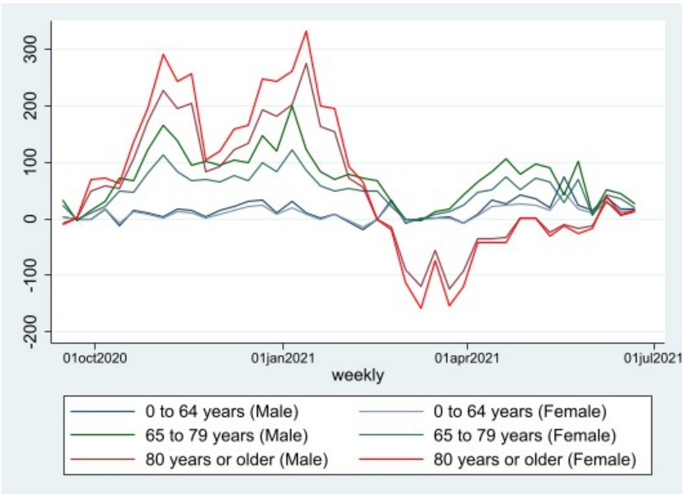


Figure 2: Excess Mortality in The Netherlands during 2020-2021 by age and gender

3.5 Estimating YLLs and QALYs lost

3.5.1 Estimating LE using a standard life table approach

The next part shifts to estimating the Years of Life Lost (YLL) and Quality Adjusted Life Years (QALYs) lost during the second wave of the pandemic. The approach is derived from that of Wouterse et al. (2022) and Briggs et al. (2021), using standard life tables accounting for the underlying health of the population.

Calculating life expectancy is a simple approach used to compare mortality at different ages over time for different sub-populations. The life expectancy for the Dutch population was derived from CBS Statline

(2022) which publishes period life expectancy tables. Life tables for male, female and the overall population in the year 2020 were extracted for Men and Women for the ages 0 to 99, displayed in *Appendix A*.

The approach to estimating Life Expectancy first starts by defining the probability of dying of any cause q(x) between the ages x and x+1. q(x) is calculated as the observed number of deaths in the selected period per 100 thousand of the average (actual) population of the same age and sex. From this we can calculate the number of persons at agex surviving to agex+1 ≥ 1 as l(x).

$$l(x) = 100000 * \prod_{a=1}^{x} 1 - q(a) \tag{8}$$

We can then calculate L(x) i.e., the life years lived between ages x and x+1. This is done for all age groups until a maximum life expectancy is assumed to be 99 years, yielding the life expectancy at each age group for the Dutch Population. T(x) is defined as the total number of person years lived above age x. Finally, Life Expectancy (LE) at age x is calculated as the ratio between T(x) and l(x), as represented in eq.11.

$$L(x) = \frac{l(x) + l(x+1)}{2} \tag{9}$$

$$T(x) = \sum_{u=x}^{99} L(u) \tag{10}$$

$$LE(x) = \frac{T(x)}{l(x)} \tag{11}$$

3.5.2 Adjusting for survival and underlying health

COVID-19 deaths are mostly concentrated in older individuals with pre-existing conditions such as COPD, Diabetes, Chronic Heart Disease, and amongst the remaining population. Under the RIVM COVID-19 death comorbidity prevalence rates published as a monthly report, 27.8 percent had diabetes, 25.5 percent COPD, and 16.5 percent had chronic heart failure. These proportions were characterized in a monthly report obtained from RIVM (2022).

Besides those with comorbidities, many persons who died of COVID-19 resided in nursing home facilities. Nursing home inhabitants have disabilities and multiple chronic conditions. Looking at the excess mortality in nursing homes during this same period, around 50 percent of the total excess deaths can be assumed to be from nursing homes. This data is obtained from the Ministry of Health, Welfare and Sport, who provide a weekly estimate of deaths occurring in care homes. Only looking at comorbidities does not capture their poor health and survival compared to the general population. Hence, living in a nursing home is listed as a separate condition.

For nursing homes, already generated figures from Wouterse et al. (2021) are used to calculate the remaining life expectancy. These figures were available from ages 65 and above for both male and female. The data can be found in *Appendix B*. To adjust for survival for comorbidities, a standardised mortality ratio (SMR) is used to capture the increased risk of dying due to a given comorbidity. The SMR is defined as the ratio between the observed death for a disease at age x and the expected deaths without the disease at the same agex.

The SMR rates for Diabetes and heart Disease are derived from Hoogenveen et al. (2017) and the SMR for COPD is derived from Hoogenveen et al. (2000). A Web plot Digitizer was used to extract the data from the graphs depicting excess mortality for the respective comorbidities. The excess mortality estimates are the same as Standardised mortality rates defined earlier. These graphs showed the variation in mortality for ages 50-100. For Ages 0-50 a constant rate is assumed, as the prevalence of disease in these age groups is extremely minimal. These rates are also listed in *Appendix C*

$$SMR(standard\ mortality\ rate) = \frac{Observed\ deaths\ for\ disease\ at\ age_i}{Expected\ deaths\ without\ disease\ at\ age_i} \tag{12}$$

Applying the SMR to probability of dying q(x), would risk the probability of dying exceeding one. Thus the instantaneous death rate i(x) is first estimated, before applying the SMR parameter to estimate the impact of the pre-existing comorbidity.

$$i(x) = -ln1 - q(x) \tag{13}$$

We then multiply the SMR of the disease derived for each age with the corresponding Life years lived between age x and x+1 i.e. L(x). Similar to the method in the previous sub-section, the SMR adjusted Life Expectancy at age x is calculated as a ratio of the sum of SMR* L(x) to the l(x) at age x. Thus, the number of life Years Lost per person is value of the remaining life expectancy at age x. Looking at the data again as a reference, a person with diabetes who died of COVID-19 on average loses 20 life years.

To adjust for differences in health, the quality of life for the different underlying health states are determined. The health states are calculated for different ages, ranging from 0 to 1, with 0 being poor health and 1 being perfect health. First, Quality of Life(QoL) estimates for the healthy population were derived from Janssen et al. (2019) for age group using time-trade off (TTO) to value health utility. These estimates are available in *Appendix D*. The estimates of QoL for the various underlying health conditions are derived from Wouterse et al. (2022) who calculated the EQ-5D values for these comorbidities in the Dutch population. The value for diabetes is assumed to be 0.8, representing that diabetic patients have a quality of life

80 percent of that of a healthy person. The various papers these assumptions are derived from are listed in *Appendix E*. Similarly, values for COPD and Heart Disease are 0.73 and 0.63. After obtaining, the SMRs, the QoL for different ages and comorbidities, the QALE at age a, for health condition h can be estimated as shown in eq.14.

$$\text{QALE}_{a,h} = \sum_{g=G}^{x} [\; q_{a,h} \prod_{a=1}^{x} e^{-(i(a)+SMR_h)} \;] \tag{14}$$

4 Results

The first research question to be answered in this thesis was, what were the number of YLLs and QALYs lost during the second wave of Covid-19 in The Netherlands during 2020-2021. Another subject this thesis also aimed to address, were the health outcomes under different mitigation scenarios. To answer these questions, this chapter first provides an analysis of the QALYs lost as a result of Excess Mortality in the pandemic using the methods mentioned in the previous chapter. Next, the health outcomes from various mitigation strategies are forecasted using a SEIR model framework as previously described. The final part of this chapter is a comparison of the YLLs and QALYs lost of the estimated policy scenarios with the actual scenario.

4.1 YLLs and QALYs lost in the Netherlands in 2020-2021

To assess the first research question, a number of steps were previously performed to ensure a systematic analysis of the data. Excess Mortality estimates are used instead of actual deaths to calculate the mortality burden during the second wave. Calculating Years of Life Lost then involved using standard life tables and adjusting for comorbidities in the population based on the gender and age distribution of these comorbidities in the population. Finally it was ensured that Quality of Life at different ages and due to prevailing comoribidites are adjusted in order to calculate QALYs Lost in the population.

First the YLLs was estimated for men, women. These estimates were then combined to reflect the outcomes for the total population. The estimate of YLL shows the remaining life expectancy due to Covid-19 based on the underlying health, age and sex of a person. At an individual level, the age and sex of a deceased person helps determine the Years of Life he/she has lost. At a population level, it helps to determine YLLs lost in the population. The results from the analysis show that a total of 76900 life years were lost during this period. That means an average of 7.052 Life Years were lost, assuming there were 10898 deaths in the population. *Figure 3* below shows the distribution of YLLs in the total population.

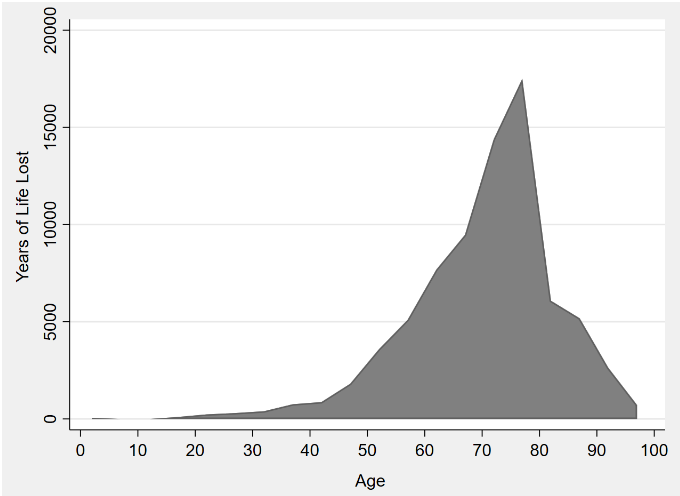
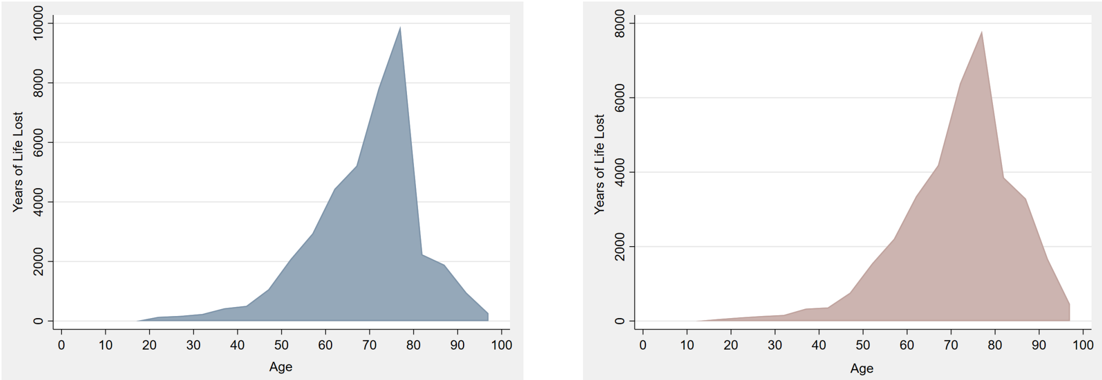


Figure 3: Years of Life Lost due to COVID-19 in the Dutch Population in 2020-21

The number of Life Years Lost varied across the population by age group. For age groups 0-20, there were hardly any Life years Lost, as there were almost no excess deaths in the population arising. For age groups 20-40, although the excess deaths assumed were close to 40, around 1700 Life years were lost. Looking at the data of this age class closely, the distribution of deaths amongst the 35-40 age group was the same as the 20-35 age group. From age group 40 onwards, the Life Years lost starts to exponentially increase, owing to the increased mortality risk for the general population and increased standard mortality rate for comorbidities. From ages 40-65, there are more than 19000 Years of Life Lost.

The largest share of YLLs however, occurred in the 70-80 age group, with close to 32000 QALYs being lost for this age class. Looking at the excess deaths, around 4100 people died in this age class. Alternatively, the 80-90 group experienced a steep drop in YLL lost but had a slightly lesser estimate of excess deaths of 3312. A total of around 11000 Life Years were lost for this population. This is less than half the number of YLLs compared to the 70-80 age group. This can be simply explained by the increased proportion of these deaths occurring in nursing homes and the lower remaining life expectancy associated with deaths in nursing homes.

When looking at the differences in YLL due to gender, 40260 Life Years are lost for males, whereas 36650 Life years are lost for females. On average 7.027 and 7.086 Life years are Lost for men and women respectively. This means that totally more Life Years were lost for men in the second wave, but since more men died than women during the second wave, the average for men was lesser than the average for women. The estimates are presented in *Figure 4* below.



(a) Male

(b) Female

Figure 4: Years of Life Lost due to COVID-19 in the Dutch Population in 2020-21 by Gender

It is noticeable that more YLLs are lost for females in the 80-90 age group compared to males. This can also be attributed to the fact that there were more excess deaths in this age category for females compared to males, with 2709 females and 2175 males deceased in this age category. Particularly during the first half of the second wave, most deaths also consisted of women in nursing homes during this period. Looking at the YLL estimates for gender gives us clues in the differences in the underlying health of the population. More women died than men in nursing homes, however women also had longer remaining life expectancy in these care homes compared to men. Thus, the remaining life expectancy was lower compared to the rest of the population, but there was a steeper drop in the total YLL for men compared to women.

After estimating YLLs, the QALYs lost were estimated, accounting for the Quality of Life at different ages and due to underlying disease. For the total population, 49500 QALYs are lost due to the second wave of Covid-19 in The Netherlands. An average of 4.546 QALYs were lost per Covid-19 death. The distribution of QALYs can be found in Figure 5 below. Once again, the 70-80 age group has the largest number of QALYs Lost and there is a sharp decrease in the QALYs lost after age 80, owing to the decrease in deaths, and a higher proportion of these deaths occurring in long term care. The rate at which QALYs are lost tends to decrease after age 60, owing to the decrease in Quality in Life brought on by an increase in persons developing complications. The slope of the QALYs Lost curve is more steeper compared to the YLL curve in *Figure 3*.

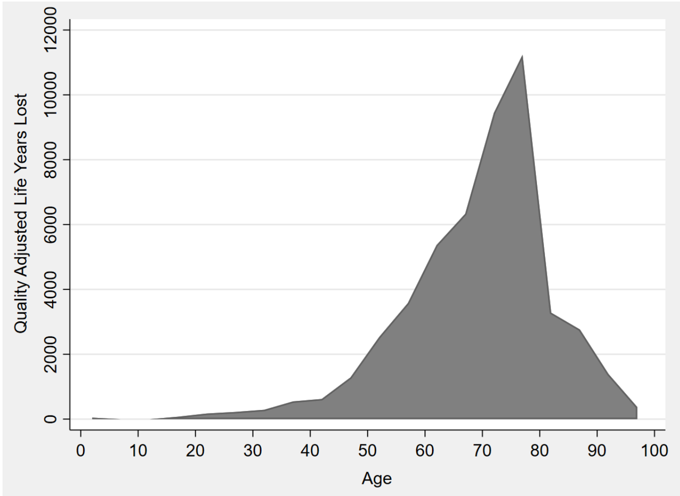
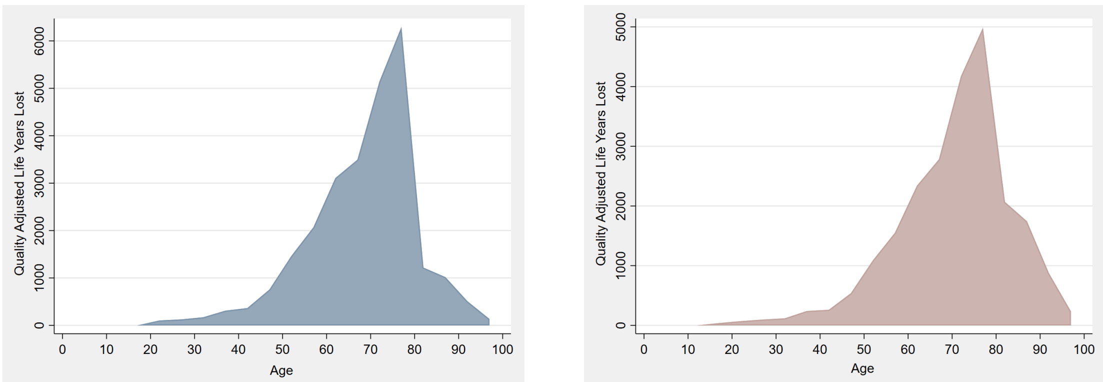


Figure 5: Quality Adjusted Life Years Lost due to COVID-19 in the Dutch Population in 2020-21

Observing the distribution of QALYs lost based on gender, in total, more QALYs are lost for men compared to women. Around 26300 QALYs are lost for men and around 23200 QALYs are lost for women during the second wave. On average however, this figure is 4.588 and 4.489 QALYs lost for men and women respectively. In contrast to the average YLL, the average QALYs lost is higher for men than women. The explanation for this polarity is that those remaining life years would have relatively had a lesser QoL compared to women, owing to the relatively higher risk for men of developing underlying diseases at older ages. This lower QoL is captured in the 80-99 age group, where there is a steep decline in the number of QALYs Lost compared to that of women for the same age group.



(a) Male

(b) Female

Figure 6: Quality Adjusted Life Years Lost due to COVID-19 in the Dutch Population in 2020-21 by Gender

4.2 Results from SEIR model simulations

The next subsection looks at 3 different scenarios that were derived using a SEIR Model. These scenarios include an *Unmitigated Pandemic*, *No Lockdown* and an *Early Lockdown*.

4.2.1 Unmitigated Scenario

The first scenario forecasted was an unmitigated second wave, assuming the government did not enforce any measures at the start of the second wave. This includes no efforts by the government to vaccinate individuals. A result of not having any measures would have led to increase in contacts, and a higher of 0.232. This is similar to the start of the first wave, where there were no measures in place. A result of these unmitigated measures would have led to the around 85 percent of the Susceptible population being infected at the end of the second wave.

What is noticeable in such a scenario is the rising rate of persons in the infectious population as a result of a faster spread of infection. As shown in Figure 7, The Susceptible population decreases at a rapid rate initially as persons move from a Susceptible to a Exposed/infected state. The persons then move from a Infected to Recovered state leading to a rapid increase in the recovered population. At the same time, the infections rise fast at the start leading to a higher peak of infections early on. The peak of the second wave would occur on 1-12-2020 after 90 days, where a maximum of 2.03 million people are infectious. Only after this point, does the Susceptible and Recovered populations stabilise, owing to the decreasing growth of infections in the population. The total estimate of infections in the period assumed in model, generates 13.96 million infections. On applying the age-standardized CFR of 0.482 percent, it is estimated that 67,300 deaths would have occurred in this unmitigated scenario.

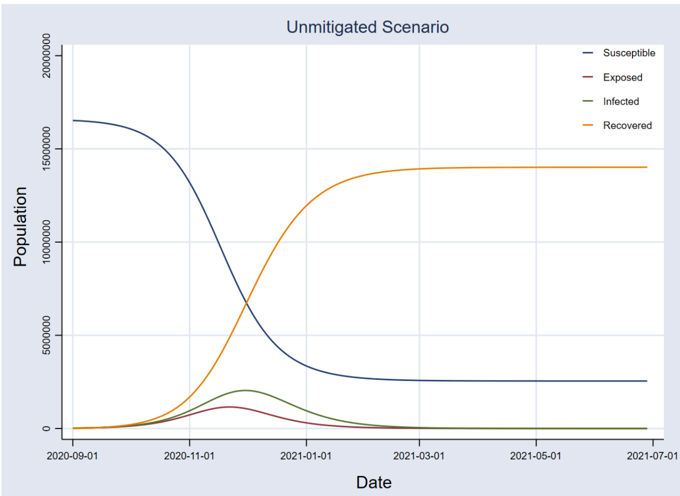


Figure 7: SEIR Model forecast of an unmitigated second wave

4.2.2 No lockdown

For this scenario, it is assumed that the number of contacts does not change at the start of the infectious period. This means that no additional measures were imposed by the government, which includes no additional measures such as a partial lockdown or a complete lockdown. What this scenario aims to measure is a situation which the mitigation measures were put into place before the start of the second wave remain fixed. Assuming that is 0.142 at start of the wave, A SEIR Model is forecasted, with only the number of infectious persons being shown in *Figure 8*.

Within this simulation, we assume that the government has an option to vaccinate individuals from January 1st. This results in two sub-scenarios, one with vaccination and one without vaccination. Also displayed in *Figure 8* is the size of the infectious population over time for the actual scenario. In can be noticed that the infectious population waxes and wanes over certain periods of time, as opposed to the SEIR model scenarios where there is a single peak. The SEIR model displays a situation where the number of contacts per infectious persons remain constant as opposed to the actual situation where the number of contacts per infectious persons increase/decrease every day.

For the scenario without vaccination, the results show that a total of 7,374,567 infections are generated, with around 55 percent of the Susceptible population remaining at the end of the wave. On applying the age-standardized CFR of 0.482 percent, it is estimated that 35545 deaths would have occurred in this unmitigated scenario. For the scenario with vaccination, a total of 4,992,712 infections are generated. Before 1st January a total of 1,661,616 infections occur. After 1st of January until the end of June, there are 3,331,096 infections in the population and 4,992,712 persons move from an Susceptible state to a Recovered state through vaccination. Applying the age-standardized CFR of 0.482, a total of 24065 deaths are estimated in this scenario.

Looking at *Figure 10* which compares both scenarios, vaccination leads to around 2.3 million less infections and around 11,500 lesser deaths. The peak of the infection also occurs 27 days before with vaccination, and this peak is 20 percent smaller in terms of total number of infectious persons in the population.
An alternative sub-scenario where the vaccination program started on 1st of February instead of 1st of January was also estimated. The scenario with delayed vaccination lead to 90,000 more infections and 4000 more deaths in the population compared to the earlier vaccination program.

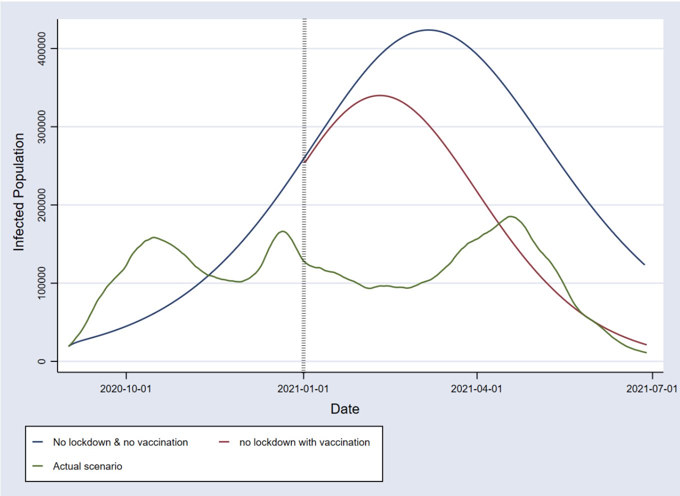


Figure 8: SEIR Model forecast of a scenario with no lockdown with and without vaccination

4.2.3 Early lockdown

For this scenario, it is assumed that the government imposes an early lockdown to prevent the rise of infections. AS discussed earlier in the previous chapter, the lockdown here assumes the same set of restrictions the Dutch government would have taken in December 2020. Assuming the lockdown is imposed on 15th October 2020, the is reduced to 0.108. As reflected in *Figure 9*, the number of infectious persons peaks on 19th November 2020 with 59,896 persons in the infectious population. On January 1st, 2021 it is once again assumed that the government starts vaccinating individuals. The infectious population continuous to decline at a steady rate after this point, reduced to only 2878 persons at end of June 2021.

Figure 9 shows the change in the total infectious population, with the early lockdown introduced 45 days after the start of the wave. In this scenario, a total of 1,241,780 infections are generated. This results in a total of 5,985 deaths. The peak of the infections occurs 77 days after the start at 67,950 persons in the infectious population. In this scenario, vaccination leads to 5.8 million persons being moved from a susceptible state to a recovered state. Compared to the actual scenario which is also visible in *figure 9*, the peak of the infectious population is lower and the slope of the decline in infectious persons is less steep compared to the actual scenario.

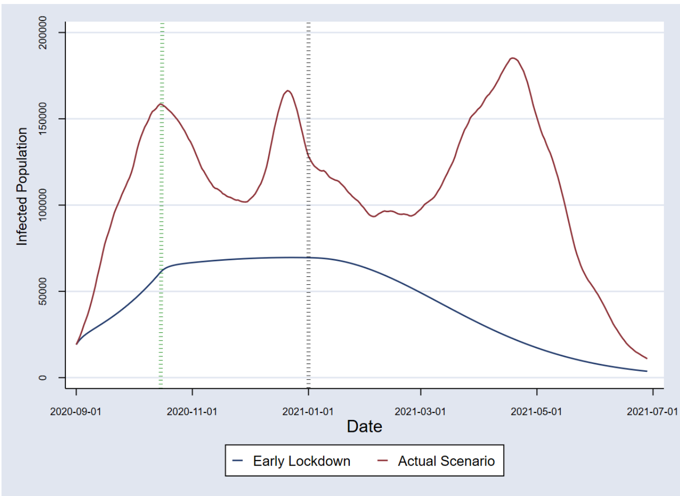


Figure 9: SEIR Model forecast of an early lockdown with vaccination

4.3 Comparing Health Outcomes under different scenarios

The final part of this results sections applies the average Life Years Lost and QALY lost estimates we earlier derived to the various scenarios generated in the SEIR Model. The main outcomes generated from these models was the number of deaths, however comparing the Life Years and QALYs Lost provides an more comprehensive overview of the health burden under these scenarios. The results of this comparison is presented in the table below.

The actual scenario is the value of Life years Lost for the overall population obtained in the previous section. The actual scenario resulted in 76,852 Life years being lost. Assuming the average YLLs and QALYs lost person, the total YLLs and QALYs can be calculated for the SEIR Model scenarios. Assuming an unmitigated pandemic, there would have been 474,641 Life Years Lost as a results of no mitigation measures in place. Not having a lockdown, would have led to 169,705 Life years being lost, which is double the amount of Life Years Lost under the actual scenario. Finally, imposing only an early lockdown after 45 days would have led to 42,209 Life Years being lost, which is less than the actual scenario. These figure are rounded up to the nearest hundred and compared in *Table 3*.

Table 3: Health Outcomes under different scenarios

Scenario	Infections	Deaths	YLL	QALYs Lost
Actual Scenario	–	11,000	76,900	49,500
Unmitigated Pandemic	13.9 million	67,300	474,500	305,600
No Lockdown	4.9 million	25,100	169,700	109,300
Early Lockdown	1.2 million	6,000	42,200	27,200

5 Discussion and conclusion

5.1 Key findings

This thesis aimed to estimate health burden from the second wave of Covid-19 in The Netherlands and also predict the health outcomes under various mitigation scenarios. The main findings from this thesis suggests that during the second wave, over 76,000 Life Years were Lost and close to 50,000 Quality Adjusted Life years were Lost. The results are also consistent with similar research, that the 70-80 age group had the most Life Years Lost and Quality Adjusted Life Years Lost in the population. On average, women lost more Life years than men, but men lost more quality adjusted years than women. An additional finding was that the number of Life Years Lost in the 0-64 population was substantially high owing the relatively high number of deaths in this age group in the second wave compared to the first wave of the pandemic.

In the different scenarios forecasted, more stringent mitigation measures led to a decrease in Life years Lost and QALYs Lost in the population. Implementing no mitigation measures on average would have lead to more than 400,000 Life years being lost in the population compared to the actual scenario that occurred in 2020-2021. Conversely, an early lockdown which continues throughout the remainder of the second wave, on average would have lead to 27,200 lesser QALYs being lost in the population. These scenarios when compared to the actual situation suggested that measures taken by the Dutch government were sufficient to reduce the spread of COVID-19 and reduce the health burden of the pandemic.

5.2 Strengths and limitations of study

The research methods used in this paper are novel and have been previosuly used to model the impact of vaccination strategies on the YLL and QALYs lost. This thesis adds to the existing literature, estimating the impact measures such as lockdowns and vaccinations may have on the mortality burden during an epidemic.

What makes this research unique is that it is a ex-post analysis of NPIs, while also investigating the overall health burden due to these NPIs. The mitigation scenarios forecasted are valuable in understanding the spread of Covid-19 and the extent of the mortality burden. Particularly, deriving parameters used in the model based on public health data sources and causal estimates help to provide a better understanding about the impact of mitigation measures.

Another strong point of this research includes the analysis of the health burden in the population, accounting for the underlying health amongst Covid-19 deaths. Calculating a naive estimate that does not account for underlying health would lead to significantly overestimating the loss of Life Years in the population due to Covid-19. Hence, by accounting for the underlying health this thesis provides an adjusted estimate of Life Years Lost and QALYs Lost.

This study does however have limitations, some of which can be addressed with better information and data sources. Firstly, the approach used to derive the Years of Life Lost assumes a fixed number of comorbidities in the population. In actuality, most Covid patients had other comorbidities such as obesity, autoimmune diseases, hypertension, chronic kidney disease and more than one comorbidity. The prevalence of these comorbidities also would have differed by gender and age, which was difficult to estimate without the appropriate data sources. This may lead to overestimating the YLLs and QALYs lost at younger ages and underestimating them at an older age.

Another limitation of this study, is that The SEIR model used does not account the for the capacity of the healthcare system in this setting. This means that the deaths estimated in the scenarios may be underestimated as it is assumed that persons move directly from an infectious state to a deceased state, without hospitalisation or being in an intensive care unit (ICU). Since the IFR was derived from actual COVID-19 data, using the same IFR for these SEIR model scenario does not account for the limited capacity of ICUs in the Netherlands, which would then increase the overall IFR if crossed.

Along with advanced compartmentalisation of health states, using a age-structured SEIR model would have allowed to test the impact of interventions on the change in number of contacts for each age group. This would lead to more accurate predictions of the number of infections. Using such a model would have also allowed for using different IFR rates for different age groups, the estimates for which were also available from cov (2022). These losses of deaths at each age could have then been used to forecast QALYs lost using the same method as done for the actual scenario in this paper. In context of the main findings of this thesis, using a age-structured SEIR model would have allowed to test the impact of interventions that could have reduced the large loss of Life years in the younger age groups during the second wave.

This study is supplementary to many other recent studies done on exploring the mortality burden of Covid-19. When comparing these results to Wouterse et al. (2022) the total QALYs Lost and YLL lost were moderately lesser than their total estimates. The average estimates for YLL and QALYs lost were higher than their paper, owing to the relatively lesser excess deaths occurring in the period examined in this paper. The average YLL was higher for women than men and the average QYLL was higher for men than women for both papers. In their paper, the age group with the highest estimate of QALYs lost is the 75-80 age group, which is line with the results reported in this thesis. The authors find that the age for the highest number of QALYs Lost is higher for men than women. In this thesis, it was only noticeable that women had more QALY losses in the higher age classes compared to men, but there was not sufficient data to show the QALYs lost at each age. There was however a difference in the magnitude, as the estimates for YLL and QYLL reported in this thesis were higher than their paper, which was done for the entire year of 2020. The supposition behind this is more Life Years were lost in for the age group 0-64 in the latter half of the second wave, which could also explain why the average YLL and QYLL estimates were higher.

The results can also be compared to Ainslie et al. (2021), who measure health burden in YLLs and Disability Adjusted Life Years Lost. Their results suggest that a total of around 105,000 Life years were lost between 27th February 2020 and 31st December 2020. Their estimate is much higher than Wouterse et al. (2022) as it does not account for underlying health. The authors however do highlight an important point that YLL contribution to disease was much lower in the second wave due to improvements in patient management and care. In addition to estimating the mortality burden, their paper also compared different vaccination scenarios in terms of YLLs and DALYs Lost. In a scenario where there is no vaccination at all, they estimate that 98,000 Life years will be lost from February 2021 onwards. Compared to one of the scenarios estimated in this thesis (*Figure 8*), no vaccination would result in close to 81,000 Life years being Lost. The results of the unmitigated scenario can also be compared to estimates of Ferguson et al. (2020) who find that an unmitigated pandemic with a R_0 of 2.2 would result in 460,000 deaths in the U.K during the first wave. When compared to the estimate in this paper, relative to population size, their estimate is almost twice the size.

5.3 Policy implications of study

Considering that a part of this research is focused on analysis of health policy, this thesis as a whole has several policy implications. First, an inquisition into the mortality burden suggested that the number of Life Years and QALYs Lost in nursing homes contributed to more than 25 percent of the total QALYs Lost during the second wave. Stricter policies for infectious disease control in nursing homes can prevent the spread of infection and considerably reduce the loss of life years in this vulnerable group. A policy recommendation to prevent the spread of infectious diseases in nursing homes as mentioned by van den Besselaar et al. (2022) would be to promote collaboration between public health services and nursing homes during epidemics and provide required training to staff and management of these care homes.

The majority of the QALYs lost in the population occurred in older individuals with underlying health conditions. Around 10 percent of the total QALYs Lost occurred in the middle aged men (40-60 years old). It is evident from other scientific papers such as Stefan et al. (2021) conducted that the onset of conditions such as hypertension, diabetes and obesity in the population has mainly contributed to the increased risk of dying from Covid-19. If the government focus on policies that supports better health and nutrition in adults, the risk of developing these conditions would considerably reduced.

The outcomes from the scenarios suggests that mitigation measures prolong the duration of an infectious wave but reduce the peak of the infectious population. This is also dependent on the compliance of these mitigation policies, something that could not be tested in the model. While it is not expected that every person in the population is expected to comply with these stringent policies, governments must aim to still implement them in a timely manner. The results from the SEIR Model simulations also show that an effective and timely vaccination program can undoubtedly reduce the mortality burden due to an infectious disease. Even a month in delay in the start of a vaccination program can lead to thousands of lives being lost.

Finally, this research may have implications on the way health policy are enacted for future epidemics. What these models consistently showed was the timely intervention of NPIs combined with an early and effective vaccination program resulted in a lower health burden in the population. There will still exist however compliance issues when such measures, therefore policy must strive to also improve compliance within the population.

What was particularly noticeable in this pandemic was the inconsistency in the message sent by the government when imposing these measures. As mentioned by Wallenburg et al. (2022), at the start of the second wave the Dutch government opted for a more tailored approach by providing regional authorities a greater say in the decision making process. For example, instead of implementing a national policy of the use of face masks in public areas, these were tasked to regional authorities who refused to take on this responsibility. This delayed the implementation of the use of face masks as a policy and could have contributed to reducing compliance in the population. Thus, a unwavering central message is also important when implementing these NPIs.

5.4 Unanswered questions and recommendations for further research

This research explored a novel infectious disease, the scientific knowledge of which is rapidly changing every day. It is acknowledged that Covid-19 also leads to long-term symptoms, leading to other physical and mental illnesses. Based on the severity of a COVID-19 infection, persons can even experience multi-organ effects or autoimmune conditions with symptoms lasting weeks or months after infection. From a health economic perspective, Long Covid has several implications on the quality of life of those who were severely infected by the disease. Accounting for future QALYs Lost due to infections can significantly alter the health burden of Covid-19 in the population.

A 'known unknown' is the duration of immunity post recovery. Limited data from other coronavirus infections suggest full immunity to reinfection is a matter of months rather than years for SARS and but it is not clear if those reinfected are again infectious to others or exhibit symptoms of infection that result in measurable morbidity. This makes models such as SEIR models less accurate as it assumes the susceptible population completely recovers from a virus. Thus incorporating re-infection period in an epidemiological model can be useful to generate more accurate outcomes of infections and deaths.

Further suggestions for research include a more detailed analysis of the proportion of comorbidities in the population. In the report by RIVM (2022) it was seen that pre-existing conditions in Covid-19 deaths also included various other comorbidities than Diabetes, COPD and heart Disease. Deriving the Standard Mortality rates for other these comorbidities, while also adjusting for the fact that some patients may have more than one would lead to a more accurate estimate of the adjusted QALYs Lost in the population.

In conclusion, this paper conceptualizes the overall health burden during the second wave of the pandemic in The Netherlands and also compares the outcomes of mitigation strategies to the actual scenario that unfolded during 2020-2021. This paper highlights the effects mitigation strategies have on reducing the health burden in the population, suggesting that timely implementation of mitigation strategies are essential.

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6 Appendix

6.1 Appendix A: Life table for Dutch Population without comorbidities

x	q(x)	d(x)	smrl(x)	smrL(x)	smrLEx	smrqL(x)	QALE	dQALY
0	0.00351	0.003516	100000	99824.5	81.84255	99824.5	75.51385485	44.394407
1	0.00042	0.00042	99649	99628.07	81.12906	99628.07	74.77808092	44.202254
2	0.00013	0.00013	99607.15	99600.67	80.16294	99600.67	73.80929082	43.868926
3	0.00013	0.00013	99594.2	99587.72	79.1733	99587.72	72.81882226	43.517683
4	0.00009	9E-05	99581.25	99576.77	78.18353	99576.77	71.82822493	43.161126
5	0.00006	6E-05	99572.29	99569.3	77.19052	99569.3	70.83464505	42.79744
6	0.00009	9E-05	99566.31	99561.83	76.19512	99561.83	69.83886538	42.426978
7	0.00004	4E-05	99557.35	99555.36	75.20194	99555.36	68.84510644	42.052213
8	0.00007	7E-05	99553.37	99549.89	74.20492	99549.89	67.84784036	41.669683
9	0.00003	3E-05	99546.4	99544.91	73.21008	99544.91	66.85255504	41.282653
10	0.00005	5E-05	99543.42	99540.93	72.21227	99540.93	65.85454567	40.888135
11	0.00006	6E-05	99538.44	99535.45	71.21585	99535.45	64.85781356	40.488507
12	0.00006	6E-05	99532.47	99529.48	70.22009	99529.48	63.86167526	40.08327
13	0.00009	9E-05	99526.49	99522.02	69.22428	99522.02	62.86547719	39.67193
14	0.00015	0.00015	99517.54	99510.07	68.23046	99510.07	61.87109059	39.255587
15	0.00014	0.00014	99502.61	99495.64	67.24062	99495.64	60.88029763	38.835323
16	0.00015	0.00015	99488.68	99481.22	66.24997	99481.22	59.88875206	38.408301
17	0.00016	0.00016	99473.76	99465.8	65.25983	99465.8	58.89766171	37.975198
18	0.0002	0.0002	99457.84	99447.89	64.2702	94475.5	57.90700683	37.535913
19	0.00023	0.00023	99437.95	99426.51	63.28295	94455.19	56.96849553	37.142226
20	0.00027	0.00027	99415.08	99401.66	62.2974	94431.57	56.03149202	36.743671
21	0.00031	0.00031	99388.24	99372.83	61.31409	94404.19	55.09649633	36.340519
22	0.00027	0.00027	99357.43	99344.01	60.33294	94376.81	54.16343424	35.932665
23	0.00024	0.00024	99330.6	99318.68	59.3491	94352.75	53.22793403	35.517125
24	0.00028	0.00028	99306.76	99292.86	58.36323	94328.21	52.29059778	35.09417
25	0.00027	0.00027	99278.95	99265.55	57.37944	92019.17	51.35511021	34.666174
26	0.00025	0.00025	99252.15	99239.74	56.3948	91995.24	50.44185465	34.254637
27	0.00035	0.00035	99227.34	99209.97	55.40878	91967.64	49.52735237	33.836129
28	0.00035	0.00035	99192.61	99175.25	54.428	91935.45	48.61753073	33.414625
29	0.0003	0.0003	99157.89	99143.01	53.44688	91905.57	47.70739054	32.98665
30	0.00043	0.00043	99128.14	99106.83	52.46277	91872.03	46.79456796	32.550451
31	0.00037	0.00037	99085.52	99067.19	51.48513	91835.28	45.88749889	32.111813
32	0.00038	0.00038	99048.85	99030.04	50.504	91800.84	44.97731199	31.664475
33	0.0005	0.0005	99011.22	98986.46	49.52301	91760.45	44.06723367	31.210576
34	0.00048	0.00048	98961.71	98937.96	48.54753	91715.49	43.16204644	0.9267775
35	0.00058	0.00058	98914.21	98885.52	47.5706	91666.88	42.25555159	30.288602
36	0.00057	0.00057	98856.84	98828.66	46.59792	92404.8	41.35280504	29.819595
37	0.00058	0.00058	98800.49	98771.84	45.62421	92351.67	40.44112296	29.334855
38	0.00079	0.00079	98743.19	98704.18	44.6504	92288.41	39.52932111	28.842857
39	0.00073	0.00073	98665.18	98629.17	43.6853	92218.27	38.62520435	28.349245
40	0.00076	0.00076	98593.15	98555.69	42.71685	92149.57	37.71807982	27.846133
41	0.00089	0.00089	98518.22	98474.38	41.74896	92073.55	36.8114118	27.335936
42	0.00093	0.00093	98430.54	98384.77	40.78571	91989.76	35.90878669	26.821243
43	0.00099	0.00099	98339	98290.32	39.82321	91901.45	35.00677777	26.299437
44	0.00113	0.001131	98241.64	98186.14	38.86218	91804.04	34.10600554	25.770886
45	0.00116	0.001161	98130.63	98073.72	37.90557	91698.92	33.20906005	25.237479
46	0.00148	0.001481	98016.8	97944.27	36.94901	87170.4	32.31208437	24.696214
47	0.00151	0.001511	97871.74	97797.84	36.00304	87040.08	31.46931756	24.199792
48	0.00174	0.001742	97723.95	97638.93	35.05673	86898.65	30.62623513	23.695902
49	0.00187	0.001872	97553.91	97462.7	34.11696	86741.8	29.78884201	23.189125

x	q(x)	d(x)	smrl(x)	smrL(x)	smrLEx	smrqL(x)	QALE	dQALY
50	0.00196	0.001962	97371.48	97276.06	33.17994	86575.69	28.9538178	22.676862
51	0.00242	0.002423	97180.64	97063.05	32.24412	86386.11	28.11980482	22.15798
52	0.00261	0.002613	96945.46	96818.94	31.32113	86168.86	27.29694031	21.640463
53	0.00283	0.002834	96692.43	96555.61	30.40178	85934.49	26.47720728	21.118017
54	0.00292	0.002924	96418.79	96278.02	29.48665	85687.44	25.6610875	20.590988
55	0.00315	0.003155	96137.25	95985.83	28.57153	85427.39	24.84493411	20.056386
56	0.00339	0.003396	95834.42	95671.98	27.66024	85148.06	24.03203678	19.516782
57	0.00381	0.003817	95509.54	95327.59	26.75263	84841.56	23.22226882	18.972031
58	0.0042	0.004209	95145.65	94945.84	25.85303	84501.8	22.41938211	18.425182
59	0.0049	0.004912	94746.03	94513.91	24.95996	84117.38	21.62206378	17.875182
60	0.00536	0.005374	94281.78	94029.1	24.08041	83685.9	20.83634236	17.327076
61	0.00622	0.006239	93776.43	93484.78	23.20748	83201.46	20.05622895	16.775972
62	0.00684	0.006864	93193.14	92874.42	22.3496	82658.23	19.28897427	16.22801
63	0.00749	0.007518	92555.7	92209.08	21.50008	82066.08	18.52875475	15.678409
64	0.00877	0.008809	91862.46	91459.64	20.65856	81399.08	17.77522423	15.126919
65	0.00915	0.009192	91056.82	90640.24	19.83692	80307.25	17.03855501	14.582321
66	0.01029	0.010343	90223.65	89759.45	19.01548	79526.87	16.30580659	14.034294
67	0.01123	0.011294	89295.25	88793.86	18.20799	78671.36	15.58473195	13.488947
68	0.01243	0.012508	88292.47	87743.73	17.40911	77740.94	14.87070485	12.942383
69	0.01367	0.013764	87194.99	86599.01	16.62193	76726.72	14.16629843	12.396912
70	0.01451	0.014616	86003.03	85379.08	15.84537	75645.87	13.47049592	11.851735
71	0.01676	0.016902	84755.13	84044.88	15.07131	74463.77	12.77630808	11.300719
72	0.01835	0.01852	83334.63	82570.04	14.31969	73157.05	12.10053778	10.758793
73	0.02015	0.020356	81805.44	80981.25	13.57802	71749.39	11.43245233	10.216611
74	0.02171	0.021949	80157.06	79286.96	12.84697	70248.25	10.77244351	9.6745731
75	0.02607	0.026416	78416.85	77394.69	12.12097	68571.7	10.11567229	9.1283397
76	0.0293	0.029738	76372.53	75253.67	11.43203	62460.55	9.488588808	8.6019499
77	0.03195	0.032472	74134.81	72950.51	10.76201	60548.92	8.932469669	8.1393541
78	0.03644	0.037121	71766.2	70458.62	10.1007	58480.66	8.383584442	7.6777569
79	0.04109	0.041958	69151.04	67730.34	9.463784	56216.18	7.854941095	7.2292568
80	0.04528	0.046337	66309.63	64808.38	8.847889	53790.95	7.343748053	6.7916215
81	0.05198	0.05338	63307.13	61661.78	8.243809	51179.27	6.842361376	6.3580096
82	0.05726	0.058965	60016.42	58298.15	7.668402	48387.47	6.36477403	5.9416732
83	0.06627	0.068568	56579.88	54705.11	7.103796	45405.24	5.896150508	5.5290617
84	0.07576	0.078784	52830.33	50829.12	6.57249	42188.17	5.455166438	5.1379545
85	0.08282	0.086452	48827.91	46805.94	6.070252	38848.93	5.038309138	4.7655217
86	0.09764	0.102742	44783.98	42597.63	5.573238	35356.03	4.625787128	4.3932929
87	0.11273	0.119606	40411.27	38133.49	5.122188	31650.8	4.251415985	4.0536712
88	0.12577	0.134412	35855.71	33600.92	4.709449	27888.77	3.908842782	3.7412636
89	0.1428	0.154084	31346.14	29108.02	4.315036	24159.66	3.581480082	3.4406392
90	0.16312	0.178075	26869.91	24678.4	3.950579	20483.07	3.278980497	3.1613972
91	0.17785	0.195832	22486.89	20487.24	3.623147	17004.41	3.007211663	2.9097103
92	0.19759	0.220136	18487.6	16661.11	3.298755	13828.72	2.73796681	2.6586643
93	0.21697	0.244584	14834.63	13225.3	2.987937	10977	2.479987364	2.4168743
94	0.24174	0.276729	11615.96	10211.94	2.67732	8475.911	2.222175285	2.1736978
95	0.26143	0.303039	8807.919	7656.592	2.371468	6354.971	1.968318763	1.932952
96	0.2832	0.332958	6505.265	5584.119	2.033908	4634.819	1.688143592	1.6648621
97	0.3166	0.380675	4662.974	3924.825	1.639939	3257.605	1.361148985	1.3485992
98	0.33196	0.403407	3186.676	2657.752	1.16804	2205.934	0.9694732	0.9653761
99	0.38587	0.487549	2128.827	1064.414	0.5	883.4633	0.415	0.415

6.2 Appendix B: Years of Life lost (LEx) estimates for Nursing Homes

x	Males	Females	Total
65	4.559644225	6.799603053	5.545226
66	4.44853231	6.633906591	5.410097
67	4.336328503	6.466581837	5.27364
68	4.223254323	6.297959133	5.136124
69	4.109527864	6.128363713	4.997816
70	3.995363132	5.958114715	4.858974
71	3.880969415	5.787524241	4.719854
72	3.766550691	5.616896476	4.580703
73	3.652305079	5.446526865	4.441763
74	3.538424324	5.276701351	4.303266
75	3.425093335	5.107695677	4.165438
76	3.312489753	4.939774756	4.028495
77	3.20078358	4.773192103	3.892643
78	3.09013684	4.608189335	3.75808
79	2.980703289	4.444995746	3.624992
80	2.872628177	4.283827939	3.648788
81	2.766048045	4.124889532	3.513411
82	2.661090576	3.968370932	3.380095
83	2.557874477	3.814449164	3.248991
84	2.456509421	3.663287778	3.120238
85	2.357096016	3.515036805	2.993963
86	2.259725819	3.369832781	2.870285
87	2.164481388	3.227798821	2.749306
88	2.071436372	3.089044756	2.631121
89	1.980655635	2.953667313	2.515812
90	1.892195408	2.821750347	2.403451
91	1.806103476	2.693365119	2.294097
92	1.722419395	2.568570616	2.187803
93	1.641174724	2.447413901	2.084606
94	1.562393294	2.329930514	1.984539
95	1.486091489	2.216144885	1.887621
96	1.412278546	2.10607079	1.793864
97	1.340956874	1.99971182	1.703272
98	1.272122382	1.897061878	1.615839
99	1.205764827	1.798105684	1.531552
100	1.141868158	1.702819305	1.450391

6.3 Appendix C: Standard mortality rates for comorbidities

Age	Diabetes		COPD		Heart Failure	
	Male	Female	Male	Female	Male	Female
0-4	0.001017	0.001017	0.014	0.014	0.0292	0.0292
5–9	0.001017	0.001017	0.014	0.014	0.0292	0.0292
10–14	0.001017	0.001017	0.014	0.014	0.0292	0.0292
15-19	0.001017	0.001017	0.014	0.014	0.0292	0.0292
20-24	0.001017	0.001017	0.014	0.014	0.0292	0.0292
25-29	0.001017	0.001017	0.014	0.014	0.0292	0.0292
30-34	0.001017	0.001017	0.014	0.014	0.0292	0.0292
35-39	0.001017	0.001017	0.014	0.014	0.0292	0.0292
40-44	0.001017	0.001017	0.014	0.014	0.0292	0.0292
45-49	0.001017	0.001017	0.014	0.013	0.0292	0.0292
50-54	0.001017	0.001017	0.013	0.013	0.0292	0.0292
55-59	0.001736	0.00098	0.014	0.014	0.0387	0.0359
60-64	0.002874	0.00157	0.017	0.017	0.051	0.045
65-69	0.008802	0.00513	0.03	0.03	0.0632	0.0566
70-74	0.015508	0.00976	0.04	0.04	0.0755	0.0728
75-79	0.062	0.0433	0.07	0.07	0.0968	0.0933
80-84	0.028742	0.02641	0.11	0.11	0.124	0.1195
85-99	0.040838	0.052	0.15	0.15	0.155	0.1379

6.4 Appendix D: Quality of Life Estimates for The Netherlands

Quality of life estimates for comoribidities

Age band	index	NL
0-17	0	1
18-24	18	0.95
25-34	25	0.927
35-44	35	0.935
45-54	45	0.89
55-64	55	0.89
65-74	65	0.886
75+	75	0.83

6.5 Appendix E: Quality of Life Estimates for Comorbidities

Quality of life: comorbidities

Comorbidity	Value	Source
Diabetes	0.799	Clarke et al. (2016)
COPD	0.733	Moayeri et al. (2016)
Heart Disease	0.639	King et al. (2016)
Nursing Homes	0.490	Makai et al. (2012)

6.6 Appendix F: STATA code for Simulations of Mitigation Scenarios

```
ssc install epimodels
ado update epimodels

*Unmitigated scenario*
  epi_seir, beta(0.232) gamma(0.105) sigma(0.2) mu(0.00) nu(0.00) susceptible(16524000) exposed(19145) infected(19145)
  recovered(0) days(300) day0(2020-09-01) steps(1)
  clear

 *No lockdown (without vaccination)
  epi_seir, beta(0.142) gamma(0.105) sigma(0.2) mu(0.00) nu(0.00) susceptible(16524000) exposed(19145)
  infected(19145) recovered(0) days(300) day0(2020-09-01) steps(1) nograph
  drop S E R
  tempfile nolockdown
  save `"`nolockdown'"'
  clear
 *No lockdown (with vaccination)
  epi_seir, beta(0.142) gamma(0.105) sigma(0.2) mu(0.00) nu(0.0027) susceptible(14830124) exposed(152363.08)
  infected(255274.34) recovered(1324528.4) days(180) day0(2021-01-01) steps(1) nograph
  drop   S E R
  rename I I_nv
  merge t using `"`nolockdown'"'

 *early Lockdown*
local interventiondate=30
local modelwindow=121
local betaA=0.142
local betaB=0.108

local notetxt = "Note: social distancing policy reducing intensity of "///+ "spread of the disease from {&beta}=
`betaA' to " /// + "{&beta}=`betaB' after `interventiondate' days."

local inicond0 "susceptible(16524000) "///+ "exposed(19145) "///+ "infected(19145) "///+ "recovered(0)"

epi_seir, beta(`betaA') gamma(0.105) sigma(0.2) mu(0.00) nu(0.00) `inicond0' ///days(`modelwindow') day0(2020-09-01) nograph

local mA `r(maxinfect)'
local d1=t[`interventiondate']
local inicond1 = "susceptible(`=S[`interventiondate']') " ///+ "infected(`=I[`interventiondate']') " ///
+ "recovered(`=R[`interventiondate']')"

label variable I "Infected, no intervention ({&beta}=0.142)"
sort t
tempfile tmp
save `"`tmp'"'
clear

local day1=string(`d1',"%tdCY-N-D")

epi_seir, beta(`betaB') gamma(0.105) sigma(0.2)`inicond1' ///days(`=`modelwindow'-`interventiondate'+1')
///clear day0(`day1') nograph

local mB `r(maxinfect)'

label variable I "Infected, with intervention ({&beta}=0.108)"

rename S SB
rename E EB
rename I IB
rename R RB

sort t
merge t using `"`tmp'"'
sort t
use actual_infections.dta
tsset t
tsline IB I
```