Modelling the Social Return on Investment

A System Dynamics approach for the Support of Patients with Cardiovascular Disease

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by

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I hope you enjoy reading my thesis.

Jeremy den Otter
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Executive Summary

Cardiovascular diseases (CVDs) are a leading cause of death globally, causing 38% of all premature deaths. Providing care for the patients who survive is considered a priority for healthcare managers. In the Netherlands, 1.7 million people currently are diagnosed with cardiovascular diseases. After experiencing and surviving a CVD event, patients require support to get their lives back on track. However, over the next years, the number of patients is expected to increase to 2.6 million people, creating a burden on the healthcare system. Moreover, the costs of healthcare have been increasing over the last few years, decreasing the accessible and affordable for the patients to receive care. Intervention is needed to keep the quality of life of patients high. However, most interventions focus on the prevention of CVDs, with no attention to patients that already diagnosed with cardiovascular diseases.

This research presents a model for the support of patients with cardiovascular diseases within the Netherlands. It is done in conjunction with Harteraad, a non-profit Dutch patient organisation that represents the interests of the 1.7 million patients. The model aims to explore the effect of interventions on the lives of patients while keeping the investment cost-efficient. As such, this research aims to answer the following research question:

Which interventions increase the social returns on investment for a patient organisation?

To successfully answer this question, four steps were taken. First, a literature study was conducted to find potential candidate interventions that Harteraad can implement. The results from the literature study suggest that the priority lies in interventions on physical activity, mental health and medication adherence.

In the second step, a causal loop diagram (CLD) was built that maps the interventions to outcomes. For this research, the main outcome variable is the social returns on investment (SROI). SROI measures value creation on a social, environmental and economic level. Secondary outcomes include deaths, hospitalisations, and quality of life. All three of which are used to calculate the SROI. The CLD shows that the interventions affect the outcomes by improving patient behaviour. Whether that is in more exercise, seeking mental support or medical adherence.

In the third step, a System Dynamics model was developed to simulate the economic effect of different interventions. Population data were retrieved from the Hartstichting, whereas data sources on input values were found in academic literature. The latter being a source of uncertainty, as healthcare systems across countries cannot be directly compared. So in the fourth step, uncertainties were incorporated into the SD model and tested systematically.

The results for the simulation show that the SROI is positive for six interventions. As such, the recommendation is to invest in either of those interventions. More specifically, for physical activity, the efficient interventions are *"Active-at-Home"*, *"Video Gaming"*, and *"Group-Based Training"*. For mental health, the efficient interventions are *"Care Coordination"*, *"Cognitive Behavioural Therapy"*, and *"Telemedicine"*. Lastly, for *"CombiConsult"*, the recommendation is to offer additional mental support as well to create social return.

Although the model is able to give insights into potential interventions, more research is required. The model is only a simplified representation of the real world. Data was either lacking or outdated, creating nuance in the model results. As such, the model cannot be used to give the optimal solution. These nuances thus need to be addressed in future research.

Despite the limitations of the model, the research provides societal and scientific contributions. The research shows that system dynamics modelling is a suitable method to model the support of patients. Moreover, the model is able to determine if interventions are cost-efficient while increasing social benefits to the patient. This research furthermore adds a contribution by performing a systematic uncertainty analysis and so on, offering aid in robust decision-making. Lastly, the model is suitable to be used in different countries under different healthcare systems. As such, this research contributes to the research on patient support.

Contents

List of Figures

List of Tables

Nomenclature

Abbreviations

Abbreviation	Definition
CVD	Cardiovascular disease
WHO	World Health Organization
SROI	Social Return on Investments
NPV	Net Present value
QoL	Quality of Life
SD	System Dynamics
EMA	Exploratory Modelling and Analysis
NVVC	Dutch Society of Cardiology
VGZ	Stichting Volksgezondheidszorg
CC	CombiConsultation
IZA	Integraal Zorgakkoord

1
Introduction

Cardiovascular diseases (CVDs) are a leading cause of death globally (Namara et al., 2019). According to the World Health Organization (WHO), an estimated 17.9 million people died from CVDs in 2019, representing 32% of all global deaths. Of these deaths, 85% were due to heart attack, stroke and heart failure. Out of the 17 million premature deaths (under the age of 70) due to non-communicable diseases in 2019, 38% were caused by CVDs (World-Health-Organization, 2021). A large portion of CVD-related deaths occur in low- and middle-income countries (Walli-Attaei et al., 2020; Yuyun et al., 2020) where the death rate has remained unchanged over the last thirty years (Jagannathan et al., 2019). However, this does not mean that the problem does not exist in the Western world. Mehta et al., 2020 argue for example that the stagnation of the US life expectancy is caused by CVDs, outpacing the effects of all other causes of death. In recent years, the outbreak of COVID-19 made it worse for these patients, since patients with cardiovascular deceases proved most vulnerable to severe infection (Chilazi et al., 2021; Clerkin et al., 2020). Despite the outbreak of COVID-19 and its subsequent limitations on personal contact, providing care for patients with CVDs remained a priority for healthcare managers (Ganatra et al., 2020).

CVDs are common in the Netherlands as well. 1.7 million people (or 9.7% of the Dutch population) suffers from CVDs (Hartstichting, 2021). Around 27% of the total deaths in the Netherlands can be attributed to CVDs, making it the second most common cause of death after cancer (Leening et al., 2014). Patients with one type of CVD have a high risk of another, co-occurring CVD or other chronic diseases (Kendir et al., 2018). As such, around 400,000 people are hospitalised due to CVD every year (Leening et al., 2014).

In the Netherlands, however, there is the ongoing issue of increasing costs. So in 2022, the Dutch government enacted the *Integraal Zorgakkoord* (IZA). The goal of IZA is to keep healthcare at high quality while still being accessible and affordable for the patients (Ministry of Health and Sport, 2022). In many countries, including the Netherlands, patient representative organisations exist that act as collective bodies representing the needs and interests of patients with certain conditions. One such organization representing those patients is Harteraad. Harteraad is a Dutch patient organisation representing the interests of the 1.7 million people with cardiovascular diseases. Harteraad aids those people in getting their lives back on track and helps them in their daily life (Harteraad, n.d.-c). Harteraad furthermore can offer guidance to the patients they represent to change the patients' behaviour for their own safety. These so-called interventions aim to improve the lifestyle of patients by reducing risk factors for further CVD-related complications. Risk factors include smoking, alcohol abuse, obesity, and lack of physical activity (Kilkenny et al., 2017). For patients that already experienced and survived a CVD-related event, poor medication compliance is another risk factor (Frishman, 2007).

Different solutions to improve the lifestyle of the Dutch population have already been taken. For example, the Dutch Government has enacted the *Nationaal Preventieakkoord* with ambitions for the year 2040 (Ministry of Health and Sport, 2018). Measures include partial smoking bans (Willemsen and Been, 2022), stricter control on unhealthy food advertising (Van Trier et al., 2021) and so on. In general, the health-related decisions made by the government focus on the entire Dutch population. Yet the responsibility for decision-making among specific patient groups, such as CVD patients, does not lie on the government. This project, however, does focus on a single patient group. The final decision hereby is made by Harteraad, not the government. Moreover, Harteraad is a non-profit patient association. As such, the income comes from donations (Harteraad, n.d.-c) and the budget is limited. So for Harteraad, it is important that intervention should be problem-solving and cost-efficient. Yet it remains unclear what the impact of those interventions is.

1.1. Problem statement

This project is done in conjunction with Harteraad. Harteraad wants to support the CVD patients they represent. However, the financial burden of investing lies on Harteraad themselves. The first problem is that currently, it is unclear what kind of intervention Harteraad can implement. Furthermore, it is unclear if these interventions – when found – will be cost-efficient. An intervention is only considered useful if the benefits outweigh the costs; and have positive social gains. Furthermore, the social gains for the patients need to be higher than the costs of investments by Harteraad. The interventions thus need to be evaluated on an economic scale in order to choose the most efficient intervention. Different approaches of economic evaluations are being used in the healthcare system. Therefore, in the next sections, the different approaches are described, including their usefulness within the healthcare sector.

1.2. Economic Evaluation in the Health Interventions

Economic evaluation is a technique that was developed by economists to aid in the decision-making process when a choice has to be made between multiple options (Robinson, 1993b). Common techniques include cost-minimalization analysis (CMA), cost-effectiveness analyses (CEA), cost-utility analyses (CUA) and cost-benefit analyses (CBA) (Evers et al., 1997). In the health care system, additional attention is given to promoting efficiency and equity (Shiell et al., 2002). Therefore, not only costs, but also the benefits – in for example Quality of Life (QoL) – are important to measure. As a result, this leaves CBA as the only potential option (Robinson, 1993b). Over time, however, other types of economic evaluation techniques have surfaced, including ROI (Masters et al., 2017) and later SROI (C. M. Laing and Moules, 2017). In this section, all three types of economic evaluation are described in light of this project.

1.2.1. Cost-Benefit Analysis

Cost-Benefit Analysis is an economic evaluation method that seeks to compare the inputs (costs) and the output (benefits) with each other (Robinson, 1993a). Since both costs and benefits are measured in monetary units, it is possible to determine if an intervention is desirable from a societal viewpoint (Johannesson and Jönsson, 1991). This means that the foundation of CBA lies in welfare economics, which seeks to evaluate the overall well-being of a society (Boadway, 1974). The selection criteria for the decision-maker is to choose interventions for which the benefits exceed the costs (Robinson, 1993a). To evaluate a project using the CBA technique, it is important to build a model that predicts the total effect on the state of the total economy (Drèze and Stern, 1987). This whole process however is not easy (Robinson, 1993a). It is especially difficult to measure health changes in monetary terms (Johannesson and Jönsson, 1991). An often-taken shortcut to this problem was to introduce a Willingness to Pay (WtP) or Willingness to Accept (WtA) metric (Bala et al., 1999) in the form of a survey.

All in all, CBA might not be a suitable evaluation technique for healthcare modelling. First, CBA expects the modelling of the total economy, while this project only focuses on a narrow topic, namely CVD patients within the health care system. We need a technique that models just a local economy. The second issue arises in the use of WtP. WtP is defined as the maximum price a buyer, customer, or user accepts to pay for a given good or service (Le Gall-Ely, 2009). However, the costs of services Harteraad offer are not paid by the patients. Moreover, since the group consists of patients with deceases, the whole metric is prone to bias (Loewenstein, 2005). Yet, the most important disadvantage of CBA is that it only works when every impact can be monetized (Browne and Ryan, 2011). As a result, CBA may not quantify all impacts correctly, as not every variable has a market price. This project regards the life of patients with deceases, which includes factors like deaths. A wrong assessment of quantifying impacts may have disastrous results (Malla et al., 2011). As such, it should be clear that this project requires a different economic evaluation method.

1.2.2. Return on Investment

A second tool to evaluate the impact of interventions in the health sector is the return on investment (ROI) (Masters et al., 2017. Where CBA compares the benefits with the costs, The ROI seeks to compare the profits following an intervention with the total costs (Gargani, 2017). This means that ROI can be seen as purely for financial analyses focusing on profit maximization and cost-savings (Goetzel et al., 2005; Edwards and Lawrence, 2021). Consequently, the ROI sees its usage in the health care system to find room for cutbacks (Masters et al., 2017). Furthermore, this technique solely takes economic metrics into account; all social and cultural factors are left out (Gargani, 2017).

While the ROI measures the creation of economic value, it excludes the social context. Since Harteraad is non-profit – and ROI is used for profit maximization – it is not a suitable evaluation tool for this project. What is needed is a tool that includes other types of factors and which suits a patient organization. This tool is known as the social return on investment (Gargani, 2017).

1.2.3. Social Return on Investments

A third tool to measure the performance of an intervention is the Social Return on Investments (SROI). SROI is used to assess the value created by human activity on a social, environmental and economic level (Nicholls, 2017). The combination of those types of factors is also known as the 'triple bottom line' approach (Millar and Hall, 2013; Banke-Thomas et al., 2015) and thus might include factors that are not easily monetizable (Edwards and Lawrence, 2021). Because the SROI measures social impact, it is increasingly being used by non-profit (voluntary) organizations (Maier et al., 2015). This includes the medical sector, where SROI analysis includes both health and non-health factors (Hopkins et al., 2023). These two properties are what make the SROI tool different from the standard cost-benefit analysis (CBA). Yet, according to Edwards and Lawrence, 2021, an SROI can be considered as a localised CBA. In the end, performing an SROI analysis can be used for (1) priority setting; (2) resource allocation; (3) stakeholder relationship building and (4) offering a management tool (Banke-Thomas et al., 2015).

Carrying out an SROI analysis involves six stages, as described by C. M. Laing and Moules, 2017:

1. **Establishing scope and identifying key stakeholders**. Also known as the recruitment of participants. Stakeholders are those who experience change. In this research, they consist of Harteraad itself and the patients with CVDs that Harteraad represents. Furthermore, support can be offered by nurses, therapists, and trainers.
2. **Mapping outcomes**. This part considers data collection in the form of developing an impact map. Hereby the relationship between input, output, and outcomes is described to visualise what differences an intervention makes.
3. **Evidencing outcomes and giving them a value**. In this stage, all variables are being monetised. In an SROI, proxy variables are used to monetise factors without a market price (Arvidson et al., 2013).
4. **Establishing impact**. Changes that would have happened anyway or were the result of other factors including actors outside the scope of the research are taken out of consideration.
5. **Calculating the SROI**. In this stage, the SROI ratio is calculated, by taking the net present value (NPV) of the investment and dividing it by the total costs of the investment. Hereby, the NPV is the difference between the social benefits and the social costs, see equations 1.1 and 1.2.

$$SROI\ ratio = \frac{Net\ Present\ Value\ (€)}{Value\ of\ Investment\ (€)} \tag{1.1}$$

With:

$$NPV = Present\ Value\ of\ Benefits\ (€) - Present\ Value\ of\ Costs\ (€) \tag{1.2}$$

The SROI ratio describes the social value creation in monetary units per one monetary unit of investment. The last step in stage five is the sensitivity analysis.

6. **Reporting, using and embedding**. Finally, in the final step, all the findings are shared with the stakeholders.

1.3. Prior Work

The usage of an SROI analysis for patient groups in the health sector is still relatively new. A literature research on SROI analysis in healthcare only shows 26 articles in total. Hereby, only two articles were published before 2018 (Bhaumik et al., 2013; Daems et al., 2014). These studies include a wide variety of patient groups. This includes diseases such as cancer (Pazderka et al., 2022; Merino et al., 2022) and diabetes (Daems et al., 2014; Jalkanen et al., 2021); disorders like haemophilia (Soto et al., 2022), epilepsy (DiLorenzo, 2021) and dementia (Hartfiel et al., 2022; Jones et al., 2020; Prendergast et al., 2022; Willis et al., 2018), and patients suffering from mental illness (Makanjuola et al., 2022; Piper et al., 2021; A. Foster et al., 2021; Pazderka et al., 2022). Regarding CVDs, there is a single article from Spain (Merino et al., 2020) that focuses on patients with heart failure.

Of the 26 projects, most were conducted in Europe, with most of them in the UK (n = 8), Spain (n = 7), Italy (n = 2) and Finland (n = 1). SROI also sees its usage in the Anglo-Saxon countries of the USA (n = 2), Australia (n = 1) and Canada (n = 1). Only the articles from Lophongpanit et al., 2019 and Tanaree et al., 2019 were conducted outside the aforementioned regions, with these case studies focusing on Thailand.

For the actual SROI analysis, different methods are being used. The most common method is the standard economic model, in which the research team go through the six steps as described in section 1.2.3. The most common way to do the calculation is by spreadsheet models using Microsoft Excel (Hyatt et al., 2022; DiLorenzo, 2021). Hartfiel et al., 2022 on the other hand, used a Theory of Change model, while Jalkanen et al., 2021 developed a Markov Model. The main focus of such models lies more on the strength of the connection between input and output, and not on the monetary value per se. The models ineffectively show the underlying behaviour of patients that Harteraad sees to change for the better. Furthermore, depending on the focus of the research, the most common objective of doing an SROI analysis is to estimate or forecast the cost-effectiveness of interventions. However, it is also possible to determine the SROI ratio after an investment has already been made (Pazderka et al., 2022, Piper et al., 2021, and Jones et al., 2020). So it can be concluded that there are two types of SROI analysis: (1) evaluative, which is conducted retrospectively and (2) forecast, which predicts how much social value will be created. This matches with the distinction found by Gosselin et al., 2020. This research fits better in the former group of articles, whereby SROI will be used for estimations and forecasting of proposed interventions. However, one thing that is lacking in these articles is the trade-off between healthcare support and healthcare costs. Only one article (Bhaumik et al., 2013) specifies the limited budget for making investments.

One important aspect of performing an SROI analysis is to be aware of uncertainty. The higher the level of uncertainty is, the lower the reliability of the results (Macdonald and Strachan, 2001). Consequently, reducing the strength of the SROI (Nielsen et al., 2021). The first major uncertainty regards the use of financial proxies to monetize non-monetary factors (Nielsen et al., 2021). Consequently, the development of proxy factors is prone to bias and perceptions of the organization itself (Maier et al., 2015). Cooney and Lynch-Cerullo, 2014 have shown that a small variation in proxy values can drastically change the outcome of the SROI analysis. A second form of uncertainty lies in the choice for social discount values. As seen in equation 1.1, all benefits are discounted into the present value. To accurately estimate the present value, a sound choice for the social discount rate needs to be made. In the case that benefits accrue long into the future, the magnitude of the benefits is highly influenced by the choice of the discount rate (Kousky et al., 2019). Furthermore, this value depends on the country where the case study is conducted. For example, in the UK a discount value of 3.5% is recommended (Banke-Thomas et al., 2015), while in the USA the Office of Management and Budget suggested 7% (Kousky et al., 2019). In the healthcare system, a third type of uncertainty is prevalent, uncertainty in human behaviour and psychological functioning among patients (Rosen et al., 2007).

Due to these types of uncertainties, assumptions have to be made in either the proxy value, the discount rate or other input variables (Lingane and Olsen, 2004). A common technique to deal with uncertainty in economic evaluation is a sensitivity analysis (sa) (Yates and Marra, 2017). Some articles contain an extensive sensitivity analysis (Lawson et al., 2022, Fowler et al., 2020 and Y. Wang et al., 2021). However, for the prior studies using SROI, the quality of the uncertainty analysis is lacking. The detailed steps taken in the SA differ across the articles. For example, Merino et al., 2022 and Carretero et al., 2020 both used SA to develop three scenarios (one where all model parameters are set to the worst value, one for the best possible values and the reference scenario). Another method is doubling and halving each uncertain variable (Pazderka et al., 2022). However, some articles completely skip the sensitivity analysis (Hartfiel et al., 2022; DiLorenzo, 2021) despite its clear importance in the SROI analysis (Krlev et al., 2013).

In conclusion, there is a wide variance in the quality of different SROI analyses. To aid Harteraad in their support for patients in a cost-efficient way, we need a model that also captures the behavioural choices made by patients and different types of uncertainties that come into play.

1.4. Research Gap & Research Question

1.4.1. Research Gap

Multiple research gaps can be identified. The first research gap is a lack of a complete overview of possible interventions regarding the support of patients. Most research focuses on profit-maximizing or prevention of CVDs among the healthy population. This differs from the goal of Harteraad to support and care for the patients they represent. As a result, a knowledge gap exists in the economic evaluation of those interventions when found. Hereby, the goal is to know if the interventions are cost-efficient for Harteraad since they are the main investor. The third research gap relates to the uncertainty that underlay in an SROI analysis. A full exploration of uncertainties in modelling SROI is lacking, as such there is a gap in the usage of a thorough sensitivity analysis in studies regarding calculating the SROI.

1.4.2. Research Question

The overall objective of this project is to explore different interventions from Harteraad to see which increases the social returns of CVD patients and furthermore, how it does so. Hence, the following research question has been formed.

Which interventions increase the social returns on investment for a patient organisation?

To aid Harteraad in their decision-making, a model will be developed that maps the impact of their interventions to different outcome metrics that all attribute to the social returns. The result will be a value, the SROI. The effects will be clear in both the short-term and in the long-term. Moreover. the results will be tested for uncertainty to see when changes in output happen. Consequently, different strategies can be formed to offer the best guidance to their patients.

1.5. Thesis Outline

Chapter 2 is the methodology. The RQ will be split into different sub-questions and the research approach to answer those will be described. This chapter also introduces the modelling method chosen for this project. In Chapter 3 an extensive literature review will be conducted. This literature review aims to identify useful interventions for Harteraad. Chapter 4 describes the system on a conceptual level. Within this chapter, the relationship between the interventions and outcome measures is identified. Based on the conceptualisation, a formal model is built. The description of this model (and how it works) can be found in chapter 5. The model verification and validation of the base model can also be found here. Chapter 6 then contains the specifics on how to implement and choose interventions for experimentation. In chapter 7, the experiments are described, including the value range of uncertainty within input variables. Chapter 8 is the results, whereby the SROI is determined for the different types of intervention under uncertainty. The results are analysed and discussed in 9. Finally, chapter 10 is the conclusion, whereby the main research question is answered and the contribution of this research on societal and scientific level is detailed.

2
Methods

This chapter describes the methods used to answer the research question as stated in chapter 1.4. Since the RQ is quite broad, it is split into multiple sub-questions. These sub-questions are chosen in such a way that answering all of them results in answering the main RQ. In section 2.1 the sub-questions are stated as well as the method to answer each of them. Section 2.2 describes the background of the chosen modelling technique and a general understanding of the type of interventions employed in healthcare. This will include a first overview of the metrics employed in the model.

2.1. Sub-Questions

First, let us repeat the main research questions:

Which interventions increase the social returns on investment for a patient organisation?

In this particular project, the patient organisation is Harteraad who focus on patients with cardiovascular disease. This leads to the first sub-question:

Sub-question 1: *What are the available different interventions from Harteraad for the treatment and support of CVD patients?*

To find the options Harteraad has to offer guidance to their patients, a literature review is conducted. First, it is important to find out what Harteraad already does for their support in patients and where their priorities lie. For which their website (Harteraad, n.d.-c) is used. Secondly, the literature review explores which interventions are also being invested in between similar organisations in different countries. This will result in a list of potential interventions that Harteraad can implement. Lastly, interviews with people from Harteraad will show which other interventions might be of interest. All in all, answering sub-question 1 outputs a full list of potential interventions.

With a full list of interventions complete, it is important to show how they increase social returns. In other words, the second sub-question is:

Sub-question 2: *How do different interventions from Harteraad create social return?*

The goal of answering this sub-question is a mapping which shows the relationship between the interventions from sub-question 1 and different performance metrics described in section 2.2. We are furthermore interested in the mechanisms that alter the behaviour or lifestyle of patients following an intervention.

Since this project contains an SROI analysis, all the inputs (interventions) and outputs (performance metrics) need to be monetized (Edwards and Lawrence, 2021). So proxy variables are included in the model to show how the SROI ratio is determined. As such, this sub-question matches with stages two and three of an SROI analysis (C. M. Laing and Moules, 2017).

The specific method to answer the second sub-question is by developing a Causal Loop Diagram (CLD). A CLD aims to map complexity within a system utilizing causal relationships (McGlashan et al., 2016). The relationships between these variables in a CLD are shown with arrows, which indicate how one directly affects the other. Furthermore, a CLD shows polarity, which indicates if connected variables move in the same direction (positive or) or opposite direction (negative or). So a CLD allows us to see not only understand the effect of interventions on social gains but also if this effect is beneficial or not for the patients.

A CLD is thus a method to show the structure of the system. By including feedback loops (in which one variable eventually loops back to itself) and delays (in which an effect is only seen after a certain period has passed) a CLD shows the dynamics of a system (G. P. Richardson, 1999). However, for modelling this problem in an uncertain world, we need to go one step further (Stankov et al., 2021). This leads to the third sub-question:

Sub-question 3: *How can a system dynamics approach be used to test the effect of different interventions?*

For this sub-question, a System Dynamics (SD) model is developed using Vensim. SD is a simulation modelling technique to develop, understand and analyse a simplified representation of a real-world system (Sterman, 2002; Forrester, 1994). This method is often used for forecasting, resource allocation and health management within the health care system (Recio et al., 2018). Other than feedback loops and delays, an SD model incorporates stocks and flows to show accumulation or depletion over time.

For the development of an SD model, a modelling cycle is followed. The cycle consists of six stages (Martinez-Moyano and Richardson, 2013) of which there is overlap with the stages of an SROI analysis:

1. **Problem Identification and Definition**: This step includes the problem of the client, the scope, and purpose of this research. So this step is already complete.
2. **System Conceptualisation**: This step consists of the formulation of a dynamic hypothesis and the development of a CLD. Both aspects will already have been undertaken to answer sub-question 2.
3. **Model Formulation**: The development of the actual SD model happens in this step. The model should strive for clarity and simplicity (Martinez-Moyano and Richardson, 2013)
4. **Model testing and Evaluation**: First the model is tested, which includes the verification and validation of the model (Kleijnen, 1995). In the verification, it is checked if the final model is consistent with the CLD and description of the model. With validation, the SD model is checked to see if it is an accurate representation of the real-world system. The last aspect of this step is the sensitivity analysis. In this research, the SA is used to deal with uncertainty. As such, major attention is given to the sensitivity analysis. A separate sub-question will be formulated, and the method to answer this sub-question will be as well.
5. **Model Use, Implementation, and Dissemination**: The last step of the modelling cycle corresponds with the last step of the SROI analysis. The model is run, and the results will be documented and shared with Harteraad.

As stated in step 4 of the modelling cycle, a sensitivity analysis will be performed. The model however contains uncertainty. Due to the limited duration of this project, multiple assumptions need to be made. Examples include assumptions regarding values of parameters, equations between variables and possible future states. Collaboratively, these uncertainties are known as deep uncertainty (Walker et al., 2012). Specifically to this project, there is also uncertainty in connecting a single intervention with certain outcomes (Kousky et al., 2019). Factors outside the scope of the organization might affect the outcome value as well. Consequently, new assumptions will have to be made, which then come back in the SD model as well. All these examples induced uncertainty in the model, hindering the validity and usability of the model. This leads to the fourth sub-question:

Sub-question 4: *How does uncertainty regarding the effect of different interventions affect the social return on investments?*

With all different types of uncertainty, the whole system can be considered as complex and uncertain (J. Foster, 2005). So, to analyse the SD model, an Exploratory Modelling and Analysis (EMA) approach is used (Bankes et al., 2013). An open-source Python toolkit for exploratory modelling is the EMA Workbench (Kwakkel, 2017), which allows for coupling with a Vensim SD model. EMA has been developed mainly for model-based decision support under uncertainty while designing robust interventions (Kwakkel and Pruyt, 2013). As such, the output of the last sub-question is the results of analysing the SD model.

2.2. Background in SD Modelling

The chosen modelling technique for this research is system dynamics. SD can be applied to any type of economic evaluation (Hoang et al., 2016) in the healthcare sector. The main usage of SD modelling lies in ROI analysis. ROI, unlike SROI, focuses more on cost saving and profit maximisation than on maximizing achievement in healthcare (Edwards and Lawrence, 2021). However, SD is still used to evaluate different interventions to form policies for the decision makers (Lawson et al., 2022; Fowler et al., 2020; G. B. Hirsch et al., 2012).

Regarding SROI analysis, an SD model involving CVD patients has been developed in Australia (Peng et al., 2021). However, the focus of their study lies upon the prevention of CVD-related deceases. This is unlike Harteraad, who focuses on the support of patients after they are diagnosed (Harteraad, n.d.-c). Other studies (Y. Wang et al., 2021; Braithwaite et al., 2018) show a similar pattern where SD is used for prevention, not for support. Jadeja et al., 2022 argues that SD is indeed not used to its full potential; lacking in the decision-making on innovations used for support.

To find evidence that SD might be a suitable method to simulate the effect of different interventions in the support of CVD patients, a preliminary literature review is conducted. This literature review details the background of SD modelling in health care and what type of policies or interventions have been used. The database selected was PubMed, since it focuses on biomedical articles. To gain a general understanding of different types of policies, the following search query was used:

(CVD OR cardiovascular) AND (polic* OR intervention) AND ”system dynamic*”

This search query resulted in 52 different articles being found. Based on the title and abstract, only 11 articles were considered to be relevant. One other article was excluded due to the main text being in Japanese. Consequently, 10 articles were considered to be relevant enough for identifying different interventions. A flowchart of this process is shown in appendix A in figure A.1.

The ten articles contain case studies in different countries on different continents, such as Australia (Peng et al., 2021, Spain (Recio et al., 2018) and Bangladesh (Kabir et al., 2022). As such, it becomes clear that there are different social norms and values in play. As well as different ways in which the health care system is organized. For example, the later articles describe the challenges of patients with non-communicable diseases (which includes CVD patients) within the population of Bangladesh. They describe problems such as a lack of an electronic medical record system and a lack of good infrastructure for the supply of medicines. As such, since Harteraad is a Dutch patient representative organization, we prioritise articles conducted in first-world countries with an emphasis on Europe and Anglo-Saxon countries. Ultimately, six articles were kept.

The first article, Peng et al., 2021 developed an SD model to inform strategies that reduce the burden of CVDs in Australia. More specifically, primary outcomes concern the number of deaths and number of hospitalisations. Secondary outcomes on the other hand were the economic net benefits. This requires clinical treatments and lifestyle changes. They focused on primary (the “healthy” population) and secondary prevention (the population that already are CVD patients) of CVDs. They identified the following possible interventions:

1. Supportive environment. This intervention focuses on improving the lifestyle of the patients including (1) reducing the consumption of salty foods, (2) improving physical activity and (3) reducing smoking prevalence.
2. Preventive medications and treatments. This intervention regards the adherence to preventive medication and the implementation of cardiac rehabilitation programs.

Both type of interventions from Peng et al., 2021 are relevant to Harteraad. Especially since Harteraad already has so-called “Beweegclubs” (Harteraad, n.d.-a). However, the article does not explain how physical activity can further be increased, and as such does not include an economic evaluation of the intervention. Furthermore, only the total number of deaths and hospital admissions are measured as outcomes, thus leaving out the quality of life.

A different article provided a Prevention Impacts Simulation Model (PRISM), which simulates outcomes related to CVDs (Yarnoff et al., 2021). PRISM includes a broader range of risk factors for CVD events. So it not only includes physical activity and promoting healthy food but also includes the effect of stress and smoking on CVD-related events. Their interventions mostly regard the entire population (initiatives to promote fruit and vegetable consumption or anti-smoking campaigns). However, one intervention can be generalized for a smaller subgroup and is interesting for Harteraad. That intervention is “Increase use of counselling and support services for distress”. Furthermore, the primary outcome measured is economics-based, namely ’Total consequence costs’. However, social benefits for patients are missing.

One model actually includes only the ‘post-CVD’’ population; the patients that already had an CVD event and survived (G. Hirsch et al., 2010). The identified risk factors for those patients are (1) high blood pressure, cholesterol, and diabetes; (2) smoking; (3) stress; (4) inactivity and (5) unhealthy diet. The model also captured the costs of the services and products used to manage the risk factors, that is, the costs of preventive medical care, smoking cessation, weight loss, and stress management. In total, G. Hirsch et al., 2010 measures the number of CVD events, the costs, and the number of people using primary care. For Harteraad, one new intervention that might be interesting is to provide social support to reduce sources of stress.

Yarnoff et al., 2019 aims to prevent chronic disease, improve quality of life, and reduce medical costs and death associated with chronic disease. They argue that determining the impact of interventions is challenging because interventions take time to affect health- and economic outcomes. As such, the model runs for 25 years. However, in the end, only the cost-effectiveness in relation to premature deaths is determined. Unlike the previous articles, Yarnoff et al., 2019 separates the “Improving physical activity” into two interventions:

- Physical activity access: % of people with access to safe and affordable walking, biking, social, and green space opportunities for physical activity in community locations.
- Physical activity promotion: The extent of local communication, placement, and pricing of physical activity options.

One article focuses on the population that never experienced a CVD event (Loyo et al., 2013). They, however, do argue the importance of reducing stress to prevent complications. Furthermore, a concrete example of a physical activity intervention is given, namely walking programs.

From the background on using SD in healthcare, we found three main types of interventions have been found that might be of relevance to Harteraad. Namely, that of providing mental support, improving physical activity and improving medication compliance. Regarding outcomes, the number of deaths, quality of life and total costs are important measures for the SROI analysis. Lastly, the quality of care, which can be measured by the patient’s satisfaction, is important as well (Lich et al., 2014).

In chapter 3, a more in-depth literature review is conducted to find specific interventions for Harteraad to implement.

2.3. Evidence of System Dynamics

As mentioned in the previous section, this research will apply a modelling approach in the form of System Dynamics. It has also been found that the model should focus should include physical activity, mental health and medical adherence, since they are all risk factors for experiencing new CVD events. What is left is to show that this model will actually be suitable for the problem.

System Dynamics is considered a suitable modelling approach when the system contains feedback, delays, and accumulation. First, feedback indicates that the output of a certain variable routes back to the input of the same variable. The Prevention Impacts Simulation Model (PRISM) shows for example feedback between physical inactivity and stress (Yarnoff et al., 2019). The model shows that when physical activity changes, the amount of stress changes as well. Then, as a result, it causes a change back in the level of physical activity. Similarly, feedback loops are seen between patients with depressive symptoms and morbidity (IsHak et al., 2021). In short, the healthcare system contains feedback loops. The second aspect of SD modelling is the presence of delays. They represent the time – or lag – between a change in some part of the system and the moment the effect takes in (Sterman, 2002). An example in the system is that stress does not immediately lead to depression. Only if long-term stress remains unmanaged can it cause depressive symptoms (Restrepo and Lemos, 2021). As such, an example of time delay also is present in the healthcare system. Lastly is the accumulation of flows into stocks. For stocks, examples include different population groups, such as patients living with CVD or patients currently in the hospital (Peng et al., 2021). Accumulation by the former is the flow of patients discharged from the hospital, while for the latter, accumulation is caused by experiencing and initially surviving a CVD event. Stocks can also be more abstract, such as total costs or total value creation

(L. Wang et al., 2020). Hereby, accumulation is the result of flows such as the investment rate and the yearly value creation.

In conclusion, the Dutch healthcare system contains feedback loops, time delays and the accumulation of flows into stocks. All of which are requirements for system dynamics modelling. This means that system dynamics is a suitable method to simulate this system.

3
Literature Review on Interventions

In section 2.2 it was found that physical activity, mental health, and medication compliance are important factors for the support of patients. Literature suggests the importance of these three factors, since physical activity, mental health, and medication compliance are risk factors for further CVD-related complications (Service, 2022). As such, a literature review is conducted for each type of intervention to find specific examples.

3.1. Mental Health interventions

Immediately after a CVD event or diagnosis of a CVD disease, patients often experience a mental health problem such as anxiety or fear caused by a fear of dying. While the mental problems usually are in the form of a short-term peak, they can develop into depression if unmanaged over a long time. These mental problems, however, increase the risk of a second CVD event (Kandola and Stubbs, 2020). It is thus important that patients retrieve psychological care immediately after a CVD event to reduce the peak and offer long-term guidance. Harteraad is able to offer mental care, as such to find relevant interventions, the following search string was used:

(CVD[Title/Abstract] OR cardiovascular[Title/Abstract]) AND ("mental health care"[Title/Abstract] OR "mental health service*"[Title/Abstract] OR "mental health intervention"[Title/Abstract])

Due to time constraints, only Meta-Analysis, Reviews and Systematic Reviews were included in the search. We ended up with 41 articles. Based on the title and the abstract, 24 of those 41 articles were considered relevant. Then, by citation chaining, one more article was found (Kasparian et al., 2019). Thus resulting in 25 papers being used. Two types of articles were found using this search string: (1) CVD risks among mental care patients and (2) mental risks among CVD patients. We primarily focus on the second type of articles, but don't discard the first type if they mention interventions that can be generalized to CVD patients as well. This leaves us with 15 relevant articles. The flowchart of this process is shown in Appendix A in figure A.2.

Table 3.1: List of identified intervention on mental health support

Intervention	Description	Source	Quality
Promoting Physical Activity	Use physical activity as a mean to support patients with mental health problems such as anxiety and depression.	Kandola and Stubbs, 2018	-
Telemedicine (TM)	Telemedicine (TM) is the use of telecommunication systems to deliver health care at a distance. Category: monitoring of a chronic condition to detect early signs of deterioration and prompt treatment and advice.	Flodgren et al., 2016; Golinkoff, 2007	+/-; +
Music therapy	The intervention provided the user with a relaxing music experience and judged the effect by measuring dynamic changes	Alneyadi et al., 2021	-
Monitoring for Patients Prescribed Antipsychotic Medication	Additional mental health support for patients with a severe mental illness. Since antipsychotic medications have adverse cardio metabolic effects, potentially contributing to CVD and diabetes risk.	Scott et al., 2012	+
Care coordination intervention (group therapy)	Organizing patient mental care activities and sharing information among all the participants concerned. Most effective in combination with education.	Kastner et al., 2018	-
Cognitive behavioural therapy (CBT) (Lifestyle therapy)	Provide mental health support with the intention of guiding patients to a more healthy lifestyle (less smoking, less alcohol consumption, healthy diet and more physical activity)	Pedersen et al., 2021; Doherty & Gaughran, 2014; Scott and Happell, 2011; Williams & Williams, 2011	+; +/-; +; -
Family Therapy	Mental health support with a patient together with their nearby family members. Improving the interactions, communication, and understanding among your family members.	Barbui et al., 2014	+/-
Parental support	Family therapy but specifically for parents of babies/young children with CVDs.	Kasparian et al., 2019	+/-
Promote autonomy and recovery	Aid patients in treatment adherence (attending PA or taking their medicines) in times of anxiety or depression.	Solmi et al., 2021	+/-
Integrating Mental Health Services and PA	Combine mental health care with physical activity. Most effective in groups.	Richardson et al., 2005	+/-

A total of 11 different interventions were identified, see table 3.1. The table provides a description and source of the intervention. Column four includes the quality of the paper. The quality (or trustworthiness) is determined by factors such as the journal it was published in, the number of citations and the geographical location of the described studies. From Table 3.1 we can see that the interventions with the most evidence of usefulness regard changing the lifestyle of CVD patients, the so-called Cognitive behavioural therapy (CBT) or lifestyle therapy (Pedersen et al., 2021; Doherty and Gaughran, 2014; Scott and Happell, 2011; R. B. Williams and Williams, 2011). Mental care support is hereby used to reduce anxiety and fear to encourage treatment adherence to increase the recovery rate. This includes participating in physical activities under supervision. Other than encouraging a healthy lifestyle, mental care is also used to increase the understanding and support of nearby family members on how to help their sick relative (Barbui et al., 2014; Kasparian et al., 2019). Lastly, patients should be able to monitor their own psychological health (Gaffey et al., 2022), so they can see themselves what should be done for a faster recovery. Which then goes back to a healthy lifestyle including enough physical activity.

One interesting identified intervention for Harteraad is that of Telemedicine (TM) to offer health care to their patients at a distance (Flodgren et al., 1996; Golinkoff, 2007). Harteraad already hands out advice on their website to aid patients in dealing with emotions and stress immediately after a CVD event (Harteraad, n.d.-b). In the case of heart failures, Harteraad also has a programme in collaboration with the 'Hartstichting' to increase adherence to therapy Harteraad, 2020. This goal matches the intervention of "promote autonomy and recovery" (Solmi et al., 2021. As such, it might be interesting to explore what else is possible to increase the effectiveness of the TM intervention.

In conclusion, table 3.1 includes a wide variety of interventions regarding mental health support. Some of these interventions are already in action, but it might be interesting to see what else is possible. Furthermore, the interventions show a clear connection between mental health and physical activity (Kandola and Stubbs, 2020; Pedersen et al., 2021; Solmi et al., 2021; C. R. Richardson et al., 2005). Consequently, different interventions regarding physical activity will be explored as well.

3.2. Physical Activity interventions

Based on section 3.1, it becomes clear that physical activity is an important factor for patients suffering from CVDs. Harteraad focuses on physical activity (PA) as well. In so-called "Beweegclubs", patients are supported to exercise in a safe and responsible manner (Harteraad, n.d.-a). So to find relevant interventions regarding PA, the following search string is used:

(CVD[Title] OR cardiovascular[Title]) AND ("physical activity intervention"[Title/Abstract] OR "exercise intervention*"[Title/Abstract] OR "sport intervention"[Title/Abstract] OR "gym"[Title/Abstract])

Again, by only using Meta-Analysis, Reviews and Systematic reviews, 58 articles were initially identified. Note that a restriction was added that CVD should appear in the title. This was done to avoid articles that mention PA has multiple advantages including on CVD, instead of using CVD-related symptoms as its main focus. Without this restriction, we would find 339 different articles. The relevancy of the reduced 58 articles was determined by reading the title, abstract, and introduction. Hereby, we were looking for articles that use PA for treatment or secondary prevention (the population that already has experienced a CVD event). In the end, 18 articles were considered to be relevant. One was a duplicate already covered by the mental health interventions (Kandola and Stubbs, 2020), one article did not test any intervention and penultimately, two more articles were added by citation chaining (Focht et al., 2004; Okwose et al., 2019). Thus, we have a total of 18 relevant articles. The flowchart of this process is shown in figure A.3.

From these 18 articles, 15 different interventions regarding PA have been identified in a wide variety of exercises. A summary of the interventions can be found in table 3.3. One set of interventions focuses on muscles, these include aerobic exercises (Y.-Y. Lin and Lee, 2018; Jakovljevic, 2018; Loyo et al., 2013), anaerobic exercises (Y. Wang et al., 2015) or a combination of both (Goncalves et al., 2021). Aerobic exercise (also known as endurance training) is a type of repetitive, structured physical activity involving large muscle groups in which oxygen is required to produce the energy needed (Yang et al., 2014). Examples include brisk walking, swimming, and cycling (Jakovljevic, 2018). This also includes slow-pace walking (Loyo et al., 2013). On the other hand, anaerobic exercises are activities in which the isolated single muscle groups are used to move a weight or to work against a resisting load (Yang et al., 2014).

Coordinative training is generally used to improve motor skills, but can be considered as a useful training regime if it sees an increase in energy expenditure. Examples includes dancing and Tai Chi (Grässler et al., 2021). Other projects laid the focus instead on flexibility by stretching to reduce the risk of injury (Crozier et al., 2018; Eijsvogels et al., 2016).

A special form of exercise is the High-Intensity Interval Training (HIIT). This training regime sees brief high-intensity bursts of exercise interspersed with bouts of recovery, aiming to maximize cardiovascular exercise intensity in a time-efficient manner (Crozier et al., 2018).

So far, these interventions focus on group-based activities. However, it is also possible to tailor the intervention to the needs of a single person (Marcus et al., 2006; Hansen et al., 2010; Rowley et al., 2018; Okwose et al., 2019) instead of exclusively focussing on groups (Focht et al., 2004; Kandola et al., 2018). One intervention, "Active-at-Home-HF" regards the improvement of PA at home (Okwose et al., 2019). The additional benefit is that no specific location has to be found before the training exercises can start.

One intervention takes it into a different direction. Instead of increasing the level of exercise, the focus is laid on relaxation to help reduce stress and depressive symptoms (Franklin et al., 2021). They consider PA as a double-edged sword, as there is a risk of acute CVD events after intensive exercising (Kalra and Roitman, 2007). However, Crozier et al., 2018 argues that this risk is only high immediately if patients start exercising too soon after a CVD event. Lastly, one intervention regards the promotion and education of PA (D'Isabella et al., 2017). This is a similar intervention as by Kandola et al., 2018 in table 3.1. As such, the last two interventions again show a clear link between PA and mental health.

Table 3.3: List of identified interventions on physical activity, including examples of exercises.

Intervention	Description	Source	Quality
Coordinative Training	Intended to improve specific motor skills. Examples: Dancing, Tai Chi	Grässler et al., 2018	-
Aerobic Exercise (Endurance or Isotonic Training)	Any physical activity involved with large muscle groups. Examples: Swimming, Brisk Walking, Rowing, Cycling	Lin & Lee, 2018; Jakovljevic, 2018	+; -
Walking programs	Specific form of aerobic exercise focusing on walking under supervision.	Loyo et al., 2013	–
Anaerobic exercise. (strength or resistance training)	Maintain, strengthen, and tone the muscles, as well as promote bone strength, balance, and coordination ability. Gym Workouts.	Wang et al., 2015	+
Aerobic + Resistance Training	Combination of Aerobic exercise and Anaerobic exercise.	Son et al., 2017	+
Flexibility exercise	Stretch and lengthen the muscles of our body, which aims to reduce the risk of injury.	McKune et al., 2017	+/-
High-Intensity Interval Training	Brief high-intensity bursts of exercise interspersed with bouts of recovery, aiming to maximize cardiovascular exercise intensity in a time-efficient manner. Main Example: treadmill Walking	Eijsvogels et al., 2016; Crozier et al., 2018	+/-; +
Educational Programs	Promote exercise among the CVD patients to educating them on the benefits.	D'Isabella et al., 2017	+/-
Cognitive-behavioural intervention	CVD patients check their own PA and based on the monitor, advise the patients on reaching a target goal.	Marcus et al., 2006	-
Group-mediated cognitive behavioural physical activity intervention program (GMCB)	Combines PA with discussion sessions to promote long-term PA even after the intervention stops.	Focht et al., 2004	+/-
Use of EXPERT Tool	Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool. Tailoring the exercise training program to each single patient according to his/her specificity.	Hansen et al., 2017	+/-
Exercise referral schemes (ERS).	Specified set of exercises tailored to the individual needs of each participant and health disorder in a gym-based setting.	Rowley et al., 2018	-
Relaxation Technique Training Groups	Focussed on relaxation instead of exercises by meditation and deep breathing	Franklin et al., 2021	+
Active-at-Home-HF	Personalised home-based physical activity intervention aiming to increase daily number of steps by 2000 from baseline.	Okwose et al., 2019	-
Video games for PA	Using video games (Wii fit and Just Dance) to keep a patient group active in a generally considered more fun way. Also helps with the mental health of patients.	Kandola et al., 2018	+/-

3.3. Medication Compliance interventions

A major change that a patient also has to make after a first-time CVD event is medicine intake. While most CVDs are incurable, taking the right medicine with the right dose slows down the risks of further complications (Al-Ganmi et al., 2016). It is therefore important that patients adhere to the prescription from the health care provider (Jimmy and Jose, 2011). Hereby, adherence is defined as a patient taking at least 80% of the advised dose (Al-Ganmi et al., 2016). The average adherence rate among CVD patients in Europe is only 57% (Chowdhury et al., 2013). This low adherence rate is directly attributed to 9% of all second-or more time CVD events (Naderi et al., 2012).

A Major reason for non-compliance is a patient's dissatisfaction with either the practitioner nurse (PN) or the general practitioner (GP) (Jimmy and Jose, 2011). The dissatisfaction hereby is often the result of miscommunication or communication barriers (Gandapur et al., 2016). Another factor is time, whereby patients reduce their medicine intake over time without consultation from the GP (Jimmy and Jose, 2011). Lastly, negative side effects are considered a drug-related problem that reduces the adherence rate of patients (Meijvis et al., 2023). From an interview in the form of an online meeting with people from Harteraad, one specific intervention for medication compliance was found, namely CombiConsult (CC). CombiConsult is a new service in which the GP, PN and pharmacist collaborate to contribute to effective and safe drug therapy (Meijvis et al., 2021). This is done by offering patients consultation from the pharmacist right before the regular check-up with the GP, for more effective tailored care (ZonMw, 2021; Meijvis et al., 2023). A schematic overview of the three steps of CombiConsult is visualised in 3.1. Figure 3.1 shows the three steps for CombiConsult. The first step is the medication check. Patients first have a consultation with their pharmacist. During this consultation, the patient is given the chance to address drug-related problems. Examples of drug-related problems include adverse effects, under/over treatment and noncompliance. Furthermore, the pharmacist and patient try to find personal health-related goals. This includes a reduction of the number of drugs and a reduction of specific adverse effects such as muscle complaints and dizziness. After the consultation, the pharmacist passes their recommendations on to the PN or GP. In the second step, the patient has a consultation with the PN or GP. If the PN/GP agrees with the recommendations from the pharmacist, the actions are accepted and implemented. Finally, in the third step, the patient has a follow-up with either the PN/GP or the pharmacist. In this meeting, it is determined if the chance of action has helped to reduce drug-related problems and whether health-related goals have been achieved.

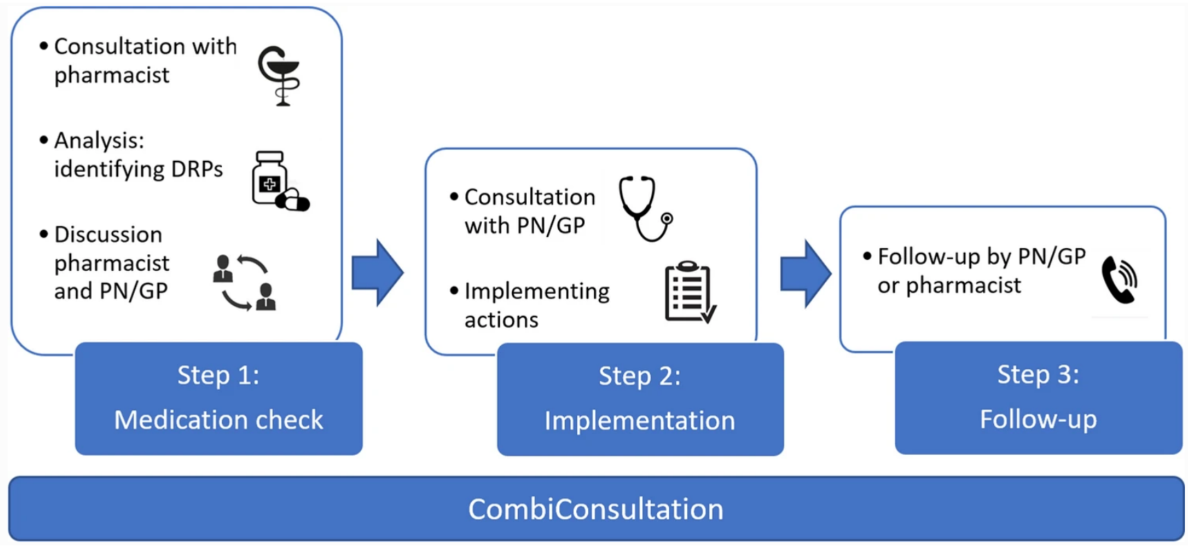


Figure 3.1: Schematic overview of the CombiConsult steps. Source: Meijvis et al., 2023.

3.4. Exclusion of other interventions

Physical activity, mental health and medication compliance are not the only risk factors for CVD events and/or complications. Other examples of risky behaviour include smoking and an unhealthy diet (Yarnoff et al., 2019). However, in an interview with the client, it was revealed that Harteraad is currently not involved – nor are there plans to be involved in the short-term – in interventions focussing on smoking cessation and dietary help. Therefore, it was decided that those interventions will not be included in this project and will not be taken into further consideration. Hereby, this also means that the model will be built on the assumption that no other investment programs are started by stakeholders outside the scope of this project.

In conclusion, the intervention taken into consideration for the support of CVD patients by Harteraad focuses on physical activity, mental health and medication. In the next chapter, a conceptual model is built that visualises the relationship between the interventions and the output measures by means of changing patients' behaviour.

4 Mapping Outcomes: The Conceptual Model

In this chapter, the conceptualisation of the CVD patient health care system is described. Chapter 3 gave an overview of different interventions that Harteraad can implement, while chapter 2 explained which performance metrics are interesting to measure. However, what is currently missing is the link between interventions and performance metrics. Thus, this chapter aims to answer the second research question: *How do different interventions from Harteraad create social return?*.

4.1. Causal Loop Diagram

For the conceptualisation of the health care system, a Causal Loop Diagram (CLD) is developed. A CLD maps a shared understanding of complex problems and provides a visual tool to guide interventions by showing how an intervention will eventually lead to outcome measures. This system is complex due to the appearance of feedback loops and delays.

Within the CLD, different variables are linked together with arrows. An arrow from variable A to variable B means a causal relationship exists between the two factors. Every arrow has a polarity, which is indicated by either a + or a - symbol. A + symbol indicates a positive causal link, which indicates if one variable A increases, then variable B increases as well. Similarly, a decrease of variable A will cause a decrease in variable B. A - symbol indicates a negative causal link, which indicates if one variable A increases, then variable B decreases. Similarly, a decrease in variable A will cause an increase in variable B. This effect does not have to happen immediately but can occur after a certain time has passed. This means that there is a delay, which is indicated by two bars going through the arrow. An example of a delay is that long-term stress complaints can cause depression or depressive symptoms (Van Praag, 2004). Lastly, a CLD is able to show feedback loops. Feedback loops simply mean that a change in variable A will eventually lead to itself and cause further changes. A feedback loop can be reinforcing (positive feedback loop, indicated with a +) or balancing (negative feedback loop, indicated with a -). The polarity of a loop is determined by counting the number of negative links within the loop, whereby an even number indicates a reinforcing loop while an odd number indicates a balancing loop.

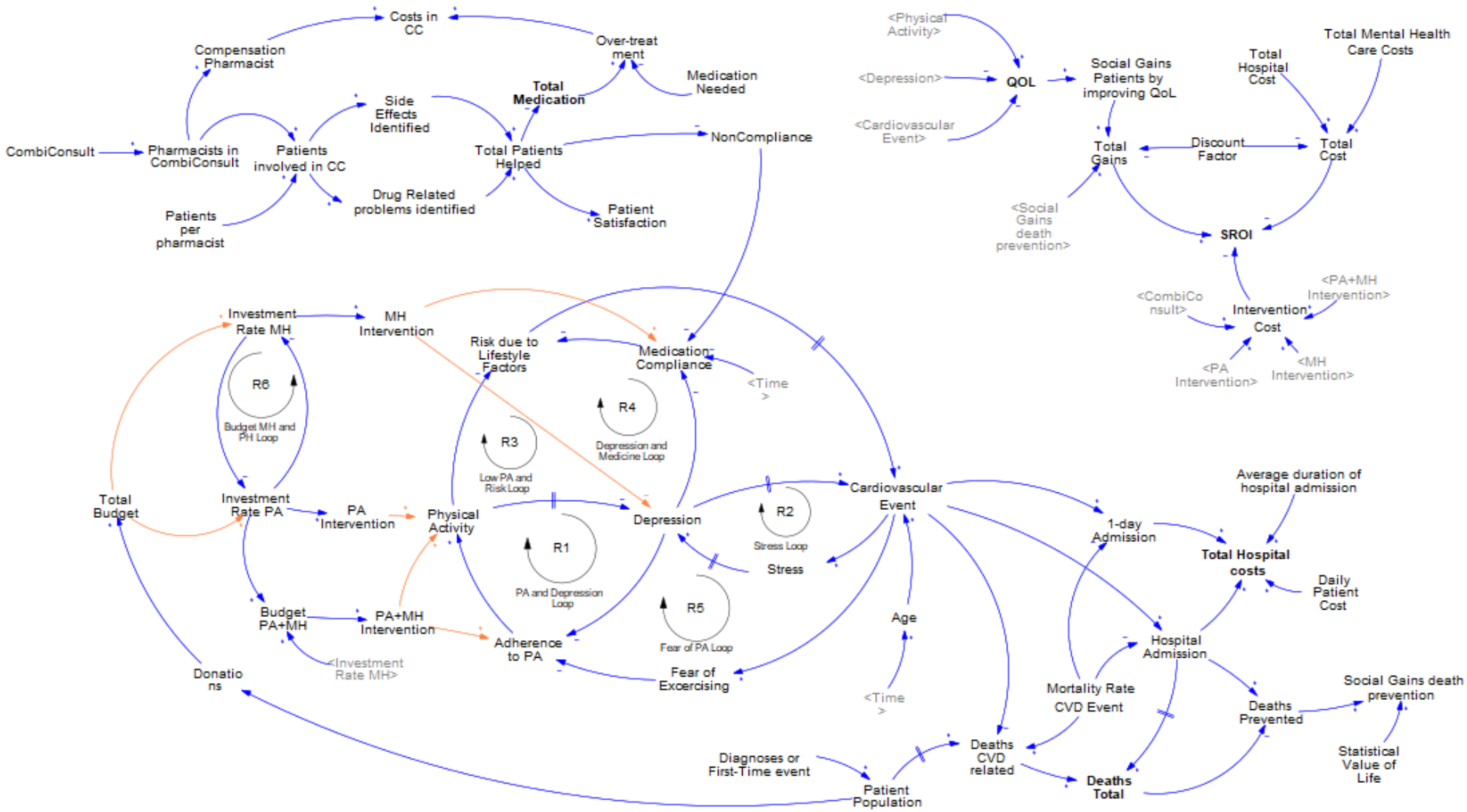


Figure 4.1: Causal Loop Diagram of the health care system for CVD patient support.

A complete overview of the CLD in this section of the health care system is visualised in figure 4.1. Other than the blue line indicating causal relationships, orange arrows indicate that this relationship is related to a specific type of intervention. Thus, this arrow only exists if this intervention is chosen. Hereby, it should be noted in this research, that only one intervention is tested at a time. Now, it should also be noted that this CLD regards only the CVD patients and not relatives and other nearby family members. For our system, figure 4.1 shows six feedback loops. Five of these are related to the CVD events and risk factors for further CVD events. This indicates that the number of CVD events is a crucial factor to understand the system. The one feedback loop outside this subsystem focuses on the selection of interventions from Harteraad (which are PA and MH interventions). With a limited budget, a choice needs to be made for which intervention priority is given (L. Wang et al., 2020). The CombiConsult intervention lies outside the influence of Harteraad, but is still very important for patients in their support. The effect of CC is also included in figure 4.1. All in all, for the CLD, every type of intervention is shown as one single variable that affects the CVD subsystem at different points. Other than CVDs and risk factors for CVDs, figure 4.1 also shows the effect of CVDs on the population in the form of deaths, hospital admission and one-day admissions Hartstichting, 2021.

4.1.1. Risk factors of CVD

In order to understand the CLD even better, we will zoom in on the CVD events part of the CLD. This part is shown in figure 4.2. Survivors of a CVD event may experience significant psychological distress following the acute event (Musey Jr et al., 2020). As mentioned before, long-term stress is then related to an increase in depressive symptoms, which may cause depression (Van Praag, 2004). This however is a risk factor for CVD incidence, severity and outcomes (Elderon and Whooley, 2013). Thus, CVD, stress and depression form a reinforcing feedback loop.

Other than being a risk factor itself, depression has other consequences that themselves further increase the risk for more CVD events. People diagnosed with depression are less likely to adhere to lifestyle changes such as physical activity changes (Sumlin et al., 2014), thus reducing the adherence rate to the new PA regime. Furthermore, Depression causes a lack of adherence to medicine intake or treatment (Eze-Nliam et al., 2010). Since both are risk factors for CVD prevalence, they describe the reinforcing loops R3 and R4. Based on the literature review of section 3.1, it shows a link between PA and depression, thus forming a reinforcing feedback loop R1. One factor that hasn't been described yet is the Fear of Exercising. Fear of Exercising, also known as kinesiophobia, is commonly seen in patients who were recently hospitalised for an acute CVD (Brunetti et al., 2017). Dias et al., 2018 argue that this is due to fear of exercise-induced adverse events. As such, the fear of exercising decreases the adherence rate to the new PA regime and in total creates a fifth reinforcing feedback loop.

Since all five feedback loops are reinforcing, an increase in the number of CVD events will lead to an even higher number of CVD events. What this means for the patients is that without help from others, their health enters a declining spiral. This is due to the patient's behaviour being negatively affected by an acute CVD event. From here the purpose of the interventions became clear. The identified interventions all focus on improving the behaviour of patients to minimize the risk of new CVD events. To understand the benefits of reducing the CVD incidence rate, it is important to understand what happens physically after a CVD event occurs. This process is shown in figure 4.3.

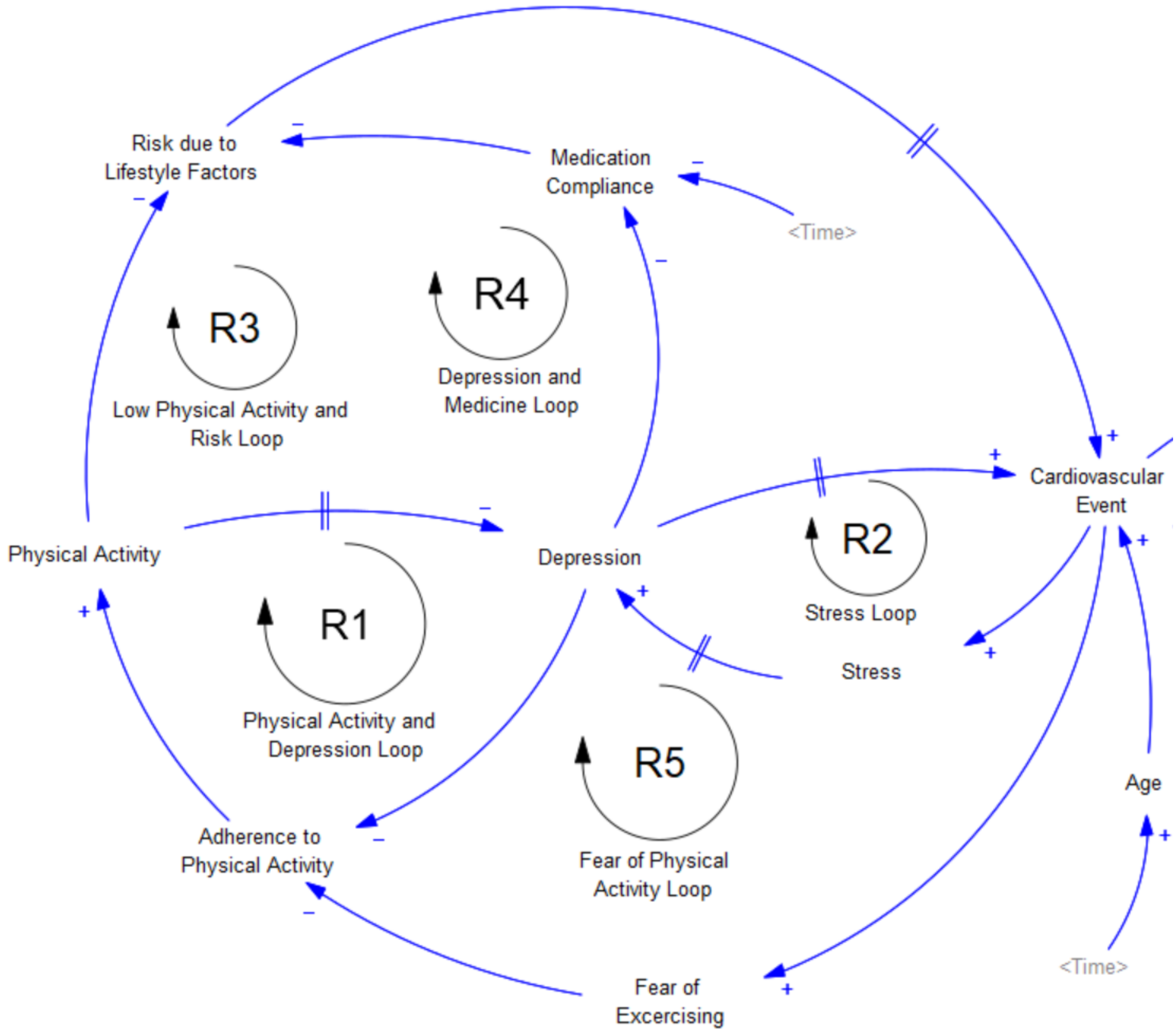


Figure 4.2: CVD event part of the CLD.

4.1.2. Consequences of CVD

After an acute CVD event, three things can happen to the patient (Hartstichting, 2021). In the worst-case scenario, the patient dies immediately. However, western rich countries see a relatively high survival rate (Byberg et al., 2016), including the Netherlands. Those who survive are instead being hospitalised. Depending on the severity of the event, the patients are either hospitalised for multiple days or are released within the same day. This however does not mean that patients are out of risk. A major number of CVD-related deaths occur a long time after hospitalisation, which can be attributed to the acute CVD event from multiple years ago (Dudas et al., 2012).

One factor that contributes to the occurrence and survivable rate of a CVD event is age. The Hartstichting reports data of all CVD patients in the Netherlands, grouped into five age groups. Their two youngest age groups (age 0 to 44 and age 45 to 55) see a relatively low amount of CVD events and deaths compared to hospitalisations. Yet, for the age group of patients between 75 and 84, the numbers are relatively the largest (Hartstichting, 2021).

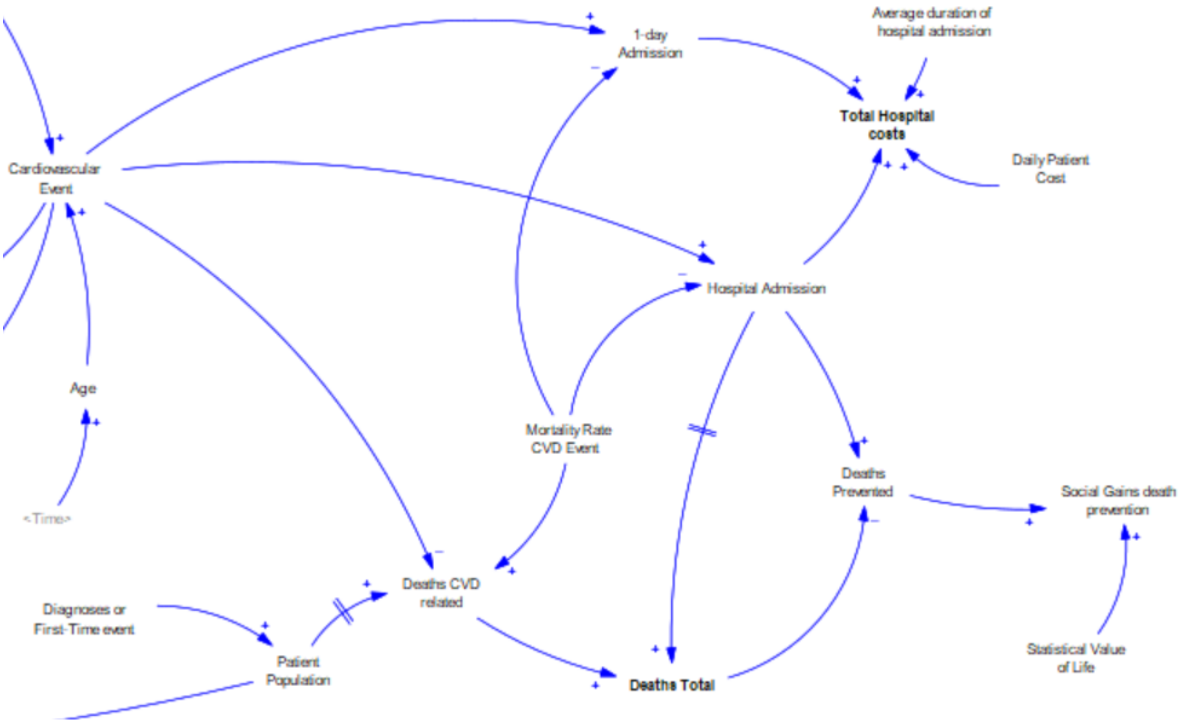


Figure 4.3: Consequences CVD events part of the CLD.

4.1.3. Conceptualisation of CombiConsult

The identified interventions have a direct effect on factors within the CVD. One intervention however has multiple other effects, which are interesting for the support of patients. This intervention is CombiConsult (see figure 4.4), whereby the pharmacists and GP/PN work together during a patient's yearly check-up (Meijvis et al., 2021). The more pharmacists are involved, the more patients follow as well. Then by consultation, different drug-related problems as well as health-related goals (as the effect of side effects) are identified. Which consequently are being solved, increasing the number of patients helped by CombiConsult.

With improved communication and the fact that patients are being helped more easily, patient satisfaction increases. More importantly, however, is that the noncompliance regarding following the treatment plan decreases. This is because side effects such as dizziness and practical problems with medicine intake decrease (Meijvis et al., 2023). Lastly, the drug-related problem of patients believing they take too many kinds of medicines can be identified. If a change in treatment plan is agreed upon with the GP, this leads to a lower total number of medications.

With CombiConsult, two types of costs are involved. First is the cost of compensation for the pharmacist because they need to be at the GP and cannot directly help patients other than CVD patients. The second type of cost is the social cost of over-treatment that with CC being implemented should decrease (Kurani et al., 2022).

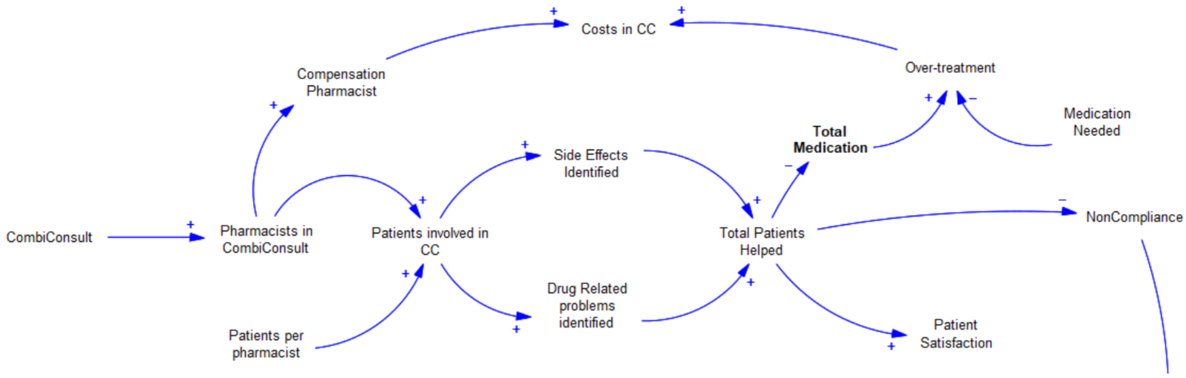


Figure 4.4: Conceptualisation of CombiConsult intervention within the CLD.

4.1.4. Quality of Life and SROI

For the Quality of Life, health is an important metric (Burckhardt and Anderson, 2003). So with lower CVD events, the patient's self-reported QoL increases. The health metrics for measuring QoL can be divided into physical health and mental health (Hoekstra et al., 2013). Section 5.1.4 describes the way of measuring in more detail. An increase in physical activity increases the QoL, while an increase in depression decreases the QoL. The social gains by improving the patient's QoL can be measured from here, and by including the social gains of death prevention, the total gains are determined. The discount rate devalues further cash flows and also decreases the total gains over time.

On the cost side, the total costs for society are determined by adding the hospital and mental health care costs. These are also discounted. To then determine the SROI ratio, the difference between social gains and social costs is divided by the intervention costs. Thus, more spending on interventions decreases the SROI. The whole process is visualised in figure (4.5).

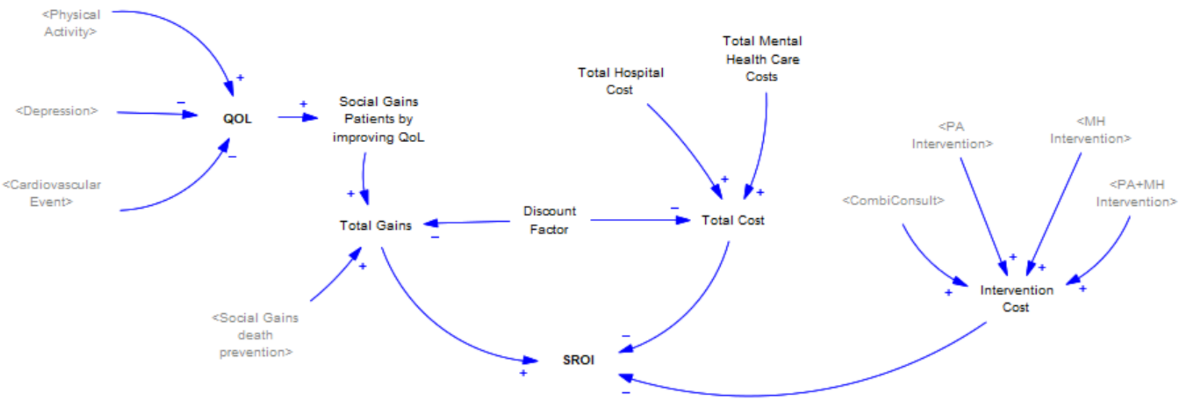


Figure 4.5: Quality of Life and SROI of the CLD

4.1.5. Dynamic Hypothesis

With the feedback loops within the CVD part of the model and the consequences of patients on the health care system, a dynamic hypothesis can be formed. Without any interventions, patients find it difficult to adjust their behaviour for the better, further increasing the CVD incidence. This will lead to a burden on the healthcare sector. Hospital costs will be unmanageable while patients are not getting the support they need. The dynamic hypothesis thus states that different interventions can be used to break the downward spiral by improving the patient's behaviour. Increasing the support patients receive while keeping the costs for the system manageable. Thus, the hypothesis is that the SROI is positive for the interventions.

To test the dynamic hypothesis, a System Dynamics model is developed based on the CLD. Instead of just a mapping between input and output, the SD model enables us to measure the impact of interventions and the performance metrics. The different parts of the CLD will be translated into different sub-models. Sub-models include (1) population sub-model including deaths and hospitalisation, (2) behaviour sub-model which focuses on PA and depression, (3) CombiConsult sub-model for which the compliance rate is modelled, (4) Intervention sub-model which adds the choice that has to be made for which intervention is implemented and for how long and lastly (5) the QoL sub-model, which models the effect of interventions on the patients' life to finally determine the SROI ratio.

5 Evidencing Outcomes and Establishing Impacts: Model Formulation

In this chapter, the model formulation is described. The conceptual model from chapter 4 is translated into a system dynamics model. Input and output variables are given a numerical value, and the causal links will be described in equations. As such, this step matches with stages three (Evidencing outcomes and giving them a value) and four (Establishing impact) of an SROI analysis (C. M. Laing and Moules, 2017).

5.1. The System Dynamics Model

Before delving deep into the model structure, a simplified overview is shown first, see figure 5.1. The system dynamics model consists of seven smaller submodels. First is the patient population and CVD event submodel. This submodel describes the Dutch population with CVDs from diagnosis to death due to CVD-related events. The second and third submodels focus on physical activity and mental health, respectively. These two submodels describe the risk factors of CVD events as well as how they affect the quality of life among the patient population. The quality of life is hereby the fourth submodel. Those four submodels form the base model, in which no intervention is implemented yet, and no SROI can be calculated

The intervention submodel is the fifth submodel. Hereby it describes which interventions are included and how they can be chosen for simulations. CombiConsult is given its own submodel and describes how it affects medical adherence as well as how it relates to deaths among the CVD population. Lastly, all submodels relate in some way to the final step of calculating the SROI ratio.

All seven submodels will be detailed more thoroughly through section 5.1.1 to 5.1.7.

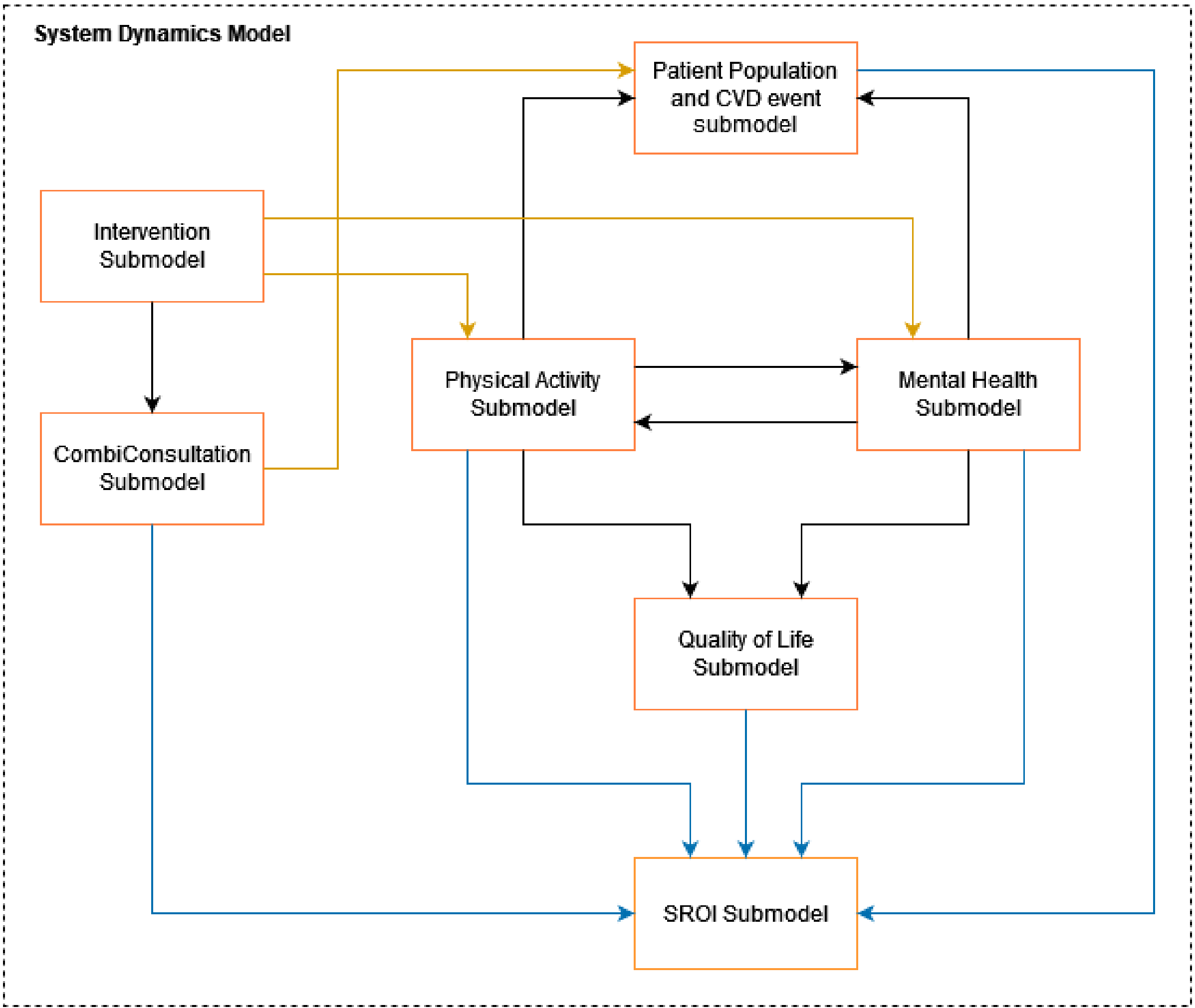


Figure 5.1: High-level overview of the system dynamics model, including the submodels. The black lines indicate the interaction between submodels within the base model. Gold/Brown lines indicate the interaction between interventions and the corresponding submodel. Lastly, blue lines indicate how the submodels interact with the SROI ratio.

5.1.1. Patient Population and CVD event Submodel

The first submodel is the patient's population and CVD event submodel. This model describes the population of the Netherlands with CVDs and the CVD events they experience. The data is based on the results of a yearly report by the Hartstichting (Hartstichting, 2021). In 2020, Hartstichting reported 1,503,100 CVD patients divided among five age groups. For privacy reasons, the data for patients between 0 and 44, and between 45 and 55 are combined into one age group. In this project, four age groups are taken into consideration: 0-54, 55-75, 75-84, and older than 85.

A trend analysis by the Ministry of Health and Sport, 2020, has shown that for 2040 an increase in patients with CVDs is expected. Mostly caused by a sharp increase in coronary heart deceases, arrhythmias, and strokes. In total, including other CVDs as well, the Netherlands will have approximately 2.6 million people suffering from CVD by 2040. Due to the way the Hartstichting measures the number of CVD patients (which leads to only counting 1.5 million patients), this leads to a yearly increase in CVD patients by 40704. Thus:

$$TotalDiagnoses - TotalDeaths = 40704 \tag{5.1}$$

The result of the yearly patients increase in this model is that by 2040, the amount of CVD patients has increased to 2.32 million, see figure 5.2.

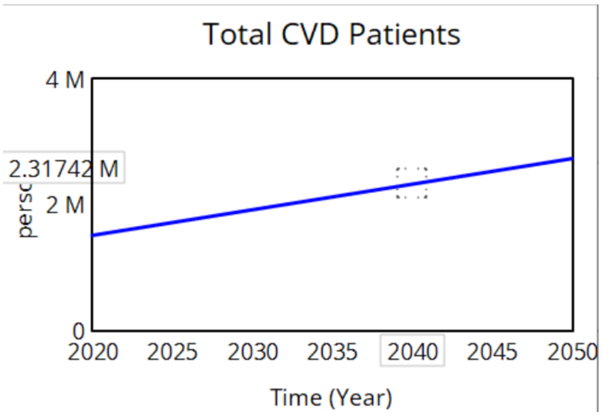


Figure 5.2: Increase in patients till 2040.

The Hartstichting furthermore reports the total deaths and hospitalisations for each age group. Hereby, for hospitalisations, a distinction is made between a long-term hospital stay and a one-day visit. Based on this data, the CVD prevalence can be calculated before model implementation by assuming the restriction that:

$$\%deaths\ after\ CVD\ + \%hospilatisation\ after\ CVD\ + \%1day\ visit\ after\ CVD\ = 100\% \tag{5.2}$$

Lastly, by using the average time of hospital stay (Hartstichting, 2021) and the average price of a hospital bed of €800 (Kiers, 2018) the total costs for the hospitals are determined.

A complete overview of all variables, equations, and units within the Population submodel can be found in tables (C.1) and (C.2) in appendix C.

5.1.2. Physical Activity Submodel

The second submodel regards physical activity. This model divides the total population into three groups. The first group are the patients that follow physical activity either individually or from home. The second group prefers to exercise in groups, which is assumed to occur under the guidance of trainers at Beweegclubs (Harteraad, n.d.-a). The third group are the patients that do not meet the requirements for physical activity. The third group entails 44% of all patients (Ten Have et al., 2011).

Patients can move from one group to another by either stopping with exercise or starting with exercising. In the former case, it is assumed that it naturally happens over time. With this process being accelerated once a patient has depressive symptoms. In the latter case, it is assumed that patients only see the need to increase PA after a CVD event. However, limiting factors are the *fear of exercise* and the preference to either exercise alone or in groups. As mentioned earlier, group exercises are organised in Beweegclubs, of which there are 230 across the Netherlands (Harteraad, n.d.-a). This forms a capacity constraint in the total amount of patients that can join Beweegclubs. A complete overview of all variables, equations, and units within the PA submodel can be found in tables (C.5) and (C.6) in appendix C.

5.1.3. Mental Health Submodel

A second major risk factor of CVD events is mental health problems, which are described in the third submodel. Three causes of depression are taken into account. First is the standard depression rate. This type of depression can occur to everyone without a special trigger, or in case the trigger falls outside the scope of this project. The data for the prevalence rate of depression among the entire Dutch population (Ten Have et al., 2023) is assumed to also be true for CVD patients.

A second cause of depression in the model is the result of long-term stress after experiencing a CVD event. In the model, this long-term effect is set at 1 year. It is furthermore assumed that there is a peak of stress right after a CVD event and that on average the decrease of level of stress is exponential. The following formula was used to measure the ratio of patients still stressed after a year:

$$EXP(-DecreasecConstant * (Time - Initial\ Time)) \tag{5.3}$$

Hereby, the *Decrease Constant* is an external variable that can be changed for experiments. When this variable is set to be equal to 2, 13.5% of all patients develop depressive symptoms a year after CVD. It is hereby important to note that this inflow of new depressive patients only contains the groups of patients that were not depressed yet.

The last cause of depression included in the model is depression caused by a lack of exercise. The occurrence rate of this influence is based on the results from Mammen and Faulkner, 2013 and only affects the patients in the PA-lacking group as described in section 5.1.2. Since the lack of PA is also a risk factor for CVD events, a function is implemented to prevent the double counting of new depressed patients.

The duration of depression can differ widely among the population, depending on factors such as the strength of the depressive episodes or the mental state of the person. As such, depression can take somewhere between a few weeks and a few years to be cured (Ten Have et al., 2017). For this project, the base duration of depression is set to 1 year, which will be altered during the experimentation. Patients with depression also form a burden on society, as such this submodel also calculated the social costs of mental healthcare.

A complete overview of all variables, equations, and units within the Mental Health submodel can be found in tables (C.3) and (C.4) in appendix C.

5.1.4. Quality of Life Submodel

The fourth submodel focuses on the Quality of Life among CVD patients. The measurement of QoL provides a meaningful way to determine the impact of health care on a personal level (Burckhardt and Anderson, 2003). Originally starting with the Flanagan Quality of Life Scale (QoLS) (Burckhardt et al., 2003), the RAND-36 is now the most widely used Health-related quality of life (HRQoL) survey instrument (Hays and Morales, 2001). RAND-36 consists of 36 health-related items on a scale from 0 to 100. Physical and mental health summary scores can be derived from those 36 items. The initial score on the physical level is set at 34 while the initial score on the mental level is set at 70 (Hoekstra et al., 2013). Since this data regards (1) only heart failure patients and (2) the state of New York, those initial values will still be varied during experimentation.

This project measures effects on a high aggregation level, therefore it is assumed that our metric does not capture the entire QoL measure. So the Quality of Life measure is determined over time by using a weighted average between the two summary scores, while including noise to a certain level. This score is compared with the initial total QoL score of 63 (Hoekstra et al., 2013).

In the last step of this submodel, the difference between the current and initial QoL score is monetised by using the quality-adjusted life years (QALYs) metric. A QALY is a self-reported measure that contains the benefits of being alive for a year multiplied by the QoL of that patient (A. Williams, 1996). For the Netherlands, a single point of QALY is worth €50,000 (Pomp, 2010).

A complete overview of all variables, equations, and units within the QoL submodel can be found in tables (C.8) in appendix C.

5.1.5. Intervention Submodel

The fifth submodel regards the choice of intervention to be tested. First, a choice can be made between testing a PA intervention, an MH intervention, CombiConsult or no interventions. Second, two more choices can be made for either the specific PA intervention or the specific MH intervention. Each specific intervention has certain effects. These effects alter variables in one of the previously described submodels. The specifics of this submodel are described in more detail in chapter 6.

The costs of investments are also included in the intervention submodel. Each intervention has its own set of costs involved, most often in the form of equipment cost (Salai et al., 2016) or wages/fees (Tan et al., 2012). In chapter 3, a total of 32 interventions were identified. However, this list needs further shortlisting. The model operates on a high aggregation level, and such different interventions may either lead to similar effects or are outside the scope of the model. For example, the different types of group-based training lead to different effects on heart rate or lung volume (Y.-Y. Lin and Lee, 2018), which then affects the risk of CVD. On this aggregation level, we can use the immediate effect. Thus, it makes sense to combine all group-based activities into one single intervention that is then used for testing. On the contrary, certain interventions no longer fall within the scope. For example, the model only includes patients with CVD and not nearby family members, so “Family Therapy”(Barbui et al., 2014) and “Parental support”(Kasparian et al., 2019) are dropped.

All shortlisted interventions still included for modelling can be found in table 5.1.

Table 5.1: Shortlist of interventions modelled used for testing

Type of Intervention	Specific Example
Physical Activity	Active-at-Home
	Video game
	Relaxation Technique Training
	High-Intensity Interval
	Group Based Training
Mental Health	Music Therapy
	Care Coordination
	Cognitive Behavioural Therapy
	Promote Autonomy and Recover
	Telemedicine
Medical Adherence	CombiConsult

5.1.6. CombiConsult Submodel

The sixth submodel is a specific intervention described in more detail, namely CombiConsult. Within CombiConsult, pharmacists are assumed to be able to make the choice to participate in this intervention. In a pilot study, 21 pharmacists are already involved in the intervention (Meijvis et al., 2023). In this study, it is explored what happens if CC is enrolled for (almost) all CVD patients in the Netherlands. If pharmacists join, all of their CVD patients are included into the program as well. Generalising the pilot study results, this leads to the identification of drug-related problems among 71.6% of all patients, and the identification of attainment of personal health-related goals among 41.7% of all patients. 72% of all recommendations on drug-related problems are accepted and of the drug-related problems, 53% is achieved (Meijvis et al., 2023). By combining those patient groups, while counting for patients that both have drug-related problems and drug-related problems, the total number of patients helped by CombiConsult can be determined. By further dividing this by the total population involved in CC, the effectiveness can be measured.

The ratio of patients helped by CC and total patients can be used to measure weighted averages of three variables: (1) patient satisfaction, (2) compliance rate and (3) the costs of spending on unnecessary medicine. The baseline satisfaction is already reported to be high (Naik Panvelkar et al., 2009) and is set at 8.5. Meanwhile, for the patient satisfaction after CC, it is assumed that half of the patients rate it with a 9 and the other half with a 10, thus averaging at 9.5. Regarding the compliance rate, the baseline value is only 50% (Jimmy and Jose, 2011), indicating that only half of the patients adhere to the advice from either the pharmacist or GP/PN. The assumption in the model is that patients helped by CC will adhere to the treatment plan completely. As such, the weighted average adherence rate can be determined, whereby full adherence prevents at most 10% of all deaths (Naderi et al., 2012). For the costs of unnecessary medicine, the difference between the current average medicine intake and the needed medicine intake is determined. Currently, a patient uses on average 5.9 different medicines (Meijvis et al., 2023). So the necessary number of medicine intake is assumed to be less than that and is set to 4.85. On average, the per capita prescribed medicine spending in Western Europe is equal to 552 dollars (Kurani et al., 2022), which is equal to €504.14 (at the time of modelling). As such, it can be determined what the overspending on medicine is.

A complete overview of all variables, equations, and units within the QoL submodel can be found in tables (C.9) trough (C.11) in appendix C.

5.1.7. SROI Submodel

In the final submodel, the SROI is being calculated. First, all the social costs and benefits from the previous six submodels are combined and discounted into a single value, the net present value (NPV). Next, the deadweight is determined. Deadweight is the effect that would have happened even when no intervention was implemented (Ruiz-Lozano et al., 2020). For example, deaths will eventually occur because people cannot live forever. In this model, the deadweight is assumed to be the NPV of a base model without intervention and is subtracted from the NPV found by the model. This difference is the social gains of the intervention. Then to calculate the SROI, the social gains are divided by the total investment costs.

5.2. Model Settings

In this project, the aim is to see what the long-term effects are of the interventions. Furthermore, most population data from the Hartstichting including deaths, hospitalisations, and the inflow of new patients, are measured in years. As such, the unit of time in the model is in years as well. The model run-time is from 2020 to 2050. The former again because most available data is from 2020. With a Final time of 2050, this means the model runs a 30-year difference, which is close to the average simulation time for an SD model in health care (Davahli et al., 2020). However, since the model starts with no investment, the SROI ratio may be inaccurate for the first five years. This leaves us with effectively a simulation run-time of 25 years. For the time step, different values were tested. Some variables – most noticeable wages and training frequency – are measured in weeks. These variables are however input variables and converted into years before they affect other variables. In the end, a time step of 0.0625 was chosen. The integration technique was set to Euler. The justification is that one of the interventions used look-ups, which require Euler integration to handle properly. Then, for consistency, all experiments will be performed under Euler integration. Lastly, the model was developed in Vensim DSS X64 9.4.2.

5.3. Verification

The objective of model verification is to check that the implementation of the model is correct and that the formalisation of the model is consistent with the conceptual model described in chapter 4.

The first test to check the correctness of the model is the dimensional check. Every variable in the model has been given a unit that describes what it measures. If there is an error, it means that one of the variables has a wrong unit or that the equation is simply wrong. Using the Unit Check function within Vensim shows "Units are OK". A second way of testing the units within the model is to manually check certain factors. Ratios and Percentages for example should be dimensionless. Furthermore, population groups should have the "type" of people. This means that the patient population model should be measured in patients. A similar reasoning also applies to variables involving pharmacists and therapists. By manually checking the model, no such errors are prevalent, which means that the units are consistent.

A second test to check the correctness of the model is to find negative stocks or divisions by zero. In the former case, stocks involving population groups and costs, for example, cannot go beneath zero. Running the model under different policies and input variables shows that this is indeed the case; these stocks never reach negative values. However, the model does have two stocks that can go negative: "Death Prevention Gains" and "Social Gains Differences". These variables are monetized versions of death prevention and cost to society. Moreover, the flows into these stocks are cashflows. In this case, these variables measure the difference between the base case and the intervention. So if an intervention has a net negative effect, it is expected that the cash flow is negative and thus that the stock becomes negative as well. This is thus not an error. For the division by zero, one instance is found. Namely, in the variable that measures the SROI. At the start of a model run, investments have yet to be made. In other words, the denominator as in equation 1.1 is zero, resulting in an error. A failsafe is implemented, setting the SROI to a value of zero when the total investments are still zero. Consequently, no SROI ratio can be calculated in the base case, since that scenario describes the situation whereby no interventions are implemented.

5.4. Validation

Validation is the process of determining the degree to which a model is an accurate representation of the real world from the perspective of the intended uses of the model. Validation is thus about building confidence that the model is fit for its intended purpose. Two tests are used for model validation: (1) Extreme Condition Test and (2) Sensitivity Analysis.

5.4.1. Extreme Condition Test

The extreme condition test explores the behaviour of the system under extreme conditions. Input parameters will be changed to both extremely high and extremely low values to explore how the behaviour of the model changes. The extreme condition test furthermore helps in identifying non-linearities and asymptotes (Senge and Forrester, 1980). Another advantage of a model passing the extreme condition test is that it shows that the model can be useful in regions other than the Netherlands as well since varying the input variables into values corresponding to those countries will not lead to nonsensical results. For each of the three major submodels (patient population, physical activity and mental health) a variable is chosen to perform the test.

Inflow of new patients

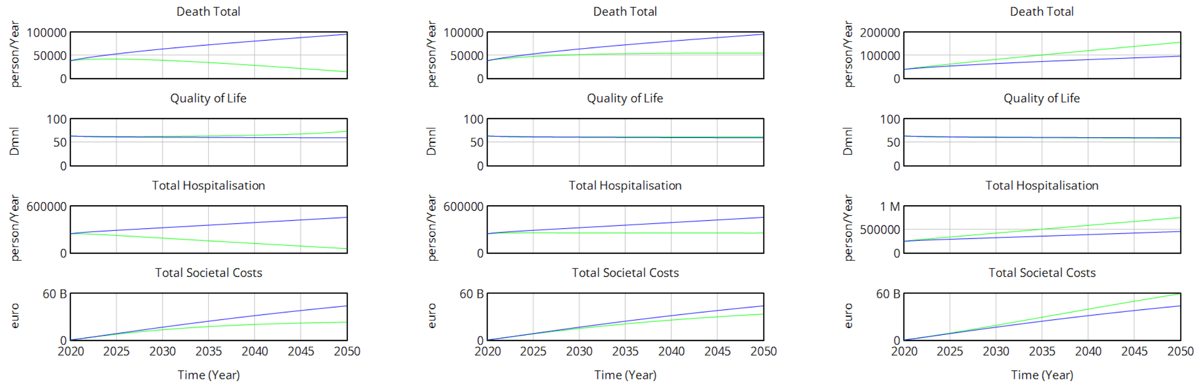
The first test relates to the patient population sub-model. The base scenario assumes that over the next 30 years, the patient population is increasing. So in this test, we check what happens in case the patient population is either decreasing or stays stable. Furthermore, the model is tested when the inflow of new patients is set at a high value.

Table 5.3: Extreme Condition Test for the inflow of new patients

Variable	Base value	Decreasing Population	Stable Population	Increasing Population
Relative Yearly Patient Increase	40704	-40704	0	100000

The results of the extreme condition test can be seen in figures 5.3a, 5.3b and 5.3c. The blue lines indicate the base scenario, while the green lines represent the behaviour of the model when the input variable is changed.

The results show predicted behaviour. In case the patient population decreases, it makes sense that the total number of deaths and hospitalisations also decreases. The quality of life eventually starts to increase. This also makes sense, as with a smaller population, the capacity constraint of therapy and clubs for physical activity are removed. This leaves us with a relative decrease in depressed patients and a relative increase in patients adhering to physical activity. In the case of a stable patient population, the output variables start to level out. The model reaches a state of equilibrium. As a result, the total societal costs flatten out due to the discounting factor. So in this scenario, the model also behaves as expected. Lastly, in the situation of an increasing patient population, the outcome measures increase in value. More deaths and hospitalisations eventually create a burden on the healthcare system, increasing societal costs. However, the quality of life remains largely unchanged. This indicates that regarding this factor, the model is already in one of the worst-case scenarios.



(a) Extreme Condition Test when the number of patients decreases

(b) Extreme Condition Test when the number of patient stays equal

(c) Extreme Condition Test when the number of patient increases

Figure 5.3: Extreme Condition Test for the inflow of new CVD patients

Duration of depression

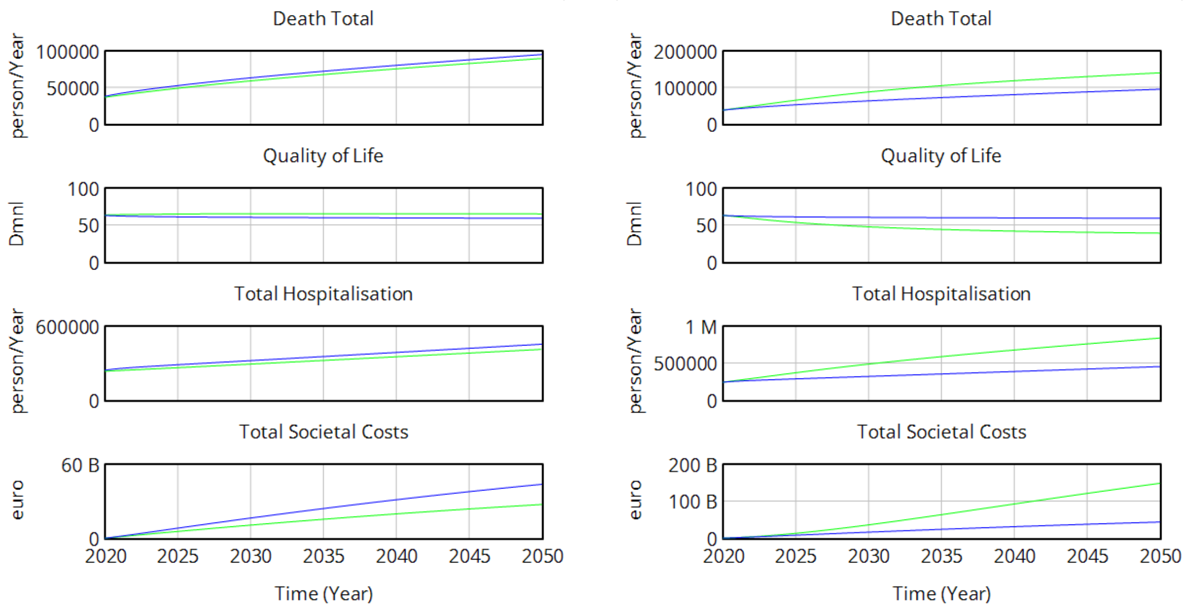
The second test relates to the mental health of the patient. The variable that is changed is the duration of depression.

Table 5.4: Extreme Condition Test for the duration of depression

Variable	Base value	Short Duration	Long duration
Average Length of Depression	1	0.001	10

The results of the extreme condition test can be seen in figures 5.4a and5.4b. The blue lines indicate the base scenario, while the green lines represent the behaviour of the model when the input variable is changed.

In case of near-immediate recovery, the population with mental health issues stays low. Despite depression being a major risk factor for CVD, it is not the only one. Furthermore, CVD events occur also in the patient population that is currently healthy. As a result, the total number of CVD events stays roughly the same, causing the total deaths and hospitalisations to barely change. With less need for therapy, the total costs for society however do decrease noticeably. For a similar reason, the quality of life is higher than in the base case. In the second scenario, depression takes 10 years to cure. The result is an ever-increasing population of patients with mental health issues. Now the effect on deaths and hospitalisation is visible. In total, the costs to society increase, and it does so exponentially. As there is no balancing factor, the quality of life does decrease as well.



(a) Extreme Condition Test when depression is solved within a day

(b) Extreme Condition Test when depression stays for long-term

Risk factor of depression

The third test relates to the risk factor that mental problems have of the chance of experiencing a CVD event.

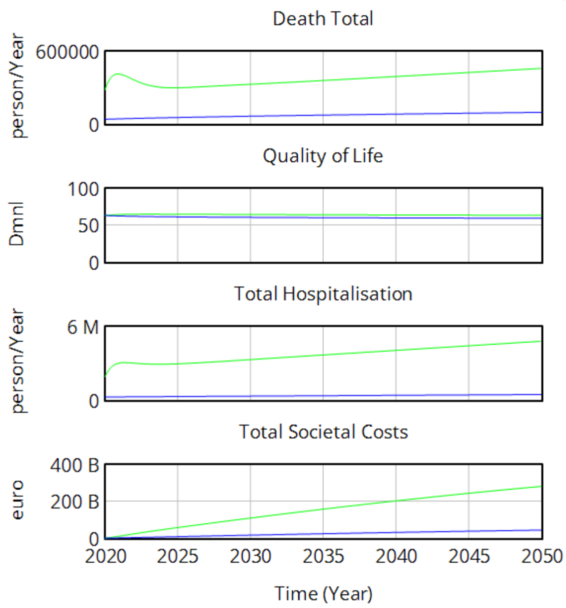
Table 5.5: Extreme Condition Test for the risk factor of depression

Variable	Base value	Short Duration	Long duration
Risk due to Depression	1.5	1	10

The results of the extreme condition test can be seen in figures 5.5a. The blue lines indicate the base scenario, while the green lines represent the behaviour of the model when the input variable is changed. In this particular case, only the test with a high-risk factor has noticeable effects on the outcome variables. The figure for the test with a low risk factor can be seen in appendix D

What is interesting in this test is that the behaviour of the model does change. From figure 5.5a it can be seen that the total deaths and hospitalisations have a noticeable jump at the start. This can be explained, however. Due to the high-risk factor, more CVD events will occur, resulting in more deaths in the short term. Only then after some years does the total patient population find its new equilibrium. From that point onwards, the model behaviour is similar to that of the base case, although with higher valued outcomes. One key point to notice here is that with a higher risk factor of depression, the quality of life starts to increase. This seems contra-dictionary. This effect however can also be explained. What happens is that with a higher risk factor, deaths are more common in the population group with mental health issues. Who generally have a lower quality of life. The increase is thus caused by the fact that the ratio of patients with a higher quality of life increases.

So in total, the extreme condition test on the risk factor of depression shows either expected behaviour or behaviour that can be logically explained.



(a) Extreme Condition Test when depression is solved within a day

Fear of exercise

The fourth and last test relate to the fear of exercise patients experience after a CVD event. Or more specifically, the percentage of how often it occurs.

Table 5.6: Extreme Condition Test for the fear of exercise

Variable	Base value	Short Duration	Long duration
Fear of Exercise Occurrence	0.116	0	1

The model outcomes are insensitive when changing these variable parameters, see appendix D figures D.2a and D.2b.

What happens is that in the case of low fear of exercise, this value is already quite close to the actual occurrence of fear of exercise (Torriani-Pasin et al., 2021). In case of high fear of exercise, an increasing amount of patients is indeed lacking in physical activity. However, the depression that follows gets cured, motivating patients to start exercising again. The result is thus a balancing effect.

5.4.2. Sensitivity Analysis on the Base Model

A sensitivity analysis is a validation test which investigates the effect of small changes in model parameters. By convention, the parameters are changed by about +/- 10% (Borgonovo and Plischke, 2016). Three types of sensitivity exist: Numerical sensitivity, Behavioural sensitivity and Policy sensitivity (Pruyt, 2013). Numerical sensitivity means that the values of outcomes change when the parameters change. This type of sensitivity should always be present, otherwise, it would mean that a parameter has no use and should be discarded. Behavioural sensitivity indicates that the dynamics of the model change. This can be useful to show the strength of certain interventions. Lastly, the policy sensitivity indicates a change in the preference order of policies. So the ranking of the outcomes changes depending on the change in input variables.

The parameters subject to change in the sensitivity analysis are the input variables. Which includes initial conditions for stocks. Table 5.7 provides an overview of all variables used for the sensitivity analysis, including the range of values.

To eventually compare different policies under different scenarios, the sensitivity analysis will be conducted by changing all parameters at once. This process is known as the multivariate sensitivity analysis. The method chosen for sampling the parameters within the uncertainty range is Latin Hypercube Sampling (LHS). LHS ensures that the samples are evenly distributed (Loh, 1996). For this test, the Exploratory Modelling and Analysis (EMA) Workbench was used. The EMA workbench enables us

Table 5.7: Sensitivity analysis for the Base Case

Variable	Base value	-10%	+10%
Relative Yearly Patient Increase	40704	36634	44774
Fear of Exercise Occurrence	0.166	0.1044	0.1276
Choice for Beweegclub	0.15	0.135	0.165
Initial QoL Score	63	56.7	69.3
Initial QoL Score Physical	34	30.6	37.4
Initial Score MH	70	63	77
People per Beweegclub	640	576	704
Decrease QoL due to Lack PA	11.8	10.62	12.98
Decrease QoL due to MH	20	18	22
Risk due to Depression	1.5	1.35	1.65
Average Length of Depression	1	0.9	1.1
Event per person	2	1.8	2.2
Mental Health Care Costs per Person	2000	1800	2200
Daily costs Hospital	800	720	880
Discount rate	0.035	0.0315	0.0385

to not only visualise the outcomes but also the distribution of the outcomes. The results of the sensitivity analysis can be found in appendix D.

In the base case scenario, the only type of sensitivity visible is numerical sensitivity. In each run, the graphs for each of the outcome variables show similar behaviour. Furthermore, the distribution graph shows that the variation in outcomes is quite small as the values in the last time step are bundled closely together. Figure D.4 in appendix D compares the outcome variables with each other. It shows that the only correlation between outcomes is that between the total deaths and total hospitalisations. This is correct since both are consequences of experiencing a CVD event and the hospitalisation rate is unchanged.

Feature Scoring

The EMA workbench is also able to visualise which parameters are most effective in changing the outcome variables. This analysis is known as feature scoring and is used to identify the most relevant features to include in a model. The results are shown in figure 5.6. Over 50% of the Quality of Life of patients depends on the initial QoL score. Indicating that especially the initial conditions are important for this outcome variable. The most influential parameter for both the total deaths and total hospitalisation is the inflow of new patients. Both parameters regarding mental health have a notable score as well. Finally, the total social costs are primarily influenced by the daily costs of hospitals for the healthcare of their patients.

The sensitivity analysis shows that the base model is robust, with only numerical changes present. The results for the feature score further match that with the results found by the extreme condition test. In total, this means that the model is fit for purpose. With a robust base model, the model can be run for the different interventions described in section 5.1.5. Hereby, a comparison can be made with the base model with the primary outcome variables. Especially if the interventions do change the model behaviour. Furthermore, with interventions enabled, the SROI ratio can be calculated.

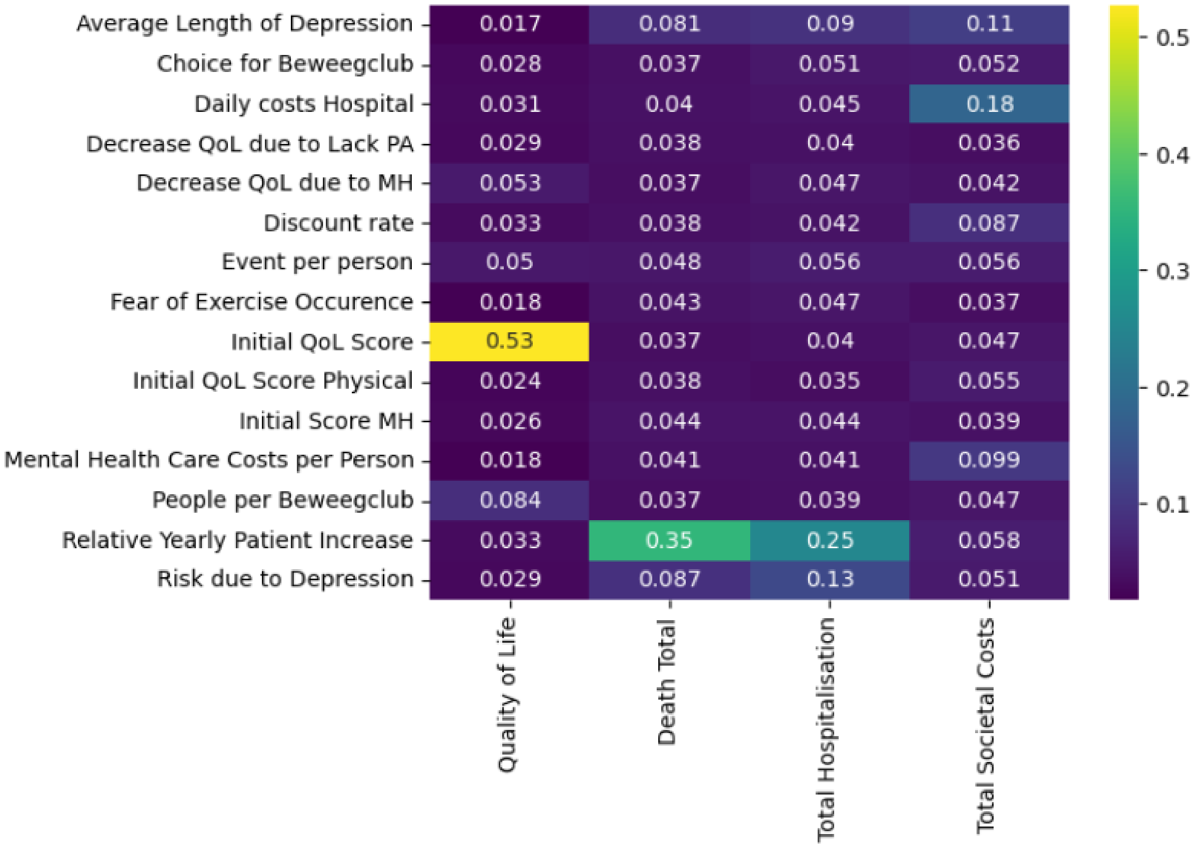


Figure 5.6: Feature scoring to find the most relevant parameters

5.5. From base model to experiments

In this chapter, the entire model formulation was described. Then the base model – the model without any investment – was verified and validated using multiple kinds of tests. An uncertainty analysis was performed to explore how much the model outcomes changed when uncertainty in model parameters was taken into account. Despite this, the SROI ratio can not be calculated in the base case, as it requires an investment to be made. So in the next chapter, a description is made of how the investments were added to the model and how new potential investments can be added as well.

6
Implementation of interventions

In section 5.1.5 from chapter 5 it was mentioned that the model contains a submodel that enables the user to select an intervention for simulation. This chapter contains a more detailed description of how the interventions were implemented and how to choose the correct one for experimentation. Moreover, a guide is handed out on how a modeller can add interventions to the model.

6.1. Implementation of Interventions

With each intervention, two elements are added to the model. First is the effect the intervention has on one of the variables within the model. For example, the intervention of music therapy sees an average reduction in stress levels of around 13.23% (Li and Xiong, 2016). As such, the variable *"Stress Reduction Music Therapy"* is given a value of 0.8677. So at each time, the level of stress is 13.23% less than that it would be under the base scenario. However, if this specific intervention is not chosen, the value is set back at 1, so that it does not influence the model at all. The second effect that needs to be included in the model is the costs involved with the intervention. Each intervention has costs in either equipment or wages/fees. In the case of music therapy, these costs come in the form of wages for the therapist who leads the session. Then by using the average group size (Li and Xiong, 2016), the number of groups and the number of sessions per group, the total costs can be calculated. Each of the interventions has its own costs involved and so, they each add their own small sub-model to the system. Then at the end, all the costs are combined in one variable that is then used to determine the SROI ratio.

6.2. The Choice of Interventions

In this project, the impact of each intervention is measured independently. However, the SD model contains sub-models for each intervention and a few additional steps have to be taken to run the model for one single intervention. To do so, multiple switches were implemented that incorporate IF THEN ELSE statements. Figure 6.1 gives an overview of how that looks in the SD model.

First is the variable *"Priority Switch"*. Hereby, the modeller can indicate to focus on either PA, MH, both PA and MH, or on CombiConsult. Moreover, it is possible to select the base scenario. Second, are the variables *"Chooser Physical Activity Intervention"* and *"Chooser Mental Health Intervention"*. These variables are needed since multiple interventions are included that focus on either PA or MH. When the priority is given to either PA or MH, there is still more to choose, since they both contain five more different interventions. Third, and most importantly, are the variables *"PA intervention switch"* and *"MH intervention switch"*. These variables make sure that only one single intervention is active at the same time. For PA, equation 6.1 specifies how this is done.

$$IF\,THEN\,ELSE(Priority\,Switch = 0, Chooser\,Physical\,Activity\,Intervention, IF\,THEN\,ELSE(\\ Priority\,Switch = 2, Chooser\,Physical\,Activity\,Intervention, Intervention\,not\,Chosen)) \quad (6.1)$$

What it means is as follows. First, it checks if priority is given to PA alone. If so, it selects the chosen PA intervention. If not, it then checks if priority has been given to both PA and MH. Based on the second check, it either still selects the chosen intervention, or it turns the entire PA selection off via the variable *"Intervention not Chosen"*.

From here on, more IF THEN ELSE statements are used to change the effects and costs of the previously described submodel per intervention.

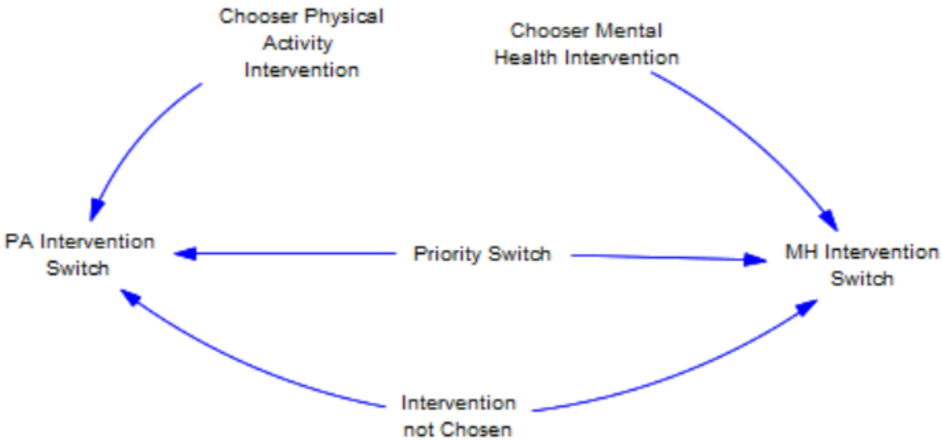


Figure 6.1: Snippet of the SD model that involves the selection of the intervention.

6.3. Adding New Interventions into the Model

In the two previous sections, it was described how the interventions from chapter 5 can be implemented into the SD model and how to select said intervention for experimentation. To add new interventions into the model, a similar approach can be taken. However, it is also important to add the new interventions in a fashion suitable for SROI by using the six stages of SROI analysis (C. M. Laing and Moules, 2017).

The first stage is to identify the scope and stakeholders. On a patient level, it is important to indicate for which patient group this intervention is intended. Hereby, a division can be made by for example age, gender, specific decease, level of PA and so on. The for the other stakeholders, it should be established who are involved in the intervention. Examples are nurses, pharmacists, and trainers.

The second stage contains the mapping of outcomes. This comes in the form of adding a new variable into the model. This variable needs to be coupled with a variable already present in the base model. As such, this step requires that there already exists data that shows which variable is affected when implementing a new intervention.

The third stage is evidencing outcomes. This step contains the parametrisation. More importantly, however, is that these effects should be monetised as well. The model already includes proxies for hospital care, deaths and QoL. What is only needed then is the cost of the investment themselves, which often occurs due to equipment or wages. The total costs of this intervention then need to be connected with the variable *"Total Investment Costs"* so it can be used to calculate the SROI in a later stage.

Stage four is the establishment of the impact. First, the newly added effect needs to be given a numerical value on its effect. Secondly, deadweight and attribution need to be taken into account. The former is already done, since the model measures the SROI per intervention by comparing the social benefits and costs with that of the base case. Moreover, since we are measuring per intervention, attribution poses no problem as well. The last step of stage four is enabling the option to choose the intervention. This requires more IF THEN ELSE statements to be included in the model. Otherwise, the process is the same as described in section 6.2.

At this point, the new intervention is included in the model with both costs and effect and, furthermore, is correctly chosen. Running the model will then output the corresponding SROI ratio, including a graph of how it evolves over time.

This chapter provided an overview of how to implement and choose an intervention into the model to calculate the SROI ratio. In the next chapter, we go back to the interventions identified in chapter 5 and describe how the interventions will be tested.

7 Experimental Set-up

In this chapter, the experimental set-up is described. In chapter 3 different examples of interventions were found for the support of patients in either physical activity, mental health and medical adherence via CombiConsult. In chapter 5, the list of interventions was shortlisted to just eleven different interventions. In the same chapter, the base model has been tested for several uncertain model parameters. However, each intervention adds a small submodel into the model with its own set of uncertain variables. Uncertainty hereby can lie in the effect of the intervention or the costs involved, or even both. As such, it can be concluded that we are modelling under deep uncertainty (Walker et al., 2012).

The first step to structure the analysis for decision-making under deep uncertainty is by using the "XLRM framework" (Lempert, 2003). The "L" stand for Policy **L**evers. These are the decisions Harteraad can make. In our model, those are the types of interventions. E**X**ternal are the critical uncertainties that are outside the control of any involved actor. The Performance **M**etrics are the model outcomes used to evaluate each chosen policy lever. In this project, the main performance metric is the SROI ratio. Lastly, the "R" stands for **R**elations in the system and describes how these elements relate to each other. In other words, the "R" is the SD model described in chapter 5. A high-level XLRM framework for this project is shown in figure 7.1. Each element of the XLRM framework has already been described, except for the range of uncertain parameters.

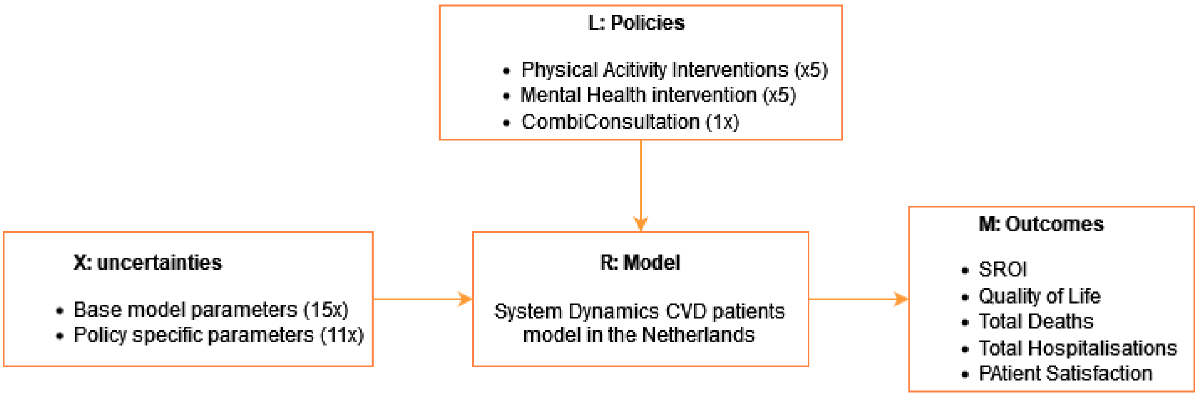


Figure 7.1: XLRM framework for modelling SROI for Harteraad

7.1. Uncertainties for all Interventions

In the sensitivity analysis on the base model, see section 5.4.2, the model was tested by changing uncertain parameters by either plus or minus 10%. It was found that the model behaviour (in the base case) is robust under uncertainty. So for the experimentation, these ranges are mostly kept unchanged. However, to add more realism to the model, the variables with evidence of a wider range are modified. Those variables are *"Average Length of Depression"* (Trimbos-instituut, 2022), *"Event per person"* and the *"Discount rate"* (Banke-Thomas et al., 2015). As such, the list of ranges for uncertain parameters for all experiments can be seen in table 7.1.

Table 7.1: Uncertainties under all experiments

Variable	Base value	-10%	+10%
Relative Yearly Patient Increase	40704	36634	44774
Fear of Exercise Occurrence	0.166	0.1044	0.1276
Choice for Beweegclub	0.15	0.135	0.165
Initial QoL Score	63	56.7	69.3
Initial QoL Score Physical	34	30.6	37.4
Initial Score MH	70	63	77
People per Beweegclub	640	576	704
Decrease QoL due to Lack PA	11.8	10.62	12.98
Decrease QoL due to MH	20	18	22
Risk due to Depression	1.5	1.35	1.65
Average Length of Depression	1	0.5	1.5
Event per person	2	1	3
Mental Health Care Costs per Person	2000	1800	2200
Daily costs Hospital	800	720	880
Discount rate	0.035	0.025	0.04

With each intervention, new variables and connecting links between variables are added to the model. As such, this adds more uncertainty to the model. So in the next section, the intervention-specific uncertainties are described, including the assumed range for experimentation.

7.2. Uncertainties for Physical Activity Interventions

The first intervention focusing on physical activity is Active-at-Home. The primary effect of it is an increase in the QoL metric (Okwose et al., 2019) by four points. However, the pilot group of this research are patients with heart failure. So the effect may be either higher or lower when the intervention is implemented for all patients. The range is therefore set to [2, 8]. The Costs come in the form of wages for the therapist, which are based on the session costs (Tan et al., 2012) and the time per patient (Kraal et al., 2013). The main uncertainty lies in the costs of heart monitors for the patients. The cost for a single heart monitor is in the range [63.48, 453.40] (Salai et al., 2016).

Table 7.3: Uncertainties for Active-at-Home

Variable	Range	Unit
QoL increase AaH	[2, 4]	Dmnl
Heart rate Monitor Costs	[63.48, 453.40]	euro/monitor

For the video gaming interventions, two types of uncertainty may alter the results. First is the price for video gaming consoles which depending on the console are somewhere in the range [200, 500]. The second uncertain variable relates to the attendance rate of video gaming compared to no intervention. An Irish pilot study shows that video games decrease drop-out by a factor of 2.5 Ruivo et al., 2017. However, since different healthcare systems are not comparable, this value can be different in the Netherlands. The range is therefore set between [2, 5].

Table 7.4: Uncertainties for Video games

Variable	Range	Unit
Price per Game Console	[200, 500]	euro/console
Video Games Enjoyment Factor	[2, 5]	Dmnl

For the Relaxation Technique Training, the main uncertainty is the effect (Van Dixhoorn et al., 1983). There is a positive result on well-being, but in certain cases, a person's anxiety may actually increase during rehabilitation. So the range is set between [1.05, 1.25] assuming it has an effect, yet small.

Table 7.5: Uncertainties for Relaxation Technique Training

Variable	Range	Unit
Effect Relaxation Technique Training Groups	[1.05, 1.25]	Dmnl

A link exists between HIIT and mortality among CVD patients Eijsvogels et al., 2016. However, HIIT also causes patients to drop out of training programmes (Wewege et al., 2018). So the main uncertainty regards the most optimal level of HIIT training per week, which can range between 0 and 80 hours per week.

Table 7.6: Uncertainties for HIIT

Variable	Range	Unit
HIIT intensity	[0, 80]	hour/week

The last intervention focusing on physical activity is group-based training. This intervention combines certain types of training, which can be approximated by altering the program duration and its effectiveness in CVD event prevention. The program duration differs between a quarter of a year and a full year (Grässler et al., 2021; Y. Wang et al., 2015). Moreover, the effect on reducing CVDs can reach values between 10% and 50% Grässler et al., 2021.

Table 7.7: Uncertainties for GBT

Variable	Range	Unit
Exercise Program Duration	[0.25, 1]	Year
Effectiveness of PA Intervention	[0.1, 0.5]	Dmnl

7.3. Uncertainties for Mental Health Interventions

Regarding mental health interventions, the effects are way less uncertain. For music therapy, it has been measured that it decreases anxiety and stress by around 14% (Li and Xiong, 2016). Cognitive Behaviour programs affect mental health, but the literature suggests it ultimately causes a reduction of deaths by 30% (Scott et al., 2012). lastly, telemedicine decreases the length of depression by around 8% (Rachas et al., 2015). The only uncertainties in these interventions deal with the *"Average Length of Depression"*. As such, that variable is just to last between half a year and 1.5 years.

Table 7.8: Uncertainties for Mental health interventions

Variable	Range	Unit
Exercise Program Duration	[0.25, 1]	Year
Average Length of Depression	[0.5, 1.5]	Year

7.4. Uncertainties for CombiConsult

The main source of uncertainty regarding CC is the costs involved. Since this intervention is relatively new, with the start of the project in 2021 (Meijvis et al., 2021), no economic analysis has been performed yet. It is only mentioned that training costs are needed before full implementation (Meijvis et al., 2023).

A second type of uncertainty focuses on the satisfaction level of patients before and after CC, as the results are not publicly available yet. Table 7.9 shows the ranges and units of the deep uncertainties within CombiConsult.

Table 7.9: Uncertainties for CombiConsult

Variable	Range	Unit
Exercise Program Duration	[0.25, 1]	Year
Duration of Pharmacist Training	[8, 40]	Hour
Daily Compensation	[10, 50]	euro/ (day*Pharmacist)
Base Pharmacist Satisfaction	[6.5, 8.5]	Dmnl

7.5. Experimentation

With each element of the XLRM framework described, all experiments can be performed. Hereby using the base model parameters from the base sensitivity analysis, as well as using the policy-specific parameters if necessary. Latin Hypercube Sampling was used to generate random samples of the parameter values. Lastly, for each experiment, 50 replications were performed. Thus resulting in a total of 550 experiments. The results of which will be shown in chapter 8.

8 Results

In this chapter, the results from the experiments are shown. For each intervention, the development of the SROI ratio over time is shown till the year 2050. Three figures are shown, first for the standard scenario using the base parameter values, and then the results are shown when uncertainty is taken into account. The third figure shows which variable caused the most variance in model output over time. With the results, an answer can be given to the fourth subquestion: *How does uncertainty regarding the effect of different interventions affect the social return on investments?*.

The main focus of this section is the SROI ratio, the results for the secondary outcomes (deaths, hospitalisations, Quality of Life) as well as additional figures can be found in appendix E.

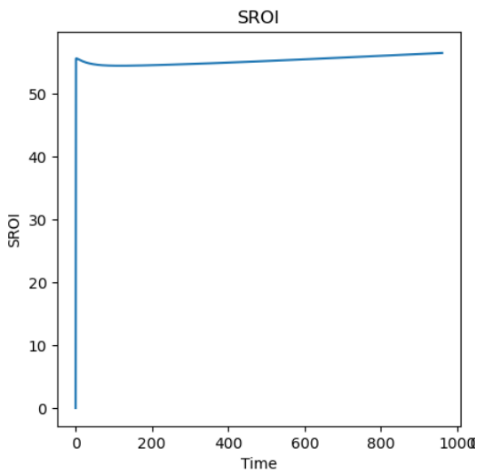
An intervention is considered worth the investment if in the long-term, here the year 2050, the SROI is positive and above 1. That indicates that the intervention has net benefit results on the patients and the health care system as a whole. If the SROI ratio is positive but below 1, then there are still net benefit results. However, the net benefit results do not outweigh the total costs of the investment. In the worst-case scenario, the SROI ratio may end up negative. This happens if there are net negative results on either the patient or the health care system as a whole; the social costs are higher than the social benefits.

8.1. Results for Physical Activity Interventions

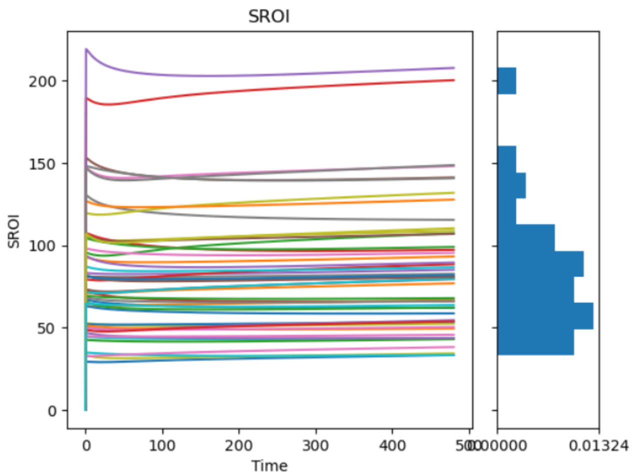
8.1.1. Results for the Active-at-Home Intervention

Figure 8.1a visualises the SROI ratio for the Active-at-Home intervention under standard circumstances. The SROI starts at zero because, at time zero, an investment has yet to be implemented. At the next time step, the graph jumps to 55.54 before slowly decreasing. The decreasing SROI ratio is only short-term, as the graph eventually increases till it reaches a value of 56.44 in the year 2050.

Figure 8.1b visualises the SROI ratio for the Active-at-Home intervention when uncertainty is taken into account. This includes uncertain parameters regarding (1) the Heart rate Monitor Costs and (2) the QoL increase Active-at-Home. The graphs of figure 8.1b all show similar shapes as of figure 8.1b. However, the behaviour is slightly different among the scenarios. In certain cases, the graphs only increase after the start-up phase, while in other scenarios they only decrease. The main variables causing this change are the *costs of heart rate monitors* and the *increase in the quality of life after Active-at-Home* is implemented. Yet in 2050, all scenarios show positive SROI with a cluster between the values of 50 and 70. Therefore, even with uncertainty taken into account, this intervention is worth the investment.



(a) SROI of Active-at-Home intervention



(b) SROI of Active-at-Home intervention under uncertainty

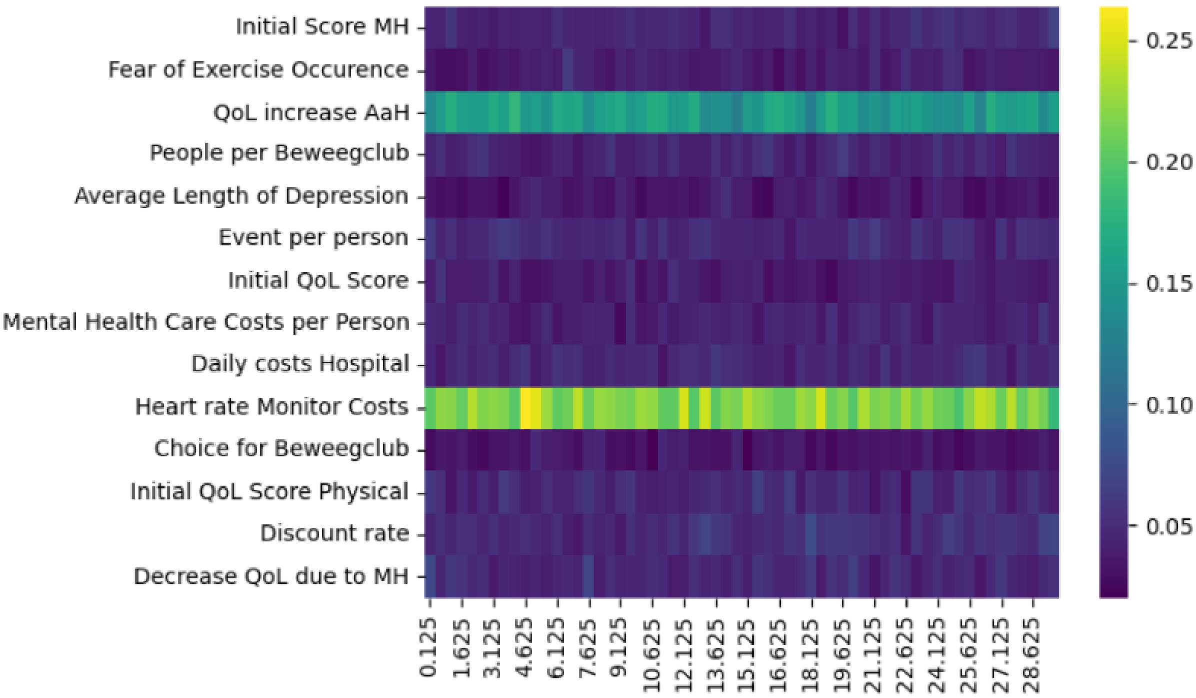
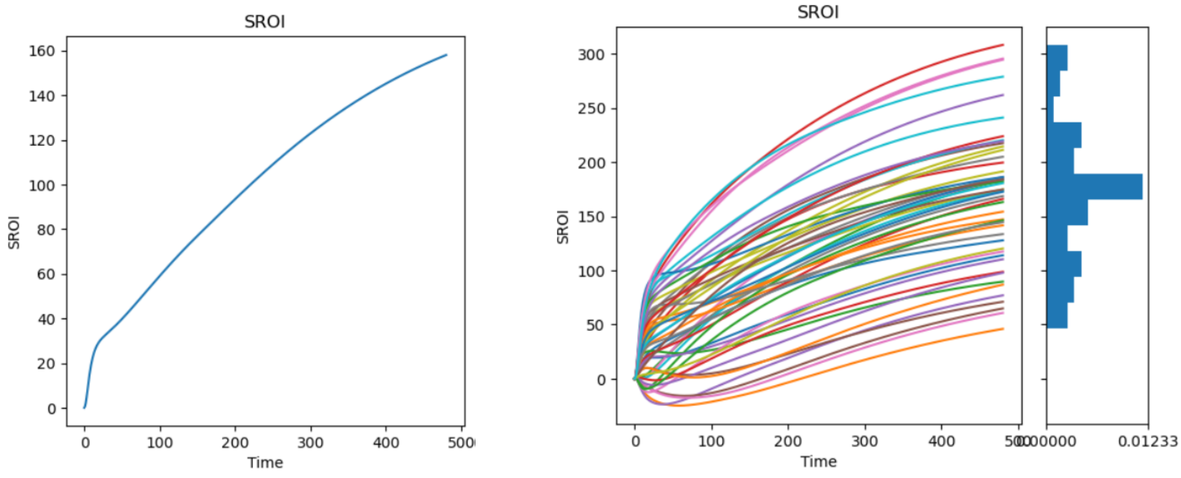


Figure 8.2: Feature Scoring over time for Active-at-Home.

8.1.2. Results for the Video Games for Physical Activity intervention

Figure 8.3a visualises the SROI ratio for the Video Games for Physical Activity intervention under standard circumstances. With this intervention mostly a one-time investment at the start of the intervention, most costs occur near the year 2020. In fact, the SROI ratio in the first time step is below 1. Then, due to the long-lasting benefits of physical activity, the SROI ratio remains to increase to reach a value of 157.98 by the year 2050.

Figure 8.3b visualises the SROI ratio for the Video Games for Physical Activity intervention when uncertainty is taken into account. The uncertainty contains the type of video game console chosen by Harteraad, which affects the SROI ratio. High console prices cause the SROI ratio to temporarily drop below zero. However, most of the variance in SROI is initially caused by the variable *"Decrease QoL due to MH"*. Which over time is replaced by the variable *"decrease QoL due to lack PA"*. In 2050 all SROI ratios are positive, varying between around 50 and 300 with the highest cluster between 170 and 190. The variance in SROI ratios



(a) SROI of Video Games Intervention

(b) SROI of Video Games Intervention under uncertainty

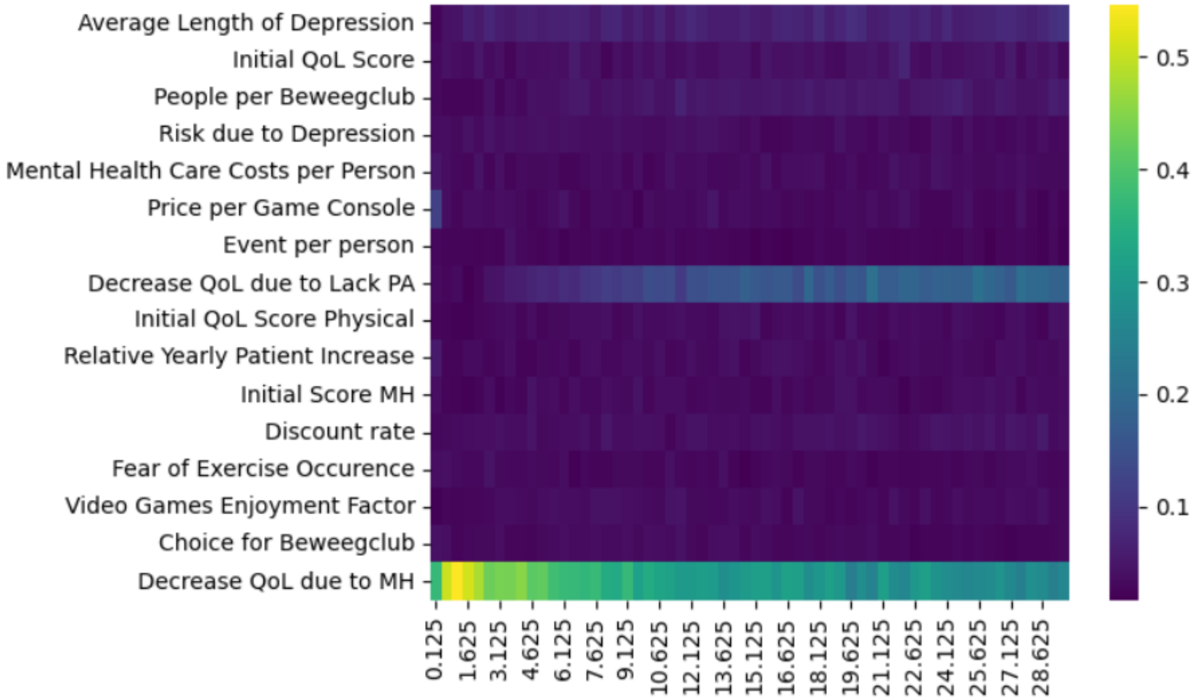
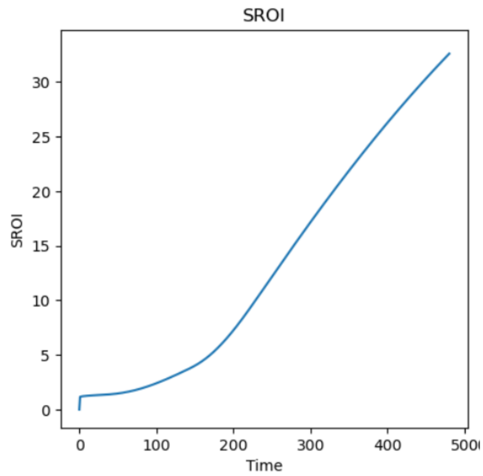


Figure 8.4: Feature Scoring over time for video games.

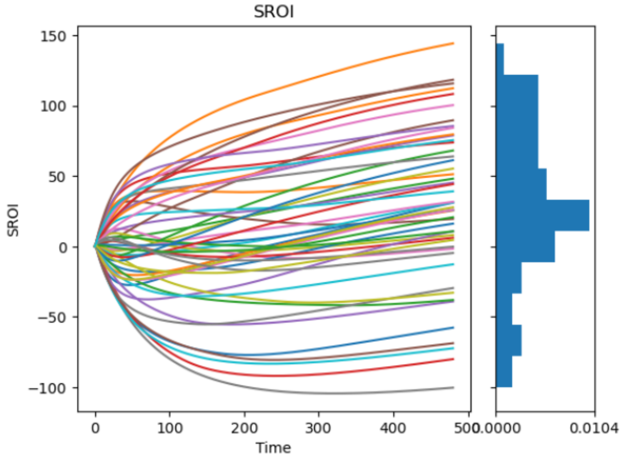
8.1.3. Results for the Relaxation Technique Training Groups Intervention

Figure 8.5a visualises the SROI ratio for the Relaxation Technique Training Group intervention under standard circumstances. The graph shows the SROI ratio starting off low at around 1.1 before the long-term effects become visible. At the end, the SROI ratio reaches a value of 32.60.

Figure 8.5b visualises the SROI ratio for the Relaxation Technique Training Group intervention when uncertainty is taken into account. The figure shows that uncertainty can alter the feasibility of this intervention. Both positive and negative SROI ratios occur. Despite the majority (n = 37) of the scenarios resulting in a positive SROI, the select few negative SROI ratios indicate that no immediate conclusion can yet be made. Hereby, the main effects on the SROI ratio are *"decrease QoL due to lack PA"* and *"Decrease QoL due to MH"*. This intervention thus shows policy sensitivity, as the intervention is not worth the investment if the SROI ratio is below 1.



(a) SROI of Relaxation Technique Intervention



(b) SROI of Relaxation Technique Intervention under uncertainty

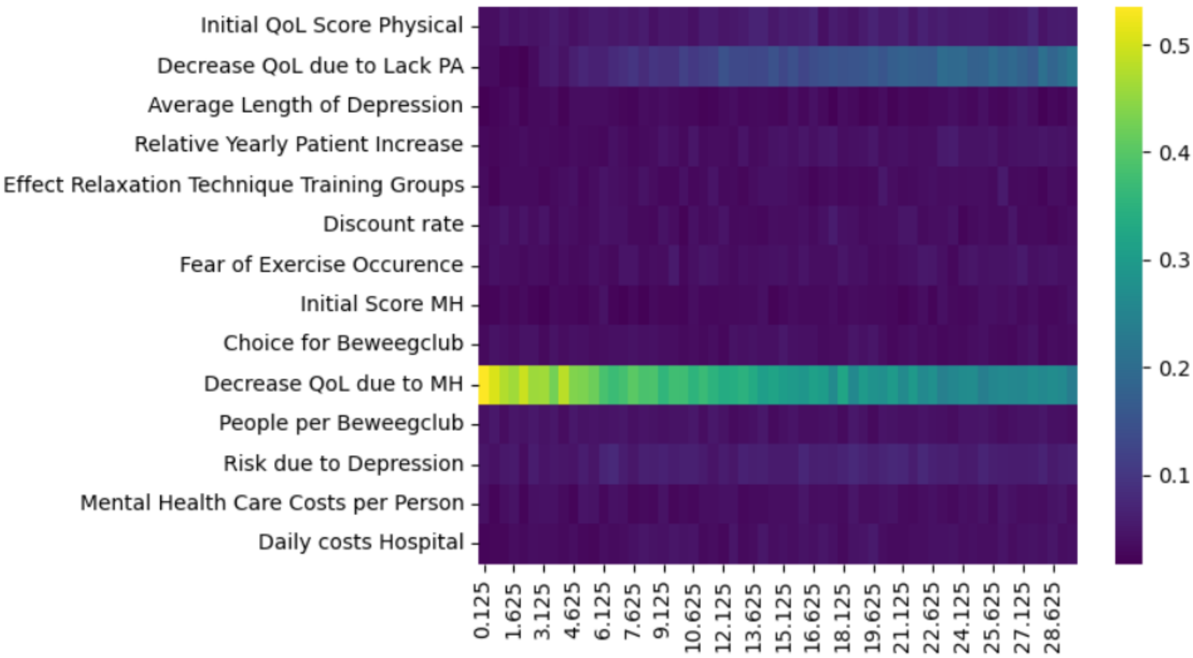
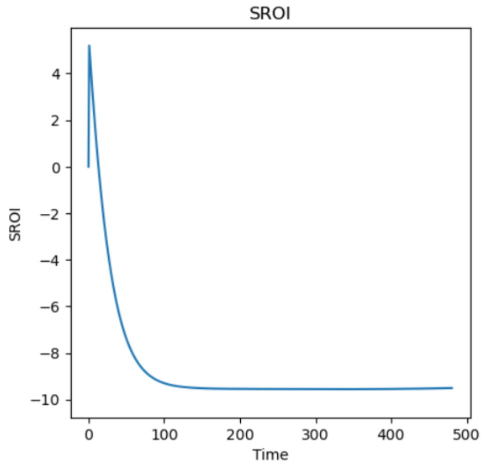


Figure 8.6: Feature Scoring over time for relaxation techniques.

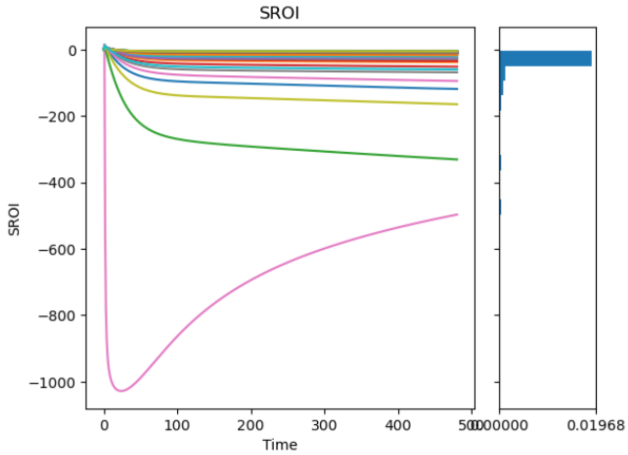
8.1.4. Results for the High-Intensity Interval Training Intervention

Figure 8.7a visualises the SROI ratio for the High-Intensity Interval Training intervention under standard circumstances. High-Intensity Interval Training can be considered a high-risk, high reward due to the intensity of the program. As such, the SROI after investment is positive in the short-term. However, the SROI soon starts to drop below zero to never becomes positive again. In the year 2050 is the SROI ratio -9.51.

Figure 8.7b visualises the SROI ratio for the High-Intensity Interval Training intervention when uncertainty is taken into account. Similar to the standard situation, all SROI ratios turn negative and stay negative. Hereby, the intensity of HIIT is the main cause of variance within the SROI ratio. Most scenarios result in an SROI ratio between 0 and -50, with two noticeable outliers reaching values in the negative hundreds. Since no scenario shows positive SROI in the long term, it indicates that the HIIT intervention is not worth any investment.



(a) SROI of High-Intensity Interval Training Intervention



(b) SROI of High-Intensity Interval Training Intervention under uncertainty

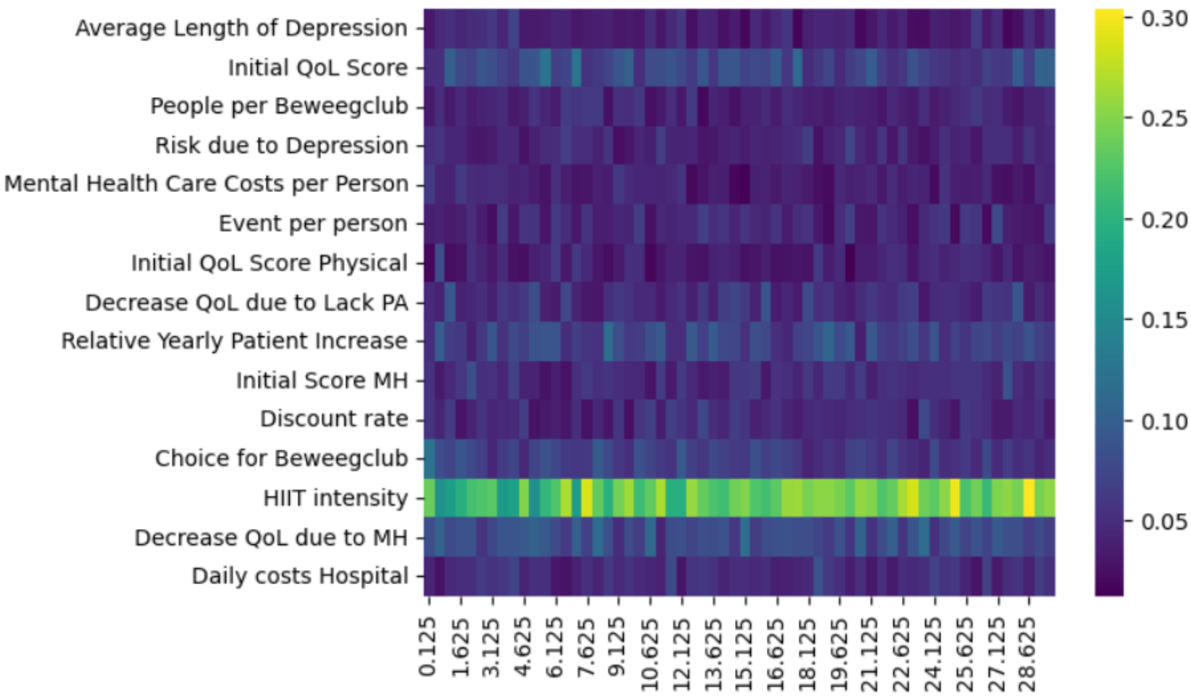
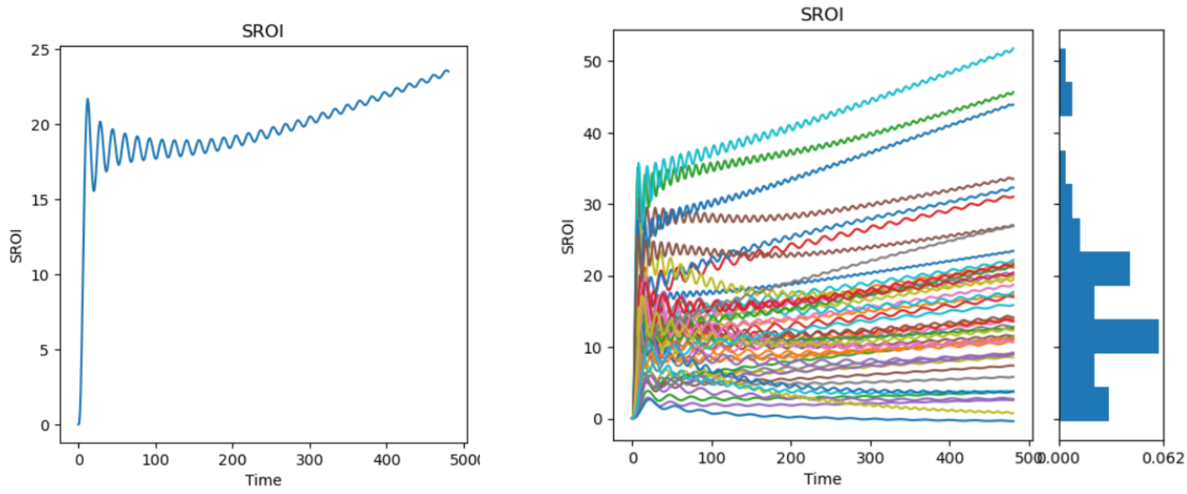


Figure 8.8: Feature Scoring over time for HIIT.

8.1.5. Results for the Group Based Training Intervention

Figure 8.9a visualises the SROI ratio for the Group Based Training intervention under standard circumstances. The SROI ratio fluctuates matching the time periods in which an investment is made and when the effects of group-based training still exist among the patient population. Over time, the amplitude of the waves decreases and the average value starts to increase. By the year 2050 the SROI ratio has reached a value of 23.53.

Figure 8.9b visualises the SROI ratio for the Group Based Training intervention when uncertainty is taken into account. The training frequency and the duration of the program influence the SROI ratio, with the effectiveness of group-based training being an influential factor as well. Yet ultimately, all SROI ratios turn out to be positive. However, in the worst-case scenario, the SROI is less than 1. This indicates that the social gains are less than the costs of the investment.



(a) SROI of Group Based Training

(b) SROI of Group Based Training under uncertainty

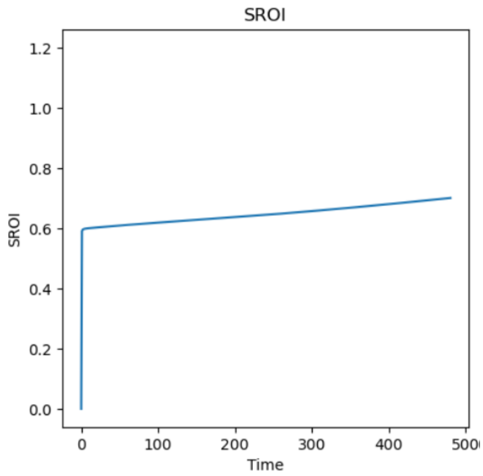
Figure 8.10: Feature Scoring over time for group training.

8.2. Results for Mental Health Interventions

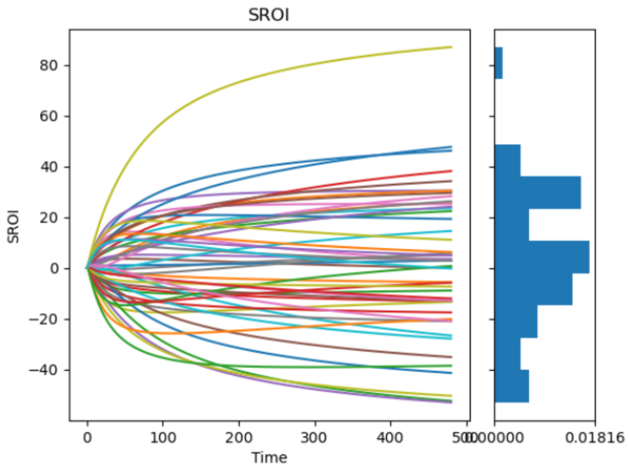
8.2.1. Results for the Music Therapy Intervention

Figure 8.11a visualises the SROI ratio for the Music Therapy intervention under standard circumstances. This intervention aims to reduce stress among patients that just experienced a CVD event. The gains of music therapy thus lie in the patient population with depressive symptoms, while the costs regard the wages for therapists providing this type of therapy. In the end, the wages outweigh the gains, resulting in an SROI ratio of 0.70.

Figure 8.11b visualises the SROI ratio for the Music Therapy intervention when uncertainty is taken into account. Uncertainty is the number of hours of music therapy needed, as well as the effect of music therapy on the patients, causes the SROI ratio to vary widely. Similar to the Relaxation Technique Training Groups from section 8.1.3 the SROI reaches both positive (n = 27) and negative values (n = 23) with the variable *"Decrease QoL due to MH"* explaining 34% of all variances. Considering the whole decision space, the SROI is negative more often than not. So it is most likely that music therapy does not provide the support patients need.



(a) SROI of Music Therapy Intervention



(b) SROI of Music Therapy Intervention under uncertainty

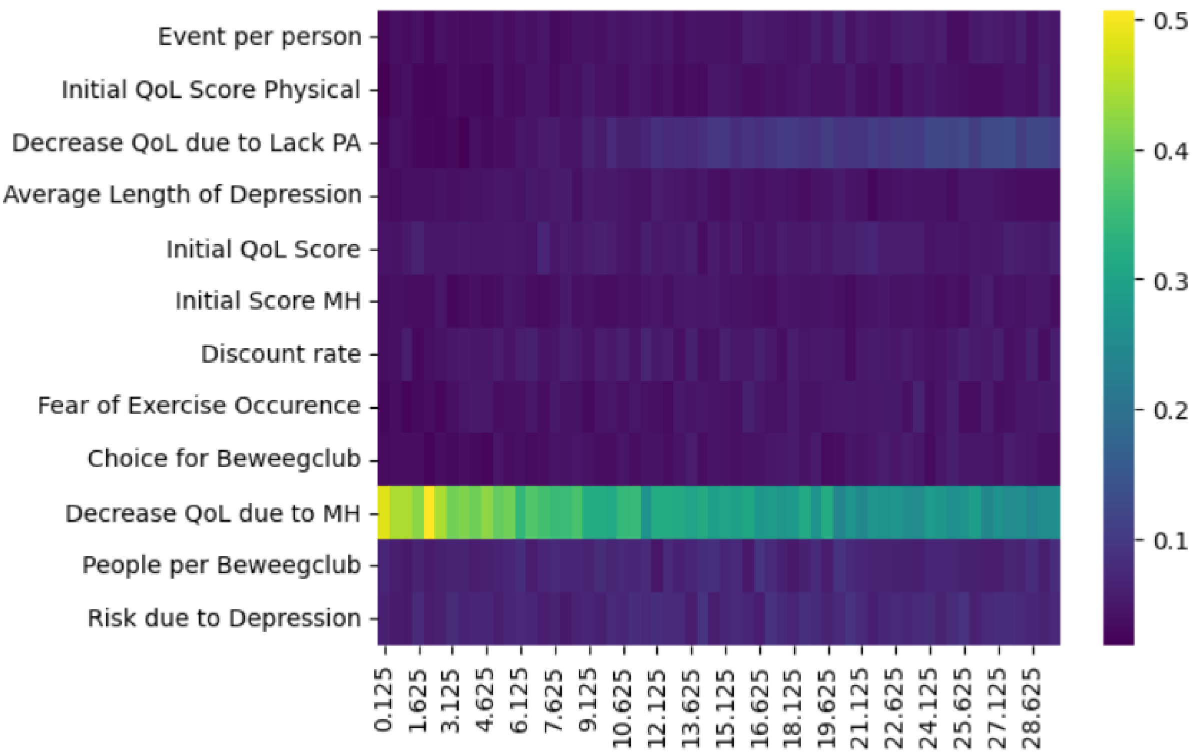
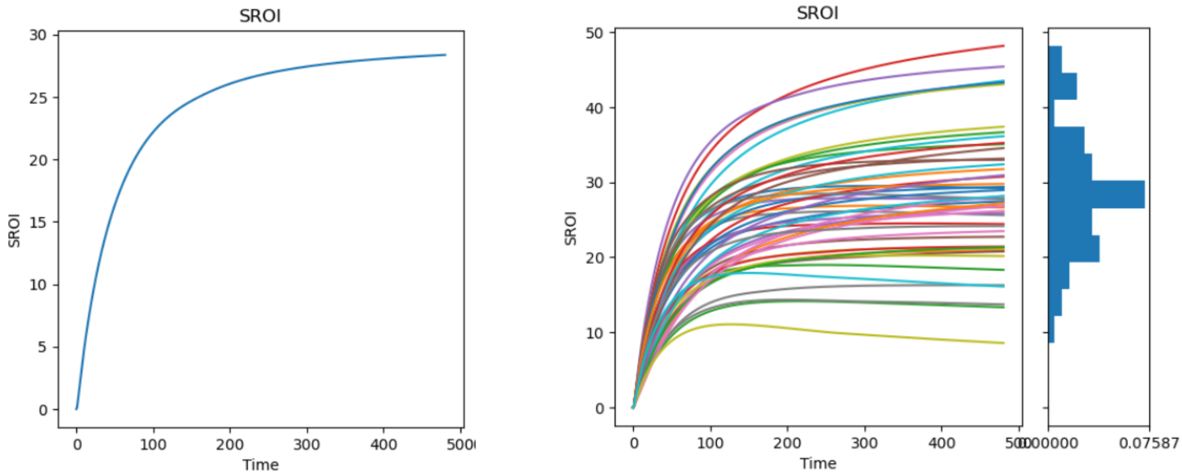


Figure 8.12: Feature Scoring over time for music therapy.

8.2.2. Results for the Care Coordination Intervention

Figure 8.13a visualises the SROI ratio for the Care Coordination intervention under standard circumstances. This intervention assumes organising information days in which all patients participate and apply the information received. This results in more awareness among the patient population to exercise, causing a net positive result. The graph shows a sharp increase in the first few years, which flattens over time. Despite the flattening of the curve, the SROI ratio remains to increase. By the year 2050, it has reached a value of 28.36.

Figure 8.13b visualises the SROI ratio for the Care Coordination intervention when uncertainty is taken into account. Uncertainty regards the costs of organizing the events and how well the patients participate. Nonetheless, figure 8.13b shows that all SROI ratios are positive in the year 2050. Only in a select few scenarios is the slope of the SROI ratio clearly decreasing. Since most benefits in this intervention are made at the start, however, the SROI ratio remains positive even in the long-term. So the SROI is still positive and thus worth the investment.



(a) SROI of Care Coordination

(b) SROI of Care Coordination under uncertainty

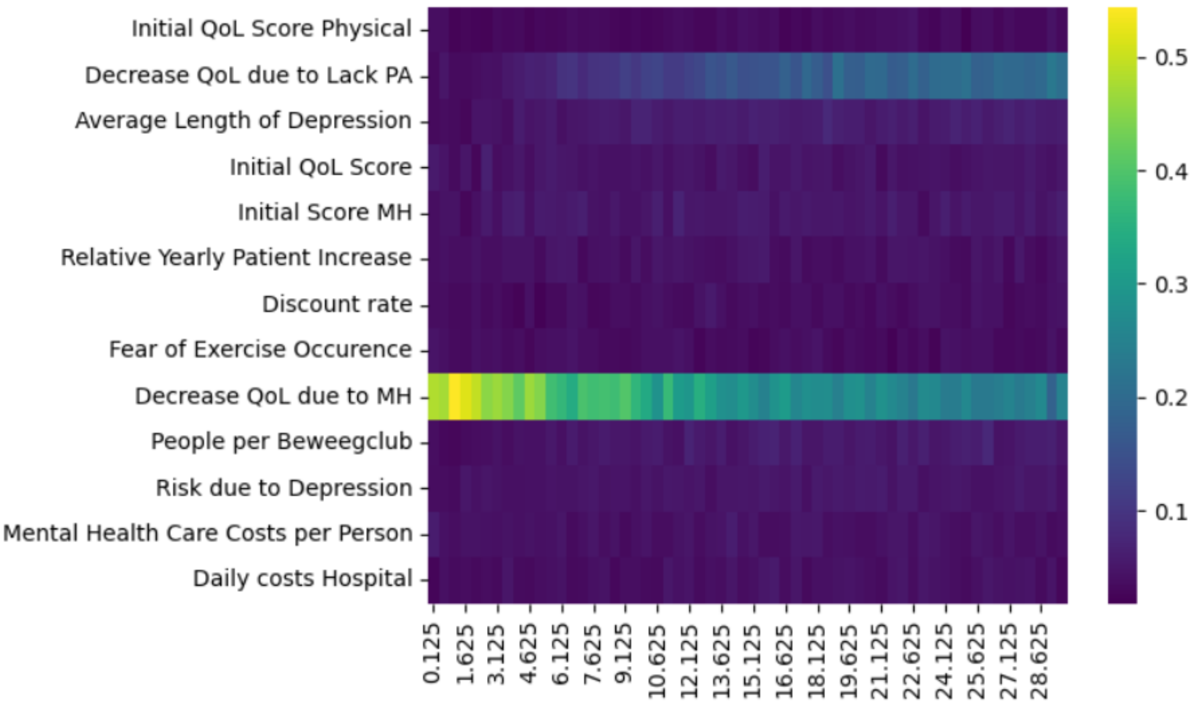
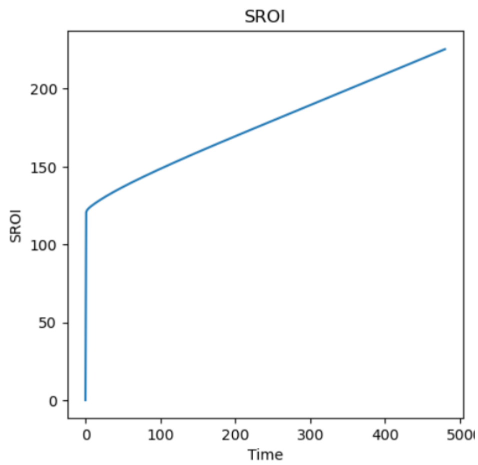


Figure 8.14: Feature Scoring over time for care coordination.

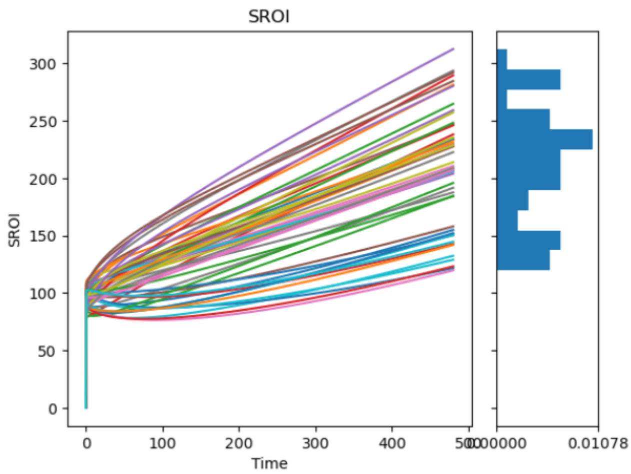
8.2.3. Results for the Cognitive Behavioural Therapy Intervention

Figure 8.15a visualises the SROI ratio for the Cognitive Behavioural Therapy under standard circumstances. In this intervention, there are initial investment costs in the training programs for therapists. However, Cognitive Behavioural Therapy has a slightly delayed effect when promoting a healthy lifestyle. So the SROI ratio starts at zero before jumping towards a higher value. Which value is reached depends on the initial QoL score. In the end, the benefits outweigh the costs and the investment. As a result, the SROI is positive, reaching a value of 225.41 by the year 2050.

Figure 8.15b visualises the SROI ratio for Cognitive Behavioural Therapy when uncertainty is taken into account. The behaviour of the model changes depending on the scenario. In the worst case scenarios – when the wages are high – the SROI actually decreases for the first 10 years before increasing. However, the ratios never drop below zero, showing that Cognitive Behavioural Therapy is an intervention worth investing in.



(a) SROI of Cognitive Behavioural Therapy



(b) SROI of Cognitive Behavioural Therapy under uncertainty

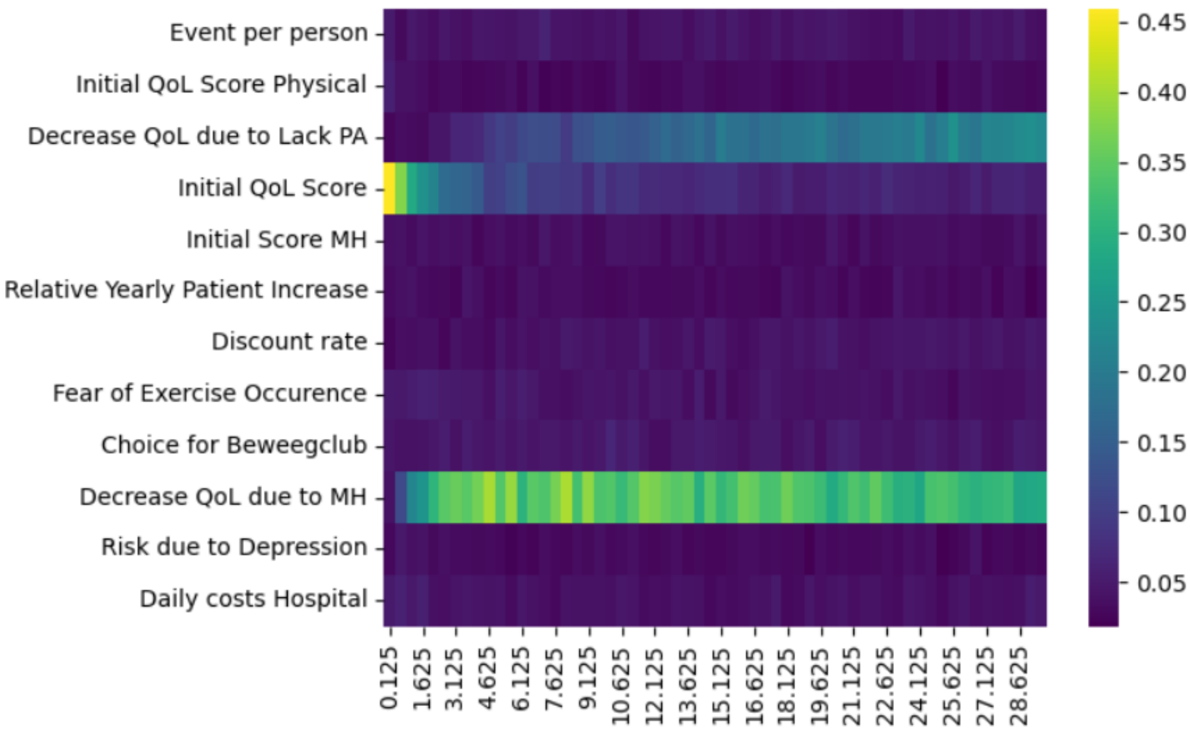
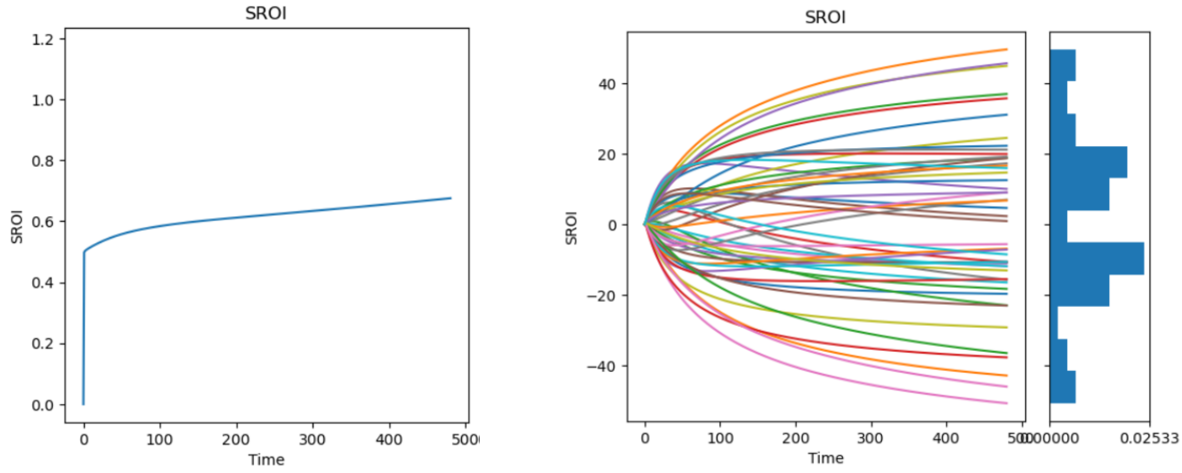


Figure 8.16: Feature Scoring over time for CBT.

8.2.4. Results for the Promote Autonomy and Recovery Intervention

Figure 8.17a visualises the SROI ratio for the promotion of autonomy and recovery under standard circumstances. The focus of this intervention is providing mental support with the aim of increasing medical usage. However, with therapy being personalised and not every patient seeking help, the cost is relatively high compared to the benefits. As a result, the SROI by the year 2050 is equal to 0.68.

Figure 8.17b visualises the SROI ratio for the promotion of autonomy and recovery when uncertainty is taken into account. The figure shows that the SROI ratio is sensitive to the uncertainty of parameters within the model. As with the music therapy intervention, the SROI is positive in some scenarios while negative in others. In other words, the model shows both behavioural and policy sensitivity. The graphs show quite a symmetry around zero, indicating that positive results occur with the same frequency as negative results. In fact, in 24 scenarios out of 50, the SROI is negative, indicating a pretty even distribution. Consequently, this indicates that the use-ability of the promotion of autonomy and recovery is not conclusive.



(a) SROI of Promote Autonomy and Recovery

(b) SROI of Promote Autonomy and Recovery under uncertainty

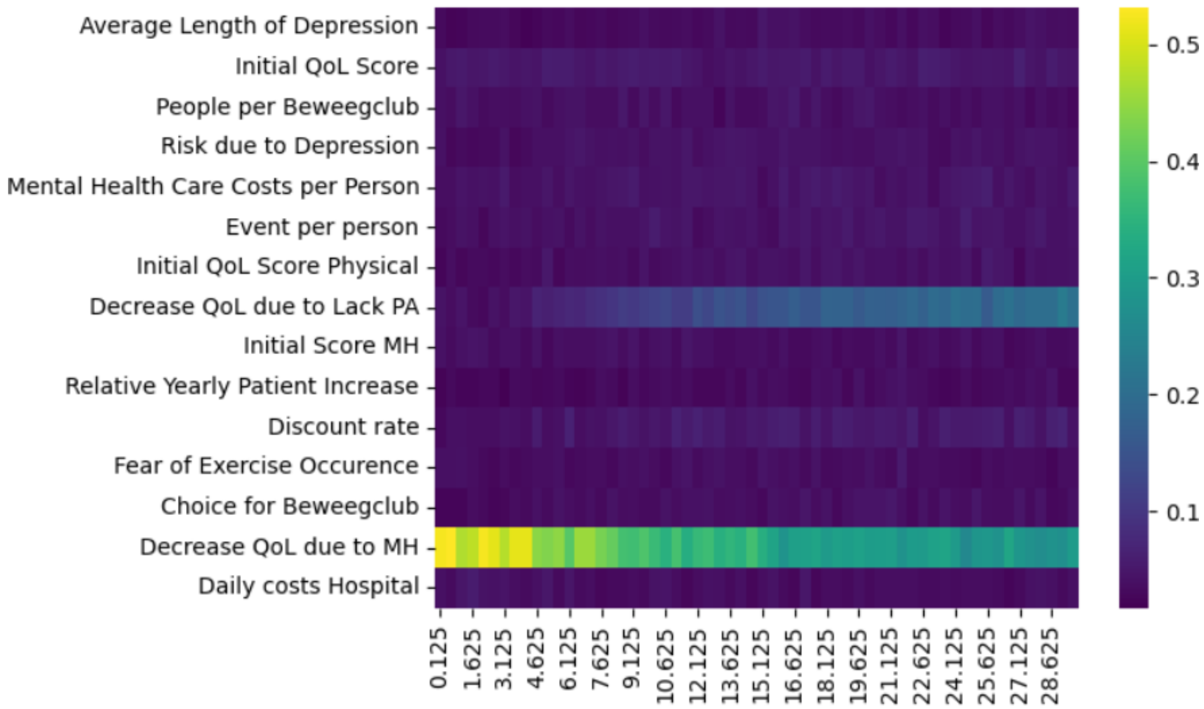
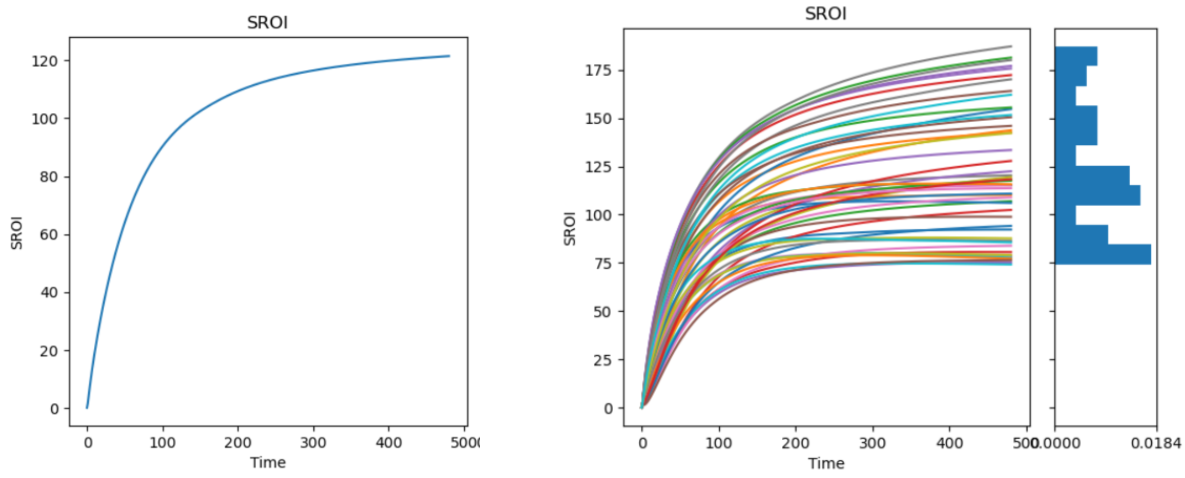


Figure 8.18: Feature Scoring over time for PAR.

8.2.5. Results for the Telemedicine Intervention

Figure 8.19a visualises the SROI ratio for the Telemedicine intervention under standard circumstances. With Telemedicine, therapists can immediately offer help regarding mental health when the first symptoms of depression appear. Depression is cured faster than without this intervention, removing a burden on the costs of mental health support. The SROI started to increase almost instantly, flattening out after 25 years. In the year 2050, the SROI has reached a value of 121.48.

Figure 8.19b visualises the SROI ratio for the Telemedicine intervention when uncertainty is taken into account. All graphs show similar behaviour, resulting in a positive SROI ratio under all scenarios. In fact, the results are relatively evenly spread between SROI ratios of 75 and 180. Consequently, Telemedicine is an intervention worth investing in.



(a) SROI of Telemedicine

(b) SROI of Telemedicine under uncertainty

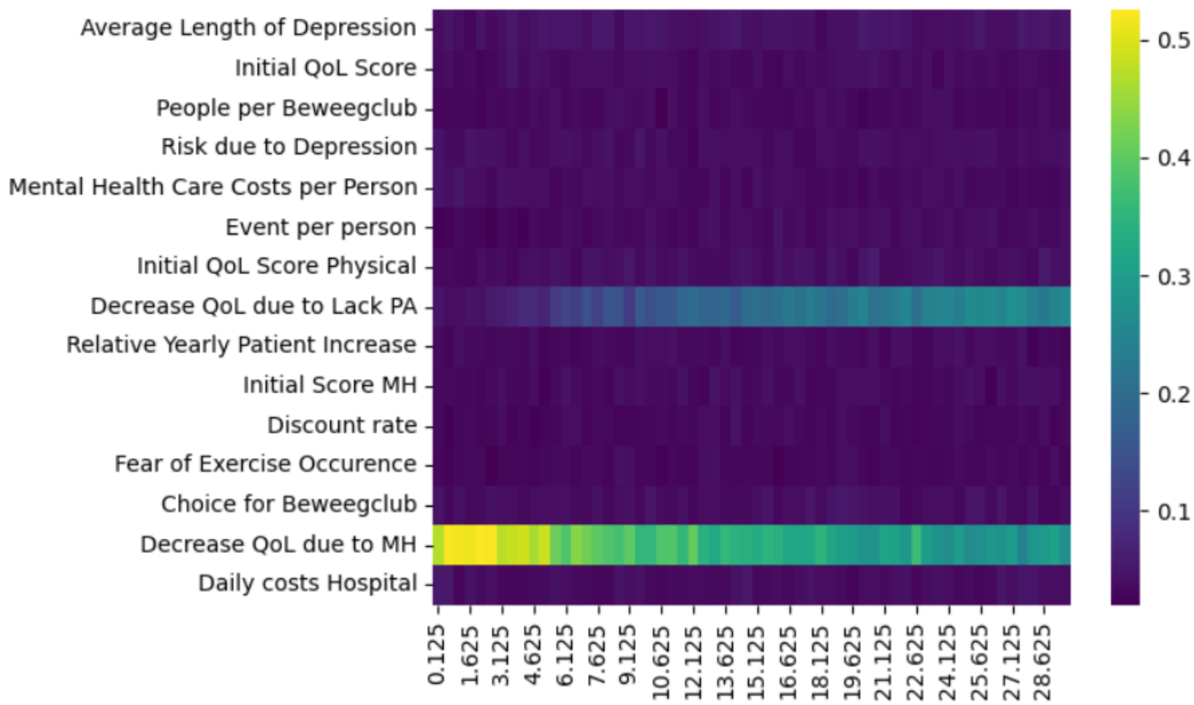
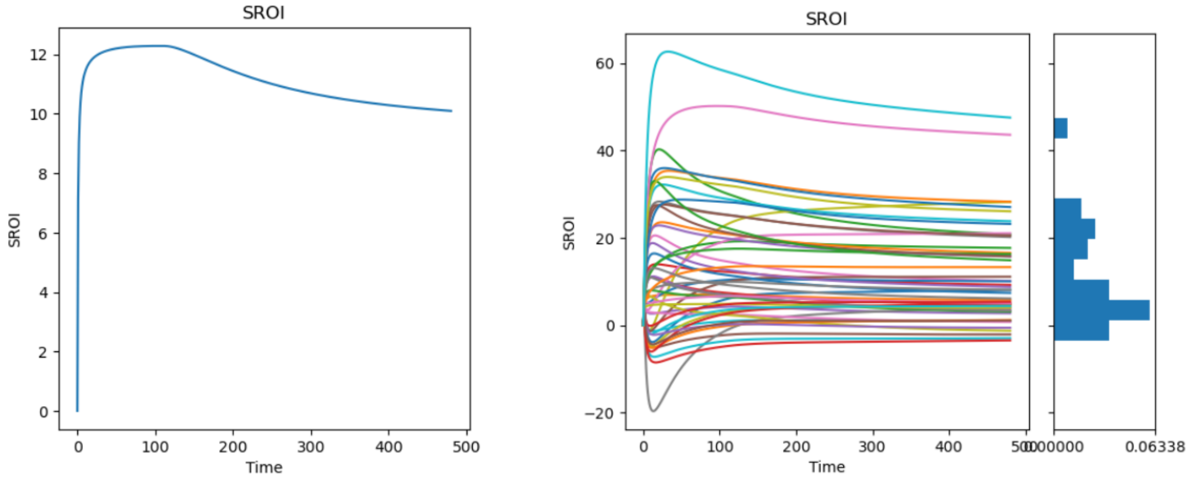


Figure 8.20: Feature Scoring over time for Telemedicine.

8.3. Results for CombiConsultation

Figure 8.21a visualises the SROI ratio for when CombiConsult (CC) is chosen in the standard circumstances. The main costs for CC are the training costs for pharmacists when joining the program, as well as financial compensation for the pharmacists. The main effect of CC is an increase in medical adherence, resulting in the prevention of unnecessary deaths. The maximum effect is seen in the year 2026 with a SROI ratio of 12.29. However, the graphs show a decrease from then on. By the year 2050, the SROI will have reached a value of 10.10 which is still positive.

Figure 8.21b visualises the SROI ratio for the CC intervention when uncertainty is taken into account. Uncertainties include the costs of training for each pharmacist and the financial compensation the pharmacists get for participating in the CombiConsult intervention. The biggest change in SROI is caused by the variable *"daily compensation"*. The strength of this variable increases over time, corresponding with the increase of pharmacists involved in CC. Furthermore, depending on the scenario, the SROI may drop to negative values in the short term before increasing and passing zero again. However, for five scenarios (10%)) the SROI ratio remains negative. All other scenarios show positive SROI by 2050 with the biggest cluster between one and five. in conclusion, CombiConsult is most likely to be worth the investment.



(a) SROI of CombiConsult

(b) SROI of CombiConsult under uncertainty

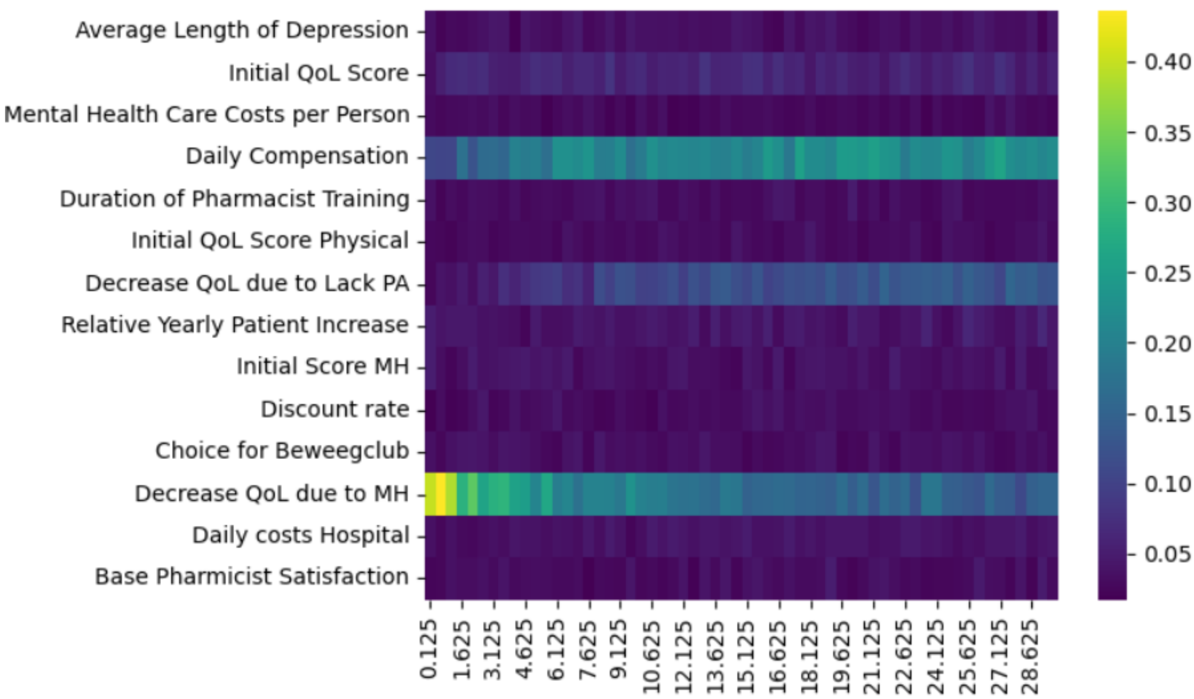


Figure 8.22: Feature Scoring over time for CombiConsult.

8.4. Summary of results

In this research, the SROI ratio was determined for eleven different interventions. Since decisions have to be made under uncertainty, the EMA workbench was used to explore the effect of including uncertainty in the model. The results show that Active-at-Home; Video Gaming; Group Based Training; Care Coordination; Cognitive Behavioural Therapy and Telemedicine have a positive SROI under all scenarios. On the contrary, High-Intensity Interval Training has negative SROI for all scenarios. Lastly, Relaxation Technique Training; Music Therapy; Promote Autonomy and Recovery and CombiConsult show mixed results. Hereby, it should be noted that for Relaxation Technique Training and CombiConsult, a positive scenario is more likely. One factor that eight of the eleven results have in common, is the importance of variables that relate to the Quality of Life. Only for High-Intensity Interval Training, Group-Based Training and CombiConsult can the variance over time be explained by other variables as well.

9 Discussion

In this chapter, the results are analysed and compared with existing literature. Additionally, a discussion is held on the approach of this research. This includes a discussion on the SROI methodology, the availability of data and the model itself. Lastly, this chapter ends with a recommendation for future research and policymakers.

9.1. Interpretation of the results

The results from chapter 8 indicate that seven interventions have a positive (and larger than one) SROI ratio. This means that those interventions have a net benefit effect which furthermore outweighs the total cost of investment. Three of the interventions show varying results. Lastly, one intervention has consistently negative SROI ratios, meaning the costs are higher than the benefits even without including the investment costs. Table 9.1 shows all the results in one table.

Table 9.1: Summarised Results

Intervention	Results on SROI
Active-at-Home	Positive and larger than 1
Video game	Positive and larger than 1
Relaxation Technique Training	Mixed Results
High-Intensity Interval	Negative results
Group Based Training	Positive Results (1 scenario less than 1)
Music Therapy	Mixed results
Care Coordination	Positive and larger than 1
Cognitive Behavioural Therapy	Positive and larger than 1
Promote Autonomy and Recover	Mixed results
Telemedicine	Positive and larger than 1
CombiConsult	Mostly positive and larger than 1, few scenarios with negative SROI

9.1.1. Interpretation of the interventions with positive results

The Active-at-Home intervention enables patients to exercise from home, even patients who cannot leave their house due to their condition. As a result, the barrier to exercise gets removed. Originally created for patients with heart failure (Okwose et al., 2020), this project explores what happens if the intervention is enabled for all CVD patients. The net effect is an increase of four points in the physical health component of the Quality of Life metric (Okwose et al., 2019). However, when comparing the base case with the intervention, the difference in QoL is only 0.5 or 0.83%. This leads to a social gain of 250 euros per patient, and with a population group of over 1.5 million, it results in a large increase in social gains. In the pilot study, the effects are smaller. However, so are the costs of heart monitors and the wages of the involved employees.

Video games for Physical Activity Intervention have positive SROI for all scenarios as well. This intervention regards a form of group exercise and is thus centred around the Beweegclubs. Research from Warburton et al., 2007 has shown that the main advantage of video games for physical activity is the increased attendance rate. The number of Beweegclubs within the Netherlands is limited as well as the capacity they can offer. So the positive effect should only reach a small part of the patient population. What happened is that the high SROI ratio is caused by the low costs of the intervention. Buying game consoles and video games is a one-time investment and according to Sutanto et al., 2019 the primary source for costs. This is shown in the model as the total costs for the video game intervention only reaches about 574k euro, whereas other interventions may cost more than millions of euros per year. So the SROI ratio calculates limited social gains with even smaller (relatively) investment costs, resulting in a high SROI ratio. As such, it is important to be aware that measuring the SROI ratio only does not show the whole story and can lead to a one-dimensional focus (Gibbon and Dey, 2011).

The third intervention – and the last for the physical activity interventions – with consistent positive SROI is the Group Based Training Intervention. In the model, this intervention is assumed to take half a year of weekly training. After which the most beneficial results are met. In this intervention, different types of group-based training are combined into one single variable. In a comparative study by Grässler et al., 2021 and D'Isabella et al., 2017 it is shown that the different regimes affect the same or similar outcome variables for different patient groups. The effects on the target groups were positive. On the other hand, King et al., 1991 group-based exercise training only increases fitness and not heart disease risk, especially among older patients. In that case, CVD events will occur as in the base case, keeping the social cost high. In that case, the SROI ratio would be lower, as the only net benefit result is the benefit to mental health Mikkelsen et al., 2017.

The fourth intervention with positive SROI is the Care Coordination Intervention. Activities within this intervention include developing a care plan, sharing knowledge, linking to community resources and aligning resources with patient and population needs (Murphy et al., 2021). Financing those activities is often a problem (Murphy et al., 2021), especially since there is uncertainty in the costs involved. However, research by Berkowitz et al., 2018 shows that Care Coordination does lead to better health outcomes and lower costs for the healthcare system. However, the article does not perform a formal cost-effectiveness analysis Khullar and Chokshi, 2018. As such, the uncertainty regarding this intervention remains high, indicating that more research is needed on this intervention.

The fifth intervention with positive SROI is Cognitive Behavioural Therapy. Mental health support is provided to better the lifestyle of patients. This intervention thus relates to both physical activity and mental health. Consequently, a net positive effect is as was expected. International studies on CBT show cost-effectiveness for both mental support and behavioural activation (Myhr and Payne, 2006; Richards et al., 2016). The costs for this intervention lie mostly in wages and training of therapists, which is similar to the costs of other interventions. So with this intervention, the high SROI ratio is primarily caused by the duality of having positive effects on mental health and exercise.

The sixth and last intervention with positive SROI is telemedicine. According to Farabi et al., 2020 this intervention is a cost-effective solution for almost all types of cardiovascular disease. The only costs lie in wages, since the costs of communication equipment such as smartphones lie on the user. In high-income countries such as the Netherlands, most people already have a smartphone (Bastawrous and Armstrong, 2013). Furthermore, a monitoring session takes only between 10 and 20 minutes Kraal et al., 2013 further reducing costs. As a result, the SROI is indeed expected to be high, which is what is shown in section 8.2.5.

9.1.2. Interpretation of the interventions with varying results

Three of the 11 investigated interventions show mixed results. Here the SROI ratio depends largely on the uncertainty of the input variables, showing both behavioural and policy sensitivity. These interventions are (1) Relaxation Technique Training Groups, (2) Music Therapy, (3) Promote Autonomy and

Recovery and (4) CombiConsult.

Relaxation and meditation cause a temporary reduction in mental health and physical activity (Walton et al., 2004). The main aim hereby is to minimize stress and the consequences of high stress levels (Mask Jr, 2000). However, in the CVD patient model, stress is only one of the three factors causing depression. As such, the positive effect on society regarding depression and the following CVD events should be limited. As Walton et al., 2004 explains, treatment for CVD deceases is not the primary intention of relaxation. In fact, this intervention has its basis in pseudo-science as alternative medicine, summarised as "mind–body medicine"(M. C. Lin et al., 2001). As such, whether this intervention is suitable for CVD patients remains debatable, which is supported by the generated results. More specifically, on the model results, the SROI is negative in thirteen scenarios. In seven of which, the main culprit is a large input value for *"Decrease QoL due to MH"*. This intervention is only used on patients who are stressed out due to their condition. So while those patients get help, the large population still see a reduction in their QoL, including on the aspect of mental health. The social costs of the QoL decrease of the large population do outweigh the social gains of this intervention. Similarly, on eight scenarios is the negative SROI caused by a large value for *"Decrease QoL due to lack PA"*. Hereby, the same argument holds true. The gains of patients who were helped with relaxation technique training, do not outweigh the consequences of patients who were not helped by relaxation technique.

Music therapy is used for a similar reason as Relaxation Technique Training Groups, namely the reduction of stress and anxiety (Mozaffari et al., 2020). Thus, the same conclusions can be made on the reason the results are inconclusive. The only difference is that music therapy is not necessary in groups or with people only in Beweegclubs. Thus reaching more people but with relatively higher costs. Consequently, the SROI ratio for music therapy behaves the same as for relaxation training groups, but with the ratio bounded between lower intervals. However, unlike the relaxation technique, the main culprit of negative SROI is only *"Decrease QoL due to MH"*. Furthermore, in all but two scenarios, this variable causes the SROI to drop below zero immediately, for which it never recovers. In those two scenarios, the drop to negative SROI occurred only in the last year and is caused by an unfortunate combination of input variables.

Lastly, is the Promote Autonomy and Recovery Intervention. The aim of this intervention is to improve the patient's lifestyle through therapy. The main focus hereby lies on correct medication intake (Solmi et al., 2021). The sole variable it influences is the adherence rate, which in turn only affects the deaths and hospitalisations. The uncertainty in social costs regarding these factors determines whether the SROI is positive or not. Despite this, the costs are relatively low as well. Only patients with high stress levels will reach a therapist. As a result, this intervention is able to reach high values of SROI. Now for the negative SROI ratios, the main culprit again is the variable *"Decrease QoL due to MH"* where the social costs of patients that do not seek help outweigh the social gains for the patients that do. Similarly to the results for music therapy, the SROI for those scenarios already dropped below zero at the start of the simulation. Despite this, in three scenarios it only drops below zero after respectively seven years (2x) and ten years (1x). Hereby, the cause lies in the PA factor of QoL.

CombiConsult is the fourth and last intervention investigated with an inconsistent positive SROI. However, it only remains negative in five of the fifty scenarios. The main factor of costs in this intervention is training in consultation skills Meijvis et al., 2021 and compensation for the pharmacists for joining CombiConsult. The wages for pharmacists can be excluded from the model due to attribution. The reason for this is that the CombiConsult is a program with already existing pharmacists. The work hours will not change for the pharmacists, meaning that their wages are paid anyway whether they join CombiConsult or not and only some additional compensation is included. Social gains come in two factors, a decrease in spending on an excess of medicines (Meijvis et al., 2023) and a decrease in deaths due to medication non-adherence (Jimmy and Jose, 2011). These effects are only quite small. For example, only 9% of deaths can be prevented (Al-Ganmi et al., 2016). On a large population group, this still accounts for over 20,000 prevented deaths per year. However, instead of dying after a CVD event, patients who survive are hospitalised, thus paradoxically increasing hospital costs. In scenarios where the hospital costs are indeed way higher than in the base case, the graph is less steep. The same holds true for the daily compensation. Even though this variable influences the final SROI ratio, it is a component of total investment costs. Meaning that it can only change the absolute value and not the sign. Further analysis shows that only in scenarios where both the decrease of QoL due to mental health and the yearly inflow of new CVD patients, is the SROI negative at the year 2050. Hereby, the reason mental health decreases can be explained by the fact that over time, more and more patients are getting involved in the CombiConsult program, leading to better support for the patient.

From the interventions with varying results, a pattern is clearly recognisable. All negative SROI ratios can be attributed to a single variable: *"Decrease QoL due to MH"*. If mental health problems see a sharper decrease in the quality of life than in the base case, is the SROI prone to become negative, especially if the intervention only focuses on a subgroup of the total population. As such, this model demonstrates the importance of mental health even for patients who fall outside the target group for the intervention.

9.1.3. Interpretation of the interventions with negative results

High-intensity interval training is the only intervention that reaches negative SROI ratios for all simulated runs. This means that the net present value of the benefits is lower than the net present value of the social costs. The two outliers related to the scenario whereby the level of HIIT is at maximum value. This is beyond the level of minimum mortality rate. Yet, due to the intensity, the non-adherence to PA increases. So even though there is still a slight reduction in mortality compared to the base case, the non-adherence takes effect after a slight delay, causing a negative feedback loop. Compared to other types of exercises, HIIT has been shown to drastically decrease mortality by over 40% Eijsvogels et al., 2016. According to Karlsen et al., 2017 HIIT can be used for maximizing health outcomes. However, HIIT is a double-edged sword. Due to the intensity, HIIT is associated with a lower adherence due to potential safety concerns (Wewege et al., 2018). In an article by Ekkekakis and Biddle, 2022, they claim that without supervision, the prescribed levels of HIIT are not met. Effectively reducing the impact even more. A negative effect can thus be expected.

Based on the results, a comparison can be made with the dynamics hypothesis described in chapter 4.1.5. It was hypothesized that all interventions would eventually lead to a positive SROI ratio. This conclusion can however only be made for six of the eleven tested interventions. In the case of high-intensity interval training, it was caused by a decreasing adherence to physical activity, an effect not taken into consideration during the conceptualisation phase. On the other hand, three interventions can have SROI ratios being less than one or even negative. This was primarily caused by the uncertainty in certain input parameters. The most influential being *"Decrease QoL due to MH"*. So a comprehensive conclusion can not be made on the usability of said interventions. However, it does show the importance of mental healthcare among patients with CVD, even when no specific intervention for MH is incorporated. Furthermore, the inability to make a full conclusion shows that the approach has limitations that need to be reflected on.

9.2. Limitations

It should be acknowledged that every research including this one has several limitations that need to be addressed. Limitations were identified from three perspectives: (1) the data collection, (2) the modelling approach including the model itself and (3) the SROI methodology.

9.2.1. Limitations on data gathering

One of the limitations of this project is the lack of data. Preferably, outcomes variable in the health care system should be measured by patient-reported outcome measure (PROM) and patient-reported experience measure (PREM) (Wolff et al., 2021). Both PROM and PREM are questionnaires filled in by the patients measuring the perception of their health (Kingsley and Patel, 2017). The problem with PROM and PREM is twofold. The first limitation is that they are self-reported and, therefore, are prone to bias. The second limitation is that special permission is needed to get and use those datasets, as the data might contain sensitive information (Lohiniva et al., 2023). For example, PREM data was needed to measure the effect of CombiConsult. However, all involved actors including all pharmacists, the GPs and the financier of the projects (ZonMw, 2021) need to agree to share their data. This process can take months, which constraints the deadline of this project. Consequently, we were not able to get those datasets in time.

Instead, literature was used to find sensible data as input for the model. This creates even more limitations with the data collection. Primarily, research may focus on different scopes. Examples being research in other countries (Hyatt et al., 2022; Merino et al., 2022; Carretero et al., 2020) or even completely different patient groups (Pazderka et al., 2022; Hartfiel et al., 2022). Healthcare systems around the world show differences in the way the system functions. This makes a comparison between countries a primary source of difficulty, since the results for one country cannot be generalized for the Dutch healthcare system. So for the data collection, grey literature was used as well. This includes Dutch websites such as the Hartstichting (Hartstichting, 2021).

9.2.2. Limitations on the model

Due to the lack of available data, several assumptions have to be made for the model. First, the patient population only contains the population of all CVD patients in one single group. While the Hartstichting (Hartstichting, 2021) has data on the patient population for each of the common CVDs in the Netherlands, no such distinction is made for patients with mental health issues or for patients lacking in physical activity. Furthermore, it is assumed that patients diagnosed with CVDs no longer immigrate or emigrate. According to S. Laing et al., 2003 however, immigration still takes place even among the sick population.

Another limitation of the model regarding patient population is the distinction of age cohorts. The Hartstichting gathered data for seven different age groups. However, due to privacy reasons, the data made public by them combines certain age groups together. Consequently, the most limited variable is measured in only four age groups.

For the model, several interventions identified in chapter 3 were combined into one single intervention. For example, all types of group-based exercises were bundled together. The validation of this choice lies in the aggregation level of this project. The aggregation level is high, meaning we are looking at averages of the population instead of measuring the impact on single patients. As such, biological influences are excluded from the model and only the end results from the paper are used (Amadio et al., 2020; Grässler et al., 2021). However, the underlying cause of this type of limitation on the corresponding choice to manage it is due to the limitation in the literature review. Due to the limited time for this project, the literature review was not systematic, hence the range of interventions found that could be modelled was limited. Moreover, there may be more studies with clear causation pathways from interventions that were not included in this project.

9.2.3. Critique and limitations of SROI

In section 1.2 of the introduction, a comparison was made between different types of economic evaluation. In the end, the choice was made to use SROI for this project. The main advantage mentioned in the introduction is that it includes social variables as well as purely economic ones (Millar and Hall, 2013; Banke-Thomas et al., 2015). Furthermore, SROI has been used as a localised CBA (Edwards and Lawrence, 2021), meaning it is usable as a method for a target population such as CVD patients. Other than advantages, SROI also has limitations in its use that need to be reflected on.

First is the meaning of the ratio itself. An SROI ratio measures the net present value of an intervention and compares that with the costs of investment (C. M. Laing and Moules, 2017). A high SROI ratio can thus mean two things: either there are major benefits for the health care system, or the benefits are low and the high SROI is simply the result of even lower investment costs. In this project, the healthcare system of all CVD patients is taken into consideration. Hereby, hospital costs and social costs of deaths are major components of total costs. Prevention of those costs, even with just a small population group affected by an intervention, inflates the SROI ratio. Subsequently, the SROI ratio does not tell the whole story. The consequence is that the SROI should not be the only factor used to determine which intervention should be given priority to.

Other types of disadvantages of the SROI framework is the subjectivity of the method (Mook et al., 2015). SROI uses monetized variables to determine the benefits, even for variables that are not easily monetised (Banke-Thomas et al., 2015). Whereas a Cost-Benefit Analysis has its roots in welfare theory (Boadway, 1974), SROI analysis uses financial proxies. Data collection on finding the right proxies is time-consuming and thus leads to uncertainty in the accuracy of the value of the proxy (Muyambi et al., 2017). Secondly, the process of determining the deadweight (the amount of impact that would have happened without the activity anyway), attribution (the percentage of impact attributable to the organization), and drop-off (the degree to which impacts diminish over time) are also embedded in subjectivity (Mook et al., 2015; Krlev et al., 2013). Due to the subjectivity, different projects working with the same datasets may still result in different SROI ratios Cooney and Lynch-Cerullo, 2014. Replication is thus a common issue with projects using SROI analysis.

In conclusion, SROI has certain advantages and disadvantages. On one hand, it monetises all different outcome variables including social variables, but on the other hand, this causes the analysis to be embedded with uncertainty. Consequently, the SROI ratio is not suitable to be the only decision criterion. Instead, the focus of SROI should be used as a learning tool (Arvidson et al., 2013), increasing knowledge and understanding of the system.

9.3. Recommendations

9.3.1. Recommendations for Future Research

In this project, only a proof-of-concept was explored for modelling the SROI using a system dynamics approach. As such, multiple suggestions for future research can be made. The first recommendation is to reassess the uncertain variables used in the model. Input variables found in the literature are limited to the scope and location of said project, due to the discrepancy between healthcare systems across countries. Expert interviews need to be conducted to find “Dutch” values for the input variables. Furthermore, it will help increase the understanding of the total system. These interviews will be conducted with policymakers within the healthcare system or other involved actors such as project financiers (ZonMw, 2021).

The second recommendation is to include more population groups. The Hartstichting has data not on just the total number of CVD patients but also data per CVD (Hartstichting, 2021). Interventions may have different results depending on the specific disease a patient suffers from (Okwose et al., 2019; Eijsvogels et al., 2016). Furthermore, death rates, hospitalisation numbers and even the length of hospital stay have notable differences between patient groups. These differences among deceases are currently not included in the model. As such, the model currently only measures the average forecasted effect on CVD patients. A second distinction to be made to measure the effect of interventions is by dividing the population further based on gender. Differences are reported among men and women (King et al., 1991). A third and last way to include more population groups is to increase the number of age cohorts. The Hartstichting measures the number of patients, deaths etc. in seven different age groups. Due to privacy reasons, however, groups are combined into just four of them (Hartstichting, 2021). For ethical reasons, using the data for all seven groups required special permission from the Hartstichting. So for this project, only the publicly available data was used, but using all seven groups would increase the realism of the model. In fact, this can even be extended to modelling on the individual level. An example is a simple SD model on worker’s burnout by Homer, 1985. Hereby, personal experiences were used to find values for input. In our project, this translates to incorporating PREM and PROM variables. Except, instead of using averages, the entire range should be added, which can be done in Vensim by importing datasets. A major disadvantage, however, is that looking at individual behaviour requires data on all model variables, which is difficult and time-consuming to gather on large models. Yet in the end it would mean that the model is even more suitable for the support of patients since it enables one-to-one support.

In the last step of the SROI calculation, the NPV of the project is divided by the investment costs. However, the investment costs come with its own set of uncertainties. The costs can be truly uncertain (Salai et al., 2016). Such is the case when the market price of equipment varies widely. The costs can also be outdated (Tan et al., 2012). The costs of wages for therapists and trainers – while being values used in the Netherlands – are based on the costs as they were in 2012. A new update on the wages is required. Implementing the updated costs would change the SROI ratio value. It would not change the sign, as the investment costs are only used in the denominator of the SROI calculation. So an intervention with net benefit results would still have net benefit results and vice versa. However, it would again increase the realism in both the model and the outcome values. In the intervention of CombiConsult, the intervention has only been created in 2021 (Meijvis et al., 2021) and as a result, no full cost-analysis has been performed yet. As such, doing so is another recommendation for future research.

A final recommendation is to implement feedback from the CVD patients. The System Dynamics model does a mathematical analysis of the usefulness of different interventions. Patients need to be involved as well, as to explore what they prioritise. In other words, the SROI should only be used as a guide to find what is important, well the patients should have the last word.

9.3.2. Recommendations for Policymakers

The recommendations for the policy-makers are based on the decision rule for SROI. An intervention is worth the investment if the SROI ratio is positive and larger than one. The most successful interventions were the ones that consistently showed positive SROI even under deep uncertainty. However, it should be noted that a direct comparison between interventions cannot be made, due to different model behaviour and different uncertainties attached to each intervention. In the end, interventions that show consistent positive SROI are “Active-at-Home”, “Video Gaming”, “Group-Based Training”, “Care Co-ordination”, “Cognitive Behavioural Therapy” and “Telemedicine”. The results show that the NPV in these interventions is positive (meaning the social benefits are larger than the social costs) and that an improvement is made in the healthcare system compared to the base scenario. Furthermore, the social gains are larger than the investment cost, resulting in the SROI being large. As such, all of these interventions have evidence of increasing social returns and are recommended for implementation.

CombiConsult is a unique case, as it is mostly positive, with just a select few scenarios where the SROI ends up negative. This is caused by both a high daily compensation for the pharmacists and the decrease in QoL due to mental health issues. With a more thorough assessment of uncertainties and costs, a positive SROI is still realistic. As such, implementation of CombiConsult is recommended only after it becomes clear in what scenario we are in.

Lastly, for the interventions with mixed results, the analysis shows that the negative SROI ratios are caused if mental health problems play a larger role in the quality of life assessment. Hereby, the decrease in mental health for the patients not supported by the intervention outweighs the patients that are helped with it. As such, the recommendation for these interventions is to further offer support in mental healthcare outside the target group of said intervention.

10
Conclusion

This chapter answers the main research question by first answering the sub-questions.

10.1. Answer Research Question

To answer the main research question, we need to first answer the sub-questions.

10.1.1. Answers Sub-Question

Sub-question 1: *What are the available different interventions from Harteraad for the treatment and support of CVD patients?*

Based on existing studies regarding SROI modelling in healthcare systems, three general types of usable interventions were found: intervention focusing on physical activity, intervention focusing on mental health and intervention focusing on medical adherence. The relevancy of these types of interventions was then later confirmed with interviews with experts from Harteraad,

In chapter 3, a literature review was conducted to find specific examples of interventions used for the support of patients. For physical activity, 15 different interventions were identified. For mental health support, the total number of different interventions turned out to be 11. For medical adherence, the choice was set for CombiConsult based on the priories of patients.

Sub-question 2: *How do different interventions from Harteraad create social return?*

A causal Loop Diagram was developed to map the system from intervention implementation to relevant outcome measures. The main outcome measure is the SROI, with deaths, hospitalisations, and Quality of life as secondary outcomes. The CLD shows behavioural mechanisms that – when not satisfied – create risks for more CVD events. Immediately, deaths or hospitalisations are direct effects after experiencing a CVD event. Which in turn leads to costs for the healthcare system and a decrease in the Quality of Life. Furthermore, a patient's behaviour also influences the QoL directly by itself.

The main aim of the interventions, is to change the behaviour of patients for the better. Hereby the interventions influence the risk factors of lack of physical activity, mental health problems and medical non-adherence. All effects can be monetized using financial proxies to calculate the SROI.

Sub-question 3: *How can a system dynamics approach be used to test the effect of different interventions?*

A system dynamics model in Vensim was built to explore the effects on the outcome measures of each intervention. SD models process on a continuous time instead of discrete time, as in a model developed in Excel. The main advantage of SD is that it enables the modeller to define clear stocks and flows, delays, feedback loops and specific look-up data. All of these exist in the healthcare system, justifying the use of SD. The model enables the implementation of even more interventions if data on the parametrisation is available. As such, all parameters and equations are defined before the modelling phase. To expand the time horizon, only a simple change in the model settings is needed. Furthermore, it is possible to expand the model to be used for different countries. To do so, only the input variables need to be adjusted to make them fit the data corresponding to that country.

The downside of using Vensim is that the method is not suitable for modelling the results on a short-time scale. In the first few time steps, no investments have been made yet. This causes a division by zero when calculating the SROI ratio. The SROI then approaches (negative) infinity, which causes the simulation to get stuck. The simple fix for this was to implement a failsafe that sets the SROI to zero in case of no intervention.

A second disadvantage of using SD is that the SROI ratio requires a comparison of outcomes between the model with intervention and the base model without any intervention. So a major part of the model is repeated twice, effectively doubling the simulation run-time. While Vensim runs fast, this may cause issues for large models.

Sub-question 4: *How does uncertainty regarding the effect of different interventions affect the social return on investments?*

In this project, decision-making happens under deep uncertainty. Types of uncertainties identified include the effect on patient behaviours, as well as the effect on the total investment costs. These uncertainties (mostly due to outdated or lack of data) affect the SROI ratios and thus the answer if an intervention is worth the investment.

The results for not including uncertainty show that only High-Intensity Interval training has negative SROI, showing that the social costs are higher than the social benefits, even before taking the investment costs into account. Two interventions (Music Therapy and Promote Autonomy and Recovery) show an SROI between zero and one, indicating that the investment costs outweigh the social returns.

When uncertainty is added to the model, changes in the model output appear. The SROI ratios for each intervention diverge to different end values. For Music Therapy and Promote Autonomy and Recovery, the results are mixed. Depending on the scenario, the SROI may end up positive or negative. Similarly, the results for Relaxation Technique Training are mixed as well. Despite the base case showing a positive SROI ratio of 32.60. This means that more research is needed before a grounded conclusion can be made regarding the usability of those interventions. A conclusion can be made for the HIIT intervention, which is consistently negative across the uncertainty space. This disproves the dynamic hypothesis that all the intervention will end up with positive SROI, as this intervention actually cause negative effects on the adherence rate to physical activity.

10.1.2. Answers Main Research Question

With all sub-questions being answered, a final conclusion can be made which answers the main research question. The research question for this thesis was as follows:

Which interventions increase the social returns on investment for a patient organisation?

The social returns on investments can be increased by investing in certain investments. These interventions support patients with CVD by changing the patients' behaviour to (1) increase the level of physical activity, (2) decrease depression and mental health problems and (3) increase the medical adherence rate.

Using a System Dynamics model, a quantitative method was used to evaluate the SROI for different interventions. Based on the results, six interventions show consistently positive results: “Active-at-Home”, “Video Gaming”, “Group-Based Training”, “Care Coordination”, “Cognitive Behavioural Therapy” and “Telemedicine”. As such, these interventions are worth the investment. A seventh intervention, CombiConsult, shows mostly positive results except for a few worst-case scenarios where mental health problems result in higher-than-average social costs. More research is needed to determine the usability of this intervention.

The model has several limitations, which limit a direct comparison between interventions. A qualitative analysis is needed as well to deal with the limitations as well as setting priorities. The aim of this report is however to increase understanding of the system. As such, this report shows the first step of increasing the support of patients with cardiovascular deceases.

10.2. Contribution of the Research

This research is associated with the MSc of Engineering and Policy Analysis (EPA) at the TU Delft, the Netherlands. The focus of the EPA MSc lies in the analysis of complex sociotechnical systems. It incorporates modelling, policy and data analysis in its mission of solving grand challenges, which includes challenges within the healthcare system. As such, the following section will describe the societal and scientific contributions of the findings of this thesis.

10.2.1. Societal Contribution

In the Netherlands, there are over 1.7 million people with CVDs (Hartstichting, 2021). After experiencing a CVD event, the patients deserve the care and support they require to keep their quality of life as high as possible. However, the number of CVD patients is expected to increase over the following twenty years, creating a burden on the healthcare system, and thus less time available per patient. Moreover, healthcare managers such as Harteraad face increasing costs in keeping the quality of care high. As such, there is a need for cost-efficient interventions.

The aim of this thesis was to explore the effect of different interventions on the patient's life, including deaths, hospitalisations, and quality of life. The outcomes were compared with the outcomes in case of no investments and based on the differences, the SROI was determined. This research then investigated which interventions under which scenarios lead to a positive SROI. Based on the results, policy recommendations for Harteraad have been presented. These policy recommendations can be implemented to aid patients in their daily lives while also reducing the risk of experiencing more CVD events. As such, this thesis aid in the support of CVD patients in the Netherlands.

10.2.2. Scientific Contribution

This thesis consisted of the exploration and modelling of different potential interventions. As such, it combines SD modelling, economic evaluation in the form of SROI and support for CVD patients who have already experienced their first CVD event. The combination of those three aspects is novel. Most research so far focuses on either different types of models (Hyatt et al., 2022; DiLorenzo, 2021; Lophongpanit et al., 2019), different types of evaluation methods (Robinson, 1993a; Masters et al., 2017), or prevention instead of support (Peng et al., 2021). As such, this thesis provides an exploration that can be used to fill the research gap in the existing scientific research. Moreover, the use of a modelling technique on a continuous timescale provides new insights by showing how the SROI and QoL change over time.

Furthermore, the existing literature on SROI lacks a systematic sensitivity analysis, which poses a problem especially in an SROI analysis due to the use of proxy variables (Maier et al., 2015). This research includes a novel and more thorough exploration of the uncertainties involved in an SROI analysis. The uncertainties in the base case were also included in the experiments for each intervention. Moreover, intervention-specific uncertainties were added as well. Therefore, instead of one specific value, the results in this thesis show a range of possible end values for the SROI ratio. As such, this thesis makes a scientific contribution by offering aid in the robust decision-making within the public healthcare sector.

This research does not only add knowledge and understanding for the support of patients but also to the application of system dynamics within the healthcare system. The model shows the relation between input variables and output measures, and how the output variable changes by making investments in potential interventions. As a result, the model does offer a good communication tool for the healthcare manager. One keynote of an SROI analysis is to understand it as a localised cost-benefit analysis (Edwards and Lawrence, 2021). As such, the model is specifically built with the Dutch healthcare system in mind, with the main focus on patients with CVDs. Therefore, extending this model to different sections of the healthcare system is difficult to do. However, extending the model to be used in different countries is possible. The model relationships are namely based on general literature, with only the input values – including the proxy values – being specific to the Dutch healthcare system. So to make the model work for different countries, only the numerical inputs need to be changed to the values true for said country. As a result, researchers from other countries can use the model to test interventions for the support of CVD patients in their country of origin. Therefore, this thesis contributes to the general research on support for CVD patients after experiencing a CVD event.

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A

Literature Review Flowcharts

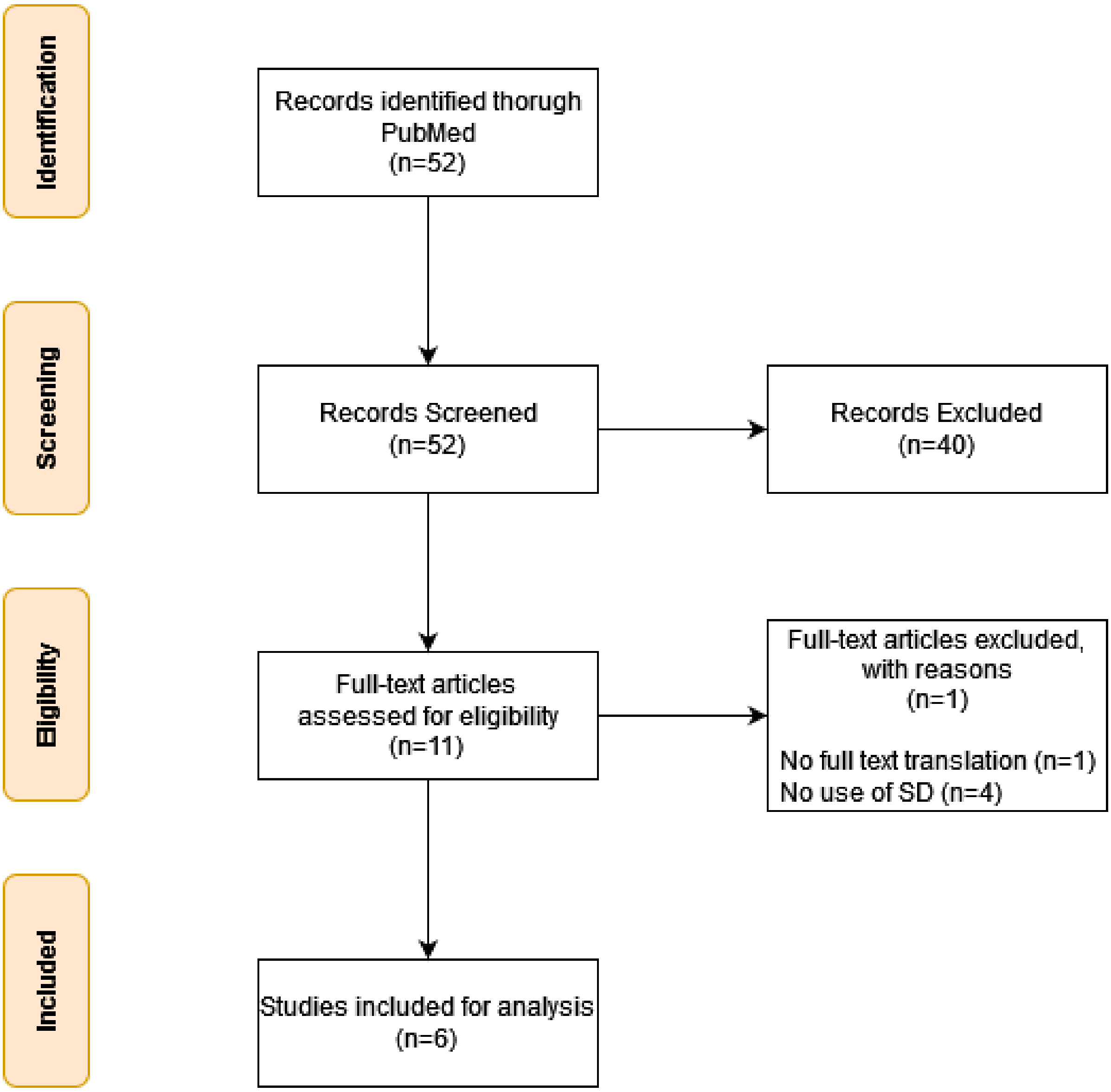


Figure A.1: Flowchart of the literature review on general interventions

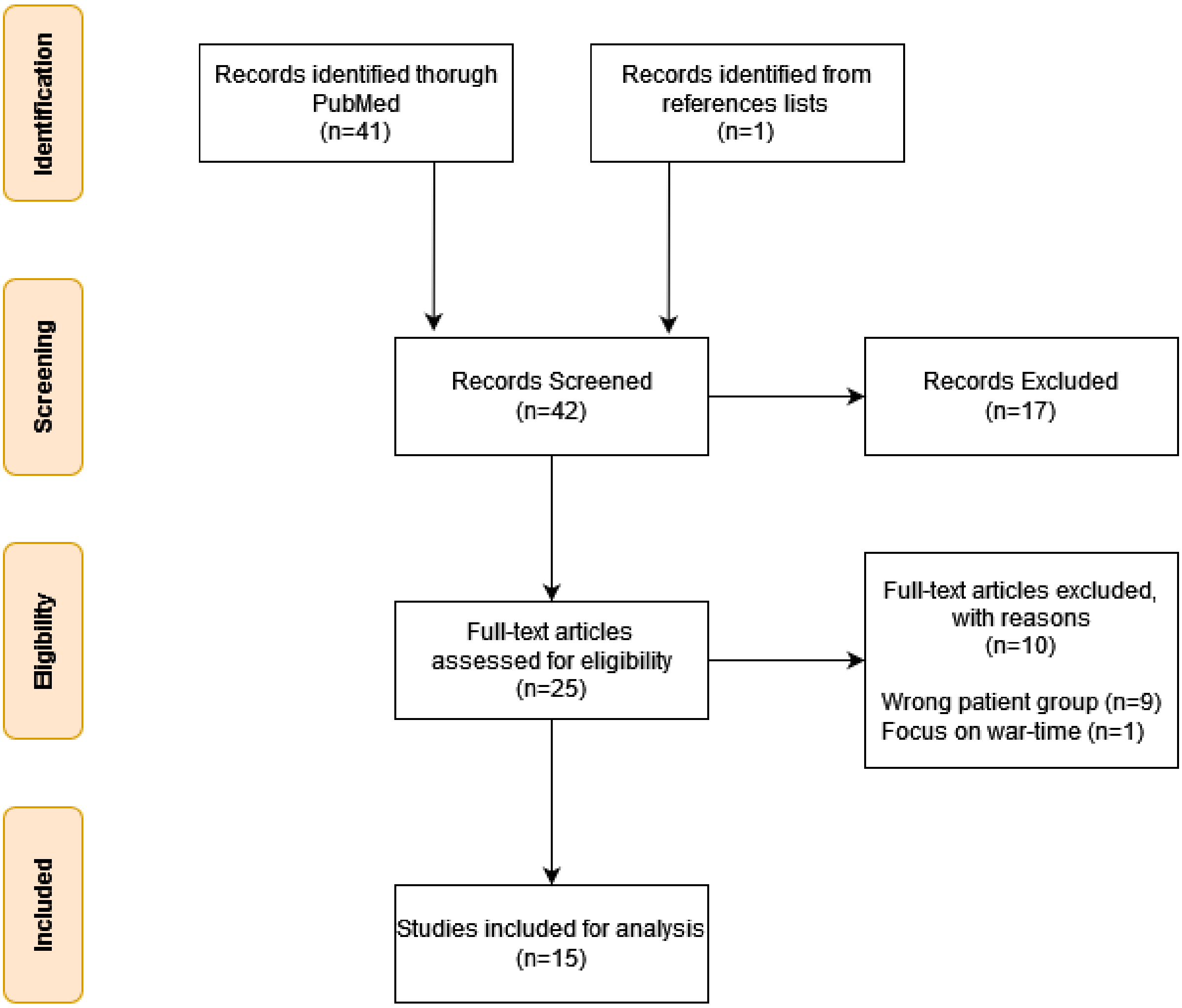


Figure A.2: Flowchart of the literature review on mental health support interventions

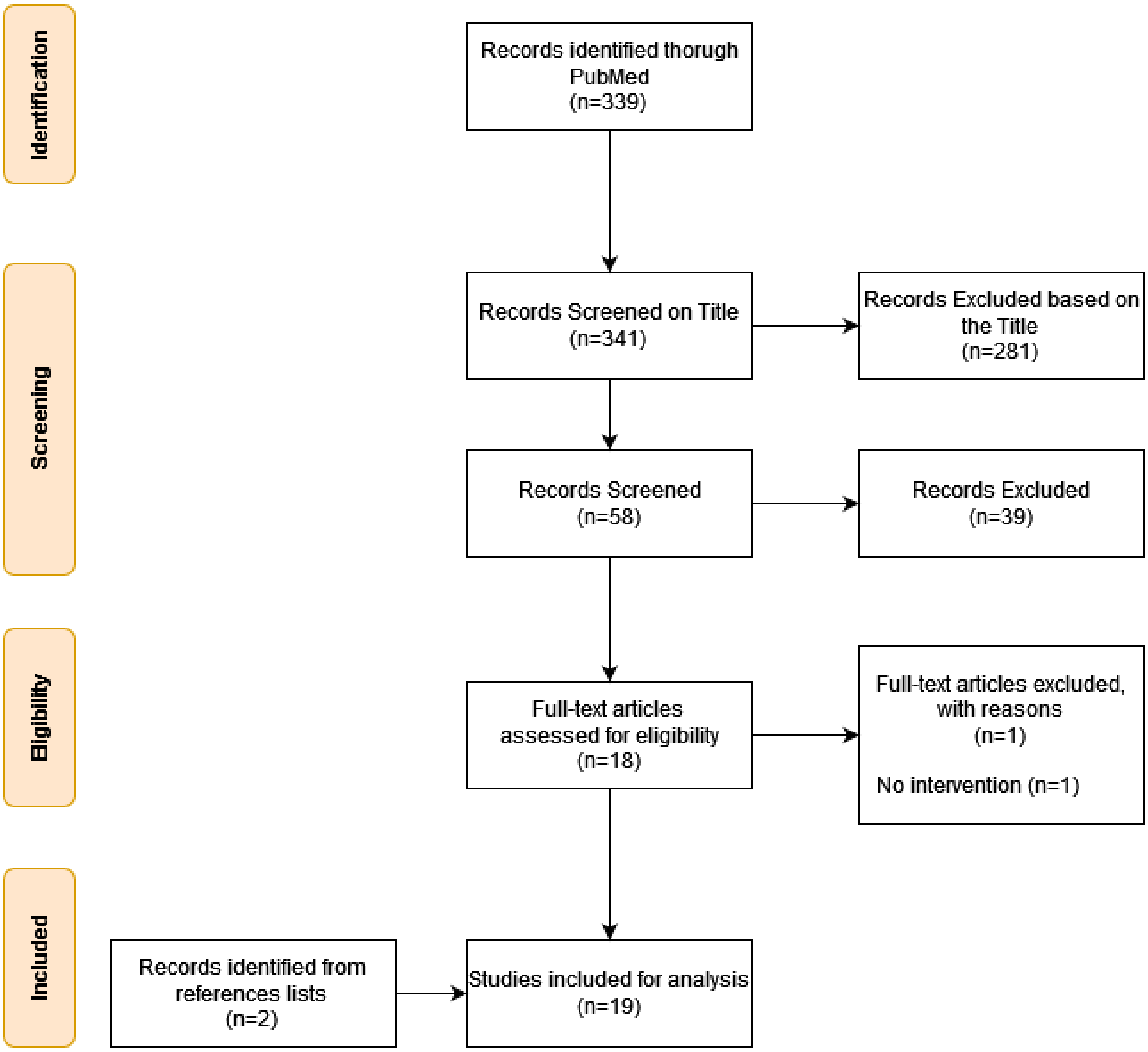


Figure A.3: Flowchart of the literature review on physical activity interventions

B

Model Conceptualisation

Table B.1: Conceptualisation of risk factors for CVD events

From	To	Relation	Reason
Cardiovascular Event	Stress	+	A high peak of stress is noticeable right after experiencing a CVD event.
Cardiovascular Event	Fear of Exercising	+	Depending on the type of event a patient experienced, patient may experience fear for exercise and physical activity due to the fear of experience yet again a CVD event.
Stress	Depression	+	Long term stress and anxiety (here combined into a single factor stress) is a cause for developing depressive symptoms.
Fear of Exercising	Adherence PA	-	The fear patients experience will show itself by them being less motivated to exercise.
Depression	Cardiovascular Event	+	Depression is one of the risk factor for even more CVD events.
Depression	Adherence PA	-	Depression is a cause for non-compliance is getting the required physical activity.
Adherence PA	Physical Activity	+	With a lower adherence, patient may stop exercising on their own or stop attending work-out groups. In both cases, the amount of physical activity decreases.
Physical Activity	Depression	-	A lack of physical activity can cause depressive symptoms that later develop in actual depression.
Physical Activity	Risks due to Lifestyle	-	A lack of physical activity is a negative type of lifestyle behaviour,
Depression	Medical Compliance	-	Depression can intentionally or unintentionally affect the adherence rate of patients in the medication intake.
Medical Compliance	Risks due to Lifestyle	-	Risks are involved in case patients stop taking their medication correctly.
Risks due to Lifestyle	Cardiovascular Event	+	Risky lifestyle (low physical activity and medication non-compliance) is a risk factor for more CVD events.
Age	Cardiovascular Event	+	The older population groups on average experiences more CVD events relative to younger populations groups.

Table B.3: Conceptualisation of the aftermath of CVD

From	To	Relation	Reason
Diagnoses	Patient Population	+	The population in this model is patients that already had experienced an CVD event, so the inflow of new patients comes from people after they experienced a first-time event and the following diagnoses.
Patient Population	Deaths	+	In a larger patient group, more deaths are expected. Especially when the death rate stays the same.
Cardiovascular Event	Deaths	+	One of the three consequences of an CVD event. In this case, the patient does not survive the event.
Cardiovascular Event	Hospital Admissions	+	One of the three consequences of an CVD event. In this case, the patient survived in and is hospitalised for several days for immediate care.
Cardiovascular Event	1-day Admissions	+	One of the three consequences of an CVD event. In this case, the patient survived and is released form the hospital in the same day.
Mortality Rate	Deaths	+	With a larger mortality rate, more patients would not survive a CVD event. Resulting in more deaths and vice versa.
Mortality Rate	Hospital Admissions	-	Based on the relationship between deaths and hospitalisation
Mortality Rate	1-day Admissions	-	Based on the relationship between deaths and 1-day hospital admissions.
Hospital Admissions	Total Hospital Costs	+	Hospital costs include immediate care and the costs of hospital beds when a patient has to stay overnight. Thus an increase in Hospital admission increases the total costs.
1-day Admissions	Total Hospital Costs	+	Same reasoning as the previous established relation, except the costs now come in the form of immediate treatment only.
Average Duration of Hospitalis admission	Total Hospital Costs	+	The longer a patient has to stay in the hospital, the more costs involved for the hospital.
Daily Patient Costs	Total Hospital Costs	+	The hospital will have higher costs, if the daily costs per hospitalised patients is higher and vice versa.
Deaths	Deaths Prevented	-	Deaths prevented measure the numerical difference in deaths after a CVD event and the survivors after a CVD event.
Hospital Admissions	Deaths Prevented	+	Deaths prevented measure the numerical difference in deaths after a CVD event and the survivors after a CVD event.
Deaths Prevented	Social Gains Death Prevention	+	he social gains death prevention is a monetised version of the deaths prevented.
Statistical Value of Life	Social Gains Death Prevention	+	The social gains death prevention is a monetised version of the deaths prevented and is determined by the statistical value of life.

Table B.5: Conceptualisation of budget and interventions

From	To	Relation	Reason
Patient Population	Donations	+	More patients means more awareness and thus more donations.
Donations	Total Budget	+	As a charity organisation, one of the inflows of budget comes in the form of donations.
Subsisides	Total Budget	+	Harteraad receives subsidies from the Hartstichting and other actors to be used for investments.
Total Budget	Investment Rate PA	+	More investments can be made when the budget increases.
Total Budget	Investment Rate MH	+	More investments can be made when the budget increases.
Investment Rate MH	Investment Rate PA	-	Within a given budget, a choose has to be made regarding the investment to be implemented. Investing more on mental health thus means less investments in physical activity interventions.
Investment Rate PA	Investment Rate MH	-	Investing more on physical activity thus means less investments in mental health interventions.
Investment Rate MH	Budget PA and MH	+	A third option is to investment in both mental health and physical activity interventions.
Investment Rate PA	Budget PA and MH	+	A third option is to investment in both mental health and physical activity interventions.
Investment Rate MH	Mental Health Intervention	+	With enough investments in mental health, an actual intervention can be implemented.
Mental Health Intervention	Depressions	-	Certain interventions focus on preventing patients for developing depressive symptoms.
Mental Health Intervention	Medication Compliance	+	Interventions such as therapy can be used to find reasons for medical non-compliance and as such, increase it.
Investment Rate PA	Physical Activity Intervention	+	With enough investments in physical activity, an actual intervention can be implemented.
Physical Activity Intervention	Physical Activity	+	The interventions focus mainly on setting patients up to increase their physical activity.

Table B.7: Conceptualisation of CombiConsultation

From	To	Relation	Reason
CombiConsult	Pharmacist Involved	+	The CombiConsutation Intervention indicates a collaboration with pharmacists and the GP.
Pharmacist Involved	Patients in CC	+	Pharmacist can decide to join the CombiConsultation programme. Then their patients are involved as well.
Patients per Pharmacist	Patients in CC	+	In case a pharmacist has more patients than other pharmacist, them joining CombiConsultation will lead to a relative larger ammount of patients joining CC. So how larger the average ammount of patients a pharmacist has, the larger the inflow of patient into CC.
Patients in CC	Patients with Side Effects	+	CC gives patients the opportunity to share side effects with the pharmacists before the yearly GP check
Achievement Side-Effect Reduction	Patients helped with Side-Effects	+	A higher rate of GP accepting measure to reduce side-effects, the larger the group of patients is that were succesfully helped.
Patients in CC	Patients with Drug Related Problems	+	CC gives patients the opportunity to share problems related to medication use with the pharmacists before the yearly GP check.
DRP Implementation	Patients helped with DRP	+	The higher rate of GP's changing the treatment plan of patients based on the results from the Pharmacist, the larger the group of patients with DRP helped by CC is.
Patients helped with Side-Effects	Total Patients Helped	+	Total Patients Helped is the sum of patients helped with side-effects and patients helped with DRPs
Patients helped with DRP	Total Patients Helped	+	Total Patients Helped is the sum of patients helped with side-effects and patients helped with DRPs
Total Patients Helped	Total Medication	-	A potential solution to patients with drug-related problems can be to reduce the number of drugs the patient has to take. Especially since a fair share of patients believe their drug intake is too high.
Total Medication	Over-treatment	+	Patients already feel like the drug intake is too high, an increase in total medication would therefore lead to an even higher over-treatment.
Total Patients Helped	Medication Compliance	+	With problems being solved by the pharmacist and GP, major factors of medication non-compliance are taken away.
Total Patients Helped	Patient Satisfaction	+	The more a patients feels like their problems are being heard, the more satisfaction a patient is with the pharmacist and GP. Thus their overall satisfaction increases.

C
Model Formulation

Table C.1: Formulation of the patient population sub-model

Variable	Equation	Value	Unit	Description
Relative Yearly Patient Increase	-	40704	person/Year	Based on the expected increase of patients till 2040 adjusted per year.
Expected Yearly Increase	Relative Yearly Patient Increase+Death Total	-	person/Year	The actual inflow of new patients.
Diagnoses [AgeGroup]	Expected Yearly Increase*Relative New Diagnoses [AgeGroup]	-	person/Year	The inflow of new patients adjusted for age group.
Relative New Diagnoses [AgeGroup]	-	0.169051, 0.448473, 0.248819, 0.133724	Dmnl	The relative occurence of diagnoses per age group.
CVD Patients [YoungPatients]	Diagnoses[YoungPatients] - Aging[YoungPatients] - Deaths[YoungPatients]	-	person	The actual inflow of new patients under the age of 55.
CVD Patients [Patients55to74]	Diagnoses[Patients55to74] + Aging[YoungPatients] - Aging[Patients55to74] - Deaths[Patients55to74]	-	person	The actual inflow of new patients between 55 and 74.
CVD Patients [Patients75to84]	Diagnoses[Patients75to84] + Aging[Patients55to74] - Aging[Patients75to84] - Deaths[Patients75to84]	-	person	The actual inflow of new patients between 75 and 84.
CVD Patients [PatientsOldest]	Diagnoses [PatientsOldest] + Aging[Patients75to84] - Deaths [PatientsOldest]	-	person	The actual inflow of new patients older than 85.
Aging [AllButOld]	CVD Patients [AllButOld]/Time in Age Group [AllButOld]	-	person/Year	This concerns the flow of patients from one AgeGroup to another
Time in Age Group [AllButOld]	-	55, 20, 10	Year	Based on the length of each age-group
Initial CVD Patients [AgeGroup]	-	254100, 674100, 374000, 201000	Person	Retrieved from Hartstichting
Deaths [AgeGroup]	CVD Complications [AgeGroup] * Death Rate after CVD [AgeGroup] * Cognitive behavioural therapy * Mortality Reduction	-	person/Year	Retrieved from Hartstichting, determined by reducing hospitalisation from the group of patients with CVD events.
Death Rate after CVD [AgeGroup]	Consequences after CVD events [AgeGroup] - Hospitalization Rate after CVD [AgeGroup] - ”1-Day Admission Rate” [AgeGroup]	-	person/event	Data retrieved from Hartstichting
Consequences after CVD events [AgeGroup]	-	1, 1, 1, 1	person/event	Assuming every CVD events leads to either deaths or hospitalisations.
Death Total	Sum(Deaths [AgeGroup!])	-	person/Year	All deaths combined

Table C.2: Formulation of CVD events and its aftermath

Variable	Equation	Value	Unit	Description
CVD Complications [AgeGroup]	CVD Patients [AgeGroup] - Patients with Depression [AgeGroup]) * CVD Prevalence [AgeGroup] *"Effect Group-Based Training" + Patients with Depression [AgeGroup] * CVD Prevalence[AgeGroup] * Risk due to Depression * "Effect Group-Based Training"	-	event/Year	All risks combined to determine the change of experiencing a CVD event.
CVD Prevalence [AgeGroup]	-	0.176242, 0.253471, 0.263484, 0.240169	event / (Year*person)	Based on data from the Hartstichting.
CVD Events[AgeGroup]	INTEG (CVD Complications [AgeGroup], Initial CVD events [AgeGroup])	-	event	The total CVD events combined
Initial CVD events [AgeGroup]	-	0, 0, 0, 0	event	Assuming the model starts at zero
"1-Day Admission Rate" [AgeGroup]	-	0.301967, 0.317332, 0.216799, 0.0615238	person/event	
"1-Day Admission"[AgeGroup]	CVD Complications [AgeGroup] * "1-Day Admission Rate" [AgeGroup]	-	person/Year	Data from Hartstichting
"Initial 1-day patients" [AgeGroup]	-	37, 149, 59, 8	person	Data from Hartstichting
"1-Day patients" [AgeGroup]	INTEG ("1-Day Admission" [AgeGroup], "Initial 1-day patients [AgeGroup])	-	person	
Hospitalisation Rate after CVD [AgeGroup]	-	0.673447, 0.638896, 0.67262, 0.584207	person/event	Data from Hartstichting
Hospitalisation [AgeGroup]	CVD Complications [AgeGroup] * Hospitalisation Rate after CVD [AgeGroup] + Additional Deaths Prevented [AgeGroup]	-	person/Year	The total number of patients per year that is being hospitalised after a CVD event.
Initial Patients in Hospital [AgeGroup]	-	331, 1495, 908, 386	person	Data from Hartstichting divided by the days per year and lengt of stay.
Patients in Hospital [AgeGroup]	INTEG (Hospitalization [AgeGroup], Initial Patients in Hospital [AgeGroup])	-	person	The total sum of patients ever hospitalised
Deaths no CBT [AgeGroup]	CVD Complications [AgeGroup] * Death Rate after CVD [AgeGroup]	-	person/Year	Base deaths per year
Additional Deaths Prevented [AgeGroup]	Deaths no CBT [AgeGroup] - Deaths [AgeGroup]	-	person/Year	Indicates the population for which death is prevented
Total Hospitalisation	Sum(Hospitalization [AgeGroup!])	-	person/Year	All age-groups combined.

Table C.3: Formulation of the mental health sub-model

Variable	Equation	Value	Unit	Description
Standard Depression Prevalence rate [AgeGroup]	-	0.099, 0.069, 0.07, 0.063	1/Year	Based on data from Statistics Netherland.
Depression Regular [YoungPatients]	CVD Patients [YoungPatients]*Standard Depression Prevalence rate [YoungPatients]	-	person/Year	The occurrence of depression among the youngest patient group.
Depression Regular [Patients55to74]	CVD Patients [Patients55to74] * Standard Depression Prevalence rate [Patients55to74]	-	person/Year	The occurrence of depression among the patients age 55 to 74.
Depression Regular [Patients75to84]	CVD Patients [Patients75to84] * Standard Depression Prevalence rate [PatientsOldest] * Care coordination intervention	-	person/Year	The occurrence of depression among the patients age 75 to 84.
Depression Regular [PatientsOldest]	CVD Patients [PatientsOldest] * Standard Depression Prevalence rate [PatientsOldest] * Care coordination intervention	-	person/Year	The occurrence of depression among the oldest patient group.
Initial Depressed Patients [AgeGroup]	-	25156, 45165, 26180, 12663	person	The standard depression rate applied to the total CVD patients.
Patients with Depression[AgeGroup]	INTEG (Depression due to PA [AgeGroup] + Depression due to Stress [AgeGroup] + Depression Regular [AgeGroup] - Depression Cured [AgeGroup], Initial Depressed Patients [AgeGroup])	-	person	The stock of all depressived patients divided among the age groups.
Average Length of Depression	-	1	Year	The typical duration of depression.
Adjusted Length of Depression	Average Length of Depression * Telemedicine	-	Year	Potential increase if Tm is implemented
Depression Cured [AgeGroup]	Patients with Depression [AgeGroup] / Adjusted Length of Depression	-	person/Year	The yearly patients cured of depression.
Non Already Depressed Patients[AgeGroup]	CVD Patients [AgeGroup]-Patients with Depression [AgeGroup]	-	person	the total patient populaton not depressed
Patient Ratio [AgeGroup]	Non Already Depressed Patients [AgeGroup] / CVD Patients [AgeGroup]	-	Dmnl	Previous variable but as a ratio.
Event per person	-	2	event/person	How often a patient experience an event in a year.

Table C.4: Formulation of the mental health sub-model cont.

Variable	Equation	Value	Unit	Description
”CVD events non-depressed patients” [AgeGroup]	CVD Complications [AgeGroup] * Patient Ratio [AgeGroup] / Event per person	-	person/Year	The number of CVD events for the non-depressed patients.
Time from Stress to Depression	-	1	Year	Assumption.
Depression due to Stress [AgeGroup]	DELAY1(”CVD events non-depressed patients” [AgeGroup] * ”Stress Prevalence after 1-year”, Time from Stress to Depression)	-	person/Year	The inflow of depressed patients due to stress
”Stress Prevalence after 1-year”	EXP(-Adjusted Decrease Constant * (INITIAL TIME + Time from Stress to Depression - INITIAL TIME)) * Stress Reduction Music Therapy	-	Dmnl	An assumed figure used to determine the level of stress after a year.
Adjusted Decrease Constant	Decrease Constant*Relaxation Technique Training Groups	-	1/Year	Assumption
Decrease Constant	-	2	1/Year	
Population Distribution [YoungPatients]	CVD Patients [YoungPatients] / Sum(CVD Patients [AgeGroup!])	-	Dmnl	The ratio of patient younger than 55.
Population Distribution [Patients55to74]	CVD Patients [Patients55to74] / Sum(CVD Patients [AgeGroup!])	-	Dmnl	The ratio of patient between 55 and 74.
Population Distribution [Patients75to84]	CVD Patients [Patients75to84] / Sum(CVD Patients [AgeGroup!])	-	Dmnl	The ratio of patient between 75 and 84
Population Distribution [PatientsOldest]	CVD Patients [PatientsOldest] / Sum(CVD Patients [AgeGroup!])	-	Dmnl	The ratio of patient 85 years and older
Risk of developing depression [AgeGroup]	-	0.267592, 0.18108, 0.18919, 0.17028	1/Year	Adjusted from Mammen and Faulkner, 2013
Depression due to PA [AgeGroup]	Patients Lacking Physical Activity * Risk of developing depression [AgeGroup] * Population Distribution [AgeGroup] - Depression due to Stress [AgeGroup]	-	person/Year	The inflow of depressed patients due to lack of PA.

Table C.5: Formulation of physical activity from home

Variable	Equation	Value	Unit	Description
Starting Home Exercises	Sum(Diagnoses [AgeGroup!]) - Joining New Beweegclubs	-	person/Year	Number of patients who are going to exercise from home
Patients with Home Exercises	INTEG (Starting Home Exercises + Starting Home Exercises after Events - Active Population Deaths - Quiting Home Exercises, Initial People PA from Home)	-	person	Total number of patients from home.
Initial People PA from Home	-	514208	person	Number determined by subtracting patients lacking PA from total population.
Active Population Deaths	Sum(Deaths [AgeGroup!]) - Deaths Patients lacking PA	-	person/Year	Deaths of people with enough PA
Non Compliance PA	Sum(Patients with Depression [AgeGroup!]) / Sum(CVD Patients [AgeGroup!])	-	Dmnl	The percentage of patients stopping with home exercise.
Adjusted Non Compliance Rate	IF THEN ELSE(”High-Intensity Interval Training” = 1 , Non Adherence HIIT , Non Compliance PA)	-	Dmnl	Non Compliance Rate if HIIT is implemented
Non Adherence HIIT	-	0.5	Dmnl	Assumption.
”Time from depression to non-adherence”	-	0.5	Year	the length between developing depression and fully stopping exercise.
Quiting Home Exercises	(Patients with Home Exercises * Adjusted Non Compliance Rate) / ”Time from depression to non-adherence”	-	person/Year	The flow of patients quitting exercise programs
Initial Patients lacking PA	-	841792	person	Based on general population data adjusted for CVD patients.
Patients Lacking Physical Activity	INTEG (Leaving Beweegclubs + Quiting Home Exercises-Deaths Patients lacking PA-Starting Home Exercises after Events - Starting with Beweegclubs after Event, Initial Patients lacking PA)	-	person	The stock of patients lacking PA.
Ratio patients lacking PA	Patients Lacking Physical Activity / Sum(CVD Patients [AgeGroup!])	-	Dmnl	And here as a ratio compared to the total CVD patiant number.
Risky patients affected	Sum(CVD Complications [AgeGroup!]) * Ratio patients lacking PA / Event per person	-	person/Year	Number of patients at higher risk for CVD events
Event rate patients lacking PA	Risky patients affected/Patients Lacking Physical Activity	-	1/Year	How often CVD event occur among PA-lacking patients.

Table C.6: Formulation of physical activity in groups in Beweegclubs

Variable	Equation	Value	Unit	Description
Fear of Exercise Occurrence	-	0.116	Dmnl	The percentage of patient afraid of PA after CVD.
Choice for Beweeg-club	-	0.15	Dmnl	The percentage of patients prefering to exercis in groups.
Starting Home Exercises after Events	Patients Lacking Physical Activity * Event rate patients lacking PA * (1-Choice for Beweegclub) * (1 - Fear of Exercise Occurrence)	-	person/Year	The flow of patients from inactive to active after CVD events.
People per Beweegclub	-	640	person/club	Assumption.
Joining New Beweegclubs	MIN(Starting new Beweegclub * People per Beweegclub, Sum(Diagnoses [AgeGroup!]))	-	person/Year	
Initial Beweegclub Patients	-	147200	person	Determined via the number of beweegclubs and patients per beweegclub.
Patients at Beweegclubs	INTEG (Joining New Beweegclubs + Starting with Beweegclubs after Event - Leaving Beweegclubs, Initial Beweegclub Patients)	-	person	The number of patients currently enrolled in Beweegclubs
”Drop-Out Rate”	-	0.15	1/Year	The percentage of patient dropping out of Beweegclubs per year. Assumption.
”Adjusted Drop-Out Rate”	”Drop-Out Rate” / Video games for PA	-	1/Year	Drop-out when video gaming is implemented.
Leaving Beweeg-clubs	Patients at Beweegclubs * ”Adjusted Drop-Out Rate”	-	person/Year	The flow of patients stopping with group activities.
Beweegclub Capacity	Beweegclub*People per Beweegclub	-	person	
Capacity Remaining per Year	(Beweegclub Capacity-Patients at Beweegclubs) / Year	-	person/Year	Indicating a capacity constraint within the Beweegclubs.
Starting with Beweegclubs after Event	MIN(Patients Lacking Physical Activity * Event rate patients lacking PA * Choice for Beweegclub * (1-Fear of Excercis Occurence), Capacity Remaining per Year)	-	person/Year	Checking if there is room for patients joining after CVD event.
Deaths Rate lacking PA	-	0.042	1/Year	Assumption.
Deaths Patients lacking PA	Deaths Rate lacking PA * Patients Lacking Physical Activity	-	person/Year	Deaths of population lacking PA.

Table C.7: Formulation of Harteraads budget

Variable	Equation	Value	Unit	Description
Yearly Subsidy Increase	-	1	Dmnl	Base value.
Subsidy Increase factor	Yearly Subsidy Increase □ ((Time - INITIAL TIME) / Year)	-	Dmnl	The yearly increase of subsidy.
Base Subsidy	-	600000	euro/Year	Based on data retrieved from Harteraad.
Project Subsidy	-	400000	euro/Year	Based on data retrieved from Harteraad.
Funds	-	180000	euro/Year	Based on data retrieved from Harteraad.
Subsidies to Harteraad	(Base Subsidy + Project Subsidy + Funds) * Subsidy Increase factor	-	euro/Year	
Base Donation Rate	-	10000	euro/Year	Based on data retrieved from Harteraad.
Patient Number Multiplier	Total CVD Patients / Sum(Initial CVD Patients [AgeGroup!])	-	Dmnl	The percentage increase of patients over time.
Donating to Harteraad	Base Donation Rate * Patient Number Multiplier	-	euro/Year	Assuming more patients = more awareness = more donations.
Initial Budget Harteraad	-	1.2e+06	euro	Based on data retrieved from Harteraad
Budget Harteraad	INTEG (Donating to Harteraad + Subsidies to Harteraad - Other Investments - Spendings Harteraad, Initial Budget Harteraad)	-	euro	the total amount Harteraad is able to spend on interventions
Spendings Harteraad	MIN(Donating to Harteraad + Subsidies to Harteraad, Spendings MH Total + Spendings Total PA)	-	euro/Year	The totoal investment made by Harteraad.
Other Investments	Donating to Harteraad+Subsidies to Harteraad-Spendings Harteraad	-	euro/Year	Investments outside of this scope.
Budget Remaining for Other Investments	INTEG (Other Investments - Spendings Harteraad Other Investment- Spendings Other than PA and MH, Initial Investments other)	-	euro	What is left for other investment.
Spendings Harteraad Other Investments	Starting new Beweegclub * New Club Costs	-	euro/Year	What is spend on other investments
Initial Costs for Harteraad	Initial Costs CBT+Initial gaming Costs	-	euro	All initial costs combined.
Total Costs for Harteraad	INTEG (Spendings Harteraad + Spendings Harteraad Other Investments, Initial Costs for Harteraad)	-	euro	
Spendings Other than PA and MH	IF THEN ELSE (Priority Switch = 1, Other Investments , IF THEN ELSE (Priority Switch = 3, Other Investments , 0))	-	euro/Year	Logical operator determining if intervention investment has to be made.

Table C.8: Formulation of the Quality of Life meassure

Variable	Equation	Value	Unit	Description
Initial QoL Score	-	63	Dmnl	Starting value of QoL.
Decrease QoL due to Lack PA	-	11.8	Dmnl	Hoekstra et al., 2013
Base Weight of PA Lack	(Base Patients Lacking Physical Activity - Initial Patients lacking PA) / Sum(Base CVD Patients [AgeGroup!])	-	Dmnl	The importance of PA on QoL.
Initial Score MH	-	70	Dmnl	Hoekstra et al., 2013
Weight of MH	(Sum(Patients with Depression [AgeGroup!]) - Sum(Initial Depressed Patients [AgeGroup!])) / Sum(CVD Patients [AgeGroup!])	-	Dmnl	The importance of MH on QoL.
Decrease QoL due to MH	-	20	Dmnl	Hoekstra et al., 2013
Quality of Life Mental	Initial Score MH - Decrease QoL due to MH * Weight of MH	-	Dmnl	the score exclusively for MH
Initial QoL Score	-	63	Dmnl	Hoekstra et al., 2013
QoL score without PA and MH	Initial QoL Score - (Initial QoL Score Physical + Initial Score MH) / 2	-	Dmnl	The QoL without MH and PA.
Quality of Life	QoL score without PA and MH + (Quality of Life Mental + Quality of Life Physical) / 2	C	Dmnl	The true average QoL score of patients.
Difference in QoL	Quality of Life - Initial QoL Score	-	Dmnl	Measures the differences between starting QoL and current QoL
Quality Adhusted Life Year	50000	-	euro / (person*Year)	Monetization of QoL
Social Gains	Quality Adhusted Life Year * Difference in QoL / 100 * Sum(CVD Patients [AgeGroup!]) * Discount Factor	-	euro/Year	The total social gains by change of QoL.
Discount rate	-	0.035	1/Year	The interest rate.
Discount Factor	EXP(-Discount rate * (Time - INITIAL TIME))	-	Dmnl	Devaluates future cash flows.

Table C.9: Formulation of pharmacists and patients within CombiConsult

Variable	Equation	Value	Unit	Description
Total Number of Pharmacists	-	2000	Pharmacist	The toal number of pharmacists in the Netherlands
Initial Number of Pharmacists	-	21	Pharmacist	Involved in CC
Join CombiConsult Program	IF THEN ELSE (Priority Switch = 3, INTEGER((Total Number of Pharmacists - Pharmacists Involved) * Join Rate Pharmacists) , No CombiConsult)	-	Pharmacist / Year	The rate of which pharmacists join CC
Join Rate Pharmacists	-	0.2	1/Year	The rate of which pharmacists join CC
Pharmacists Involved	INTEG (Join CombiConsult Program, Initial Number of Pharmacists)	-	Pharmacist	A stock of pharmacists in CC
Average Patient Population Pharmacists	Sum(CVD Patients[AgeGroup!])/Total Number of Pharmacists	-	person / Pharmacist	the average patients per pharmacist.
Patients involved in ComboConsult	Pharmacists Involved * Average Patient Population Pharmacists	-	person	Assuming that patients follow the pharmacist in joining CC.
Side Effect Occurence	-	0.417267	Dmnl	Meijvis et al., 2023
CC Patients with Side Effects	Patients involved in ComboConsult * Side Effect Occurence	-	person	Generalized for the entire patient population.
Achievement reducing Side-Effects	-	0.53	Dmnl	Meijvis et al., 2023
Co-Occurence SE and DRP	-	0.322353	Dmnl	Assumption.
Patients helped with SE Only	CC Patients with Side Effects * ”Achievement reducing Side-Effects” * ”Co-Occurence SE and DRP”	-	person	
Patients helped with SE and DRP	CC Patients with Side Effects * ”Achievement reducing Side-Effects” * (1-”Co-Occurence SE and DRP”	-	person	
DRP Occurence	-	0.715827	Dmnl	Meijvis et al., 2023
CC Patients with DRP	Patients involved in ComboConsult * DRP Occurence	-	person	
DRP Implementation	-	0.72	Dmnl	Meijvis et al., 2023
”Co-Occurence DRP and SE”	-	0.613419	Dmnl	Assumption.
Patients helped with DRP and SE	CC Patients with DRP*DRP Implementation*(1-”Co-Occurence DRP and SE”)	-	person	
Patients helped with DRP Only	CC Patients with DRP * DRP Implementation * ”Co-Occurence DRP and SE”	-	person	

Table C.10: Formulation of the effects of CombiConsult

Variable	Equation	Value	Unit	Description
Total Patients helped by CC	Patients helped with SE Only + Patients helped with DRP Only+Patients helped with DRP and SE + Patients helped with SE and DRP	-	person	The number of patients helped by CC.
CC Effectiveness ratio	Total Patients helped by CC / Sum(CVD Patients [Age-Group!])	-	Dmnl	The ratio of patients helped.
Base Pharmacist Satisfaction	-	8.4	Dmnl	The standard satisfaction with the pharmacist.
Satisfaction After CC	-	9.5	Dmnl	Assumption.
Average Satisfaction	Base Pharmicist Satisfaction + (Satisfaction After CC - Base Pharmicist Satisfaction) * CC Effectiveness ratio	-	Dmnl	Weighted average of patient in and out of CC.
Compliance Rate after CC	-	1	Dmnl	Assumingperfect adherence after CC.
Standard Compliance Rate	-	0.55	Dmnl	Starting adherence rate.
Compliance Rate	Standard Compliance Rate*Promote autonomy and recovery	-	Dmnl	Or after PAR is implemented.
Average Compliance Rate	Compliance Rate + (Compliance Rate after CC - Compliance Rate) * CC Effectiveness ratio	-	Dmnl	Weighted average of compliance rate.
Maximal Death Prevention	-	0.1	Dmnl	Al-Ganmi et al., 2016
Standardized Increase in Death Prevention	Maximal Death Prevention / (Target Compliance Rate - Compliance Rate)	-	Dmnl	
Target Compliance Rate	-	0.8	Dmnl	Assuming that an average of 80% is satisfactory.
Compliance Rate Max Effect	MIN(Average Compliance Rate, Target Compliance Rate)	-	Dmnl	Assuming that an average of 80% is satisfactory.
Death Prevention Increase	Base Death Rate + Standardized Increase in Death Prevention * (Compliance Rate Mac Effect - Compliance Rate)	-	Dmnl	The additional numbers of death prevention.
Base Death Rate	-	1	Dmnl	The death prevention of CC over time.

Table C.11: Formulation of costs and gains of CombiConsult

Variable	Equation	Value	Unit	Description
Average Number of Medications	-	5.9	medication / person	Meijvis et al., 2023
Medication Necesary	-	4.85	medication / person	Assumption.
Total Medication Needed	Sum(CVD Patients [AgeGroup!]) * Medication Necesary	-	medication	All necessary medication that need to be taken.
Unnecesary Medication	Total Medication - Total Medication Needed	-	medication	The over-treatment.
Total Medication	(1 - CC Effectiveness ratio) * Sum(CVD Patients [AgeGroup!]) * Average Number of Medications + CC Effectiveness ratio * Sum(CVVPatients [AgeGroup!]) * Medication Necesary	-	medication	Weighted average after CC implementation.
Medicine Cost per patient	-	504.14	euro / (person*Year)	
Spendings Unnecesary Medication	(Unnecesary Medication / Total Medication) * Sum(CVD Patients [AgeGroup!]) * Medicine Cost per patient * Discount Factor	-	euro/Year	Costs per medicine converted to euros
Unnecessary Medicine Costs	INTEG (Spendings Unnecessary Medication, Initial Costs medicine)	-	euro	The yearly costs of overtreatment.
Cost per Training Hour	-	14.09	euro / (hour * Pharmacist)	Assumption.
Duration of Pharmacist Training	-	8	hour	Assuming the training can be completed in 1 day.
Spending on CC	Join CombiConsult Program * Cost per Training Hour * Duration of Pharmacist Training * Discount Factor	-	euro/Year	The yearly spendings on CombiConsult.
CC Costs	INTEG (Spending on CC, Initial CC Costs)	-	euro	The total spending of CC.

Table C.12: Formulation of indirect costs

Variable	Equation	Value	Unit	Description
Length of Day Admission[AgeGroup]	-	1, 1, 1, 1	Day	One day since the patient can leave the same day.
Avg Time in Hospital[AgeGroup]	-	4, 5, 5, 5	Day	Based on data from the Hartstichting.
Daily costs Hospital	-	800	euro / (day*person)	Receievd from Zorgenstelsel.nl
Spendings Hospital [AgeGroup]	Hospitalization [AgeGroup] * Avg Time in Hospital [AgeGroup] * Daily costs Hospital * Discount Factor + ”1-Day Admission” [AgeGroup] * Length of Day Admission [AgeGroup] * Daily costs Hospital * Discount Factor	-	euro/Year	The total yearly spendings of CVD patient care for hospitals
Total Hospital Costs[AgeGroup]	INTEG (Spendings Hospital [AgeGroup], Initial Hospital Costs)	-	euro	The toal costs for society on healthcare
Mental Health Care Costs per person	-	2000	euro / (person*Year)	Costs of curing a patient depressive state. Richtlijnendatabase.nl
Spendings Mental Health Care	Sum(Patients with Depression [AgeGroup!]) * Mental Health Care Costs per person * Discount Factor	-	euro/Year	Total yearly spendings on mental health care.
Total Mental Health Care Costs	INTEG (Spendings Mental Health Care, Initial Mental Care Costs)	-	euro	Total costs meantal health care.
Yearly Burden	Sum(Spendings Hospital [AgeGroup!]) + Spendings Mental Health Care + Spendings Unnecesary Medication	-	euro/Year	Total societal costs regarding health care on the whole system.
Total Societal Costs	INTEG (Yearly Burden, Initial Costs to Society)	-	euro	All social costs combined.
Conversion Factor Percentage	-	100	Dmnl	From percentage to ratio.
Quality of Life Factor	Quality of Life / Conversion Factor Percentage	-	Dmnl	Convert the QoL metric to an number between 0 and 1.
Differences in Deaths	(Sum(Base Deaths [AgeGroup!]) - Sum(Deaths [AgeGroup!])) * Year	-	person	Death prevention due to implementation intervention.
Gains Death Prevention	Differences in Deaths *Quality Adhusted Life Year * Discount Factor * Quality of Life Factor	-	euro/Year	Social gains of death prevention.
Death Prevention Gains	INTEG (Gains Death Prevention, Initial Deaths Prevented)	-	euro	Total gains death prevention.

Table C.13: Formulation of calculating the SROI ratio

Variable	Equation	Value	Unit	Description
Societal Costs Difference	(Base Total Societal Costs - Total Societal Costs) + Death Prevention Gains	-	euro	The difference in social costs for QoL
Increase Social Gains	Social Gains - Base Social Gains	-	euro/Year	The difference in social gains with the no intervention case.
Initial Social Gains	-	0	euro	Assuming the model starts at zero gains.
Social Gains Differences	INTEG (Increase Social Gains, Initial Social Gains)	-	euro	
Investing	Spending on CC+Spendings MH Total+Spendings Total PA+Spendings Harteraad Other Investments	-	euro/Year	The total investment per year.
Initial investment Costs	Initial Costs CBT + Initial gaming Costs + Initial CC Costs	-	euro	
Total Investment Costs	INTEG (Investing, Initial investment Costs)	-	euro	Stock of total cost.
No Intervention SROI	-	0	Dmnl	SROi with no intervention.
SROI	IF THEN ELSE (Priority Switch=4, No Intervention SROI , (Social Gains Differences + Societal Costs Difference) / Total Investment Costs)	-	Dmnl	Calculating the SROI ratio when the base case is not selected.

Table C.14: Formulation of the Physical Activity Interventions

Variable	Equation	Value	Unit	Description
Priority Switch	-	4	Dmnl	0 = Priority on PA, 1 = Priority on MH, 2 = Priority on PA+MH, 3 = CombiConsult, 4 = No Intervention (Base Case)
Chooser Physical Activity Intervention	-	1	Dmnl	1 = ”Active-at-Home-HF”, 2 = Video Games, 3 = Relaxation Technique Training Groups, 4 = HIIT, 5 = Group Based Training
QoL increase AaH	-	4	Dmnl	increase in QoL after AaH
QoL increase No AaH	-	0	Dmnl	When AaH is not chosen
”Active-at-Home”	IF THEN ELSE(PA Intervention Switch = 1 , QoL increase AaH , QoL increase No AaH)	-	Dmnl	Operator choosing AaH
Video Games Enjoyment Factor	-	2.5	Dmnl	Reduction is drop-out rate after video gaming
Video games for PA	IF THEN ELSE(PA Intervention Switch = 2 , Video Games Enjoyment Factor , No Intervention Multiplier)	-	Dmnl	Operator choosing VG
Effect Relaxation Technique Training Groups	-	1.15	Dmnl	Assumptions
Relaxation Technique Training Groups	IF THEN ELSE(PA Intervention Switch = 3 , Effect Relaxation Technique Training Groups , No Intervention Multiplier)	-	Dmnl	Operator choosing RTTG
Group Based Training	IF THEN ELSE(PA Intervention Switch = 5 , 1 , 0)	-	Dmnl	
Exercise Program Duration	-	0.5	Year	Assuming length of group-based activities
Effectiveness of PA Intervention	-	0.4	Dmnl	Maximum effect on CVD due to training.
Reduction CVD Events Training	(COS(Time Passed * (1 / Exercise Program Duration) * Pi) /2 + 0.5) * Effectiveness of PA Intervention + (1 - Effectiveness of PA Intervention)	-	Dmnl	Function assumed to be a sine wave with period being the duration and amplitude due to the effect.
”Effect Group - Based Training”	IF THEN ELSE(Group Based Training = 1 , Reduction CVD Events Training, No Intervention Multiplier)	-	Dmnl	Operator choosing GBT.

Table C.15: Formulation of the Active-at-Home Intervention

Variable	Equation	Value	Unit	Description
Heart rate Monitor Costs	-	285.44	euro/monitor	
Monitors per person	-	1	monitor/person	Assumption
Equipment Costs	Heart rate Monitor Costs * Monitors per person * Starting Home Exercises	-	euro/Year	Yearly costs for equipment.
No Yearly Costs	-	0	euro/Year	If no equipment costs is made.
Spending on Equipment	IF THEN ELSE(PA Intervention Switch = 1 , Equipment Costs , No Yearly Costs)	-	euro/Year	Only spend if intervention is chosen.
Session Costs	-	35	euro/hour	The wages for monitoring patients.
Time per Monitoring	-	0.25	hour/person	How long consultation with a patient takes.
Monitoring Costs	Patients with Home Exercises * Time per Monitoring * Session Costs	-	euro	Total costs of wages.
Spending on Monitoring	IF THEN ELSE(PA Intervention Switch = 1 , Monitoring Costs/Year , No Yearly Costs)	-	euro/Year	
”Initial Active-at-Home Costs”	-	0	euro	Set costs to zero if intervention is not chosen.
”Active-at-Home Costs”	Spending on Equipment + Spending on Monitoring, ”Initial Active-at-Home Costs”	-	euro	Total costs of AaH intervention.

Table C.16: Formulation of the Video Game and Relaxation Interventions

Variable	Equation	Value	Unit	Description
Price per Game Console	-	320	euro/console	Assumption based on market price consoles.
Consoles per Beweegclub	-	2	console/club	Assumption.
Potential Costs Video Console	Initial Number of Beweegclubs * Consoles per Beweegclub * Price per Game Console	-	euro	Costs of buying consoles if intervention is chosen.
New Beweegclubs Console Costs	Starting new Beweegclub*Price per Game Console*Consoles per Beweegclub	-	euro/Year	Costs made when new Beweegclubs are using video games.
Spendings on Gaming	IF THEN ELSE(PA Intervention Switch=2, New Beweegclubs Console Costs , No Yearly Costs)	-	euro/Year	
Initial gaming Costs	IF THEN ELSE(PA Intervention Switch=2, Potential Costs Video Console , Initial Costs if not Chosen)	-	euro	Set costs to zero if intervention not chosen.
Gaming Costs	INTEG(Spendings on Gaming, Initial gaming Costs)	-	euro	Total costs of VG intervention.
Group Size	-	32	person/group	Average group for relaxation.
Groups Needed	Patients at Beweegclubs / Group Size	-	group	
Hourly Costs Occupational Therapist	-	22	euro/hour	Wages for the therapist.
Session per group	-	12	hour/ (group * Year)	Assumption.
Budget Needed	Groups Needed*Session per group*Hourly Costs Occupational Therapist	-	euro/Year	Totoal budget needed for implementation RTT.
Spendings Relaxation	IF THEN ELSE(PA Intervention Switch = 3 , Budget Needed , No Yearly Costs)	-	euro/Year	Set costs to zero if intervention not chosen.
Initial Relaxation Costs	-	0	euro	
Costs Relaxation	INTEG(Spendings Relaxation, Initial Relaxation Costs)	-	euro	Total costs of relaxation intervention.

Table C.17: Formulation of the HIIT and Group-based Training Interventions

Variable	Equation	Value	Unit	Description
Program Duration HIIT	-	12	week/ (group * Year)	Duration in weeks for HIIT
Hourly Costs Trainer	-	35	euro/hour	Wages for trainer
Costs per HIIT group	HIIT Intensity * Hourly Costs Trainer * Programme Duration HIIT	-	euro / (Year * group)	Total costs due to wages
Budget Needed for HIIT	Costs per HIIT group * Groups Needed	-	euro / Year	What is needed to pay for the wages.
Spendings HIIT	IF THEN ELSE("High-Intensity Interval Training"=1, Budget Needed for HIIT , No Yearly Costs)	-	euro/Year	Set costs to zero if intervention is not chosen.
Initial Costs HIIT	-	0	euro	
Costs High-Intensity Interval Training"	INTEG(Spendings HIIT, Initial Costs HIIT	-	euro	Total costs HIIT intervention.
Training Frequency	-	6	hour / (week * group * Year)	Total costs HIIT intervention.
Weeks per year	-	52	week/Year	
Costs per group	Total hours per group * Hourly Costs Trainer	-	euro/ (Year * group)	Total costs per group.
"Budget Needed for Group-Based Training"	Costs per group * Groups Needed	-	euro/Year	Total budget needed to pay for GBT.
Spendings on Training	IF THEN ELSE(PA Intervention Switch=5, "Budget Needed for Group-Based Training" , No Yearly Costs)	-	euro/Year	Set costs to zero if intervention is not chosen.
"Initial Costs Group-Based"	-	0	euro	
"Costs Group-Based Training"	INTEG(Spendings on Training, "Initial Costs Group-Based")	-	euro	Total costs of GBT intervention.
Spendings Total PA	(Spending on Equipment + Spending on Monitoring + Spendings HIIT + Spendings on Gaming + Spendings on Training + Spendings Relaxation) * Discount Factor	-	euro/Year	All yearly spendings combined.
Initial Costs PA Interventions	Initial gaming Costs	-	euro	
Total Costs Physical Acitivities	INTEG(Spendings Total PA, Initial Costs PA Interventions)	-	euro	All yearly spendings added and combined into one single stock.

Table C.18: Formulation of the Mental Healthcare Interventions

Variable	Equation	Value	Unit	Description
Chooser Mental Health Intervention	-	1	Dmnl	1 = Music Therapy, 2 = Care co-ordination intervention, 3 = CBT, 4 = Promote autonomy and recovery, 5 = TM
MH Intervention Switch	IF THEN ELSE (Priority Switch=1, Chooser Mental Health Intervention , IF THEN ELSE (Priority Switch=2, Chooser Mental Health Intervention , Intervention not Chosen))	-	Dmnl	Logical operator to choose for MH interventions.
Stress Reduction Factor	-	0.8677	Dmnl	Li and Xiong, 2016
Stress Reduction Music Therapy	IF THEN ELSE (MH Intervention Switch = 1 , Stress Reduction Factor , No Intervention Multiplier)	-	Dmnl	Only reduce stress if intervention is chosen.
Reduction Depression CCI	-	0.59	Dmnl	Assumption
Care coordination intervention	IF THEN ELSE (MH Intervention Switch = 2 , Reduction Depression CCI , No Intervention Multiplier)	-	Dmnl	
CBT Factor	-	0.7	Dmnl	Scott et al., 2012
Cognitive behavioural therapy	IF THEN ELSE (MH Intervention Switch = 3 , CBT Factor , No Intervention Multiplier)	-	Dmnl	Only reduce deaths if intervention is chosen.
Benefit of PAR	-	1.1	Dmnl	
Promote autonomy and recovery	IF THEN ELSE (MH Intervention Switch = 4 , Benefit of PAR , No Intervention Multiplier)	-	Dmnl	Own Assumption.
Reduction Telemedicine	-	0.91863	Dmnl	Rachas et al., 2015
Telemedicine	IF THEN ELSE (MH Intervention Switch = 5, Reduction Telemedicine, No Intervention Multiplier)	-	Dmnl	Only reduce stress if intervention is chosen.

Table C.19: Formulation of Music Therapy and Care Coordination

Variable	Equation	Value	Unit	Description
Group Size Music Therapy	-	30	person / group	Li and Xiong, 2016
Groups Needed for Music Therapy	Patients Affected by CVD Events / Group Size Music Therapy	-	Group	Divide patient into groups.
Duration Music Therapy	-	5	hour / (Year * group)	Assumption
Hourly Rate Therapist	-	77	euro/hour	Tan et al., 2012
Spendings Music therapy	IF THEN ELSE(MH Intervention Switch=1, Costs per group Music Therapy * Groups Needed for Music Therapy , No Yearly Costs)	-	euro/Year	Only spend money if intervention is chosen.
Costs Music Therapy	INTEG(Spendings Music therapy, Initial Costs Music Therapy)	-	euro	Total costs MT intervention
Patients eligible for Care Coordination	CVD Patients[Patients75to84] + CVD Patients[PatientsOldest]	-	person	Intervention only applied to the older generations.
Group Size Care Coordination	-	171	person/group	Average of Kastner et al., 2018
Groups Needed for Care Coordination	Patients eligible for Care Coordination / Group Size Care Coordination	-	group	Divide the patient into groups
Costs organizing Care Coordination	-	2000	euro / (Year * group)	Costs of organising a one-day event.
Spendings Care Coordination	IF THEN ELSE (MH Intervention Switch=2, Groups Needed for Care Coordimation * Costs organizing Care Coordination , No Yearly Costs)	-	euro/Year	Only spend money if intervention is chosen
Initial Costs Care Coordination	-	0	euro	
Costs Care Coordination	INTEG(Spendings Care Coordination, Initial Costs Care Coordination)	-	euro	Total costs CC intervention.

Table C.20: Formulation of CBT and Promotion of Autonomy

Variable	Equation	Value	Unit	Description
Number of Psychotherapists	-	703	therapist	Data from ZorgkaartNedelrand
Wages per session	-	70	euro/session	Tan et al., 2012
Sessions per Year	-	52	session / (Year * therapist)	Sssuming 1 session per week with the therapist
Budget Needed CBT	Number of Psychotherapists * Sessions per Year * Wages per session	-	euro/Year	Total budget need to pay for CBT
Spendings CBT	IF THEN ELSE (MH Intervention Switch=3, Budget Needed CBT , No Yearly Costs)	-	euro/Year	Only spend money if intervention is chosen
Training Costs CBTH	-	264.19	euro / therapist	Henrich et al., 2023.
Training Cost	Training Costs CBTH * Number of Psychotherapists	-	euro	Totoal cost of wages for trainers.
Initial Costs CBT	IF THEN ELSE (MH Intervention Switch=2, Training Cost , Initial Costs if not Chosen)	-	euro	
Cognitive behavioural therapy Costs	INTEG(Spendings CBT, Initial Costs CBT)	-	euro	Total costs CBT intervention
Average Costs per session	-	68.5	euro / session	Tan et al., 2012
Sessions per Patient	-	2	session / person	Assuming two session are needed.
Budget Needed Autonomy	Sum(Depression due to Stress[AgeGroup!]) * Average Costs per session * Sessions per Patient * Attendence Rate	-	euro/Year	Total budget needed to pay PAR
Spendings Promotion	IF THEN ELSE (MH Intervention Switch=4, Budget Need Autonomy , No Yearly Costs)	-	euro/Year	Only spend money if intervention is chosen
Initial Costs Promotion	Initial Costs CBT	-	euro	Starting with already spend training costs.
Costs Promotion Autonomy	INTEG(Spendings Promotion, Initial Costs Promotion)	-	euro	Total costs for PAR intervention.

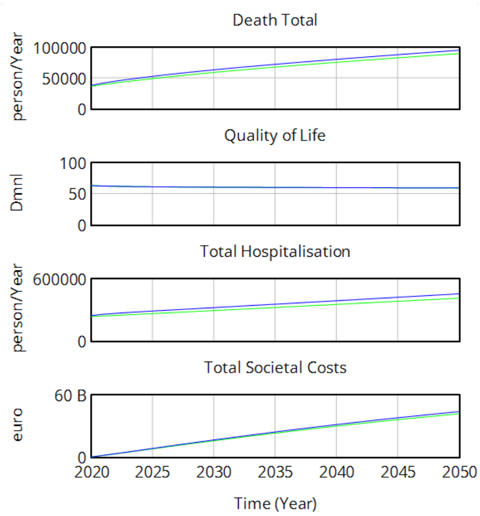
Table C.21: Formulation of Telemedicine

Variable	Equation	Value	Unit	Description
Participation Rate	-	1	1/Year	
Monitoring Costs TeleMedicine	Sum(Patients with Depression [AgeGroup!]) * Session Costs * Time per Monitoring * Participation Rate	-	euro/Year	Total monitoring costs per year.
Spending TeleMedicine	IF THEN ELSE (MH Intervention Switch=5, Monitoring Costs TeleMedicine , No Yearly Costs)	-	euro/Year	Only spend money if intervention is chosen.
Initial Costs TeleMedicine	-	0	euro	
Costs TeleMedicine	INTEG(Spending TeleMedicine, Initial Costs TeleMedicine)	-	euro	Total costs Telemedicine
Spendings MH Total	(Spending TeleMedicine + Spendings Care Coordination + Spendings CBT + Spendings Promotion + Spendings Music therapy) * Discount Factor	-	euro/Year	Total spendings for mental health interventions
Initial Costs MH Interventions	-	0	euro	Initial costs MH.
Total Costs MH	INTEG(Spendings MH Total, Initial Costs MH Interventions)	-	euro	Total costs of mental health interventions.

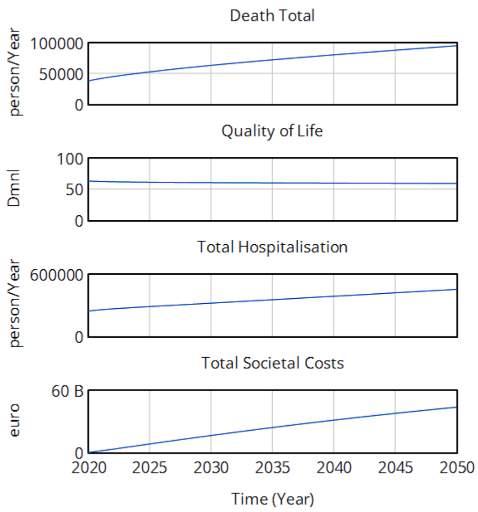
D

Model Validation Figures

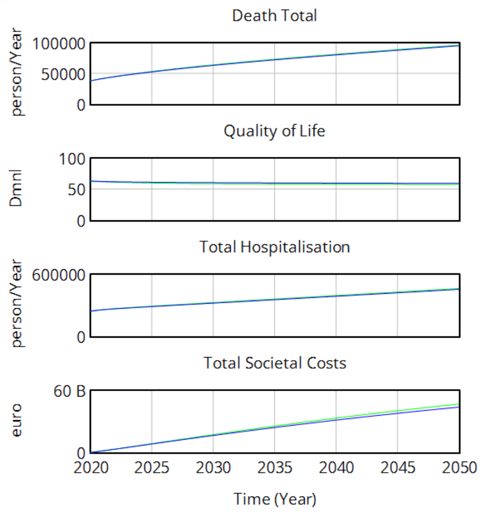
D.1. Extreme Condition Test Figures



(a) Extreme Condition Test when depression is solved within a day

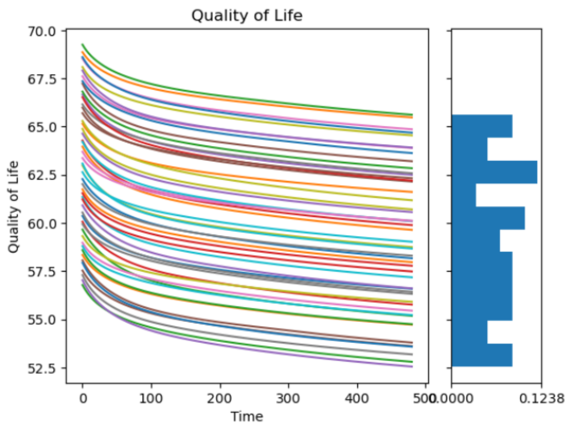


(a) Extreme Condition Test when depression is solved within a day

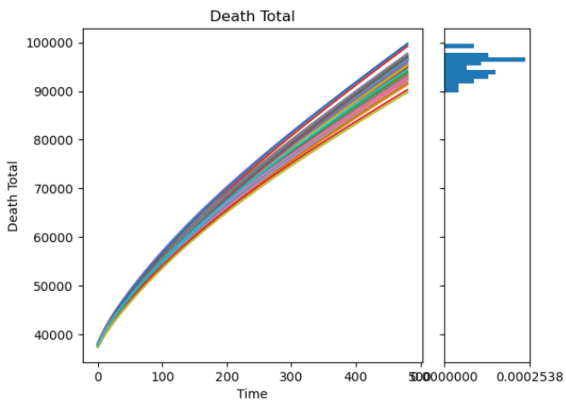


(b) Extreme Condition Test when depression stays for long-term

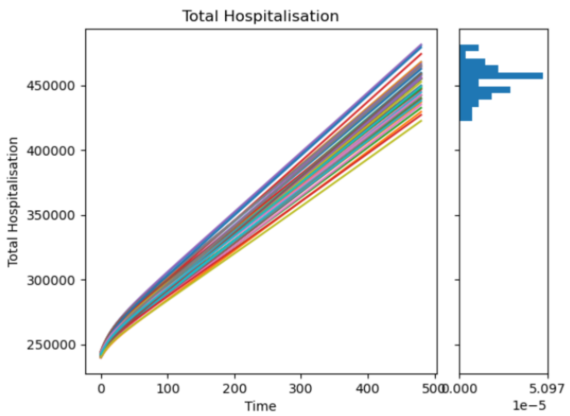
D.2. Sensitivity Analysis Figures



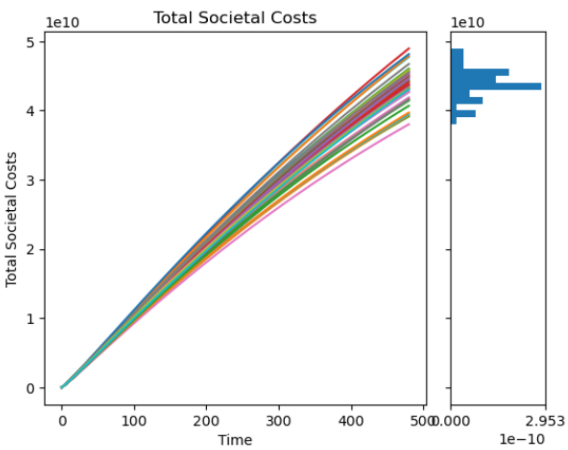
(a) Flowchart of the literature review on general interventions



(b) Flowchart of the literature review on general interventions



(c) Flowchart of the literature review on general interventions



(d) Flowchart of the literature review on general interventions

Figure D.3: The average and standard deviation of critical parameters: Region R4

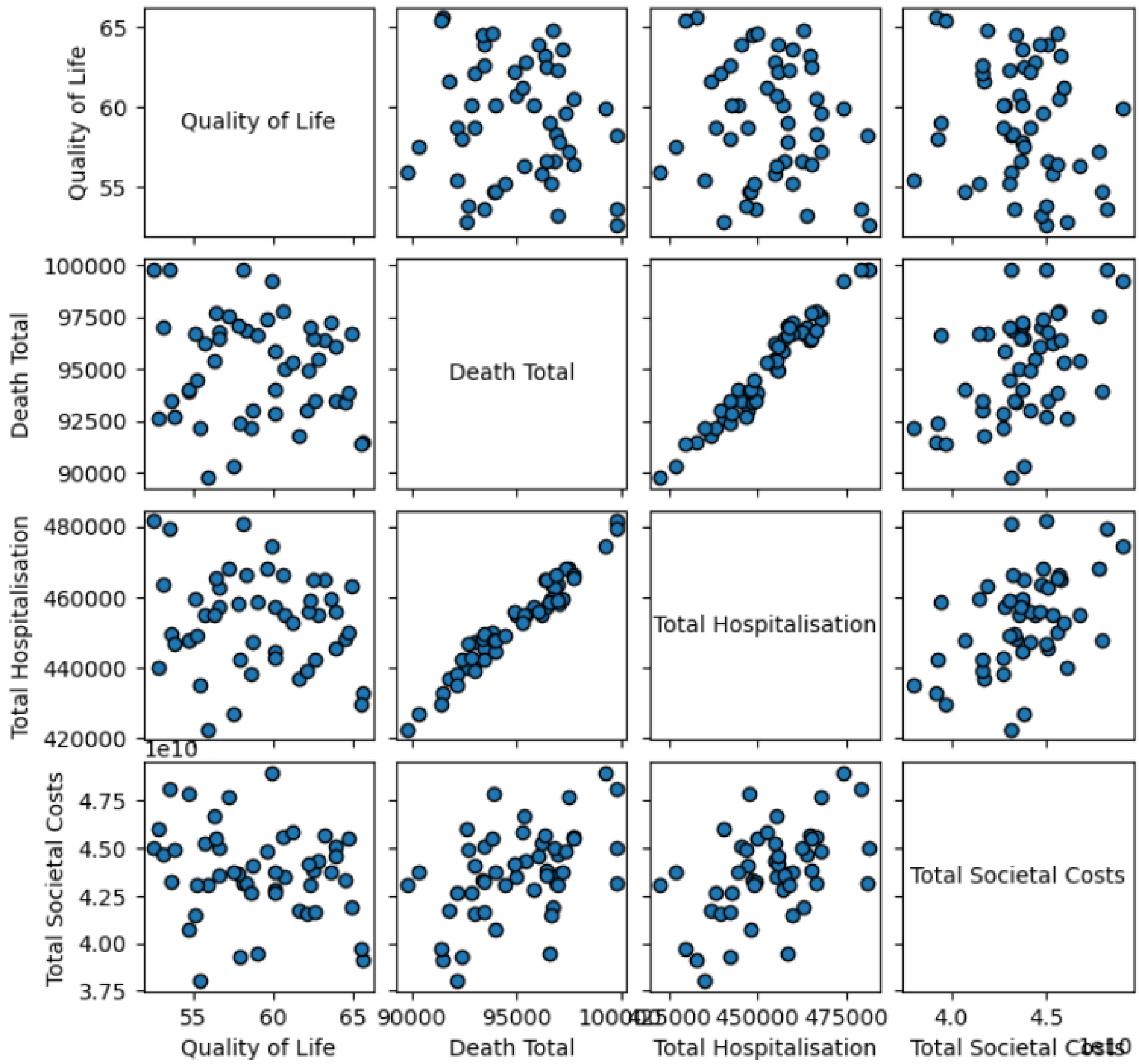
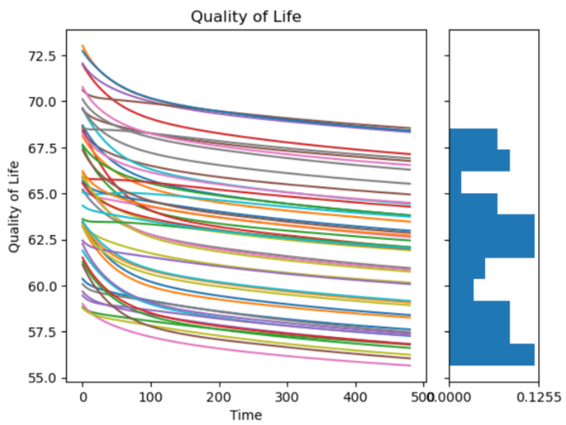


Figure D.4: Flowchart of the literature review on general interventions

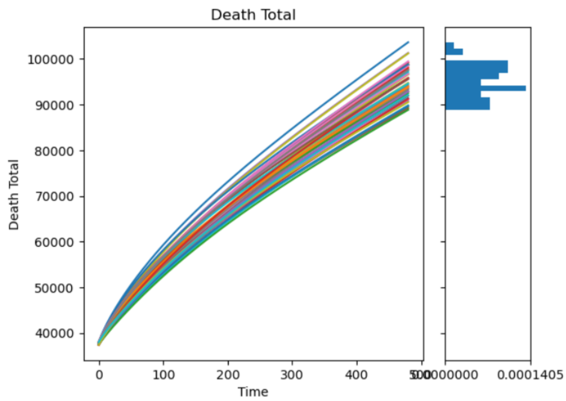
E
Graphs of Results

E.1. Graphs for Physical Activity Interventions

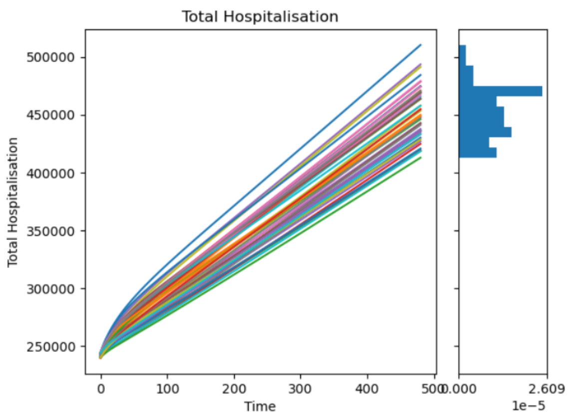
E.1.1. Graphs for the Active-at-Home Intervention



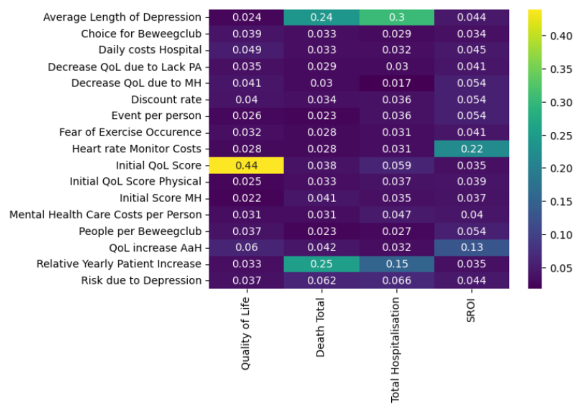
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.1: The graphs for Active-at-Home on quality of life, deaths and hospitalisation as well as the factors influencing the results.

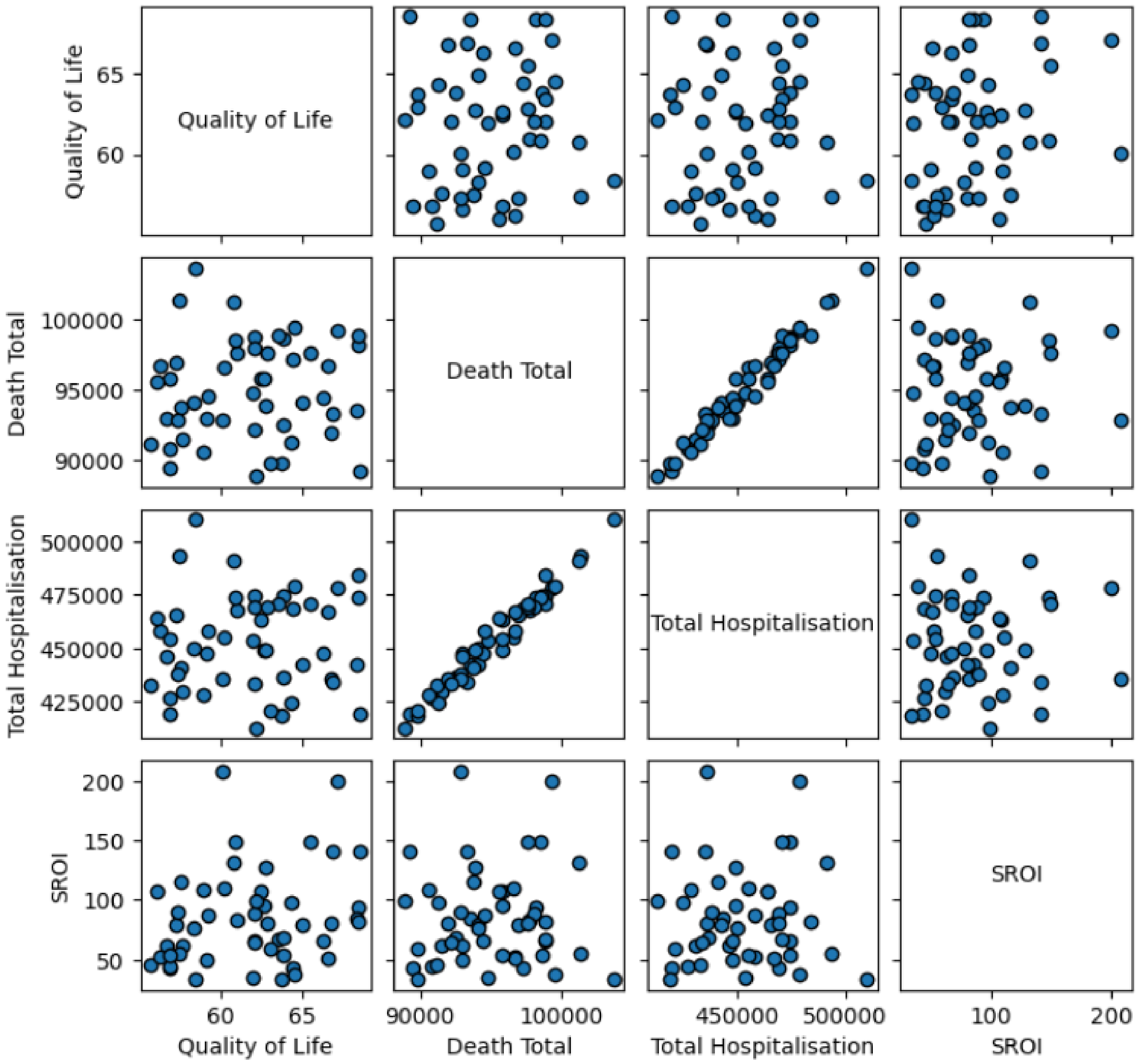
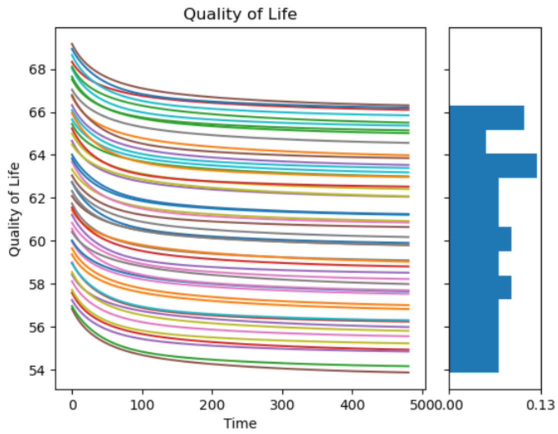
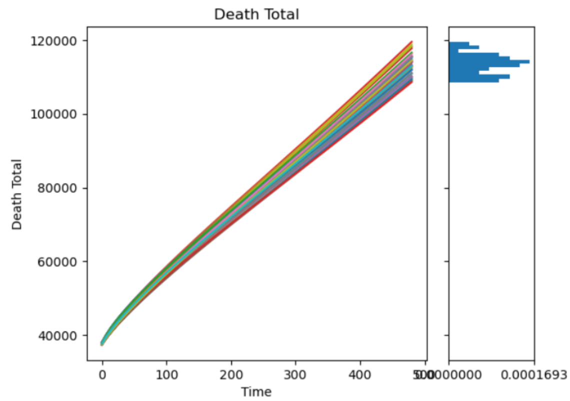


Figure E.2: Scatter plot of the results in the Active-at-Home Intervention

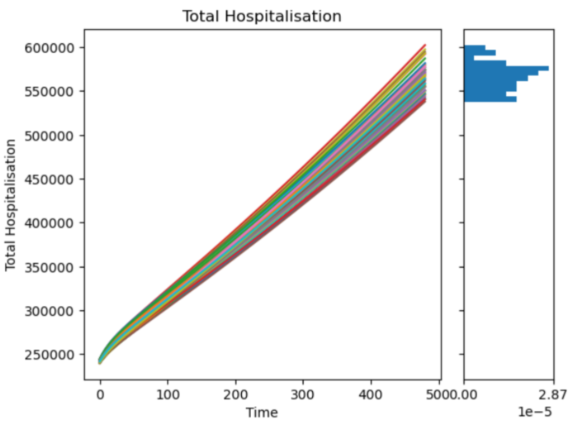
E.1.2. Graphs for the Video games Intervention



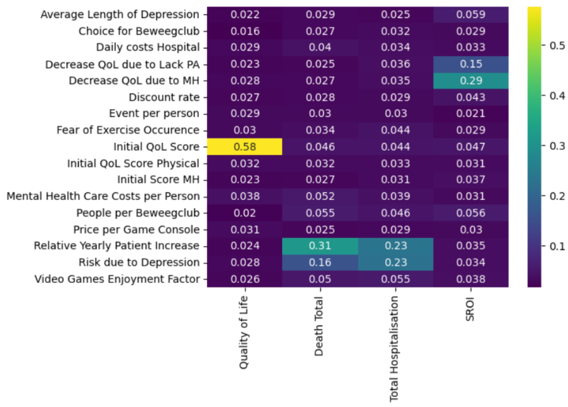
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.3: The graphs for Video Games on quality of life, deaths and hospitalisation as well as the factors influencing the results.

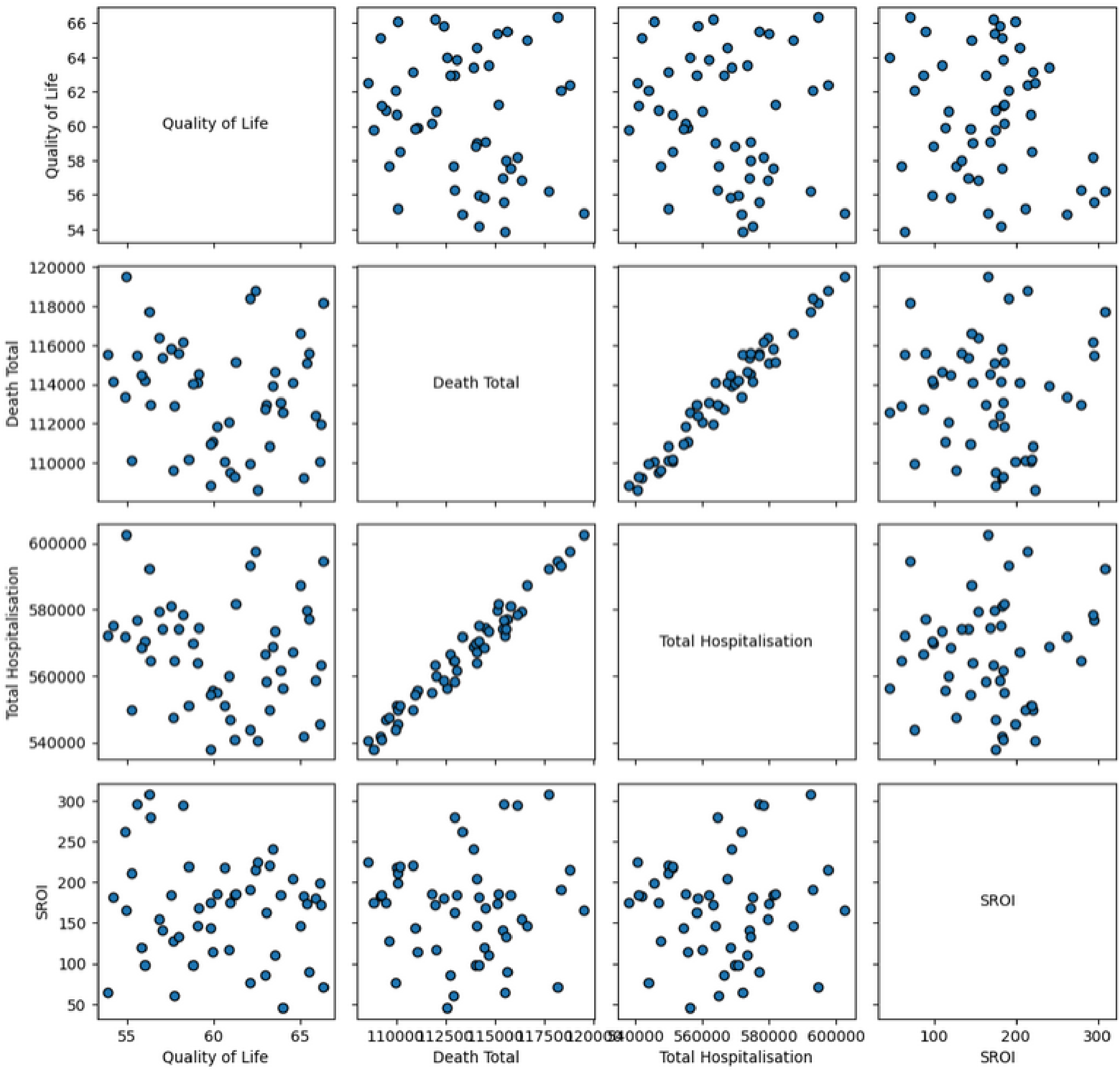
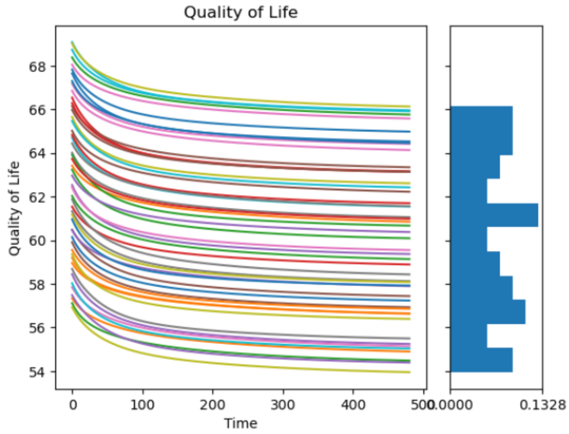
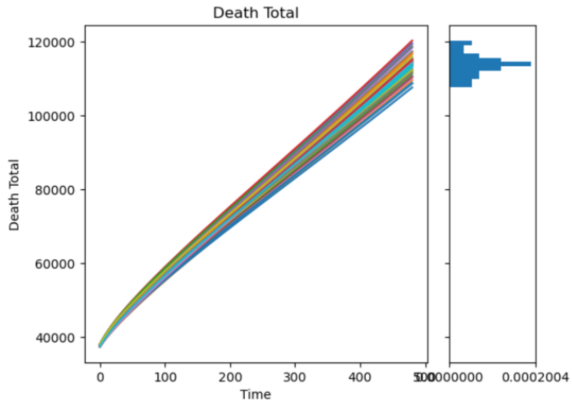


Figure E.4: Scatter plot of the results in the video gaming intervention

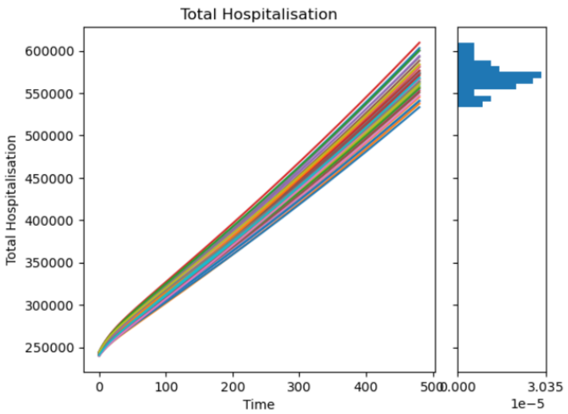
E.1.3. Graphs for the Relaxation Technique Training Intervention



(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty

(d) Feature Scoring for all outcome variables

Figure E.5: The graphs for Relaxation Technique Training on quality of life, deaths and hospitalisation as well as the factors influencing the results.

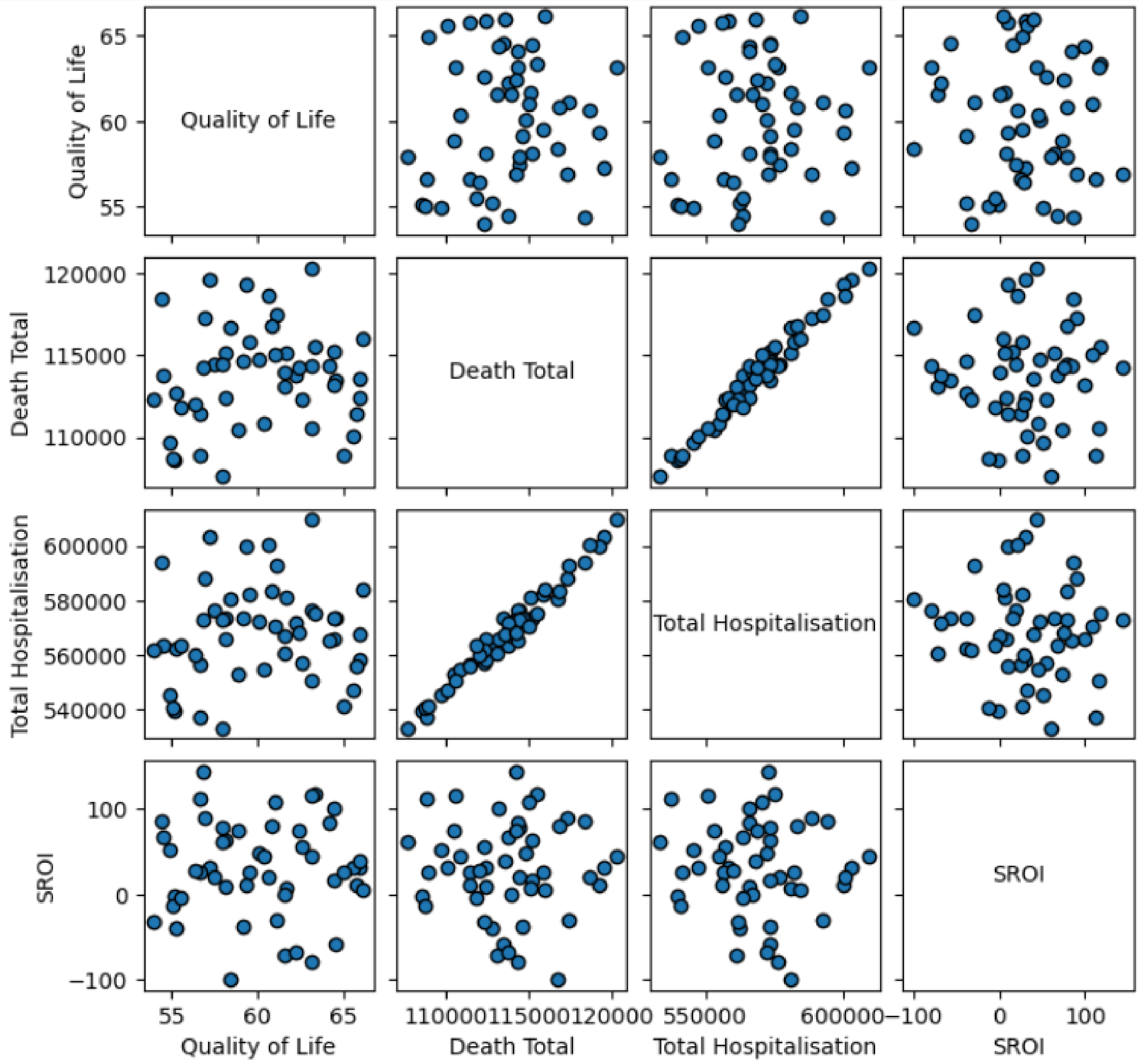
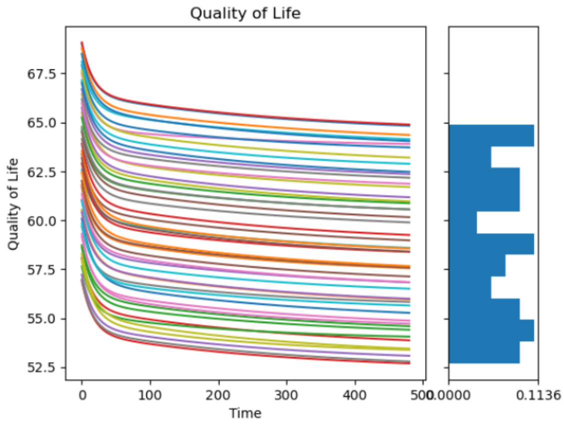
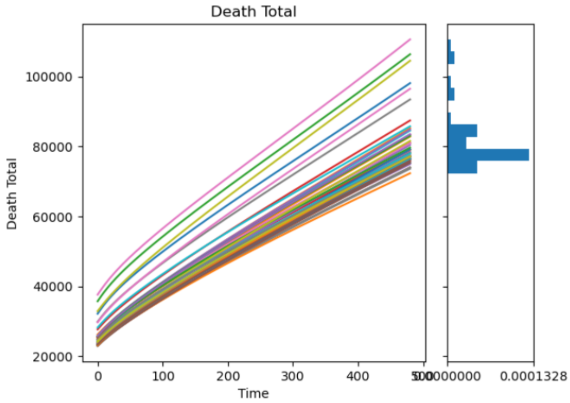


Figure E.6: Scatter plot of the results in the relaxation technique intervention

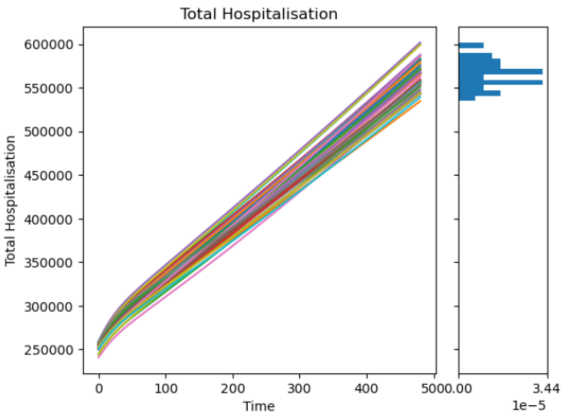
E.1.4. Graphs for the High-Intensity Interval Training Intervention



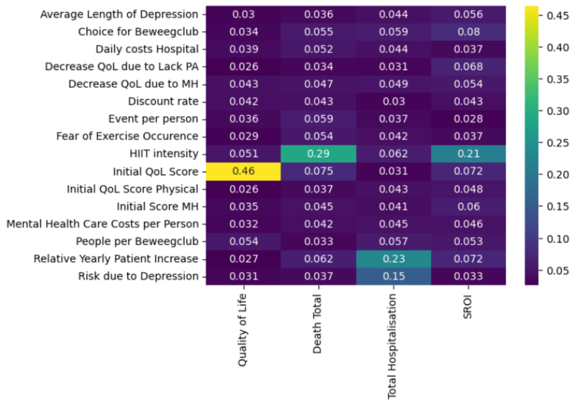
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.7: The graphs for HIIT on quality of life, deaths and hospitalisation as well as the factors influencing the results.

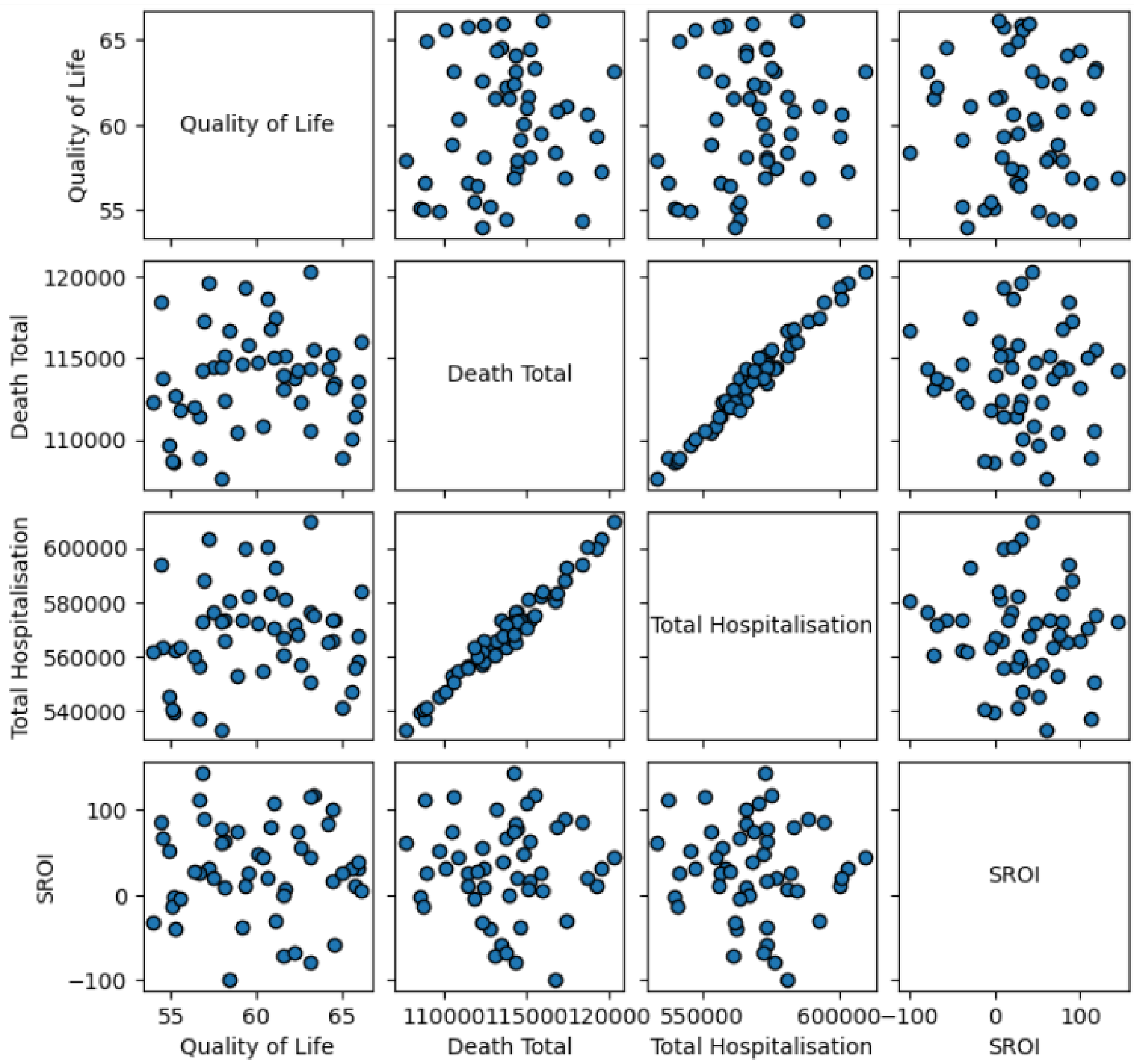
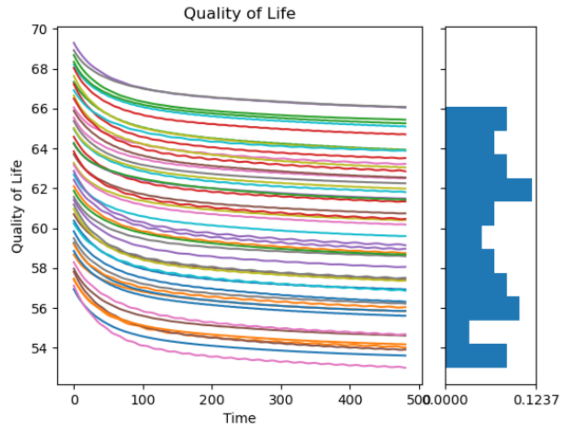
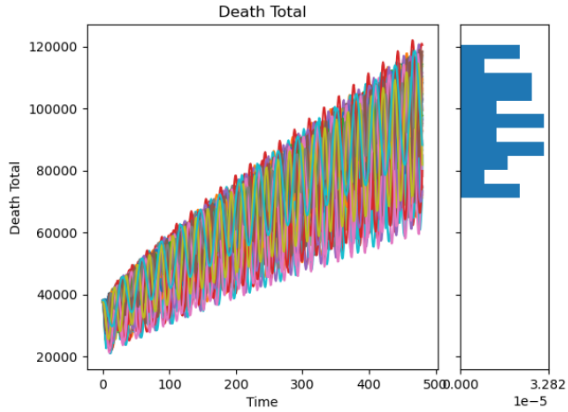


Figure E.8: Scatter plot of the results in the HIIT intervention

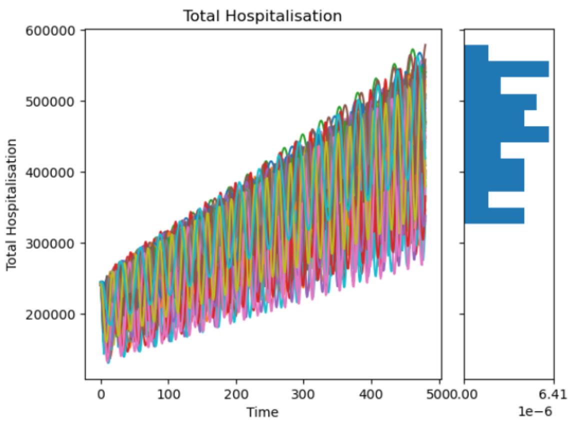
E.1.5. Graphs for the Group Based Training Intervention



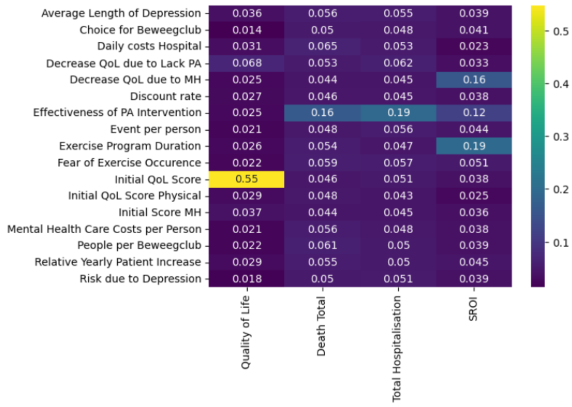
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.9: The graphs for Group Based Training on quality of life, deaths and hospitalisation as well as the factors influencing the results.

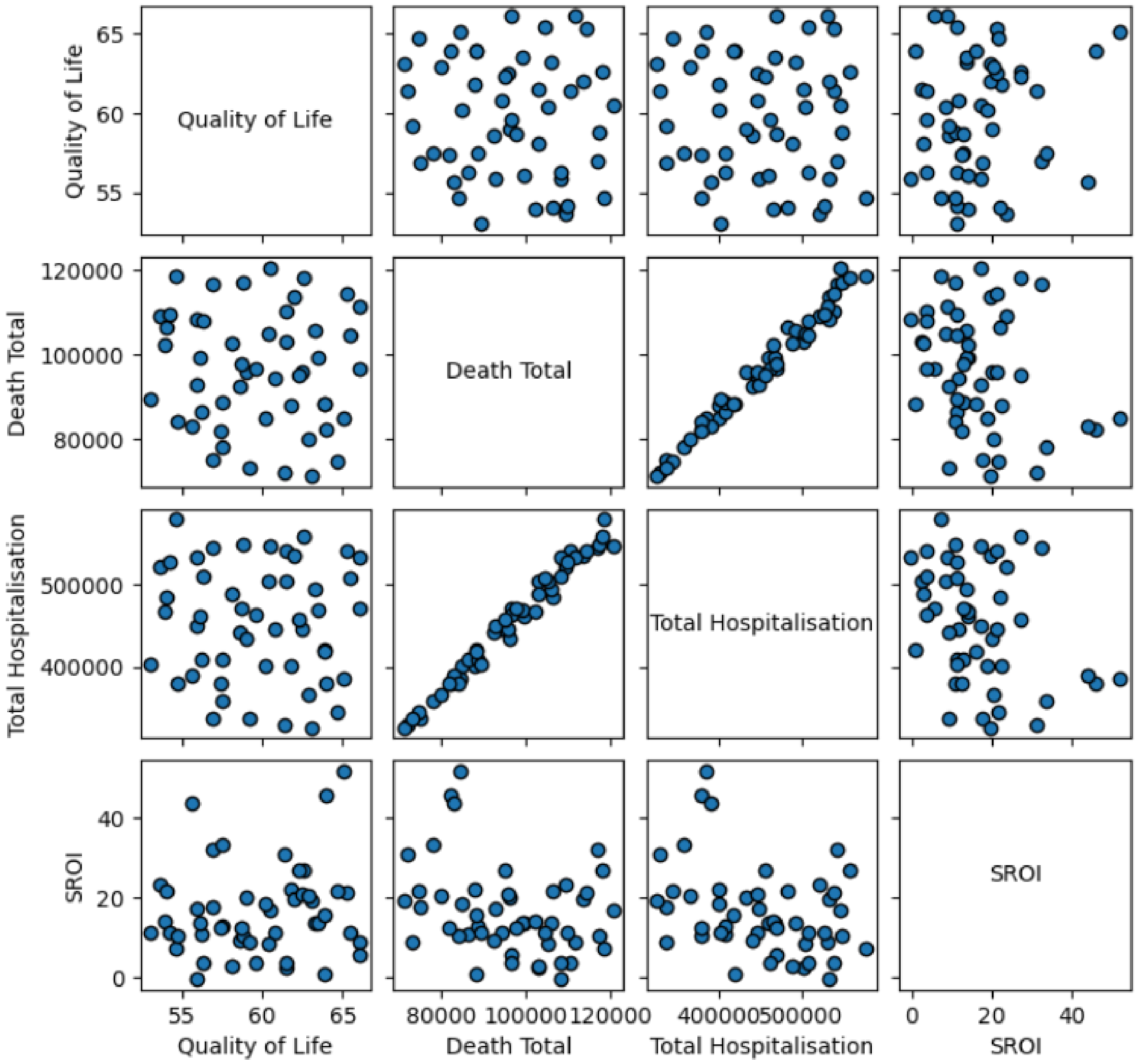
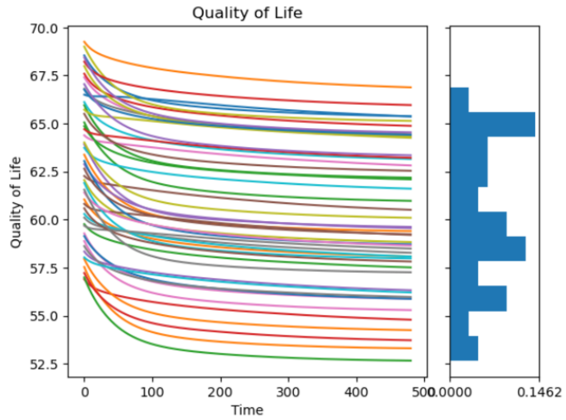


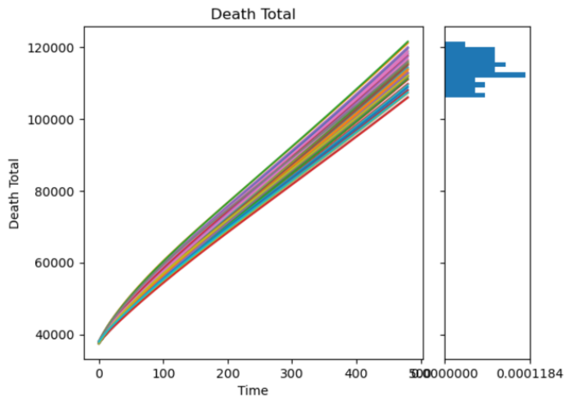
Figure E.10: Scatter plot of the results in the group training intervention

E.2. Graphs for Mental Health Interventions

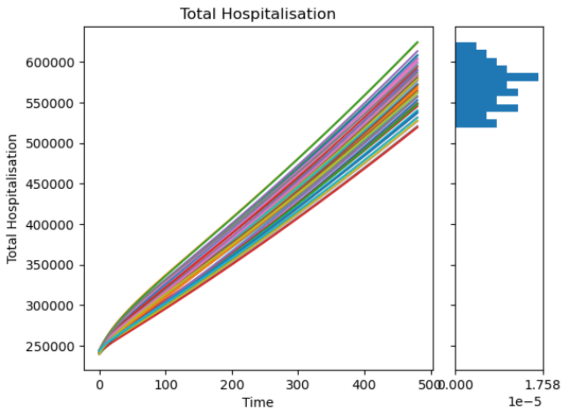
E.2.1. Graphs for the Music Therapy Intervention



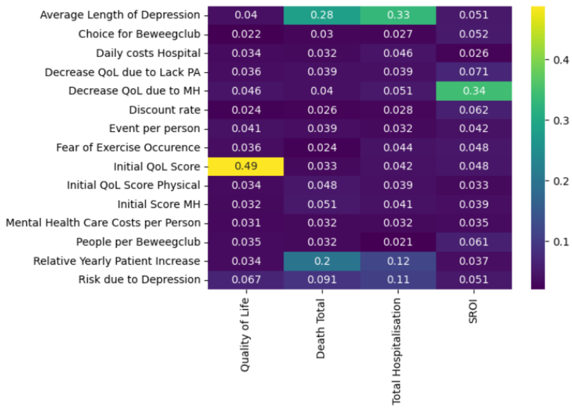
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.11: The graphs for Music Therapy on quality of life, deaths and hospitalisation as well as the factors influencing the results.

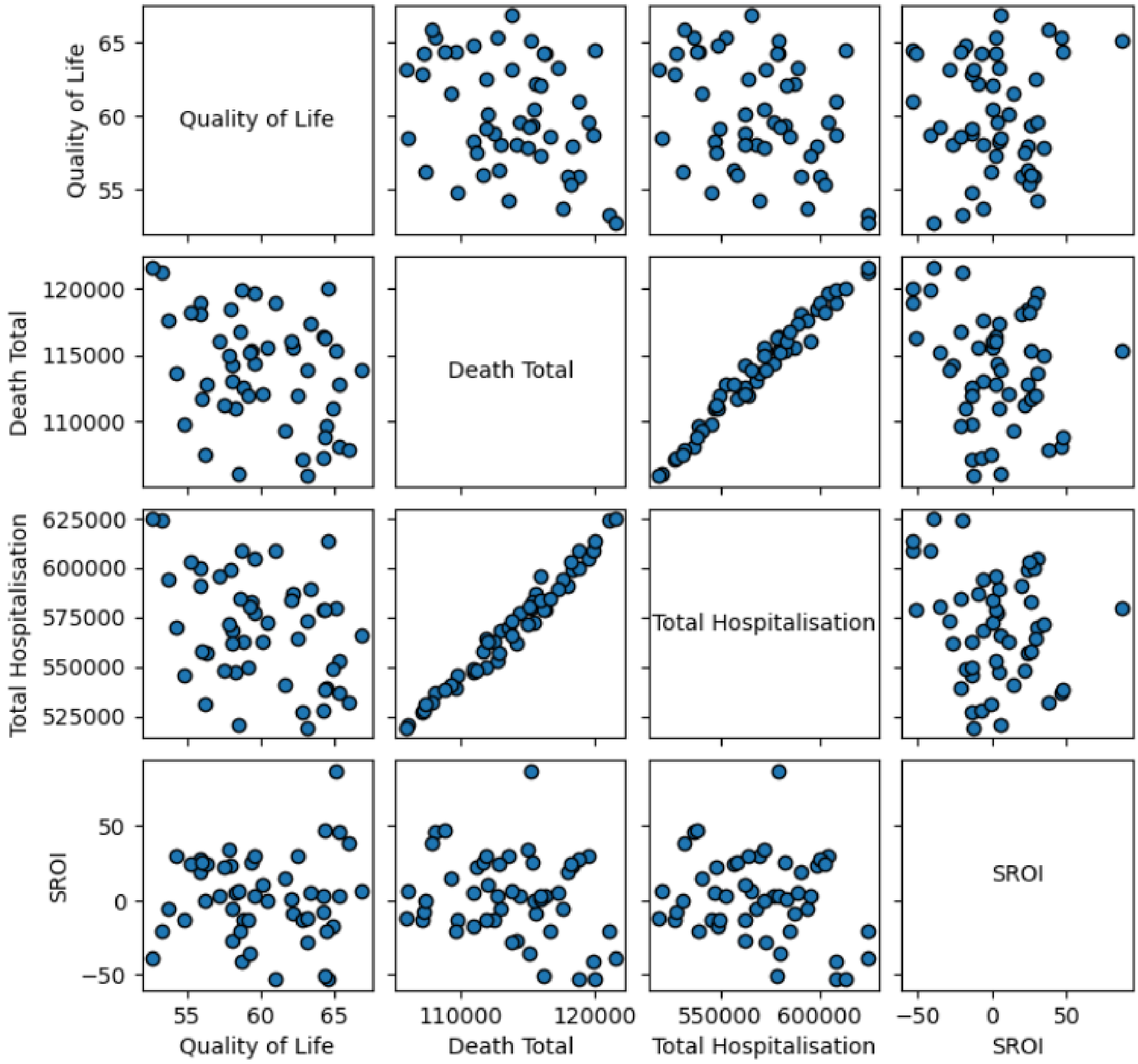
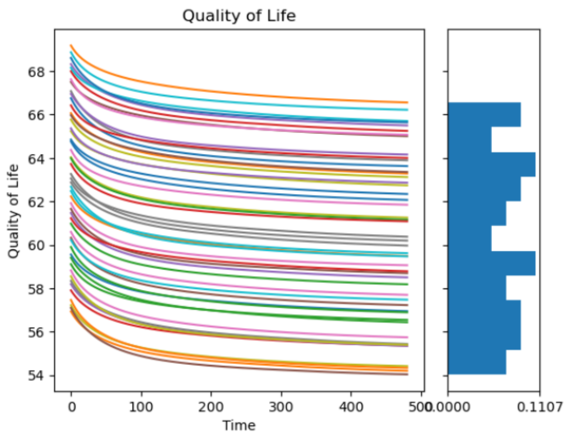
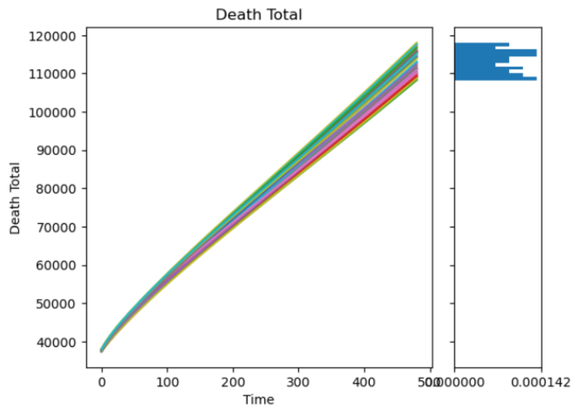


Figure E.12: Scatter plot of the results in the music therapy intevrention

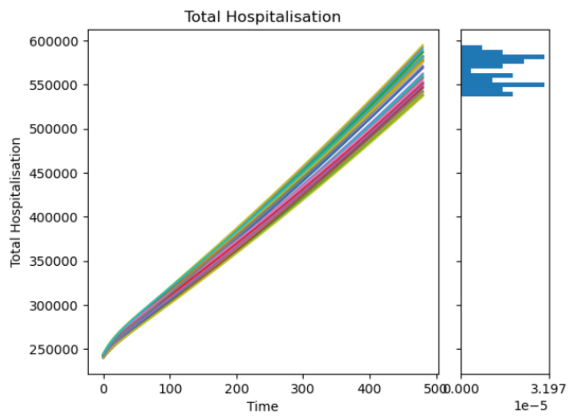
E.2.2. Graphs for the Care Coordination Intervention



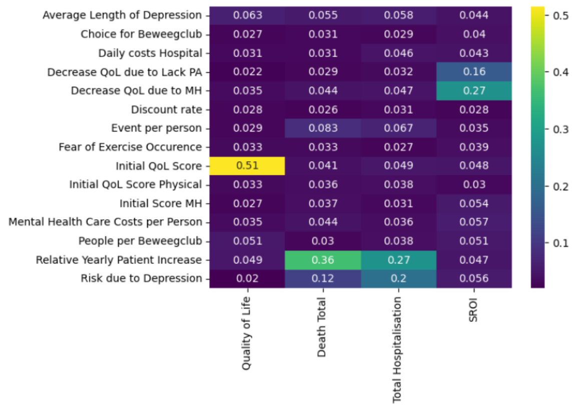
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.13: The graphs for Care Coordination on quality of life, deaths and hospitalisation as well as the factors influencing the results.

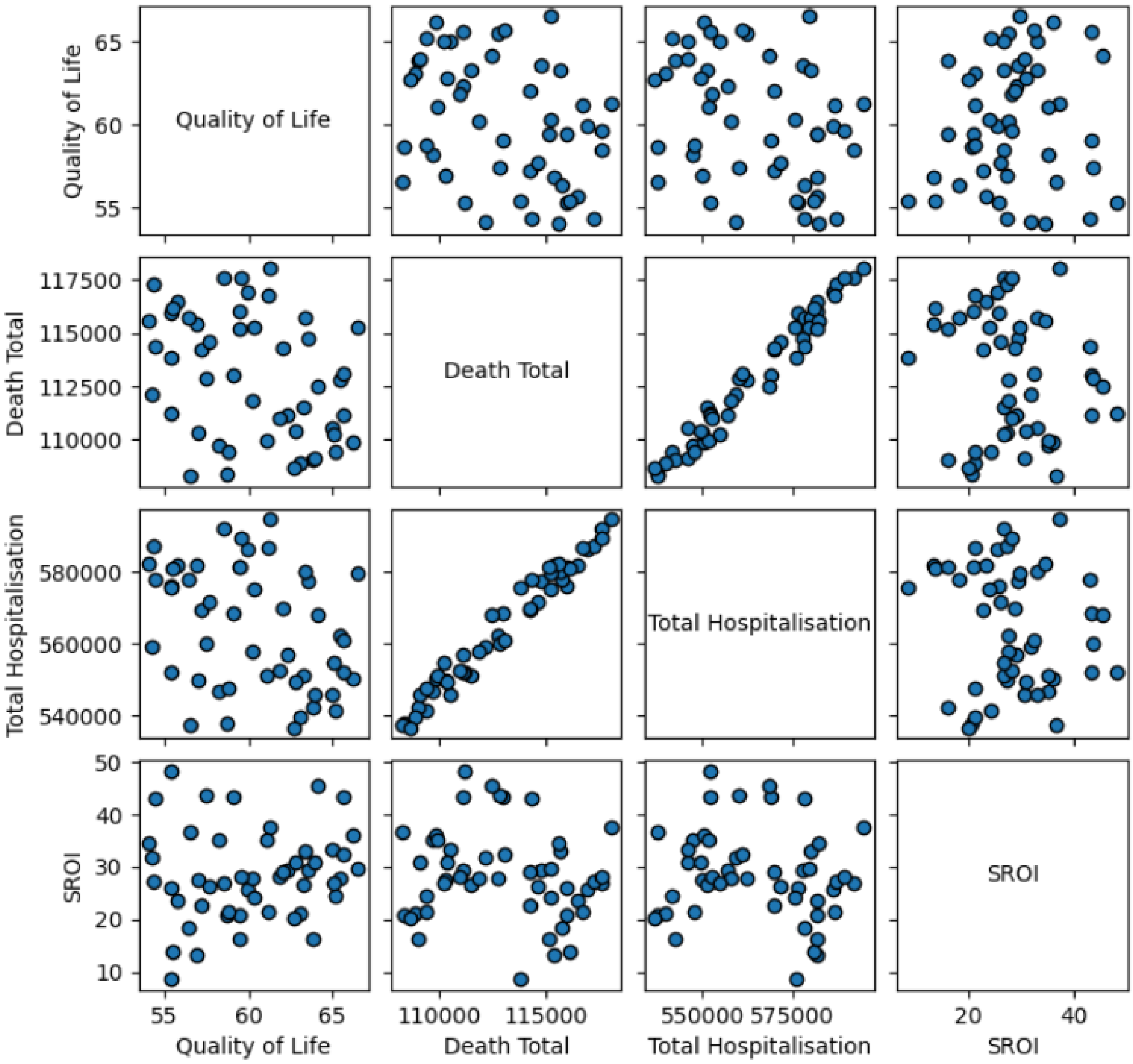
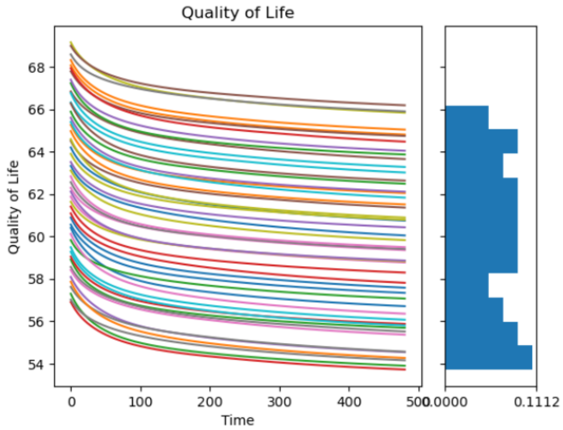
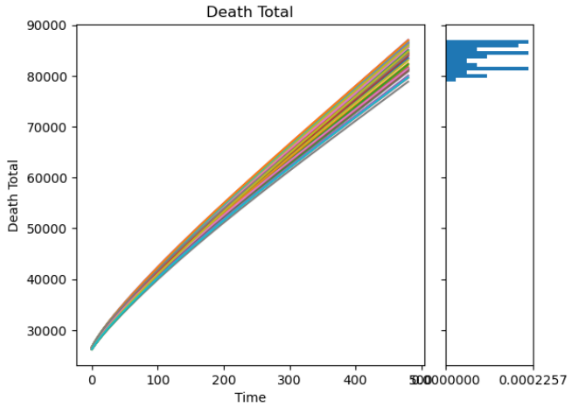


Figure E.14: Scatter plot of the results in the care coordination intervention

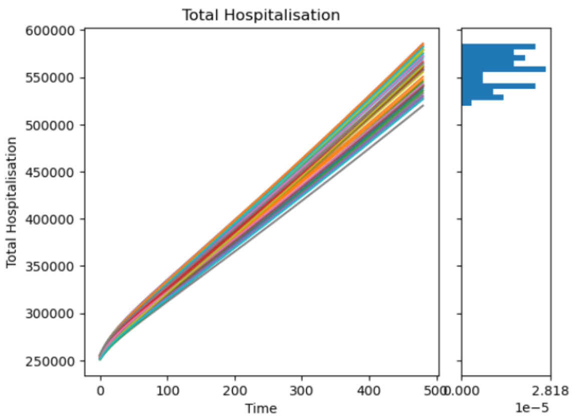
E.2.3. Graphs for the Cognitive Behavioural Therapy Intervention



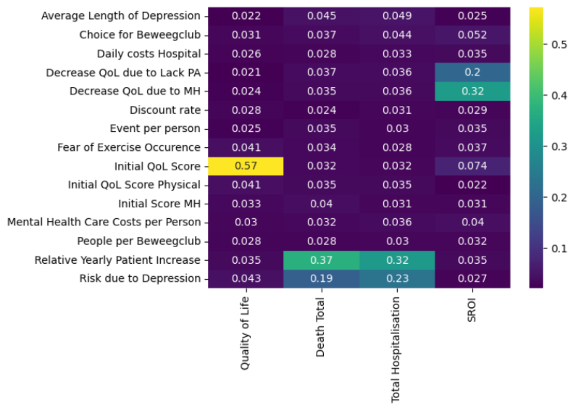
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.15: The graphs for Cognitive Behavioural Therapy on quality of life, deaths and hospitalisation as well as the factors influencing the results.

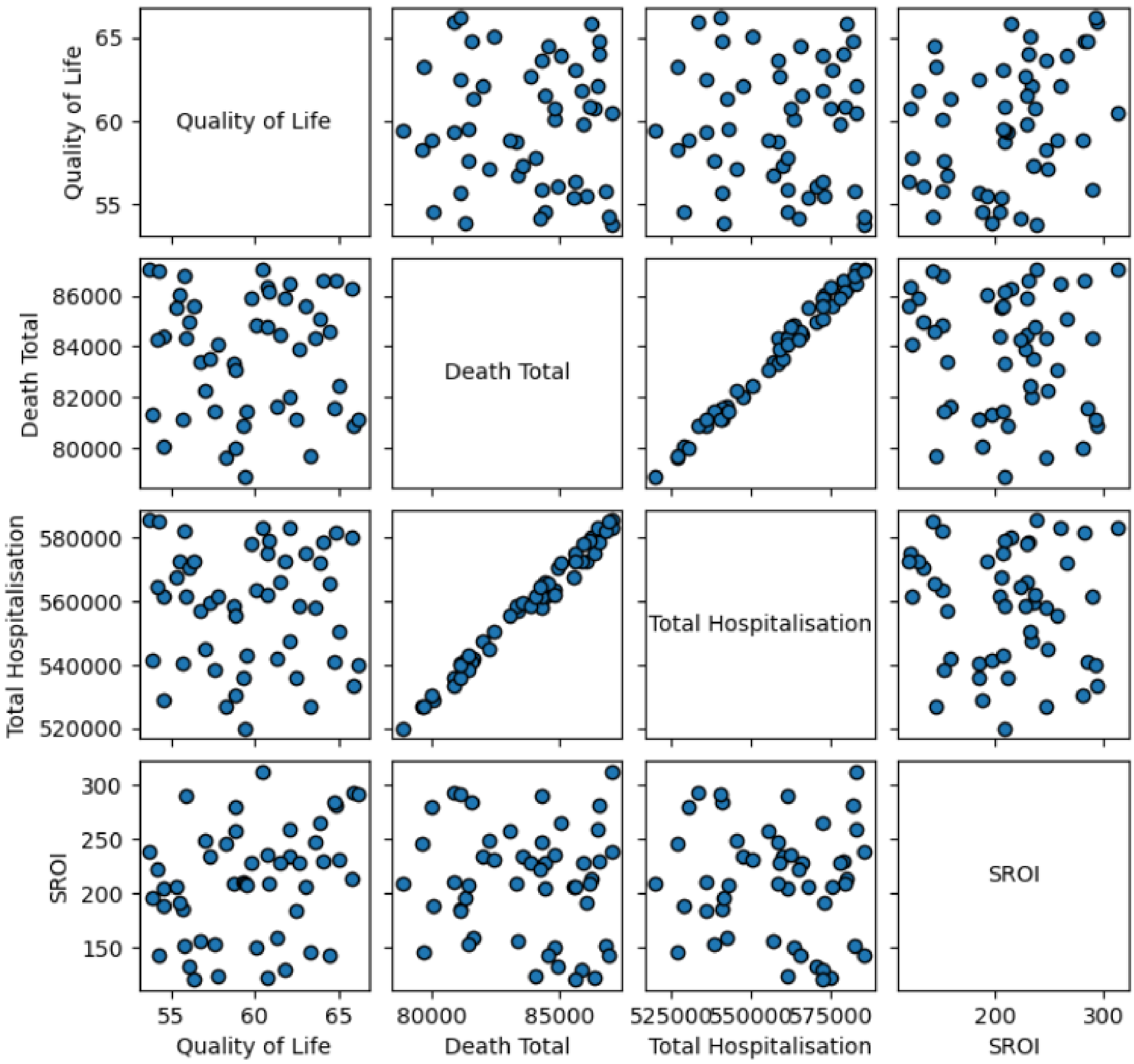
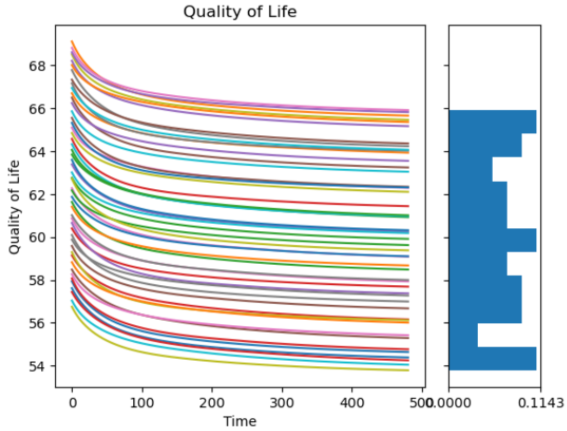
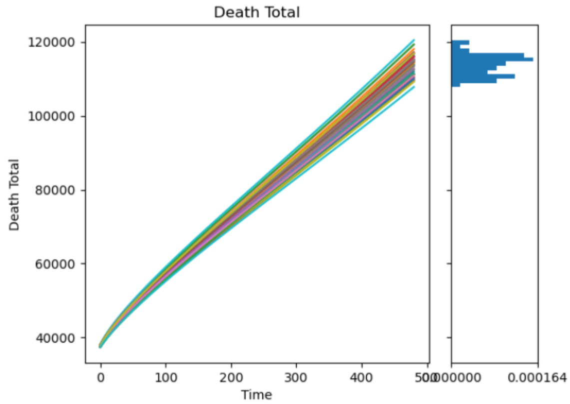


Figure E.16: Scatter plot of the results in the CBT intervention

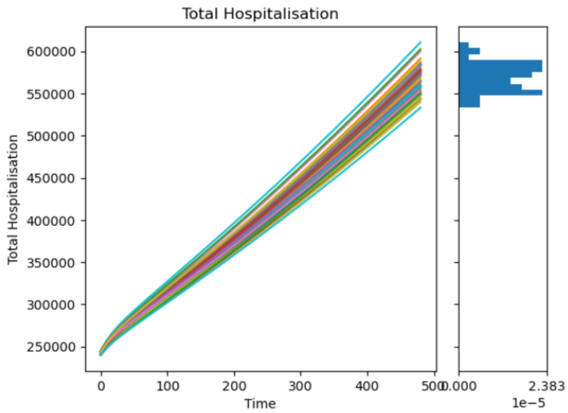
E.2.4. Graphs for the Promote Autonomy and Recovery Therapy Intervention



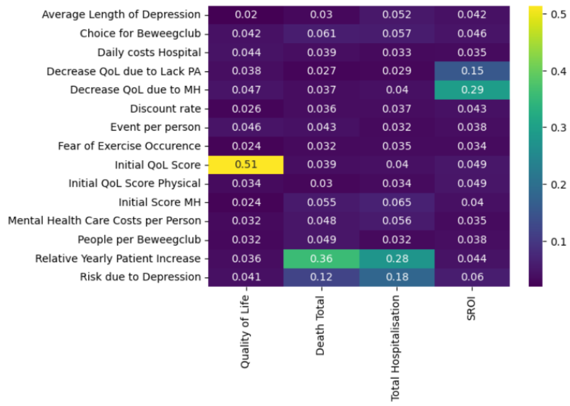
(a) Quality of Life under uncertainty



(b) Total deaths under uncertainty



(c) Total Hospitalisation under uncertainty



(d) Feature Scoring for all outcome variables

Figure E.17: The graphs for Promote Autonomy and Recovery on quality of life, deaths and hospitalisation as well as the factors influencing the results.

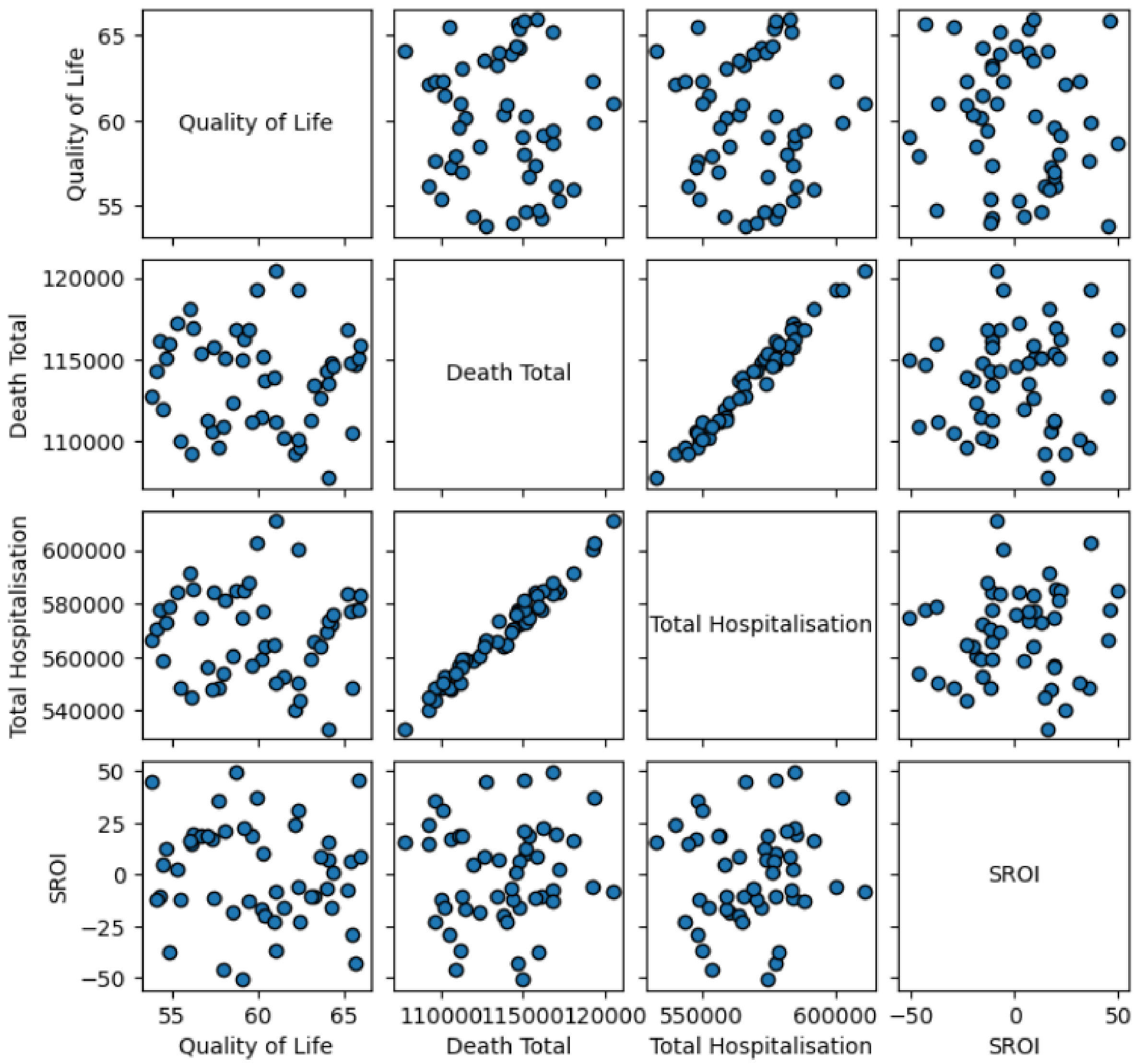
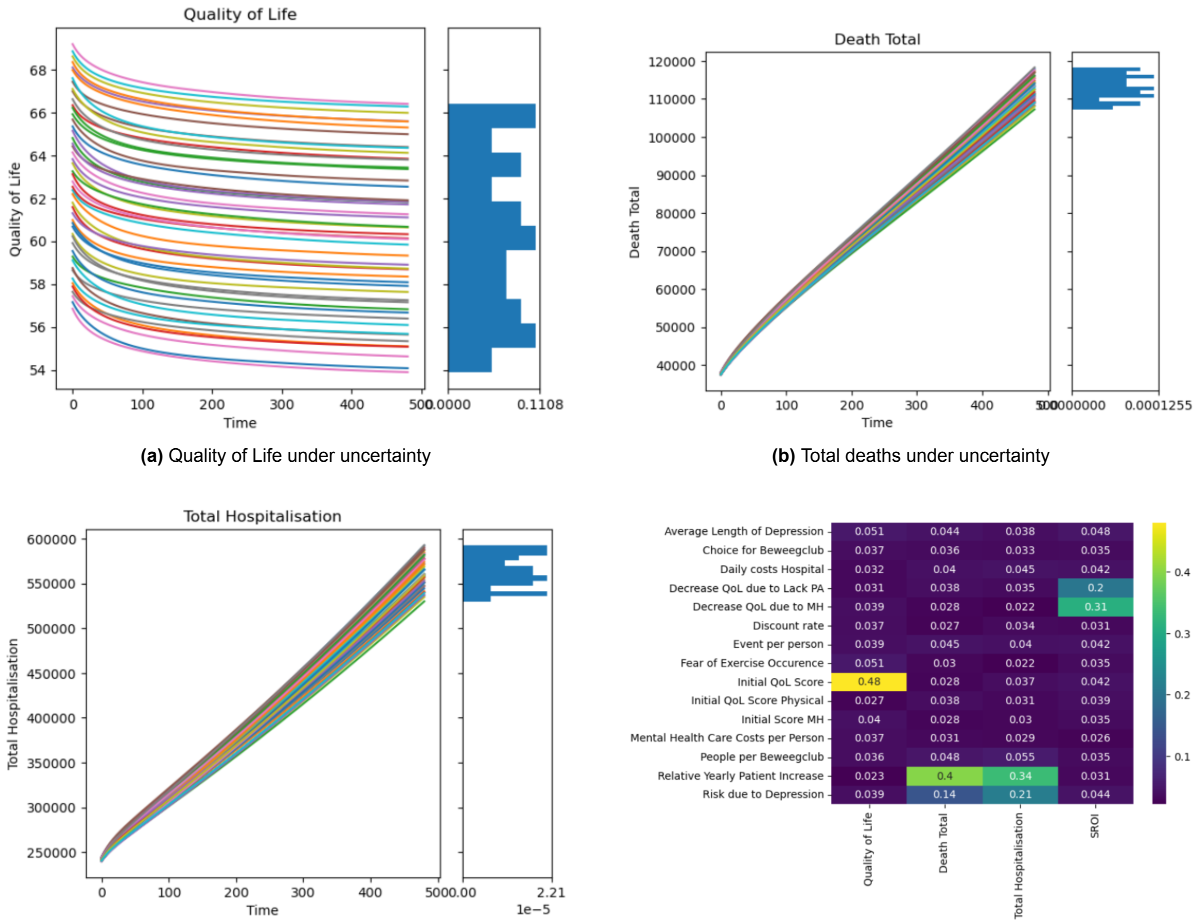


Figure E.18: Scatter plot of the results in the promote autonomy and recovery intervention

E.2.5. Graphs for the Telemedicine Intervention



(a) Quality of Life under uncertainty

(b) Total deaths under uncertainty

(c) Total Hospitalisation under uncertainty

(d) Feature Scoring for all outcome variables

Figure E.19: The graphs for Telemedicine on quality of life, deaths and hospitalisation as well as the factors influencing the results.

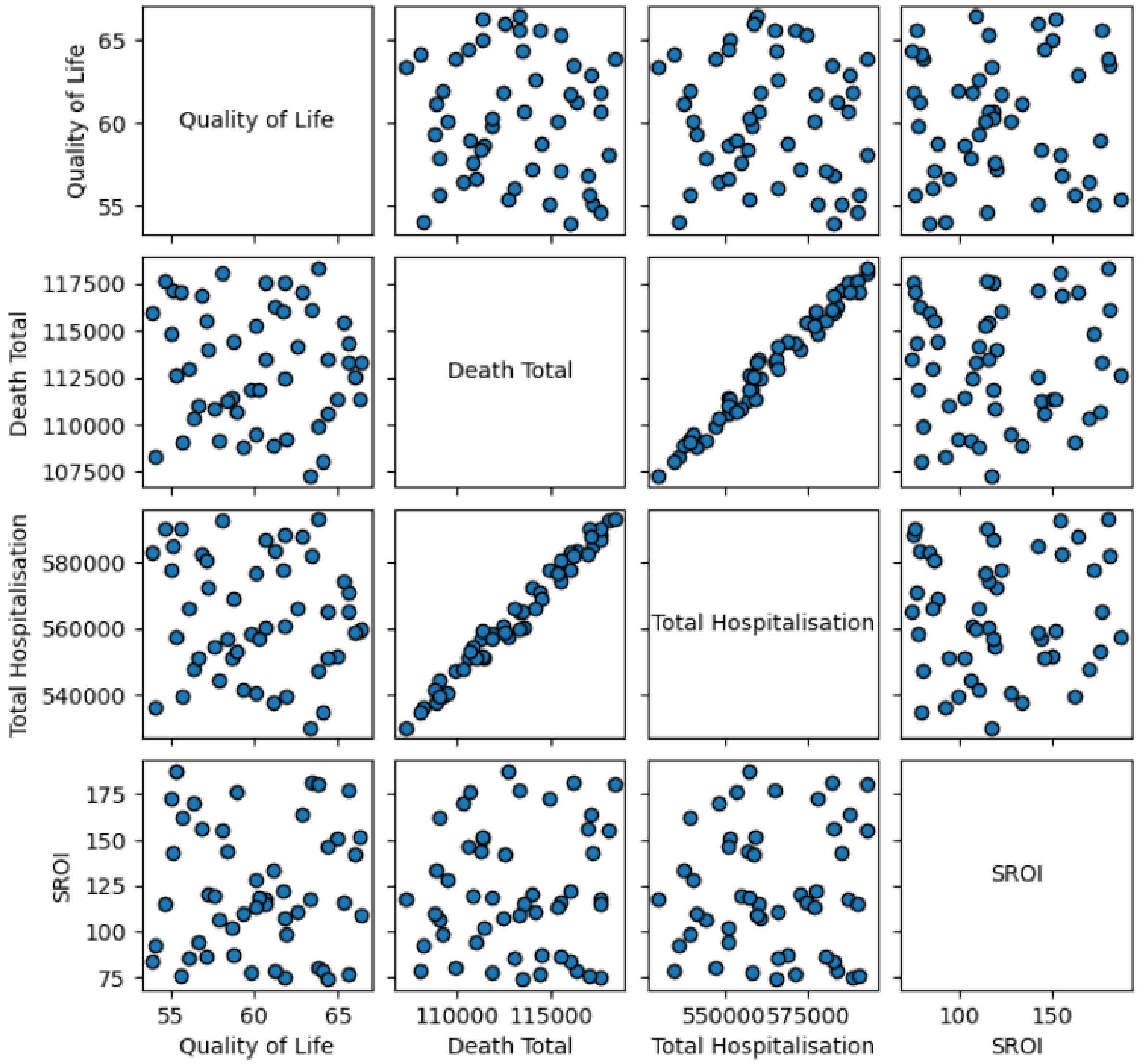
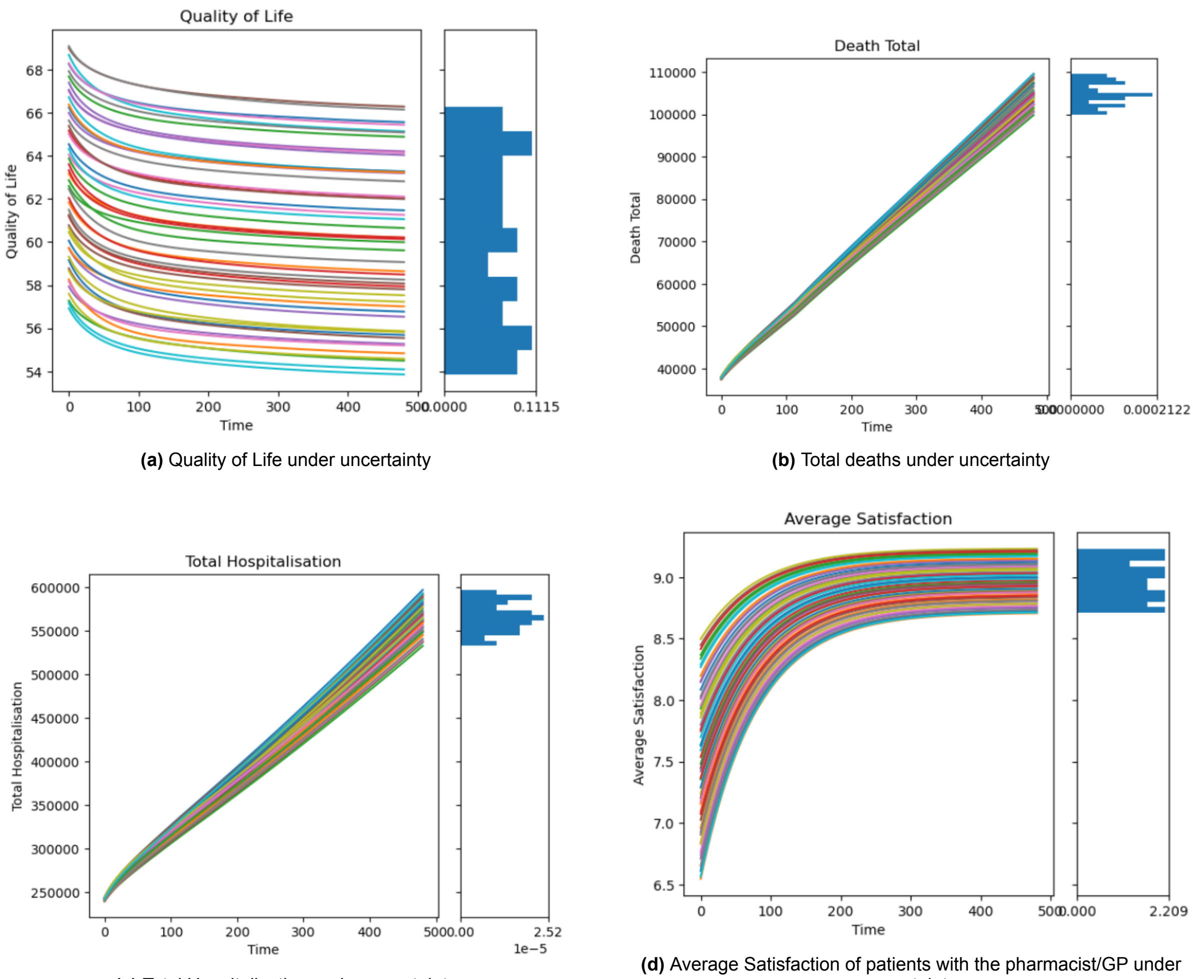


Figure E.20: Scatter plot of the results in the telemedicine

E.3. Graphs for CombiConsult Interventions



(a) Quality of Life under uncertainty

(b) Total deaths under uncertainty

(c) Total Hospitalisation under uncertainty

(d) Average Satisfaction of patients with the pharmacist/GP under uncertainty

Figure E.21: The graphs for CombiConsult on quality of life, deaths and hospitalisation as well as the factors influencing the results.

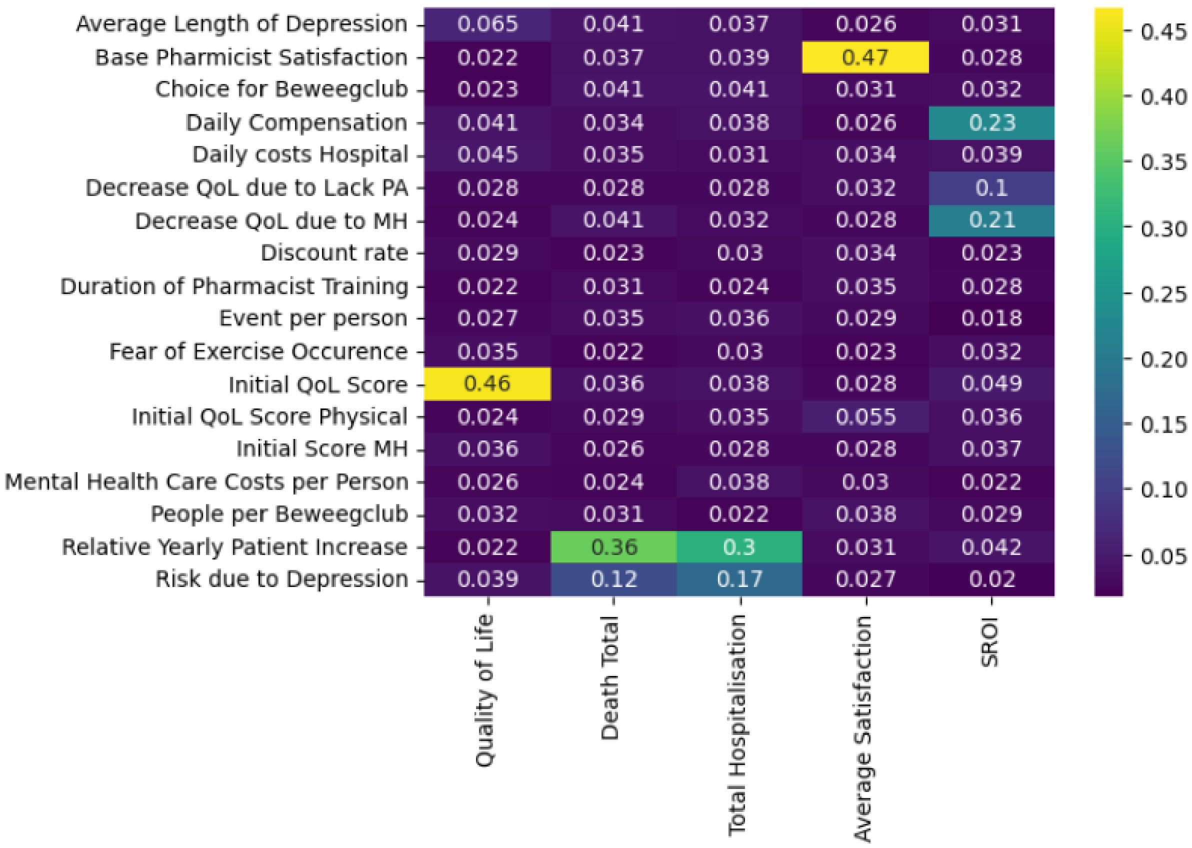


Figure E.22: Feature scoring indicating the relevancy of the uncertainties on the outcome measures for CombiConsult

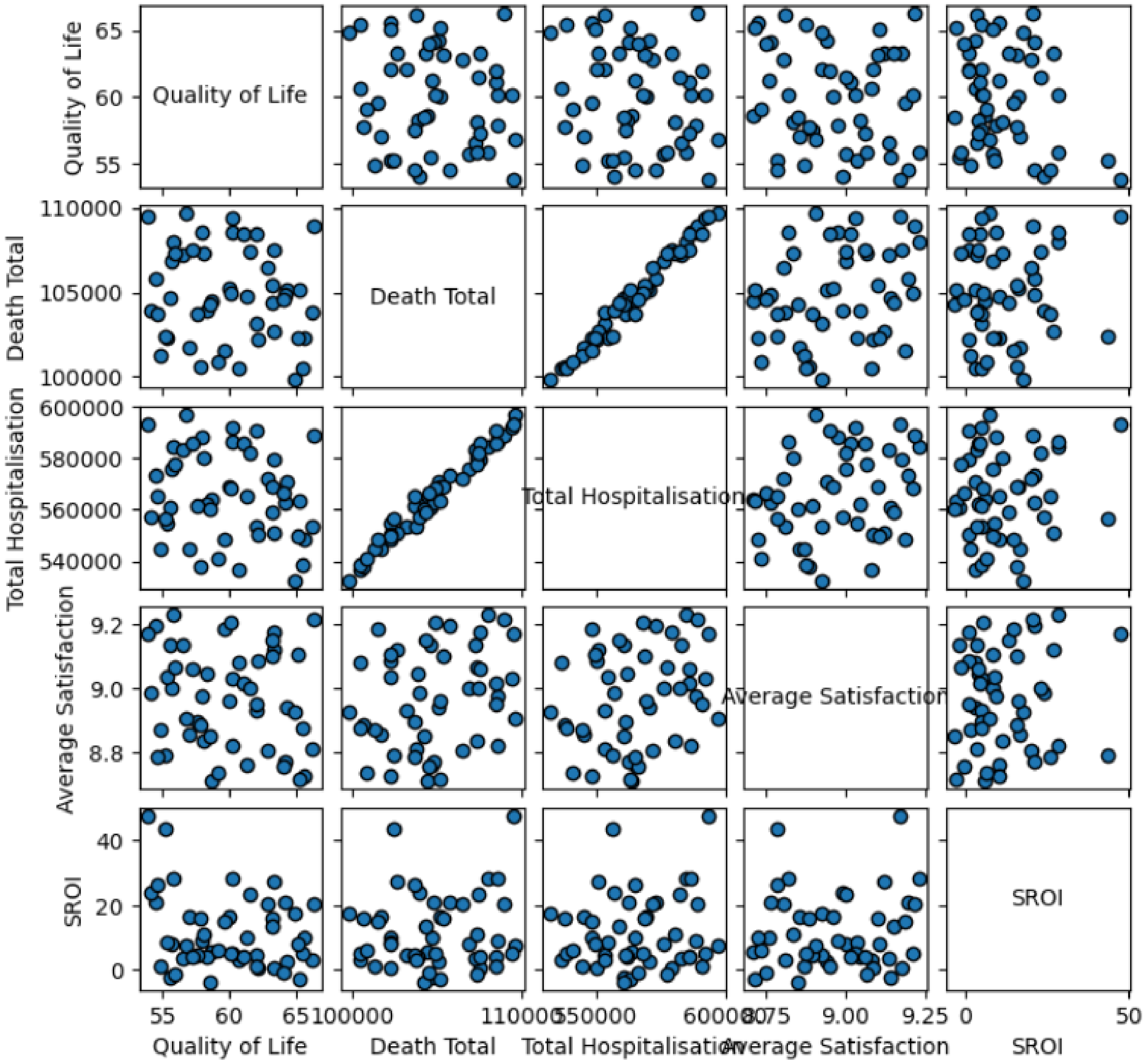


Figure E.23: Scatter plot of the results with CombiConsult