Priority setting in health care and public health

The role of health economics

Linda Ryen

Department of Public Health and Community Medicine Institute of Medicine Sahlgrenska Academy, University of Gothenburg



UNIVERSITY OF GOTHENBURG

Gothenburg 2018

Priority setting in health care and public health © Linda Ryen 2018 linda.ryen@msb.se

ISBN 978-91-7833-087-4 (PRINT) ISBN 978-91-7833-088-1 (PDF) http://hdl.handle.net/2077/56329

Printed in Gothenburg, Sweden 2018 Printed by BrandFactory

I love deadlines. I like the whooshing sound they make as they fly by. Douglas Adams

Priority setting in health care and public health

The role of health economics

Linda Ryen

Department of Public Health and Community Medicine, Institute of Medicine Sahlgrenska Academy at University of Gothenburg, Sweden

ABSTRACT

The aim of this thesis is to analyze the role of health economics for priority setting in health care and public health. Four papers provide the basis for the analysis. Paper I contains an application of a typical cost-effectiveness analysis, where the cost per QALY for an injury prevention strategy is assessed. Paper II reviews and analyzes the literature on estimates of the willingness to pay for a QALY. Paper III describes the burden of injury fatalities both in terms of 'number of fatalities' as well as 'sum of potential years of life lost', to study the priority-setting implications of the different metrics. In paper IV, public preferences for priority setting criteria in health care are explored based on a population survey.

Results show that, despite being cost-saving from the societal perspective, there is a risk that interventions are not being implemented due to lack of incentives when different actors carry costs and enjoy benefits. Reviewing the literature on the willingness to pay for a QALY displays a wide spread of the estimates, indicating that there is not much hope of finding *one* monetary value of a QALY from the current literature to inform a demand-based threshold value in cost-effectiveness analyses. The choice of using life-years lost or fatalities ("lives lost") carries substantial implications for priority setting among injury types and must be carefully considered in evaluations of interventions. Finally, the survey results on public preferences indicate a reluctance to accept any criteria for priority setting, which makes it difficult to assess how the criteria actually used by decision-makers align with the preferences of the payers (i.e. the population).

Keywords: prioritizing, preferences, QALY, cost-benefit analysis, cost-utility analysis, cost-effectiveness analysis, willingness to pay

ISBN 978-91-7833-087-4 (PRINT) ISBN 978-91-7833-088-1 (PDF)

SAMMANFATTNING PÅ SVENSKA

Hälso- och sjukvård liksom folkhälsoarbete är nyttigheter som i Sverige huvudsakligen finansieras med skattemedel. Eftersom medborgarnas behov av och efterfrågan på hälso- och sjukvård är större än vad tillgängliga resurser räcker till, är prioritering en nödvändighet. Att prioritera handlar om att bestämma vilka behov som ska ges företräde och vilka som får stå tillbaka. Hälsoekonomi innebär en tillämpning av nationalekonomisk teori och metod på frågor som rör liv och hälsa. Gemensamt för de metoder som används vid hälsoekonomiska utvärderingar är att de jämför kostnader och konsekvenser av olika alternativ på ett strukturerat sätt.

Den här avhandlingen syftar till att analysera hälsoekonomins roll för prioritering inom hälso- och sjukvård och folkhälsa. Fyra delstudier ligger till grund för analysen. Delstudie 1 innehåller en analys av kostnadseffektiviteten av en skadeförebyggande åtgärd och fungerar som ett typfall för hur hälsoekonomisk utvärdering kan tillämpas som prioriteringsunderlag. Det primära utfallet i studien är kostnaden per vunnet kvalitetsjusterat levnadsår (QALY). Delstudie 2 omfattar en översikt av litteraturen som skattat betalningsviljan för en QALY, vilket kan användas för att avgöra var gränsen för kostnadseffektivitet ska dras. I delstudie 3 beskrivs konsekvenserna av att skifta perspektiv på bördan av dödsfall till följd av skador: är det primära att minimera dödsfall eller förlorade levnadsår? I delstudie 4 undersöks allmänhetens preferenser för olika kriterier som kan ligga till grund för prioritering i sjukvården med hjälp av en enkätundersökning.

Resultaten visar att även om åtgärder är kostnadsbesparande på samhällsnivå, dvs. att de förbättrar hälsan till en lägre kostnad, finns en risk att de inte införs om det är olika aktörer som bär kostnaderna respektive drar nytta av fördelarna. Genomgången av betalningsviljan för ett kvalitetsjusterat levnadsår påvisade en stor spridning av estimaten, vilket tyder på att det inte finns något större hopp att hitta *ett* monetärt värde som skulle kunna användas som gräns för att avgöra vad som är kostnadseffektivt utifrån ett samhällsekonomiskt perspektiv. Att skifta fokus från antalet döda till förlorade levnadsår förändrar den relativa betydelsen av olika skadetyper. Detta är en aspekt att tänka på vid valet av utvärderingsmetodik och utfallsmått. Slutligen indikerar enkätresultaten avseende preferenser för prioritering att det tycks finnas en allmän motvilja mot att överhuvudtaget prioritera inom sjukvården, vilket gör det svårt att avgöra om befolkningens preferenser kring prioriteringar överensstämmer med de faktiska prioriteringsgrunder som används.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

- Ryen, L, Svensson M. Modelling the cost-effectiveness of impact-absorbing flooring in Swedish residential care facilities.
 European Journal of Public Health, 2016; 26: 407–411.
- II. Ryen, L, Svensson M. The willingness to pay for a qualityadjusted life-year. A review of the empirical literature. Health Economics 2015; 24: 1289-1301.
- III. Ryen L, Bonander C, Svensson, M. From loss of life to loss of years. A different view on the burden of injury fatalities in Sweden 1972-2014. Forthcoming in European Journal of Public Health.
- IV. Ryen, L, Jakobsson N, Svensson M. What should guide priority setting in health care? A study of public preferences in Sweden. Manuscript.

Reprints were made with kind permissions of the publishers.

AUTHOR CONTRIBUTIONS

Paper I: Linda Ryen (LR) obtained the data and created the model constituting the basis for the analysis. The manuscript was written in co-operation with main supervisor Mikael Svensson (MS) with LR as the primary author.

Paper II: LR obtained the data and conducted the statistical and econometric analyses. The manuscript was written by LR and MS in co-operation.

Paper III: LR obtained the data, wrote the manuscript, and conceptualized the study with inputs from MS and co-supervisor Carl Bonander (CB). CB conducted the statistical analyses.

Paper IV: Co-supervisor Niklas Jakobsson (NJ) conducted the statistical analyses on the survey data. LR was responsible for writing the manuscript in co-operation with NJ and MS.

CONTENT

ABBREVIATIONSX			
DEFINITIONS IN SHORTXI			
1 INTRODUCTION			
2 AIM			
3 ECONOMIC EVALUATION METHODS			
3.1 Economics and health			
3.2 Different choices, different methods			
3.3 Different methods, different assumptions			
3.3.1 CBA and welfarism			
3.3.2 CEA, CUA and extra-welfarism			
3.3.3 Implications by choice of method 11			
4 VALUING LIFE AND HEALTH			
4.1 Valuing health outcomes in monetary terms			
4.2 Valuing a QALY			
5 PRIORITY SETTING IN SWEDEN AND ABROAD 16			
6 Results			
6.1 Modelling the cost-effectiveness of impact-absorbing flooring			
6.1.1 Methods			
6.1.2 Results			
6.2 Reviewing the willingness to pay for a qaly			
6.2.1 Methods			
6.2.2 Results			
6.3 From loss of life to loss of years			
6.3.1 Methods			
6.3.2 Results			
6.4 Public preferences for priority setting			
6.4.1 Methods			
6.4.2 Results			

7	DISCUSSION	29	
8	CONCLUSIONS	34	
9	FUTURE PERSPECTIVES	35	
Ac	CKNOWLEDGEMENT	36	
Re	References		

ABBREVIATIONS

CBA	cost benefit analysis	
CEA	cost effectiveness analysis	
CUA	cost utility analysis	
ICER	incremental cost effectiveness ratio	
NPV	net present value	
PYLL	potential years of life lost	
RP	revealed preferences	
SP	stated preferences	
VSL	value of statistical life	
WTP	willingness to pay	
WTP-Q	willingness to pay for a QALY	
QALY	quality adjusted life year	

DEFINITIONS IN SHORT

Health care	The organized provision of medical care to individuals or a community [1]. This includes the maintaining, improving or restoring of health by prevention, diagnosis and treatment of diseases, injuries or other physical and mental impairments which are delivered by health professionals [2].
Health economics	The application of economic theory, models and empirical methods to the analysis of decision-making by individuals, health care providers and governments with respect to health and health care [3].
Priority setting	Deciding who gets what at whose expense [4]. In order to control the allocation of scarce resources, it is decided which beneficial treatments are more important than others and which are not important at all [5].
Public health	Public health concerns the protection and improvement of health of people and their communities, including promoting healthy lifestyles, researching disease and injury prevention, and detecting, preventing and responding to infectious diseases [6].

1 INTRODUCTION

People have different and innumerable wants but resources are scarce and have alternative uses. This applies to health care and public health services as well as to standard market goods. For example, we can always imagine an improvement in the number of patient-staff contact hours in long term care, or earlier or more extensive access to new oncology drugs, or a higher number of publicly available defibrillators etc. At the same time, the resources needed to provide these services (nurses, physicians, physical capital, human capital) are in limited supply. This means that available resources will never suffice to cover all needs, and that choices and priority setting is inevitable. Obviously, some of these choices will involve very difficult decisions [7].

As individuals, we are constantly facing choices and setting priorities affecting our own health, but numerous choices need to be made collectively. These social choices are frequently made by politicians or other decision-makers on behalf of the general public, whose risk and well-being as payers and patients are affected by decisions made [8]. In reality, the saying "health above all" does not apply since we clearly choose to satisfy other wants on a daily basis, both as individuals and collectively. For instance, people risk their lives for the sake of pleasure, comfort or thrill [9].

On the most general level, the question is how much resources should be devoted to health care and how much should be allocated to other ends. Resources spent on improving health cannot be used in other sectors and vice versa. This illustrates the core concept of opportunity cost: the cost for using resources is the value of their best alternative use, since this is what we need to sacrifice when deciding to use them to a specific end. No society is as healthy as it could be or wealthy enough to avoid all preventable deaths [10].

Once resource allocation is decided on at a general level, choices remain on how to distribute these resources within the health sector and, given that distribution, decide how they should be used. Many choices ultimately boil down to questions of value. Should diseases and/or injuries be treated or prevented? Which diseases should have priority? Should we go for treatment today or invest in research for finding new cures that might benefit future generations? Do we prioritize elderly or children, men or women, aim at "saving" lives, life years or improving quality of life? Deciding on what services to provide or, often more controversially, not to provide, raise questions about values and principles in society in general and more specifically regarding health and health care. The choices made and priorities set will ultimately affect whose lives are saved, which fatalities are prevented and which diseases are cured or treated.

Since the allocation of scarce resources as to best satisfy human wants is the definition of the basic economic problem, using health economics to aid priority setting in health care and public health follows naturally (at least to economists). Some might however shy away from promoting economic reasoning of costs and consequences as a tool for making choices within areas where decisions, more or less directly, affect mortality and morbidity. On the other hand, costs are reminding us that resources have alternative uses, which implies that decisions and priority setting in health care and public health will always implicitly place monetary estimates on life. From an efficiency and ethical perspective, it must be argued that it is better to provide transparent and systematic input to decision makers considering costs and consequences due to alternative courses of action [11].

Health economics can be used as an aid to make more rational choices and to use resources efficiently, but it cannot deliver the values or ethics to guide difficult decisions. Given the values, health economics can provide useful analytical tools, by recognizing the scarcity of resources and allocating them as efficiently as possible [10].

As will be discussed in the following, there are different forms of economic evaluation methods used in health care and public health. These methods allow for different conclusions in different decision contexts and are also based on different normative assumptions about what we aim to maximize. Hence, policy decisions can be viewed as a combination of analysis and values, implying that methodology as well as preferences are of importance when using health economics to support priority setting in health care and public health.

2 AIM

The overarching aim of this thesis is to analyze the role of health economics for priority setting in health care and public health. Specifically, implications for policy and practice from the normative assumptions made indirectly by methodological choices are analyzed.

To provide a basis for this analysis, paper I starts out with the application of a typical cost-effectiveness analysis (CEA), often performed for interventions or strategies in health care and public health. The following papers relate to the overall aim through questions arising in relation to the application of the typical CEA.

The CEA presents the results in terms of the (incremental) cost per qualityadjusted life year (QALY) gained, which does not in itself say anything about the welfare or efficiency effects of introducing an intervention. In practice, results are compared to threshold values to decide whether they should be introduced. Paper II studies how much society are willing to pay for a QALY, based on a review of the literature on the willingness to pay for a QALY, and discusses the possibilities to use such estimates to judge the welfare effects from interventions.

Depending on methodological choices, either lives or life years gained will be more important. For the analysis in paper I, the number of gained (qualityadjusted) life years is what enters the analysis. In paper III, the differences in interpretation and priority setting that may arise depending on focusing on "saving lives" or "saving life-years" are analyzed. Specifically, the burden of injury fatalities is described both in terms of the commonly used metric 'number of fatalities' as well as the 'sum of potential years of life lost' (PYLL) to study how a change of perspective alters the relative importance of injury types.

By using economic evaluation methods, we strive to allocate resources efficiently, implementing cost-effective treatments and interventions to maximize the value given the resources. There are however other ways to think about priority setting, like fairness or need. The theme for paper IV is to assess the public preferences for priority setting criteria used in health care.

Table 1 contains an overview of the specific aims and methods for each paper.

	Aim	Methods
Paper I : Modelling the cost-effectiveness of impact-absorbing flooring in Swedish residential care facilities.	To examine the conditions under which installing impact- absorbing flooring is cost-effective from a societal perspective.	Application of an incremental cost- effectiveness analysis using a Markov decision model.
Paper II : The willingness to pay for a quality adjusted life year. A review of the empirical literature.	To test the possibilities of finding <i>one</i> monetary value for a quality- adjusted life year to be used in health economic analyses.	After reviewing the published literature estimating the monetary value of quality adjusted life years, descriptive statistics as well as regression analysis are applied to explore the impact of methodological differences on estimates.
Paper III : From loss of life to loss of years. A different view on the burden of injury fatalities in Sweden 1972-2014.	To present the impact of changing the way of describing the burden of injury from number of fatalities to the sum of potential years of life lost.	By combining life-expectancy tables with data on external causes of injury, the number of injury fatalities are converted to a sum of potential years of life lost. Spline regression models are then used to estimate temporal trends in both fatality counts and potential years of life lost.
Paper IV : What should guide priority setting in health care? A study of public preferences in Sweden.	To explore public preferences on age, disease severity and treatment cost as priority setting criteria.	Data from a web survey are analysed using multinomial logistic regression analysis and one-sample proportion tests.

Table 1. Aims	and methods	of the	included papers
10000 1110000	chier hieriteeus	0, 1110	memaca papers

3 ECONOMIC EVALUATION METHODS

3.1 ECONOMICS AND HEALTH

The economic perspective is based on three fundamental ideas: resources are scarce in relation to human wants, available resources have alternative uses and different people want different things. Given that, the economic problem is how to allocate resources in a way that best satisfies wants [10]. Health care and public health interventions are generally not traded on markets, but publicly regulated and/or provided, implying that there are no market forces achieving an optimal (efficient) allocation of resources [9]. Also, health is of particular importance to most of us since good health is a major component of our well-being [5]. Hence, there are reasons to study the allocation of resources both to and within the health sector.

Economics can be divided into positive and normative analyses, which has been described as a dichotomy, i.e. a distinction between two fundamentally different things [12]. Positive economics describes the world as it is and normative economics tells how it ought to be. Determining what *is* is a matter of facts, what *ought to be* will always depend on values and perceptions of right and wrong. Within health economics, the positive branch for instance deals with explaining (describing) individual health behaviour on the basis of micro-economic theory while the normative branch aims at determining whether introducing a certain health policy is welfare-improving [9]. Thus, economic evaluations, i.e. the comparison of costs and consequences of alternative courses of actions, are normative by definition in their prescription of preferred courses of action from an economic perspective.

The line between positive and normative is however not always sharp. The aim of normative economics is not necessarily to state what should be done or which values should be assigned to things but rather to have an analytical function, helping to make clear - describing - what would be the implications of using different values or choosing different strategies [13].

In addition, what appears to be positive (descriptive) analyses, often also include normative components. This relates to paper III, where two different perspectives of presenting the burden of injury are explored; in terms of the mere number of fatalities or by aggregating the sum of potential years of life lost. Both perspectives are positive - describing the state of the world based on facts - but still resulting in different pictures. A normative part enters due to questions arising when comparing these pictures. Should we dedicate resources to reduce the number of fatalities due to falls, since falls cause a high number of fatalities each year? Or should we use resources to reduce the number of suicides or poisonings, injury types causing a greater loss in terms of life years, since those affected on average are younger? This illustrates how values and preferences might affect the health economic evaluation setting: should we aim at saving lives or life years?

3.2 DIFFERENT CHOICES, DIFFERENT METHODS

There are different forms of health economic evaluation methods, sharing a common feature: the comparison of benefits to costs resulting from of a health policy or intervention. The methods are categorized as cost-benefit (CBA) and cost-effectiveness (CEA) analyses [14]. Depending on which type of choice we face, different methods allow us to draw different conclusions, which is illustrated in figure 1. Paper I contains an application of a typical CEA performed on an injury prevention strategy.

This difference between evaluation methods, in terms of what conclusions they allow for, is a rationale for paper II. The search for a monetary value of a quality adjusted year (QALY) also implies searching for a link between CEA to CBA and a possibility to say something about the welfare economic consequences of interventions, i.e. allowing for conclusions about whether resources should be allocated to health or used to achieve other goals.

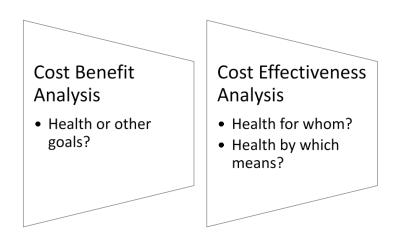


Figure 1. Conceptual illustration of the scope of different health economic evaluation methods

CBA has the potential to say something about whether an intervention is worthwhile from a societal perspective, i.e. be an aid in deciding how to allocate resources between health and other sectors [11].

CEA comes in two forms, depending on whether consequences are expressed in terms of a composite health metric or in natural units. When health consequences (in the most common case) are described in terms of qualityadjusted life years (QALYs), a generic measure combining effects on length of life and quality of life, the CEA is by some authors referred to as cost-utility analysis (CUA) [15]. A CUA results in a cost per QALY gained, making comparisons of different interventions affecting health across different groups of patients or disease areas possible, i.e. allowing for answering the question 'health for whom?'. Although still common in the literature, economists typically do not prefer to use the term CUA since QALYs are not theoretically considered to be proper utilities [11, 16].

When a CEA expresses consequences in natural units, the cost of achieving an effect, like lowering the cholesterol level or the number of hip fractures avoided, is compared between different strategies [14]. This means that only interventions resulting in the same type of effectiveness outcome are compared, allowing the identification of the most cost effective way to achieve a certain result.

The methods share the same basics: 'to identify, measure, value and compare the costs and consequences of the alternatives being considered' [11]. While measuring costs similarly, consequences are dealt with in different ways as summarized in table 2. When performing a CBA, all consequences are translated into monetary units, allowing for comparisons between different areas [14]. CEA and CUA, which are the most commonly used methods within the health care and public health sectors, are mainly useful in setting priorities and making choices within a given budget or by referring to external standards [17]. This will be discussed further in the next section.

easured.			
Method	Costs	Consequences	

Table ? Health economic evaluation methods by costs and consequences

Method	Costs	Consequences
Cost-effectiveness analysis (CEA)	Monetary units	Natural units, the same unit for policies compared.
Cost-utility analysis (CUA)	Monetary units	One or multiple effects (not necessarily the same for policies compared), summarized in a common health measure, typically QALYs.
Cost-benefit analysis (CBA)	Monetary units	One or multiple effects (not necessarily the same for policies compared), translated into monetary units.

3.3 DIFFERENT METHODS, DIFFERENT ASSUMPTIONS

As described in the previous section, there are differences between evaluation methods in terms of in which decision context they are useful and how consequences are measured or valued. These differences are rooted in the normative assumptions underlying the methods, which will be discussed in the following.

3.3.1 CBA AND WELFARISM

CBA is grounded in welfare economic theory, where the key assumptions are that (i) social welfare is a function of the welfare of all individuals and (ii) individuals are the best judges of their own welfare [18]. Based on that, all policies should be judged by how much utility or welfare they generate, since health is only one of many components of people's welfare. The fact that people keep doing things that are not good for their health is seen as proving that focusing only on health is not relevant [9, 10].

The theoretical basis for deciding whether an intervention is increasing social welfare or not is the Pareto principle, stating that social welfare increases if introducing a policy makes at least one person better off and no one worse off [19]. Since that rarely is the case, Hicks and Kaldor reinterpreted the Pareto principle to a more practically applicable statement of potential welfare

improvement [20, 21]. This means that a policy increases social welfare if winners could compensate losers, and still be better off than before introducing the policy [22].

The criterion of potential Pareto improvement forms the basis for CBA, where costs and consequences are measured in monetary units and then compared to evaluate whether benefits exceed costs. Compensation is hypothetical due to an aim of separating the efficiency and equity aspects from each other [23]. This means that finding the most efficient way to achieve something is one problem, and that equity or distributional concerns should be discussed separately.

One major challenge in performing CBA in health care is to convert health outcomes to money. According to welfare economic theory, the value of enhanced health is what those gaining from an intervention would be willing to give away to achieve the benefits, i.e. their (collective) willingness to pay for what is achieved. This willingness to pay resembles the compensation criterion of the potential Pareto improvement [24]. It is important to note that this money-for-health trade-off should focus on decisions under uncertainty [11]. Under scenarios with certainty, individuals might very well demand infinite compensation to avoid loss of life, which would make CBA pointless. Hence, what is valued is the money-for-health risk trade-off implying that values of statistical lives rather than actual lives are used as inputs in CBA.

The fact that CBA measures and values both costs and benefits in monetary terms implies that the decision-rule is relatively straightforward. The net present value (NPV) is the outcome of relevance and is calculated as:

$$NPV = \sum_{t=0}^{T} \delta^{t} \times (Benefits - Costs)_{t}$$

The NPV gives the present value of the difference in benefits and costs of an intervention, compared to some relevant comparator, over the life-time (T) of the intervention. Often, a discount factor ($\delta = 1/(1 + discount rate)$) is also used to adjust benefits and costs that occurs in the future. The potential Pareto-criterion states that if the NPV is positive, the intervention increases social welfare.

The fact that all outcomes are measured in monetary units allows informing allocation decisions. Decision-makers can assess the return on investments in the health sector compared to investments in other sectors of society, thus answering the question 'health or other goals?'.

3.3.2 CEA, CUA AND EXTRA-WELFARISM

CEA, and by definition CUA, is based on the extra-welfarist approach, aiming to maximize health (in terms of the greatest number of QALYs or some other health metric) according to a given resource allocation [25]. Health itself should be maximized, rather than the individual utility to which it may give rise. This means that only consequences related to health are considered and that the focus is on measuring the cost for achieving a particular health state. It also means stepping away from the focus on individual preferences as manifested in welfarism, instead applying a more paternalistic perspective in deciding that health is the most important goal [18].

The QALY concept, which is the most commonly used health outcome in CEA/CUA (and will henceforth be used as a generic illustration of the health outcome in CEA in this thesis), combines effects on life length with effects on quality of life into a single index, thus providing a common currency enabling comparisons across different diseases [15]. The strength of QALYs is that it captures quality and quantity simultaneously, i.e. changes in morbidity as well as mortality [14].

The primary outcome of relevance from a CEA is the incremental costeffectiveness ratio (ICER). In an example where a new treatment is compared to some current treatment, the ICER is calculated as:

$$ICER = \sum_{t=0}^{T} \delta^{t} \times \frac{(Cost_{new \ treatment} - Cost_{current \ treatment})_{t}}{(QALYs_{new \ treatment} - QALYs_{current \ treatment})_{t}}.$$

The ICER is thus the present value of the difference in cost divided by the present value of the difference in QALYs, and can be seen as the "price tag" (cost) per gained QALY with the new treatment compared to the current treatment.

CEA is useful when health-related quality of life is the important outcome or when policies affect both mortality and morbidity, and you need a unit combining these effects [11]. This is the case in paper I, where the installation of impact-absorbing flooring in residential care facilities is evaluated. Hip fractures among the elderly lead to both fatalities as well as pain and suffering, meaning that preventing hip fractures affects both mortality and morbidity.

CEA is also used for comparing policies with different kind of outcomes, where a common unit is needed. The way to decide whether an intervention is worthwhile from a societal perspective is either to choose interventions in ascending order of ICER until the budget is exhausted or to select all interventions with an ICER lower than or equal to a specific threshold value [26]. This closely relates to the theme of paper II, as a social monetary value of a QALY potentially could be considered a threshold value for deciding on which interventions may be defined as cost-effective.

3.3.3 IMPLICATIONS BY CHOICE OF METHOD

The primary difference between the methods is the metric used to estimate (health) consequences – the monetary willingness to pay or QALYs (or something similar to QALYs) [25]. Since both costs and consequences are measured in monetary units in CBA, the decision rule is, as described, relatively simple: adopt all interventions for which the monetary value of the health consequences are greater than the costs (NPV>0).

Because CEA yields estimates of the cost per gained QALY, the decision rule is, as described, somewhat different: adopt all interventions with cost per gained QALY (ICER) below some cut-off (threshold) value [26]. The major practical advantage of CBA is that it directly answers the question of whether or not a policy should be introduced at all [27]. By contrast, CEA takes the budget devoted to health for granted, giving no guidance as to how this budget is set.

But, CBA and CEA differ not only technically and in terms of their decision rules. Above all, they differ in the incorporation of the welfare of those affected. As described in the previous section, CEA focuses on health, CBA focuses on utility. They are thus based on different value judgments.

The welfarist position, underlying CBA, claims that collective decisions should be based on the total utility of the affected persons. The extra-welfarist position underlying CEA, according to which health is the only relevant outcome for particular collective decisions, argues that individual utility is not a relevant basis for collective decision-making. This means, that applying different methods to the same problem might (and does) yield different results [28].

It should be stressed, that neither of the methods addresses distributional concerns or equity in themselves. CBA takes the present distribution of resources for granted and CEA seeks to maximize the number of QALYs from a given budget, ignoring who experiences the increase [9].

More and more CEAs are performed in a wider context than concerning medical technologies and health care, for instance in public health, but also in social care and regarding environmental regulations affecting health, as discussed in paper II. This has its merits, since it allows for comparisons on how health is valued in different sectors - is a QALY gained from treating patients with a disease worth more than a QALY gained from public health interventions aimed at preventing the same disease? However, if the interventions being evaluated can be thought to have broader benefits than just pure health effects, there might be a reason to consider performing a CBA instead, being able to incorporate a wider range of effects.

4 VALUING LIFE AND HEALTH

Decisions affecting life and health are made regularly, not only by individuals but also by parliaments, public authorities and other decision-makers on behalf of the public. This involves balancing the protection and lengthening of human life against the input of scarce resources [9]. These decisions are not only made in health care and public health, but also in other sectors like transportation and the environment. Measures that bring benefits usually come with a cost, and rational decisions cannot be made unless costs and consequences from the specific measures are compared. The fact that such decisions are made, means that implicit values for life and health can be estimated, whether it has been deliberately taken into account or not.

Also, it should be pointed out that both valuing health in monetary terms, as in the case of CBA, and attaching quality weights for health states, as in CEA, are connected with uncertainty and are associated to methodological difficulties in obtaining reliable values.

4.1 VALUING HEALTH OUTCOMES IN MONETARY TERMS

When using CBA, consequences are measured in monetary terms. There are three different approaches that have been or are used to assign monetary values to health outcomes [11]. Those are the human capital approach, revealed preferences (RP) and stated preferences (SP).

The human capital approach, valuing health in terms of production losses, has largely been abandoned for not being compatible to the theoretical foundation of welfare economics because of the narrow view of utility as restricted to impacts on labor productivity [29].

An idea more in line with welfare economics is what those benefitting from an intervention are prepared to pay for it. This collective willingness to pay for health benefits is the monetary value of health focused on in CBA [11]. The value of a statistical life (VSL) is defined as the amount an individual is willing to pay for a specified reduction in the probability of death [30]. The reason for valuing a statistical life is that the outcome metric should measure the uncertain outcome incorporated in health interventions and the monetary value of benefits should indicate the value of this probability reduction.

Since there are no markets for trading changes in the probability of death (or getting ill or injured), there are no market prices available. Thus, monetary values are established through RP or SP studies.

In RP studies, economists try to estimate such values from contexts where individuals are trading off risk for money. One such context is the labor market, where individuals take on riskier jobs while getting a wage premium in return [31]. Another context revealing preferences where risk is traded off for money is consumer behavior in connection to products with differing safety features, like the willingness to pay for safer cars. There are however difficulties in using for instance money-risk trade-offs for estimating the VSL. One problem is that people taking risky jobs or buying a new car do not necessarily perceive the actual risk level objectively, which of course will distort the resulting estimate.

SP studies are based on the creation of hypothetical scenarios that respondents are asked to value. The most common form is contingent valuation studies (CV). Respondents are asked to imagine the contingency of a market for a suggested intervention and then state their maximum willingness to pay for such an intervention [11]. In choice experiments (CE), respondents are instead offered bundles of prices and benefits and are asked to say 'yes' or 'no' to those bundles. Based on repeated choices, this allows for estimating the willingness to pay.

The individuals' average willingness to pay are then aggregated to a whole statistical life and used as a measure of consequences in a CBA. Performing a CV to identify the willingness to pay requires a presentation of risk levels, which implies that the resulting estimate is related to the risk. In turn, this means that a VSL estimate stemming from one risk setting cannot be readily transferred to another setting, with different baseline risks [32].

4.2 VALUING A QALY

A number of metrics have been developed in order to summarize the effects of health interventions [9]. The best known are probably QALYs and disability-adjusted life years (DALYs).

DALYs combine the years of life lost due to disability (premature death) and years of life lived with disability [5]. QALYs combine health-related quality of life and years of life. Hence, QALYs measure health benefits whereas DALYs measure disease burden. Another difference lies in who evaluates quality of life. For DALYs, experts make the assessment whereas QALY values are based on potential or actual patients. As DALYs are mainly used for international comparisons of disease burden and QALYs are the most common metric used in CEA, this section focuses on QALYs.

QALYs provide a common unit for measuring health benefits by incorporating an intervention's effect on both quality and quantity of life [30]. Using a scale where death is assigned 0 and perfect heath is calibrated to the value 1, quality weights are multiplied with the time spent in different health states [9]. Hence, QALYs represent the number of years in full health that is equivalent to a health profile including years of less than full health.

For CBA, the crucial issue is to value health outcomes in monetary terms. For CEA, it is about measuring preferences for different health states and converting them to quality weights. There are three techniques being widely used: the rating scale, standard gamble and time trade off [11]. In a rating scale, respondents are asked to rank health outcomes from the least to the most preferred. This is done on a scale where the intervals between outcomes indicate the size of the difference in preference. For standard gamble, respondents are offered two alternatives. The first alternative is a treatment with two possible outcomes: return to full health living for an additional number (t) of years with a possibility of p or immediate death with a possibility of (1-p). The second alternative is a certain outcome of a chronic state for t additional years. The probability of p is then altered until the respondent is indifferent between the two alternatives, and p defines the preference score. The time trade off technique also offers respondents two alternatives. The first alternative is to live in state 1 for time t followed by death. The second alternative is to be healthy for time x (less than t) and then die. Time x is then altered until the respondent is indifferent between the two alternatives and the preference score is indicated by x/t.

Apart from the difficulty of establishing quality weights capturing differences in health states, there is a need to consider who should be asked to judge the different health states. In most cases, there will be different results if asking a patient population experiencing a certain illness or if asking respondents from the general population to imagine the quality of life in hypothetical health states. Polsky et al. [33] have for instance shown that quality weights based on patient responses were significantly higher than those derived from the general population.

5 PRIORITY SETTING IN SWEDEN AND ABROAD

The general issue behind priority setting discussions in health care is how to balance the demands that demography, technological advances and increased public expectations create within the resources available [34].

Approaches to health care priority setting can be broadly divided into two categories; outlining principles to guide priority setting efforts (e.g. Norway, the Netherlands, Sweden, and Denmark) or establishing expert bodies to recommend what services to provide within the system (e.g. UK, Israel, New Zealand and the state of Oregon) [35].

In Sweden, parliament has decided on guiding principles by establishing an ethical platform [36]. This platform is based on three principles that are explicitly ranked: the human value principle takes precedence over the needand solidarity principle which in turn takes precedence over the cost effectiveness principle:

- (i) The human value principle states that the equal value of all human life should be respected and that people have the same right to receive health care without consideration of their abilities, social status, income, chronological age, ethnicity or else.
- (ii) The need and solidarity principle states that those with the most pressing medical needs should have more of the health care system's resources than other patient groups and that the needs of vulnerable groups and of those who cannot speak for themselves, including children and elderly are to be specifically considered.
- (iii) The cost-effectiveness principle implies that the relationship between cost and health effects should be reasonable from a medical, humanitarian and socioeconomic perspective, allowing more people to be treated within a limited budget.

Health economic research efforts have been devoted to economic evaluation of costs and benefits to provide a basis for ranking health care services in terms of their relative value for money [37]. However, in many countries there is skepticism when it comes to basing priorities on economic criteria, not least due to the political and social context in which priority setting is made (ibid). The sole use of economic criteria for priority setting implies that overall societal health is the only goal when setting priorities but in the publicly financed health care, additional objectives in terms of equity and concerns for severity are of interest as well [38]. The principle of equity is a distinct feature of health systems in Nordic countries and this principle has been one of the main driving forces behind discussions of priority setting [34].

One way to explain the normative basis in health care priority setting is by using theories of distributive justice. Three theories relating to this subject are utilitarianism, egalitarianism and maximin [38]. Whereas utilitarianism reflects the economic reasoning of maximizing health within a given budget, egalitarianism argues for the most equal distribution of resources and the maximin theory states that all solutions should be evaluated from the interest of the least advantaged, i.e. from a health care perspective the interest of those with the most severe conditions.

There is generally a reluctance to put weight on cost-effectiveness [35]. In both Sweden and Denmark, it was specified that cost should only be considered when comparing treatments for the same illness [39]. In Sweden, it is however being discussed whether the cost-effectiveness principle in reality has been given an extended role, allowing for comparisons with threshold values due to changes in the law regulating pharmaceutical reimbursements [40, 41]. Only New Zealand lists cost-effectiveness as a primary consideration [42]. The UK expert body, NICE, explicitly integrates cost in guideline development and technology assessment decisions by considering the overall cost of adding a new treatment to the existing treatments [43].

6 RESULTS

In this section, the methods and main results from each paper are summarized. For more details, the reader is referred to the appended papers and the more general discussion and conclusions are found in section 7 and 8, respectively.

6.1 MODELLING THE COST-EFFECTIVENESS OF IMPACT-ABSORBING FLOORING

Fall-related injuries, especially hip fractures, among elderly cause morbidity, mortality and high costs [44]. As the risk for sustaining fall injuries increases with old age and ill-health, those living in residential care facilities are especially vulnerable. In paper I, a typical CEA using QALYs as an outcome measure, i.e. a CUA as described in section 3.3.2, is performed on the installation of impact-absorbing flooring in Swedish residential care facilities. Compared to standard flooring, impact-absorbing flooring reduces the force transferred to the bone in case of a fall and even small reductions have been shown to decrease the number of fractures [45]. Thus, this is a public health intervention aimed at preventing injuries.

6.1.1 METHODS

The prevention effect considered in the analysis is a decreased probability of suffering hip fractures for those living in facilities with impact-absorbing flooring. However, as the flooring was rather new at the time of the study, the size of this effect was not established. The effect used in the study was thus based on laboratory results on the peak force reduction in combination with results from the use of hip protectors. The analysis was conducted as a modelling study, aiming at exploring the conditions under which the intervention is cost-effective from a societal perspective. Data on costs, probabilities and quality of life measures were retrieved from the published literature and from Swedish register data. A social discount rate of 3 per cent was applied and the time horizon was set to a maximum of 10 years due to the very small probability of someone living in residential care longer than that, given that the average age of entering residential care is 85 years.

A societal perspective was taken, which implies that all costs and effects are considered regardless of who is affected. This further means that consumption and production costs were included and because of the age of the target population for this particular intervention, the implication is that the cost of added life years were taken into account. There is no consensus whether this cost should be included or not [46], and the issue is further discussed in section 7.

To estimate the cost-effectiveness of installing impact-absorbing flooring, an incremental cost-effectiveness analysis was performed, comparing (the more expensive) impact-absorbing flooring to standard flooring in terms of costs and QALYs. This means, that the result is expressed as the incremental cost/effectiveness ratio (ICER), measuring the difference in costs divided by the difference in QALYs resulting from the intervention as shown in the formula below. Hence, the result expresses the change in cost resulting from a change in QALYs due to the intervention, in most cases that is the cost of one additional QALY.

 $(Cost_{impact-absorbing} - Cost_{standard})/(QALY_{impact-absorbing} - QALY_{standard}) = \Delta Cost/\Delta QALY$

To perform the analysis, a Markov cohort model was applied. Markov modelling is suitable when the risk is on-going, as is the case here, since every individual may suffer zero, one or repeated hip fractures over a number of years [7]. A Markov model consists of a finite number of health states depending on the intervention at hand. In this case, three different states are included: 'healthy', 'hip fracture' and 'dead' as shown in figure 2. Every individual included will be in one (and only one) of those states at any given time and, depending on the transition probabilities entered into the model, individuals remain in a state or move to another state.

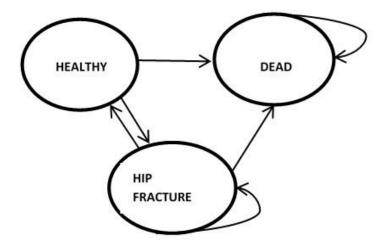


Figure 2. Markov decision diagram.

One cohort enters a care facility with standard flooring and one cohort enters a facility with impact-absorbing flooring. In this case, the cohorts will differ in terms of the probabilities to move between the states, since the risk for suffering a hip fracture is what is affected by the intervention¹.

In each of the states included, for every one-year cycle, QALY estimates (0-1) and cost estimates are assigned, as well as probabilities for moving between states.

After running the base-case model, a probabilistic sensitivity analysis (PSA) by a Monte Carlo simulation was performed. This allows for joint uncertainty in all parameters of the model, which is important since the assumptions made are crucial for the conclusions, and is a generally recommended approach for sensitivity analysis in CEA [47]. Probability distributions are imposed on the parameters included in the model, illustrating the uncertainty attached to them [7]. The Monte Carlo simulation is then performed by repeatedly running the model (in this case, 10,000 times), every time randomly selecting values from the distributions assigned to the parameters, and recording the resulting pairs of costs and effects. These cost-effect pairs are then used to estimate confidence ranges around the results, to illustrate the reliability of the base-case result.

6.1.2 RESULTS

The results indicate that impact-absorbing flooring reduces costs and increases QALYs, i.e. that the intervention, under the base-case assumptions, is "dominant" (cost-saving and improving health). The average incremental saving is SEK 2,786 for 0.02 QALYs. The sensitivity analysis shows that installing impact-absorbing flooring is cost-saving in 60 per cent of the 10,000 iterations made. In another 20 per cent of the iterations, the QALY gain comes with a cost, but it is still cost-effective compared to the threshold value of a QALY commonly used in Sweden, SEK 500,000 [48]. In 15 per cent of the iterations, the ICER is above SEK 500,000 and in the remaining 5 per cent of the iterations it is an inferior strategy, i.e. the cost is higher but there is a loss of QALYs.

One-way sensitivity analysis, i.e. altering one parameter at the time, indicate that the effectiveness of the impact-absorbing flooring needs to go below 25 per cent (to be compared to the 60 per cent effectiveness assumed for the base case) for the ICER to be over SEK 500,000. Also, doubling the assumed cost of the flooring, which could be the result either from higher installation costs

¹ When analyzing some other intervention, the difference might as well be in terms of costs or effects attached to different states.

or due to facilities offering more space per person, yields an ICER of about SEK 250,000. Also, the results show that the intervention is dominant and costsaving both including and excluding the cost of added life years.

Paper I illustrates one of the difficulties commonly attached to performing CEA on public health interventions, i.e. interventions aimed at preventing injuries or illnesses. As previously mentioned, the analysis is performed from a societal perspective and the result should be interpreted from that perspective as well. In the Swedish setting, most residential care facilities are operated at the local level and health care at the regional level. The implication is that the cost of installation is carried by one actor and the benefits from the reduction in hip fracture costs by another. Thus, the local level lacks the financial incentives to install the more expensive flooring.

Evaluating by the CEA framework, aimed at maximizing health, means that non-health effects are not taken into account. In the case of impact-absorbing flooring for instance, it has been suggested that the flooring brings (both positive and negative) effects for the working environment of nurses at the care facilities [49]. Those kinds of effects are not included in paper I.

Further, interventions aimed at fragile elderly people naturally have a low potential for substantial QALY gains since the initial quality of life often is low and the remaining life length is short, even in the absence of hip fractures.

6.2 REVIEWING THE WILLINGNESS TO PAY FOR A QALY

There has been a rapid increase in the use of CEA with QALYs as a health outcome measure, like the one performed in paper I, in the evaluation of medical technologies as well as public health interventions. As described in section 3.3.2, the resulting cost per QALY, i.e. the ICER referred to in section 6.1, can be compared to alternative interventions or to a specified threshold value, thus answering the question 'health for whom?' presented in figure 1. The question 'health or other goals?' can however not be answered unless a monetary value could be assigned to a QALY.

Paper II contains a review of the literature estimating the willingness to pay for a QALY, identifying published estimates as well as exploring the impact of methodological differences on estimates.

6.2.1 METHODS

The review was based on searches in the databases PubMed, Econlit, and Google Scholar using the search terms 'willingness to pay', 'WTP', 'value' and 'monetary value' in combinations with 'QALY', quality-adjusted life year' and 'life year'. In total, 24 papers met the inclusion criteria:

- Original and explicit estimates of the willingness to pay for a QALY (WTP-Q).
- Published in peer-reviewed journals in English.

In those 24 papers, a total of 383 unique estimates were identified. In order to render values comparable across time and countries, all estimates were converted to 2010 Euros.

The main methodological difference lies in whether estimates were based on stated preference (SP) studies or on VSL-conversions, as described in section 4.1. In SP studies, respondents are directly asked to state their willingness to pay for small health increases/QALYs, and their answers are then transformed to estimates on the WTP for a full QALY. For VSL-conversions, the WTP-Q is implicitly derived from VSL estimates by assuming a certain life expectancy and discount rate for the sample on which the VSL was derived.

SP-based estimates were more common, and were used in 21 out of 24 studies. Estimates also differ in terms of whether the QALYs that respondents are asked to value are based on changes in quality of life or on changes in length of life.

Mean, median and trimmed mean were estimated for the total number of estimates and by methodological approach. A logarithmic transformation was then performed to adjust for the highly skewed data. Next, linear regression analysis was applied examining the impact on the estimates from the methodological differences identified in the studies. The factors analyzed were:

- VSL conversions compared to SP studies.
- Estimates based on length of life changes compared to quality of life changes.
- Size of the change in QALY that respondents were asked to value.

6.2.2 RESULTS

The results do not support the existence of *one* societal monetary value of a QALY, due to a wide spread of estimates ranging from less than \notin 1000 to \notin 4,800,000. The mean estimate amounts to \notin 118,839 and the trimmed mean, i.e. disregarding the 2.5 per cent highest and lowest estimates, respectively, amounts to \notin 74,159. The median estimate to \notin 24,226 and about 75 per cent of all estimates are below \notin 75,000.

There are numerous factors to explain the wide range of estimates: studies differ in methodology, preferences are elicited in different ways, differences in the countries studied, whether the perspective taken is social or individual and so on. Several violations of the view that 'a QALY is a QALY is a QALY' are found since the WTP-Q seems to be related to different contextual factors. This is also illustrated by the regression results:

- It turns out that WTP-Q estimates based on VSL conversions are significantly higher than those obtained from SP studies. According to the regressions, a WTP-Q estimate that is based on a VSL conversion will on average be 5.4 to 7.5 times higher than if based on SP studies.
- When looking at SP studies separately, estimates based on changes in life length yield estimates that are 1.4 to 3.5 times higher than estimates based on quality of life changes alone.
- For the cases where the magnitude of the quality of life change is explicitly stated in the article, we find that larger quality of life changes give lower WTP-Q estimates, i.e. scale bias is a problem.

It is however relevant for decision-makers to have an idea about people's preferences for the allocation of resources, which is the information contained in a WTP-based threshold value. If the WTP for a QALY is much higher than what can be afforded within a given budget, or the other way around, there is reason to think about the allocative efficiency of the economy. The fact that it is difficult to achieve a smaller band of values is shared with non-market valuation research in general, for example VSL estimations.

6.3 FROM LOSS OF LIFE TO LOSS OF YEARS

As described in section 3.1, the line between positive and normative analyses is not as sharp as it might seem. The choice of measure to describe a problem will affect how it is perceived in relation to other problems. This may also impact priority-setting and economic evaluations.

The most common way to describe the burden of injury fatalities in a population is by simply counting the number of fatalities [50]. But, as a large share of fatalities occur in older age-groups, it can be argued that the frequency does not fully acknowledge premature mortality as an indicator of the health status of a population [51, 52]. Paper III explores the implications of changing the perspective in describing the burden of injury fatalities in Sweden, from counting the number of fatalities to aggregating the number of potential years of life lost (PYLL) due to injuries. In addition, the trends for both measures in 1972-2014 were studied. This also directly relates to Paper I and II, that focuses on life-years (as part of the QALYs), which is the standard approach in CEA.

6.3.1 METHODS

The sum of PYLL is defined as the sum of life years lost due to premature fatalities from a particular cause in a given population [52]. As each year lost is given weight, the implication is that fatalities at young years are valued higher than those occurring at old age. There are large differences between injury types in terms of the age of the fatalities. In 2014, the average fall fatality lost approximately 9 life years while the average poisoning fatality lost 40 years.

To calculate the sum of PYLL, it is necessary to estimate the average time a person would have lived if the injury had not happened. Here, the remaining life expectancy at time of death is used and data is collected from age- and sex specific life tables. In combination with injury fatality statistics, the number of fatalities is converted to a sum of PYLL, using the below formula, where i=age at death, d= number of deaths at age i and L_i =life expectancy at age i.

$$\sum_{i=0}^{\infty} d_i(L_i)$$

Cause- and group specific spline regression models are then fit to the data in order to estimate temporal trends in both the number of fatalities and the sum of PYLL for 1972-2014. The fitted values from the regression models are used in all calculations to minimize the impact of for example outlier events.

6.3.2 RESULTS

The overall trends for the number of fatalities and the sum of PYLL are similar in the time period 1972-2014. There is a steady reduction from the early 1970's to around the year 2000. Since then, both the number of fatalities and sum of PYLL increase.

When comparing the number of fatalities to the sum of PYLL, there are some results that deserve to be highlighted:

- The number of fatalities due to suicides, unknown intent and poisonings are increasing whereas other external causes are decreasing. This trend is strongly enhanced when studying the sum of PYLL, indicating that relatively young people are the victims.
- For both poisonings and suicide, the share of PYLL is larger than the share of fatalities, which implies that other factors are the driving force behind the increase rather than an aging population.

The results indicate an on-going transition from technical to social injury risks, bringing forward new challenges for injury prevention, as behavioural risk factors have been shown to be more difficult to handle [53].

If it is possible to prevent injury fatalities among young people, i.e. where there is a great loss in terms of potential life years, efficient interventions have a greater potential to be cost-effective in terms of cost per QALY compared to interventions aimed at preventing injuries among older people. However, no matter how great the burden of injury from fatalities, there is no escaping the necessity to find interventions that really works.

6.4 PUBLIC PREFERENCES FOR PRIORITY SETTING

Priority setting is to decide who gets what at whose expense [4]. From an economic point of view, *whose expense* relates to the opportunity cost, implying that priority setting concerns who will not get health care in order for others to have it. In a publicly financed health system, *whose expense* from a financial point of view is the public sector, in other words the tax payers, i.e. all of us. Thus, it is reasonable to argue that the criteria used for setting priorities should be in line with public preferences.

In paper IV, public preferences on priority setting criteria are explored by a web survey in the general population in Sweden. Respondents are asked about their views on age, treatment costs and disease severity as criteria for setting priorities in healthcare.

6.4.1 METHODS

In 2014, a web survey was conducted asking respondents to take a stand on statements related to priority setting in health care. The data collection was performed using a web panel among Swedish residents aged 18 years and older. In total, 1,160 respondents answered all of the questions included in this study. Respondents were asked to state which claim (out of three) was closest to their own opinion of how a health care budget should be distributed. In all domains, supporting statement 1 corresponded to agreeing that age, disease severity or treatment cost are valid for setting priorities. The statements are shown in table 3.

Which claim is closest to your opinion on how a health budget should be allocated?		
Age	Disease severity	Treatment cost
<u>Statement 1</u> : Among patients who are equally ill, younger age groups should have priority over older age groups, since those who are younger can be supposed to benefit from the treatment over a longer period.	<u>Statement 1</u> : Treatment for mild diseases should have lower priority than treatments for severe diseases even if the health enhancements are of equal size.	<u>Statement 1</u> : Among patients who are equally ill, those who can be treated at low cost should have priority over those who can be treated at high cost, allowing more people to be treated when resources are limited.
<u>Statement 2</u> : Priority among patients should not depend on age.	<u>Statement 2</u> : Priority among patients should not depend on disease severity.	<u>Statement 2</u> : Priority among patients should not depend on the cost of treatment, although this might mean that fewer patients can be treated.
Statement 3: Priority among patients should not depend on age, unless the remaining life span of older patients is very short.	<u>Statement 3</u> : Priority among patients should not depend on disease severity, with exception for very mild diseases, which should be given lower priority.	<u>Statement 3</u> : Priority among patients should not depend on the cost of treatment, unless the cost is extremely high.

Table 3. Priority setting statements for respondents

Descriptive summary statistics show that the sample corresponds well to the Swedish population in terms of sex and age, but has a higher share of persons with university education and a higher net of tax household income. Those differences are not uncommon when using web panels [54].

When analysing the collected data, one-sample tests of proportions were conducted to test if there was a majority support for the suggested priority setting criteria (statement 1). Secondly, those showing weak support (statement 3) were added and a new one-sample test of proportions was performed. Thirdly, the association between individual characteristics like age, sex, level of education, and priority setting preferences are analysed by using multinomial logistic regression analysis. This regression analysis methodology is suitable when the dependent variable is categorical with more than two levels, which was the case here [55].

6.4.2 RESULTS

The distribution of answers to the priority setting questions are presented in figure 3. A higher share of respondents think that younger individuals should not have priority over older ones than the other way around, but a majority are prepared to make exceptions if the remaining lifespan for the older person is very short. Less than one out of five respondents agree that disease severity should guide priority setting in health care. About 50 per cent of respondents do however state that severity could be considered if very mild diseases are considered. When it comes to treatment costs, 13 per cent agrees that treatment costs are valid to use as a priority setting criterion while 41 per cent reject that.

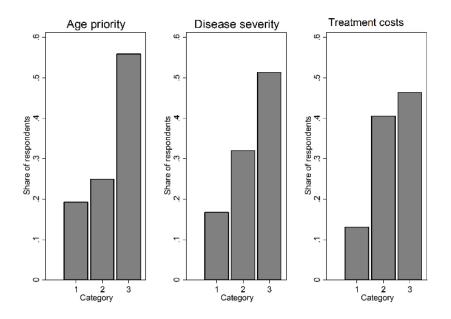


Figure 3. Distribution of answers to the prioritizing questions. Categories 1-3 corresponds to statements 1-3 in table 2.

The results signal a reluctance to priority setting in health care in general, and even more so to economic reasoning. It is a limitation of the study that respondents were not required to take a stand on how to actually set priorities in health care and there is a clear tendency to go for statement 3, which is less categorical than statement 1 or 2. However, denying the need for making choices is not an option for decision-makers and there seems to be a need to be more transparent about the grim reality of priority setting. Further, as preferences are divergent, there will always be a need for balancing and compromising different interests among groups. As also pointed out by Mason et al., there seems to be no set of preferences shared by majorities in populations [56].

It also turns out, that some individual characteristics are clearly related to priority setting preferences. There are indications of self-interest, which is not surprising, but highlights that there will be trade-offs in priority setting when balancing the interests of different groups in the population.

- Women are less likely than men to agree that treatment costs are relevant, to give priority to the young or to treatment of severe diseases.
- Those above 65 years of age are less likely than others to give priority to the young and more likely to state that disease severity should not be considered when setting priorities.
- Those younger than 45 years of age are more likely to give priority to the young and to severe diseases.

7 DISCUSSION

To recall: the overall aim of this thesis is to look further into the role of health economics for priority setting in health care and public health. First, some differences regarding the use of health economics for health care and public health are discussed, illustrated by paper I. Next, the issues concerning the appropriate threshold value for CEA results, the impact of valuing lives or life years and the public preferences for priority setting in health care are addressed.

First, it might be useful to consider the differences between the health care and public health sectors when using health economic methods. As health promotion and prevention efforts compete with health care in the allocation of resources, this is an important distinction to address. In health care, people who are ill or injured get treated while public health policies are concerned with preventing people from getting ill or injured in the first place. In other words, public health interventions aim at non-events and resources are invested to gain (more or less) uncertain future benefits among (more or less) unidentified individuals [57].

Health care interventions are often more specific in terms of the expected outcome: health gain is the one and only effect aimed for and this will be captured by QALYs or equivalent metrics. This corresponds to the extra-welfarist approach underlying CEA. For some public health interventions, this works fine as well and CEA is increasingly being used in wider contexts than medical technologies and health care. But in many cases, public health interventions can be expected to bring a range of outcomes, including non-health effects that might be realised in a rather distant future compared to most health care procedures [57]. These effects might be difficult to incorporate in the QALY metric, meaning that the extra-welfarist approach might not be suitable since all effects are not included. In those cases, the welfarist approach, using CBA, would offer the possibility to capture and include the non-health effects. Evaluating by the CEA framework, aimed at maximizing health, means that non-health effects are not taken into account.

CBA is often used for evaluating environmental and transport policies whereas CEA/CUA dominates in the health sector [58]. A literature review by Buchanan and Wordsworth indicates that applying both methods to same problem in many cases leads to different recommendations [28]. This means that awareness of the implications by choice of methodology is recommended.

A wider use of the same methodology would allow for studying the allocation of resources by comparing how much we are prepared to pay for a QALY gained within different sectors. This could be interpreted as an indicator of the allocative efficiency of the economy. Would resources used to prevent road traffic fatalities and injuries save more lives if used in suicide prevention?

In paper I, installing impact-flooring is a public health intervention where the outcome is captured in the QALY metric: decreasing the number of hip fractures leads to decreases in mortality and morbidity. However, even in that case, non-health effects can be imagined. It has been suggested that the flooring brings (both positive and negative) effects for the working environment of nurses at the care facilities [49].

Economic research with clear results do not always translate into policy [10]. This is not necessarily a problem - evaluation outcomes are not substitutes for decisions, but rather a way to describe costs and consequences of alternative actions which should be considered alongside with values in terms of for example equity. Thus, there can be distributional or normative reasons why cost-effective policies are considered inappropriate. The results in paper I do however highlight another issue in relation to that. Even though the intervention was likely to be cost-saving on the societal level, i.e. QALYs are gained at a decreased cost, the cost-savings mainly occur in the health care sector while the investment costs occur in the long-term care sector (municipalities). This may of course reduce the likelihood of the intervention being implemented.

Due to how health care and long term care are organized in Sweden, this is probably a common situation when it comes to interventions benefiting frail elderly people. This is a dilemma that deserves more thorough consideration. Similar situations can arise when it comes to public health interventions that are financed by actors outside the health care sector but aiming at effects in particular benefiting the health care sector. This could be the case for actors within sectors such as school and social services that do not have health as their main objective.

When performing a CBA, willingness to pay estimates for health outcomes are used to value benefits in monetary units in order to judge whether an intervention is worthwhile from the societal perspective [11]. When performing a CEA, knowledge about the appropriate threshold value would allow for conclusions about which interventions could be considered to increase social welfare.

The results in paper I indicated that installing impact-absorbing flooring was cost-saving, thus implying that the intervention would increase welfare: there would be more health for less resources used. Acknowledging the uncertainty of the assumptions, the cost-saving properties remained for 60 per cent of the cases whereas another 20 per cent of the cases were below the threshold value of SEK 500,000 commonly referred to in Sweden [59]. According to that, there was a high possibility that installing the flooring is welfare enhancing. But do we know that SEK 500,000 is the appropriate threshold value?

The review results in paper II did not support the existence of *one* social value of a QALY. Instead, a wide spread of estimates were found. The result further implied that estimates obtained from quality of life improvements might not be suitable when evaluating policies affecting life length and vice versa. At the time of the review, there was a lack of studies combining quality of life and length of life changes, which is the relevant case in paper II and in many other cases as well. Also, as all estimates in the review were based on hypothetical settings, revealed preference studies might be of importance in this field of research. Besides from the possibility to identify an appropriate threshold level, identifying the willingness to pay for a QALY would be a help to judge whether too much or too little resources are allocated to health, thus helping to answer the question 'health or other goals'.

As described in paper III, every premature death can be considered a social and economic loss to society. When counting the number of fatalities, the loss to society is considered to be of the same size for each fatality. However, every fall fatality in Sweden 2014 resulted in a loss of on average 9 years, whereas the average road traffic fatality lost 32 years and the average poisoning fatality lost 40 years. As some studies indicate preferences for saving younger lives [8], estimating the number of life years lost due to injuries is one way to acknowledge that preference. There is no ideal way to measure the burden of injury, but it seems wise to combine several measures to provide different perspectives [50].

The different perspectives, loss of life and loss of years, also relates to the choice of methodology in health economic evaluations. In CEA, the number of life years saved is part of the QALY metric. This means that interventions preventing fatalities among young persons will be more cost-effective than interventions preventing fatalities among older persons, all other things equal, unless VSL estimates for specific risk settings are established and used. In the case of paper I, those living in residential care rarely live more than a few years even in the absence of hip fractures. Using the VSL estimate from the transportation sector will thus assign very high values to the years gained. The results in paper III show that there are quite large differences in age profiles of

those affected by different injury types. CEA will be more appropriate for evaluation with regard to incorporating those differences, as long as risk-specific VSL estimates are not available.

Two central ideas in priority setting with respect to health are benefit maximisation and fairness [5]. Benefit maximization requires measurement of benefits (for instance, QALYs or in monetary terms) and the use of economic evaluation methods like CBA or CEA to identify the most efficient way to allocate resources. It might be useful to think about fairness as a constraint on the maximisation of benefits. However, there is no generally accepted definition of fairness and what is considered fair depends on the values and preferences in the population. For instance, is it fairer to give everyone an equal share of resources available or to aim at equal outcomes?

Many people are uncomfortable with the idea of setting priorities regarding health, which is indicated in paper IV and in other studies [60]. But whatever we might feel about it, the fact is that resources are scarce and that some kind of rationing or priority setting will take place anyhow. In order to gain acceptance for priority setting and rationing in health care, the criteria used need to be in line with public preferences [61]. If there is a general reluctance to priority setting in health care, as indicated in paper IV, this can make it more difficult to identify true preferences for priority setting criteria. In an open discussion of these issues, however, the implications of priority setting need to be faced: if there are diseases or patient groups with high priority there will inevitably be others with low priority. Paper IV further indicated that costs are not considered to be a valid priority setting criteria. Ironically, the fact that resources are scarce does however imply that this avoidance of cost considerations might be increasingly difficult to retain in practice.

However, one limitation in paper IV was that respondents were not obliged to take a stand on how to actually set priorities. Respondents were allowed to disagree with all criteria without stating an alternative. Qualitative studies making trade-offs more explicit might be one way to explore preferences more thoroughly. A recent study on preferences for health care priority setting in nine countries (including Sweden) indicated that multiple factors need to be considered in order to reflect population preferences, and that differences seem to be country-specific [56]. This means that studies might not be directly transferable between countries.

One question, related to paper I, concerns whether the so-called *cost of added life years* should be included when evaluating interventions. Cost of added life years is the net cost (production minus consumption) for people living longer due to the intervention at hand. The implication is, that when saving

individuals beyond their productive years, there is an extra cost arising. This is true from a purely economic perspective, but of course a much more delicate question from a normative perspective. What standpoint you take might depend on what role you consider economic evaluations to have. If you think they tell you exactly what should be done, including the cost of added life years probably appears ethically doubtful. On the other hand, considering economic evaluations as one of many bases for decision, it would be odd not to clearly report all economic consequences – and apply values judgements separately.

There are sometimes ethical objections to economic reasoning in the health domain. However, one might refer to the sixth section of the Helsinki declaration, since it specifically points out the significance of evaluation [62]. As resources are limited, it is of great importance to use them efficiently. In some cases, health economists could benefit from stressing that performing economic evaluations actually is in line with the Helsinki declaration. As valuing lives and discussing cost-effectiveness in health care sometimes is considered somewhat hardhearted, it can be useful to highlight that using scarce resources wisely in itself is beneficial for society.

Health economics has multiple possible roles in terms of priority setting in health care and public health. It can be used to describe the need to set priorities and the consequences of priority setting, performing economic evaluations to draw conclusions about what should be done and also, identifying value judgments needed to take a stand on. Economic evaluations are not a substitute for decisions, but rather a way to describe costs and consequences of alternative actions which should be considered together with values in terms of for example equity. Hence, knowledge about preferences is also needed for decision-making.

One important strength of using health economics as an aid in the priority setting process, is the systematic framework and array of concepts available in general economic theory, concepts that are especially relevant to the choices facing policy-makers [10]. Policy depends on analysis and values. Sensitivity to that interaction will make economists more useful contributors to health policy. Given the values, health economics can be a useful analytical tool, by recognizing the scarcity of resources and allocating them as efficiently as possible.

8 CONCLUSIONS

- The mere fact that interventions are cost-effective or even costsaving - from the societal perspective does not mean that they are always implemented. This is especially the case for public health interventions where different actors are carrying costs and enjoying the benefits. The incentive structure would need to be altered to change this condition.
- A high burden, whether in terms of lives or life years lost, does not in itself mean that there are savings waiting to be realized unless there are cost-effective interventions. However, high burdens indicate problems where there might be a potential to find such interventions. Problems causing a great loss of potential years of life further indicate an increased possibility for a lower cost per QALY, due to the fact that a high quantity of life years might be saved.
- Public preferences for priority setting are crucial as resources used by public actors are resources stemming from taxes paid by the public. The results in paper IV do however indicate a reluctance to priority setting which might make it more difficult to find out true preferences for the hard choices involved in priority setting.
- Although the same methods often are applied to both health care and public health measures, there are differences that might affect the choice of methods and comparison of results.

9 FUTURE PERSPECTIVES

There are opportunities for using health economics to improve the allocation of resources to and within the health care and public health sectors. The need for priority setting is increasing because of a growing pressure on the health system, for instance due to demography and technological advances. At the same time, there are indications of a reluctance to priority setting in general and to economic reasoning in specific. Hence, it would be valuable to perform a qualitative study on preferences for priority setting, exploring whether the negative attitudes to economic reasoning is persistent even when inevitable trade-offs are made clearer.

Health economic evaluations can also be used to shed light on the allocative efficiency of the economy. In cases where the same methodology is used, results can be compared to see whether there are differences in what we are prepared to pay for health in within different sectors. If there are significant differences, are those in line with public preferences?

There is also a need to discuss the incentives for performing public health interventions in cases where different actors pay and benefit from interventions that are cost-effective on the societal level. This is especially relevant in the Swedish setting due to the regional organization of health care.

Finally, although not being a health economic issue, the worrying trend in suicides and poisonings, specifically for young men, identified in paper III, needs to be addressed.

ACKNOWLEDGEMENT

I am very grateful for having had the opportunity to combine the writing of this thesis with my regular work at the Swedish Civil Contingencies Agency (MSB). It has been an inspiring and rewarding time, although there never seemed to be enough time to keep up with the 'to-do list'. I would like to express my gratitude to a number of people who have played important roles in making sure that the rewards by far outweighed the challenges.

My main supervisor, **Mikael Svensson**, for excellent support and guidance over the years, from the very beginning to this thesis. Thank you for sharing your expertise and for your persistence in finding a way allowing me to complete this thesis while still working at MSB.

My co-supervisors, **Carl Bonander**, **Niklas Jakobsson** and **Henrik Jaldell**, for constructive criticism, encouragement in moments of need, and for being so generous with your time and expertise.

My former head of unit at MSB, **Thomas Gell**, and my present ones, **Per Sundström** and **Marianne Stålheim**, for being supportive and patient, and for so generously agreeing to let me go ahead with this project.

My highly valued colleagues and friends at the Knowledge Development Unit, for always being encouraging, helpful and supportive. A special thanks to **Colin McIntyre** for kindly, and at very short notice, taking the time to review the English language in the thesis frame.

Last but not least, **Henrik**, **Hanna** and **Ella** for love, patience and the support in finding just the right balance between the necessary time in front of the computer and the complete letting go of work.

REFERENCES

- 1. *Oxford Dictionaries*. 2018; Available from: https://en.oxforddictionaries.com/definition/healthcare.
- 2. *Wikipedia*. 2018; Available from: https://en.wikipedia.org/wiki/Health_care.
- 3. Morris, S., et al., *Principles of economic evaluation in health care*. Economic Analysis in Health Care (2nd ed.). Chichester: John Wiley & Sons, 2012: p. 232-50.
- 4. Williams, A., *Priority setting in public and private health care: a guide through the ideological jungle.* Journal of health economics, 1988. **7**(2): p. 173-183.
- 5. Hirose, I. and G. Bognar, *The ethics of health care rationing: an introduction.* 2014: Routledge.
- 6. *CDC Foundation*. 2018; Available from: <u>https://www.cdcfoundation.org/what-public-health</u>.
- 7. Gray, A.M., et al., *Applied methods of cost-effectiveness analysis in healthcare*. Vol. 3. 2010: OUP Oxford.
- 8. Carlsson, F., D. Daruvala, and H. Jaldell, *Preferences for lives, injuries, and age: A stated preference survey.* Accident Analysis & Prevention, 2010. **42**(6): p. 1814-1821.
- 9. Zweifel, P., F. Breyer, and M. Kifmann, *Health economics*. 2009: Springer Science & Business Media.
- 10. Fuchs, V.R., *Who shall live? Health, economics, and social choice.* 1998: World Scientific.
- 11. Drummond, M.F., et al., *Methods for the economic evaluation of health care programmes*. 2015: Oxford university press.
- 12. Hands, D.W., *The positive-normative dichotomy and economics*. Handbook of the Philosophy of Science, 2012. **13**: p. 219-239.
- 13. Fleurbaey, M., *Economics and economic justice*. 2004.
- Rudmik, L. and M. Drummond, *Health economic evaluation: important principles and methodology*. The Laryngoscope, 2013. 123(6): p. 1341-1347.
- 15. Whitehead, S.J. and S. Ali, *Health outcomes in economic evaluation: the QALY and utilities.* British Medical Bulletin, 2010. **96**(1): p. 5-21.
- 16. Hammitt, J.K., *Admissible utility functions for health, longevity, and wealth: integrating monetary and life-year measures.* Journal of risk and uncertainty, 2013. **47**(3): p. 311-325.
- Johannesson, M. and M.C. Weinstein, On the decision rules of costeffectiveness analysis. Journal of health economics, 1993. 12(4): p. 459-467.

- 18. Birch, S. and C. Donaldson, *Valuing the benefits and costs of health care programmes: where's the 'extra'in extra-welfarism?* Social science & medicine, 2003. **56**(5): p. 1121-1133.
- 19. Johansson, P.-O., *Evaluating health risks: an economic approach*. 1995: Cambridge University Press.
- 20. Hicks, J.R., *The foundations of welfare economics*. The Economic Journal, 1939. **49**(196): p. 696-712.
- 21. Kaldor, N., *Welfare propositions of economics and interpersonal comparisons of utility*. The Economic Journal, 1939: p. 549-552.
- Nash, C., D. Pearce, and J. Stanley, *An evaluation of cost-benefit analysis criteria*. Scottish Journal of Political Economy, 1975. 22(2): p. 121-134.
- Zerbe, R.O., Y. Bauman, and A. Finkle, An aggregate measure for benefit–cost analysis. Ecological Economics, 2006. 58(3): p. 449-461.
- 24. Olsen, J.A. and R.D. Smith, *Theory versus practice: a review of 'willingness-to-pay'in health and health care.* Health economics, 2001. **10**(1): p. 39-52.
- 25. Kenkel, D., *WTP-and QALY-based approaches to valuing health for policy: common ground and disputed territory.* Environmental and Resource Economics, 2006. **34**(3): p. 419-437.
- 26. Weinstein, M. and R. Zeckhauser, *Critical ratios and efficient allocation*. Journal of Public Economics, 1973. **2**(2): p. 147-157.
- 27. Brent, R.J., *Cost-benefit analysis and health care evaluations*. 2004: Edward Elgar Publishing.
- Buchanan, J. and S. Wordsworth, Welfarism Versus Extra-Welfarism: Can the Choice of Economic Evaluation Approach Impact on the Adoption Decisions Recommended by Economic Evaluation Studies? PharmacoEconomics, 2015. 33(6): p. 571-579.
- 29. Mishan, E.J., *Evaluation of life and limb: a theoretical approach*. Journal of Political Economy, 1971. **79**(4): p. 687-705.
- 30. Hurley, J., *An overview of the normative economics of the health sector*. 2000. 55-118.
- 31. Viscusi, W.K., *The value of risks to life and health.* Journal of economic literature, 1993. **31**(4): p. 1912-1946.
- Carlsson, F., D. Daruvala, and H. Jaldell, *Value of statistical life and cause of accident: A choice experiment*. Risk Analysis, 2010. **30**(6): p. 975-986.
- Polsky, D., et al., A comparison of scoring weights for the EuroQol© derived from patients and the general public. Health Economics, 2001. 10(1): p. 27-37.
- 34. Calltorp, J., *Priority setting in health policy in Sweden and a comparison with Norway*. Health Policy, 1999. **50**(1): p. 1-22.

- 35. Sabik, L.M. and R.K. Lie, *Priority setting in health care: Lessons from the experiences of eight countries.* International Journal for equity in health, 2008. **7**(1): p. 4.
- 36. SOU, Vårdens svåra val. Slutbetänkande av prioriteringsutredningen. 1995, Socialdepartementet Stockholm.
- 37. Robinson, R., *Limits to rationality: economics, economists and priority setting.* Health Policy, 1999. **49**(1): p. 13-26.
- 38. Olsen, J.A., *Theories of justice and their implications for priority setting in health care.* Journal of health economics, 1997. **16**(6): p. 625-639.
- 39. *Priorities in health care: ethics, economy, implementation.* 1995: Sweden. Health Care and Medical Priorities Commission
- 40. Sandman, L., et al., *Etiskt problematiskt att begränsa rollen för kostnadseffektivitet*. Läkartidningen, 2018. **118**.
- 41. Carlsson, P. and S. Waldau, *Att välja rättvist: Om prioriteringar i hälso-och sjukvården.* 2013: Studentlitteratur.
- 42. *Core health and disability support services for 1993/94.* Wellington: Core Services Committee (PO Box 5051), 1992.
- 43. Devlin, N. and D. Parkin, *Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis.* Health economics, 2004. **13**(5): p. 437-452.
- 44. Heinrich, S., et al., *Cost of falls in old age: a systematic review*. Osteoporosis international, 2010. **21**(6): p. 891-902.
- 45. Robinovitch, S., et al., *Hip protectors: recommendations for biomechanical testing—an international consensus statement (part I)*. Osteoporosis international, 2009. 20(12): p. 1977-1988.
- 46. Meltzer, D. and M. Johannesson, *Inconsistencies in the*" societal perspective" on costs of the Panel on Cost-Effectiveness in Health and Medicine. Medical Decision Making, 1999. **19**(4): p. 371-377.
- 47. Briggs, A.H., *Handling uncertainty in cost-effectiveness models*. Pharmacoeconomics, 2000. **17**(5): p. 479-500.
- 48. *Hälsoekonomiska utvärderingar. SBU:s handbok, kap 11.* 2017, Statens beredning för medicinsk utvärdering (SBU).
- 49. Gustavsson, J., et al., *Effects of Impact-Absorbing Flooring in Residential Care from the Perspectives of Enrolled Nurses.* Journal of Housing For the Elderly, 2017. **31**(4): p. 367-381.
- 50. Hendrie, D. and T.R. Miller, *Assessing the burden of injuries: competing measures*. Injury control and safety promotion, 2004. **11**(3): p. 193-199.
- 51. Dranger, E. and P. Remington, U YPLL: A Summary Measure of Premature Mortality Used in Measuring the Health of Communities. planning, 1998. **113**: p. 55-61.
- 52. Gardner, J.W. and J.S. Sanborn, *Years of potential life lost (YPLL) what does it measure?* Epidemiology, 1990: p. 322-329.

- 53. Lund, J. and L.E. Aarø, *Accident prevention. Presentation of a model placing emphasis on human, structural and cultural factors.* Safety Science, 2004. **42**(4): p. 271-324.
- 54. Schonlau, M., et al., *Selection bias in web surveys and the use of propensity scores*. Sociological Methods & Research, 2009. **37**(3): p. 291-318.
- 55. Hedeker, D., *A mixed-effects multinomial logistic regression model.* Statistics in medicine, 2003. **22**(9): p. 1433-1446.
- 56. Mason, H., et al., From representing views to representativeness of views: Illustrating a new (Q2S) approach in the context of health care priority setting in nine European countries. Social Science & Medicine, 2016. **166**: p. 205-213.
- 57. *Hälsoekonomi och folkhälsoarbete*. 2011, Sveriges kommuner och landsting.
- 58. Svensson, M. and L. Hultkrantz, A Comparison of Cost-Benefit and Cost-Effectiveness Analysis in Practice: Divergent Policy Practices in Sweden. Nordic Journal of Health Economics, 2017.
- 59. Nationella riktlinjer för sjukdomsförebyggande metoder 2011. Hälsoekonomiskt underlag (Bilaga). 2011, Socialstyrelsen.
- 60. Busse, R., *Priority-setting and rationing in German health care*. Health Policy, 1999. **50**(1): p. 71-90.
- 61. Landwehr, C. and D. Klinnert, *Value congruence in health care priority setting: social values, institutions and decisions in three countries.* Health Economics, Policy and Law, 2015. **10**(2): p. 113-132.
- 62. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. The Journal of the American College of Dentists, 2014. **81**(3): p. 14.