# Health Care Priorities and Severity – An Explorative Study of how to Compare Across Patient Groups

by

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# Abstract

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This thesis looks at health care priorities across patient groups, and compares two interventions for two different patient groups with base in the defined Norwegian priority criteria of severity, effect and cost-effectiveness. The comparison takes base in existing studies, and a methodological "gold standard" is defined to enable a comparison across the groups of heroin abuse and metastatic colorectal cancer. The aim of the thesis is to illustrate how an operationalization of severity can affect priority decisions, and the severity measure of absolute QALY loss (AQL) is compared to the severity measure of relative QALY loss (RQL).

The methadone intervention for heroin abuse proved to be both more effective and more cost-effective than the cancer intervention of bevacizumab, both when considering a societal and a provider perspective. The two severity measures provided opposing results. With AQL, heroin abuse was almost twice as severe as cancer with a loss of 41 QALYs compared 23 QALYs. RQL resulted in a ratio of 0.66 for heroin abuse and 0.96 for cancer, which indicates the opposite conclusion.

The main results rests on undiscounted QALYs. When discounting the QALYs, AQL becomes almost equal for the compared groups, mainly due to the age difference. Since the severity measures are based on the patients' quality-adjusted life expectancy (QALE), a possible gender effect is relevant because women on the average live longer than men. The use of a fixed innings threshold is also depicted as an alternative to QALE. A final choice of severity measure was difficult to make, but some arguments are provided in favour of AQL as this measure has some inbuilt elements that have the ability to reduce a possible ageism critique. In addition, the argument is made that age actually does matter.

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# Chapter 1: Introduction and contextual framework

## 1.1 Introduction

Health care expenditures in the western part of the world have grown significantly for the last decades, both in absolute terms, and as a share of the gross domestic product. Norway is one of the countries in the world that use the most resources on health care services (see Figure 1.1), and in 2009 the estimated GDP share was 9.6 % (OECD 2011).

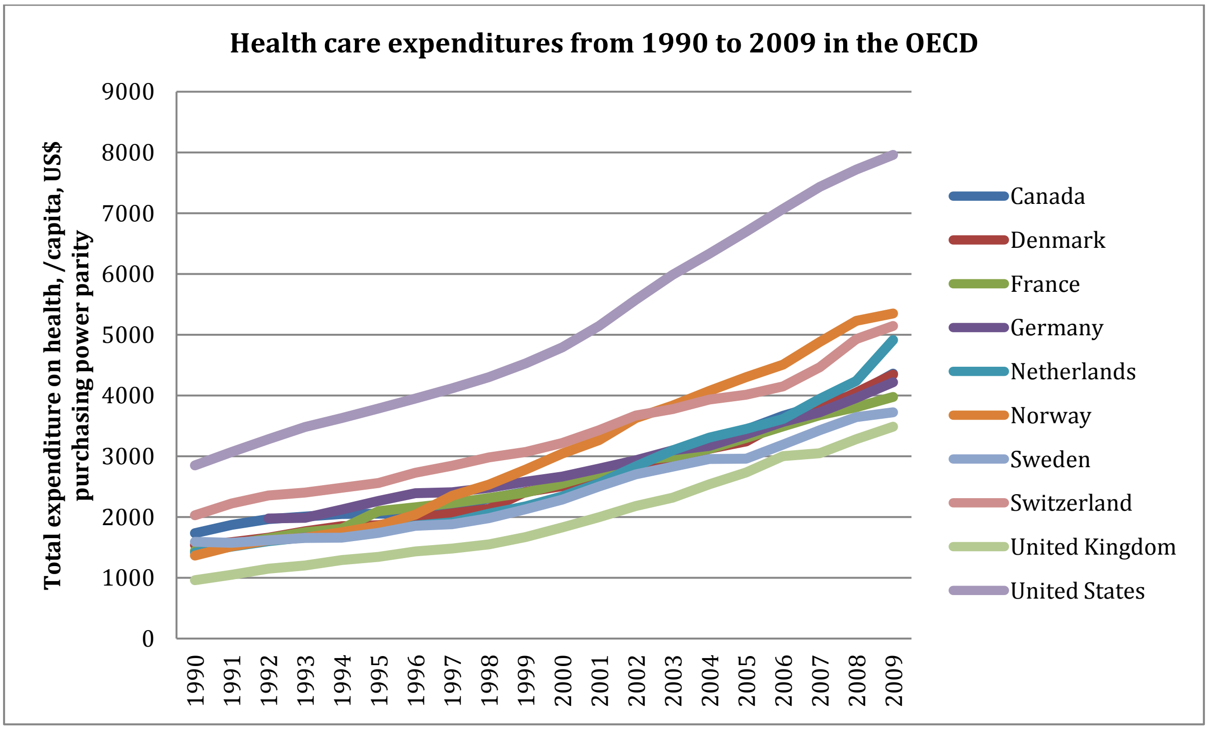


*Figure 1.1: Health care expenditures per capita in some of the OECD countries.*

Despite the wealth in Norway and despite the growth in health care expenditures, the health care sector still has to compete for labour and resources against other sectors (Helsedirektoratet 2012a, p. 8). In addition there remain a lot of unsolved tasks within the health care sector. There are not enough health care personnel or other resources to cover every health care need that exists in society. With an aging population, health care needs are bound to increase in the future, and lifestyle choices challenge the capacity and further fuels the need for health services. In addition there are constant technological improvements and innovations that enhances the supply side of the health care sector, thus pushing the limits of what is achievable. With improving living conditions the demand for quality also grows (Helsedirektoratet 2012, p. 16).

In addition to these expense growths, the market for health services is also has distinguished imperfections. Kenneth Arrow pointed out the “nonmarketability” of the market for health care services, where several characteristics make general market theory and the pricing mechanisms of supply and demand insufficient for describing this specific market (Arrow 1963). The demand for health services is irregular and unpredictable, and there is asymmetric information between the supplier and the consumer. There are barriers to entry as licensing is required, and suppliers (doctors) stand in a unique position with the possibility of inducing demand as the production of the product and the consumption happens simultaneously. There is also significant government intervention and external effects are highly present. These factors give rise to inefficiencies and market failures.

All of these elements characterising the health services, creates the need for rationalization and making priority decisions of which health services that should be offered and which patients that should be treated first. Even if this need for making priority decisions is contested, decisions like these are still made every day in the health care sector. In the context of health care priorities, every decision to treat a patient brings along the consequence of saying no to another patient. Despite this being a harsh reality, avoiding these challenges can lead to arbitrary decisions and increase the risk for not treating first those who are most sick (Helsedirektoratet 2012a, p. 16). Priority decisions within health care are inevitable.

*This thesis deals with priority decisions across patient groups on an overall system level. The aim is to compare two interventions for two different patient groups – heroin abusers and metastatic colorectal cancer patients – in the context of health economic evaluations. The framework for the comparison is the priority criteria defined in Norwegian law and regulation: severity, effect and cost-effectiveness,* *and how these compare across the two groups. Great emphasis will be given to the severity consideration that is suggested operationalized in a newly suggested official guidance. Specific attention will be given to the methodological choices that become relevant when conducting comparisons across patient groups. The following research question is asked: how does an explicit measure of severity compare across patient groups in the context of priority decisions?*

The basis for looking at this research question lies in this recently suggested guidance on economic evaluations in the health care sector. In this document the Norwegian Directorate of Health establishes a methodological framework for how economic analyses should be conducted on an overall system level. The aim of this guidance is to ensure that the economic analyses are uniform and of adequate quality so that they can provide useful information in priority decisions (Helsedirektoratet 2011a). This guidance triggered the choice of topic for this thesis, but there are several other reasons why this is an interesting subject to pursue.

How to make priority decisions *within* specific patient groups has received a lot of attention in the Norwegian health care system. 32 guidelines have been developed to aid decision makers in determining which patients should get prioritized treatment within the specific disciplines (Helsedirektoratet 2011b). When considering decisions made on an overall system level, however, very little research has been done. At the MTV-conference in 2011 on priorities in Norway, Berit Mørland from the Norwegian Knowledge Centre for the Health Services emphasized this. She stated that there are no priority tools for making priority decisions across disciplines, and that horizontal prioritization (priorities made across patient groups as opposed to vertical priorities that are made within disease groups) is still a huge challenge (Mørland 2011). The newly suggested guidance is an important contribution to this challenge.

The notion that there are some major differences between how different patient groups are affected by today's priority practice, poses another important reason for choosing this as a topic. In an article in Aftenposten in 2010, the Director

General of Health Bjørn-Inge Larsen is rather clear in his declaration. He states that the weaker patient groups, like drug addicts, chronic patients or individuals with dementia, suffer with todays implicit decision making regime, and that the stronger groups like cardiac and cancer patients gain on this lack of systematic decision making (Aftenposten 2010). A further statement in the same article from the Director is that implicit and discretionary priority practice leads to the outcome that some groups come out as winners and some groups end up as losers, which deems unfair as all patients have equal rights.

There is also a lack of public debate on the topic of health prioritization (Aftenposten 2010) and a distrust among the public that priority decision “are guided solely by the “bottom line,” not patient welfare” (Daniels 2000). Audacious comments by politicians enhance negative attitudes among the public. The leader of the Progress Party, Siv Jensen, calls statements from the Norwegian Director General of Health of not providing expensive treatments for those who need it, for morally and ethically reprehensible (own translation) (VG 2010). According to Jensen, it puts a price on a human life. Such comment can create the expectation that there are no real economic factors to consider in health, and that more money is the solution to everything, which the Norwegian society apparently has in abundance.

The newly suggested guidance is an attempt to provide aid in the difficult decision processes of health care priorities, but it received a lot of comments and critique from the hearing responses, and has for the time being (May 25$^{th}$ 2012) been withdrawn for further revision. Especially the suggestion of an explicit severity measure received a lot of attention: 14 out of the 30 responses commented explicitly on severity (Helsedirektoratet 2012b). The discussion goes in the direction of how one should define severity, that the different measures have adverse effects, and that a measurement in itself is problematic. One of the critiquing arguments by the pharmaceutical industry was that no real life data was provided on how an explicit severity measure would unfold in an actual priority situation. Only illustrative scenarios were presented, and it is necessary to put such a measure into a real life context to see what possible consequences this can have for the patients (Hearing response Pharmaceutical Industry 2011). The case illustration in this thesis can shed some light on the different outcomes resulting from an operationalization of severity.

Severity is a concept that is difficult to define. When considering a case of progressed cancer against extensive drug addiction, the immediate and intuitive reaction is that a progressed cancer diagnosis is much more severe. Through the discussion in this thesis it is showed that with an operationalization of severity based on a plausible definition, heroin abuse can actually be defined as more sever than cancer. This reasoning rests on the foundation that it is loss of good life years that makes a disease severe, as opposed to immediate death.

## 1.2 The institutional framework in Norway

Norway took a relatively early position in the debate on prioritization in health care. A public commission chaired by professor Inge Lønning (Lønning 1) initially put the priority issues on the agenda in 1985. The commission was set up by the Norwegian government to consider principles and guidelines for how priority decisions should be conducted in the health care sector, and to establish criteria for how scarce resources should be allocated. In 1996 a second commision (Lønning 2) was appointed to revise these guidelines.

The work from the first commission from 1985 resulted in the Norwegian Public Report with the title “Guidelines for priority setting in the Norwegian health care system”(NOU 1987:23). The goals and guidelines of the report took base in ideals and values that have widespread support in the Norwegian society, namely justice, equality and freedom. This lead to the agreement that the focal point should be on those who are considered to be the weakest members of society. The official report made a clear statement that severity was the most important criteria when making priority decisions.

The follow-up commission from 1996 published a new report in 1997 (NOU 1997:18). In addition to severity, they also pointed out the equal importance of the effect of the intervention and its cost-effectiveness. In the report's description of severity, three relevant dimensions are emphasized: prognosis, reduction of physical and mental function status, and disabling pain (NOU 1997: 18, p.14). When considering effect, the intervention has to alleviate at least one of the severity issues, and the cost criteria states that there should be a reasonable relation between cost and effect. These three criteria put together decide whether or not patients have the right to so called "necessary health services" which is defined as the topmost priority group. Four subsequent groups describe lower priority levels.

The discussions resulting from these two reports formed the value foundation for a Patients' Rights Act[1], (today called the Patient and User Rights Act) and the priority regulations[2]. The regulation that gives access to specialized health care, § 2-1, second paragraph, includes the same three criteria defined by Lønning 2 – severity, benefit and costs-effectiveness. The first criteria states that a patient has right to specialized health care when: "The patient has a condition with reduced prognosis related to the life expectancy or quality of life if health care is delayed" (Norheim 2005, p. 645). The priority regulation further explains the meaning of reduced prognosis with regards to quality of life: "..the patients quality of life without treatment is significantly reduced as a result of pain or suffering, problems regarding vital life functions like nutrition intake, or impaired physical or mental function level" (own translation).

The way the law and regulation is articulated leaves a lot of room for interpretation, but some of it is made clearer through the NOU 1997: 18. "A certain prognosis" is defined in the NOU 1997:18: "The risk of death as a result of the disease is more than 5-10 % in the course of five years" (own translation) (NOU 1997: 18, p. 151).  This clearly states that severity is linked to the probability of death due to the disease in question, and consideration of length of life is in this way defined. Quality of life is also further explained in the NOU

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[1] Pasient- og brukerrettighetsloven (1999) Lov om pasient og brukerrettigheter 2. juli 1999 nr. 64.

[2] Regulation from December 1st 2000 nr. 1208, statuated in the Patients' Rights Act § 2-1 seventh subsection.

1997:18 on page 151 with specification of pain or suffering and impaired function level as main elements. Evaluating quality of life is not an easy task and it is an important element to discuss, but this will receive limited attention in this thesis.

The fundamental intention of these reports was to ensure a fair and reasonable set of rules and guidelines for how scarce resources should be allocated in society, both on an overall level and within the same patient groups. In vertical interdisciplinary priority setting maximum individual waiting times for treatment was explicitly defined in 2004, creating the foundation for actually following through the priority regulations (Norheim 2005). By enabling sanctions when maximum waiting times were exceeded, the law gained much more interest, and priority decisions were likely to be taken seriously when there were consequences. An open priority procedure gives patients the opportunity to appeal violations of the law.

## 1.3 The suggested guidance

The suggested guidance: "Economic analyses in the health care sector – a guidance" (own translation), was sent out for a hearing process in the autumn of 2011. The guidance was an attempt at providing a systematic approach for horizontal decision-making across patient groups (Helsedirektoratet 2011a). An important specification is that it is meant for use in overall decisions, and not to be used for isolated treatment decisions. It is meant to contribute to the decisions of what the public health care system should be offering of treatments in the future. To conduct horizontal and overall priority decisions, different patient groups have to be lined up and compared against each other.

As mentioned in the introduction, the guidance' intention is to create a uniform way of conducting economic analyses in the health care sector and to achieve analyses of adequate quality. These are important elements when economic considerations are used in priority decisions, and especially within health care. A consistent element throughout the guidance is that the suggested methods are in accordance with the fundamental values of priority decisions in Norway defined by the two Lønning commissions.

The new guidance goes a long way in establishing specific “rules” for how economic analyses of health care interventions should be conducted. These range all the way from specifying the type of economic analysis down to the specific discount rates. A brief review of the most important elements in the guidance will be provided here. Further theoretical specifications will be given in the next chapter.

The suggested type of analysis is either a cost-utility or a cost-benefit analysis. The cost utility analysis produces the outcome of cost per quality-adjusted life years (QALYs), which is an output measure comparable across patient groups. A cost-benefit analysis converts all variables into monetary terms. QALYs are recommended as a main outcome measure, and benefits of the treatment are the amount of QALYs gained. The cost-effectiveness measure is the incremental cost-utility ratio (ICUR) – additional cost per additional QALY gained. The recommended measure of severity is the absolute loss of QALYs compared to the quality-adjusted life expectancy (QALE) of the specific age and gender group. The guidance also provides some methodological recommendations: the analysis should take a societal perspective, the time horizon should be that of a lifetime, the new intervention should be compared to what is the standard intervention for that disease (not no intervention), future costs should be discounted with a an annual rate of 4 %, and future benefits should be discounted with an annual rate of 2 %. The recommended reference value for a QALY should be 500 000 2005-NOK when evaluating cost-effectiveness.

There are well-established techniques for evaluating an intervention’s clinical effect and the belonging costs of the intervention. The effect can be measured through clinical randomized controlled trials, and costs can be defined and calculated. The third priority criterion of severity, however, is not intuitively something that is measurable. But if severity can be mapped as a specific value, all three criteria – severity, effect and cost-effectiveness, are made explicit. The guidance still emphasizes the importance of providing a description of severity in addition to the explicit measure, and repeatedly it is stated that economic evaluations are only to be used as input in the decision-making process, and are not to receive standalone significance (Helsedirektoratet 2011a, p. 8).

With generalized, explicit decision variables, cross comparisons between patient groups and treatment schemes can be done in an open and assessable manner. Because of the numerous hearing responses critiquing the guidance, the end result is still to be published.

## 1.4 The explicit severity measures

With base in the suggested guidance, the severity measure for the main analysis is defined as the absolute QALY loss (AQL)– the number of quality-adjusted life years an individual is expected to lose when receiving standard treatment. This measure is a direct result of an individual's life expectancy, and with the use of utility weights, the quality adjusted life expectancy (QALE). The guidance also includes the suggestion of a relative severity measure – relative QALY loss (RQL). Here the level of severity is defined as the number of QALYs lost as a share of QALE. Other calculations are also suggested, but these two capture the important differences in how severity can be valued. The severity measures of absolute and relative QALY loss are illustrated in Figure 1.2.

Life years are depicted along the x-axis and utility weights along the y-axis. This framework is also the basis for the QALY-calculations, but this will be explained in more detail later. The QALE-line illustrates the expected health profile of a healthy 30-year old individual. In this diagram the individual is assumed to live until 80 years with reduced life quality from the age of 70. Then this individual gets a disease at $T_0$ = 30, represented by the straight vertical line. If this patient receives the standard treatment, the health profile looks like the innermost bent line. This is called "health profile with standard intervention". Here both length and quality of life is reduced compered to QALE. With a new intervention the individual can move to the middle bent line – "health profile with new

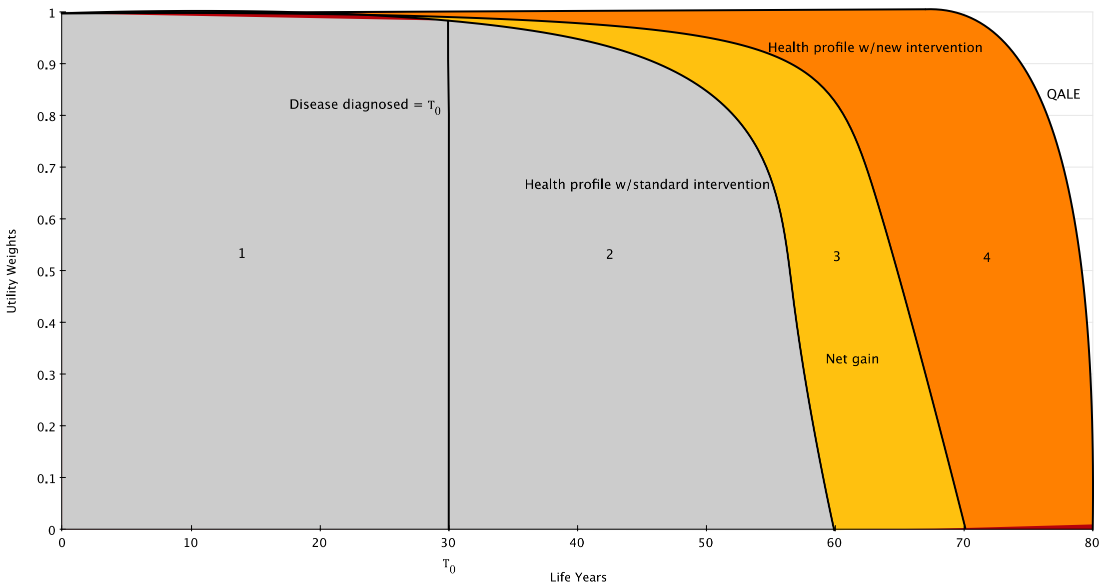


*Figure 1.2: A health profile depicting the two severity measures and the profiles achieved with different interventions.*

intervention". Both length and quality of life is improved compared to the standard intervention. There will most likely also exist an even worse health profile where the individual does not get any treatment at all, but this is not depicted here. The severity measure of absolute QALY loss is displayed in areas 3 and 4. This is, as defined above, the QALE at 30 minus the QALYs achieved with standard intervention. The amount of quality-adjusted life years an individual loses when receiving standard treatment for that disease decides the severity of the disease. The the more QALYs he or she loses, the more severe is the disease. In this illustration the individual loses somewhere above 20 QALYs. The relative severity measure is also depicted in this diagram. This is the absolute QALY loss as a share of QALE at 30. The relative loss of this individual seems to be just below half of what he or she has left – a measure of maybe 0.45. How severe this disease is requires some external definition of severity levels, but this disease can with good reason be defined as severe according to both measures. Relative severity between patient groups further demands that groups are lined up against each other and compared.

## 1.5 The case illustration: Drug abuse vs. cancer

To get across the issue of health care prioritization, it was of some interest to start off with a patient group that might suffer under today's decision-making. The patient group of drug abusers can prove to be a very interesting group, both due to its nature and its history. Drug abusers are a difficult group to offer treatment to, and they often have secondary diagnosis and live poor lives. Up to 2004 this group of clients/patients were mainly the responsibility of the social services. From January 1st 2004 they became the responsibility of the regional health authorities and the specialized health services (Helse- og Omsorgsdepartementet 2006-2007). They went from being clients to patients, and received the same rights as other patient groups. According to professor Helge Waal, drug abusers were provided these patient rights to ensure more openly that they received sufficient health services. In addition to this it was an attempt to reduce judgment among the public by using the concept of illness in describing drug abuse (Bergens Tidende 2010a). The patient group of drug abusers, here under heroin abusers, stands as the main group in the comparison.

If there exists some kind of scale or ranking of the amount of treatment offered to different patient groups, the comparison and the implication of health priorities is made clear by choosing a comparable patient group that is on the high end of this scale. As mentioned in the introduction, cancer seems to be such a patient group. This discipline receives a lot of focus from researchers and has very strong interest groups that promote their rights and need. It is a disease area that gets a lot of media coverage, almost on a daily basis. There is also the statistical factor that many individuals develop cancer in Norway. 27 520 individuals were diagnosed with cancer in 2009 (Cancer Registry of Norway 2011) which is a lot when considering the relative small population of 5 million in Norway. Cancer will pose as the reference group in the comparison.

For the cross comparison to be relevant for the Norwegian setting, an important criterion is that both these patient groups are offered treatment in today's health care system. In economic evaluations it is the interventions that are being evaluated, and not the patient groups themselves. Both drug abusers and cancer patients do have several treatment options in the Norwegian health care system, and are thus suitable when discussing Norwegian health care priorities.

Other groups could easily have been chosen to get across the issue of health care priorities. The idea of choosing drug abuse and cancer rests on an article published in Bergen Tidende where heroin abuser were compared to lung cancer patients in a context of health priorities and productivity considerations (Bergens Tidende 2010b). The CEO of the University Hospital in Bergen, Stener Kvinnsland, has promoted similar comparisons both in this and in other newspaper articles, and states that there is a need for making cross comparisons of this kind (Bergens Tidende 2010c). He points out that it is not the disease itself, but rather the severity of the disease and if the treatment is able to affect the prognosis that should decide where resources should be allocated.

Health economic evaluations will constitute the theoretical foundation for enabling this cross-comparison, together with theory on severity and equity. This will be elaborated upon in the following chapter.

# Chapter 2: Theoretical framework

## 2.1 Health economic evaluations: a framework

A major part of health economics is to enable the measuring of effects and costs of health care interventions. The purpose of such measuring is to establish a foundation for decision-making and to make more rational choices when there are scarce resources.

In considering why economic evaluations are important, three elements are specified by Drummond et al. (2005)[3]. 1) "Without a systematic analysis, it is difficult to identify clearly the relevant alternatives" (Drummond et al. 2005, p. 8). Of course, a complete evaluation of all possible alternative treatments, from preventive and health promoting interventions to surgery, will be a difficult, if not impossible task, but with a more systematic approach a decision is more likely to be a better one, and it allows for thorough scrutiny of the choices made. 2) "The viewpoint in an analysis is important"(Drummond et al. 2005, p.8). The different viewpoints can lead to opposite results, and the specification is thus important when making concluding statements. 3) "Without some attempt at measurement, the uncertainty surrounding orders of magnitude can be critical" (Drummond et al. 2005, p. 9). Every single decision of health care provision comes along with an alterative cost and the fact that resource could be spent elsewhere, maybe even more efficiently.

The effect of a health care intervention is related to the improvement of a health state. This is directly linked to the lengthening of life expectancy and improvement of quality of life. A treatment scheme can also have adverse negative effects such as pain or discomfort, and the end result or effect measure should incorporate all of this. From an economic viewpoint, there is also the cost of the intervention to consider. The cost of a treatment can include those for

[3] The health economic methodology referred to in this thesis rests to a large extent on the contents of this book. Its systematic approach makes it both useful and easy to use, and the orientating towards other sources is extensive throughout the book.

medication, staff time, treatment facilities etc. The cost concept can be expanded to include societal or external costs as well.

In economic evaluations, it is the additional or incremental effect of the treatment that is compared to the incremental cost. This is the appropriate form of evaluation as it is the additional cost-effectiveness ratio that is of interest when evaluating a new intervention (Drummond et al. 2005). In itself, most treatments incur a positive health effect to a certain amount of costs, but with established treatment in place, it is the additional value of the new intervention that is of interest. There are several methods for measuring and evaluating health care interventions, and the specific choice of inputs and outputs can be of highly varying kind.

### Type of analysis

There are three main types of economic analyses that are used for health care evaluations: cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis (Drummond et al. 2005). The main difference between the methods is the output measure. In cost-effectiveness analyses (CEA) the measure of output is a specific single-dimensional measure, like life years, cholesterol level or clean urine samples. Such measures can be informative in its self, but can come to short in cross comparison of different patient groups as the output measure may only be applicable to one of them. The use of life years, however, does not have this limitation. In cost-utility analyses (CUA), the output is a multidimensional measure, the most commonly used being quality adjusted life years (QALYs). This is a measure that incorporates both length and quality of life. Such a measure is generalized and allows for comparison across patient groups. Finally there is the cost-benefit analysis (CBA), which converts the benefit of the treatment into monetary value through for example willingness-to-pay – a valuation technique based on individuals' preferences. This is not without controversy, but it also produces comparable figures across disciplines.

Since the task at hand is to compare interventions for two different patient groups, the most appropriate type of analysis is either a CUA or a CBA, or CEA if life years are used as the output measure.

CBA is the only one of the methods that, on its own, can say if something is actually worthwhile. The output measure of net social benefit is the present value of the difference between the discounted benefits and costs. With a positive output, the intervention is worth its costs – it gives more in return than what you have to pay for it. In this regard, CBA is the only method that can make one-at-a-time conclusions of cost-effectiveness (Drummond et al. 2005). A CUA can never in itself state whether an intervention or a program is cost-effective. This will always have to be in relation to an external criterion of cost-effectiveness like a threshold level or league tables decided upon by decision-makers. CUA are in this respect based on discretionary assessments, and are not evidential.

Despite the convenience of using cost-benefit analyses, there are ethical objections to valuing life and health in monetary terms. "Many decision-makers find this difficult or unethical or do not trust analyses that depend on such valuations" (Weinstein and Fineberg 1980 referred to in Drummond et al. 2005, p. 215). Valuations of human life does not resonate well to many, but it is commonly done in the insurance world and when calculating benefits of political decisions in other sectors than the healthcare sector (e.g. the transport sector). The CUA avoids these difficulties, and may even make the economic evaluation more transparent – every single element is not reduced to one single figure as in CBA.

In the Norwegian context, the Norwegian Official Report from 1997 on cost-benefit analyses state that there is much discussion on whether or not individuals' willingness-to-pay should affect priority decisions in the healthcare sector (NOU 1997:27). WTP is the standard approach of evaluation in CBA, and it is based on subjective utility and how much individuals are willing to give for this utility (Zweifel et al. 2009). The NOU states that it is unclear whether we can achieve WTP for health care interventions in a meaningful way, partly due to the involvement of taking a standpoint based on small probabilities for a health situation to occur. In addition, in a Norwegian setting where health services are mainly covered by the government, individuals are even less accustomed to such considerations. It is also doubtful that individual preferences are equal to the preferences of a society.

The NOU concludes that due to the difficulties in using WTP within the health care sector, cost-effectiveness analysis with QALYs as the output measure emerges as a possible alternative. It also states that it can be difficult to convert health care assessments into monetary terms (NOU 1997: 27, p. 11). Drummond et al. (2005) make no general recommendation on type of analysis, only that each serve their own purpose.

For the purpose of comparing the three priority criteria, and with emphasis on the operationalization severity, the cost-utility analysis using quality-adjusted life years emerges as the most appropriate form. The newly suggested economic guidance also rests on the use of CUA and QALYs. Alternatively cost-effectiveness analyses using life years as the output measure can be used, where own conversion into QALYs will have to be included.

### The need for QALYs

The output measure of quality-adjusted life years take into account both length and quality of life. In the context of health and health care, the phrasing “quality of life” (QoL) should be substituted with the more appropriate phrasing “health related quality of life” (HRQoL). There are a multiple of other elements that affect the quality of life, such as the environment, the surrounding community and working conditions. These are, however, not normally included in the quality evaluation when establishing QALYs. For simplicity “quality of life” will be used as a substitute for the narrower notion of “health related quality of life”.

QALYs are the most commonly used health measure, and it allows for disease burdens to be compared across diagnosis. The use of QALYs as a measure of health benefit has the aim of maximizing health across a population subject to budget constraints (Weinstein et al. 2009).

The diverse aspects affecting health and quality of life are the workhorse parameters of the different MAU-instruments – multi attribute utility instruments, which measure utility weights. These instruments consist of two elements: a questionnaire that gives a description of the disease and an element of valuation that establishes the utility weights. There exists several different instruments; EQ-5D, SF-6D, etc., and several valuation techniques. The EQ-5D for example, tracks the five dimensions of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Different instruments and different versions of the same instrument track these and/or other dimensions, and can understandably be more or less suited for different disease areas. No single instrument stands out as the best one amongst researchers and policy makers (KILDE), but even so, they are well established and of frequent use (Universitetet i Oslo 2011).

The different MAU-instruments are disease independent and provide a general consideration of the disease. The embedded valuation techniques can themselves be used to establish utility weights. These are, however, disease specific methods for establishing the weights, and they are often time-consuming techniques. The most common of these methods are time trade-off (TTO), visual analogue scale (VAS) and standard gamble (SG). In all of these methods, individuals are faced with a hypothetical situation and asked to state their preferences (Universitetet i Oslo 2011).

TTO asks the individual how many years he/she is willing to give up to go from a specific disease for T years and then die, to perfect health. If the individual is willing to give up 7 years out of say T = 10 years, he/she prefers to live the remaining 3 (t) years in perfect health. The utility weight is then (t / T) = (3/10) = 0.3. The VAS technique asks the individual to place the value of a disease on a scale, the commonly used scale ranging from 0 to 100, where 0 is the worst and 100 is the best. If the individual places the disease at 70 (h), the utility is equal to 0.70 (h/100). SG is a technique where an individual is presented with two alternatives. One alternative is to do nothing and live with the hypothetical health state. The second alternative gives the individual the opportunity to take a magic pill and become completely healthy, but with a probability of immediate death. SG then asks how high the probability of becoming completely healthy must be for the individual to become indifferent to taking the pill or not. The EQ-5D is valued with TTO, and the SF-6D is valued though SG. The resulting utility weights are used as input when calculating quality adjusted life years.

The QALY concept is a relatively easy concept. One QALY is equal to one life year lived in perfect health. A life year is adjusted with a utility weight, and a year in perfect health has a utility weight of 1. Death has a utility weight equal to 0, and everything in between denotes a health state. To live in a state with utility 0.5 for two years is in QALY terms equal to one year in perfect health: (0.5 x 2) = (1 x 1) = 1 QALY. Even though the concept is easy, it is not without flaw. To try and quantify health benefits in this way is, understandably, critiqued and maybe even ethically wrong as it translates life and health into a single measure.

The first conflicting element to point out is that the different MAU-instruments can lead to different utility weights (Weinstein et al. 2009). Even different version of the same instrument can lead to varying utility weights (Nord 1992). The different methods for posing the questions also have an impact. Such diverging results makes it almost impossible to safely rest on any of the utility weights produced. When the results of a cost-utility analysis are used in priority decisions, this is not without consequence either. The measured health gain will always be a result of the choices made in the analysis.

Secondly there is the element of whom to ask when establishing the utility weights, and the generalization of utility weights. Some suggest to ask the patients themselves, and others suggests asking a representative group in society who could possibly get the disease (Whitehead and Ali 2010). The original valuations of the utility weights of EQ-5D and SF-6D were from randomized populations of 3000 British citizens and 836 British citizens, respectively (Universitetet i Oslo 2011) (SF-6D has also been valued in a few other countries.). To make the preferences of a group of British citizens applicable to everyone else in the world does seem like a bold assumption and a vast simplification. Utility is a subjective matter, and very much so in the case of health and disease burdens. In addition to groups of the population, doctors and scientists have also been used to define the relevant utility weights. When all these sources are used, it is easy to imagine that the validity of the weights is of varying kind. Neither preferences nor demographics are equal across countries, and an overall generalization can deem inappropriate. However, "Differences that might exist from this geographic factor are small compared to the differences that exist among instruments" (Drummond et al. 2005). More concern should be put on the choice of instrument and valuation technique.

In order to equate QALYs with utility, some important and restrictive assumptions are needed. This is important from a decision-theoretic perspective since QALYs are used as input for resource allocation in health care (Zweifel et al. 2009). Firstly, the use of QALYs as utility requires utility independence. That is, the two elements of quality (utility weights) and quantity (life years) must be mutually utility independent (Drummond et al. 2005). Preference for one of them must not depend on the level of the other. Then there has to be risk neutrality with respect to length of life or time. This means that the individual is indifferent between a certain length of life equal to T and the lottery with uncertain length of life equal to the life expectancy T (Zweifel et al. 2009). Finally there is the element of constant proportional trade-off behaviour. Preferences for health states has to be stable over the individual's entire life (Zweifel et al. 2009), and trade-off decisions between quality and quantity have to be independent of age and life years remaining (Drummond et al. 2005). To speak of QALYs as utility, these three theoretical assumptions have to apply.

Another element worth mentioning is that measuring utility requires cardinal preferences as opposed to ordinal preferences. If the preferences were ordinal they would simply have to be ranked in accordance with preferences. Higher rank means more utility compared to an alternative. With utility at a cardinal level, a specific number representing the strength of the preference has to be attached to the utility. In general microeconomics' syllabus, students are taught that cardinal utility is unnecessary, probably immeasurable or may not even exist (Drummond et al. 2005, s. 142). However, the axioms defined by von Neaumann and Morgenstern (NM) have provided the foundation for modern decision theory, and their normative definition of cardinal utility under uncertainty is both widely used and discussed. The calculations of QALYs rest upon these NM-utilities, as well as the restrictive assumption mentioned above.

A final element worth including is the health distribution among the recipients of health care. Distributional considerations are not made through cost-utility analyses and the maximization of QALYs in a population. Such an evaluation approach makes no differentiation of who is gaining in health and who is not – a gain is a gain irrespective of anything else. This is what Culyer refers to as "QALY egalitarianism" (Culyer 1992 referred to in Whitehead and Ali 2010, p. 14). The loss or gain of QALYs is not concerned with factors like health condition, severity of disease, social role of individuals and so on (Whitehead and Ali 2010). Considerations for equity can in this sense be set aside for efficiency considerations. If equity is to receive greater concern, a trade-off between equity and efficiency might be necessary in order to achieve a more equitable distribution. This is where welfare economics enter as a discipline and political decisions ensure that more resources are provided to the weaker societal groups. Efforts are taken to alleviate differences in society, but possibly and most likely at the expense of achieving greater utility gains elsewhere.

Despite these elements of critique, the measuring of health benefits through QALYs is a widely used approach and an internationally accepted method of evaluation. For this reason, and for the purpose of focusing on the task at hand – the potential effect on priority decisions of defining explicit severity measures – no further questioning of this method will be made here.

## 2.2 Severity and the foundation for an explicit measure

Both of the explicit severity measures exemplified in this thesis are founded in well-know theories. The moral concern of severity is anything but a straightforward specification, and diverging definitions compete for a final agreement. The intangibility of actually specifying severity lies in the nature of the concept, and thus makes an explicit measure both very interesting and highly controversial.

Severity takes base in the ethical consideration of those who are considered to be worse off. Egalitarianism constitute an ethical starting point for such consideration, and the egalitarian view supports whichever solution that gives the most equal distribution of a good, or in this case health (Olsen 1997). Both Olsen and Parfit (1997) state that a pure interpretation of egalitarianism is absurd as it supports any solution where everyone is equal. Elster (1992) (referred to in Olsen (1997), p. 627) calls this type of egalitarianism "strongly envious", and Olsen concludes that the maximin view of Rawls "emerges as a more sensible rule" (Olsen 1997, p. 628). With maximin as the foundation, priority should be given to those who are worse off. In cases where this is done, inequalities are accepted. Parfit refers to a pure interpretation of egalitarianism as "telic egalitarianism", and criticises it for supporting a "levelling down" of health (Parfit 1997). If equality is the only considered factor, then a situation where someone is made worse off can be better because everyone is equal. Parfit therefore suggested another theory, which can be juxtaposed with Rawls' maximin view, namely prioritarianism. This view states that when concerned with equality, more priority should be given to those who are worse off from a moral standpoint. This theory does not support the notion that equality in itself is of value, and thus avoids the levelling down critique of telic egalitarianism (Norheim 2009).

These theories of equity are the underlying ethical consideration for the different definition of severity, which to a greater extent establishes a gradation of severity levels than the underlying ethical concepts. The chosen theories constitute the theoretical backdrop for the more easily quantifiable severity concepts.

### The fair innings approach

The fair innings argument constitutes the theoretical framework for the main measure of severity suggested in the economic guidance. This straightforward theory of fairness is based on the reasoning that there is some length of life that is considered a reasonable lifespan (Harris 1985). Each individual has the right, as far as this right is possible to ensure, to a certain number of life years, the common threshold mentioned being 70 years (three score years and ten) (Harris 1985; Williams 1997). Those who do not reach this limit are somehow cheated of a fair innings of life years, and those who live beyond this threshold are considered to be “”living on borrowed time”” (Williams 1997, p. 119).

The fair innings argument enters the priority debate because it implies that every individual has the right to reach his or her fair inning. Pushed to it’s limits, the argument states that if you are only able to save one individual and you have to choose between a 50-year old and a 71-year old, you save the one who has not reached 70 (if this is the limit).

However, this approach is ambiguous when the two “competing” individuals are 25 and 35 years old and you can only save one of them. A pure interpretation would lead to the conclusion that the youngest should always get first priority on the basis that anyone who is older have had more of an opportunity to reach their fair innings. Another way to interpret the approach would be to say that neither have reached their fair innings, so neither should have priority before the other. In this case the fair innings approach does not help with the priority decision.

Ambiguous results like these can lead to questioning of the validity of this equity measure. How will it help in deciding what to do in difficult situations like the one above?  This is not necessarily a flaw, however, as the big task of making priority decision is based of several elements put together, and never rests on a single decision criterion.

### The generalized fair innings approach

Williams (1997) makes the suggestion of incorporating quality of life in the fair innings measure, which Nord calls "the generalised fair innings approach" (Nord 2005). Williams states that it is not only the age at death that is relevant, but also the quality of the life that is lived (Williams 1997). The fair innings threshold should be based on quality adjusted life expectancy, "Otherwise it will not be possible to reflect the view that a lifetime of poor quality health entitles people to special consideration in the current allocation of health care, even if their life expectancy is normal " (Williams 1997, p. 121). This suggestion then takes base in the use of QALYs instead of life years.

In fine-tuning his argument, Williams makes two suggestions of how to measure a fair innings. The first suggestion is a more dynamic approach where it is the present age that determines the expected lifetime QALYs and not the fair innings as defined at birth. With this way of determining a fair innings, the lifetime QALYs increases with age, and the QALE is constantly recalculated. The older an individual gets, the higher is the QALE for the individual, but the significant differences only becomes evidential late in life. This is what later will be referred to as a "moving innings threshold". The other suggestion is to introduce age weights, where the weights are decreasing with increasing average age, thus directly providing higher value to younger individuals, and giving more weight to loss of QALYs at young ages.

### The proportional shortfall approach

The alternative measure of severity that is presented in the suggested economic guidance, but only for illustrative purposes and not suggested for use in future analyses, is the relative loss of QALYs. Stolk et al. present this severity measure as the "proportional shortfall" approach (Stolk et al. 2004). They make the argument that this approach includes two partially contradicting criteria, namely the fair innings criteria and the severity-of-illness criteria.

The basic concept of severity-of-illness is that whoever has the lowest quality of life at point of intervention, is the one who is worse off and should get priority, all else equal (Nord 1999). To be in a state of 0.5 on a quality scale is regarded as more severe than being in a state of 0.7. If a new intervention can change both states by 0.1 for 10 years, they both get 1 extra QALY. If you have to choose between the two patients, priority should be given to the first one. The approach implicates the use of some sort of severity weight where states low on the quality scale are given more weight than higher values, thus making sure that the life years get less influence than quality when calculating QALYs. The severity approach has concern for those who are worse off now and in the future (Nord 2005), as opposed to fair innings, which incorporates a whole lifetime. The element of age thus becomes less relevant when using the severity approach.

Both the fair innings approach and the severity-of-illness approach make important equity arguments (Stolk et al. 2004). A fair innings coincide with the equity concept of giving priority to those with the lowest quality-adjusted life expectancy, implicitly leading to priority of the young before the old. The severity concept only emphasizes the future health profile without treatment as relevant for an equitable decision, and additional weight is given to "low quality"-conditions (to avoid using the term "severe"). Both concepts originate from equity theory, and they both make important arguments of who is considered to be "worse-off", but they can lead to opposing results. The proportional shortfall is argued to better reflect societal preferences because it balances these two concepts by measuring severity in relative terms instead of absolute outcomes (Stolk et al. 2004).

The proportional shortfall concept considers the individuals' remaining lifetime as point of departure. Whoever is facing a large future relative loss is considered to be worse off. This means that two individuals facing immediate death can be considered equally worse off even if they are fifty years apart in age. The relevant issue is the QALY loss as a fraction of the remaining quality adjusted life expectancy. If an individual is 60 years old with a life expectancy of 80 years, and he dies at 65, the proportional shortfall is 15/ 20 = 0.75. He loses 75% of what he has left. In comparison, a 40 year old, who is also expected to live until 80, and who dies at 60, has a proportional shortfall of 20/40 = 0.50. With this approach the 60 year-old with a larger relative loss, gets priority before the 40 year-old who has a smaller loss in relative terms. In absolute terms, the 40-year old suffer the greatest loss.

The balancing of the two equity concepts is as follows. The fair innings consideration is preserved through the assumption that all individuals want to reach a common or specific target of health. Each individual wants to reach his or her own potential for health improvement, and when you are cheated of a large amount of the rest of your life, this is considered to be severe and unfair. This target for health looks both in retrospect and to the future. Proportional shortfall also assumes that from the moment you get sick, you want to maximize the time you have left. This represents the severity-of-illness concept that only considers the prospective health – age is irrelevant.

These different approaches of considering and measuring severity can and will lead to diverging results of who is considered to be worse off. The choice of method will thus be important for the priority debate, and the case illustration provided in this thesis is meant as input in that debate.

# Chapter 3: Methodology and choice of studies

The methodological approach of this comparison consists to a large extent of finding two appropriate cost-effectiveness evaluations, one for each of the patient groups of drug abuse and cancer (these two simplified "names" will from here on be used when referring to the two compared patient groups). An important element for this context is to choose evaluations that enable the calculation of severity. Economic evaluations of health care interventions can be different in a numerous ways: what they seek to evaluate, how the evaluation is conducted, which interventions that are compared, varying discounting rates for both costs and effects, whether or not quality of life is included, how quality of life is measured, the time horizon used, the perspective of the study, and so on. A cross-comparison can therefore be very difficult, and maybe even impossible. Because this comparison is performed in the context of priority decisions, the quality of the chosen studies is also of great relevance.

To be able to carry out a credible comparison between a drug abuse intervention and a cancer intervention, these differences will have to be taken into account and made as uniform as possible. Gold et al. (1996) (referred to in (Drummond et al. 2005, p. 46) first proposed a "reference case" on methodological principles for economic evaluations. They defined some main features of a good methodological approach, and Drummond et al. continue this work and present a ten-point checklist for *assessing* economic evaluations. The Norwegian official report on cost benefit analyses makes the fundamental contribution on this subject for the Norwegian setting (NOU 1997:27). This set of literature forms the basis when defining a "gold standard" for the studies used in this comparison. The suggested guidance is, as previously pointed out, an attempt to carry on this idea of a cohesive approach for economic evaluations in the health care sector.

## 3.1 The "gold standard"

To conduct a cross-comparison, some features of the economic evaluations should be present. The composition of these features will be called the "gold standard", which will stand as a template in the search for good studies on the cost and effect of medical interventions. This "gold standard" will enable the calculation of severity. In addition, it will provide the two other priority criteria of effect and cost-effectiveness, thus leading to a transparent comparison and evaluation of the three defined priority criteria. To this effect, the main features of this "gold standard" are output, perspective and time. These three features make up some of the criteria defined by Drummond et al. (2005) as to what a proper economic evaluation should contain. In addition, the element of sensitivity, hereunder the enabling of verification and inspection is highly essential for the quality of the studies and the presented results.

### Output

The first important feature that should be present in both of the chosen studies is the health profile of the patient in question. A health profile consists of both the remaining life years and the corresponding utility weight of the disease. Out of the three different types of analyses, as determined earlier, the cost-utility analysis with QALYs as the measured output stands out as the appropriate form for this comparison. If this is not accessible, life years are an alternative resulting from cost-effectiveness analyses, and a search for proper utility weights will have to be done to convert life years into QALYs.

To be able to calculate severity in accordance with the guidance, one specific health profile is necessary, and that is the profile with standard intervention. This illustrates for how long and with what utility an individual is expected to live with the treatment that is offered at the present time. To calculate the QALY gain, which is the benefit of the treatment and the second of the priority criteria, a second health profile is also needed, and that is the health profile with new intervention. The new intervention is what is being evaluated when conducting a cost-utility analysis (or a cost-benefit or cost-effectiveness analysis for that matter).

### Perspective

The second feature that is important when comparing interventions both within patient groups and across disciplines, is the perspective used in the evaluations. The perspective defines the viewpoint of the evaluation, and determines to some extent what costs to include in the cost-effectiveness evaluation. This can have a crucial impact on the cost-effectiveness ratio presented in the results.

There are mainly three different perspectives: patient, health care provider and societal perspective (Drummond et al. 2005). A patient perspective is based on welfare economics and the individuals' values, and as the name suggests, it is the individual's costs that are relevant (like travel costs, co-payments and time). This is referred to as the "welfarist" perspective. The perspective of the health care provider takes account of the costs that the actual treatment brings along, and it is often referred to as the "extrawelfarist" perspective. The much broader societal perspective can incorporate both of the above, in addition to other external costs induced on society, like for example crime. This perspective is called the "decision-making" perspective. The important thing is not which of the perspective that is used as they all can serve a useful purpose in different contexts. The important thing is that the studies being compared use the same perspective, since the choice of perspective can give highly diverging outcomes on both the cost levels and the resulting cost-effectiveness ratios.

The economic guidance stresses the fact that both a provider perspective and a societal perspective should be provided, and does not make a specific choice of either one of them (Helsedirektoratet 2011a). However, it does point out that a provider perspective gives a limited outline of the use of resources, and states that this is not considered relevant for making priority decisions on the public health care system's treatment options. In first-order priority decisions a societal perspective gives the extensive foundation needed to make the best decisions possible (Helsedirektoratet 2011a). As a student in economics, it is the broader, overall, societal perspective that is the area of interest for this discipline. Priority decisions within health care can have significant opportunity costs, and such broad effects can only be captured through a societal perspective.

In addition to the importance of considering the costs on a system level to make overarching decisions, this specific case study of drug abuse also makes for a societal perspective. Drug abuse brings along several socio-economic problems like crime, incarceration, reduced ability to work and increased use of social services, which will be included when taking a societal perspective. With a provider perspective only the direct costs of treatment are included.

Studies presenting a societal perspective are therefore preferred for this comparison, but with the awareness that this is a comprehensive perspective to take, and that there is a lot of room for discretion when stating what a societal perspective actually includes. A provider perspective can therefore prove to be a more reasonable and a straightforward choice.

### Time

The final feature of time requires the evaluations to be done with a lifetime horizon. To be able to evaluate severity and benefit throughout a whole lifetime, the health profile must also illustrate a whole life. It is not enough for the study to present 6 months or a year in a patient's life. This becomes especially important when considering the effect of the treatment amongst drug abusers, which often can be characterized as a life style as well as a disease. If such data is not available, extrapolations of short-term data can be done.

The desired time horizon in new economic guidance is also that of a lifetime. The time horizon should be so long that it enables to capture all the important differences in costs and effects of the comparing alternatives (Helsedirektoratet 2011a).

### Managing uncertainty

Even with these three features in place, maybe the most important element of cost-effectiveness evaluations is the element of managing the sensitivity and uncertainty of the results. This is often done through sensitivity analyses. Different elements are varied one at a time to establish the effects of the different parameters and presumptions made in the main analysis. An underestimation of the costs will for example lead to a more cost-effective result. If for example the difference between the lowest and the highest possible cost levels are large, great weight should be put on presenting both these scenarios.

### Concluding remarks

These three features of a QALY output for both the standard and the new intervention, the aim for a societal perspective and a lifetime horizon, constitute the main elements when trying to find appropriate, comparable studies. In addition to these three features, the opportunity to illustrate some sensitivity considerations is also of importance. Studies of cost and effect can, and are being done in a multiple of different ways. To find some that are an exact match with this "gold standard" will probably be impossible. The goal will therefore be to get as close a possible, and make reasonable adjustments and compromises with the studies that are available.

The data used in this comparison will be based on existing economic evaluations, and is therefore a result of what data that is actually available for use. If it were possible, own estimations of cost and effect designed to meet these exact criteria of the "gold standard" would be preferable, but that would mean insurmountable obstacles for this thesis. The comparison is based on the methodological approach of finding appropriate existing studies.

## 3.2 Choice of studies

In addition to aiming for the "gold standard", a few other elements should be in place for the comparison to be relevant in the context of health care priorities. Firstly, both of the treatments in the comparison should be relevant for the

Norwegian health care setting. If not, any results indicating more or less priority of these treatments, will be irrelevant in the context of Norwegian health care priorities. The linkage to an actual priority debate should be as real as possible. This might be an obvious statement, but none the less an important one. Secondly, the intervention for treating drug abuse should fulfil the two priority criteria of utility and cost-effectiveness, or at least not be discharged due to these two criteria. Otherwise the effect of operationalizing a severity measure might not be meaningful in a comparative discussion. What would make an interesting case was if the cancer treatment was offered even though the effect was minimal and the costs were not proportional, and if the drug treatment proved to be both beneficial and cost-effective. Then the effect of an operationalized severity measure could receive some standalone attention. This reasoning is based on the already stated notion that drug abusers are an under-prioritized patient group, while cancer patients receive both a lot of attention and have a lot of treatment options.

### The search for a drug study

To get an overview of the existing literature on studies of cost and effect of heroin abuse treatment, an initial search was done in the Medline database. The search terms used were methadone and economics or buprenorphine and economics, and titles indicating information on cost and effect of treatment were extracted. The different types of analyses were all relevant in this first search: cost-utility, cost-effectiveness or cost-benefit. This first search was to get an impression of what kind of analyses that had been done, rather than a final decision to look at a medicinal treatment like methadone or buprenorphine as the only possible treatment options for drug abuse. The search was limited to go only as far back as 1990.

A similar search was made in the Cochran library, and a search in Google Scholar was also made to cross check the findings.

An additional search was made within the publications of the Norwegian Knowledge Centre for Health Services, to see if any Norwegian studies had been done on this topic. No specific studies on cost and effect of drug treatment were found here, but a report from the Norwegian Institute for Alcohol and Drug Research (SIRUS) has evaluated different interventions for drug abuse (Melberg et al. 2003).

In addition to this attempt at a systematic search, a general search was made in Google Scholar of the different terms for the "disease" of drug abuse, hereunder heroin abuse: drug dependence, opioid dependence or heroin dependence, together with cost-effectiveness. This was to find out if there existed analyses of cost and effect of other kinds of treatments than those of methadone or buprenorphine. Other possible treatments could be detox, therapy and bed services.

### *Search results*

An important source of information resulting from this search was a review study by Connock et al. from 2007. They have done a systematic review of the studies on cost and effect of methadone or buprenorphine treatment on opioid dependence (Connock et al. 2007). They did a systematic literary search in the major electronic databases MEDLINE, EMBASE, Cochrane Library, Wiley and Health Economic Evaluation Database (HEED), a search among industry submission and a search on Internet sites of national economic units. The search was made from 1996 or from the inception of the databases up until August 2005. Inclusion and exclusion criteria were applied by an experienced health economist and checked by another health economist. They also conducted their own economic evaluation. Through this systematic approach they ended up with twelve different studies that got through their thorough evaluation of quality.

Nine of these twelve studies were found in the search made here. Two of those that were not found were from 1975 and 1976, which this search did not cover, and one was not found at all. By choosing one of the nine overlapping findings, it is with relative good confidence that the choice is adequate for this purpose of comparison.

The search for other kinds of interventions than those found in the main search, did not provide relevant results. The SIRUS-report evaluated the effect and costs of several interventions within the different therapies of inpatient treatment, outpatient treatment and maintenance treatment. Measurements of the treatments effect were disease specific in this report and therefore not useful for cross comparison of different patient groups. The results were, however, positive in the sense that the treatment resulted in reduction in drug use at a reasonable cost (Melberg et al. 2003).

The most relevant intervention thus seems to be the maintenance treatments of either methadone or buprenorphine. There has been done several analyses of cost and effect on these interventions, and this gives an opportunity to apply the predetermined selection criteria.

### *Choice of intervention*

The different studies from the search show that there are multiple choices when considering what kind of intervention to analyse and what to compare it to, even within maintenance treatment; methadone vs. no treatment, methadone vs. drug-free treatment, buprenorphine vs. methadone, methadone plus heroin vs. standard methadone treatment and so on. The economic guidance clearly states that the comparative intervention should be the established treatment of the disease, and that comparing the new intervention to placebo or no treatment at all should be used for illustrative and sensitivity purposes (Helsedirektoratet 2011a). The regional health authorities in Norway offer a couple of different treatment schemes to drug abusers today: emergency treatment, in- and outpatient treatment, maintenance treatment, treatment for those with a dual diagnosis and forced admission (Helse Bergen 2010). There are also low-threshold services and self-help groups for those with drug problems. A reasonable choice of the compared interventions should therefore be some of these established treatments.

### *The drug treatment studies*

The nine overlapping findings from the search are listed in Table 3.1. The choice of study is one that enables a comparison, namely fulfilling the "gold standard", and that can be several of them.

The review study by Connock et al. (2007) is assumed to provide a filter for ensuring the quality of the studies. When considering the results of the studies, almost all of them showed cost effective results of the evaluated interventions – they were all within the commonly accepted American threshold of USD 50 000 per QALY (Ubel et al. 2003) (which is lower than the suggested Norwegian threshold), and often far below. The utility or benefit of the treatments was also positive, but often not to a very large extent. Whichever study is chosen, they all fulfil the above-mentioned additional criteria that will allow for the severity measures to be the centre of the discussion. This leaves a very good basis for applying the selection criteria of the "gold standard". A required output in QALYs eliminates the cost-effectiveness studies not presenting life years, and this only leaves out study number 5 in Table 3.1 (because number 9 presents life years despite being a CBA). The rest either produces the cost-effectiveness ratio of cost per QALY or cost per life year, which can be converted with utility weights. The perspective does not directly eliminate any of the studies, but a societal perspective is preferred, and since some of the studies do take this perspective, it is preferable to choose one of them. This reduces the studies down to number 7, 8 and 9. The final feature of time was a lifetime horizon. Heroin abuse and treatment is a life long situation for many. As Zarkin et al. (2005) points out, anything but a lifetime evaluation of treatment ignores the chronic nature of heroin abuse. Extrapolation of monthly or yearly data is an alternative to demanding a lifetime horizon, but when taking base in existing studies with limited presentation of the underlying models, this is especially challenging. Two of the studies present a lifetime horizon, namely studies number 1 and 9.

| Number | Year | Author | Title | Type of analysis | New vs. comparator | Output | Perspective | Time |
|---|---|---|---|---|---|---|---|---|
| **1** | 1999 | Barnett | The cost-effectiveness of methadone maintenance as a health care intervention | CEA | MMT vs. drug-free treatment | Life years | Provider | Lifetime |
| **2** | 2000 | Zaric et al. | HIV transmission and the cost-effectiveness of methadone maintenance | CUA | Increased MMT vs. MMT | QALYs | Provider | 10 y |
| **3** | 2000 | Zaric et al. | Methadone maintenance and HIV prevention: a cost-effectiveness analysis | CUA | Expansion of MMT vs. MMT | QALYs | Provider | 10 y |
| **4** | 2001 | Barnett et al. | The cost-effectiveness of buprenorphine maintenance therapy for opiate addiction in the United States | CUA | BMT vs. conventional treatment | QALYs | Provider | 10 y |
| **5** | 2003 | Doran et al. | Buprenorphine versus methadone maintenance: a cost-effectiveness analysis | CEA | BMT vs. MMT | Heroin-free days | Provider | 1 y |
| **6** | 2004 | Masson et al. | Cost and cost-effectiveness of standard methadone maintenance treatment compared to enriched 180-day methadone detoxification | CEA & CUA | MMT vs. MDT | Life years and QALYs | Provider | 10 y |
| **7** | 2005 | Dijkgraaf et al. | Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials | CUA | MMT + heroin vs. MMT | QALYs | Societal | 1 y |
| **8** | 2005 | Harris et al. | A randomised trial of the cost effectiveness off buprenorphine as an alternative to methadone maintenance treatment for heroin dependence in a primary care setting | CEA & CUA | BMT vs. MMT | Heroin-free days & QALYs | Societal | 1 y |
| **9** | 2005 | Zarkin et al. | Benefits and costs of methadone treatment: results from a lifetime simulation model | CBA | Increased MMT vs. MMT* | Life years | Societal | Lifetime |

*Table 3.1: Overview of the nine overlapping drug abuse studies.*

(MMT: methadone maintenance therapy, BMT: buprenorphine maintenance therapy, MDT: Methadone detoxification therapy.
*There are two other scenarios compared, but this is the one used for this specific comparison.)

The final choice of study landed on study number 9, the lifetime simulation model by Zarkin et al. (2005). The main reason for choosing this study was exactly the simulation of a whole lifetime, and in addition the inclusion of societal costs as well as provider costs so that both perspectives could be illustrated in the comparison. Even though this study states to be cost-benefit analysis, all of the costs are presented separately, and the effect of the treatment in life years is provided as well. This enables an extraction of the treatment costs, and the life years can be converted to QALYs by using utility weights from the literature.

### The drug study

The article by Zarkin et al. from 2005 calculates the cost-benefit ratio of methadone treatment using a lifetime simulation model. The model simulates costs and benefits across the lifetime to a cohort of 1 million men and women using a Monte Carlo simulation model. Throughout life the individuals can be in either of five different states every month: non-user, user, in treatment, incarcerated non-user and incarcerated user. The authors state several reasons for choosing a dynamic model for their calculation. It gives flexibility when incorporating multiple variables, it keeps track of the individual's attributes, and it captures the stochastic variations of individual behaviour (Zarkin et al. 2005). The model keeps track of the variables heroin use, methadone treatment, employment, crime, incarceration and the use of health care. The different individual attributes included are age, gender, current heroin use, history of heroin use and methadone treatment, and current employment status. Several attributes are not included, like social status, and the authors acknowledge the simplifications they have made, but make convincing arguments of including the most important variables and attributes (Zarkin et al. 2005, p. 1136 – 1137). What the authors also point out is that, of all the parameters needed to calculate the transitions between states and the associated costs and benefits, as many as possible are from the existing literature. The rest are assumed, calculated or derived from existing data. Examples of these parameters are the probability of using heroin at a specific age, the probability of committing a crime, the cost of criminal activity and so on. The individuals enter the model at age 18 and leave at age 60 or at death.

The comparator in this study is called the baseline model. The baseline is supposed to represent the situation that best captures the key characteristics of heroin use and methadone treatment observed in previous studies. Such a definition lacks an exact description of what exactly the baseline is, and this kind of ambiguous phrasing is common throughout several cost and effect studies. The interpretation made here is that the baseline represents a modelled society where methadone is offered to a certain extent, and costs, benefits and life years at baseline are presented. This falls in under the criterion of the guidance that the comparator should be the existing treatment practice, and not placebo or no treatment at all, to be able to establish the additional costs and effects that the new intervention will have.

Three "new" interventions are evaluated in this study. One of these seems highly relevant for the treatment options in Norway: a 100 % increase in the probability of going into treatment. This is the intervention that will be used in this comparison, since the two other interventions were no treatment (used as comparator to the baseline) and a 25 % increase in length of treatment stay, which had no significant effect (but which is also relevant). As mentioned in the article, an increase in the probability of going into treatment can correspond to a policy measure set to increase the provision of treatment, examples being a program to educate abusers on the benefit of treatment or an increase in the number of treatment slots available (Zarkin et al. 2005, p. 1143).

The measured cost-benefit ratio of an increase in the probability of going into treatment was 76. This result states that for every single dollar of costs, there are 76 dollars in benefit. The main reason for this high ratio is an increase in earnings, as well as a reduction in crime costs (but this is not a significant change). The new intervention also led to an increase of 3.65 life years.

These positive results of cost and effect, together with the appropriate time line, the effect presented in life years and a presentation of both the direct and the indirect costs, makes this an appropriate study for a cross-comparison with specific emphasis on severity.

### The search for a cancer study

The same features as for the drug study will apply for the cancer study. The "gold standard" features of output, perspective and time will have to be applied. The output will have to be in QALYs, or life years with own conversion, which is the case with the drug study. The perspective should be societal to match the choice of drug study, but presentation of a provider perspective as well would be preferable so that both perspectives can be evaluated and compared. Finally, the time horizon should be that of a lifetime.

The comparative cancer study will take the role of being a reference study in this case. A published study of cost and effect of a cancer treatment is in its simplicity the aim of this section. A quick search with the terms "cancer" and "cost-effectiveness" in Google Scholar resulted in more than 400 000 hits (May 31$^{st}$ 2012). A similar search with the terms "heroin abuse" and "cost-effectiveness" resulted in just over 23 000 hits (May 31$^{st}$ 2012). Economic analyses of cancer interventions seem to be of a much larger scope, and much more comprehensive. In order of limiting the search process, and with the cancer study only being a reference case, a search for a Norwegian study was first done. A further limitation was then made with regards to type of cancer.

### *Search results*

A quick search within the publications of the Norwegian Knowledge Centre for the Health Services, limiting the subject to health economics and using the search term "cancer", resulted in no more than 12 hits, and where most of them were irrelevant. The types of cancer emerging from this search were breast cancer and colorectal cancer. In order of not limiting the comparison to apply for only one gender, breast cancer was not an option. With colon cancer being one of the three most common cancer types for both genders in Norway (Cancer Registry of Norway 2011), a decision of looking at colorectal cancer seems to be an appropriate choice. This limitation of cancer type makes the search task more manageable. Colorectal cancer is an often-used collective term for cancer in the colon and rectum (Store Norske Leksikon 2012).

Only one health economic study resulting from this simple search seemed relevant for this purpose of comparison (Aaserud et al. 2007). In this study the pharmaceutical bevacizumab was evaluated as an addition to first-line chemotherapy for metastatic colorectal cancer. This specific pharmaceutical was then used as a renewed search term. An important element also for the reference study is the treatment's relevance for the Norwegian health care setting. With rapidly changing treatment programs in the context of cancer, evaluations can soon enough become out-dated.

A follow up search was made in the Medline search engine using the search terms "bevacizumab" and "cost effectiveness" resulting in just over fifty hits. By looking for colon or colorectal cancer in the titles, a couple of results emerged as relevant (Asseburg et al. 2011; Hedden et al. In press; Shiroiwa et al. 2007, 2010; Tappenden et al. 2007b), and an important source was a review study and economic evaluation of bevacizumab and cetuximab (Tappenden et al. 2007a).

A general search in Medline using the terms "colon cancer" and "cost effectiveness" was also done, resulting in over two hundred hits. A couple of health economic evaluations resulted from this search, but mostly these evaluations had a new intervention that was equal to the baseline of the studies from the previous findings, and thus seem to be of less relevance to the Norwegian setting.

None of the findings from the search on bevacizumab fulfilled all of the selection criteria. The review study found in Medline provided some useful information (Tappenden et al. 2007a), as the results were not very different from the Norwegian study. The results, however, were exactly the same as another cost-utility publication by the same authors (Tappenden et al. 2007b), but they had both different time horizons and different approaches with regards to discount rates, thus making it difficult to interpret the results. The final choice of a reference study can therefore with reason be the report by the Norwegian Knowledge Centre for the Health Services from 2007 found in the initial search (Aaserud et al. 2007).

### The reference cancer study

The reference study conducts a health economic evaluation of using bevacizumab in treatment for metastatic colorectal cancer (Aaserud et al. 2007). As described in the report, colorectal cancer was the second most common type of cancer in Norway at the time of the report, and the 5-year survival rate was approximately 5 % in 2007 according to the Cancer Register. The commonly used first line treatment for this patient group is 5-FU and calcium folinate combined with oxaliplatin or irinotecan (Aaserud et al. 2007). The report sets out to evaluate the additional effect and the additional costs of adding bevacizumb (Avastin®) to the first line treatment. Bevacizumb is a costly pharmaceutical, and was at the time of the report registered for use in combination with the existing treatment.

The economic evaluation takes base in an assumed average patient with metastatic colorectal cancer that is younger than 70 years. The new intervention of adding bevacizumb to the standard treatment was compared to the standard treatment itself. The adding was done only in the first-line treatment. The second- and third-line treatment was the same for both interventions. The calculations were done in a Markov model, which tracked the two treatment options. The report did a cost-effectiveness analysis with life years as the output. The report states that there were no good and relevant utility weights available for a QALY calculation (Aaserud et al. 2007, p.27).

According to the study, average remaining life years with metastatic colorectal cancer is 2 years, and some live up to 3 years. The treatment given at this stage of the disease is palliative care of chemotherapy. The time horizon of the study is from the start of bevacizumab treatment and until the end of complete treatment or until death occurs. A lifetime perspective would have been preferable, but this will be commented upon later.

The costs were presented from both a provider perspective and a societal perspective, but the only thing separating the two perspectives was the inclusion of value added tax (VAT). The societal perspective was without VAT as this only constitutes a transfer of money in this case. The study included costs relating to the following: pharmaceuticals, pharmacy time for mixing the pharmaceuticals, administrating the treatment, CT scans, policlinic consultation, prevention and treatment of side effects, the patients and their families expenses on travel, food and accommodation and symptomatic treatment.

The resulting output measures of the study was 668 000 NOK per life year gained with a health service (provider) perspective, and 549 000 NOK per life year gained with a societal perspective. Both costs and life years were discounted with an annual rate of 4 %, and the costs were presented in 2007-NOK.

## 3.3 Contextualizing the chosen studies for the Norwegian setting

To view the chosen interventions in a Norwegian context is both of interest and importance when discussing health care priorities within the Norwegian society. It is of relevance to provide some indication of the number of individuals that are actually prevailing these kinds of treatments in Norway, and an approximation of the cost levels.

### Methadone

The number of injection drug users (IDUs) in Norway is estimated to be between 8 700 and 12 300 (Amundsen and Bretteville-Jensen 2010). These are crudely estimated numbers from 2007, the last year with complete data for the Norwegian Institute for Alcohol and Drug Research (SIRUS). An average estimate would be about 10 000 IDUs and most of these abuse heroin. Some of the statistics presented online by SIRUS looks at the offer of medically assisted treatment, hereunder methadone. In 2010 there were 6015 patients in treatment across the country, the highest number over a period of 11 years. The number of patients on a waiting list or applying for treatment was 241, indicating a rather high coverage rate. The similar statistics for the Health Region West was 1277 and 35 respectively (SIRUS 2011).

In the recent report by the Norwegian Directorate of Health it is presented that the average annual cost per patient in maintenance treatment is 90 500 Norwegian kroner (Helsedirektoratet 2012a, p. 109). At the baseline of the drug study used in this comparison, the cost level with a provider perspective was just above 21 000 USD in 2001, which is within the same cost range. The cost level referred to in the report included drug costs and the expenses for disclosure of these drugs. For the Health Region West this would amount to an annual cost of over 115 million Norwegian kroner (90 500 * 1277).

### Bevacizumab

The report from the Norwegian Knowledge Centre for Health Services provides a very specific amount of patients that are eligible for being treated with bevacizumab. The rationalization is as follows: "The number of individuals in Norway with colorectal cancer is 3500, of whom 50 per cent have metastases and out of which 40 per cent are younger than 70 years. Of these 700 patients, 60 per cent will be obsolete for bevacizumab… We therefore assume that approximately 280 patients will be candidates for treatment with bevacizumab in the course of a year" (own translation) (Aaserud et al. 2007, p. 43-44). They also make a projection of the total costs of offering this treatment. With the added cost of 247 000 Norwegian kroner per patient from a provider perspective, the total additional costs are assumed to be about 70 million Norwegian kroner (247 000 * 280), where 56 million constitute the direct costs of bevacizumab.

A different article draws a parallel to the actual budgetary situation of hospitals in connection with cancer treatment (Johansson et al. 2009). This article looks at cetuximab, a pharmaceutical similar to bevacixumab, in the context of colorectal cancer. According to the article, 700 patients yearly have this diagnosis in the Health Region West, and 200 of these could be eligible for the treatment. With a minimum cost of 400 000 Norwegian kroner per patient, this would total to about 80 million Norwegian kroner if all were to receive treatment. The drug budget for the oncology unit at the University Hospital in Bergen, the largest hospital in this region, was about 30 million kroner in 2005.

These expense numbers for both methadone and bevacizumab show that there is a significant amount of money tied up in treating both of these groups, which in turn can give a slight indication of what the alternative costs can be. The total consecutive budget for the Health Region West in 2012 is approximately 21.9 billion Norwegian kroner (Helse Vest 2012), and with the estimates done here, methadone and bevacizumab constitute almost 1 % of the total budget (115 million + 70 million

/ 21.9 billion = 0.0084) (assuming that all the colon cancer patients were treated in this region). Keeping in mind that the expense figures are from two to seven years back, they have probably in real terms increased since then, and can thus make up an even larger share of the total budget.

These numbers leave a good foundation for discussing these two interventions in the context of health care priorities, and indicate the scope that is undertaken in dealing with such priorities.

## 3.4 The priority criteria and some needed tools

Even though the chosen studies create the foundation for extracting the explicit priority criteria, and the use of a "gold standard" constitute a framework for making the criteria comparable, some additional tools are needed. These are mainly needed to enable the calculation of severity, as this is not normally included in cost-effectiveness evaluations. Some cost tools are also needed to make the costs comparable across the patient groups.

### Life table

The most important tool for the calculation of severity is the Norwegian life table. This table, produced by Statistics Norway provides a couple of different parameters, among those the average remaining life years at every age level for both genders. It is the expected remaining life years at a given age that is used in the calculation of severity, here used as a proxy for quality-adjusted life expectancy (QALE). See Appendix 1.[4]

[4] The life table used in this thesis is from 2009. A life table from 2011 was published by Statistic Norway in April 2012, but the changes are so small that effects on the results provided in this comparison would be minimal.

## Utility weights

The second group of tools needed are the utility weights in order to convert life years into QALYs. Separate utility weights for drug abuse and cancer are needed, and sensitivity analysis will have to be done to establish how prone the results are to the specific weights used.

### *Drug abuse utility weights*

Utility weights used to define the quality of life with drug abuse were provided in several of the drug studies from the literature search (Barnett et al. 2001; Zaric et al. 2000a; Zaric et al. 2000b). Barnett et al. (2001) used their own adjustments for defining maintenance treatment and IDU weights. Zaric et al. (2000a) assume their weights, and remark on the lack of research done on mental illness, and that they are aware of no weights determined for substance abuse disorders. Zaric et al. (2000b) makes the same assumption. However, these three articles all assume identical utility weights – 0.8 for injection drug user, and 0.9 for receiving maintenance treatment. They all similarly refer to the literature for other weights that limit activities, and which can therefore be seen in relation to drug abuse: moderate angina (0.92), migraine (0.87), ulcer (0.84) and severe angina (0.82).

These weights of 0.8 and 0.9 state that if you are an injection drug user, you have a health related quality of life equal to 0.8. If you get maintenance treatment, like methadone, your quality of life increases with 0.1 up to 0.9.

The Handbook of Disease Burdens and Quality of Life Measures did not provide any additional information of the quality of life weights in connection with drug abuse. It does, however, state that substance abuse impairs quality of life and treatment improves quality of life (Preedy and Watson 2010, p. 3703). This supports the assumption that maintenance treatment provides higher weighting than being an IDU.

### *Cancer utility weights*

The utility weights in the literature on colorectal cancer were not equally unanimous as for drug abuse. In an overview article by Earle et al. (2000) the authors make a critical review of the cost-utility analyses conducted in the field of oncology. They have done a literature search from 1975 to 1997 to get an overview of the results of all the studies done. According to this article the utility weights in connection with colon cancer range from 0.75 and up to 0.97, but none of the weights are linked to adding bevacizumab to the first line treatment.

The review study evaluating bevacizumab and cetuximab for treating metastatic colorectal cancer comments on the “crucial gap in the current evidence base” with regards to the utility assessment (Tappenden et al. 2007a, p. 56). The different studies referred to present very different utility weights, and the review study’s own economic assessment of bevacizumab end up using the weights 0.8 and 0.6 for “progression free” and “post-progression” health states respectively. The weights are thus linked to the health state, and not the response of the treatment.

An appraisal-guidance from the NHS in the UK also provides a couple of utility weights in direct link to bevacizumab (NICE 2007). The appraisal-guidance presents the results of two different providers: the manufacturer of the pharmaceutical and the assessment group. The manufacturer use similar weights for the intervention group who got bevacizumab plus standard treatment and the control group who only got standard treatment. A pre-progression health state was given the weight of 0.8 and the post-progression health state was given the weight of 0.5. The assessment group also gave both groups similar utilities. The pre-progression state was similar to that of the manufacturers (0.8) and the post-progression state was 0.6. Also here the weights are linked to the health state irrespective of the evaluated treatment.

The choice of which utility weights to use should take base in the findings in the literature, but in the end it simply has to be a pragmatic choice within sensible boundaries since the findings are not unanimous. The literature gives diverging results, thus limiting the quality of the choice. The specific utility impact of receiving bevacizumab in connection with metastatic colorectal cancer seems to be lacking in the literature.

With base in the findings in the literature, the following utility weights for metastatic colorectal cancer are used: the weight corresponding to the outcome of the standard intervention will be 0.6, and weight of the outcome relating to the new intervention of adding bevacizumab will be 0.8. These weights lie within what can be said to be a reasonable range, and still constitute a significant difference in utility between the two interventions. It is the distance between the weights that matters when calculating the change in QALYs – the effect of going from 0.3 to 0.5 is equal to the effect of going from 0.7 to 0.9. These choices will be subjected to sensitivity evaluations, and they are most likely an overestimation of the intervention's effect.

### Cost tools

Finally, some tools are needed on the cost side to ensure a reasonable comparison. The costs have to be converted to the same index year, and a change in currency is needed for the American drug study.

#### *Inflation calculators*

The suggested economic guidance states that the costs and the cost-effectiveness ratios should be provided in 2005-NOK to achieve comparable figures. The reason for choosing exactly 2005 as the index year seems to be founded in the attempt to establish a unified method of evaluation. Both the Ministry of Finance and the Directory of Health refers to values in 2005-NOK in official documents according to the guidance (Helsedirektoratet 2011a). However, the most important element is to compare figures that are actually comparable, and for that costs have to be presented in the same reference year. If this reference year is 2005 or 2008 does not make a difference, and even less of a difference in this context of an isolated comparison for illustrative purposes.

Since the two studies are presented in different time values, the value of the costs will have to be inflation adjusted. To be in accordance with the suggested time value of the guidance, the cost will be converted to a 2005-level. Online inflation calculators were used to achieve the correct values[5].

The costs of the drug study are presented in 2001-USD, and the costs of the cancer study are presented in 2007-NOK. It might have been an easier approach to simply use 2007-NOK in the comparison, and this without any loss of important information, but a decision is made to stay with the somewhat established reference value. From the American study the costs are simply adjusted, and from the Norwegian study the costs are first changed to today's value, and then to a 2005-level. With these recalculations the costs are converted to similar time values, and an appropriate comparison can be conducted.

### *Historical exchange rate*

Since the drug study is an American study, a change of currency from USD to NOK is necessary. The average historical exchange rate between US Dollars and Norwegian Kroner in 2005 was 6.45 (Norges Bank 2012).

[5] American inflation calculator:
http://www.bls.gov/data/inflation_calculator.htm <downloaded May 5th 2012>
Norwegian inflation calculator:
http://www.abcnyheter.no/penger/kalkulatorer/2009/01/25/inflasjonskalkulator<downloaded May 5th 2012>

With all these tools in place the task of establishing the three priority criteria can begin. All of the calculations are done in MS Excel.

# Chapter 4: Results

## 4.1 Main results for drug abuse

The main results emerging from the study of the drug abuse intervention are summed up in Table 4.1. In the following, a more detailed review of the calculations is provided.

| MAIN RESULTS FOR HEROIN ABUSE: A 100 % increase in the probability of receiving methadone treatment vs. baseline methadone treatment | EFFECT | COST-EFFECTIVENESS | | SEVERITY | |
|---|---|---|---|---|---|
| | QALY gain | Provider perspective | Societal perspective | AQL | RQL |
| | 3 | 4 673 | - 210 530 | 41 | 0.66 |

*Table 4.1: The main results for the drug abuser – effect, cost-effectiveness and the two severity measures.*

### Effect

The effect of an intervention is defined as the QALY gain; the difference between the QALYs achieved with the standard intervention and the new intervention. The model used in the underlying drug study tracks what the authors call ever-users and never-users. The focus here will be on the ever-users as they are the ones that are evaluated as a patient group, even though the never-users also experience changes as a result of the new intervention. The individuals enter the model at age 18, and an ever-user is expected to live for an additional 27.13 years at baseline. With the new intervention of a 100 % increase in the probability of going into treatment, the ever-user is expected to live for an additional 30.78 years. The gain in life years is then 3.65 years. When converting to QALYs, a further assumption has to be applied in order to decide which of the utility weights to use. Since the baseline scenario is also a situation where maintenance treatment is offered, it is an important element what the distribution among the recipients look like.

With the standard intervention, the model uses the following probabilities for a user to enter treatment: 1 % for the age groups 18-25 and 35-60, and 1.5 % for the age group 26-34. These will be referred to as groups 1 to 3. The new intervention of a 100 % increase in the probability of going into treatment changes these probabilities to 2 % and 3 %, respectively. The probabilities represent monthly conditions. To equate these with the annual probabilities needed here, the assumption that the probability of going into treatment is the same every month, is applied. The individuals receiving treatment have a utility weight of 0.9, and the untreated IDUs have a utility weight of 0.8. Equation (1) is used to calculate the baseline QALYs.

$$\begin{aligned} QALYs\ at\ baseline \\ &= \{p(treatment) * MMT\ utility\ weight * life\ years\ groups\ 1\ \&\ 3\} \\ &+ \{p(treatment) * MMT\ utility\ weight * life\ years\ group\ 2\} \\ &+ \{p(treatment) * IDU\ utility\ weight * life\ years\ groups\ 1\ \&\ 3\} \\ &+ \{p(treatment) * IDU\ utility\ weight * life\ years\ group\ 2\} \end{aligned} \quad (1)$$

$$\begin{aligned} QALYs\ at\ basline \\ &= \{0.01 * 0.9 * 18.13\} + \{0.015 * 0.9 * 9\} + \{0.99 * 0.8 * 18.13\} \\ &+ \{0.985 * 0.8 * 9\} \approx 21.7 \end{aligned} \quad (2)$$

With the new intervention, the probabilities and the number of life years change, but the equation is identical to that of the baseline.

$$\begin{aligned} QALYs\ with\ new\ internvention \\ &= \{0.02 * 0.9 * 21.78\} + \{0.03 * 0.9 * 9\} + \{0.98 * 0.8 * 21.78\} \\ &+ \{0.97 * 0.8 * 9\} \approx 24.7 \end{aligned} \quad (3)$$

The results are summed up in Table 4.2.

| EFFECT | Baseline | New intervention | Gain |
|---|---|---|---|
| Life years from age 18 | 27.13 | 30.78 | 3.65 |
| QALYs from age 18 | 21.74 | 24.69 | 2.96 |

*Table 4.2: The effect of the new intervention presented both in life years and in QALYs.*

This conversion from life years to QALYs results in 21.7 QALYs at baseline and 24.7 QALYs with the new intervention as additional QALYs after age 18. The QALY gain with the new intervention is 3 QALYs, which is lower than the gain in life years due to the reduction in quality. The underlying study makes no comment of whether or not the life years have been subjected to discounting. The assumption is therefore made that the life years have not been discounted based on the reasoning that if they were, this would have been specified.

### Costs

The underlying study is stated to be a cost-benefit analysis, which means that all the output data are converted into monetary values – the costs as well as the benefits (even though life are presented on its own). To get from the total benefit to simply the "negative" costs, the social costs in connection with employment have been excluded. This is partly due to the controversy of including productivity factors, and it is also in accordance with the guidance suggestion of not to include such factors in the main analysis (Helsedirektoratet 2011a).

Three main blocks of costs were extracted for the ever-users. The data used is per ever-user and not per treatment participant since the rest of the data are presented per ever-user. This is also in accordance with calculating the effect as applying to the users of heroin. The costs extracted from the study are the cost of heroin-treatment (methadone), the crime costs incurred by ever-users and health care costs. The inclusion of crime costs represent the societal perspective, and the exclusion of these represents the provider perspective, but this is recognised as a bold simplification.

The heroin treatment costs increases with the new intervention. This is in accordance with the new intervention being an increase in the probability of entering treatment due to for example an increase in treatment facilities. The crime costs are reduced due to a reduction in the percentage of ever-users committing crimes and a reduction of the percentage being incarcerated for a crime. This also seems to be a reasonable correlation (even though the study states that this is not a significant change). The difference in health care costs is almost 0 in this specific study. All the costs are discounted with an annual rate of 3 % (the guidance suggests a 4 % discount rate for costs). The choice of specific discount rates is subjected to sensitivity considerations.

By subtracting the costs at baseline from the costs of the new intervention, the incremental cost of the new treatment is established. The incremental societal costs are negative due to the reduction in crime costs. The results are depicted in Table 4.3.

| COSTS | Baseline | New intervention | Incremental costs, 2001-USD | Incremental costs, 2005-USD | Incremental costs, 2005-NOK |
|---|---|---|---|---|---|
| Heroin-treatment | 3 830 | 5 788 | 1 958 | 2 159 | 13 927 |
| Crime | 1 061 639 | 972 115 | - 89 524 | - 98 724 | - 636 770 |
| Health care | 17 431 | 17 417 | - 14 | - 15 | - 100 |
| Total societal costs (w/crime) | 1 082 900 | 995 320 | - 87 580 | - 96 580 | - 622 943 |
| Total provider costs (w/o crime) | 21 216 | 23 205 | 1 944 | 2 144 | 13 827 |

*Table 4.3: Overview of the drug abuse costs at baseline and with the new intervention. The incremental costs are presented in US Dollars both in 2001 and 2005 values, and in Norwegian kroner in 2005 values.*

### Cost-effectiveness

With both the effect in terms of QALY gain and the incremental costs with both a societal and a provider perspective, the incremental cost-utility ratios can be easily calculated. This is the output measure that states how much additional costs it takes to achieve one additional QALY. The equation is simple:

$$ICUR = \frac{Incremental\ cost}{Incremental\ QALY} \quad (4)$$

The calculated ratios for the two perspectives are depicted in Table 4.4.

| ICUR | ICUR: Cost per QALY |
|---|---|
| **Provider perspective (w/o crime)** | 4 673 |
| **Societal perspective (w/crime)** | Cost saving (- 210 530) |

*Table 4.4: The cost-effectiveness of the new drug abuse intervention with both a societal and a provider perspective. The ratios are cost-utility ratios due to an effect in QALYs and not life years.*

## Severity

The final priority component, and the central focus of this comparison, is severity. Calculations are done for both of the severity measures. One important assumption that enters at this point is that all life years lived without the disease in question, is a life year lived in perfect health. That means that nothing but the analysed disease affects the quality of life. The postulation that a life year at 80 is lived in perfect health is likely an overestimation, but for this isolated comparison, it is of lesser importance. Also, with the uncertainty resting on the disease specific weights, to include additional utility weights based on similar uncertainty, might only disturb the results, and leave ground for even more vagueness. This will be further discussed in the next chapter.

Since the individuals in the drug study enter the model at age 18, this is also used as point of departure for the calculation of severity. The remaining life years for an average 18-year-old individual when considering both genders are 63.29 years according to the Norwegian life table (see Appendix 1). For these main results, separation according to gender is not done. Gender differences will enter in the sensitivity discussion.

The absolute QALY loss is simply the difference between the QALE and the QALYs achieved with standard intervention.

$$AQL = QALE - QALY\ with\ standard\ intervention \tag{5}$$

$$AQL = 63.29 - 21.47 \approx 41 \tag{6}$$

The relative QALY loss is equal to the absolute QALY loss as the fraction of QALE:

$$RQL = \frac{AQL}{QALE} \tag{7}$$

$$RQL = \frac{41}{63.29} \approx 0.66 \tag{8}$$

The severity measures are summarized in Table 4.5.

| SEVERITY | QALE at age 18 | AQL | RQL |
|---|---|---|---|
| Both genders | 63.29 | 41 | 0.66 |

Table 4.5: The two measures of severity for the average drug abuser.

The health profile for the drug abuser is illustrated in Figure 4.1. The graph is again a joint illustration of both men and women. The absolute severity measure constitutes areas 3 and 4. The main element affecting this severity measure is the early onset of death, and to a lesser extent the reduction in quality of life. However, the potential for quality of life to play an important role in the severity measure, is definitely present. The severity measure of relative QALY loss can be viewed as areas 3 and 4 as a share of the square from age 18 up to 81 (areas 2, 3 and 4), which constitutes more than half of the total area. The graph also illustrates the QALY gain shown as area 3, which is the effect of the new intervention as calculated above.

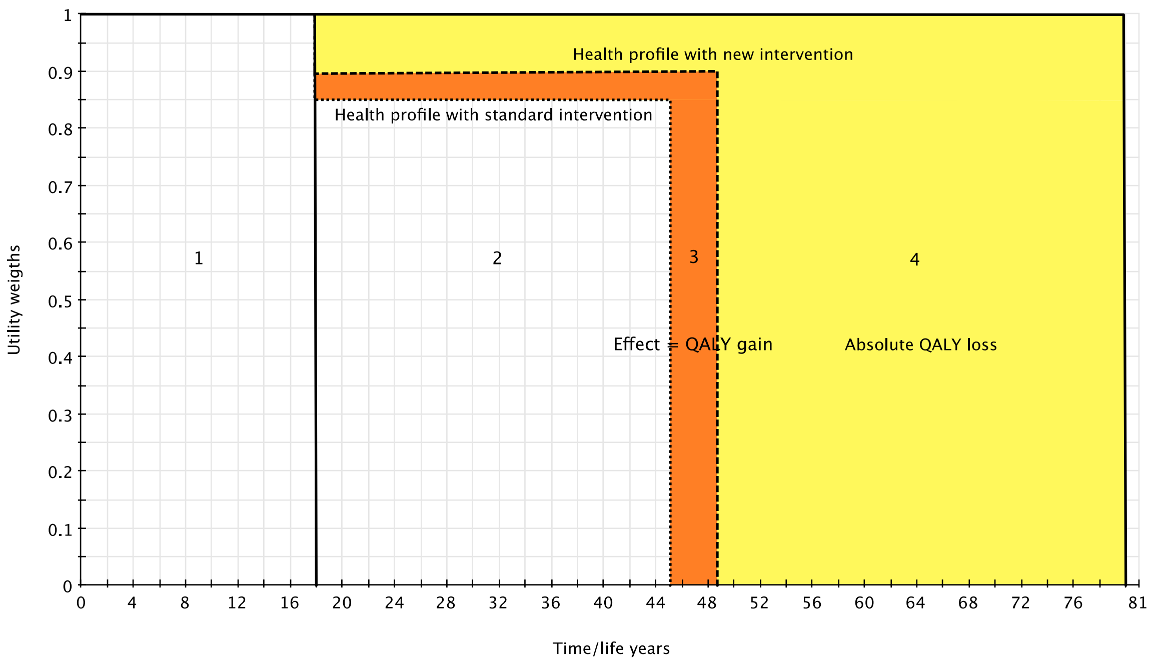


*Figure 4.1: The health profile for an average drug abuser with disease occurring at age 18.* [6]

## 4.2 Main results for cancer

The equivalent main results for the cancer intervention are presented in Table 4.6. Again a profound review of the calculations will follow.

| MAIN RESULTS FOR METATATIC COLORECTAL CANCER: The adding of bevacizumab to standard intervention vs. standard intervention | EFFECT | COST-EFFECTIVENESS | | SEVERITY | |
|---|---|---|---|---|---|
| | QALY gain | Provider perspective | Societal perspective | AQL | RQL |
| | 0.64 | 373 382 | 306 868 | 23 | 0.96 |

*Table 4.6: The main results for the cancer patient – effect, cost-effectiveness and the two severity measures.*

[6] The vertical distance between the utility weights is not in accordance with the actual calculations of the QALY gain due to the composition of the population, and the illustration should therefore be interpreted with moderation.

### Effect

The cancer study presented the effect of the treatment in life years, both discounted with a 4 % discount rate and undiscounted life years. Both the discounted and undiscounted life years are recalculated with the use of utility weights to achieve the effect in QALYs. The life years with standard and with new intervention are simply multiplied with their respective utility weights. The results are shown in Table 4.7.

| EFFECT | Standard intervention | New intervention | Gain |
|---|---|---|---|
| **Life years** | 1.57 | 1.98 | 0.41 |
| **Life years, discounted** | 1.51 | 1.88 | 0.37 |
| **QALYs** | 0.94 | 1.58 | 0.64 |
| **QALYSs, discounted** | 0.91 | 1.50 | 0.60 |

*Table 4.7: The effect of the new intervention is presented both in life years and in QALYs, and both discounted and undiscounted.*

Because the effect for the drug abuser is presented in undiscounted QALYs, this will also be the comparable effect measure for the cancer patient. The main result of the new intervention's effect will thus be 0.64. The effect of discounting the QALYs is included as a sensitivity consideration in the next chapter.

### Costs

In the study, the costs were presented in 2007-NOK, and conversion is made to 2005-NOK. The costs with a societal perspective are lower than with a health service (provider) perspective due to the exclusion of value added tax (VAT). The VAT only constitutes a transfer of money when the broader perspective is taken. The underlying cost groups were provided in the previous chapter, so only the sums are presented in Table 4.8.

| COSTS | Standard intervention | New intervention | Incremental costs, 2005-NOK |
|---|---|---|---|
| Provider perspective | 207 685 | 447 396 | 239 711 |
| Societal perspective | 180 511 | 377 520 | 197 009 |

*Table 4.8: The costs with the standard and the new intervention, and the difference in costs as the incremental cost level.*

With a 4 % discount rate of the costs, the study is in accordance with the recommended rate of the guidance, but as mentioned above, the effect of the rate level will be subject to sensitivity considerations.

### Cost-effectiveness

With both the gain in QALYs and the incremental costs in place, calculations of the cost-utility ratios are again easily obtained with the equation (4). The results are shown in Table 4.9.

| ICUR | ICUR: Cost per QALY |
|---|---|
| Provider perspective (w/VAT) | 373 382 |
| Societal perspective (w/o VAT) | 306 868 |

*Table 4.9: The cost-effectiveness of the new cancer intervention with both a societal and a provider perspective. The ratios are again cost-utility ratios due to an effect in QALYs.*

### Severity

In calculating the severity measures for the cancer treatment, an additional and important assumption also has to be made here – the average age of the patient. Without establishing a specific age, one cannot extract the right QALE from the life table. The study does not specify the age of the assumed average cancer patient, but state that bevacizumab is only given to younger patients, which are those younger than 70 years, and who have good general health. To be in line with this age specification, 60 years is chosen as the starting point and the average age. The assumption of not weighing the life years not affected by the relevant disease also applies here.

When the average age is established, remaining life years are extracted from the life table, and severity calculated from that. An average 60-year old have 23.64 remaining life years (see Appendix 1). Also here no specification of gender is made.

The calculations for both absolute and relative QALY loss are similar to equation (5) and (7).

$$AQL = 23.64 - 0.94 = 23 \tag{9}$$

$$RQL = \frac{22}{23.64} = 0.96 \tag{10}$$

The results are summed up in table 4.10:

| Severity | QALE at age 60 | Absolute QALY loss | Relative QALY loss |
|---|---|---|---|
| Both genders | 23.64 | 23 | 0.96 |

*Table 4.10: The two severity measures for the average cancer patient.*

For the purpose of a direct comparison with the drug abuse intervention, the health profile for the average cancer patient can be illustrated as in Figure 4.2.


*Figure 4.2: Health profile for the average cancer patient with disease occurring at age 60.*

Also here, areas 3 plus 4 depict the severity measure of absolute QALY loss, while area 3 alone depicts the effect of the new intervention. Again it is the loss of complete life years due to the early onset of death that has the biggest impact on the absolute QALY loss. A major difference from the drug abuser is that the life years weighed with utility weights are minimal for the cancer patient. The choice of utility weights thus seems to be of minimal importance for this severity measure. The relative severity measure constitutes areas 3 plus 4 as a share of the square from age 60 up to 83 (areas 2,3 and 4), which is almost all of it. This is in direct accordance with the relative measure being 0.96 – the cancer patient loses almost all of his or her remaining lifetime.

A joint illustration of the prognosis for the two groups is shown in Figure 4.3. This figure clearly depicts the differences between the patient groups: the absolute loss of QALYs for the drug abuser is much greater than for the cancer patient, but the relative loss for the cancer patient is substantially larger than for the drug abuser (remembering that the starting point for the drug abuser is 18 years).

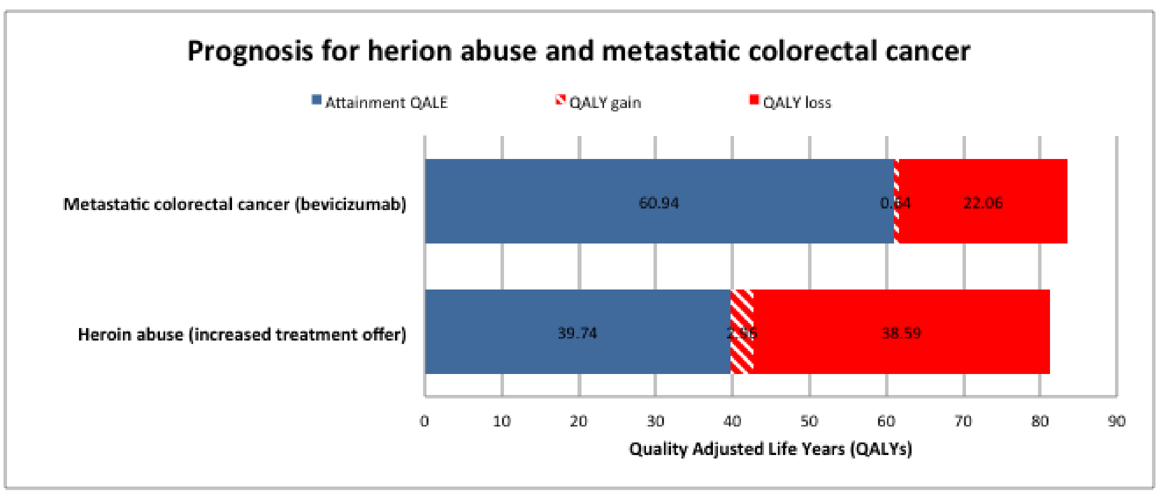


*Figure 4.3: The prognosis depicted for the compared patient groups. The attainment QALE is the QALYs achieved with standard intervention. The QALY gain is the striped areas, and the QALY loss constitutes both the rightmost parts of the columns and the striped areas.*

## 4.3 Comparing the results

With all the assumptions and recalculations made, the final results are meant to be as equivalent and unified as possible, thus providing a set of information that is comparable across the patient groups. With comparable outcome measures it should be possible to state which intervention has the highest effect, which intervention is more cost-effective, and which of the patients that have the most severe disease. Such information can be used as input in decision-making processes that decides upon overall budgetary allocations and health care priorities. The results presented here, however, should be interpreted with great caution.

In considering the cost-effectiveness of the interventions, some external threshold for what is considered to be cost-effective has to be established. The suggested guidance recommends that the reference value for an intervention should be 500 000 2005-NOK per QALY (Helsedirektoratet 2011a). According to Kristiansen, the World Bank has suggested a pragmatic threshold level of the gross national product per inhabitant (Kristiansen 2003), which in Norway was equal to 412 000 NOK in 2005 (Kristiansen and Gyrd-Hansen 2007). The USA have used USD 50 000 as a limit (Ubel et al. 2003), and NICE in England have used between 20 000 and 30 000 GBP (Appleby et al. 2007).

Both of the cost-effectiveness ratios for drug abuse are well within all of these limits. With a societal perspective, the study even states cost saving – the new intervention is both less costly and more effective than the alternative, and with a provider perspective the ratio is very low. The cost-effectiveness ratios for cancer are also within the accepted limit of the guidance's, but these are definitely higher than for drug abuse.

The suggested guidance has set up a preliminary table, Table 4.11, to illustrate how the different priority criteria can be weighed against each other. It is emphasized in the guidance that the limits between what should and should not be offered of health services are for illustrative purposes only (Helsedirektoratet 2011a). The definitions of the different levels are based on own translations.

In Table 4.11, both severity and cost-effectiveness are divided into four categories describing the different levels of the measures. The severity level depicted here is the one of absolute QALY loss. The table is an illustration of how trade-offs can be made between the priority criteria, but it is not a foundation for an explicit decision rule. With regards to severity, the highest level is categorized as a QALY loss larger than 10 QALYs, which is the case for both of the disease groups in this comparison.

| **TRADE-OFF BETWEEN SEVERITY AND COST-EFFECTIVENESS** | | **Cost effectiveness (NOK/QALY)** | | | |
|---|---|---|---|---|---|
| | | **Extremely good: 0 – 50 000** | **Very good: 50 000 – 250 000** | **Quite good: 250 000 – 500 000** | **Not so good: More than 500 000** |
| **Severity** | **Not/not so severe: QALY loss < 1** | ? | Not offered | Not offered | Not offered |
| | **A little/somewhat severe: 1<QALY loss<5** | Offered | ? | Not offered | Not offered |
| | **Very severe: 5<QALY loss<10** | Offered | Offered | ? | Not offered |
| | **Extremely severe: 10<QALY loss** | Offered | Offered | Offered | ? |

*Table 4.11: A depiction of the possible trade-offs between the absolute severity measure and the cost-effectiveness of the intervention. The table is transferred from the Directorate of Health's suggested guidance.*

However, the drug abuser is faced with almost twice the loss of QALYs compared to the cancer patient – 41 compared to 23 QALYs.

The cost-effectiveness ratios of the drug abuser is either cost-saving or categorized as "extremely good" – between 0 and 50 000 NOK/QALY. The level of severity is definitely higher than 10 QALYs. With this table as a template, treatment should clearly be offered to these patients. The conclusion in the original drug study was a positive cost-benefit ratio, which support these results. In addition, the costs were based on a 3 % discount rate. If the costs were rather subjected to a 4 % discount rate, this would only result in a lower cost level, and in turn even lower (better) cost-effectiveness ratios. It is with good certainty that the conclusion for the drug abusers is that the treatment is cost-effective.

For the cancer patient, both of the cost-effectiveness ratios lie within the category of “quite good”. With base in the trade-off table, this cost-effectiveness ratio is dependent on a high severity level for offering the treatment, which is the case with cancer, and the decision here would also be to offer the treatment. The underlying cancer study concluded with cost-effectiveness ratios of 668 000 and 549 000 NOK with a provider and a societal perspective respectively (Aaserud et al. 2007). These ratios lie in the highest cost category, and the study stated high uncertainty around the cost-effectiveness of the treatment. These results were based on the effect in life years (not QALYs) being discounted with a 4 % discount rate, and a currency in 2007-NOK. To have equal purchasing power in 2005 and 2007, less money is needed in 2005, and the costs are therefore lower. These methodological elements could have easily been the standard in the main results, which would have altered the conclusion of cost-effectiveness and the placement in Table 4.11. Awareness of such effects is crucial when making concluding statements.

The effect on an intervention has not been set up in the same way as severity and cost-effectiveness, at least not in terms of a QALY gain. But again the numbers lean towards a greater priority for the drug abuser. Their QALY gain is calculated to be 3 QALYs, while the cancer treatment had a QALY gain of only 0.64. With an economic perspective this would not be of particular relevance as the effect of the intervention is taken account for in the cost-effectiveness measure. Clinicians on the other hand would likely tend to put greater emphasis on the effect itself. A suggestion by Buyx et al. is to introduce a minimum clinical threshold where interventions that do not reach this predetermined level, are not offered (Buyx et al. 2011).

All of the three priority criteria give a rather clear indication that when comparing these two treatment schemes for drug abusers and cancer patients, a greater degree of priority speaks in favour of drug abuser. However, it does not state that priority should not be given to the cancer patients, and the relative severity measure speaks in favour on the cancer patient. Again, though, all results should be interpreted with caution.

### The foundation for discussing severity and priority

The task at hand was to illustrate the potential effect of operationalizing a severity measure in the context of health care priorities across patient groups. The final results from this comparison have provided an interesting foundation for the discussion. Substance abuse treatment has been a politically prioritized area in Norway for several years, but there is still a lack of monitoring for those on maintenance treatment and others with substance abuse problems (Helsedirektoratet 2012a). For cancer patients on the other hand, it is a defined standard today that for at least 80 % of cancer patients it shall take only 5 days for a referral to be assessed, no more than 10 days before the evaluation is started, and not more than 20 days to start treatment (Helsedirektoratet 2012a, p. 98). This gives a clear indication of the level of priority that is established for those who are cancer patients within the Norwegian health care system. The results of effect and cost-effectiveness for both of the patient groups are within acceptable limits – the intervention both provide a positive effect and are cost-effective within a threshold of 500 000 2005-NOK. The explicit severity considerations can therefore receive focused attention. In addition, due to the results for the drug abuse intervention being both more effective and more cost-effective than the cancer intervention, an explicit severity measure can potentially have an interesting impact in the context of priority decisions.

With particular focus on the severity measures, a difficult question is which of the measures to use – absolute QALY loss or relative QALY loss. Even though the guidance suggests absolute QALY loss as the standard measure of severity, this should be up for a thorough discussion. From the calculations in this comparison, the choice proves to be an important one – the two severity measures give opposite results of who is considered to be worse off. Using absolute QALY loss states that drug abuse is almost twice as severe as the evaluated cancer disease – a loss of 41 QALYs compared to 23. The relative severity measure states the exact opposite – that drug abuse is almost half as severe as cancer with 0.66 compared to 0.96. Focused attention will therefore be on the choice of severity measure.

# Chapter 5: Sensitivity considerations and calculations

With the main results resting on many assumed parameters and methodological choices, it is of great importance to look at the effect of some of the choices made. To evaluate the sensitivity of the different parameters is a fundamental part of economic evaluations, and important for determining the validity of the results and conclusions. Because this comparison rests upon existing studies, the ability to conduct such sensitivity evaluations is dependent on what data the studies themselves choose to present. Where there are no possibilities of running sensitivity calculations, general considerations will be done in order to establish the potential effect and magnitude for the output measures. This can be equally informative as specific results, mostly because the results themselves are uncertain. Again the main focus will be on the severity measures and the different parameters affecting these measures, but some attention will also be given to the two other priority criteria of effect and cost-effectiveness.

## 5.1 Utility weights

The utility weights used for weighing the life years for the drug abuser, were extracted from the literature, and similar weights were found in several studies. No other assumptions of weights therefore stand out as more appropriate than the ones already chosen. For the cancer treatment, an evaluation of the utility weights is more natural as these weights varied in the literature.

The valuation technique is an element that should receive some attention. Without any specific valuation techniques to comment upon, no reasonable direction (higher or lower) could be decided upon for the sensitivity evaluation. A note should, however, be made for the time trade-off technique. An important factor to keep in mind when using this specific valuation technique is that time trade off incorporates the individual's time preferences, and when discounting the effect of a treatment, it can be argued that this is actually double discounting (Drummond et al. 2005). An assessment of time preference is incorporated in this technique.

With this said, the effect of changing the utility weights is still of some interest, since the chosen weights are established with a great amount of uncertainty. To evaluate the effect of the chosen weights, a 50 % change of the distance between the weights will be made in both directions. This relatively large change was chosen to achieve a significant variation in the distance.

### Drug abuse

For the drug abuse intervention, the distance in utility between the standard and the new intervention was 0.1. A 50 % reduction and a 50 % increase result in the respective differences of 0.05 and 0.15. An important factor that needs to be determined is which of the weights that are changed. Because there is a much larger share of individuals who do not enter treatment than those who do, a change in those who are IDUs without maintenance treatment will have a much stronger impact on the results than a change in MMT. Equal change will be made on both weights. For a 50 % reduction in the distance the weights will be 0.825 and 0.875, and for a 50 % increase, the weights will be 0.775 and 0.925. The results are show in Table 5.1:

| DRUG ABUSE: Change in distance between the utility weights | Severity | | Effect | Cost-effectiveness | |
|---|---|---|---|---|---|
| | AQL | RQL | QALY gain | Provider | Societal |
| - 50 % | 40.89 | 0.646 | 3.03 | 4 562 | -205 543 |
| + 50 % | 42.22 | 0.667 | 2.89 | 4 789 | - 215 764 |
| No change | 41.55 | 0.657 | 2.96 | 4 673 | - 210 530 |

*Table 5.1: Changes in the utility weights in connection with drug abuse and the impact on the three priority criteria.*

The changes in the difference between the utility weights seem only to have a minor impact on the evaluated output measures. As stated in the previous chapter, and with the focus being on the severity measures, it is the loss of full life years that constitute the main impact for the drug abuser. Small changes in utility do not have significant influence.

Even though the impact of these changes is minimal, a few comments are appropriate. The changes in the societal cost-effectiveness ratios are not what they appear, namely that reduced effect leads to more cost saving and vice versa. When costs are negative and effect is positive, there are no trade-offs between the two criteria, and it is only of interest to maximize the effect. To present the ratios is therefore not necessary, and either "dominant" or "cost saving" should be written instead. The change in QALY gain is also not as expected – a decrease in the weights distance leads to a higher effect and vice versa. This is a result of the population distribution as mentioned above, and even though the distance is reduced, the lower weight is increased from 0.8 to 0.825, and this affects the result. The changes in severity are as expected – increased (decreased) distance means more (less) to lose and higher (lower) severity, and this applies for both measures.

### Cancer

Similar recalculations are done for the utility weights in connection with cancer – a 50 % change in the distance between the weights. In which end the change is made also affect these parameters, and both ends are therefore equally changed. Since for example the severity measures are a direct result of the baseline situation, the results are affected by whether the changes are made here or not. The initial weights were 0.6 and 0.8 for the standard and new intervention respectively, which equals a distance of 0.2.  For a 50 % decrease, the weights 0.65 and 0.75 are used, and for a 50 % increase, 0.55 and 0.85. The changes are depicted in Table 5.2.

| CANCER: Change in distance between the utility weights | Severity | | Effect | Cost-effectiveness | |
|---|---|---|---|---|---|
| | AQL | RQL | QALY gain | Provider | Societal |
| - 50 % | 22.62 | 0.96 | 0.46 | 516 062 | 424 131 |
| + 50 % | 22.78 | 0.96 | 0.82 | 292 509 | 240 401 |
| No change | 22.70 | 0.96 | 0.64 | 373 382 | 306 868 |

*Table 5.2: Changes in the utility weights in connection with cancer and the impact on the three priority criteria.*

As shown in Table 5.2, the utility weights have a minimal impact on the severity measures for cancer because there are a minimum number of life years that are weighed with utility weights. The relative change in the effect, though, is significant as the initial level was very low. The cost-effectiveness ratios are therefore also sensitive to the choice of weights, thus being in accordance with the results of the original study, which concluded on uncertainty around the cost-effectiveness of the treatment (no weights were used here). The changes in the cost-effectiveness ratios are a direct consequence of the change in effect. The provider perspective has actually exceeded the 500 000-level when the weights' distance is decreased.

### Comments on utility weights

The amount of life years that are weighed with utility weights is very low for the cancer intervention, and to use other utility weights than the ones chosen here will have minimal impact on the severity measures for this group. For drug abuse the potential effect is much greater. About 30 life years are weighted for this group, but for the weights to play an important role in the measuring of severity, the utility weight used for injection drug user would have to be much lower, and the distance much greater than what is calculated here. In relation to the weights used for other slightly similar diseases as mentioned earlier, it is not likely that the utility could be very much lower than what is used in this sensitivity evaluation.

With these sensitivity results, it can be stated with relatively good certainty that the chosen utility weights are good enough for illustrating the explicit severity measures. The weights play little or no impact at all on this specific evaluation criterion, and this is true for either of the severity measures. For the cancer intervention, however, the impact on effect and cost-effectiveness was significant, thus indicating great uncertainty in relation to these two priority criteria.

## 5.2 Gender

When using remaining life years (which have been juxtaposed with quality-adjusted life expectancy (QALE)) as the basis for calculating severity, gender enters as a factor of some potential influence. Women live on average longer than men, and have therefore more life years to lose at any given age. This gives room for a possible gender variation in favour of women when calculating severity. According to Tsuchiya and Williams (2005), findings in the literature also confirm this difference when including factors of quality of life. In their article, they touch upon several reasons for why there is a difference between the genders, one of them being a natural, biological cause for a shorter life expectancy for men. This might be viewed as a justified difference, and therefore not a source for unfairness or an argument against "fair innings".

To see how gender can affect the results when considering severity in this comparison, calculations are done based on the remaining life year for men and women separately, instead of being based on average remaining life years. A flaw in this consideration is that the studies are based on average individuals, while there might be a difference between men and women in the specific treatment scenarios as well. This is not captured here.

| DRUG ABUSE: Gender and severity | AQL | RQL |
|---|---|---|
| Male | 39.4 | 0.64 |
| Female | 43.7 | 0.67 |
| Both | 41.5 | 0.66 |

*Table 5.3: The severity measures for drug abuse when incorporating gender differences.*

| CANCER: Gender and severity | AQL | RQL |
|---|---|---|
| Male | 21 | 0.96 |
| Female | 24.3 | 0.96 |
| Both | 22.7 | 0.96 |

*Table 5.4: The severity measures for cancer when incorporating gender differences.*

As shown in Table 5.3 and 5.4, the absolute QALY loss is affected by gender differences, and men come to short both compared to women and compared to a joint evaluation. The relative losses also show some differences, but not to the same extent, and the use of RQL instead of AQL might prove to be less prone to difference based on gender. These results also show the importance of using similar gender-specifications when making comparisons across patient groups.

What becomes clear through these calculations, and what the life table shows as well, is that the difference between men and women seem to be approximately 4 years for almost every age level – both for remaining life years, and thus absolute QALY loss. Women will always be able to lose four more years or QALYs than men. Awareness of this almost constant difference can make it easy to take into account, for example by using average figures, or always adding four years when evaluating men. The element of gender thus seems to generate easily controllable effects.

## 5.3 Discounting

The discounting of costs and benefits is done to take account of the time preferences of these values. "…individually and as a society we prefer to have dollars or resources now, as opposed to later, because we can benefit from them in the interim." (Drummond et al. 2005, p. 38). The discounting of costs is directly linked to the existence of interest rates and that there is an actual monetary value to paying later rather than sooner. With regards to benefit, the argument is that we as human beings are impatient and desire the benefits now rather than in the future (though maybe not an agreed upon argument).

The consequences of discounting future values in cost-effectiveness evaluations depend on the nature of what is being evaluated. Any element of cost or effect occurring at point of intervention/evaluation or soon after will have much more impact on the results than what occurs in the future. With preventive treatments like cholesterol lowering medication, the benefit will (possibly) be realized far into the future, and by discounting these benefits, the end results might underestimate the actual effect of the treatment. Also, if the cost of an intervention to a large part arises far into the future, the cost-effectiveness of the treatment might give a distorted picture of the "real" cost level, for example that the intervention actually is very costly and that the cost evaluation should be done in the future. Even though using discount rates, at least for costs, is an appropriate way of going about evaluations, the consequences should not be overlooked. The point of departure for the evaluation becomes very important.

### Discounting costs

With regards to the specific discount rates used in the studies, some comments can be made.

The drug abuse study use a 3 % discount rate for costs. With the model being a simulation of several parameters over a lifetime, and with a handful of probabilities that will or will not prevail every single month depending on the state of the individual, the recalculation of the costs to a for example 4 % discount rate can prove to be a very difficult task. However, with the cost-effectiveness ratios being what they are, there is a lot of room for increases in the cost levels, and a continued conclusion of cost-effectiveness. Only a reduction in the discount rate would lead to higher costs, and with the rate at 3 %, it would be more natural to increase the rate. The NOU suggests an annual rate 3.5 % (NOU 1997: 27, p. 18) and the guidance defines 4 % as the rate for the standard analysis. It therefore seems reasonable to conclude that the drug abuse treatment is cost-effective, and that this conclusion is maintained despite of a different discount rate.

The same cannot be said for the cancer intervention. The study uses a 4 % discount rate. The results in this comparison concluded with cost-effectiveness, but the study itself questioned the cost-effectiveness of the treatment. With the results being somewhat close to the commonly accepted thresholds, a lower discount rate might push the results above what can be considered as cost-effective. However, since the evaluation takes place over a very short period of time, the costs are barely subjected to future discounting, and the effect of using a different discount rate is likely to be marginal.

### Discounting QALYs

As mentioned earlier, the drug study makes no comment on whether or not the effect in life years has been discounted, and the assumption was therefore made that they are not. The cancer study presented both discounted and undiscounted life years. The main results of this comparison rest upon the undiscounted effect measures.

A noteworthy weakness of this comparison becomes visible in the context of discounting: the analyses used do not cover a complete life span, but some reasonable assessments of how the discounting of QALYs might turn out can still be made. The discounting of QALYs can affect both the severity measures and the effect of the treatment, which in turn also can affect the cost-effectiveness ratios. Since the main results are not discounted, a sensitivity assessment will be based on discounting the QALYs with a 2 % discount rate, as suggested by the guidance. All calculations of discounting are done in MS Excel with a present value function, see equation (11), where PV is the present value, n = number of periods, $A_n$ = annuity in period n (which is equal to 1 every year), and r = discount rate.

$$PV = -\sum_{t=0}^{n} A_n(1+r)^{-n} \qquad (11)$$

### *Impact on effect and cost-effectiveness*

The impact of discounting the QALYs gained with standard and new intervention is shown in Table 5.5.

| IMPACT ON EFFECT: Discounting QALYs with an annual rate of 2 % | Standard intervention | New intervention | QALY gain/effect |
|---|---|---|---|
| **Drug abuse** | | | |
| QALYs - not discounted | 21.74 | 24.69 | 2.96 |
| QALYS - discounted | 17.49 | 19.34 | 1.84 |
| % Reduction | | | 37.8 % |
| **Cancer** | | | |
| QALYs - not discounted | 0.94 | 1.58 | 0.64 |
| QALYS - discounted | 0.92 | 1.54 | 0.62 |
| % Reduction | | | 3.4 % |

*Table 5.5: The impact of an annual discounting of 2 % on the QALYs achieved with standard and new intervention, and thus the gain in QALYs.*

The initial QALY gains for the two treatment schemes were not great for either of them: 3 QALYs for the new methadone treatment and just above half a QALY for the new cancer treatment. But since the incremental effect of the new methadone treatment was actualized well into the future, it is to a large extent subjected to the test of time when making use of a discount factor. With a 2 % discount rate, the incremental QALY gain is reduced with almost 40 % from 2.95 to 1.84 QALYs for the drug abuser. The cancer patient only gets a reduction of about 3 % from 0.64 to 0.62 QALYs gained with a 2 % discount rate. Even with the use of a relatively low discount rate, this seems to have a great impact for drug abuse in the comparison.

The subsequent impacts on the cost-effectiveness ratios of discounting the QALYs are summed up in Table 5.6.

| IMPACT ON COST-EFFECTIVENESS: Discounting QALYs with an annual rate of 2 % | Original ICUR | New ICUR |
|---|---|---|
| Drug abuse | | |
| Provider | 4 673 | 7 515 |
| Societal | - 210 530 | - 338 556 |
| Cancer | | |
| Provider | 373 382 | 386 631 |
| Societal | 306 868 | 317 756 |

*Table 5.6: The impact of discounting the gain in QALYs on the cost-effectiveness ratios.*

The cost-effectiveness ratios of the new cancer intervention are not greatly affected by the discounting as it only resulted in a 4% reduction in the incremental effect, but the changes are still worth a closer look. Because the effect itself is so small (under 1 QALY), small changes in the incremental effect can have a potentially significant impact on the cost-effectiveness ratios, but most likely not to the extent of pushing the ratios over the limit for cost-effectiveness.

For drug abuse, discounting the gain in QALYs does seem to have an impact on the cost-effectiveness ratios. With a provider perspective, the ratio goes from 4673 to 7515, which is a relatively huge increase only due to the inclusion of a discount factor. Even though the conclusion of cost-effectiveness is not altered in this scenario, a higher original cost level might have pushed the ratios over the thresholds. For the societal perspective the same reasoning as before apply – the effect should be maximized when the costs are negative. The reduced effect does not lead to more cost saving.

As shown in Tables 5.5 and 5.6, the discounting of QALYs can have a huge impact on both the output measures of effect and cost-effectiveness. This is therefore an important element to keep in mind when comparing different patient groups. For this comparison, though, the changes due to the discounting of QALYs did not alter the relative differences between the to groups when considering effect and cost-effectiveness. The drug treatment is still both more effective and more cost-effective. A more important question is therefore how the discounting of QALYs can affect the severity measures.

### *Impact on severity*

In making an assessment of how the severity measures are affected by discounting future QALYs, the approach taken here takes base is discounting the individual QALEs for the two patient groups. Because the QALEs are different for the two groups due to the age difference, the future discounting will also have varying impact. An alternative approach could be to discount the QALE at birth for both groups, which would equate the amount of QALYs being discounted. But for the sake of taking base in the initial differences between the two groups, the first approach is taken.

The 18-year old drug abuser has many life years ahead of him or her and therefore also has a lot of lifetime to actually discount. The 60-year old cancer patient has nowhere near the same amount to lose, and the discounting will in this respect have much less to say. The 18-year old have approximately 63 remaining QALYs to start off with, and with a 2 % annual discount rate, this amounts to only about 36 QALYs. This highly affects how many QALYs the individual can actually lose, and thus the severity level. The 60-year old cancer patient has approximately 23 QALYs left, and discounting these with a 2 % rate, leaves the individual with almost 19 QALYs to potentially lose. By subtracting the discounted QALYs with the standard intervention from the discounted QALE, both severity measures are obtainable. The results are presented in Table 5.7.

| IMPACT ON SEVERITY: Discounting QALYs with an annual rate of 2 % | | Age | Remaining life years/QALYs | QALYs w/std. treatment | AQL | RQL |
|---|---|---|---|---|---|---|
| Drug abuse | Not discounted | 18 | 63.29 | 21.74 | 41.5 | 0.66 |
| | Discounted | 18 | 35.72 | 17.49 | 18.23 | 0.51 |
| | % Reduction in severity | | | | 56.1 % | 22.3 % |
| Cancer | Not discounted | 60 | 23.64 | 0.94 | 22.7 | 0.96 |
| | Discounted | 60 | 18.69 | 0.92 | 17.77 | 0.95 |
| | % Reduction in severity | | | | 21.7 % | 1 % |

*Table 5.7: The impact of discounting the achieved QALYs with standard and new intervention on the calculated severity measures.*

What clearly emerges from these calculations is that the discounting of QALYs has a major impact on the severity measure of absolute QALY loss. For the drug abuser AQL is reduced with over 55 %, from 41.5 to 18.2 QALYs. For the cancer patient the reduction is 22 %. This major difference in reduction between the two patient groups leads to the outcome that they are now characterized as almost *equally severe*. This is a major contrast to the main results where drug abuse is almost twice as severe as cancer using the absolute severity measure. The change in the relative QALY loss is minimal for the cancer patient, but for the drug abuser the reduction is almost 22 %. The initial relation is therefore maintained with this measure. Discounting the QALYs over a lifetime has for this comparison the ability of completely altering the conclusion of who is characterized as the most severe. These calculations take base in the main results where both genders are included.

## 5.4 Disease independent QoL

Throughout this comparison, the continued assumption of equalizing remaining life years with quality-adjusted life expectancy has been made. However, if QALE was more properly defined, more than just the disease specific factors would assert themselves.

Quality of life is likely to deteriorate with age, as older people do not experience the same level of quality as younger individuals. Mobility is reduced, hearing and memory often declines, and old age is a fact. This comparison rests on the chronic states of utility – the weights are the same for the whole length of the evaluation. This is most likely an overestimation of the QALYs for both patient groups.

One Swedish and one Finnish study have tried to establish the health related quality of life for an average population (Burström 2006 and Sintonen 2010 referred to in Helsedirektoratet 2011a, p. 21). The results are transferred into Table 5.8.

| Age | 18-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| EQ-5D (Sweden) | 0.85 | 0.86 | 0.86 | 0.84 | 0.83 | 0.81 | 0.81 | 0.80 | 0.80 | 0.81 | 0.78 | 0.76 | 0.71 |
| 15D (Finland) | 0.97 | 0.95 | | 0.95 | | 0.92 | | 0.90 | | 0.87 | | 0.80 (85+: 0.70) | |

*Table 5.8: Health related quality of life measured for different age groups with two different multi attribute utility instruments in Sweden and Finland. According to these studies, no life years after age 18 are lived in perfect health.*

The results from these two studies clearly depict that health related quality of life deteriorates with age, but they also show that no life years are lived in perfect health. Different valuation instruments also lead to different results, as commented upon in Chapter 2. To equalize QALE with remaining life years is an overestimation of QALE, and not just in the final life years, but most likely throughout life as well. A hypothetical variation of the comparison is set up to try to illustrate the impact of incorporating disease-independent reduction of quality of life in the comparison. The example is based on reduced health related quality of life as a result of old age.

Lets say from the age of 70 that quality slowly starts to deteriorate. At 70 the drug abuser has about 11 remaining life years, while the cancer patient has about 13 when taking base in the remaining life years from ages 18 and 60 for the two groups. If they each lost 1/3 of these life years due to quality reduction, they would lose about 3.5 and 4.5 QALYs respectively. The changes in the severity measures are shown in Table 5.9.

| Health related quality reduction with older age | Reduced QALYs after 70 | AQL | | | RQL | | |
|---|---|---|---|---|---|---|---|
| | | Main | New | Reduction | Main | New | Reduction |
| Drug abuse | 3.76 | 41.5 | 37.8 | 9 % | 0.66 | 0.63 | 3.4 % |
| Cancer | 4.55 | 22.7 | 18.15 | 20 % | 0.96 | 0.95 | 1 % |

*Table 5.9: Incorporation of reduction in disease-independent quality of life and the impact on the severity measures.*

The inclusion of age-dependant quality reduces all of the severity measures as the patients now have less QALYs to lose. The absolute severity measure is affected the most for both groups. For the older cancer patient, the percentage reduction in absolute loss of QALYs is 20 %. This is because these last years constitute a larger part of the total remaining life years for the cancer patient. For the drug abuser the reduction is under 10 %. The relative severity measures are minimally affected for both groups since both the QALE and AQL is reduced, and the relative change between these two are minimal.

## 5.5 Fixed innings threshold

One element that is important to highlight specifically in connection with the suggested severity measures, and for the purpose of taking account of some of the existing theory and opinions of how severity should be measured, is the use of a fixed innings threshold. With the use of QALE, the relevant starting point changes with every age level, and it is a constantly moving threshold. With a fixed innings level the threshold is defined in advance. Williams (1997) refers to a fair innings and a normal life span as usually being expressed as three score years and ten, which is equal to 70 years. A conversion into QALYs would normally mean a somewhat lower number, say maybe 65 QALYs, but since this element of non-disease specific quality of life is not included in the main calculations, remaining life years are still used as a proxy for QALE.

In one of the hearing responses to the suggested guidance sent in by the research group for prioritization in health care at the University of Bergen, it is expressed that a QALY loss should be measured in relation to a more closely defined “norm” for a normal life span (Hearing response University of Bergen 2011). A suggestion is made that this should be decided from the QALE at a certain level or certain age, and they mention an example of 90 QALYs. Another suggestion they make is to define the norm of a life span equal to the QALE within a 95% percentile of the Norwegian society.

To illustrate the effect of using a fixed innings threshold when calculating the severity measures, the thresholds of 70, 80 and 90 QALYs will be used. Both 70 and 90 are referred to above, and 80 QALYs is the threshold closest to the life expectancy of the two patient groups in this specific comparison, and closer to the average in Norway (Statistics Norway 2012).

| Fixed innings threshold | AQL | | RQL | |
|---|---|---|---|---|
| | Drug abuse | Cancer | Drug abuse | Cancer |
| 70 QALYs | 30.3 | 9 | 0.58 | 0.9 |
| 80 QALYs | 40.3 | 19 | 0.65 | 0.95 |
| 90 QALYs | 50.3 | 29 | 0.7 | 0.97 |

*Table 5.10: The severity measures of absolute and relative QALY loss when based on fixed innings thresholds.*

Table 5.10 shows the two severity measures when taking base in different fixed innings thresholds. The absolute QALY loss is directly linked to the threshold level – the higher the level, the higher is the potential loss. The difference between the patient groups is still maintained where the drug abuser lose significantly more QALYs than the cancer patient. An interesting result for the cancer patient is that with a threshold of 70 QALYs, the AQL is 9 QALYs, which changes the placement in Table 4.11 from “extremely severe” down to “very severe”. This can be important in the context of priority decisions. The directions for the changes in relative QALY loss are also as expected – it increases with the threshold level. For all thresholds, cancer is still characterized as the most severe disease with this measure.

A fixed threshold demands the difficult decision of choosing an appropriate threshold, and the choice is relevant for both the severity measures. To use a moving innings threshold like QALE is also a decision that need to be taken, and it all comes down to what the basis for the severity calculations should be. Both approaches demand a normative choice, and to illustrate some of the different effects of these choices, can be of relevance.

## 5.6 The summarized sensitivity considerations

As shown through these sensitivity considerations, the element most likely to affect the main results is the discounting of future QALYs. Due to the great age difference between the patient groups, the impact of discounting future benefits turn out very differently. The much younger drug abuser is subjected to more discounting than the much older cancer patient, and the impact on absolute QALY loss resulted in an almost equalized severity level. A fixed innings threshold is also a methodological element that should receive outstretched attention, as the severity measures are prone to large changes depending on the foundation for the severity evaluations. Utility weights, gender, discounting of costs and disease independent quality of life are factors that to a certain extent affect the three priority criteria, but none of them to the extent where the priority considerations alter between the two groups. This is also true for the fixed innings threshold, but this should receive special focus in the context of operationalizing severity.

# Chapter 6: Discussion

The main part of the discussion is dedicated to the choice of severity measure, as the compared measures of absolute and relative QALY loss gave contradictory results as to which of the patient groups were considered to have the most severe disease. There are several other ways of considering severity, but this comparison is set out to evaluate these two explicit measures, and continued focus will therefore be on them. In addition, the appropriateness of the chosen studies is discussed, and some considerations are made in the context of the Norwegian priority practice.

## 6.1 Choice of studies

This comparison has taken base in other published studies on cost and effect of specific interventions, and the results presented here are therefore a direct consequence of the results presented in the underlying studies. The methodological approach and the use of a "gold standard" was an attempt to make a systematic choice of studies based on reasonable criteria, but the results in the studies themselves have not been subjected to any systematic evaluation. Despite the use of a "gold standard", the underlying studies are based on different methods. The drug study is a simulation model based on reasonable assessments and findings in the literature, while the cancer study is a health economic evaluation based on a hypothetical average patient. Some comments should therefore be given to the reasonableness of the results in the underlying studies.

Almost all of the results in the nine studies on drug abuse interventions listed in Table 3.1 in Chapter 3 provided reasonable cost-effectiveness ratios, and are therefore fully in line with the provider perspective presented in this comparison. The societal perspective might stand in a unique position with its cost-saving result, but a study by Bukten et al. (2012) does underpin these results. They showed that crime is halved when heroin dependents enter maintenance treatment, but that the level of crime reduction depend on whether or not the patients stay in treatment. This does support the result of the drug study where crime reduction was the main driving factor for a cost saving cost-effectiveness ratio with the societal perspective.

An average drug abuser receiving maintenance treatment can with reason be described like this: the disease of drug abuse can and often do occur at an early age, maintenance treatment has no curative effect, but does have a positive, though small effect, on both length and quality of life. The corresponding costs of this treatment are not very high, and the potential external effects to society of providing treatment to these patients might be significant. Old age is also rarely achieved for those who do not get out of the drug abuse. These characteristics are not stating anything of controversy, and the characteristics for the drug abuse do seem to be appropriate.

Some reasonable comments can also be provided for an average cancer patient. The progression of the health state to metastases means reduced prognosis for most individuals as the cancer has spread to other parts of the body. The treatment at this stage of the disease can be uncertain and of minor effect. The relatively low effect of the intervention thus seems reasonable. With the study specifying that the pharmaceutical is considered to be expensive, and that new cancer treatments in general are very costly, the relatively high cost-effectiveness ratios also seem reasonable. That the difference between a provider perspective and a societal perspective was minimal can seem like an oversimplification, but beside the fact that productivity considerations might not be of particular significance for these "older" patients (and this has not been a focal point in this comparison), there are no other obvious external effects of treating cancer. The disease can affect anyone.

With these general comments, it does seem like the comparison is based on what can be considered as reasonable characteristic for these two patient groups. The choices of age for the two groups, however, are only indirectly linked to the studies, and the choice of age should receive some specific attention.

## 6.2 AQL vs. RQL: Returning to the theoretical starting point

### Fair innings and absolute QALY loss

Absolute QALY loss as a measure of severity has its theoretical foundation in the fair innings-argument presented in the theory chapter. The main characteristic of fair innings is that it includes a whole lifetime perspective when considering the situation of a patient, which leads to the common critique of age being the main driver behind the severity conclusion. Williams (1997) suggests incorporating quality of life as well as quantity in terms of life years, and thus resting the fair innings-argument on QALYs instead of life years. Williams does try to convince the reader of this equity concept, but recognises that ethical principles in nature are contestable with each having convincing arguments (Williams 1997, p. 120). He refers to various surveys that have tried to establish people's preferences. A main result of these surveys is that the younger individuals generally deserve priority before the old, which is a driving factor for severity as shown in this comparison. One of the main arguments from Williams in this article is the need for more explicit decision making processes within health care priority settings, and that the fair innings concept is easily quantifiable, thus making it an explicit measure that leaves room for clarification and accountability (Williams 1997, p. 120).

The generalized fair innings approach (which uses QALYs instead of life years) needs more theoretical clarification and empirical research (Nord 2005). This is based on the reasoning that current and future suffering and illness are significant in formal theories of justice, in Norwegian government guidelines, and is evidential from a number of public surveys (Nord 2005, p. 262). The fair innings argument's inclusion of foregone health states as well is not equally well established. Both severity-of-illness and proportional shortfall have in this respect a stronger theoretical foundation. Another serious problem with the generalized fair innings argument according to Nord is that in the context of pain relief, this approach implies that an 80-year old individual has less moral claim for pain relief than a 50-year old, and that “this runs counter to both moral intuition and official government guidelines in Norway and Sweden” (Nord 2005, p. 262). Despite of this critique, Nord also refers to Amartaya Sen as one of the few who have discussed fair innings, and Sen’s position that it is an approach that “deal with social class in a fulsome way” (Nord 2005, p. 258). By including a life time perspective, more fundamental inequalities are given significance, and severity is considered in a much more comprehensive way.

### Proportional shortfall and relative QALY loss

The relative QALY loss is based on the equity concept of proportional shortfall. This measure of severity considers prospective health and not what lies previous of the current health state. Stolk et al. (2004) makes some arguments in favour of this concept. The defence mainly rests on the concept of proportional shortfall incorporating both fair innings and severity-of-illness. Since both of these equity concepts have received support in empirical studies, it is possible to argue in favour of an intermediate concept (Stolk et al. 2005). The other argument Stolk et al. (2004) makes is that this relative measure is more in line with actual principles realized in society. This reasoning rests on the experiences from the Netherlands where elderly patients receive extensive health care services.

This equalizing of observed priority practice with what are actually people’s preferences seem like a bold assumption. A more appropriate statement would be to say that proportional shortfall is a positive theory that describes what is real practice, but whether it has some normative value or not is unclear. The appropriateness of using proportional shortfall as an equity concept thus seems to depend what the aim of the evaluation is. If the aim is to establish how equity enters the current decision making regime, then proportional shortfall might be appropriate. But if the aim is to establish a reasoning and methodology for what future priority decisions should be based on, then to rest in what best describes current practices seems bold if based on that reasoning alone.

### The suggested guidance

As stated several times, the suggestion in the now-withdrawn guidance is to use absolute QALY loss as the measure of severity in the standard evaluation of health care interventions, and several reasons for this are put forward (Helsedirektoratet 2011a, p.70-71). The first reason given is that AQL is in accordance with the severity concept of the second Lønning commission (Lønning 2), namely "…a condition with reduced prognosis related to the life expectancy or quality of life if health care is delayed" (Norheim 2005, p. 645). The use of QALYs as the measured unit, and the magnitude of QALYs lost, definitely fulfils this description. But it cannot be said that the relative measure does not incorporate these considerations. This would be dependent on the definition of "reduced prognosis", since both AQL and RQL are based on QALYs.

Six more reasons are presented in the guidance, but only one of them seems to be relevant for absolute QALY loss alone: the intention of the severity measure to characterize a deadly cancer diagnosis as more severe for a 30-year old individual than for a 90-year old individual. This is an outcome that is not captured through the relative QALY loss, which considers a sudden occurrence of disease or death equally severe for both these individuals. Another argument by the guidance is that severity measured as AQL has the ability of clarifying the potential of disease prevention if that is an option for the evaluated disease, but it will later be discussed that this is not an argument supporting AQL.

The four other reasons supporting AQL as the severity measure seem to be applicable for both measures; the established intervention as the reference point instead of no treatment; prognosis compared to QALE; that the measure is easily obtainable within the framework of economic evaluations and thus suffer under the similar restrictions; and finally that they are for use only in first-order priority decision on an overall level. These reasons seem to be common for both measures, and does not provide convincing arguments for using AQL before RQL.

## 6.3 Some factors affecting the severity measures

### Average ages of the two patient groups

Because the calculation of severity is not normally built into economic evaluations, the average age of both groups had to be assumed. In the case of drug abuse, the underlying simulation model started at age 18, which in turn was a natural choice for the starting point of the severity calculations. But 18 years is very young, and not many 18 year olds are actually eligible for maintenance treatment as this is provided for those with heavy dependencies. However, due to the drug study being a simulation model covering more than 40 years, and that all the other output figures took base in this starting age, this was also done for the severity measures. An important consideration will therefore be how the choice of a different age might affect the severity results. This is done through an illustrative graph as more of a general reflection as opposed to an exact recalculation. A natural choice for a different age is one higher than 18 years.

The average age mentioned for opioid dependants receiving methadone treatment is 40 years (Ravndal and Lauritzen 2004), which will be depicted as the new starting age as shown in Figure 6.1. Because nothing else is altered except for the starting point of the evaluation, the effect or utility of the new intervention is in this case minimally affected. The area between years 18 and 40 and between the utility weights of standard and new intervention (area 5), constitute the reduced effect of the new intervention as a consequence of the new starting age. This amounts to less than one third of the initial QALY gain. The QALE does not change notably, as it is

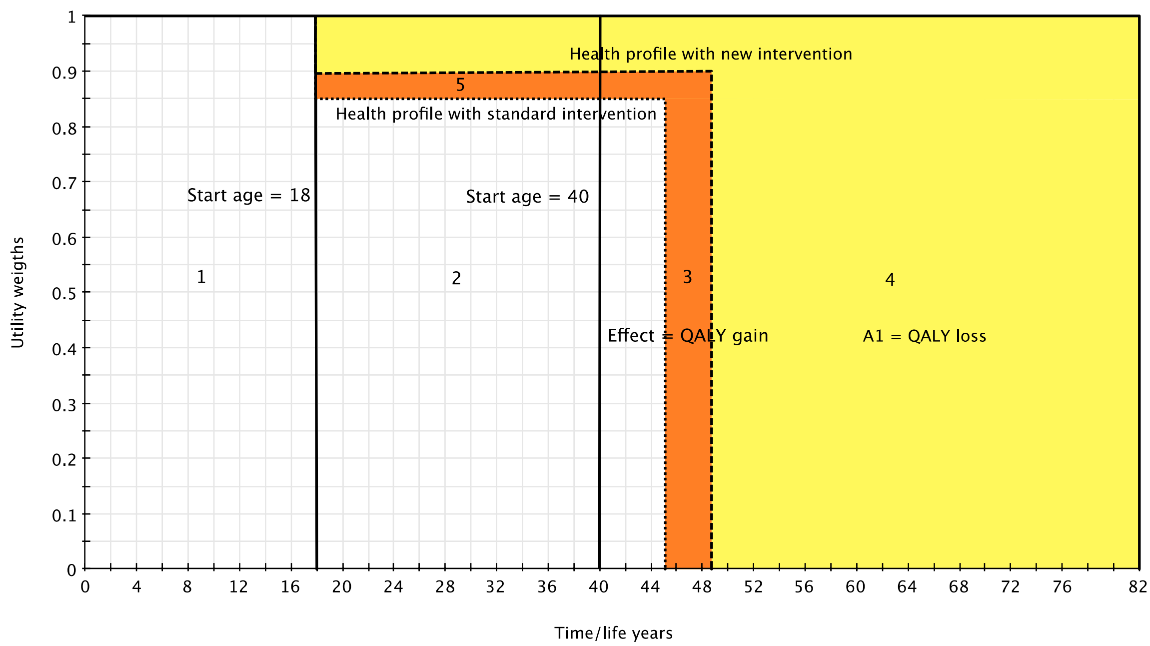


*Figure 6.1: Health profile of an average drug abuser with the disease occurrence/point of departure is increased from 18 to 40 years.*

almost equal for 18 and 40-years olds: looking at both genders, 18 year-olds have 63.29 remaining life years and 40 year-olds have 42.02, which add up to 81.3 and 82 respectively. This similarity in QALE seems to be valid up to about 50 years, where it slowly starts to increase (see Appendix 1). With a new starting age at 40, there is a slight change in the absolute QALY loss, but only to the extent of the quality of life reduction from age 18 to 40 not being included. AQL does not change significantly in this specific case. The relative QALY loss however, looks to be much more affected. At age 18 there is a significant amount of time before death occurs – 21 QALYs as calculated in the comparison. This constituted about one third of what was potentially left of remaining QALYs, and RQL was therefore 0.66. At age 40, the amount of QLAYs lost constitutes a larger share of the remaining life years, thus increasing the relative loss significantly. The illustration is dependent on the whole setup not moving towards the right in the figure, but only that the starting point for the evaluation move to the right. This is assumed to be the most natural approach when taking base in the underlying drug study.

For the cancer intervention the original choice of starting age fell on 60 years. According to the Norwegian Cancer Registry, the probability of developing cancer before the age of 75 is 35 % for men and 28 % women (Cancer Registry of Norway 2011). Based on these numbers, the choice of 60 years as the average age for a cancer patient seems to be too low. The underlying cancer study made the distinction that those eligible for the new treatment were younger than 70 years. For the specific pharmaceutical of bevacizumab, another appropriate age would perhaps be 65 years, but also younger ages than 60 can be depicted. In choosing 60 years for the main comparison, the average age was at least not a choice made to achieve a low absolute QALY loss, but rather an attempt not to make a preconceived conclusion. In considering a different starting age for this average cancer patient, a lower age of 50 years is chosen. This is based on this specific pharmaceutical being used only for some eligible patients that might be of this age, and because to use 65 years will presumably not give very different results than 60. The age of 50 years for an average cancer patient is depicted in Figure 6.2.

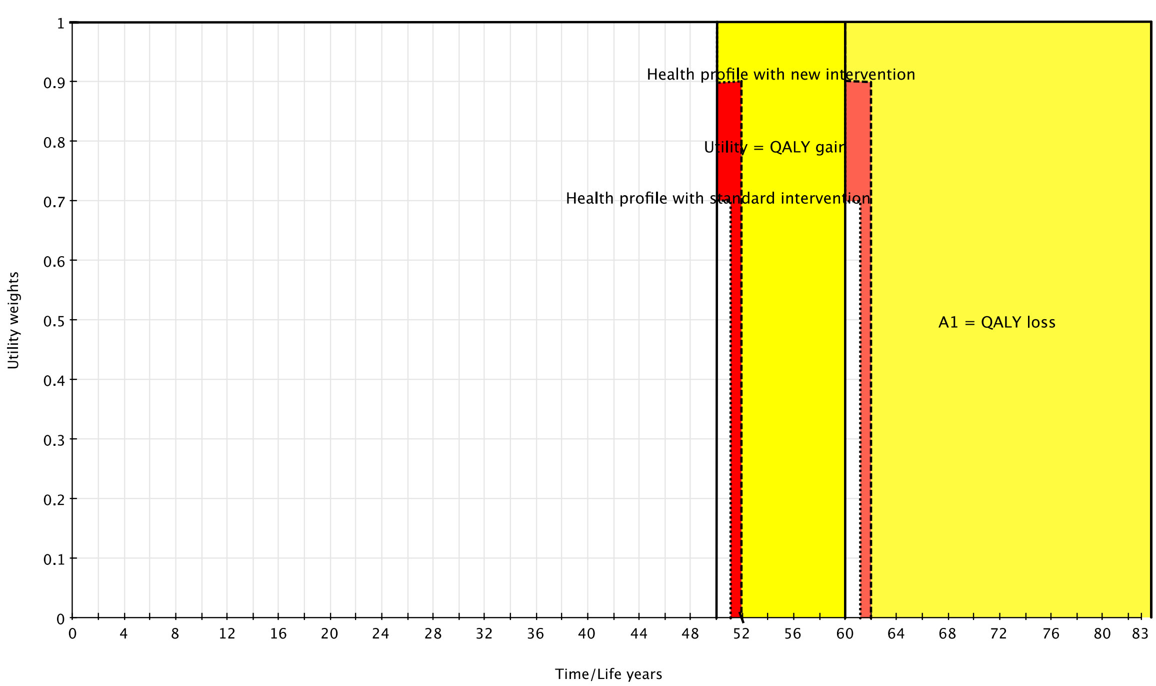


*Figure 6.2: Health profile of an average cancer patient where the disease occurrence/point of departure is reduced from 60 to 50 years.*

The average remaining life years for a 50 year-old and 60-year old are 32.55 and 23.64 respectively, resulting in a slight difference in QALE, but for this illustration it is assumed to be 83 years for both ages. Since the evaluation started at the inset of the treatment, which now is at 50, all the lines are moved leftwards in the figure. A direct result of this change is an increase in the absolute QALY loss with about 10 QALYs (because of a 10 year age difference), which would now add up to about 32 QALYs. This confirms the ageism critique that younger individuals have a higher severity level AQL, even though the disease is the same. The relative loss will also increase as the remaining life years now constitute a smaller share of the total QALE, but this change will be minor as the original level was already as high as 0.96.

As shown through these graphs, the average age or point of departure does have an impact on the severity measures. The most controversial choice seems to be 18 as the average age for a drug abuser as this is very low. An increased age affects the relative severity measure, but not to the extent that it reaches the level of cancer (but much closer). The absolute loss for the cancer patient also increases with a lower average age, but not to the extent that it reaches the level for drug abuse. The original results are therefore maintained – AQL characterizes drug abuse as the most severe disease, and RQL favours cancer. Also, when considering the age of an average cancer patient, 60 years seems like a reasonable choice, as it should be below 70, and there are no other convincing arguments of choosing an even lower age of 50.

The important thing to keep in mind is that the choice of age level can affect the main results, and these illustrative graphs show that both measure of severity are prone to these changes.

### Meeting the ageism critique

Even though the relative severity measure also can be subjected to changes due to the age of the patient, it is the absolute severity measure and the fair innings reasoning that is generally mentioned is the context of age, and criticized for supporting the young over the old. Ageism is criticized for making age alone a priority factor. The impact of age on the severity measures has also been confirmed through the main results of this comparison. When defining severity based on a lifetime horizon an old individual have already achieved a respectable amount of life years, and thus have little or less to lose than a younger individual. And for a younger individual, the potential for loss is on the average much greater than for an older person. When comparing individuals of different age groups, the critique of ageism does pose as a reasonable argument.

The severity measure of absolute QALY loss as suggested in the guidance does have two elements that seem to lessen the over-emphasis on age. Firstly, through the QALY concept, great emphasis is also put of the quality of life, and not just the quantity of life. It is not age alone that creates a large loss of QALYs, but the quality of life is important as well. In this comparison of drug abuse and cancer, the element of quality was not a stand-alone factor for the end results, and this was also shown through the sensitivity evaluation. But in theory, and in other cases, quality can be a dominating factor, especially if considering chronic impairments that reduces quality of life for many years. If for example a 40-year old individual is expected to live until 80, but does so with poor quality (0.5) due to a chronic disability, this person will lose 20 QALYs. This is less than what the 60-year old cancer patient loses (22.5 QALYs), even though he or she is older. To base the evaluation on QALYs instead of life years, balances quantity with quality, and reduces the emphasis on age. It is not the age of the patient that is important, but the health experienced by the patient throughout a lifetime.

The other element that seems to contradict the focus on age is the use of a moving QALE as opposed of a fixed innings threshold when determining the potential loss of QALYs. With a moving innings threshold everyone has something to lose. The younger you are the more you have to lose, but no matter how old you get, you still have some remaining life years. The average 90 year old has 4.22 remaining life years (see Appendix 1), and thus have an absolute QALY loss of just above 4 QALYs if he/she dies tomorrow. This approach supports the notion that everyone is entitled to some kind of treatment, and this is an important element for those who criticize fair innings for indirectly implicating that older people should not receive treatment or even pain relief (Nord 2005). The subject of pain relief, however, should stand in a unique position and not be included in general priority discussions, just like experimental medicine, which would never make it through the same economic evaluations as established treatments.

With a fixed innings threshold, the outcomes also depend on the choice of threshold, whether it is a high threshold like 90 QALYs or lower like 70 QALYs. A low threshold can with reason be criticized for supporting ageism. Any disease you get after the age of 70 is not considered to be severe. With a higher threshold, the innings limit might be above the life expectancy for most individuals, and everyone stands to lose some amount of QALYs and have some level of severity. If the threshold is so high that it covers most patients, though, it becomes less helpful when difficult priority decisions has to be made.

### The relevance of age as opposed to immediate death

The operationalization of severity can understandably be perceived as very mechanical and lacking important discretionary assessments, and an exact number defining the severity level is most likely far from what is normally thought of when considering the severity of a disease. But by establishing severity as a determining factor for providing treatment to patients, the term should be properly and explicitly defined.

Severity is meant to say something about the prognosis of the specific disease. In making assessments of the prognosis, are such considerations actually independent of age? Take for example Alzheimer's. This is a disease that often is a direct result of old age, and is in some way one of the courses a natural life can take. But

Alzheimer's can also occur with not so old individuals, maybe between ages 50 and 60. Not many would disagree that Alzheimer's at 55 is more severe than Alzheimer's at 80. The same can be said for cancer. Cancer at 20 will by most be considered more severe than cancer at 70. But what about intermediate cases like 40 vs. 50? These are very difficult assessments to make, but the main point is that age does matter. The disease's severity level is not just an independent factor easily established when the name of the disease is known. The element of age and time of disease occurrence is also relevant. This is captured through the absolute QALY loss, but ignored in the relative measure.

Even though the relative severity measure is also based on the QALY concept, it is how soon the death occurs that has the potential of affecting the measure the most – at least in the high levels of severity. This might not be the intention of the measure – it is the relative loss that is important. This is recognised as a counterintuitive implication of proportional shortfall (van de Wetering et al. 2011). The cancer patients who had a severity level of 0.96 is a result of these patient dying soon after diagnosis. If the drug abuser were to reach the same level of severity, the utility weight would have to be close to zero, which is highly unlikely. With the use of the relative measure, immediate death seems to undermine all other disease implications in a severity context. Even though an unexpected death is a tragedy no matter how old you are, an unexpected death at 30 is more of a tragedy than at 80. The point to get across is that there are also other elements than a sudden death that is negative or unwished for in a severity context. Also, a sudden death might be more of a burden for those surrounding the individual than for the individual itself if it is a painless death. The feelings of those surrounding the individual are not an element of interest in the definition of severity. In the upper end of the severity scale the relative measure seem to be somewhat one-dimensional.

Age as an element relevant in a priority setting is also commented upon in the NOU 1997:18, and an important consideration is made in the context of treatment. Age is relevant insofar as it is considered as a prognostic criterion and not considered independently. Older age will often reduce the ability of the body to make use of the treatment and increase the risk of side effects (NOU 1997: 18). In the context of evaluating the ability to gain from the treatment, age is of relevance and of legitimate concern.

### Gender

When considering gender, the results in the sensitivity chapter showed that men falls short compared to women with the fair innings concept of absolute QALY loss. This is one of the adverse effects of using fair innings as an equity concept – men have a shorter life expectancy than women, and therefore have less to lose when including a lifetime horizon (Tsuchiya and Williams 2005). Because of this difference between the genders, men will always have of lower severity than women of the same age. The same is in principle true when considering the relative severity measure, though it might not be as evident as with the absolute measure.

What can be said in the context of the absolute severity measure is that by using a common fixed threshold level, the gender differences can maybe be alleviated. This can, however, favour the male patients. For low fixed threshold levels both genders have lower absolute QALY losses than with the use of QALE. For higher fixed levels, however, it is more likely that men are located above their life expectancy, and therefor get higher severity values, while women are more likely to be below and get lower severity values. Neither AQL nor RQL seem to handle the gender difference in a way that makes one measure more appropriate than the other.

### Discounting of benefits

The results in the sensitivity chapter proved that the discounting of QALYs is highly relevant for the severity measures when comparing different patient groups .The appropriateness of discounting future health benefits has been widely discussed in the context of cost-effectiveness evaluations (Drummond et al. 2005; Nord 2011). The discussion is based on whether benefits should be discounted with an equal rate as the costs, at a lower rate or not discounted at all, but an in-depth review of this discussion provides enough material for another thesis all together.

The impact on severity of discounting QALYs was established by discounting the QALE as well as the gain in QALYs with standard intervention from a specific age. Since the two patient groups had different QALEs, the effect of discounting turned out very differently. This can almost be viewed as a kind of inverse age weighing where an older patient has a QALE that is not subjected to the same amount of discounting as a younger patient's QALE. This comparison provides a contributing example of the possible effects such methodological choices can have. The absolute measure seems to be most prone to the discounting of QALYs, and the relative measure is not equally affected due to exactly the relative difference between AQL and QALE not being particularly altered.

### Preventive interventions

One of the arguments in the suggested guidance for choosing absolute QALY loss as the main measure of severity was the clarification it provided in connection with preventive treatments. Van de Wetering et al. (2011) who supports the severity consideration of proportional shortfall also comment on this "shortcoming" of the relative measure, but they suggest some sort of normative choice that can alleviate this shortcoming. Out of the many who receive preventive treatment, only a smaller group will actually experience the negative health state that is being treated. "Calculating proportional shortfall over the entire group would result in a very low *average* proportional shortfall since only a small percentage of the treated group would actually experience a health loss. This in turn results in low priority for (primary) preventive action, but the very aim of the intervention is to avoid health loss for those who would experience it without the preventive intervention." (van de Wetering et al. 2011). With this reasoning, the authors suggests that the proportional shortfall should be calculated with base in the subgroup only, who are those who actually experience the negative health effect. This approach is taken in the Netherlands. In principle, the same problem arises with the absolute severity measure when considering an average patient: the average patient will have a low absolute loss, but if only the affected subgroup was considered, the absolute loss would be much larger. It seems that there are no arguments in connection with preventive interventions that gives more support to either of the severity measures.

### Absolute QALY loss vs. relative QALY loss: A final choice

Both the suggested measures of severity are founded in ethical considerations that have valid arguments in their favour. Throughout the discussion provided herein, the finale choice of a severity measure does seem to speak in favour of the absolute QALY loss based on the reasoning that age does matter in the context of health care priorities.

A group of Dutch researches, who strongly supports the equity concept of proportional shortfall and RQL, gives a reasonable conclusion: “The highlighted shortcomings of proportional shortfall clearly should not be misinterpreted as a plea to replace it with a different equity concept such as fair innings. Indeed, whatever principle is chosen, similar shortcomings and normative choices will arise in transitioning from principle to practice. Since different notions of equity—all of which have some support in some instances—will always conflict in certain circumstances, conflicts with societal preferences will be inevitable” (van de Wetering et al. 2011, p. 7). The final choice of an explicit severity measure should in the end be based on the population’s priority preferences, as well as empirical research and knowledge, and a legitimate process for making priority decisions.

# Chapter 7: Conclusion

## 7.1 The Norwegian priority setting revisited

The different statements from the Director General of Health Bjørn-Inge Larsen and CEO Stener Kvinnsland, referred to in the introductory chapter, strongly indicate that the stronger group of cancer patients seem to triumph over the weaker group of drug abusers in relation to health care priorities. There seem to be a kind of agreement in the Norwegian society that cancer treatment should be offered whatever the cost and whatever the effect of the treatment. There is an enormous focus on ensuring treatment for cancer patients, which stand in strong contrast to the unwillingness so to speak, to talk of the health care needs of the equally rightful drug abusers. Why is it like this?

One explanation may be that the situation that drug abusers are positioned in, to a large extent is perceived as being their own responsibility, and that they can simply stop abusing these substances that ruin their lives. The element of "fault" or "own responsibility" is a very difficult assessment criterion (Cappelen and Norheim 2005). Firstly, previous behaviour shall not be of relevance when seeking help. Risky behaviour undoubtedly both increases the need for health care and further limits the effect of the care given. Secondly, if one should include the element of own responsibility, this should be applicable for all diseases. There is a general awareness today that smoking can lead to lung cancer, that obesity can be linked to eating habits, and that lack of physical activity can have an impact on heart conditions. Some of these conditions are located within the disease areas that seem to gain on today's decision-making. If own responsibility is an argument for providing less treatment to drug abusers, then this argument should apply for other prioritized patient groups as well.

Drug abusers are also a patient group that create a lot of discontent among other individuals in society. People living with drug abusers in their local community may be exposed to robbery, theft, threats, vandalism and other criminal actions. Drug abuse and imprisonment have a high correlation (Friestad and Hansen 2004, p. 61), thus resulting in a significant burden for taxpayers. There is believably a discontent among many when the discussion of providing treatment to this group arises, and in comparison the "innocent" cancer patient will always be subjected more goodwill.

Apart from this notion of innocence and feeling of some deserved justice towards those who are affected by cancer, possibly one of the most important elements of this slight bias towards supporting treatment for cancer is the close proximity to the disease, and also high probability of developing cancer at some point in life. The media is overflowing with information on cancer: how to prevent it, what can cause it, what the recent research is showing and so on. Heart breaking stories of children, husbands or wives, parents or close friends being ripped away by cancer can be read or heard daily in the media. Cancer is everywhere. It can with reason be stated that there are some sort of common interest that cancer treatment is always ensured and that researchers find new and better treatments in the future. One recent media headlines stated that 2 out of 3 now survive cancer (NTB 2012).

To end up as a drug abuser is in comparison a very unlikely scenario for most people. Those who are in the risk zone are often young, experimental and risk seeking individuals, but after reaching a certain age, say the early twenties, there is very small chance of ending up as a heroin abuser. The individuals most prone to such a destiny may also those without a political voice, and the basis for voicing their needs and rights as a group, is minimal compared to those speaking on behalf of cancer.

This is also the foundation for yet another very important difference between these two patient groups. Interest groups are important participants when it comes to priority questions (Helsedirektoratet 2012a), and they have a great deal of power.

The Norwegian Cancer Society has a very strong position in Norway, with both a lot of support in society and with a great deal of money and resource, and consequently also a great influential significance. The interest organizations for drug abuser are not nearly in the same position. Money and resources does not find its way with the same ease, and in the field of health care, as in most other areas, money plays a significant role.

With relevance to some of the highly visible support for cancer, an example can be made of the recent attention around Matias – a 20-year old man with malignant melanoma. The media attention is a result of the public health care system not providing Mathias with the pharmaceutical Ipilumumab that has a cost of 800 000 Norwegian kroner (TV2 2012a). The established effect of the treatment is between two and four months of increased life expectancy, and it can also have extensive and even deadly side effects. Because the treatment is offered in Denmark, and since there is proof of other patients who have lived for several years after receiving the treatment, the media attention and the outstretched support among people have been enormous. Several people have even initiated to collect money for Matias so that he can get the treatment that he needs (TV2 2012b). This is an example of how immersive cancer is. It outplays all other diseases. The individuals who took initiative to collect money had themselves lost family members to cancer. It seems that it is this close proximity to cancer that makes it such a cared about disease. Treatment was in the end offered to Matias through a clinical trial (TV2 2012c).

It can possibly be concluded that today's priority practice is in close relation to what society actually prefers and what they/we expect of the public health care system. There is, however, a numerous amount of other disease areas and destinies that also deserve support and attention, and which can often be marginalized through an over focus on a single disease like cancer.

## 7.2 Summarizing main arguments

An articulated and well-founded explicit priority practice could be a step towards bringing out in the open that every decision to treat a patient brings along a decision of not treating someone else. Despite this harsh and brutal reality, health care priorities are still something positive. "It is to make the most of opportunities: When we say no to something, we also say yes to something better. It is unethical not to prioritize. Not to prioritize implies arbitrariness and increases the risk of the sickest not being treated first. To actively prioritize is justice as good prioritization means using the resources where the needs are greatest, where the intervention have great benefit and where the costs are in reasonable relation to what we obtain" (own translation) (Helsedirektoratet 2012a, p. 16).

This thesis conducts a cross-comparison of two very different patient groups in the context of health care priorities. Established priority criteria in Norway are severity, effect and cost-effectiveness, and these have created the foundation for the comparison. Special emphasis has been given to the severity criterion, and the operationalization of an explicit severity measure, which assumes that severity is a concept that can actually be measured. The two measures of absolute QALY loss (AQL) and relative QALY loss (RQL) have been calculated and compared for the two patient groups of heroin abusers and metastatic colorectal cancer patients.

The specific results of the comparison indicate that more priority should be provided to the heroin abuser. An increase in the offer of methadone treatment resulted in a positive health effect at a highly acceptable cost. With a societal perspective the result was actually cost saving due to the reduction in crime costs. The cancer intervention of bevacizumab proved to have only a slight positive effect, and more uncertainty rest around the cost levels. The two measures of severity gave contradictory results as to who was considered to have the most severe disease. AQL deemed heroin abuse as most severe with the loss of 41 QALYs compared to 23 QALYs for cancer. The conclusion was the exact opposite with the use of RQL with

0.66 as the relative loss for the heroin abuser and 0.95 for cancer. More priority to the heroin abuser rests of the argument that age does matter, and that AQL might be a more suitable severity measure.

The results should not be over-interpreted, and they are not themselves suitable for making priority decisions. These main results are based on existing studies that have their own shortcomings and flaws, and in addition, further recalculations have been done to make the data comparable across the two groups. The results from the severity calculations can, however, provide some useful input as to how the two opposing measures can actually unfold if used as input in priority decisions.

The contribution of this thesis is the discussion of how methodological choices can affect the different severity measures. The element of discounting future QALYs has the potential of completely alternating the compared results when using AQL. Awareness of this is of relevance, especially when cross-comparisons are done for diverse patient groups.

In calculating severity, the use of an individual, moving innings threshold, specified according to age and gender, as opposed to a predetermined fixed threshold, is also highly relevant. This choice can and will affect both severity measures, and poses as another important methodological challenge. A moving QALE ensures that everyone has some life years to lose, but there is still a need for making a normative choice as to what the loss should be in relation to.

The difference between genders when it comes to life expectancy is also illustrated through the sensitivity considerations. Women live on average longer than men, and when severity takes base in a lifetime horizon, men will always come out short. Managing this difference is important when making priority considerations.

An important specification to make is that this is a thesis in economics. The end results and conclusions are in this respect based on this subject's framework and the corresponding tools and methods. The issue of health care priorities, however, stretches far beyond the economic field. Medicine is one of the main subject areas, and also Law, ethics, social sciences and politics are essential part takers when discussion and implementing health care priorities. But economics does have a unique role in the context of health and priorities. Economics is used for rationalizing the choices of providing treatment to different patients and to ensure that money is spent where they provide the most value. To ignore the economic factors in health care can leave room for unjust and even unethical decisions. The economic field's ability to visualize and define premises for making decisions, are unique, and of great importance in these decision-making processes.

# Appendix 1: Life Table

Norwegian life table from 2009 (Statistics Norway 2010).

| Age x | Survivors at age x | | | Death at age x to x+1 | | | Life expectancy – remaining years at age x | | | Probability of death at age x, per 1000 (Ungraduated) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | lx | | | dx | | | ex | | | qx | | |
| | Both sex | Males | Females | Both sex | Males | Females | Both sex | Males | Females | Both sex | Males | Females |
| 0 | 100 000 | 100 000 | 100 000 | 313.00 | 376 | 245 | 80.86 | 78.60 | 83.05 | 3.13 | 3.76 | 2.45 |
| 1 | 99 687 | 99 624 | 99 755 | 21.00 | 29 | 14.00 | 80.11 | 77.89 | 82.26 | 0.22 | 0.29 | 0.14 |
| 2 | 99 666 | 99 595 | 99 741 | 17.00 | 19 | 14.00 | 79.13 | 76.92 | 81.27 | 0.17 | 0.19 | 0.14 |
| 3 | 99 649 | 99 575 | 99 728 | 13.00 | 10 | 17.00 | 78.14 | 75.93 | 80.28 | 0.13 | 0.10 | 0.17 |
| 4 | 99 636 | 99 566 | 99 711 | 10.00 | 7 | 14.00 | 77.15 | 74.94 | 79.29 | 0.10 | 0.07 | 0.14 |
| 5 | 99 626 | 99 559 | 99 697 | 15.00 | 20 | 10.00 | 76.16 | 73.94 | 78.30 | 0.15 | 0.20 | 0.10 |
| 6 | 99 611 | 99 539 | 99 687 | 10.00 | 13 | 7.00 | 75.17 | 72.96 | 77.31 | 0.10 | 0.13 | 0.07 |
| 7 | 99 601 | 99 526 | 99 680 | 12.00 | 10 | 14.00 | 74.18 | 71.97 | 76.32 | 0.12 | 0.10 | 0.14 |
| 8 | 99 589 | 99 516 | 99 666 | 2.00 | 3 | 0.00 | 73.19 | 70.97 | 75.33 | 0.02 | 0.03 | 0.00 |
| 9 | 99 587 | 99 513 | 99 666 | 15.00 | 13 | 17.00 | 72.19 | 69.98 | 74.33 | 0.15 | 0.13 | 0.17 |
| 10 | 99 573 | 99 500 | 99 649 | 8.00 | 9 | 7.00 | 71.20 | 68.99 | 73.34 | 0.08 | 0.10 | 0.07 |
| 11 | 99 564 | 99 491 | 99 643 | 8.00 | 6 | 10.00 | 70.21 | 67.99 | 72.34 | 0.08 | 0.06 | 0.10 |
| 12 | 99 556 | 99 484 | 99 633 | 13.00 | 18 | 6.00 | 69.21 | 67.00 | 71.35 | 0.13 | 0.18 | 0.07 |
| 13 | 99 544 | 99 466 | 99 626 | 6.00 | 3 | 10.00 | 68.22 | 66.01 | 70.36 | 0.06 | 0.03 | 0.10 |
| 14 | 99 538 | 99 463 | 99 617 | 13.00 | 9 | 16.00 | 67.23 | 65.01 | 69.36 | 0.13 | 0.09 | 0.16 |
| 15 | 99 525 | 99 454 | 99 601 | 9.00 | 12 | 6.00 | 66.23 | 64.02 | 68.37 | 0.10 | 0.12 | 0.07 |
| 16 | 99 516 | 99 442 | 99 594 | 31.00 | 39 | 23.00 | 65.24 | 63.02 | 67.38 | 0.31 | 0.40 | 0.23 |
| 17 | 99 484 | 99 402 | 99 572 | 43.00 | 51 | 35.00 | 64.26 | 62.05 | 66.39 | 0.43 | 0.51 | 0.35 |
| 18 | 99 441 | 99 352 | 99 536 | 49.00 | 71 | 25.00 | 63.29 | 61.08 | 65.42 | 0.49 | 0.72 | 0.25 |
| 19 | 99 392 | 99 280 | 99 511 | 62.00 | 84 | 38.00 | 62.32 | 60.12 | 64.43 | 0.62 | 0.85 | 0.38 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | 99 330 | 99 196 | 99 473 | 62.00 | 83 | 39.00 | 61.36 | 59.17 | 63.46 | 0.62 | 0.84 | 0.39 |
| 21 | 99 269 | 99 113 | 99 434 | 47.00 | 67 | 27.00 | 60.40 | 58.22 | 62.48 | 0.48 | 0.68 | 0.27 |
| 22 | 99 222 | 99 045 | 99 408 | 40.00 | 66 | 14.00 | 59.42 | 57.26 | 61.50 | 0.41 | 0.66 | 0.14 |
| 23 | 99 181 | 98 980 | 99 394 | 42.00 | 49 | 35.00 | 58.45 | 56.30 | 60.51 | 0.43 | 0.50 | 0.35 |
| 24 | 99 139 | 98 930 | 99 359 | 61.00 | 96 | 24.00 | 57.47 | 55.33 | 59.53 | 0.61 | 0.97 | 0.24 |
| 25 | 99 078 | 98 834 | 99 335 | 57.00 | 76 | 38.00 | 56.51 | 54.38 | 58.54 | 0.58 | 0.77 | 0.38 |
| 26 | 99 021 | 98 758 | 99 297 | 43.00 | 58 | 27.00 | 55.54 | 53.42 | 57.56 | 0.43 | 0.59 | 0.27 |
| 27 | 98 979 | 98 701 | 99 271 | 63.00 | 96 | 30.00 | 54.56 | 52.45 | 56.58 | 0.64 | 0.97 | 0.30 |
| 28 | 98 916 | 98 605 | 99 241 | 75.00 | 107 | 42.00 | 53.60 | 51.50 | 55.60 | 0.76 | 1.09 | 0.43 |
| 29 | 98 840 | 98 498 | 99 199 | 71.00 | 96 | 45.00 | 52.64 | 50.56 | 54.62 | 0.72 | 0.98 | 0.46 |
| 30 | 98 769 | 98 401 | 99 154 | 55.00 | 68 | 42.00 | 51.68 | 49.61 | 53.65 | 0.56 | 0.69 | 0.42 |
| 31 | 98 714 | 98 333 | 99 112 | 69.00 | 112 | 23.00 | 50.71 | 48.64 | 52.67 | 0.70 | 1.14 | 0.23 |
| 32 | 98 645 | 98 221 | 99 089 | 76.00 | 96 | 55.00 | 49.74 | 47.70 | 51.68 | 0.77 | 0.97 | 0.56 |
| 33 | 98 569 | 98 125 | 99 034 | 53.00 | 74 | 31.00 | 48.78 | 46.74 | 50.71 | 0.54 | 0.76 | 0.32 |
| 34 | 98 516 | 98 051 | 99 003 | 63.00 | 88 | 36.00 | 47.80 | 45.78 | 49.72 | 0.64 | 0.90 | 0.36 |
| 35 | 98 453 | 97 962 | 98 967 | 74.00 | 94 | 52.00 | 46.83 | 44.82 | 48.74 | 0.75 | 0.96 | 0.53 |
| 36 | 98 380 | 97 869 | 98 914 | 84.00 | 118 | 48.00 | 45.87 | 43.86 | 47.77 | 0.86 | 1.20 | 0.49 |
| 37 | 98 295 | 97 751 | 98 866 | 73.00 | 99 | 44.00 | 44.91 | 42.91 | 46.79 | 0.74 | 1.02 | 0.45 |
| 38 | 98 223 | 97 652 | 98 822 | 87.00 | 97 | 78.00 | 43.94 | 41.96 | 45.81 | 0.89 | 0.99 | 0.78 |
| 39 | 98 135 | 97 555 | 98 744 | 85.00 | 106 | 63.00 | 42.98 | 41.00 | 44.85 | 0.87 | 1.09 | 0.64 |
| 40 | 98 050 | 97 449 | 98 681 | 84.00 | 112 | 54.00 | 42.02 | 40.04 | 43.88 | 0.86 | 1.15 | 0.55 |
| 41 | 97 966 | 97 337 | 98 627 | 101.00 | 150 | 50.00 | 41.05 | 39.09 | 42.90 | 1.04 | 1.54 | 0.50 |
| 42 | 97 865 | 97 187 | 98 577 | 115.00 | 146 | 81.00 | 40.09 | 38.15 | 41.92 | 1.17 | 1.50 | 0.83 |
| 43 | 97 750 | 97 041 | 98 496 | 141.00 | 180 | 99.00 | 39.14 | 37.20 | 40.95 | 1.45 | 1.86 | 1.01 |
| 44 | 97 608 | 96 861 | 98 396 | 120.00 | 143 | 95.00 | 38.20 | 36.27 | 40.00 | 1.23 | 1.48 | 0.96 |
| 45 | 97 489 | 96 718 | 98 302 | 137.00 | 161 | 111 | 37.24 | 35.33 | 39.03 | 1.40 | 1.66 | 1.13 |
| 46 | 97 352 | 96 557 | 98 191 | 158.00 | 160 | 156 | 36.29 | 34.38 | 38.08 | 1.63 | 1.66 | 1.59 |
| 47 | 97 193 | 96 397 | 98 034 | 171.00 | 194 | 147 | 35.35 | 33.44 | 37.14 | 1.76 | 2.01 | 1.50 |
| 48 | 97 022 | 96 203 | 97 887 | 198.00 | 242 | 152 | 34.41 | 32.51 | 36.19 | 2.05 | 2.52 | 1.55 |
| 49 | 96 824 | 95 961 | 97 736 | 202.00 | 251 | 149 | 33.48 | 31.59 | 35.25 | 2.08 | 2.61 | 1.52 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | 96 622 | 95 710 | 97 587 | 245.00 | 280 | 207 | 32.55 | 30.67 | 34.30 | 2.54 | 2.93 | 2.12 |
| 51 | 96 377 | 95 430 | 97 380 | 270.00 | 296 | 243 | 31.63 | 29.76 | 33.37 | 2.80 | 3.10 | 2.49 |
| 52 | 96 107 | 95 134 | 97 137 | 307.00 | 356 | 254 | 30.72 | 28.85 | 32.45 | 3.19 | 3.75 | 2.62 |
| 53 | 95 800 | 94 778 | 96 883 | 312.00 | 372 | 249 | 29.82 | 27.95 | 31.54 | 3.26 | 3.93 | 2.57 |
| 54 | 95 488 | 94 406 | 96 634 | 381.00 | 424 | 336 | 28.91 | 27.06 | 30.62 | 3.99 | 4.50 | 3.48 |
| 55 | 95 107 | 93 981 | 96 298 | 359.00 | 467 | 246 | 28.03 | 26.18 | 29.72 | 3.78 | 4.97 | 2.56 |
| 56 | 94 748 | 93 515 | 96 052 | 403.00 | 489 | 314 | 27.13 | 25.31 | 28.80 | 4.26 | 5.23 | 3.27 |
| 57 | 94 345 | 93 026 | 95 738 | 432.00 | 542 | 315 | 26.25 | 24.44 | 27.89 | 4.58 | 5.82 | 3.29 |
| 58 | 93 913 | 92 484 | 95 423 | 505.00 | 597 | 406 | 25.37 | 23.58 | 26.98 | 5.38 | 6.45 | 4.26 |
| 59 | 93 408 | 91 888 | 95 017 | 544.00 | 679 | 399 | 24.50 | 22.73 | 26.09 | 5.82 | 7.39 | 4.20 |
| 60 | 92 864 | 91 209 | 94 617 | 573.00 | 724 | 412 | 23.64 | 21.90 | 25.20 | 6.18 | 7.94 | 4.35 |
| 61 | 92 290 | 90 485 | 94 205 | 605.00 | 751 | 450 | 22.78 | 21.07 | 24.31 | 6.56 | 8.30 | 4.78 |
| 62 | 91 685 | 89 734 | 93 755 | 742.00 | 881 | 594 | 21.93 | 20.24 | 23.42 | 8.09 | 9.82 | 6.33 |
| 63 | 90 943 | 88 853 | 93 162 | 794.00 | 903 | 678 | 21.11 | 19.44 | 22.57 | 8.73 | 10.16 | 7.28 |
| 64 | 90 149 | 87 950 | 92 484 | 838.00 | 990 | 678 | 20.29 | 18.63 | 21.73 | 9.30 | 11.25 | 7.33 |
| 65 | 89 311 | 86 960 | 91 806 | 908.00 | 1069 | 739 | 19.47 | 17.84 | 20.89 | 10.17 | 12.29 | 8.05 |
| 66 | 88 403 | 85 891 | 91 067 | 994.00 | 1226 | 753 | 18.67 | 17.05 | 20.05 | 11.25 | 14.28 | 8.27 |
| 67 | 87 409 | 84 665 | 90 314 | 1116.00 | 1385 | 842 | 17.87 | 16.29 | 19.22 | 12.77 | 16.36 | 9.32 |
| 68 | 86 292 | 83 280 | 89 472 | 1132.00 | 1440 | 820 | 17.10 | 15.56 | 18.39 | 13.12 | 17.29 | 9.17 |
| 69 | 85 160 | 81 840 | 88 652 | 1299.00 | 1515 | 1 081 | 16.32 | 14.82 | 17.56 | 15.25 | 18.51 | 12.20 |
| 70 | 83 861 | 80 325 | 87 570 | 1288.00 | 1420 | 1 160 | 15.56 | 14.09 | 16.77 | 15.36 | 17.68 | 13.24 |
| 71 | 82 573 | 78 905 | 86 411 | 1522.00 | 1858 | 1 197 | 14.80 | 13.33 | 15.99 | 18.44 | 23.54 | 13.85 |
| 72 | 81 051 | 77 047 | 85 214 | 1513.00 | 1850 | 1 187 | 14.07 | 12.64 | 15.21 | 18.66 | 24.02 | 13.92 |
| 73 | 79 538 | 75 197 | 84 027 | 1786.00 | 2232 | 1 365 | 13.33 | 11.94 | 14.41 | 22.46 | 29.68 | 16.24 |
| 74 | 77 752 | 72 965 | 82 662 | 1905.00 | 2324 | 1 517 | 12.62 | 11.29 | 13.64 | 24.51 | 31.84 | 18.35 |
| 75 | 75 847 | 70 642 | 81 146 | 2108.00 | 2465 | 1 772 | 11.93 | 10.65 | 12.89 | 27.80 | 34.90 | 21.84 |
| 76 | 73 739 | 68 176 | 79 373 | 2164.00 | 2547 | 1 805 | 11.25 | 10.01 | 12.17 | 29.34 | 37.36 | 22.74 |
| 77 | 71 575 | 65 629 | 77 568 | 2468.00 | 2912 | 2 068 | 10.58 | 9.38 | 11.44 | 34.49 | 44.37 | 26.66 |
| 78 | 69 106 | 62 717 | 75 500 | 2736.00 | 3375 | 2 155 | 9.94 | 8.80 | 10.74 | 39.59 | 53.81 | 28.55 |
| 79 | 66 371 | 59 342 | 73 345 | 2858.00 | 3125 | 2 627 | 9.33 | 8.27 | 10.04 | 43.07 | 52.65 | 35.82 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 80 | 63 513 | 56 218 | 70 718 | 3185.00 | 3482 | 2 943 | 8.72 | 7.70 | 9.39 | 50.15 | 61.94 | 41.62 |
| 81 | 60 328 | 52 736 | 67 775 | 3370.00 | 3674 | 3 137 | 8.16 | 7.18 | 8.78 | 55.86 | 69.67 | 46.29 |
| 82 | 56 957 | 49 062 | 64 637 | 3590.00 | 3939 | 3 327 | 7.61 | 6.68 | 8.18 | 63.04 | 80.29 | 51.47 |
| 83 | 53 367 | 45 123 | 61 311 | 3921.00 | 4114 | 3 802 | 7.09 | 6.21 | 7.60 | 73.47 | 91.18 | 62.02 |
| 84 | 49 447 | 41 009 | 57 508 | 3876.00 | 3908 | 3 913 | 6.61 | 5.79 | 7.07 | 78.39 | 95.30 | 68.04 |
| 85 | 45 570 | 37 100 | 53 595 | 4307.00 | 4390 | 4 333 | 6.13 | 5.35 | 6.55 | 94.52 | 118,316 | 80.85 |
| 86 | 41 263 | 32 711 | 49 262 | 4078.00 | 4034 | 4 228 | 5.72 | 5.00 | 6.08 | 98.83 | 123,335 | 85.83 |
| 87 | 37 185 | 28 676 | 45 034 | 4274.00 | 3996 | 4 643 | 5.29 | 4.63 | 5.60 | 114,937 | 139,334 | 103,108 |
| 88 | 32 911 | 24 681 | 40 391 | 4107.00 | 3742 | 4 548 | 4.91 | 4.30 | 5.19 | 124,779 | 151,617 | 112,600 |
| 89 | 28 804 | 20 939 | 35 843 | 4148.00 | 3545 | 4 765 | 4.54 | 3.97 | 4.78 | 144,010 | 169,290 | 132,937 |
| 90 | 24 656 | 17 394 | 31 078 | 3653.00 | 3348 | 4 029 | 4.22 | 3.68 | 4.44 | 148,160 | 192,452 | 129,632 |
| 91 | 21 003 | 14 047 | 27 049 | 3644.00 | 2804 | 4 427 | 3.87 | 3.44 | 4.03 | 173,512 | 199,609 | 163,656 |
| 92 | 17 359 | 11 243 | 22 622 | 3378.00 | 2546 | 4 159 | 3.58 | 3.17 | 3.71 | 194,626 | 226,446 | 183,832 |
| 93 | 13 980 | 8 697 | 18 464 | 2967.00 | 2218 | 3 674 | 3.32 | 2.96 | 3.44 | 212,202 | 255,008 | 198,983 |
| 94 | 11 014 | 6 479 | 14 790 | 2498.00 | 1693 | 3 202 | 3.08 | 2.80 | 3.17 | 226,781 | 261,279 | 216,527 |
| 95 | 8 516 | 4 786 | 11 587 | 2217.00 | 1385 | 2 919 | 2.84 | 2.61 | 2.91 | 260,294 | 289,358 | 251,947 |
| 96 | 6 299 | 3 401 | 8 668 | 1678.00 | 1049 | 2 213 | 2.67 | 2.47 | 2.72 | 266,383 | 308,284 | 255,309 |
| 97 | 4 621 | 2 353 | 6 455 | 1418.00 | 698 | 1 997 | 2.45 | 2.35 | 2.48 | 306,872 | 296,821 | 309,310 |
| 98 | 3 203 | 1 654 | 4 458 | 953.00 | 618 | 1 244 | 2.32 | 2.13 | 2.36 | 297,667 | 373,454 | 279,102 |
| 99 | 2 250 | 1 037 | 3 214 | 788.00 | 355 | 1 132 | 2.09 | 2.10 | 2.08 | 350,440 | 342,791 | 352,130 |
| 100 | 1 461 | 681 | 2 082 | 532.00 | 261 | 750 | 1.94 | 1.93 | 1.95 | 364,085 | 383,389 | 360,091 |
| 101 | 929 | 420 | 1 332 | 358.00 | 155 | 518 | 1.77 | 1.82 | 1.76 | 385,667 | 369,687 | 388,585 |
| 102 | 571 | 265 | 815 | 238.00 | 112 | 339 | 1.57 | 1.60 | 1.56 | 416,859 | 422,484 | 415,913 |
| 103 | 333 | 153 | 476 | 166.00 | 67 | 242 | 1.33 | 1.40 | 1.31 | 497,607 | 435,282 | 508,902 |
| 104 | 167 | 86.00 | 234 | 59.00 | 35 | 80.00 | 1.15 | 1.09 | 1.16 | 354,351 | 406,513 | 342,327 |
| 105 | 108 | 51.00 | 154 | 42.00 | 31 | 50.00 | 0.50 | 0.50 | 0.50 | 393,469 | 602,705 | 324,402 |

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