

## Why Should Economic Evaluations of Medical Innovations Have a Societal Perspective?

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### 1. INTRODUCTION

The aim of medical innovations is to improve health. A medical innovation can be defined as the application of new medical knowledge, often but not always embodied in a product, for example a pharmaceutical drug.

Improved medical knowledge is the product of investments in medical research and/or knowledge created during the use of health technologies; for example from systematic evaluations and follow-up studies.

Studies have shown that improvements in health have created enormous value for society (Luce et al. 2006). Some of this value has been created from investments in medical research and the development of new medical technology, and some through the experiences gained from using these technologies in clinical practice. Some of the increased medical knowledge has improved health through changes in consumption and production patterns, for example reduced smoking and less use of hazardous chemicals.

Increasingly questions are asked about the value of new technologies for health improvements in relation to the price and cost of using them within the health care system. The quest for "value for money" in spending health care resources has led to the establishment of formal institutions and mechanisms for making choices on access and use of new technologies. Pharmaceutical drugs have been leading this trend, but similar demands are increasingly put on other products, diagnostic measures and different activities for prevention and health promotion.

While it has been widely accepted that economic evaluations should include all potential health effects, positive as well as negative (side effects), there have been different approaches to the inclusion of the other consequences of using the technology. While the basic principles behind economic evaluation state that all consequences, both costs and benefits, should be included, a common practice has been to limit the perspective on cost to that of a specific “payer”.

Health technology assessment and reimbursement agencies usually recommend a “health care” perspective for the economic evaluation. For example, the Canadian guidelines for the economic evaluation of health technologies state that “in the reference case, use the perspective of the publicly funded health care system”. Other costs may be considered “where it is likely that they have a substantial impact on the results” (CADTH 2006). NICE guidelines on methods for technology appraisal in the UK and Wales state, in the reference case, that “the perspective adopted on costs should be that of the NHS (National Health Service) and PSS (Personal Social Services)” (NICE 2008). Before the last revision of the NICE guidelines, if a wider perspective was expected to influence the results significantly, additional analyses should be presented. The Swedish Dental and Pharmaceutical Benefits Agency (TLV), on the other hand, recommends a societal perspective and states that “all relevant costs associated with treatment and illness, should be identified, quantified and evaluated”. Accordingly TLV also recommends the inclusion of costs of loss of production and mortality costs, which are defined as total consumption less total production during gained life years (LFN 2003).

A societal perspective for economic evaluation is the classical approach to assessing the profitability of societal investments, assuming that governments normally should and do look at overall social returns. Cost-benefit analysis was invented to provide guidance on the use of resources that will maximise societal welfare, just because individual decisions in some cases are suboptimal because the decision maker does not take all relevant costs and benefits into account. Cost-benefit analysis is also the standard approach in the assessment of environmental and transport safety programmes affecting health. While there may be arguments for a different approach to economic evaluation of programmes within the health care sector, this may lead to suboptimal decisions about allocation of resources. Abandoning the societal perspective for economic evaluation in health care will create inefficiencies in the use of resources and discriminate against investments for improved health within the health care sector, compared to within other sectors of the economy.

One argument against a social perspective, and for a more limited payer perspective, is that the resources available to the payer are specifically allocated for the improvement in health per se, and that consideration of other potential gains from the intervention is not appropriate. This makes the very strong assumption that for the specific payer resources are totally flexible to be reallocated between different projects, since cost-savings for the payer are considered in the calculation of the cost-effectiveness ratio. This may be to some extent realistic when NICE takes a limited NHS and PSS perspective in England and Wales, but is rather implausible when applying a payer perspective to all health care expenditures, in short as well as long run, for Canada or Sweden with a regionalized health care, or the US with a fragmented system of both public and private payers. In the same way, this approach assumes that there is no possibility, in short or long run, to reallocate resources from other sectors to projects that improve health. While a societal perspective may unrealistically assume that such reallocations may and will take place, there is from an analytical point of view a strong case to maintain this perspective as the general principle. Specific restrictions on allocation of resources can always be considered and analysed as a special case.

Another argument against a societal perspective in economic evaluations of improvements in health focuses on the distributional consequences, arguing that, for example, considering indirect costs and costs in added years of life discriminates against specific population groups, in particularly the elderly outside the labour force. This argument also implicitly assumes that no transfer of benefits from improved earnings can be translated to improved health care for the elderly. As an example, vaccination against the swine flu is mainly based on the large potential costs for the economy of an epidemic. A national vaccination programme may prevent not only morbidity and mortality related to the flu, but also prevent a reduction in GDP.

In a societal perspective, net cost of consumption minus production from an increase in survival should be included since such costs are real for society as a whole. This can easily be criticized for discrimination against life extending treatments for the elderly, and this is probably the major reason why it is excluded. But a consequence of this is underinvestment in life saving innovations for the younger population, and a bias against quality of life improving interventions among the elderly. Excluding net costs in added years of life is a non-transparent and questionable way to make priorities for life saving innovations. The method recently suggested by NICE, to adopt a higher threshold value for cost per QALY gained for patients with a short life expectancy (less than 24 months) regardless of age may be a better alternative

(NICE 2009). It is also easy to present estimates of cost-effectiveness both with and without costs in added years of life, to give the decision maker explicit information about the impact on the result of the different assumptions.

Investments in improved health have important distributional and ethical implications which should be presented and taken into account when a decision is made, but this does not take away the argument for a societal perspective as the base case in economic evaluations.

In this paper we argue for using a societal perspective for the economic evaluation for all investments in health improving technologies, both inside and outside the health care system. Adopting a societal perspective implies that not only the costs that refer to a specific payer or the health care system should be considered. Also costs for informal care, loss of production, and mortality costs, should be included. A societal perspective is required for the economic evaluation to assist decisions on the efficient allocation of societal resources for health care. This is not in contradiction to also looking at costs and benefits from the point of view of different stakeholders, such as payers, or assessing distributional (equity) aspects of a specific investment. But this is secondary to the primary analysis of the benefits and costs for society as a whole.

To illustrate the importance of adopting a societal perspective and including all relevant costs, examples will be given from the disease areas of Alzheimer's disease (AD) and multiple sclerosis (MS). The examples highlight the importance of also including indirect productivity costs and costs for informal care in economic evaluation of medical interventions.

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## 2. THE SOCIETAL PERSPECTIVE IN METHODS FOR ECONOMIC EVALUATION OF HEALTH TECHNOLOGIES

### 2.1 In the beginning was cost-benefit analysis (CBA)

*“Cost-benefit analysis is a widely used technique of applied welfare economics, which is used to throw light on the social desirability of undertaking an economic project. A project can be defined as an act of investment, introduction of a new commodity or a change in policy”.*

The New Palgrave Dictionary of Economics, (Eatwell et al. (eds) 1987, page 687).

Welfare economics is a theoretical framework for the analysis of the optimal allocation of resources from a societal perspective, as opposed to from the perspective

of an individual consumer or producer. The social value of the construction of a bridge, as an example, is not equal to the price paid for the crossing, or the total revenue that the owner can derive from its services. It is the consumer and producer surplus that is generated, i.e. the value for the consumer above what he is paying, and the profit for the producer, that represents the value.

Welfare economics also gives qualitative guidance on pricing and the rationale for public policies, for example when public subsidies are necessary, to maximise the social value. Dupuit (1844) used the construction of a bridge to illustrate the concept of consumer surplus. Investing in new medical technologies, for example drugs, has the same basic economic characteristics: high investment costs to produce the necessary knowledge, but low marginal costs for its use. In both cases there is of course the need to finance the investment, either through public funds or through user charges (prices). For a recent application of these concepts to drug development, see Jena and Philipson (2008). Their study shows that the manufacturers of drugs for treatment of HIV/AIDS have only been able to capture a small part of the consumer surplus created by these innovations. Their argument is that use of economic evaluations, particularly with a narrow and limited definition of value of innovation, will lead to underinvestment to develop such innovations. While the argument is complicated, and both the calculations and the distribution of the benefits of innovation between developers and users can be discussed, these studies point to the importance of the perspective of the analysis if it is to provide correct incentives for innovation.

The societal perspective in economic evaluation also goes back to early applications in the 1930s to flood control projects, where the inclusion of all benefits – wherever and whenever they occur – was important for a correct assessment to inform decisions about investment (Eckstein 1958). Many investments in improved health carry the same characteristic. Prevention and treatment of infectious diseases produce a benefit not only for the person undergoing vaccination or treatment, but also for other people by reducing the risk of infection. Without a societal perspective, we cannot make correct assessments and decisions about investment in such programmes. It is interesting to note, that while the recent “swine flu pandemic” is a serious threat to the health of some of the people affected, a major argument for the huge investments in vaccination programmes has been the potential effect on the economy.

In the 1960s the theory and application of cost-benefit analysis was focused on investment projects (programmes) for economic development (Little and Mirrlees 1974). In this work the focus was not on externalities but on distorted prices, or the absence of

prices and thus the need to define “shadow prices”. While there is a large literature about the theoretical and methodological foundations of cost-benefit analysis, in particular the merits of the “surplus” versus the “programming” approach, both approaches are firmly grounded in the objective to find criteria and estimates of social value and profitability. When cost-effectiveness analysis is mentioned as an alternative in situations when some precise, usually non-pecuniary, objective is exogenously stipulated, the societal perspective is maintained.

### **COST-BENEFIT ANALYSIS**

In a CBA costs and benefits are measured in monetary units. Benefits are defined as the amount of money gainers of the programme are willing to pay to make sure that the programme is undertaken (willingness to pay (WTP)) and costs are defined as the compensation the losers of the programme require to accept that the project is carried out (willingness to accept (WTA)). A project (e.g. a medical intervention) should be implemented if the benefits exceed the costs. In the case of mutually exclusive programmes (i.e. the case when only one programme can be implemented) the programme with the greatest level of net benefits (benefits minus costs) should be implemented. All independent programmes with a positive net benefit should be implemented. If there is a budget constraint the net benefit should be maximised given the budget constraint. CBA implies that a one dollar benefit or cost is given the same weight for everyone in society.

## **2.2 Human capital and cost of illness**

The theory of human capital started to take shape during the 1950s, and health was identified as an important contributor to economic growth together with education. The value of investments in health could thus be measured as improvement in productivity. Health benefits were thus given a monetary valuation which could be directly compared with the costs for such investments. Health care and education were now seen as investments in human capital, with an economic return, rather than “unproductive” consumption. It was also possible to make estimates of the economic losses from different health problems; what are called burden of disease or cost of illness studies. This perspective was not new, however, and studies using capitalised earnings to estimate the cost of illness, with or without deduction for consumption, had long been performed. For a review see Dublin and Lotka (1946). But new studies were now published that used this framework to provide arguments for investments in prevention and treatment to improve health, for example Weisbrod (1961), and later for estimates of the return to investments in medical research, using the polio vaccine as an example (Weisbrod 1971).

*“Quantitative data on disease losses would seem to be valuable in educating a population to the importance of support for health activities”*  
Weisbrod (1961, p. 86)

While it was recognised that productivity gains were an important outcome from improved health, use of this concept was met by objections – one being to the valuation of human life only from the production side. What about the value of health and education which is not translated into employment and income? Gains in productivity are important but we are also willing to pay for improvements in health “per se”.

### **MEASUREMENT OF WTP FOR IMPROVEMENTS IN HEALTH**

The measurement of health changes in monetary terms can be based either on revealed preferences or on stated (expressed) preferences. The revealed preference approach is based on observing how individuals trade health risks against money (wealth). Examples are labour market studies where individuals get wage premiums to accept more risky jobs (Viscusi 1992). In the stated preference approach, also named the contingent valuation method (CVM), survey methods are used to measure the hypothetical WTP for a good or a service. The CVM was originally developed in the environmental field to measure the value of changes in the environment (Hanemann 1994). The monetary valuation of observed or hypothetical health changes in the health care sector is usually based on contingent valuation studies (Diener et al. 1998; Zethraeus 1998). However, revealed preferences may also be useful for deriving the societal WTP for a quality adjusted life year (QALY).

The economic importance of changes in health levels flows first from the importance of health as a consumption goal in itself and second from the effect of health on production (Fuchs 1966). The scene was thus set for the development of evaluation methods that took into account both types of outcome. The extensive research around the value of a statistical life (VSL) is one example of this; see Schelling (1968) and Jones-Lee (1976) for two of the most important early contributions. Value of life estimates are directly relevant as comparators to costs in programmes that focus on reductions in fatalities, for example investments in road or workplace safety. Since they estimate the value of life from a societal perspective, “the life you save may be your own”, the relevant cost concept to compare to VSL estimates is a social cost concept. For more information on the methodology of estimating VSL and empirical estimates from private and public decision makers, see the boxes on the next page.

## THE VALUE OF A STATISTICAL LIFE (VSL)

The value of a statistical life (VSL) is an outcome measure used to provide guidance on the value of benefits in terms of reduced mortality and increased survival (life saved). In particular, the VSL is widely used to assess the survival benefits of programmes in the environmental (e.g. reducing the pollution of the air) and transport (e.g. increasing the road safety) sectors. If a programme saves lives in a large population, the sum of willingness to pay in the population divided by the number of lives saved will define the VSL. E.g. if the average individual in a population of 100,000 individuals is willing to pay US\$100 to reduce the probability of dying by 1 in 100,000 (save one life in a large population), then the population is willing to pay

$$\text{US\$10,000,000} = \left( \frac{100,000 \times 100}{1} \right)$$

to prevent one member of that population from dying prematurely. If the willingness to pay is \$10 rather than \$100 then the VSL is \$1m rather than \$10m. The life is denoted a statistical life because ex ante it is not possible to identify which life will be saved.

There are no explicit markets for mortality risk reductions, where it is possible to observe a price or value. On the other hand individuals make implicit valuations on mortality risk reductions in many decisions, e.g. when

paying more for safer products, or accepting a more risky job if compensated with a higher wage.

A first approach to estimate the VSL is to use studies on actual choices, using indirect methods such as wage risk studies or consumption good studies (e.g. fire alarms and seatbelts). This approach infers the VSL from actual behaviour with respect to willingness to accept an increased risk for higher payment or willingness to pay to reduce a risk. A problem with these methods is to isolate the risk-income trade off from other confounding factors. Furthermore, the absolute change in risk is small, and often it is claimed that individuals overstate these risks, implying that VSL may be overstated. On the other hand there may also be a selection bias in that people more willing to accept risk tend to take more risky jobs. This will work in the opposite direction.

The second approach to estimate the VSL is using direct questions in surveys. The survey approach means people are asked to state how much (maximal) they would pay for a specified risk reduction. Well designed surveys may play a role in deriving VSL for environmental commodities and health outcomes for which good market data are not easily accessible. A problem with this approach is a risk that hypothetical choices fail to take into account a binding budget constraint leading to a reported WTP that may overestimate the "true" value.

## EMPIRICAL ESTIMATES OF VSL

A majority of studies have used labour market data from the US and other countries to derive the VSL. The empirical evidence with respect to the VSL is mixed and problematic due to the wide range of estimates of VSL they reveal (Johansson 2002). The studies summarised below reflect the huge variation in the VSL but also that the range of reasonable estimates of VSL has been narrowed over time. Kniesner et al. (2006) suggest that it is reasonable to conclude that the VSL varies between US\$5.5 to 7.5 million (in 2001 US dollars).

Viscusi (1992) claims that reasonable estimates based on labour market studies are in the range of US\$4 to 9 million (in 1998 US dollars). In a meta-analysis by de Blaeij et al. (2000), including both studies using direct and indirect methods, the magnitude of the VSL varies between US\$400 000 - 30 million (1998 US dollars). De Blaij et al. (2000) show that studies using indirect methods come to lower values than studies using direct methods. This may be explained by a risk that hypothetical choices lead to hypothetical bias so that reported WTP overestimates the "true" value. Miller (2000) presents mean VSL by country (based on revealed and stated preferences) and shows that e.g. the Sweden average from four studies is US\$3.1 million, while seven UK studies average US\$2.3 million, and 39

US studies average US\$3.5 million (1995). Miller (2000) further shows that the VSL averages at least 120 times GDP per capita. Using this relationship based on the GDP per capita levels (PPP US\$) for 2005 (41 890 (US), 33 238 (UK), and 32 525 (Sweden)) would imply that the predicted VSL is US\$5.0 million in the US, 4.0 million in the UK, and 3.9 million in Sweden.

In a meta-analysis by Mrozek and Taylor (2002) based on labour market studies it is claimed that a reasonable VSL is approximately US\$2 million (year 1998). In a critical review of market estimates of the VSL (labour, housing and product markets), Viscusi and Aldy (2003) showed that the range of VSL was extremely wide from US\$0.5 million to \$21 million (year 2000). The median value of statistical life was estimated at US\$6.7 million. Kniesner et al. (2006) express concern over the wide range of estimates for VSL based on labour market studies. By using the best available data and econometric practice, Kniesner et al. (2006) narrows the range on reasonable estimates for VSL to US\$5.5-7.5 million (at 2001 prices). Some of the large variation in VSL may reflect real differences and may be explained by differences in risk levels, risk changes, income levels and kinds of risk. Differences in VSL between countries may be explained by income, cultural and institutional differences (Johansson, 2002; Johansson, 2006).

## OFFICIAL VSL IN DIFFERENT COUNTRIES

In many countries, governments recommend or require economic analysis of proposed regulations and changes in public policies. In particular regulatory agencies in the US, UK and Canada use VSL to assess the value of environmental, health and safety rules (Viscusi and Aldy 2003). The VSL used by US regulatory agencies (usually based on indirect methods), varied in the period 1985-2000 between US\$1.0–6.3 million (US\$ 2000). In the end of that period (1996-2000) most regulatory analyses used a VSL in the range of US\$5-6 million. The US Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) used a value of US\$6.3 million and 5.5 million respectively in analyses of water health risk reduction and of medical devices. In UK regulatory agencies usually base their VSL estimates on contingent valuation (CV) studies. The UK Department of the Environment, Transport and Regions (DETR) has employed a CV based value of preventing a fatality of US\$1.2 million in year 1987 (£ 500 000). This value has been used by the department since 1988 for regulatory

and policy analyses. The UK Health and Safety Executive uses a double value for cancer related fatalities (Viscusi and Aldy 2003). The VSL for transportation related projects in Canada varied between \$400 000 and 3.2 million in the period 1982 – 1993. An analysis of a Canadian rule on tobacco products used VSL estimates of between \$1.7 and \$5.7 million (Viscusi and Aldy 2003). Further, to assess the survival benefits of traffic safety measures, the Swedish Road Administration (SRA) initially used a value of SEK13 million (1999 prices), which was adjusted upwards to SEK16.3 million in the prices of 2001, and to SEK17.1 million in the prices of 2005 (US\$1.9 million using the PPP exchange rate of 2005, US\$1 = SEK9.2 ; SIKA 2002, SRA 2006). In a sensitivity analysis the SRA recommended to use a range of VSL between SEK10 and 30 million (US\$1.1-3.3 million; SIKA 2002). In a recent study by the EU's Directorate-General (DG) Environment, the recommendation is to use a value in the interval €0.9 – 3.5 million. The best estimate according to this study is €1.4 million (Johansson 2006).

## COST-EFFECTIVENESS ANALYSIS

CEA is a method based on the objective to maximise outcome in terms of health subject to a budget constraint (Weinstein and Zeckhauser 1973). Costs are measured in monetary units and health improvement in a non-monetary unit such as gain in life expectancy (years). The most frequently used health outcome measure including both quantity and quality of life is QALYs (Drummond et al. 2005). When QALYs are used the analysis is also referred to as cost-utility analysis (CUA). QALYs are computed by multiplying each life year with a quality weight between 0 (dead) and 1 (full health). The weight reflects the individuals' quality of life in each life year. QALYs may be interpreted as equivalent to the number of years in full health. For QALYs to be a useful effectiveness measure in CEA they should reflect individual preferences, i.e. individuals should prefer treatments with more QALYs. Some support for QALYs reflecting individual preferences is found in Doctor et al. (2004).

To determine whether programmes are cost-effective or not we need to determine how much society is willing to pay for a QALY or for another effectiveness measure used in the CEA. This means that for independent health care programmes, those which have costs per unit of gained effectiveness below this price should be adopted. Further for mutually exclusive programmes the programme with the highest cost per unit of gained effectiveness that is below the price should be implemented (Johannesson, 1996). The willingness to pay for a QALY will determine which projects should be undertaken and thus the budget that is devoted to health care. A higher willingness to pay for a QALY results in a higher total spending on medical interventions, i.e. the more society is willing to pay for improvements in health, the more society is willing to spend on programmes that improve health.

The theory of human capital and estimates of cost of illness and the production value of improvements in health were developed with a societal perspective. The same basic idea as in other areas of applied welfare economics prevailed; all costs and benefits should be counted whenever (returns are often very long term on investments in human capital) and wherever they occurred. It is difficult for the investor to capture all benefits from the investment; e.g. because increased incomes from education go partly into taxes.

## 2.3 Cost-effectiveness analysis

One of the first, and probably one of the most influential, cost-effectiveness analyses of a new and expensive medical technology addressed the following question: what is the best mix of centre dialysis, home dialysis and kidney transplantation (Klarman et al. 1968)? This study calculates cost per life year gained for different treatment strategies and, as a sensitivity analysis, cost per quality-adjusted life year gained, and concludes that "transplantation is economically the most effective way to increase life

expectancy of persons with chronic kidney disease". The authors are well aware of the limits of their study, and cost-effectiveness analysis in general. The methodology, while elegant and well adapted to address the question asked, raises a number of issues. We note here only that there is no discussion about the definition of costs included; they are rough estimates of the direct treatment costs, discounted to present value with a 5% annual discount rate. No indirect costs are included, and no shadow price for the limited availability of kidneys for transplantation.

This study showed that cost-effectiveness analysis, particularly if outcome is measured as increases in (quality adjusted) life expectancy, can address important economic questions in the choice of treatment and allocation of resources. Despite the limitations - that the chosen outcome measure may not take all relevant outcomes into account, and that it is implicitly assumed that the desired outcome can be afforded - it gives guidance for decisions that have to be made. But there are two key issues that are not explicitly addressed, first which principles should be used for defining which costs should be included, and second how to avoid double counting a defined consequence on both the cost and the effect side. For example, does the quality of life adjustment take into account changes in the patient's income or expenses?

#### **2.4 Milton Weinstein and the US approach**

Milton Weinstein published in 1976 together with a cardiologist, an important study of the cost-effectiveness of hypertension treatment that for a long term set the standard for cost-effectiveness analysis in the US (Weinstein and Stason 1976, Weinstein and Stason 1977; Stason and Weinstein 1977). The costs included in the estimates of cost per life year saved from treatment of hypertension were: the intervention costs, the costs of treating side effects, the reduction in costs from fewer cardiovascular events, and the increased health care costs from the increase in survival. Indirect costs were not included, meaning that the study was done from the perspective of an imaginary US health care budget. The inclusion of "unrelated" health care costs has been debated along two different lines of argument: one being that they should be excluded and the other that not only health care costs but also all other costs related to changes in survival should be counted, i.e. total consumption minus production.

These issues are discussed at length in a very thorough review of the methods and application of "Cost-effectiveness in Health and Medicine" by a panel of leading US health economists appointed by the US Public Health Service, see Gold et al. (1996). The Panel was unable to reach a conclusion, even after long deliberations, as to whether all health care

costs should be included, regardless of whether they are directly related to the treated disease or not, and regardless of whether they occur during the "original" or the "extended" life span. Instead, departing from their goal of achieving consistency across analyses, the Panel leaves this matter to the discretion of the analyst. This conclusion seems to be very influenced by the first version of the paper by Garber and Phelps (1995), indicating that it does not matter if unrelated non-health care costs are included or not, only that there is consistency in the method (Garber and Phelps 1997). This result is only correct under very specific assumptions which have been pointed out in later research (Meltzer 2003).

The Panel also makes a distinction between "time costs" and "productivity costs", concluding that time costs should be included in the numerator of the reference case, but that productivity costs should not. The Panel defines "time costs" as the opportunity cost of time spent receiving health care services, such as time in the hospital, or waiting to see a doctor, or filling a prescription. "Time costs" include not only the patient's time but also the time of unpaid caregivers, including family members. The principle underlying the recommendation to include time costs is that these are direct medical care costs just like the time spent by doctors and nurses, and the fact that the time is not compensated is not important from a societal perspective.

In contrast, the Panel discussed at length the more difficult question of whether "productivity costs" should be included in the numerator (C) or the denominator (E) of the cost-effectiveness (C/E) ratio. "Productivity costs" reflect lost productive time caused by the illness itself. The most important principle invoked by the Panel is to avoid double counting, and the Panel decided the issue in order to achieve consistency across analyses, and not because one approach had more theoretical merit than the other. The final conclusion for the Reference Case was that the "morbidity cost" of an intervention (its impact on productive time and leisure time) should be excluded from the numerator of the cost-effectiveness ratio, because it is fully captured in the utilities in the denominator in the Reference case". However, "time spent during care and intervention" and "effects of lost productivity borne by others" should be included in the numerator because those are regarded as direct costs of providing health care.

This distinction between "time costs" and "productivity costs" leaves some ambiguity regarding the definition of "time spent during care" and who is included in "others". If we assume that only post-tax income is considered in the outcome estimate, all taxes and other external costs must be included among others.

Moreover, the assumption that the utilities for impaired health states reflect lost productivity of the individual is questionable. While the utility assessment questionnaires associated with some quality-of-life scales, such as the EQ-5D, are ambiguous regarding whether the utility response should reflect income losses, others such as the utility assessment procedure for the Health Utilities Index explicitly instruct respondents not to consider lost income owing to the health state. The Panel considered an alternative Reference Case recommendation that would include productivity costs in the numerator, and that would require the use of utility instruments that explicitly instruct respondents not to consider income effects. However, because the Panel did not wish to be prescriptive regarding the choice of a particular source of utilities, they opted for the recommendation to exclude productivity costs from the numerator and to presume that income losses are reflected by the utilities.

The assumption that the measurement of utilities should include income effects only, leads to problems both for empirical studies aimed at measuring health related quality of life, and for the interpretation of the results. The proportion between the income effect and the pure health effect will differ between studies. It is more practical and straightforward approach to estimate QALYs without income effects, and show them separately on the cost side. Empirical studies also indicate that respondents in studies in most cases will not include income effects when valuing health states, unless specifically asked to do so, see Sendi and Brouwer (2005) and Davidsson and Levin (2008). However, it is recommended to inform the respondents that it is the “pure” health effect that should be valued.

Details in recommendations aside, different Panel members had different views and it is not easy to interpret the compromise reached, there is reason to quote the first recommendation from the Panel on estimating costs in cost-effectiveness analysis: “Resource use and costs should be identified and valued from the societal perspective for the Reference Case analysis.” (Gold et al. 1996, p. 209)

## **2.5 Alan Williams and the European approach**

The European approach to cost-effectiveness analysis was developed from cost-benefit analysis, and Alan Williams was the leading economist in the search for a “scientific, yet practical” method to help decision makers in health care to “do better” (See Jönsson 2008 and Sugden 2008). We take the liberty of calling this the European approach because at that time Alan Williams and the UK Health Economists

Study Group was the leading actor in the European development of health economics in general, and economic evaluation in particular.

The major contribution from Alan Williams was the further development of an explicit measure of health benefit, the quality-adjusted life year (QALY), to be used as a composite effectiveness measure. This version of cost-effectiveness analysis is often called cost-utility analysis, to distinguish it from other forms of cost-effectiveness analysis where outcome is measured in physical units. This is not the place to review the debate around the pros and cons of welfare economics as the theoretical foundation for cost-effectiveness analysis in health care. Most of that discussion focuses on the role of individual preferences and willingness to pay in assessing the value of health improvements. We will instead focus on the less observed and, for Alan Williams probably less interesting, questions about how to define costs in cost-effectiveness analysis.

While Alan Williams, as many others, insisted that valuation of health benefits should not be based on individual willingness to pay in a market, he accepted market based valuation of resources used for health care. He advocated the “decision maker approach”, but also noted that an important role for health economists was to assist in defining the “relevant questions” and to “make sure that all relevant costs/benefits are included, but only once”. He noted that “CBA is not the same as financial appraisal”, it should have a “GNP [Gross National Product] orientation (opportunity cost of time)”, and that also “resources not in GDP [Gross Domestic product] (time lost for persons not in the labour force) should be included”. In a later paper he stated, that “all changes in real resources should be measured and they can be classified in: changes in service production, changes in resources used by patients and their helpers, and changes in the gross domestic product” (all quotations in this paragraph are from Williams 1981).

The societal perspective has continued to be strong in Europe, where most health economists interested in economic evaluation came from a background in economics, rather than medicine or decision sciences, which was the case in the US, and lately has been the case also in Europe. The strong influence of this is seen for example in the Swedish guidelines for economic evaluation for reimbursement of pharmaceuticals, which recommend a societal perspective (LFN 2003). But it is also possible to see a development towards a more restricted payer perspective when economic evaluation increasingly has become an element in health technology assessment (HTA) used by specific decision makers.



The cost per QALY approach, with or without a societal perspective, has not been endorsed for use in Germany and France, for example, in the same way as it has in UK, the Netherlands and the Nordic countries. Decision analysts with a medical, epidemiological and statistical background are, not surprisingly, more interested in modelling outcomes than in the costing aspects of an economic evaluation. This has also improved the quality of the studies in many respects. But since the final result is a ratio (ICER) that includes costs, the overall quality of the study demands full attention is also given to the definition, measurement and valuation of costs.

## 2.6 Guidelines for economic evaluation

Despite the increasing interest among decision makers from the mid 1970s in HTA and cost-effectiveness analysis, empirical studies were mainly academic exercises with limited relation to actual decision making. This changed in the 1990s, first with the direct use of cost-effectiveness criteria for drug reimbursement in Australia in 1993 and later in Canada in 1995. This was followed by similar requirements in several other countries, but probably the most important push for economic evaluation of medical technologies came with the establishment of NICE in England and Wales in 1999. NICE does not make reimbursement decisions, but the direct link between NICE and resource allocation within the NHS gave economic evaluation a direct link to decision making.

With economic evaluation gaining a more direct link to decision making, guidelines for economic evaluations started to be published. It is not surprising that the decision making bodies like to see guidelines in line with what they interpret as their interests. Guidelines will also reflect the interests of other stakeholders with an influence over their development; for example the interest in probabilistic sensitivity analysis by academic members of the NICE guideline committee, and the interest in the “friction method” by Dutch health economists involved in the guidelines for the Netherlands.

We can see that even if there are great similarities between the guidelines from different jurisdictions, there are also noticeable differences. A frequent feature is that regulators and payers, with some exceptions, have limited the type of costs that are considered when calculating the cost of the intervention. The most restricted example is New Zealand, where only reimbursed drug costs are considered. There are restrictions to defined health care costs in Australia and Canada, as well as for England and Wales (NICE). Indirect costs are included in the Netherlands, but calculated with the friction cost method which makes their impact minimal, and in Sweden, where in principle all relevant costs can and should be included (Table 1).

The academic community of health economists, at least those who are directly involved with the different agencies, have to a large extent accepted the

**Table 1. Perspectives in guidelines for economic evaluation**

Country	Authority	Perspective
Australia	Pharmaceutical Benefits Advisory Committee	Health care sector
Belgium	Drug reimbursement committee	Health care payer (government + patients)
Canada	Canadian Agency for Drugs and Technologies in Health	Publicly funded health care system
England & Wales	National Institute for Health and Clinical Excellence	National Health Service (NHS) and Personal Social Services (PSS)
Germany	Institute for Quality and Efficiency in Health Care	German citizens who belong to the Statutory Health Insurance (SHI)
The Netherlands	Ministry of Health, Welfare and Sports	Societal (note that productivity costs are estimated based on the friction method)
New Zealand	Pharmaceutical Management Agency	Perspective of the funder (health budget and direct patient health care costs)
Sweden	The Dental and Pharmaceutical Benefits Agency	Societal

restricted perspectives on cost in the guidelines. The pharmaceutical industry has, at the individual company level, accepted the different guidelines and adapted to the situations in different countries. They have challenged the methods only in individual cases, where the restricted methodology has worked against their interests. From an industry policy perspective the position has been that prices should be market based and HTA and economic evaluation should not be used as criteria for pricing and reimbursement. However, a change in position seems under way, at least in Europe, where the European pharmaceutical industry trade association, EFPIA, has during the last three years collaborated within the High Level Pharmaceutical Forum (HLPF) to develop principles and practices that can be jointly accepted by industry, regulators, payers and policy makers (EFPIA 2005).

This means that there are several reasons to have a renewed discussion of the principles for economic evaluations, and in particular of how to define which sources of value, including potential cost savings, should be included in the calculation of the cost-effectiveness ratio. There are two major objectives for this. The first is to facilitate international cooperation in assessments and avoid unnecessary duplication of work and thus economize on scarce resources and competences for undertaking studies. While decisions are national, and studies need to be tailored to national conditions, a significant part of an assessment is the same regardless of jurisdiction. A societal perspective on costs is a natural starting point for making a study transferable from one jurisdiction to another. The second objective is to provide correct incentives for innovation. Cost-effectiveness analysis as currently performed has been criticized for curbing health care expenditures for medical innovation in a way not consistent with long terms objectives (Jena and Philipson 2008). It is important that cost-effectiveness studies provide correct incentives for innovation, and one step in that direction is to take all costs and benefits of innovation into account; in particular long term consequences. A societal perspective is essential for this.

## **2.7 The theoretical basis for medical cost-effectiveness analysis**

In view of the rapidly increasing application of medical cost-effectiveness analysis, it may be surprising to note that there are very few contributions to the development of the basic methods. One reason may be that the theory of social choice is complicated and there are no obvious roads to success, which makes the project risky for an economist who would like to make a career in the profession. Alan Williams' contribution to the measurement of outcome is practical and pragmatic in nature, and not based on a coherent theory (but on some very important principles). Attempts to formulate

a more general theory of "extra welfarism" have not yet provided any direct guidance for methodological development of medical cost-effectiveness analysis. For an excellent introduction and review of the issues see Brouwer et al. (2008), and Culyer (2008).

While the "perspective on costs" of the "decision maker" has not been much discussed in this debate, since focus has been on what should be maximized, it would be surprising if a broad societal perspective were not the recommendation also from the general theory of "extra welfarism". The role of the health economist is not only to make the calculations, but also to help the decision maker to "ask the right question", and there should not be unnecessary restrictions on this process.

Within the model of expected utility maximization for a representative consumer, an important result was derived in two papers addressing the issue of how to account for costs following a medical intervention (Garber and Phelps 1997, Meltzer 1997). The results have important consequences for which costs to include in a medical cost-effectiveness analysis. The main conclusion is that all costs should be included, also unrelated costs from reduction in mortality and improved survival. It is not double counting, and it is not unimportant, that the net cost of production and consumption in added years of life is added to the numerator when the C/E ratio is calculated.

One consequence is that the omission of these costs will favour interventions that extend life over those that improve quality of life for the elderly, while the opposite is the case for younger. These results have so far only made it into the guidelines for economic evaluation in Sweden. Partly this is due to the difficulty of calculating the effect on consumption and production from medical interventions. But that is something that will improve over time, and even approximations can give useful information. A reasonable standard would at least be that cost-effectiveness studies publish cost-effectiveness ratios both with and without costs in added years of life, as is shown in Figure 1, to inform decision makers about the likely impact. Figure 1 shows that including future net costs has little effect in the younger age group (<45 years), but substantially increases the cost-effectiveness ratio at older ages. However it does not change the conclusion that treatment of hypertension is cost-effective at ages 45 and above.

It is difficult to speculate how quantitatively important it will be to include costs in added years of life compared to including a broader definition of non-medical costs. But it relates to the valuation of improvements in quality of life versus improvement in survival at end of life, which is a very much debated issue at the

moment. It may be overshadowed by the more important issue of valuation of life extension, but in the same way as discussion about pensions take life expectancy into account, it is difficult to just ignore the implications for private and public expenditures on services related to mortality and ageing.

Another important area of methodological development is how to address uncertainty about the benefits and costs of medical interventions. There are several aspects of uncertainty: around the expected values and for individual patients or groups of patients. But most important for future development of the methods of medical cost-effectiveness analysis, is addressing questions about the value of further medical research. Estimates of the expected value of information (EVI) can be used to inform decisions about where it is most valuable to collect more information to reduce uncertainty (Claxton and Thompson 2001).

In addressing issues about incentives for and investments in development of new technologies, where the money is not coming from a specific health payer's budget, it seems more relevant to take a societal perspective.

## 2.8 The net benefit approach to cost-effectiveness – return to cost benefit analysis?

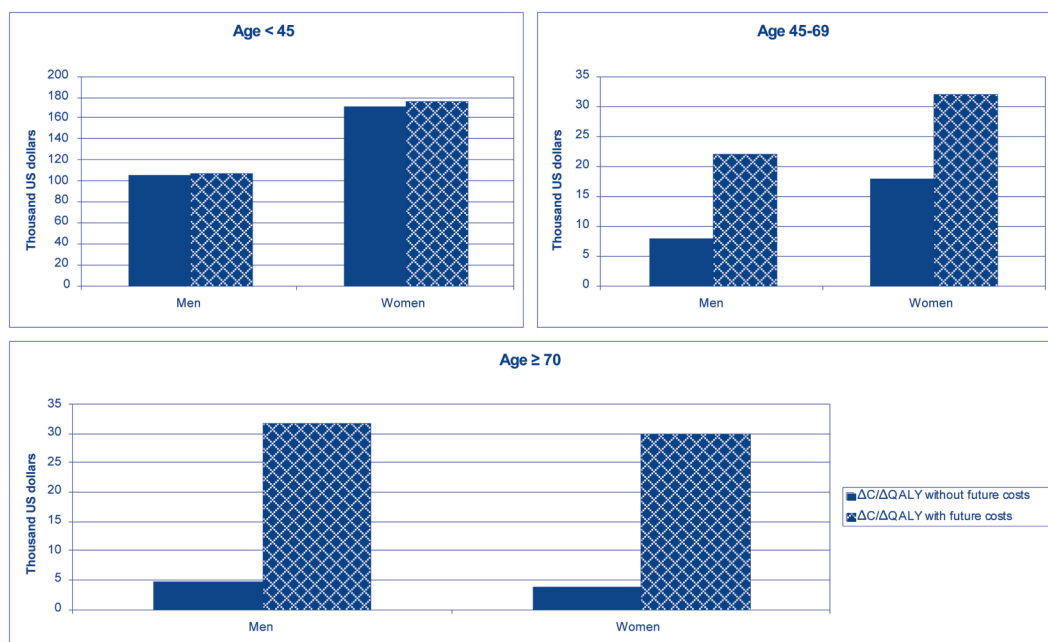
The net benefit approach to cost-effectiveness analysis was developed as a response to the need to estimate

confidence intervals around cost-effectiveness estimates (Tambour et al 1998). Estimating confidence intervals for ratios has some complications, but by multiplying the QALYs by a factor representing the value of a QALY in monetary terms, the ratio can be re-arranged as a difference between benefits and costs both expressed in financial terms and traditional statistical estimates of uncertainty around the central value can then be applied.

But discussion was also stimulated by the debate around what should constitute a “bench mark value” for when a project could be considered cost-effective. The estimation of a cost per QALY does not indicate whether a programme should be adopted or not, until you know the willingness to pay (WTP) for an additional QALY. While it is possible to take the view that decision makers will “do better” by choosing technologies with lower rather than higher costs per QALY, and that the decision making process can be described as “QALY searching”, the interest in answering the question “what is a QALY worth?” will not vanish, see Culyer et al. (2007).

If we assume that there is a fixed price or WTP for a QALY, cost-effectiveness analysis will in principle be transformed into a cost-benefit analysis. The only difference is that benefits are assessed with a particular two step method; first the gain in QALY is estimated, and second this gain is multiplied by a monetary amount which represents the WTP or value of the health benefits produced by the programme. There are

**Figure 1. Effect of including future costs on the cost per QALY gained ( $\Delta C/\Delta QALY$ ) for the treatment of hypertension (diastolic blood pressure 90-94), 1995 prices, Thousand dollars (Johannesson et al. 1997).**



many ways to estimate the QALY gain, and the two main research areas will be how to estimate the QALYs, and secondly how to estimate WTP for a QALY.

You may wonder why it is necessary to take this “detour” via the QALY instead of estimating the WTP for a more direct experience or description of the programme effects. There are probably a number of situations where it is difficult to take the two step process, for example when the benefits of a new technology include a significant amount of process utility, or for specific diseases where the outcome cannot easily be described by QALYs gained; erectile dysfunction and obesity perhaps being two examples. We will thus probably see a greater acceptance of direct WTP estimates of health gains as the net benefit approach to QALY gains is more firmly established.

This has consequences for the choice of perspective in economic evaluation. It is not logical to compare a monetary measure of benefit based on WTP for a QALY with an arbitrary measure of costs. It is thus necessary to define a cost measure that has the same comprehensive property as the outcome measure. Within this framework it is possible to analyze the consequences for specific budgets, as is done routinely in many public administrations, and such a budget impact analysis is an important complement to the economic evaluation, but not a replacement for it.

An alternative view is to search for the benchmark value implied by decisions by the budget holder from whose perspective the analysis is done. In a commentary on NICE, Alan Williams stated that “it is widely believed that the “shadow price” is much lower than the NICE benchmark of £30k”, see Williams (2004). This would imply that there are many decisions within the NHS where more health (QALY) can be purchased at a lower price than the official threshold, and that in successive turns the threshold will be driven down to this value. A first question is whether this is correct or not. It is complicated to carry out research of the implicit threshold, see for example Appleby et.al. (2009). They conclude, as Alan Williams did, that “A definitive finding about the consistency or otherwise of NICE and NHS cost-effectiveness thresholds would require very many decisions to be observed, combined with a detailed understanding of the local decision making processes”. Apart from the empirical problems involved in identifying the incremental cost and QALY effect of different spending decisions, there is the problem of interpretation. The cost-effectiveness ratio is only one factor that determines spending decisions. It is also impossible, without detailed analysis, to make a judgment whether differences in cost per QALY are the result of variations in “x-efficiency”, i.e. to what extent the provider is “doing things right”, as opposed to “doing the right things”.

If the implicit threshold were lower, it would imply that more health (QALYs) could be bought at a lower price. This would call for more investments in health within the NHS compared to spending in other sectors. It thus takes us back to the question of what is an acceptable threshold for spending within the NHS, and this question cannot be answered by investigating internal spending decisions. In addressing this question, what the budget for NHS should be rather than how a defined budget should be spent, a social perspective is relevant.

## **2.9 The practical importance of a societal perspective in economic evaluation**

Using a societal perspective for economic evaluation of medical interventions increases the likelihood of achieving an optimal investment level of social resources in health care and further, given the optimal level of health investments, of implementing the most efficient medical interventions. Using a societal instead of a health care payer perspective increases the probability of producing more health given limited health care resources.

We argue that considerations of costs are neglected in economic valuations in health care. While more resources are needed for better cost estimates, the extra costs are modest, for example to translate changes in working time to income, or time for informal care to costs. Also, many of the calculations can be standardized and re-used from study to study, for example calculations of cost in added years of life. The extra costs of obtaining better estimates must also be seen in relation to the benefits.

Following a narrow *health care perspective* would likely lead to problems with sub-optimisation compared to a societal perspective (Johannesson 1996). This can be exemplified by a study by Berggren et al. (1996), who assessed the cost-effectiveness of laparoscopic versus open cholecystectomy. From the viewpoint of society laparoscopic surgery was shown to be a cost-saving strategy, while from the point of view of health care (the hospital), when excluding the effects on production or the indirect costs, laparoscopic surgery was more expensive. Given that the health effects were assumed to be the same for the two alternatives, implementing laparoscopic surgery instead of the open surgery would be profitable for society, but not for the hospital (or health care system). Replacing open with laparoscopic surgery implied lower costs for society, and that resources could instead be used in the production of more health for other treatment and patient groups. This example illustrates that a health care perspective (hospital) may lead to the wrong conclusions from a societal point of view. Using a health care perspective instead of a societal perspective implied that less health

## THE SOCIAL VALUE OF A QALY

Interpreting CEA as a special case of CBA and using a fixed price per unit increase in effectiveness as the decision rule for CEA, means that the social value per effectiveness unit must be determined. In practice this means that the price per QALY gained, which is the most widely used outcome measure in economic evaluation, has to be decided. If the price per QALY gained is set at the optimal level, CEA will lead to a maximisation of social welfare.

There is no consensus of the social value of a QALY gained. The value or price is usually based on some arbitrary rule set to around US\$50 000 (Hirth et al. 2000). Sometimes a range of values is suggested. Laupacis et al. (1992) argue that the evidence for adoption is strong if the cost per QALY gained is below Can\$ 20 000, moderate between Can\$20 000 and Can\$100 000 and weak if above Can\$100 000 (1990 Canadian dollars). Johannesson (2001) uses a value of a QALY gained in the range of US\$40,000 and US\$100 000 (1999 prices).

Reimbursement and HTA organisations usually do not explicitly state the value of a QALY gained, or equivalently, which maximal cost per gained QALY they find acceptable. For example the accepted threshold for a gained QALY is not commented upon at all in the Canadian guidelines for economic evaluation of health technologies (CADTH 2006). There are exceptions, and NICE (2008), for example, states that to support technologies the cost per gained QALY should not in general exceed £20 000–30 000 (US\$30 000–46 000). To support technologies above this value, NICE argues that other factors may be important, such as the inclusion of wider societal costs. It is not clarified what is required to support technologies with costs above this value.

One approach to define whether a medical intervention is cost-effective, followed by Laupacis (1992) for example, is to assess whether the cost per QALY gained for the intervention of interest is below the cost per QALY gained for interventions already implemented in the health care system. The argument is that society must be willing to pay the cost per QALY gained for implemented programmes; otherwise they would not have been implemented. This is a doubtful approach based on an arbitrary rule that depends on which other treatments and patient groups the comparison is made against. In fact any programme can be made to appear cost-effective by comparing it with the “right” alternative. Further, it does not say anything about whether already implemented programmes are themselves cost-effective or not.

Alternatively, the value of a gained QALY (or of a life year gained) can be derived from estimates of the VSL. This means that the WTP per gained QALY is calculated by

dividing the VSL by the (discounted) QALYs gained for a saved life. For example, based on the value of SEK17.1 million set by SRA, a value per QALY gained of SEK670 000 (US\$73 000) is obtained. This value is obtained by first dividing the VSL by the expected number of discounted life years (at a 3% discount rate) lost at a traffic death in Sweden, which is 19.6 years (30.5 without discounting). The discounted life years are then adjusted with quality of life in the Swedish general population (0.85), which results in 16.7 QALYs lost. After adjusting for the treatment of taxes by the SRA (all costs are multiplied by a factor of 1.53 to reflect excess burden of taxes and value added taxes) a value per QALY gained of SEK670 000 (US\$73 000) is obtained. Using the VSL recommended in a sensitivity analysis (SEK10–30 million) will generate a value per QALY in the range of SEK600 000–1 800 000 (US\$65 000–200 000) before adjusting for taxes and SEK390 000–1 170 000 (US\$42 000–130 000) after adjusting for taxes. Performing the same calculations but instead using the estimated VSL suggested by Kniesner et al. (2006) of US\$5.5–7.5 million (SEK51–69 million), based on wage-risk studies, would yield a value per gained QALY of SEK3 100 000–4 100 000 (US\$330 000–450 000) before adjusting for taxes and SEK2 000 000–2 700 000 (US\$220 000–290 000 US\$) after adjustment for taxes. Adjusting for a lower income level per capita for Sweden compared to the US by using the relationship in Miller (2000) and a VSL of US\$3.9 million, implies a value of a gained QALY of US\$230 000 (SEK2 150 000) before adjustment for taxes, and US\$150 000 (SEK1 400 000) after adjustment for taxes.

Hirth et al. (2000) found that 80% of identified VSL studies implied a value of a QALY gained in excess of US\$100 000. The median value per study type in Hirth et al. (2000) were \$93 000 (revealed preference non-occupational safety studies), US\$161 000 (contingent valuation studies), and US\$428 000 (revealed preferences occupational studies). Thus, values of willingness to pay per QALY gained based on VSL estimates are well above the values based on rules of thumb and set by, for example, NICE in the UK. In particular, the value of a QALY gained derived from wage risk studies markedly exceeds values based on rules of thumb. This indicates that thresholds used by HTA and reimbursement agencies underestimate the optimal societal value of a QALY gained, implying that fewer resources than optimal are invested in health care. It may be argued that it is inappropriate to transfer WTP estimates based on VSL studies and claim that derived values of QALYs are valid for health care. On the other hand there is no reason to believe that arbitrary rules of thumb more accurately reflect the societal value of a QALY gained. Still, there is a lot of uncertainty about the “true” value of a gained QALY and collecting more information about the willingness to pay for a QALY gained should be a research priority.

was produced, i.e. that health was not maximised. This is also an example where in Sweden resources were transferred from the National Social Insurance System, paying for sickness benefits, to the county councils responsible for paying for hospital care.

Cost-effectiveness is also likely to be affected by the inclusion of costs of informal care. This may significantly affect the cost-effectiveness of interventions in e.g. Alzheimer's disease. In a review by Jönsson (2003) it is concluded that the increased drug costs incurred by the use of cholinesterase inhibitors will be partly offset by savings in costs of informal care.

Finally, including costs in added life years may also change the cost-effectiveness across and within age groups. E.g. cost-effectiveness ratios for the treatment of hypertension are generally lowest among older men and women, but after including costs in added years of life, the cost-effectiveness ratios are generally lowest among middle aged men and women (Johannesson et al. 1997).

Thus, a narrow health care perspective significantly increases the risk of sub-optimisation from a societal point of view. To minimize the risk of sub-optimisation we conclude that cost-effectiveness analysis should be based on a societal perspective, which means that all costs, no matter where and to whom they accrue, should be included in the analysis (Gold et al. 1996, Johannesson 1996).

To further illustrate the importance of adopting a societal perspective, we now consider examples from the disease areas of Alzheimer's disease (AD) and multiple sclerosis (MS). The examples highlight the importance of including indirect productivity costs and costs of informal care in economic evaluation of medical interventions.

### 3. TWO CASE STUDIES: ALZHEIMER'S DISEASE AND MULTIPLE SCLEROSIS

#### 3.1 Alzheimer's disease

##### *Disease background*

Alzheimer's disease (AD) is a neurodegenerative disorder and the most common cause of dementia in the elderly (Fratiglioni and Qiu 2009). The disease leads to gradual cognitive impairment and loss of functional capacity. In advanced stages of AD patients are often completely dependent on caregivers, and mortality is high (Winblad et al. 1999). Behavioural disturbances are frequent in

moderate to severe disease, increasing the burden of disease for caregivers and patients (Winblad 1996). There is also a small proportion of AD patients who develop dementia at a young age; many of these experience rapidly progressing dementia with a complete loss of work capacity at an early stage.

Possible or probable AD is a clinical diagnosis based on criteria (e.g. ICD-10 or DSM-IV). The diagnosis can be confirmed post mortem by the hallmark neuropathological findings of beta-amyloid plaques and neurofibrillary tangles in the brain (Alzheimer 1991).

There is currently no curative treatment for AD. Currently available therapy for AD (cholinesterase inhibitors and the NMDA receptor antagonist memantine) has only demonstrated a limited, transient symptomatic effect (Kaduszkiewicz et al. 2005). There is hope that new treatment strategies under development will demonstrate disease-modifying properties by interfering with the pathological processes of AD and slowing disease progression (Nitsch 2004).

AD is a major cause of mortality and morbidity in the elderly, and involves high costs of care. The total worldwide cost of AD has been estimated at over US\$300 billion annually, of which direct costs are approximately US\$156 billion (Wimo et al. 2006). AD is probably one of the diseases with the largest impact on public health and with profound economic consequences - but also opportunities for novel therapeutic strategies. Ageing populations worldwide are expected to bring increased prevalence of AD and further strain on care systems and caregivers. At the same time, research in treatments for AD is highly active with a number of new molecular entities (NMEs) undergoing late-stage clinical testing at the time of writing. AD is therefore likely to be a focus of health technology assessment and economic evaluation during coming years.

##### *Cost-of-illness*

There is a growing literature on the health economics of AD. Cost-of-illness studies have described the magnitude and distribution of costs for AD patients in several countries (Jönsson and Berr 2005) and identified determinants of care (Ernst et al. 1997, Jönsson et al. 2006a, Wolstenholme et al. 2002). Table 2 presents a summary of studies with costs converted to €(2005) PPP.

Total cost per patient ranges from €6,614 to €64,426 per year, almost a 10-fold difference reflecting, among other things, differences in the costing perspective. Medical care costs constitute a relatively small share of total costs, 10-25% in most studies. Informal care costs, where included, range from 8% to 78% of total costs. This variability reflects

**Table 2. Estimates of annual cost per patient with Alzheimer's disease for different countries**

Country		Medical care	Formal non-medical care	Informal care	Total costs
		€ (2005) PPP	€ (2005) PPP	€ (2005) PPP	€ (2005) PPP
Belgium	Cost % of total	8,218 56%	5,222 36%	1,233 8%	14,673 100%
France, 1995	Cost % of total	2,198 33%	2,047 31%	2,369 36%	6,614 100%
France	Cost % of total	4,910 21%	4,151 18%	13,898 61%	22,959 100%
Germany	Cost % of total	1,850 15%	5,494 46%	4,696 39%	12,040 100%
Italy	Cost % of total				52,406 100%
Italy	Cost % of total				28,691 100%
Denmark	Cost % of total	3,330	7,422		10,752 100%
Nordic countries 2006	Cost % of total	3,113 22%	7,167 51%	3,757 27%	14,038 100%
Sweden, 1999	Cost % of total	74	27,161		27,236 100%
Finland	Cost % of total				33,333 100%
Spain	Cost % of total	2,851 10%	3,377 12%	21,366 77%	27,595 100%
Spain	Cost % of total				30,525 100%
Spain	Cost % of total	4,230 13%	2,178 7%	25,385 78%	32,517 100%
UK, 1999	Cost % of total	15,913 25%	4,317 7%	44,196 69%	64,426 100%
UK	Cost % of total	1,818	30,650		32,468 100%
UK	Cost % of total				35,287 100%

differences in the methodology for data collection, in the methods used for valuation of informal care and in the structure of dementia care in different health care systems.

Figure 2 shows data for the amount of informal care time per patient from the ICTUS study, where the same data collection methodology has been applied across 12 European countries (Reynish et al. 2007).

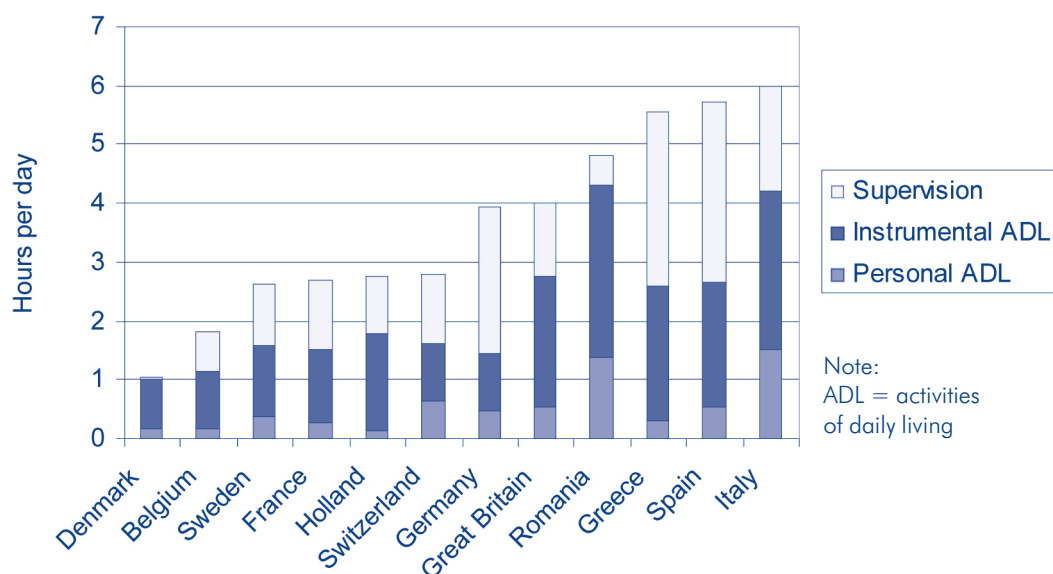
The average number of hours of informal care ranges from 1 hour per day in Denmark to 6 hours per day in Italy, reflecting differences in the structure of dementia care and availability of formal and institutional care. The importance of including informal care costs clearly varies from country to country depending on the way in which the disease is managed.

The valuation of informal care is controversial (McDaid 2001). Several approaches have been proposed which

yield substantially different results. The opportunity cost of the caregiver's time can be estimated through the value of lost production for caregivers of working age (the human capital method). For the loss of non-working (leisure) time, there is no market price and so information on the opportunity cost has been taken mostly from stated-preference studies. An alternative approach has been proposed to value the caregiver's time by the cost of a replacement worker (nurse or home aid). This method is clearly limited by the absence of a perfect replacement, and the fact that the method does not consider the opportunity cost of the resource being valued.

To illustrate the costs of AD, data are presented in Table 3 from a prospective observational study in the Nordic countries. 272 patients with AD and their caregivers were followed for a year. Data on costs of care, disease severity and health-related quality of life was collected every six months. The cost of informal

**Figure 2. Informal care time by country**



care was valued at SEK196 per hour for lost production and SEK28 per hour for lost leisure time.

Community care represents the largest cost component, in particular in advanced AD (low MMSE score); over half of the cost in the most advanced

stages. 59% of caregivers were spouses to the patient, most over the retirement age, and 31% were children to the patient, many of working age. The lost production component of the caregiving time was relatively small in this sample in comparison with the value of lost leisure time.

**Table 3. Costs per patient in SEK by disease severity measured with MMSE**

	MMSE 26-30	MMSE 21-25	MMSE 16-20	MMSE 10-15	MMSE 0-9
<b>Medical care</b>					
Pharmaceuticals	10,148	10,720	11,189	10,322	9,814
Outpatient care	4,715	6,419	8,085	7,029	6,208
Inpatient care	13,903	5,930	13,603	15,017	71,729
<i>Medical care, share of total</i>	47%	25%	18%	14%	23%
<b>Community care</b>					
Special accommodation	7,214	17,131	68,105	106,814	164,136
Other community care	6,049	18,765	35,441	20,985	46,131
<i>Community care, share of total</i>	22%	38%	56%	56%	56%
<b>Informal care</b>					
Lost production	0	6,394	6,720	7,317	11,698
Lost leisure time	18,702	28,601	40,939	59,393	65,247
<i>Informal care, share of total</i>	31%	37%	26%	29%	21%
<b>TOTAL</b>	60,730	93,959	184,081	226,876	374,962

Note: MMSE = Mini Mental State Examination, which is the most commonly used test for complaints of memory problems or when a diagnosis of dementia is being considered; the lower the score, the more severe is the condition  
Source: Jönsson et al. 2006a



### Quality of life and health utilities in dementia

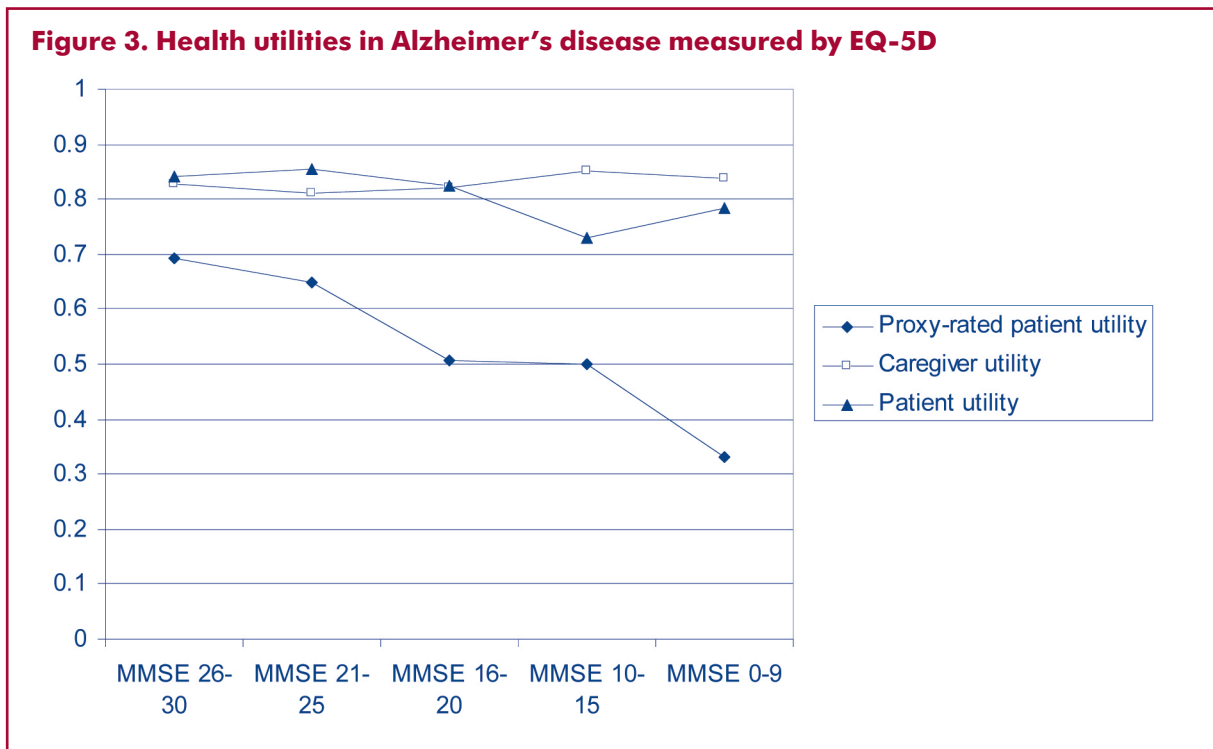
In standard cost-utility analyses, only patient health benefits are usually included. In AD however, caregivers are expected to benefit from treatment to perhaps even a greater extent than patients, since awareness of symptoms is often compromised in patients with moderate to severe dementia. The benefits to caregivers may be included and valued as quality of life improvements but perhaps also health improvements, since relative to the general population there is an increased morbidity in caregivers to AD patients. Since there may be an interaction between the health effects and how much caregivers spend in terms of time and other resources, a societal perspective is necessary to make sure that all consequences are captured and that there is no double counting.

QALYs (or the equivalent outcome measure) may in some cases be too crude to pick up the full impact of a treatment on the quality of life. Aspects such as the relationship between patient and carer, which may be fundamental to the quality of life of those involved, are

seldom captured by standard elicitation techniques. Also the impact of the provision of informal care on the quality of life of caregivers is often ignored. In the NICE technology appraisal of cholinesterase inhibitors, a utility increment of 0.06 (on a scale from 0.00 to 1.00) was added to the utility derived from treating the patient to reflect caregiver utility. Figure 3 shows data from the same Nordic observational study on utilities rated with the EuroQoL EQ-5D instrument for caregivers, for patients and for patients by caregivers as proxies (Jönsson et al. 2006b). Patients as well as caregivers rated their own utility highly, in line with what would be expected from a healthy normal population. Only the proxy-rated patient utilities showed a response to disease severity.

### Modelling cost effectiveness in AD – the importance of a societal perspective

Treatment in AD is not focused on saving or prolonging life, but on preventing or postponing disease progression. The cost-effectiveness of AD treatment has been modelled with different



**Table 4. Model simulation: lifetime costs of care, with and without treatment, SEK**

	No treatment	Treatment	Difference	% of total cost savings
Pharmaceuticals	49,159	49,393	235	0%
Direct medical	146,371	128,670	-17,701	17%
Community care	515,476	448,490	-66,986	66%
Informal care	245,371	228,604	-16,767	17%
Total	956,377	855,158	-101,219	100%

	<b>WTP SEK600,000/QALY</b>	<b>WTP SEK zero</b>
Pharmaceutical costs	18,700	(negative)
Direct medical costs	23,300	4,600
Direct costs	41,000	22,300
Societal costs	45,400	26,700

techniques, including survival models, regression models and Markov models (Jönsson 2003). These models have in common that they apply an effect from treatment on baseline progression rates estimated from longitudinal observational studies, and then link the estimated disease progression (with and without treatment) to costs and outcomes (e.g. health utilities). Most models have been based on disease states defined by MMSE scores obtained from a commonly used type of brief cognitive assessment. The modelling of AD with disease states based only on cognition has been criticised; the results would likely be comparable if states were based on other indicators of disease severity.

To illustrate the importance of which costs are included in the cost-effectiveness ratio, we have run simulations using a previously published Markov model for a novel treatment which we assume reduces disease progression by 50% for a duration of three years (Jönsson et al. 1999). After three years treatment is stopped and disease progression returns to the same as for untreated patients. Patients are assumed to have the same age and gender distribution as the Swedish observational study (mean age 76 years, 37% male).

Table 4 shows that the majority of the cost savings (83%) would be found outside the health care system: in community care and informal care costs.

The annual drug cost, which indicates the potential price for the hypothetical innovation, at which the cost per QALY gained is SEK600,000, varies from SEK18,700 (QALY gains only are valued) to SEK45,400 (cost savings included from a social perspective) depending on the costing perspective. (see Table 5). If QALY gains are not considered, which means that increased treatment costs must be offset by savings of other costs, the break-even treatment cost is SEK26,700 from the societal perspective, but only SEK4,600 from a health care cost perspective. The reward to innovators and thus the incentives for innovation will thus strongly depend on the perspective used when assessing the value of an innovation for AD.

Figure 4 shows the distribution of net benefits (QALY gained x WTP per QALY minus cost difference), assuming SEK600,000/QALY and no treatment cost. The net benefit from treatment increases as additional cost items are added. The distributions also become flatter, reflecting increased uncertainty around the estimates. It is not obvious how this should be interpreted by decision makers, who may be risk averse, and thus have a trade-off between higher return and more uncertainty. The expected value may still be the most important for a public decision maker.

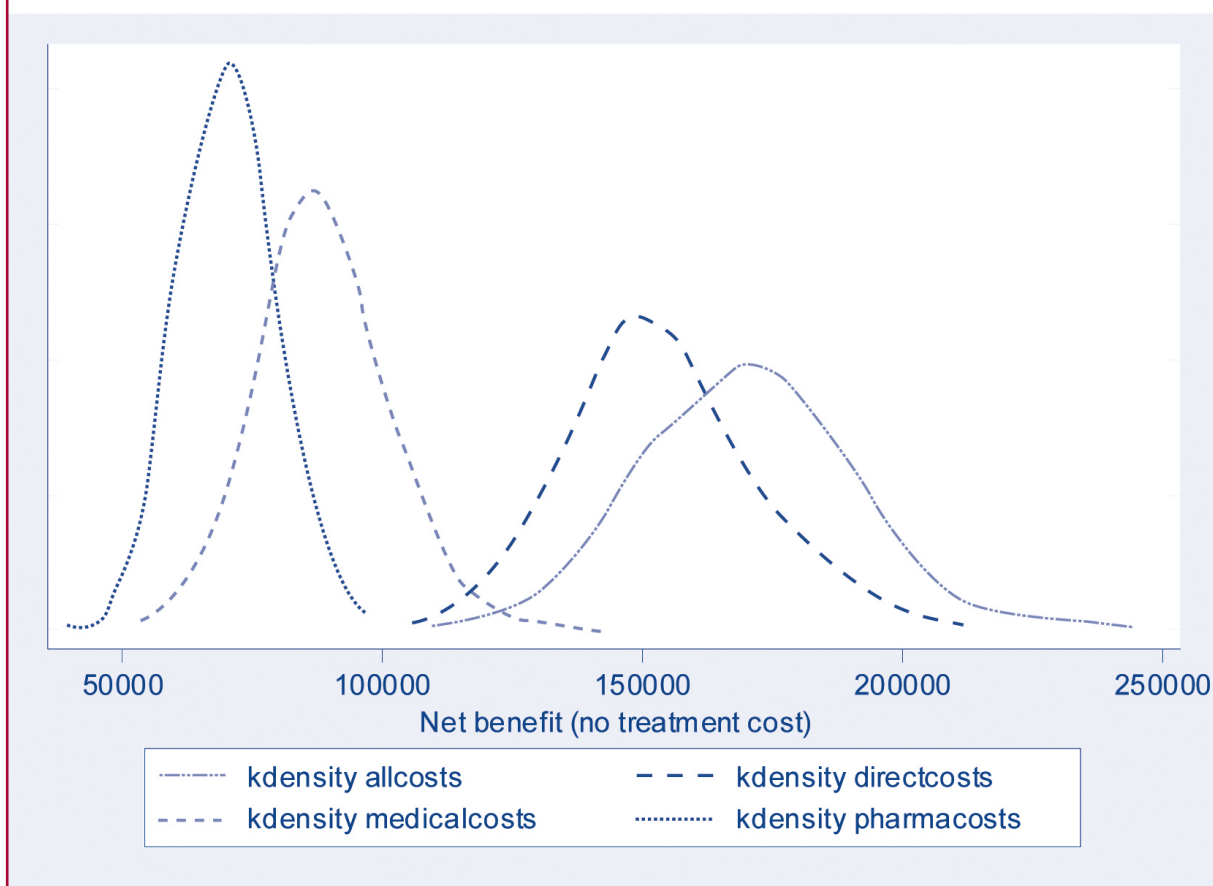
### **Discussion**

Dementia care is organized in very different ways in different countries and regions. It commonly involves more than one care provider, and social services as well as medical services, and the costs for dementia care are typically split across several budgets. In Sweden for example, the county councils are responsible for all medical care, but all community care is the responsibility of the municipalities.

Traditionally the focus has been on supportive care services to compensate for the loss of functional abilities and to manage behavioural disturbances. There has been little or no specific medical therapy to offer. With the introduction of novel treatment options comes the issue that these are delivered and paid for through the health care system, while the majority of the economic benefits will fall on other stakeholders. This may lead to disincentives for investments in new health care technologies if a narrow health system perspective is taken since benefits will be mainly incurred in the social care systems.

There is a growing body of literature on contingent valuation (CV) methods for eliciting the value of treatment benefits as well as the value of informal care in dementia (Nocera et al. 2002, van den Berg et al. 2006, van den Berg and Ferrer 2007, van den Berg et al. 2008). Such studies may better capture the full value of the benefits from AD therapies than estimates of costs per QALY. We still need more empirical studies to judge that, but a societal perspective is still essential to make sure that all benefits and costs are included, but only once.

**Figure 4: Net benefit distribution by costing perspective**



### 3.2 Multiple Sclerosis

#### Disease background

Multiple sclerosis (MS) is a chronic progressive and potentially disabling disorder with considerable social impact and economic consequences despite its relatively limited prevalence ranging between 0.04-0.15% in published studies (Dean 1994). Disease onset is usually in the thirties, making MS the major cause of non-traumatic disability in young adults.

MS is an inflammatory and neurodegenerative immuno-mediated disorder of the central nervous system, characterized by inflammation, demyelination and primary or secondary axonal degeneration. It is clinically manifested by multiple neurological dysfunctions (e.g. visual and sensory disturbances, limb weakness, gait problems and bladder and bowel symptoms) that increase over time and often lead to irreversible functional disability. The disease is also associated with a high degree of fatigue which affects a majority of patients, regardless of their disease status and functional disability, and interferes significantly with patients' ability to participate in daily activities and with their work capacity (Johnson 2008).

The early disease stage is usually characterized by a relapsing-remitting course (RRMS), where patients

experience incapacitating disease exacerbations, but recover to a large extent between these episodes. Over time, increasing demyelination and the axonal degeneration lead to incomplete recovery after exacerbations and hence to a secondary-progressive disease course (SPMS). Between 10% and 20% of patients present with a primary progressive disease course from clinical onset (PPMS) (Hauser 1994).

In the mid-1990s, several first-line biological disease-modifying treatments (DMT) were introduced (Betaferon®, Avonex®, Copaxone®, Rebif®) for the treatment of RRMS, based on their ability to reduce the number of exacerbations. More recently, a further agent was approved as second-line treatment, or for patients intolerant to the previous biologics: Tysabri®. The expectations for these treatments is that by reducing the frequency and severity of relapses and improving recovery after an episode – both identified as indicators of a bad prognosis – the disease progression will be delayed.

These treatments were introduced in a field where limited treatment options existed, at a substantially higher cost. The proportion of direct costs represented by drug treatment, estimated at around 1-3% in the early 1990s, was estimated to have increased to around 25-35% in recent studies (Andlin-Sobocki et

al. 2005, Kobelt et al. 2006). Consequently, the question arises whether investing in these newer treatments represents an efficient use of resources. The past decade has produced a substantial number of studies on the cost of MS and on the cost-effectiveness of these treatments, including several health technology assessment reports (Kobelt 2004, Kobelt 2006, Patwardhan et al. 2005). In all of these studies, costs other than health care costs have been found to represent the majority of costs and hence the largest opportunities for cost-savings with effective treatment.

MS is thus a very good example to illustrate the costs to society of a progressive and severely disabling disease, and the importance of adopting a societal viewpoint when evaluating the potential changes that can occur with disease modifying treatments:

- The total costs of MS have been explored in a large number of European countries, making MS one of the diseases with the best data as far as its economic impact and health burden (quality of life) are concerned (Kobelt et al. 2006).
- The majority of costs of MS are found outside the health care system, in terms of productivity losses, family support and private investment to adapt the environment to better suit a patient with functional limitations.
- All types of costs increase with worsening disease, but the steepest increase is seen for indirect costs as patients have to leave the workforce soon after disease onset, and for informal care costs as patients become increasingly dependent on their family.

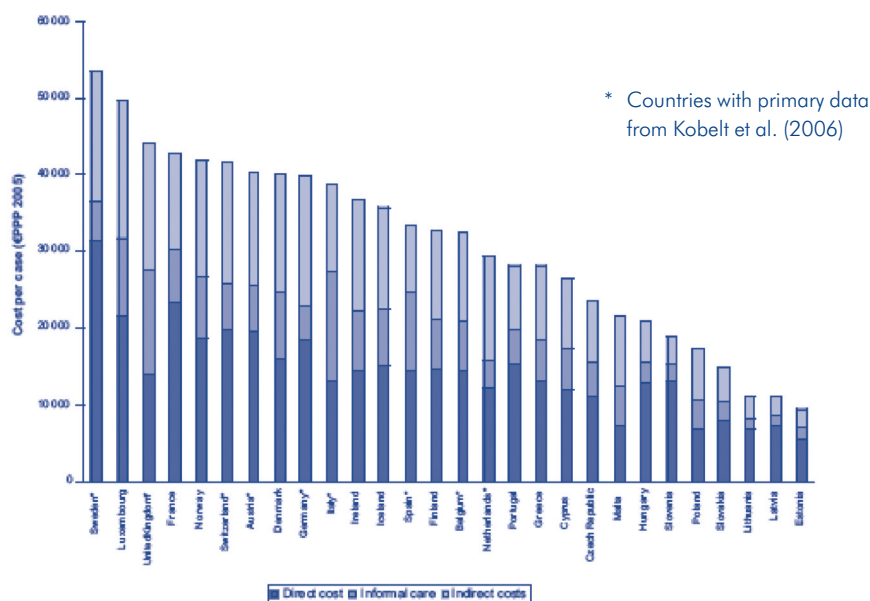
- Thus, the major economic benefit of treatments that slow disease progression will occur in societal costs, while the treatment costs will occur in the health care system.
- Finally, a number of economic evaluations for new DMTs have been performed during the past decade, exploring the long term effect on outcome (utility) and costs from different perspectives.

### The cost of MS

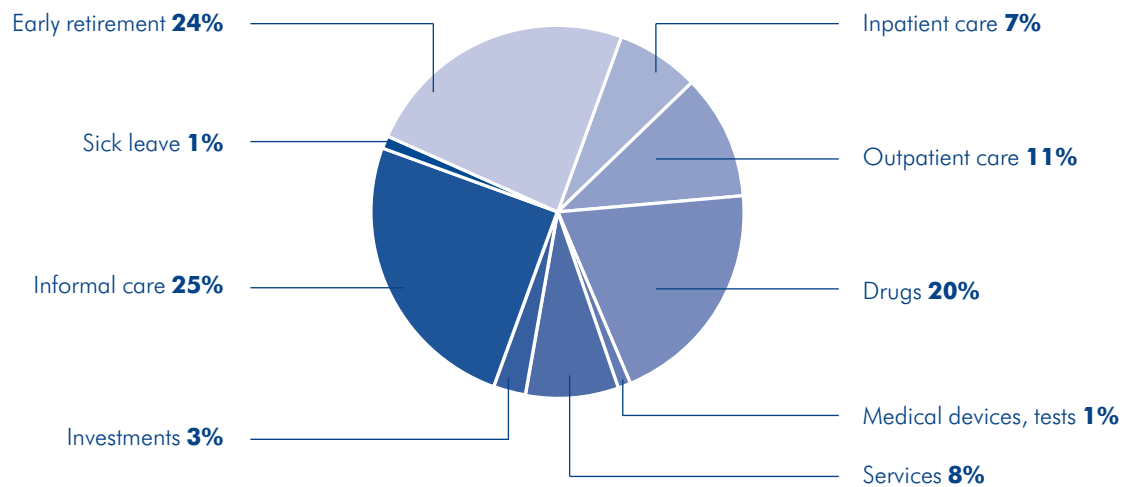
There is a wealth of different types of studies on the health and economic burden of MS, and it would go beyond the purpose of this paper to review that literature. Rather, studies are selected to illustrate the points made. A recent study of the costs of 12 disorders of the brain in Europe (EU 25 plus Iceland, Norway and Switzerland) estimated the number of patients with MS in Europe at 380,000 (Andlin-Sobocki et al. 2005). MS had the second lowest prevalence among the diseases studied, and hence relatively low total costs, but the mean annual cost per case in 2004 was second only to brain tumours. Taking into account that patients with MS often live 40 years or more with the disease, while survival with brain tumours is limited, MS could easily qualify as having the highest cost per patient.

The total cost of MS in Europe was estimated using a model that permitted imputing the costs per patient, according to disease severity, from available studies to countries where no data existed using economic and health indicators (Andlin-Sobocki et al. 2005). The first estimate was however based on a limited

**Figure 5. Mean cost per patient across Europe, estimated from published data (Sobocki et al. 2007)**



**Figure 6. Estimated total cost of MS in Europe by resource type**



Source: Adapted from Sobocki et al.(2007)

number of studies from the mid-1990s, and the calculations were repeated in 2005 when the results of a large study in Western Europe became available (Kobelt et al. 2006, Sobocki et al. 2007). The cost per patient ranged from €10,000 to €54,000 (Figure 5) and was dominated in almost all countries by non-health care costs (Sobocki et al. 2007).

The total cost of MS in Europe was estimated at €12.5 billion, of which less than half was health care costs: informal care and productivity losses amounted to €3.2 billion each, together representing 51% of total costs. Adding to this the patients' private investments, non-health care costs represent 54% (Figure 6).

The survey underlying these calculations included over 13,000 patients in nine countries (Kobelt 2006). The structure of the mean cost per patient in these countries illustrates a number of points related to productivity losses and in particular to informal care (Figure 7):

- Resource use will depend on the sample included in the analysis. Although in this study the same questionnaire and identical analytical methods have been used, the samples in the Netherlands and Germany were earlier in the disease process, resulting in less use of informal care.
- Informal care use and the provision of help from the health care system are interlinked and to some extent substitutes for one another. Sweden provides extensive formal help to disabled people, resulting in almost no need for informal care, despite the fact that the Swedish sample was the most severely ill. Similar is true for Switzerland, albeit to a lesser extent.

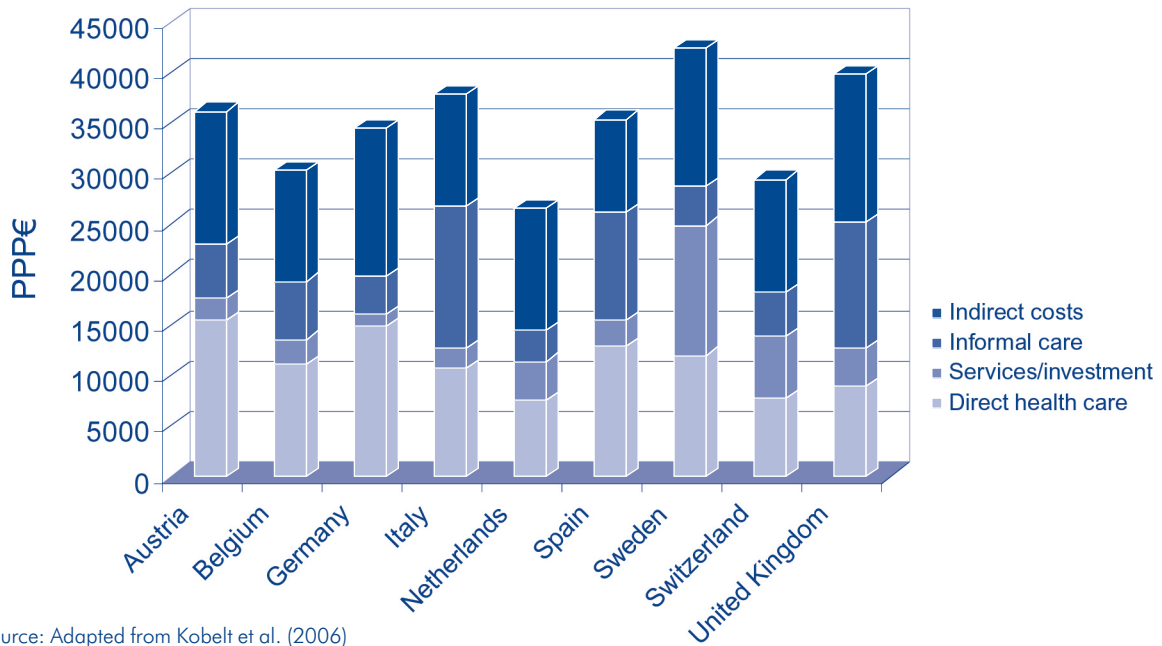
- Indirect costs are a large part of costs, almost irrespective of the severity of disease in the sample. Early in the disease process, productivity losses will be caused by frequent and long sick leaves. After some time, there will be a mix of sick-leave and early retirement, followed by patients leaving the work force. Very late in the disease, indirect costs will decrease as patients attain normal retirement age.

Both of these processes, informal care and productivity losses, can theoretically be influenced by treatments that slow the disease process, and should therefore be included in any decisions on resource allocation.

Contrary to non-health care costs, there is limited potential for changing costs in the health care system with new treatments in a chronic progressive disease such as MS, where exacerbations happen on average less than once a year. Patients will, as soon as diagnosed, have regular follow-up and be, for many of them, in need of hospitalization for severe relapses. Treatment may indeed reduce these relapse costs but these have been estimated at only around €3,000 per relapse (Kobelt et al. 2006). As shown in Figure 8, the increase in direct medical costs as a patient becomes more disabled is rather limited. . The increase in costs with advancing disease severity stems mainly from the use of devices such as walking sticks, stair lifts and wheel chairs, and from informal care and productivity losses.

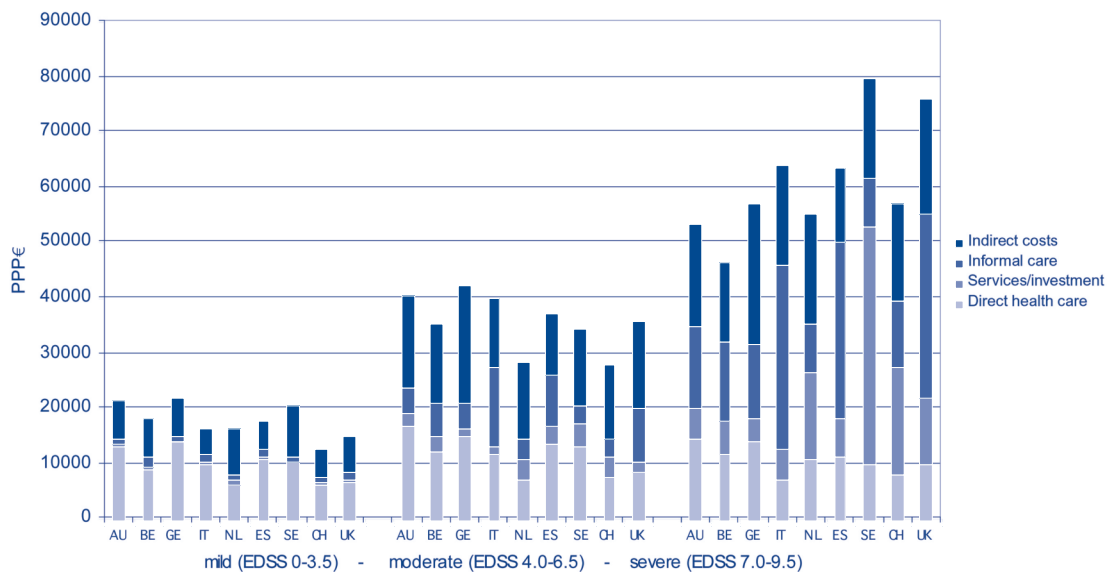
In this situation, new treatments aimed at preventing disease worsening will not provide cost off-sets within the limited perspective of the health care system. As on the outcome side, where dramatic effects on

**Figure 7 – Cost structures in 9 countries (N=13,186, mean annual cost/patient, PPP€ 2005)**



Source: Adapted from Kobelt et al. (2006)

**Figure 8 – Cost increase with progressing disease (mean annual cost per patient, PPP€ 2005)**



Source: Adapted from Kobelt et al. (2006)

quality of life are elusive due to the irreversibility of the disease, cost-effectiveness ratios from the payer perspective are unlikely to meet any of the current (unofficial) thresholds used by different decision makers. An exception to this is Sweden with its generous provision of services to disabled people as part of the health care system.

Yet, when looking at costs and their increase over the course of the disease from the societal perspective, it is equally obvious that there is a large potential for DMTs to be cost-effective from that perspective. However, as treatment of MS is in the preventive setting – maintaining patients for a longer time in milder disease states with early treatment – it takes

time for such effects to be measurable and modelling of those effects is unavoidable.

### Cost-effectiveness estimates

A number of models have estimated the cost-effectiveness of DMTs in the past decade. The majority of these studies were performed at introduction of a new treatment, using the limited knowledge available from clinical trials. All models have been based on disease progression measured with the Expanded Disability Status Scale (EDSS). This measure of functional capacity, largely based on ambulation, is included in all clinical studies, epidemiological cohorts and treatment registries. It has also been shown to correlate extremely well with both costs and utility in all studies and countries, making it an ideal measure to estimate the long term effect of an intervention for cost-effectiveness analysis (Kobelt et al. 2006).

Using the latest analysis published, we can explore a number of issues related to the need to use a societal perspective (Kobelt et al. 2008). We can then perform a number of comparisons for other countries using the same model (unpublished data).

The study was performed in Sweden, comparing results of a clinical trial with a new DMT indirectly to treatment with current DMTs as observed in the Stockholm MS registry. If we compare Sweden to the other countries in Figure 8, we can see that health care and service costs are very similar for the mild and moderate disease stages, but diverge greatly in the severe stages due to the extensive services offered by the Swedish health care system. This is important in two respects:

- a) the time horizon of the analysis is crucial, as it must include a timeframe within which patients can actually reach the severe disease stages with high cost and low utility; a long timeframe is hence important in all analyses everywhere;
- b) treatments should be more cost-effective in Sweden than in other countries even when considering only the health care perspective due to the steep direct cost increase in late disease.

Table 6 illustrates the importance of the perspective and the time horizon in Sweden (Kobelt et al. 2008).

With a societal perspective, over 20 years, the new treatment dominates previous DMTs for the type of patients included in the clinical trial. It also dominates no treatment. When we include only health care costs, the cost per QALY gained is €38,000, which in Sweden is considered acceptable. However, if we shorten the timeframe to 10 years, we lose almost half of the treatment benefit in terms of QALYs gained, as well as some of the late savings, leading to a cost per QALY of €124,000, which would exceed what Sweden is willing to accept.

A further conclusion that can be drawn from the costs presented in Figure 8 is that treatments are likely to be more cost-effective in the Swedish system than elsewhere, even when using health care costs. When comparing the above numbers to the health technology assessment performed by the National Institute for Health and Clinical Excellence (NICE) in the UK, we observe that the cost per QALY for

**Table 6 – Cost per QALY of a DMT in Sweden under different assumptions (€ 2005)**

	Timeframe years	Incremental cost (€)	Incremental effect (QALY)	ICER €/QALY
<b>Comparison to current DMTs<sup>1)</sup></b>				
Health care perspective (including services)	20	13,010	0.34	38,000
Societal perspective	20	-3,830	0.34	dominant
Societal perspective	15	7,840	0.27	28,000
Societal perspective	10	22,217	0.18	124,000
<b>Comparison to no treatment<sup>2)</sup></b>				
Health care perspective (including services)	20	22,400	1.05	21,300
Societal perspective	20	-30,900	1.05	dominant

Sources:

1) Adapted from Kobelt et al. (2008);

2) Unpublished data.

interferon treatment ranges from €53,200 to €90,800 after discounting costs at 6% p.a. and effects at 1.5% p.a. (Chilcott et al. 2003). Ratios for the societal perspective are not available from the paper. However, using data from one of the manufacturers' submissions, we can estimate that using the societal perspective reduces the ratios by 35-40%. This would produce a range of cost-effectiveness ratios in the theoretically acceptable range (€33,500-€57,000).

We can observe such differences in the ICERs across countries, the magnitude depending on a number of factors such as the extent to which countries provide services in late disease, the salary levels and the proportion of the population in the workforce at different ages. Figure 9 illustrates these differences, estimated by using the above model for the latest DMT introduced.

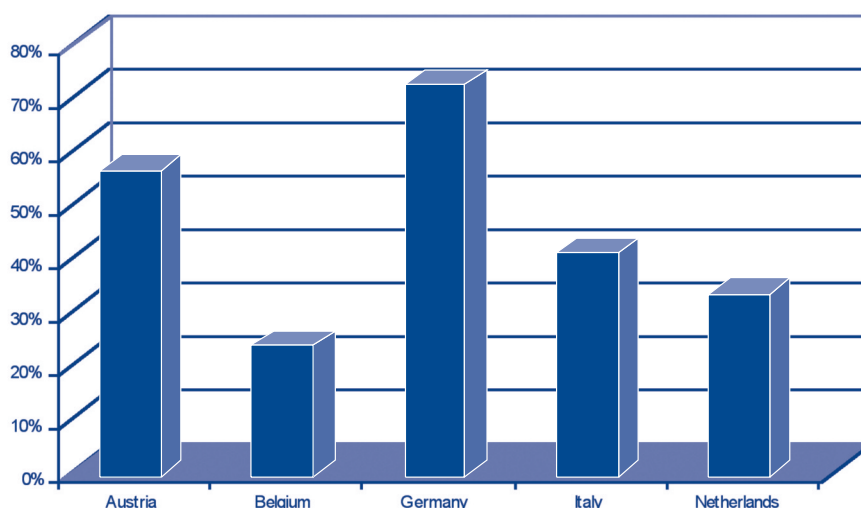
### Discussion

The goal of treatment in MS is to avoid exacerbations, thereby ultimately slowing the speed of progression to severe disability, where quality of life is low and costs high. Costs in moderate and severe disease are

essentially caused by the inability to work, and the need for extensive external help. Health care costs have historically been low, and caused by extended hospital stays. With the general move in recent years from inpatient to more outpatient care, hospitalization costs have been reduced (Henriksson and Jönsson 1998). In a disease such as MS this means simply that a large part of these costs have been shifted to families, as rehabilitation is shifted to the outpatient setting with patients staying at home even during exacerbations or when the disease has advanced to severe functional disability.

In the light of this, it appears contrary to social responsibility to fail to take into account informal care costs when making decisions on treatments that will act in the long term. It appears equally illogical from an economic standpoint to ignore the loss of productivity caused by the disease. Excluding both of these impacts will lead to decisions that reject potentially cost-effective treatments. One might argue that we are in need of a more precise guideline on how exactly informal care costs and productivity losses should be estimated, but excluding them in a disease like MS simply denies the consequences of the disease.

**Figure 9 – Increase in ICER when only using health care cost perspective**



Source: Unpublished data, using costs from Kobelt et al. (2006)



## 4. DISCUSSION AND CONCLUSIONS

A societal perspective for economic evaluation is the classic approach to assessing the profitability of societal investments. This is the standard approach in the assessment of different environmental, transport and safety programmes affecting health using cost-benefit analysis. Cost-benefit analysis provides guidance on how to allocate resources in order to maximise societal welfare. Departing from a societal perspective increases the risk of societal inefficiencies in the use of resources for health and the risk that maximal health is not produced.

There are several reasons why economic evaluation in health care has developed away from a societal perspective towards a more restricted payer perspective. One is the critique of welfare economics and cost-benefit analysis as a basis for economic evaluation of resource allocation to and within the health care sector. The search for alternative methods, based on a theory of “extra welfarism” is acknowledged, but the aim of this briefing is not a full discussion of the general methodology for economic evaluation. The paper is restricted to addressing the societal versus health care payer perspective on costs in economic evaluation of investments in health care technologies. The arguments apply to different approaches to benefit evaluation, for example both willingness to pay or QALY gained. We argue that a “decision maker approach” to economic evaluation should take a societal perspective.

Another reason is the success of economic evaluation as an instrument to help decision makers in the health care system – clinicians, budget managers and policy makers responsible for funding and reimbursement decisions – to make rational allocative decisions. This gives a focus on the specific budget they are responsible for. But we should also acknowledge that health economists have been ready to accept this as a prerequisite to get entrance to and influence over the decision making processes. Some principles have been given up in order to gain access to a field where many stakeholders hold strong opinions. Advising governments on methodology involves compromises as is evident from guidelines from all over the world, which is an argument to keep alive the debate about the key principles. Many “decision maker perspectives” include definitions of “imaginary” rather than real budgets. It is the rule in all countries, rather than the exception, that health care spending is divided into many different “budget silos”, and an important aim of economic evaluation is to reduce the risk that this will lead to sub-optimal decisions. It should also be clear that the ethical and

distributional arguments for restricting the cost perspective in order to not discriminate against certain groups, for example the elderly, are relevant. But we argue that restricting the perspective so that important costs are neglected is not a good method for addressing these issues. The consequences cannot be predicted and the risk of suboptimal decisions is great.

Adopting a societal perspective in a systematic way should not unfairly benefit specific stake holders, for example the innovative health technology industry. The social versus private perspective is not about profits, but about what types of innovations are developed. The threshold for adopting technologies is of course affected by how costs are defined, but also by many other factors that determine the returns to investments in new health care technologies.

In our view, an economic evaluation is not the decision; but it is an input to the decision process. We share the view that decisions about health care technologies can be seen as “deliberate processes” where several different inputs to health care decision making are combined, see Culyer (2009). The cost-effectiveness algorithm is an important input, but not the only one, and we argue that this algorithm is more useful if calculated from a societal perspective than from a more restricted payer perspective.

We acknowledge that a wider societal perspective requires more work and input of scarce resources in terms of qualified health economists and others. But we think the extra investment is justified by the improved usefulness of the resulting study. If there are serious omissions in the cost estimates, even the best outcome assessments may lead to a wrong decision. It is also likely that adopting a societal perspective may lead to an increase in uncertainty about the cost-effectiveness estimates, but this must be seen in relation to the uncertainties in the estimates of outcome. It is also “better to be vaguely right than precisely wrong” as Ezra Mishan so well argued for an imprecise measurement of the right concept rather than a precise estimate of the wrong one.

To improve decision making on the societal efficiency of the allocation of health care resources, economic evaluations should be based on a societal perspective. Adopting a societal perspective implies not only that the costs that refer to a specific payer or the health care system should be included. The costs of informal care, loss of production, and mortality costs should also be accounted for. Using a societal perspective instead of a health care perspective in economic evaluation implies that more health may be produced given available resources. Further, information is provided on the optimal social level of spending on health care.

The importance of using a societal perspective is illustrated by the two examples from the Alzheimer's and multiple sclerosis disease areas. In particular they show the importance of including productivity costs and costs of informal care, which usually are not considered in economic evaluation of medical interventions. Departing from a societal perspective may have significant implications for the assessment of cost-effectiveness.

To increase the understanding and comparability of the results of economic evaluation of health care programmes, a common framework should be adopted. A societal perspective for economic evaluation should be the standard approach adopted by health technology assessment and reimbursement organisations world-wide.

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