Societal perspective on the cost of illness

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Societal perspective on the cost of illness

Kosten van ziekten vanuit maatschappelijk perspectief

Proefschrift

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Chapter 4 Roijen L. van, Essink-Bot M.L., Koopmanschap M.A., Bonsel G. and Rutten F.F.H.. Labour and health Status in economic evaluation of health care. International Journal of Technology Assessment in Health care, 1996 , 12 (3): 405-415.

Chapter 5 Koopmanschap M.A., Roijen L. van, Bonneux L., Barendregt J.J.M.. Current and future costs of cancer. European Journal of Cancer, 1994; 30A(1): 60-65.

Chapter 6 Beeck E.F., Roijen L. van, Mackenbach J.P.. Medical costs and economic production losses due to injuries in the Netherlands. The Journal of Trauma, 1997; 42 (6): 1116-1122.

Chapter 7 Roijen L. van, Beckers A., Stevenaert A., Busschbach J.J. van, Eijk W. van, Rutten F.F.H.. The burden of hypopituitarism in Adults after pituitary surgery. Endocrinology and Metabolism, 1997, 4 (suppl. B.), 139-142.

Chapter8 Roijen L. van, Gageldonk A., Arends L., Smit F., Donker M.. Setting priorities for cost-effectiveness analyses in mental health care in the Netherlands. (Submitted).

Chapter 9 Roijen L. van, Essink-Bot M.L., Koopmanschap M.A., Michel B., Rutten F.F.H. Societal perspective on the burden of migraine in the Netherlands. Pharmacoeconomics 1995; 7(2): 170-179.

Chapter 10 Roijen L. van, Nijs H.G.T., Avezaat C.J.J., Karlsson G., Linquist C., Pauw K.H. and Rutten F.F.H.. Costs and effects of microsurgery versus radiosurgery in treating acoustic neurinoma. Acta Neurochirurgica 1997;139(10), 942-948 .

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Contents

1. INTRODUCTION

1.1. The Cost of illness

The rising costs of health care during the last decades enhanced the importance of economic evaluations in support of decisions on resource allocation. Questions may be raised as to whether the allocation of resources is optimal when measured against the total health gain that an investment brings. Many health economists have emphasised that the high costs of disease may be a necessary but certainly not a sufficient condition for priority-setting in health care (e.g. Drummond, 1992). Additionally, data on the effectiveness of interventions themselves is needed. In health policy the high cost of diseases may lead to priority being given to those health care programmes which are already costly. Whereas if past resource allocation decisions have been made in an irrational manner, then subsequent policy decisions perpetuate and amplify the initial mistake (Sheill et al., 1987). From a policy point of view, the equitable distribution of costs and consequences across socio-economic groups is a competing dimension upon which decisions are made. Therefore, apart from information on cost-effectiveness, health policy should also be based on ethical considerations (e.g. equity).

Cost-of-illness studies may serve several purposes:

Firstly, the results of cost-of-illness studies may be applied as inputs for scenario analyses. Planning future provisions of health care requires insight into demographic developments, the epidemiology and other relevant components of the cost of illness such as technological developments. In general, epidemiological and technological developments are not included in scenario analyses as they are difficult to estimate.

Secondly, the results of cost-of-illness studies may be used as a first step towards setting priorities in health care research. This may be fundamental research into more effective treatment of a disease or applied research into the operational aspects of the treatment. Several criteria for priority-setting were proposed by the Dutch Minister of Health. The substantial societal burden of diagnostic categories, high costs and a high prevalence rate respectively, are

important but not the only selection criteria. Additionally, there should be a high degree of uncertainty regarding the cost-effectiveness of an intervention, together with a probability of contributing towards a reduction of morbidity or mortality and/or the improvement of health-related quality of life.

Thirdly, the results of cost-of-illness studies may be used to distinguish between cost increase due to demographic, price and epidemiological developments, and other reasons. Furthermore, cost-of-illness studies may serve as a point of reference for cost-effectiveness analyses. A cost-effectiveness study of a new intervention analyses changes in costs and effects compared to the current situation, which is described in the cost-of-illness study.

Lastly, the results of cost-of-illness studies can be used as an input for cost-effectiveness analyses. On the one hand to indicate which cost items and aspects of quality life should be included, as cost-of-illness studies provide information on which costs are important and which aspects of quality of life are at issue. On the other, the results may serve as input for estimating the cost-effectiveness ratio of an intervention. For instance, the estimates of production losses in certain patient groups may be input to estimate the reduction of indirect costs as a consequence of a successful intervention.

1.2. Methodology

'Cost-of-illness' or 'burden-of-illness' studies produce systematic information on the cost to society of disease. These studies consist of one or more of the following components:

- The direct costs, representing the value of resources, within and outside health care, used to prevent, detect, treat and monitor the disease or its effect;
- The indirect costs due to lost production or costs to prevent a production decrease (for paid and unpaid work) as a consequence of morbidity or premature death from the disease;
- Reduced health-related quality of life as a consequence of the disease;
- Premature death.

A complete cost-of-illness study should consist of all four components, presenting an overall view of the societal burden of a disease. However, general studies concentrate on the direct cost

estimates (the first component). In this thesis all studies will be referred to as 'cost-of-illness' studies.

This thesis contains papers on general and specific cost-of-illness studies. The latter estimate the costs of illness for a specific disease, whereas general studies include the cost of all illnesses and further allocate these total costs across diagnostic categories. Dorothy Rice was one of the important pioneers in this research field (Rice, 1966). Ideally, all specific studies should add up to the grand total of diseases and figures should be comparable. However, due to methodological differences this is not the case.

Cost of illness can be estimated according to the incidence or prevalence based method (Hartunian et al., 1980). The incidence based method is longitudinal and requires estimates of incidence, expected disease course and treatments most likely to be used. In principle, estimates based on the incidence approach include all present and future direct costs and losses of output. The prevalence method is more simple and estimates the economic burden resulting from the prevalence in a given year. While prevalence or annual cost-of-illness studies estimate the burden of illness during a year, incidence costs more appropriately measure the benefits of changes in incidence of disease, as may result from prevention or successful intervention during the course of disease (Hodgson, 1988). Estimating effects of an intervention applying the prevalence method is a valid approach in the case of acute conditions with a short duration. The prevalence method will also be satisfactory for estimating the cost of chronic diseases having a constant incidence or stable course of the disease and where no rapid changes in medical technology are to be expected which may have a significant influence on medical care costs. Finally, the prevalence method is appropriate to estimate the share of a disease category in the total costs for a given year.

1.3. Comparability

In addition to methodological differences between cost-of-illness studies, variations in health care systems and social security systems make comparisons very difficult. For instance, in comparing figures of the total costs (direct and indirect costs) for the Netherlands, Sweden and the US, large differences were found in the share of GDP (The Netherlands 28%, Sweden 23% and United States 16%). With respect to health care costs both total and disease-specific costs are very similar in the Netherlands and Sweden, but differ substantially from those in the United States. This appears to be due to differences in medical practice and financing of health care; demographic or epidemiological aspects are less important (Koopmanschap et al., 1994).
Differences in social security systems are probably responsible for the large differences in indirect costs due to absence from work and disability, a subject dealt with in chapter 3 of this thesis. The liberal criteria for entitlement for social security benefits probably enhanced absence from work rates in the two European countries as compared to the United States. In addition, the average duration of disability in the Netherlands is relatively long (15 years).

1.4. Health and Labour Questionnaire

There is still a lot of discussion about the proper way of quantifying and valuing indirect costs (Koopmanschap et al., 1995). Production losses due to illness may occur in the paid or unpaid section of the economy, depending on the particular characteristics of the patients concerned, such as age and gender. Furthermore, production losses due to a specific illness also depend on the type of manifestation (acute, chronic or sporadic) and on the severity of the disease. Disease may cause permanent disability or may be responsible for only a temporary reduction of productivity at work or at home. For some diseases indirect costs constitute a substantial part of the total costs, for instance for migraine. In chapter 8 of this thesis we estimated that 80% of the total costs of migraine are due to indirect costs.

Quantifying these production losses we can distinguish two types of data, national data and patient specific data on absence from work, reduced productivity, disability and mortality. In

chapter 3 we estimated the indirect cost of disease using national data on absence from work, disability and mortality by age and gender for all diseases. In chapter 6 we assessed the direct and indirect cost of injuries based on national data. When performing specific economic evaluations we were often confronted with a lack of (diagnostic specific) data on key parameters for estimating production losses. The Dutch national registry on short-term absence became less complete due to changes of the prioritisation of the sickness benefits scheme. Hence, we have developed the Health and Labour Questionnaire (HLQ) to collect individual data on absence from work, reduced productivity and disability. The HLQ data enable the estimation of production losses and describe the ability to use work as an indicator of health status in the social domain.

Estimates of indirect costs should incorporate production losses in relation to unpaid labour to prevent adverse equity implications. National data on production losses for the unpaid sector are scarce. However, for specific patient groups (e.g. the elderly and women) household production may be relatively important compared to paid production. The HLQ also quantifies production of unpaid labour. For measuring unpaid production losses, four productive activities were distinguished: household work, shopping, caring for children and odd jobs around the house (see chapter 4).

Most studies use the human capital approach for valuing the indirect costs (Koopmanschap et al., 1993). This method estimates the value of potentially lost production as a consequence of illness, whereas the actual loss for society may be much smaller (Drummond et al., 1986). For short term absences, a person's work may be covered by others or made up by the sick person on his return to work. For long-term absences, an individual's work can be covered by someone drawn from the ranks of unemployment or reallocating employees over jobs (Drummond, 1992). The institute for Medical Technology Assessment (iMTA) developed the friction cost method which seeks to estimate the real amount of indirect cost attributable to disease, taking into account the situation in the labour market and within firms (Koopmanschap et al., 1995). Estimates of indirect costs based on the latter are about 10% to 20% as compared with costs estimates according to the human capital method. The huge difference is due to the costs of disability and mortality, which are assumed to cause production losses in the long term using

the human capital approach. In chapter 6 the influence of the method applied on the level of indirect costs and the distribution by diagnostic subcategory are assessed for injuries. This study indicates that the indirect costs are one-fifth according to the friction cost method when compared to the human capital approach. In calculating the potential production losses for society, traffic injuries are a major source of indirect cost, whereas occupational injuries are by far the largest subcategory when the actual production losses are computed.

1.5. Study scope and objectives of this thesis

In summary, this thesis aims to:

- Indicate the relevance of general and specific cost-of-illness studies for health policy.
- Discuss the comparability of estimates of cost-of-illness studies.
- Present the contents, operational design and validation of the Health and Labour Questionnaire (HLQ).
- Demonstrate the influence of the application of the HLQ in cost-of-illness and cost-effectiveness studies.

1.6. Structure of this thesis

Part I consists of results of a general cost-of-illness study for the Netherlands. Chapter 2 provides a comprehensive description of the total direct costs generated by all diseases in the Dutch population. Estimated direct costs are distributed by type of care, 48 disease categories, age and gender in 1988 and a demographic projection of future costs is made. In chapter 3 indirect costs by age, gender and main disease category for the Netherlands are compared with estimates for Sweden and the United States based on the human capital approach.

Cost-of-illness studies for specific diseases have been performed more often. Part II of this thesis will discuss the results of partial costs-of-illness studies. In chapter 4 the HLQ is presented. We applied the HLQ in several studies and the results are presented for the general population, migraine patients, patients with a spinal cord injury and patients with hip or knee problems. In chapter 5 the cost of five types of cancer are presented. These costs were linked to

incidence and mortality and prevalence for prediction of the future costs. Chapter 6 of this thesis presents the direct and indirect cost for injuries, using both the human capital approach and the friction cost method. In chapter 7 we assessed the burden of hypopituitarism in adults after pituitary surgery. Direct and indirect costs and the health-related quality of life of these patients are compared to estimates for the general population. In this study module 1, 2 and 4 of the HLQ were applied (absence from work, reduced efficiency and labour related problems).

In the previous discussion it is stated that cost-of-illness studies may be used as a first step to set research priorities. Chapter 8 concerns a paper on a study for targeting future research in mental health care. The direct cost of mental disorders are estimated for the Netherlands in 1993. Subsequently, a brief description is given of the international literature study on effectiveness of treatments for schizophrenia. We conclude with recommendations for cost-effectiveness analyses on schizophrenia.

In a large survey the societal burden of illness of migraine is assessed. Direct medical costs and indirect costs are estimated, and are presented in chapter 9. Production losses are assessed by applying the HLQ.

Chapter 10 analyses costs and effects of treating acousticus neurinoma patients by using microsurgery compared to radiosurgery. Cost and effects estimates of the conventional treatment are based on a retrospective study in the Netherlands. Similar data for a comparable group of patients in Sweden were collected for radiosurgery, as this treatment option is currently not available in the Netherlands. The HLQ is applied for assessing production losses. In chapter 11 a number of conclusions are presented.

Part I General cost-of-illness studies

2 COST OF ILLNESS IN THE NETHERLANDS

2.1. Summary

This study is an essential prerequisite to gain more insight into the complex relationship between public health and the cost of medical care. It offers a first tentative but comprehensive description of the total direct costs generated by all diseases in the Dutch population. We classified estimated direct cost of illness (39.8 thousand million guilders) by type of care, sex, age and 48 diagnostic categories for 1988.

In order to estimate the costs of health care in the year 2030, we linked this information with demographic development.

We were able to allocate 75% of all costs to diseases. Ranking by major disease categories revealed that mental disorders account for the highest proportion of costs (20%), followed by diseases of the circulatory system (9%), and diseases of the digestive system (8%). Cost of medical care increased significantly with age and were presumably incurred by non fatal ailments. Health care costs for men and women were almost similar.

In the year 2030 the costs of dementia and diseases of circulatory system will increase the most. A reliable estimate of the costs should also take epidemiological and economic considerations into account.

2.2. Introduction

The task of the health care system is to safeguard the health of citizens, and to promote public health. At first sight this opening statement would seem too trivial to be included in a serious medical-scientific article. However, through an examination of the history of the Dutch health care system, as well as its concomitant policies over the last few decades, one could draw the conclusion that this seemingly simple truth has often been lost sight of. Issues such as policy on volume, cost control, personnel planning and alike could be discussed without any reference at

all being made to their contribution to health care. As a source of information the Health Care Financial Review, published annually by the Dutch Ministry of Welfare, Health and Culture, has become an increasingly indispensable and informative document, even though it does not, in fact, establish a bridgehead between health care and public health. Furthermore, it quickly becomes apparent to anyone studying the development of public health that health care is but one of a number of factors having an important and demonstrable influence on public health.

Now that demand for health care is slowly outstripping the available supply, the contribution made by various sections of the health care system has become a matter of current discussion. Questions may be raised on the possible advantages to general health care by investing in a particular medical technology, or whether the expenditures on resources is optimal when measured against the total gain to health that this investment brings. In the future, the relationship between public health, use of resources and cost will become an increasingly important field of research. It will also be necessary to gain insight of the correlation between these three determinant factors in order to study the expected increase in demand for health care services and the costs that this will incur.

The research presented in this chapter forms a first step on the path towards a better understanding of this correlation. Here, an attempt will be made to answer the following two questions:

- How are the total costs of health care distributed over the various health care sectors, over various age groups, between men and women and between various illness groups?
- How will these costs be divided in the year 2030 when only the influence of the aging population is taken into account?

The results of this research have been more thoroughly described in a separate research report containing all the relevant tables and more detailed information (Koopmanschap et al., 1991).

2.3. Methodology

Our analysis is based upon the year 1988. This year was chosen because at the time of this study the data on this year proved to be the most recent and complete. The total cost of health care (not including the cost of care of the elderly or social services) as described in the Health Care Financial Review serves as the point of departure in our cost calculation.

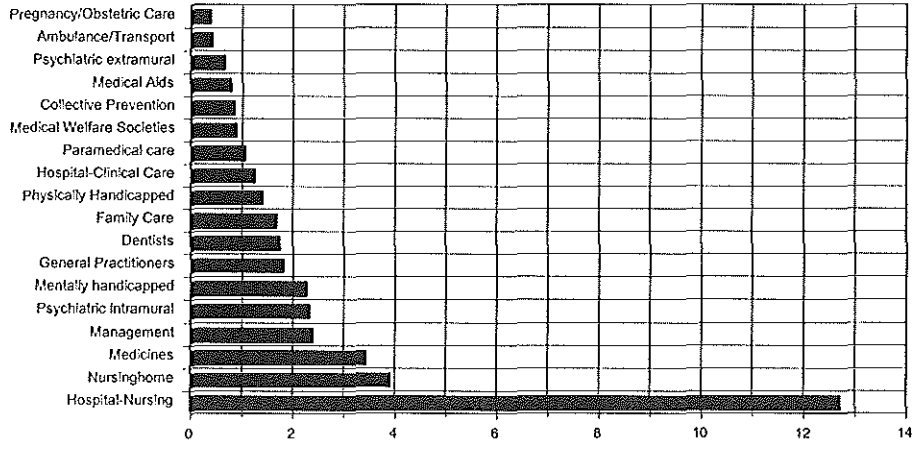
Costs: Only the costs incurred within the health care services are considered in this study. These costs relate to the resources utilised in diagnosis, care, treatment, prevention, revalidation and organisation. This definition of costs is in agreement with that put forward in the Health Care Financial Review (WVC, 1990). In addition to these direct costs, ill health also bring indirect costs to society in the form of a decline in productive capacity. This share of the costs we have represented in the degree of work-related sick leave, invalidity and death, although we have left the costs hereby incurred out of consideration for the present study.

Diagnosis: The users of care services were divided into diagnosis groups, age-sets and gender groups. The diagnosis groups were arranged in accordance with the guidelines of the International Classification of Diseases (ICD)(WHO, 1977). The seventeen sections of this classification were sub-divided into forty-eight diagnosis groups on the basis of the number of fatalities, the burden of ill health, its economic consequences, the expectations regarding the disease's development, and its treatment. Only the cost division in the seventeen sections of the ICD are given in this chapter. The division into forty-eight groups is to be found in the detailed report mentioned earlier.

Data: Over the last few years, Dutch society has used nine percent of its annual Gross National Product on health care which, in international terms, gives the Netherlands a medium ranking. This level of expenditure must also be seen in light of a relatively good level of public health (Mackenbach et al., 1991). In 1988 the total expenditure on health care amounted to 44.3 thousand million guilders (approx. USD 27.6 billion). If geriatric care and social work are not including then the total figure was 39.8 thousand million guilders (approx. USD 24.8 billion). In our research the figure of 44.3 thousand million guilders was sub-divided by diagnosis group, age-set and gender.

We sub-divided health care into as many sub-sectors as possible (see figure 2.1). For each (sub-) sector the costs have been calculated for diagnosis group, age-set and gender with the help of a common denominator. This common denominator mostly contains information on the amount of services that were delivered per diagnosis group. For example, the costs of physiotherapy were sub-divided according to the number of contact with a physiotherapist. It has been assumed that each contact involved the same costs. Although this assumption is not altogether correct, the common denominator replicates the division of costs as close as possible where both illness and age-related data on the length of contact between patient and practitioner is lacking.

Figure 2.1 Costs of the Dutch Health Care system in 1988 per sector in thousand million guilders (cost in 10^9 guilders).



The sector 'hospitals' delivers a whole range of services but lack of information meant that we could only divide it into two sub-sectors: 'clinical treatments' and 'other hospital care'. In this sub-division the cost of polyclinic treatments were included under the heading 'other hospital care' and were estimated pro rata the number of nursing days. One consequence of this approach was that while conditions requiring relatively little nursing care but a great deal of polyclinical

treatment were being underestimated, conditions requiring the reverse of this therapeutic regime were being greatly overestimated.

In sub-dividing the costs only the primary diagnosis was used as our point of reference. Generally speaking, it is these conditions which bring about the most expenditure, although secondary ailments may also substantially influence the consumption of medical resources. This means in practice that our estimates of the costs incurred by diagnosis groups where a secondary condition appeared relatively often were probably somewhat under their true level.

2.4. Results

Seventy-five percent of the total costs of Dutch health care may be attributed to conditions contained within the diagnosis groups. Of the other 25%, 6% went to policy and management while lack of sufficient data made it impossible to ascribe the remaining 19% to any particular category of illness. These categories include the sectors 'medicines', 'home care' and 'ambulances/ transportation'. The results are discussed for each user variable.

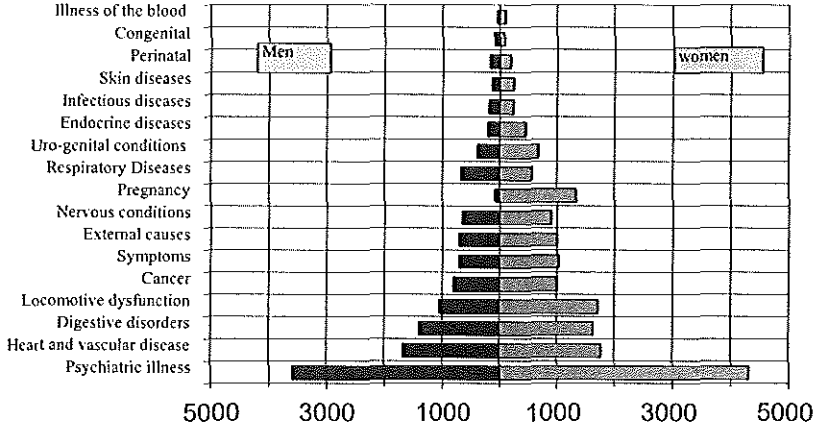
Costs per sector. Taking the Health Care Financial Review as our point of reference, seventeen care sectors were distinguished, with the sector 'hospitals', at 35%, consuming the lion share of resources (see figure 2.1). Fairly far behind came the sectors 'convalescence' and 'medicines', both at 10% of the costs.

Costs per diagnosis and gender. Women consumed 57%, around 22 thousand million guilders (approximately USD 13.75 billion), of the total costs (figure 2.2). Using the guidelines of the International Classification of Diseases (ICD), little difference could be discovered between men and women in their respective share of the costs. For both genders the costs incurred for psychiatric illnesses, heart and vascular disease, digestive disorders and locomotive dysfunction's were the greatest. Locomotive dysfunction was more prevalent among women and heart and vascular disease among men.

The diagnosis groups with the highest costs concerned conditions with a lengthy trajectory and a low mortality rate. Only heart and vascular disease formed an exception to this rule (see figure 2.2). The picture changes when the category 44-64 years is examined, with psychiatric illnesses,

heart and vascular disease, locomotive dysfunction's and cancer becoming more prevalent. In the category 65-79 years, heart and vascular disease becomes the diagnosis group consuming the greatest proportion of expenditure. The sharp increase in costs in the category 80 years and older can be primarily attributed to diagnoses such as 'dementia', 'strokes/apoplexy', 'locomotive dysfunction' and 'non-traffic accidents' (see table 2.1).

Figure 2.2 **Costs per diagnosis group (sub-divided into the seventeen sections of the International Classification of Diseases) according to gender in 1988 in millions of guilders.**



Costs per age-set and gender. Figure 2.3 shows that little variation is to be found in costs per individual or per age-set between men and women. The average costs only slowly increase until the age category 55-59 years is reached. While in the category 5-9 years the average cost was one thousand Dutch guilders (USD 625), this sum had leapt threefold by the time the category 55-59 years is reached. Above this age group costs begin to escalate rapidly with the 85 and over averaging no less than 18,000 Dutch guilders (approximately USD 11,250) per head. The higher costs for women of 80 years and over than for men of the same age can partly be explained by the fact that the women in this category of our research population were slightly

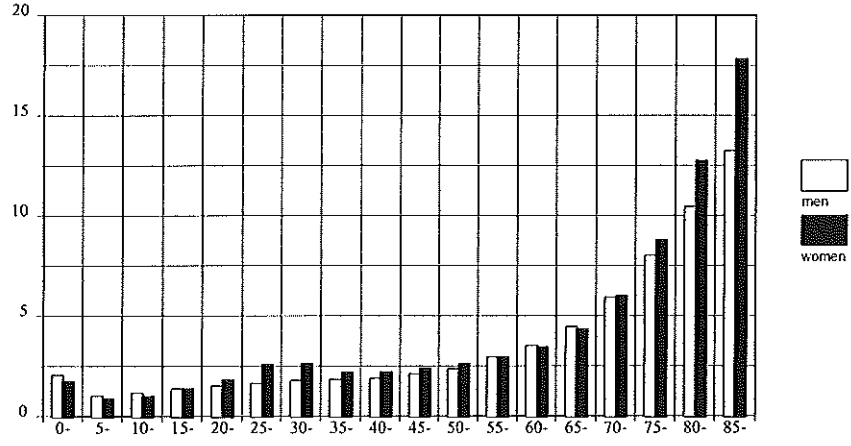
older than the men. The high cost of women in the category 20-44 years can be almost entirely accredited to pregnancy and childbirth. These costs are assigned to women which is something of an arbitrary decision (see figure 2.3).

Table 2.1 The average cost of health care in 1988 per person according to age and diagnosis group (in Dutch guilders).

Diagnosis Group*	Age					
	0-19	20-44	45-64	65-79	>=80	total
Infectious diseases	36	19	21	40	84	28
Cancer	9	36	184	503	678	123
Endocrine Illnesses	9	5	47	174	380	45
Blood disorders	4	3	7	32	90	9
Psychiatric Illnesses	210	615	550	847	3279	592
Nervous disorders	59	41	97	321	722	104
Cardiovascular diseases	4	30	277	1023	2306	234
Respiratory diseases	66	40	75	227	435	83
Digestives disorders	158	192	199	307	544	206
Uro-genital conditions	20	50	92	194	306	72
Pregnancy	45	202	1	0	0	94
Skin diseases	13	16	20	61	181	25
Locomotive dysfunction	48	143	232	413	1043	187
Congenital	31	6	3	4	3	12
Perinatal	91	0	0	0	0	24
Symptoms	74	76	123	262	565	117
External causes	60	619	88	279	1057	116
Not assignable	233	289	571	1114	2019	416
Never assignable	161	161	161	161	161	161
Total per person	1332	1994	2748	5960	13854	2693

*Diagnoses have been categorised following the seventeen guidelines of the ICD (WHO, 1977).

Figure 2.3 **The average costs per person according to age and gender in thousands of guilders.**



Costs per diagnosis and sector. Often the cost of a diagnosis group appear to be concentrated within a single or small cluster of care sectors. As the prevalence of a particular diagnosis increases, it brings with it a concomitant rise in costs for the care sector(s) concerned with its treatment. This factor is of utmost importance to the planning of health care services.

Heart and vascular diseases took 13% (3.4 thousand million guilders; USD 2.125 billion) of the resources available in intramural care, second only to psychiatric illnesses. By further sub-dividing the diagnosis group 'heart and vascular diseases' it appears that, in hospitals, ischemic heart disorders represented a large share of the costs, while 'strokes/apoplexy' form a major diagnosis group in convalescent homes. This demonstrates the importance of further sub-dividing the seventeen ICD guidelines. Of note was the fact that the cost of nervous disorders, excluding eye and ear conditions, were mostly met by the convalescent home sector. These expenditures mostly concerned the treatment of Parkinson's disease and Multiple Sclerosis. Of the total costs of acute lung diseases, 35% (139 million guilders; USD 86.8 million) were taken up by the 'general practitioner' sector, and hypertension accounted for 70% (100 million guilders; USD 62.5 million) of resources. As information becomes available on the cost of

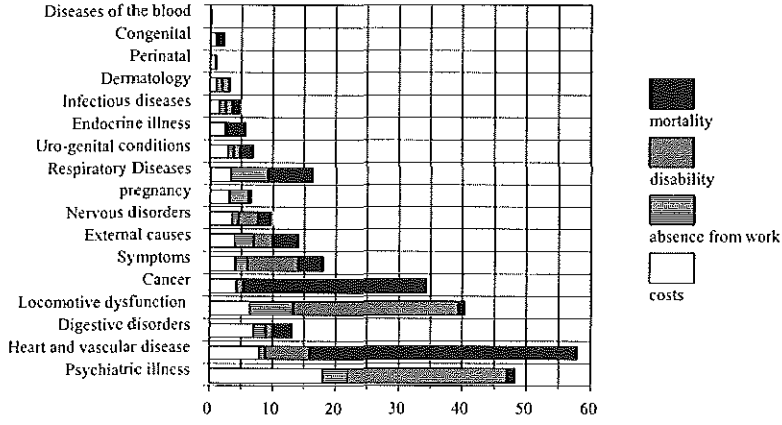
medicines vis-à-vis diagnosis groups, the share of the costs for hypertension met by the general practitioner sector will diminish.

The Consequences of Illnesses. Apart from the direct medical costs, illness also leads to a loss of productive capacity which has its indirect financial consequences for society as a whole. To create a more comprehensive picture of the cost of illness to society, the peripheral factor of production loss also has to be included in calculations. Loss of productivity is measured by the amount of registered sick leave, invalidity and mortality, but production losses occurring through unpaid labour (work in the household, for example) are not included here.

The quantification and evaluation of these production losses may be done in a number of ways (Koopmanschap et al., 1992). Here the categories 'sick leave', 'invalidity' and 'mortality' are only reproduced in their volumes. Figure 2.4 shows that diagnosis groups with high direct costs were not unduly influenced by the three aforementioned categories. 'Psychiatric illnesses' and 'locomotive dysfunction's' were, however, well represented in the categories 'sick leave' and 'invalidity', but not in 'mortality'. 'Cancer' and 'heart and vascular diseases' were diagnosis groups with a high mortality but were relatively unimportant in the scales 'sick leave' and 'invalidity' (see figure 2.4).

With regard to 'absence from work' it must be said that in 70% of the cases no diagnosis was made because they involved only short-term absences from work with no medical practitioner being consulted.

Figure 2.4 **Percentage share of the diagnosis group (the seventeen sections of the International Classification of Diseases) in costs, absence from work, disability and mortality.**



Cost projection 1988-2030. The data available to us for 1988 forms the basis upon which we have built a cost model, the construct of which allows us to make long-term projections on expenditure (CBS, 1990b). A first step is a cost calculation based upon demographic trends, together with data on the developments in prevalence and incidence. In addition to estimates on total cost, insight may also be gained of the cost development within particular sectors.

With the help of the population prognosis for the Netherlands to the year 2030, a global projection of costs is possible (den Toom, 1988). The average cost per head of population in relation to diagnosis, age-set and gender - the categories previously described - are also used as our point of departure here. The results will certainly not be predictions, but rather projections because, in reality, not only is the size and composition of the population influential to cost development but epidemiological and economic factors also play an important role. Changes in patterns of consumption, a shift from intramural to extramural care for example, has an influence upon the level and distribution of costs. Table 2.2 gives the projected cost

development of diagnosis in line with the demographic prognosis for the years 2010 and 2030, expressed in indices. The year 1988 is 100; costs are also given in 1988 prices.

Table 2.2 **Development of health care costs according to diagnosis group (projections for the years 2010 and 2030, based on demographic development, index costs 1988=100).**

	2010	2030
Diagnoses with a low index (<110)		
Pregnancy	82	86
Fertility	87	89
Perinatal	91	95
Congenital	98	98
Dental diseases	103	99
Appendicitis	104	103
AIDS	106	103
Other lung diseases	109	118
Diagnoses with a high index (>131)		
Dementia	148	203
Cardiovascular diseases	139	182
Male sexual organs	136	181
Duodenal ulcers	136	171
Rheumatism	135	173
Cancer	135	174
Diabetes Mellitus	134	174
Liver diseases	134	162
Nephritis/Nefrose	133	165
Index total costs	121	139

The first four diagnosis groups with a relatively low index: fertility, perinatal abnormalities and congenital abnormalities, are strongly dependent on the number of live births. This prognosis is given with great caution as the number of live births in any given year is very difficult to predict. Furthermore, developments in the medical technology connected to fertility, such as the diagnosis and treatment of infertility, will most probably lead to increases in costs, although these too cannot easily be predicted. AIDS is a case in point. As very little insight exists on the epidemiological development of this disease, a cost estimate becomes extremely problematic. The examples given here make clear that, in addition to demographic factors, epidemiological and economic factors must also be included in analyses if any plausible projection of costs in the future is to be achieved (see table 2.2).

The list of diagnosis groups with a relatively high index is headed by 'dementia', followed by 'heart and vascular disease'. The demographic projection indicates that costs will rise substantially for illnesses related to the male sexual organs, duodenal ulcers, rheumatism, cancer and diabetes mellitus. A strong increase in these costs is most noticeable in the year 2030 as a consequence of the 'baby boom' years between 1946 and the early 1960's. The members of this cohort will be well advanced in years by then and it is thought that, for example, the costs involved in the treatment of dementia will double by the year 2030. In 1988, the costs for the category 20-44 years are the most consuming. By 2010 the projection indicates that the category 45-64 years will take over the top position, with the high costs being incurred by the 65-79 years category in the year 2030.

The group with the highest cost index are related to illnesses that generally take hold in later life. Projections on the composition and population level within this age-set are then more reliable than those for younger age-sets. Furthermore, illnesses at great age involve far more care, a factor that make cost reductions for conditions related to age rather improbable. The cost projections for these elderly conditions may, therefore, be given with some degree of certainty.

2.5. Discussion

Our research does, for the first time, offer a total overview of the costs of ill health in the Netherlands from the perspective of age, gender and diagnosis group. Using this method the costs incurred by all diagnosis groups are calculated using the same premise, which thus allowed the results to be mutually compared. Until now research in the Netherlands on cost has been limited to a single or small cluster of diagnosis groups. The results of research into the costs of heart and lung disease, accidents and lung cancer already conducted in the Netherlands are in general agreement with our findings. The greatest variation between our results and the findings of others is for lung cancer, but this may be explained by the fact that we underestimated the cost of polyclinic help for this ailment due to this data being unavailable to us.

While our research has been able to pinpoint the data still lacking which would be able to increase the accuracy of cost estimates, most notably in the sectors 'hospital' and 'medicines', it has nevertheless been possible to attribute seventy-five percent of the costs of Dutch health care to particular categories of illness.

Some research has also been carried out in other countries on the total cost of health care. Comparison with these results is more difficult due to differences in the composition of the population, the epidemiological data available and the type of care that each sector provides. While the findings of Lindgren for Sweden showed great similarity to ours, this cannot be said of Rice et. al. and Berk et. al. in the United States (Lindgren, 1990; Rice et al., 1985; Berk et al., 1975). Table 2.3 shows the percent points division of the seventeen ICD categories. The low level of expenditure on psychiatric services in the American samples is in marked contrast to those indicated in European research. Although this probably reflects the limited availability of psychiatric services in the United States, this does not necessarily mean that the prevalence of psychiatric disorders is any lower in the USA than in Europe (see table 2.3).

Table 2.3 Division of direct costs in health care according to diagnosis group for a number of foreign research projects compared with the present study.

Diagnosis group	USA, 1975[a]	USA, 1980[b]	Sweden, 1983[c]	The Netherlands, 1988[d]
Infectious diseases	1.7	2.0	1.6	1.0
Cancer	4.5	6.2	5.1	4.6
Endocrine illnesses	2.8	3.5	2.3	1.7
Blood disorders	0.5	0.5	0.5	0.3
Psychiatric illness	7.9	9.4	21.1	22.0
Nervous disorders	6.3	8.1	4.2	3.8
Heart and vascular disease	13.5	15.4	12.3	8.7
Respiratory Diseases	6.4	7.9	5.0	3.1
Digestive disorders	12.3	14.7	3.8	7.6
Uro-genital conditions	4.7	5.8	3.0	2.7
Pregnancy	2.9	-	2.7	3.5
Skin diseases	1.8	2.8	1.7	0.9
Locomotive dysfunction	4.3	6.2	3.9	7.0
Congenital	0.4	0.6	0.5	0.4
Perinatal	0.1	-	0.5	0.9
Symptoms	2.7	1.8	5.1	4.3
External causes	5.8	8.8	4.8	4.3
Other illnesses	0.0	4.1	0.0	0.0
Not assignable	21.4	2.0	21.9	23.1
Total	100.0	100.0	100.0	100.0

a. Berk et al., 1978; b. Rice et al., 1985; c. Lindgren, 1990; d. Koopmanschap et al., 1991.

Diagnoses which involve high costs are, generally speaking, not life-threatening conditions, with the exception of heart and vascular disease. Costs increase with age, and the costs

differences between men and women are minimal, except for the cost of female patients aged 80 and over. The sub-division into forty-eight diagnosis groups proved to be a valuable method as the seventeen IC guidelines often contain diagnosis groups with strongly variant cost compositions over sector, age-set and gender.

The data offers an insight into the current state of illnesses vis à-vis the costs they bring about. When incorporated into demographic data they would seem to provide a good basis for a global cost projection. The next step would be to incorporate epidemiological and economic data into calculations on the future state of financial affairs.

In calculating costs a number of choices have been made which we feel should be discussed and clarified here. While a large proportion of the cost of the elderly is consumed by housing costs - and is therefore unrelated to illness - shortfalls in nursing home capacity has led to an increase in ill people remaining in old peoples homes, and data on this factor is currently lacking.

Furthermore, the provision of care carried out by social services is, for the most part, related to social and not health problems. If further research indicates that the costs of the sectors 'care of the elderly' and 'social services' do indeed derive from illnesses, then these too must be included in analysis.

In the research of Rice the direct costs involved in pregnancy and the conditions which may arise in the perinatal period have not been separated; their share has been subsumed in the category 'other illnesses'.

The decision to include the costs of pregnancy was also an arbitrary one. In the first place, as it is not an 'illness', pregnancy cannot be easily compared with other diagnosis groups. Secondly, the level of medical consumption is determined not by the care of the mother but by the care of the unborn child. The medical costs related to having children could also be seen as costs in the process of child delivery. From this perspective the cost should rather be attributed to the envisioned product: the child.

Finally, the addition of indirect costs of illness incurred through paid and unpaid work to the calculations will undoubtedly has an influence upon both their composition and level.

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3. INDIRECT COST OF DISEASE; AN INTERNATIONAL COMPARISON

3.1. Summary

Results of economic evaluations are often strongly influenced by estimates of indirect costs. International comparability of these estimates may contribute to rational decision-making in health care policy. Hence, estimates should be international comparable. Comparability of these results between countries may be hampered due to variation in methodology, data sources, valuation of production losses, and social security arrangements. Furthermore differences in epidemiology, demography and economic environment may cause variation in the level and the distribution by diagnosis of indirect costs. In this study indirect cost of disease for the Netherlands are compared with estimates for Sweden and the United States. We found large differences: both in the share of indirect costs in GDP as in the constituting elements, absence from work, disability and mortality. The level of indirect costs due to absence from work and the distribution according to diagnosis are quite similar for the two European countries. The cost of disability are particularly high for the Netherlands. Comparison of disability costs between the three countries is hampered due to lack of quantitative information on the influence of social insurance arrangements on the level of indirect costs and the distribution by diagnosis. The large number of deaths at young age in the U.S. is responsible for the higher mortality costs compared to the two European countries.

3.2. Introduction

The economic cost of disease generally are divided into direct costs and indirect costs. Direct costs represent the value of resources used to prevent, detect and treat a health impairment or its effect. Indirect costs represent the value of output lost due to illness or premature death. Indirect costs bear a more implicit relation to illness because they do not directly influence

expenditures from treating disease and they are not easily measurable. Nevertheless production losses due to illness and production gains due to health care influence the wealth of society and should therefore be incorporated in economic evaluations of health care programmes. Indirect costs are often substantial compared to direct costs and strongly influence the cost-effectiveness. A literature review on studies considering indirect costs of diseases indicated that on average indirect costs represented 52% of the total disease costs or total costs saved by health care interventions (Koopmanschap et al, 1993). Comparability of results of economic evaluations between countries may be hampered due to variation in methodology, data sources, valuation of production losses and social security arrangements. If these aspects are comparable, it is possible to analyse the contribution of differences in epidemiology, demography and economic environment to the level of indirect costs and the distribution by diagnosis. In this study indirect cost of disease are calculated for the Netherlands and compared with estimates for Sweden and the United States. The total costs are divided into costs of absence from work, disability and mortality, because different processes and causes are at the root of each of these cost components. We will attempt to trace the contribution of each of the factors mentioned to differences in results across the countries. Finally, we will give recommendations to extend comparability, allowing for a better interpretation of international differences in indirect costs.

3.3. Methodology

Indirect cost of disease are defined as the value of production lost to society due to absence from work and disability and death. It should be emphasised that we do not value human life itself, but we analyse only the economic effects of disease. Other important aspects of illness, like pain and suffering are not dealt with here and should preferably be measured in terms of quality of life.

We estimate indirect costs for the Netherlands in 1988, and compare these with Sweden in 1983 and the U.S. in 1980, the most recently published estimates of indirect costs for these countries (Lindgren, 1990; Rice et al., 1985).

The three studies use the human capital approach to estimate indirect costs. This method calculates the potential indirect costs of diseases. If, for example, someone dies at the age of 35, it is assumed the total earnings from that age until the age of retirement represent the value of production lost. So, the human capital method assumes that all potential years of life lost, short-term absence and long-term disability would have been spent in full productivity. This concept of indirect costs in the economic appraisal in health care is not uncontroversial. Many authors have suggested that the production losses for society are overestimated due to the current methodology used due to economic circumstances (Lindgren, 1990; Drummond, 1992; Gerard et al., 1989). For short-term absenteeism, work may be taken over or postponed. For long-term absences, work can be taken over by unemployed or by reallocation of employees over jobs. An alternative approach called the friction cost method takes into account these economic circumstances that limit production losses to disease. According to this approach production losses are assumed to be confined to the period needed to replace a sick worker: the friction period. The length of this period and the resulting indirect costs depend on the situation on the labour market (Koopmanschap et al., 1992). Estimates of the indirect costs according the friction cost method are only available for the Netherlands. So, for reasons of comparison with the studies of Rice and Lindgren we only present the estimates based on the human capital approach. The share of absence from work, disability and mortality in the total indirect costs and the distribution according diagnosis may be useful tools in health care decision making.

In most studies the production loss of paid and unpaid labour is valued at average market earnings and imputed values of housekeeping services. The estimates of indirect costs are the result of average earnings by age and sex and the number of days from work lost, disabled and death by diagnosis, age and sex. The indirect costs are distributed according to the seventeen chapters of the International Classification of Diseases, Injuries and Causes of Death (WHO, 1977). All studies made a distinction between absence from work, disability and mortality. The study of Lindgren is based on the cost of the incidence of illness in one year. Rice used the prevalence method; for the Netherlands we will present results of both methods. The prevalence approach estimates the indirect costs due to the total number of days of absence, disabled and deaths in a year. The incidence method includes only the indirect

cost of new cases but takes into account the present and future indirect costs during the expected course of disease. Hence, here this will only make a difference for the cost of disability because absence is defined as a period of sickness shorter than 1 year.

3.3.1. The Netherlands

Table 3.1 presents an overview of data sources used in the studies. We have used national disease-specific statistics on absence from work, disability and mortality for 1988. Data on absence from work by diagnosis, age and sex were derived from the Central Office for Statistics (CBS, 1988a). This register covers over 50% of the labour force, except for the self-employed and a part of the public employees. Cost of absence from work are based on numbers of days of sickness for periods of absence less than one year. Unfortunately, in 70% of the cases of short-term illness the diagnosis is unknown because the patient had no contact with a doctor.

The Mutual Medical Service provided data on incidence and prevalence of disabled employees and early disabled persons by diagnosis, age and between the sexes (GMD, 1990). There is not much difference in the duration of the disability period between diagnoses and sex (van Eck et al., 1986). The average disability period amounts to 15 years and decreases with age. Data on the number of deaths before the age of 65 in the entire population by primary diagnoses, age and sex are also provided by the Central Office for Statistics (CBS, 1989a). The average number of days of household production lost per person due to sickness is derived from a Time Use Survey on a representative sample of the Dutch non-institutionalised population (CBS, 1992). There was no information available about the underlying diagnosis, therefore we have assumed the distribution by diagnosis to be equal to paid labour. Household production years lost are based on the number of deaths before the age of average life expectancy (74 for men and 80 for women). We used the market alternative approach, assuming the value of household production to be equal to the costs of hiring personal to do the housework (Harwryslyshyn, 1977). This is valued as the weighted average gross earnings of occupations that correspond to the main household tasks (LTD, 1992). We valued the production loss of paid labour by using the gross average earnings per

worker by sex and age taking into account the proportion of full time and part time labour (CBS, 1988b). Future earnings per person, based on average earnings and labour force participation rates by sex and age plus imputed household values, are discounted at 5% per year.

Table 3.1 Overview of data used for estimates of indirect costs for the Netherlands 1988, Sweden 1983 and the United States 1980

	Netherlands	Sweden	United States
Absence paid labour	National Registry	National Registry	Survey
Absence non paid labour	Survey	National Registry	Survey
Disability	National Registry	National Registry	National Registry
Mortality	National Registry	National Registry	National Registry
Value production loss due to morbidity	Average earnings per worker by age and sex	Average earnings per worker by age and sex	Average earnings per worker by age and sex
Value production loss due to mortality	Life time earnings per person by age and sex, disc. 5%	Life time earnings per person by age and sex, disc. 5%	Life time earnings per person by age and sex, disc. 4% and 6%
Value household production loss due to morbidity	Weighted average earnings of corresponding occupations	Average earnings per worker by age and sex	Weighted average earnings of corresponding occupations

3.3.2. Sweden

The National Social Swedish Insurance Board provided data on the number of sickness days for periods less than 1 year by diagnoses, age and sex. In Sweden nearly all persons in the productive age range are entitled to a sickness benefit cash transfer. So, the estimates do not only refer to employed people but also include people without paid jobs. For periods less than 1 working week, the recorded illness may be based on either a self-reported diagnosis or a doctor's diagnosis; if absence from work lasts longer than 6 days, a doctor's examination is required for receiving sickness benefits.

Data on disabled by diagnosis, age and sex were derived from the National Social Swedish Insurance Board. Lindgren assumed that none of the disabled returns to the labour force, so they stay disabled until the age of retirement (65 years).

The Swedish National Bureau of Statistics provided data on the number of deaths before the age of retirement by primary diagnosis, age and sex.

The average gross earnings per worker in the relevant age and sex groups were used to estimate the value of production loss due to absence, permanent disability and mortality. Lindgren assumed the value of household production to be equal to the gross average earnings in market employment. The future earnings are discounted at 5% per year and labour force participation rates are taken into account.

3.3.3. United States

Rice calculated the costs of absence from work, disability and mortality by diagnosis, age and sex for the U.S. in 1980. The number of sickness days by diagnosis of currently employed and housewives is based upon estimates by the National Health Interview Survey (NHIS). The NHIS is a household sample survey of the civilian non-institutionalised population. The number of persons unable to work due to long-term physical or mental illness is based on the publication of the Bureau of Labour Statistics and the number of persons in institutions. The number of persons in institutions is reported by the U.S. Bureau of Census and is allocated to

diagnoses according to the type of institution. Rice excluded the influence of the duration of the disability. So, this estimate calculates the loss in 1 year, based on the prevalence of disability during that year. Production losses due to morbidity are valued by the gross earnings for men and women by age and sex. The value of housekeeping was imputed by multiplying hours spent in each kind of domestic task by the wages for corresponding occupations by age and sex. The present value of life time earnings is discounted at 4% and 6%. For our comparison we used the mean unweighted estimates of mortality costs discounted at 4% and 6%, which comes close to 5%.

3.4. Results

3.4.1. Total indirect costs

For reasons of comparison we present direct costs and indirect costs as share of the GDP. For the Netherlands the total cost of illness in 1988, direct and indirect, amounted to 126 billion Dutch guilders, 28% of the GDP. For Sweden and the U.S. the total costs of illness accounted for 23% and 16% of GDP respectively (see table 3.2). Note that this does not imply that GDP would be increased by this percentage if all diseases would be eradicated. It only indicates the potential loss of GDP due to illness. The relatively high total cost of illness in the Netherlands are mainly due to indirect costs, which are more than twice the size of the direct costs. For Sweden this ratio is 1.5 and for the U.S. slightly more than one. Expressed as a percentage of the GDP indirect costs due to mortality show the smallest differences between the three countries.

Table 3.3 shows that the distribution of indirect costs according to disease is very similar for the two European countries; non-fatal diseases (mental disorders and locomotor diseases) have the largest share in the costs. For the U.S, fatal diseases, like cardiovascular disease, accidents and violence, are far more important.

For both the U.S. and the Netherlands indirect costs for men are about 70% higher than for women, but in Sweden men and women have an equal share of costs.

Table 3.2 Direct and indirect costs* as share in GDP in % and indirect costs of disease due to absence from work*, disability and mortality* (annual discount rate 5%) as % of total indirect costs, for the Netherlands 1988, Sweden 1983 and U.S. 1980

	Netherlands	(%)	Sweden	(%)	U.S.	(%)
Share in GDP						
Direct costs	8.9		9.0		7.9	
Indirect costs	19.2		13.8		8.3	
absence	3.8		5.2		1.2	
disability	10.9		5.1		1.2	
mortality	4.4		3.5		5.8	
Total costs	28.1		22.8		16.2	
Share in indirect costs	1988	1990	1975	1983	1970	1980
absence	20	19	40	38	28	15
disability	57	58	35	37		15
mortality	23	22	25	25	71	70
Total indirect costs	100	100	100	100	100	100

*including the indirect costs due to production losses of unpaid labour.

For the Netherlands about 75% of the total costs of illness for persons over age 65 are due to direct costs, reflecting increasing need of medical care with age and decreasing value of production after the age of 65 (in general only unpaid production). For the U.S. this percentage amounted to 79%. For the U.S and Sweden the share of indirect costs in GDP decreased in time. This percentage amounted to 9.3% for the U.S in 1972 compared to 8.3% in 1980. For Sweden this share was 16.8% in 1975 and 13.8% in 1983. Finally, the share of

morbidity and mortality costs in the total indirect costs did change much over time, see table 3.2.

Table 3.3 Distribution of indirect costs by main disease categories (17 ICD-chapters) in the United States, Sweden and the Netherlands in percentages of total indirect costs

	Netherlands 1988	Sweden 1983	US 1980
Infectious diseases	0.9	1.6	2.4
Neoplasms	4.3	8.0	15.4
Endocrine/metab.dis.	1.3	1.9	2.3
Diseases of the blood	0.1	0.2	0.4
Mental disorders	18.7	14.9	4.5
Dis.nervous system	4.0	3.9	2.4
Cardiovascular diseases	10.2	12.2	21.5
Respiratory diseases	3.8	10.3	6.8
Dis.digestive system	2.7	3.6	4.7
Genito-urinary diseases	0.9	1.3	1.3
Pregnancy and delivery	1.1	0.7	-
Diseases of the skin	0.7	1.0	0.3
Locomotory diseases	23.5	21.8	3.1
Congenital anomalies	1.4	1.3	2.0
Perinatal diseases	0.3	0.5	-
Symptoms	8.4	3.6	2.8
Accid., pois. And voilence	7.6	13.2	26.4
Other diseases	0.0	0.0	3.8*
Unallocated	10.3	0.0	0.0
Total	100.0	100.0	100.0

* Includes complications of pregnancy, childbirth, and puerperium and certain conditions originating during the perinatal.

3.4.2. Absence from Work

Table 3.2 shows that absence from work accounts for 38% of the total indirect costs for Sweden, as compared to 20% for the Netherlands and 15% for the U.S.. The average number of work days lost rank highest for the Netherlands (17 days per worker), followed by Sweden (14 days per worker) and the U.S. (5 days per worker), see table 3.4.

The high number of days of absence from work could indicate a worse health state of the European workers. However, national health surveys, studies on health, medical consumption and health related quality of life indicate that U.S workers are even less healthier than European workers (Adams, 1991). The striking difference between the average number of absence days is partly the result of the social security arrangements. Study indicated that the highest increase in time of absence from work rates occurred in countries with more liberal criteria and procedures for entitlement (Enterline, 1966; Prins, 1990). In the Netherlands the arrangements became more permissive in 1968. This change has been thought to induce an increase in absence of over 16% for 1968 compared to 1966 and 1967 (Taylor, 1972). The sickness benefits became equal to 100% of the normal income from the first day on. The Swedish insurance system resembles the Dutch system except for a obligatory doctor's examination. For the U.S. generally a waiting period applies, which provides a clear incentive to go to work, even during illness. The method of collecting data also influences the recorded level of absence. Contrary to the Dutch and Swedish national registries, the NHIS is based on self-reporting. Study indicates that the number of long-term sickness is underestimated in health surveys compared to national registries (Prins, 1990). Finally, the U.S. law is relative liberal in case of firing a sick worker. Table 3.5 shows that the distribution of the costs of absence from work by diagnosis is quite similar for Sweden and the Netherlands, but for the U.S. the pattern deviates. Both for Sweden and the Netherlands locomotor diseases are the main reason for absence from work, 26% and 20% of the costs.

Table 3.4 Number of work days lost, disabled persons and mortality rates for the Netherlands 1987, Sweden 1983 and the U.S. 1980

	Netherlands	Sweden	U.S.
Number of work days loss per worker	17[a]	14[b]	5[c]
Incidence of disabled per 100 000 employed	1263[d]	794[e]	
Prevalence of disabled per 100 000 employed	13 047[d]		7300[f]
Mortality rate for homicide (males)	1.2	1.6	17.0
per 100 000 persons (females)	0.6	0.9	4.4
Mortality rate for suicide (males)	13.7	27.3	18.6
per 100 000 persons (females)	8.4	10.9	5.4
Mortality rate for motor (males)	13.5	13.9	34.4
vehicle accidents (females)	5.6	5.5	12.0
per 100 000 persons			

a. Central Office for Statistics, CBS 1988.
b. The national Social Swedish Insurance Board, 1983.
c. National Health Interview Survey (NHIS, 1981)
d. Common Medical Service, 1988.
e. The National Social Swedish Insurance Board, 1983.
f. Bureau of Labour Statistics, 1980.
g. WHO World Health Statistics Annual 1989, 1986 and CBS 1990.

For the U.S. locomotor diseases rank fifth, representing only 8% of the costs. Respiratory diseases are the most important reason for absence in the U.S. (24%). The strikingly low share of cost of respiratory diseases for the Netherlands is probably the result of the lack of information on short-term absence from work in the Dutch records, as supported by the Swedish data on short-term illness. Accidents, poisoning and violence are the second reason for short-term illness in the U.S. (23%), which is partly the result of the much higher incidence rate of violence and motor vehicle accidents in the U.S. (see table 3.4).

Table 3.5 Distribution of indirect costs due to absence from work by main disease categories and sex in percentage of costs for the Netherlands 1988, Sweden 1983 and the U.S. 1980

	The Netherlands 1988			Sweden 1983			U.S. 1980		
	M	F	T	M	F	T	M	F	T
Infectious diseases	0.9	1.0	0.9	2.8	2.9	2.9	5.2	6.2	5.6
Neoplasms	0.7	0.8	0.8	1.7	1.5	1.6	6.3	7.2	6.7
Endocrine metab. dis.	0.3	0.4	0.3	1.3	1.5	1.4	2.6	2.5	2.6
Diseases of the blood	0.1	0.2	0.1	0.2	0.3	0.2	0.2	0.5	0.3
Mental disorders	12.5	13.2	12.7	9.0	8.5	8.8	2.7	3.5	3.0
Dis. Nervous system	1.7	1.3	1.6	2.8	2.7	2.8	3.0	3.2	3.1
Cardiovascular	3.1	1.1	2.5	6.7	4.4	5.6	8.4	9.6	8.9
Respiratory diseases	4.1	4.4	4.2	21.2	22.7	21.8	23.6	24.5	24.0
Dis. digestives system	3.8	2.3	3.4	6.4	4.8	5.6	8.6	7.4	8.0
Genito-urinary diseases	0.9	2.6	1.4	1.1	4.4	2.7	2.9	6.4	4.4
Pregnancy and delivery	0.0	13.6	4.0	0.0	3.8	1.8	0.0	0.0	0.0
Disease of the skin	0.9	0.8	0.9	1.3	1.8	1.5	1.8	0.8	1.4
Locomotory	22.4	12.4	19.5	26.0	25.7	25.7	8.0	8.0	8.0
Congenital anomalies	0.1	0.1	0.1	0.1	0.2	0.1	0.0	0.0	0.0
Perinatal diseases	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Symptoms	2.1	1.7	2.0	6.1	8.1	7.1	2.5	4.1	3.2
Accidents	8.6	4.1	7.3	13.3	7.3	10.4	24.3	12.4	19.3
Other	-	-	-	-	-	-	0.0	3.6	1.5a
Unallocated	37.6	40.1	38.4	-	-	-	-	-	-
Total	100	100	100	100	100	100	100	100	100

For Sweden and the Netherlands, the cost share of accidents, poisoning and violence are in third place, 10% and 7% of the costs. Nearly 13% of the cost of absence from work is due to

mental diseases for the Netherlands, for Sweden mental illness is responsible for 9% and for the U.S. only 3%. The U.S. data are based on self reporting and because mental illness is a less socially accepted disease, this could influence the distribution by disease (Rubin, 1992). For all three countries cardiovascular diseases, accidents, poisoning and violence and locomotor diseases are relatively more important for men than women. In both the U.S and the Netherlands, men are responsible for the main share of the costs (72% and 70% respectively), although the share of men in the number of work loss days is only 54% for the U.S. and 59% for the Netherlands. This difference is the result of the higher average income of men compared to women in these two countries. In Sweden both sexes are responsible for about half of the number of days lost as well as the costs.

The loss of unpaid production due to sickness is of minor significance for the U.S (6.7 billion U.S. $) and the Netherlands (1.6 billion Dutch guilders), 3% and 2% respectively of the total indirect costs. Data of the Dutch Time Use Survey shows that people feeling ill still spend time on household activities. In some age categories, especially for persons having a paid job, household production even increased due to illness. The Swedish estimates incorporates the costs of unpaid production loss but the data did not allow us to estimate these costs.

3.4.3. Disability

The share in the total indirect costs based on the prevalence of disability is 15 % for the U.S and 57% for the Netherlands. The strikingly high share in the Netherlands is due to a high prevalence of disability, which is the result of high incidence and long average duration of disability (see table 3.4). Both the level and the length of the period of receiving disability benefits are relatively attractive in the Netherlands. As a consequence, a disability benefit is often preferred to an unemployment benefit. Dutch studies indicate that 15-20% of the persons receiving a disability benefit should actually be considered as unemployed (Roodenburg, 1985; Vrooman, 1990). In the U.S. a benefit is only paid in the case of invalidity, i.e. persons unfit for any other job (SSB, 1989). In addition, the waiting period of 5 months is a clear incentive to continue working. Although, the distribution of the costs by

diagnosis is maybe influenced by the level of indirect costs, some striking differences can be observed. For the Netherlands mental illnesses (29%) and locomotory diseases (24%) rank highest. For the U.S. cardiovascular diseases are the main reason for disability (25%) followed by mental diseases (24%).

Women have a relatively low share of in the cost of disability, 25% for the U.S. and 16% for the Netherlands. This reflects the low labour force participation rates for women, 60% for the U.S. and 41% for the Netherlands and the lower average income of women compared to men for both countries (OECD, 1988).

We compared the estimates for the Netherlands with the estimates for Sweden using the incidence method. For the Netherlands 63% of the indirect costs are due to disability compared to 37% for Sweden. The Swedish government pursues an active policy against disability, towards preventive arrangements as substitutes. However, the distribution of disability costs by diagnosis is quite similar for the two European countries. Locomotor diseases and mental illnesses rank highest, see table 3.6. Diseases of the circulatory system are the third main reason for disability in Sweden (12%) and the Netherlands (8%). Neoplasms account for 3.4% of the costs for Sweden and only 1,7% for the Netherlands. The latter difference is partly implied by the method used. In our calculation we have made corrections for the average duration of disability by diagnosis, age and sex. The average duration of disability for neoplasms is relatively short (6 years), compared to the mean duration of 15 years. The share of cancer in these costs for the Netherlands would amount 3,1% applying the method comparable to Lindgren (Lindgren, 1990). He assumed that disability will proceed until the age of 65, irrespective of diagnosis. This caused an overestimation of the Swedish costs of disability due to cancer. Contrary to the Dutch situation the share of both sexes in the cost of disability is not significantly different in Sweden, 47% for women. On the other hand men are responsible for 58% of early retirements. This is caused by the fact that women on average retire earlier than men and consequently the total number of work years lost for women is higher. Besides the participation rate of women is relative high in Sweden, 78% (OECD, 1988).

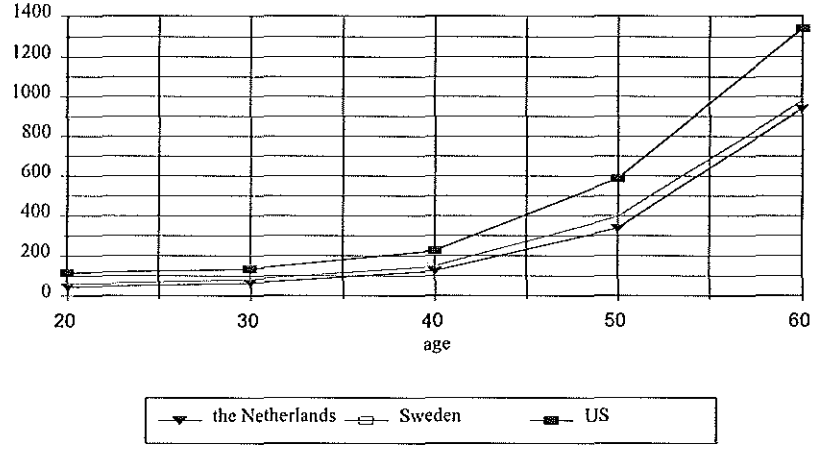
Table 3.6 **Distribution of indirect costs due to disability by main disease categories and sex in percentage of costs for the Netherlands 1988, Sweden 1983 and the U.S. 1980**

	The Netherlands 1988			Sweden 1983			U.S. 1980		
	M	F	T	M	F	T	M	F	T
Infectious diseases	0.7	0.8	0.8	0.9	1.0	1.0	6.4	7.4	6.5
Neoplasms	1.4	3.0	2.0	2.0	4.2	3.4	10.2	12.1	10.5
Endocrine metab. dis.	1.5	1.9	1.6	2.6	2.7	2.7	4.1	4.2	4.1
Diseases of the blood	0.1	0.2	0.1	0.1	0.1	0.1	0.5	0.6	0.5
Mental disorders	22.3	31.7	24.3	31.7	27.5	29.7	23.0	28.8	23.8
Dis. Nervous system	5.2	6.2	5.4	6.1	6.6	6.3	4.6	5.0	4.7
Cardiovascular	12.4	5.9	11.0	15.8	7.0	11.7	26.4	17.7	25.3
Respiratory diseases	4.3	2.3	3.9	3.2	2.7	3	5.9	2.8	5.5
Dis. Digestives system	2.4	1.7	2.3	1.4	1.4	1.4	1.9	2.2	1.9
Genito-urinary diseases	0.6	1.3	0.7	0.6	0.6	0.6	0.7	0.8	0.7
Pregnancy and delivery	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Disease of the skin	0.7	0.8	0.8	0.9	1.4	1.1	0.2	0.0	0.2
Locomotory	30.0	25.3	29.0	26.8	38.0	32.0	12.5	13.6	12.6
Congenital anomalies	1.6	1.9	1.7	1.2	1.6	1.4	0.0	0.0	0.0
Perinatal diseases	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Symptoms	10.7	13.7	11.3	0.7	1.8	1.2	2.2	2.4	2.2
Accidents	5.8	3.3	5.3	5.2	3.5	4.4	1.5	2.4	1.6
Other	-	-	-	-	-	-	-	-	-
Unallocated	-	-	-	-	-	-	-	-	-
Total	100	100	100	100	100	100	100	100	100

3.4.4. Mortality

Mortality costs are responsible for 23% the total indirect costs in the Netherlands, 25% for Sweden and nearly 70% for the U.S.. The comparison of the mortality costs clearly demonstrates the influence of expected life-time earnings on the results. Figure 3.1 presents the number of deaths per 100,000 inhabitants by age and sex for the Netherlands, Sweden and the U.S. (CBS, 1989; WHO, 1986; WHO, 1983). The high share of mortality costs for the U.S. is due to the high mortality in the younger age groups, accounting for considerably higher expected life-time earnings forgone. The patterns of the costs distributed to diseases due to mortality for Sweden and the Netherlands are less similar than for short-term illness and disability (table 3.7). For the Netherlands the main share of the cost of mortality is caused by cancer (28%), followed by cardiovascular disease (24%), also responsible for the highest incidence of deaths before the age of 65. Accidents, poisoning and violence come third with 22% of the mortality costs. Both for the U.S. and Sweden, accidents, poisoning and violence rank highest, 32% and 31% respectively of the cost of mortality.

Figure 3.1 Death rates per 100,000 persons for the Netherlands (1988), Sweden (1983) and the U.S. (1980) (CBS, 1989; WHO, 1986; WHO, 1983).



The high cost of accidents, poisoning and violence in the U.S. are mainly caused by the high incidence of deaths due to violence and traffic accidents compared to European countries (see table 3.4). These victims are relatively young and have high expected life-time earnings. The number of reported suicides is relatively high for Sweden. The average number of suicides per million decreased for Sweden in the last decade, for the Dutch population it increased (WHO, 1991). This probably indicates an increase in the fraction of reported suicides in the Netherlands.

For both men and women the mortality costs due to neoplasms rank highest in the Netherlands (26.3% and 40.3%). For Sweden neoplasms also rank highest for women and account for 40% of the mortality costs for women. Cardiovascular diseases and accidents, poisoning and violence are relatively more important for men in all three countries.

For the Netherlands men account for 60% of the mortality costs. For both the U.S. and Sweden this share is 70%.

Table 3.7 **Distribution of indirect costs due to mortality by main disease categories and sex in percentage of costs for the Netherlands 1988, Sweden 1983 and U.S. 1980**

	The Netherlands 1988			Sweden 1983			U.S. 1980		
	M	F	T	M	F	T	M	F	T
Infectious diseases	2.1	0.9	2.0	0.9	1.2	1.0	0.9	1.3	1.0
Neoplasms	26.3	40.3	27.8	18	39.3	24.4	15.5	26.5	18.8
Endocrine metab. dis.	2.3	2.0	2.3	1.6	2.3	1.8	1.5	2.9	1.9
Diseases of the blood	0.2	0.3	0.2	0.2	0.2	0.3	0.3	0.5	0.3
Mental disorders	0.7	0.5	0.7	3.0	1.2	2.5	1.3	0.8	1.1
Dis. Nervous system	2.6	3.3	2.7	2.0	2.8	2.2	1.6	2.1	1.8
Cardiovascular	25.0	13.1	23.7	26.7	14.7	23.1	24.5	24.6	24.5
Respiratory diseases	1.7	1.9	1.7	3.4	3.7	3.5	3.4	4.2	3.6
Dis. Digestives system	3.5	3.1	3.4	3.8	3.2	3.6	4.7	4.8	4.7
Genito-urinary diseases	0.3	0.5	0.3	0.4	0.5	0.4	0.6	1.1	0.8
Pregnancy and delivery	0.0	0.6	0.1	0.0	0.0	0.0	0.0	0.0	0.0
Disease of the skin	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1
Locomotory	0.3	0.6	0.3	0.1	0.8	0.3	0.1	0.7	0.3
Congenital anomalies	2.6	6.2	3.0	2.4	3.8	2.8	2.1	3.3	2.5
Perinatal diseases	2.3	3.8	2.4	1.6	3.1	2.0	0.0	0.0	0.0
Symptoms	7.4	5.2	7.2	1.4	1.7	1.5	2.6	2.9	2.7
Accidents	22.8	17.6	22.2	34.5	21.5	30.6	37.1	18.7	31.7
Other	-	-	-	-	-	-	3.7	5.5	4.2a
Unallocated	-	-	-	-	-	-	-	-	-
Total	100	100	100	100	100	100	100	100	100

a. Includes complications of pregnancy, childbirth, and puerperium and certain conditions originating during the perinatal period

3.5. Discussion

In comparing the estimates of indirect costs for the Netherlands, Sweden and the U.S. the following remarks can be made. Health care costs rose significantly more rapidly than the average earnings in the U.S. between 1980 and 1988 (OECD). Thus the distribution of direct and indirect costs in 1988 may be expected to be quite different from that in 1980. However, when comparing the share of absence from work, disability and mortality in the total of indirect costs and the distribution of the indirect costs according to diagnosis, there is no indication of major changes in this respect for this period.

In estimating life-time earnings all three studies assumed that people will be working during their expected life-time in accordance with the pattern of labour force participation rates for their age and sex group for the base year. There is evidence of changes in employment rates for women during time. However, in absence of information on future developments we assumed constant rates.

Changes in age, sex and diagnosis specific death rates, especially before the age of retirement, may partly explain the differences observed for the different base years across countries. For the U.S. and Sweden death rates for cardiovascular disease for men and women aged 35-74 decreased between 1979 and 1989. However, for other diagnosis, like homicide, these rates increased. Consequently, it is difficult to predict what kind of influence these changes will have on the indirect costs.

We have assumed that the costs of loss of unpaid production are similarly distributed by diagnosis as in the case of paid labour. The composition by age and sex of non-professionally employed is quite different from that of the paid workers. Further study should indicate whether the distribution by diagnosis differs between the two groups. Data on the number of persons incapable of performing household production are lacking for all three studies. These costs are probably low because it has been shown that in general people still spend time on productive activities like household work, childcare and shopping, even when they are ill.

Lindgren assumed that the value of household production losses is equal to the gross average earnings. This may be an overestimation of these costs for Sweden, because the average earnings of paid work are higher than the average production value of unpaid work. However,

the household production losses for the U.S. and the Netherlands account for only a small amount of the total indirect costs. This indicates that both the number of days of absence and the valuation of these losses are low. Therefore, it would probably make a relatively small difference in the total indirect costs for Sweden when valuing these losses at a lower rate.
Finally, the present estimates ignore production losses without absence. These efficiency losses are difficult to quantify but may play an important role in morbidity costs, especially in case of relatively rigid social insurance systems.

3.6. Conclusions

Our analysis illustrates the possibilities and limitations of comparing indirect cost of disease across countries.
Estimates of morbidity costs should be treated with caution. The cost of absence from work and the distribution by diagnosis are quite similar for the Netherlands and Sweden. A comparison with the U.S. is complicated due to differences in social security arrangements and because the U.S. data on absence are based on interviews, whereas data for the Netherlands and Sweden are registry based.
The cost of disability are high for the Netherlands, which is presumably not caused by differences in morbidity, but is mainly due to the favourable social insurance arrangements. Comparison of disability costs between the three countries is hampered due to insufficient quantitative information on the influence of these arrangements on the level of indirect costs and the distribution by diagnosis.
Estimates on mortality costs are comparable and express potential years of life lost, weighted by country-specific differences in labour costs and participation rates. The large number of deaths at young age in the U.S. is responsible for the high mortality costs as compared to the two European countries.
The following recommendations can be made for making estimates of indirect costs more uniform. First, valuation of production losses and discount rates used should be similar. In addition, because the influence in social insurance systems on absence and disability appears to be considerable, longitudinal study is required to quantify its impact on morbidity costs.

Study is also required on the interaction between unemployment and absence from work and disability.

Estimates of indirect costs should preferably be based on national registries. For the Netherlands the registration of diagnosis on short-term illness should be improved. A national registry on absence from work for the U.S. would increase the reliability of the estimates of indirect costs. After correcting for differences mentioned above, the remaining variation in absence, disability and mortality costs should be analysed in relation to economic, demographic, epidemiological or cultural differences.

Our calculations are based on estimated potential production losses. We would prefer comparing estimates of indirect costs which really occur in society, for instance based on the friction cost method. Additional data for Sweden and the U.S. is needed to calculate indirect costs according to this method. Very likely there will remain differences in the contribution of the different diagnosis groups to the direct and indirect costs between countries.

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Part II Specific cost-of-illness studies

4. LABOUR AND HEATLH STATUS IN ECONOMIC EVALUATION OF HEALTH CARE

4.1. Summary

A health care program may influence both costs and health effects. We developed the Health and Labour Questionnaire (HLQ), which consists of 4 modules to collect data on absence from work, reduced productivity, unpaid labour-production and labour-related problems. We applied the HLQ in several studies and the results are encouraging.

4.2. Introduction

Economic evaluations examine both costs and benefits of health care interventions. The impact of a health care program on patients' labour performance may substantially influence both costs and health effects of the program. In the early US literature on health status assessment, labour performance was used as a dominant indicator of health status and its position still is more emphasised in the United States compared with the European literature. In currently available generic health outcome measures, such as the MOS 36-item Short Form Health Survey (SF-36), the health effects in the social (role) domain are partly operationalized as limitations in performing paid and/or unpaid work (Ware et al., 1992).

Production losses have an implicit relation to illness because they do not directly influence expenditures. Nevertheless, indirect costs due to illness influence the wealth of society and should therefore be incorporated in economic evaluations of health care programs. Production losses may occur in the paid and/or unpaid sector of the economy, depending on the particular characteristics of the patients, such as age and gender. The production losses due to a specific illness also depend on the type of manifestation (acute, chronic or sporadic) and on the severity of the disease. Disease may cause permanent disability or may be responsible for only a

temporary reduction of productivity at work or at home. Economic evaluation requires a standardised method of measuring production losses due to illness and reduced labour performance (Koopmanschap et al., 1994; Leving et al, 1992; van Roijen et al.,1995; Ware et al., 1992). So far, no standard instrument appears to be available (Koopmanschap et al., 1993; Koopmanschap et al., 1994; Leving et al., 1992). Hence, we developed the Health and Labour Questionnaire (HLQ) to collect quantitative data on the relationship between illness and treatment and labour performance. The HLQ data should permit the estimation of production losses (costs) and the ability to use work as an indicator of health status in the social domain. The present chapter addresses on the following issues; (i) the contents and the operational design of the HLQ; (ii) the feasibility of the HLQ in various groups of patients and non-patients; and (iii) the validity of the HLQ in several unrelated disease-groups.

4.3. Questionnaire

In developing the HLQ the following requirements had to be met:

- the questionnaire must produce data on the economic effects of illness on labour performance from a societal perspective;
- the questionnaire must produce data on health-effects on paid and on unpaid work;
- the format of the questionnaire must allow for application in a broad range of diseases (e.g. both sporadic diseases and chronic diseases);
- the questionnaire must be suitable for self-assessment by patients;
- the questionnaire must be fairly short and easy to understand to avoid interference with other research tasks of the patient; and
- the questionnaire must be modular to permit leaving out questions that are not applicable to the study population (e.g. paid work in retired patients).

These starting points were operationalized as follows.

Module 1: Absence from paid work

In general, absence from work reduces the effective labour time and consequently decrease of productivity (CPB, 1987; Koning et al., 1984). Respondents with paid jobs are asked to mark on a bar for each (half) day(s) of the two weeks preceding assessment, whether they performed their work or were absent due to health problems or to other reasons. They are requested to fill in one of the three letters in each of the boxes, B "performed paid work", Z "unable to perform paid work due to illness" and V " no paid work due to other reasons" (weekend, holidays etc.). If they worked for only half a day and they were absent from work due to illness in the afternoon they had to fill in B/Z. Figure 4.1 shows module 1 of the non-disease specific HLQ. If the study's interest is a specific health problem a distinction is made between absence due to that health problem and due to other health problems. If the sample is large enough the mean annual number of working days lost is derived by multiplying the results by 26.

Figure 4.1 Example of the non-disease specific module 1 of the HLQ

Imagine that you perform four days paid work, but in the last week you did not work on Thursday and Friday due to health problems. You always have Wednesday free. Then the table would appear as follows:

MO	TU	WE	TH	FR	SA	SU	MO	TU	WE	TH	FR	SA	SU
B	B	V	B	B	V	V	B	B	V	Z	Z	V	V

THE WEEK BEFORE LAST LAST WEEK

Module 2: Reduced productivity at paid work

People sometimes do go to work in spite of illness, which may cause production losses due to reduced efficiency. To enable an estimation of reduced productivity, respondents are asked to estimate the number of additional hours they should have worked to compensate for production

losses due to illness on working days. This method will be referred to as the HLQ-approach. Additionally, this module contains a descriptive instrument of seven items to evaluate specific problems for production. These items relate to the influence of health problems on concentration, working pace, need to be alone, decision making, postponement of work and taking over work by other workers. Response modalities are: 1= "never", 2= "sometimes", 3= "often", 4= "always". The efficiency score results after summing the unweighted items. So, the minimum score is 7 and the maximum score is 28. Table 4.1 shows an example of the item on problems with concentration.

Table 4.1 Example of an item on concentrating problems of module 2 of the HLQ

I did go to work but as a result of health problems.....

	(almost) NEVER	SOMETIMES	OFTEN	(almost) ALWAYS
I had a problem concentrating	☐	☐	☐	☐

Module 3: Unpaid production

Households not only consume but also produce goods and services by combining goods and time. The economic consequences of these productive activities of household have been a neglected part of the economic theory for a long time (Harwryslyshyn, 1977; Homan 1988). However, if a patient is not able to carry out household activities, this influences welfare. Unpaid production is defined as services produced in the unpaid sector of the economy, which could be provided by a third person in the market (Harwryslyshyn, 1977). Regarding unpaid work, four productive activities were distinguished; household work, shopping, care for children and odd jobs around the house. This division was derived from a national time use survey in which 109 activities were aggregated into productive and unproductive clusters (van Roijen et al., 1994).

According to module 3 of the HLQ, all respondents were asked to estimate the number of hours spent on each activity per week in the past two weeks. The number of hours of unpaid production lost is determined by comparing these data with the time spent by the general population or, if available, by a control group, matched for sex, age and labour market participation, since these variables were found to affect hours spent on household production (van Roijen et al., 1994). We ask whether household tasks, normally performed by the respondent, were postponed or taken over by other members of the household, family or friends and/or paid workers. In this way estimated production losses can be corrected for substitution. The mean annual hours of unpaid production loss are calculated by multiplying these estimates by 26.

Module 4: Paid and unpaid labour-experienced impediments

In module 4 of the HLQ subjects having a paid jobs are requested to indicate the experienced impediments while performing their job. The response categories are: "no impediment", "some impediment", "a lot of impediment". The item scores are 0, 1 and 2, respectively.

For all unpaid activities, the respondents are asked whether they have performed these in the past two weeks. A "yes" is followed by asking the amount of trouble experienced as a result of health problems. A "no" is followed by the question to what extent this was caused by health problems, see figure 4.2. The item scores are 1, 0, 2 and 0 respectively. The aggregated impediment score results after summing of the items.

Figure 4.2 Example of the non-disease specific module 4 of the HLQ

We would now like you to indicate with a cross whether you have performed any of the following unpaid activities in the LAST TWO WEEKS and whether they caused you to be hindered by health problems.

Example 1

During the LAST TWO WEEKS Mrs. Pieterse did not go shopping in the city due to her health problems. She did manage to go to her local corner shop notwithstanding her health problems. She indicates this as follows:

	DID DO		DID NOT DO	
	Was hindered by health problems	Was not hindered by health problems	Due to health problems	Other reason
Shopping	✗			

Potential confounders and descriptive characteristics were included in an added module. These questions refer to age, gender, comorbidity, education and occupation.

4.4. Methodology

4.4.1. Study samples

We have applied the complete HLQ in several studies, see table 4.2. First, the HLQ was sent to a representative sample of 995 persons from the general population.

A second study concerned the burden of migraine (van Roijen et al., 1995). We selected patients of 12 years and older from the general population using a screener questionnaire based on the criteria of the International Headache Society (IHS) (Olesen, 1988). From the 10,480 persons

who underwent a face to face interview, 992 patients met the IHS-criteria and experienced a migraine attack in the last 12 months. Additionally, a control group was selected from the subjects in the survey population who did not meet the IHS-criteria.

In an unpublished longitudinal study on electrostimulation of the bladder in patients with spinal cord injury, we analysed the amount of trouble experienced while performing unpaid activities. We measured the impediment score as a result of spinal cord injury and of micturition problems before implantation, 3 months, 6 months and 1 year after implantation. It was assumed that the impediments due to spinal cord injury would not change, whereas the impediments as a result of the micturition problems would decrease after the implantation of the electrostimulation device.

Finally, the HLQ was applied in patients with hip or knee problems, who were on a waiting list for surgery.

Table 4.2 Studies in which the HLQ was employed

Study	HLQ-Module	N	Response	Population
Survey	1,2,4	667	68%	General
Migraine	1,2,3,4	846	58%	Migraine patients
Electrostimulation	3,4	44	81%	Spinal cord injury patients
Knee surgery	3,4	57	76%	Knee patients
Hip prothesis	3,4	50	75%	Hip patients

4.4.2. Feasibility

We used the response rates, the missing values rates, the completion time and the remarks of the respondents as empirical indicators of feasibility.

4.4.3. Validity

Module 1: Absence from paid work.

Testing the validity of measuring absence from work with the module 1 of the HLQ we compared the non disease-specific absence from work in the general population with data from the Central Office of Statistics (CBS, 1993). This register covers over 50% of the labour force, except for the self-employed and a part of the public employees. We also compared absence from work due to migraine with the result of a study for the UK (Cull et al., 1993).

Module 2: Reduced productivity at paid work

Production losses due to reduced productivity are difficult to quantify. Measuring output per worker is the most direct way to evaluate reduced productivity, but this kind of research is expensive and output is often difficult to quantify. A second best solution is to use an indirect method, like estimating the time needed to compensate for reduced production due to illness (HLQ-approach). Validation of this part of the questionnaire is not possible because of lack of reference data. For reason of comparison we added questions to determine reduced productivity according to a method proposed by Osterhaus and colleagues (Osterhaus et al., 1992). This approach multiplies the number of working days impeded by health problems with the self-estimated level of performance. Pearson correlation coefficients were calculated between the number of hours at reduced productivity (HLQ-approach) and the descriptive efficiency score (Osterhaus-method).

Module 3: Unpaid labour production

To investigate the validity of measuring time spent on unpaid work, we compared the estimated number of hours spent on each productive activity in the general population sample with results from a survey in the general population based on the more appropriate but costly diary method (CBS, 1992). In this Time Use Survey (TUS) a representative sample was selected from the Dutch population of 12 years and older (n=6,289). We decided that the total time of these four clusters should not exceed 112 hours (7*16) per week. We compared time spent by the general population from our survey with time spent by the representative respondent in the TUS. For the study on migraine patients we compared the result with time spent by the control group.

Additionally, we compared time spent by hip- and knee patients with time spent by a similar age- and sex group of the general population.

Module 4: Paid and Unpaid Labour experienced impediments

We assessed the ability of the health status instrument, module 4, to discriminate between subgroups of respondents by difference in absence from work due to illness. The Mann-Withney U test was used due to the non-normal distribution of the data. For the respondents with paid jobs we grouped the subjects by no absence from work and days absence from work of 0.5 days or more.

4.5. Results

4.5.1. Feasibility

Of the 995 persons in our survey among the general population, 726 persons returned the questionnaire. Of these, 16 were returned by postal services because of wrong address and 43 questionnaires were returned blank, yielding a response rate of 68%. Since only 4,5% were missing, respondents generally were able to distinguish between absenteeism due to illness and absence for other reasons. Sixteen percent of the subjects did not answer the question about reduced productivity, so we assume the respondents experienced this part of the questionnaire as relatively difficult either as a concept or to apply in practice. For the questions on time spent on the household activities missings ranged from 8% to 11% in the general population. Missings on the questions of experienced impediment during paid and unpaid work were at an acceptable level given the complexity of these questions, ranging from 7% to 11%.

The required time for completion of the complete questionnaire was about 10 minutes.

The most frequent reported remarks of the respondents actually referred to descriptions of their health problems in more detail rather than referring to experienced difficulties with the questions. A small number of the respondents indicated that they had problems estimating the number of hours spent on household production, especially child care. Finally, some

respondents did not understand the phrase 'health problems', for instance should 'fatigue' be considered as a health problem or not.

4.5.2. Validity

Module 1: Absence from paid work

The average amount of absence from work based on the national registry was 12.9 days per year for men and 13.8 for women (CBS, 1993). Using the HLQ on the representative sample of 346 persons having a paid job, the non-disease specific absence from work was comparable to these national data, 12.2 days for men and 14.1 for women per year. The estimated mean number of days absence due to migraine were 4 days per year for women and 1 day absence from work for men respectively. These results were in accordance with a study from the UK both with respect to the absolute level and the difference between men and women. For the UK the number of days of absence from work due to migraine was 1,6 for men and 3,6 for women (Cull et al., 1993).

Module 2: Reduced productivity at paid work

We compared estimates based on the HLQ-approach with estimates of reduced efficiency according to the method proposed by Osterhaus, see methods (Osterhaus et al., 1992). According to the latter method 8,9 working days per migraine patient per year were lost due to reduced efficiency. Using the HLQ-approach, the number of days was 2,7 per patient per year. We found rather low Pearsons' correlation between the answers according to the HLQ-approach and the estimate based on the Osterhaus-method (r=.41). The correlation between estimates according to each of the methods and sum scores on the 7 items related to problems during working time because of health problems was r=.56 and r=.51 respectively.

Module 3: Unpaid labour production

For the general population the average time spent on household production by sex and labour market participation, was in good accordance with estimates from the aforementioned TUS, except for child care (CBS, 1992), see table 4.3.

As might to be expected a paid job reduced time spent on household production, while children in the household increased time spent on these activities. We found no significant differences in time spent on household production between migraine patients and the control group. We also did not found significant differences in time spent between migraine patients who did not suffer from migraine in the past two weeks and patients who had one attack or more in the same period. Patients may substitute leisure and time spent on household production or postpone non-urgent activities, while migraine is not a chronic condition.

Table 4.3 Time spent (on average, hours per week) on household production in the general population by gender and labour market participation

Household activity	Employment Status			
	Paid work		No paid work	
	TUS[a]	HLQ-4	TUS[a]	HLQ-4
Men				
Household work	5.5	5.9	8.9	7.3
Shopping	2.6	2.3	3.7	3.1
Childcare	1.7	7.0	0.8	2.6
Odd jobs	2.2	1.7	2.0	1.5
Women				
Household work	18.1	16.5	26.4	25.3
Shopping	4.5	3.6	5.1	4.8
Childcare	2.9	10.8	4.1	11.4
Odd jobs	1.4	0.9	1.0	2.5

a.Time Use Survey (CBS, 1992)

In de the study on spinal cord injury patients, there was a high variation in time spent on unpaid production, which precluded meaningful generalized interpretation of the results. We found

that knee and hip patients spent on average significant less time on household production compared to persons of similar age and sex in the general population, except for time spent on shopping by knee patients, see table 4.4. We left out time spent on child care due to the small number of patients with children in these patients groups.

Table 4.4 Time spent (on average, hours per week) on household production for hip and knee patients compared with an age/gender-matched control group from the general population

Household activity	Hip (n=46)	Control group	Knee (n=51)	Control group
Household work	13.5	18.2	8.1	15.7
Shopping	2.6	4.5	4.4	3.9
Odd jobs	1.5	6.9	1.7	5.6

Module 4: Paid- and Unpaid Labour-experienced impediment

According to module 4 of the HLQ, the experienced amount of trouble in labour performance due to spinal cord injury was constant over time as expected. With respect to micturition problems, the trouble score decreased significantly over time for household production, shopping and odd jobs, see table 4.5.

Table 4.6 shows the ability of the HLQ-module 4, to discriminate between different levels in absence from work. The average impediment score for unpaid work of persons with a paid job in the general population and no days of absence from work in the two weeks prior to the assessment was .28. In the group of persons who have been absent the mean score was significantly higher, 1.07. The same holds for the impediment score for paid work, respectively .12 and .84, see table 4.6. So, the impediment score for both paid and unpaid work discriminates highly between the two groups.

Table 4.5 **Impediment score for patients with spinal cord injury on three consecutive occasions**

Productive activities	t=0 (n=44)	t=1 (n=36)	t=2 (n=38)	t=3 (n=33)
Household work	0.4[a](0.6)[b]	0.1 (0.2)	0.1 (0.3)	0.1 (0.2)
Shopping	0.6 (0.7)	0.1 (0.2)	0.1 (0.2)	0.0 (0.0)
Child care	0.2 (0.5)	0.1 (0.2)	0.1 (0.2)	0.1 (0.2)
Odd Jobs	0.4 (0.6)	0.1 (0.2)	0.1 (0.4)	0.1 (0.2)

Abbreviations: t=0, 'before implantation'; t=1, '3 months after implantation'; t=2, '6 months after implantation'; t=3, '1 year after implantation'.

[a] X.

[b] Standard deviation is given in parentheses.

Table 4.6 **Impediment score, for paid and unpaid work in the general population between groups differing in number of days absent from work**

	Absence from work		
Impediment score	0 days (n=280)	>0.5 days (n=21)	p Value (MWU)
Unpaid work	0.28[a] (0.49)[b]	1.07 (0.73)	<.0000
Paid work	0.12 (0.24)	0.84 (0.67)	<.0000

[a] X.

[b] Standard deviation is given in parentheses.

4.6. Discussion

All questions relate to 'the past two weeks', so respondents have to answer the questions retrospectively. In our experience, two weeks is the maximum period length to allow for reliable recollection on time use and absence. Recall accuracy falls when the respondents attempt to estimate time use for a longer time period compared to the more valid, but more costly, diary method (Juster et al., 1991). We assume that this period of two weeks is representative for the period between two assessments. In general this assumption is valid if the number of subjects is large enough and the period is randomly drawn over the year. The optimal length of the period between two assessments, as well as the number of subjects required, depend (among other things) on the expected course of the particular disease studied.

With respect to reduced efficiency, HLQ-module 2, earlier research was based on the level of performance by the patient, combined with the number of working days affected by the disease (Osterhaus et al., 1992). This method estimates these number of days in a more indirect way, combining two answers on labour performance, which increases the possibility of inconsistencies and mistakes. In our study the estimates of the costs of reduced efficiency according to this method compared to the HLQ-approach was 3 times as high. Since a gold standard is missing, additional research is required in which output is objectively measurable.

The output of household production and consequently the production loss is difficult to measure, as this output is not traded on a market. Therefore, empirical research concentrates on the evaluation of time spent on unpaid production, the so called 'input-method'. This method ignores differences in production technology and efficiency between patients and controls or the general population. This is particularly true if it concerns a chronic stable disease. However, it is difficult to test this effect directly and its size is still an open question.

Joint activities is a major problem of measuring time use. The total time is usually ascribed to the productive activity. Using the survey method respondents seem to respond by adding up time when an activity was secondary to periods when this task was primary (Juster et al., 1991). The remarks of the respondents indicated that they found it difficult to separate time spent on child care and other household tasks, e.g. shopping with the children. Overestimation of time

spent on child care is probably due to the measurement method used. Changing the instruction prior to the question concerning child care may improve estimates for this part.
Indirect costs may also occur when production by relatives or friends is affected due to spending time caring for the patient. While these costs will probably increase in the future, additional research is necessary developing instruments for measuring these production losses.

4.7. Conclusion

We tested the feasibility and the validity of the HLQ-questionnaire using data from the first applications of this instrument. The small number of missing values per module indicates that the questionnaire was generally well understood by various groups of respondents (patients and non-patients). For a postal questionnaire, without any reward, the useable response rate was at an acceptable level (68%). Estimates on the number of days non-disease specific absence from work (module 1) were in accordance with national data. Estimates of days of absence from work due to migraine were comparable to an other disease specific study on this subject.
In this study we made a first attempt to measure reduced productivity at paid work using module 2 of the HLQ-questionnaire. We found a low correlation between two alternative methods of measuring reduced productivity. Additional research on reduced productivity is necessary, using methods of direct output measurement.
Except for child care, module 3 of the HLQ-questionnaire appeared to be suitable for assessing time spent on unpaid labour. The instrument did not show changes in time spent on unpaid work due to the attack-wise disease migraine. This may be a valid result, as patients may postpone non-urgent activities during the attack. Patients with knee or hip problems spent less time on household production compared to a sample matched by age and sex from the general population, which indicates unpaid production loss due to illness.
The results on the impediment score, module 4 of the HLQ-questionnaire, showed that the instrument could indicate the expected changes of impediments due to treatment. The impediment scores of paid and unpaid work were able to discriminate between groups by number of days of absence from work.

5. CURRENT AND FUTURE COSTS OF CANCER

5.1. Summary

Cancer costs in the Netherlands amounted to 4.8% of health care costs in 1988. For five cancer types, and a sixth group, covering all other malignancies, costs were broken down by age, sex and disease phase. They showed a remarkably similar pattern of medical consumption. Costs were linked to observed incidence, mortality and estimated prevalence, together allowing for prediction of future costs of cancer. In 2020, as a result of ageing, cancer costs will have increased much more rapidly than total health care costs, in particular for cancer of the lung and prostate. Colorectal cancer costs were predicted for epidemiological scenarios. Our model shows that an increase in future prevalence may bear quite different cost implications. If it is due to higher incidence, the costs will increase substantially. If due to survival improvement, the increase will be less prominent. Simply extrapolating costs based on future prevalence or mortality may produce serious errors.

5.2. Introduction

An optimal allocation of health care resources requires insight in the epidemiology and cost of diseases. Regarding cancer, we need to know both the absolute costs and the relative costs as compared to other diseases and total health care. Furthermore, the impact of demography, changes in medical practice and epidemiology on future health care costs should be analysed.

In this article we estimate the costs for five cancer categories: cancer of the lung, breast, colorectal, prostate, stomach; and all other malignancies in a sixth category. These cancer categories were selected, based on their importance for mortality, morbidity and medical consumption.

First, we will calculate the total costs per type of cancer, age-group and sex for 1988. Next, these costs will be assigned to three disease phases: the year following incidence, the year preceding death and the period in between. The estimated costs per patient by disease phase will

be combined with incidence, mortality and prevalence, as calculated by our cancer disease model. This allows for prediction of future cancer costs for several possible scenarios: a demographic scenario and scenarios concerning expected trends in incidence and survival. The costs predicted by the "three phase model" will be compared with outcomes using simple extrapolations of average costs per patient.

5.3. Methodology

5.3.1. Total costs of cancer

In a recent study we estimated total health care costs for the Netherlands in 1988, for the six cancer types mentioned, together with 42 other disease categories, covering the entire ICD 9-CM classification (see chapter 2). Total health care costs were allocated to diseases, age-groups and sex, using utilisation of services or the number of patients. Data on in-hospital and nursing home care were extracted from national registers with (nearly) complete coverage. For general practitioner's care, physical therapy and district nursing we used data from recent, large surveys. These results were used to calculate the cost of inpatient hospital care and non-hospital care for cancer.

Cost of outpatient hospital care consist of radiotherapy, chemotherapy and follow-up. Cost of Dutch radiotherapy-centres were assigned to the six cancer types, using the number of new patients receiving radiotherapy by type of cancer (Health Council, 1984). The costs of cytostatics administered in hospitals (Nepharma, 1989) were assigned to the six cancer types, in proportion to the distribution of in-hospital costs. The costs for monitoring patients without symptoms after diagnosis and primary treatment, were calculated in detail for breast cancer and were extrapolated to other cancers (de Koning et al., 1991).

5.3.2. Costs by disease phase

Several studies indicated that over the course of cancer, the costs show two peaks. The first peak, due to diagnosis and primary therapy; the second peak, due to palliation of often severe

symptoms in advanced disease (Baker et al., 1989 and Bried et al., 1989). In between, medical consumption is modest. Hence, we discerned three disease phases, inspired by Baker:

- the first year following incidence, as a result of diagnosis and primary treatment;
- the last year of life for people dying of cancer (only for people who survived the first year, who get recurrent or metastatic disease and do not die from other causes);
- the period in between: "the intermediate phase", during which people are disease free or having already diagnosed metastases (in these terms disease free is a mixture of cured patients and patients who currently have no disease symptoms, but who will later get recurrent or metastatic disease);
- Costs for patients dying within one year after incidence were assigned to the incidence phase.

The average costs per patient by type of cancer, age, sex and phase were estimated as follows. For the intermediate phase we used detailed estimates for the Netherlands of annual follow-up costs per patient for breast cancer (de Koning et al., 1991). For the other types of cancer the relative follow-up costs compared to breast cancer, calculated for 87,000 patients in the United States, were combined with the costs for breast cancer, yielding the annual follow-up costs per patient (Baker et al, 1989).

The hospital costs in the incidence phase were primarily based on the length of stay in 1988, by type of cancer, age and sex, according to nation wide Dutch hospital register. The length of stay for patients with metastases as primary cause for hospital admission determined the in-hospital cost during the last year of life. Although the last year of life and the period of metastases are not equivalent, hospital stays concerning metastases are often concentrated in the last year of life (Baker et al., 1989; Riley et al., 1987 and van Ballegooijen et al., 1992). This length of stay is assumed to be age and sex specific, but not cancer specific, because if metastases are coded as primary cause of admission, the site of the primary tumour is seldomly known.

The average hospital admission rate was derived by comparing the number of model based incident cases and deaths for 1988 (correcting for patients dying within the first year after diagnosis) to the number of hospital stays registered in 1988, for each combination of cancer, age and sex. The ratio of hospital stays versus incidence plus deceased served as the average admission rate. The admission rate was assumed to be equal for the incidence phase and the last year of life, because the data did not allow for separate estimates (see discussion). Combination

of the model-based incidence and mortality with length of stay and admission rate yielded the number of "model-based hospital days", which corresponds closely to the number of registered hospital days per cancer type, age and sex. Combining the number of hospital days with costs per day and adding other hospital costs (for surgery, radiotherapy, chemotherapy etc.) and non-hospital costs generated the average costs per patient.

5.3.3. Disease model

Our cancer model calculated the number of patients in each disease phase, per cancer type, age and sex (Bonneux et al., 1994). The model is a deterministic state transition model: it divides the population in subpopulations, defined by states. Every model year, the population "ages" one year and the states are updated. Transitions from one state to another are governed by probabilities, extracted from registries and literature. Transition probabilities depend only on the current state defined by age, sex, cancer type, and disease phase.

A demographic module reproduces the population forecasts for the Netherlands and generates first incidents of cancer by age and sex similar to the 1989 national cancer incidence rates for the Netherlands (CBS, 1989 and the Dutch Cancer Registry, 1993).

After incidence patients first run a risk of immediate death as a consequence of primary treatment. The survivors are divided into two groups: a fraction which is cured and a fraction which is not. The not cured will enter the intermediate ('disease-free') phase of the disease, and subsequently will die of the disease, provided they do not die from other causes first. In practice of course cured and disease free patients cannot be distinguished, and both will incur follow up costs.

The cancer specific mortality of the non-cured is modelled by applying a lognormal survival to the relative survival rates. Relative survival rates correct the observed mortality in the diseased population for the expected mortality in the reference population with the same age and sex (Rutqvist et al., 1984 and Rutqvist, 1961). Together this implies that survival after diagnosis can be characterised by 4 parameters: a fraction dead after treatment, a fraction cured, and the geometrical mean (equalling the median survival time) and variance of the lognormal distribution. A mathematical description of the survival is in appendix 5.1.

The demographic module takes care of all other causes of death, corrected for the studied diseases by using cause elimination life table methodology. This other causes mortality probability is applied to all states in the model, under the assumption that it is independent. Prevalences are calculated as the result from incidence, disease specific mortality and all other causes mortality.

Surviving patients run a higher risk of a second cancer episode. Therefore they are again subjected to the cancer incidence of the reference population, multiplied by the relative risks observed in the Connecticut Cancer Register (Boice et al., 1986).

The model was calibrated on aggregated data of cancer survival from Dutch and Scandinavian cancer registries, corrected for other causes of death. The fraction dead after treatment is from the Dutch hospital register, the other three survival parameters were estimated by an iterative nonlinear least squares regression, weighted for the numbers of deaths. Residual errors were small (SIG, 1992).

5.3.4. Scenarios

We have illustrated the relevance of epidemiology for future cost estimates with four scenarios for colorectal cancer. Scenario 1 only incorporates the expected demographic development. In scenario 2 we added an improving prognosis after diagnosis. In the Norvegian and Finnish registries a very significant improvement over time of 5 year relative survival rates has occurred between 1954 and 1985 of 2% per year (Cancer Registry Norway, 1980; Finnish Foundation for Cancer Research, 1989; Hakulinen et al., 1981 and Langmark et al., 1990). We extrapolated an average relative decrease of cancer specific mortality of 2 % per year to 2005. Five year survival rates thus increased from 44% (1985) to 55% (1995) to 66 % (2005).

Scenario 3 involves, in addition to demography, a 2% annual relative increase in the incidence of all stages for men, and 1% for women. The trend in incidence is assumed to be 2% higher than the observed mortality trend in most western countries and is primarily caused by earlier diagnosis and increased detection of slower growing tumours (Doll et al., 1981).

Scenario 4, in our opinion the most realistic one, incorporates demography, increasing incidence (2.5% per year for men, 1.4% for women) and improved survival. As a consequence, mortality

rates for men decrease by 0.4% annually and by 1.1% for women, as has been observed in the Netherlands over the period 1978-1989 (SIG, 1992).

5.4. Results

5.4.1. Total costs

Total cost of malignant cancer in the Netherlands amounted to 1894 million Dutch guilders in 1988 (table 5.1), representing 4.8% of total health care costs. West-Germany and Sweden have a comparable share: 4% and 5.1% respectively (Henke et al., 1986; Lindgren, 1990). For the United States it is somewhat higher: 6.2% (Rice et al., 1985). In-hospital care takes about 60% of total costs. Outpatient hospital costs consist of radiotherapy (200 mln), chemotherapy (200 mln) and follow-up costs (143 mln).

Table 5.1 Health care costs for cancer, by health care sector in millions of Dutch guilders (in parentheses as percentage of total cancer costs). The Netherlands 1988.

Health care sector	Costs for 1988 in mln Dutch guilders
In-patient hospital care	1148 (61%)
Out-patient hospital care	543 (29%)
Non hospital care	203 (11%)
Total health care	1894 (100%)

About NLG 1000 mln was assigned to the five specific cancers, leaving almost 900 mln for the other cancers (table 5.2). Lung cancer is in first place: it is responsible for 16% of the costs of cancer (300 mln), and is mainly caused by men. Colorectal and breast cancer each represent about 14% of the total cancer costs, whereas stomach cancer and prostate cancer cause about 5-

6% of the total costs. This ranking corresponds to recent estimates for Texas (Williams et al., 1992). Hospital costs predominate and costs are fairly equal for both sexes.

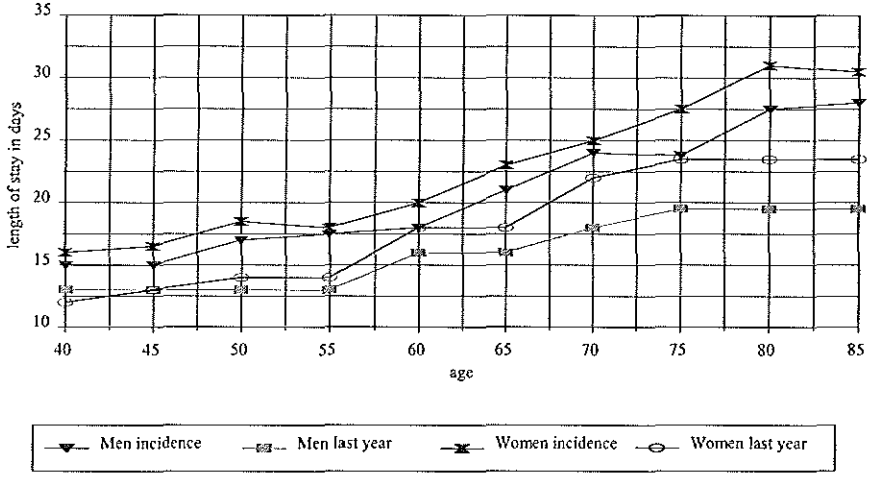
Table 5.2 **Health care costs per type of cancer, sex and health care sector, for six types of cancer in millions of Dutch guilders (in parentheses as percentage of total cancer costs). The Netherlands 1988.**

Type of cancer	Total costs	% for men	% in hospital
Lung cancer	300 (16%)	83	92
Breast cancer	253 (13%)	0	82
Colorectal cancer	250 (13%)	45	88
Prostate cancer	110 (6%)	100	87
Stomach cancer	99 (5%)	59	84
Other cancers	882 (47%)	46	92
All cancers	1,894 (100%)	49	89

5.4.2 Length of stay and admission rate

Figure 5.1 shows the average length of hospital stay by age and sex for colorectal cancer for the incidence phase and the last year of life. Only the results for colorectal cancer are shown, but the general pattern applies to all types of cancer.

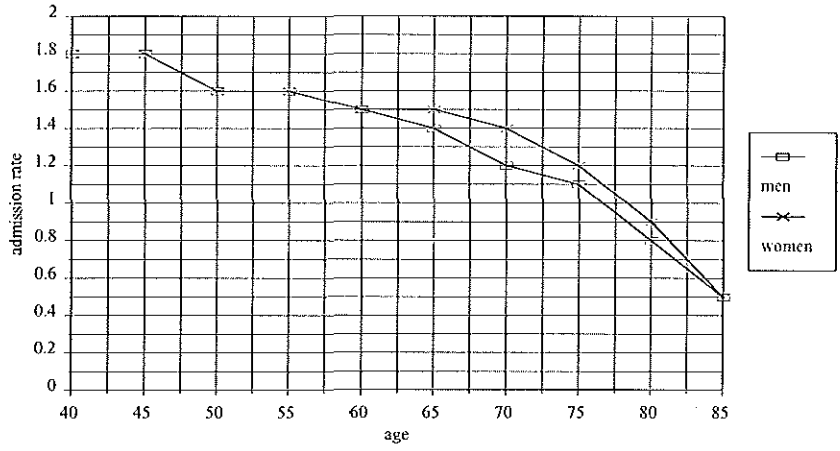
Figure 5.1 **Average length of hospital stay in days for colorectal cancer, by age-group, sex and disease phase. The Netherlands 1988.**



Until age 55, the length of stay (per stay) is stable and fairly equal for both sexes. With increasing age, hospital stays become longer for both sexes, but at a quicker rate for women. For each type of cancer, older women in the Netherlands stay significantly longer in hospital than men of the same age, irrespective of the disease phase. Subsequent analyses have shown that this holds for the majority of diseases in the Netherlands (SIG, 1990a). Older women are more often single than older men (41% versus 15% in 1987 (CBS, 1990)), limiting the opportunities for home care, which may cause longer hospital stays.

The average admission rate for colorectal cancer patients is 1.8 until age 45, but diminishes considerably with increasing age (figure 5.2). For people of age 80 and older it becomes smaller than 1, implying that a substantial number of these patients are not hospitalised. Consequently, they consume relatively more nursing home care, district nursing care and general practitioner's services, which we took into account. The admission rate is hardly sex-specific.

Figure 5.2 **Average hospital admission rate per patient having colorectal cancer, by age-group and sex (model based outcomes). The Netherlands 1988.**



5.4.3. Costs by disease phase

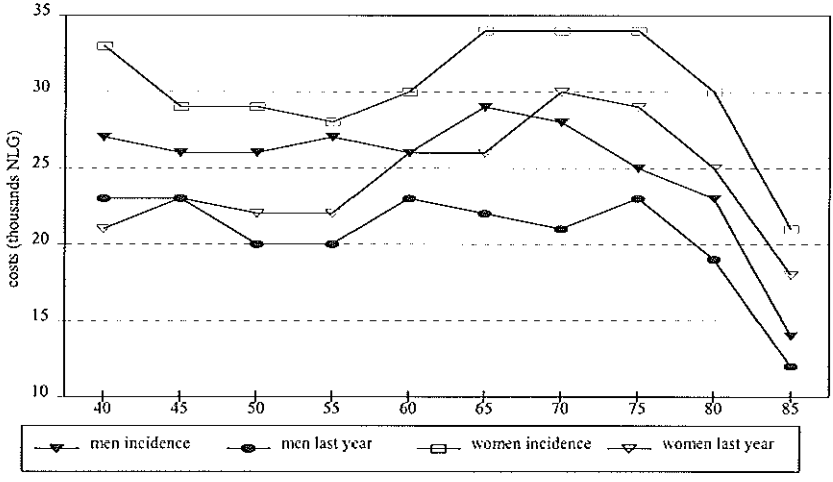
Figure 5.3 shows the average costs per patient having colorectal cancer, during the incidence phase and the last year of life respectively. Until age 55 the costs are stable, amounting to NLG 20-30,000 per patient. For women between age 60 and 75 they rise, due to the increase in length of stay which more than compensates for the falling admission rate. For people older than 80 the costs fall to 12-20,000, as the low admission rate then becomes the dominant factor. Relatively low costs for patients older than 80 years were also found by Riley (Riley et al., 1989). During the incidence phase, costs (NLG 25-30,000) are higher than during the last year of life (20,000), irrespective of age and sex. For women over 60 the costs are about NLG 5,000 higher than for men of the same age.

A considerable part of the results for colorectal cancer holds for all six cancer types, such as the lower costs for patients older than 75. The higher costs for women older than 60 apply to all four cancer types that are relevant for both sexes. Fairly stable costs until age 60 prevail for all cancers, except for "other cancers", in which patients younger than 15 years incur considerably

higher costs. This category is a mixture of very different types of cancer, both for young and for elderly patients. The high costs for people under 15 are mainly caused by leukaemia, brain cancer and non-Hodgkin's disease (Coebergh and van der Heijden, 1991) for which therapy (immuno- and chemotherapy and bone marrow transplantation) is very expensive (OTA, 1981; Black, 1982 and Office of Health Economics, 1980). The notable increase in costs between age 60 and 75 also applies to prostate cancer and lung cancer (women), but not to stomach cancer and other cancers. The incidence phase is not always more expensive than the last year of life. For breast-, prostate- and other cancers the last year of life appears to be more expensive. De Koning's study (de Koning et al., 1992) confirms this result for breast cancer.

During the incidence phase, the average costs per person are the highest for stomach cancer (NLG 30,000) and other cancers in younger people (30-50,000). Breast- and prostate cancer are relatively "cheap" (21,000), leaving colorectal- and lung cancer in the middle-range (NLG 25-30,000). The variation in costs for the last year of life is much smaller, resembling Baker's findings for U.S. Medicare cancer patients (Baket et al., 1989), as well as Dutch results for breast and cervical cancer (van Ballegooien et al., 1992; de Koning et al., 1992). We estimated these costs at about NLG 25,000. The only exception is "other cancers", causing higher costs during the last year of life.

Figure 5.3 **Average costs per patient having colorectal cancer, by disease phase, age-group and sex, in thousands of Dutch guilders (model based outcomes). The Netherlands 1988.**



5.4.4. Costs over the course of cancer

Assembling the three disease phases illustrates the costs over the course of cancer (figure 4). The costs show two peaks, the first just after clinical detection, the second in the last year of life. In the intermediate phase, annual costs are very modest. The total costs of the intermediate phase depend chiefly on the length of disease free survival. The total costs related to the prevalence of cancer only become important if the intermediate phase is very long, say 15 years.

Figure 5.4 **Average costs per patient by disease phase for colorectal cancer, in thousands of Dutch guilders (model based outcomes). The Netherlands 1988.**

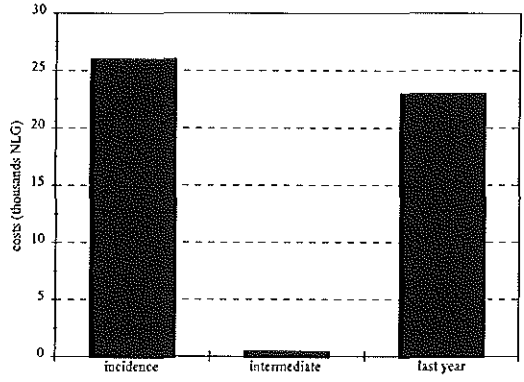


Table 5.3 **Predicted costs per type of cancer for the Netherlands in 2005 and 2020, demographic scenario, in millions of guilders in 1988 prices and as index compared to 1988 (1988=100).**

Type of cancer	Costs in 2005		Costs in 2020	
Lung cancer	377	(126)	474 mln	(158)
Breast cancer	311	(123)	352	(139)
Colorectal cancer	308	(123)	375	(150)
Prostate cancer	134	(123)	173	(157)
Stomach cancer	122	(123)	151	(150)
Other cancers	1,060	(120)	1,253	(142)
All cancers	2,312	(122)	2,778	(147)
All diseases	46,110	(116)	51,675	(130)

5.4.5. Demography and costs

Table 5.3 shows the predicted costs regarding all six cancer types, for the years 2005 and 2020, applying the demographic scenario. In 2005, the index for total cancer costs (1988=100) is 122: a 1.2% annual increase, comparable to total health care (index=116). Costs increase at about the same rate for each type of cancer. In 2020, the burden of ageing becomes heavier, as the Dutch post-war baby boom reaches ages 60-75. By then cancer costs (index=147) will have increased considerably more rapidly than total health care costs (130). The cost of lung and prostate cancer will be most seriously affected by ageing (index 158 and 157 resp.). The consequences for breast cancer and other cancers are less severe as they prevail at relatively young age. Still, their rate of cost increase is higher than for total health care.

5.4.6. Scenarios for colorectal cancer

The two-peaked cost pattern has important implications for future cancer costs. The results of four scenarios for colorectal cancer are presented for the year 2005 (table 5.4). According to our model, costs of colorectal cancer in 2005 amount to 308 million guilders, if only demography is taken into account. Improving disease-free survival (scenario 2), and consequently increasing the prevalence of cancer, will result in NLG 299 mln, since it only raises the number of patients consuming the relatively inexpensive follow-up (incidence remains the same) and cancer specific mortality declines, because of other causes mortality. On the other hand, if the same increase in prevalence of disease-free persons occurs, but due to a rise in incidence (scenario 3), the costs will rise substantially: NLG 395 mln. All extra patients will undergo expensive diagnosis and primary therapy. Furthermore, cancer mortality increases, causing extra costs as well. In case of the most realistic course of events (scenario 4), the costs will amount to NLG 417 mln.

Table 5.4 also presents the predicted costs using simple extrapolations without discerning disease phases. Three variants are shown, based on constant costs per prevalent case, per death and per incident case, respectively. In case of scenario 1, incorporating only demography, the predictions are quite accurate, although the incidence method understates the costs by 6%.

The prevalence-based method predicts the same costs for scenario 2 and 3 since either produces the same prevalence in 2005. In case of improved survival (scenario 2), this leads to overestimating the costs by 20%. If the incidence increases (scenario 3), the costs are underestimated by 9%. The mortality-based approach is quite accurate if the incidence rises (and consequently mortality) but fails completely in predicting the costs of survival improvement. For scenario 2 and 4 the costs are understated by 27-33%. The incidence-based method performs reasonably in case of scenario 1 to 3, for scenario 4 costs are overestimated by 10%.

Table 5.4 **Predicted costs for colorectal cancer for the year 2005 applying four models to four scenarios, in millions of Dutch guilders. In parentheses: differences in % compared to outcomes of the three phase model.**

	1988	2005 Scenario 1	2005 Scenario 2	2005 Scenario 3	2005 Scenario 4
Three phase model	250	308	299	395	417
No phase model prevalence-based	250	309	358 (+20%)	358 (-9%)	413 (-1%)
No phase model mortality-based	250	310	218 (-27%)	401 (+2%)	279 (-33%)
No phase model incidence-based	250	290 (-6%)	290 (-3%)	380 (-4%)	460 (+10%)

5.5. Discussion

Epidemiology and medical consumption vary considerably between types of cancer as well as between individual patients. Recognising this variability, our analysis shows that the general pattern of medical consumption coincides remarkably well for the six cancer types described. The length of hospital stay increases uniformly with age, especially for women. On the other hand, the admission rate falls with age. For patients older than 75, the second factor dominates, resulting in lower costs. Over the course of cancer, medical consumption shows two peaks: during the first year after incidence and in the last year of life. In between the costs are modest.

We assumed the same admission rate for patients in the incidence phase and the last year of life. The length of hospital stay for patients with metastases was assumed to be age and sex specific, but equal for all cancer types, which is supported by research for the U.S. and the Netherlands. Both assumptions are obviously rather crude, but sufficient to demonstrate the divergent consequences of several scenarios. Sensitivity analysis by substantially varying the most uncertain parameter -the admission rate during the incidence phase versus the last year of life- proved not to affect the basic two-peaked pattern of costs seriously. Consequently, the predictions of future costs for the scenarios described are robust.

The costs during the prevalence phase were based on Dutch calculations for breast cancer, combined with Baker's relative estimates for other types of cancer. As the costs are relatively low, errors in these estimates will not influence the results seriously.

The assumed survival improvement for colorectal cancer (scenario 2 and 4) seems high, but is the results of two processes: a true decrease of mortality due to more effective treatment and a spurious increase of survival due to earlier diagnosis (lead time) and increased detection of slow growing tumours which had passed unnoticed before (length time and pseudo-diagnosis) (Doll et al., 1981; Cole et al., 1980).

The demographic scenario described does not account for future trends in risk factor exposure, like smoking for lung cancer and the influence of screening on breast cancer. Further refinement of the disease model and cost estimates is underway, incorporating the impact of these trends on future morbidity, mortality and costs.

* In 1988, the exchange rate of one Dutch guilder (NLG) was approximately 0.3 British Pounds and 0.5 U.S. Dollar.

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Appendix 5.1.

1. The survival was modelled by using the lognormal distribution:

$$f(t) = \frac{1}{t\sqrt{(2\pi\sigma)}} \exp\left[\frac{-(\ln t - \mu)^2}{2\sigma^2}\right]$$

Where t is the time after diagnosis, m the median survival and s^2 the variance.

We used a discrete approximation with a time step of one month. The proportion of survivors at any time t_i after diagnosis t_0 is then given by:

$$P(S)_{t_i} = (1 - M_{op})\left(c + (1-c)\sum_{t_2}^{t_i}\left[\frac{1}{t_i\sqrt{2\pi\sigma}} \exp\left(\frac{-(\ln t_i - \mu)^2}{2\sigma^2}\right)\right]\right)$$

where M_{op} is the proportion dying in hospital after first admission and c is the fraction cured.

Appendix 5.2.

Average costs per patient by type of cancer, disease phase, age-group and sex, in thousands of Dutch guilders. The Netherlands 1988.

Stomach cancer

	Men		Women	
Age	Incidence phase	Last year of life	Incidence phase	Last year of life
25-44	40	37	37	32
45-49	33	30	33	27
50-54	31	27	31	25
55-59	32	25	34	24
60-64	30	25	34	26
65-69	30	24	32	23
70-74	26	23	30	25
75-79	23	21	32	29
80-84	20	19	25	24
85+	15	15	14	15

The costs during the intermediate phase are assumed to be not age and sex-specific. For stomach cancer they amount to NLG 514 per patient for each year a patient stays in this phase.

Colorectal cancer

	Men		Women	
Age	Incidence phase	Last year of life	Incidence phase	Last year of life
25-44	27	23	33	21
45-49	26	23	29	23
50-54	26	20	29	22
55-59	27	20	28	22
60-64	26	23	30	26
65-69	29	22	34	26
70-74	28	21	34	30
75-79	25	23	34	29
80-84	23	19	30	25
85+	14	12	21	18

The costs during the intermediate phase are assumed to be not age and sex-specific. For colorectal cancer they amount to NLG 443 per patient for each year a patient stays in this phase.

Lung cancer

	Men		Women	
Age	Incidence phase	Last year of life	Incidence phase	Last year of life
25-44	27	27	38	32
45-49	25	27	34	31
50-54	25	27	34	33
55-59	27	27	39	32
60-64	25	28	37	39
65-69	26	28	35	37
70-74	23	24	34	36
75-79	21	23	31	28
80-84	15	17	23	21
85+	10	11	10	10

The costs during the intermediate phase are assumed to be not age and sex-specific. For lung cancer they amount to NLG 536 per patient for each year a patient stays in this phase.

Breast cancer

Women		
Age	Incidence phase	Last year of life
25-44	19	22
45-49	22	24
50-54	23	26
55-59	23	25
60-64	22	27
65-69	22	25
70-74	21	26
75-79	21	27
80-84	18	23
85+	11	15

The costs during the intermediate phase are assumed to be not age and sex-specific. For breast cancer they amount to NLG 375 per patient for each year a patient stays in this phase.

Prostate cancer

	Men	
Age	Incidence phase	Last year of life
40-44	28	25
45-49	23	25
50-54	23	25
55-59	22	24
60-64	22	29
65-69	23	28
70-74	21	27
75-79	20	28
80-84	19	24
85+	11	13

The costs during the intermediate phase are assumed to be not age and sex-specific. For prostate cancer they amount to NLG 435 per patient for each year a patient stays in this phase.

Other cancers

	Men		Women	
Age	Incidence phase	Last year of life	Incidence phase	Last year of life
0-4	55	51	54	47
5-9	46	51	49	47
10-14	38	45	35	35
15-19	35	41	32	35
20-24	33	41	33	35
25-29	31	38	33	35
30-34	31	38	34	35
35-39	27	28	33	35
40-44	27	28	32	35
45-49	25	26	34	38
50-54	23	24	32	36
55-59	24	24	33	36
60-64	22	25	34	38
65-69	21	25	35	37
70-74	19	23	32	39
75-79	18	24	33	39
80-84	15	20	31	34
85+	14	18	25	27

The costs during the intermediate phase are assumed to be not age and sex-specific. For other cancers they amount to NLG 488 per patient for each year a patient stays in this phase.

6. MEDICAL COSTS AND PRODUCTION LOSSES DUE TO INJURIES IN THE NETHERLANDS

6.1. Summary

To support injury control, we assessed the direct medical costs and indirect costs of injuries in the Netherlands, making use of recent advances in health economics. We estimated the direct medical costs with the help of available data on health care utilisation as a consequence of injuries. In our calculations of indirect costs, we used two alternative approaches. We used the traditional human capital approach, which estimates the potential economic production losses caused by diseases or injuries. In addition, we applied the friction cost method which has recently been developed as an attempt to measure the actual economic production losses to society.

Injuries are an important source of medical costs and economic production losses. Almost two-thirds of the medical costs are the result of accidents among females (mainly domestic accidents of elderly women). On the contrary independent of the method used, more than 80% of the indirect costs are the result of injuries of males (mainly caused by a high frequency of traffic injuries, occupational injuries and sports injuries among young males). The application of the friction cost method confirms the importance of injuries as a source of production losses in comparison with other diseases, showing that they belong to the main three causes of indirect costs to society.

Estimates of the medical costs and both the potential and actual economic production losses to society clearly demonstrate that injuries should be a major concern for health policy makers and the medical profession.

6.2. Introduction

Injuries are a public health problem that is often underestimated by policy makers and the medical profession. In the Netherlands, as in many other industrialised countries, current health policy focuses on the prevention and treatment of chronic conditions, which are considered to be the major public health challenges today (Ruwaard et al., 1994).

Several indicators, however, show that injuries should not be neglected as a public health problem of major concern. Injuries, in fact, are a major challenge in both industrialised and developing countries. It has been shown that the percentage share of injuries as a cause of death ranges from 6% in the established market economies of the world to almost 12% in China (Murray et al., 1990). Perhaps even more important are recent estimates of the burden of disability in populations. These estimates show that in the highly industrialised regions, almost 10% of the number of years lived with a disability are the consequence of injuries, where this proportion reaches 15% in developing countries (Murray et al., 1994).

There is substantial evidence that many injuries and their consequences, such as premature death and disability, are potentially avoidable by preventive measures or adequate trauma care (Beeck et al. 1989). This fact only increases the challenge for public health policy.

In setting public health priorities, therefore, injuries should be taken into account. One of the possible tools for purposes of priority setting is the assessment of societal costs of diseases and injuries. Cost assessment gives an impression of the diagnostic groups that, from an economic perspective, put a high burden on society. This is important policy information in addition to available data on morbidity and mortality in the population.

The production of reliable estimates of the costs of diseases and injuries, however, is rather difficult. From the area of health economics several methods have been emerging (Drummond, 1986; Robertson, 1992; Koopmanschap et al. 1995).

This scientific area has taught us that 'cost-of-illness'estimates have to be interpreted with care. The results of specific studies are highly dependent on the elements that are taken into account and on the methods used (Drummond, 1992; Roijen et al. 1995). A major issue in the design of a cost-of-illness study is the choice whether to restrict to the direct costs (costs of health care and other expenses) or to include the indirect costs (costs of production losses to society).

In the area of injury control most attention has been given to the calculation of direct medical costs (Mackenzie et al., 1988; Harlan et al., 1990; Miller et al., 1993; Miller et al., 1996), although some studies included estimates of the indirect costs as well (Hartunian et al., 1980, Max et al., 1990)

With respect to the indirect costs, there is an ongoing debate among health economists about the appropriate methodology to estimate their magnitude accurately (Roijen et al., 1995). The indirect costs represent the economic consequences of injuries beyond the health care sector, resulting from absence from work, disability and death. It has been shown that they on average represent over 50% of the total disease costs or total costs saved by health care interventions (Koopmanschap et al., 1993). This means that novel information on these economic production losses could be very important to policy makers in the area of injury control.

Within the framework of surveillance activities to support health policy we have assessed the direct medical costs and indirect costs of injuries in the Netherlands, making use of recent advances in health economics (Koopmanschap et al., 1992).

The Netherlands is a small, industrialised country in Western Europe. Demographic information concerning the time of our cost assessment shows a population size of almost 15 million persons. One quarter of the Dutch population is younger than 20 years, whereas 13% is elderly (65 years and over). As in other industrialised countries the proportion of young people is decreasing, whereas the share of elderly people is rising.

The Netherlands has a rather high population density with more than 400 persons/km^2 of land. It has an economically active population of about 4 million males and 2 million females. As in other industrialised countries almost two-thirds of them are working in the service sector. At the time of our cost assessment the unemployment rate was 11% of the labour force in spite of a high mean level of education attainment among persons aged 20-64 years.

Our study addressed the following questions:

- What are the direct and indirect costs of injuries in the Netherlands, and how do they compare to the costs of other major diseases?
- What are the direct and indirect costs of specific subcategories of injuries in the Netherlands, and how do they compare to each other?

6.3. Methodology

Our study on injury costs used a further refinement of the classification of a comprehensive cost of illness study which divided the total Dutch health care budget among 48 diagnostic groups (Koopmanschap et al., 1994). The diagnostic groups of this comprehensive study were derived from the ninth revision of the International Classification of Diseases and included the following injury categories: 'traffic accidents', 'non-traffic accidents' (including all accidental injuries outside the traffic system with the exemption of complications of medical treatments) and 'other injuries' (including medical complications, self-inflicted injuries, and assault).

We further subdivided both categories of accidental injuries. Traffic accidents were specified according to the mode of transport of the injury victim: passenger car occupant, cyclist, moped rider, pedestrian, other modes of transport. The heterogeneous category of non-traffic accidents was broken down into the following three subclasses: occupational accidents, domestic accidents and sports accidents.

The category of 'other injuries' was not further subdivided because of lack of adequate data for the assignment of costs to specific subcategories. Data on the complete category of 'other injuries' will nevertheless be presented in order to give a comprehensive picture of injury costs in the Netherlands.

6.3.1 Direct costs

The direct costs as estimated in our study are restricted to the costs of injuries that are made within the health care sector. In this way, a picture is given of the proportion of the Dutch health care budget needed for the medical care of injuries and its specific subcategories.

Additional direct costs, such as property damage, are not included. Adequate data are not available and previous studies in the Netherlands, which included these costs, have therefore produced highly variable results (Beeck et al, 1996).

For the estimation of direct medical costs the so-called 'top down approach' has been used. This method divides the total costs of each sector in health care (hospital care, nursing home care,

general practitioner care, physiotherapy, domestic help, aids and appliances, ambulance transport and other medical care) by diagnosis, age and sex. The total costs of each sector in health care are annually published by the Dutch government (WVC, 1989). These total costs can be subdivided by diagnosis, age and sex with the help of health care registration data (CBS, 1990), and information from population surveys into medical consumption as a consequence of injuries (Consumer Safety Institute, 1988).

Health care registration data allowed us to subdivide the costs of hospital care, nursing home care and domestic help by diagnosis, age and sex. Population survey data made it possible to subdivide the costs of general practitioners, physiotherapy and aids and appliances by diagnosis, age and sex. For one important health care sector with respect to injuries, ambulance transport, we were not able to make a subdivision by diagnosis, age and sex due to the lack of adequate data. Therefore the costs of ambulance transport are not included in this study.

The 'top down approach' in principle fits the purposes of our study. A comparison of the health care costs of injuries with the health care costs of other diseases can directly be made. The validity of the method, as with other approaches to cost assessment, depends on the quality of the available data. In our study, detailed data on injuries at the end of the 1980s were available, both with regard to hospital registration data (1988) and population survey data (1987).

Table 6.1 provides a summary of the data used to divide the total costs of injuries in different health care sectors by injury category, age and sex. This table also summarizes the data underlying the calculations on indirect costs, which will be explained below.

Table 6.1 shows that for all relevant parameters in our cost calculations data were available for the years 1987 or 1988 (with the exception of the value of household production losses, for which data from 1990 had to be applied).

Table 6.1 **Overview of data used for estimates of direct medical costs and indirect costs in the Netherlands**

Cost element	Data	Source
Direct medical costs		
- Hospital care	National Registry 1988	CBS / LMR 1990
- Nursing home care	National Registry 1988	CBS / LMR 1990
- Domestic help	National Registry 1988	CBS / LMR 1990
- General practitioners	Population Survey 1987	SCV 1988
- Physiotherapy	Population Survey 1987	SCV 1988
- Aids and appliances	Population Survey 1987	SCV 1988
- Ambulance transport	Not available	
Indirect costs		
- Absence paid labour	National Registry 1987	CBS 1988a
- Absence non-paid labour	Population Survey 1987/1988	CBS 1992
- Long-term work disability	National Registry 1988	GMD 1988
- Mortality	National Registry 1988	CBS 1989
- Value production loss due to fatal injuries	Lifetime earnings per person by age and sex in 1988	
- Value market production loss due to non-fatal injuries	Average earning per worker by age and sex in 1988	CBS 1988b
- Value household production loss due to non-fatal injuries	Average earning of corresponding occupations by age and sex in 1990	LTD 1992

The data were derived from statistics that were published by several national institutions between 1988 and 1992. An important part of the information came from the Central Office of Statistics (CBS) which annually publishes the results from national registries and population surveys from different areas, including health care. Among them are data from the National Medical Registry (LMR) which annually collects detailed information from hospitals. Another part of the information came from the Consumer Safety Institute (SCV) which is a national center on injury surveillance in the Netherlands.

Most data for the calculations of indirect costs were also be derived from the Central Office of Statistics (CBS). Data on long-term work disability, however, were from the Mutual Medical Service (GMD). At the time of our study, this organisation was responsible for all medical and administrative procedures with regard to patients not returning to their jobs as a consequence of a disease or an injury. Data on household production losses were obtained from the Dutch Department of Social Affairs and Employment, which has a specific Technical Service on Earnings (LTD).

6.3.2. Indirect costs

Indirect costs refer to the lost production capacity of individuals as a consequence of diseases and injuries. It may include the lost output of employed persons, the lost nonmarket production and the future or potential loss of production. Indirect costs do not include a valuation of life or non-fatal injury (Ball et al., 1995). They do not refer to 'human costs' such as the expression in monetary terms of losses of life expectancy or physical and mental sufferings of the victims and their relatives. Estimates of indirect costs describe only the production losses for society from an economic perspective.

In our study the indirect costs of injuries have been estimated with the help of two alternative approaches. First, we used the 'human capital approach'. This method has a long tradition and has been applied in studies of the costs of injuries (Hartunian et al. ,1980; Max et al., 1990). This approach estimates losses of economic production as a consequence of disease or injury at a specific age using the total potential productive value of employed persons from that age until

the age of retirement. Moreover, the potential nonmarket productive value from that age until the mean age of death is also considered. The human capital approach ignores the fact that within production processes, everyone can be replaced. During short-term absenteeism work may be taken over by other employees or may be postponed. During long-term absences work can be taken over by unemployed persons or employees can be reallocated to other jobs.

As an attempt to estimate the 'actual' production losses to society instead of the 'potential' production losses as measured by the human capital approach, health economists have recently developed the friction cost method (Koopmanschap et al., 1992). In our study, we have used this method along with the human capital approach to produce estimates of the indirect costs of injuries. The friction cost method is based on the fact that a worker who becomes the victim of premature death or disability will be replaced in the economic process after a so-called 'friction period'.

The length of this period and the resulting indirect costs depend on the situation on the labour market. The friction cost method confines production losses to this friction period (2,5 months in the Netherlands in 1988), which is usually much shorter than the period from premature death or disability up to the age of retirement or the mean age of death.

In both the human capital approach and the friction cost method the following sources of production losses have been considered: premature death, short-term absenteeism, and long term work disability (which in the Netherlands is defined as work disability after the decision is made that the patient cannot return to his job; only in a small minority of cases this decision is made within the friction period). In calculating indirect costs we used national registration data on mortality (CBS, 1989), long term work disability (GMD, 1990) and short term absenteeism (CBS, 1988).

We valued the production loss of paid labour by using the gross average earnings per worker by age and sex taking into account the proportion of full-time and part-time labour in the population (CBS, 1988). In calculating the non-market productive value we used the market alternative approach, assuming the value of household production to be equal to the costs of hiring personnel to do the housework (LTD, 1992). The average number of days of household production lost per person due to diseases or injuries was derived from a time use survey in the Dutch population (CBS, 1992). Future earnings per person, based on average earnings and

labour force participation rates by age and sex plus imputed household values, were discounted at 5% per year.

We calculated the direct medical costs and the indirect costs of injuries and other diseases in millions of Dutch guilders. These were afterwards translated into millions of US Dollars using the exchange rate between the two currencies of 1988 as provided by the Organisation of Economic Co-operation and Development (OECD).

6.4. Results

6.4.1. Direct medical costs

Table 6.2 shows the direct medical costs of injuries in comparison to other diseases which are made within several sectors of health care. The total direct medical costs of injuries are 952 million US Dollars a year, which is almost 5% of the total health care budget in the Netherlands. The direct medical costs of injuries are equal to those of cancer and about half of those of cardiovascular diseases. As with other diseases the majority of medical costs is incurred in the hospital. Other important sources of direct medical costs of injuries are nursing home care and physiotherapy.

Table 6.3 shows the direct medical costs of specific subcategories of injuries for males and females. Almost two-thirds of the direct medical costs are a consequence of injuries to females caused mainly by domestic accidents. Domestic accidents are by far the largest subcategory accounting for more than 500 million US Dollars of the total medical costs of injuries. Another striking subcategory is that of injuries to cyclists, which in the Netherlands causes more than twice the costs of injuries to passenger car occupants (in both males and females). Sports injuries are also an important subcategory, with medical costs which are much higher than, for example, the costs of occupational injuries or injuries to passenger car occupants.

Table 6.2 **Direct medical costs of injuries in comparison with other diseases by health care area (The Netherlands, 1988, in millions of US dollars; percentage share are shown in parentheses)**

	All diseases	Injuries	Cardiovascular diseases	Cancer
All medical costs	20.075 (1.00)	952 (0.05)	1.746 (0.09)	915 (0.05)
General practitioners	906 (1.00)	40 (0.04)	77 (0.08)	17 (0.02)
Physiotherapy	530 (1.00)	63 (0.11)	4 (0.01)	1 (0.00)
Hospital care	7.033 (1.00)	641 (0.09)	825 (0.12)	795 (0.11)
Mental health care	3.046 (1.00)	- -	- -	- -
Nursing home care	1.974 (1.00)	86 (0.04)	427 (0.22)	46 (0.02)
Other medical costs	6.586 (1.00)	122 (0.02)	413 (0.06)	56 (0.01)

Table 6.3 **Direct medical costs by injury category and gender (The Netherlands 1988; amounts in millions of US Dollars)**

	Males	Females	Both sexes
Traffic accidents (total)	106	76	182
- Passenger car occupants	17	12	29
- Cyclists	34	29	63
- Moped riders	17	5	22
- Pedestrians	13	13	26
- Other traffic	25	17	42
Non-traffic accidents (total)	199	387	586
- Occupational injuries	24	5	29
- Sports injuries	38	16	54
- Domestic injuries	137	572	503
Other injuries (total) (Intentional injuries/medical complications)	75	109	184
Total medical costs of injuries	380	572	952

Figure 6.1 Direct medical costs of traffic injuries by age and sex (The Netherlands 1988; amounts in millions of US Dollars)

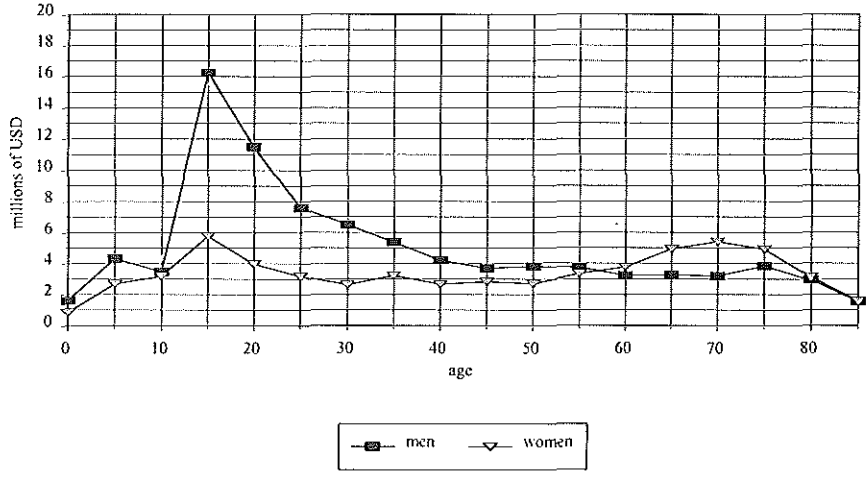


Figure 6.2 Direct medical costs of occupational injuries by age and sex (The Netherlands, 1988; amounts in millions of US Dollars)

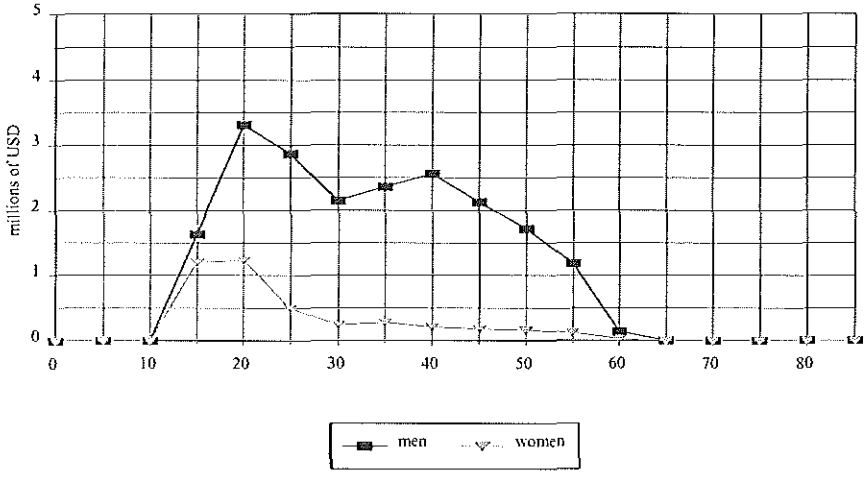


Figure 6.3 **Direct medical costs of sports injuries by age and sex (The Netherlands 1988; amounts in millions of US Dollars)**

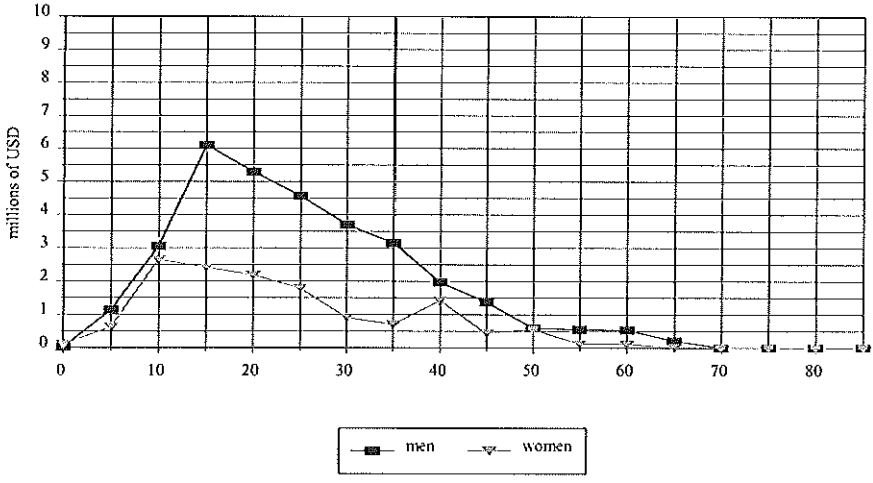
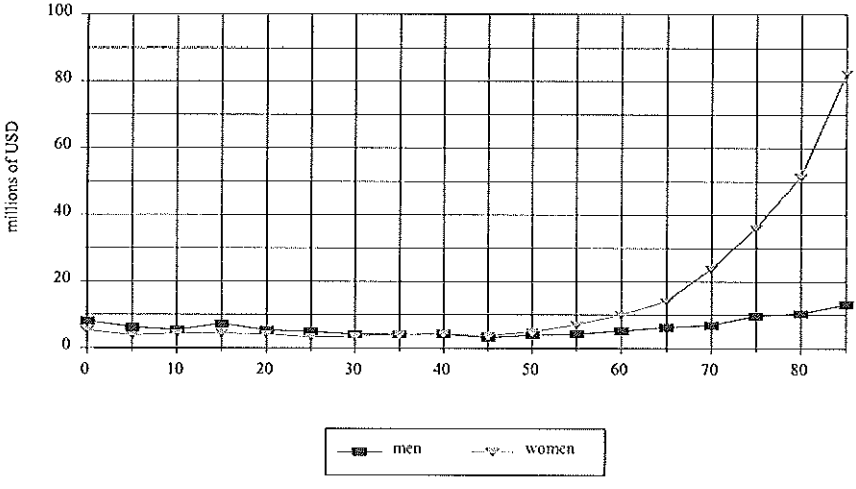


Figure 6.4 **Direct medical costs of domestic injuries by age and sex (The Netherlands 1988; amounts in millions of US Dollars)**



From figure 6.1 it can be observed at what ages the direct medical costs of injuries and its main subcategories are generated. Among males the highest medical costs of injuries are made in early adulthood (15-25 years of age). This is based on the combined effect of high costs of traffic injuries (figure 6.1), occupational injuries (figure 6.2) and sports injuries (figure 6.3) at this age. Among females on the contrary, the importance of accidents is immediately clear, particularly among the elderly. The high level of direct medical costs of injuries in females is based to a large extent on the very high costs of domestic accidents among elderly women (figure 6.4).

6.4.2. Indirect costs

The indirect costs of injuries have been calculated according to both the human capital approach and the friction cost method. Table 6.4 shows the indirect costs of injuries in comparison to other diseases according to both methods. Injuries are the source of 8% of the total indirect costs of diseases in the Netherlands. For males this percentage is 9 to 10%, whereas for females, it is somewhat lower (5%). Independent of the method used injuries rank third behind locomotor diseases and psychiatric disorders. Most strikingly, injuries account for a higher proportion of the total indirect costs of diseases than cardiovascular diseases and cancer. This difference becomes even more clear when the friction cost method is applied.

Table 6.4 **Indirect costs of injuries by gender according to the Human capital approach (HC) and Friction cost method (FC) (The Netherlands 1988; percentage shares of total indirect costs)**

	Injuries	Cardiovascular diseases	Cancer	Locomotor diseases	Psychiatric diseases
Human capital approach (HC)					
Both sexes	0.08	0.08	0.04	0.27	0.23
Males	0.10	0.09	0.04	0.29	0.21
Females	0.05	0.03	0.04	0.23	0.30
Friction cost method (FC)					
Both sexes	0.08	0.02	0.01	0.17	0.10
Males	0.09	0.02	0.01	0.20	0.10
Females	0.05	0.01	0.01	0.11	0.11

Table 6.5 provides information on the indirect costs of specific subcategories of injuries to males and females. Contrary to the direct medical costs, it appears that the indirect costs are generated mainly by males. The potential production losses as calculated by the human capital approach of males (2851 million) and females (442 million) add up to 3293 million US Dollars. The actual production losses as calculated by the friction cost method are lower for both males (579 million) and females (123 million), adding up to 702 million US Dollars. According to both approaches more than 80% of the indirect costs are the consequence of injuries of males. This observation has the following background. First, in the age category between 20 and 60 years the incidence of injuries of males is much higher than that of females. Second, in the

Netherlands males have a much higher labour force participation rate than females. For many injured women production losses are restricted to work in the household, which is valued rather low in comparison to most jobs in the market sector.

The relative proportion of the specific subcategories of injuries in the indirect costs is highly dependent on the method used. In the human capital approach traffic accidents are a major category. This is based on the high indirect costs as a consequence of traffic deaths, which often appear at younger ages. In the friction cost method the indirect costs are almost completely caused by short-term absenteeism. In this approach occupational accidents are the main cause of indirect costs, and sports injuries rank second. This is due to the high frequency of these types of injuries among males which belong to the labour force.

Table 6. 5 Indirect costs of injuries by source of economic production loss and gender according to the Human capital approach and Friction cost method (The Netherlands 1988; amounts in millions of US Dollars)

	Human capital approach		Friction cost method	
	males	females	males	females
Short-term absenteeism	876	185	566	121
Traffic accidents	157	53	85	30
Occupational accidents	359	27	240	19
Sports accidents	162	32	113	23
Domestic accidents	136	54	93	37
Other injuries	53	19	35	12
Long-term disabilities[a]	1169	179	2	0
Mortality	825	78	11	2
Traffic accidents	337	28	4	1
Nontraffic accidents[b]	114	5	2	0
Other injuries	374	45	5	1
Total indirect costs of injuries	2851	442	579	123

[a] No information available for any specification by injury category

[b] No information available for a breakdown into occupational accidents, sports accidents and domestic accidents

6.5. Discussion

Our study has shown that injuries are an important source of medical costs (5% of the total health care budget) and economic production losses (8% of the indirect costs due to all diseases) in the Netherlands.

Almost two-thirds of the direct medical costs of injuries are the result of accidents among females, which are mainly domestic accidents among elderly women. Another major source of health care use are the sports injuries, causing almost twice the direct medical costs of either injuries to passenger car occupants or occupational injuries. Injuries to cyclists are a remarkable subcategory as well, causing by far the highest direct medical costs of all subcategories of traffic injuries in the Netherlands.

The indirect costs of injuries are characterised by complete different patterns by subcategory, age and sex. Contrary to the direct medical costs, more than 80% of the indirect costs are the result of injuries of males. This result is produced independent of the method used.

In calculating the potential production losses for society (human capital approach) traffic injuries are a major source of indirect costs, whereas occupational injuries are by far the largest subcategory when the actual production losses are computed (friction cost method).

Estimates of both the direct medical costs and the indirect costs of injuries confirm that we are dealing with a major public health problem, that should be a priority area for research and policy. Our results clearly demonstrates that cost assessment could be one of the tools in priority setting in public health policy and research. In interpreting the results of our study, however, one must be aware of some specific limitations; when using this tool in general, methodological considerations have to be considered.

A general comment, already mentioned above, is the high dependence of the results of cost of illness studies on the elements that are taken into account and on the methods that have been used. The results from our study show that it matters whether either the direct medical costs and/or the indirect costs are considered. Moreover, different approaches for the estimation of indirect costs produce different rankings of injury subcategories. One should be aware of this when using cost estimates for purposes of priority setting.

To make reliable cost estimates, the availability of adequate data on health care utilisation, mortality, short-term absenteeism, and long-term work disability by diagnosis, age and sex is of primary importance. In our study we could use data from 1987 and 1988 which provided much detail on health care utilisation due to diseases and injuries in that period. This enabled us to produce detailed estimates of the direct medical costs of injuries in 1987 and 1988. We had to use data from different years, which is unlikely to have affected the main results of our study. The data on all but one of our parameters fell within a two-year period (1987-1988). The annual fluctuations of these parameters are probably too small to exert a significant influence on the calculations.

More important seems the fact that our cost estimates do not reflect the current situation in the Netherlands. Moreover, although we used the best data which were available, information on some important health care sectors (e.g. ambulance transport) was lacking. These factors must be taken into account when interpreting the cost estimates of our study.

Our calculations of the direct medical costs in the Netherlands probably slightly underestimate the present importance of injuries in comparison with other diseases. First, the incidence of injuries in the Netherlands shows a slight overall increase in recent years, which is based to a large extent on rising numbers of domestic accidents among the elderly (Beeck et al., 1996). It was shown how important domestic accidents among the elderly are as a cause of direct medical costs of injuries. Second, the costs of ambulance transport were not included in our study. This sector occupies almost 1 % of the total health care budget in the Netherlands. Unpublished data from a local ambulance service have shown us that probably almost one quarter of the total ambulance costs should be assigned to injuries, which would lead to another 0.25% of the total direct medical costs.

Contrary to the costs of health care, the indirect costs have probably been slightly overestimated in our study, because the incidence of occupational injuries and sports injuries has slightly fallen in recent years (Beeck et al., 1996). It was shown that these are the subcategories with the highest actual production losses for society as calculated by the friction cost method.

In spite of the limitations as described above, our study has produced results which are highly comparable with the results of other studies into direct medical costs of injuries, both in the Netherlands and abroad (Toom et al. , 1988; Muizelaar, 1996; Rice et al., 1985; Lindgren, 1990). Our study has generated new information for estimating the indirect costs of injuries. The results from our study clearly demonstrate the value of new economic methods to assess the production losses for society.

The application of the friction cost method demonstrates the importance of injuries as a source of production losses in comparison to other diseases. By this method, injuries one of the three main causes of indirect costs (locomotor diseases, psychiatric diseases and injuries) and are far more important than cardiovascular diseases and cancer.

Moreover it sheds light on the economic impact of specific subcategories of injuries which only seem to have minor importance when using traditional public health indicators (mortality and morbidity). A good example is the subcategory of occupational injuries. In the Netherlands this is a minor cause of death, accounting for only a small proportion in the direct medical costs and a moderate proportion in the potential production losses as calculated by the human capital method. Occupational injuries, however, are by far the most important source of actual production losses for society within the category of injuries.

The friction cost method emphasises the production losses that results from short-term absenteeism, whereas in the human capital approach injuries at young ages leading to death or long-term work disability are more important.

From an economic perspective, the friction cost method seems to be the preferable approach in assessing the indirect costs because the dynamics of the labour market are taken into account. This leads to better estimates of the economic production losses for society than traditional methods, such as the human capital approach. One must consider, however, that in estimating economic production losses, consequences of injuries with regard to 'quality of life' (such as

loss of healthy life expectancy and physical and mental sufferings) are not taken into account. For purposes of priority setting information on these 'human costs' should be available, as should information about 'economic costs' as assessed in our study. Research in this area, therefore, should be stimulated. At present adequate data on the quality of life of injury victims are not available. Moreover, the methodology should be further developed, although some interesting studies have been performed already (Jurkovich et al, 1995; MacKenzie et al, 1993; Siosteen et al., 1990).

Returning to the results of our study, we can conclude the following. By estimating the health care costs, the potential economic production losses, and the actual economic production losses due to injuries in the Netherlands, it has been shown that this problem should be a major concern for both health policy makers and the medical profession.

Several priority areas for further research and policy can be indicated. The assessment of direct medical costs confirms the importance of domestic accidents among the elderly and females in particular. It points to the problem of accidental fall and (hip) fractures (Barret-Conner, 1995; Cox et al., 1993; Hollingworth et al., 1995) among the elderly, which can be seen as one of the important epidemics of western societies today.

Another priority area is the sports injuries, which appear to lead to both high direct medical costs and to high actual production losses for society. A priority area which seems rather specific for the Dutch situation is the problem of injuries to cyclists. In the Netherlands, a country of cyclists, injury victims within this subcategory produce direct medical costs which are twice as high as the costs of injuries to passenger car occupants. Finally, based on our estimation the actual production losses for society, it is clear that the prevention of occupational injuries should not be neglected.

7. THE BURDEN OF ILLNESS OF HYPOPITUITARY ADULTS WITH GROWTH HORMONE DEFICIENCY

7.1. Summary

Many chronic diseases have socio-economic implications in terms of lost productivity and increased medical consumption. In the present study, an attempt was made to quantify the burden of illness associated with hypopituitarism, including untreated growth hormone deficiency (GHD), after pituitary surgery.

In total, 129 adults with hypopituitarism after pituitary surgery were studied. The Short-Form 36 Health Survey (SF-36) was used to assess health status. The Health and Labour Questionnaire was applied for measuring production losses and labour performance. Data on medical consumption were also collected.

Hypopituitary patients reported a lower health status than that of the general population in all but two dimensions of the SF-36 (pain and physical functioning). Nearly 11% of the patients reported being incapacitated for paid employment due to health problems, compared with 4.8% of the Belgian population. Patients in paid employment reported that they had a mean of 19.8 days of sickness leave per year, which is twice that in the general population. The number of visits to general practitioners and specialists was also higher in the patients (9.6 and 6.5 visits, respectively, for the patients compared with corresponding figures of 2.1 and 1.5 for the general Belgian population). The average number of days spent in hospital was 3.5 for the patients, compared with 2.3 in the general population. The annual health care costs and costs due to production losses calculated for hypopituitary patients who had received pituitary surgery amounted to 135,024 BEF or USD 4,340. This compares with the mean annual cost per person for the Belgian population as a whole of 68,569 BEF or USD 2,204. Hypopituitary patients with GHD have a higher cost to society in terms of lost production and medical consumption than the average Belgian population. Hypopituitary patients reported a lower health status than that of the mean population in all but two dimensions of the SF-36 (body pain and physical

functioning). However, the contribution of GHD to the burden of illness reported is not clear because of the co-morbidity existing in the study population.

7.2. Introduction

Adults who have undergone pituitary surgery are routinely given replacement therapy for pituitary hormone deficiencies. However, until recently, growth hormone (GH) replacement therapy was not available. There is now compelling evidence that GH deficiency (GHD) in adults is associated with an increase in risk factors for premature cardiovascular death (Cuneo et al., 1991; Markussis et al., 1992; Amato et al., 1993; Rosén et al., 1993b; Johansson et al., 1994), a reduced bone mineral content (Kaufman et al., 1992; Rosén et al., 1993c), abnormal body composition with an increase in body fat and a reduction in lean body mass and extracellular fluid volume (Salomon et al., 1989; Rosén et al., 1993a;), and a lack of energy and vitality connected with poor general health (McGauley, 1989; Rosén et al., 1994).

The present study is the first to examine the burden of illness of adults suffering from hypopituitarism after pituitary surgery, who were not given GH replacement therapy. Quality of life of these patients and the costs, both direct and indirect, associated with their illness and its treatment were assessed in comparison with reference data.

7.3. Methodology

7.3.1. Patient selection and questionnaires

Patients who had undergone pituitary surgery at the Centre Hospitalier Universitaire de Liège, Belgium, between the beginning of the 1970s and April 1994 were included if a GH stimulation test (insulin tolerance test; ITT) indicated a GH level below 10 mU/l. If the ITT was performed within 2 weeks after pituitary surgery, at least one additional pituitary hormone deficiency was required before inclusion in the study. When additional hormone deficiencies were limited to

luteinizing hormone (LH)/follicle-stimulating hormone (FSH), patients were included only if they were shown to have normal prolactin levels. This criterion was added because in cases of elevated prolactin levels, LH/FSH and target hormones are deficient (even in cases of small adenoma without any compression). Patients who had not been submitted to GH testing were accepted as having GHD if at least one other pituitary hormone deficiency was present. Patients were excluded if they were below 20 years of age or if they had been treated previously with GH.

All patient who fulfilled the inclusion criteria received a questionnaire by post in October 1995. After 3 weeks, patients who had not responded were reminded by telephone. The first part of the questionnaire consisted of the Short-Form 36 Health Survey (SF-36), which is a standard questionnaire for assessing health status (Ware et al., 1992); the second part was the Health and Labour Questionnaire (HLQ), which is concerned with production losses and labour performance (van Roijen et al., 1996); and the third part contained questions relating to demography. Medical consumption was recorded by contacting the patients by telephone using an interview protocol.

7.3.2. Quality of life

The official French translation of the SF-36 was used to assess quality of life, which is related to an individual's physical, psychological and social functioning. The SF-36 consists of 36 items assigned to the domains of physical functioning, social functioning, role limitations, mental health, vitality, pain, general health and health changes (Table 7.1). The health status of the hypopituitary patients was compared with SF-36 reference data for representative samples of the US and Dutch populations, as such reference data for Belgium were not available. In addition, the influence of age and gender on the differences between reference values and scores for the patients was analysed. The results for the hypopituitary patients were also compared with SF-36 scores for other chronically ill groups of patients.

Table 7.1 The nine health status dimensions of the SF-36 (Ware, 1993).

Variable	Lowest score	Highest score
Physical functioning	Very limited in performing all physical activities, including bathing or dressing, due to health	Performs all types of physical activities, including the most vigorous, without limitations due to health
Social functioning	Extreme and frequent interference with normal social activities due to physical or emotional problems	Performs normal social activities without interference due to physical or emotional problems
Role – physical	Problems with work or other daily activities as a result of physical health	No problems with work or other daily activities as a result of physical health
Role – emotional	Problems with work or other daily activities as a result of emotional problems	No problems with work or other daily activities as a result of emotional problems
Mental health	Feelings of nervousness and depression all the time	Feels peaceful, happy and calm all the time
Vitality	Feels tired and worn out all the time	Feels full of 'pep' and energy all the time
Pain	Very severe and extremely limiting pain	No pain or limitations due to pain
General health	Evaluates personal health as poor and believes it is likely to get worse	Evaluates personal health as excellent
Health changes	Believes general health is much worse now than 1 year ago	Believes general health is much better now than 1 year ago

7.3.3. Indirect costs

Indirect costs of disease are defined as the value of production lost to society due to absence from work and reduced productivity at work, caused by the illness or its treatment. The HLQ was used to collect data on production losses and reduced labour performance (van Roijen et al., 1996). This questionnaire consists of three modules: absence from work, reduced productivity at work and labour-related problems.

Absence from work

Respondents in paid employment were asked to indicate for each half day of the 2 weeks preceding the assessment, whether they were absent from work due to health problems or other reasons (e.g. weekend, holidays). Under the assumption that this period was representative, the mean annual number of days lost as a consequence of illness was derived. If the respondents were absent because of illness for the entire 2 weeks, they were asked to indicate when the period of absence began. Belgian statistics on absence from work do not provide reference data for these findings. The Belgian Social Security System records only absenteeism from work that exceed 15 days. However, Lombaert and co-workers have estimated a figure for the total absence from work for 1994 in a sample of companies that are representative for Belgium; this figure was used as a reference for comparison (Lombaert et al., 1996).

The number of permanently disabled patients in the study population is an indicator of the health status and burden of hypopituitarism after pituitary surgery. The number of patients who indicated that they were incapacitated for paid employment was therefore compared with the number of incapacitated individuals according to the national statistics of Belgium for 1993 (RIZIV, 1996a).

Productivity at work

To provide an estimate of reduced productivity while at work, respondents were asked to estimate the number of hours that they should have worked longer to compensate for production losses due to illness on working days. Reference data, obtained using the HLQ, for reduced

efficiency are available from a large survey of a representative sample from The Netherlands (van Roijen et al., 1996).

Labour-related problems

Individuals in paid employment were requested to indicate the impediments experienced while performing their work. The response categories were as follows: 'no impediment', 'some impediment' and 'serious impediment'. The item scores are 0, 1 and 2, respectively. In the absence of reference data for Belgium, data from the aforementioned Dutch survey were used for comparison (van Roijen et al., 1996).

7.3.4. Direct costs

Direct costs are the monetary valuation of the resources used to detect and treat disease. Medical consumption was recorded by questioning patients by telephone about their utilization of health services. The questions concerned the number of visits to general practitioners and specialists in the past month and hospital admissions during the past 6 months. Direct costs for these health care providers were based on doctors' tariffs (Statute book, 1995). With regard to average medical consumption for Belgium, data on the use of healthcare services for 1992 have been extracted from the ARIS health information software package of the Centre for Health Economics and Hospital Policy in Belgium (ARIS, 1996). The Department of Social Affairs, Health and Environment systematically collects annual data on hospital stays in Belgium (Department of Social Affairs, Health and Environment, 1992). Reference data for the number of visits to general practitioners and specialists were collected by the National Institute for Illness and Social Insurance (RIZIV, 1996b). We have assumed that the use of the relevant health care provisions for the Belgian population did not change between 1992 and 1995. The average health care expenditure per person for the Belgian population was calculated by multiplying the average number of physician visits and hospital days by the corresponding tariffs for 1995.

7.4. Results

7.4.1. Patient characteristics and response rates

In total, 215 hypopituitary patients were considered for inclusion in the study. Thirty-two of them died before the start of the survey, leaving 183 hypopituitary patients with GHD to complete the questionnaires. Of these, 138 (75%) responded, although eight had been treated previously with GH and were therefore excluded. Another patient was excluded because a member of his family had completed the questionnaire. Of the 129 patients remaining for analysis, all but three had undergone surgery by the transphenoidal route. Two patients had had transcranial surgery only. Eighteen patients were operated on twice, and two patients had had three interventions. The route of surgery remains unclear for one patient. The aetiology of the patients before surgery is shown in Table 7.2, and the distribution by age, gender and employment status of the responders is shown in Table 7.3.

Table 7.2 Distribution of hypopituitary patients by diagnosis before pituitary surgery.

Diagnosis	Number of patients
Non-secreting adenoma	55
Cushing's disease	16
Acromegaly	13
Prolactinoma	36
Craniopharyngioma	6
Others*	3

*Other causes included empty sella syndrome, pituitary abscess and cordoma.

The mean time between surgery (an approximate indicator of the time of onset of GHD) and completion of the questionnaires was 10.4 years (range, 1.7–30.9 years).

Thirty-one patients received radiotherapy. Patients with thyroid and/or adrenal insufficiency were given adequate replacement therapy. LH/FSH deficiency was present in 59 of the 129 patients. The status of sex-steroid substitution is unknown in five patients. Of the other 54 patients with LH/FSH deficiency, 28 men and 10 women received sex-steroid substitution, while 10 men and 6 women did not. In the total population of 129 patients, 20 presented with isolated GHD, 33 had one additional pituitary hormone deficiency, 36 had two additional deficiencies and 40 had three or more additional hormone deficiencies.

Table 7.3 Distribution of patients by gender, age and employment status.

	Sample
Gender	
Male	63
Female	66
Age	
20–24	2
25–34	9
35–44	13
45–54	32
55–64	29
65–74	34
75+	10
Employment status	
Employed	36
Not-employed	93
Total	129

Eight of the 129 patients could not be contacted to obtain information from which the direct costs of illness could be calculated; analyses of direct cost were therefore performed on data from 121 patients.

7.4.2. Quality of life

Table 7.4 gives the SF-36 scores for the hypopituitary patients compared with US and Dutch reference scores. In all dimensions of the SF-36, the hypopituitary patients had a significantly ($p < 0.01$) lower score than the US and Dutch norms (except for 'pain' in comparison with the US reference values) (Ware et al., 1993).

Table 7.5 gives an overview of the SF-36 scores according to gender and age. The first four columns show the gender differences. The mean scores for the male hypopituitary patients were, with the exception of scores for pain, significantly lower than the US reference values (Ware et al., 1993). The mean scores for the female hypopituitary patients were all significantly lower than the US reference values. Similar differences were found when the patients were compared with reference values from The Netherlands (van der Zee et al., 1993), which may be a more suitable population to use for comparison with the Belgian patients.

Table 7.4 **SF-36 scores in hypopituitary patients (n = 129) compared with reference scores from the USA (n = 2474) and The Netherlands (n = 1063). Values are means ± SEM, with 95% confidence intervals given in parentheses for the patient group.**

	Patients	US	The Netherlands
Physical functioning	72.28 ± 2.4 (65.9–78.6)	84.2 ± 0.5	81.9 ± 0.7
Social functioning	72.61 ± 2.3 (66.6–78.6)	83.3 ± 0.5	86.9 ± 0.6
Role – physical	62.31 ± 3.6 (52.9–71.7)	81.0 ± 0.5	79.4 ± 1.1
Role – emotional	66.41 ± 3.7 (56.9–75.9)	81.3 ± 0.7	84.1 ± 1.0
Mental health	61.11 ± 1.9 (56.1–66.1)	74.8 ± 0.4	76.8 ± 0.6
Vitality	48.71 ± 2.2 (42.9–54.5)	60.9 ± 0.4	67.4 ± 0.6
Pain	67.52 ± 2.5 (61.0–74.0)	75.2 ± 0.5	79.5 ± 0.8
General health	56.15 ± 2.2 (50.4–61.9)	72.0 ± 0.4	72.7 ± 0.7
Health changes	48.67 ± 1.8 (44.1–53.2)	–*	52.4 ± 0.6

*Reference score does not exist for the US.

For all dimensions, scores for the hypopituitary patients were significantly lower ($p<0.01$) compared with the corresponding reference values, except where indicated otherwise (NS).
The reference scores in table 7.4 cover people of all ages. As the average age of the patients in the present study was 57 years, we compared them with reference data from the US for people between 55 and 65 years of age (table 7.5). For all health dimensions, the scores for the hypopituitary patients were significantly ($p<0.01$) lower than the US reference values, with the exception of physical functioning and pain.

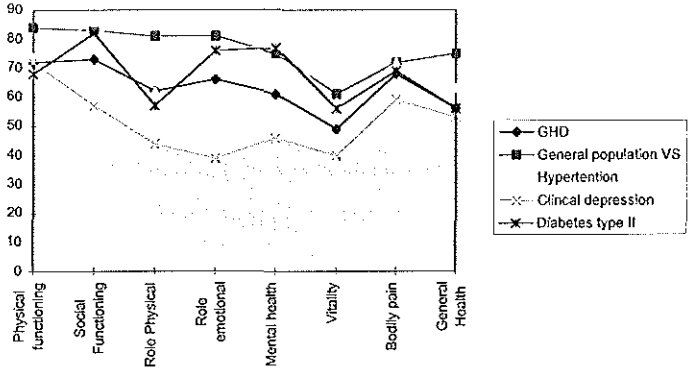
Table 7.5 **SF-36 scores by gender and age for hypopituitary patients compared with reference values for the US**

Health dimension	Hyp. patients		US		Hyp. Patients	US
	Male (n=63)	Female (n=66)	Male (n=1055)	Female (n=1412)	Age 55–64 (n=29)	(n=269)
Physical functioning	76.9	68.1	87.2	81.5	68.9 (NS)	76.2
Social functioning	76.6	68.9	85.2	81.5	79.0	81.4
Role–physical	66.8	58.1	86.6	77.7	63.7	73.7
Role–emotional	70.3	62.8	83.3	79.5	72.0	80.3
Mental health	64.2	58.2	76.4	73.3	63.2	75.0
Vitality	51.4	46.2	63.6	58.4	48.5	60.4
Pain	72.4 (NS)	62.9	76.8	73.6	63.7 (NS)	67.5
General health	54.9	57.3	73.5	70.6	56.1	64.6

The scores for the hypopituitary patients were compared with those for other chronically ill patients (Fig. 7.1, scores from Ware et al., 1993). The scores for the hypopituitary patients were lower than those for patients with either hypertension or non-insulin-dependent diabetes

mellitus. However, in all dimensions, the SF-36 scores for the hypopituitary patients were higher than those for patients with clinical depression.

Figure 7.1 Score on the SF-36 of GHD compared to scores for the general population, hypertention, depression, depression and diabetes



7.4.3. Indirect costs

Nearly 11% (n = 4) of the patients who were in paid employment (n=36) reported that they were incapacitated due to health problems. In comparison, in 1993, 4.8% of the working population in Belgium was incapacitated for paid employment (RIZIV, 1996 a).

Absence from work

Of the 36 respondents in paid employment (mean age, 48 years), four patients reported that they had been absent from work sometime during the past 2 weeks. One of them indicated that the period of illness began more than 3 months ago. On an annual basis, the average time absent from work was 19.8 days/year, compared with a mean of 8.9 days/year for the general Belgian population (Lombaert et al., 1996).

Productivity at work

Nearly all respondents (97%) in paid employment reported no reduced efficiency at work due to health problems.

Labour-related problems

Employed patients were also asked to indicate to what extent they experienced reduced performance at work. The observed distribution across the three categories (no impediment, some impediment, and serious impediment due to health problems) was no different from that of a Dutch reference population (van Roijen et al., 1996).

Although the number of patients in paid employment in the sample was small (n = 36), the indirect monetary costs of illness were estimated. As data on the gross earnings by age and sex were lacking, the valuation of the production loss was based on average gross earnings. Multiplication of workdays lost by average gross earnings gave an indirect cost per working patient of BEF 91 465/year. In this calculation, account was taken of the fact that a reduction of annual labour time causes a less than proportional decrease in productivity per year, because of diminishing returns on labour and reduction of the internal labour reserve of a company (elasticity of 0.8; CPB, 1987; Koning et al., 1984). For the Belgian population, the average indirect costs amounted to BEF 41,113/worker.

7.4.4. Direct costs

Table 7.6 gives the average number of visits to general practitioners and specialists, and the number of days spent in hospital per hypopituitary patient per year. The corresponding costs are based on the accompanying charges per specialist and tariffs for hospital days by department. Additionally, this table shows the average use of these health care provisions and average expenditures per person for the general Belgian population (ARIS, 1996). Hypopituitary patients had higher health care costs due to visits to general practitioners and specialists and to hospital admissions than the reference population.

The direct and indirect costs add up to BEF 135,024 per patient per year.

Table 7.6 **Average number of visits to general practitioners and specialists and the number of days spent in hospital by hypopituitary patients, and the associated costs, compared with average utilization and costs incurred by the general Belgian population (in BEF, 1995)**

	Hypopituitary patients	Belgian population
General practitioner		
Average number of visits	9.6	2.1
Costs	3,696	809
Specialist		
Average number of visits	6.5	1.5
Costs	4,790	825
Hospitalization		
Average number of visits	3.5	2.3
Costs	35,073	25,822

7.5. Discussion

The socio-economic implications of certain diseases, in terms of lost productivity and medical consumption, are attracting increasing attention. To our knowledge, no previous study has considered the social costs of hypopituitarism and GHD in adults. In this analysis, 129 hypopituitary adults with GHD, who had undergone pituitary surgery for various reasons, were compared with reference groups. They reported a significantly lower health status, were more often incapacitated for paid employment, had higher rates of absence when they were in employment, and consumed significantly more health care resources than the population in general.

Questions on absence from work related to 'the past 2 weeks'. In our experience, 2 weeks is the maximum period for reliable recollection of absence from work, and we have assumed that this period of 2 weeks is representative for the year. Although there was only a small number of patients in paid employment, our results regarding the number of days absent from work were in accordance with the amount of sick leave recorded in a period of 6 months in a group of 148 patients with GHD before inclusion in a therapeutic trial of GH (22 days/patient/year) (Verhelst et al., 1997).

Estimation of the direct costs should be interpreted with caution for several reasons. Firstly, in comparing the average number of visits and days spent in hospital by the hypopituitary patients with the Belgian reference population, it was not possible to correct the latter for variance in utilization by age and sex because of lack of detailed data. Secondly, the calculation is based on charges, instead of real costs, which may cause over- or underestimation. Additionally, the direct-cost estimation is restricted to utilization of a limited number of health care provisions. Finally, information collected by interview may be less reliable than data obtained from health care providers or insurance companies.

Since the early 1980s, the ITT has been used to investigate GH secretory capacity and is an integral part of the endocrinological assessment of patients undergoing pituitary surgery. Most patients included in this survey were selected on the basis of a low GH peak during an ITT. It was realized that the short period between surgery and the ITT in some patients may raise doubts concerning the accuracy of the diagnosis of GHD. Therefore, for inclusion in the study, those patients who had been tested within 2 weeks of surgery were required to have at least one additional pituitary hormone deficiency. If this happened to be a deficiency in FSH/LH, patients were included only if they had normal prolactin levels. For some patients, ITT results were not available, and they were included only if they had at least one additional pituitary hormone deficiency, as it has been demonstrated that, in this group, the probability of having GHD exceeds 80%. In the final patient population, of the 18 patients who did not have a GH stimulation test, eight presented with two additional hormone deficiencies and ten with three additional deficiencies, which means that the probability that these patients had GHD was close to 100%.

The reported differences between the hypopituitary patients and the reference population cannot be attributed entirely to GHD, as all the patients received regular medical follow-up as a result of their surgery. Moreover, part of the study population had suffered previously from Cushing's disease or acromegaly, which are themselves incapacitating. Finally, 31 patients needed radiotherapy, which may also lead to specific symptomatology. Further studies are therefore needed to compare patients who have undergone pituitary surgery, either with or without GHD, with both groups consisting exclusively of non-secreting adenomas and prolactinomas, but excluding Cushing's disease and acromegaly. Such studies would indicate more precisely the contribution of GHD to the burden of illness for these patients. With the above considerations in mind, it is likely that at least part of our observations can be attributed to the GH-deficient status of the patient group.

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8. SETTING PRIORITIES FOR COST-EFFECTIVENESS ANALYSES IN MENTAL HEALTH CARE

8.1. Summary

Aim of the study was to set priorities for economic evaluations in mental health care in the Netherlands. Direct costs of health care due to mental disorders were estimated. We selected 4 'expensive' diagnostic categories for further analysis. A literature study on effectiveness of possibly competing treatments for the selected diagnostic categories was carried out (illustrated by schizophrenia). Supplementary information was gathered from practice guidelines and from a panel of specialists. Finally, priorities were set for future cost-effectiveness research in mental health care. After dementia (31%), schizophrenia (12%), neurotic disorders (9%), affective psychose (9%) and substance abuse disorders (6%) were responsible for the highest share in health care costs. As an example, we present the results of our literature review and what is known and not known about effectiveness of current treatment categories in schizophrenia Application of the prioritisation criteria resulted in 8 recommendations for further costs-effectiveness studies for schizophrenia.

8.2 Introduction

Rising costs and budget constraints in health care have enhanced the importance of cost-effectiveness analyses to support decisions about expenditures. Optimising the total health gain of investments is at stake. Cost of illness studies may be used as a first step towards setting priorities in health care expenditures. Many researchers, however, have emphasised that high cost of disease may be a necessary but certainly not a sufficient condition for priority setting in health care (e.g. Drummond, 1992). Additionally, data on cost-effectiveness of interventions are needed.

In spite of high prevalence and high costs of mental disorders, studies on cost-effectiveness in mental health care are rare. Overall, most interventions at present have either not been evaluated

or evaluated with an incomplete research design, i.e. ignoring costs of interventions (Maynard et al., 1995). The present study was meant to set priorities for economic evaluations in mental health care in the Netherlands. To gain priority for cost-effectiveness analyses an intervention in mental health care had to meet the following requirements:

- The therapy is directed at a diagnostic group that generates high expenses (either as a group or individually);
- The interventions should have some known (or assumed) effectiveness for the particular disorder;
- The therapies 'competitiveness' is uncertain, i.e. it is not known whether this therapy has a superior effect for equal costs compared with other therapies, or an equal effect for less costs than its alternative.

The following steps were taken for targeting future research. First, the direct cost of health care due to mental disorders were estimated to determine diagnostic categories bearing substantial health care costs in the Netherlands. Based on this cost-criterion we selected four diagnostic categories for further analysis. Secondly, a literature study on effectiveness of possibly competing treatments for the selected diagnostic categories was carried out. This was done by analysing the results of treatment outcome research. We gathered supplementary information from practice guidelines and from a panel of specialists. These two steps provided us with information on the priority criteria mentioned above, and in the third step we set priorities for future cost-effectiveness research.

In this paper we will present the direct cost estimates of mental disorders for the Netherlands in 1993. Subsequently, we will give a brief description of the international literature study on effectiveness of treatments for one disorder having high costs in the Netherlands: schizophrenia. We conclude with recommending priorities for cost-effectiveness analyses on schizophrenia.

8.3. Methodology

8.3.1. Cost of mental illness in the Netherlands

Cost of illness can be divided into direct and indirect costs. Direct costs are the health service costs of patients seeking therapy. Indirect costs are the societal costs of production losses due to illness. The present cost of illness study is limited to costs incurred within the health care services. Estimates of indirect costs are not included because accurate data on absence from work and disability are lacking (see discussion). Cost of illness can be estimated according to the incidence- or prevalence based method (Hartunian et al., 1981). The incidence based method is longitudinal and requires estimates of disease progression. The prevalence method is more simple and estimates the cost of disease in a given year. Estimating only the relative contribution of different mental disorders to the total health care costs for one year, we limited ourselves to the prevalence method.

Starting point for our cost calculation were the total direct costs per relevant health care service in the Netherlands for 1993 (VWS, 1995). Diagnostic categories were based on the 9th revision of the International Classification of Diseases (WHO, 1977). The ICD-codes 290 to 316 were included, some of them aggregated into broader diagnostic categories. We excluded the cost of prevention, and of mentally disabled persons. We limited ourselves to adult and elderly patients: children and youth were excluded. For each health care service the costs were assigned to diagnostic categories, age and gender based on the number of patients on set day, the number of hospital days per year or the expenditures per year per group of patients. For instance, the distribution of the costs for inpatient care was based on the number of patients hospitalised on a given date or the number of hospital days for 1993 per patient category. For outpatient care we used the number of visits or the number of patients.

The primary diagnoses were used for assigning the costs. In general, data were extracted from national data sources with nearly complete coverage (psychiatric hospitals, nursing homes, hospitals, TBS-clinics, substance abuse clinics, CAD's, and health resorts). We also used representative data from large surveys in the Netherlands for costs assignment (outpatient

psychiatric care, general practitioners (GP), and costs of pharmaceuticals for non-hospitalised patients).

Cost of drugs prescribed to hospitalised patients were included in the cost of hospital care. For most health care services we had sufficient information on diagnosis, age and gender. These data were insufficient for sheltered housing (RIWB) and some small services for outpatient psychiatry and substance abuse. We classified these costs as 'not assignable'. Table 8.1 presents the cost criteria, data source, the availability of data, and the relative costs per health care sector.

8.3.2. A literature study of meta-analyses of effectiveness studies

After establishing costs per diagnosis our next step was to provide an overview of what is known about the effectiveness of treatments for four diagnoses. We confined ourselves to four 'expensive' mental disorders in the Netherlands (schizophrenia, depression, anxiety disorders and alcohol related disorders). Dementia had the highest costs of all mental disorders. After consultation with the Health Insurance Funds Council we excluded this diagnostic category for this part of the study because the main costs for this diagnostic category are generated outside the mental health care.

We limited our efforts to treatment outcome research. We realised that most research deals with efficacy instead of effectiveness. Because efficacy studies provide information about treatments that can be effective in treatment situations, we consider this restriction not essential for prioritising cost-effectiveness analyses on a national level. It is not efficient to make a comprehensive review of the results of the vast quantity of outcome research in mental health care. For prioritising cost-effectiveness studies, rough estimates of effectiveness will suffice. In order to get an empirically justified impression of the effects of treatments, we confined ourselves to a 'quick route' by studying meta-analyses and systematic research reviews for each of the four selected diagnostic categories.[1] Narrative reviews and professional guidelines served

[1] Research reviews evaluate and summarize the findings of several publications of primary research. In this study we used three categories of research review. Two categories are methodologically more sophisticated and therefore of special interest for us: 1) statistical meta-analyses and 2) systematic research reviews. For these categories the results can be evaluated, because procedures of data gathering and formal analysis procedures are described explicitly. For reasons of brevity we will use the term meta-analysis for both categories. We separated meta-analyses from 3) traditional or narrative research reviews. This category of research reviews is scientifically

as background material for determining relevant treatment categories and additional information on treatments. The consequence is that we did not gather recent publications of primary treatment outcome research.

For statistical meta-analyses methodological quality criteria are more extensive than for systematic research reviews. Carrying out a meta-analysis or review, it is recommended practice to use code sheets to systematically gather and evaluate the characteristics and outcomes of primary studies (Gageldonk, 1995). In the same vein we developed, pre-tested and used code sheets that enabled systematic comparison of the studied meta-analyses and reviews. Examples of criteria for methodological quality of statistical meta-analyses are: statistically independent research outcomes, homogeneity of calculated effect sizes and correction of the summary statistic for errors (Hedges et al., 1985; Hunter et al., 1990). Examples of quality criteria for systematic research reviews (including statistical meta-analyses) are: proper selection of primary research publications (e.g. research designs and specific design characteristics) and comparability of patients and treatments between studies.

We searched the following databases: Psyclit, Medline, Embase, SCI-search, SSCI, Toxline, Mental Health Abstracts, ERIC, Health Periodicals, Pharmline, Sociofile and Dissertation Abstracts. Our attention was directed to studies published from 1980 and we excluded publications of prevention, of youth problems and of mentally disabled persons. After excluding narrative reviews and double countings, our initial data-set of nearly 900 publications of different sorts of review-studies decreased to 167 statistical meta-analyses and systematic reviews of treatment outcome research for our four diagnostic categories. Most meta-analyses were found for depression and anxiety disorders. Additionally, a questionnaire was sent to a panel of specialists on the four diagnostic categories. The questionnaire was to indicate interventions relevant for future cost-effectiveness analyses which were missing on the list of interventions selected by the literature search.

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unsound, because authors do not describe their methods. Thus one can not adequately determine the efficacy of treatments (Hunter et al., 1990; Rosenthal, 1991).

8.3.3. Prioritising cost-effectiveness analyses

We used three criteria for prioritising cost-effectiveness analyses in mental health care (see introduction): health care cost for the intervention to be studied, a reasonable assumption of its effectiveness, and its possible competitiveness with other interventions in terms of effectiveness or costs (or both).

As an example, we present a summary of the results of priorities for cost-effectiveness analyses for one diagnostic category: schizophrenia. This category generates the highest cost for mental health care after dementia. Results for all four diagnostic categories are published in detail elsewhere (Donker et al., 1996; Arends et al., 1996; Gageldonk, 1996; Smit, 1996).

8.4. Results

8.4.1. Total costs of mental disorders

Total direct cost of mental disorders in the Netherlands amounted to 6,9 billion Dutch guilders (USD=NLG 1.94), 11% of the total health care costs in 1993. When we initiated this study, 1993 was the most recent year of which costs figures were available. Ninety-two per cent of these total costs could be ascribed to specific diagnoses. Costs of some sectors, i.e. 'sheltered housing' (RIWB), 'other outpatient care' and 'other substance abuse care' could not be distributed among diagnoses due to lack of information. Thirty-three percent of the total costs were generated by general psychiatric hospitals, and 30% by nursing homes (see table 8.1).

Table 8.1 Cost criteria, data source, availability of data and percentage of the total costs of mental illness per health care sector in the Netherlands in 1993

Health care service	Cost criteria (number of ...)	Data source	Availability of data on diagnosis	% of total costs of mental disorders
General psychiatric hospitals	patients	National data source	+	33
Psychogeriatric nursing home	hospital days during the year	National data source	+	30
Hospitals[1]	hospital days during the year	National data source	+	11
RIAGG[2]	visits	Survey	+	9
Pharmaceuticals	costs	Survey	+	5
Sheltered housing (RIBW)	no data	no data	_	3
General practitioner	consults	Survey	+	3
TBS-clinics[3]	patients	National data source	+	2
CAD's[4]	new patients	National data source	±	2
Substance abuse clinics/hospitals	patients	National data source	+	1
Other substance abuse care	no data	no data	_	1
Other outpatient care	no data	no data	_	0
Health resorts	admissions during the year	National data source	+	0

1. The costs of 'hospitals' include the costs of nursing and physician services in general, categoral and academic hospitals.
2. Regional Institutes for Outpatient Mental Health Care
3. In TBS clinics criminals with psychiatric problems are receiving compulsory treatment, in order to diminish the chance of future offenses or crimes.
4. CAD's provide outpatient treatment to patients with substance abuse disorders.

8.4.2. Costs by diagnosis and sector

Table 8.2 presents diagnostic groups which induce the largest costs. Dementia is obviously in first position with 31% of the total costs. Over 90% of these costs were due to 'nursing homes'. Second is schizophrenia, responsible for 12% of the total costs of mental disorders. Ninety percent of these costs were due to treatment of these patients in 'psychiatric hospitals'. The costs of neurotic disorders amounted to 9% of the total costs. Affective psychosis (a.o. major depression and bipolar disorders, ICD-9 code 296) accounted for nearly 9% of the total costs. The costs related to the latter were predominantly spread over 'psychiatric hospitals' and 'h-ospitals'. The main share of the costs of personality disorders was due to care in psychiatric hospitals. The costs of alcohol and drugs related disorders accounted for 6% of the total costs of mental disorders. Psychiatric hospitals, addiction clinics and CAD's were responsible for 78% of these costs.

The costs of other depressive disorders (ICD-9 code 311), 243 million guilders, are ranked in the eigth position. It should be noted, however, that a part of the costs of depression are included in other diagnostic categories e.g., neurotic disorders (ICD-9 code 300; third position), affective psychosis (ICD-9 code 296; fourth position), personality disorders (ICD-9 code 301) and adjustment problems (ICD-9 code 309; ninth position). Data on these diagnoses did not allow us to make a sharp distinction to estimate the total cost of depression. Therefore, total cost of 'depression' are heavily underestimated in the present study. The ICD category 'neurotic disorders', consuming 9% of the total cost of mental disorders, includes different kinds of anxiety disorders as well as dystymia. We chose 4 disorders for further study on effectiveness of treatment and prioritisation of future cost-effectiveness analyses: schizophrenia, depression, anxiety and alcohol abuse/dependency.

Table 8. 2 Direct cost of mental disorders for the Netherlands in 1993 and health care facilities contributing to more than 20% of these costs (in millions of Dutch guilders)

Diagnosis category (ICD-9 code)	Costs	% of total costs	Health care service (% of the costs)
Dementia (290)	2146	31	Nursing homes (93%)
Schizophrenia (295)	850	12	Psychiatric Hospitals (90%)
Neurotic disorders (300)	635	9	Psychiatric hospitals (33%) Hospitals (20%)
Affective psychosis (296)	600	9	Psychiatric hospitals (61%) Hospitals (34%)
Alcohol and drugs (291,291,303-305)	418	6	Psychiatric hospitals (36%) Addiction clinics (20%) CAD's (20%)
Personality disorders (301)	383	6	Psychiatric hospitals (45%)
Other psychosis (297,298)	356	5	Psychiatric hospitals (70%)
Other depression (311) [1]	243	4	RIAGG (41%)
Adjustment problems (309)	170	2	RIAGG (35%) Psychiatric hospitals (32%)
Others	520	6	
'Not assignable'	570	8	
Total (290-316)	6890	100	Psychiatric hospitals (33%) Nursing homes (30%)

[1]Some of the costs of 'depression' were included in other diagnostic categories: neurotic disorders, affective psychosis, personality disorders and adjustment problems. A clear distinction of the costs for depression within each category proved to be impossible.

8.4.3. Costs by diagnosis and gender

For both genders the sequence of diagnostic categories by costs was quite similar. Women consumed about 60% of the total cost of mental illness. Over 40% of these costs for women were related to dementia, followed by schizophrenia 11%. For men these percentages were respectively, 22% and 17%, see table 8.3. The higher mental health care costs for women may at least partly be explained by more women reaching very high age and their related higher risk of dementia.

Table 8.3 Percentages in costs by diagnosis and gender in the Netherlands 1993

	Men	Women
Dementia	22	42
Schizophrenia	17	11
Affective psychosis	10	9
Neurotic disorders	9	10
Alcohol and drugs	11	4
Personality disorders	8	4
Other psychosis	7	5
Other depression	6	4
Adaptation problems	3	2
Others	8	12
Total	100	100

8.4.4. Costs by diagnosis and age

Although the total costs of mental disorders increased with age, this is mainly due to dementia. Dementia is the only 'expensive' diagnostic category with a clear positive relationship between

age and costs. Contrary, schizophrenia and affective psychosis are the most expensive diagnostic categories in the age group of 40-50 years. When the age group of 20-40 years is examined, the costs for neurotic disorders, personality disorders, other psychosis and adjustment problems are the highest.

8.4.5. Effectiveness studies for schizophrenia

For four disorders (schizophrenia, depression, anxiety disorders and alcohol abuse/dependency) we conducted a literature review on treatment effectiveness, and subsequently prioritised future cost-effectiveness analyses. As an example we present the results on schizophrenia.
During our literature search we discovered that recently, treatment outcome research for schizophrenia had already been thoroughly evaluated by the University of Maryland in a comprehensive review of research reviews and primary research (PORT, 1994; 1995). We therefore compared the reviews in the Maryland study with our selection. Our final results are based upon 33 meta-analyses and systematic research reviews from the Maryland study that scored high on methodological quality. We added eight other studies of high standard. For statistical meta-analyses we evaluated effect sizes, summary statistics and confidence intervals. For systematic research reviews we evaluated the methodological quality and the results. We used the treatment categories proposed in the Maryland-study. These eleven categories include pharmacological treatments, electro-convulsive therapy, psychotherapy and interventions such as community support or vocational rehabilitation.

In the meta analyses and reviews we studied, we found ample evidence for the effectiveness of pharmacotherapy. Further specification of its effect, however, remains necessary, for instance specification of effective dose ranges, patient characteristics relevant for the choice of medication, and the effect of its combination with other treatment modalities. Conventional pharmaceuticals result in a reduction of positive symptoms in the acute phase of schizophrenia and prevention of relapse in the maintenance phase, but side effects may occur and their effect on long term negative symptoms is usually absent or not very well studied. New generation

pharmacotherapies show a decrease of positive as well as negative symptoms, in the acute and in the maintenance phase of schizophrenia, and they usually have less side effects. On the other hand, their costs are higher.

Psychological and community interventions are usually applied in combination with pharmacotherapy, but they often have different treatment goals (such as independent living, general competence and coping skills, reduction of inpatient episodes, vocational rehabilitation, subjective quality of life of patient and family, social functioning, etcetera). For most of these interventions (including group therapy, family therapy, social skills training, casemanagement and other community support systems) some studies do suggest effectiveness. Study design, however, is often inadequate, and on the whole the evidence is still inconclusive. Several interventions are applied in combination, but until now research has been unable to indicate the added value of each separate element. Patient characteristics relevant for the choice of a particular (combination of) intervention(s) have hardly been identified. Findings on effectiveness studies for schizophrenia were reported in more detail elsewhere (Gageldonk, 1996). Cost of these interventions in the Netherlands were unknown.

In addition to these findings from international research we consulted thirteen opinion leaders from Dutch psychiatric practice. They were asked if they could name any interventions that were (1) regularly applied in the Netherlands but not mentioned in international research literature, and (2) might be interesting candidates for cost-effectiveness analyses (for instance because of their supposedly superior effectiveness over other interventions, or their supposedly equal effectiveness at lower cost).

8.4.6. Recommendations for cost-effectiveness analyses

Application of the prioritisation criteria on our findings resulted in eight recommendations for further cost-effectiveness studies, see table 8.4.

Table 8.4 Recommendations for further cost-effectiveness studies in schizophrenia

Recommendation	Comment
Comparison of medication effectiveness in different settings (inpatient, outpatient, nature and frequency of treatment sessions, specific measures to enhance compliance).	In most research on pharmacotherapy effectiveness, medication is varied within a given (often inpatient) setting. The relevant question is what the surplus value is of inpatient over outpatient treatment (in terms of cost and effect, given a certain type of medication); what is the surplus value of more frequent outpatient contact, or of adding special types of counselling (again: given a certain type of medication)? Patient compliance may be a relevant mediating variable to measure in such studies.
Community support systems and case management	More detailed description and measurement of the actually provided different types of care is necessary, in order to distinguish effective from ineffective components. Professional background of the care providers might be a relevant variable.
Symptom management, medication management and training in identifying prodromes (early stage symptoms preceding a relapse).	Many Dutch opinion leaders mentioned this as a high priority topic for cost-effectiveness research.
Cognitive behavioural therapy and cognitive training.	These interventions were also put forward by our opinion leaders. Maybe comparison with the interventions mentioned under 3 is relevant.
Comparison between conventional and new generation pharmacotherapy.	Cost-effectiveness research in this area should use long term follow-up measurement, and measure positive as well as negative symptoms and other relevant items (such as quality of life of patient and family).
Group therapy as compared to strictly individual approaches.	For instance cognitive behavioural therapy.
Family therapy as a supplement to care as usual.	Special attention should be paid to families from ethnic minorities.
Vocational rehabilitation as a supplement to care as usual.	Different, recently developed approaches should be compared, with special attention for patient and community variables that may predict success.

8.5. Discussion

At the start of this research project we formulated three criteria for prioritising areas for cost-effectiveness analyses in mental health care. These criteria largely fit with the criteria for cost-effectiveness research in health care programmed by the Dutch minister of health in December 1995.

In the present study we first indicated diagnostic categories having high costs in health care. In a literature study on effectiveness, supplemented with information of specialists in the relevant areas, we explored interventions which have some known (or assumed) effectiveness for the diagnosis. Finally, an overview was presented of recommendations for future cost-effectiveness analyses.

In this study we estimated costs by diagnosis, age and gender. With respect to the current purpose of the study this information may seem superfluous. However, linking these estimates to demographic and, if possible, to epidemiological data would improve our ability to predict future costs. The latter may consist of relevant information for decisions to set priorities for economic evaluation in mental health care.

Despite international diversity of health care systems, Souêtre showed that most developed countries spend about 10% of their total health care expenditures on treatment of mental disorders (Souêtre, 1994). This is in accordance with our estimate: 11%.

Schizophrenia is, after dementia, the diagnostic category bearing the highest direct costs in the Netherlands. A detailed cost of illness study on schizophrenia estimated the total direct costs NLG 776 million for the Netherlands for 1989 (Ament et al., 1993). In the present study the indirect costs for this illness were not calculated due to lack of reliable data. According to the study of Ament and Everts the indirect cost for schizophrenia, using the human capital method, were relatively low (8% of the total costs). However, these costs may be relatively high for other mental disorders. Therefore, valid estimations for the indirect costs need to be explored in future research.

The literature study of effectiveness studies was limited to meta-analyses and systematic research reviews. Although we considered our approach valid for the purpose to set priorities for future CEA's we definitely not claim to present a complete, accurate and up-to-date

overview of treatment effectiveness data. The additional information of a panel of specialist prevented that we would not take into account important and/or new inventions applied in the Netherlands relevant for future cost-effectiveness analyses which were missing on the list of interventions selected by the literature search.

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9. SOCIETAL PERSPECTIVE ON THE BURDEN OF MIGRAINE IN THE NETHERLANDS

9.1 Summary

This study presents a comprehensive overview of the burden of migraine in the Netherlands. We assessed the direct and indirect costs of this disease and the health status of patients with migraine. We developed the Health and Labour Questionnaire (HLQ) to collect data on the effect of illness on labour performance. 846 Migraine patients and 834 controls were selected from the general population. Participants completed the HLQ as well as generic health status questionnaires.

The direct costs of migraine amounted to 134 million Netherlands guilders (NLG)(USD1=NLG 1.68, October 1994). Conservative calculations of the costs of absence from work and reduced productivity at work were NLG 264 and NLG 277 million per year, respectively. Our study did not indicate household productivity losses. The baseline estimate of the total societal costs of migraine in the Netherlands was NLG 675 million per year. The assessment of health status showed considerable impairment of psychological and social functioning in migraine patients.

9.2. Introduction

Migraine is a common and disabling disease. The headaches are generally unilateral and their frequency and intensity varies considerably between patients. Nausea and vomiting may accompany the headaches. Several attempts have been made to construct a definition of migraine (Blau, 1984). For example the International Headache Society (IHS) have proposed uniform diagnostic criteria for research studies (Cephalalgia, 1988). In the present study, we selected migraine patients from the general population by using these IHS criteria as strictly as possible.

Costs-of-illness studies have been subject to major criticism (Bherens et al., 1988; Hodgson, 1988; Shiell et al., 1987 and Drummond, 1992). On the one hand, such studies highlight the economic importance of a particular disease and they can help to identify research priorities. On the other hand, without additional information on effectiveness, they do not provide information that can be used for resource allocation decisions. The results of this study should be viewed in the context of these limitations. However, cost-of-illness studies may provide useful information to assess the relevance of an economic appraisal in a certain disease area, and can be incorporated into a total economic evaluation.

In this study, we investigated the burden of migraine in the Netherlands. The economic cost of migraine were divided into direct costs and indirect costs. Direct costs represent the health service costs of patients seeking therapy. Indirect costs represent the value of production loss because patients are unable to perform paid or unpaid labour or are working less efficiently because of migraine. We developed the HLQ to measure the effect of illness on labour performance. Furthermore, we studied the extent to which the health status of migraine patients is impaired by their disease, thus presenting a comprehensive overview of the burden of migraine to society.

9.3. Methodology

9.3.1. Direct Costs

We estimated the direct costs due to migraine in The Netherlands for the year 1988. The total costs of treating migraine patients for each relevant health care sector (general practitioners, hospitals, pharmaceutical services, alternative practitioners and physiotherapists) were calculated using data on utilisation of services, extracted from representative national registries for inpatient care and large surveys for ambulatory care (van Roijen et al., 1992).

No reliable data were available for the number of hospital outpatient visits. From a pilot study in two hospitals and interviews with five neurologists, we estimated: (i) the proportion of migraine patients in the total population who visited hospital outpatient departments; and (ii) the average number of visits per patient due to migraine, to calculate these costs. The number

of visits to alternative practitioners (e.g. a homeopath) was estimated using the answers to questions added to the HLQ.

9.3.2. Indirect Costs

We developed and used a questionnaire (the HLQ) to collect data from patients on the influence of illness on labour performance.

Identification of samples

Migraine patients were selected from the general population using a screening questionnaire that was based on the IHS-criteria. Furthermore, we required patients to have had at least 1 attack during the past year. Patient selection was carried out by a Survey of a representative sample of the Dutch population aged 12 years and older.

For a period of 12 weeks between October 1992 and February 1993, 10,480 persons underwent face-to-face interviews. All respondents were asked if they were willing to participate in a second investigation. 992 Patients met the IHS-criteria and experienced a migraine attack in the last 12 months. Of those patients, 853 (86%) were prepared to participate in a second survey.

The control group was selected from the population of the first survey who were willing to participate in a second survey, but who did have migraine according to the IHS-criteria. Controls were matched by age, sex and labour force participation. Questionnaires for the second survey were sent by mail in June 1993, with two consecutive reminders.

The Health and Labour Questionnaire

The HLQ was designed to be suitable for self-assessment and is intended to measure both labour performance related to health status and productivity losses. The questionnaire included items about labour performance in both paid production and unpaid (e.g. household work) productivity in the 2 weeks before assessment.

Respondents were asked to what extent their capacity to perform labour was impaired by health problems. This question was asked separately for paid work and unpaid activities. In

patients a distinction was made between migraine and other health problems. Questions on production losses were divided into absence from work, reduced productivity at work and household productivity losses. The feasibility and validity of this instrument are discussed in chapter 4 of this thesis.

Absence from work

Respondents with paid jobs were asked to mark on which day(s) or half days of the previous 2 weeks they were absent from work because of migraine or other health problems. If the respondents were absent because of illness during the entire two weeks, they were asked to indicate the start of this episode. The mean annual number of days lost was derived by multiplying the results by 26.

The first survey also contained questions on absence from work due to migraine based on three months' recall. The answers were aggregated into seven categories (0, <= 1 day, 2 days, 3 to 4 days, 5 to 6 days, 7 to 8 days and 9 days or more). The mean number of days absence from work per year was derived by multiplying the results by 4.

The total number of working days lost for the Netherlands was derived by multiplying the mean age-and gender-specific number of work days lost due to migraine by the rates of migraine prevalence and labour force participation by age and gender (CBS, 1989; CBS, 1990). The estimated number of working days lost was valued by the average production value per worker by age and gender (CPB, 1992; CBS, 1989).

Reduced productivity at work

Reduced productivity was measured by using 3 approaches. Firstly, respondents with paid jobs were asked to indicate the number of additional hours they should have worked in the past two weeks to make up for production losses due to migraine on days when they attended work despite experiencing a migraine. This method is referred to as the HLQ-approach.

For comparison, we also added questions to determine reduced productivity using 2 methods described by Osterhaus and co-workers (Osterhaus et al., 1992). The first approach estimates reduced efficiency on the basis of the number of working days with symptoms of migraine multiplied by the estimated level of performance affected by migraine. This method is referred to as 'Osterhaus method 1'. The second approach involves multiplying the number of

attacks and the number of working hours affected by migraine by the estimated level of performance ('Osterhaus method 2'). In both methods, the level of performance was measured by a visual scale rating from 1 (maximum inefficient level of performance) to 10 (normal level of performance).

To assess the feasibility and validity of the three measurement methods we added a descriptive instrument. This consisted of six items related to problems occurring during working time because of migraine. The items, which were about the influence of migraine on concentration ability, working speed, need to be alone, decision making abilities and tendency to postpone work, may be considered indicators of efficiency. The answers on each item of the respondents are weighted as follows: 1='never'; 2= 'sometimes'; 3='often'; 4='always'. The efficiency score was obtained by summing the weighted items.

The mean annual number of hours productivity loss was calculated by multiplying these two-week estimates by 26. To extrapolate reduced productivity to the Dutch labour force we used the age- and gender specific rates of migraine prevalence and labour-force participation rates. The resulting number of work days lost is valued by the average production value by age and sex.

Household productivity

Household productivity is defined as services produced in the household, which could be produced by a third person on the market (Harwrylyshyn, 1977). Household production is split up into four productive activities; household work, shopping, care for children and miscellaneous household tasks. Each activity category was described extensively in the questionnaire. For all activities, the respondents were asked if they had performed such activities in the past two weeks. A 'Yes' answer was followed by a question about time spent and the difficulties experienced in performing these activities. A 'No' was followed by the question to what extent the nonperformance of the activity was caused by migraine or other health problems. Calculating the number of hours lost due to migraine, we compared the estimates of time spent on household activities of the migraine population with that in the control group.

9.3.3. Health Status and comorbidity

Health Status and Co-morbidity

In this study health-related quality of life is referred to as 'health status' and was measured using the EuroQol questionnaire (Essink-Bot et al., 1993). Co-morbidity was measured using a list of chronic conditions (CBS, 1991). Questions on demographic variables like age, gender and education were added.

The questionnaire for the migraine group contained an additional number of questions on the frequency of migraine attacks (to avoid misclassification) and on utilisation of alternative health services. At 20 pages, the migraine booklet was about four pages longer than the questionnaire sent to the control group.

9.3.4. Valuation

Paid labour

For paid labour, hours lost were valued by the average value added per worker by age and gender, which we assumed to be proportional to gross labour income. In general, the human capital approach is used to estimate the indirect costs. This method estimates the value of potentially lost production. However, many authors have suggested that the real production losses for society may be much smaller (Drummond, 1992; Lindgren, 1981). Here, the friction cost method, which takes into account the economic circumstances that may limit production losses due to illness, was used (Koopmanschap, 1992).

Absence from work reduce effective labour time. Studies indicated that a reduction of annual labour time causes a less than proportional decrease in labour productivity per year. The elasticity for annual labour time versus labour productivity was estimated between 0.6 and 0.9 (CPB, 1987; Koning, 1984; WRR, 1977). In this study, we used a value of 0.8.

Unpaid labour

There are no prices to indicate the value of household productivity. We used the market-alternative approach for valuing these production losses. This approach uses the assumption that a paid worker is hired to perform the unpaid jobs. The number of hours household

production lost are then multiplied by the price paid to the market equivalent worker (Harwryslyshyn, 1977).

9.4. Results

9.4.1. Response

A total of 846 questionnaire were mailed to patients with migraine. Of these, 23 were returned by postal services because they were wrongly addressed, and a further 65 questionnaires were returned by patients who claimed that they did not have migraine. Both groups were excluded from the analysis. The resulting number of potential respondents in the migraine group was therefore 758. Of this number, 479 (63%) actually returned their questionnaires. However, 43 questionnaires were returned blank, giving an overall response rate of 58%. Of the controls, 585 individuals returned their questionnaire, a response rate of 71%. This difference in response is probably partly due to the differences in the length of the questionnaire (Herberlein et al., 1978). Table 9.1 shows some characteristics of the migraine group and the controls.

Table 9.1 **Overview of characteristics of the migraine group and controls. Figures in parentheses are percentage**

Characteristics	Men		Women	
	Migraine	Control	Migraine	Control
No. of patients[a]	70 (16)	120(21)	364(84)	454(79)
Mean age (years)	38	41	41	41
Employment status[b]				
paid	52(74)	71(59)	156(44)	177(39)
unpaid	18(26)	49(41)	202(56)	275(51)

[a] No data on gender were available for 2 patients in the migraine group and 11 patients in the control group.

[b] No data on employment status were available for 8 patients in the migraine group and 13 patients in the control group.

The comparatively low percentage of men without paid work in the migraine group is due to relative high nonresponse in this category. The number of migraine attacks per year based on two weeks' recall was 26, twice as high as the number based on one year recall. We used the number of attacks based on the 2 weeks recall to estimate reduced productivity, believing these estimates be more reliable, because of the shorter recall period. Nearly half of the respondents with migraine had not had a migraine in the previous two weeks.

9.4.2. Prevalence of migraine

According to our survey, the overall prevalence of migraine in the Dutch population is 9%. In agreement with other studies, the prevalence of migraine was higher for women (12%) than for men (5%), see table 9.2 (CBS, 1991; Green, 1977; IPM, 1991a; Waters, 1973).

Table 9.2 Prevalence of migraine in the Netherlands in 1993 based on the IHS-criteria

	12-19	20-29	30-39	40-49	50-65	65+	Total
Men	8%	6%	6%	6%	3%	1%	5%
Women	10%	15%	16%	16%	11%	4%	12%

9.4.3. Direct costs

About 70% of migraine patients consulted a physician for their headaches at least once, but only half of them had done so during the previous year (IPM, 1991b). The proportion of the total number of GP consultations in a representative survey that were for migraine was used to assign costs to migraine (NIVEL, 1992). The average number of consultations per patient for migraine was 1,3 per year. The total costs for general practitioners consultations was approximately 6,8 million Dutch guilders (NLG).Corresponding figures for women and men were NLG 5.3 million and NLG 1.5 million, respectively. Hospitalisation does not play an important role in the treatment of migraine, with the mean stay being 10 days (SIG, 1990). The total costs for hospital treatment were NLG 3.7 million in 1988.

Six per cent of the patients were found to consult a neurologist because of migraine. The associated costs amounted to NLG 1.6 million, with an average of 2.5 visits per patient and a unit price of NLG 68.80 per visit (COTG, 1989). The costs of techniques used in the differential diagnosis of migraine, such as electroencephalograms and computerised axial tomography scans were NLG 2.5 million based on information from medical records. Thus, the total hospitalisation costs for migraine were NLG 7.8 million in that year. The costs of drugs for migraine was NLG 11.5 million in 1988 (IMS, 1992; Nepharma, 1989). Migraine patients are often not satisfied with the outcome of orthodox health care. We found that 17% of the migraine patients visited an alternative practitioner (e.g. homoeopathist) with an average of over eight visits per year and a unit costs of NLG 70. The associated costs were relatively high at NLG 107 million. The costs of physical therapy amounted to nearly NLG 1 million (NIVEL, 1987). Table 9.3 presents an overview of the direct costs of migraine for each health care sector in 1988 .

Table 9.3 Direct costs of migraine in millions of Dutch guilders for 1988

	Costs
General Practitioners	6.8
Hospital	7.9
Pharmaceuticals	11.5
Physiotherapy	0.9
Alternative practitioners	106.7
Total	133.7

9.4.4. Indirect costs

Absence from work

As expected, migraine causes only very short term absence from work. Consequently, the estimates of indirect costs will not vary greatly irrespective of whether the human capital or the friction cost method is applied (Koopmanschap et al., 1992).

According to the HLQ, nearly 10% of women in the migraine group reported absence from work because of migraine, varying from 0.5 day to 2.5 days in the previous two weeks. In contrast, only 2% of men reported absence from work due to migraine in the same period. Using 2-week recall values, the estimated mean number days off work per year because of migraine was 4 days for women and 1 day for men per year, see table 9.4. Using the three months' recall the average number of days of absence from work is about 4 days per year for both men and women.

Table 9.5 presents estimates of the indirect costs incurred through absence from work, on the basis of the HLQ and data collected from the first survey. The indirect costs due to absence from work according to the 2 weeks' recall, assuming an elasticity value of 0.8, amounted to NLG 48 million for men and NLG 217 million for women. For women, the value of indirect costs was largely independent of whether 3 months' or based 2 weeks' recall was used. In men, costs cost calculated using 3 months' recall were nearly five times as high as those calculated using the 2-week period. On the one hand, this difference may be due to the relative small number of men in the sample in the second survey which incorporated the

question on the 2 week method. On the other hand, answers based on a three months recall may be less reliable. Furthermore, the latter estimate was based on aggregated data. Therefore, we consider the conservative estimate based on the HLQ as the baseline estimate.

The percentage of women reporting absence from work due to health problems other than migraine in the 2 weeks before completing the HLQ was relatively high for migraine patients compared with controls (14% vs 7.5%). 35 per cent of these female migraine patients and 25% of the controls were absent because of other health problems during the entire 2 weeks before questionnaire completion. 95 per cent of the migraine patients reported 1 or more chronic conditions (excluding migraine and headache) compared with 62% of the control group. Depression and skin diseases are reported respectively 2 and 1.5 times, respectively, more often in the migraine group than in the controls, which is consistent with the finding of other studies (Von Korff et al., 1992).

According the friction cost method, the total indirect costs due to other health problems in migraine patients amounted to NLG 785 million for men and NLG 585 million for women.

Table 9.4 Average production losses in days and hours per patient per year due to migraine

	Men	Women	Total
absence from work in days (*2 weeks recall*)	1,0	3,9	3,2
absence from work in days (*3 months recall*)	4,1	4,2	4,2
reduced productivity at work in hours *	18,7	22,8	21,8
efficiency on affected days	69%	73%	72%
reduced productivity at work in days **	8,9	8,9	8,9
reduced productivity at work in hours ***	93,8	93,8	93,4

* 'HLQ-approach'= estimates the number of hours patients should have worked longer to make up for reduced productivity at work due to migraine

** 'Osterhaus method 1'= days of work affected x (100 - effectiveness)

*** 'Osterhaus method 2'= hours of work affected x number of attacks last year x (100 - effectiveness)

Reduced productivity at work

The cost of reduced efficiency at work caused by migraine vary substantially, depending on the method of estimation. Overall, 25% of the migraine patients reported that they should have worked longer to make up for reduced productivity at work during migraine episodes. According to this HLQ-approach, reduced productivity was responsible for an average production loss per year of nearly 19 hours for men and 23 hours for women (see table 9.4). The total costs amounted to NLG 277 million per year (NLG 115 million for men and NLG

162 million for women)(table 9.5). For men, the costs due to reduced productivity were more than double the costs incurred by absence from work calculated from 2 weeks' recall. This may indicate a trade-off between absence and reduced efficiency for men. For women, the costs of absence from work were higher than the costs of reduced productivity. On average when a migraine was experienced, men were 69% productive and women were 73% productive (mean values), which could also indicate a more substantial trade-off between absence and reduced productivity at work for men.

Table 9.5 Indirect costs due to migraine (in millions of guilders)

	men	women	total
absence from work (2 weeks recall)	48	217	264
absence from work (3 months recall)	235	237	473
reduced productivity at work*	115	162	277
reduced productivity at work**	420	548	968
reduced productivity*** at work	590	865	1455

* 'HLQ-approach'= estimates the number of hours patients should have worked longer to make up for reduced productivity at work due to migraine

** 'Osterhaus method 1'= days of work affected x (100 - effectiveness)

*** 'Osterhaus method 2'= hours of work affected x number of attacks last year x (100 - effectiveness)

According to Osterhaus method 1, the number of days of reduced productivity was about 9 days per year per patient. Using the Osterhaus method 2 the estimated number of hours lost due to reduced productivity was over 93 working hours per year per patient. The estimated costs according to these two approaches were about 4 to 5 times higher as compared to the H&L-approach (table 9.5).

We compared the results for each of the 3 methods to investigate their feasibility and validity. In the H&L approach, 13% of the respondents were not able to estimate the number of hours they would need to work to make up for reduced productivity. For the Osterhaus method 1 and 2, 10.3% and 17.3% of the data needed were missing, respectively. Using Pearson's correlation, we found that there was little correlation between the answers obtained using the H&L-approach and the estimates based on the two Osterhaus-methods 1 and 2 ($r=0.37$ and $r=0.33$ respectively). Moreover, low correlation was found between estimates according to each of the methods and total sum scores on the 6 items related to problems during working time because of migraine ($r=0.18$; $r=0.34$; $r=0.16$).

Unpaid production

Previous research indicated that time spent on household production strongly depends on age, gender, employment status and household composition (van Roijen et al., 1994). Our results agree with these findings. We found that having a paid job reduced time spent on household productivity, except for men in the control group, while children increased time spent on these activities (see table 9.6). However, we found no significant differences in time spent on household production between migraine patients and the controls.

Table 9.6 **Time spent on household production (in hours per week) for migraine patients and the controls, according to employment status and household composition**

household composition	paid work		no paid work	
	migraine	controls	migraine	controls
With children				
Men	24	21	27	16
Women	37	41	53	59
Without children				
Men	17	16	21	15
Women	19	19	32	30

9.4.5. Health Status

The results of the EuroQol descriptive questionnaire are shown in table 9.7. Testing for statistical significance on mean score per dimension (using the Mann-Whitney-U test) showed that there were significant ($p<0.01$) differences between migraine patients and controls for usual activities, pain/discomfort and anxiety/depression. Migraine patients scored consistently worse than the controls.

Valuation of own health state, measuring using a visual analogue scale from 0 (worse imaginable health state) to 100 (best imaginable health state) was 77 for migraine patients and 83 for controls ($p<0.001$).

An interesting feature of the EuroQol instrument is the existence of a set of values on health states from a representative sample of the general population. If these societal values are attached to the results of the EuroQol descriptions of the study group, this results in mean values of 69 and 72 for migraine patients and controls, respectively ($p<0.001$).

Table 9.7 **EuroQol-description Migraine group (n=436) and Control group (n=575)**

	migraine	control	MWU (p-values)
Mobility*: X (sd)	1.18 (0.40)	1.13 (0.34)	.048
no problems (%)	83.0	87.4	
some problems (%)	16.3	12.4	
confined to bed (%)	0.7	0.2	
Self-care*: X (sd)	1.03 (0.17)	1.02 (0.14)	.386
no problems (%)	97.2	98.0	
some problems (%)	2.8	2.0	
unable to (%)	0	0	
Usual activities*: X (sd)	1.29 (0.48)	1.19 (0.44)	<.001
no problems (%)	72.4	83.3	
some problems (%)	26.4	14.8	
unable to (%)	1.2	1.9	
Pain/discomfort*: X (sd)	1.54 (0.57)	1.34 (0.50)	<.001
none (%)	49.5	67.4	
some (%)	46.6	31.2	
extreme (%)	3.9	1.4	
Anxiety/depression*: X (sd)	1.29 (0.51)	1.16 (0.39)	<.001
none (%)	73.0	85.3	
some (%)	24.6	13.7	
extreme (%)	2.5	1.1	
Valuation own health (0-100): X (sd)	76.7 (17.4)	82.9 (15.0)	<.001
Valuation general population (0-100): X (sd)	68.9 (10.3)	71.6 (9.6)	<.001

* 1=optimal level, 3=worst level

9.5. Discussion

Information produced by cost of illness studies is of limited value in health care decision making. A step forward should be the evaluation of the costs and effects of a new drug for migraine compared to the current standard therapy.

In our study, the costs of alternative practitioners were responsible for a considerable part of the direct costs (80%). Previous research, based on incomplete secondary data, indicates these costs form an important share of the total direct costs (van Roijen et al., 1993).

Preliminary results indicate that, judging by the small number of patient who did not respond either to individual items or the entire questionnaire, the questionnaire was well understood by patients. Estimates of the number of non-disease specific absences from work were in accordance with national data. Except for child care, the HLQ is suitable for assessing time lost on unpaid labour.

The number of days of absence from work due to migraine measured using the HLQ was lower than that calculated on the basis of 3 months' recall, especially for men. On the one hand, we believe that recall over a 2 weeks period is more reliable than that over 3 months. Moreover, the latter was based on aggregated data. On the other hand, there was only a small number of men in the sample in the second survey, which increases uncertainty. However, the H&L-questionnaire results are in accordance with other studies from Sweden and the U.K (Björk et al., 1991; Cull et al., 1993), showing similarities in the absolute numbers lost per year and in the differences between men and women. In the U.K study the number of days of absence from work due to migraine was 1.6 for men and 3.6 for women (Cull et al., 1993). Thus, our conservative estimate based on the H&L-questionnaire may be the most realistic estimate of the costs due to absence from work.

The feasibility of the instrument used to measure reduced productivity, as indicated by the number of missings, favoured for the HLQ-approach and the Osterhaus method 1.

The HLQ-approach and both Osterhaus methods claim to measure reduced productivity, but the assessment on validity did not yield promising results. Apart from the differences in the absolute level of reduced productivity calculated using 3 methods, statistical tests revealed low correlation between the results. Moreover, we found that there was low correlation between the total scores on 6 items indicating the level of efficiency at work during a

migraine and the results of the 3 instruments. Since there is no 'gold standard', further research is necessary in which the output can be measured objectively.

In the HLQ-approach, the respondents were asked to quantify the number of hours needed to make up for reduced efficiency. The methods used by Osterhaus et al. estimate these number of days or hours in a more indirect way, combining answers on labour performance. This increases the potential for inconsistencies and mistakes.

Estimates of indirect costs were lower using Osterhaus method 1 compared with method 2. The latter method implicitly assumes that all attacks occur during working hours, which is not always the case. Thus, this method will overestimate these costs.

No losses in unpaid productivity due to migraine were observed. On the one hand, migraine may not cause unpaid production losses. On the other hand this result may be due to the method of time measuring used. Juster and Stafford found that respondents appear to remember days when an activity was especially prominent and treat this day as an average day (Juster et al., 1991). In addition, our method is probably too unrefined to measure small differences in time spent. Should migraine cause relative small losses for unpaid production then the diary method is more appropriate for measuring these losses. Finally, patients may substitute leisure and time spent on household production or postpone non-urgent activities, while migraine is not a chronic condition. The data did not allow us to analyse this hypothesis.

9.6. Conclusion

The direct costs of migraine amounted to 134 million Dutch guilders, only 0,3% of total health care costs in 1988. Alternative practitioners were responsible for about 80% of these costs, because migraine patients often seek therapy outside established health care. Indirect costs due to migraine were high compared to direct costs. Costs due to absence from work were about two times as high, 264 million Dutch guilders. Our conservative estimate of the costs due to reduced productivity amounted to 277 million Dutch guilders. In conclusion, our baseline estimate of the total costs due to migraine is 675 million Dutch guilders per year. This estimate can be considered conservative, because higher estimates of the costs of reduced productivity were obtained by techniques other than the HLQ. Thus, the costs due to reduced productivity are important with respect to migraine and probably other diseases. Additional research is required to validate the measurements approaches.

Our study did not indicate household production losses due to migraine. The assessment of health status showed consistently a considerable impairment for psychological and social functioning of migraine patients in comparison with controls. Given the relative importance of indirect costs, economic appraisals from a societal perspective of medical interventions for migraine should focus on the possible reduction of production losses due to migraine.

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10. COST AND EFFECTS OF MICROSURGERY VERSUS RADIOSURGERY IN TREATING ACOUSTICUS NEURINOMA

10.1. Summary

This study analyses cost and effects of treating acousticus neurinoma patients by using microsurgery compared to radiosurgery. Radiosurgery is the stereotactic application of radiotherapy and an innovative medical technology. Cost and effects estimates of the conventional treatment were based on a retrospective study in the Netherlands. Similar data for a comparable group of patients in Sweden were collected for radiosurgery, as this treatment option is currently not available in the Netherlands.

Fifty-three acoustic neurinoma patients who had been operated on the University Hospital Rotterdam between November 1990 and January 1995 were included. This group was compared with 92 acoustic neurinoma patients treated with radiosurgery (Gamma Knife, Stockholm, Sweden) in the same period. Data on health care use were collected from patient files. To obtain data on production losses and quality of life, a questionnaire was sent by mail in February 1995. This booklet consists of the Health and Labour Questionnaire (HLQ), the Short Form-36 and the EuroQol.

The response rate was 92%. The direct costs for microsurgery amounted to NLG 20,072 and for radiosurgery to NLG 14,272 per patient. The indirect costs were respectively NLG 16,400 and NLG 1,020. General health rating was better for radiosurgery than for microsurgery. On the whole differences in long term clinical outcomes between the two patient groups were small. Assuming a reasonable occupancy of the expensive radiosurgery equipment we demonstrated that for the short term treating patients with an extra-meatal tumour diameter of the acoustic neurinoma less than three centimetres with radiosurgery is more cost-effective than microsurgery.

10.2. Introduction

Radiosurgery comprises the stereotactic application of radiotherapy and is regarded as an innovative medical technology. It is a treatment method in which a small target volume in the patient's body is localised with great accuracy and subsequently irradiated using a single high dose of ionising radiation. Current indications for radiosurgery include, among others, arteriovenous malformations, brain metastases and benign skull base tumours (e.g. acoustic neurinoma, meningiomas). Conventional surgery consists of craniotomy with surgical resection of the lesion. From the side of the Dutch government and the neurosurgeons there is a growing demand for an cost-effectiveness analysis in order to evaluate these two treatment modalities.

Pollock and co-workers were the first to compare the results of microsurgery and radiosurgery (Pollock et al., 1995). Stereotactic radiosurgery proved to be an effective and less costly treatment of unilateral neurinomas less than 3 cm in diameter. However, their study has some limitations. First, patients were treated with radiosurgery or microsurgery according to patients' preference, which reduces the comparability of the two groups. Second, the evaluation of the costs was limited to length of hospital stay, management charges and effect on employment status. Third, only patient satisfaction was measured to capture the patients' perspective. In the present study we also have chosen the acoustic neurinoma as an example for an evaluation. Consecutive series of eligible patients were studied. Cost and effects estimates of the conventional treatment were based on a retrospective study in the Netherlands. Similar data for a comparable of patient group in Sweden were collected for radiosurgery, as this treatment option is currently not available in the Netherlands. We calculated total direct and indirect costs. Instead of 'patients' satisfaction', we measured quality of life by generic standardised instruments. Quality of Life constitutes the common denominator from the patients' perspective, when comparing two entirely different treatment modalities. Additionally, some relevant clinical outcomes are presented.

In short, we present a comparison of costs and effects of treating acoustic neurinoma patients with microsurgery versus radiosurgery, as if radiosurgery was implemented in the

Netherlands (hence: for costs, Swedish volumes are multiplied by Dutch prices). As all parameters and assumptions are stated explicitly, our study provides a framework for making similar comparisons for other countries.

10.3. Methodology

10.3.1. Identification of samples

Radiosurgery refers to closed-skull single dose irradiation of an intracranial target with 1 millimetre precision. Since 1968, radiosurgery is performed using a Gamma Knife in the Karolinska Hospital in Stockholm. In the present paper radiosurgery by using a Gamma Knife will be referred to as 'radiosurgery'. For the comparison with conventional surgery, the diameter of target should not exceed 30 mm. Analysing conventional therapy we used data from the University Hospital Rotterdam. Costs and effects were studied retrospectively over a period of 4 years. This design was chosen because a prospective randomised study would take too long to complete. Fifty-three acoustic neurinoma patients who had been operated in the University Hospital Rotterdam between November 1991 and February 1995 were included. The Dutch patient group was compared with a group of 92 Swedish acoustic neurinoma patients treated with radiosurgery in the same period with similar age and sex composition and comorbidity, who met the same medical criteria (unilateral tumour, extra meatal diameter less than 30 mm, no prior treatment).

We analysed costs from the day of either micro or radio-surgery. The pre-treatment period is not considered because no major differences in costs are to be expected for diagnostic procedures.

The total booklet contained a questionnaire for collecting data on production losses due to illness, the Health and Labour Questionnaire (HLQ), general health status instruments and a standard set of socio-demographic questions on age, sex, education and employment status. Comorbidity was assessed by a standard list of 27 chronic conditions (CBS, 1991). For the both study groups patient questionnaires were sent by mail in February 1995, with reminders

after two weeks. In case patients did not respond after the reminder, patient were approached by phone.

10.3.2. Direct Costs

Direct costs represent the costs as a consequence of the surgical operation or radiosurgery session, hospital days, radiological procedures, laboratory tests, medication and outpatient visits (after treatment). In order to collect these data on health care use from patient files, registry-forms were developed, which were identical for Rotterdam and Stockholm.

For both treatments, the costs were calculated by multiplying the volumes by Dutch prices of 1995. The average costs presented are based on the average follow-up time, which was similar for both groups. Estimating the costs for diagnostic procedures and laboratory tests tariffs were used in case they reflect the cost price. Unit prices were calculated for the radiosurgery session, operation, hospital days and outpatient visits. Labour costs and capital cost for treatment with radiosurgery and the operation were calculated separately. Based on observations of the treatment process and the microsurgical operation we estimated the intensity of different types of labour, in terms of fraction of the session/operation time. Estimating the capital costs we calculated annuities per year, using an interest rate of 5%. A life span of 12 years was assumed for the Gamma Knife. For the modification of the building a life-span of 15 years was assumed, because the total life span of the building is estimated 50 years while the University Hospital Rotterdam has existed for about 35 years. Cobalt resources have to be replaced after 7 years. We allocated the capital costs to cases assuming that an average number of 200 patients per year, including all diagnoses, is treated with radiosurgery. Based on the percentage of costs of non-medical staff, education and general hospital services in the total costs of the department of neurosurgery, 'overhead' costs were calculated as 40% of the costs per session. Labour costs are based on the average gross earnings for employees in university hospitals for 1995.

Due to important differences in resource use between normal and intensive care hospital days, unit prices for both kinds of hospital days were calculated.

10.3.3. Indirect Costs

Indirect costs are the value of production loss because patients are unable to perform paid or unpaid work. For the valuation of the production loss of paid labour we used the average production value per working person for the Netherlands. Studies indicate that a reduction of annual labour time causes less than proportional decrease in labour productivity per year (CPB, 1987; Koning et al., 1984). We assumed this elasticity to be 0.8.

In order to collect data on production loss between the two treatment groups the HLQ was applied (van Roijen et al., 1995). The HLQ enables to estimate production losses of paid and unpaid labour and the ability to work as an indicator of health status. The complete HLQ consists of four modules (absence from work, reduced productivity at work, unpaid production and trouble experience with paid and unpaid work)(van Roijen et al., 1995). In view of this study population we applied the first, third and fourth module. According to module 1 respondents with paid jobs were asked to mark on a bar for each (half) day(s) of the two weeks preceding the assessment, whether they performed their work or were absent due to health problems or to other reasons (e.g. weekend, off days). Module 3 concerned unpaid production like household work, shopping, care for children and jobs around the house (like gardening). We asked whether household tasks normally done by the patient were taken over by other family members, neighbours and/or paid help. In module 4 of the HLQ subjects having a paid job were requested to indicate the impediments experienced while performing their job. The response categories are as follows: 'no impediment', 'some impediment' and 'a lot of impediment'. The item scores are 0,1 and 2 respectively. So, the impediment score range from 0 to 2. Consequently, a higher score means more impediment.

10.3.4. Health status instruments

We assessed health related quality of life by using non-disease specific standard questionnaires. These instruments measure basic values (physical, psychological and social functioning) which are relevant for everyone's health status (Ware et al., 1992). A

combination of two generic questionnaires, The Medical Outcomes Study 36-item Short Form-36 (SF-36) and the EuroQol (descriptive instrument and the thermometer) were applied to investigate whether differences between patients treated by radiosurgery and conventional surgery were consistent if measured by different instruments (Essink-Bot et al., 1993; Ware et al., 1992). The SF-36 consists of 36 items, assigned to the domains of physical functioning, social functioning, role limitations, mental health, vitality, pain, general health perceptions and health change. The EuroQol classification consists of five items (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each following the general form: no problems - some problems - extreme problems. In addition, evaluation of perceived health is assessed with a visual analogue scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).

10.3.5. Statistics

Standard statistical techniques were used. Multiple linear regression analyses were applied to compare quality of life outcomes, corrected for age, sex, comorbidity and educational level.

10.4. Results

10.4.1. Response

Fifty three questionnaires were mailed to the patients treated by microsurgery; 49 patients (92%) responded. Ninety-two patients treated by radiosurgery were requested to participate in the study. In Sweden the overall response rate was also 92% (90 patients).

10.4.2. Patient Characteristics

In table 10.1 patient characteristics are shown. Characteristics reflect the patients' status at study entry (follow-up time for both groups is similar). In the radiosurgery group educational level is higher than in the microsurgery group (median level 4 versus 3, $p<0.001$). Yet, some caution is warranted in comparing school systems in two countries.

Total number of reported comorbidities from a standard list of 27 most prevalent diseases and illnesses was not different. However, the radiosurgery group reported more 'serious heart disease or myocardial infarction' (14% versus 2% for microsurgery $p< 0.02$) and 'arthritis (reuma) of hands or feet' (17% versus 4% for microsurgery$p<0.01$).

Table 10.1 Patient characteristics at study entry

	Microsurgery	Radiosurgery
n	53	92
Follow-up; month (median, min-max)	24 (1-53)	24 (0.5-75)
Age; yr (mean; SD)	52 (11)	55 (14)
Sex; % male	51%	34%
Tumour diameter		
< 15 mm	52%	53%
15-30mm	48%	47%
Comorbidity		
0 - 1	51%	57%
2 - 4	43%	29%
>5	6%	13%
Educational level; median (range 1-7)	3	4
Paid work	53%	47%

10.4.3. Direct costs

Table 10.2 presents the average number and costs of the most relevant medical procedures per patient. According to the anaesthesia reports the average duration of the micro-surgical operation was 7 hours and 24 minutes. Given this duration and labour intensiveness, the average costs of the operation were over NLG 7,700 In case of treatment with radiosurgery the average duration was 7 hours, of which over 5 hours for application of the stereotactic frame, to carry out an MRI and dose planning. Table 10.2 shows the intensiveness of different types of labour in terms of their fraction of total treatment time.

The investment costs of the radiosurgery equipment amounted to 6.7 million guilders, modification of the building 3 million guilders and the replacement of the cobalt resources almost NLG 700,000. The annual costs per patient are based on 200 treatments per year, which may be considered as the base scenario. For radiosurgery nearly 70% of the direct costs were attributed to the costs of the session with the Gamma knife.

The average length of total hospital stay from the day of surgery of patients treated by microsurgery is 13 days, nearly 11 days of normal care and over 2 days of intensive care. 65% of the patients treated by radiosurgery required hospitalisation. The total length of stay varied from 1 to 5 days. The total average length of stay was 1.6 days, 1.1 days before treatment and 0.5 days after treatment. The costs of a normal hospital day on the neurosurgical department amounted to NLG 530 per day and to NLG 1,426 for intensive care. So, the mean costs for hospitalisation from the day of the treatment were nearly nine-thousand guilders per patient treated by microsurgery compared to only NLG 265 for radiosurgery, see table 10.2.

The number of post-operative MRI- and CT-scans were on average higher in the Gamma Knife group compared to the patients treated with microsurgery, see table 10.2. The total costs of outpatient visits were over NLG 700 for the microsurgery group. We assumed on average 4 outpatient visits for the Gamma Knife group. In the Dutch patient group the average costs of laboratory tests amounted to NLG 900 after the operation.

Table 10.2 **Average number of the most important procedures and costs (in Dutch guilders, 1995) per acoustic neurinoma patient from day of operation or treatment radiosurgery**

	Microsurgery		Radiosurgery	
	Number	Costs	Number	Costs
Hospitalisation				
(duration in days)				
Normal care	10.5	5,554	05	265
Intensive care	2.4	3,387		
Scans				
MRI-scan	0.3	275	1.5	1,683
CT-scan	1.2	376	2.0	705
Microsurgical operation/treament				
Capital costs[1]				5,652
Labour costs[2]		2,857		1,387
Overhead[3]		4,860		2,812
Outpatient visits	4	712	4	728
Other[4]		2,052		1,050
Total		20,072		14,272

1. Capital costs calculation is based on 200 treatments per year, see also table 10.6.
2. Labour intensiveness

(in fraction of total operation/treatment time)	Microsurgery	Radiosurgery
neurosurgeon	1	1
neurosurgeon ass.	1	-
aneasthesist	0.5	-
anaesthesia nurse	1	-
nurse	2	1.5
ENT physician	0.5	-
physicist	-	0.4
x-ray specialist	-	0.2

3. With respect to microsurgery 'overhead' consists of costs of the operation room and indirect costs. For Gamma Knife 'overhead' (non medical staff, education and general hospital services) is 40% of the costs per session.
4. Including costs of visits to eye specialist and ENT physician, medication and laboratory tests

10.4.4. Indirect costs

The Dutch patients with paid jobs were absent from work until 3 months after surgery. Patients treated by radiosurgery were on average absent from work for one working week after treatment. The average indirect costs per patient with paid work in the microsurgery group amounted to NLG 16,400. In the group who underwent radiosurgery these costs were only NLG 1,020.

Four of the patients in the surgical group recorded that they were not able to return to their job due to consequences related to the operation. This is equal to 17% of the patients with a paid job in this treatment group. Only one person in the radiosurgery group reported he was incapacitated due to the consequences of the treatment of the acoustic neurinoma, which is equal to 2% of the study population with paid work. For individuals with paid jobs the average impediment score was 0.55 for the group receiving surgery and 0.11 for those treated with radiosurgery.

Table 10.3 Average number of days and costs (in Dutch guilders, 1995) due to absence from work, number of incapacitated persons and impediment score for paid work due to treatment of acoustic neurinoma

	Microsurgery	Radiosurgery
Absence of work (in number of days)	60	5
Indirect costs (in NLG)	16,400	1,020
Number of incapicitated persons (in % of paid workers)	4 (17%)	1 (2%)
Impediment score (SD)	0.55 (0.65)	0.11 (0.32)

We asked whether household tasks, normally performed by the respondent, were postponed or taken over by other members of the household, family or friends and/or paid workers. In the patient group treated with microsurgery 27% indicated that tasks were taken over, mainly by family members, compared to 13% in the group treated with radiosurgery, see table 10.4.

Table 10.4 Patients performance of household production due to treatment of acoustic neurinoma

	No. of patients Microsurgery	No. of patients Radiosurgery
Self-performing	73%	87%
Family members	21%	10%
Others	3%	1%
Alpha	3%	1%
Home-help	5%	1%
Other paid help	5%	0%

10.4.5. Total costs

Total costs (direct and indirect costs) for microsurgery amounted to NLG 36,472 and for radiosurgery to NLG 15,292. The fact that the total costs for microsurgery were over two times higher than for radiosurgery, was mainly due to the difference in the number of days of hospitalisation and the substantial discrepancy in indirect cost. The direct costs dominate in both treatments, but to a much larger extent for radiosurgery.

10.4.6. Health related quality of life

General health rating was better for radiosurgery (excellent 16%, (very) good 65%, poor or fair 19%) than for microsurgery (excellent 4%, (very) good 65%, poor or fair 30%, $p < 0.01$). In Figure 10.1 SF-36 scores are presented. For 5 out of 8 domains no significant

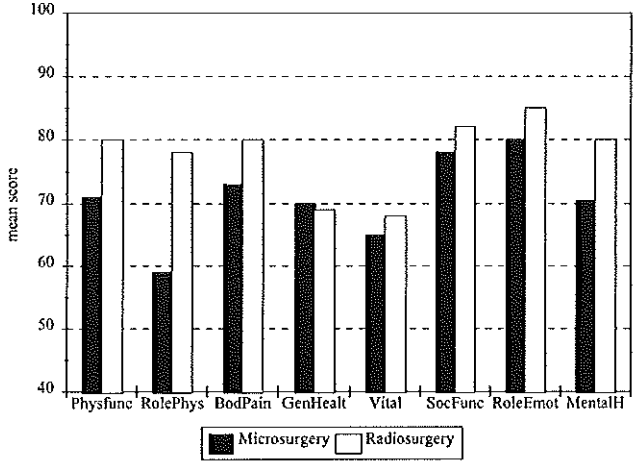
differences were found. The radiosurgery group had significantly higher scores, indicating better health related quality of life, than the microsurgery group for the domains physical functioning (eg. walking, climbing, vigorous activities), role physical (eg. performing work/activities), and mental health (happiness, nervousness, mood). Though statistically significant, the differences were moderate: within 0.5 SD difference.

Also when measured with the EuroQol, the radiosurgery group scored higher than the microsurgery group. Mean (SD) weighted EuroQol-score 0.89 (0.15) for radiosurgery versus 0.77 (0.18; $p<0.01$) for microsurgery, also a difference around 0.5 SD.

These results are consistent when analysing these data per period, with the categories <1 year, 1-2 years, and 2-4 years past treatment. No trend in time was found for either group. All differences remained significant and of similar magnitude, when corrected for age, sex, comorbidity and educational level.

Regardless the instrument used, the Radiosurgery group has significant higher health related quality of life than the microsurgery group.

Figure 10.1. Quality of life after microsurgery and radiosurgery



10.4.7. Clinical Outcomes

In table 10.5 some relevant short and long term clinical outcomes are shown. Short term outcomes in the microsurgery group reflect the typically surgery-associated complications, such as meningitis and hospital-associated complications, e.g. urinary and respiratory tract infection. These were absent in case of radiosurgery. Facial and trigeminal nerve function were dichotomised in 'affected' or 'not-affected'. Hydrocephalus and liquor cyst where scored as a complication in case of post-operative repair.

On the whole long term clinical outcomes between the two patient groups were comparable. However, facial nerve paralysis may be less frequent after radiosurgery than after micrsurgery.

Table 10.5 Clinical Outcomes

	Microsurgery	Radiosurgery
Short term outcomes		
meningitis	6,5%	0%
hydrocephalus	7,0%	0%
liquor cyst	4,8%	0%
urinary infection	3,0%	0%
respiratory infection	2,0%	0%
Long term outcomes		
N. VII; % affected	10,0%	2%
N. V; % affected	0%	0%

10.4.8. Sensitivity analyses direct cost estimates

In the base scenario we assumed 200 treatments per year for radiosurgery. Table 10.6 shows the direct costs per patient treated by radiosurgery at different occupancy rates. As in the base scenario we assumed an interest rate of 5%, a life span of 12 years for the Gamma Knife, and of 15 years for modifying the building, and a replacement of cobalt resources after 7 years.

Table 10.6 Capital costs per patient for treatment with radiosurgery assuming different utilization rates (in Dutch Guilders, 1995)

Number of treatments per year	100	200	300	400
Gamma Knife	7,542	3,771	2,514	1,885
Cobalt resource	1,062	531	354	266
Building modification	2,700	1,350	900	675
Total capital costs	11,304	5,652	3,768	2,826

A scenario of 100 treatments, including all diagnoses, would produce an average of NLG 21,850 per patient, which is slightly above the level of the costs for microsurgery. The total direct costs would decline to NLG 11,746 per treatment if 300 treatments per year are assumed. The total average direct costs would be reduced by nearly NLG 10,000 per patient if the occupancy rate would be increased to 400 treatments per year. As expected here, substantial economics of scale can be demonstrated.

10.5. Discussion

Assuming a reasonable occupancy rate of the expensive radiosurgery equipment we demonstrated that for the short term (up to 4 years) treating patients with an extra-meatal tumour diameter of the acoustic neurinoma less than 3 centimetres with radiosurgery was more cost-effective than microsurgery.

The goal of microsurgery is radical tumour removal and the goal of radiosurgery is arrest of tumour growth. A strictly clinical comparison, e.g. post-operative tumour diameter, is therefore not relevant, since microsurgery would be more favourable by definition. The study of Pollock indicates that radiosurgery can achieve long-term growth control and may, therefore, be considered as at least equivalent to cure (Pollock et al., 1995). The follow-up period of our study, four years, is too short to allow a definite conclusion regarding the efficacy of the radiosurgical treatment. Moreover, since 1988 the radiation dose of the gamma-knife unit at the Karolinska Hospital has been decreased in order to reduce morbidity, but the effect on long-term tumour control needs a longer follow-up period in view of the slowly progressive natural growth of the tumour.

From the patients' point of view also the short-term health related quality of life is important. Figure 10.2 shows the predicted time profile of health related quality of life up to 10 years after both micro- or radiosurgery. According to Noren et al. radiosurgery will succeed in tumour control. So, health related quality of life is expected to remain constant. However, in a subsample part of the patients treated with Gamma Knife tumour control may not be achieved, indicated as tumour growth: this will presumably lead to a decrease of health related quality of life. For the short term, up to 4 years, quality of life of patients is on average lower for the operated patients compared to patients treated with radiosurgery. Study indicated that tumour recurrence after complete resection will be between 0% and 9% (Pollock et al., 1995). In case of recurrence of the tumour, health related quality of life will decrease in time, see figure 10.2.

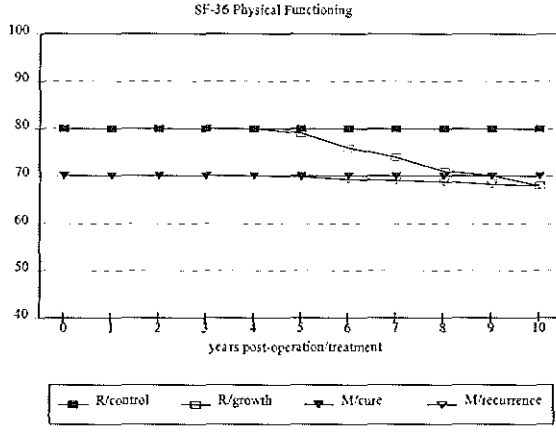
To preserve comparability of the study groups, differences in socio-demographic factors and comorbidity were controlled for in the analysis of quality of life.

Other studies support the reproducibility and the comparability of the scale score interpretations of the SF-36 in Sweden, the United Kingdom and the United States. The pattern of predictive relationships between the seven SF-36 scales and the General Health Scale was consistent across these three countries and demonstrated the importance of the SF-36 health concepts in explaining variations in personal health evaluations. Findings to data from the Netherlands indicate the same for the Dutch version of the SF-36 (Ware et al., 1995).

The average costs per patient treated by radiosurgery depend to a large extent on the number of treatments per year. In our base scenario the total number of treatments was 200 per year. According to a report of the Dutch Health Council, accepted indications for radiosurgery include, acoustic neurinoma and arteriovenous malformations (National Health Council, 1994). So, it is reasonable to assume that the number of treatments will exceed the base estimate of 200 per year, also in case a single center for radiosurgical treatment for the Netherlands would be erected.

Absence from work and incapacity for work are influenced by the social security system of a country (van Roijen et al., 1995). Study indicated that the highest level in absence from work rates occur in countries with more liberal criteria and procedures for entitlement. There are no major differences in the social security system in case of absence from work between the two countries. However, with respect to incapacity for work the social security system differs between the Netherlands and Sweden. Both the level and the length of the period of receiving incapacity for work benefits are relatively attractive in the Netherlands. As a consequence, an incapacity for work benefit is often preferred to an unemployment benefit. The Swedish government pursues an active policy against incapacity for work, towards preventive arrangements as substitutes. So, this difference in social security system may have increased the number of incapacitated in the Dutch patient group compared to the Swedish.

Figure 10.2. Conceptual time profiles of health related quality of life up to 10 years after microsurgery and radiosurgery



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11. CONCLUSION

This final chapter presents the conclusions that may be drawn with respect to the key objectives stated in the introduction of this thesis.

- Indicating the relevance of general and specific cost-of-illness studies for health policy.
- Discussing the comparability of the results of cost-of-illness studies.
- Presenting the contents, operational design and validation of the Health and Labour Questionnaire (HLQ).
- Demonstrating the application of the HLQ in cost-of-illness and cost-effectiveness studies.

11.1. Health policy

There is a growing tension between rising demand for health care on the one hand and political pressure to contain cost of health care on the other. The government is therefore in search of instruments able to both lower the cost of health care and increase efficiency in the health care system. Economic evaluations provide insight into the cost and effectiveness of new or established health care programmes. While cost-of-illness studies are not a full economic evaluation, they may nevertheless be useful for health policy. Firstly, cost of illness is a step in the process of setting priorities for topics to be studied in cost-effectiveness studies. Secondly, projections of cost of illness based on demographic, epidemiological and/or technological trends can produce estimates of future costs. Thirdly, comparisons of estimates of cost of illness in time can provide insight into the cost consequences of demographic, epidemiological and price developments and other reasons. International comparisons of the cost of illness may contribute towards a global understanding of the effects of differences between health care systems, health policies, epidemiology and social insurance systems on cost. Finally, a cost-of-illness study is a first step towards a comprehensive health policy model able to gain greater insight of the relationship between public health and the cost of disease.

11.1.1. Priority-setting

Cost-of-illness studies may provide a first step in the selection of research areas for cost effectiveness analyses. However, information on cost needs to be linked with additional information on the effectiveness of the interventions for the particular disorder. The research on mental illness (chapter 7) illustrated the prioritization process. The selection of diagnostic categories for further analysis was, in the first instance, based on a cost criterion (schizophrenia, depression, anxiety disorders and alcohol-related disorders). Next, a literature review on treatment effectiveness of possibly competing treatments for the selected diagnostic categories was conducted. We systematically gathered and evaluated the characteristics and outcomes of the studies. In addition a panel of opinion leaders from Dutch psychiatric practice was asked to name interventions that were regularly applied in the Netherlands but not yet mentioned in international research literature, and which might be interesting candidates for cost-effectiveness analyses. From the literature review and supplementary information from the panel we were able to distinguish eleven types of treatments.

For prioritisation of cost-effectiveness analyses the following requirements were set:

- The interventions should have some demonstrated effectiveness for the particular disorder and;
- It is uncertain whether the therapy has a superior effect for equal cost compared with other therapies, or an equal effect for less cost than its alternative.

Application of these prioritisation criteria resulted in eight recommendations for categories of interventions to be considered in cost-effectiveness studies for schizophrenia:

1. Comparison of medication effectiveness in different settings (inpatient, outpatient, nature and frequency of treatment sessions, specific measures to enhance compliance);
2. Community support systems and case management;
3. Symptom management, medication management and training in identifying prodromes (early stage symptoms preceding a relapse);
4. Cognitive behavioural therapy and cognitive training;
5. Comparison between conventional and new generation pharmacotherapy;

6. Group therapy as compared to strictly individual approaches (for instance cognitive behavioural therapy);
7. Family therapy as a supplement to usual care;
8. Vocational rehabilitation as a supplement to usual care

11.1.2. Future costs

Information on the expected cost of illness is one of the tools for planning future provision of health care. Cost-of-illness studies may be used to estimate future costs for demographic, epidemiological and technological scenarios. However, projections of costs based on epidemiological and technological projections are exceptional, as they require knowledge of the future epidemiological development and treatment of the disease. In chapter 2 the total direct costs of 48 diagnostic categories by age and gender were estimated for 1988. A substantial part of health care costs was due to chronic diseases, e.g. mental disorders (20%) and cardiovascular diseases (9%). These cost estimates for 1988 were used as input for future cost projections in 2030, based on demographic developments. According to the projection, the total costs increased by one percentage point per year during 1988-2030. The demographic projection indicated that costs will rise substantially for dementia, followed by cardiovascular disease. The diagnosis groups with the highest cost index were related to illnesses that generally take hold in later life. The cost projections for these elderly conditions may be given with considerable degree of certainty. Demographic projections for older age groups are more reliable than those for younger age-sets. Furthermore, illnesses at old age involve far more care, a factor that makes cost reductions rather improbable.

Adding epidemiological scenarios to the cost projections enhances the validity of future cost estimates for diseases that develop at relative young age. In chapter 5 of this thesis on the future cost of cancer, both demographic and epidemiological trends were analysed. For colorectal cancer the costs were predicted for several epidemiological scenario's. The three phase model demonstrated that an increase of future prevalence bears different cost implications, depending on the underlying reason. If the increase of prevalence is due to higher incidence, the costs will

increase substantially. If the increase is due to survival improvement, the costs will rise less sharply.

11.1.3. Comparisons

The results of general cost of illness may be used to distinguish cost increases due to demographic, price and epidemiological developments, and other reasons. Recently, an update of the 1988 study was published, describing the cost of illness by diagnosis age and gender for 1994 (Polder et al., 1997). The results for 1988 and 1994 were largely similar in terms of order of diseases. Chronic diseases involving much care, e.g. dementia and strokes, were responsible for the highest proportion of health care costs. Comparing the cost for 1988 with 1994 revealed that the total cost rose by 5.3% per year. Half of this increase was due to wage and price increases in health care. About one-quarter was due to demographic development and the other 25% increase was due to other reasons (epidemiological and technological developments, and other reasons). The development of medical technology is probably an important determining factor of future health care costs, but very difficult to estimate. Hodgson illustrated the uncertainty of the impact on future cost of changes in parameters that determine cost by trends in medical care for Coronary Heart Disease (CHD) (Hodgson,1988). On the one hand, the number of hospital days declined between 1979 and 1985. On the other, the number of Coronary Arteriography Bypass Grafting (CABG) and the number of percutaneous transluminal coronary angioplasty (PTCA) increased during this period. The number of hospitals with facilities for open heart surgery and cardiac catherization capability, and cardiac or mixed intensive care units also increased rapidly. Furthermore, the cost of medicines prescribed for CHD patients have grown rapidly. Hodgson concluded that it is difficult to foresee the substantial impact on the total costs due to these structural and contrary changes over time.

International comparisons of cost-of-illness studies may contribute to a global understanding of the influence of epidemiology, medical technological development and (health care) policy on costs. Comparison of the total cost of illness (direct and indirect costs) between the Netherlands, Sweden and the US indicated that these costs, in terms of percentage of GDP, were much higher

for the two European countries (the Netherlands 28%, Sweden 23% and US 16%). This was mainly due to differences in indirect costs.

The direct costs (both total and disease-specific costs) were similar in the Netherlands and Sweden, but differ from those in the US. Koopmanschap et al. (1995) suggested that the difference in medical practice and health care systems may explain a substantial part of the divergent results; demographic or epidemiological aspects seemed less important (Koopmanschap et al., 1995) . Institutional differences related to social security arrangements played an important role in explaining variations in indirect costs across the three countries. The costs due to disability were relatively high for the Netherlands, mainly because of favourable social insurance arrangements.

Besides general cost-of-illness research, several specific cost-of-illness studies were presented, for example, for migraine and growth hormone deficiency. A specific cost-of-illness study offers the possibility for a detailed study on different cost divisions, for instance informal care or reduced efficiency while at work due to disease. These costs were not part of the general cost-of-illness studies because national data on these aspects were lacking. Furthermore, the specific studies on growth hormone deficiency and migraine contained data on health related quality of life of the patients compared to the general population and other chronically ill patients.

Ideally, cost estimates of specific cost-of-illness studies should add up to the total cost of illness. Due to methodological problems this is not the case, however.

11.2. Comparability

Standardisation of research methodology is a prerequisite for the comparability and reliability of the use of cost-of-illness studies in health policy planning. In this paragraph we summarise some methodological problems that occurred while performing and comparing cost-of-illness studies.

11.2.1 General and specific cost-of-illness studies

Methodological differences between cost-of-illness studies may hamper comparisons of the results. The cost estimates of general cost-of-illness studies are based on the so-called 'top down' approach. The total costs are divided to diagnosis, age and gender based on a common denominator, for example hospital days. Using this method the costs incurred by all diagnosis groups were calculated using the same premise, so the results are comparable, but may be less exact. When estimating the cost of a specific disease category the direct costs are generally estimated using the 'bottom-up' approach. A detailed study on the use of resources for treatment and/or care is carried out per patient group. These volumina are multiplied by the corresponding prices and the number of patients per type.

General cost-of-illness studies proceed by allocating a given cost category to the diseases causing the costs, thereby avoiding double counting. The latter may occur in a specific cost-of-illness study when in the presence of multiple diseases, health care costs may be included for which the disease in question is reported as a secondary condition. In the general cost-of-illness study the total costs are divided by using data on the primary diagnosis. Therefore, the cost of diseases that often prevail as co-morbidity are possibly underestimated.

11.2.2. Incidence and prevalence method

The incidence-based and prevalence-based methods may lead to different estimates of cost of illness. Depending on the course of the disease and the purpose of the cost-of-illness study the prevalence or incidence method is applied. To determine the economic burden resulting from the prevalence of a disease in a given year and to indicate areas for future cost-effectiveness studies, the prevalence method is a suitable approach. However, to determine the cost consequences from an increase or decrease in the incidence and/or changes in the course of a disease, then the more complicated incidence method is more appropriate. The cost estimates of both approaches will be similar in case of acute conditions with short duration. The differences in costs estimates between both approaches will increase ceteris paribus when the incidence is declining, because the prevalence method captures the cost of chronic patients from larger

incidence cohorts of earlier years. With regard to the direct costs the estimates using the prevalence method will be higher compared to the incidence method when the annual treatment costs are declining over time. In general, the cost estimates will be higher using the prevalence approach compared to the incidence method because some of the costs are not discounted in the prevalence method which are discounted in the incidence method.

The prevalence method was applied in all cost-of-illness studies described in this thesis, except for the analysis of the future cost of colorectal cancer. We demonstrated that when estimating the future costs of a demographic scenario the results using the prevalence and incidence methods were comparable. However, if epidemiological trends are included, the incidence method provides more realistic predictions of future costs than the prevalence method. The relevance of the epidemiology for future costs is demonstrated for colorectal cancer (chapter 5 of this thesis).

11.2.3. Co-morbidity

In the presence of multiple diseases it may be difficult to indicate the burden of illness, because the contribution to the total costs of the specific disease, may not be clear. This was demonstrated in the study on the burden of hypopituitarism in adults after pituitary surgery. The underlying research question was to estimate the burden of growth hormone deficiency. In the present study design the differences in costs and in health status compared with the general population cannot be attributed entirely to growth hormone deficiency as these patients suffer from co-morbidity. Further study is therefore needed to compare patients who have pituitary surgery either with or without growth hormone deficiency.

11.2.4. Limitations data-sources

The information on medical consumption may be extracted from various sources. In the Netherlands a growing number of hospitals have computerised patient information systems. If such a system is not available or the data are not complete than the information should be gathered from patient files using a standard registration form. In additional other data sources such as judgmental assessments from experts may be incorporated. Besides volumes, the costs

are also determined by prices. In the absence of real prices, tariffs are often used for calculating the costs. However, tariffs may strongly deviate from the real costs. These limitation may cause serious errors in the estimates. In a sensitivity analysis the influence of the major possible sources of error should be studied.

11.3. Health and Labour Questionnaire

Depending on the specific diagnosis indirect costs may be an important aspect of the cost of illness. Data of national statistics on absence from work are often insufficient. Diagnosis specific data on short absence from work is lacking in the Netherlands and sick leave registration is influenced by changes in social security regulations. The Health and Labour Questionnaire (HLQ) supplied the necessary detailed information on absence from paid work, reduced productivity at work and unpaid production losses. Reduced productivity at work and unpaid production is lacking in a national statistic.

The HLQ consists of four modules to collect data on absence from work, reduced productivity, unpaid labour production and labour-experienced trouble. The HLQ was applied in a representative sample of the Dutch population, migraine patients, adult patients suffering from growth hormone deficiency, a study on electrostimulation of the bladder in patients with spinal cord injury and in patients with hip or knee problems. Finally, the HLQ was applied in a study on the costs and effects of microsurgery versus radiosurgery in treating acousticus neurinoma. We tested the feasibility and validity of the HLQ using data from these applications. Analysing the quality of the HLQ we discerned two types of criteria, that is practical and conceptual criteria (Essink-Bot et al., 1995). Practical criteria determine the feasibility of a questionnaire.

11.3.1. Feasibility

We used the response rate, the missing values rates, the completion time and the remarks of the respondents as empirical indicators of feasibility. According to these indicators the HLQ was well understood by respondents (patients and non-patients) of different age and gender.

11.3.2. Validity

Conceptual criteria relate to validity, i.e. the extend to which the instrument measures the characteristics as intended. Three types of validity are distinguished: content validity, criterion validity and construct validity. Content validity refers to theoretical testing of the content of an instrument, i.e. representative coverage of all relevant domains. Criterion validity requires a measurable superior reference criterion. Determining of construct validity requires empirical testing of a priori hypotheses about the instrument under study with an instrument of proven validity.

The HLQ attempts to produce data on the economic effects of illness on labour performance from a societal perspective. Apart from absence from work, the HLQ allows for collection of quantitative data on production losses without absence (reduced efficiency) and production loss of unpaid labour. The modular format permits the omission of questions that are not applicable to the research population. The format of the HLQ was suitable for application in a broad range of diseases.

Module 1 of the HLQ appeared to be a valid instrument for measuring disease and non-disease specific absence from work. With respect to several diseases, migraine for example, reduced productivity at work was responsible for an important part of the total indirect costs. The study on the cost of migraine indicated that there was a low correlation between the results of alternative measurement methods of reduced productivity at work using a questionnaire (module 2). Validation of this part of the questionnaire was not possible because of lack of a gold standard. Therefore, additional research on measuring reduced productivity at work using a detailed questionnaire is necessary. Measuring output (loss) per worker is the most direct way to evaluate reduced productivity and may be considered as a valid reference. Validating alternative measurement instruments used in the HLQ on reduced productivity requires comparison of these results with outcomes of direct output measurement. Currently, the Institute for Medical Technology Assessment is performing a validation study.

Except for child care, module 3 of the HLQ appeared to be suitable for assessing time spent on unpaid labour. This module attempts to quantify production losses of groups of patients who do not have a paid job, such as the elderly, women or children. In the presented studies these costs were minor compared to production loss of paid labour because of the small number of

hours lost and the relative low valuation of unpaid production. Using the HLQ in the study of acoustics neurinoma patients indicated that part of the household tasks was taken over by other members of the household, friends or neighbours. The results on the impediment score in module 4 of the HLQ showed that the instrument could reveal the expected changes of impediment due to treatment. Table 11.1 presents the main results of the application of the HLQ in several studies.

Table 11.1 Overview studies using Health and Labour Questionnaire

HLQ	Modules[a]	Results
General population	1,2,3,4	Reference data for absence from work, reduced efficiency, unpaid production and labour performance
Migraine patients	1,2,3,4	Indirect costs 80% of the total cost of illness of which 51% due to reduced efficiency. No indication of household production losses compared to the control group.
Adult GHD patient	1,2,4	Higher absence rates compared to the reference data. No indication of reduced efficiency.
Acousticus neurinoma	1,2,3,4	Patients treated by microsurgery had significantly higher indirect costs compared to radiosurgery, a higher impediment score and a higher percentage of patient of which household tasks were taken over by family members.
Spinal cord injury	3,4	High variation in time spent on household production.
Hip patients	3,4	Household production losses due to illness and a higher impediment score compared with the reference population.
Knee patients	3,4	Household production losses due to illness and a higher impediment score compared with the reference population.

[a]Module 1 'absence from work', Module 2 'reduced efficiency at work', Module 3 ' unpaid production' and Module 4 ' impediment to paid and unpaid labour'.

In the case of studies in which we did not have a control population, we used the data from the general Dutch population as reference data. In the study on hypopituitary adults with growth hormone deficiency, the application of the HLQ indicated that the indirect costs per year per patient were higher than the direct costs. We found no indication for reduced performance at work in this patient group. Applying the HLQ in the study of acousticus neurinoma patients indicated that the indirect costs were much higher in the microsurgery group compared to the group treated with radiosurgery. Assuming a reasonable occupancy of the expensive radiosurgery equipment we demonstrated that the same is true of direct costs. Furthermore, the HLQ demonstrated that in a higher percentage of the group treated by microsurgery compared to the radiosurgery group household tasks were taken over by others. Therefore, the HLQ indicated a better performance and lower indirect costs for the radiosurgery group. The results of the HLQ amplified the fact that for the short-term treatment of patients with an extra-meatal tumour diameter of the acoustic neurinoma of less than 3 centimetres with radiosurgery is more cost-effective than microsurgery.

In the study on spinal cord injury, there was a high variation in the time lost to unpaid production, which precluded any meaningful generalised interpretation of the results. Further research on this part of the questionnaire is desirable. The research on unpaid production losses due to illness should, in the first instance, emphasise the losses in terms of volumina, rather than the valuation, because the monetary value of household production is still a subject of discussion. The low valuation of unpaid production compared to paid work may underestimate the social consequences for certain patient groups as demonstrated in the study of hip and knee patients.

A cost-of-illness study is a tool for policy-makers to investigate the current and future cost of illness. For economic evaluation to have an impact on public policy, the results should relate to the real world that policy-makers are facing. Economic evaluations do not incorporate the importance of the distribution of costs and social consequences into the analyses. Therefore, the techniques of economic evaluation are just one step in the process of decision-making in health care. In this process, cost-of-illness studies may serve several purposes. The following applications were discussed in this thesis. Cost-of-illness studies may be applied as input for scenario analyses. In a steady-state situation the future costs may

be estimated by using the prevalence method. However, if it seems likely that changes in epidemiological and/or technological development may be expected, and which will have a significant influence on the future direct costs, then the much more complicated incidence method should be applied. A cost-of-illness study seemed an useful tool for setting priorities in health care research. However, high cost is just one of the criteria for setting priorities. Comparing cost-of-illness studies contributes to a global understanding of the influence of medical technology, epidemiology, health care policy and other developments on the costs. The influence of these components in future cost-of-illness studies deserves further research. The HLQ seems a useful instrument for estimating the indirect cost of paid and unpaid labour. The feasibility, reliability and validity of the module on 'reduced efficiency' and 'unpaid production' remain to be investigated.

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SUMMARY

In this thesis we indicated the relevance of general and specific cost-of-illness studies for health care policy. The comparability of results of cost-of-illness studies is discussed. An instrument for estimating production losses for paid an unpaid work in cost-of-illness or cost-effectiveness studies is presented. The feasibility and the validity of the Health and Labour questionnaire (HLQ) is discussed. Finally, we demonstrate the influence of the application of the HLQ in cost-of-illness and cost-effectiveness studies

Health Policy

The role of economic evaluations in decisions in health care policy has become more important due to the development of medical technology and health care budget constraints. Economic evaluations supply decision-makers with information on the costs and effects of health care programmes. Economic evaluations do not incorporate the importance of distribution of costs and the social consequences into the analyses. Therefore, the techniques of economic evaluation are just one step in the process of decision-making in health care. With regard to health care policy cost-of-illness studies may serve several purposes. Firstly, cost-of-illness estimates may be a first step towards targeting fundamental or applied research. Secondly, they may be applied as input for scenario analyses and produce estimates of future costs. Thirdly, a comparison of estimates of costs of illness studies may provide information on the costs consequences of demographic, price, epidemiological development and other reasons. Finally, a cost-of-illness study is a first step in constructing a multi-disease model of public health.

A complete cost-of-illness study consists of 4 components;

- The direct costs, representing the value of resources, within and outside health care, used to prevent, detect, treat and monitor the disease or its effect;
- The indirect costs, due to lost production or costs to prevent a production decrease (for paid and unpaid work) as a consequence of morbidity or premature death from the disease;
- Reduced health-related quality of life as a consequence of the disease;
- Premature death.

A general cost-of-illness study provides a comprehensive description of all diseases. Specific cost-of-illness studies, on the other hand, concentrate on one disease or disease category. This thesis comprises both general and specific cost-of-illness studies .

Prioritisation

In a study on mental illness in the Netherlands, cost of illness was used a tool as a first step towards targeting future research areas. Four disease categories - schizophrenia, depression, anxiety disorders and alcohol-related problems - were selected. However, the high cost of disease is not a sufficient condition for priority-setting. Additionally, we have made an inventory of the effectiveness of the relevant interventions and possible competitiveness with other interventions in terms of effectiveness and costs. For schizophrenia we compiled a list of 8 topics for future cost effectiveness studies.

Future costs of illness

In a general study on the cost of illness for the Netherlands, the total costs of all diseases by age and gender, categorised into 48 important disease categories, were estimated. Mental disorders (20%) and diseases of the circulatory system (9%) bear the highest health care costs (direct costs). Locomotion disease (24%) and mental disorders (19%) had the highest costs due production losses (indirect costs), applying the human capital method.

The direct cost estimates for 1988 were linked to demographic development in order to estimate health care costs for 2030. These projections show that chronic non-fatal diseases dominate in future costs. When epidemiological and medical technological changes are also taken into account the projection become more reliable. With respect to colorectal cancer a three-phase disease model was used for predicting the future costs. We presented costs estimates based on several scenario's. These costs predictions showed that an equal increase of future prevalence may bear different cost implications. If the rise is due to higher incidence, the cost will increase substantially. If the progress of prevalence is due to survival improvement, the increase will be less prominent because, in the intermediate phase, annual costs are modest .

Comparison

A comparison of the direct cost estimates for 1988 with a study from 1994 indicated that the total costs increased by 5.3% annually. Half of this increase was due to wage and price increases in health care. Demographic development was responsible for 25% of this increase and the other 25% was due to epidemiological and technological development and other reasons.

The indirect cost of all diseases for the Netherlands were compared to estimates for Sweden and the US. We found large differences in the share of the indirect costs in GDP as in the constituting elements, absence from work, disability and mortality. The level of indirect costs due to absence from work and the distribution according to diagnosis are quite similar for the two European countries. The costs of disability were particularly high for the Netherlands mainly due to favourable social insurance arrangements. The large number of deaths at young age in the US is responsible for the higher mortality costs compared to the two European countries.

Comparability

Results from general and specific cost-of-illness studies are often not comparable due to methodological differences. General cost-of-illness studies calculate the cost and distribute this total figure across disease categories. Specific cost-of-illness studies are generally calculated by multiplying volumina by the corresponding prices and the number of patients per type.

The incidence and prevalence method may lead to different estimates of cost of illness depending on the course and duration of the disease. In estimating the future costs for a demographic scenario the results of both approaches are comparable. However, the incidence approach provides the best measurements where epidemiological trends, course of the disease and/or costs of treatment are concerned. Finally, the methods for estimating the indirect cost may differ. In general, the human capital method is applied which estimates the potential economic production losses caused by diseases. The friction costs method, however, takes

into account short and long run processes in the economy which reduce the production losses substantially as compared to the potential losses.

Health and Labour Questionnaire

We developed the Health and Labour Questionnaire (HLQ) for collecting detailed data on production losses by specific disease for estimating indirect costs, which are often lacking in national registries. Furthermore, the HLQ describes the ability to work as an indicator of health status. The HLQ, consists of 4 modules to collect data on absence from work, reduced productivity, unpaid labour production and labour-related trouble. We applied the HLQ in several cost-of-illness and cost-effectiveness studies, e.g. general population, migraine, hypopituitary patients with growth hormone deficiency and acousticus neurinoma patients. The results on response, feasibility and construct validity were positive. The HLQ was well understood by patients and non-patients, and it appeared to be a valid instrument for measuring disease and non-disease specific absence from work. With respect to migraine, reduced productivity at work was responsible for an important part of the total indirect costs. This study indicated that there is a low correlation between the results of alternative measurement methods of reduced productivity at work using a questionnaire. Validation of this part of the questionnaire was not possible due to lack of reference data. Additional research on measuring reduced productivity at work using a detailed questionnaire is necessary. Currently, the institute for Medical Technology Assessment is performing a validation study. Except for child care, module 3 of the HLQ appeared to be suitable for assessing time spent on unpaid labour. Using the HLQ in the study of acouticus neurinoma patients could indicate substitution of household tasks by other members of the household. Finally, the results on the impediment score in module 4 of the HLQ showed that the instrument could reveal the expected changes of impediment due to treatment .

SAMENVATTING

In dit proefschrift wordt de beleidsrelevantie van totale en ziekte-specifieke 'kosten van ziekte'-studies onderzocht. De vergelijkbaarheid van de resultaten van 'kosten van ziekte'-studies wordt besproken. Tevens wordt een meetinstrument voor de bepaling van productieverliezen bij betaald- en onbetaald werk als gevolg van ziekte gepresenteerd. De haalbaarheid en validiteit van deze zogenaamde 'Ziekte- en Werk' (Z&W) vragenlijst wordt onderzocht. Tenslotte, is de invloed van de toepassing van de Z&W vragenlijst op de resultaten van 'kosten van ziekte'-studies en kosten-effectiviteitsanalyses bestudeerd.

Beleidsrelevantie

Het belang van economische evaluaties bij beleidsbeslissingen is toegenomen door kostenbeheersing en de ontwikkeling van medische technologie in de gezondheidszorg. Economische evaluaties verschaffen beleidsmakers informatie over kosten en effecten van gezondheidszorgvoorzieningen. Economische evaluaties geven geen inzicht in de verdeling van de kosten en maatschappelijke consequenties van beleidsbeslissingen. Daarom zijn vanuit de resultaten van economische evaluatie niet zonder meer conclusies voor beleid te trekken. In het licht van beleid kan een 'kosten van ziekte'-studie de volgende doeleinden dienen. In de eerste plaats kan een 'kosten van ziekte'-studie leidraad zijn voor de bepaling van prioriteiten in fundamenteel en toegepast onderzoek. Een tweede belangrijke toepassing van onderzoek naar 'kosten van ziekte' is die in scenario-analyses. Ten derde kan een vergelijking van resultaten 'kosten van ziekte'-studies inzicht verschaffen over de invloed van demografische-, epidemiologische-, prijs en overige ontwikkelingen op de kosten. Tenslotte, kan een 'kosten van ziekte'-studie als onderdeel dienen van de ontwikkeling van een volksgezondsheidmodel.

Een totale 'kosten van ziekte'-studie bevat meestal één of meer van de volgende vier componenten:

- de directe kosten, waarmee de kosten worden bedoeld die direct met de behandeling van de ziekte samenhangen;
- de indirecte kosten, waarmee de verloren productie wordt aangeduid ten gevolgen van ziekteverzuim, arbeidsongeschiktheid of vroegtijdige sterfte vanwege ziekte;
- de vermindering van kwaliteit-van-leven waarmee ziekte gepaard gaat;
- en vroegtijdige sterfte.

Een totale 'kosten van ziekte'-studie biedt een overzicht van de kosten van alle diagnostische categorieën. Een ziekte specifieke studie, zoals het woord al aangeeft, geeft de kosten voor één diagnose of diagnose-catogorie. Dit proefschrift bevat totale en specifieke 'kosten van ziekte'-studies.

Prioriteren

In een studie over kosten van psychische aandoeningen, wordt een 'kosten van ziekte'-studie gebruikt als eerste stap voor de selectie toekomstig onderzoeksgebieden. In deze studie zijn eerst de diagnosecategorieën geselecteerd met hoge directe kosten te weten: schizofrenie, depressie, angststoornissen en alcohol gerelateerde problemen. Hoge kosten zijn echter geen voldoende voorwaarde voor het inzetten van meer middelen. Aanvullend dient informatie over kosten-effectiviteit, van interventies die in een dergelijk ziektegebied kunnen worden ondernomen, beschikbaar te zijn. In een literatuur studie zijn gegevens over effectiviteit van interventies geïnventariseerd en geanalyseerd. In dit proefschrift is dit traject voor schizofrenie uitgewerkt en is vervolgens een lijst van 8 onderzoeksgebieden geïdentificeerd.

Toekomstige 'kosten van ziekten'

In een 'kosten van ziekte' studie voor Nederland zijn de totale kosten toegewezen aan 48 diagnostische categorieën. Psychische aandoeningen (20%), gevolgd door hart- en vaatziekten

(9%) zijn verantwoordelijke voor het hoogste aandeel in de directe kosten. Voor de indirecte kosten zijn aandoeningen van het bewegingsstelsel (24%) en psychische ziekten (19%) de belangrijkste. De indirecte kosten zijn berekend op grond van de human capital methode.
De directe kostenschatting voor 1988 hebben als basis gediend voor een projectie van de kosten in 2030 op grond van demografische ontwikkeling. De schattingen geven aan dat de kosten van niet-fatale aandoeningen zullen domineren in de toekomst. Tevens komt naar voren dat naast demografische ook epidemiologische en economische factoren in deze schatting dienen te worden opgenomen om tot betrouwbare voorspellingen te komen. Voor de bepaling van toekomstige kosten van colorectum kanker is een ziektemodel gebruikt. De kosten zijn berekend voor verschillende scenario's. De kosten voorspellingen laten zien dat een overeenkomstige toename van de prevalentie verschillende implicaties voor de kosten kan hebben. Wanneer de toename het gevolg is een stijgende incidentie dan zullen de kosten sterk toenemen. Wanneer de toename in prevalentie het gevolg is van overlevingverbetering dan zullen de kosten minder snel stijgen, omdat de kosten voor behandeling in deze fase gemiddeld lager zijn.

Vergelijking

Een vergelijking van de resultaten van de 'kosten van ziekte' -studies voor 1988 en 1994 geeft aan dat kosten jaarlijks met 5,3% zijn gestegen. Na de totale kostenstijging komt de helft voor rekening van de loon- en prijsstijging in de gezondheidszorg. De demografische ontwikkeling is verantwoordelijk voor een kwart van de kostenstijging. Het resterende deel wordt veroorzaakt door epidemiologische en technologische ontwikkelingen en overige oorzaken.
De kosten van productieverliezen als gevolg van ziekte (indirecte kosten) voor Nederland worden vergeleken met de kostenschattingen voor Zweden en de Verenigde Staten. Er blijken groten verschillen in het aandeel van de totale kosten in het BNP. Tevens bestaan er grote verschillen in het aandeel van ziekteverzuim, arbeidsongeschiktheid en mortaliteit in de totale indirecte kosten. De verdeling van de indirecte kosten over de diagnosecategorieën zijn voor de twee Europese landen vergelijkbaar. De kosten voor arbeidsongeschiktheid zijn voor Nederland hoog als gevolg van gunstige sociale voorzieningen. Een groot aantal sterfgevallen op jonge leeftijd is verantwoordelijk voor de hoge kosten voor sterfte in de Verenigde Staten.

Vergelijkbaarheid

De schattingen van totale - en ziekte specifieke 'kosten van ziekte' studies zijn vaak onvergelijkbaar als gevolg van methodologische verschillen. In totale 'kosten van ziekte'-studies worden de kosten berekend naar diagnosegroep met behulp van een verdeelsleutel. In een ziekte-specifieke 'kosten van ziekte'-studie worden de volume eenheden vermenigvuldigd met de bijbehorende prijs eenheid.
Er is een onderscheid te maken tussen de een benadering die uitgaat van prevalentiegegevens, en een die op incidentiegegevens is gebaseerd. Afhankelijk van het verloop en de duur van de ziekte kunnen de incidentie- en prevalentie methode tot verschillende kostenschattingen leiden. Projecties van 'kosten van ziekte' zijn vergelijkbaar voor beide methoden. Ons onderzoek geeft echter aan dat de incidentiemethode nauwkeuriger resultaten geeft met scenario's waarin epidemiologische trends, veranderingen in verloop van de ziekte en/of kosten van behandeling zijn opgenomen. Daarnaast kan de wijze van berekening en waardering van de indirecte kosten verschillen. Hierbij wordt nog vaak de human capital methode toegepast, waarbij de bruto inkomsten van personen over de gehele periode waarin ze tengevolge van ziekteverzuim niet kunnen werken, worden genomen als waarde voor de verloren productie. De frictiekosten-methode, waarbij rekening wordt gehouden met opvang en vervanging van arbeid, komt op realistischer schattingen die een factor 10 lager zijn dan de indirecte kosten op basis van de human capital methode.

Ziekte en Werk vragenlijst

De vragenlijst voor Ziekte en Werk (Z&W) is ontwikkeld om gedetailleerde informatie te verzamelen over productieverliezen van diagnoses voor bepaling van de indirecte kosten van ziekte, aangezien nationale registratie systemen vaak onvolledige informatie bevatten. Daarnaast beschouwt de Z&W vragenlijst het vermogen om te werken als een indicator van gezondheidstoestand. De Z&W vragenlijst bestaat uit 4 modules om informatie verzamelen over ziekteverzuim, productieverliezen zonder verzuim, productie in de onbetaalde sector (w.o. huishoudelijk werk en vrijwilligers werk) en ervaren hinder tijdens werk als gevolg van

gezondheidsproblemen. De Z&W vragenlijst is toegepast in verscheidene studies. De studiepopulaties waren onder andere; de algemene populatie, migraine patiënten, volwassen patiënten met groeihormoon deficiëntie en patiënten die zijn behandeld vanwege een brughoektumor. De resultaten met betrekking tot response, haalbaarheid en de constructie validiteit zijn positief. De Z&W vragenlijst werd goed begrepen door patiënten en niet-patienten en het blijkt een betrouwbaar meetinstrument voor ziekte-specifiek en niet-ziekte specifiek verzuim. In de studie over migraine blijkt dat productieverlies zonder verzuim verantwoordelijk is voor een aanzienlijk deel van de totale indirecte kosten. Deze studie geeft een lage correlatie aan tussen de resultaten van verschillende meetinstrumenten voor productieverlies zonder verzuim. Validatie van dit gedeelte van de vragenlijst was niet mogelijk door het ontbreken van referentiewaarden. Aanvullend onderzoek met betrekking tot meeting van productieverliezen zonder verzuim met behulp van een vragenlijst is noodzakelijk. Momenteel voert het instituut voor Medische Technology Assessment een validiteitsonderzoek uit met betrekking tot module 2 van de Z&W vragenlijst. Met uitzondering van het meten van 'kinderverzorging', onderdeel van module 3, is de Z&W vragenlijst een betrouwbaar instrument voor bepaling van de tijdsbesteding aan onbetaalde productie. In de studie bij patiënten die zijn behandeld vanwege een brughoektumor gaf de Z&W vragenlijst aan dat er substitutie plaatsvond van onbetaald werk van de patiënt naar overige leden van het huishouden. Tenslotte blijkt module 4 van de Z&W vragenlijst de invloed van veranderingen in gezondheidstoestand op het vermogen te werken in kaart te kunnen brengen.

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CURRICULUM VITEA

Leona van Roijen werd geboren op 23 september 1964 te Leiden. In 1983 behaalde zij het einddiploma atheneum (Rembrandt scholengemeenschap, Leiden). In 1989 sloot zij haar studie algmene economie aan de Erasmus Universiteit Rotterdam af. Gedurende 1990-1994 was zij werkzaam bij het instituut Maatschappelijke Gezondheidszorg, Erasmus Universiteit Rotterdam. Vanaf 1994 is zij in dienst bij het instituut voor Medische Technology Assessment, Erasmus Universiteit Rotterdam.
Leona van Roijen is getrouwd met Gerben Hakkaart en ze hebben een dochter Julia (5 januari 1997).