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The cost of multiple sclerosis in Norway – (and how certain can we be?)

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(Draft August 7. 2006)

Abstract

The research question initially formulated for this study was to attempt to set a numerical target for the total yearly cost of MS to the Norwegian society, and relate the cost and patients´ experienced quality of life to illness severity. As work progressed, the question of how much confidence may be put in this kind of information in Norway as for today turned into another main issue. It turned out that much of the information that could be used for our study was so imprecise or unreliable that giving an impression that the information could be used to give an acceptably precise *single* estimate of the cost of MS to the Norwegian society would be seriously misleading. Therefore both "conservative" and "best" estimates are given. A conservative estimate of the yearly cost of MS to the Norwegian society around year 2002 is NOK 1 836 million. A best estimate is NOK 4 033 million, more than twice the conservative estimate. Mainly three factors account for the difference between the estimates: Uncertainty on what elements should be included in cost-of-illness studies, uncertainty on how some cost elements should be valued, and a combination of differences in information on the same phenomena in different sources of information and the researchers´ choices on how to handle them. For decision making purposes the combined effect of differences in information from different sources and the researchers´ choices on how to handle them is most grave since it will usually go unrecognized.

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When related to illness severity, the total cost per patient to society seem to *in*crease, and the patients experienced quality of life to *de*crease, in a close to linear fashion with increasing EDSS-levels [1]. However, a warning should be raised that because of the uncertainties as those mentioned, Norway probably has a long way to go before studies like ours in general might be regarded as providing acceptable information for decisions as important as those that have to be made in the health sector.

[1] The EDSS, Kurtzke`s "Expanded Disability Status Scale", is the most common tool used to express illness severity in MS. The scale ranges from 0 (no disability) to 10 (dead due to MS) and is divided in 20 half-point steps

Introduction

Multiple sclerosis (MS) is a chronic, eventually progressive disorder of the central nervous system, characterized by demyelination and axonal loss with resultant accumulation of neurological impairment and disability. The progressive loss of function results in a high level of disability (Grima et al, 2000), and more than 50 % of persons with MS are unemployed within 10 years from diagnoses (Bourdette et al, 1993). The onset of the illness is normally between 20 and 40 years of age and it is the second most common cause of disability in young and middle-aged adults (Hauser, 1994). The illness also typically has a long duration, mean 40 years (Weinshenker et al, 1989), and may in rare cases also cause death. It has therefore long been acknowledged that MS brings high costs upon both patients and society, but also that successful treatment may bring comparably large gains. During the 1990s immunomodulatory drugs were introduced. These are costly and do not cure the illness, but may delay progression and reduce at least some costs. The effects are however modest and uncertain. The Norwegian Multiple Sclerosis National Competence Center has initiated work to develop a tool to be used to illuminate the combined effect on costs and gains. This article refers the findings from the first phase of this work, the setting of a numerical target for the cost of the illness to the Norwegian society, and relating the cost and patients experienced quality of life to illness severity.

Methods, material and terminology

Our study may be classified as a combined top-down/bottom-up cost-of-illness study with the human-capital method used to set a numerical target for the cost of sick absence from work, early retirement and premature death. We made no special attempt, however, to make the study fit perfectly into any given such classification scheme. Information from a wide range of sources was gathered and attempted combined in a way that might hopefully provide the best possible results.

Most of the sources used gave information of relevance for the setting of numerical targets for only one single or a limited group of cost elements. These sources will be briefly commented upon below in relation to the specific numerical targets attempted set. One of the sources, however, a postal survey among MS-patients in Hordaland County, provided a broader set of information, both information that could not be gathered from other sources, but also information to be used to check the consistency of information gathered in different ways, and is therefore given a more general comment below.

Hordaland County was chosen as geographic area for the survey because it is a county for which the files at the Multiple Sclerosis National Competence Center are assumed to be especially complete, in that they contain all persons in the county with a MS-diagnosis according to the Poser criteria (Grytten et al., 2006). These persons can be said to comprise the *total MS-population*, or the *population of registered MS-patients* in Hordaland County. It was considered possibly unethical, however, to send questionnaires asking for information about their MS to all these persons because not all of them might even be aware of their diagnoses, and some would regard themselves as free of MS even if they were aware that they had once got the diagnoses. Neither should it be necessary to send questionnaires to these persons, asking questions on the cost to society of their illness, since logically there should be none. Therefore, two neurologists at Haukeland University Hospital, one of the authors and one other, surveyed the files and removed all the persons they considered might not to be aware of or feel any consequences of their MS. The remaining persons should then be the part of the total patient population in Hordaland County that should be relevant for our study. In the study, this population is denoted "the relevant patient population in Hordaland County". The relevant patient population in Hordaland County comprised 526 persons in 2002. The questionnaire sent to these patients was structured into 7 different parts, background information, ambulatory care, institutionalization, support and assistance, drug use, employment status and quality of life [1]. To minimize the risk of recall error the questions asked were about

[1] Freddie Henriksson, Sten Fredrikson, T. Masterman and Bengt Jönsson were so kind to provide us with the questionnaire they had used in their study on costs, quality of life and disease severity in Sweden in 1998. Our questionnaire was in all important respects made identical to their questionnaire for comparison purposes. We thank Henriksson, Fredrikson, Masterman and Jönsson for their generosity

the situation at the moment the questionnaire was answered or the last preceding month, with only a few exceptions. The exceptions where mainly questions about support in the form of adaptations of houses and cars, and helping aids purchased or received, where longer perspectives were assumed more suitable. Also, some questions on illness history were for longer time periods.

423 of the patients, 81 %, responded and there were no significant differences between the groups of responders and non-responders concerning sex, age and kind of MS at outburst. Since the notion "the relevant patient population", however, was coined specifically for the gathering of information from Hordaland County for our study, no information at the outset existed on the size of the corresponding population nationally. This population, being the population that would be relevant for extrapolations of the survey findings, and for that reason denoted "the relevant national patient population" in the article, therefore had to be estimated. We did this by assuming that the ratio of patients in the *relevant patient population* to the *total MS-population* was the same in Norway as a whole as in Hordaland County. Until some time before we made our study it had generally been assumed that the prevalence of MS in Hordaland County might be approximately 20 % higher than in the rest of the country (Fuglset, Mehling, 1996). If so, that would indicate a size of the total Norwegian MS-population of approximately 6 500 patients, with 4 670 patients in the *relevant* patient population. More recently the prevalence of MS in Hordaland County and the rest of Norway have been assumed to be reasonably identical. In that case the total Norwegian MS-population should be more like a 7 740 patients, with approximately 5 570 patients in the relevant patient population.

Since a relatively wide specter of information for our study was gathered through the postal survey, two limitations of this information and our further extrapolations of it should be born specifically in mind. First, since our exclusion of patients assumed not to be aware of or not to feel any consequences of their MS was based on judgment, some patients having MS with cost effects to society may have been excluded. To the extent this has been the case, our estimates of the cost of MS to the Norwegian society may be somewhat too low. Hopefully, however, this possible underestimation should be of

modest magnitude since the exclusion of patients was done with great care by qualified neurologists. Second, the cost effects to society of the relevant MS-population in Hordaland County may not be representative for the corresponding cost effect in other parts of Norway, both because patients in Hordaland County may receive different treatment etc. than other Norwegian patients, and because the size of the relevant patient population in Hordaland County may not be representative of the size of this population in other parts of the country. Differences in treatment may for instance be due to Hordaland County containing Norway`s second largest city and being served by its own university hospital, different employment opportunities for disabled persons in different parts of Norway etc.. However, imperfect knowledge of the populations of MS-patients in different parts of the Norway made sampling aimed at providing a more representative sample difficult. On the other hand, Hordaland County comprises both rural and urban areas like most other counties in Norway, and contains approximately 10 % of the MS-patients in the country. This should contribute to make the MS-population in Hordaland County reasonably representative also for the national population what treatment etc. is concerned. The possible effect of eventual non-representativeness of our chosen survey population in this respect might therefore also, in our opinion, be expected to be modest. Similar representativeness problems have also faced researchers in other countries, and mostly, also they have chosen to rely on geographically delimitated samples. The uncertainty of the size of the relevant national MS-population is graver since it is absolute, of considerable magnitude, and will be transferred directly into all results based on extrapolations of information gathered from our sample of MS-patients in Hordaland.

Even more important is it, though, that this uncertainty on the size of the relevant national MS-population only is *one striking* example of a more general problem that we typically encountered during our work. It turned out that much of the information that could be found was so imprecise or unreliable that giving an impression that it could be used to give an acceptably precise *single* estimate of the cost of MS to the Norwegian society would be seriously misleading. Therefore, both “conservative” and “best” estimates are given for a lot of numbers. Whenever information from different sources varied, we chose the information that would contribute to the lowest cost of MS to the Norwegian

society as our conservative estimate, given that we considered it to be of reasonably good quality. If the information, however, in our opinion could be suspected to be directly erroneous, we made adjustments we considered reasonable. The "best" estimates were based on the authors´ subjective evaluation of all available information. In line with the considerations above, we chose 4 670 persons as the conservative estimate of the size of the relevant national MS-population, and 5 570 persons as the best estimate. In addition to the term "the relevant patient population", we also coined two other terms, "ideal or close to ideal information" and "volume- and value components", specifically for the purpose of our work.

Ideal or close to ideal information is used to denote information that in principle should have been collected and presented to give a true and complete picture of the phenomena under study. For example, market prices free of taxes and subsidies should in general be expected to give a true and complete picture of the cost to society in terms of units of resources consumed, and hospital records a comparable picture of for example the number of bed-days in hospitals. We have sought to use this kind of information whenever available.

The cost to society of resources used or generation of welfare lost due to for example an illness [1] is the product of the number of units of resources used or generation of welfare lost, and the cost to society of each unit. Ideally, the best information on unit costs should be combined with the best information on the number of units consumed or lost to produce the most correct numerical targets for the cost to society. The information may however be found in different sources, given for different units of measurement, so compromises may have to be struck. For hospital stays for example, information on the cost to society of each unit of the specific resources consumed during the stay, like nurses´ time, food etc., measured in natural units for each kind of resource, will normally be more correct than information on the cost to society of more aggregated unit measures

[1] The use of resources should take into account all resources, human as well as physical, to diagnose, treat or nurse etc., or to give other forms of help or support to patients due to their illness. The reduced generation of welfare should include all reductions in the patients´, and possibly also their families and friends possibilities or ability to perform activities that would have contributed to increased welfare for themselves or others.

as for example “bed-days” etc.. Often however, information on *the number of “units” consumed or lost* is recorded more systematically for more aggregated unit measures. In our work we searched for the units of measurement for which we could find or produce the most ideal *corresponding* information on both the number of units consumed or lost, and the same units´ cost to society. The number of *such measurement units* consumed, or of generation of welfare lost is denoted the “*volume component*” of the cost to society of this resource usage or loss of welfare generation in the article, and the assumed cost to society of each of these units, the “*value component*”. For hospital stays for example, since the information on unit costs to society of the individual resources might be more easily aggregated to costs per bed-day than the other way around, we chose bed-days as the compromising unit of measurement for the volume- and value components of the cost of these stays. The notation tells that the information used for the setting of the numerical target for, for example the costs to society of hospital stays, was chosen not solely because of availability, but because it was the information that was considered to be the *best* available for the purpose. The notation, in our opinion, also contributes to make the presentation of the findings of our study as simple and precise as possible.

Some information gathered both through the survey and from other sources was given in monetary values. In some cases, these values included taxes or subsidies. This has been adjusted for so that all the monetary values presented in the study are free of taxes and subsidies to make them reflect cost to *society*.

Results

Table 1-3 refers the main findings of our work.

Table 1 **Conservative and best estimates of the total yearly cost of MS to the Norwegian society around [1] year 2002**

	Conservative estimate	Best estimate
DIRECT ECONOMIC COST:		
Drugs	***196 400 000***	***285 759 000***
Ambulatory care	***105 059 000***	***156 275 000***
Institutionalization	***272 535 000***	***343 942 000***
Support and assistance	***244 861 000***	***663 402 000***
Sum direct economic costs	***818 855 000***	***1 449 378 000***
INDIRECT ECONOMIC COST:		
Patients´ reduced participation in paid work	***1 016 876 000***	***1 910 176 000***
SOCIOECONOMIC COST:		
Reduced quality of life	**0**	**673 750 000**
TOTAL	**1 835 731 000**	**4 033 304 000**

Table 2 **Average total cost per patient to the Norwegian society for EDSS-levels 1-9 around 2002 (NOK 1000)**

EDSS / Cost estimate:	1	2	3	4	5	6	7	8	9
Best	382,4	402,5	596,8	687,0	939,1	937,6	884,9	1354,7	1235,3
Conservative	233,1	234,3	370,8	424,2	620,0	580,5	536,1	815,2	711,8

Table 3 **Quality of life experienced on average by Norwegian MS-patients at EDSS-levels 1-9 (% of perfect healthy)**

EDSS	1	2	3	4	5	6	7	8	9
Quality of life	78,2	75,1	67,3	60,8	57,5	51,3	52,6	38,5	20,0

[1] In our work, we have had to utilize information from partly differing time periods. The information has, however, been treated and used so to reflect the situation in 2002 reasonably well

Table 1 gives a conservative estimate of the total yearly cost of MS to the Norwegian society around year 2002 of NOK 1 836 millions, and a best estimate of NOK 4 033 millions, more that twice as large. The direct economic cost contains the cost of all the resources, human as well as physical, used to diagnose, treat and nurse etc., or to give other forms of help or support MS-patients because of their illness. The indirect economic cost contains all the potential generation of welfare lost due MS-patients´ reduced participation in paid work, and the socioeconomic cost the cost to society due to the patients´ reduced ability to perform also unpaid work, and to pain, grief, anxiety and social handicaps caused by MS. Table 2 and 3 show how the total yearly cost to society per MS-patient, and the patients experienced quality of life, on average varied with illness severity.

Arriving at the results

Drug costs

MS-patients use a variety of drugs because of their illness. From a cost perspective the absolute most important are β-interferons and glatiramer acetate. These drugs are used by MS-patients only, and the sales are surveyed by both the Norwegian National Insurance Administration and The Norwegian Association of Pharmaceutical Manufacturers. Especially the information from the manufacturers´ association may, after a few routine adjustments, mainly by replacing the wholesale prices used in their statistics with retail prices, be said to give very close to ideal information on the cost to society of the use of these drugs. When we made our study the most recent information from the manufacturers´ association was for 2001. This information on the cost of β-interferons and glatiramer acetate was used, after the mentioned replacement of prices, as our conservative estimate of the cost of immunomodulatory drugs. To arrive at the best estimate, we increased our conservative estimate by 50 % because the information from both the Norwegian National Insurance Administration and The Norwegian Association of Pharmaceutical Manufacturers showed that the use of β-interferons and glatiramer-

acetate absolutely were on the rise and that we had not seen what might be expected to be the full use of these drugs yet.

For two of the remaining drugs used by MS-patients because of their illness, Solumedrol and Prednisolon, we gathered information on the volume components of their cost to society through the survey among the MS-patients in Hordaland and from hospital records. The information from the hospitals indicated less use of these drugs than the information from the postal survey. The information from the hospitals should in principle be routine recorded and should therefore also in principle be more ideal than the survey information. It was therefore used for the conservative estimates of the volume components of the cost to society of the use of the drugs. The information from the hospitals was however far from complete and we therefore used the information from the postal survey for the best estimates. The Norwegian Pharmaceutical Product Compendium (Felleskatalogen, 2002) gives retail prices for drug sales in Norway. We considered these prices to give reasonably ideal information on the cost to society of each unit of the drugs, and applied them unadjusted as *both* conservative *and* best estimates of the value components.

For all other drugs used by MS-patients due their illness, we gathered information on the cost of their use to the Norwegian society mainly through the postal survey. Information gathered in this way may not come especially close to ideal, but it seemed to be the only feasible way to gather it. For drugs where the patients´ outlays could be assumed to reflect the cost of their use to society, possibly after some routine adjustments, we asked for this information directly in the survey. For drugs where the patients´ outlays could not be assumed to reflect the cost to society of the use because of subsidies etc., we gathered only information on the volume components through the postal survey, and used information in Felleskatalogen to estimate the value components in the same way as for Solumedrol and Prednisolon. We made no attempt to differentiate between conservative and best estimates for the information on the use of all these unspecified drugs, and the difference between the conservative and best estimates of the total cost to society of the use of the drugs is therefore solely due to the extrapolation process where we used the

conservative estimate for the relevant national patient population to arrive at the conservative estimates of the cost, and the best estimate for the relevant national patient population to arrive at the best estimates of the cost. Table 4 summarizes the estimates of the cost to society of MS-patients´ use of drugs due to their illness.

Table 4 Total yearly cost to the Norwegian society of drug use due to MS around year 2002

	Conservative estimates			**Best estimates**		
Drug:	Volume-compo-nents	Value-compo-nents	**Cost to society**	Volume-compo-nents	Value-compo-nents	**Cost to society**
Solumedrol	870	690	**600 000**	1 390	690	**959 000**
Prednisolon	870	136	**118 000**	1 390	148	**206 000**
B-interferon/ glatiramer acetate	Without meaning	Without meaning	**165 000 000**	Without meaning	Without meaning	**248 000 000**
Other drugs bought at Pharmacies	Without meaning	Without meaning	**24 051 000**	Without meaning	Without meaning	**28 685 000**
Non-pharmacie drugs	Without meaning	Without meaning	**6 631 000**	Without meaning	Without meaning	**7 909 000**
Total			**196 400 000**			**285 759 000**

The cost of ambulatory care

MS-patients visit a range of professionals for consultation and treatment that do not require institutionalization, most often physicians, nurses and physiotherapists, but also occupational therapists, incontinence advisors, speech therapists, psychologists, social workers, social welfare workers, opticians, chiropodists, acupuncturists, homeopaths, ergo therapists, chiropractors, healers and foot zone therapists mainly. We found no information that could be said to come especially close to ideal for the setting of numerical targets for the *volume* components of the cost to the Norwegian society of these visits.

We chose to gather most of the information on the *volume* components through the survey among the MS-patients in Hordaland County. Here we asked the patients for the number of visits they had made to each category of professionals the last month. For polyclinic visits to neurologists in hospitals, we gathered in addition information on the volume components from the Norwegian Patient Register. This information should in principle be routine recorded and should therefore also in principle be more ideal for the setting of numerical cost targets than information from the survey. It seemed, however, to be somewhat incomplete. For visits to physicians in general, some information was also available from an earlier attempt to set a numerical target for the cost of MS-to the Norwegian society (Fuglset and Mehling, 1996).

The information gathered through the postal survey on polyclinic visits to neurologists in hospitals indicated a higher number of such visits than the information from the Norwegian Patient Register, and even still higher than the information in Fuglset and Mehling´s study. The information in Fuglset and Mehling´s study was based on very simplifying assumptions, however, and we used the information from the Norwegian Patient Register, which was somewhat mid-way between the information gathered through the postal survey and the information in Fuglset and Mehling´s study, as our conservative estimate of the volume component of the cost to the Norwegian society of these visits. As our best estimate, we used the best estimate based on the information from the postal survey. For visits to physicians in private practice, even the *conservative* estimate based on the information gathered through the postal survey was more than four times higher than the estimate in Fuglset and Mehling´s study. Because of this, we chose the conservative estimate of the volume component of the cost of visits to or by physicians in private practice as 50 % of the conservative estimate based on the results from the postal survey. As our best estimate, we used the best estimate based on the information from the postal survey unadjusted. For all other visits, we based both our conservative and best estimates of the *volume* component of their cost to society on the information from the survey. The difference between the estimates also here being due solely to the extrapolation process where we used the conservative estimate for the

relevant national patient population to arrive at the conservative estimates of the volume component, and the best estimate for the relevant national patient population to arrive at the best estimate of the volume component.

While we found no information that could be said to come especially close to ideal for the setting of numerical targets for the volume components of the cost to society of MS-caused ambulatory care, for the value components, the picture was more mixed. For the value components of the costs to society of the visits to physicians, psychologists and physiotherapists, we could use information in official price- or tariff lists for services typically provided during such visits, negotiated between Norwegian health authorities, and hospitals and the professionals´ organizations. The listed prices and tariffs were exclusive of sales tax, and we considered them to give reasonably close to ideal information on the value components of the cost to society of visits to psychologists, physiotherapists and doctors in private practice. For polyclinic visits to neurologists in hospitals, however, they seemed to be somewhat farther from ideal, because the negotiation of this tariff is complicated both by political considerations and defective information availability. Bearing this in mind, we set the conservative estimates like the prices/tariffs of short and uncomplicated visits. We set the best estimates as weighted averages of the prices and tariffs for visits of varying content and duration, assumed to be typical for MS-patients. We assumed the value components of the cost to society for the rest of the visits, which together accounted for only 26 % of the number of visits to physiotherapists, to be identical to the value components of the cost of visits to physiotherapists, except for the visits to or by nurses. The value components of the cost of visits to or by nurses were estimated from information on nurses´ salaries, typical health-sector overhead costs, and duration of visits. For home visits, transport costs were also included. More information on the volume- and value components and the total cost to society of ambulatory care due to MS is given in table 5.

Table 5 Conservative and best estimates of the yearly cost to the Norwegian society of ambulatory care due to MS around year 2002

	Conservative estimates			Best estimates		
Visits:	Value-compo-nents	Volume-compo-nents	**Cost to society**	Value-compo-nents	Volume-compo-nents	**Cost to society**
To/by physicians in private practice:						
General practitioners	224	7 705	**1 726 000**	344	18 380	**6 323 000**
Specialists	201	1 635	**329 000**	326	3 900	**1 271 000**
Home visits	639	935	**597 000**	770	2 230	**1 717 000**
Contact by telephone etc.	35	3 200	**112 000**	35	7 800	**273 000**
***Sum* physicians in private practice:**		***13 475***	***2 764 000***		***32 310***	***9 584 000***
Neurologists in hospitals	175	6 085	**1 065 000**	605	10 000	**6 050 000**
Sum physicians		***19 560***	***3 829 000***		***42 310***	***15 634 000***
To/by nurses:						
Home visits	213	275 630	**58 709 000**	320	328 630	**75 585 000**
At nurses´ office	128	9 810	**1 256 000**	170	11 700	**1 989 000**
Contact by telephone etc.	43	9 340	**402 000**	57	11 140	**635 000**
Sum nurses		***294 680***	***60 367 000***		***351 470***	***78 209 000***
To other professionals:						
Physiotherapists	235	135 430	**31 826 000**	300	161 530	**48 450 000**
Occupational therapists	235	4 200	**987 000**	300	5 010	**1 503 000**
Incontinence advisors	235	930	**219 000**	300	1 110	**333 000**
Speech therapists	235	930	**219 000**	300	1 110	**333 000**
Psychologists	245	3 270	**801 000**	386	3 900	**1 505 000**
Social welfare workers	235	470	**110 000**	300	560	**168 000**
Social workers	235	1 870	**439 000**	300	2 230	**669 000**
Opticians	235	4 670	**1 097 000**	300	5 570	**1 671 000**
Chiropodist	235	6 540	**1 537 000**	300	7 800	**2 340 000**
Acupuncturists	235	7 940	**1 866 000**	300	9 250	**2 775 000**
Homeopaths	235	1 400	**329 000**	300	1 670	**501 000**
Ergo therapists	235	2 360	**555 000**	300	2 790	**837 000**
Chiropractors	235	470	**110 000**	300	560	**168 000**
Healers	235	930	**219 000**	300	1 110	**333 000**
Sone therapists	235	470	**110 000**	300	560	**168 000**
Various other professionals	235	1 870	**439 000**	300	2 230	**669 000**
Sum other professionals		***173 750***	***40 863 000***		***206 990***	***62 432 000***
Total		**487 990**	**105 059 000**		**600 000**	**156 275 000**

Cost of institutionalization

Institutionalization of MS-patients because of their MS takes mainly three forms, hospital stays, nursing-home stays and stays at rehabilitation centers. The hospital stays are either day-and-night stays, denoted "bed-days" in this article, or stays only during daytime, denoted "day-stays". Information on the volume components of the cost to the Norwegian society of the hospital stays should in principle be routine recorded by the Norwegian Patient Register. Further, much effort is made by a related organization unit, Samdata, to estimate the corresponding unit costs. Therefore, information that should come reasonably close to ideal for the setting a numerical target for the cost to society of these stays should in principle exist. It turned out, however, that this information lacked somewhat in reliability. Therefore, we also gathered supplementing information through the postal survey among the MS-patients in Hordaland County.

The information from the Norwegian Patient Register on both bed-days and day-stays in *hospitals* indicated a lower number of such stays than the information from the survey. For *bed-days* the differences were in the area 25 % to 50 %. Since information from the survey was gathered from a convenience sample, we made checks to see whether there could be any obvious fallacies in this information. We found no such fallacies, and we chose the best estimate of the volume component of the cost to the Norwegian society of these stays mid-way between the number of bed-days indicated by the information from the Norwegian Patient Register, and the best estimate of this number based on the information from the survey. We chose he information from the Norwegian Patient Register as it was for our conservative estimate. For *day-stays* the information from the two sources was more dramatically different. The information from the survey indicated a number of day-stays more than ten times higher than the number indicated by the information from the Norwegian Patient Register. Further checks on the information from both sources indicated important weaknesses of both. Therefore, we chose the conservative and best estimates of the volume component of the cost to society of MS-patients´ day-stays in hospitals mid-way between the number of such stays indicated by

the information from the Norwegian Patient Register, and the conservative and best estimates, respectively, based on the information from the survey.

We collected information on *unit costs* of MS-patients´ *bed-days* in hospitals mainly from the National Insurance Administration, but also checked it against information from Samdata. Both the National Insurance Administration and Samdata have put much effort in trying to set a numerical target for this cost, and their information on this topic may therefore be said to come reasonably close to ideal, even if not perfect due to some weakness in the basic data for their calculations. The information from the two sources corresponded reasonably well. The information from the National Insurance Administration, however, appeared to fit our needs best and we therefore used this both as conservative and best estimates of the value component of the cost to society of bed-days in hospitals due to MS. We found no information on the unit cost of day-stays, and assumed somewhat arbitrarily, the value component of their cost to society to be 1/3 of the cost of bed-days.

For stays in nursing homes and rehabilitation centers, in our opinion no sources of information appeared to exist, that could give even close to ideal information for the setting of numerical targets for their cost to society. We therefore found we would have to rely on less satisfactory information sources, and we considered the best alternative to be to try to gather information on the volume components of the cost through the survey among MS-patients in Hordaland. For stays in rehabilitation centers, this information could also be checked roughly against information gathered by the Norwegian Patient Register. The information from the patient register seemed to confirm the information gathered through the postal survey reasonably well, and we therefore chose the conservative and best estimates based on the information gathered through the postal survey, unadjusted as estimates of the volume components of the cost to the Norwegian society of both nursing home and rehabilitation center stays. Our estimates of the value components were solely rough assumptions based on information from different sources touching on the theme. Table 6 summarizes the information on the cost to the Norwegian society of institutionalization due to MS.

Table 6 **Conservative and best estimates of the yearly cost of hospital stays, nursing-home stays and stays at rehabilitation centres to the Norwegian society around year 2002**

	Conservative estimate			Best estimate		
Stays at:	Volume-compo-nents	Value-compo-nents	**Cost to society**	Volume-compo-nents	Value-compo-nents	**Cost to society**
Hospitals as:						
Bed-days	5 970	7 450	**44 477 000**	7 475	7 450	55 689 000
Day-stays	1 760	2 480	**4 365 000**	2 080	2 480	5 158 00
Nursing homes	60 710	1 275	**77 405 000**	72 410	1 500	108 615 000
Rehabilitation centers	32 690	4 475	**146 288 000**	38 990	4 475	174 480 000
Total			***272 535 000***			***343 942 000***

Cost of support and assistance

Many MS-patients are in need of assistance and support for the carrying out of daily activities. This can be given directly as human assistance in the carrying out of the activities, and more indirectly as equipment and adaptations that may make it easier for the patients to carry out the activities themselves. Setting a numerical target for the cost to the Norwegian society of this assistance, equipment and adaptations poses special problems, especially for equipment and adaptations.

Equipment and adaptations

We found no existing sources that contained information that might be said to come even close to ideal for the setting of a numerical target for the cost to the Norwegian society of equipment and adaptations for MS-patients. The information would, in our opinion, also be difficult to procure more directly, because the equipment and adaptations will often be

tailored to the individual patients. We found our best alternative, though, to be to try to gather somewhat rough information on the volume components of the cost of equipment and adaptations in two ways, both through the survey among the MS-patients in Hordaland, and also by eliciting expert opinions, and combine this information with similarly rough information on the value components. In the survey, we asked the patients for the number of units they had received or bought the last 12 months within broad categories of equipment and adaptations. We extrapolated this information to conservative and best estimates of the volume components of the cost to the Norwegian society of the equipment and adaptations, using the conservative and best estimates of the size of the relevant national patient population. However, since each patient typically will receive much of such equipment and adaptations only once, or very few times during their lifetime, if at all, that may specifically reduce the reliability of information procured as described above, where a prevalence approach was used. Therefore, we also attempted to use an incidence approach. We asked two neurologists, two ergotherapists and one nurse, all with expert knowledge of the effects of MS, to give their judgment of how large percentage of persons hit by MS would be in need of the different kinds of equipment and adaptations during their life-time, and if so also of how many units they might need. They were asked to give both conservative and their best estimates. Three would not answer the question, claiming that it would be an impossible task. Two, however, the nurse and one of the ergotherapists, joined forces and gave their common estimates. Because of the limited response to this attempt to gather information on the volume components of the cost to the Norwegian society of equipment and adaptations for MS-patients, we chose not to use the information received through this request in our attempt to set a numerical target for the cost to the Norwegian society of equipment and adaptations. It should be noted however, that the information gathered through the experts´ opinions was dramatically different from that given in the responses to the survey among the MS-patients in Hordaland County.

To arrive at the *value* components of the cost, we chose to assume that the cost of construed standard units within each of the specified categories of equipment and adaptations, would to be representative for the costs of units typically provided to MS-

patients, and we attempted to estimate this cost mainly from information in the previously mentioned study on the cost of MS in Sweden (Henriksson, 2001). To some extent, though, this information was also supplemented with information on corresponding Norwegian prices in 2002. Comparisons indicated that Norwegian 2002 NOK-prices typically could be as much as 50 % higher than the 1998 SEK-prices given in the Swedish study. Based on this information, for most of the equipment and adaptations, we used the SEK costs as conservative estimates of the cost to the Norwegian society of equipment and adaptations for MS-patients around 2002 because the combined effect of currency translation and Norwegian inflation from 1998 to 2002 seemed to "cancel each other out". For our best estimates, we increased the Swedish 1998 SEK prices by 50 %.

Human assistance

In addition to equipment and adaptations that may make it easier for patients to carry out daily activities themselves, MS-patients may also receive human assistance directly for the carrying out of the activities. This may be assistance that is paid for from professionals, mainly personal assistants, home helpers and babysitters, and unpaid assistance mainly from relatives and friends. We found no existing sources that contained information that could be said to come close to ideal for the setting numerical targets for the volume components of the cost to the Norwegian society of this assistance. We chose to provide also this information through the survey among the MS-patients in Hordaland County. Here we asked the patients how many hours of paid help and assistance of the different kinds they had received last month. Concerning help and assistance from relatives and friends, we also asked whether relatives or friends had had reduced posts, and if so, the percentage reduction, and if they had had short term absences from work or used their spare time, and also if so, how many hours, to provide the assistance. We arrived at our conservative and best estimates of the volume components of the cost to society of the help and assistance, measured as lost work-years for reduced posts, and hours for short term absences and use of spare time, by extrapolating this information using the conservative and best estimates of the relevant national MS-population.

When we chose to use work-years and hours like this as the unit of measurement for the volume component of the cost to the Norwegian society of the help and assistance, we could also extract information on some of the value components, that might be said to come reasonably close to ideal, from wage- and labor cost information, routine gathered by the Norwegian Bureau of Census. This concerned mainly the value components of the cost to society of paid assistance and assistance from relatives and friends during time they would else have used to perform paid work.

The information from the Norwegian Bureau of Census indicated, however, that females performed fewer hours of paid work daily than males, and were also less productive the hours they performed such work. To arrive at conservative estimates, we assumed that these differences reflected real differences in productivity. To arrive at the best estimate, however, we assumed that the differences in productivity between sexes indicated by the information from Norwegian Bureau of Census did not reflect real differences in productivity, but were caused by females typically performing more unpaid work, especially at home, than males. Therefore, for our best estimates, we assumed that the bureau of census´ wage- and labor costs for males reflected also females´ productivity. This explains why the conservative and best estimates of the cost of relatives´ and friends´ help and assistance differs more for females than for males. This way of taking care of females performing more unpaid work than males may deviate somewhat from how this is more typically handled in cost-of-illness studies, where reductions in performance of unpaid work, like house-keeping and child-rising etc., is often treated as a cost category of its own. This may be principally more correct, but will not affect the estimated total costs to society. Further, introducing reductions in unpaid work as a cost category of its own may also necessitate more speculative assumptions to arrive at the final estimates of total costs to society. For the best estimates of the cost to society of relatives´ and friends´ help and assistance to MS-patients during spare time, we assumed that the wage- and labor costs for males reflected the unit cost to the Norwegian society, also of this help and assistance. For the conservative estimate of this cost, the cost to society was assumed to be zero. More detail on the setting of the numerical targets set is given in table 7.

Table 7 Conservative and best estimates for the yearly cost to the Norwegian society of support and assistance to MS-patients around year 2002

	Conservative estimates			Best estimates		
	Volume-compo-nents	Value-compo-nents	**Cost to society**	Volume-compo-nents	Value-compo-nents	**Cost to society**
Adaptations						
Adaptation of kitchen	98	30 000	**2 940 000**	117	45 000	**5 265 000**
Adaptation of bathroom	234	30 000	**7 020 000**	279	45 000	**12 555 000**
Ramps	145	10 000	**1 450 000**	173	15 000	**2 595 000**
Roof lift	56	25 000	**1 400 000**	67	37 500	**2 513 000**
Stair- or pit lift	79	75 000	**5 925 000**	95	112 500	**10 688 000**
Other adaptations of house	243	30 000	**7 290 000**	290	45 000	**13 050 000**
Safety alarm	163	5 000	**815 000**	195	7 500	**1 463 000**
Adaptation of car	285	130 000	**37 050 000**	334	195 000	**65 130 000**
Adaptation on the job	145	30 000	**4 350 000**	173	45 000	**7 785 000**
Sum adaptations			***68 240 000***			***121 044 000***
Equipment						
Wheelchair	509	6 000	**3 054 000**	607	9 000	**5 463 000**
Electric wheelchair	388	110 000	**42 680 000**	462	165 000	**76 230 000**
Elektric moped	145	30 000	**4 350 000**	173	45 000	**7 785 000**
Rollator	220	1 000	**220 000**	262	1 500	**393 000**
Special furniture	121	10 000	**1 210 000**	145	15 000	**2 175 000**
IT equipment	42	10 000	**420 000**	50	15 000	**750 000**
Surgical splints etc.	84	400	**34 000**	100	600	**60 000**
Walking stick/crutch	616	100	**62 000**	735	150	**110 000**
Special kitchen devices	201	2 000	**402 000**	240	3 000	**720 000**
Special writing devices	131	2 000	**262 000**	156	3 000	**468 000**
Other minor equipment	22	2 000	**44 000**	26	2 000	**52 000**
Sum equipmentr			***52 738 000***			***94 206 000***
Paid assistance						
Personal assistant	126 090	272	**34 296 000**	150 390	390	**58 652 000**
Support worker	9 340	272	**2 540 000**	11 140	390	**4 345 000**
Home care	116 750	298	**34 792 000**	139 250	490	**68 233 000**
Domestic help	4 670	298	**1 392 000**	5 570	490	**2 729 000**
Child care	65 380	272	**17 783 000**	77 980	390	**30 412 000**
Unspecified paid assistance	4 670	272	**1 270 000**	5 570	390	**2 172 000**
Transport	- 410 970	85	**- 34 932 000**	- 490 160	150	**- 73 524 000**
Sum paid assistance			***57 141 000***			***93 019 000***
Unpaid assistance from relatives and friends, in form of relatives´ and friends´:						
Sick absence form work:						
Women	4 600	1 283	**5 902 000**	5 490	1 778	**9 761 000**
Men	14 180	1 778	**25 212 000**	16 910	1 778	**30 066 000**
Reduced posts						
Women	35	295 200	**10 332 000**	42	408 000	**17 136 000**
Men	62	408 000	**25 296 000**	74	408 000	**30 192 000**
Spare time used	948 010	0	**0**	1 130 710	237	**267 978 000**
Sum unpaid assistance			***66 742 000***			***355 133 000***
Total			**244 861 000**			**663 402 000**

The cost of MS-patients reduced participation in paid work

MS may cause not only the patients´ relatives and friends, but even more the patients themselves of course, to reduce their participation in paid work. These reductions will mainly take the form of short term sick absences from work, absences because of rehabilitation, reduced posts, early retirement or reductions due to premature death because of MS. Information on *work-days* lost because of short term sick absences and absences due to rehabilitation, and on *work-years* lost because of reduced posts and early retirement is routine recorded by the National Insurance Administration for the part of the reductions reimbursed by them. We considered that this information, with a few routine adjustments, could be transformed to information on the volume component of the cost to the Norwegian society of the reductions. The value components would be similar to the value components in the preceding paragraph of the cost to society of relatives´ and friends´ reduced participation in paid work. This combined information on the volume- and value components of the cost to the Norwegian society due to MS-patients reduced participation in paid work might, at least in principle, be said to be reasonably ideal for the setting of a numerical target for the cost. We also gathered information on the volume components, however, through the postal survey among the MS-patients in Hordaland County. It turned out that with one exception the numbers derived from the information from The National Insurance Administration were markedly higher than the numbers derived from the survey. In these cases, we used the numbers derived from the information from The National Health Administration as conservative estimates of the volume components, while we chose the best estimates mid-may between these conservative estimates and the best estimates derived from the information in the postal survey.

The information from The National Insurance Administration did not cover information on reductions in paid work due to premature death because of MS. Neither would it, for obvious reasons, be possible to gather such information through the postal survey among MS-patients in Hordaland County. Some information on these reductions, that might be

used to estimate the volume component of the cost to society is gathered by the Norwegian Bureau of Census, but does not cover the relevant time span completely. In addition, the information seems to be somewhat incomplete also for the part of the time span covered, especially for the first part. Since the information from The Bureau of Census, however, was the only information that seemed to exist on this topic, we used this information with only a marginal upward adjustment as both conservative and best estimates of the volume component of the cost to the Norwegian society of the reductions in paid work due to premature death because of MS. As the best estimate of the *value* component of the cost, we used the same information as for the value component of the cost to society of relatives working in reduced posts. As the conservative estimate, zero was chosen since it can be argued that people in general will consume approximately the values they create during their lifetime. Table 8 gives details.

Table 8 Conservative and best estimates for the yearly cost of MS-patients reduced performance of paid work to the Norwegian society around year 2002

	Conservative estimate			Best estimate		
Reduced performance of paid work due to:	Value-compo-nents	Volume-compo-nents	**Cost to society**	Value-compo-nents	Volume-compo-nents	**Cost to society**
Sick absence from work						
Women	1 283	40 000	**51 320 000**	1 778	73 000	**129 794 000**
Men	1 778	30 000	**53 340 000**	1 778	37 000	**65 786 000**
Sum sick absence from work		*70 000*	***104 660 000***		*110 000*	***195 580 000***
Rehabilitation:						
Women	1 283	5 200	**6 672 000**	1 778	12 000	**21 336 000**
Men	1 778	6 000	**10 668 000**	1 778	6 000	**10 668 000**
Sum rehabilitation		*11 200*	***17 340 000***		*18 000*	***32 004 000***
Reduced post/early retirement						
Women	295 200	1 905	**562 356 000**	408 000	2 600	**1 060 800 000**
Men	408 000	815	**332 520 000**	408 000	1 000	**408 000 000**
Sum reduced posts and early retirement		*2 720*	***844 876 000***		*3 600*	***1 468 800 000***
Premature death due to MS	*0*	-	-	*408 000*	*524*	***213 792 000***
Total			**1 016 876 000**			**1 910 176 000**

Socioeconomic costs

In addition to the effect MS may have for the patients´ ability to perform *paid* work, the illness may also reduce their ability to perform *unpaid* work like housekeeping, bringing up children and so on, and to perform leisure activities. The patients may further experience pain and both the patients and their relatives may have worries because of the patients´ illness. We have considered this last group of effects as reductions in the patients´ and relatives´ experienced quality of life, and the cost to society due to these reductions as a socioeconomic cost, in line with the choice described in the paragraph on

support and assistance to MS-patients, of not treating reductions in *unpaid* work as a cost category of its own.

We could not find any information that could be said to be ideal or close to ideal, neither on the volume- nor on the value components of the cost to the Norwegian society of these reductions in quality of life. We considered the best alternative to be to gather the information for the volume component of the cost through the postal survey among the MS-patients in Hordaland County, and for the value components from other cost-of-illness studies. In the postal survey, we asked the patients to indicate on a visual analogue scale how they would characterize their own health situation compared to what they would consider "perfectly healthy". The distance they indicated from "100 % perfectly healthy" was interpreted as their felt percentage reduction in quality of life. From this reduction, we deducted the reduced quality of life normally felt by adult persons, and assumed the remaining differences to represent the patients´ loss in quality of life because of their MS (Canadian Burden of Illness group, 1998). We arrived at conservative and best estimates of the volume component of the cost to the Norwegian society of the reduced quality of life by applying this percentage to the conservative and best estimates of the relevant national patient population, giving quality-adjusted life-years lost as the result. In addition, we added 10 % to account approximately for relatives´ reduced quality of life due to the patients´ illness.

As our *best* estimate of the value component of the cost, we chose a value given as typical in the Swedish cost of MS study by Henriksson et al.. We set the *conservative* estimate to zero both for the patients and their relatives because of the enormous uncertainty attached to estimates of the economic value of quality of life, and also because there is much disagreement on whether losses of quality of life should be regarded as a *cost* to society.

Table 9 Conservative and best estimates of the total yearly socioeconomic cost to Norway due to MS around year 2002

	Conservative estimates			Best estimates		
	Volume-compo-nents	Value-compo-nents	**Cost to society**	Volume-compo-nents	Value-compo-nents	**Cost to society**
Patients	0	0	**0**	1 225	500 000	**612 500 000**
Relatives	0	0	**0**	123	500 000	**61 250 000**
Total	0	0	**0**	1 348	500 000	**673 750 000**

Costs, quality of life and disease severity

To relate the per patient costs and Norwegian MS-patients experienced quality of life to the severity of their disease, disease severity was expressed by patients´ EDSS-levels, and whether they had experienced a relapse or not. We could gather information on the patients´ EDSS-levels from the Multiple Sclerosis National Register for 400 of the patients who answered the survey among the MS-patients in Hordaland County, and information on the occurrences of relapses, costs and patients experienced quality of life through the survey among MS-patients in Hordaland County ,as described above. Table 9, 10 and 11 show the average experienced quality of life and costs per patient in the relevant patient population, for the patients at each EDSS-level from 1-9, and the additional cost of relapses. In table 10, direct economic cost is exclusive cost of immunomodulatory drugs, but aside from that includes the cost of all the resources, human as well as physical, used to diagnose, treat and nurse etc., or to give other forms of help or support MS-patients because of their illness. The indirect economic cost contains all the potential generation of welfare lost due MS-patients´ reduced participation in paid work, and the socioeconomic cost the cost to society due to the patients´ reduced ability to perform also unpaid work, and to pain, grief, anxiety and social handicaps caused by MS. The information on the cost of MS to the Norwegian society *in general* was, as described in the first part of this article, gathered from a wide range of sources to provide the best impression of this cost. To relate the cost information to illness severity, we

needed cost information on individual patients. This had to be gathered solely through the survey among the MS-patients in Hordaland County. Therefore there is not 100 % correspondence between the cost figures in table 1 and table 10 and 11. The reason that the cost of immunomodulatory drugs is not included in the numbers in table 10 is that this information is planned to be used in our further work to analyze the cost-utility of the use of these drugs. There the cost of these drugs has to be treated separately.

Table 9 Quality of life experienced on average by Norwegian patients in the relevant patient population, at EDSS-levels 1-9 (percent of "perfect healthy")

EDSS	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Experienced quality of life	78,2	75,1	67,3	60,8	57,5	51,3	52,6	38,2	20,0

Table 10 Average direct economic cost, total economic cost and total cost to society per patient in the relevant patient population, at EDSS-levels 1-9 around 2002 (NOK 1000)

EDSS / Estimates	1	2	3	4	5	6	7	8	9
Direct economic cost									
Best	105,2	102,2	184,7	212,0	376,7	375,8	344,9	656,5	552,3
Conservative	103,2	99,7	169,9	199,6	338,1	329,5	271,0	503,5	386,5
+ Indirect economic cost:									
Best	159,7	165,7	249,6	280,1	352,1	314,7	332,4	391,0	408,0
Conservative	129,8	134,7	200,9	224,6	281,8	251,1	265,1	311,7	325,3
= Total economic cost									
Best	265,0	268,0	434,3	492,1	728,8	690,5	677,3	1 047,5	960,3
Conservative	233,1	234,3	370,8	424,2	620,0	580,5	536,1	815,2	711,8
+ Socioeconomic Cost									
Best	117,4	134,5	162,5	195,0	210,3	247,1	207,6	307,2	275,0
Conservative	0	0	0	0	0	0	0	0	0
= Total cost to society									
Best	382,4	402,5	596,8	687,0	939,1	937,6	884,9	1 354,7	1 235,3
Conservative	233,1	234,3	370,8	424,2	620,0	580,5	536,1	815,2	711,8

In addition to the averages given in tables 9 and 10, we also performed several regressions to try to find underlying patterns in the data material. These indicated a rather close to linear relation between the patients EDSS-levels, and the total cost per patient to society and patients experienced quality of life. For the direct economic cost, the relation was more of an exponential kind. The differences are explained by both indirect economic and socioeconomic costs exhibiting relatively steep rises at low EDSS-levels, and then flattening more out.

We estimated the cost of a relapse as the difference in average monthly costs between patients with and without relapse. Table 11 gives the results.

Table 11 Cost of a relapse around 2002 (NOK)

Cost category	Patients with relapse	Patients without relapse	Difference
Direct economic cost			
Best	24 975	20 329	4 646
Conservative	22 901	17 677	5 224
Total economic cost			
Best	51 993	40 986	10 007
Conservative	44 632	34 229	10 403
Total cost to society			
Best	72 692	55 578	17 114
Conservative	44 632	34 229	10 403

Experienced quality of life differed with 0,12 on the visual analogue scale (0,54 versus 0,66) between those experiencing a relapse and those not.

Comparisons with Sweden

The questionnaire we used in our study was structured so to facilitate comparisons of our results with the results obtained for Sweden in the study on the cost of MS to the Swedish society in 1998 (Henriksson et al., 2001). Their study was of special interest to us since it was for our closest neighboring country and also seemed to have been carried out in a way that corresponded well with the way we planned to arrive at our *best* cost estimates. Because of differences in the size of the two countries, costs *per patient* had to be compared. Henriksson et al. arrived at their per patient costs by dividing the national costs with the assumed number of persons in the *total MS-population* in Sweden - (not the *relevant* patient population). To arrive at comparable Norwegian figures we had to do the same.

Our best estimate of the total cost of MS to the Norwegian society around 2002 was NOK 4 033 million. Divided with our best estimate of the total Norwegian MS-population, 7 740 patients, this gave approximately NOK 521 000 per patient. Henriksson et al. found the Swedish total cost per patient to be SEK 688 136 in 1998, when the cost of reduced quality of life was included. Adjusted for an exchange rate of approximately SEK 100 = NOK 95 in 1998 and Norwegian inflation of approximately 10 % from 1998 to 2002, the Swedish SEK 1998-figures should be directly comparable to our own NOK 2002-figures, indicating a 32 % higher cost per patient in Sweden. From a health-economic point of view, this figure is only interesting to the extent it may reflect underlying real differences in the way MS-patients are taken car of, or economic conditions in the two countries. In this perspective, a closer analysis of the difference gives mixed results. Below, the difference is broken down to more detailed information on the individual subgroups of costs.

Table 12 Cost per patient information for the main subgroups of costs in Norway and Sweden. (NOK 2002)

	Norway	Sweden	Swedish costs as % of Norwegian costs
Drugs	36 920	48 455	131
Ambulatory care	20 191	33 119	164
Institutionalization	44 347	59 029	133
Support and assistance	85 711	156 287	182
MS-patients reduced participation in paid work *	219 299	145 577	66
Reduced quality of life	87 048	245 455	282

* Exclusive cost of premature death due to MS

The information in table 12 shows that the difference of 32 % between the Swedish and Norwegian total cost per patient conceals larger differences for some such subgroups, and if the cost numbers in table 12 are disaggregated further, even more striking differences are revealed.

Drugs

Our best estimate of Norwegian MS-patients total drug costs was NOK 285 759 000 or NOK 36 920 per patient. Henriksson et al. found the cost per patient to be SEK 48 445 in 1998. Adjusted for exchange rates and inflation, this is approximately 30 % higher than the Norwegian number. Henriksson et al. split the drug cost in three subgroups, the cost of immunomodulatory drugs, other prescribed drugs and OTC-drugs. We used a slightly different categorization of drugs used by Norwegian MS-patients. Direct comparisons of the information on drug use in the two studies are therefore somewhat problematic. However, if the information in the studies is recasted to information on the cost of immunomodulatory drugs, and of all other drugs, as is done in table 13, comparisons may be made

Table 13 Swedish and Norwegian drug costs per sub-group (2002 NOK)

	Sweden	**Norway**
Immunomodulatary drugs	46 992	32 041
Other drugs	1 453	4 795

Table 13 shows that the cost of immunomodulatory drugs per patient in Sweden was close to NOK 15 000, or slightly less than 50% higher than in Norway. This makes the difference in cost to immunomodulatory drugs larger than the total difference in drug costs. The difference in cost to immunomodulatory drugs was, however, to some extent offset by NOK 3 342, or 230 % higher cost to “other drugs” in Norway.

Ambulatory care

Our best estimate of the total cost to the Norwegian society of ambulatory care was NOK 156 275 000, or NOK 20 191 per patient. Henriksson et al. found the cost per patient in Sweden to be SEK 33 119 in 1998, close to 65 % more than in Norway, adjusted for exchange rates and inflation. In both studies specific information was gathered on the cost of visits to, or contact with a vide variety of professionals. Table 14 shows details of the number of visits per patient and year in the two countries [1].

Table 14 Number of visits per patient and year to ambulatory care practitioners in Norway and Sweden

Ambulatory care practitioner:	Visits of Norwegian MS-patients	Visits of Swedish MS-patients
Neurologist	4,1	1,8
General practitioner	0,8	2,4
Other specialists	0,9	-
Physician home visit	0,1	0,3
Nurse	9,2	1,5
Nurse home visit	6,5	42,5
Physiotherapist	26,4	20,9
Occupational therapist	6,9	0,6
Chiropodist	1,5	1,0
Speech therapist	0,8	0,1
Continence advisor	0,7	0,1
Psychologist	1,1	0,5
Social worker	2,0	0,3
Optician	0,7	0,7
Other paramedical practitioners	1,7	2,5
Total	63,4	75,1

The information in table 14 indicates that the by far most frequently visited ambulatory care practitioners in both countries were physiotherapists, and that these were visited somewhat more frequent in Sweden than in Norway (26,4 versus 20,9 visits per patient and year). The most striking difference is for nurse home visits. The average number per

[1] The figures for Norway have been calculated from information in table 5

patient of such visits were 6,5 in the Swedish study and 42,5 in the Norwegian. This may be explained, as will be showed later, by much more extensive use of personal assistants in Sweden. It might be noted, though, that Swedish MS-patients seem to visit nurses in the nurses´ office more often than Norwegian patients (9,2 versus 1,5 visits). Swedish patients also seem to visit neurologists more often (4,2 versus 1,8 visits), and general practitioners less often (0,8 versus 2,4 visits) than Norwegian patients. In addition, Swedish patients seem to make much heavier use of occupational therapists than Norwegian (6,9 versus 0,6 visits). For visits to other ambulatory care practitioners, the average number of visits per patient and year were around one or less, making the information on the number of such visits very uncertain, and also detailed comparisons of little value. The average total number of visits to ambulatory care practitioners was slightly less than 20 % higher for the Swedish patients. The difference of 65 % in the average cost per patient for the total number of visits is therefore primarily caused by generally much higher assumed costs per visit in the Swedish study (Henriksson et al. 2000).

Institutionalization

Our best estimate of the total cost to the Norwegian society of MS-caused institutionalization was NOK 44 347 per patient. In Henriksson et al.´s study the cost was SEK 59 047. Adjusted for exchange rates and inflation the number for Sweden is approximately 33 % higher than the Norwegian. There is some uncertainty, however, as to the comparability of these figures. The Norwegian number contains the cost of inpatient hospital care, rehabilitation and nursing home stays. The Swedish number contains inpatient hospital care and rehabilitation. The figures are only comparable to the extent that nursing home stays are included in the Swedish number for “rehabilitation”. If not, the cost of nursing home stays should be removed from the Norwegian number before comparisons, and if so, the Swedish number will exceed the Norwegian by close to 100 % (1998-SEK 59 047 versus 2002-NOK 30 404). Also some differences of even larger magnitudes can be found by a closer look at the underlying data for the two

countries. The average Swedish MS-patient spent 5 days a year in hospitals and close to 20 days in rehabilitations centers. For Norwegian patients the numbers were 1,2 and 5,0 if the number of days in nursing homes is removed from the Norwegian figure. The Swedish number exceeds the Norwegian by approximately 300 %. Therefore, when the total cost per patient number exceeds the Norwegian by less than this, the reason is that the unit cost numbers in the Swedish study are much lower than the Norwegian for inpatient hospital care and rehabilitation stays (Henriksson et al., 2000).

Support and assistance

Also when it comes to support and assistance, the Swedish estimate of the total cost to society exceeds the Norwegian by close to 100 %, seemingly reflecting the huge problems attached to estimate this cost element. The best cost estimate for Norway was NOK 663 402 000, or NOK 85 711 per patient. Henriksson et al. found the corresponding cost per patient to be SEK 156 287. However, the main part of this difference may to a large extent be explained by the cost of one specific kind of support, namely the cost of personal assistants. Leaving this cost element out, the cost per patient was NOK 78 133 in our study and SEK 66 725 in the Swedish study, a difference of a modest 15 %, which might seem to be a rather close fit. But also here a closer look at the underlying information reveals several striking differences. The cost per patient for home help, home care and child care was almost 60 % higher in our study than in Henriksson et al.´s study, even if the number of hours of such services received was more than 100 % higher in Sweden. The reason is that the cost per hour of such services used in our study was three to four times higher than in the Swedish study. The same pattern could also be found for informal care, adaptations made and items purchased. The cost per patient of informal care according to our study exceeded the Swedish cost by more than 120 %, even if number of hours of such care was more than twice as large for the Swedish patients. The cost per hour of informal care used in our study was four to five times larger than in the Swedish study. For adaptations made and items purchased, the costs per unit were set

50 % higher in our study than in Henriksson et al.´s study. Still the total cost per patient of adaptations and items purchased in the Swedish study exceeded the Norwegian cost by more than 130 %, due to much more extensive use of adaptations and helping aids in Sweden. Table 15 shows the difference in the percentage of the patients receiving specific adaptations and helping aids in the two countries.

Table 15 Percentage of the patients receiving adaptations and helping aids in Norway and Sweden

	Used/made by percent of the patients in:	
Kind of adaptation/items:	**Sweden**	**Norway**
Adaptation of kitchen	6	2
Adaptation of bathroom	17	5
Adaptations of other parts of the house	8	5
Roof lift	8	1
Lift	8	2
Ramps	10	3
Safety alarm	12	4
Adaptations at the job	1	3
Adaptation of the car	8	6
Wheelchair	23	10
Electric wheelchair	9	8
Electric moped	10	3
Walking stick	17	13
Rollator	11	5
Special kitchen utensils	11	4
Special writing devices	6	3
Other	13	9

MS-patients reduced participation in paid work

Our best estimate of the total cost of Norwegian MS-patients reduced participation in paid work was NOK 1 910 176 000, and NOK 246 793 per patient. Henriksson et al. found the corresponding cost per patient to be much lower, SEK 145 577. The Norwegian number includes the cost of early death because of MS with NOK 27 622. This cost was

not included in the Swedish study. Even adjusted for this however, the Norwegian cost number exceeds the Swedish by 50 %. Most of this remaining difference is due to a higher cost of labor used in our study (NOK 237 versus SEK 180 per hour).

Reductions in quality of life

The best estimate of the total cost of MS-patients reduced quality of life is NOK 673 750 000 in in our study, NOK 87 048 per patient. Henriksson et al. found the corresponding cost per patient to be SEK 245 455, nearly three times as large. The cost per QUALY lost is identical in the two studies and the difference is solely due to greater MS-caused quality of life losses in the Swedish study (0,49 versus 0,17 quality-adjusted life years lost per patient and year). In the Norwegian number, an assumed quality of life loss for relatives is included. When this is removed, the Swedish number is slightly *more* than three times higher than the Norwegian. Close to 65 % of this difference is due do measurement method differences, in that the loss was measured by the use of a visual analogue scale in our study and by combining the descriptive part of the questionnaire with population based quality of life values in the Swedish study. Close to another 20 % of the difference is explained by different corrections for normal quality of life losses felt in the general population, and the rest by Norwegian MS-patients reporting lower quality of life losses than the Swedish, as indicated in table 16.

Costs and quality of life for various EDSS-categories

The information on costs per EDSS-level from our study is given in tables 9 and 10.The Swedish study used broader EDSS-categories when costs and quality of life were related to illness severity. In tables 16 and 17 the results from our study are recasted to partly fit the format used by Henriksson et al.

Table 16 MS-patients experienced quality of life in different EDSS-categories in Norway and Sweden

EDSS-level / Studie:	1	2	3	4	5	6	7	8	9
Norway *)	82				71			62	
Sweden [1]	68				52			17	

[1] Henriksson et al., 2001
*) Precise comparisons with Sweden are difficult because precise corrections for differences in the patient inclusion criteria in the two studies is difficult

Table 17 Total cost the Norwegian and Swedish societies, total economic and direct economic cost per patient at different EDSS levels (NOK 1000)

EDSS / Cost category	≤ 3,0	3,5 -6,0	≥ 6,5
Total economic cost			
Norway *)	205,8	426,7	578,7
Sweden **)	109,1	256,2	717,4
Direct economic cost			
Norway *)	79,8	212,9	323,7
Sweden **)	28,2	118,2	464,8

*) Precise comparisons with Sweden are difficult because precise corrections differences in the patient inclusion criteria and different treatment of the cost of interferons in the two studies are difficult
**) Estimated from the Swedish data

Even if the information for the two countries in tables 16 and 17 is far from perfectly comparable, some patterns still seem to emerge. The experienced quality of life is higher for the Norwegian patients for all EDSS categories. The Swedish numbers are lower than the Norwegian for low and medium, but higher for higher EDSS-levels both for or direct and total economic cost per patient.

We started the comparison of our own study and the Swedish study by Henriksson et al. by stating that our findings on the total cost to society per patient differ by 32 %, the Swedish numbers being the highest. The difference may be characterized as modest, given the uncertainty that at least as for today, surrounds all such studies. An explanation may however be that the Swedish study was chosen for comparison because it seemed to have been carried out in a way that we found sound, and that we also wanted to follow in our own work. Closer comparisons, however, revealed much larger differences in the findings on more specific cost elements, often of more than 100 %. The closeness of the main result may therefore very well be said to be a result of pure luck, caused by many of the more detailed differences canceling each other out.

The Norwegian numbers may have been systematically somewhat understated, because of the assumption that for the patients who were excluded from the survey for ethical reasons, no cost would accrue to the Norwegian society because of their potential illness, even if the level of this understatement should hopefully be modest.

Discussion

The objective of this study has been to provide information for further economic analysis of the treatment of multiple sclerosis with immunomodulatory drugs. The study has provided information on the cost of MS to the Norwegian society in general, and on the cost and quality of life per patient at different EDSS-levels. Several studies have been carried out the last 20 years on the cost of multiple sclerosis to society. The results varies tremendously. For instance, in three studies on the yearly cost of an average MS-patient to society in Germany, United Kingdom and Sweden around 2000 the estimates varied from € 28 000 for UK (Kobelt et al, 2000 - I), through € 33 000 for Germany (Kobelt et al, 2001), and to € 45 000 for Sweden (Henriksson et al, 2001). By itself this should not cause concern if the estimates should be expected to reflect real differences in the costs between the countries. It may seem unreasonable though, that the costs should be that different. The clinical effects of the disease should not vary much between the countries, and neither do the treatment and help to the patients seem very different in general. The

problem is that if the estimates are not correct, but still are used for decisions that may be of outmost importance to the patients, as for example on treatment, these decisions may be quite arbitrary. The problem is further highlighted by looking at the variation in results over time, even within each country. For Sweden, the total yearly cost of MS to society was estimated to SEK 1 688 million in 1991 and SEK 1 876 million in 1994 (Henriksson, Jönsson, 1998), and to SEK 4 499 million in 1999 (Henriksson et al., 2001). In Germany it was estimated to DM 1 432 million in 1997/98 (Upmeier, Miltenburger, 2000) and to DM 2 977 million and DM 7 850 million in 1999 in two separate studies (Kobelt et al., 2001), (Kobelt et al., 2000 - II), and in UK it was estimated to GBP 118 million in 1986/87 (O´Brien, 1987), to GBP 283 million in 1993/94 (Blumhardt, Wood, 1996), to GBP 487 million in 1994 (Holmes et al., 1995) and to GBP 1 337 million in 1999 (Kobelt et al., 2000 - I). Even if it may be given good explanations for the differences, obviously not all the studies can have given "the truth" about the cost of multiple sclerosis in the three countries, and possible decisions made on the basis of the information might therefore not have been optimal. This is especially serious since such decisions might affect both the welfare and even survival of seriously ill people. One example of such decisions may be the different decisions made by UK and other countries´ health authorities on the use of β-interferons in the treatment of MS-patients during the 1990´s, partly on the basis of economic analyses that varied far beyond any reasonable levels (Jacoby et al., 1998), (Kobelt, 2000). This rise the question of how much or little confidence may be put in this kind of information, especially for our purpose, in Norway as for today.

In the health-economic literature it is usually stressed that no more effort should be put into the gathering of data and information for health-economic analyses than will be reflected in a comparable increase in the value of the studies results (Drummond et al., 2003). This is of course undisputable correct in principle. It may also be used by researchers, however, as an excuse to stop data search prematurely, especially since it is almost impossible to calculate the effect of more extensive data search on the value of the studies results. To try to avoid become victims of such temptations we chose a rather basic approach to our research question. We started by raising the question: "Concerning

information, how must the situation have had to be if it should have been possible to set a numerical target for the total cost of an illness to society 100 % correctly?" After that, the best answer that could be found to this question guided our work. This answer was that ideally, all the use of resources and all reduced generation of welfare due to the illness should have been routine recorded, together with their alternative values to society, somewhat in the same way as parts, material and mechanics´ time etc. are recorded and priced in car workshops. For MS, this would for instance mean that whenever a MS-patient took an aspirin or two because of the MS this should have been recorded and related to MS together with the aspirins´ alternative value to society, while aspirins taken for other purposes should not be recorded. Similarly, if relatives had taken a day off from work to nurse a patient, this should have been recorded as a MS-cost, but not if they had dropped work for other reasons. Such recording of all use of resources and their alternative values to society, and all reductions in potentially welfare-generating activities, is of course not done systematically in any country for any illness or disease. Still it is done, though, for some cost elements due to some illnesses and diseases. In our work we made considerable effort to use such information whenever it could be found. Further, for cost elements where such information could not be found, the same effort was made to try to find information that might be expected to come as close as practically possible to the ideal. In addition we have tried to follow a philosophy of not excluding any cost element on the assumption that it would probably be of so modest magnitude that checking it further would be a waste of time and resources. Also, no data or information has been accepted to be of acceptable quality without closer evaluation. Finally, we have also gathered information from different sources where practical, to check for consistency. Still after all this effort, our results are very uncertain.

Table 1 showed a conservative estimate of the total yearly cost of MS to the Norwegian society around year 2002 of NOK 1 836 million, and a best estimate of NOK 4 033 million, the best estimate being more than twice as large as the conservative. Our work indicates that the difference may be explained by three factors: Uncertainty on what elements should be included in cost-of-illness studies. For example, should "the cost of reduced quality-of-life be included? Uncertainty on how some cost elements should

valued. For example, what is the economic value of quality-of-life or leisure time? And finally, the combined effect of differences in information on the same phenomena in different sources of information, and the researchers´ choices on how to handle them.

It is difficult to separate the effect of the factors 100 %. For example is the difference between the conservative and the best estimates of the cost of reduced quality-of-life due both to uncertainty on how quality-of-life should be valued economically, and on whether it should be included in cost-of-illness studies at all. Similarly is the difference between the conservative and best estimate of the cost of visits to neurologists in hospitals due both to differing information in different sources on the number of such visits, and on uncertainty on how numerical targets for the cost to society of each visit should be set. If, in such cases, the differences that may be attributed to two or more factors in combination are allocated evenly to each factor, slightly less than 50 % of the difference between the conservative and the best estimate of the total cost of MS to the Norwegian society can be said to be due to uncertainty on how cost elements should be valued, and slightly more than 25 % to each of the remaining two factors: uncertainty on what elements should be included in cost-of-illness studies and differences in information from different sources, and the researchers´ choices on how to handle them.

Even though the part of the difference that is explained by the two first factors accounts for approximately 75 % of the total difference, this part of the difference may not be the most important from a decision making point of view. This is so because these two causes of uncertainty in the results are well known, and in well presented cost-of-illness studies there should also be clearly stated what choices have been made with respect to how cost elements have been evaluated and which ones are included or excluded. The most grave part of the difference is that which can be explained by differing information in different sources of information, and the researchers´ choices on how to handle them, since the only reason it surfaced in our study is that we had the opportunity and patience to gather and compare such information. Had this not been done, this uncertainty for the setting of a numerical target for the cost of MS to the Norwegian society would not have been known, and decision makers might have run the risk of using incorrect information

as a basis for their decisions without being aware of it. Decision makers would probably have put the same confidence in numbers "collected through a postal survey among a sample comprising 10 % of the total national patient population", especially when also assured that the sample was chosen to be reasonably representative, as they would have put in numbers "provided by the Norwegian Bureau of Census" or the National Patient Register. The problem is, however, that the numbers gathered from these sources might differ by several 100 %, as illustrated in the text.

Because of dissimilarities in methodology, perspective, definitions, evaluation principles and data sources used in different quality of life and cost of MS-studies, comparisons of findings from different studies may in general be of limited value. Still, we found the Swedish study by Henriksson et al.from 2001, to be of special interest for comparisons with our work because their study was for our closest neighboring country and also seemed to have been carried out in a way that corresponded well with the way we planned to arrive at our own best cost estimates for Norway. Also, the total cost per MS-patient turned out to be reasonably similar in the two countries. A closer look beneath this surface, however, revealed dramatic differences in several instances.

Relating the information on cost of MS and the patients´ experienced quality of life to illness severity adds still more uncertainty both because less information will be available for each individual level of severity, and because of additional methodological imperfections and difficulties.

Conclusion

The huge uncertainty found for almost all the results of our study, indicates that at least Norway, but probably also other countries have a long way to go before studies like our in general might be regarded as providing acceptable information for decisions as important as those in the health sector.

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