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Costs and quality of life in multiple sclerosis in Europe

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ABSTRACT

Objectives: To assess overall resource consumption, work capacity, and quality of life (QoL) of patients with multiple sclerosis (MS) in nine European countries.

Methods: Information on resource consumption related to MS, informal care by relatives, productivity losses, as well as overall QoL (utility) was collected with a standardized pre-tested questionnaire from 13186 patients enrolled in national MS societies or followed in neurology clinics. Disease information collected included disease duration, self-assessed disease severity, and relapses. Mean annual costs per patient (€, 2005) were estimated from the societal perspective.

Results: The mean age ranged from 45.1 to 53.4 years, and all levels of disease severity were represented. Between 16% and 29% of patients reported having experienced a relapse in the 3 months preceding data collection. The proportion of patients in early retirement due to MS ranged from 33% to 45%. The use of direct medical resources (e.g. hospitalisation, consultations, drugs), varied considerably across countries, while the use of non-medical resources (e.g. walking sticks, wheelchairs, modifications to house and car), and services (e.g. home care, transportation) was comparable. Informal care use was highly correlated with disease severity, but was further influenced by health care systems and family structure. All types of costs increased with worsening disease. The total mean annual costs per patient (adjusted for GDP purchasing power) were estimated at €18,000 for mild disease (EDSS <4.0), €36,500 for moderate disease (EDSS 4.0-6.5) and €62,000 for severe disease (EDSS >7.0). Utility was similar across countries at ~0.70 for a patient with an EDSS score of 2.0 and ~0.45 for a patient with an EDSS score of 6.5. Intangible costs were estimated at around €13,000 per patient.

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Introduction

Treatment of multiple sclerosis (MS) has changed over the past 10 years as a number of new potent therapies were introduced in an area where treatment options had been limited. Compared to the old and inexpensive symptomatic treatments, the new disease-modifying drugs (DMDs) appear costly, and it must be expected that health care costs for MS have increased. Also, the new treatments are likely to lead to more intensive patient management, thus potentially, further increasing costs. Finally, as knowledge of MS has improved, pathological and therapeutic criteria have been modified and diagnosis often occurs earlier, increasing the patient population that is eligible for treatment, thus potentially increasing treatment costs. As a consequence, the interest in economic evaluation of MS has intensified.

The relevant economic question today is whether investment in more costly treatments is a good use of scarce resources. Evidence of the cost-effectiveness of new treatments must be demonstrated in order for these agents to be adopted and paid for by health care services. However, cost-effectiveness analysis in MS is not straightforward. The objective of MS therapy is to avoid temporary disability due to relapses, and more importantly, to delay progression to more permanent disability. Thus, the major economic benefit of treatment lies

in the future; savings will come from delaying or preventing patients' progression to more severe disease, which is associated with high costs and low quality of life (QoL). However, clinical trials are too short to provide full evidence of the benefits of DMDs, and modelling has become the accepted standard for economic evaluation in MS.

Cost-effectiveness models in MS combine epidemiological data on the natural history of the disease, consumption of health care and other resources, work capacity over the entire course of the disease, QoL related to disease severity, and data on the effectiveness of treatments to change the disease course.¹⁻⁹

Current data on the overall burden of MS in Europe are scarce. A number of cost studies were performed in the early and mid-nineties,¹⁰⁻¹⁶ when DMDs were not yet established as part of standard treatment. Thus, the findings of these studies may no longer be accurate. Other studies have focused on patients treated with DMDs,^{17, 18} and findings are therefore not representative of the total patient population.

The objective of this European-wide observational study was to establish the current cost of MS at different levels of disease severity, in order to provide a basis upon which the economic impact of new treatments can be estimated. It is possible to combine this information with good data on the prevalence of MS including prevalence at different levels of severity, to estimate the total cost of MS in a given country or geographic area.

Patients and Methods

The study is based on the methodology used in several earlier studies of MS in Europe and the United States.^{15, 16, 19,20} Information on demographics, resource utilisation, work capacity, and QoL was collected in a cross-sectional anonymous mail survey. The aim was to enrol patients at all levels of disease severity to allow estimation of the effect of progressing disease on costs and QoL.

Study Subjects

The study was performed in nine European countries, in collaboration with neurology clinics and national MS societies. In six countries, the questionnaire was mailed by the MS societies to their members (Austria, Italy, Spain, Sweden Switzerland, United Kingdom). In the three remaining countries (Belgium, Germany, Netherlands) MS societies had other ongoing surveys at the time of this study, and patients were therefore enrolled solely through neurology clinics, with appropriate ethical approvals.

The questionnaire informed patients about the purpose of the study and about how data would be used. Patients provided written consent to use the information they provided for research and publication.

Data

The questionnaire asked for background information on age, gender, marital status, living situation, education level, employment status, and QoL. Disease information was limited to age at first MS symptoms, year of diagnosis, type of MS, exacerbations during the past 3 months, and a self-assessment of disability. A description of disease severity was developed and tested in a small sample of patients prior to inclusion in the questionnaire. This scale focused on ambulation, and was based on the original description in the Expanded Disability

Status Scale (EDSS)²¹ and on the Patient Determined Disease Steps (PDDS) instrument²².

The objective of the study was to determine the cost of *MS*, as opposed to the cost of a *patient* with MS. Patients were therefore asked to include only consumption related to MS. Different recall periods were used for different resources, based on experience in previous studies. Questions regarding inpatient admissions, consultations, investigations and short-term absences from work related to the past 3 months; medication, services such as home care, informal care from family and friends related only to the past month; and major investments such as wheel chairs, scooters, or transformations to the house and car related to the past year. In addition, working patients were asked to indicate whether they had to change their type of work or working hours because of MS, and patients on early retirement were asked to confirm that it was due to MS.

Data on QoL was collected as utility using a generic preference-based instrument, the EQ-5D.²³ The EQ-5D covers five domains of health-related QoL (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with three levels of answers (no, some, and severe problems). The resulting combination of answers can then be translated into utilities via a social tariff established with the general population using decision-analytic methods (time-trade-off).²⁴ Although reference scores for the EQ-5D are available in a number of countries, the tariff for the United Kingdom is the only one in Europe based on decision-analytic methods (time-trade-off),²⁵ and has been widely used, including in MS. In order to compare results across countries and to earlier studies, it was used for all countries in this study.

Data Management and Analysis

Completed questionnaires were entered into an online database that included both numerical and logical checks in order to minimise errors. Prior to analysis, missing answers and outliers were systematically verified. In a small number of situations (e.g., when a patient had indicated having used a resource, but had omitted the quantity), the mean quantities for users of the same resource were imputed. For some items (e.g., investments), patients were asked to indicate the cost because no standard unit costs would have been available. To avoid problems with potential outliers, we assumed that no such costs would be higher than the sample mean + one standard deviation.

Unit costs were obtained from a number of publicly available sources and telephone interviews, and if necessary, adjusted to 2005 prices using the consumer price index. Utilisation was annualised and the main analysis was performed from the societal perspective, using opportunity costs regardless of payment. In countries with social insurance systems, costs are also presented from the payer perspective (health care and social services).

Hospitalisation was generally based on admissions using diagnosis-related groups (DRG), while inpatient stays in nursing homes or rehabilitation centres were based on *per diem* costs. Consultations were based on a cost per visit, while sessions with health care professionals such as physiotherapists were estimated using the average duration of a session. The cost of medication was estimated from average public prices across pack sizes, dosage strengths, and recommended doses. Where generics were available, the prices of branded and generic products were weighted according to the estimated generics penetration in each country. MS-specific drugs were generally assumed to be self-injected (except for a small proportion of patients using once-per-week intramuscular interferon beta-1a, where injections were performed by a nurse). Over-the-counter medication and investments were based directly on patients' indications.

Production losses were valued using the human capital approach where the production of an individual is valued at the market price (in this case the gender specific average salary including employers' costs). For short-term sick leave, labour costs were adjusted to individual patients' working hours, while for long-term sick leave and early retirement due to MS the national average annual working time by gender was used. This method of estimation of indirect costs is the most commonly used in economic studies, although it has been suggested that it may overestimate costs, as particularly in times of unemployment, a worker would be rapidly replaced and hence no production loss would occur. A different method of calculation (friction cost method²⁶) has therefore been proposed, but it is not generally used.

Informal care was valued using the net disposable income after taxes. Other methods to estimate informal care include the replacement method, where the care would be provided by a professional rather than a family member, or production losses for family members that are working. The former may lead to an overestimation, as not all informal help would be performed by a professional, while the latter assigns no value to time spent by non-working family members.

The mean cost of an MS relapse was calculated as the difference in costs during the preceding 3 months between patients with a relapse and those without. Calculations were based on patients below EDSS 5.0, as relapses are more frequent in early disease and may have a larger impact on patients with limited permanent disability.

Finally, an estimate of intangible costs (i.e., costs due to pain, grief, anxiety, and social handicap) is also presented. These costs are generally omitted in cost-of-illness studies, while in cost-effectiveness analyses they are included in the outcome assessment. We calculated the loss of quality-adjusted life-years (QALYs) from the difference in utility scores between MS patients in the samples and the general population in the respective country matched for gender and age. By assigning a monetary value to a QALY (e.g. €50,000 or three times gross domestic product (GDP) per capita²⁷), intangible costs can be calculated.

Results

Patients

The study included a total of 13186 patients at all levels of disability (**Figure 1**). However, due to the survey methodology used, and the difficulty of completing an extensive questionnaire, the number of patients with very severe disability (EDSS 9.0-9.5) was somewhat limited at slightly over 1% of the sample and the prevalence of these patients may be underestimated.

Table 1 presents the main characteristics of the samples. The sample size in the different countries ranged from 799 to 2793 patients, with response rates varying between 19% and 75%. Patients recruited in neurology clinics tended to have a shorter disease duration and less permanent disability (lower mean EDSS scores) than patients recruited by patient associations. In contrast, patients recruited by neurology clinics had a higher number of relapses. This is not unexpected because such clinics are most likely to follow patients with active disease.

The proportion of patients who were working ranged between 25% and 40%, depending to some extent on the proportion of patients over 65 years in the samples. However, no obvious relation with disease status of the sample was evident. Similarly, while on average 35% of patients were in early retirement due to MS, the proportion was considerably higher (around 45%) in Austria, Netherlands and the United Kingdom. The reasons for this were not obvious. Likely, these results reflect differences in general workforce participation and

handling of long-term sick leave and invalidity pensions in different countries, rather than differences in the samples or disease severity. However, the effect of the disease on employment is very pronounced (**Figure 2**). While at EDSS scores between 0.0-1.0 approximately 70-80% of patients below 65 years are employed, this proportion is below 10% for patients with EDSS scores of 8.0-9.0. In addition, a number of employed patients were on long-term sick leave at the time of the survey, reducing the number of patients actually able to work. Lastly, more than 50% of patients indicated that they had had to reduce the number of hours worked or change their type of work. Most often this was associated with a loss of income (not included in this analysis).

Resource Use

The utilisation of direct medical resources is often not only influenced by the disease, but also by the organisation of the health care system, medical tradition, ease of access, and availability. This becomes evident when comparing consumption across the countries. Despite the relative similarity of the samples, there is substantial variation in inpatient admissions and length of stay, medical consultations, physiotherapy and the use of DMDs (**Table 2**). Similarly, although the proportions of patients that use services such as home help or that make investments such as modifications to the house or the car are more comparable across the countries than the proportions using other health care resources, their availability and/or their cost nonetheless influences consumption. Thus, there are considerable differences in the intensity of the usage of services, as different countries provide different levels of service. A good example is Sweden, where patients with severe diseases are offered extensive support through personal assistants employed by the health care system. Other countries appear to provide very limited support and patients therefore require substantial help from friends and families (e.g., in Italy or the United Kingdom). Also, informal care is influenced by tradition and family structures. In countries where the proportion of women at home is larger, the use of informal care may be higher due to both availability and the type of activities that are reported as informal care by respondents.

Table 1 – Characteristics of the Samples

	Austria	Belgium	Germany	Italy	Netherlands	Spain	Sweden	Switzerland	United Kingdom
Recruitment *	NMSS	Clinics	Clinics	NMSS	Clinics	NMSS	NMSS	NMSS	NMSS
Response rate (%)	35	38	38	31	52	32	75	45	19
Sample size (No)	1019	799	2793	921	1549	1848	1339	1101	2048
Proportion women (%)	70.4	68.0	72.2	65.8	69.1	64.2	73.0	63.8	74.5
Proportion living alone (%)	28.1	18.8	21.1	12.5	15.5	9.7	27.9	22.6	14.3
Mean age	50.0(12.2)	48.1(12.6)	45.1(11.1)	46.1	46.7(11.1)	44.7(10.8)	53.4(12.0)	52.5(12.8)	51.4(10.7)
Proportion aged 65+ (%)	13.0	12.4	17.7	8.5	7.6	5.5	16.1	21.4	10.3
Proportion employed and working (%)	28.5	33.9	35.3	40.6	32.2	26.2	24.3	31.3	24.9
Proportion employed but on long term sick leave (%)	1.9	5.8	5.6	1.5	5.2	3.8	16.5	3.4	3.3
Proportion on early retirement due to MS	44.5	32.9	33.9	33.3	42.2	34.1	35.6	33.9	44.3
Mean age at diagnosis	34.7(10.4)	35.3(10.8)	35.0(10.2)	33.8(10.3)	37.0(10.2)	33.0(9.9)	39.3(10.7)	36.2(10.6)	38.8(10.0)
Mean age at first symptoms	31.5(10.2)	31.8(10.7)	31.8(10.0)	29.9(10.0)	31.2(9.9)	29.5(10.0)	32.0(10.7)	33.4(10.9)	32.2(10.4)
Mean EDSS	4.4(2.4)	4.2(2.4)	3.8(2.3)	4.6(2.3)	3.9(2.2)	4.5(2.3)	5.1(2.2)	4.5(2.4)	5.1(2.0)
Proportion with relapse (past 3 months) (%)	16.8	21.5	24.4	21.5	29.2	22.6	18.0	16.3	28.9
Proportion unsure regarding relapse or missing (%)	13.0	16.1	16.3	29.3	27.4	17.2	26.7	14.5	0

* NMSS = National MS Societies (patient associations), Clinics = Neurology clinics

Table 2 – Resource consumption

	Austria	Belgium	Germany	Italy	Netherlands	Spain	Sweden	Switzerland	United Kingdom
<u>Hospitalisation</u>									
% patients with admissions	25.8	19.0	24.5	15.6	7.9	17.0	12.2	13.2	6.7
Mean (SD) number of inpatient days per year	27.9(70.1)	20.9(66.8)	20.6(51.2)	12.1(46.1)	5.7(31.6)	8.4(33.1)	10.5(46.7)	20.0(71.8)	5.0(32.4)
Of which neurology	8.1	7.0	10.4	3.0	1.2	2.8	1.0	0.6	0.7
Of which rehabilitation	11.1	8.3	7.6	5.3	0.8	3.2	6.1	3.9	1.1
Of which nursing home	6.6	4.6	1.4	2.3	3.4	1.5	2.4	14.2	2.0
<u>Consultations</u>									
Mean (SD) number of medical and paramedical visits per year	35.6(58.0)	37.5(73.7)	37.0(50.8)	28.8(44.1)	17.3(28.1)	46.5(79.1)	14.7(28.7)	21.2(35.1)	45.4(36.6)
Mean (SD) number of physiotherapy sessions per year	11.6(25.7)	67.6(89.9)	41.4(47.3)	31.3(48.1)	25.5(44.7)	29.1(52.5)	13.9(27.2)	26.0(38.9)	8.2(18.8)
<u>Medication</u>									
% patients using disease modifying drugs	39.8	49.7	50.3	42.6	35.5	52.4	42.6	37.9	20.6
<u>Investments, services</u>									
% patients with investments	25.6	31.7	27.4	20.5	28.7	40.0	29.3	33.5	46.0
% patients using services	24.5	37.3	25.0	30.6	40.6	28.2	40.4	39.5	19.8
<u>Informal care</u>									
% patients using informal care	57.9	51.3	47.5	56.4	52.2	52.9	56.6	48.0	62.2
Mean (SD) number of hours/year	1024(1956)	664(1521)	497(1175)	1668(2400)	434(1017)	1341(2453)	498(1064)	601(1514)	1144(2149)

Costs

Total costs per patient are a function of both the quantity of a given resource used and its unit cost, as well as the patient sample included in the study; therefore, comparisons across countries should be made with great care. This is the case even in a study like ours where both data collection and analytical methods have been standardised (except for the United Kingdom where data handling and analysis were slightly different). Unless the results are linked to detailed prevalence data by severity, costs for the total MS population and the mean cost per patient cannot be accurately estimated. Therefore, we present overall results for patients with mild, moderate, and severe disease (**Figure 3**), proportions of costs represented by different resource types (**Figure 4**), and more detailed consumption for given levels of disability (EDSS 2.0 and 6.5) as examples (**Table 3**).

DMD usage varied between 21% (United Kingdom) and 52% (Spain) among the countries, and was concentrated in early disease (**Figure 5**). This had a considerable influence on the average cost per patient in the samples. However, it did not influence other costs, as it was found that these were not different for patients with or without DMDs at the same level of EDSS and in the absence of a relapse. Thus, any effect on costs of these treatments will be through a reduced relapse rate and slower disease progression.

The cost of an MS relapse was similar across the countries, ranging between €2800 and €4000 with one exception (€5800 in Austria).

Utility and Intangible Costs

Unlike costs, utilities were almost identical across countries (**Figure 6**), illustrating the consistency of disease definition across geographies and the strong correlation between disability and QoL. Similarly, the loss of utility during a relapse was comparable across countries, at around 0.1.

The utility loss due to MS translated into a mean QALY loss per patient of 0.27 (range 0.21 to 0.32) and an intangible cost of €13 400 (range €10 300 to €15 400) yielding a willingness to pay for a QALY of €50 000. When three times GDP per capita is used, the mean intangible cost is estimated at € 19 800, with an expected larger variation (€12 100 to €33 000).

Table 3 – Mean costs per patient at EDSS 2.0 and EDSS 6.5 (2005 €)

Patients at EDSS 2.0	Austria	Belgium	Germany	Italy	Netherlands	Spain	Sweden	Switzerland	United Kingdom
Utility	0.719	0.649	0.721	0.677	0.694	0.717	0.696	0.767	0.725
Total costs	26348	22276	27910	21683	20517	19604	27254	18538	19679
(SD total costs)	(22818)	(20254)	(21905)	(19472)	(18849)	(21025)	(31396)	(21877)	(19170)
Direct costs	18132	13582	18305	15067	9676	13604	16462	10707	9537
Inpatient care	2979	1387	1807	1840	544	2240	4449	417	94
Outpatient care	4528	1902	2205	1215	1370	1131	2750	1419	3512
Tests	307	221	155	669	210	348	368	212	63
Drugs	8807	7426	12881	7610	5027	7964	7459	6919	4324
Services	192	319	79	493	1176	155	139	518	102
Investments	133	466	171	169	259	231	211	120	160
Informal care	1185	1861	809	3071	1089	1534	1086	1102	1282
Indirect costs	8216	8694	9605	6616	10842	6000	10792	7831	10142
Patients at EDSS 6.5	Austria	Belgium	Germany	Italy	Netherlands	Spain	Sweden	Switzerland	United Kingdom
Utility	0.447	0.384	0.440	0.442	0.477	0.431	0.462	0.540	0.477
Total costs	54821	43790	55344	53717	44196	44104	52457	49274	53724
(SD total costs)	(31791)	(25295)	(20761)	(32016)	(26744)	(30198)	(47567)	(37477)	(41532)
Direct costs	31634	26000	28948	37355	23093	31517	32630	26804	33179
Inpatient care	7886	2784	4989	5316	2175	3284	6913	3652	1340
Outpatient care	6380	5194	4785	2196	2239	3564	3003	2461	5440
Tests	197	306	366	397	155	332	126	207	78
Drugs	7218	7724	7377	4089	4245	5505	5572	5904	2962
Services	742	2028	946	1702	4876	1714	8978	3479	2368
Investments	2189	2691	2769	1439	2564	1714	1592	6046	2609
Informal care	7022	8545	7715	22215	6839	14715	6445	7196	18382
Indirect costs	23187	17790	26396	16362	21103	12588	19827	22471	20545

Exchange rates: 1€ = 9.07 SEK, 1.56 CHF, 0.688 GBP

Discussion

This is the largest burden of illness study performed in MS to date. Resource consumption amongst patients is highly variable and the large samples included in the individual countries lead to less uncertainty in the results compared with earlier analyses. However, there are a number of issues that merit discussion.

The inclusion of several countries with historical differences in their approach to health care and disease presents a challenge. As data collection must be standardised to a large extent, there is a risk of losing information on some country-specific particularities. However, the advantages of standardisation prevail, and for the first time it is possible to analyse differences between countries, be they due to the organisation of the health care systems, traditions, consumption, prices or the economic environment. All of these factors strongly influence the outcomes, and even in a standardised study such as ours, it is not possible to compare the mean annual cost per patient without explaining the underlying differences.

There were differences among our national samples in patient demographics, consumption patterns, handling of early retirement and sick leave, and the price of individual resources including the cost of employment. Analytical methods, usually one of the largest factors leading to differences in study results, play a limited role when comparing results among the countries within our study. However, they will explain some of the differences compared with earlier studies.

Selecting a patient sample that is fully representative of the prevalence of a disease is difficult because estimates of prevalence differ. The objective of this study was to estimate costs at each level of severity rather than to obtain a true population sample. Nevertheless, by adjusting to prevalence by severity, it is possible to estimate the total burden of the disease in each country.

Patients were recruited either through MS patient associations or through neurology clinics, and the two approaches may have led to slightly different samples. The average EDSS score was 4.8 in the six countries where patients were recruited from patient associations, compared to 3.9 in the three countries with samples from neurology clinics. This can be interpreted in two ways. Patient associations may include people with more advanced disease, since it may take some time for patients to join these associations, and because patients with more severe disease may be more likely to look for support. Neurology clinics, on the other hand, may see more patients who are earlier in their disease process, particularly in MS where DMDs are indicated for relapsing disease and early treatment is advocated. Thus, such samples are likely to be biased toward earlier disease. The truth may lie somewhere in between. Whatever the reason, however, there was a considerable difference with only 6.8% of patients in the three clinic samples having an EDSS score of 8.0 or higher, compared with 12.9% of patients in the samples from patient associations. Regardless, since the main purpose of our study was to estimate costs and utility stratified by disease severity, the number of MS patients at each EDSS level does not pose a problem for our analyses because members of a patient association would not have more severe disease at a given EDSS level.

Another bias in the samples recruited in neurology clinics could arise from selecting patients on the dependent variable (consumption). Indeed, it could be

that patients who are currently being followed are patients with a high consumption of health care resources. However our study included all patients on file in the clinics, rather than patients with recent contacts. Consumptions should therefore be representative.

As expected, health care utilisation was quite variable across countries, reflecting differences in the organisation of health care systems, financial incentives, access, and traditions. For instance, in countries where hospitalisation is, or has until recently been paid by a daily rate, both the number of admissions and the length of stay are substantially higher (e.g., Austria, Belgium, Germany). Similarly, the number of medical visits is high in countries with more office-based medical or paramedical practices and hence easier access, often combined with fee for service payment. Good examples of this are Belgium, Germany, and Spain, which have a high frequency of both medical visits and physiotherapy sessions. Contrary to this, in countries where specialist consultations are mostly limited to hospitals, as in Sweden, or are capitated as in the Netherlands, the number of visits is lower. The proportion of patients who had to make investments or required services such as home help or transportation was more similar across countries. It appears that these requirements are driven to a large extent by the disease and disease severity, with patients assuming all or part of the cost. The intensity of usage does differ, however, likely as a consequence of availability.

Informal care appears to be influenced by several factors. Although the proportion of patients using informal care was strikingly similar across the samples, the number of hours was very different. While patients in the three samples with earlier disease (Belgium, Germany, Netherlands) received around 500 hours of informal care per year, this amount was double or triple that in some of the countries with more severe patients. This difference cannot be explained by a difference in disease severity alone. The amount of informal care is generally a function of the extent of services offered by the health care systems. A good example of this is Sweden, where patients with severe disability have access to personal assistants who are funded by the system. As a consequence, the use of services is highest in Sweden, while the use of informal care is among the lowest, despite of the fact that the sample has the highest EDSS. Contrary to this, countries like Italy or the United Kingdom appear to offer limited services, leading to more use of informal care. There also appears to be an influence of the family structure. In countries where fewer women are employed outside the home, informal care is more readily available and usage therefore higher. Also, in these countries, fewer patients live alone (around 10-12% in Italy and Spain compared to over 25% in some of the other countries). Similar results were found in some of the earlier studies.^{15, 16,14, 19} Lastly, it is possible that patients in different cultures include different things under the concept of informal care.

Finally, the cost per patient is driven by quantities of resources used and their price, and these prices differ across countries and settings. In countries with a national health system such as Sweden and the United Kingdom, unit costs are derived from overall usage and are likely to represent opportunity costs, while in fee for service systems they represent tariffs which may include other incentives. In general, the former are considerably higher, e.g. the cost of a medical consultation with a neurologist in Sweden or the United Kingdom has a cost of over €200, compared to €19.18 in Germany. Quantities, prices, and availability

also drive the share of costs represented by different types of resources (Figure 4).

Productivity losses still represent the highest single contributor to societal costs, but the proportion is lower than found in studies in the early nineties when direct costs were very low. Despite this, costs borne by payers such as the health care sector or social services represent only around half of the total cost per patient in most countries.

All information in our study was collected from patients, with no opportunity to clarify or verify responses due to the anonymity of the answers. However, we have shown earlier that patient reporting is highly accurate despite potential cognitive difficulties in this patient group and general recall bias.¹⁹ For instance, in a study in Germany, the difference between the mean number of hospitalisation days reported by 200 MS patients and the mean abstracted from their medical records was half a day.¹⁹

Patients were also asked to assess their EDSS based on descriptions from the original instrument focusing primarily on ambulation.²¹ This may appear to be a limitation in the validity, but a pre-test of the questionnaire in a small sample had shown a good correlation with EDSS, and in particular the PDDS has been found to have a very high correlation.²² Patients did appear to have difficulties in distinguishing between relapsing and progressive disease, however, and we did not include this distinction in the analysis. Earlier studies have shown that costs were not different for patients with different courses of MS at the same level of EDSS, when controlling for relapses.⁵

A very striking finding in the study is that utility scores by EDSS are virtually the same across the countries. This confirms the overwhelming impact of MS on QoL, but is obviously also the consequence of the fact that the same health state tariff for the utility instrument (EQ-5D) was used.²⁴ Over 1 year, patients lose on average a third of a QALY compared to the general population, leading to an average cost increase of €15000 or 30% due to intangible costs.

Conclusion

Costs for patients with MS in Europe increase more than three- to four-fold for patients with severe disease (EDSS >7.0) compared to patients with earlier disease (EDSS <4.0), and there is a substantial detrimental effect of advancing disease on QoL. Using drugs that slow disease progression early on, thus avoiding or delaying the severe disease states where patients are unable to work and become dependent on help from their family, will provide large benefits to society.

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Legend to figure 1

All levels of disease severity (EDSS) were represented. Patients with limited disability were overrepresented in the German sample, where in addition to patients in specialized clinics a panel of patients with early disease who had earlier expressed an interest to participate in surveys was included.

Legend to figure 2

The proportion of patients employed or on long-term sick leave is calculated as a percentage of patients aged 65 or below. The reduced work-capacity particularly at EDSS 2-3 compared to EDSS 4 is explained by an increased frequency of relapses in this group and hence a concentration of sick-leaves. A similar finding can be seen in Figure 6 where utility at EDSS 3 is relatively low.

Legend to figure 3

Patients are grouped into mild disease (EDSS 0 – 3.5), moderate disease (EDSS 4.0 – 6.5) and severe disease (EDSS 7.0 – 9.5) and total mean annual cost per patient calculated from the societal perspective. Local currencies have been transformed using the GDP purchasing power parity index (OECD 2004).

Sweden and UK have the highest costs, particularly in advanced disease. In Sweden, this is clearly a consequence of the special service of personal assistants provided to people with disability, which e.g. in the severe patient group represents 43% of total costs, while in the UK it is a consequence of a very high use of informal care associated with high revenues and a strong currency.

Legend to figure 4

Costs are presented as percentages of total cost per patient in each country, from the societal perspective (all costs regardless of who pays). Other direct costs include all medical care (hospitalization, consultations, tests, prescription and OTC drugs excluding DMDs), services (home care, home help, transportation) and investments (devices, appliances, changes to house and car). Informal care is calculated as loss of leisure time for the carer, using the disposable income (net after social contribution and taxes) as the cost of leisure time.

Legend to figure 5

Treatment with DMDs is presented as a proportion of patients treated at each level of EDSS. DMDs include interferon-beta 1a (Avonex), interferon-beta 1b (Betaferon, Rebif), glatiramer acetate (Copaxone).

The Belgian sample at EDSS 3 appears as an outlier with a number of untreated patients in severe relapse, translating into low work capacity (Figure 2), low utility (Figure 6) and high costs.

Legend to figure 6

Utility scores are calculated in all countries using the original EQ-5D health status system²⁴, in order to obtain comparable values. The EQ-5D allows negative scores (i.e. health states worse than death) and negative scores have been set to 0 in our study

Figure 1 – Patients by EDSS per country (N = 13186)

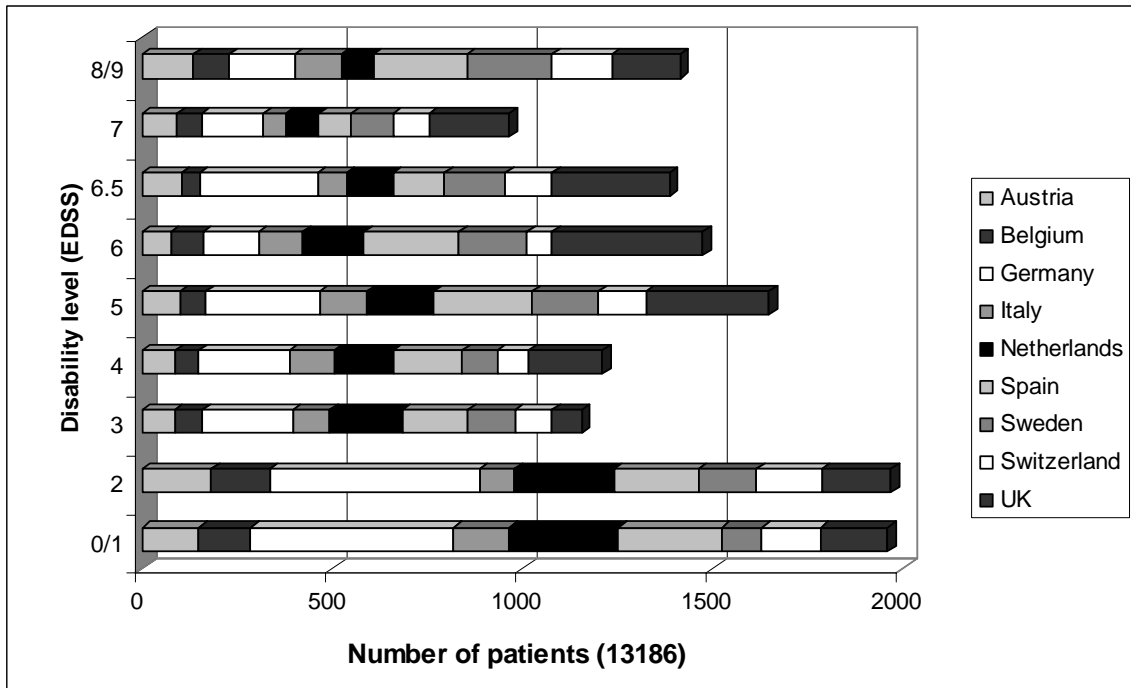


Figure 2 – Employment of patients with MS

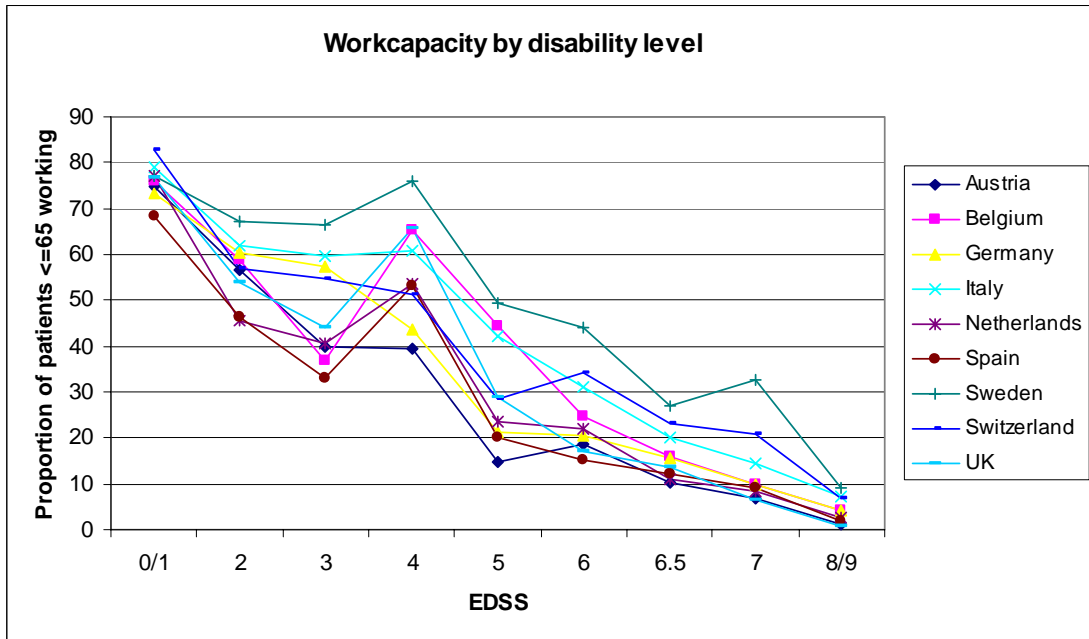


Figure 3 – Mean total annual cost per patient by level of disease severity

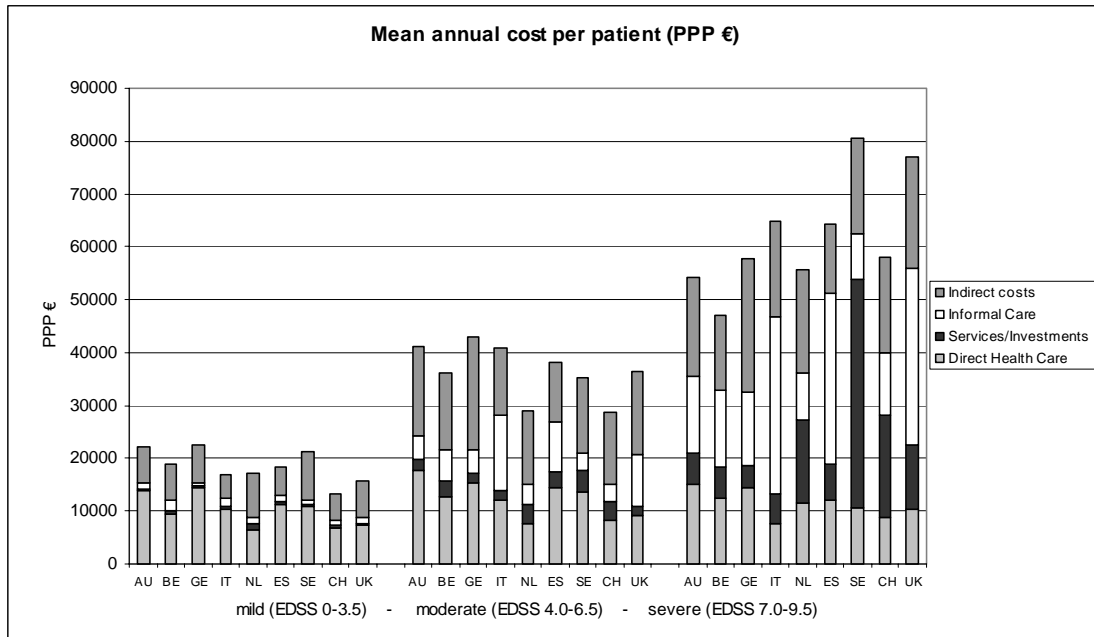


Figure 4 – Proportions of costs represented by different resource types

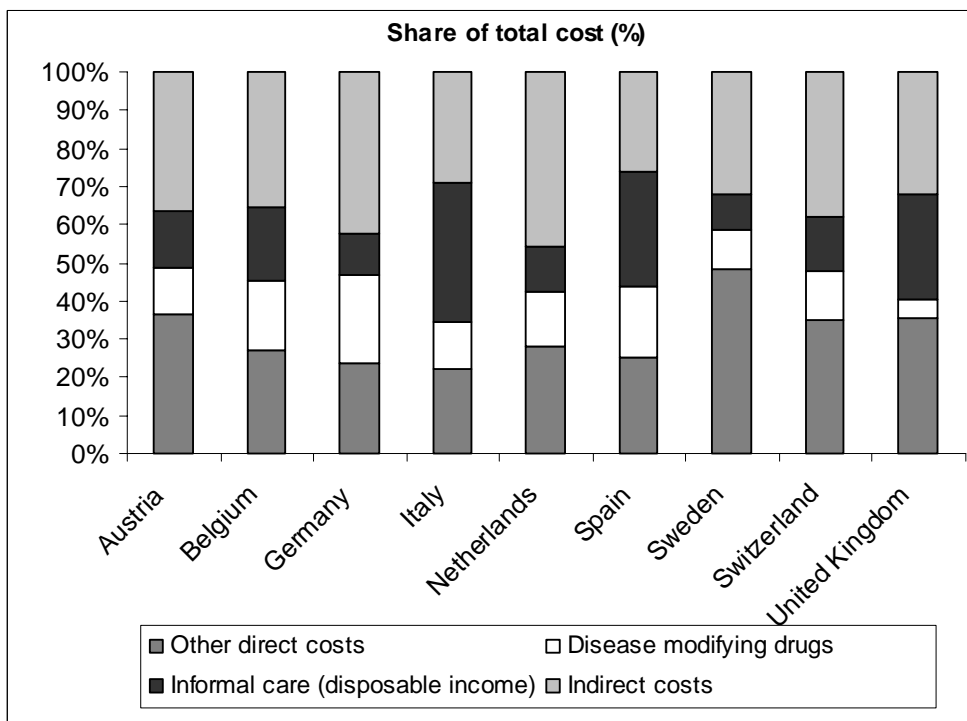


Figure 5 – Patients treated with DMDs

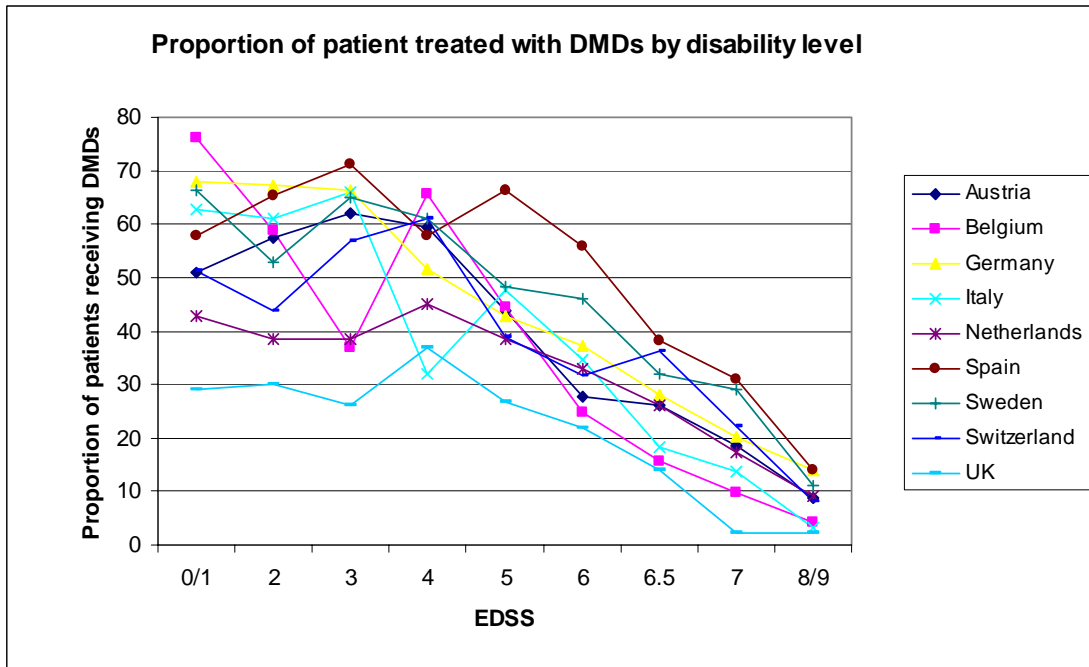


Figure 6 – Utility scores by disability level

