COSTS AND QUALITY OF LIFE IN MULTIPLE SCLEROSIS

A Cross-Sectional Observational Study in the UK

Gisela Kobelt [1], Peter Lindgren[2], David Parkin [3], David Francis [4],

Michael Johnson [5], David Bates[6], Bengt Jönsson [7]

Stockholm School of Economics

Working Paper Series in Economics and Finance, No

(This report is part of an observational study in three countries)

ABSTRACT

We performed a cross-sectional, "bottom-up" observational study of resource consumption and quality of life of patients with multiple sclerosis (MS) in the United Kingdom. Three centers participated in the study. Patients received a questionnaire either by mail or during a clinic visit, and a total of 619 patients returned the questionnaire (the answer rate being around 70%). Patients provided information on all resource consumption, medical and non-medical, work absence and informal care related to their MS. Disease scores (Expanded Disability Status Scale, EDSS) were available for a majority of patients from the study centers, and were assigned using a matrix of disease (mobility) descriptions and EDSS scores.

Mean total cost per patient and year was 16'717 £. When this cost is extrapolated to an estimated patient population in the UK of 80'000, total costs to society are estimated at 1.34 billion £.

Direct costs represented 28%, informal care accounted for 26% and indirect costs amounted to 46%. Of the direct costs, an estimated £ per patient or % of total costs are paid for by the NHS. Intangible costs were estimated at 5000 £ per patient and year.

The mean age of the cohort was 44 years (disease onset 34), the mean utility measured with EQ-5D was 0.487 (0.919 to –0.594), and the mean EDSS score 5.1 (1.0 to 9.5). All costs (direct, informal care, indirect) increased with increasing EDSS scores, while utilities decreased.

KEYWORDS: multiple sclerosis, cost-of-illness, quality of life, EDSS, utility

---

[1] Health Dynamics International, Fox House, Temple End, High Wycombe, Bucks HP13 5DR, UK
[2] Stockholm Healtheconomics, Stockholm, Sweden
[3] University of Newcastle, Department of Public Health, Newcastle-upon-Tyne, UK
[4] University Hospital Birmingham, Queen Elizabeth Neurosciences Center, Birmingham, UK
[5] St James's University Hospital, Department of Neurology, Leeds, UK
[6] Newcastle Hospitals NHS Trust, Royal Victoria Infirmary, Newcastle-upon-Tyne, UK
[7] Stockholm School of Economics, Centre for Health Economics, Stockholm Sweden

CONTENTS

0. SUMMARY

This report presents a cross-sectional, "bottom-up", prevalence-based observational study of the cost of multiple sclerosis (MS) in the United Kingdom and an analysis of how this cost relates to disease severity and quality of life. The study includes all costs caused by the disease, regardless of where and to whom they occur. Thus, direct and indirect costs are included, and intangible costs are estimated. Disease severity is measured with the Expanded Disability Status Scale (EDSS) and quality of life with the EuroQol (EQ-5D and VAS).

The mean total cost per patient and year is estimated to 16'717 £, of which indirect costs represent 46% or 7'695 £. Direct medical costs are estimated at 2665 £ (16% of total costs). Interferons represent approximately 10% of direct costs (241 £ or 1.4% of total cost), while OTC medications account for a very small part (78 £ or 0.5% of total costs). Investments and house adaptations represent 11.8% of total costs, or 1'984 £, and more than half of these costs is borne by the patient. Informal care is the largest direct cost and represents 26.1% of total costs or 4'373 £. Thus, total direct costs are estimated at 9'022 £ per patient and year, of which an estimated 3'420 £ (20% of total costs, or 38% of direct costs, or 74% of direct costs excluding informal care) are paid for by the NHS. Intangible costs are estimated at 5'000 £, using a value of 13'500 £ (20'000 $) for a QALY lost.

All costs (direct, informal, indirect) increase and quality of life (QoL) decreases as the disease progresses. When patients are grouped into mild, moderate and severe MS, total costs per patient and year are 7'273 £, 12'875 £ and 26'679 £ respectively. Utility scores (QoL) are 0.70, 0.57 and 0.28 respectively.

This study attempts to estimate ALL relevant costs due to MS that occur to society, using the same methodology as a recent study in Sweden [1].

Comparing the cost per patient, total costs in Sweden are substantially higher, mostly due to the use of far more social services than in the UK. Thus, direct costs in Sweden are far higher and informal care costs far lower than in the UK, while indirect costs are similar.

The total cost of MS in the UK, assuming a patient population of 88'000, is 1'470 million £ according to our estimates. Of these, approximately 210 million £ are for patients with mild disease (EDSS <=3.0), 320 million £ for patients with moderate disease (EDSS 3.5 – 6.0), and 940 million £ for patients with severe disease (EDSS >=6.5). Around 300 million £ of these costs fall on the NHS. Only one study has presented an estimate exceeding 1 billion £ [2], with costs to the NHS of 153 million £, but it is difficult to compare our results to the figures in that study due to the methodology it used (which might have included transfer costs). Other studies have presented lower figures, and this is likely due to the fact that they have not included informal care costs and other costs borne by the patient.

In conclusion, this study appears to be the most complete study performed in the UK so far, using standard and up-to-date cost-of-illness methodology, and the results indicate that the cost burden of MS to society is higher than previously indicated.

1. INTRODUCTION

1.1. Background

It is estimated that multiple sclerosis (MS), an inflammatory demyelinating disease of the central nervous system, affects over 1 million people worldwide [3]. In industrialized countries, prevalence rates vary considerably between 15 and 145 per 100'000 [4]. Disease onset is typically between 20 and 40 years of age, with a higher incidence in females, and MS is the most common cause of disability in young adults [5].

The course of the disease is unpredictable, although a high frequency of severe exacerbations in the first two years after onset has been related to a poor prognosis [6]. A majority of patients (~80%) will have relapsing-remitting disease (RRMS) at onset, and a high proportion of these patients will convert to secondary progressive disease (SPMS), with a gradual progression of functional impairment punctuated by exacerbations (recurrent relapses) particularly in the earlier years of SPMS. A small proportion of patients (15-20%) will have progressive disease at onset (PPMS).

At present, the etiology of the disease is poorly understood and no cure exists. Current treatments focus on reducing and managing exacerbations, and research has focused on treatment that can affect the progression of the disease. Several new treatments have recently been introduced that have shown a clear effect on the frequency of exacerbations in RRMS [7-9]. Of three clinical trials with interferons in SPMS, one has shown a significant effect on disease progression [10], and all three have shown an effect on relapse rates.

These new agents are more expensive than previously used treatments, and there has been a concern about rising costs [11]. The cost-effectiveness of the new interventions has been questioned, and as a consequence, there is need for better knowledge of the actual cost of care and total cost caused by MS, as a basis for cost-effectiveness assessments and decisions about resource allocation.

Several cost of illness studies have been performed in different countries [1 2 12-17], but most of them have some limitations for use in cost-effectiveness analyses, due to either the size of the samples, or the type of costs included or excluded [18]. (For a comparison of the studies, see [1]). Other studies have assessed the impact of different disease variables such as disability levels or the presence of an exacerbation on costs and quality of life (QoL) [19-21]. In summary, these studies have shown that the burden of MS to society is substantial, and that

- indirect costs account for a high proportion
- informal care constitutes a substantial part of costs
- costs increase with increasing severity of the disease
- costs are higher during a relapse
- quality of life and employment status are significantly affected

1.2. Multiple sclerosis in the United Kingdom

It is estimated that in the UK a total of 88'000 patients are affected [2]. Of these, 45% are estimated to have RRMS and the remainder one of the types of progressive disease [11]. Several population-based surveys have been performed, but a large part of these data is not yet in the public domain.

It has been estimated that the National Health Service (NHS) spends over 150 billion £ on MS [2]and there has been a debate regarding a potentially large cost increase caused by the introduction of the new treatments. As a consequence, the National Institute for Clinical Excellence (NICE, the UK institute for technology assessment in health care) is currently performing an overall evaluation of their benefits and the costs with the objective to produce clinical guidelines for the NHS. Currently, it appears that fewer patients in the UK receive these treatments than in some other European countries or in North America.

1.3. The objective of this study

Several of the available cost of illness studies were performed in the UK or have included the UK [2 12 13 16 19]. They provide a wealth of information, but also a somewhat scattered picture of the total cost of care, as none of the studies has included both a large representative sample and all costs regardless of to whom they occur. In addition, patients were generally defined as mild, moderate and severe and grouped accordingly. This may make it difficult to relate these studies to currently published clinical trials where small incremental changes in disease severity are investigated.

There is an ongoing debate concerning the costs that should be considered when estimating the cost-effectiveness of interventions, for instance at the level of a national health service, and the official guidelines for economic evaluation introduced in several countries differ in their requirements. However, to give an accurate description of costs caused by and related to a disease, all costs (direct medical and non medical as well as indirect costs) must be included.

In MS, a large part of the costs is borne by the patients or their relatives, and top-down cost of illness studies using registries or patient charts will not allow such data to be collected. Also, as available studies have shown, the disease has a large effect on patients' ability to participate in the workforce, and such data are rarely available from databases. Lastly, any effect of the disease and the different levels of disease severity on QoL will be missing. Data in such detail can only be collected from patients directly, in a bottom-up observational study.

The objective of this study was hence to collect detailed data on all costs related to MS, in a representative sample of patients in the United Kingdom, and to investigate how costs and QoL relate to different levels of disease severity, measured by the Expanded Disability Status Scale (EDSS) [22]. A further objective was to compare data to the recently performed large observational study in Sweden [1].

2. MATERIALS AND METHODS

2.1. Theories and methods used

This study follows closely the methodology used in the most recent population-based study in Sweden [1]. It is hence a descriptive cost of illness study, based on the human-capital theory [23 24] and relates all cost to the disease (MS). As MS is a chronic disease with an average duration of around 40 years, a prevalence- rather than incidence-based approach was used, estimating the cost per patient and year. This allows calculating the cost for all patients with the disease in a given year in a geographically defined area and relating the estimates to measures of annual health care expenditure in the area.

Data collection strategies for cost of illness studies can be "top-down" (i.e. using aggregate figures on resource consumption related to diagnoses from registries or published sources), or "bottom-up" (i.e. estimating costs in a sample of patients and extrapolating to the national level). Both approaches have advantages and drawbacks, the major drawbacks being data availability in the top-down approach and difficulties relating to the selection of a representative sample in the bottom-up approach. As the purpose of this study was to include <u>all</u> costs, regardless of where they occur, the bottom-up approach was used.

The objective of the study was to estimate costs related to MS, not costs for patients with the disease, and only MS-specific resource consumption was therefore included. It is possible that patients with a severe disease consume more resources also for other diseases and thus have overall higher costs. In these cases it is generally difficult to separate what part of total costs relates to the disease that is being investigated and what part to co-morbidities. For patients with MS, this is less of a problem, as the consequences of the disease are rather well defined, and in addition patients are in an age group where co-morbidities are generally limited. It was thus felt possible to collect only MS specific costs.

Data on resource utilization, QoL and disease severity was collected directly from patients, cross-sectionally, during the fall of 1999.

2.2. Study centers and subjects

Three centers with well established MS clinics and a large number of patients attending these clinics were approached for this study and all agreed to participate:

- The Royal Victoria Infirmary in Newcastle upon Tyne
- The St James's University Hospital in Leeds
- The Queen Elizabeth Neurosciences Center in Birmingham.

In two centers (Leeds and Birmingham), all patients registered in the files of the MS clinics and who had been in contact with the clinic recently were contacted by mail for study participation. In the third center (Newcastle) patients were approached consecutively when visiting the MS clinic and asked for their willingness to participate. As a consequence, it could be argued that patients in the Newcastle center were in a more active disease phase, which had prompted their coming to the clinic. However, MS patients have rather regular contact with their physician, and there is no indication that this difference in sample selection would have influenced the results. In addition, the sample from Newcastle was quite obviously smaller than the samples from the other two centers.

On the other hand, it is likely that this method of sampling results in a reduced number of patients with very severe disease, particularly patients who are bed-bound or live in residential care. This was less likely to be the case in the two centers where all patients on file were included, but certainly in Newcastle these patients were excluded. In order to verify this, we compared the prevalence of severely disabled patients in this study to the estimates in other studies or databases. A similar comparison was performed for patients living in residential care.

2.3. Data collection

2.3.1. Background variables and resource consumption

Patients were asked, either in writing or during a clinic visit, to answer questions regarding resource consumption, disease severity and QoL by completing a questionnaire. The questionnaire contained 3 sections with general and disease information, 5 sections with resource utilization:

- background variables (age, education level, living arrangements)
- hospitalization (overnight stays and day hospitalization) and medical visits to physicians, nurses, physiotherapists or home visits by these professionals
- visits to other professionals (psychologist, incontinence advisor, optician, social worker, other therapists)
- medication (interferons, other POMs, OTC drugs)
- community and other services (home help, child care, meals on wheels, etc)
- investments (house adaptations, devices, etc)
- employment situation and changes in employment situation due to MS
- disease related information (type of disease, ability to move around, etc.) and information on relapses

For health care resources and community services, patients were asked for their consumption during the past 3 months. An exception to this was hospitalization, where patients were asked for utilization during the past year. This was based on the assumption that it is possible to recall severe events such as hospitalization over a relatively long period of time, while it might be difficult to assign such events to a specific month. Similarly, large investments such as transformations to the house etc. were related to the past year. Patients were reminded at each question what the relevant time frame to consider was.

2.3.2. Quality of life (utilities)

Quality of life data was collected with a generic preference-based instrument, the EQ-5D [25], from the descriptive part of which utility values on a scale between 0 (death) and 1 (full health) for different health states can be developed. In addition, a visual analogue scale (VAS) gives a score between 0 (worst imaginable state) and 100 (best imaginable state).

The EQ-5D is based on questions concerning 5 domains, with answers at 3 levels, yielding 243 possible combinations of answers. From these, health state descriptions were created and utilities assigned with the time trade-off method in the UK population [25]. A health state classification system was then developed from which utilities for the different combinations can be derived. For the development of utilities, interviewees had been specifically asked to ignore any effect on their economic or working condition, in order to separate health-related QoL from cost implications.

2.3.3. Disease severity (EDSS)

Disease severity was expressed as EDSS levels. However, in addition to grouping patients into mild, moderate, severe, we also used smaller groupings (essentially by 1 full EDSS point) that have been used in cost-utility models [26 27]. EDSS scores were available from the medical records for the majority of patients. When no scores were available, they were derived from the specific disease section in the questionnaire. This section included specific questions regarding mobility, derived from the EDSS scoring system. We developed a matrix to assign an EDSS score (based on full EDSS points) and a grouping, and verified the accuracy of the matrix by comparing the actual scores from the charts and scores assigned from the questionnaire for a sub-sample of 100 patients for which both were available. The matrix predicted the groupings with over 90% accuracy, and considering the uncertainty and inter-rater variability involved in EDSS scoring, we considered it unnecessary to attempt to complete the missing values by telephone-interview or by calling the patients to the clinic for a visit.

2.4. Costing

In cost of illness studies or economic evaluations, data collection focuses on resource consumption, and each resource unit is then multiplied with its unit cost. Unit costs for a resource are the opportunity cost of that resource (or its value in its best alternative use). In normal well-functioning markets, market prices will reflect the opportunity cost, but in health care this is not always the case, and in a national health system such as the UK, no market prices are available. However, within the NHS, opportunity costs for the majority of resources are available from several sources and specific studies. For this study, we have used a number of sources for valuing health service and other public resources, while costs for investments and out-of-pocket expenses have been largely based on patients' estimates. Costs relate to the year 1999 and details on the major unit costs can be found in Annex 1.

2.4.1. Direct costs

Direct costs relate to the cost of detection, treatment, rehabilitation and long-term care of an illness, and the purpose of this study was to include all costs related to MS from a societal point of view. Thus costs borne by the patient for services not available on the NHS, as well as informal care provided by family and relatives are also included, but a separate estimate for costs to the NHS is provided as well.

Direct medical costs are grouped into inpatient care, ambulatory care, social services, drugs, investments and informal care. Unit costs for the resources were assigned as follows:

- Inpatient and ambulatory care as well as social services were valued using the PSSRU survey from the University of Canterbury [28] and the internet site of the Department of Health [29]
- Prescription drug prices were based on average recommended daily doses and average package size prices in the British National Formulary [Pharmaceutical, September 1999 #61]
- OTC drug costs were taken mainly from patients' indications (available for approximately 90% of the items), verified with prices in the Boots price list available on internet

(http://www/boots.co.uk). When a patient had omitted to indicate a price, the item was costs by using indications for the same item from other patients or when not available, the Boots price list.

- Investment costs were used as indicated by the patients, and the full cost of an investment was assigned to the year. As this was a cross-sectional study, it would be impossible to obtain information regarding earlier investments in order to calculate annuities; however, in any given year, a proportion of patients would make such investments. When patients had not indicated any cost, we used the average cost indicated for the same investment by all other patients, excluding however large outliers. Several patients indicated that they had to move to a different house and indicated the full purchase price of the new house. This cost was excluded from our calculations, and only a mean estimate for the cost of moving and re-installation, as indicated by several patients, used for all these cases.
- The cost of informal care was considered to be a direct cost, as in the absence of family or relatives, someone else would have to provide the service, likely on a paid basis. However, rather than using the full hourly wage rate as a shadow price, we used 35%, as in other published studies. The national average hourly gross wage for adults was taken from the New Earnings Survey (April 1999).
- Residential care had to be valued using a proxy cost, as there are no specific institutions for young disabled patients. We used the cost of long-term care for the elderly in the private sector, as there did not seem to be a difference between costs for residents requiring different levels of assistance. The average cost per week was thus estimated at 403 £.

2.4.2. Indirect Costs

Indirect costs are constituted by sickness absences, early retirement or premature mortality due to the disease. The questionnaires provided information concerning short-term sickness absence, early retirement due to MS, or changes in working hours due to MS. Information on premature mortality would have to be obtained from other sources, but this was excluded from the study, as the impact of MS on mortality is relatively small and very difficult to estimate. The loss of production due to sickness absence was calculated for each patient, based on her/his

current working status, and an average cost per patient calculated. Indirect costs due to early disease-related retirement was calculated as one full year at the average national salary, as again in any given year, a number of patients would have to take early retirement. The annual production loss was calculated as the gross hourly wage of 9.61 £ from the New Earnings Survey, increased by 5% for employers' contributions, and based on a 35 hour week, for 52 weeks.

2.5.3. Intangible costs

Intangible costs, i.e. costs due to pain, grief, anxiety, social handicap, etc., are usually omitted in cost of illness study. However, Henriksson et al provided an interesting estimate of these costs in the recent population based study in Sweden [1]. We have used a similar approach, calculating the difference in utilities between our sample and an age and sex-matched sample of the normal population in the UK, and the number of quality-adjusted life-years (QALYs) lost by the MS sample in one year. By assigning a value to (or willingness to pay for) a QALY, intangible costs due to MS can calculated. Although there is no agreed value for a QALY, the Swedish study used a theoretical value equivalent to US $ 60'000, based on a recent survey amongst health economists [30 31]), for illustrative purposes. We felt that this value was probably high for Europe and used a theoretical value for the UK of 13'500 £ (20'000 US $), but also illustrate the calculations when using the same value as the Swedish study.

2.6. Analysis

Resources used by each individual patient were valued with the relevant costs and an average cost per patient in the sample, and an average cost per patient at different levels of disability computed (mild, moderate, severe). Costs for smaller groupings will be reported at a later stage, with the cost-effectiveness analysis.

We indicate mean cost per patient for the sample as a whole, but also mean costs for those patients using the different resources. We omit extrapolation to the full estimated prevalence in the UK, as it might be more useful to perform these calculations for patients in different health authorities, rather than at a national level.

3. RESULTS

3.1. Patient sample

A total of 619 patients were included in the study. Nine patients had participated in the testing of the questionnaire, and as no changes to the questionnaire were found to be necessary, they were included in the resource analysis (although they had not completed the EQ-5D for which no testing was performed). Eleven questionnaires were received after completion of the analysis and could therefore not be included.

The response rate in the centers that contacted all patients by letter was 66.3% and 72.2% (the higher rate being likely due to about 100 reminders being mailed). The response rate in the third center was 100%, as no patient refused to participate, and the overall response rate was 73%.

There was very little missing data, but 20 patients had omitted the section with background variables and 14 patients the section on employment status. The sections on resource consumption and disease variables were completed by all patients and only some questions were omitted. The EuroQol was completed by 585 patients; 570 answers could be analyzed for the EQ-5D (patients with missing answers were excluded, as the EQ-5D does not provide a system to integrate missing answers); the VAS was completed by 564 patients.

3.2. Background variables

As expected, the proportion of female patients was around 70%. The mean age was 44 years with a disease onset around 34 years. Around one third of patients had an educational level above the minimum required and the vast majority was married or lived with their family. 37% of patients were employed or self-employed, and of these, 44% indicatd to work full-time and 35% part-time, while 21% provided no answer. 38% of patients were early retired due to MS, and around half of the patients indicated that they have had to modify their working situation since being diagnosed with MS.

Table 1 – Descriptive statistics, background variables (n=599)

Variable	Proportion (%) or Mean (SD)
Gender	
Male (%)	29.4
Female (%)	70.6
Age	
Mean, SD	44.3 (11.3)
Marital status	
Single (%)	26.2
Married (%)	70.6
widowed (%)	1.5
no answer (%)	1.7
Education level	
minimum time (%)	60.4
degree or equivalent (%)	34.9
Living	
Alone (%)	13.9
With family (%)	81.7
Long term care (%)	1.0
other (%)	3.2
no answer (%)	0.3

Table 2 - Descriptive statistics, employment situation(n = 619)

Variable	Proportion (%)
Employed during last 3 months (%)	37.2
full time	37.0
self employed	7.0
reduced time	35.2
no answer	20.9
Changed work situation	
no	23.5
changed work	9.6
changed hours	11.7
changed work and hours	11.7
stopped working	16.5
no answer	27.0

Employment situation	
early retired	39.2
house work	7.3
Part-time work	0.2
retired	2.6
seeking work	1.1
unemployed	11.6
student	0.8
other	8.2
Retired due to MS	38.0

A few patients (2%) did not complete the section on disease states, and valid answers were received for 605 patients. Slightly over 10% of the patients indicated that they had benign disease, 21.5% had relapsing/remitting disease and 10% relapsing/progressive disease, while 27% and 26% had secondary and primary progressive disease. About one third of the cohort reported few limitations with full ability to walk, around 15% of patients were able to walk between 100 and 500 meters, around 30% could walk between 20 and 100 meters but with walking aids. Over 16% indicated that they always required a wheelchair, but some of them also indicated that they were sometimes bed-bound. 22 patients (3.7%) indicated that they were bed-ridden, and 6 patients (or 1%) lived in long-term care. When the actual EDSS scores, including for missing patients, and patients answers are combined, 37 patients or around 6% of the patients in the cohort are partly or completely bed-bound. 3% if patients provided no answer on their mobility.

Exactly half of the patients had a relapse during the past year, and 19% of patients had a relapse during the past 3 months. We estimated the cost of a relapse by comparing resource consumption most likely associated with a relapse (hospitalization, day-hospitalization, visits to neurologists or GPs, medication, the need for informal care and sick leave) for patients with or without a relapse. We excluded patients with an EDSS above 6.5 from this calculation, as relapses were very infrequent in this group. Total costs differed by 292 £, of which relapses 92 £ were direct costs and 200 £ informal care, while sick leave was not different.

Table 3 - Descriptive statistics, disease information (n = 605)

Variable	Proportion (%) or Mean (SD)
Age at first symptom of MS mean (SD)	34.4 (10.4)
Disease situation	
- 1 – no limitations (%)	1.8
- 2 – very slight disturbances in vision or mobility, or muscle weakness (%)	14.9
- 3 – moderate limitations, but fully able to walk without help (%)	14.4
- 4 – some limitations, but able to walk without help for up to 500 meters, and only slight limitations in daily activities (%)	7.8
- 5 - moderate limitations, but able to walk without help or rest for up to 200 meters, and many limitations in daily activities (%)	6.9
- 6 – substantial limitations and requiring often walking aids (sticks, crutches) to walk 100 meters (%)	12.6
- 7 – substantial limitations and always requiring walking aids to walk 20 meters (%)	18.7
- 8 – severe limitations and requiring a wheel chair (%)	16.4
- 9 – very severe limitations, mostly bed-ridden, but able to use the arms (%)	2.0
- 10 – always bed-ridden (%)	1.7
- no answer (%)	3.0
Course of disease	
- benign (%)	10.7
- relapsing-remitting (%)	21.5
- secondary progressive (%)	26.8
- relapsing-progressive (%)	10.2
- primary progressive (%)	26.1
- no answer (%)	4.6
Relapses	
- relapsing during the past year	50.5
- relapsing during the past month	18.9
Patients with concomitant illness/es (%)	13.4

3.3. Direct costs

3.3.1. Inpatient care

126 patient (20.4 %) were hospitalized, the majority of them in the neurology ward (63.2 %). 6 patients (1%) lived in long-term care facilities.

Table 4 – Mean costs of inpatient care (n = 619)

Inpatient care	**Proportion using the resource**	**Average number of inpatient days per patient and year**		**Mean cost per patient and year £ (1999)**	
		Entire sample	Patients using	Entire sample	Patients using
Total inpatient days	20.4 %	2.1	10.4	448	2255
• *of which neurology*	*63.2 %*	1.1	5.4	253	1272
Long-term care	1%	3.6	365.0	217	22360
Total inpatient care	**20.4 %**	**5.7**	-	**685**	**3240**

3.3.2. Ambulatory care

Table 5 – Mean costs of ambulatory care (n = 619)

Practitioner	**Used by (%)**	**Mean number of visits per patient and year**		**Mean cost per patient and year in £ (1999)**	
		Entire sample	Patients using	Entire Sample	Patient using
Day stays	9.0	0.9	10.0	111.40	1231.10
GP	47.5	4.2	8.8	75.60	159.20
Neurologist	45.7	2.4	4.9	220.00	481.40
Urologist	4.8	0.3	5.6	19.90	410.00
Other specialist	15.7	1.7	10.8	107.90	688.50
Home visit, physician	13.2	1.2	8.4	60.20	453.10
Nurse or physiotherapist	38.4	7.2	18.8	63.40	174.40
Home visits, nurse	35.8	5.0	18.3	90.60	349.20
Occupational therapist	14.4	1.44	10.0	21.60	150.30
Chiropodist	9.9	0.7	6.0	4.70	47.20
Speech therapist	3.7	0.2	6.4	3.30	87.60
Continence advisor	7.4	0.52	6.8	11.60	156.00
Psychologist	3.7	0.4	11.0	10.60	284.00
Social worker	7.3	0.72	5.8	13.00	179.20
Optician	12.3	0.64	5.2	8.490	69.10
Other paramedical	7.9	0.54	5.3	43.60	435.80
Total	**100**	**28.26**	-	**869.00**	**1036.40**

When the entire sample is considered, the average number of any type of outpatient visit was around 28, or slightly more than one visit per fortnight. All patients had ambulatory care visits of one type or the other and a large number of different practitioners were involved. However, the majority of visits were to general practitioner, nurses or physiotherapists, on average one visit per month. Home visits by either a physician or a nurse were rather frequent (around six per patient and year). Consultant visits were slightly more than 4 per year, the majority of them to neurologists. Mean total cost per patient was 869 £. (This estimate excludes time cost and travel expenses and thus underestimates the total opportunity cost of visits.)

3.3.3. Drugs

Prescription drugs account 87.5% of all drug costs and were used by 74% of the patients. A large proportion (44%) of prescription drug costs were due to interferons, although only very few patients (2.6%) received interferons. This proportion is substantially lower than in other countries, where the proportions are around 10%, but is representative of the United Kingdom. When the cost of interferons is considered within total direct costs of care, they represent only 1.4 %.

The most frequently used prescription drugs were

- muscle relaxants (~20% of all patients in the cohort), predominantly baclofen followed by diazepam
- vitamins (~20% of patients of all patients), predominantly B12
- antispastic, anti-parkinson, andi-epileptic, anti-convulsant drugs (~10% of all patients) predominantly carbamazepine, amantadine, gabapentin
- anti-depressants (~10% of all patients), two thirds TCAs, one third SSRIs
- incontinence drugs (~10% of all patients), almost exclusively oxybutynin
- steroids (~6% of all patients), almost exclusively prednisolone
- others: NSAIDs, analgesics

Table 6 - Mean cost of prescription and OTC medication (n=619)

Drugs	Used by (%)	Cost per patient and year (£)	
		Whole sample	Only patients using the resource
Interferons	2.6	240.85	9318.00
Azathioprine	3.4	11.73	346.00
Other prescribed drugs	54.3	295.56	544.50
OTC drugs	47.0	78.31	166.60
All drugs	**74.3**	**626.45**	**842.90**

3.3.4. Community and other services

Around one quarter of patients made use of community and other services, and the use was dominated by home care and home help, as well as by other non-specified services. Patients who made use of such services spent around 2500 £ on home care or child care, and around 700 £ on home help, and around 1600 £ on other services, with a mean expense for the users of around 2000 £. The mean cost per patient in the cohort was 488.40 £ per year.

Table 7 – Cost of using different community services as a consequence of MS

Services	Used by (%)	Cost per patient and year (£)	
		Entire sample	Only patients using the resource
Home care	10.0	266.60	2653.30
Home help	9.7	68.60	705.80
Child care	1.6	36.50	2249.60
Day care	2.4	11.10	458.40
Meals	0.5	0.60	121.30
Other	6.6	104.90	1578.90
Total	**24.3**	**488.40**	**2008.80**

3.3.5. Adaptations and investments

Investment costs were dominated by adaptations needed in the house, most frequently the bathroom; almost 20% of the patients in the cohort required bathroom changes and 17% adaptations to other parts of the house including the kitchen. 5% of patients required stair elevators. Car adaptations were made by 8.6% of the patients, at a relatively high cost. Over one fifth of the patients purchased a wheelchair during the year and one third required other types of walking aids.

Overall, mean investment costs were substantial, at 1984 £ per patient in the cohort, and over 3000£ for those patients requiring such adaptations. Patients indicated that 53% of these costs were paid for by themselves.

Table 8 - Adaptations made and items purchased/received.

Adaptations and items	**Used/made by (%)**	**Cost per patient and year**	
		Whole sample	Only patients using resource
Adaptation of kitchen	5.5	99.00	1799.00
Adaptation of bathroom	19.5	286.00	1468.00
Adaptation of other part of the house	11.5	386.00	3350.00
Bed elevator	3.1	46.00	1480.00
Stair lift	5.2	248.00	4765.00
Stair rail	11.0	19.00	175.00
Ramps	6.2	41.00	669.00
Alarm	3.1	10.00	324.00
Adaptations at work	3.1	81.00	2630.00
Adaptations of car	8.6	175.00	2035.00
Walking aids	30.4	10.00	33.00
Wheelchair	22.6	138.00	611.00
Spectacles	17.9	25.00	141.00
Special kitchen utensils	9.1	28.00	311.00
Special hygiene utensils	10.2	14.00	145.00
Special writing devices	2.9	13.00	439.00
Other	14.1	363.00	2573.00
Total	**65.7**	**1984.00**	**3018.00**

3.3.6. Informal care

Patient in this cohorts lived predominantly at home, with their family, and thus informal care use was very frequent. 55.6% of all patients received care from family members, relatives or friends, for an average of 45 hours per week or 25 hours per week for the entire sample. Using a rate of 35% of the national average hourly gross wage for adults, the weekly cost per patient using informal care was 151.40 £ or 84.10 £ per patient in the entire cohort. The total mean cost of informal care per patient was 4373 £.

3.4. Indirect costs

3.4.1. Short term sickness absence

37.2 % of patients in the sample were employed. The average number of sickness-absence days for these working patients was 51 days per year. Correcting for reduced time employment, the average number of hour lost per year was 193 hours which at a gross hourly cost of 10.09 £ yields an average yearly cost of 1947.40 £ per person for the working patients, or £723.40 considering the entire sample.

3.4.2. Long term sickness absence

Of the non working patients, 38% were early retired. Of these 97%, or 235 patients, were retired due to MS. At an annual cost of 18'365 £, the average cost per patient in the cohort was £ 6972.

3.5. Total costs (direct and indirect)

Direct costs constitute 54% of total costs and amount to 9022 £ per patient and year. About half of these costs (48.5 % or 26% of total costs) represent informal care, and excluding informal care, direct costs amount to 4649 £ per patient and year. Indirect costs represent 46% of total costs, which is lower than in previously published

studies. The reason for this is that most studies have excluded informal care. When informal care is excluded from our calculations, direct costs amount to 4649 £ and indirect costs represent 62% (of a total of 12'344 £). This is still lower than the ranges published, but is likely due to the fact that few studies have included OTC medication and investment costs and services borne by the patient. In this study these costs amounted to 7.4% of total costs, and when these are also excluded, indirect costs represent 69%.

Thus, it can be seen that a large part of costs is borne by the patients, around 5600 £, representing 62 % of direct costs, and almost 33.5 % of total costs. The remaining direct costs are rather evenly distributed on inpatient stays, ambulatory care, drugs and community services, and direct costs paid for by the NHS are estimated at 3420 £ per patient and year.

Table 9 – Mean total cost per patient and year

Costs	**Cost per person and year £ (1999)**	**Share of total cost (%)**
Hospital inpatient care	685	4.1
Ambulatory care	869	5.2
- day stays	111	0.7
- physicians	484	2.9
Nurses/physiotherapists	154	0.9
- paramedical	117	0.7
Drugs	626	3.7
- interferons	241	1.4
Services	488	2.9
Adaptations	1984	11.8
Informal care	4373	26.1
Total direct costs	**9022**	**53.9**
Total indirect costs	**7695**	**46.1**
Total cost	**16'717**	**100.0**

3.6. Quality of life (utilities)

The EQ-5D was completed by 585 patients completed and the mean utility for the sample derived from the EuroQol health status matrix was 0.487. There was no difference between women and men, the values being 0.49 and 0.48 respectively. Values ranged from 0. 919 to -0.594. Negative values are possible with the EQ-5D, as some patients may judge a health states as being worse than death, and we used these negative values in our calculations of mean utilities.

6 patients were excluded from the analysis of the VAS, as their answers were not interpretable. The mean values on the VAS were 54.62 covering the range of the scale from 1 to 100.

Patients with a relapse during the past year or the past month had lower utilities at the time of the study.

Table 10 – Mean utilities (EQ-5D and VAS)

	N	Mean values (SD)	Range
EQ-5D			
All patients	585	0.487 (0.328)	-0.594, 0.919
Relapses during the past year			
• patients with	297	0.542 (0.287)	-0.484, 0.919
• patients without	287	0.430 (0.358)	-0.594, 0.919
Relapses during the past 1-2 months			
• patients with	115	0.457 (0.344)	-0.594, 0.919
• patients without	469	0.497 (0.325)	-0.594, 0.919
Visual Analogue Scale			
All patients	564	54.62 (22.57)	1 – 100

3.7. Functional status

Recent EDSS scores were available for approximately two thirds of the patients, and these were used for the groupings, regardless of patients' answers on the mobility questionnaire. For the remainder, the matrix developed from the disease descriptions in the questionnaire was used to assign scores. The cohort covered the entire spectrum of the EDSS, and the mean score for the cohort is estimated at 5.1.

Table 11 – Functional status according to EDSS (n=597)

EDSS	Disease description	Number of patients	Proportion %
<= 3.0	1, 2, 3	157	26.2
3.5, 4.0	4	58	9.7
4.5, 5.0	5	56	9.4
5.5, 6.0	6	93	15.6
6.5	7	109	18.3
7.0	8	87	14.6
>= 7.5	9, 10	37	6.2

3.8.The effect of functional status and QoL on costs

As in previous studies, costs increase as disability increases, and QoL decreases as the disease progresses. In order to make our results comparable to published studies, results are presented for definitions of mild, moderate and severe patients.

Table 11 - Annual cost per patient by disability level

	Utilities	Costs (£, 1999)			
Disability level	EQ-5D	Direct costs	Indirect costs	Informal care costs	Total costs
Mild (31.1%) (EDSS <= 3.0)	0.698	2117	4013	1143	**7273**
Moderate (27.3%) (EDSS 3.5 – 6.0)	0.574	3041	7097	2737	**12875**
Severe (38.8%) (EDSS >= 6.)	0.277	7980	10868	7849	**26697**

Note: 3% of EDSS scores missing

3.8. Intangible costs

The cohort of 619 patients lost a total of 220.6 QALYs due to MS during the year, or an average of 0.383 QALYs per patient and year (0.394 for men, 0.379 for women). Using 13'500 £ (20'000 US$) as a value for a QALY lost, intangible costs per patient and year were 5'170 £. Using the same value as in the Swedish study (60'000 US$), the cost per patient and year is 15'320 £.

Table 12a– QALYs lost (women)

Age Group	Mean utility (population)	Mean utility (sample)	Difference	Number of patients	QALYs lost
20-29	0.936	0.673	0.263	29	7.627
30-39	0.914	0.607	0.307	123	37.761
40-49	0.875	0.451	0.424	119	50.456
50-59	0.817	0.393	0.424	94	39.856
60-69	0.814	0.415	0.399	37	14.763
70-79	0.741	0.139	0.602	8	4.816
>80	0.690	-	-	0	-
Total	**n.a.**	**n.a.**	**n.a.**	**410**	**155.279**

Table 12b– QALYs lost (men)

Age Group	Mean utility (population)	Mean utility (sample)	Difference	Number of patients	QALYs lost
20-29	0.941	0.398	0.543	12	6.516
30-39	0.915	0.564	0.351	44	15.444
40-49	0.890	0.521	0.369	61	22.509
50-59	0.804	0.380	0.424	43	18.232
60-69	0.782	0.345	0.437	6	2.622
70-79	0.773	-	-	0	-
>80	0.736	-	-	0	-
Total	**n.a.**	**n.a.**	**n.a.**	**166**	**65.323**

4. Discussion

This study used the same methodology as a recent observational study in Sweden, with the objectives to estimate the total burden of multiple sclerosis, to relate disease severity to costs and to quality of life, and to compare to the Swedish study.

Although the study was only performed in three centers, the sample appears to be representative of the MS population: Patients are distributed across the entire spectrum of the disease, with about one quarter of the sample with very mild disease (EDSS <= 3.0), slightly less than 15% of patients wheelchair bound and 6% bed-ridden. Thus, despite the process of sampling, particularly in one center, the cohort includes a representative sample of very severely disabled patients.

Very few patients in the cohort were living in nursing homes or long-term care facilities (6 of 619), and the sampling process may indeed have excluded such patients, as they may not have been in recent contact with the MS clinics. Thus, it is possible that the mean cost for the severely disabled patient group has been underestimated in our study. However, it is known that the vast majority of patients with MS in the UK are cared for at home, and it is difficult to ascertain whether, and how much, costs have been underestimated. If we were to assume that 3% rather than 1% of patients lived in long term care, the total mean cost per patient would be higher by about 450 £.

Few patients in the cohort were treated with interferons (2.6%), but this proportion corresponds to the national average in the UK, which is lower than in other countries. Comparing to the Swedish study, the difference is large, as in the Stockholm area over 40% of patients received interferons (the national average in Sweden being 10%).

The comparison to the Swedish study is interesting from several other points of view:

- Costs are clearly much higher in Sweden, at 409'000 SEK or about 31'500 £ (corrected for a proportion of 12% rather than 42% of patients receiving interferons), compared to 16'700 £ in the UK. (Figure 1)

- All types of costs are higher, with the exception of informal care. However, a substantial part of the difference is due to more services being made available to patients in Sweden, particularly "personal assistants". As a consequence, services represent 22 % of total costs in Sweden, and 3% in the UK (approx. 7600£ compared to 500£. Conversely, informal care in the UK is far higher, at 4400 £ compared to 1600 £ in Sweden, as patients' relatives fulfill the roles of "personal assistants". Patients in Sweden also used rehabilitation facilities rather intensively, representing 8.6% of costs or around 3000 £, while this was entirely absent in the UK study.
- Thus, direct costs are far higher in Sweden, while informal care costs are substantially higher in the UK. (Figures 2 and 3)
- The difference in indirect costs is less pronounced, and similar amounts of patients indicated that they had to stop working or change their employment because of their MS. (Figure 4)
- The UK sample was younger than in Sweden, but the sex distribution was identical. Far fewer patients lived along in the UK than in Sweden, which can be explained by the fact that little social support is available to patients in the UK and the majority of the care burden falls on family. Contrary to this, patients in Sweden can live alone, with the help of the "personal assistants".
- The proportions of benign or RRMS, SPMS and PPMS were also identical.
- The average EDSS scores were the same, and the proportion of patients with mild, moderate and severe disability very similar.
- Utility values with the EQ-5D were slightly lower in Sweden, while the VAS was very similar. The average QALY loss due to MS was 0.49 in Sweden, and 0.39 in the UK. This is likely due to the fact that population values with the EQ-5D are considerably higher in Sweden than in the UK, while the health states system was derived from the UK population, rather than to a difference in the effect of the disease on patients. This is illustrated by the fact that the slope of the utility curve in the two populations is virtually the same. (Figure 5)

Overall, the two studies differ very little in terms of the cohorts' background and disease variables, but resource consumptions is very different.

Figure 1 – Comparison UK and Sweden – Mean total costs by disease level

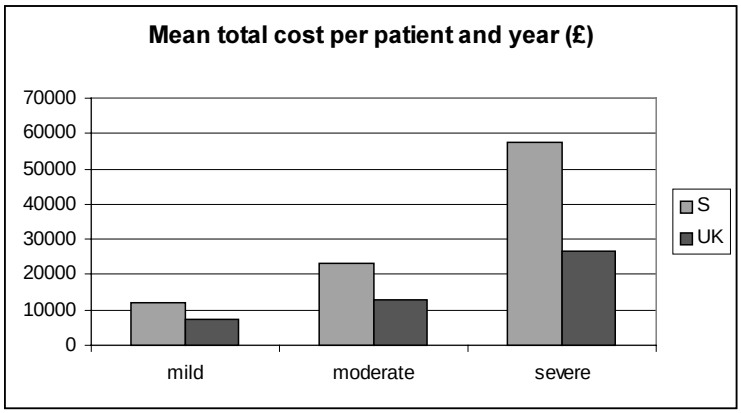


Figure 2 – Comparison UK and Sweden – Mean direct costs by disease level

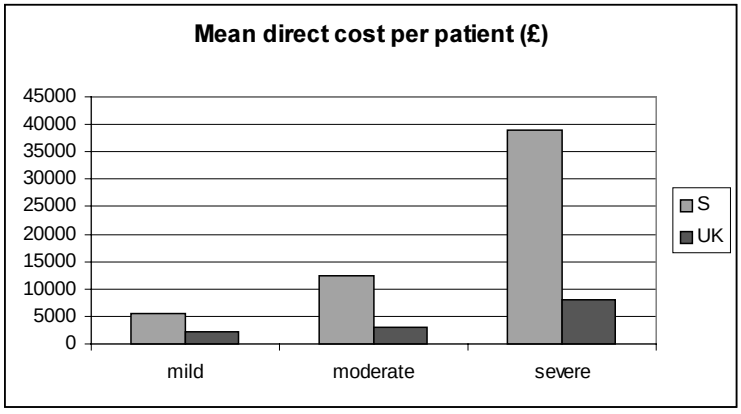


Figure 3 – Comparison UK and Sweden – Mean informal care costs by disease level

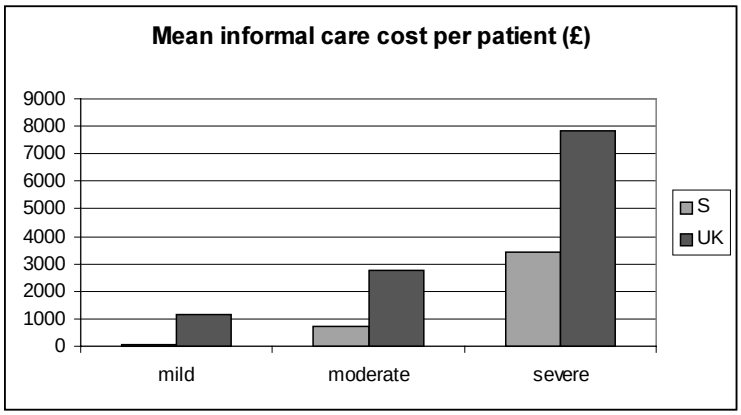


Figure 4 – Comparison UK and Sweden – Mean indirect costs by disease level

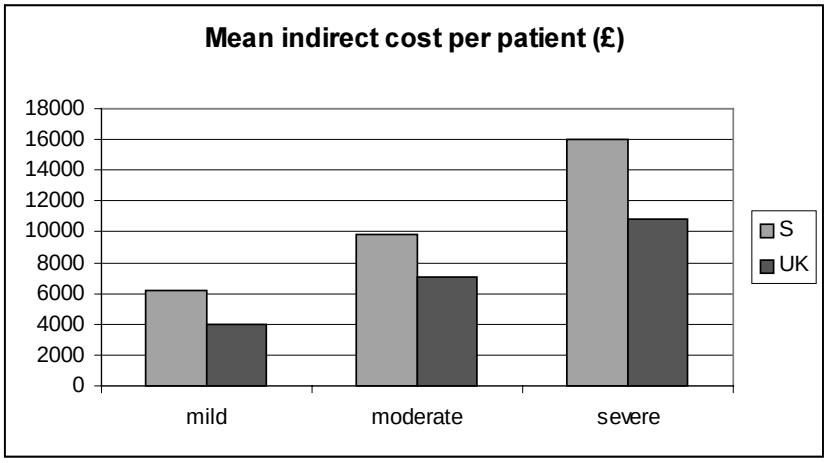
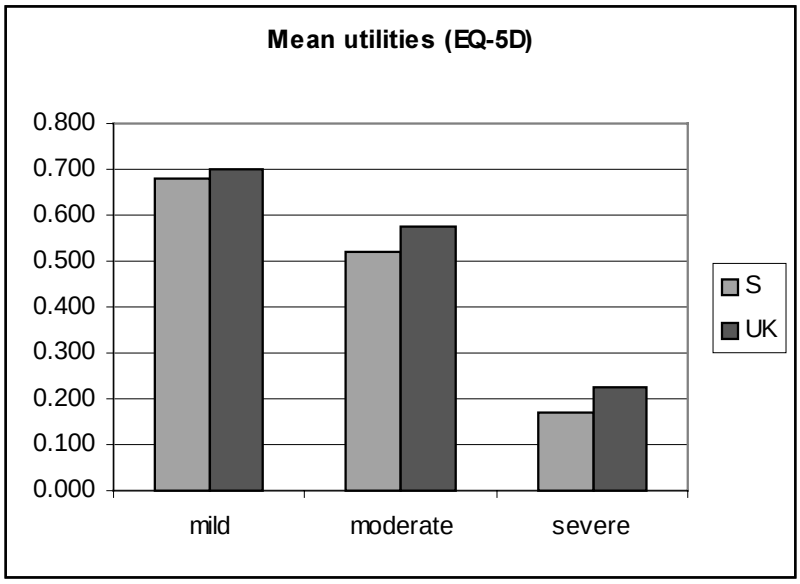


Figure 5 – Comparison UK and Sweden – Mean utilities by disease level



5. REFERENCES

1. Henriksson F, Fredrikson S, BJonsson. Costs, quality of life and disease severity in Multiple Sclerosis - a cross-sectional study in Sweden. Stockholm: Stockholm School of Economics, 2000.
2. Holmes J, Madgwick T, Bates D. The cost of multiple sclerosis. *British Journal of Medical Economics* 1995(8):181-93.
3. Dean G. How many people in the world have multiple sclerosis? *Neuroepidemiology* 1994;13:107.
4. Goodkin D. Interferon beta 1-b. *Lancet* 1994;344:1057-1060.
5. Hauser S. Multiple Sclerosis and other demyelinating diseases. In: Isselbacher K, Braunwald E, Wilson J, al. e, editors. *Harrison's principles of internal medicine*. New York: McGraw-Hill Inc, 1994:2281-94.
6. Runmarker B, Andersen O. Prognostic factors in a multiple sclerosis incidence cohort with 25 years follow-up. 1993(116):117-134.
7. The IFNB Multiple Sclerosis Study Group. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis: clinical results of a multicenter, randomized, double-blind, placebo-controlled trial. *Neurology* 1993;43:655-661.
8. Jacobs L, Cookfair D, Rudick R, Herndon R, Richert J. Intramuscular Interferon Beta-1a for Disease Progression in Relapsing Multiple Sclerosis. *Annals of Neurology* 1996;39:285-294.
9. The PRISMS Study Group. Randomised double-blind placebo-controlled study of interferon beta-1a in relasping/remitting multiple sclerosis. *Lancet* 1998;352:1498-1504.
10. The INFB Multiple Sclerosis Study Group. Interferon Beta-1B delays progression of disability in secondary progressive multiple sclerosis: Results of a European multicentre randomised study. *Lancet*, 1998:1491-1497.
11. Tolley K, Whynes D. Interferon-b in multiple sclerosis. Can we control its costs? *Pharmacoeconomics* 1997(11):210-215.
12. O'Brien B. Multiple Sclerosis. London, UK: Office of Health Economics, 1987.

13. Blumhardt L, Wood C. The economics of multiple sclerosis: a cost of illness study. *British Journal of Medical Economics* 1996(10):99-118.

14. Henriksson F, Jönsson B. The economic cost of multiple sclerosis in Sweden in 1994. *Pharmacoeconomics* 1998(13):597-606.

15. Midgard R, Rise T, Nyland H. Impairment, disability and handicap in multiple sclerosis. A cross-sectional study in Möre and Romsdal County, Norway. *Journal of Neurology* 1996(243):337-344.

16. Murphy N. Economic evaluation of multiple sclerosis in the UK, Germany and France. *Pharmacoeconomics* 1998(13):607-622.

17. K Whetten-Goldstein FS, LB Goldstein, ED Kulas. A comprehensive assessment of the cost of multiple sclerosis in the United States. *Multiple Sclerosis* 1998;4:419-425.

18. Henriksson F. *Multiple Sclerosis* 2000.

19. Parkin D. A cost-utility analysis of interferon beta for multiple sclerosis. Report to the National Health Service Technology Assessment programme. Newcastle: University of Newcastle, 1997.

20. The Canadian Burden of Illness Study Group. Burden of Illness of Multiple Sclerosis: Part I: Cost of Illness. *Canadian Journal of Neurological Sciences*, 1998:23-30.

21. The Canadian Burden of Illness Study Group. Burden of Illness in Multiple Sclerosis. Part II: Quality of Life., 1998:31-38.

22. Kurtzke J. Rating neurological impairment in multiple sclerosis and expanded disability status scale (EDSS). *Neurology* 1983(33):1444-1452.

23. Rice D. *Estimating Cost of Illness*. Washington, DC, USA: US Government Printing Office, 1966.

24. Hodgson T, Meiners M. Cost of illness methodology: A guide to assessment practices and procedures. *Milbank Memorial FUnd Quarterly/Health and Society* 1982;60:429-491.

25. The EuroQol Group. EuroQol - a new facility for the measurement of health-related quality of life. *Health Policy*, 1990:199-208.

26. Jönsson B, Jönsson L, Kobelt G. Modelling disease progression and the effect of treatment in secondary progressive MS. Stockholm: Stockholm School of Economics, 1999.

27. Kobelt G, Jönsson L, Henriksson F, Fredrikson S, Jönsson B. Cost-utility of interferon beta-1b in secondary progressive multiple sclerosis. *Int Journal of Technology Assessment in Health Care* 2000;16(3):in print.

28. Netten A, Dennett J, Knight J. Unit costs of Health and Social Care, 1999. Canterbury: Personal Social Services Research Unit (PSSRU), 1999.

29. The National Health Services Executive. The new NHS: 1999 reference costs.: Department of Health : http://www.doh.gov.uk/nhsexec/refcosts.htm, 1999.

30. Fuchs V. Economists, values and health care reform. *American Economic Review* 1986;86:1-24.

31. Newhouse JP. US and UK health economics: two discipline separated by a common language? *Health Economics* 1998;7:79-92.