

Quality of life and cost of multiple sclerosis

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1. Introduction

It is estimated that multiple sclerosis (MS) affects over one million people worldwide [1] and around 120 000 people in Germany [2]. In industrialized countries, prevalence rates vary between 15 and 145 per 100 000. Disease onset is typically between 20 and 40 years of age, with a higher incidence in women. MS is the most common cause of disability in young adults [3].

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 alter the progression of the disease. Several new treatments have recently been introduced that have shown an effect on the frequency of exacerbations in RRMS [4–6]. Of three clinical trials with interferons in SPMS, one has shown a significant effect on disease progression [7], and all three have shown a reduction on relapse rates.

These new agents are more expensive than previously used treatments, and there has been a concern about rising costs [8]. The cost-effectiveness of the new interventions has been questioned, and as a consequence, there is need for more accurate information of the actual cost of care, and total expenditures due to MS as a basis for cost-effectiveness assessments and decisions about resource allocation.

Patient reported outcomes (PRO) are increasingly seen as important additional sources of information on the safety and efficacy of treatments from the perspective of patients' organisations, HTA and regulatory agencies [9]. The outcomes measured in trials of treatments of MS, however, have mainly focused on clinical endpoints such as relapse rate and assessments of disability by the physician and on paraclinical para-

meters of disease such as the MRI. It has been suggested that evaluation of outcome based solely on these measures may be of limited usefulness because of its failure to consider the patient's point of view, and because other important aspects of MS are not sufficiently addressed. Hence, additional outcomes such as the assessment of depression, fatigue, cognition and quality of life (QoL) have been suggested and are now used as secondary or tertiary endpoints of efficacy. Health related quality of life (HrQoL) as a patient-reported outcome is particularly relevant in chronic progressive disabling diseases in which treatment cannot cure the illness but may improve and prolong functional independence. It is also an important outcome in that the patient evaluates the benefit of treatment taking into consideration both perceived efficacy and side effects.

2. Cost of illness

Several cost of illness studies have been performed in different countries [10–19]. The main objectives were to estimate the economic burden for society as a whole, and on different payers, as well as to generate cost data for cost-effectiveness analyses. The general findings of all studies were that (1) costs dramatically increase as patients progress to higher levels of disability [15,16]; (2) indirect costs are the dominant overall cost driver as 80% of patients lose their ability to work within the first 10 years after onset of MS [20]; and (3) that inpatient care is the dominant direct cost driver. Another significant finding was that a large proportion of the economic burden is not incurred within the health care system, but borne by social systems, communities or families [12,15].

Current knowledge on the economic burden of MS in various countries is limited due to a number of methodological problems; many studies have used only small samples, no disability measurements have been employed, different designs have been followed, i.e.

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either a “top-down” (using available statistics) or “bottom up” (primary data collection through chart reviews and questionnaires) approach, or included and excluded different costs. Severely disabled patients were almost never included. For some countries no cost of illness data exist. With this background three cost of illness studies were performed in Sweden [21], the UK [22] and Germany [23] using the same methodology on large representative samples. All three studies were prevalence-based observation studies, using a “bottom-up” approach; MS related resource use was correlated to EDSS status, quality of life and other aspects of MS. Sources of data included patient charts and a patient questionnaire. The objective of this study was to collect detailed cost-related data and to investigate how costs and QoL relate to different levels of disease severity, measured by the EDSS. This paper will focus on the German cost of illness study and will draw comparisons with the findings in the other two countries. In Germany six centers (five ambulatory neurology wards in university hospitals and one rehabilitation clinic) participated in the study. Patients were asked to complete a questionnaire which were returned by a total of 737 patients, a return rate of 66%. In the UK 619 patients (73% return rate) were included and 413 in Sweden (return rate of 76%). The questionnaire provided information on both medical and non-medical resource consumption, sick leave and informal care related to MS, as well as on QoL [24]. Simultaneously, medical charts were also abstracted for a subsample of 202 patients in order to allow comparison between answers in the questionnaires and recorded data. Levels of disability were assessed using the EDSS.

The mean age of the cohort was 41.9 (SD 14.1) years, the mean age of disease onset was 33.4 years, and the mean EDSS score 4.4 (range 1.0–9.5). The samples were very similar in all three countries with respect to demographic data. This was also true for the distribution of patients according to the clinical course of disease. The mean HrQoL score measured with the EQ-5D was 0.552 (SD 0.331), the mean total cost per patient per year was 65400 Deutsch marks (DM), adjusted for usage of interferons, which was higher in this sample than the current average use in Germany. When this cost is extrapolated to an estimated patient population of 120 000, the total costs to society are estimated at 7.85 billion DM. Direct costs represented 57.5%, informal care accounted for 12.1% and indirect costs amounted to 42.5%. Public payers pay for an estimated 24800 DM per patient or 38% of total costs. All types of costs (direct, informal care, indirect) increased with increasing disability.

It is interesting to compare these results with those of the two other countries, Sweden and the UK. For the UK the cost per patient are estimated at £16700 per patient per year, and at £1.47 billion for the annual

societal costs; the respective costs for Sweden are estimated at Swedish kroner 409 000 and SK 1.47 billion per year for society. The major differences are due to the costs of inpatient care, ambulatory visits, interferon use and informal care. Far more patients were admitted to hospital in Germany than in the other two countries, 58 versus 3 and 20% in Sweden and the UK, respectively, with a substantially higher length of stay, 16 days versus 5 and 2. Medical visits to neurologists and general practitioners were much more frequent, 13.6, respectively, versus 4.9 and 6.6. Interferon use in Germany and Sweden exceeded 40% in the samples, while in the UK it was only 2.6%. German patients also purchased far more OTC drugs. Probably the most interesting comparison relates to the provision of home care and home help. A similar proportion of patients needed and used these services in all three countries, but Sweden appears to provide the highest level of service and the UK the lowest, with Germany somewhere in the middle. As a direct consequence, the amount of informal care needed differed, and represented 11% of total costs in Germany, 5% in Sweden and 26% in the UK.

In all three countries costs markedly increased with increasing disability. Table 1 displays the mean total cost per patient per year for three different disability levels.

In all three studies the main cost driver is inpatient care of which hospital care accounts for more than 80%; indirect costs are significant but lower than previously estimated. This study was the largest international survey of the cost of MS in three countries based on representative samples. Reliable cost of illness data are essential for any cost benefit comparison. All studies so far have shown that disability and costs are closely related and the present study also shows that a considerable increase in costs is incurred in patients with an EDSS above 7.0. If progression can be delayed, the QoL and functional independence of patients will improve, and costs to health care systems, society and patients will also be diminished.

3. Quality of life

HRQoL as “the individual’s assessment of how a health problem and its treatment affect his/her ability to perform activities and roles that he/she values” [24] is an

Table 1
Mean total costs per disability level (EDSS)

EDSS	≤ 3.0	3.5–6.0	≥ 6.5
Germany (DM)	14.214	36.430	61.227
Sweden (SK)	122.620	269.572	712.903
United Kingdom (BP)	7.273	12.875	26.697

important outcome particularly in chronic progressive, disabling diseases for which there is no cure. There is general agreement that HrQoL is a multidimensional concept comprising physical, psychological and social aspects. The assessment should always be made by the patient and is hence always subjective. The use of validated questionnaires is essential and a number of new disease specific measures were developed for MS since the mid 1990s [25–27], but very few studies have used them to evaluate the impact of treatments in MS; furthermore, very few measures are suitable for clinical practice. The main focus of most published studies to date has been to establish the psychosocial burden for patients with MS compared to the general population through observational studies [15–17] and to validate new questionnaires. International observational studies have consistently shown that all aspects of HRQoL are much impaired in patients with MS, even at low levels of disability or when patients are still fully ambulatory; HrQoL further deteriorates during relapses [16]. While physical aspects of HrQoL also deteriorate with increasing disability, there are inconsistent findings for overall HrQoL or psychosocial aspects. Findings from a Canadian burden of illness study in 197 patients suggest that mental health (as measured by the SF-36) stabilises and even improves with higher levels of disability as patients are coping better with their illness over time [15]. Recent findings of the German, Swedish and British cost of illness studies, however, suggest that HrQoL dramatically decreases associated with progression to higher EDSS levels: health states > 7.0 on the EDSS were rated as “worse than being dead” by most of the patients in this group. Prospective controlled studies to evaluate treatment are scarce and focus mainly on rehabilitation [28,29]. HrQoL was prospectively included as a tertiary outcome of efficacy in the European study with interferon beta-1b in patients with secondary-progressive MS [7]. As no MS-specific questionnaire of HrQoL was available at the time the study was initiated, the Sickness Impact Profile (SIP) [30] was used. The SIP has been widely used for a broad range of indications, MS among them. Hutchinson and Hutchinson [31] have shown that changes in SIP scores were closely associated with changes on the EDSS. Petajan and colleagues [28] used the SIP to evaluate the outcome of a physical fitness program in patients with MS and showed a positive effect in the physical domain. The SIP comprises 136 items grouped in two categories, a physical and a psychosocial domain. It was self-completed in validated native language versions by all 718 patients at baseline and at 6-monthly intervals. The data show a trend for a better HrQoL in the interferon treated group for all three different scores, physical, psychosocial score and total [32], but only group comparisons for the physical dimension reached statistical significance at consecutive visits. As expected from

previous studies, physical HrQoL deteriorated in both groups with increasing disability although there had been no difference between groups at baseline. The deterioration was delayed in the Betaferon-treated group, in other words, more patients were kept stable in that group. At months 6,12 and at the patient's last visit, this difference reached statistical significance at the 5% level.

The trial was followed by an open-label extension of treatment with interferon beta-1b for another 18 months. There was a positive effect on physical HrQoL at all times in patients who were treated with interferon beta-1b during both the double-blind and the open-label period. This effect was again statistically significant at the end of the open-label treatment. A similar effect was observed for the total score of the questionnaire which includes all aspects of QoL. An important issue is whether this difference is clinically meaningful. Considerable score changes, by eight points on the SIP, were observed in patients who progressed but not in those who remained stable. However, more studies into the QoL of patients with MS are needed to better understand what patients would feel to be a meaningful difference.

This was the first large randomized, controlled clinical trial in MS showing a modest positive effect of treatment on HRQoL. As expected this effect is most clearly seen on the physical status. The effect was maintained during the open-label extension of treatment and was in line with the clinical measures of efficacy.

4. Conclusion

The psychosocial and economic burden of MS has been investigated through cross sectional observational studies using different methodological approaches. On a cross-sectional basis, progression to higher EDSS levels has been shown to be closely associated with an increase in costs and a decrease in HrQoL. Future studies should investigate both issues using longitudinal designs that should also include MS-specific questionnaires. Consensus on methodology is needed to enable comparisons between studies.

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