

The Manifold Economic Impact of Multiple Sclerosis – Indirect and Direct Costs of Managing Patients

David W Brandes¹ and Peter Rieckmann²

1. Neurologist, Hope Neurology, Knoxville, Tennessee, US; 2. Professor and Director, Department of Neurology, Bamberg Academic Hospital, University of Erlangen, Bamberg, Germany

DOI: 10.17925/ENR.2013.08.S1.17

Abstract

Multiple sclerosis (MS) is associated with a significant economic burden, not only in terms of direct costs (drugs, hospital admissions, healthcare aids), but also indirect costs including loss of income, reduction of productivity, burden on caregivers and family members, and a reduction in patient quality of life (QoL). The disease has a marked effect on employment, with less than 20 % of patients of working age in employment at higher disability levels (Expanded Disability Status Scale [EDSS] 6.0–8.0). Disabilities, fatigue, cognitive impairments, transportation difficulties, speech impairments and bladder and bowel problems all impact on the patient's ability to work and their QoL. The economic costs of MS do not just impact the patient. The stress and physical burden of caring for a friend or relative with MS may also impact on the finances and health of caregivers and increase their own requirement for healthcare resources. The increasing availability of disease-modifying drugs (DMDs) and earlier diagnosis of the condition has resulted in an increase in the direct costs of MS related to expenditure on DMDs. However, due to the significant increase in costs that are associated with increasing disease severity, interventions aimed at delaying disease progression may help to reduce the economic burden of MS. This article will review the direct, indirect and intangible costs of MS and discuss the economic impact of drug development on these costs.

Keywords

Multiple sclerosis, disease-modifying drugs, direct costs, indirect costs, intangible costs, economic impact

Disclosure: David W Brandes has been a member of the Speakers' Bureau for Acorda, Avanir, Bayer, Biogen Idec, EMD/Serono, Genzyme/Sanofi, Novartis, Questcor and Teva. He has participated on advisory boards for Avanir, Biogen Idec, Genzyme/Sanofi, Novartis, Questcor and Teva, and has received research support from Biogen Idec and Teva. Peter Rieckmann has served on scientific advisory boards for Merck Serono, Novartis, Teva and Bayer-Schering Pharma. He has also received speaker and/or consulting honoraria from Bayer-Schering Pharma, Biogen Idec, Merck Serono, Novartis and Teva.

Acknowledgements: Editorial assistance was provided by Janet Manson at Touch Medical Media and was funded by Genzyme.

Received: 30 November 2012 **Accepted:** 10 December 2012 **Citation:** *European Neurological Review*, 2012;7(Suppl. 2):17–23

Correspondence: David W Brandes, Hope Neurology, 10800 Parkside Drive, Suite 202, Knoxville, TN 37934, US. E: dwbnorth@sbcglobal.net

Multiple sclerosis (MS) is the most prevalent neurological disease among young adults, affecting 30 out of 100,000 people globally; prevalence is particularly high in Europe, North America and parts of Australia, with rates over 100 per 100,000.¹ The incidence of the disease is considered to rise with increasing distance from the equator though recent data suggest this may be changing.² The incidence of MS is also generally increasing, especially in females and has been attributed to various factors including the increasing urbanisation of populations.³

MS is associated with both high direct and indirect medical costs, and all costs increase with worsening disability. Patients with more severe disability (Expanded Disability Status Scale [EDSS] >7) may have annual costs four to five times higher than patients living with less disability (EDSS <4).⁴ MS displays a wide range of clinical symptoms that negatively impact patients' and caregivers' health related quality of life (HRQoL). Regardless of disability level, relapses significantly increase the cost of the disease, mainly due to associated hospitalisations and medications. Because the onset of MS usually occurs during the years of an individual's highest productivity and earning potential, MS has a severe and long-term effect on income and employment and ultimately quality of life (QoL). Direct medical costs of MS in the US

are estimated to total in excess of US\$10 billion per year^{5,6} and a recent European study showed that the total cost of MS in Europe was approximately US\$18.9 billion (€14.6 billion).⁷

Disease-modifying drugs (DMDs) have been available since the mid 1990s and are offered as subcutaneous injections (interferon beta-1a [IFN β -1a], interferon beta-1b [IFN β -1b], glatiramer acetate [GA]), intramuscular injections (IFN β -1a), intravenous infusions of monoclonal antibodies (natalizumab) or more recently as oral agents (such as fingolimod or teriflunomide). These medications modify the natural course of the disease by decreasing relapses and the inflammatory lesion load and to some extent also slowing disability progression. However, as mainly biological preparations, they are expensive compared with older symptomatic treatments (e.g. the antispastic agent baclofen), most are intended for long term treatment and some have significant side effects requiring more intensive patient management. As a result the proportion of the cost of MS represented by drug expenses has risen significantly in the last two decades. A recent study noted that the direct cost per MS patient nearly quadrupled in Italy during the period 1996-2004 and attributed this change to the availability of DMDs and the cost of diagnostics.⁸

Table 1: Summary of Studies of the Economic Impact of Multiple Sclerosis

Country	Year	Number of Patients	Summary of Findings	Reference
Australia	2007	100	Average annual direct and indirect costs per patient US\$19,532 and US\$14,446 (AU\$20,396 and AU\$15,085), respectively. Greatest uses of resources were for immunomodulating drugs, consultations and district nursing	52
Austria	2006	1,019	Mean total annual costs per patient US\$31,132 (€40,300)	53
Belgium	2006	799	Mean total annual costs per patient ranged from US\$9,270 (€12,000) per year (EDSS 0–1) to US\$39,784 (€51,500) per year (EDSS 8–9)	54
Germany	2006	2,793	Mean total annual cost per patient ranged from US\$14,291 (€18,500) (EDSS 0–1) to US\$54,440 (€70,500) (EDSS 8–9)	55
Italy	2002	552	Mean direct cost over three months was US\$1,408 (ITL 2,134,000) mean indirect cost was US\$5,132 (ITL 7,775,000)	29
Italy	2006	921	Mean total annual cost per patient ranged from US\$9,270 (€12,000) (EDSS 0–1) to US\$54,848 (€71,000) (EDSS 8–9)	19
Netherlands	2006	1,549	Mean total annual cost per patient US\$7,184 (€9,300) (EDSS 0–1), US\$64,725 (€50,000) (EDSS 7) and US\$100,803 (€78,000) (EDSS 8–9)	56
Poland	2008	120	All EDSS <3.5. Total annual direct and indirect costs per patient US\$13,495 (€10,425) and US\$9,162 (€7,078) respectively for those taking IFN; US\$1,401 (€1,082) and US\$10,137 (€7,831), respectively for those taking steroids	57
Spain	2006	1,848	Mean total annual cost per patient US\$13,495 (€10,425) (EDSS 0–1), US\$58,594 (€45,264) (EDSS 7) and US\$85,039 (€65,693) (EDSS 8–9)	20
Spain	2006	200	Mean total annual cost per patient US\$18,456 (€14,327) (EDSS 0), US\$24,384 (€18,837) (EDSS 1–3), US\$36,077 (€27,870) (EDSS 3.5–5.5), US\$53,330 (€41,198) (EDSS 6–7) and US\$68,402 (€52,841) (EDSS>7.5)	58
Sweden	2006	1,339	Mean total annual cost per patient ranged from US\$20,712 (€16,000) (EDSS 0–1) to US\$150,161 (€116,000) (EDSS 8–9)	18
Switzerland	2006	1,101	Mean annual cost per patient in the sample US\$54,369 (€42,000) corresponds to costs for a patient at the median EDSS score of 5	59
UK	2006	2,048	Mean annual costs ranged from US\$19,462 (€12,000) (EDSS <4) to almost US\$97,312 (€60,000) (EDSS ≥7). Employment rates reduced from 82 % in early disease to 2 % at EDSS of 8	60
UK	2008	1,942	Mean service cost per patient over 6 months was US\$13,619 (£8,397), 71.6 % due to informal care. Only 8.1 % due to the use of DMDs and drugs for spasticity. Lost employment costs amounted to a mean of US\$6,877 (£4,240)	61
US	2006	4,000	Mean annual cost per person US\$47,215 (€36,474), 53 % for direct medical and non-medical costs, 37 % for production losses and 10 % for informal care	12
France, Germany, Italy, Spain and the UK	2012	1,261	Mean total annual cost per patient ranged from US\$17,618–US\$29,242 (€13,534–€22,461) (EDSS ≤3), US\$37,135–US\$57,216 (€28,524–€43,948) (EDSS 4–6.5) and US\$51,545–US\$85,137 (€39,592–€65,395) (EDSS ≥7)	13

AU = Australian; DMD = disease-modifying drugs; EDSS = Expanded Disability Status Scale; IFN = interferon; ITL = Italian lire.

Greater awareness of MS by physicians, revision of the McDonald criteria for MS diagnosis,⁹ the widespread availability of magnetic resonance imaging (MRI) and a consensus by most neurologists concerning the importance of early treatment of MS have resulted in a willingness to investigate suspected neurological symptoms and have led to earlier diagnosis of MS. This improves patient prognosis but also increases the population of patients receiving treatment and therefore potentially further increases costs of disease management. However, early treatment of MS patients with DMDs results in increased cost-effectiveness of these drugs.¹⁰ Treatment for MS aims at limiting temporary disability due to relapses and more importantly, in some cases delays the progression to more permanent disability. Thus, the major economic benefit of treatment lies in the future and can be derived from the analysis of indirect costs. Such indirect costs however, are difficult to assess accurately and are rarely taken into account when considering treatment costs.

The guidelines in treating MS do not directly address the issue of limiting the economic impact of MS and minimising treatment costs. Consequently, the economic impact of multiple sclerosis is a subject of intense current interest. This article will review the direct, indirect

and intangible costs of MS and discuss the economic impact of drug development on these costs.

Total Costs of Multiple Sclerosis

Because of differences in the availability and costs of medical care, the use of paid and unpaid home and community-based services and the extent to which people withdraw from the work force (with resultant loss of income), it is difficult to compare worldwide costs of MS directly, particularly between the US and Europe, even when the same methodology is used. A large European study by Kobelt et al. (n=13,186) encompassing nine countries estimated the total mean annual cost of hospitalisations, consultations and medications used in MS at US\$23,300 (€18,000) in patients with mild disease (EDSS <4), US\$46,602 (€36,000) in patients with moderate disease (EDSS 4–6.5) and US\$80,258 (€62,000) in patients with severe disease (EDSS >7).¹¹ The total costs comprise direct, indirect and intangible costs associated with QoL. Kobelt et al. also performed a US study (n=1,909) of MS patients taking DMDs and estimated the mean total cost at US\$47,215, (€36,474) ranging from US\$32,297 (€24,950) for mild disease to US\$64,492 (€49,820) in severe disease.¹² The recent TRIBUNE study, which explored the total costs of MS in five European Countries, found the mean total

annual cost per patient ranged from US\$17,618–\$29,242 (€13,534–€22,461) for patients with mild disease (EDSS ≤3), US\$37,135–\$57,216 (€28,524–€43,948) for patients with moderate disease (EDSS 4–6.5) and US\$51,545–85,137 (€39,592–€65,395) for patients with severe disease (EDSS ≥7).¹³ A summary of worldwide studies on the costs of MS is given in *Table 1*.

Most recent studies on the economic impact of MS include direct and indirect costs. Both the direct and indirect costs of MS increase with disability severity.^{4,14} Regardless of disability level, relapses significantly increase the cost, mainly due to associated hospitalisations and medications. While direct medical costs are highest at the early stages of MS treatment, they are outweighed by indirect costs at the later stages of the disease.¹⁵ The relative contributions of direct and indirect costs in the US and Europe are illustrated in *Figures 1, 2* and 3.

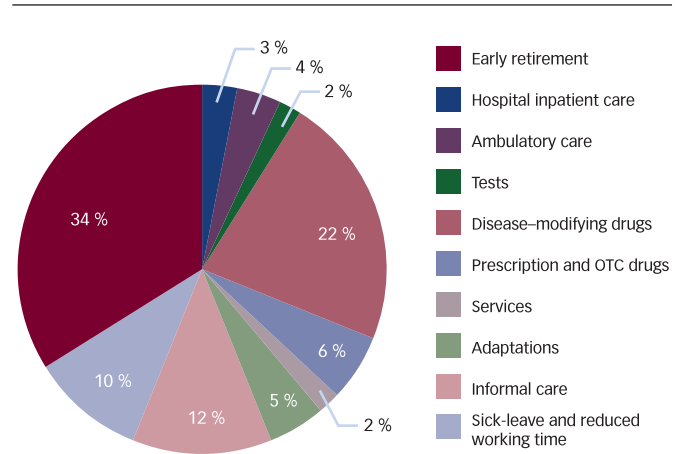
Direct Costs of Multiple Sclerosis

Direct costs refer to all resources consumed to diagnose, treat, or manage patients with MS. The direct healthcare costs of MS are high and include diagnostic tests, hospital costs, physician costs, nursing home care, medication, rehabilitation, physician costs and assessments. Prompt diagnosis has an impact on the cost as a delay can result in unnecessary referrals to other specialists, as well as additional diagnostic testing. Monitoring of disease progression is also expensive, often involving an annual MRI. Disease management involves consultation costs, the highest being associated with physiotherapy, followed by neurologists, psychiatrists and psychologists.¹² Hospitalisations due to relapse incur a large direct cost. However, the greatest direct cost of MS is associated with DMDs, some of which require frequent injections (≥ 3x weekly) and have long treatment duration (over 20 years).

Previous studies on the costs of MS have estimated the cost of drugs at up to 80 % of the total costs of MS.^{16,17} However these have only considered direct costs incurred in MS and have failed to take into account the impact of DMDs on disease progression and relapse rate, and consequent saving in indirect costs. When interpreting studies of the cost-effectiveness of DMDs, it is also important to be aware of the disparity of drug costs between the US and Europe: for example, in 2011 the annual cost of IFNβ-1a in the UK was approximately US\$12,920 (£8,000, €9,981) compared with about US\$34,000 (£20,963, €26,265) a year in the US,¹⁰ and the costs have continued to rise significantly throughout the US since that time. The cost of other prescription drugs/concomitant medications is also significant. In the Kobelt US study estimate of total costs, 77.6 % of patients also used other prescription drugs including antidepressants (52.7 %) and anti-spasticity drugs (48.5 %), followed by anti-fatigue medication (38.4 %). Over-the-counter drugs were used in addition by 58.1 % of the sample.¹²

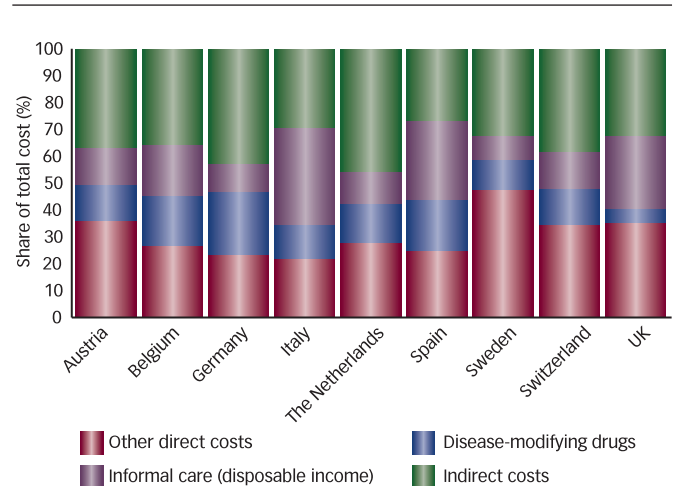
In addition to medical expenses, direct nonmedical costs refer to other resources required in the care for MS patients. These include paid home care, informal care provided by family and friends, MS adult day care, home or automobile modifications, disability aids, transportation and other resources (e.g. childcare, housekeeping). The level of informal care can vary significantly between countries and is often hard to quantify. In Sweden, the government provides in-home personal assistance resulting in high costs¹⁸ whereas in countries with a lower proportion of female participation in the workforce such as Spain and Italy the costs are much lower.^{19,20} As

Figure 1: Distributions of Costs Incurred in Multiple Sclerosis in the US



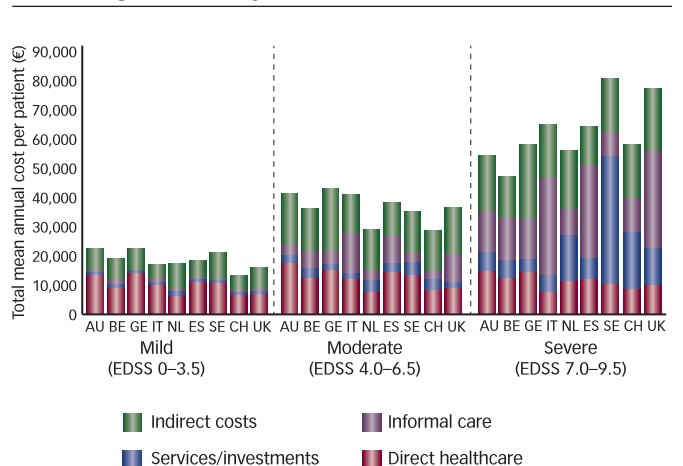
OTC = over-the-counter. Source: Kobelt et al., 2006.¹²

Figure 2: Proportion of Direct and Indirect Costs of Multiple Sclerosis Per Patient in Europe



Costs are presented as percentage of total cost per patient. Direct costs include medical care (hospitalisation, consultations, tests, prescriptions and over-the-counter drugs excluding disease-modifying drugs, services (home care, home help, transportation) and investments (devices, appliances, changes to house and car). Informal care is calculated as lack of leisure time for the carer, using the disposable income (net after social contribution and taxes) as the cost of leisure time. Source: Kobelt et al., 2006.¹¹

Figure 3: Costs of Multiple Sclerosis in Europe According to Severity of Disease



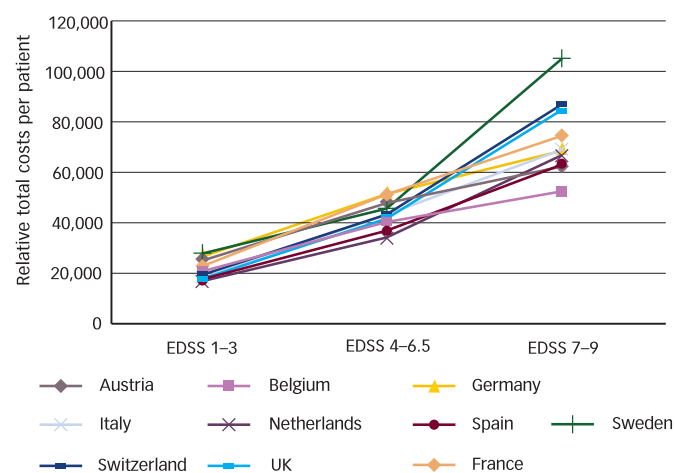
AU = Austria; BE = Belgium; CH = Switzerland; EDSS = Expanded Disability Status Scale; ES = Spain; GE = Germany; IT = Italy; NL = The Netherlands; SE = Sweden; UK = United Kingdom. Source: Kobelt et al., 2006.¹¹

Table 2: Percentage of Workforce Participation, Sick Leave and Early Retirement in Multiple Sclerosis Patients by Country

Characteristics	Austria	Belgium	Netherlands	Spain	UK	Sweden	Switzerland	Germany	Italy
Currently employed	30.4	39.7	37.4	30.0	28.2	40.8	34.7	40.9	42.1
Working full time	20.4		10.6	17.9	5.5	12.4	0	17.1	14.1
Working reduced hours		33.9				21.7			
Long-term illness leave	0.6	5.8	1.9	3.8	0.9	6.7	1.2	2.3	0.6
Short-term sick leave (3 months)	26.5		14.0	5.5	11.5	24.9	4.5	11.0	22.4
Changed working hours	6.7		15.7	3.9	10.9	52.0*	16.3	9.7	12.3
Changed type of work	5.6		10.4	6.8	10.8	38.8*	7.6	6.6	11.8
Retired early because of MS	44.5	32.9	42.2	34.1	44.3	35.7	33.9	33.9	33.9

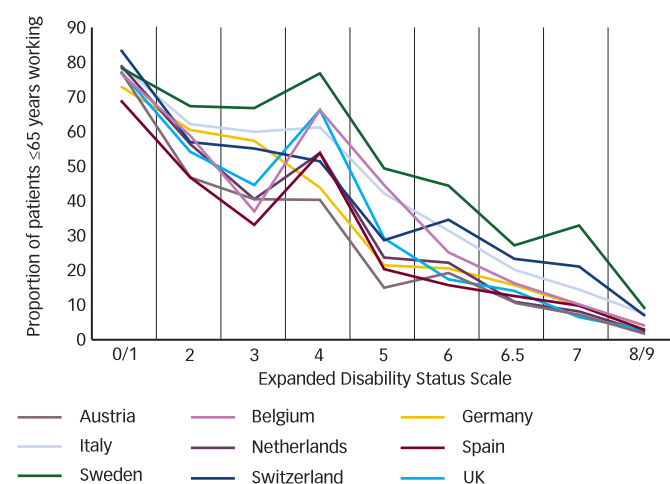
* Of those currently employed. MS = multiple sclerosis. Source: Trisolini et al., 2010.¹⁴

Figure 4: Patient Costs as Compared to Expanded Disability Severity Scale



EDSS = Expanded Disability Status Scale. Source: Patwardhan et al., 2005.⁴

Figure 5: Proportion of Patients Employed or on Long-term Sick Leave as a Percentage of Patients Aged ≤65 years



The reduced capacity at Expanded Disability Status Scale (EDSS) 2–3 compared with EDSS 4 is explained by an increased frequency of relapses in this group and hence a concentration of sick leave. Source: Kobelt et al., 2006.¹¹

fewer females work in these countries, there are more people available to provide a care-giving role. Direct costs of MS such as medications and treatment costs, rise with increasing EDSS category and the direct cost for those with the highest EDSS scores can be up to seven times those for the lowest EDSS scores (see Figure 4).⁴

Indirect Costs of Multiple Sclerosis

Indirect costs associated with MS include lost productivity, the economic impact of early mortality and the impact on the family. People with MS often have difficulty continuing to work and lost productivity due to loss of employment or early retirements is the largest single factor contributing to the financial cost of MS.¹⁴ Indirect costs represent a higher proportion of total costs at moderate levels of disability, as more people at these levels are of working age.^{12,19}

The impact of MS on employment is marked. The Kobelt European study demonstrated that among patients with EDSS scores of 0–1.0, about 70–80 % of those aged 65 years or below were employed. The employment rate for patients with EDSS 4.0 varied between countries from 40–76 %, however for patients with EDSS 8.0–9.0 this proportion was <10 %. Moreover, over half of the respondents had to reduce the number of hours worked or change their type of work (see Table 2, Figure 5).¹¹ Early retirement was noted in 35 % of participants (see Table 2).¹¹

In the Kobelt US study of MS patients taking DMDs, 41 % were working (63 % full time). Around one fifth of patients had changed their work or reduced their working hours, while 31.5 % had taken early retirement because of MS. An additional 10.9 % reported that they had stopped working because of MS, without indicating that they received an early retirement pension.¹²

Income loss in MS patients is accompanied by a corresponding increase in disability/incapacity claims to government welfare programmes and insurance companies. A US study of MS patients found that health insurance covered 51 % of costs for services, excluding informal care, with compensation for earnings loss representing only 27 %.²¹ This imposes a high economic burden on medical and social security budgets worldwide.

In a literature review, it was found that of those employed, MS patients have a significantly increased occurrence of long and short-term sick leave, particularly associated with relapses.¹⁵ In a US study (n=989) employees with MS had more than 6 times the number of sick leave days per year than those without. Annual costs for disability were nine times higher for employees with MS than employee controls. In addition, indirect costs (such as loss of earnings due to unpaid leave), were >4 times higher for employees with MS than for employee controls.²²

In a recent survey carried out by the Multiple Sclerosis International Federation involving 8,681 participants from 125 countries, fatigue (85 %) and mobility issues (72 %) were reported as the symptoms most detrimental to their ability to remain working. When unemployed

participants were asked what factors might have enabled them to carry on working, the top responses given were flexible work hours (48 %), the ability to take regular breaks to rest (42 %), a place to rest (34 %) and better awareness of MS among work colleagues (34 %).²³ Furthermore, people with MS are more likely than all other disabled employees to complain of discrimination related to benefits, health insurance, demotion, reasonable accommodations, and the terms of employment.²⁴

Premature death from MS or complications associated with the disease causes an economic burden due to the value of the lost years of life. MS is usually considered a disease that does not have a dramatic impact on life expectancy. However, recent studies across multiple countries show that MS reduces life expectancy by 5–15 years due to high levels of disability or co-morbidities.^{25–27} Treatments that improve MS symptoms and prevent and manage complications in more severely disabled patients may result in improved survival.

The economic impact of MS is not restricted to the patient. People with MS often require help performing daily tasks because of healthcare problems as well as functional and cognitive impairments. Informal caregivers, principally spouses and other relatives often provide patient care. Several studies have found that the stress and physical burden of caring for a friend or relative with MS may also impact on the health of caregivers and increase their own requirement for healthcare resources. In one study (n=62), 64.5 % of participants reported work adjustments, for example having to take time off and 12 % of caregivers were receiving treatment for depression.²⁸ In Italy, where the level of informal care is high, the cost of working days lost by the caregiver is similar to the cost of working days lost by the patient: 39.3 % of caregivers lost an average of 7.8 days working days over three months.²⁹ In a US study (n=1,461), 53 % of informal caregivers had missed an average of 7.3 days work over the past year due to care giving responsibilities.³⁰ A total of 7 % reported changing their employment as a result of their role as a caregiver. Of the participants, 28 % reported high blood pressure, 26 % reported high cholesterol, 13 % reported chronic headache, 13 % reported persistent trouble sleeping and 17 % reported depression or anxiety, however the incidence was not compared to the general population.³⁰

In summary, from early in the disease MS has profound implications on employment and financial status for many people, including patients, care partners and other family members.

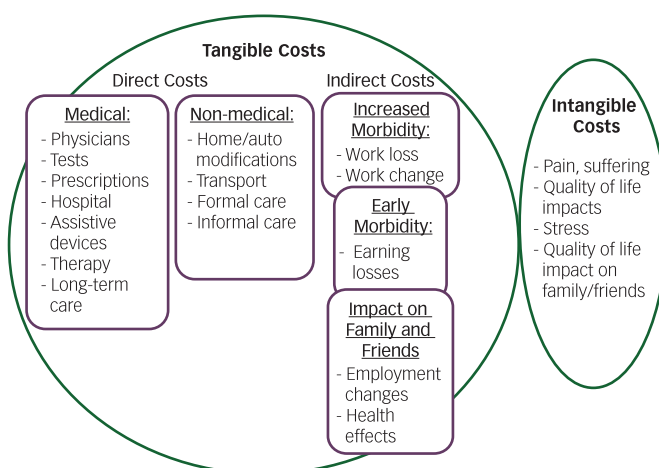
Intangible Costs of Multiple Sclerosis

A significant component of the economic burden of MS, frequently underestimated in cost-of-illness studies of MS, is the intangible cost related the impact of MS on QoL. Numerous studies have documented adverse effects of MS on QoL, including physical, social and mental functioning.^{1,31,32} Other impacts of MS not included in generic QoL measures include cognitive dysfunction.³³ Although it is difficult to quantify intangible costs, a Spanish study calculated the intangible costs per patient-year as US\$1,424 (€1,100) (EDSS = 1–3), US\$10,680 (€8,250) (EDSS = 3.5–5.5), US\$12,815 (€9,900) (EDSS = 6–7) and US\$14,239 (€11,000) (EDSS >7.5).³⁴

Economic Impact of Advances in Drug Development

An important question to address when assessing the economic impact of advances in drug development is, to what extent do DMDs provide cost saving in the treatment of patients with MS? In a study

Figure 6: Model of Multiple Sclerosis Costs Categories



Source: Trisolini et al., 2010.¹⁴

comparing the direct and indirect costs of MS, initiation of DMD therapy was associated with substantial medical and indirect savings for employees with MS. Risk-adjusted total annual medical costs and indirect costs were significantly lower for treated MS employees than for untreated MS employees.³⁵ These findings are important, as the majority of healthcare interventions across other disease states do not result in cost savings.

Various models have been used to calculate the cost-effectiveness of DMDs in MS and as a consequence there is a lack of consistent comparative data between different DMDs. Several studies have found that GA is associated with a reduction in cost of MS care relative to IFN β -1a and IFN β -1b,^{16,36,37} although another study found no significant difference between them.³⁸ A comparison of GA and natalizumab found GA to be the more cost-effective drug, although natalizumab was associated with a slower disease progression and relapse rate over two years.³⁹ Multiple papers have suggested that natalizumab is the most effective in relapse rate reduction of the currently available DMDs.^{40–42} In a study of the cost-effectiveness of natalizumab compared to other DMDs, the two-year costs of therapy were highest for natalizumab (natalizumab, US\$72,120 [€55,713]; intramuscular [IM] IFN β , US\$56,790 [€43,871]; IFN β -1b, US\$56,773 [€43,857]; subcutaneous [SC] IFN β , US\$58,538 [€45,221]; and GA \$57,180 [€44,172]). The cost per relapse avoided, however, was much lower for natalizumab than other DMDs (natalizumab, US\$56,594 [€43,719]; IFN β , US\$87,791 [€67,819]; IM IFN β -1a, US\$93,306 [€72,079]; SC IFN β -1a, US\$96,178 [€74,298]; and GA, US\$103,665 [€80,082]).^{41,43} It should be noted that, these studies used relapse rate reduction rather than sustained disability progression as a primary outcome measure, have assumed full patient adherence and have not captured adverse events in the models. It is difficult to compare the relative effects of DMDs across clinical trials because of heterogeneity in inclusion criteria and baseline disease severity.

Treatment adherence has a significant impact on patient outcome in patients with MS. Patients who are more adherent with their therapy have better outcomes. A recent study (n=2,446) found that patients who adhered to their DMD treatment were significantly less likely to have MS-related hospitalisations (odds ratio [OR]=0.63, 95 % confidence interval [CI]=0.47–0.83) and MS relapses (OR=0.71, 95 % CI=0.59–0.85) than the non-adherent group.⁴⁴

The adherent group incurred lower overall medical costs than the nonadherent group (US\$3,380 (€2,611), 95 % CI, US\$3,046–\$3,750 versus. US\$4348 (€3,359), 95 % CI, US\$3,828–\$4,940, $p=0.003$).

In addition to their effect on disease progression, MS drugs may bring about a reduction in the costs of MS by their functional effects. In one study, natalizumab treatment resulted in improvements in cognitive function that are maintained at two years.⁴⁵ Symptomatic treatments that improve function, for example, fampridine, which improves walking ability,⁴⁶ could have a significant impact in reducing indirect costs by allowing patients to continue working for longer.

It has recently been suggested that the price of DMDs would have to be cut by at least two-thirds in the US to make them cost effective in terms of improving quality of life. The DMDs examined in the study (IFN β -1a, IFN β -1b and GA), were estimated to cost more than US\$800,000 (€618,000) per quality adjusted life year (QALY). While there is no formal definition of cost-effectiveness in the US, this is an order of magnitude above what is generally considered acceptable. However, the effectiveness varied significantly among individuals. Prescribing DMDs at an earlier stage of the disease was associated with improved cost-effectiveness.¹⁰ However, some people have criticised the study, pointing out that data was taken over a 10-year period, whereas the disease can span 25–30 years.⁴⁷ Since early treatment delays the onset of progressive disease, the savings can only be fully assessed over a longer interval.

Several new therapeutic options for MS have emerged in the last few years, including new oral drugs either launched (fingolimod and teriflunomide),⁴⁸ or are in development, including BG-12 and laquinimod.⁴⁹ Other new drugs such as alemtuzumab⁵⁰ and ocrelizumab,⁵¹ are effective

and require short and infrequent treatment courses, and may offer cost-effective approaches.

Concluding Remarks

MS imposes a substantial economic burden on MS patients, caregivers, and on healthcare resources. These burdens include direct costs, indirect costs, and other intangible costs (see *Figure 6*). The apparent cost of healthcare is variable according to the perspective of the viewer. For example, private healthcare insurers utilise only the direct costs of care, while governments that provide for the cost of medical care utilise their direct costs of care, loss of tax income due to unemployment and long-term care costs. On the other hand, patients and families utilise direct and indirect medical costs not paid by insurance, as well as loss of income and costs related to quality of life. Each view is valid, but the overall cost of care must include all viewpoints when making decisions about healthcare funding.

Better information about disability rights and the availability of services are necessary to help people with MS continue working longer and thus reduce the economic impact of the disease. Campaigns are also needed to raise awareness that MS is a treatable disease and that physical accommodations and flexibility in workplace along with effective therapy can extend an individual's gainful employment.

In addition, further studies are required to compare currently available DMDs and to evaluate the benefits of early treatment. The increased choice to patients offered by newer, possibly less expensive drugs with shorter treatment courses has the potential to affect both the direct and indirect costs of MS. The continued development of drugs with increasing efficacy and which reduce disability and disease progression will hopefully change the course of this disease and its associated economic burden. ■

- Olek MJ, The Canadian Burden of Illness Study Group, Burden of illness of multiple sclerosis: Part II: Quality of life. The Canadian Burden of Illness Study Group, *Can J Neurol Sci*, 1998;25:31–8.
- Benito-Leon J, Are the prevalence and incidence of multiple sclerosis changing?, *Neuroepidemiology*, 2011;36:148–9.
- Kotzamani D, Panou T, Mastorodemos V, et al., Rising incidence of multiple sclerosis in females associated with urbanization, *Neurology*, 2012;78:1728–35.
- Patwardhan MB, Matchar DB, Samsa GP, et al., Cost of multiple sclerosis by level of disability: a review of literature, *Mult Scler*, 2005;11:232–9.
- Zwibel HL, Smrtka J, Improving quality of life in multiple sclerosis: an unmet need, *Am J Manag Care*, 2011;17(Suppl. 5):S139–45.
- Fox RJ, Sweeney PJ, Multiple sclerosis. Cleveland Clinic Disease Management Project. The Cleveland Clinic Foundation, 2002. Available at: www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/neurology/multsclerosis/multsclerosis.html (accessed 24 October 2012).
- Fattore G, Lang M, Pugliatti M, The Treatment experience, burden, and unmet needs (TRIBUNE) study - measuring the socioeconomic consequences of multiple sclerosis, *Mult Scler*, 2012;18:5–6.
- Patti F, Amato MP, Trojano M, et al., Multiple sclerosis in Italy: cost-of-illness study, *Neuro Sci*, 2011;32:787–94.
- Polman CH, Reingold SC, Banwell B, et al., Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria, *Ann Neurol*, 2011;69:292–302.
- Noyes K, Bajorska A, Chappel A, et al., Cost-effectiveness of disease-modifying therapy for multiple sclerosis: a population-based study, *Neurology*, 2011;77:355–63.
- Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of patients with multiple sclerosis in Europe, *J Neurol Neurosurg Psychiatry*, 2006;77:918–26.
- Kobelt G, Berg J, Atherly D, et al., Costs and quality of life in multiple sclerosis: a cross-sectional study in the United States, *Neurology*, 2006;66:1696–702.
- Karampampa K, Gustavsson A, Miltenburger C, et al., Treatment experience, burden and unmet needs (TRIBUNE) in MS study: results from five European countries, *Mult Scler*, 2012;18:7–15.
- Trisolini M, Honeycutt A, Wiener J, Lesense S, Global economic impact of MS, Multiple Sclerosis International Federation, 2010; Literature Review, available at: http://www.msif.org/docs/Global_economic_impact_of_MS.pdf (accessed 11 December 2012).
- Naci H, Fleurence R, Birt J, et al., Economic burden of multiple sclerosis: a systematic review of the literature, *Pharmacoeconomics*, 2010;28:363–79.
- Ollendorf DA, Jilinskaia E, Oleen-Burkey M, Clinical and economic impact of glatiramer acetate versus beta interferon therapy among patients with multiple sclerosis in a managed care population, *J Manag Care Pharm*, 2002;8:469–76.
- Russo P, Capone A, Paolillo A, et al., Cost-analysis of relapsing-remitting multiple sclerosis in Italy after the introduction of new disease-modifying agents, *Clin Drug Investig*, 2004;24:409–20.
- Berg J, Lindgren P, Fredrikson S, et al., Costs and quality of life of multiple sclerosis in Sweden, *Eur J Health Econ*, 2006;7(Suppl. 2):S75–85.
- Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of multiple sclerosis in Italy, *Eur J Health Econ*, 2006;7(Suppl. 2):S45–54.
- Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of multiple sclerosis in Spain, *Eur J Health Econ*, 2006;7(Suppl. 2):S65–74.
- Whetten-Goldstein K, Sloan FA, Goldstein LB, et al., A comprehensive assessment of the cost of multiple sclerosis in the United States, *Mult Scler*, 1998;4:419–25.
- Ivanova JI, Birnbaum HG, Samuels S, et al., The cost of disability and medically related absenteeism among employees with multiple sclerosis in the US, *Pharmacoeconomics*, 2009;27:681–91.
- Chandraratna D, MSIF survey on employment and MS, Multiple Sclerosis International Federation, 2010; available at: www.msif.org/document.rm?id=648 (accessed 11 December 2012).
- Unger DR, Roessler RT, Stacklin R, A comparative analysis of employment discrimination complaints filed by people with multiple sclerosis and individuals with other disabilities, *Journal of Vocational Rehabilitation*, 2004;20:165–70.
- Ekestern E, Lehart G, Mortality from multiple sclerosis in Austria 1970–2001: dynamics, trends, and prospects, *Eur J Neurol*, 2004;11:511–20.
- Grytten Torkildsen N, Lie SA, Aarseth JH, et al., Survival and cause of death in multiple sclerosis: results from a 50-year follow-up in Western Norway, *Mult Scler*, 2008;14:1191–8.
- Ragonese P, Aridon P, Salemi G, et al., Mortality in multiple sclerosis: a review, *Eur J Neurol*, 2008;15:123–7.
- Khan F, Pallant J, Brand C, Caregiver strain and factors associated with caregiver self-efficacy and quality of life in a community cohort with multiple sclerosis, *Disabil Rehabil*, 2007;29:1241–50.
- Amato MP, Battaglia MA, Caputo D, et al., The costs of multiple sclerosis: a cross-sectional, multicenter cost-of-illness study in Italy, *J Neurol*, 2002;249:152–63.
- Quig ME, Simsarian J, Cutter G, et al., MS CarePartner Stress: a NARCOMS study, *Multiple Sclerosis Quarterly Report*, 2007;29:6–10.
- Murphy N, Confavreux C, Haas J, et al., Quality of life in multiple sclerosis in France, Germany, and the United Kingdom. Cost of Multiple Sclerosis Study Group, *J Neurol Neurosurg Psychiatry*, 1998;65:460–6.
- Vickrey BG, Hays RD, Harooni R, et al., A health-related quality of life measure for multiple sclerosis, *Qual Life Res*, 1995;4:187–206.
- Bagert B, Camplair P, Bourdette D, Cognitive dysfunction in multiple sclerosis: natural history, pathophysiology and management, *CNS Drugs*, 2002;16:445–55.
- Casado V, Romero L, Gubieras L, et al., An approach to estimating the intangible costs of multiple sclerosis according to disability in Catalonia, Spain, *Mult Scler*, 2007;13:800–4.
- Birnbaum HG, Ivanova JI, Samuels S, et al., Economic impact of multiple sclerosis disease-modifying drugs in an employed population: direct and indirect costs, *Curr Med Res Opin*, 2009;25:869–77.
- Bell C, Graham J, Earnshaw S, et al., Cost-effectiveness of four immunomodulatory therapies for relapsing-remitting multiple sclerosis: a Markov model based on long-term clinical data, *J Manag Care Pharm*, 2007;13:245–61.
- Sanchez-de la Rosa R, Sabater E, Casado MA, et al., Cost-effectiveness analysis of disease modifying drugs (interferons and glatiramer acetate) as first line treatments in relapsing-remitting multiple sclerosis patients, *J Med Econ*, 2012;15:424–33.
- Goldberg LD, Edwards NC, Fincher C, et al., Comparing the cost-effectiveness of disease-modifying drugs for the first-line treatment of relapsing-remitting multiple sclerosis, *J Manag Care Pharm*, 2009;15:543–55.
- Earnshaw SR, Graham J, Oleen-Burkey M, et al., Cost effectiveness of glatiramer acetate and natalizumab in relapsing-remitting multiple sclerosis, *Appl Health Econ Health Policy*, 2009;7:91–108.

40. Bakhshai J, Bleu-Laine R, Jung M, et al., The cost effectiveness and budget impact of natalizumab for formulary inclusion, *J Med Econ*, 2010;13:63–9.
41. Chiao E, Meyer K, Cost effectiveness and budget impact of natalizumab in patients with relapsing multiple sclerosis, *Curr Med Res Opin*, 2009;25:1445–54.
42. O'Day K, Meyer K, Miller RM, et al., Cost-effectiveness of natalizumab versus fingolimod for the treatment of relapsing multiple sclerosis, *J Med Econ*, 2011;14:617–27.
43. Brandes DW, Shaya FT, Pill MW, Quantifying the role of natalizumab in health and economic outcomes in multiple sclerosis, *Am J Manag Care*, 2010;16:S171–7.
44. Tan H, Cai Q, Agarwal S, et al., Impact of adherence to disease-modifying therapies on clinical and economic outcomes among patients with multiple sclerosis, *Adv Ther*, 2011;28:51–61.
45. Mattioli F, Stampatori C, Bellomi F, et al., Natalizumab efficacy on cognitive impairment in MS, *Neurol Sci*, 2011;31(Suppl. 3):321–3.
46. Goodman AD, Brown TR, Krupp LB, et al., Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial, *Lancet*, 2009;373:732–8.
47. Valeo T, This way in: the cost of MS drugs, *Neurology Now*, 2011;7:12–3.
48. Brinkmann V, Billich A, Baumruker T, et al., Fingolimod (FTY720): discovery and development of an oral drug to treat multiple sclerosis, *Nat Rev Drug Discov*, 2010;9:883–97.
49. Gasperini C, Ruggieri S, Pozzilli C, Emerging oral treatments in multiple sclerosis – clinical utility of cladribine tablets, *Ther Clin Risk Manag*, 2010;6:391–9.
50. Coles AJ, Fox E, Vladoic A, et al., Alemtuzumab more effective than interferon beta-1a at 5-year follow-up of CAMMS223 Clinical Trial, *Neurology*, 2012;78:1069–78.
51. Kappos L, Li D, Calabresi PA, et al., Ocrelizumab in relapsing-remitting multiple sclerosis: a phase 2, randomised, placebo-controlled, multicentre trial, *Lancet*, 2011;378:1779–87.
52. Taylor B, McDonald E, Fantino B, et al., The cost of multiple sclerosis in Australia, *J Clin Neurosci*, 2007;14:532–9.
53. Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of multiple sclerosis in Austria, *Eur J Health Econ*, 2006;7(Suppl. 2):S14–23.
54. Kobelt G, Costs and quality of life for patients with multiple sclerosis in Belgium, *Eur J Health Econ*, 2006;7(Suppl. 2):S24–33.
55. Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of multiple sclerosis in Germany, *Eur J Health Econ*, 2006;7(Suppl. 2):S34–44.
56. Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life in multiple sclerosis in The Netherlands, *Eur J Health Econ*, 2006;7(Suppl. 2):S55–64.
57. Matschay A, Nowakowska E, Hertmanowska H, et al., Cost analysis of therapy for patients with multiple sclerosis (MS) in Poland, *Pharmacol Rep*, 2008;60:632–44.
58. Casado V, Martinez-Yelamos S, Martinez-Yelamos A, et al., Direct and indirect costs of Multiple Sclerosis in Baix Llobregat (Catalonia, Spain), according to disability, *BMC Health Serv Res*, 2006;6:143.
59. Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of multiple sclerosis in Switzerland, *Eur J Health Econ*, 2006;7(Suppl. 2):S86–95.
60. Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of multiple sclerosis in the United Kingdom, *Eur J Health Econ*, 2006;7(Suppl. 2):S96–104.
61. McCrone P, Heslin M, Knapp M, et al., Multiple sclerosis in the UK: service use, costs, quality of life and disability, *Pharmacoeconomics*, 2008;26:847–60.