

New insights into the burden and costs of multiple sclerosis in Europe: Results for Portugal

Maria José Sá, Gisela Kobelt, Jenny Berg, Daniela Capsa, Johan Dalén and The European Multiple Sclerosis Platform

Abstract

Background: In order to assess the value of management strategies in multiple sclerosis (MS), outcome data have to be combined with cost data. This, in turn, requires that cost data be regularly updated.

Objective and methods: This study is part of a cross-sectional retrospective study in 16 countries collecting current data on resource consumption, work capacity and health-related quality of life (HRQoL). Descriptive analyses are presented by level of severity; costs are estimated in the societal perspective, in EUR 2015.

Results: A total of 535 patients (mean age 48.5 years) participated; 92% were below retirement age and of these, 43% were employed. Employment was related to disease severity, and MS was felt to affect productivity at work by 72% of patients, most often through fatigue. Overall, 98% and 74% of patients felt that fatigue and cognition were a problem. Mean utility and costs were 0.756 and €16,500 at the Expanded Disability Status Scale (EDSS) 0–3, 0.572 and €28,700 at EDSS 4–6.5 and 0.206 and €34,400 at EDSS 7–9. The average cost of a relapse was estimated at €2930.

Conclusion: This study illustrates the burden of MS on Portuguese patients and provides current data that are important for the development of health policies.

Keywords: Multiple sclerosis, burden of illness, fatigue, cognition, costs, HRQoL, Portugal

Introduction

Portugal was one of the first countries in Europe to include economic evaluation into decisions about reimbursement and pricing. The National Authority of Medicines and Health Products (Infarmed) issued specific guidelines as early as 1998.¹ Despite this, no comprehensive assessment of the burden of multiple sclerosis (MS) has been published so far.

The availability of disease-modifying treatments (DMTs) has led not only to changes in patient management but also to focus on earlier and better diagnosis and adjustments in the diagnostic criteria themselves. One of the consequences in this regard is that the recorded prevalence of the disease is quite different from that estimated two or three decades ago.² The prevalence of MS in Portugal has been recently estimated at around 56.2 per 100,000,³ and the vast majority of patients are followed in hospitals of the National Health Service. With earlier diagnosis after a clinically

isolated event,⁴ one must also expect a different distribution of the type of MS and the severity of the disease: a larger proportion of patients with relapsing-remitting multiple sclerosis (RRMS) disease and thus of patients in the early stages of the disease, with less disability.

It is therefore important to update the information on the burden of MS, and this study is part of a European-wide effort in 16 countries, endorsed by the European Platform of MS Societies (EMSP) and carried out with the support of national MS societies.⁵ It uses a similar methodology as the last European survey in 2005 that, however, did not include Portugal.⁶

Materials and methods

The detailed methodology of the European survey is published separately.⁷ We therefore only provide a short summary of the general methods and issues specific to Portugal.

Multiple Sclerosis Journal

2017, Vol. 23(2S) 143–154

DOI: 10.1177/
1352458517708667

© The Author(s), 2017.
Reprints and permissions:
[http://www.sagepub.co.uk/
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Correspondence to:
G Kobelt
European Health Economics,
15 Rue Victor Schoelcher,
68200 Mulhouse, France.
kobelt.gisele@wanadoo.fr

Maria José Sá
Department of Neurology,
Centro Hospitalar de S. João,
Porto, Portugal

Gisela Kobelt
European Health Economics,
Mulhouse, France

Jenny Berg
Daniela Capsa
Johan Dalén
Mapi Group, Stockholm,
Sweden

Data

The study aimed to estimate all costs related to MS: hospitalisation, rehabilitation, consultations, diagnostic procedures and tests, medication, community care, family support and production losses (sick leave, early retirement, invalidity). In addition, information on major symptoms such as fatigue and cognition using visual analogue scales (VAS), health-related quality of life (HRQoL), as well as self-assessed disability using descriptions based on the Expanded Disability Status Scale (EDSS) were included.

Data were collected with a standard questionnaire, at a single point in time, for a retrospective period of time. The latter was varied depending on the question in order to minimise recall bias: 1 month for use of drugs, community services and family help; 3 months for hospitalisation, consultations, tests, sick leave and relapses; and 12 months for major investments. Resource utilisation is reported for these time periods, while cost calculations are annualised.

Disease information such as the type of MS, disability (EDSS), HRQoL, utility (EuroQol-5 dimensions (EQ-5D)⁸), symptoms (fatigue, cognition) and the effect of MS on work related to the current week. For comparability across countries, utilities are estimated with the original value set developed in the United Kingdom.⁹ In Portugal, a specific national value set as well as population norms were established very recently, and we therefore also present utilities established with the local tariff.^{10,11}

Costs

Costs are calculated from the societal perspective, including all costs regardless of who ultimately is responsible for them. Patient co-payments and patients' out-of-pocket expenses are thus included.

The cost of a relapse is calculated as the difference in quarterly costs between patients with or without a relapse and an EDSS score between 0 and 6. Patients who were unsure were excluded from the estimation. Invalidity, early retirement and DMT costs are not considered in this calculation, as they are unlikely to be affected within 3 months.

Unit costs for the individual resources were taken from public sources and are reported in the paper on methodology.⁶ Results are reported in 2015 EUR.

Patients

The objective was to include a sample where all levels of disease severity (defined by EDSS) were

represented in sufficient numbers to allow analysis. This highlights how costs and HRQoL change as the disease progresses and provides the necessary data for cost-effectiveness analysis of treatments that are expected to change the course of the disease. As a consequence, our study population does not represent national prevalence of MS in Portugal and mean results for the sample are not meaningful. They can neither be extrapolated to national costs without careful adjustment, nor can they be compared directly to the results in other studies. We therefore report results by disease severity only.

Data collection

In anonymous surveys, participation will depend heavily on the methods used: collecting data in clinical MS centres tends to overestimate the number of patients with early but severe disease and those on treatment with DMTs; collecting data from members in a patient organisation may be influenced by the structure and the activities of the organisation. Internet surveys will bias towards younger patients and those with better education, while postal mailings may bias towards older patients. In Portugal, the vast majority of patients participating were members of the Sociedade Portuguesa de Esclerose Múltipla (SPEM), but a small number was recruited in a clinical centre.

The Portuguese data were collected between October 2015 and March 2016, after approval by the National Committee for Data Protection (Comissão Nacional de Proteção de Dados, Lisboa). SPEM invited 1930 of their members by postal mail to participate in the survey.

Results

A total of 535 evaluable responses were received (46 online, 489 on paper). All geographical regions were represented, reflecting population levels in these areas, except for Lisbon, that was slightly overrepresented (31% in the sample vs 21% in the population).

Age and EDSS in our samples drive the proportion of patients with relapsing disease indicated for DMT treatment, the number of patients actually on DMTs, to some extent the proportion reporting a relapse and the proportion of patients of working age.⁵ The Portuguese respondents were among the younger groups in the European study, with a high proportion of patients of working age and a large group with early disease and consequently a high proportion on treatment with DMTs. Table 1 provides details on demographics, employment and disease.

Table 1. Sample characteristics.

	Sample	Mild MS EDSS 0–3	Moderate MS EDSS 4–6.5	Severe MS EDSS 7–9	Missing EDSS
<i>N</i> (percentage of total sample)	535	274 (51.2)	160 (29.9)	75 (14)	26
Proportion women	66.5%	–	–	–	–
Proportion living alone	12%	34 (12.4%)	21 (13.1)	6 (8.0)	3
Mean age (SD)	48.46 (11.01)	45 (9.4)	50 (10.9)	58 (10.6)	–
<i>Education</i>					
Primary school	10.1%	–	–	–	–
High school degree	5.8%	–	–	–	–
Professional diploma	42.4%	–	–	–	–
University education	38.9%	–	–	–	–
<i>Employment</i>					
Patients of working age	493 (92.1% ^a)	264 (96.4%)	146 (91.3%)	60 (80.0%)	23
Total currently employed or self-employed	216 (40.4% ^a)	173 (63.1%)	37 (23.1%)	4 (5.3%)	2
Working age, employed or self-employed	213 (43.2% ^b)	172 (65.2%)	37 (25.3%)	3 (5.0%)	1
Working full time	86 (39.8% ^c)	70 (40.5%)	15 (40.5%)	0	1
On long-term leave (>3 to ≤12 months)	11 (5.1% ^c)	–	–	–	–
Sick leave (past 3 months)	16 (7.4% ^c)	–	–	–	–
Not working due to MS	230 (46.7% ^b)	–	–	–	–
Invalidity pension	174 (35.3% ^b)	45 (17.0%)	79 (54.1%)	40 (66.7%)	10
Early retired	39 (7.9% ^b)	14 (5.3%)	13 (8.9%)	11 (18.3%)	1
<i>Disease information</i>					
Mean age at diagnosis (SD)	35.93 (11.29)	34 (9.8)	37 (12.5)	40 (11.8)	–
Mean age at first symptoms (SD)	29.69 (10.36)	28 (9.2)	31 (11.6)	32 (11.1)	–
Mean EDSS (SD)	3.8 (2.5)	1.8 (1.1)	5.3 (0.9)	7.8 (0.5)	–
Proportion with RRMS	288 (53.8%)	–	–	–	–
Proportion with relapses	96 (17.9%)	42 (15.3%)	32 (20.0%)	15 (20.0%)	7
Proportion using DMTs	422 (78.9%)	84.3%	81.9%	53.3%	20

MS: multiple sclerosis; SD: standard deviation; EDSS: Expanded Disability Status Scale; RRMS: relapsing-remitting multiple sclerosis; DMT: disease-modifying treatment.

^aOf total sample (*N* = 535).

^bOf patients of working age (*N* = 493).

^cOf patients working (*N* = 216).

Demographics and employment

The age of respondents in Portugal ranged from 20 to 80 years (mean: 48.5; median: 47.0; standard deviation (SD): 11.0); women represented 67%; 85% lived with their family; and only four patients were in a nursing home at the time of the survey. Education levels were slightly higher in comparison to the general population: 10% of patients had basic education, 48% a secondary or a professional degree and 39% a university degree of some type. This compares to 15% of the Portuguese population over 20 years of age who completed a university education (17% for women).¹²

In the sample, 493 patients (92%) were below effective retirement age (66 years for women and 68 years for men¹³) and of these, 43% patients were employed or self-employed at the time of the survey. Three

patients above retirement age also worked, bringing this group to 216 patients (or 40% of the full sample) with a mean age of 42.6 years. It is difficult to relate this to the situation in Portugal, as employment rates are only published as a proportion of the total population (54.4% in 2015).¹⁴ More than half of the patients worked part-time (58%) for an average of 13.2 hours/week. This is considerably higher than in the general population where 14.4% of women and 10.6% of men worked part-time.¹⁴ A total of 40% indicated that MS was the cause for part-time work.

Very few patients (*N* = 11; 5%) reported to be on long-term sick leave (>3 to ≤12 months) or having had a short-term absence during the past 3 months (*N* = 16; 7%). Short-term sick leave lasted on average 16.9 days.

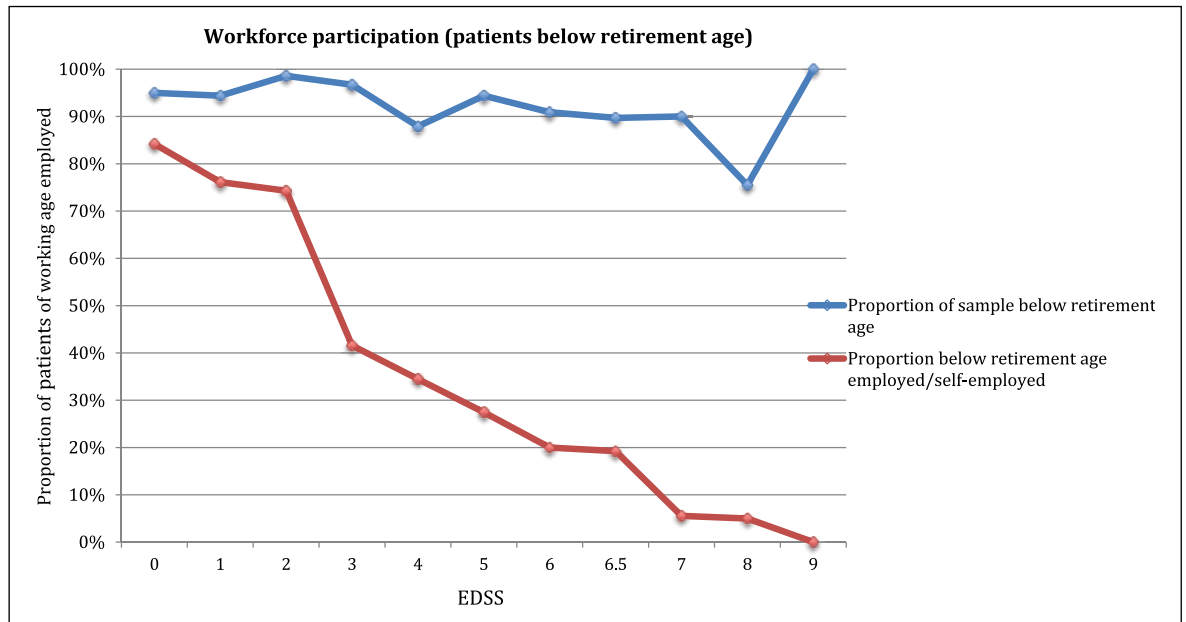


Figure 1. Employment by disease severity.

EDSS: Expanded Disability Status Scale.

Proportion of patients of working age employed or self-employed. Working age was defined as effective retirement age (66 years for women and 68 years for men; www.oecd.org). A total of 493 patients (92%) were below retirement age and of these, 43% were employed or self-employed. The group at EDSS 9 comprised only two patients, both below retirement age and not working.

Employment decreased rapidly with advancing disease, as shown in Figure 1. MS was the reason for 77% of patients who were not employed.

Most patients felt that MS affected their productivity at work (72%) and only 13% indicated that they had no problems, while 14% had not answered the question. The severity of the effect covered the entire VAS range from 0 to 10, with a mean of 3.8 (SD: 2.8) (Figure 2). Fatigue was considered the most bothersome symptom (71%), followed by difficulty thinking (31%), low mood (23%), mobility (23%) and pain (20%).

Disease information

The mean EDSS was 3.8 (SD: 2.5), and all levels of EDSS were well represented yielding a stable analysis, except for EDSS 9 where only two responses were received. Our results for the severe group of patients (EDSS 7–9) thus represents only patients with EDSS 7 and 8 and may be underestimating costs for this group (Table 1). The proportion of patients with RRMS was 54% and patients with secondary-progressive multiple sclerosis (SPMS) disease represented 21% of the sample. A total of 14% of patients had primary-progressive multiple

sclerosis (PPMS) disease and 11% did not answer the question. In view of the age and low mean EDSS of the sample, this distribution appears reasonable, although the proportion with PPMS may be somewhat overrepresented. This attests to the apparent difficulties for patients in all countries to distinguish between disease types, particularly SPMS and PPMS. Thus, we did not include the disease type in our analyses and focus instead on EDSS levels, despite the fact that DMTs are mostly indicated for relapsing disease.

DMTs were used by 79% of the sample, with usage declining with higher EDSS levels, as expected (Table 1). Among users, 39.6% were on their first DMT treatment. First-generation DMTs were used by 69%, newer DMTs were used by 25.8%, while responses were missing for 5.2% of the sample (Table 2).

Relapses in the preceding 3 months were reported by 96 patients (18%) of which slightly over half occurred in the past month (Table 1). However, 12% of respondents were unsure whether they had a relapse or not, and 4% did not answer the question. We assumed that the answer was no. The mean number of relapses over a period of 3 months in the sample was thus estimated at 0.2 (SD: 0.6). Corticosteroids were used by 52% of patients with relapses.

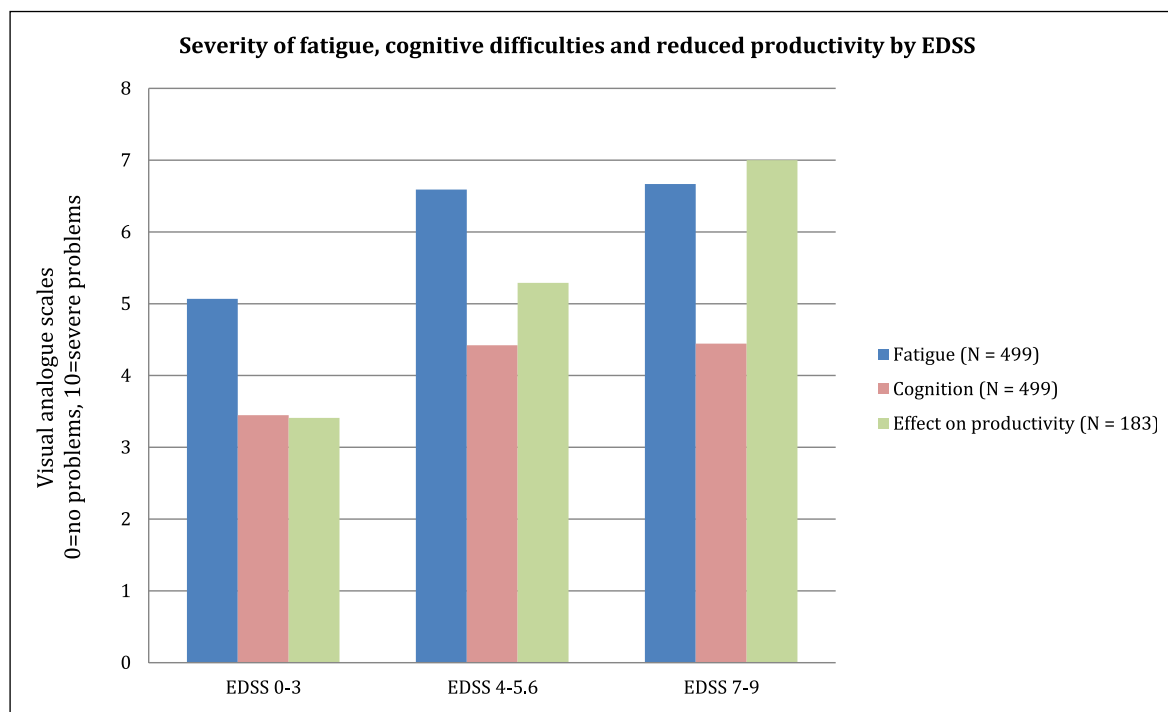


Figure 2. Fatigue, cognitive difficulties and effect of MS on productivity at work.

EDSS: Expanded Disability Status Scale.

Mean score on the visual analogue scales (0 = no problem; 10 = severe problems) for fatigue, cognitive difficulties and impact of MS at work (only for patients working). Patients with missing EDSS ($N = 26$) or missing answers are excluded. Of 499 valid answers for fatigue and cognition, 487 and 397, respectively, indicated problems; of 183 answers for productivity at work, 154 indicated problems. Patients reporting no problems are assigned zero for the analysis.

Table 2. Type of DMT used ($N = 422^a$).

First-generation treatments	Percentage of total users	Second-generation treatments	Percentage of total users
Interferon-beta 1b (Betaferon [®] /Extavia [®])	20.4	Natalizumab (Tysabri [®])	8.3
Interferon-beta 1a (Avonex [®])	17.8	Fingolimod (Gylenia [®])	15.2
Interferon-beta 1a (Rebif [®])	16.1	Dimethyl fumarate (Tecfidera [®])	2.1
Glatiramer acetate (Copaxone [®])	14.5	Mitoxantron (Novantrone [®])	0.2
Peginterferon-beta 1a (Plegridy [®])	0.2		

DMT: disease-modifying treatments.
^aMissing information on DMT for 22 patients.

Symptoms and HRQoL

Fatigue was an issue for 98% patients who answered the VAS ($N = 523$). The mean score was 5.8 for the sample, and 5.1, 6.6 and 6.8 for patients with mild, moderate and severe disease, respectively (Figure 2).

Similarly, a majority of patients felt that they suffered from cognitive difficulties (74%). The mean VAS score among this group with issues was 5.3 and was

correlated with disease severity: 4.8 in the mild, 5.4 in the moderate, and 6.0 in the severe group (Figure 2). For the full study sample (assigning 0 to the group with no problems), the mean score was 4.

Among the five domains of HRQoL included in the EQ-5D, only self-care did not represent problems for a majority of patients. Both the severity and the type of domain affected changed with advancing disease (Figure 3).

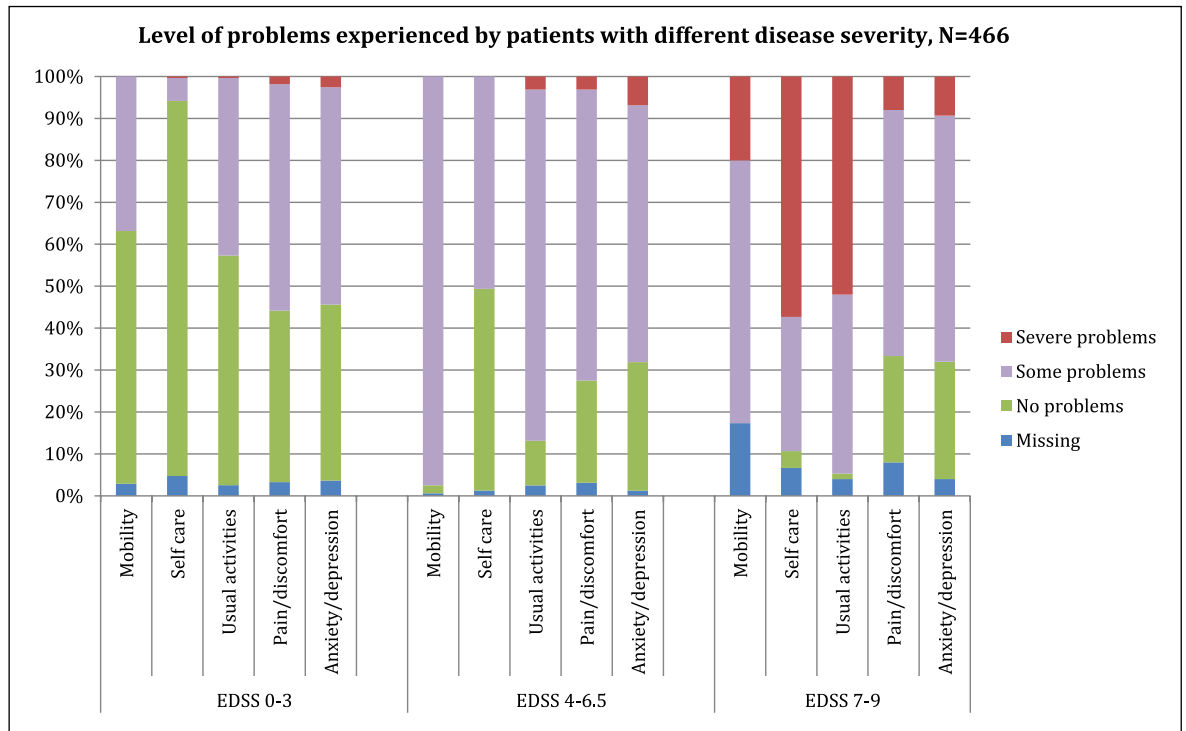


Figure 3. Problems in different domains of QoL (EQ-5D). EQ-5D: EuroQol-5 dimensions; EDSS: Expanded Disability Status Scale. Proportions of patients at different levels of disease severity experiencing difficulties in the five domains of the EQ-5D. The ability for self-care and usual activities declines rapidly with advancing disease, mobility affects all patients in the moderate and severe groups, while pain and anxiety appear more severe in the mild group.

Utility

Mean utility in the sample was 0.628 and 0.497 using the UK and Portuguese value sets, respectively, and declined with increasing EDSS (Figure 4).

Resource utilisation

Resource utilisation is presented in Table 3. Healthcare resources (except medication) were collected for a 3-month period. Hospitalisation was rare (24 patients, 4.5%), while day admissions and use of rehabilitation were 14% and 4%, respectively. A total of 73% of patients had consultations, most often with the neurologist, and 48% had investigations and tests. Medication for MS and MS symptoms was used by 92% of patients during the past month. Prescription drugs other than DMTs and corticosteroids were used by 49% of patients, while 48% purchased non-prescription drugs. Medical devices or specific investments for MS were required by 23% of patients during the past year, most often for walking aids.

Community and social services were used by only 13% of patients in the past month, most frequently transportation. Help from family was used by 32% of

patients, on average 19.9 days/month and 7.3 hours/day. Services and informal care were concentrated in the group with severe disease (Figure 5).

Costs

Total mean annual costs per patient for patients with mild, moderate and severe disease and by EDSS score are presented in Figure 6 and Table 4.

The average cost of a relapse during a 3-month period was estimated at €2931, of which 74% were due to hospital care (Figure 7).

Discussion

This study is an important contribution to the knowledge of the burden and management of MS in Portugal, where published material addressing these issues is very scarce. As a whole, these data represent a snapshot that may alert health professionals and governmental entities to difficulties encountered by patients and to the costs of MS in general, and thereby contribute to improving healthcare planning and resource allocation.

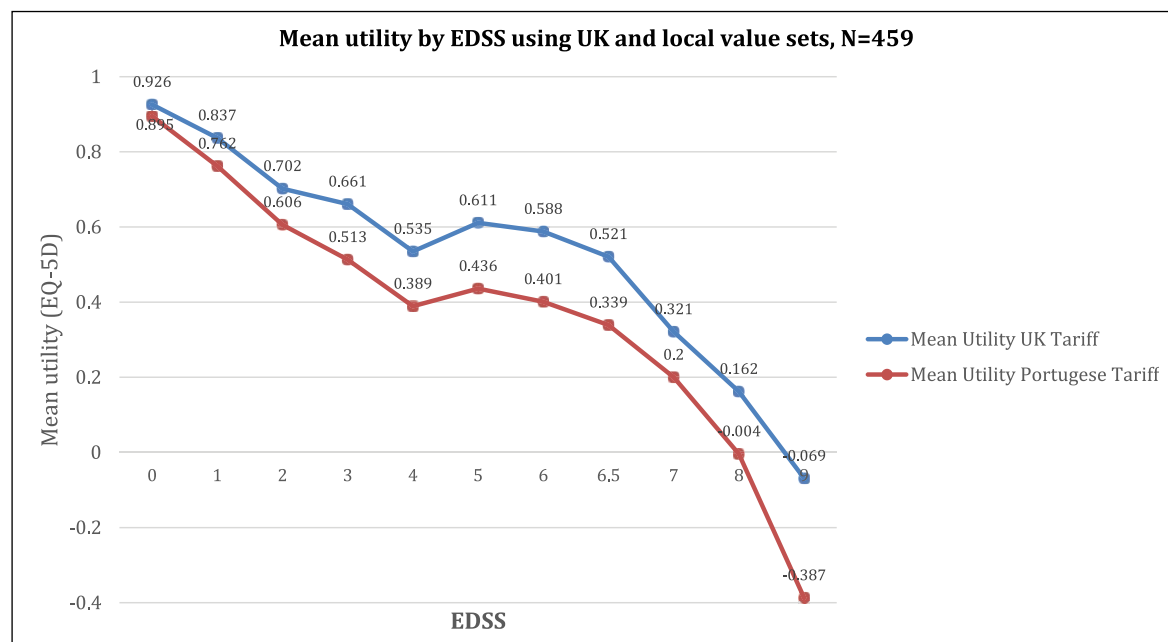


Figure 4. Utility by disease severity.

EQ-5D: EuroQol-5 dimensions; EDSS: Expanded Disability Status Scale.

Utility by EDSS level estimated with the UK and Portuguese value sets of the EQ-5D established with the general population.⁷⁻⁹ Utility is calculated by relating the scores (1 = no problem; 2 = some problems; 3 = severe problems) of the five domains of the EQ-5D to a health state valuation system established with the general population.

Table 3. Resource utilisation, health care and community services.

	Users	Percentage of sample	Mean number of times (SD)	Mean number of days (SD)
<i>Hospitalisation (3 months)</i>				
Inpatient admission	24	4.5		
Neurology ward	17	3.2	2.1 (1.7)	6.6 (4.8)
Other wards	6	1.1	1.8 (1.6)	22.7 (38.8)
Day admission	77	14.4		
Neurology ward	51	9.5	–	3.8 (4.1)
Other wards	18	3.4	–	4.0 (4.6)
Rehabilitation centre	20	3.7		
Inpatient admission	4	0.7	–	15.8 (30.3)
Day admission	9	1.7		7.7 (12.6)
Nursing home	9	1.7		39.5 (38.8)
<i>Consultations (3 months)</i>				
Any type of consultation	390	72.9		
Neurologist	322	60.2	1.5 (1.5)	–
Internist	6	1.1	2.8 (1.9)	–
Urologist	51	9.5	1.2 (0.5)	–
Ophthalmologist	50	9.3	1.4 (0.9)	–
Psychiatrist	33	6.2	1.5 (0.9)	–
General practitioner	95	17.8	1.9 (2.0)	–
MS nurse	103	19.3	2.3 (2.6)	–
Continence advisor	18	3.4	2.2 (2.4)	–
Physical therapist	120	22.4	19.8 (13.0)	–

(Continued)

Table 3. (Continued)

	Users	Percentage of sample	Mean number of times (SD)	Mean number of days (SD)
Occupational therapist	23	4.3	26.3 (19.1)	–
Speech therapist	2	0.4	3.0 (1.4)	–
Acupuncturist	27	5.0	8.6 (9.5)	–
Counsellor	41	7.7	3.5 (3.0)	–
Homeopath	10	1.9	3.3 (3.4)	–
Massage therapist	28	5.2	8.6 (8.5)	–
Telephone consultation MS nurse	71	13.3	1.8 (1.4)	–
Telephone consultation neurologist	38	7.1	1.7 (1.0)	–
<i>Tests (3 months)</i>				
Any kind of test	259	48.4		
MRI (brain)	12	23.2	–	–
MRI (spine)	75	14	–	–
Ultrasound	35	6.5	–	–
Blood tests	209	39.1		
<i>Medication (1 month)</i>				
Any kind of medication	491	91.8	–	–
DMT	422	78.9	–	–
Corticosteroids	50	31.3	–	–
Symptomatic prescription drugs	260	48.6		
Walking, spasticity, pain	175	32.7	–	–
Urological	49	9.2	–	–
Fatigue	55	10.3	–	–
Depression	124	23.2	–	–
OTC drugs	255	47.7	–	–
<i>Equipments, aids, modifications (12 months)</i>				
Any kind of equipment	121	22.6		
Lifts, elevators, ramps, rails	22	4.1		–
Walking aids	53	9.9		–
Wheelchairs	42	7.9		–
House and car modifications	59	11		–
<i>Community services (1 month)</i>				
Any kind	69	12.9		
Home help (days)	26	4.9	–	16.7 (11.3)
Transportation (trips)	38	7.1	–	7.5 (7.2)

MS: multiple sclerosis; SD: standard deviation; MRI: magnetic resonance imaging; DMT: disease-modifying treatment; OTC: over the counter drug.

The distribution of the disease types in our sample is somewhat different from what has been shown in other studies. In particular, the proportion of patients with RRMS is considerably lower than what has been observed in studies based on hospital cohorts (82%–85.3%).^{15–17} This is not surprising as patients on treatment with DMTs, hence the majority with early and predominantly relapsing-remitting MS, are followed in hospitals. The sample in our study was recruited from a wider population in different settings, including therefore also more advanced patients. However, it is also

known that patients find it difficult to judge their type of MS. Therefore, we used only EDSS and not disease type for our analyses and may assume that all disease types are represented, at least in the moderate group.

Healthcare costs are, as expected, dominated by the cost of DMTs, particularly in early disease. The mean annual cost per patient in our study increases three-fold from €12,660 to €36,600 between EDSS 0 and EDSS 7, but decreases slightly at EDSS 8. This is entirely due to a much lower or no use of DMTs in the

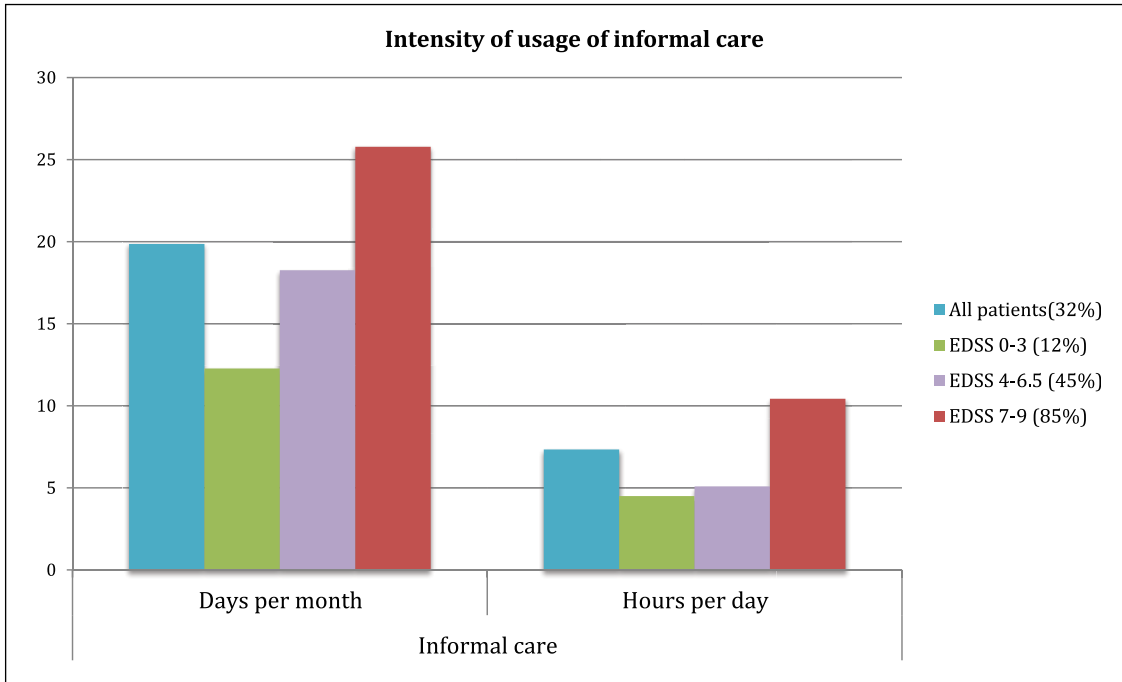


Figure 5. Use of informal care (days per month and hours per day, per user). EDSS: Expanded Disability Status Scale. Intensity of use of informal care (number of days and hours per day during the past month). Use is concentrated in the severe group: 12% of patients in the mild, 45% in the moderate and 85% in the severe group are relying on family support.

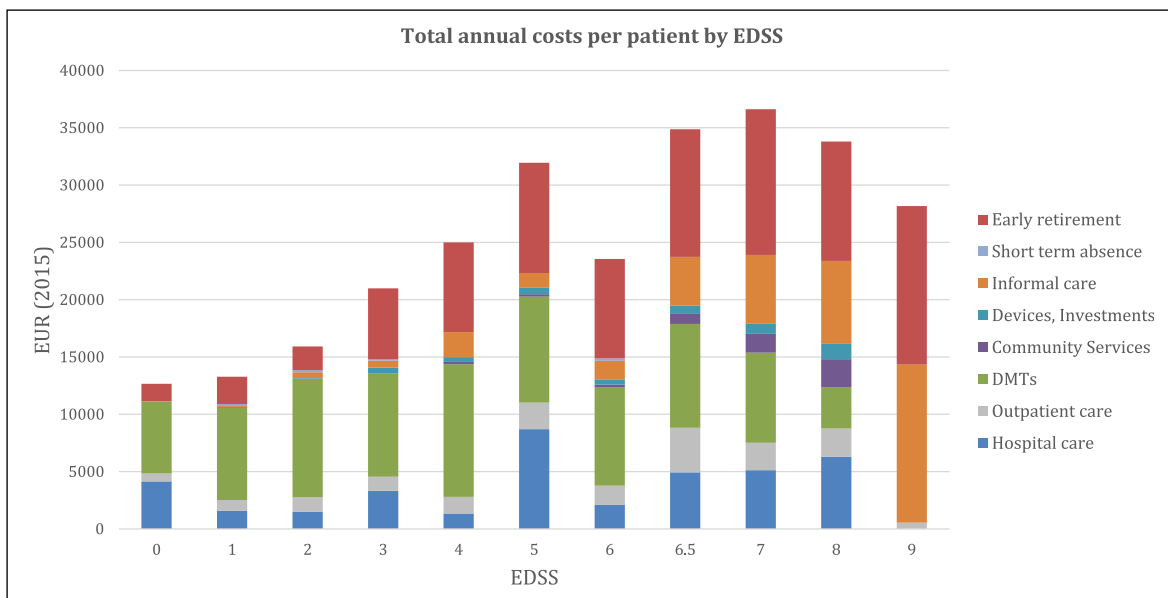


Figure 6. Total mean annual cost per patient by disease severity ($N = 535$). EDSS: Expanded Disability Status Scale. Mean total annual costs per patients by level of EDSS. Total costs increase with disease severity, but the type of resources changes. Healthcare costs dominate in early disease, while production losses and informal care dominate in more severe disease.

severe group that offsets the increase in community and informal care. The sample at EDSS 9 (two patients) is too small to draw any conclusion.

Among other healthcare resources, hospital care represents around 70% of the total at all levels of severity. This reflects the fact that patients with MS are mainly

Table 4. Total mean annual cost per patient by disease severity (mild, moderate and severe), $N = 535$ (EUR 2015).

	Mild	Moderate	Severe
	EDSS 0–3	EDSS 4–6.5	EDSS 7–9
	Mean (SD)	Mean (SD)	Mean (SD)
Total costs	16,500 (16,200)	28,700 (22,800)	34,400 (240,400)
<i>Healthcare costs</i>	<i>12,303 (14,844)</i>	<i>16,451 (20,703)</i>	<i>12,860 (21,151)</i>
Inpatient care	1317 (10,080)	2264 (16,011)	3791 (15,368)
Day admission	1203 (4013)	2422 (6760)	2027 (7737)
Consultations	442 (819)	1073 (1599)	1513 (2113)
Tests	329 (615)	272 (428)	159 (316)
Medication	316 (540)	903 (1129)	719 (955)
DMTs	8696 (7348)	9516 (8767)	4652 (6947)
<i>Services and informal care costs</i>	<i>570 (2516)</i>	<i>2961 (4909)</i>	<i>10,418 (8677)</i>
Community services	21 (256)	327 (1085)	2160 (5086)
Investments	185 (1992)	535 (1995)	1174 (2408)
Informal care	364 (1512)	2099 (3954)	7084 (5719)
Total direct cost	12,873 (15,204)	19,412 (21,305)	23,278 (22,793)
Short-term absence	131 (990)	56 (642)	0 (0)
Long-term absence, invalidity, early retirement	3454 (6317)	9267 (7451)	11,122 (6934)
Total indirect cost	3585 (6323)	9323 (7408)	11,122 (6934)

EDSS: Expanded Disability Status Scale; SD: standard deviation; DMT: disease-modifying treatment.

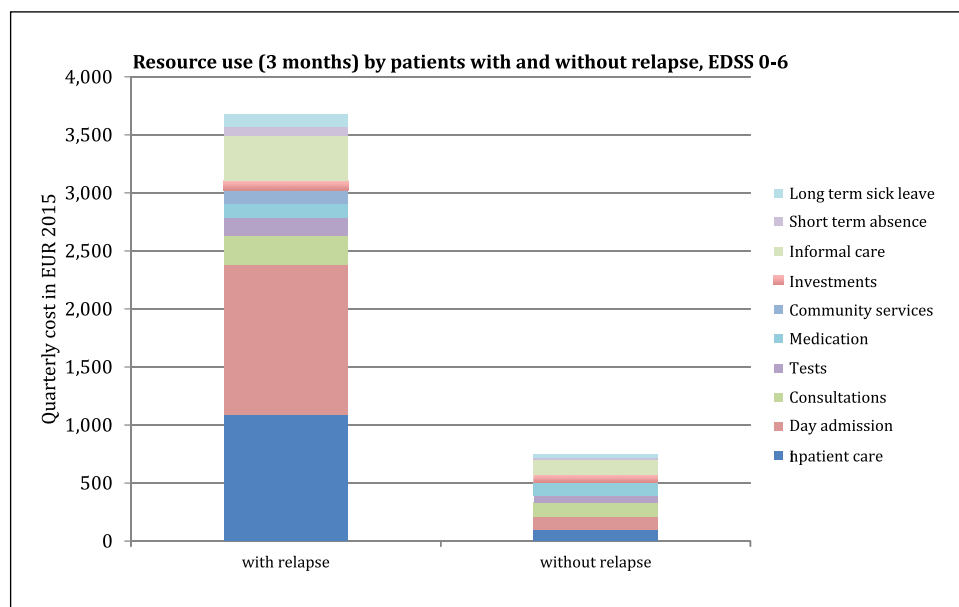


Figure 7. Relapse costs (3 months).

EDSS: Expanded Disability Status Scale; DMT: disease-modifying treatments.

Mean 3-month cost of a relapse (Euro 2015), estimated as the difference of costs of patients below EDSS 6.5 with and without a relapse ($N = 75$ and $N = 289$, respectively). Patients who were unsure ($N = 64$, 12%) were excluded from the estimation. Invalidity, early retirement and DMT costs are not considered in this calculation, as they are unlikely to be affected within 3 months. The cost of a relapse is thus estimated at €2931, of which 74% are due to hospital care and 9% to informal care.

followed in public hospitals. Among non-medical direct costs, the low use of community services and

the substantial rate of family help is representative of the pattern of socio-familial organisation and the

insufficiency of formal support in Portugal. In effect, the National Post Hospital Care Project created in 2006 (Law 101/2006) to provide continuity care to functionally dependent people irrespective of age has up to now been used mainly by elderly people, which implies the need for expansion and improvement strategies (Development Plan for 2016–2019, Ministry of Work, Solidarity and Social Security and Ministry of Health).

Almost all patients in our sample are below retirement age (92%), but less than half of them continue working. The majority of those not working indicate that this is due to their disease. Patients appear to leave the workforce very rapidly, with the proportion working dropping from around 75% at EDSS 1–2 to 40% at EDSS 3. These results fit those obtained in a recent multicenter study where 74.1% of the non-active MS population was retired due to disease. Additionally, the rates of activity and employment were similar to the general population in mildly incapacitated patients, but much reduced in patients with moderate and high incapacity.¹⁸ Our data do not allow analysis of the reasons for early retirement from work, as many factors may contribute. The high level of fatigue is most certainly one factor, but the economic conditions with high unemployment in recent years (increased from 4% in 2004 to 14% in 2014) are likely to have played a role as well. Among patients not working because of MS, 75% receive an invalidity pension. In the general population, the proportions with invalidity pensions are 5.5%, 8.2% and 14.2% in the age groups 40–44, 45–49 and 50–54 years, respectively.¹⁹ Overall, the number of people on invalidity pensions in the Portuguese population has decreased by more than half since 1990.¹⁹ The comparison of our results with these national statistics illustrates the severity of MS and its very severe impact on working life.

When comparing the utility values by EDSS estimated with the recent Portuguese and UK value sets, the similarity of the curves is striking. The same results are seen in the other countries in our study that have developed a value set with the same method as Dolan *et al.*⁹ in the United Kingdom. However, the Portuguese values are somewhat lower at all levels of EDSS.

In conclusion, information on the burden of illness in Portugal is limited.²⁰ This study provides the first comprehensive assessment of the burden of MS for Portuguese patients, the healthcare system and society overall.

Acknowledgements

The authors are grateful to Manuela Duarte Neves, Luísa Sacchetti Matias and Susana Protásio (Portuguese MS Society, SPEM) for support with data collection, to Luis Lopes Madureira Silva Miguel (CISEP Lisbon) for providing unit costs, to Jennifer Eriksson and Mia Gannedahl (MAPI Group) for organisational and statistical support, to Markas Gedminas (Medscinet) for construction of the online platform, to Barbara Rosengren for language editing and to Cara Harley for formatting.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: M.J.S. has received consulting fees from Bayer, Biogen, Merck Serono, Novartis, Sanofi Genzyme and Teva. G.K. has received consulting fees from Almirall, Bayer, Biogen, Merck Serono, Novartis, Oxford PharmaGenesis, Sanofi Genzyme and Teva. J.B., D.C. and J.D. were at the time of the study employed by the MAPI Group, a research company acting as consultants to pharmaceutical companies.

Funding

The author(s) declared receipt of the following financial support for the research, authorship and/or publication of this article: European Health Economics and MAPI have received funding for the full research and production of the manuscripts from Biogen.

References

1. INFARMED. *Guidelines for economic drug evaluation studies*. 1998, <http://www.infarmed.pt/>
2. Pugliatti M, Rosati G, Carton H, *et al.* The epidemiology of multiple sclerosis in Europe. *Eur J Neurol* 2006; 13: 700–722.
3. De Sa J, Alcalde-Cabero E, Almazan-Isla J, *et al.* Capture-recapture as a potentially useful procedure for assessing prevalence of multiple sclerosis: Methodologic exercise using Portuguese data. *Neuroepidemiology* 2012; 38: 209–216.
4. 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.
5. Kobelt G, Thompson A, Berg J, *et al.* New insights into the burden and costs of multiple sclerosis in Europe. *Mult Scler* 2017; 23(8): 1123–1136.

6. 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: 918–926.
7. Kobelt G, Eriksson J, Phillips G and Berg J. The burden of multiple sclerosis 2015: Methods of data collection, assessment and analysis of costs, quality of life and symptoms. *Multiple Sclerosis* 2017; 23(2S): 4–16.
8. The EuroQol Group. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 1990; 16: 199–208.
9. Dolan P, Gudex C, Kind P, et al. The time trade-off method: Results from a general population study. *Health Econ* 1996; 5: 141–154.
10. Ferreira LN, Ferreira PL, Pereira LN, et al. EQ-5D Portuguese population norms. *Qual Life Res* 2014; 23: 425–430.
11. Ferreira LN, Ferreira PL, Pereira LN, et al. The valuation of the EQ-5D in Portugal. *Qual Life Res* 2014; 23: 413–423.
12. PORDATA. *População residente, segundo os Censos, com o ensino superior completo em % da população residente*. 2015, <http://www.pordata.pt/>
13. OECD. *Average effective age of retirement 2007–2012*. 2012, <http://www.oecd.org> (accessed 1 March 2016).
14. PORDATA. *Taxa de emprego: Total e por sexo (%)*. 2016, <http://www.pordata.pt/> (accessed 1 December 2016).
15. Barros P, de Sa JM and Sa MJ. Month of birth and risk of multiple sclerosis in a Portuguese population. *Clin Neurol Neurosurg* 2013; 115: 1762–1765.
16. Costa DC, Marques Sa MJ and Calheiros JM. Social characteristics and quality of life of Portuguese multiple sclerosis patients. *Neurol Ther* 2013; 2: 43–56.
17. Tomás J, Dias Ferreira J, Sequeira J, et al. Demography, clinical characteristics and socioeconomic status of the Portuguese patients with Multiple Sclerosis. *Eur J Neurol* 2015;22: 395.
18. Samoes R, Varanda S, Grilo M, et al. Economic activity and employment in the Portuguese patients with Multiple Sclerosis in 2014 – results of the national cross-sectional PORT-MS study. *Eur J Neurol* 2015; 22: 755–756.
19. PORDATA. *Social security disability pensioners: Total and by age group*. 2015, <http://www.pordata.pt/> (accessed 2 December 2016).
20. De SA J, Rio EM, Monteiro E, et al. Health care costs and disease severity of relapsing remitting multiple sclerosis in Portugal. *Mult Scler* 2004; 10: S135.

Visit SAGE journals online
[journals.sagepub.com/
home/msj](http://journals.sagepub.com/home/msj)

 SAGE journals