Health and Economic Impact of Relapsing Forms of Multiple Sclerosis in Greece: The Storms Study

Yfantopoulos J1, Grigoriadis N2, Hatzikou M3, Iliopoulos I4, Karageorgiou K5, Chantzaras A6, Kyritsis AP7, Papathanasopoulos P8, Rombopoulos G9, Tsimourtou V10, Velikis M11, Treska X12, Tzortzis D13, Kostadima V14, Dimisianos N15 and Raill S16

1School of Economics and Political Science, University of Athens, Greece
2Department of Neurology, Aristotle University of Thessaloniki, Greece
3Novartis Hellas S.A.C.I., Greece
4Department of Neurology, University of Patras, Greece
5Department of Neurology, Iatriko Medical Centre of Athens, Greece
6Department of Neurology, University of Ioannina, Greece
7Department of Neurology, University of Patras, Greece
8Department of Neurology, University of Thessalia, Greece

Abstract

Background: Little information on costs and quality of life (QoL) of patients with Multiple Sclerosis (MS) has been published for Greece so far.

Objective: The objective of the study was to assess the socio-economic burden that MS imposes to Greek patients with relapsing forms of multiple sclerosis.

Methods: Information on demographics, disease history, resource consumption and productivity losses was collected from 200 patients recruited in six MS centres throughout Greece. Annual costs were estimated in 2011 unit costs. Health-related QoL (HRQoL) was measured with the EQ-5D questionnaire. Using the Expanded Disability Status Scale (EDSS), patients were stratified into those with mild (EDSS 0-3), moderate (EDSS 3.5-6.0) and severe (EDSS 6.5-7.5) disability. The perspective of the analysis was that of the national security fund (EOPYY).

Results: The mean annual cost per patient was estimated at €26,118. Higher disability increased costs substantially: €20,702 for mild, €32,126 for moderate and €45,442 for high severity patients. HRQoL was considerably impaired by disease progression. Patients with Secondary Progressive (SPMS) as expected had higher costs and lower HRQoL than Relapsing Remitting Multiple Sclerosis (RRMS) subjects, attributed to higher mean disability.

Conclusion: In accordance with other studies, MS imposes a considerable health and economic burden in Greece, which increases significantly with advancing disability.

Keywords: Multiple sclerosis; Economic impact; Health, Quality of life; EQ-5D; Greece

Introduction

Multiple sclerosis (MS) is the second most common non-traumatic cause of neurological disability in adults worldwide, with a considerable socioeconomic impact, which is disproportionate to the relatively limited prevalence of the disease [1]. In Greece, the estimated prevalence varies with location, ranging between 10.2/100,000 individuals in southern areas [2] and 119.61/100,000 people in western areas [3], with the most recent estimation being 23 cases per 100,000 individuals in northern areas [4]. Several epidemiological studies have demonstrated a gradual increase in prevalence and incidence of MS in Greece, placing most geographical areas in the medium and high-risk zone [3-7]. This gradual increase has been ascribed to the advances in diagnostic modalities and overall improved awareness [4].

The socio-economic burden of MS is particularly high both for patients, their families, as well as the national health system. The average annual cost per patient with MS is higher than for patients with many other, more common, chronic conditions [8,9]. The economic burden of MS is largely driven by the progression of disability and relapses, while MS-related symptoms of fatigue, depression, cognitive deterioration and behavioral disorders, pain, urinary and sexual dysfunction and comorbidities are also factors in the overall economic impact [10-15]. MS typically starts in early adulthood, so the disease has considerable economic consequences through lifelong decreased work capacity and productivity [16-20].

Furthermore, MS patients have lower health-related quality of life (HRQoL) than the general population, with the magnitude being similar to that of other chronic diseases [21,22]. Greater disability and relapses [16-20] other MS-related symptoms (fatigue, depression, cognitive deterioration and behavioral disorders, pain, urinary and sexual dysfunction), as well as treatment side effects and injection problems for some therapies, have been found to exert a detrimental influence on patients’ quality of life (QoL) [23-24]. Additionally, MS has an adverse impact on the social and family life of patients, as well as on the lives of their caregivers [25].
Although information about costs and QoL of MS patients is available for a number of European countries, no such data have been published for Greece so far. The objective of the study was to assess the health and economic burden that relapsing forms of MS impose to Greek MS patients and the Greek social security fund (EOPTY), respectively.

**Materials and Method**

**Study design and data collection**

This was a multicentre, cross-sectional, retrospective, burden of disease study. The subjects were identified from six MS centres from various areas of the country. Adult patients suffering from either remitting-relapsing or secondary progressive MS with relapses were included in the study, provided they had given written informed consent. Patients that had limited capacity to participate in the study procedures, due to cognitive impairment or other factors, or were participating in another clinical study were excluded.

During a single visit, trained researchers completed a case report form by interviewing each patient on: i) demographics, ii) disease data (year of diagnosis, year of first symptoms, type of MS, Expanded Disability Status Scale [EDSS] score, number of relapses), iii) MS related comorbidities, iv) treatment-related information, v) resource utilization (inpatient and outpatient care, diagnostic and laboratory tests, medication, disability equipment, productivity loss and informal caregiving). Additionally, patients self-assessed their HRQoL with the EQ-5D questionnaire.

**Costs calculation**

This study adopts a bottom-up approach to estimate the mean annual costs per MS patient in Greece, from a social security fund perspective. Since MS is a chronic disease, a prevalence-based approach was selected, taking into account the use of resources during the previous year, using information which was gathered at a single point in time. A prevalence-based economic evaluation provides estimates of costs and health benefits of a certain population for a specific time horizon. Only MS specific resource utilization was collected. Costs were computed as the monetary value of resource utilization, i.e. the number of resource units consumed multiplied by the respective unit cost. Unit costs were obtained from publicly available sources in Greece (Table 1). MS related comorbidities’ economic burden was estimated as the total mean annual cost per patient related to each comorbidity, based on previous relevant literature [9,26]. Productivity loss of patients was approximated as the income reduction due to MS and the cost related to the early disability pension. The informal care cost was estimated by taking into account the total weekly hours spent for informal care (extrapolated to year), and using the mean gross income for Greece in 2011 (€19,018), divided by the number of hours worked, equally for working and non-working caregivers.

Costs were grouped as: 1) direct medical costs (inpatient and outpatient care, consultations, investigations, treatments and MS-related comorbidities), 2) direct non-medical costs (equipment investment, professional assistance, informal care) and 3) indirect costs (productivity loss, i.e., disability pension, percentage of income reduction).

**QoL**

The EQ-5D [27] is a widely used generic instrument for measuring HRQoL. It consists of a descriptive health state classification system with five dimensions, including: 1) mobility, 2) self-care, 3) usual activities, 4) pain/discomfort and 5) anxiety/depression, and a Visual Analogue Scale (VAS) assessing the overall perception of the subject’s health state. Each dimension of the descriptive system is measured with an ordinal three-point scale describing three levels of severity: i) no problems, ii) some problems, and iii) extreme problems. Together, these five dimensions with three levels for each dimension define a total of 243 health states, ranging from full to worst health. Health utilities were obtained based on time trade-off valuations from a general population study conducted at the United Kingdom, which have been found applicable in the Greek setting [28].

**Analysis**

Descriptive statistics (frequency, percentage, mean, standard deviation, median, interquartile range) were used for the analysis of the demographic and clinical characteristics of the sample, as well as the resource utilization and costs. To assess the effect of disability on costs and QoL of MS, along with demographic and clinical data, three categories were created based on EDSS score, as in previous studies [10-13,15], i.e., those with mild (EDSS 0-3), moderate (EDSS 3.5-6) and severe disability (EDSS 6.5-7.5). We conducted Jonckheere trend tests to examine whether a significant trend existed (ordered pattern of alternatives) in continuous data with advancing severity of the disease, as it was measured with the EDSS groups described; Cochran-Armitage tests were used for categorical responses. Similarly, the differences between MS type groups were compared with Mann-Whitney and χ² tests, for continuous and categorical data respectively. All comparisons were evaluated on the α=5% level. Confidence intervals (95%) of the costs were estimated by non-parametric bootstrapping. Statistical analysis was carried out with IBM SPSS Statistics 21 software package.

**Results**

**Patient demographics and disease information**

A total of 200 patients completed the study and were included in the analysis. Patients’ socio-demographics and disease information are presented in (Table 2). The sample had a mean age of 39.5 years, with 70.4% being females. The overall mean EDSS level was 3.1 (± 2.0), and the majority of subjects (62.5%) belonged to the mild disability subgroup (EDSS ≤ 3). Patients with less severe disease were younger (p<0.001); also the time period since first appearance of symptoms and diagnosis was shorter for less afflicted subjects (both p<0.001). A proportion of 86.5% was diagnosed as having RRMS, and 13.5% with SPMS. Finally, only 32% of the participants were employed or self-employed at the time of the study.

The most frequently reported comorbidities were depression (50%), urinary problems (34.5%), sleep disturbance (27.5%) and cognitive impairment (21.5%). Urinary tract infections and osteoporosis increased with the EDSS disability level (p<0.05). On average, RRMS patients were experiencing comorbidities to a lesser extent, though the difference was found statistically significant only for osteoporosis (p<0.05).

**Resource utilisation**

About 30% of the patients had required a hospital admission due to MS during the previous year (Table 3); a proportion of 46% had received outpatient care in a hospital and 4.5% in a rehabilitation centre, while 64.5% had consulted a specialist. The majority of patients had received a Disease Modifying Treatment (DMT; 84%), and 29% non-prescription medicines in the previous 3 months and 1 month of the study, respectively; a proportion of 76% had at least one Magnetic
Table 1: Overall (n=200) Severity EDSS 0-3 (n=125) EDSS 3.5-6 (n=58) EDSS 6.5-7.5 (n=17) RRMS (n=173) SPMS (n=27) p-value\* p-value\*

Subjects (female: male ratio) 200 (70.0:30.0) 125 (26.4:73.6) 58 (36.2:63.8) 17 (35.3:64.7) 172 (72.7:27.3) 27 (55.6:44.4) 0.078

Age, years
Mean ± SD 39.5 ± 10.3 35.9 ± 8.7 44.4 ± 9.9 49.8 ± 9.1 37.9 ± 9.5 50.3 ± 8.6 <0.001
Median (IQR) 39.5 (14.7) 35 (13.5) 43.5 (12.0) 50 (12.0) 38.0 (13.0) 50.0 (12.0) <0.001

Cohabits with family/spouse, n (%) 177 (88.5%) 111 (91.4%) 53 (91.4%) 13 (76.5%) 154 (89.0%) 23 (85.2%) 0.503

Employment status, n (%) Full time 53 (26.5%) 34 (27.2%) 17 (29.3%) 2 (11.8%) 0.868 49 (28.3%) 4 (14.8%) 0.347
Part time 11 (5.5%) 8 (6.4%) 2 (3.4%) 1 (5.9%) 0.116 11 (6.4%) 0 (0%) 0.001
Employed 44 (22.0%) 25 (20.0%) 17 (29.3%) 2 (11.8%) 0.841 41 (23.7%) 3 (11.1%) 0.142
Self-employed 20 (10.0%) 17 (13.6%) 2 (3.4%) 1 (5.9%) 0.058 19 (11.0%) 1 (3.7%) 0.241
Housekeeping 29 (14.5%) 16 (12.8%) 9 (15.5%) 4 (23.5%) 0.256 24 (13.9%) 5 (18.5%) 0.524
Student 15 (7.5%) 14 (11.2%) 1 (1.7%) 0 (0%) 0.014 15 (8.7%) 0 (0%) 0.001
Unemployed 27 (13.5%) 21 (16.8%) 5 (8.6%) 1 (5.9%) 0.083 25 (14.5%) 2 (7.4%) 0.319

Type of MS, n (%) RRMS 173 (86.5%) 124 (99.2%) 45 (77.6%) 4 (23.5%) <0.001 n.a. n.a.
SPMS 27 (13.5%) 1 (0.8%) 13 (22.4%) 13 (76.5%) n.a. n.a.

Years since first diagnosis
Mean ± SD 9.2 ± 5.9 7.4 ± 5.2 11.7 ± 6.1 14.2 ± 5.2 8.5 ± 5.7 14.1 ± 5.2
Median (IQR) 8.0 (7.0) 6.0 (7.0) 11.0 (9.0) 12.0 (5.0) <0.001 8.0 (7.0) 13.0 (7.0) <0.001

Years since first symptoms
Mean ± SD 11.9 ± 6.7 9.9 ± 6.1 15.1 ± 6.7 16.2 ± 5.5 11.1 ± 6.5 17.2 ± 5.6

Median (IQR) 11.0 (10.0) 9.0 (8.5) 15.0 (11.3) 15.5 (9.0) <0.001 10.0 (9.0) 17.0 (10.3) <0.001
EDSS
Mean ± SD 3.1 ± 2.0 1.7 ± 0.8 4.8 ± 1.0 6.8 ± 0.4 2.7 ± 1.7 5.9 ± 1.4
Median (IQR) 2.5 (2.9) 2.0 (1.0) 4.5 (2.0) 6.5 (0.8) <0.001 2.0 (2.3) 6.0 (2.5) <0.001
Relapses in previous year
Mean ± SD 1.5 ± 1.0 1.4 ± 0.8 1.8 ± 1.2 1.8 ± 1.0 1.6 ± 1.0 1.3 ± 0.7
Median (IQR) 1.0 (1.0) 1.0 (1.0) 1.5 (1.0) 1.5 (2.0) 0.070 1.0 (1.0) 1.0 (0) 0.223
Relapses requiring steroids in previous year
Mean ± SD 0.9 ± 0.9 0.8 ± 1.0 1.2 ± 1.0 0.5 ± 1.0 1.0 ± 1.0 0.6 ± 0.8
Median (IQR) 1.0 (1.0) 1.0 (1.0) 1.0 (2.0) 0 (1.0) 0.351 1.0 (2.0) 0 (1.0) 0.128
MS related Comorbidities, n (%)

<table>
<thead>
<tr>
<th></th>
<th>Overall (n=200)</th>
<th>Severity</th>
<th>Type of MS</th>
</tr>
</thead>
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<tr>
<td></td>
<td>EDSS 0-3 (n=125)</td>
<td>EDSS 3.5-6 (n=58)</td>
<td>EDSS 6.5-7.5 (n=17)</td>
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<tr>
<td>Inpatient care (length of stay in days)</td>
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<td></td>
<td></td>
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<tr>
<td>Hospital, n (%)</td>
<td>60 (30.0%)</td>
<td>36 (28.8%)</td>
<td>23 (39.7%)</td>
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<tr>
<td>Mean ± SD</td>
<td>1.8 ± 3.7</td>
<td>1.7 ± 3.4</td>
<td>2.5 ± 4.3</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0 (3.0)</td>
<td>0 (3.0)</td>
<td>0 (4.0)</td>
</tr>
<tr>
<td>Hospital due to relapses</td>
<td></td>
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<tr>
<td>Mean ± SD</td>
<td>2.2 ± 3.4</td>
<td>2.0 ± 3.3</td>
<td>2.9 ± 3.5</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0 (4.0)</td>
<td>0 (3.0)</td>
<td>3.0 (5.0)</td>
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<tr>
<td>Outpatient care (visits)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital, n %</td>
<td>92 (46.0%)</td>
<td>49 (39.2%)</td>
<td>32 (55.2%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>3.8 ± 6.8</td>
<td>3.6 ± 7.5</td>
<td>4.2 ± 9.9</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0 (4.0)</td>
<td>0 (4.0)</td>
<td>4.0 (4.0)</td>
</tr>
<tr>
<td>Rehabilitation centre, n %</td>
<td>9 (4.5%)</td>
<td>1 (0.8%)</td>
<td>5 (6.8%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.2 ± 9.1</td>
<td>0 ± 0.4</td>
<td>3.7 ± 16.7</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Consultations (public &amp; private), n %</td>
<td>129 (64.5%)</td>
<td>79 (63.2%)</td>
<td>41 (70.7%)</td>
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<tr>
<td>Physiotherapist</td>
<td></td>
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<tr>
<td>Mean visits ± SD</td>
<td>12.4 ± 38.0</td>
<td>3.9 ± 19.4</td>
<td>24.6 ± 48.6</td>
</tr>
<tr>
<td>Median visits (IQR)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (34.0)</td>
</tr>
<tr>
<td>Ergotherapist</td>
<td></td>
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<tr>
<td>Mean visits ± SD</td>
<td>0.7 ± 10.2</td>
<td>0 ± 0</td>
<td>2.5 ± 18.9</td>
</tr>
<tr>
<td>Median visits (IQR)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Neurologist</td>
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<td></td>
<td></td>
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<tr>
<td>Mean visits ± SD</td>
<td>3.7 ± 5.7</td>
<td>3.9 ± 6.2</td>
<td>3.5 ± 4.9</td>
</tr>
<tr>
<td>Median visits (IQR)</td>
<td>0 (4.0)</td>
<td>0 (6.0)</td>
<td>0 (5.0)</td>
</tr>
<tr>
<td>Psychologist</td>
<td></td>
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<tr>
<td>Mean visits ± SD</td>
<td>0.7 ± 4.2</td>
<td>0.2 ± 1.6</td>
<td>1.7 ± 7.3</td>
</tr>
<tr>
<td>Median visits (IQR)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Other specialist</td>
<td></td>
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</tr>
<tr>
<td>Mean visits ± SD</td>
<td>2.0 ± 4.9</td>
<td>1.9 ± 5.4</td>
<td>2.5 ± 4.2</td>
</tr>
<tr>
<td>Median visits (IQR)</td>
<td>0 (4.0)</td>
<td>0 (0)</td>
<td>0 (4)</td>
</tr>
</tbody>
</table>

* Comparing patients with mild, moderate and severe disability; Jonckheere–Terpstra or Cochran-Armitage test for examination of trend.
†Comparing patients with RRMS and SPMS type of MS; Mann-Whitney or X2 test for examination of difference.
MS: Multiple Sclerosis; EDSS: Expanded Disability Status Scale; RRMS: Relapsing-remitting multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; SD: Standard deviation; IQR: Interquartile range; n.a.: Not Applicable.

Table 2: Socio-demographics and disease information of the sample by EDSS level and MS type.
Resonance Imaging Scan and 5.5% a Lumbar Puncture performed, in the previous 3 months. Advancing disability appears to increase significantly the utilisation of outpatient care (both hospital and rehabilitation centre) and co-medication, though statistical significance is not established in all cases. RRMS patients utilise medical resources to a greater extent compared with SPMS subjects (with the exception of immunosuppressants). Apparently, due to higher disability level and lower relapse rate, SPMS patients require more informal care support rather than health care services utilisation.

Modification of living space or vehicle or use of walking aids due to MS was necessary for 14% of the subjects (Table 4). The frequency of patients reporting any MS-related investment ($p<0.001$) and use of professional or informal care due to MS (both $p<0.001$) increased significantly with worsening severity of the disease; notably, utilization of informal care was much more frequently reported (39%) than professional care (6.5%). RRMS patients were receiving less informal and professional assistance (both $p<0.001$), and had less overall MS-related modifications and equipment investments than the SPMS subjects ($p<0.001$). Apparently, due to higher disability level and lower relapse rate, SPMS patients require more informal care support rather than health care services utilisation.

About one third of the patients (31%) had been retired due to MS, and 33.5% reported receiving MS-related disability benefits during the study; patients in a more severe condition recorded more sick days on average, though not statistically significant. A proportion of 9% of the study; patients in a more severe condition recorded more sick days on average, though not statistically significant. A proportion of 9% of the sample reported a permanent reduction in work hours, and 5% listed a work change and/or income reduction due to the disease. About one third of the patients (31%) had been retired due to MS, and 33.5% reported receiving MS-related disability benefits during the study; patients in a more severe condition recorded more sick days on average, though not statistically significant. A proportion of 9% of the sample reported a permanent reduction in work hours, and 5% listed a work change and/or income reduction due to the disease.

### Costs

The mean cost per patient per year was estimated at €26,118, with
MS treatments being the largest contributor to the overall cost (48.4%) and for all disability and MS type subgroups (Tables 6 and 7). Total cost increased significantly (p<0.001) across the EDSS disability level groups; €20,702 for mild disability (EDSS 0-3), €32,126 for moderate disability (EDSS 3.5-6) and €45,442 for high disability patients (EDSS 6.5-7.5). Total direct medical and non-medical, and indirect costs all increased significantly with advancing disability (all p<0.05). The component costs of outpatient care, MS treatments, MS-related comorbidities, MA-related investments, professional and informal assistance and economic burden due to early retirement (disability pension) all enlarged significantly (all p<0.05) with increasing disability. Notably, the share of informal care in the total cost rose from 5.7% in patients with mild condition to 32.6% in subjects with severe disability. Notably, the share of informal care in the total cost rose from 5.7% in patients with mild condition to 32.6% in subjects with severe disability. Notably, the share of informal care in the total cost rose from 5.7% in patients with mild condition to 32.6% in subjects with severe disability (14.6% overall contribution).

MS related investments previous 12 months, n (%) | Overall (n=200) | Severity | Type of MS
---|---|---|---
| | EDSS 0-3 (n=125) | EDSS 3.5-6 (n=58) | EDSS 6.5-7.5 (n=17) | p-value* | RRMS (n=173) | SPMS (n=27) | p-value†
| House modifications, n (%) | 28 (14.0%) | 4 (3.2%) | 15 (25.9%) | 9 (52.9%) | <0.001 | 18 (10.4%) | 10 (37.0%) | <0.001
| Car modifications, n (%) | 10 (5.0%) | 2 (1.6%) | 3 (5.2%) | 5 (29.4%) | <0.001 | 6 (3.5%) | 4 (14.8%) | 0.012
| Gait aids, n (%) | 6 (3.0%) | 1 (0.8%) | 3 (5.2%) | 2 (11.8%) | 0.307 | 4 (2.3%) | 2 (7.4%) | 0.149
| Manual wheelchair, n (%) | 20 (10.0%) | 0 (0%) | 11 (19.0%) | 7 (41.2%) | <0.001 | 13 (7.5%) | 7 (25.9%) | 0.003
| Electric wheelchair, n (%) | 3 (1.5%) | 0 (0%) | 2 (3.4%) | 1 (5.9%) | 0.18 | 1 (0.6%) | 2 (7.4%) | 0.007
| Professional assistance, n (%) | 13 (6.5%) | 4 (3.2%) | 3 (5.2%) | 6 (35.3%) | <0.001 | 7 (4.0%) | 6 (22.2%) | <0.001

Nurse at home:
- Mean hours per week ± SD: 2.0 ± 0
- Median hours per week (IQR): 2.0 (0)
- Percent of income reduction: 0%

Mediator help:
- Mean hours per week ± SD: 2.2 ± 11.1
- Median hours per week (IQR): 2.5 ± 12.3
- Mean days ± SD: 0 ± 0
- Median days (IQR): 0 (0)

Table 4: Indirect resource utilisation data of the sample by EDSS level and MS type.

Table 5: Productivity loss of the sample by EDSS level and MS type.
<table>
<thead>
<tr>
<th>Inpatient care</th>
<th>Outpatient care</th>
<th>Consultations</th>
<th>Investigations</th>
<th>MS treatments</th>
<th>MS related Comorbidities</th>
<th>OTC</th>
<th>Direct medical costs</th>
<th>MS related Investments</th>
<th>Professional assistance</th>
<th>Informal care</th>
<th>Direct non-medical costs</th>
<th>Income reduction</th>
<th>Retirement due to MS</th>
<th>Indirect costs</th>
<th>Total costs</th>
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</thead>
<tbody>
<tr>
<td>129 ± 261</td>
<td>294 ± 626</td>
<td>630 ± 868</td>
<td>261 ± 211</td>
<td>12643 ± 4982</td>
<td>5644 ± 6290</td>
<td>17 ± 76</td>
<td>19618 ± 8161</td>
<td>68 ± 648</td>
<td>188 ± 1214</td>
<td>3816 ± 839</td>
<td>4072 ± 8677</td>
<td>418 ± 2109</td>
<td>2010 ± 2839</td>
<td>2428 ± 3324</td>
<td>26118 ± 14922</td>
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<tr>
<td>(n=125)</td>
<td>(n=216)</td>
<td>(n=900)</td>
<td>(n=237)</td>
<td>(n=10207)</td>
<td>(n=10210)</td>
<td>(n=10)</td>
<td>(n=125)</td>
<td>(n=0)</td>
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<td>(n=4638)</td>
<td>(n=0)</td>
<td>(n=0)</td>
<td>(n=0)</td>
<td>(n=14922)</td>
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<td>78-159</td>
<td>143-280</td>
<td>379-594</td>
<td>237-237</td>
<td>10844-12671</td>
<td>3717-5567</td>
<td>14 ± 50</td>
<td>16087-18702</td>
<td>0</td>
<td>28 ± 173</td>
<td>1171 ± 3106</td>
<td>1199 ± 3101</td>
<td>472 ± 2341</td>
<td>1632 ± 2681</td>
<td>2104 ± 3388</td>
<td>22090 (17302)</td>
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<tr>
<td>0 (211)</td>
<td>0 (216)</td>
<td>300 (720)</td>
<td>0 (12)</td>
<td>8942 (8562)</td>
<td>3377 (5946)</td>
<td>7-21</td>
<td>17399 (9474)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (515)</td>
<td>750-1740</td>
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<td>1200-2084</td>
<td>0 (6000)</td>
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<td>495 ± 969</td>
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<td>7091 ± 7323</td>
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<td>119 ± 852</td>
<td>28 ± 155</td>
<td>6299 ± 10500</td>
<td>6446 ± 10522</td>
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<td>54 ± 222</td>
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*p-value* Comparing patients with mild, moderate and severe disability; Jonckheere–Terpstra test for examination of trend.

MS: Multiple Sclerosis; EDSS: Expanded Disability Status Scale; OTC: over-the-counter drugs; SD: Standard deviation; IQR: Interquartile range.

**Table 6:** Costs per patient per year by EDSS level (in € 2011), 95% CI.
Discussion

The objective of this study was to estimate the health and economic burden of MS in Greece, while offering valuable insights into the way disease severity and MS type affect the related costs.
The mean annual cost per patient was estimated at €26,118. This is comparable to the results of a recent study across 5 European countries, in which the mean annual cost per patient ranged between €20,738 and €29,400 [10-15]. Worsening disability was associated with a substantially increased economic impact of the disease, which is in accordance with the findings of most published studies [10-13,15, 19,29-36]. According to the existing literature [10-20], severe disability, when compared to mild, is associated with increased costs for hospitalizations, consultations, laboratory tests and other drugs, although the cost of immunomodulatory drugs is reduced. In our research, total direct medical and non-medical as well as indirect costs indeed increased considerably with advancing disability, with statistical significances established for the majority of their components. Furthermore, treatment cost retained its prominence in all disability and MS type subgroups, though its share in the total cost gradually decreased, which may be attributed to the patient recruitment, as it is discussed subsequently. Informal care contributed significantly to the total cost (14.6%); its contribution increased from 5.7% in patients with mild to 32.6% in subjects with severe disability, confirming the importance of informal care for MS patients, which is strongly associated with the severity of the disease [10-15,18,19,29-36]. Higher mean disability in patients with SPMS compared with RRMS subjects resulted in almost doubled total costs, in congruence with what is observed in other European countries [10,12-15]; total direct medical and non-medical as well as indirect costs all were significantly different between the 2 groups.

HRQoL was found considerably impaired by MS. Psychological and mobility problems and difficulties related to usual activities were reported by the majority of the patients. The mean utility score in the sample was 0.601 (VAS mean score 67.9), which is lower than the corresponding value in the general population, though somewhat higher than in other similar reports [16-20,37], which could be attributed to the lower mean EDSS level of this study. Finally, higher severity and SPMS type of MS decreased HRQoL, which is consistent with the international literature [10-15,18,19,29-36].

There are several limitations related to the recruitment of patients from hospital MS centres, as it might result in a sample of subjects with higher mean disability [38]. Nevertheless, in our study, the number of patients which were assigned to the high disability group (EDSS 6.5-7.5) was relatively low (n=17). In fact, patients with EDSS >7.5 were not represented in our study, hence costs might has been actually underestimated due to the lack of high resource consuming patients. Currently, there are no country-scale studies of MS in Greece with epidemiological data concerning different patient disability categories, which could have been used as a demographic guide in the study design. Additionally, we approximated the productivity loss due to MS by the patient-reported reduction in their income, which may not be an appropriate proxy for estimating productivity losses, if there is a benefit to mitigate the fall in income.

Furthermore, the questionnaire explicitly requested resource utilization due to MS, but it still might have captured consumption unrelated to MS, thus yielding inflated costs. This possible limitation is particularly relevant to the comorbidities’ economic burden, which was estimated as the total mean annual cost per patient, and not only as co-medication costs. Nevertheless, MS is a well-defined condition, and unrelated comorbidity is relatively low due to the young age of the patients [19,38]. A degree of recall bias introduced by participants regarding their reports about past events or experiences may also be present, as it is a common peril among studies with a retrospective design [41]. Finally, the sample size of patients without a recent relapse was not large enough to estimate the specific cost related to relapses, which would have been a valuable piece of information.

In conclusion, the STORMS study contributes to the scarce information on costs and health of MS patients in Greece. In view of the increasing economic and HRQoL burden with worsening disability, the use of MS treatments that can effectively delay the progression of the disease may reduce the detrimental impact of the disease on patient and caregiver lives, as well as on society as a whole.

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Disclosures and Conflict of Interest

J Yfantopoulos has received honoraria and research grants from Novartis. N Grigoriadis has received honoraria and research grants from Novartis, Teva, Biogen Idec, Bayer, Merck-Serono and Sanofi-Genzyme. K Karageorgiou is a member of advisory boards of Genzyme, Teva, Genesis Pharma and Novartis. P Papanathanasopoulos has participated as a member of Advisory Boards and got unrestricted research grants from Novartis, Genesis, TEVA, Serono and Bayer. D Tzortzis has received research grants from Novartis. V Tsimourtou and S Ralli has received research grants from Novartis, Bayer and Genesis and Novartis. N Dimianos has received honoraria from Novartis, Genesis Pharma and Merck, travel expenses from Teva, Merck, Novartis and an unrestricted research grant from Genesis Pharma. I Iliopoulos, V Kostadima, AP Kyritsis, X Treska and A. Chantzaras have nothing to disclose. M.Chatzikou and G. Rombopoulos are employees of Novartis Hellas and M. Vikelis was working in Novartis Hellas during the analysis of the study.

Reference


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