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## Background

- Multiple sclerosis (MS) is a chronic neurodegenerative disorder that typically affects young and middle-aged adults, leading to substantial health and socioeconomic burden.<sup>1</sup> In Spain, the prevalence of MS is estimated between 0.10% and 0.13% of the total population.<sup>2,3</sup>
- MS imposes substantial clinical and financial burden on both the patient and society. Previous studies have not estimated the total societal burden, including extra costs, foregone income and production losses endured by MS patients, their caregivers, and employers in Spain.<sup>4,5</sup>
- Therefore, the present study was undertaken to address the existing gap and estimate the cost burden imposed by MS in Spain.

## Objective

- To estimate the total societal cost (i.e., the cost to the National social security system [Seguridad social], employers, patients, and caregivers) of MS for the year 2020 in Spain, including extra costs incurred related to childcare, salary shortfalls, and unemployment benefits.

## Methods

### Study Design

- This was a cost-of-illness study that estimated the direct and indirect costs associated with MS in Spain.

### Data Source

- Data on the MS population was sourced from the MS International Federation.<sup>3</sup> For the distribution of MS population by EDSS, the distribution reported in a Spanish nationwide study was used.<sup>4</sup>
- Estimates reported from a Spanish nationwide study were used to calculate the cost data.<sup>4</sup> Data that had not previously been counted (i.e., childcare costs, unemployment benefits, foregone income) and other missing information were drawn from the socioeconomic impact of MS study in France.<sup>6</sup>
- Table 1** summarises the data sources and the methodology used to calculate different components of direct and indirect costs.

**Table 1. Data sources and the calculation used to derive cost estimates**

Data	Source and Calculation
MS population	MS International Federation <sup>3</sup>
EDSS-wise distribution	Oreja-Guevara, 2017 <sup>4</sup>
OOPE	
SS costs	<ul style="list-style-type: none"> <li>Estimates from Sicras-Mainar (2017)<sup>5</sup> were extrapolated to numbers of patients in each EDSS stage</li> <li>Increased by 6% per year (2015-2020) following hypothesis that annual SS costs in Spain evolve in the same direction and dimension as those in France<sup>7</sup></li> <li>As Sicras-Mainar (2017)<sup>5</sup> does not provide distinction for costs between EDSS stages 4-6 and 7-9, the cost differences between Assurance maladie spendings according to EDSS levels was applied<sup>8</sup></li> <li>Annual number of patients with early retirement x average retirement pension in Spain</li> </ul>
Consumables	<ul style="list-style-type: none"> <li>% of MS patients who purchased consumables at each EDSS.<sup>6</sup> The difference between the consultation OOPEs for Spanish and French patients (=38% higher) were replicated</li> <li>Adapted to the size and distribution of the Spanish MS population<sup>3</sup></li> </ul>
Consultations	<ul style="list-style-type: none"> <li>Costs for consultations from Oreja-Guevara (2017).<sup>4</sup> Part of the costs attributable to SS spendings (estimated at 19.5%) were increased by 6% per year (2015-2020) following hypothesis that yearly SS costs in Spain for MS evolve in the same direction and dimension as those in France<sup>7</sup></li> <li>The inflated SS costs were then added to the OOPE share (19.5% of the original figure)</li> <li>Total OOPE+SS costs x (0.195 x number of patients in each EDSS stage)</li> </ul>
Specialised transportation	<ul style="list-style-type: none"> <li>Cost per person<sup>4</sup> x number of persons in each EDSS stage x share of patients having resorted to Specialised transportation (assumed to be 2% for all stages)<sup>4</sup></li> </ul>
Adapted vehicle & mobility equipment	<ul style="list-style-type: none"> <li>As per Oreja-Guevara et al, 25% of patients were assumed to have invested in mobility equipment, home or automobile modifications<sup>4</sup></li> <li>Cost per person<sup>4</sup> x number of persons in each EDSS stage that invested in mobility equipment, home, or automobile modifications</li> </ul>
Home help	<ul style="list-style-type: none"> <li>Cost per person<sup>4</sup> x number of persons in each EDSS stage who resorted to home help</li> </ul>
Childcare	<ul style="list-style-type: none"> <li>Costs incurred for childcare at each age (derived from EUROSTAT assuming that Spanish MS patients are distributed along age brackets the same way French patients)<sup>9</sup></li> <li>Inflated by 20% (to reflect the differences between France and Spain)</li> <li>OOPEs were adapted according to the income difference between Spain and France</li> </ul>

**Table 1 (Continued)**

Sick leaves (for patients, employers, caregivers, and SS)	Data from Cleiss was used <sup>10</sup>
	<b>Patients</b>
	<ul style="list-style-type: none"> <li>Number of persons taking sick leave at each EDSS stage x (average net income x the first 3 days)</li> <li>Slower salary progression = Estimates from the French study<sup>6</sup> were adjusted by salary levels along average income</li> </ul>
	<b>Employers' production losses</b>
	<ul style="list-style-type: none"> <li>Costs for exits from the labour market = total inoccupation periods stemming from premature departures from the labour market x share of productivity foregone during an employee's absence</li> <li>Production per person = Spanish GDP/ number of persons on the labour market</li> </ul>
	<b>Loss of income for caregivers</b>
	<ul style="list-style-type: none"> <li>% of MS patients receiving informal help at each EDSS stage<sup>4</sup></li> <li>Average Spanish income x (total number of days off work<sup>4</sup> extrapolated to the total MS population<sup>3/3</sup>)</li> </ul>
Early retirement and invalidity pension costs	<ul style="list-style-type: none"> <li>% of MS patients retiring early annually<sup>6</sup></li> <li>Patients' income loss = annual number of patients with early retirement x average salary for each age bracket</li> <li>Patient's forgone income = income they would have earned - retirement benefits</li> </ul>
Unemployment benefits	<ul style="list-style-type: none"> <li>Data from the French study<sup>6</sup> was adjusted to the number of Spanish MS patients who left the labour market every year and unemployment benefit amounts, adjusted to the average Spanish income</li> </ul>
Foregone income for workers	<ul style="list-style-type: none"> <li>Estimates from the French study<sup>6</sup> were used and applied to the Spanish MS population, adjusted to the average Spanish income</li> </ul>

EDSS, Expanded Disability Status Scale; GDP, gross domestic product; MS, multiple sclerosis; OOPE, out-of-pocket expenses; SS, Seguridad Social.

## Study Measures

- Total costs including direct and indirect costs attributed to MS were calculated.
- Direct costs included costs incurred to the healthcare system, extra expenses, and patient out-of-pocket expenses (OOPE).
- Indirect costs included loss of income through lost productivity of MS patients and caregivers as well as benefits and health-related aid (**Table 1**).
  - Productivity loss (defined as foregone production for employers whose employees temporarily or permanently cease work) was estimated using a new, more precise method that was developed to monetise productivity loss associated with MS
  - The new method is based on exact job inoccupation periods of absence, updated work compensation ratios by colleagues and possibilities of replacement by unemployed workers.
- Costs reported were derived by extrapolating the data to the Spanish MS population.
- All costs were inflation-adjusted to 2020 Euros (€) and specific evolution rates were applied to costs relative to the healthcare system, as it was posited that those increased yearly, with the number of people treated for MS and variation of costs for drugs and treatments.

## Statistical Analysis

- All study variables were summarised using descriptive statistics. Data for categorical variables were summarised as counts and percentages while those for continuous variables were presented as means and standard deviations (SD).
- A p<0.05 was set as the threshold for statistical significance.

## Results

### Study Population

- Based on the data from MS International Federation, an estimated 55,000 patients have MS in Spain.<sup>3</sup> **Table 2** summarises the EDSS-wise distribution of MS patients that was considered for analysis.

**Table 2. Distribution of the MS patients by EDSS stage**

EDSS stages	Original distribution <sup>4</sup> n (%)	Estimated Spanish distribution n (%)
1-3	270 (58.4%)	32,267 (58.7%)
4-6	135 (29.2%)	16,317 (29.7%)
7-9	50 (10.8%)	6,417 (11.6)
<b>Total</b>	<b>455 (98.5%)*</b>	<b>55,000 (100%)**</b>

EDSS, Expanded Disability Status Scale; MS, multiple sclerosis.

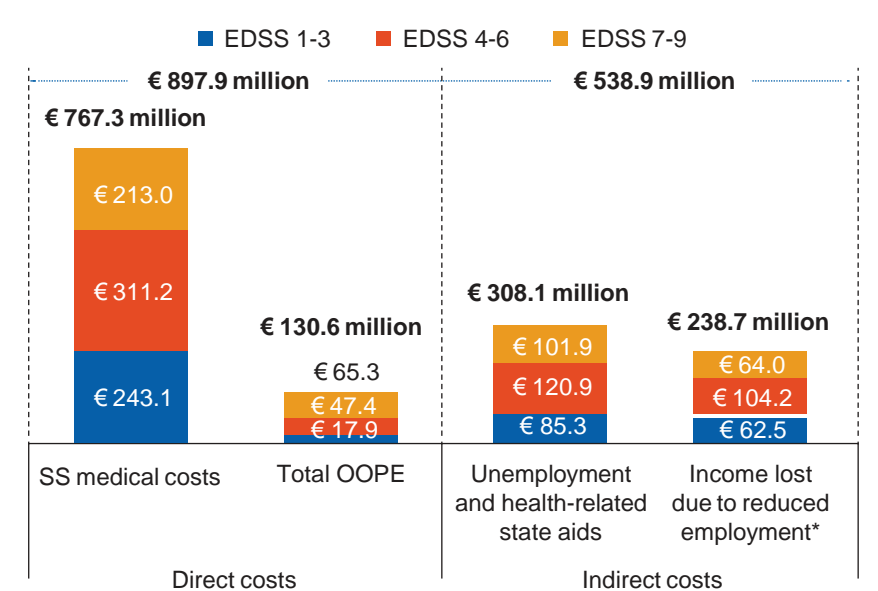
**Notes:** \*Of 462 MS patients who participated in the original study, data on EDSS stages were missing for seven patients; \*\* For this study, 7 (1.5%) patients were equally distributed across the EDSS stages.

### Annual costs of MS in Spain

- The annual total cost of MS in Spain was estimated at €1.4 billion (€26,123 per person/year). Direct costs contributed 64.1% of the costs, and the remaining were driven by indirect costs (35.9%) (**Figure 1**).

- Of the €897.9 million total annual direct costs (€16,325.7 per person), the Seguridad social spends €767.3 million per annum on MS-related medical reimbursements (€13,951.3 per person). OOPEs accounted for €130.6 million (€2,374 per person), the majority of which were driven by costs related to home help (€64.3 million), adapted vehicle and mobility equipment (€37.5 million), and consultations (€18.8 million). Costs for childcare (€8.0 million), specialised transportation (€1.3 million), and consumables (€0.6 million) contributed to the remaining OOPEs.
- Indirect costs accounted for €538.9 million of the total annual costs (€9,797.6 per person) and were driven by unemployment and health-related state aids, loss of income due to lost productivity for patients and caregivers, and foregone income for patients (**Figure 1**).
  - Most of the indirect costs due to sick leaves, retirement pensions, and health-related aids and unemployment benefits (€314.8 million) were borne by the Seguridad social. Income lost for patients and caregivers due to MS accounted €12.0 million and €176.9 million, respectively. Income shortfall for employers due to reduced working time contributed €16.5 million to the total annual costs.
- The total annual costs were €408.8 million, €583.8 million, and €444.2 million for EDSS ≤3, EDSS 4-6 and EDSS 7-9 groups, respectively. As the disability progressed, the total annual total costs per patient also increased from €12,670.2 per person (EDSS ≤3) to €35,778.6 (EDSS 4-6) and €69,221.2 (EDSS 7-9).

**Figure 1. Annual costs of MS in Spain**



EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; OOPE, out-of-pocket expenses; SS, Seguridad Social.

**Notes:** \*Includes income lost due to sick leaves, exit from the labour market, and early retirement for patients and employers + forgone income for patients and caregivers + sick leaves and early retirement costs for the Seguridad social + unemployment benefits

## Conclusions

- The results from this study highlight that MS exerts a substantial socio-economic impact and can hamper the personal and professional lives of MS patients and their caregivers, while negatively impacting productivity for employers and the economy.
- These findings are very relevant to healthcare providers, payers, and policymakers in Spain for future healthcare decision-making, particularly with the increasing advances in scientific innovation relating to the availability of high-efficacy treatments (HETs) for the effective management of MS.
- Timely diagnosis, holistic disease management and timely intervention with HET options available in MS in relapsing-remitting MS, has the potential to reduce the burden and societal cost of the disease.

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## Disclosures

This study was funded by Novartis Pharma AG, Basel, Switzerland. Marta Aguirre, Elizabeth Karpf, and Antonios Petropoulos are employees of Novartis. Alice Bouleau and Charles-Antoine Schwerer are employees of Asterès. María Duato has nothing to disclose.

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