A Retrospective Matched-Cohort Study to Assess the Clinical and Economic Burden in People with Secondary Progressive Multiple Sclerosis in the United States

Nupur Greene[1], *Ashis K. Das*[2], *Ines Hemim*[1], *Eunice Chang*[2], *Marian H. Tarbox*[2]

[1]Sanofi, Cambridge, MA, USA; [2]ADVI Health, Washington, DC, USA

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BACKGROUND

- Multiple sclerosis (MS) is classified into distinct phenotypes—either relapsing-remitting MS (RRMS) or other progressive forms, which includes primary progressive MS (PPMS) and secondary progressive MS (SPMS)[1]
- At least 50% of people diagnosed with RRMS develop SPMS within 20 years of disease onset, which is characterised by irreversible disability progression.[2] This transition can occur with relapses (active SPMS [aSPMS]) or without relapses (non-relapsing SPMS [nrSPMS])[3]
- Early diagnosis of SPMS is difficult due to the absence of clear diagnostic criteria and variability in symptoms, often leading to a retrospective diagnosis; which delays appropriate intervention and contributes to increased healthcare resource utilisation (HCRU) due to prolonged disease management and frequent clinical assessments.[1,2] Data specifically on the clinical and economic burden of SPMS in the United States (US) remains limited[4]

OBJECTIVE

- To understand the real-world clinical and economic burden in people with SPMS in the US

CONCLUSIONS

- Overall, comorbidities, HCRU, and HCCs were significantly higher in people with SPMS versus MS-free matched-controls, leading to a substantial clinical and economic burden in the SPMS population, which currently has very limited approved therapies.

METHODS

Study design and population

- This retrospective, matched-cohort study was conducted using a large, integrated US-based administrative claims database from 01 January 2018 to 30 June 2023 (**Figure 1**)
- The index date was defined as a randomly selected date with an MS diagnosis during the identification period between 01 January 2018 and 30 June 2021
- For the present analysis, people with SPMS were identified as per the inclusion/exclusion criteria illustrated in **Figure 2**
- People with SPMS were then matched (1:1) to unique MS-free controls based on age, gender, insurance type, and region
  - The index date for these MS-free matched-controls was the same as that for the matched SPMS cohort

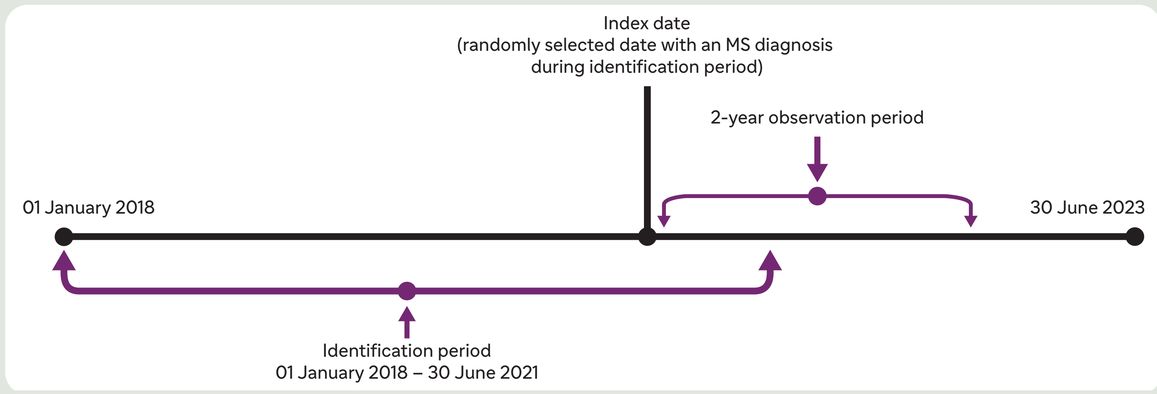
Study measures

- During the 2-year observation period, baseline demographics, Charlson Comorbidity Index (CCI), specific comorbidities of interest, HCRU, and healthcare costs (HCCs) were compared between the SPMS cohort and the MS-free matched-controls
  - Inpatient admissions, emergency department (ED) visits, non-ED outpatient service visits, medical and pharmacy costs, cost of infections, and use of specific services were included in HCRU and HCC calculations

Statistical analysis

- Descriptive statistics were used to compare all study variables
- All HCCs were reported in US dollars, adjusted to 2023 values
- All statistical tests were two-sided, with a significance threshold of $P<0.05$

Figure 1: Study time frame



MS, multiple sclerosis.

RESULTS

Baseline demographics

- The final cohort included 5,111 people with SPMS and 5,111 MS-free matched-controls (**Figure 2**)

Figure 2: Attrition chart for SPMS cohort

People with an MS diagnosis (ICD-10-CM codes: G35.xxx) during the identification period (01 January 2018, to 30 June 2021)	*N*=75,492
People with ≥1 inpatient claim or ≥2 outpatient claims with a diagnosis of MS during the 2-year observation period	*N*=49,542
People who were continuously enrolled in both medical and pharmacy plans during 2-year observation period	*N*=24,229
People who were ≥40 years old	*N*=19,600
People who had ≥2 signs, symptoms, or medications anytime during the 2-year observation period	*N*=5,628
People who either were not newly diagnosed with MS or had a clinical relapse	*N*=5,324
People who had no diagnosis of myasthenia gravis or NMO	*N*=5,201
People with SPMS who had a matched MS-free control[a]	*N*=5,111

N is the number of patients. [a]MS-free matched-controls were matched by age, gender, region, and insurance type. The index date of the matched-controls was the same as that of the people with SPMS. ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; MS, multiple sclerosis; NMO, neuromyelitis optica; SPMS, secondary progressive multiple sclerosis.

- The mean±standard deviation (SD) age of the SPMS cohort was 58.1±10.2 years, with majority being female (77.0%) and covered by commercial insurance (74.5%) (**Table 1**)

Table 1: Demographics of people in the SPMS cohort versus MS-free matched-controls

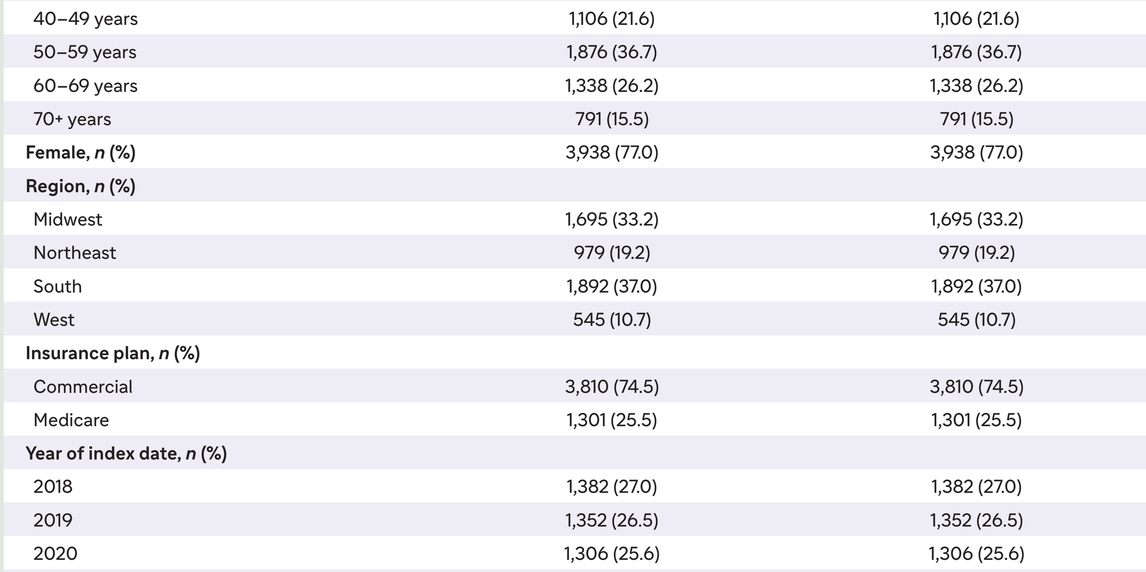
Variables	People with SPMS (*N*=5,111)	MS-free matched-controls (*N*=5,111)
Age, years (mean±SD)	58.1±10.2	58.1±10.2
Age group, *n* (%)		
40–49 years	1,106 (21.6)	1,106 (21.6)
50–59 years	1,876 (36.7)	1,876 (36.7)
60–69 years	1,338 (26.2)	1,338 (26.2)
70+ years	791 (15.5)	791 (15.5)
Female, *n* (%)	3,938 (77.0)	3,938 (77.0)
Region, *n* (%)		
Midwest	1,695 (33.2)	1,695 (33.2)
Northeast	979 (19.2)	979 (19.2)
South	1,892 (37.0)	1,892 (37.0)
West	545 (10.7)	545 (10.7)
Insurance plan, *n* (%)		
Commercial	3,810 (74.5)	3,810 (74.5)
Medicare	1,301 (25.5)	1,301 (25.5)
Year of index date, *n* (%)		
2018	1,382 (27.0)	1,382 (27.0)
2019	1,352 (26.5)	1,352 (26.5)
2020	1,306 (25.6)	1,306 (25.6)
2021	1,071 (21.0)	1,071 (21.0)

N is the total number of patients. *n* is the subset of patients. MS, multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis.

Clinical Burden

- The mean±SD CCI score was significantly higher in the SPMS cohort than in the MS-free matched-controls (2.0±2.4 vs. 0.9±1.7; $P<0.001$)
- The proportion of people with infections, leucopenia, and elevated liver transaminase levels was significantly higher ($P<0.001$) in the SPMS cohort than in the MS-free matched-controls (**Figure 3**)

Figure 3: Infections, leucopenia, and elevated liver transaminase levels in the SPMS cohort versus the MS-free matched-controls

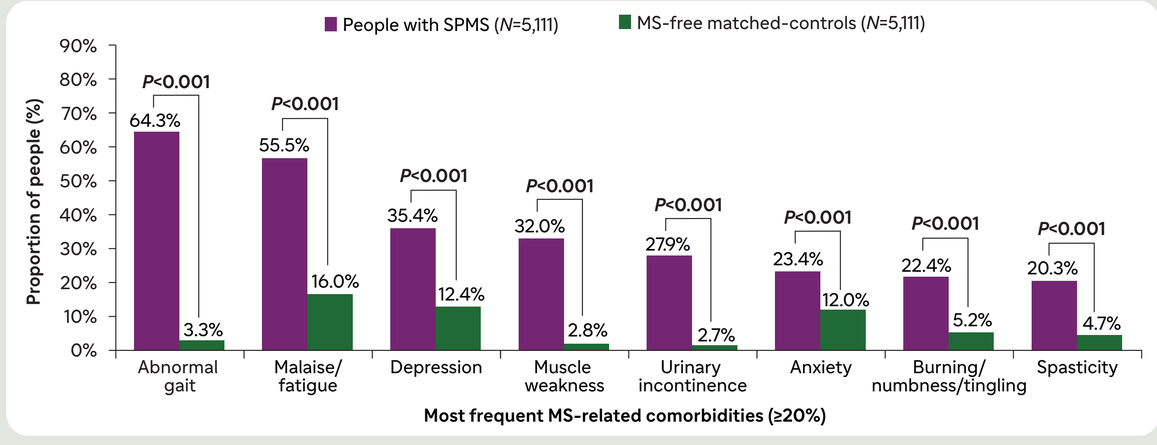


N is the total number of patients. MS, multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Specific comorbidities of interest

- The most frequent MS-related comorbidities (≥20%) in the SPMS cohort versus the MS-free matched-controls included abnormal gait, malaise/fatigue, depression, muscle weakness, urinary incontinence, anxiety, burning/numbness/tingling, and spasticity (all $P<0.001$; **Figure 4**)
- Other comorbidities (84.2% vs. 58.6%; $P<0.001$) and autoimmune comorbidities (31.2% vs. 18.0%; $P<0.001$) were significantly higher in the SPMS cohort than in the MS-free matched-controls

Figure 4: Most frequent MS-related comorbidities (≥20%) in the SPMS cohort versus the MS-free matched-controls



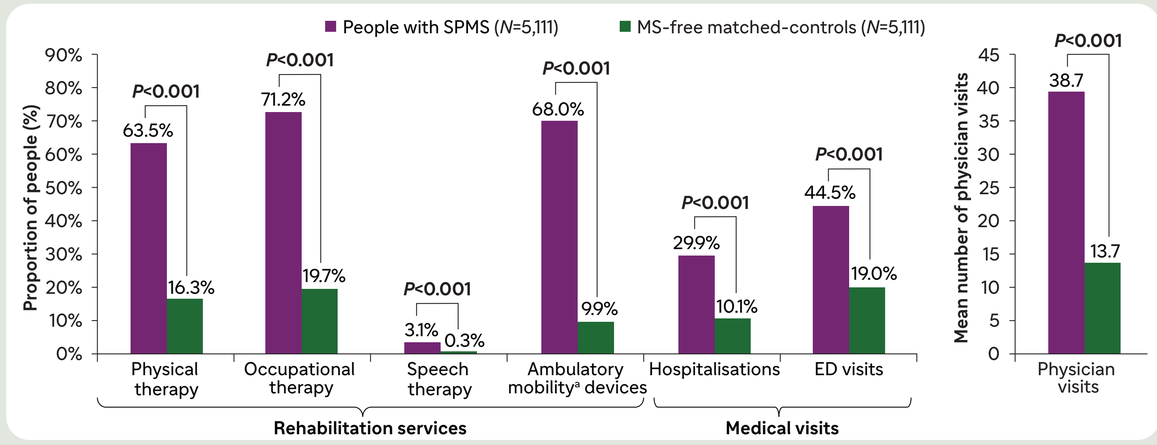
N is the total number of patients. MS, multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Economic Burden

All-cause healthcare resource utilisation and healthcare costs

- During the follow-up period, a significantly higher proportion of people with SPMS required rehabilitation services (ambulatory devices and physical, occupational, and speech therapies) than the MS-free matched-controls (all $P<0.001$; **Figure 5**)
- At follow-up, the rates of hospitalisations and ED visits, and the mean number of physician visits were significantly higher in people with SPMS versus MS-free matched-controls (all $P<0.001$; **Figure 5**)
- The length of hospital stay was also significantly higher in the SPMS cohort than in the MS-free matched-controls (mean±SD: 12.8±21.1 days vs. 7.8±12.1 days; $P<0.001$)

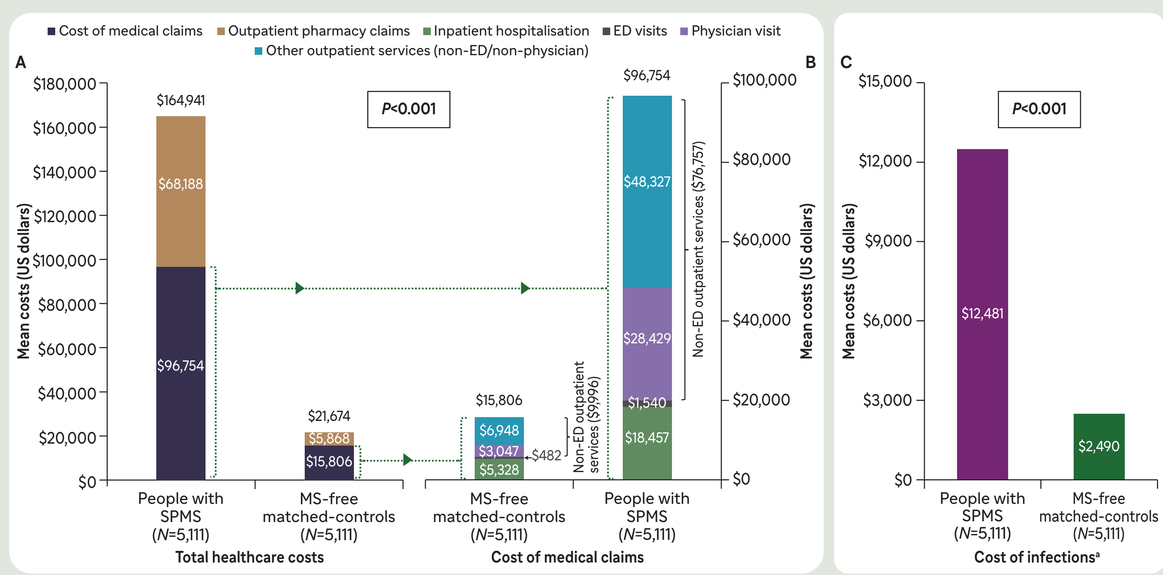
Figure 5: All-cause healthcare resource utilisation in the SPMS cohort versus the MS-free matched-controls



N is the total number of patients. [a]Ambulatory mobility devices included cane, walker, wheelchair, orthotics, other walking aids. ED, emergency department; MS, multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

- The mean total all-cause HCCs were significantly higher ($P<0.001$) in the SPMS cohort than in the MS-free matched-controls, which were primarily driven by the cost of medical claims and non-ED outpatient services (**Figure 6**)

Figure 6: (A) All-cause total healthcare costs inclusive of cost of medical claims and outpatient pharmacy claims, (B) Cost of medical claims derived from all-cause total healthcare costs, and (C) Cost of Infections.



N is the total number of patients. Costs were adjusted to 2023 US dollars. The all-cause total healthcare costs were significantly higher in the SPMS cohort than those for the MS-free matched-controls (all $P<0.001$). [a]Cost of infections: Costs of medical claims with a diagnosis of infections in any field plus the costs of antibiotics or antivirals pharmacy claims, with days of supply <21, filled within 7 days of an infection medical claim. ED, emergency department; MS, multiple sclerosis; SPMS, secondary progressive multiple sclerosis; US, United States.

LIMITATIONS

- As this study provides a cross-sectional view of the burden of illness among people with SPMS,
  - It may not fully capture the progressive and variable nature of disease management over time
  - A potential misclassification of the SPMS cases might have influenced patient identification and associated outcomes
- The absence of mortality data in retrospective claims analyses limits the assessment of true disease burden by omitting critical information about survival outcomes and ultimate disease progression
- Additionally, findings may not be generalisable to populations outside of commercial insurance coverage, including uninsured individuals and those over 65 years of age

References

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Disclosures

Nupur Greene and **Ines Hemim** are employees of Sanofi and may hold stocks or stock options in the company.

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