Understanding the Burden of Illness in People with Nonrelapsing Secondary Progressive Multiple Sclerosis in the United States: A Matched-cohort Study

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BACKGROUND

- Multiple sclerosis (MS) is categorized into relapsing or progressive forms based on its clinical course[1]
  - Relapsing-remitting MS (RRMS) is the most common form of MS representing around 85% of the total MS cases[1]
  - Approximately 50% of people with RRMS progress to secondary progressive MS (SPMS) over 10–15 years[2,3]
  - However, many people with SPMS continue to accumulate disability in the absence of clinical relapses and can be termed as nonrelapsing SPMS (nrSPMS)
- Although several disease-modifying therapies (DMTs) are available for relapsing MS in the United States (US), there are no DMTs approved for nrSPMS[4]
- While it is known that people with MS have a substantially lower quality of life and higher healthcare costs (HCCs) than the general population,[5,6] data on the clinical and economic burden in people with nrSPMS are lacking

OBJECTIVE

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

METHODS

Study design

- A retrospective, matched-cohort study was conducted using the Optum Market Clarity linked EHR and claims database, i.e. a large, integrated US-based administrative health database from 01/01/2012 to 12/31/2021 (Figure 1)
- People with nrSPMS were matched to unique MS-free controls based on age, sex, race, region, and insurance (1:1). The index date of control was the same as matched MS patients

Figure 1: Study time frame

MS, multiple sclerosis; Y, year.
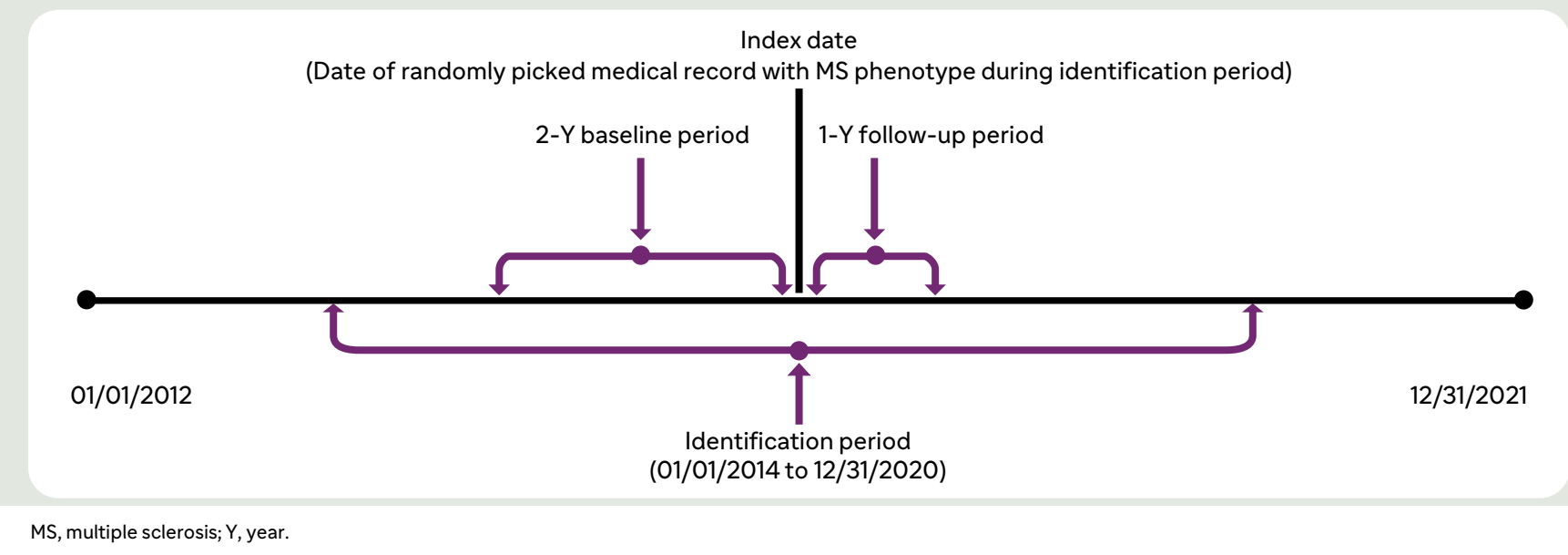
Study population

- The nrSPMS cohort consisted of people with MS who had an SPMS electronic health record (EHR) during the identification period (Figure 1)
  - An additional continuous enrollment during a 2-year baseline period was required to classify people with SPMS into nrSPMS (defined as no relapse in prior 2 years) and active SPMS (defined as ≥1 relapse in prior 2 years)
- The identification of the nrSPMS cohort was also carried out using a validated claim-based nrSPMS algorithm[7]
  - People were excluded if they were aged >70 years, OR had a primary diagnosis of other neurological disorder (Alzheimer's, Parkinson's disease, myasthenia gravis, or stroke), OR had evidence of relapse during the 2-year baseline period

Study measures

- Demographics, Charlson Comorbidity Index (CCI), specific comorbidities of interest, healthcare resource utilization (HCRU), and HCCs were compared with the controls during the 1-year follow-up period
  - HCRU and HCCs included inpatient admissions, emergency room visits, outpatient services, pharmacy costs, use of specific services, and cost of infections
- Treatment patterns were observed for people with MS during the 1-year follow-up period

Statistical analysis

- Descriptive statistical analyses were used to compare all study measures
- All costs were reported in US dollars (adjusted to Year 2021)
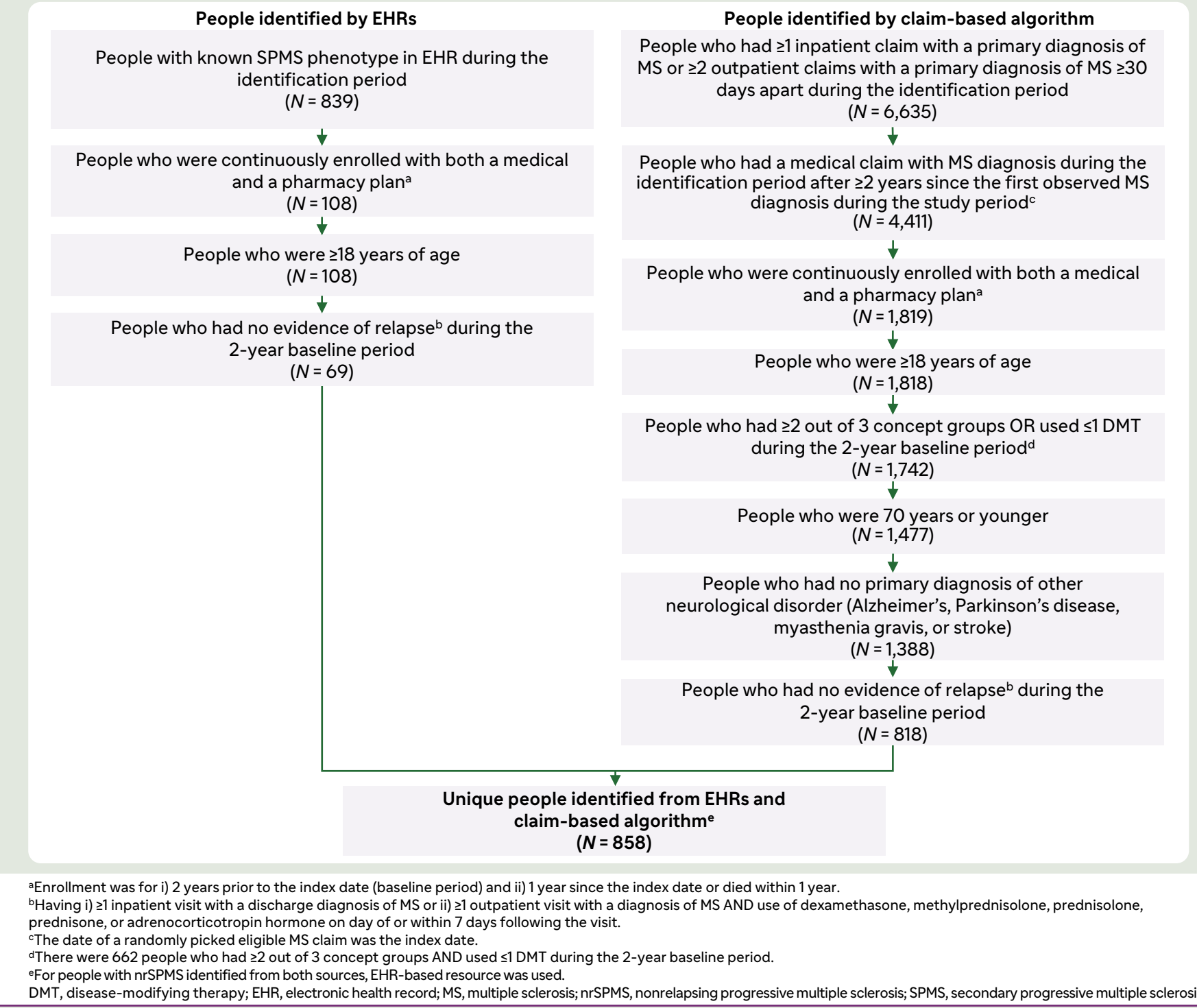- All tests were 2-sided, and $P < 0.05$ was considered significant

RESULTS

Demographics

- A total of 858 people with nrSPMS were identified, out of which 856 were included in the final cohort (Figure 2) along with the 856 matched MS-free controls. Two people with nrSPMS were excluded as they had no matched controls

Figure 2: Attrition chart for nrSPMS cohort

aEnrollment was for i) 2 years prior to the index date (baseline period) and ii) 1 year since the index date or died within 1 year.
bHaving i) ≥1 inpatient visit with a discharge diagnosis of MS or ii) ≥1 outpatient visit with a diagnosis of MS AND use of dexamethasone, methylprednisolone, prednisolone, prednisone, or adrenocorticotropin hormone on day of or within 7 days following the visit.
cThe date of a randomly picked eligible MS claim was the index date.
dThere were 662 people who had ≥2 out of 3 concept groups AND used ≤1 DMT during the 2-year baseline period.
eFor people with nrSPMS identified from both sources, EHR-based resource was used.
DMT, disease-modifying therapy; EHR, electronic health record; MS, multiple sclerosis; nrSPMS, nonrelapsing progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

- The mean (standard deviation [SD]) age of the nrSPMS cohort was 54.4 (10.7) years; majority were female (79.8%) and Caucasian (87%; Table 1)

Table 1: Demographics of people in the nrSPMS cohort versus controls

Variable	nrSPMS cohort (N = 856)	Control cohort (N = 856)
Age (years), mean ± SD	54.4 ± 10.7	54.4 ± 10.7
18–34	43 (5.0)	43 (5.0)
35–54	343 (40.1)	343 (40.1)
55–64	312 (36.4)	312 (36.4)
65+	158 (18.5)	158 (18.5)
Female	683 (79.8)	683 (79.8)
Race		
Caucasian	745 (87.0)	745 (87.0)
African American	63 (7.4)	63 (7.4)
Other/Unknown	48 (5.6)	48 (5.6)
Region		
Midwest	398 (46.5)	398 (46.5)
Northeast	180 (21.0)	180 (21.0)
South	109 (12.7)	109 (12.7)
West	140 (16.4)	140 (16.4)
Other/Unknown	29 (3.4)	29 (3.4)
Plan type		
Commercial	442 (51.6)	442 (51.6)
Medicaid	26 (3.0)	26 (3.0)
Medicare	324 (37.9)	324 (37.9)
Unknown	64 (7.5)	64 (7.5)

Data presented as n (%) unless otherwise specified.
nrSPMS, nonrelapsing progressive multiple sclerosis; SD, standard deviation.

Clinical characteristics

- The mean CCI score was significantly lower in the nrSPMS cohort than that in matched controls (1.02 vs. 1.21; $P = 0.032$)
- A higher proportion of people in the nrSPMS cohort reported infections and leukopenia compared with matched controls (Figure 3)
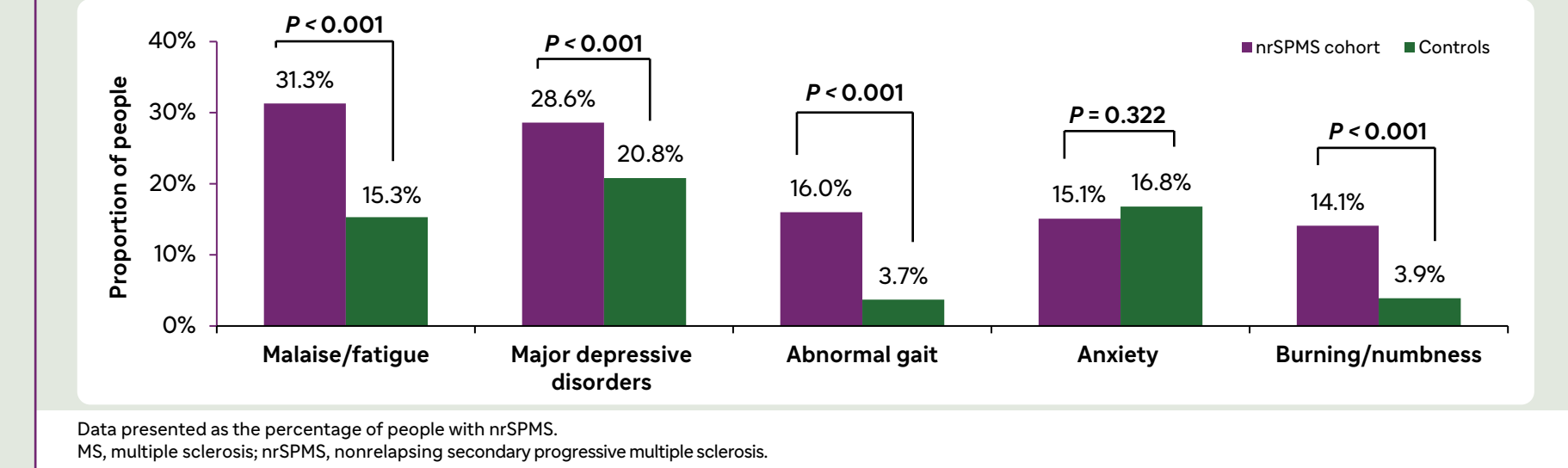
Figure 3: Proportion of people with infections and leukopenia in the nrSPMS cohort versus matched controls

Data presented as the percentage of people with nrSPMS.
nrSPMS, nonrelapsing secondary progressive multiple sclerosis; NS, non-significant.
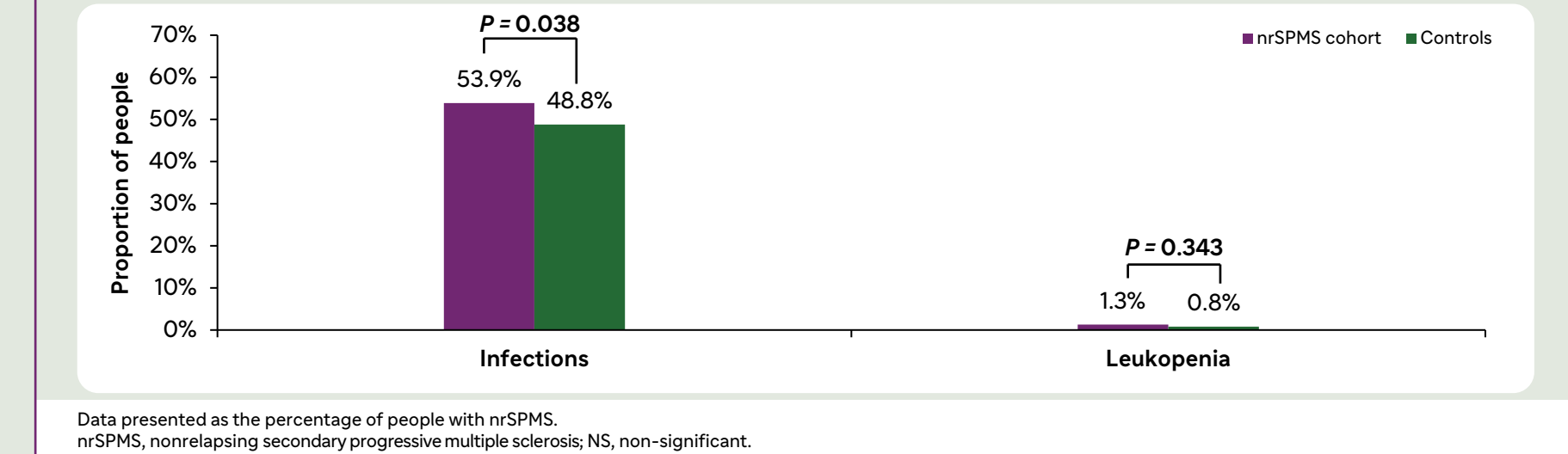
Specific comorbidities of interest

- The top five most frequent MS-related comorbidities in people with nrSPMS vs. controls included malaise/fatigue, major depressive disorders, abnormal gait, anxiety, and burning/numbness (Figure 4)
- Other comorbidities were reported by 63.6% in the nrSPMS cohort and 60.6% in the matched controls ($P = 0.213$); autoimmune comorbidities were reported by 17.9% in the nrSPMS cohort and 20.4% in the matched controls ($P = 0.177$)
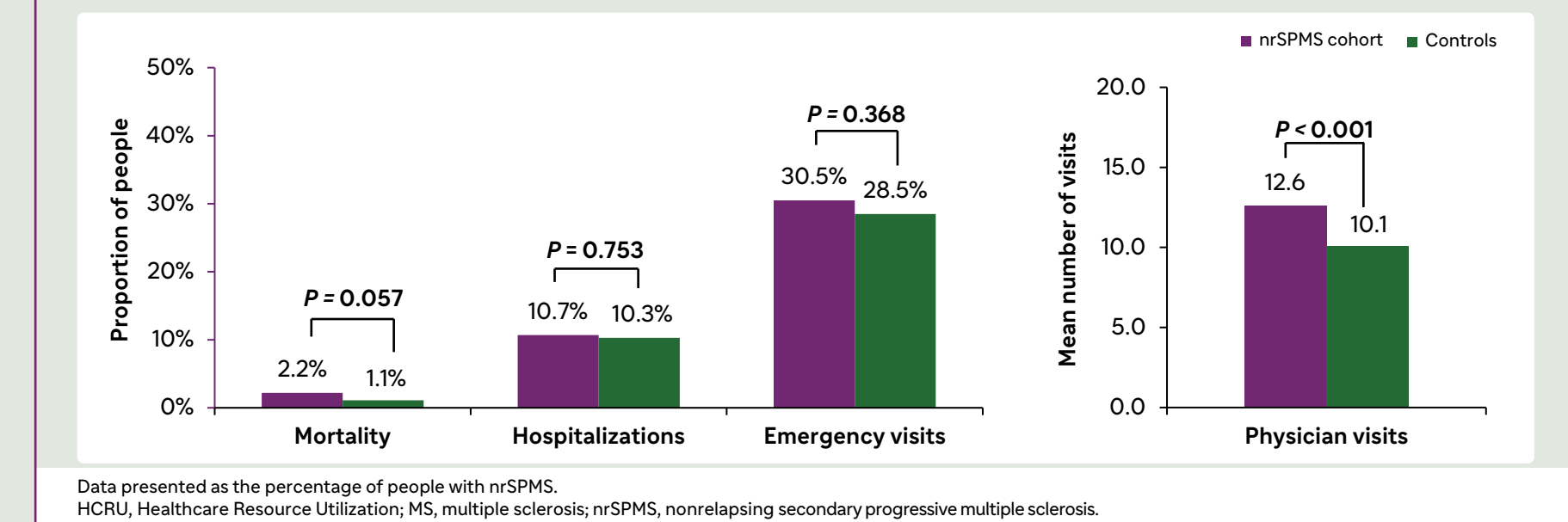
Figure 4: Most frequent MS-related comorbidities in the nrSPMS cohort versus matched controls

Data presented as the percentage of people with nrSPMS.
MS, multiple sclerosis; nrSPMS, nonrelapsing secondary progressive multiple sclerosis.

Healthcare resource utilization and healthcare costs

- The nrSPMS cohort had a higher proportion of people with mortality, hospitalizations, emergency visits, and a significantly higher mean number of physician visits versus matched controls during the follow-up period (Figure 5)
  - The mean (SD) length of hospital stay was 13.8 [22.8] days in the nrSPMS cohort and 12.4 [17.6] days in the matched controls ($P = 0.630$)
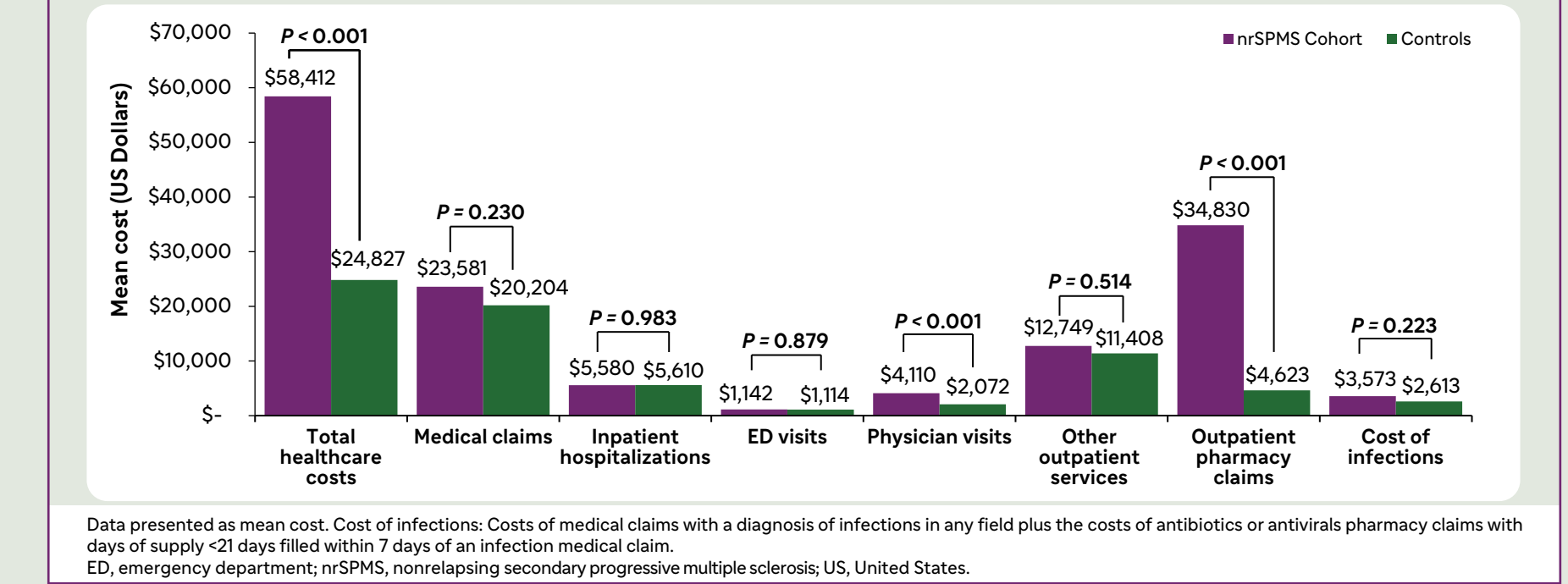
Figure 5: All-cause HCRU in the nrSPMS cohort versus matched controls

Data presented as the percentage of people with nrSPMS.
HCRU, Healthcare Resource Utilization; MS, multiple sclerosis; nrSPMS, nonrelapsing secondary progressive multiple sclerosis.

- The mean total HCCs were significantly higher in the nrSPMS cohort than that in matched controls, which were primarily driven by outpatient pharmacy and physician visit costs (Figure 6)
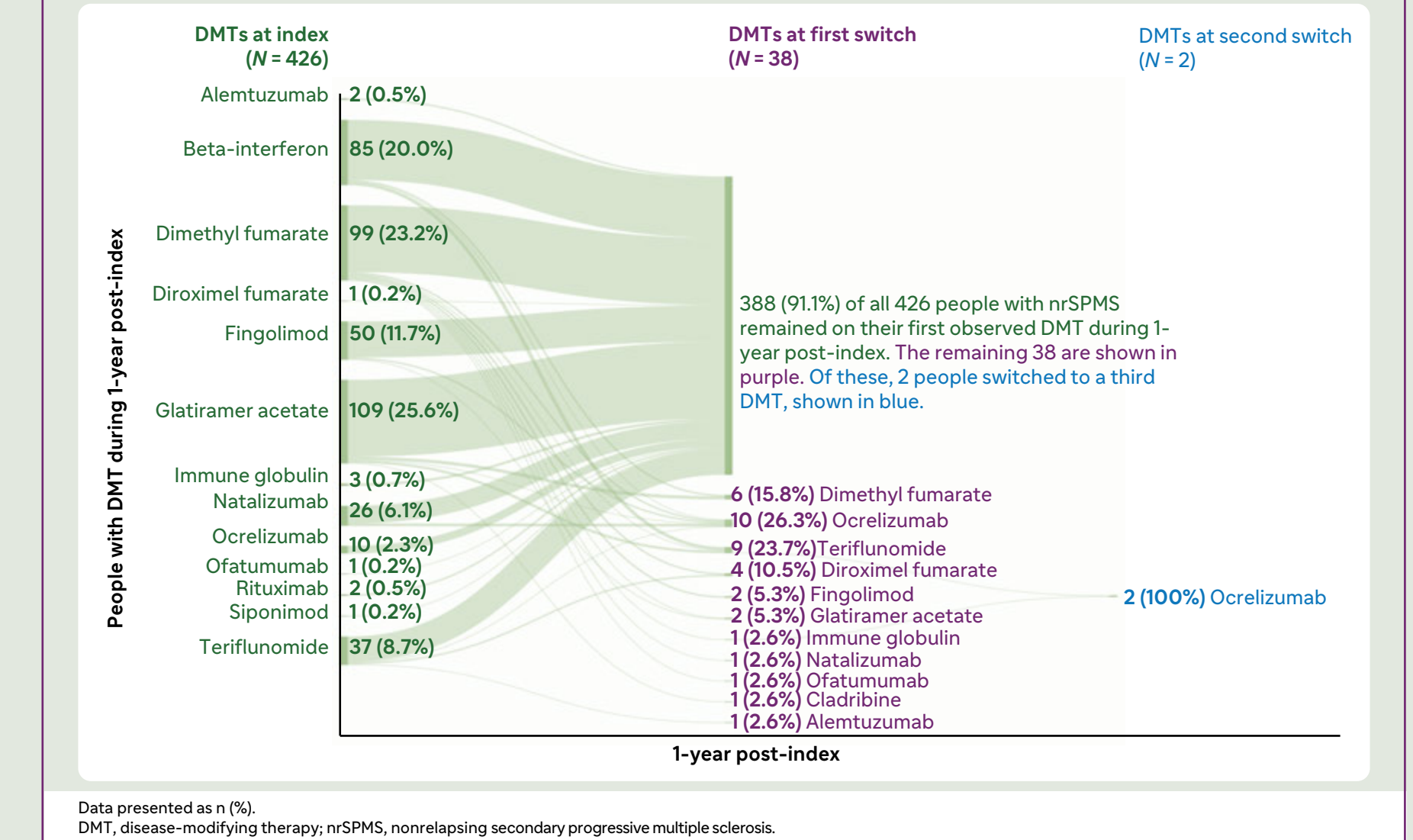
Figure 6: Healthcare costs in the nrSPMS cohort versus matched controls

Data presented as mean cost. 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 days filled within 7 days of an infection medical claim.
ED, emergency department; nrSPMS, nonrelapsing secondary progressive multiple sclerosis; US, United States.

Treatment pattern

- Around 41.1% and 49.8% of people with nrSPMS were treated with a DMT at index and after 1-year follow-up
- The most used DMTs among people with nrSPMS at index and after 1-year follow-up were glatiramer acetate (11.1% and 13.0%), dimethyl fumarate (9.6% and 12.3%), and beta-interferon (8.8% and 99%)
- Among the 426 people on a DMT at index, 388 (91.1%) remained on their first observed DMT and 38 switched to a second DMT during the 1-year post-index period; of which 2 switched to a third DMT (Figure 7)

Figure 7: DMT switch pattern, by individual drug among people with nrSPMS using DMT

Data presented as n (%).
DMT, disease-modifying therapy; nrSPMS, nonrelapsing secondary progressive multiple sclerosis.

LIMITATIONS

- This study may have potentially under-represented the proportion of people with nrSPMS treated with DMTs as it does not encompass individuals who may have previously received such treatments
- The random selection of index date and 1 year follow-up may not fully capture the true extent of treatment in this population due to the limited approved treatment options for nrSPMS
- As this study offers a cross-sectional look at the burden of illness for people with nrSPMS, a static perspective may not fully capture the dynamic nature of managing people with nrSPMS over time, including potential treatment discontinuation and lack of consistent treatment due to limited treatment options

CONCLUSIONS

Overall, people with nrSPMS exhibit a higher prevalence of comorbidities and a substantially increased HCRU compared to matched controls, resulting in additional clinical and economic burden in a population with no approved therapies

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