A Longitudinal Analysis of Multiple Sclerosis Phenotype Transitions Using Medical Charts in the United States

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BACKGROUND

- Relapsing-remitting multiple sclerosis (RRMS) is the most common form of multiple sclerosis (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]
  - For people with SPMS who still experience relapses, their disease remains "active," and can be termed active SPMS (aSPMS).
  - However, many people with SPMS show progression in the absence of relapses, which can be termed nonrelapsing SPMS (nrSPMS).
  - Conversion from RRMS to SPMS cannot be defined by a sharp threshold but represents a gradual process.[4-6]
- Transitional MS has been poorly characterized in terms of patient characteristics, disease course, or interventions that may delay conversion to SPMS.[8]
  - Our understanding of predictors of transitioning to aSPMS or nrSPMS is also currently lacking.
- By investigating patterns and predictors of transitions between MS phenotypes and exploring MS progression in the real-world setting, we aimed to highlight unmet clinical needs in patients with MS (PwMS).

OBJECTIVES

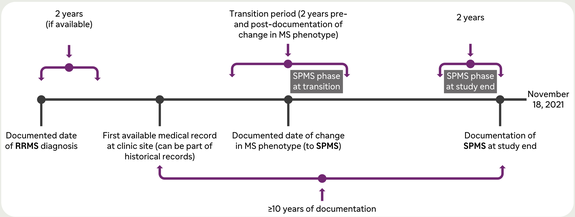
- This study aimed to investigate transitions between MS phenotypes over time and to explore predictors of these transitions.

METHODS

Study design and population

- This was a multi-center, retrospective medical chart review of PwMS conducted across various clinical sites in the United States.
- Adult patients (≥18 years) diagnosed with MS according to the updated 2017 McDonald diagnosis criteria and having ≥10 years of documented medical records, including date and MS phenotype at onset and during transition and associated onset symptoms (follow-up cutoff date: November 18, 2021), were included (**Figure 1**).
- PwMS were classified based on the following MS phenotypes:
  - RRMS: diagnosed by treating neurologist;
  - SPMS: diagnosed by treating neurologist;
  - aSPMS: prior RRMS and current SPMS diagnosis; experiencing ≥1 relapse in the past 2 years before index;
  - nrSPMS: prior RRMS and current SPMS diagnosis; evidence of disease progression but no clinical relapse in 2 years before index; and
  - Primary progressive MS (PPMS): diagnosed by treating neurologist.

Figure 1. Study design



MS, multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Assessments

- Demographics and patient characteristics, MS phenotype history, MS clinical history, disability scores (Expanded Disability Status Scale [EDSS]), and disease-modifying therapy (DMT) use were abstracted at following time periods: at MS diagnosis, during transition from RRMS to SPMS, and at study end.

Statistical analysis

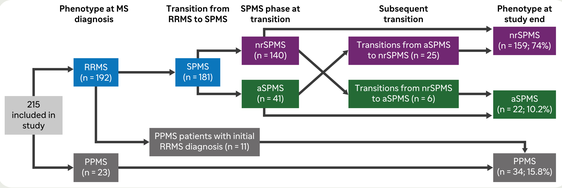
- Descriptive statistical analyses were used to compare clinical characteristics of the study population (nrSPMS and aSPMS) over time.
- Time to transition from RRMS to SPMS was analyzed using the Kaplan-Meier method to evaluate time from diagnosis of RRMS to SPMS transition among patients who transitioned to nrSPMS versus those who transitioned to aSPMS.
- Predictors of transition from RRMS to nrSPMS were analyzed using logistic regression models.
- All tests were 2-sided, and $P < 0.05$ was considered significant.

RESULTS

Phenotype transition analysis

- A total of 215 medical charts of PwMS were included in this study (RRMS = 192 and PPMS = 23 at diagnosis; **Figure 2**).
  - Of the 192 patients diagnosed with RRMS, 181 (94.3%) transitioned to SPMS which included 159 (87.8%) patients with nrSPMS and 22 (12.2%) patients with aSPMS.

Figure 2. Phenotype transitions through study



aSPMS, active secondary progressive multiple sclerosis; MS, multiple sclerosis; nrSPMS, nonrelapsing secondary progressive multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

- Patients with nrSPMS at study end were older, had a longer follow-up duration, and reported higher employment rates post-SPMS transition than patients with aSPMS at study end. Moreover, ambulatory devices and DMTs were less utilized by nrSPMS patients compared to aSPMS patients (**Table 1**).

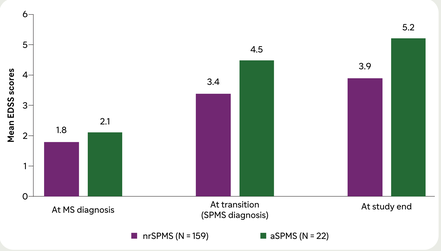
Table 1. Demographics and clinical characteristics of patients with nrSPMS and aSPMS at study end

Variables, mean (SD) unless otherwise specified	nrSPMS (N = 159)	aSPMS (N = 22)	All SPMS (N = 181)
Age at MS onset (years)	34.4 (6.1)	33.0 (7.6)	34.3 (6.3)
Female, n (%)	105 (66.0)	12 (54.5)	117 (64.6)
Race, n (%)			
White	115 (72.3)	16 (72.7)	131 (72.4)
Black or African American	37 (23.3)	6 (27.3)	43 (23.8)
Multiple races	4 (2.5)	0 (0)	4 (2.2)
Others	1 (0.6)	0 (0)	1 (0.6)
Ethnicity, n (%)			
Hispanic, Latino, or Spanish origin	40 (25.2)	0 (0.0)	40 (22.1)
Non-Hispanic, Latino, or Spanish origin	106 (66.7)	22 (100.0)	128 (70.7)
Insurance status at study end, n (%)			
Private insurance	125 (78.6)	12 (54.5)	137 (75.7)
Medicare	16 (10.1)	9 (40.9)	25 (13.8)
Medicaid	14 (8.8)	1 (4.5)	15 (8.3)
Employment (full- or part-time, self-employed), n (%)			
At MS diagnosis	144 (90.6)	21 (95.5)	165 (91.2)
At transition (SPMS transition)	132 (83.0)	14 (63.6)	146 (80.7)
At study end	98 (61.6)	7 (31.8)	105 (58.0)
Loss of employment due to MS, n (%)	36 (22.6)	14 (63.6)	50 (27.6)
Time from MS diagnosis to study end (years)	18.7 (5.8)	14.1 (3.8)	18.1 (5.8)
Any selected comorbidities documented at MS diagnosis, n (%)	66 (41.5)	13 (59.1)	79 (43.6)
Number of relapses in 2 years following MS diagnosis	0.6 (0.8)	2.0 (2.1)	0.7 (1.1)
Number of patients using any ambulatory devices, n (%)	58 (36.5)	14 (63.6)	72 (39.8)
Time to any/first ambulatory device use (years)	13.9 (6.5)	71 (4.5)	12.6 (6.7)
Number of DMTs used at MS diagnosis	0.9 (0.4)	1.2 (0.5)	1.0 (0.4)
Number of patients using any DMT at MS diagnosis, n (%)	145 (91.2)	22 (100.0)	167 (92.3)

aSPMS, active secondary progressive multiple sclerosis; DMT, disease-modifying therapy; MS, multiple sclerosis; nrSPMS, nonrelapsing secondary progressive multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis.

- In terms of disability outcomes, nrSPMS patients reported lower EDSS scores throughout the study period than that reported by aSPMS patients (**Figure 3**).

Figure 3. Mean EDSS scores by SPMS transitions over time



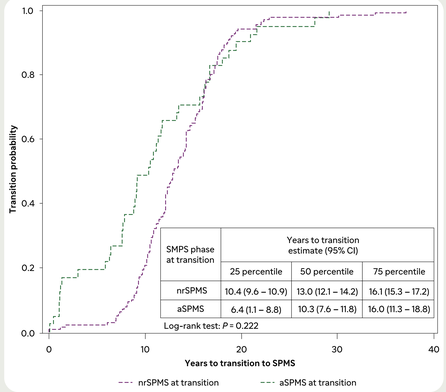
aSPMS, active secondary progressive multiple sclerosis; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; nrSPMS, nonrelapsing secondary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Time to transition from RRMS to SPMS

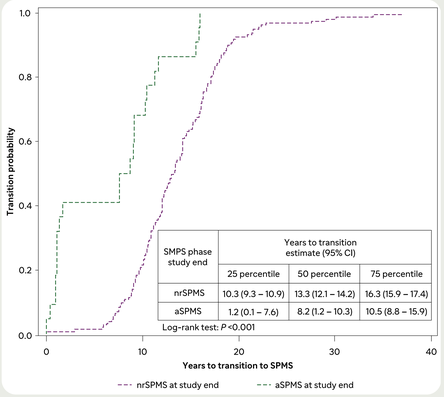
- The median time from MS diagnosis to SPMS was longer in patients with nrSPMS than that in patients with aSPMS at transition (13.0 years vs. 10.3 years; **Figure 4a**) and study end (13.3 years vs. 8.2 years; **Figure 4b**).

Figure 4. Time to transition from RRMS to SPMS

a) By SPMS phase at transition



b) By SPMS phase at study end

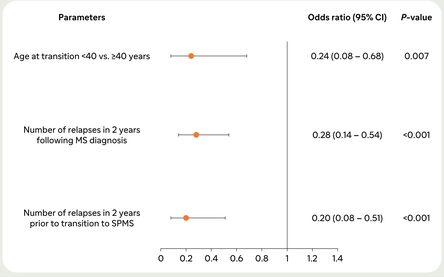


aSPMS, active secondary progressive multiple sclerosis; CI, confidence interval; nrSPMS, nonrelapsing secondary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis

Predictors of transition from RRMS to nrSPMS

- Patients who were younger at SPMS transition (<40 years vs. ≥40 years, $P = 0.007$), had more relapses in 2 years following MS onset ($P < 0.001$), and had more relapses in 2 years prior to SPMS transition ($P < 0.001$) were associated with lower odds of RRMS to nrSPMS transition (**Figure 5**).

Figure 5. Factors associated with transition from RRMS to nrSPMS



CI, confidence interval; MS, multiple sclerosis; nrSPMS, nonrelapsing secondary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

LIMITATIONS

- Due to the small sample size, patients in this study may not be representative of all patients with SPMS.
- Imaging studies, procedures, and laboratory tests may not be thoroughly documented as records of care that occurred outside the clinic were included only to the extent that they were incorporated into the patient's medical record at the participating clinic.

CONCLUSIONS

- In this real-world study, the majority (87.8%) of patients with SPMS at study end had no relapses (nrRSPMS).
- Patients who were older at their initial SPMS transition with fewer relapses following MS diagnosis as well as prior to their SPMS transition were more likely to transition to nrSPMS.
- These data support the emerging view that smoldering inflammatory processes drive disability accumulation independent of relapse activity across the spectrum of MS.

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Disclosure

NG and KH are employees of Sanofi and may hold stocks/stock options in Sanofi.
SNG, MSB, EC, and CC are employees of PHAR, which was paid by Sanofi to conduct the research described in this poster. PHAR also discloses financial relationships with the following entities outside of the submitted work: Akcea, Amgen, Boston Scientific Corporation, Eisai, Genentech, Greenwich Biosciences, Ionis, Jazz, Novartis, Prothena, Recordati, Regeneron, Sanofi, Sunovion, and Takeda Pharmaceutical.

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