

# Characteristics, burden of illness, and physical functioning of patients with relapsing-remitting and secondary progressive multiple sclerosis: a cross-sectional US survey

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**Background:** Although most patients with relapsing-remitting multiple sclerosis (RRMS) will develop secondary progressive multiple sclerosis (SPMS), little is known about the burden of multiple sclerosis by disease subtype. This study describes the burden of disease in terms of demographics, disease severity, symptoms, health care resource and disease-modifying therapy (DMT) utilization, work and activity impairment, and physical functioning of SPMS and RRMS patients.

**Methods:** SPMS and RRMS patient responses from the 2012 and 2013 waves of the US National Health and Wellness Survey were evaluated to detect differences in demographics, disease severity, symptoms, and health care resource and DMT utilization. In addition, data from the Work Productivity and Activity Impairment and Short Form-36 questionnaires were analyzed.

**Results:** SPMS patients were older than RRMS patients (mean age 55.7 vs 48.9 years;  $P < 0.001$ ); a lower proportion were female (56.2% with SPMS vs 71.6% with RRMS;  $P = 0.002$ ), and fewer SPMS than RRMS patients were employed (20.0% vs 39.7%;  $P < 0.001$ ). SPMS patients described their disease as more severe, reporting several neurological symptoms more frequently and higher hospitalization rates than RRMS patients. A lower percentage of SPMS than RRMS patients reported DMT use. SPMS patients had greater overall work and activity impairment than RRMS patients. After controlling for baseline characteristics, impairment in physical functioning was greater in SPMS patients.

**Conclusion:** Overall, SPMS patients had a higher burden of illness than RRMS patients, underscoring the need to treat RRMS patients early to delay disability progressing using therapies that are effective in real-world settings.

**Keywords:** multiple sclerosis, disease-modifying therapy, US National Health and Wellness Survey

## Introduction

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system with a variable and often unpredictable clinical course characterized by neurological impairment and progressive disability.<sup>1</sup> The disease is classified as relapsing-remitting MS (RRMS) when relapses and remissions occur. The majority of patients present with a relapsing-remitting course;<sup>2</sup> however, it is possible for MS patients to present with primary progressive MS (PPMS), in which clinical disability progression occurs continuously without remissions.<sup>3</sup> When an initial relapsing-remitting phase is followed by a progressive phase – defined as an accumulation of disability regardless of relapses, with or without persistence of superimposed relapses – the

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disease is classified as secondary progressive MS (SPMS).<sup>3</sup> The proportion of patients with RRMS who develop SPMS increases with longer disease duration, and the majority of RRMS patients develop SPMS over the long term.<sup>4</sup> Although difficult to detect in clinical practice,<sup>5</sup> the transition from RRMS to SPMS occurs in the absence of treatment in ~50% of RRMS patients within 10 years and in up to 90% of RRMS patients within 20–25 years.<sup>4</sup> The use of disease-modifying therapies (DMTs) may affect these transition rates, but this has not been quantified.

Throughout the disease course, patients with MS experience a variety of symptoms, including fatigue, depression, bowel and bladder dysfunction, weakness, impaired mobility, cognitive problems, and sexual dysfunction.<sup>6–8</sup> These symptoms often lead to restricted physical activity, reduced work productivity, and increased health care resource utilization.<sup>9</sup> Patients with MS frequently report diminished health-related quality of life (HRQoL), not only compared with the general population<sup>10</sup> but also relative to patients with other chronic diseases, such as inflammatory bowel disease and rheumatoid arthritis.<sup>11</sup> Longer duration of MS and increasing disability have shown significant association with worse physical functioning scores.<sup>12</sup> SPMS carries a particularly poor prognosis.

Despite the severe, irreversible disability associated with SPMS, there is considerably more information in the medical literature about RRMS than about SPMS.<sup>13</sup> A number of studies have identified potential risk factors for progression in patients with RRMS,<sup>2,14–18</sup> and the findings suggest an association between progression to SPMS and demographic characteristics such as age at RRMS onset and, to a lesser extent, sex.<sup>2,14,15,18–22</sup> A recent Canadian study (an analysis of the London Ontario Database) of patients with RRMS reported that male sex, older age at MS onset, and high early relapse frequency predicted a significantly higher risk of progression to SPMS and a shorter latency to progression.<sup>14</sup> However, burden of illness and demographic data on patients with SPMS remain limited. Similarly, while the number of effective treatment options indicated for relapsing forms of MS in the USA has increased over the years,<sup>23</sup> the number of agents approved specifically for SPMS (including non-relapsing forms) is limited, with mitoxantrone being the only DMT currently approved specifically for SPMS. The extent and patterns of use of DMTs by patients with SPMS are unknown.

This study used data from the US National Health and Wellness Survey (NHWS), an annual, online, self-administered survey developed and managed by Kantar

Health (New York, NY, USA) to gain insight into the characteristics of patients with SPMS and their perceived burden of illness relative to patients with RRMS. The objectives of the study were to describe the demographics and self-reported disease severity, symptoms, health care resource utilization, extent and patterns of DMT utilization, work and activity impairment, and physical functioning of SPMS and RRMS patients.

## Methods

### Sample and procedures

This cross-sectional study utilized data from the 2012 (March–August) and 2013 (April–August) waves of the US NHWS. The US NHWS provides data from a representative sample (71,157 in 2012, 75,000 in 2013) of adults aged  $\geq 18$  years on demographic characteristics, medical history, health care resource utilization, health care attitudes and behaviors, and outcomes across a large number of health conditions. Respondents are drawn from an internet panel maintained by Lightspeed Research (Warren, NJ, USA). Members of the panel register through unique email addresses and passwords and complete an in-depth demographic profile. US NHWS respondents are recruited from the internet panel using a stratified random sampling framework that ensures that the sex, age, and race/ethnicity distribution of the sample matches that reported by the US Census Bureau.

For this study, data from the 2012 and 2013 US NHWS waves were pooled to increase the number of patients contributing data for analysis. Only the most recent response was included for patients who responded to both annual surveys, resulting in a total sample of 130,089 unique respondents. Only responses from patients with a self-reported physician diagnosis of RRMS or SPMS were included in this study.

### Ethics, consent, and permissions

All respondents provided informed consent electronically before answering any survey questions. Institutional Review Board approval for the 2012/2013 US NHWS was granted by Essex Institutional Review Board (Lebanon, NJ, USA) to Kantar Health, who owns the rights to the data.

## Measures

### Patient characteristics

Patients self-reported their MS by type (RRMS or SPMS). Self-reported demographic data included age, sex, ethnicity (white, Hispanic, African American, Asian, or other), education level (high school or less, some college, or college

degree or higher), annual income group (<\$25K, \$25K–\$49K, \$50K–\$74K, ≥\$75K, or declined to answer), and employment status.

## MS severity and symptoms

Patients self-reported the severity of their MS (mild, moderate, or severe) and their symptoms (“yes” or “no” responses to a predefined list).

## Health care resource and DMT utilization

Patients were asked how many times they had visited a traditional health care practitioner (respondents were provided with a list of traditional health care practitioners, which included neurologists), an emergency room, or had been hospitalized in the previous 6 months. In addition, patients were given a list of MS medications and asked to indicate which they were using currently. DMTs included interferons (ie, intramuscular interferon beta-1a, subcutaneous interferon beta-1a, and interferon beta-1b), glatiramer acetate, natalizumab, fingolimod, and teriflunomide. Patients who reported taking more than one DMT simultaneously were excluded from the analyses. All patients, regardless of DMT use, were asked specific questions regarding their attitudes and beliefs about medications. Patients were asked if they agreed or disagreed with the following statements: “Unless there is a good reason to change my medication, I think it is best to continue taking my medication as I currently do,” and “I am not willing to tolerate side effects from my prescription medication(s).”

## Work and activity impairment

Work and activity impairment were assessed using the general health version of the Work Productivity and Activity Impairment (WPAI) questionnaire.<sup>24</sup> For employed patients, three metrics were computed: absenteeism (percentage of work time missed because of health problems), presenteeism (percentage of productivity impairment, while working, because of health problems), and overall work productivity loss (percentage of overall work impairment because of health problems). Activity impairment was computed for all patients, regardless of employment status, and was evaluated using a single item on the WPAI questionnaire. This item provided the percentage of impairment due to health problems experienced by patients during daily activities in the previous 7 days.

## Physical functioning and general health

Physical aspects of HRQoL were assessed using the Physical Component Summary (PCS) score and the physical health

domain scores of the Short Form-36 version 2.0 (SF-36v2) health questionnaire.<sup>25</sup> The physical health domains included in the SF-36v2 are physical functioning, role limitations due to physical health, bodily pain, and general health. PCS and domain scores are calculated as norm-based scores ranging from 0 to 100. In the general US population, the mean score is 50, with a standard deviation (SD) of 10. Higher scores indicate better HRQoL. Patients were also asked to rate their general health on a scale of 1–5, where 1 was excellent and 5 was poor.

## Statistical analyses

Data for patients with RRMS and SPMS were compared using a chi-square test for categorical variables (sex, ethnicity, education level, annual income, employment status, disease severity, symptoms, use of DMTs, and patients’ attitudes and beliefs about medications) and an independent-sample *t*-test for continuous variables (age, health care visits, hospitalization and work, and activity impairment). Scores for the PCS and physical health domains of the SF-36v2 and the general health rating were analyzed using a multivariable linear regression model controlling for age (continuous), sex, and ethnicity (white/non-white).

## Results

### Patient characteristics

A total of 810 survey respondents, representing 0.6% of the total 2012/2013 US NHWS sample (N=130,089), self-reported a physician diagnosis of RRMS or SPMS and were included in this study. Of these 810 patients with MS, 458 (56.5%) reported having RRMS and 105 (13.0%) reported having SPMS. The remaining patients with MS reported having benign MS (n=85, 10.5%), PPMS (n=45, 5.6%), chronic progressive MS (n=30, 3.7%) or malignant MS (n=4, 0.5%), or did not know or did not provide their type of MS (n=83, 10.2%).

Demographic information for respondents reporting a diagnosis of RRMS or SPMS is shown in Table 1. A lower proportion of patients with SPMS than of those with RRMS were female (56.2% vs 71.6%;  $P=0.002$ ), and patients with SPMS were older than patients with RRMS (mean age 55.7 vs 48.9 years;  $P<0.001$ ). Ethnicity also differed significantly between MS subtypes ( $P=0.006$ ), although the small number of patients in some categories precludes any meaningful interpretation. Neither education level nor annual income differed significantly between patients with RRMS and those with SPMS. A total of 39.7% of patients with RRMS were employed (25.1% full time, 9.2% part

**Table 1** Patient characteristics by multiple sclerosis subtype

Characteristic	RRMS (n=458)	SPMS (n=105)	P-value
Age, years, mean (SD)	48.9 (12.0)	55.7 (11.9)	<0.001
Sex, n (%)			0.002
Female	328 (71.6)	59 (56.2)	
Male	130 (28.4)	46 (43.8)	
Ethnicity, n (%)			0.006
White	363 (79.3)	92 (87.6)	
Hispanic	19 (4.1)	8 (7.6)	
African American	60 (13.1)	3 (2.9)	
Asian	4 (0.9)	2 (1.9)	
Other	12 (2.6)	0 (0.0)	
Education level, n (%)			0.355
High school or less	74 (16.2)	19 (18.1)	
Some college	201 (43.9)	52 (49.5)	
College degree or higher	183 (40.0)	34 (32.4)	
Annual income, n (%) <sup>a</sup>			0.077
<\$25,000	108 (23.6)	36 (34.3)	
\$25,000–\$49,000	128 (27.9)	30 (28.6)	
\$50,000–\$74,000	95 (20.7)	13 (12.4)	
≥\$75,000	100 (21.8)	23 (21.9)	
Declined to answer	27 (5.9)	3 (2.9)	
Employment status, n (%)			<0.001
Employed	182 (39.7)	21 (20.0)	
Long-term disability	116 (25.3)	33 (31.4)	
Short-term disability	1 (0.2)	0 (0.0)	
Not employed but looking for work	18 (3.9)	2 (1.9)	
Not employed and not looking for work	16 (3.5)	4 (3.8)	
Homemaker	32 (7.0)	4 (3.8)	
Retired	86 (18.8)	40 (38.1)	
Student	7 (1.5)	1 (1.0)	
Work/activity impairment, %, mean (SD)			
Absenteeism	9.6 (24.0) <sup>b</sup>	21.6 (29.4) <sup>d</sup>	0.039
Presenteeism	26.3 (27.8) <sup>c</sup>	39.0 (33.0) <sup>e</sup>	0.066
Overall work impairment	31.2 (32.6) <sup>b</sup>	47.6 (38.0) <sup>d</sup>	0.038
Activity impairment	45.9 (31.2)	69.1 (24.0)	<0.001

**Notes:** P-values are for testing differences between RRMS and SPMS using a chi-square test for categorical variables and an independent-sample t-test for continuous variables. Percentages may not add up to 100% because of rounding. <sup>a</sup>Rounded to the nearest thousand. <sup>b</sup>n=173. <sup>c</sup>n=167. <sup>d</sup>n=20. <sup>e</sup>n=19.

**Abbreviations:** RRMS, relapsing-remitting multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis.

time, and 5.5% self-employed), compared with only 20.0% of patients with SPMS (8.6% full time, 8.6% part time, and 2.9% self-employed) ( $P<0.001$ ).

### MS severity and symptoms

Patients with SPMS rated their MS as being of greater severity than did patients with RRMS ( $P<0.001$ ). Among patients with SPMS (n=105), 21.9% considered their MS severe, 72.4% characterized their MS as moderate, and 5.7% rated their MS as mild. In contrast, 5.7%, 52.0%, and 42.4%

of patients with RRMS (n=458) rated their MS as severe, moderate, and mild, respectively.

MS-related symptoms reported by a statistically significantly higher proportion of patients with SPMS than with RRMS included difficulty balancing or walking (88.6% vs 69.9%), muscle spasms (74.3% vs 54.1%), urinary incontinence or urgency (67.6% vs 41.7%), stiffness (56.2% vs 34.9%), constipation (51.4% vs 28.3%), sexual dysfunction (33.3% vs 22.7%), and tremor (25.7% vs 15.3%) (Table 2).

### Health care resource and DMT utilization

The mean (SD) number of hospitalizations in the previous 6 months was higher for patients with SPMS than with RRMS (0.30 [0.80] vs 0.17 [0.56];  $P=0.047$ ). Patients in the RRMS and SPMS groups reported similar numbers of visits over the previous 6 months to a traditional health care professional (6.0 vs 6.6;  $P=0.387$ ), a neurologist (1.2 vs 1.3;  $P=0.666$ ), and an emergency room (0.3 vs 0.4;  $P=0.203$ ).

**Table 2** Proportion of patients with MS-related symptoms by MS subtype

Symptom, n (%)	RRMS (n=458)	SPMS (n=105)	P-value
Breathing problems	27 (5.9)	8 (7.6)	0.509
Constipation	129 (28.2)	54 (51.4)	<0.001
Depression	164 (35.8)	31 (29.5)	0.222
Diarrhea	43 (9.4)	14 (13.3)	0.227
Difficulty balancing or walking	320 (69.9)	93 (88.6)	<0.001
Difficulty concentrating	205 (44.8)	37 (35.2)	0.075
Difficulty remembering	233 (50.9)	38 (36.2)	0.007
Difficulty with speech	115 (25.1)	32 (30.5)	0.259
Dizziness	150 (32.8)	33 (31.4)	0.794
Fatigue	364 (79.5)	89 (84.8)	0.218
Hearing loss	44 (9.6)	11 (10.5)	0.787
Irritability	129 (28.2)	26 (24.8)	0.481
Itching	66 (14.4)	19 (18.1)	0.342
Mood swings	126 (27.5)	24 (22.9)	0.331
Muscle spasms	248 (54.1)	78 (74.3)	<0.001
Numbness of face, body, arms, or legs	282 (61.6)	71 (67.6)	0.248
Pain	249 (54.4)	52 (49.5)	0.370
Seizures	15 (3.3)	5 (4.8)	0.458
Sexual dysfunction	104 (22.7)	35 (33.3)	0.023
Stiffness	160 (34.9)	59 (56.2)	<0.001
Swallowing problems	75 (16.4)	22 (21.0)	0.263
Tremor	70 (15.3)	27 (25.7)	0.011
Urinary incontinence or urgency	191 (41.7)	71 (67.6)	<0.001
Vision problems	185 (40.4)	42 (40.0)	0.941

**Note:** P-values are for testing differences between RRMS and SPMS using a chi-square test.

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

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A higher proportion of patients with SPMS than with RRMS reported not using a DMT (50.0% vs 26.5%;  $P<0.001$ ) (Figure 1). The majority of patients with RRMS or SPMS who reported using a DMT were using an interferon or glatiramer acetate.

Patients with RRMS and SPMS had similar attitudes and beliefs about MS medications. The majority of patients with RRMS (77.1%) or SPMS (79.0%) agreed with the statement “Unless there is a good reason to change my medication, I think it is best to continue taking my medication as I currently do” ( $P=0.663$ ). Similar proportions of patients in the two groups (RRMS, 27.5%; SPMS, 32.4%) agreed with the statement “I am not willing to tolerate side effects from my prescription medication(s)” ( $P=0.318$ ).

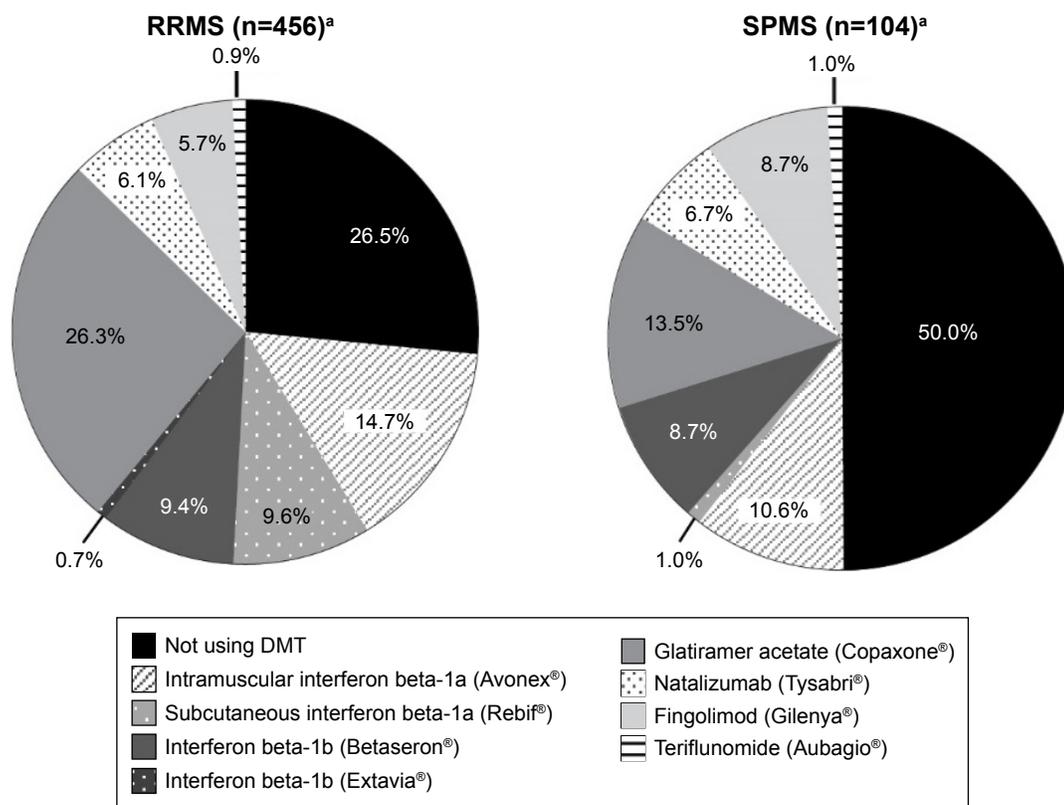
## Work and activity impairment

Analyses for absenteeism, presenteeism, and overall work productivity loss due to health problems included only the 182 patients (39.7%) with RRMS and 21 patients (20.0%) with SPMS who were employed. Patients with SPMS had a significantly higher mean percentage of missed

time from work (absenteeism) than patients with RRMS (21.6 vs 9.6;  $P=0.039$ ), although the number of working patients with SPMS was small (Table 1). The difference in mean percentage of productivity impairment while working (presenteeism) between the SPMS and RRMS groups was not statistically significant (39.0 vs 26.3;  $P=0.066$ ). The mean percentage of overall work impairment (overall work productivity loss) was significantly higher in the SPMS group than in the RRMS group (47.6 vs 31.2;  $P=0.038$ ). Similarly, the mean percentage of activity impairment was significantly higher in the SPMS group than in the RRMS group (69.1 vs 45.9;  $P<0.001$ ).

## Physical functioning and general health

Patients with RRMS reported significantly better physical functioning than patients with SPMS both before and after adjustment for age, sex, and ethnicity. The mean PCS score was significantly higher in patients with RRMS than in those with SPMS (40.4 vs 32.6;  $P<0.001$  after adjustment) (Figure 2A). Mean scores for the domains of physical functioning, role limitations due to physical health, and general

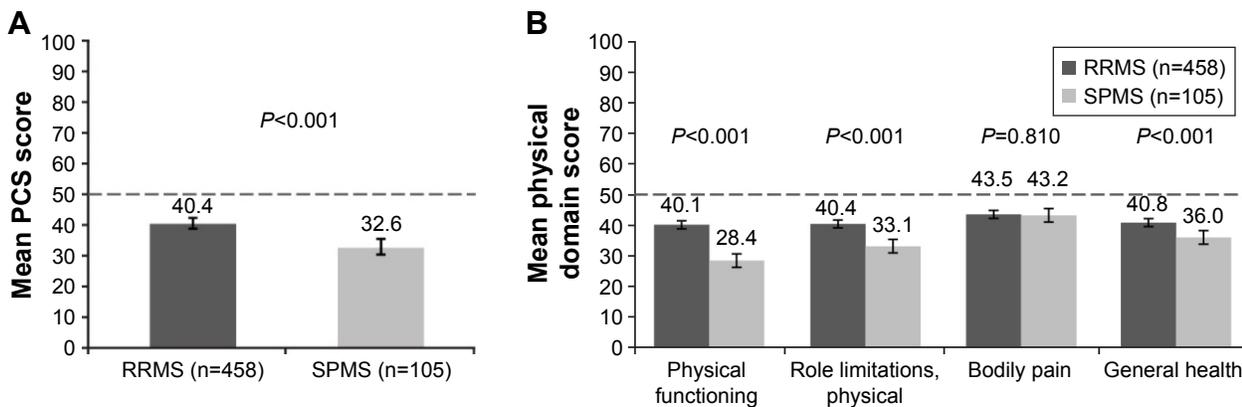


**Figure 1** Use of DMTs by multiple sclerosis subtype.

**Notes:** Percentages of patients using specific types of DMT are shown. Percentages may not add up to 100% because of rounding. <sup>a</sup>Two RRMS patients and one SPMS patient were taking more than one DMT and were excluded from the analysis.

**Abbreviations:** DMT, disease-modifying therapy; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

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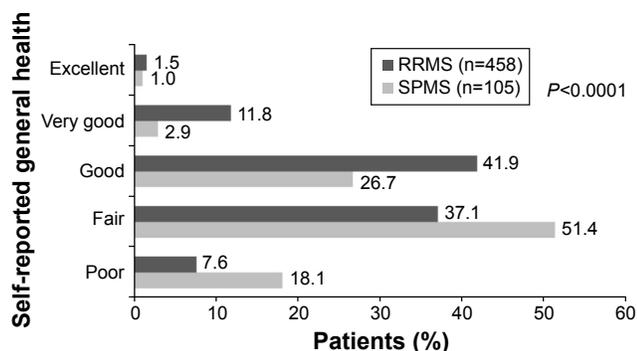


**Figure 2** Physical aspects of health-related quality of life.

**Notes:** (A) PCS scores from the SF-36v2 questionnaire; (B) SF-36v2 physical domain scores. Mean scores are shown. Error bars represent 95% CIs. *P*-values are for testing differences between RRMS and SPMS using a multivariable linear regression model controlling for age, sex, and ethnicity. Dashed horizontal lines indicate mean scores in the general US population.

**Abbreviations:** CIs, confidence intervals; PCS, physical component score; RRMS, relapsing-remitting multiple sclerosis; SF-36v2, Short Form-36; SPMS, secondary progressive multiple sclerosis.

health were also significantly higher in patients with RRMS than in those with SPMS (all  $P < 0.001$  after adjustment) (Figure 2B). Within the physical functioning domain, patients with SPMS reported more limitations in all activities, including vigorous activities (eg, running, lifting heavy objects, or participating in strenuous sports); moderate activities (eg, moving a table, pushing a vacuum cleaner, bowling, or playing golf); lifting or carrying groceries; climbing one or several flights of stairs; bending, kneeling, or stooping; walking any distance; and bathing or dressing. Within the domain of role limitations due to physical health, patients with SPMS reported increased time spent and increased difficulty in performing work or other activities, limitations in the kind of work or activities in which they could engage, and a sense of accomplishing less than they would like compared with patients with RRMS.



**Figure 3** Patient-reported general health rating.

**Notes:** Percentages of patients reporting general health ratings from 1 (excellent) to 5 (poor) are shown. *P*-value is for testing difference in distribution of responses between RRMS and SPMS using a multivariable linear regression model controlling for age, sex, and ethnicity.

**Abbreviations:** RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Patients with SPMS perceived their general health (1=excellent, 5=poor) as significantly worse than did patients with RRMS both before and after adjustment for age, sex, and ethnicity (mean rating 3.74 [95% confidence interval {CI} 3.57–3.92] vs 3.36 [95% CI 3.26–3.47];  $P < 0.001$  after adjustment) (Figure 3).

## Discussion

In this study, US patients with RRMS and SPMS had different demographic characteristics. Patients with SPMS were older and the higher proportion of females over males seen in RRMS (71.6% female) was less pronounced in SPMS (56.2% female). Previous studies have shown that the strongest consistent predictor of MS evolution is age at MS onset, with shorter progression times for older patients.<sup>14,15,19–22</sup> Some studies have shown that male sex is also associated with a higher risk of progression to SPMS, although this finding is not consistent across studies.<sup>14,15,20,21,26</sup>

Patients with SPMS in this study described their disease as significantly more severe than patients with RRMS. The symptom profile differed between the two patient groups, with a significantly greater proportion of patients with SPMS than with RRMS reporting several neurological symptoms, including difficulty balancing or walking, and bladder dysfunction. Additionally, patients with SPMS in this study had a significantly higher rate of hospitalization than patients with RRMS, a finding consistent with published reports of increased hospitalization and associated costs in patients with severe MS.<sup>27,28</sup>

A significantly lower proportion of patients with SPMS than with RRMS reported using DMTs, with half of the patients with SPMS reporting no DMT use. Among users

of DMTs, the majority of patients with RRMS and SPMS reported using an interferon or glatiramer acetate, suggesting that conversion to the SPMS disease phenotype was not associated with therapy change. In the USA, all DMTs are approved for relapsing forms of MS aside from mitoxantrone, which was approved for RRMS and SPMS based on results of a small placebo-controlled study in which a combined group of 28 patients with worsening RRMS and 32 patients with SPMS were randomized to receive the currently approved dose of mitoxantrone.<sup>29</sup> This underscores the importance of earlier use of effective treatments in real-world settings that will significantly delay the progression of disability from RRMS to SPMS.

Lower employment rates were reported for patients with SPMS than for patients with RRMS in this study. This likely reflects the higher burden of illness that they experience; employment levels among patients with MS have been shown to be inversely correlated with disability.<sup>30</sup> Alongside the lower rates of employment observed among patients with SPMS, this study also found that work and activity impairment were significantly greater in patients with SPMS than in those with RRMS. These data show that patients with SPMS suffer greater disruption to their working lives and everyday life activities than patients with RRMS. Other studies in the USA and elsewhere have shown that the later stages of MS represent a significant socioeconomic burden, due principally to patients' reduced work capacity and the costs associated with increased activity impairment and the need for personal care.<sup>9,31–33</sup>

SPMS was also associated with greater impairment in physical aspects of HRQoL than RRMS was, which is consistent with results of other studies.<sup>12,34</sup> Observed differences in SF-36v2 PCS and physical domain scores between the MS subtypes may, at least in part, be explained by differences in patient characteristics such as age. A negative association between physical SF-36 scores and age has been reported in general populations.<sup>35–37</sup> Consequently, physical SF-36 scores would be expected to be lower in patients with SPMS because they tend to be older than patients with RRMS. Similarly, in the general population in Canada and the USA, men have been shown to have substantially higher physical SF-36 scores than women.<sup>35</sup> Differences in physical SF-36 scores have also been observed among ethnic groups.<sup>38</sup> Given the association of physical functioning with age, sex, and ethnicity, physical functioning data in this study were subjected to multivariable analysis to control for these patient characteristics. In this multivariable analysis, patients with RRMS and SPMS scored lower on

measures of physical functioning and, therefore, suffer a greater loss of physical functionality compared with the general US population. In addition, after controlling for these characteristics, impairment in physical aspects of HRQoL remained significantly greater in patients with SPMS than in patients with RRMS. Patients with SPMS experienced a greater decrease in physical functioning and more physical limitations in daily activities and reported poorer health in general than did patients with RRMS. It should be noted, however, that although the multivariable analysis controlled for the influence of age, sex, and ethnicity on physical HRQoL and general health rating, some of the differences in measures between RRMS and SPMS may have been due to unreported variables.

As the course of MS is variable and unpredictable, if worsening of symptoms could be predicted, patients might feel better prepared to manage changes in function.<sup>39</sup> The clinical significance of measuring functional aspects of HRQoL in patients with MS has been highlighted by two previous 2-year studies.<sup>40,41</sup> These studies found an increased risk of clinically meaningful deterioration of disability in MS patients with poor physical HRQoL. This suggests that identifying MS patients with poor physical HRQoL may be important in assessing the risk of future disability progression. While further research is needed to identify predictors of progression to SPMS, earlier treatment to delay the loss of functionality and progression from RRMS to SPMS should remain a high priority in clinical settings.

This study has several limitations. The cross-sectional design of the study prevents the drawing of causal inferences from the data.<sup>42</sup> Participation in the US NHWS survey is voluntary and may result in self-selection bias, potentially capturing healthier respondents (ie, those who are well enough to take a lengthy Internet survey and are not institutionalized). The RRMS and SPMS groups were of unequal size, with considerably fewer SPMS than RRMS patients recruited. While this generally reflects the natural history and differences in prevalence of RRMS and SPMS in the US population, it may also be related to age, and the lack of a well-established definition of SPMS in the MS community. Older patients, who are more likely to have SPMS than younger patients, may have been underrepresented because data collection involved a web-based survey. Older patients are less likely to be familiar with computers or to have access to them.<sup>42</sup> As a consequence, the results of this study may not be generalizable to all patients with MS in the USA.

Another limitation is that the use of patient self-reports may have allowed for inaccuracies in patient responses and

response bias, particularly as the measures included in this study were not verified clinically. A further factor to consider when interpreting the results of the study relates to medical diagnosis, as the distinction between RRMS and SPMS can be imprecise at certain stages of disease progression. Finally, as the study utilized US data exclusively, the findings may not be generalizable globally to all patients with MS.

In conclusion, the results of this study of data from a large US survey increase our understanding of the burden of illness of RRMS and SPMS on patients. Compared with patients with RRMS, patients with SPMS have a greater burden of illness, characterized by significantly increased disease severity, neurological symptoms, hospitalizations, and overall work and activity impairment. When controlling for baseline characteristics, patients with SPMS continued to have significantly lower physical functioning than patients with RRMS. While approximately half of the patients with SPMS were using DMTs, some therapies have not proved effective in preventing or delaying disability progression. Therefore, it is important to treat RRMS patients early with treatments proven in real-world settings to delay disability progression and preserve or increase functionality for patients.

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## Author contributions

HJG and CW contributed to study design, supervision, and coordination; data collection, analysis, and interpretation; and drafting and revising the manuscript for content.

## Disclosure

At the time of the analysis, Ms Gross was an employee of Kantar Health, which was contracted by Biogen to perform the analysis on previously collected data. She is currently employed by Adelphi Research Global, which was not in any way associated with this study. Ms Watson is an employee of the study sponsor, Biogen.

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