# A Qualitative Exploration of Fatigue in Patients With Progressive Multiple Sclerosis

F McDougall,<sup>1</sup> D Miller,<sup>2</sup> M Brown,<sup>3</sup> C Slota,<sup>3</sup> L Doward,<sup>4</sup> S Belachew,<sup>5</sup> L Julian<sup>6</sup>

¹Roche Products Limited, Welwyn Garden City, UK; ²Cleveland Clinic, Mellen Center, Cleveland, OH, USA; ⁴RTI-HS, Manchester, UK; ⁵F. Hoffmann-La Roche Ltd, Basel, Switzerland; <sup>6</sup>Genentech, Inc., South San Francisco, CA, USA



### **BACKGROUND**

- Fatigue is one of the most prevalent and debilitating symptoms of multiple sclerosis (MS), with a significant impact of patients' quality of life<sup>1</sup>
- It is estimated that 75% of patients with MS experience fatigue during their disease course<sup>2</sup> Immune-mediated processes, including inflammation and neurodegeneration, are believed to contribute to the clinical
- manifestation of fatigue in MS<sup>3</sup> While fatigue is a common symptom of MS, the patient-focused qualitative literature on fatigue in progressive forms of
- MS is sparse Patient-focused research such as this contributes to the selection and interpretation of patient-reported outcome data

# in ongoing progressive MS trials, ensuring that treatment benefit can truly be captured from the patient perspective

#### **OBJECTIVE**

 To characterize the burden of fatigue associated with MS from the perspective of patients diagnosed with primary and secondary progressive forms of MS

# **METHODS**

#### Study Design

- Adult patients (N=44) with primary progressive multiple sclerosis (PPMS; n=21) and secondary progressive multiple sclerosis (SPMS; n=23) were recruited via a medical recruitment agency in the United States
- Adults recruited for the interviews met the following self-reported screening criteria:
- Aged 18 to 65 years
- Clinician-confirmed diagnosis of PPMS, SPMS or progressive relapsing MS (PRMS)<sup>a</sup>
- Not restricted to a wheelchair for short distances (able to walk 25 feet)
- Able to read, speak and understand English
- Willing to participate in a telephone interview and complete a secure online version of a patient-reported questionnaire on fatigue
- Patients participated in a 45-minute semi-structured telephone interview, targeting the following topic areas:
- Current clinical characteristics and MS symptoms
- Most bothersome MS symptom
- Description, characterization and nature of fatigue (e.g. severity, duration, progression)
- Impact of fatigue
- See example interview questions <sup>a</sup>Individuals who were previously diagnosed with PRMS are now considered PPMS.

# Example Interview Questions From the Progressive MS Patient Interviews

- For you, what it is like living with MS?
- a. What is the hardest thing about living with MS? Why? (impact)
- What symptoms do you commonly experience with MS?
- [Obtain general exhaustive listing of current symptoms (e.g., any other symptoms?); if fatigue not mentioned, probe, "do you ever experience fatigue as related to your MS?"]
- Which symptoms do you find most bothersome? [ask for 3 most bothersome symptoms if necessary with a long listing
- a. [For each] What makes this symptom so bothersome for you? (probe to understand the role of intermittent symptoms vs those more constant/persistent, such as fatigue)
- b. [If not mentioned] What about fatigue? How does it compare to these other symptoms? (probe to understand the role of intermittent symptoms vs those more constant)
- How would you describe the severity of your fatigue? Is it consistent? Does it vary?
- a. At its worst, how would you describe your fatigue?
- b. When it is mild, how would you describe it? How does fatigue impact you?
- [Obtain spontaneous mentions overall and then for each: daily activities, cognition, work, emotions, social activities/role, family activities/role, sleep (need naps, good night sleep), personal/intimate relationships, independence/doing things for self (preparing meals, drinks, looking after self, others)]
- (For each impact area, probe to understand how/what and secondary impacts and how the respondent feels about impacts [i.e. emotional reactions])

# For all interview questions, please scan here



#### Qualitative Data Analysis

- Qualitative descriptive analysis methods were used to identify, characterize and summarize patterns found in the interview data
- Qualitative themes were coded to allow the assessment of frequencies and comparison of percentages across MS subtypes:
- Current MS symptoms
- Fatigue progression Fatigue frequency
- Factors that improve/worsen fatigue
- Fatigue impact areas (i.e. daily activities, work/financial, social, family, partner/spouse relationships, cognition, emotional)
- Fatigue impact area intensity (i.e. low, high)

## **RESULTS**

#### Patient Characteristics

- Patient characteristics are presented in **Table 1**
- The mean age of patients was 52.5 years, mean time since diagnosis was 14.7 years and the majority were female (81.8%)
- The current age and percentage of females were similar between PPMS and SPMS populations — More than half of the participants were college educated (52.2%), married (63.6%) and most were white (86.4%) Nearly 80% of patients were unemployed, receiving disability benefits or retired

#### Table 1. Demographics and characteristics for study participants at baseline

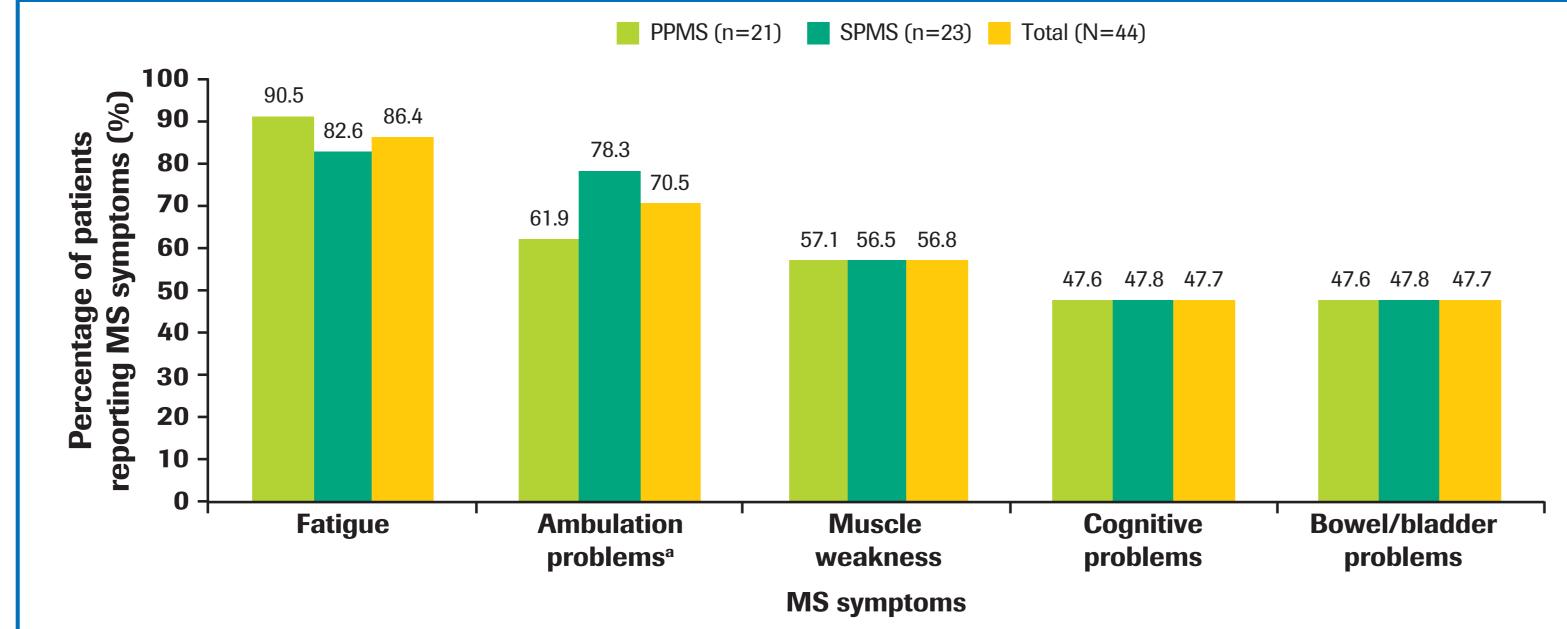
Parameter	PPMS (n=21)	SPMS (n=23)	Total (N=44)
Current age, years, mean (SD)	53.0 (7.4)	52.0 (8.2)	52.5 (7.8)
Female, n (%)	18 (85.7)	18 (78.3)	36 (81.8)
Age experienced first MS symptom, years, mean (SD)	33.8 (8.9)	30.7 (10.3)	32.2 (9.6)
Time diagnosed, years, mean (SD)	13.0 (8.2)	16.3 (8.4)	14.7 (8.4)
Education, n (%) High school Some college College degree Advanced degree	1 (4.8) 6 (28.6) 8 (38.1) 6 (28.6)	3 (13.0) 11 (47.8) 5 (21.7) 4 (17.4)	4 (9.1) 17 (38.6) 13 (29.5) 10 (22.7)
Marital status, n (%) Single Married Divorced/separated Widowed	1 (4.8) 16 (76.2) 4 (19.0) NA	5 (21.7) 12 (52.2) 5 (21.7) 1 (4.3)	6 (13.6) 28 (63.6) 9 (20.5) 1 (2.3)
Race/ethnicity, n (%) White Black Other/Hispanic	20 (95.2) 1 (4.8) NA	18 (78.3) 2 (8.7) 3 (13.0)	38 (86.4) 3 (6.8) 3 (6.8)
Employment status, n (%) Employed full-time Employed part-time Unemployed, receiving disability benefits or retired  MS, multiple sclerosis; NA, not applicable; PPMS, primary progre	4 (19.0) 3 (14.3) 14 (66.7)	1 (4.3) 1 (4.3) 21 (91.3)	5 (11.4) 4 (9.1) 35 (79.5)

ivis, multiple scierosis, NA, not applicable, Privis, primary progressive multiple scierosis, Srivis, secondary progressive multiple scierosis.

#### Current MS Symptoms

- Of all spontaneously reported MS symptoms, fatigue was the most common (86.4%) (Figure 1)
- Patients (N=42) used the words "tired" (61.9%), "low/no energy" (28.6%) and "exhaustion" (19.0%) to describe
- their fatigue (**Table 2**) Metaphors and phrases used by patients include:
- Body shutdown
- Hitting a wall Like you have the flu
- No life force in body, like dying
- Other than fatigue, the most frequently reported MS symptoms were ambulation problems (70.5%), muscle weakness (56.8%), cognitive problems (47.7%) and bowel and/or bladder problems (47.7%) (Figure 1)
- More patients rated fatigue as their most bothersome MS symptom (38.6%) compared with other MS-related symptoms (**Figure 2**)
- Consistent with the reported frequency of current symptoms, fatigue, ambulation problems (25.6%), muscle weakness (13.6%), cognitive problems (9.1%) and bowel and/or bladder problems (4.5%) were described as the most bothersome MS symptoms (Figure 2)
- Interestingly, while the report of fatigue was similar between progressive MS subtypes (**Figure 1**), more patients with PPMS reported fatigue as their most bothersome symptom, compared with patients with SPMS (61.9% vs 17.4%; **Figure 2**)
- Patients commonly reported that they considered fatigue to be bothersome because of its impact on many different aspects of their daily lives
- Additionally, fatigue influenced, and was influenced by, their other MS symptoms, resulting in a cycle that significantly affected patients' abilities to perform daily activities, in particular patients' ability to move their muscles or walk
- Participants explained why they identified fatigue as one of their most bothersome MS symptoms (Figure 3) and described their fatigue (Figure 4)

#### Figure 1. Most frequently reported current MS symptoms



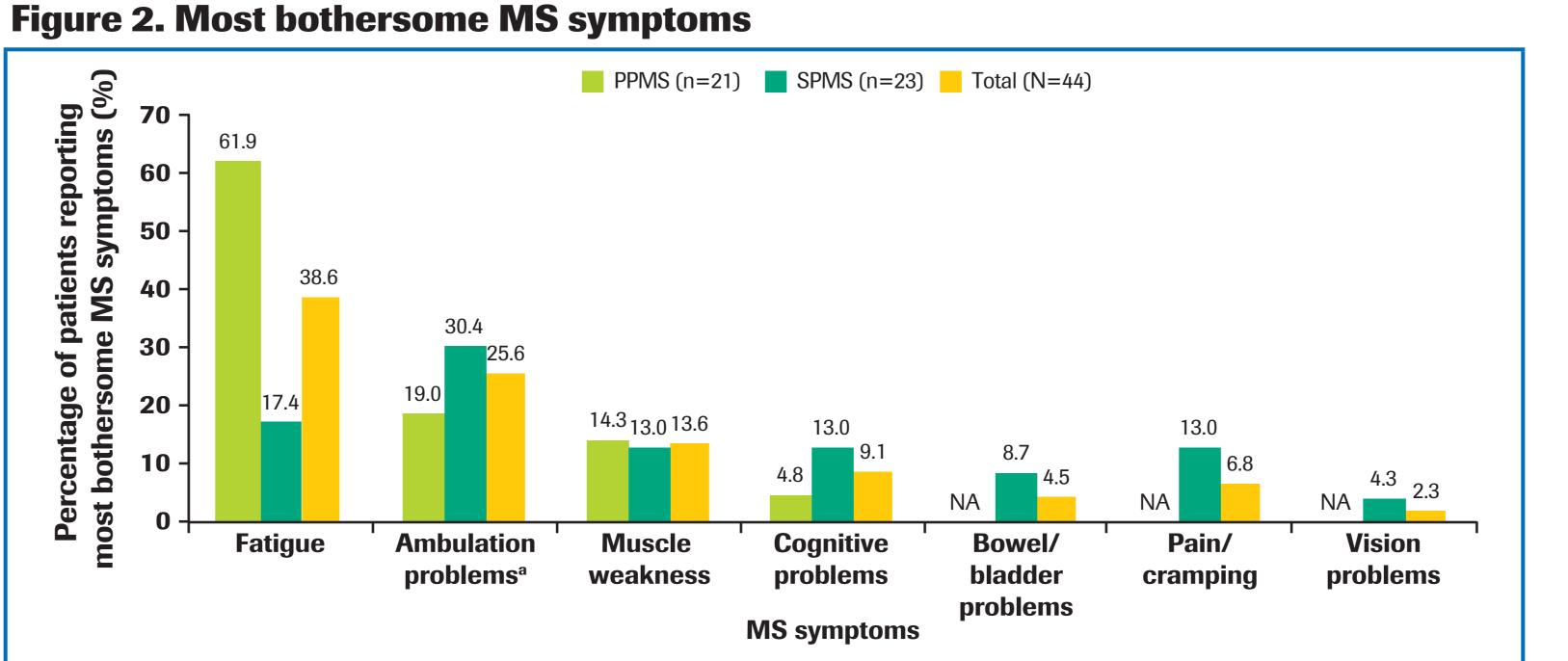
Patients' report of current symptoms was spontaneous, not probed, nor designed to be exhaustive. As such, the symptom report cannot necessarily be interpreted as comprehensive or valid in terms of symptom prevalence or burden.

MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

#### Table 2. Participant description of MS-related fatigue

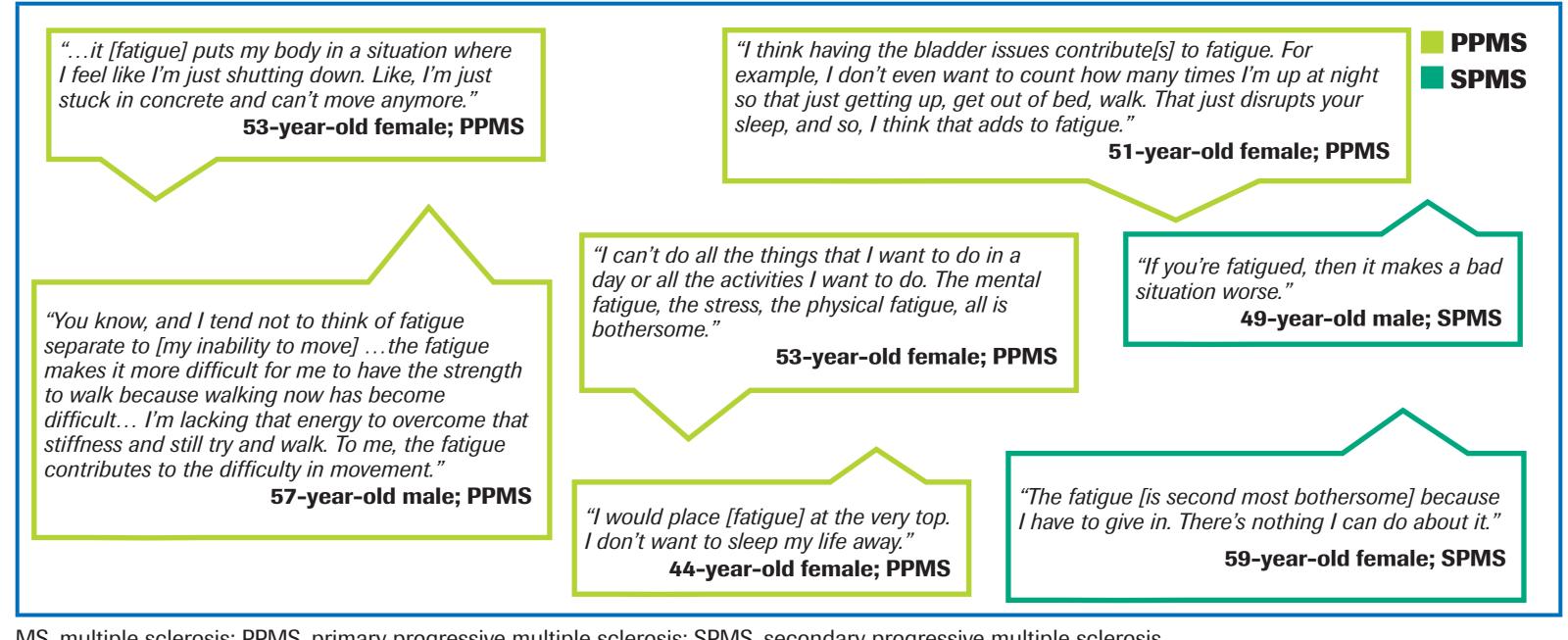
Fatigue language	N=42,ª n (%)	Patient-provided examples and descriptions	
Tired	26 (61.9)		
Low/no energy	12 (28.6)	<ul><li>End of energy</li><li>Lack of energy</li></ul>	<ul><li>Energy sucked out</li><li>Drained of energy</li></ul>
Exhaustion	8 (19.0)	<ul> <li>Exhaustion that is not easy to rebound from</li> </ul>	<ul> <li>Overwhelming kind of exhaustion</li> </ul>
"Wiped out"	3 (7.1)		
<b>Others</b> <sup>b</sup>	18 (42.9)	<ul> <li>A weight</li> <li>Can't rebound</li> <li>Crash</li> <li>Debilitated</li> <li>Done</li> <li>Down</li> <li>Dragging</li> </ul>	<ul> <li>Drowsy</li> <li>Heavy body</li> <li>Helpless</li> <li>Listless</li> <li>No motivation</li> <li>Out</li> <li>Paralyzing</li> </ul>

<sup>a</sup>This analysis was based on N=42; data for this analysis were not obtained for one patient; another patient did not report fatigue and was excluded from this analysis; <sup>b</sup>Each word/phrase reported once. MS, multiple sclerosis.



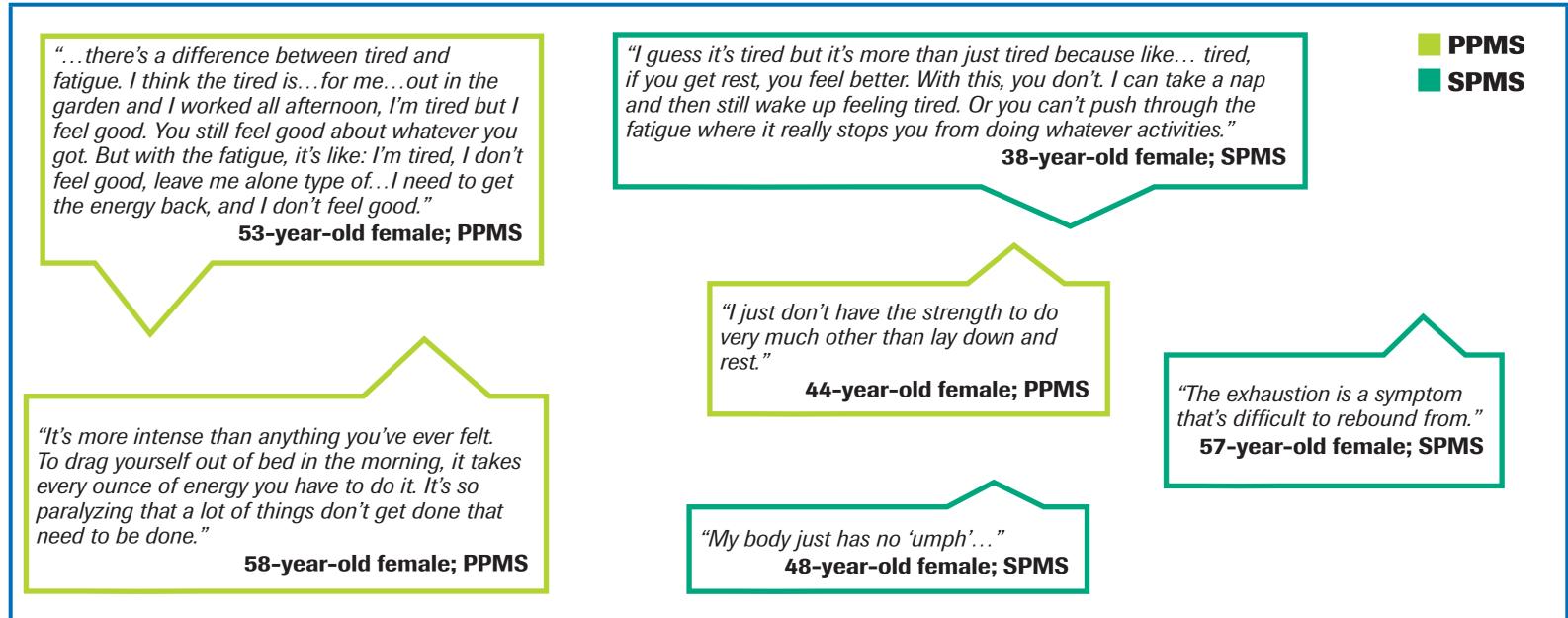
MS, multiple sclerosis; NA, not applicable; PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

#### Figure 3. Quotes about why fatigue was one of the most bothersome MS symptoms



MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

#### Figure 4. Patient's descriptions of their fatigue

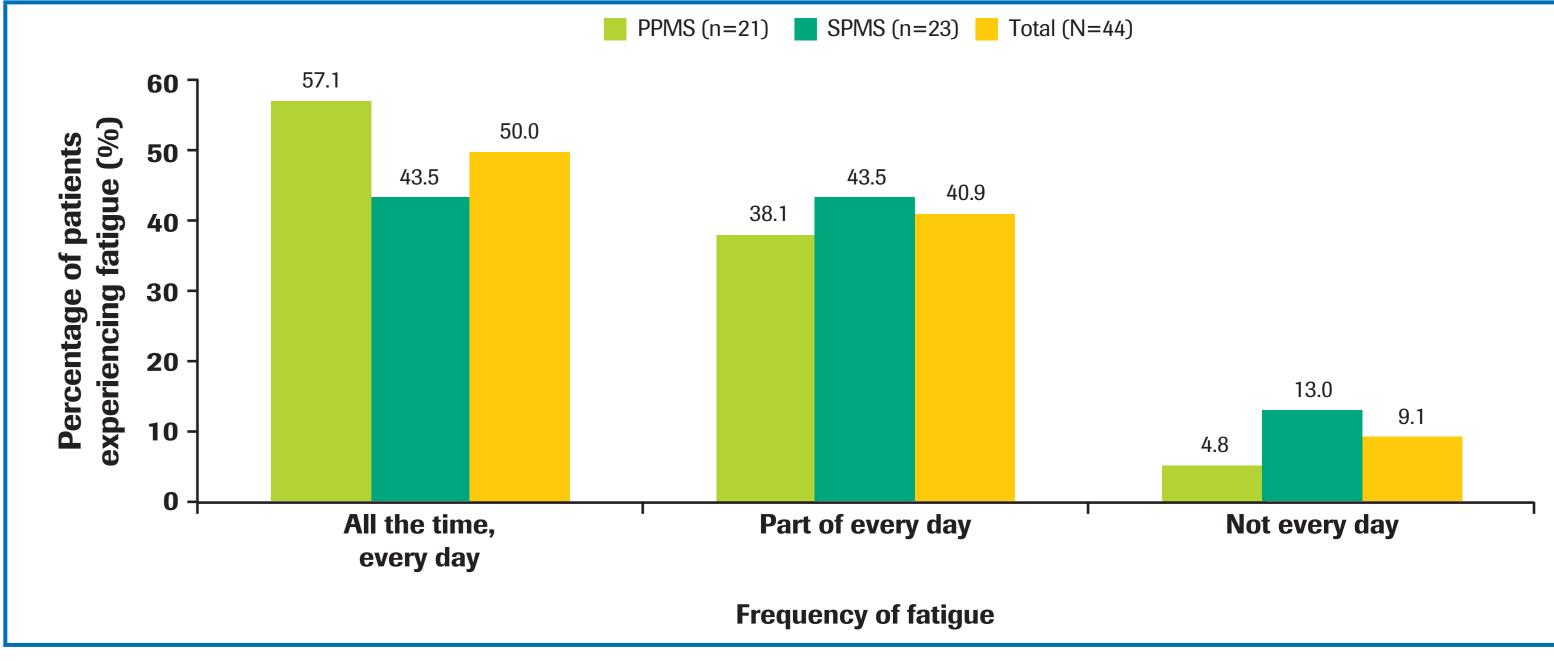


PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis

#### Other Fatigue Characteristics

- Half of patients reported feeling constantly fatigued, and more than 90% reported experiencing fatigue at least daily (**Figure 5**)
- Typically, the morning hours were when patients had more energy than the afternoon or evening (56.8%; data not shown)
- Across all patients, fatigue was often reported as exacerbated by hot weather or humidity (70.5%; data not shown)
- There was no apparent difference between MS subtypes in the reported frequency of fatigue (**Figure 5**)

#### Figure 5. Frequency of experiencing fatigue

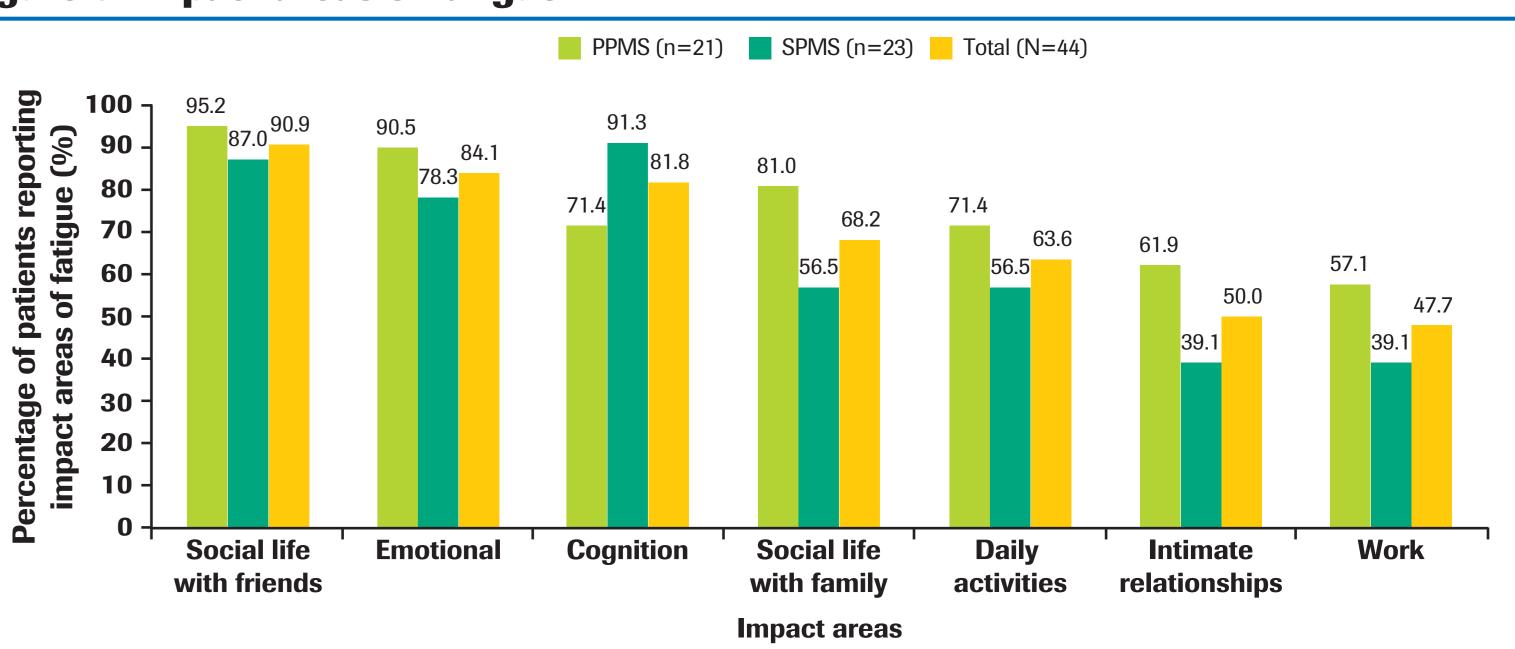


PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

#### Impacts of Fatigue

- The top three most frequently reported negative impacts of fatigue were social functioning (90.9%),
- emotional wellbeing (84.1%) and cognitive functioning (81.8%) (Figure 6)
- Patients described themselves as "homebodies", as fatigue limited their social interactions with friends (90.9%) and family (68.2%), and impacted the types of activities they could participate in (data not shown)
- Patients with SPMS reported more cognitive effects (91.3%) compared with those with PPMS (71.4%) (**Figure 6**) Conversely, patients with PPMS reported a numerically greater impact on social interactions with family compared with patients with SPMS (81.0% vs 56.5%, respectively), and on intimate relationships (61.9% vs 39.1%, respectively) (Figure 6)
- Patients attributed their inability to think clearly or focus for long periods of time to their fatigue
- Patients also reported experiencing depression and anxiety, which some patients attributed to their fatigue

#### Figure 6. Impact areas of fatigue



PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis

#### Limitations

- Due to small MS subtype sample sizes, the data should be interpreted with caution
- The gender ratio observed in this study population (85.7% female) is atypical for patients with PPMS where a 1:1 male/female ratio is the norm
- Patients were aware that the focus of the interview was on fatigue, so we cannot rule out the possibility that patients were primed to place greater emphasis on this symptom compared to others

# CONCLUSIONS

- Fatigue is a common, troublesome and disabling symptom in progressive forms of MS that
- has a profound impact on patients' daily lives These findings provide insights into the varied consequences of fatigue and can inform its measurement in both clinical and research settings
- Treatments that improve the symptoms of fatigue or prevent fatigue worsening are needed for patients with progressive MS

### **ACKNOWLEDGMENTS**

We would like to thank all patients and the investigators who participated in this project. T study was run by RTI Health Solutions, and sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance for this presentation was provided by Articulate Science, UK, and funded by F. Hoffmann-La Roche Ltd, Basel, Switzerland.

#### REFERENCES

Janardhan V. Bakshi R. J Neurol Sci 2002:205:51-58 2. Lerdal A, et al. Eur J Neurol 2007;14:1338–1343. 3. Patejdl R, et al. Autoimmune Rev 2016;15:210-220.

#### **DISCLOSURES**

F McDougall is an employee and shareholder of F. Hoffmann-La Roche Ltd. D Miller has served as a consultant for, and receive any of those funds directly nor is his/her salary contingent upon the study sponsor, on a contract basis; however, the author does not receive any of those funds directly nor is his/her salary contingent upon the results of the work for those entities. C Slota is an employee of RTI Health Solutions. RTI Health Solutions performs work for multiple pharma and biotech companies, including the study sponsor, on a contract basis; however, the author does not receive any of those funds directly nor is his/her salary contingent upon the results of the work for multiple pharma and biotech companies. Including the study sponsor, on a contract basis; however, the author does not receive any of those entities. L Doward is an employee of RTI Health Solutions. RTI Health Solutions performs work for multiple pharma and biotech companies, including the study sponsor, on a contract basis; however, the author does not receive any of those entities. L Doward is an employee of RTI Health Solutions performs work for multiple pharma and biotech companies. companies, including the study sponsor, on a contract basis; however, the author does not receive any of those funds directly nor is his/her salary contingent upon the results of the work for those entities. S Belachew is an employee and shareholder of F. Hoffmann-La Roche Ltd.