

## **SUPPLEMENTARY MATERIAL**

### **Results from Patient Interviews on Fatigue in Progressive Multiple Sclerosis and Evaluation of Fatigue Patient-Reported Outcome (PRO) Instruments**

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# Concept Elicitation Interviews on Fatigue in Patients with Progressive MS

## Concept Elicitation Discussion Guide Flow

<b>Introduction</b> [~5 minutes]	<ul style="list-style-type: none"><li>• Introduce the research topic</li><li>• Review what to expect during the research session</li></ul>
<b>Discussion</b> [~50 minutes]	<ul style="list-style-type: none"><li>• Brief description of MS signs and symptoms</li><li>• Characterization of MS-related fatigue</li><li>• Impacts of MS-related fatigue</li><li>• Key areas for improvement in MS-related fatigue</li></ul>
<b>Conclusion</b> [~5 minute]	<ul style="list-style-type: none"><li>• Elicit any final thoughts</li><li>• Thank respondents and close interview</li></ul>

**Note:** This discussion guide is semi-structured in nature and meant to serve as a basis for the discussion. The moderator will actively listen, probe as necessary, and take note of nonverbal communication (e.g., long pauses, facial expressions, gestures). Specifically, the moderator will be aware of the following:

- Probes (i.e., specific, targeted questions) are to be used to clarify ideas reported spontaneously by participants, as well as to explore concepts that participants have not reported in response to an open-ended line of questioning. Participants will be given enough time to respond to questions before more specific probes are used.
- Non-verbal cues (e.g., facial expressions indicating rejection or acceptance of a question) and communication (e.g., nodding or shaking their head, pointing to identify the location of a sign or symptom) can be informative, especially when discussing potentially uncomfortable or sensitive information. The moderator will comment on the non-verbal cue or communication and invite the participant to explain his/her feelings or actions to ensure the action is properly recorded and interpreted.

## Introduction (~5 minutes)

### *What to expect*

Thank you for your interest and willingness to be a part of this discussion today. My name is *[first name]* and I am the moderator for today's discussion. I am working on this project as a consultant to help identify important aspects of multiple sclerosis (MS) from your perspective. I work for ZS Associates, a company that works with pharmaceutical companies to understand the patient perspective on various health conditions.

Our purpose here today is to understand your experience with progressive MS. This is a free-flowing discussion and we are trying to capture many different points of view; there are no right or wrong answers.

This conversation will be audio-recorded in order to help me write a more accurate report of what you have said. You will not be cited by your full name and any sort of personally identifying information will only be accessible to our research staff.

*[If applicable]* Some people have been invited to observe this research session. Although they are observing, they will not participate in this discussion and are here to listen to what you have to say. *[If video streaming]* This research session will be live streamed for observational purposes, video recording will not take place and **only** the audio for this conversation will be recorded.

*[If focus group]* Since we are in a group setting, please feel free to excuse yourself to go the restroom or get a drink at any time. I ask that only one person be up or out at a time to limit distractions. Additionally, I find it is helpful to set some basic ground rules to make sure the discussion stays on track:

- If you haven't done so already, please silence your cell phone.
- As we start getting into the conversation, please speak one at a time.
- Since this is being recorded, try to talk about as loud as loud as I am so that you can be heard.
- Don't feel like you must answer every question, but I do ask that you are an active participant in the conversation.
- Please avoid side conversations with your neighbors and share what you have to say with all of us.
- Remember that there are no right or wrong answers and we are not trying to achieve consensus – rather, we are aiming to hear as many viewpoints as possible, so please say what you believe.
- I may have to interrupt you to keep us on the timeline and to ensure we hit all the discussion topics.

Do you have any questions before we begin?

### *Icebreaker*

I will go first, but before we dive into the conversation, I would like you to please introduce yourself and tell me:

- Your first name
- Your favorite hobby
- Something you did recently for fun

## Concept elicitation (~50 minutes)

Thank you. I would like to start out by talking through some topics that may be relevant to you. Please keep in mind your experience specifically as it relates to progressive MS while talking through these topics.

### **General description of MS**

I would like to begin by learning a little bit more about your experience with MS.

- What type of progressive MS do you have?
- How long ago were you diagnosed with progressive MS?
  - *[If SPMS, ask:]* When were you first diagnosed with MS?
- What it is like to have progressive MS?
- What are the main signs and symptoms you experience because of your progressive MS?
  - What is the most bothersome sign/symptom of your progressive MS?
- What is a typical day for you in terms of your progressive MS?
- What is the most challenging aspect of living with progressive MS?

### **Characterization of fatigue**

*[If not spontaneously reported, state:]* This conversation will be focused on understanding fatigue you may experience because of your MS.

- *[If not spontaneously reported, ask:]* Do you experience fatigue because of your MS? Please explain.
- How would you describe the fatigue you experience because of MS?
- What does fatigue feel like to you?
  - Do you think of fatigue as physical? Please explain.
    - What does physical fatigue feel like? For example, does fatigue feel like weakness?
  - Do you think of fatigue as mental? Please explain.
    - What does mental fatigue feel like? For example, does fatigue feel like a change in your alertness?
- How would you describe fatigue to someone who has never experienced it?
- How do you know your fatigue is because of MS? Is it easy or difficult to tell what is causing your fatigue?
- What is a typical day for you in terms of your fatigue because of your MS?
- What would you consider a bad day in terms of your fatigue because of your MS?
- Has your fatigue changed over time? Please explain.

- *[If SPMS, ask:]* Was your fatigue different when you were in the relapsing-remitting stage of MS?
- Do you notice that the fatigue occurs at a certain time of day? Does it occur more/less frequently under certain circumstances? Is there a pattern?
- How often does fatigue happen?
  - Within a day? Within a week? Within a month?
- How long does the fatigue last?
- How bad does the fatigue get at its worst?
  - On a scale from 0 to 10, where 0 is no fatigue and 10 is fatigue as bad as you can imagine, how bad does it get? How long does it last when it's at its worst?
  - *[If SPMS, ask:]* Would you answer this question the same or differently if you were thinking about the fatigue you experienced during the relapsing-remitting stage of your MS?
- Now, I would like you to think about ways in which your fatigue could get better. Would it be meaningful to you if ...
  - You experienced fatigue less often? Please explain.
  - Your fatigue did not last as long? Please explain.
  - Your fatigue was less severe? Please explain.

## ***Impacts of fatigue***

Now that we have talked about what it feels like to experience fatigue caused by MS, I would like to hear more about how fatigue impacts your life.

**Note:** After discussing impacts spontaneously described by the respondents, ask the following questions.

- Does your fatigue change the way you do things? If so, how?
  - How often does this happen?
  - How long does this typically last?
- Does your fatigue stop you from doing things? What things? Why?
  - How often does this happen?
  - How long does this typically last?
- Does your fatigue affect your daily activities (for example, doing household activities)? If so, what activities?
  - Are you able to go about your usual activities when you are feeling fatigued? Please explain.
  - How often does this happen?

- How long does this typically last?
- Does your fatigue affect activities you do in your free time? If so, how?
  - How often does this happen?
  - How long does this typically last?
- Does your fatigue affect you physically (for example, difficulty walking)? If so, how?
  - How often does this happen?
  - How long does this typically last?
- Do you currently or have you ever taken any medication to help with your fatigue? If so, please describe.
  - How often do you take medication for your fatigue?
- Does your fatigue affect your relationships? If so, how?
  - Does it affect your romantic relationships? If so, how often?
  - Does fatigue affect your relationships with family? If so, how often?
- Does your fatigue affect your social life (for example, spending time with friends)? If so, how?
  - How often does this happen?
- Does your fatigue affect you at work or school? If so, how?
  - How often does this happen?
  - How long does this typically last?
- Does your fatigue affect you emotionally (for example, feeling sad or frustrated)? If so, how?
  - How often does this happen?
  - How long does this typically last?
- Does your fatigue affect your sleep (for example, requiring more sleep or having difficulty falling or staying asleep)? If so, how?
  - How often does this happen?
  - How long does this typically last?
- Does your fatigue affect your wake-up routine (for example, having difficulty starting your day)?
  - How often does this happen?
  - How long does this typically last?
- *[If not spontaneously reported and time permitting, ask:]* Do you have a caretaker or caregiver that assists you with daily activities?
  - *[If yes, ask:]* Does your fatigue impact the amount of support you need from your caretaker or caregiver? Please explain.
- Does your fatigue impact you in any other way that we have not yet discussed?

## ***Key areas for improvement***

Now that we have had a chance to discuss how you experience fatigue and how it impacts your life, I would like you to reflect on which areas in your life has been most affected by fatigue.

- What impacts of fatigue are most important to improve?
- If you could improve one aspect of your fatigue, what would it be and why?

## ***Closing***

Now that our time together is coming to a close, I wanted to briefly pause and ask you if there are other things you would like to share about your experience with MS that would be helpful for us to know.

Thank you so much for your time. I really appreciate you sharing your experience with me.

**Table S1.** Frequencies and descriptions of fatigue-related symptoms reported by patients with progressive MS (PPMS and SPMS)

Concept	n (n%)			Exemplary patient quote
	PPMS (n=14)	SPMS (n=16)	Total (n=30)	
<b>Aspects of physical fatigue</b>				
Physically tired	14 (100.0%)	16 (100.0%)	30 (100.0%)	"I hate to keep using the word <b>tired</b> but I mean, I'm just tired and I feel overwhelmed with having to do the smallest of tasks" (GA-02, SPMS)
Physical fatigue	14 (100.0%)	16 (100.0%)	30 (100.0%)	"I just experience that <b>extreme physical fatigue</b> " (NC-01, SPMS)
Low energy	10 (71.4%)	13 (81.3%)	23 (76.7%)	"I just feel really shaggy and just <b>not energy, no energy at all</b> " (AZ-01, PPMS)
Physical exhaustion	11 (78.6%)	11 (68.8%)	22 (73.3%)	"Like <b>physical exhaustion</b> , not like it's suddenly sleepy or something, I guess this is what they call the lassitude when you just feel like you don't have it in you to be" (WA-01, SPMS)
Physical weakness	9 (64.3%)	13 (81.3%)	22 (73.3%)	"I think a part of fatigue is <b>physical weakness</b> . ... I just don't have the strength to lift it as easily, so it feels heavier" (CO-03, PPMS)
Drained	10 (71.4%)	8 (50.0%)	18 (60.0%)	"It's like <b>drained</b> , it's like I have no -- it's like <b>somebody pulled the plug out of the wall</b> and I just can't even rest to the point where I feel like all right, now I can, you know, lie down for 20 minutes and get up and go" (NJ-04, SPMS)
Body feels heavy	9 (64.3%)	6 (37.5%)	15 (50.0%)	"It's hard to move around my kitchen without <b>feeling this weight, the heaviness of the fatigue</b> . It's like a blanket that gets wrapped around you and lulls you to just stop what you are doing and rest for a bit because it feels like I just can't go on" (MA-01, SPMS)
Sleepy	6 (42.9%)	6 (37.5%)	12 (40.0%)	"I'm having a <b>physical response</b> where I just want to close my eyes and lie down. ... my eyes are closing and <b>I'm falling asleep</b> " (IL-02, PPMS)
Wiped out/ worn out	2 (14.3%)	3 (18.8%)	5 (16.7%)	"I just get <b>worn out</b> so quick" (CO-01, SPMS)
Physically uncomfortable	1 (7.1%)	2 (12.5%)	3 (10.0%)	"It has made me <b>physically uncomfortable</b> ... you're just not comfortable in what you're doing because of the fatigue is weighing you down" (PA-01, SPMS)
Shut down	2 (14.3%)	0 (0.0%)	2 (6.7%)	"My body feels like it's just <b>shutting down</b> sometimes when I'm severely fatigued" (GA-03, PPMS)
Malaise	1 (7.1%)	0 (0.0%)	1 (3.3%)	"It's like a <b>malaise</b> . It's like you don't just feel tired, it takes you over. It just, you -- it's almost like a fear that you're not going to get up again" (FL-03, PPMS)



Concept	n (n%)			Exemplary patient quote
	PPMS (n=14)	SPMS (n=16)	Total (n=30)	
<b>Aspects of mental fatigue</b>				
Mentally tired	12 (85.7%)	12 (75.0%)	24 (80.0%)	<i>"You get <b>mentally tired</b> too because I still think that I can get up and I can do things and I'm still going to have the stamina that I used to have" (NJ-01, PPMS)</i>
Mentally fatigued	12 (85.7%)	12 (75.0%)	24 (80.0%)	<i>"When I get <b>fatigued mentally</b>, I'll drift off and I won't be able to do what I want to do" (FL-01, SPMS)</i>
Difficulty communicating clearly	6 (42.9%)	9 (56.2%)	15 (50.0%)	<i>"When I'm fatigued, I can't get my words out. <b>I can't think of the word I want to say</b> that'll be right on the tip of my tongue and <b>I can't have a conversation</b> in that moment" (GA-04, SPMS)</i>
Loss of focus	6 (42.9%)	8 (50.0%)	14 (46.7%)	<i>"<b>I can't focus</b>. I can barely talk when I'm that tired" (OH-01, PPMS)</i>
Loss of concentration	6 (42.9%)	7 (43.8%)	13 (43.3%)	<i>"You <b>can't concentrate on anything</b>. Your mind just won't work to concentrate on things, to be aware of things and tired enough; it is checked out" (NJ-03, SPMS)</i>
Slowed thinking	6 (42.9%)	5 (31.3%)	11 (36.7%)	<i>"Just <b>feeling slower</b>, like things would take you longer to absorb. It's almost like <b>your reaction time is slower</b>. I'm still alert and processing fine. I can hold a conversation fine, it's just a <b>little slower</b>" (NJ-06, PPMS)</i>
Difficulty thinking clearly	5 (35.7%)	6 (37.5%)	11 (36.7%)	<i>"<b>I can't think very, very clearly</b> and so forth. ... It is real mental fatigue" (FL-04, SPMS)</i>
Mentally exhausted	3 (21.4%)	6 (37.5%)	9 (30.0%)	<i>"It's a <b>mental exhaustion</b> that is not about being smart and it's not about having knowledge; it's about being able to turn that -- to turn your brain on" (NJ-02, PPMS)</i>
Less alert	2 (14.3%)	4 (25.0%)	6 (20.0%)	<i>"It's definitely a <b>change in alertness</b> because I just can't think anymore ... it just kind of affects everything" (NJ-05, SPMS)</i>
Forgetfulness	2 (14.3%)	3 (18.8%)	5 (16.7%)	<i>"<b>I forget things</b> ... I'm trying to converse with somebody and the words are there, but I can't say them or they don't come out because ... I'm having that mental fatigue" (TX-01, SPMS)</i>
Mentally worn out	2 (14.3%)	2 (12.5%)	4 (13.3%)	<i>"It's a more of a mental cloudy sort of it takes over you, makes you feel like <b>mentally worn out</b>" (PA-01, PPMS)</i>

Abbreviations: MS, multiple sclerosis; PPMS, primary progressive MS; SPMS, secondary progressive MS

**Table S2.** Frequencies and descriptions of fatigue-related impacts reported by patients with progressive MS (PPMS and SPMS)

Concept	n (n%)			Exemplary patient quote
	PPMS (n=14)	SPMS (n=16)	Total (n=30)	
<b>Emotional wellbeing</b>				
Low motivation	11 (78.6%)	13 (81.3%)	24 (80.0%)	<i>"I am <b>less motivated</b> to do anything when I have fatigue. It's hard to do those daily errands or even focus on a puzzle. I can get them done if I have to but it takes more of a push from me to really get to the point where I won't procrastinate"</i> (TX-02, PPMS)
Frustration	8 (57.1%)	12 (75.0%)	20 (66.7%)	<i>"It's more, <b>you get frustrated with yourself</b> and then your body just says, alright, well, if you think you can do this, then we're going to prove to you that you can't, and you just get tired"</i> (NJ-01, PPMS)
Depression/ sadness	10 (71.4%)	9 (56.3%)	19 (63.3%)	<i>"I mean emotionally because it makes <b>you feel sad and makes you feel down</b>... It really <b>makes you get down, depressed</b> and you can't be happy when you're feeling so tired all the time. It does, it can really wear you out mentally"</i> (PA-01, SPMS)
Anger	4 (28.6%)	3 (18.8%)	7 (23.3%)	<i>"Well, it <b>makes you angry</b> because it's like I should know how to do this or else I should not need help with this, and if I'm not focusing, I'm just lost"</i> (GA-03, PPMS)
Misunderstood	2 (14.3%)	3 (18.8%)	5 (16.7%)	<i>"It's <b>not something that other people really understand</b> well either so you can't really explain it and have people understand ... I think is maybe <b>one of the hardest parts of fatigue is like nobody understands it, nobody</b>"</i> (NJ-02, PPMS)
Fear/anxiety	2 (14.3%)	3 (18.8%)	5 (16.7%)	<i>"I'm <b>afraid to go anywhere</b>, to do anything. You know, just say okay, and <b>[the fatigue] has made me a chicken</b>"</i> (NJ-03, SPMS)
Self-conscious	2 (14.3%)	1 (6.3%)	3 (10.0%)	<i>"I'm always <b>self-conscious</b> of my fatigue"</i> (CA-01, PPMS)
<b>Work/school</b>				
Loss of productivity	5 (35.7%)	9 (56.3%)	14 (46.7%)	<i>"I know especially recently it has been getting worse and I've been <b>getting less and less done in the time frame</b> that I have to work"</i> (NJ-06, PPMS)
Loss of accuracy	5 (35.7%)	7 (43.8%)	12 (40.0%)	<i>"I couldn't think and I was <b>making a lot of mistakes</b> [at work]. I wasn't able to complete things without – like things are taking longer to complete and everything"</i> (CO-01, SPMS)
Loss of employment	5 (35.7%)	7 (43.8%)	12 (40.0%)	<i>"I loved my last job, it was probably my least paid job, but it was my favorite job that I had ... and I hated leaving my job and the reason I <b>had to leave my job</b> was ... I would <b>get too tired</b>"</i> (NJ-01, PPMS)
Absenteeism	6 (42.9%)	5 (31.3%)	11 (36.7%)	<i>"I <b>can't even work</b> some days. If I <b>wake up exhausted</b> even though I slept for enough hours, I'll call my boss and tell her I <b>can't make it in</b>"</i> (NJ-06, PPMS)

Concept	n (n%)			Exemplary patient quote
	PPMS (n=14)	SPMS (n=16)	Total (n=30)	
Arriving late/leaving early	4 (28.6%)	5 (31.3%)	9 (30.0%)	"I know there have been days when I did used to go into the office where I literally would have to just, you know, <b>leave for the day because I just couldn't make it</b> " (NC-01, SPMS)
Missed opportunities	4 (28.6%)	3 (18.8%)	7 (23.3%)	"I mentioned that I had started a business and so I'm not as – <b>there have been some potential clients that I've had to turn down</b> because the thought of all that I had to do I knew that I could not do it alone because I would be too tired to accomplish what I wanted" (GA-02, SPMS)
<b>Mobility</b>				
Difficulty walking	11 (78.6%)	13 (81.3%)	24 (80.0%)	"It makes it <b>harder to walk</b> . It feels like, because like my legs are really heavy" (OH-01, PPMS)
Requires a walking aid	11 (78.6%)	12 (75.0%)	23 (76.7%)	"Originally I <b>started out with a cane</b> , with a walker, a cane, then it <b>progressed to a walker</b> , then it <b>progressed to crutches</b> , then now it has <b>progressed to wheelchair</b> " (WA-02, PPMS)
Clumsiness	8 (57.1%)	13 (81.3%)	21 (70.0%)	"I'm <b>very clumsy and uncoordinated</b> ... I think it's a combination of the way my muscles work but when I'm tired, they work even worse ... I am like struggling to make sure I <b>don't trip or fall anytime</b> I'm like taking a step to do anything ... I'm holding onto the chair to make sure that I don't trip" (CO-03, PPMS)
Trouble with balance	4 (28.6%)	10 (62.5%)	14 (46.7%)	"Sometimes, you can tell when I'm needing to get in bed soon, because I'll <b>just get like really goofy and really balance issues</b> " (GA-03, PPMS)
Difficulty standing	9 (64.3%)	5 (31.3%)	14 (46.7%)	I have noticed that I'm <b>like sitting more now than I ever was prior</b> . Like, I mean, there were times where I would stand out in front of my store for hours just, you know, talking to people ... but now I don't do that, I just sit down and wait (GA-01, SPMS)
<b>Activities of daily living</b>				
Difficulty completing household chores	13 (92.9%)	15 (93.8%)	28 (93.3%)	"... <b>making my own breakfast in the morning is like running a marathon</b> , by the time I'm done cooking, I'm exhausted. Isn't that crazy? Like 6:30 AM in the morning <b>and I've already spent all the energy I have</b> " (NJ-06, PPMS)
Difficulty running errands	9 (64.3%)	8 (50.0%)	17 (56.7%)	"Shopping like going grocery shopping, anything with is like, I <b>definitely don't like going</b> no more as that stuff is like <b>really exhausting</b> . I try to <b>limit that as much</b> . I do a lot of online shopping for certain stuff" (PA-01, SPMS)
Difficulty driving	3 (21.4%)	3 (18.8%)	6 (20.0%)	"There are <b>times that I did pull over if [fatigue] happened in a car</b> , because it has happened in a car often, but it seems -- again like that 20 minutes just rejuvenate, get it together, has always been a standby" (IL-03, SPMS)

Concept	n (n%)			Exemplary patient quote
	PPMS (n=14)	SPMS (n=16)	Total (n=30)	
<b>Social life</b>				
Skipping events	8 (57.1%)	14 (87.5%)	22 (73.3%)	<i>“Socially though with friends, that’s another issue. I don’t attend events or parties or go out to dinners or celebrations as much as I used to because I just experience <b>this fatigue that makes it not worth it</b>” (CO-02, SPMS)</i>
Negative impact on friendships	8 (57.1%)	11 (68.8%)	19 (63.3%)	<i>“I’ve <b>lost friends who got tired of me cancelling on them</b> all the time. And especially right when the fatigue first got really bad, it was all I ever wanted to talk about. So I’m sure they also got sick of that” (NJ-06, PPMS)</i>
Arriving late/leaving early	5 (35.7%)	7 (43.8%)	12 (40.0%)	<i>“I <b>usually have to go home earlier</b> because I just get tired and I can’t stay as late as they do sometimes or <b>even like functions and stuff</b>, I’m one of the first people to leave, you know, a lot of the time” (CO-01, SPMS)</i>
<b>Active leisure activities</b>				
Difficulty exercising	12 (85.7%)	10 (62.5%)	22 (73.3%)	<i>“When I <b>have fatigue, I can’t exercise</b>, so it’s the opposite. ...fatigue kind of stops me from exercise, stops me from being healthy” (CA-01, PPMS)</i>
Difficulty completing home improvement projects	3 (21.4%)	6 (37.5%)	9 (30.0%)	<i>“I <b>have one room that I want to redo the floor</b> and my husband and I are kind of thinking well, maybe we’ll try doing it ourselves. And I’m just sort of trying to budget whether or not I can commit the amount of time because that’s one of those things that, you know, when you start you can’t really stop, you can’t do half the room and then say, you know, well, I’m tired I think I’m going to go lie down for a little while” (NJ-04, SPMS)</i>
Difficulty traveling	4 (28.6%)	3 (18.8%)	7 (23.3%)	<i>“I <b>don’t take trips anymore</b> ... like before the quarantine, thinking about driving up to Maine to my dad’s house, the thought of driving up there, being in the car that long, having to get out and going to a rest stop to use the bathroom, just thinking about it is tiring, and <b>physically doing it is exhausting</b>” (NJ-01, PPMS)</i>
Difficulty hiking/camping	3 (21.4%)	4 (25.0%)	7 (23.3%)	<i>“I just <b>don’t do, you know, the major hikes anymore</b>. So, we’ll just go up to, you know, <b>little mountains or whatever</b>, but it hasn’t been – I mean, we used to go every weekend” (AZ-01, PPMS)</i>
Difficulty attending concerts/sporting events	3 (21.4%)	4 (25.0%)	7 (23.3%)	<i>“I <b>used to like to go out and see bands play music</b> and even after I had gotten diagnosed, but I don’t do that anymore, I don’t go ... <b>I’m too tired</b>” (NJ-01, PPMS)</i>
Difficulty gardening	3 (21.4%)	3 (18.8%)	6 (20.0%)	<i>“I <b>no longer do any gardening</b>. I used to raise roses and it just I – I don’t do that to myself.... <b>Because of the fatigue</b>” (FL-03, PPMS)</i>

Concept	n (n%)			Exemplary patient quote
	PPMS (n=14)	SPMS (n=16)	Total (n=30)	
<b>Wake-up routine</b>				
Difficulty starting day	8 (57.1%)	14 (87.5%)	22 (73.3%)	<i>"I <b>wake up just exhausted</b> and I sleep fine. But the second I open my eyes, just like <b>this wave of fatigue hits me</b> and it <b>makes it difficult to even do something as simple as getting out of bed</b>" (NJ-06, PPMS)</i>
<b>Family life</b>				
Negative impact on family members	11 (78.6%)	8 (50.0%)	19 (63.3%)	<i>"Fatigue <b>changes the way I parent</b> for one because if the kids give me much pushback I'm going to quit, like <b>I'm too tired to fight with you</b> like, you know, okay, do what you want" (NJ-02, PPMS)</i>
<b>Sleep</b>				
Requires more sleep than normal	7 (50.0%)	6 (37.5%)	13 (43.3%)	<i>"I <b>need more sleep now than I ever did before</b>. I think it's even better for me to <b>sleep 9 hours</b>" (CA-01, PPMS)</i>
Difficulty falling asleep	1 (7.1%)	3 (18.8%)	4 (13.3%)	<i>"I feel so tired I lie down but I <b>can't sleep</b> and one might think I'm so tired and I lie down I should just immediately go off to sleep, but sometimes I <b>just lie there even after I take a sleeping aid</b>. ... I think my -- sometimes <b>my fatigue impacts my ability to get adequate rest</b>" (GA-02, SPMS)</i>
Difficulty staying asleep	0 (0.0%)	2 (12.5%)	2 (6.7%)	<i>"... then by the time it's time for me to go to bed, then I'm <b>not sleeping through the night because I'm in those patterns of a couple hours here, a few hours there</b>" (NC-01, SPMS)</i>
<b>Physical functioning</b>				
Ability to bathe/dress	7 (50.0%)	9 (56.3%)	16 (53.3%)	<i>"A bad day for me [with fatigue] would be the days where <b>it's just hard for me to take care of myself</b>. It's hard for me to ... get dressed or to do and the days when I can't even put on a shirt because my arms are so tired, those are the days that I have to just stay home and I mean stay in and do nothing" (GA-04, SPMS)</i>
<b>Romantic relationships</b>				
Negative impact on romantic partner	8 (57.1%)	7 (43.8%)	15 (50.0%)	<i>"I <b>can't be the spouse I want to be</b> because all I can focus on is how tired I feel. ...I just feel like I <b>am a burden on my wife</b>. We used to be this couple who could go out and conquer the world together, but now, I just sit at home. I know she loves me but there are a few days that I think <b>she questions the part of her vows about caring through sickness and in health</b>, because everyone always makes those vows when they are young and healthy" (NJ-06, PPMS)</i>

Concept	n (n%)			Exemplary patient quote
	PPMS (n=14)	SPMS (n=16)	Total (n=30)	
<b><i>Resting leisure activities</i></b>				
Difficulty reading	2 (14.3%)	7 (43.8%)	9 (30.0%)	<i>"I try and read and so forth in the afternoon, and I have difficulties sometimes <b>concentrating on what I'm reading</b>, and I get really tired. ... I kind of <b>lose interest in what I'm reading</b>" (FL-04, SPMS)</i>
Difficulty crafting/knitting	4 (28.6%)	2 (12.5%)	6 (20.0%)	<i>"I just get <b>frustrated with the knitting</b> ... because ... <b>I keep messing up</b>. ... because I'm too tired" (OH-01, PPMS)</i>
Difficulty watching TV	2 (14.3%)	1 (6.3%)	3 (10.0%)	<i>"If I'm <b>watching something on TV</b> and the mental fatigueness comes it, it's like I can't even recall what I just watched. It makes it really <b>difficult to follow a plot</b>" (TX-02, PPMS)</i>
Difficulty playing boardgames	0 (0.0%)	2 (12.5%)	2 (6.7%)	<i>"Sometimes like a <b>Scrabble game</b> or something right to think of good words and things like that. <b>I'll be too tired</b>, I'm like why am I doing – I'm too tired <b>I'm not effective at this</b>" (NJ-03, SPMS)</i>

Abbreviations: MS, multiple sclerosis; PPMS, primary progressive MS; SPMS, secondary progressive MS