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Patient and Physician Perspectives on the Wearing-Off Effect in Multiple Sclerosis: Results From Structured Interviews

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KEY FINDINGS & CONCLUSIONS

- Perception and comprehension of the WOE differ between pwMS and clinicians, indicating the need for effective health communication and further work to elucidate the mechanisms of WOE
- Fatigue was reported as the most bothersome symptom by both patients and clinicians; some patients indicated fatigue as a trigger to other symptoms such as weakness and cognitive difficulties
- Clinicians' perceptions of the WOE were variable, suggesting that the care or attention provided by clinicians could be influenced by their perceived importance of the WOE
- Studies with a larger sample size are needed to further characterize the mechanisms and patient impact of the WOE among pwMS receiving DMTs

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INTRODUCTION

- The wearing-off effect (WOE) refers to symptoms such as fatigue, cognitive dysfunction, sensory symptoms, and pain that occur toward the end of treatment cycles and can influence patient satisfaction[1,2]
- Studies have reported the wearing-off phenomenon in people with multiple sclerosis (pwMS) receiving various disease-modifying therapies (DMTs)[1-7]
- Limited information is available on peoples' and clinicians' perspectives regarding the wearing-off phenomenon of DMTs in multiple sclerosis (MS)

OBJECTIVE

- To identify the key symptoms reported by pwMS and observed by clinicians due to the WOE associated with MS DMTs, and to better understand pwMS and physician perspectives on the WOE

METHODS

- Qualitative interviews were conducted among pwMS and clinicians treating MS (NCT05627271)
- Participants from the UK, USA, and Germany were recruited to participate in a one-time, semi-structured, virtual one-on-one interview; interviews were based on a modified version of a previously published questionnaire[2]
- The interviews were recorded and transcribed; all transcripts were checked for completeness and accuracy
- Both pwMS and clinicians were interviewed on disease experience, relapse and remission, and WOE symptoms
- In addition, pwMS were interviewed on their symptom experience and experience with their neurologist
- Clinicians were also asked on their perspective around the WOE
- Both pwMS and clinicians were requested to score the severity of each reported symptom on a scale of 0 (not severe at all) to 10 (extremely severe)
- Participants were also asked to fill in a short sociodemographic and clinical questionnaire shared via email
- Key inclusion/exclusion criteria for participants are outlined in **Figure 1**

Figure 1. Key inclusion/exclusion criteria

Eligibility criteria for pwMS

Key inclusion criteria
- pwMS receiving DMTs (natalizumab, ocrelizumab, or ofatumumab) and aged ≥18 years
- Confirmed diagnosis of RRMS
- Experienced WOE symptoms[a]

Key exclusion criteria
- Currently participating in an interventional MS clinical trial

Eligibility criteria for clinicians

Key inclusion criteria
- Specialists in neurology who have prescribed DMTs at least once during the last year
- Treated ≥16 patients with MS in the last month
- Treated patients who have experienced WOE

Key exclusion criteria
- Currently involved as an HCP in an MS trial or receives funding from one of the drug manufacturers of the DMTs included in the survey

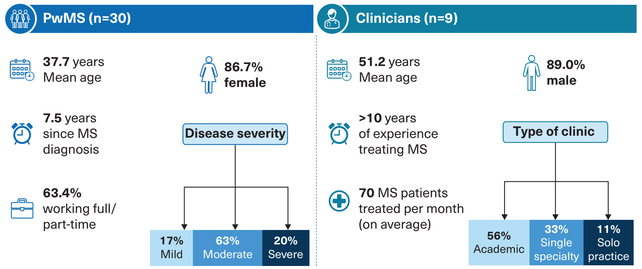
[a]pwMS who experienced WOE symptoms toward the end of treatment cycles were recruited to minimize association bias.
DMT, disease-modifying therapy; HCP, healthcare professional; MS, multiple sclerosis; pwMS, people with MS; RRMS, relapsing-remitting MS; WOE, wearing-off effect.

RESULTS

Sociodemographic and clinical characteristics

- Responses from 30 pwMS (n=10 per country) and 9 clinicians (n=3 per country) were collected during the survey
- Sociodemographic and clinical characteristics of pwMS and clinicians are summarized in **Figure 2**

Figure 2. Sociodemographic and clinical characteristics



MS, multiple sclerosis; pwMS, people with MS.

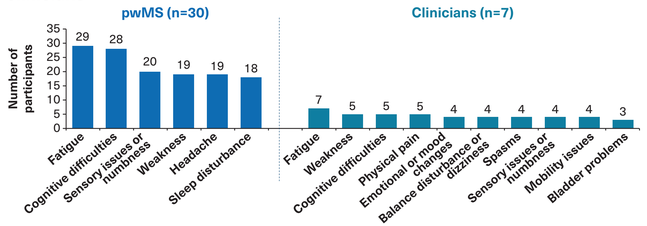
pwMS and clinician perspectives on the WOE

- All pwMS recognized ≥1 WOE-associated symptoms, irrespective of the type, route of administration, and frequency of DMT received, whereas 7 of 9 clinicians reported observing WOE in their practice
- Most patients (22/30) were able to differentiate WOE from relapse-related symptoms
- Clinician perspectives on WOE were variable, describing it as psychosomatic manifestations, lack of efficacy, or placebo effect

Commonly reported WOE symptoms

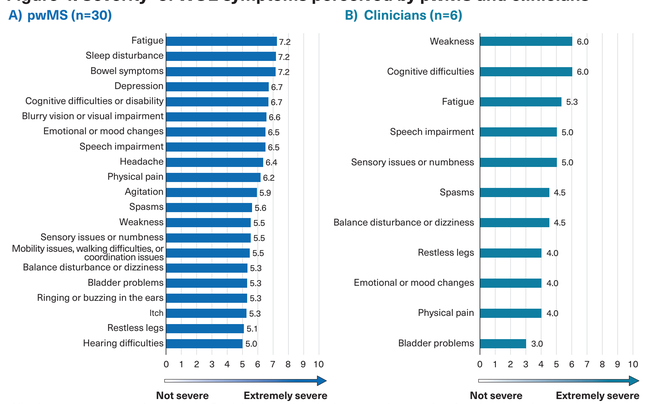
- Fatigue was the most common WOE symptom reported by patients (29/30) and clinicians (7/7; **Figure 3**) and was also described as the most bothersome symptom
- Other common symptoms reported by pwMS were cognitive difficulties (28/30) and sensory dysfunction or numbness (20/30)
- In comparison, clinicians most often identified weakness, cognitive difficulties, or pain (5/7 each) as related to WOE
- Fatigue was the most spontaneously reported symptom (without the need for probing) among pwMS; some pwMS also identified fatigue as a potential trigger for other symptoms such as weakness and cognitive difficulties (8/30)
- pwMS perceived fatigue as the most severe WOE symptom, whereas clinicians perceived weakness and cognitive difficulties as the most severe WOE symptoms (**Figures 4A** and **4B**)

Figure 3. Commonly reported WOE-associated symptoms by pwMS and clinicians



pwMS, people with multiple sclerosis; WOE, wearing-off effect.

Figure 4. Severity[a] of WOE symptoms perceived by pwMS and clinicians



[a]All values are represented as average. Participants were asked to score the severity of each reported symptom on a scale of 0 (not severe at all) to 10 (extremely severe).
pwMS, people with multiple sclerosis; WOE, wearing-off effect.

Time to onset of WOE-associated symptoms

- pwMS mostly reported experiencing WOE-associated symptoms within 4 to 7 days prior to the next dose; however, most were unsure or said the time to resolution of WOE-associated symptoms varied after the last administration of DMT
- Clinicians perceived that the time to onset of WOE symptoms and time to symptom resolution after receiving the next DMT treatment varied across patients

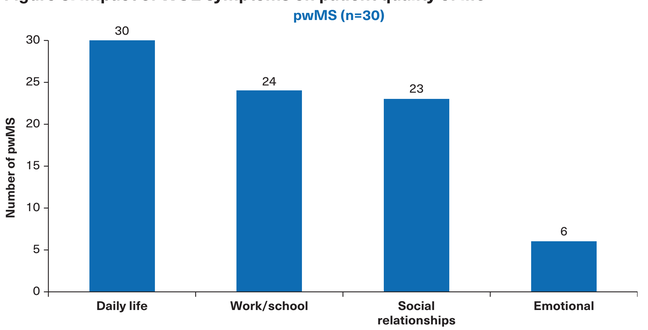
Coping mechanisms

- The primary coping mechanisms recommended to pwMS included stress management (16/30), prescription of medications (7/30), taking supplements (4/30), physical rehabilitation (3/30), or others including planning and preparation, wearing tight clothing, and tips from patient support group (4/30)
- Many pwMS (18/30) were not willing to switch to a different DMT because of WOE symptoms
  - Seven pwMS were willing to switch; reasons for switching included preference for a more effective treatment, side effects, or physician recommendation
- In comparison, 6 of 9 clinicians were willing to switch to a different medication because they perceived the appearance of WOE symptoms as a lack of effect from the current medication

Impact of WOE on patient quality of life

- All pwMS reported that WOE negatively impacted their daily activities (**Figure 5**). When stratified by commonly reported WOE-associated symptoms, pwMS most frequently reported an impact on daily activities

Figure 5. Impact of WOE symptoms on patient quality of life



pwMS, people with multiple sclerosis; WOE, wearing-off effect.

Experience of pwMS with neurologist

- Overall, 25 of 30 pwMS discussed WOE-associated symptoms with their neurologists
- Among these 25 pwMS, 15 perceived that the attention received was appropriate

Strengths and limitations

- The questionnaire was designed to not ask questions on WOE directly but rather on the underlying symptoms at the beginning of the interview to minimize association bias
- Application of study results is limited by the small sample size and inclusion of participants from only three countries

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Abbreviations

DMT, disease-modifying therapy; **HCP**, healthcare professional; **MS**, multiple sclerosis; **pwMS**, people with multiple sclerosis; **RRMS**, relapsing-remitting multiple sclerosis; **WOE**, wearing-off effect.

Disclosures

Enrique Alvarez received compensation for consulting from Alexion, Biogen, Celgene/Bristol Myers Squibb, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Motric Bio, Novartis, Sanofi, Scionic, and TG Therapeutics, and for research from Atara, Biogen, Genentech/Roche, Novartis, Sanofi, TG Therapeutics, Patient-Centered Outcomes Research Initiative, National Multiple Sclerosis Society, National Institutes of Health, and Rocky Mountain MS Center. **Joanne Fielding** has received support for contracted research from Biogen Australia and Genzyme Corporation and honorarium from Novartis Pharmaceuticals, Australia. **Dorsa Khazaei**, **Cecilia Jimenez-Moreno**, and **Donald M. Bushnell** are employees of Evidera-PPD who received funding to complete this research study. **John Parratt** has received honoraria and research grants from Biogen, Novartis, Sanofi, Roche, and Teva Pharmaceuticals. **Diogo Pata** was associated with Novartis during the study. **Ivan John Clement** is an employee of Novartis.

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