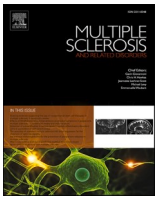
Multiple Sclerosis and Related Disorders 58 (2022) 103475

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard



Patient perspectives on patient-reported outcomes in multiple sclerosis treatment trajectories: A qualitative study of why, what, and how?

Katrine Westergaard [a,c,*], Lasse Skovgaard [a], Melinda Magyari [b,c], Maria Kristiansen [d]

[a] The Danish Multiple Sclerosis Society, Valby, Denmark
[b] Danish Multiple Sclerosis Center, Department of Neurology, Copenhagen University Hospital Rigshospitalet, Denmark
[c] The Danish Multiple Sclerosis Registry, Copenhagen University Hospital Rigshospitalet, Denmark
[d] Department of Public Health & Center for Healthy Aging, University of Copenhagen, Copenhagen, Denmark

ARTICLE INFO

Keywords:
Patient-reported outcomes
Multiple sclerosis
Clinician-patient relationship
Patient perspective
Patient involvement

ABSTRACT

Background: Interest in patient-reported outcomes has been growing in multiple sclerosis research and clinical care in recent years. This situation reflects the need for developing, testing, and integrating measures that adequately capture patients' perspectives on symptoms, functional capacity, health status, and health-related quality of life. However, the patient perspective on the relevance, content, and use of patient-reported outcomes is yet to be investigated. Hence, this study aims to investigate the perspectives of people with multiple sclerosis on the value of patient-reported outcomes in clinical encounters, the most important aspects of living with multiple sclerosis that should be reflected in these reports, and possible opportunities and barriers for integrating this data into clinical care.

Methods: A qualitative study was conducted to capture patient perspectives in a Danish population of people with multiple sclerosis. Initially, two focus group interviews were conducted with a total of 11 participants to explore their perspectives on patient-reported outcomes and related prospects and barriers. Subsequently, nine individual interviews were conducted to further investigate the identified aspects, opportunities, and barriers to use patient-reported outcomes in clinical care and treatment.

Results: In general, the informants were motivated to report patient-reported outcomes, and they believed these reports to be relevant in clinical encounters as well as to have potential to promote patient involvement by focusing on current challenges for others with this disease. However, differences in the perceived need for reporting patient-reported outcomes were detected regarding the stage in the multiple sclerosis care trajectory and in relation to the disease phenotypes. In terms of domains to be incorporated into patient-reported outcomes, a total of 28 were identified by the informants, including neurological symptoms, cognitive impairments, mental health and well-being, self-care activities, and social challenges. Several factors for integrating patient-reported outcomes into clinical care emerged as important, in particular related to timing and frequency of reporting patient reported outcomes, considerations of cognitive impairments, the need for individualized approaches to patient-reported outcomes, and the need for active use of these reports for adjustment of treatment approaches in clinical encounters.

Conclusion: From the perspective of people with multiple sclerosis, patient-reported outcomes hold important potential for enhanced patient involvement leading to a more multifaceted agenda in clinical consultations. However, patient-reported outcomes need to be comprehensive and encompass a broad range of measures regarding neurological symptoms, cognitive impairments, mental health and well-being, self-care activities, and social challenges to adequately capture and support the needs of people with multiple sclerosis in clinical encounters. It is important to address barriers for integration of patient-reported outcomes into clinical care, with the aim of preventing misuse. Future studies should focus on the synergy between perspectives from both patients and clinicians to understand how integration of patient-reported outcomes in clinical care can succeed.

* Corresponding author at: The Danish Multiple Sclerosis Society, Poul Bundgaardsvej 1, DK-2500 Valby, Denmark
E-mail address: kwe@scleroseforeningen.dk (K. Westergaard).

https://doi.org/10.1016/j.msard.2021.103475
Received 25 February 2021; Received in revised form 22 December 2021; Accepted 23 December 2021
Available online 27 December 2021

1. Introduction

Multiple sclerosis (MS) is an autoimmune neurological disease in the central nervous system, causing increasing disability and symptom burden over time (Dobson and Giovannoni, 2019). Several MS-related symptoms, such as fatigue, spasticity, and pain, are associated with lower health-related quality of life among people with MS (pwMS) (Barin et al., 2018; Giovannoni, 2006).

The commonly used objective disability assessment by clinicians is the Expanded Disability Status Scale score, which also serves as the outcome measure to evaluate the effect of disease-modifying treatments in randomized controlled trials (Meyer-Moock et al., 2014; Cheschmavar et al., 2020; Kapoor et al., 2018). However, this score does not adequately capture patients' experience of the disease and their associated needs for treatment and support (Benito-León et al., 2003). Therefore, patient-reported outcomes (PROs) have become of growing interest in MS research and patient counseling in clinical contexts, as they aim to systematically capture patients' perspectives on symptoms, function, health status, and health-related quality of life (Nowinski et al., 2017; Gunn et al., 2021; Zajicek et al., 2012). For example, in recent years, national MS registries in the Nordic countries have been developed; to varying degrees, these registries have adopted PRO measures including fatigue, physical and psychological impact of MS, and health-related quality of life (Hillert and Stawiarz, 2015; Myhr et al., 2015). The use of PROs is relevant in clinical care, as they may be used as a supportive communication tool for health professionals in understanding patients' experience of a treatment, leading to a more comprehensive and individualized approach to clinical encounters (Black, 2013). Hence, integration of PROs in clinical practice may have the potential to enhance patient-centered care (Snyder et al., 2012).

A systematic review was conducted in the preliminary work of the present study and identified a limited number of MS-specific PRO instruments where pwMS had explicitly contributed to the development of the instrument (SR Gunnersen et al., 2012SR). Research suggests that patient involvement in the development of PRO measures are of significant importance to ensure that the operationalization of aspects of PRO into questionnaire items reflect the patients' perspectives (Wiering et al., 2017). Involving patients in developing PROs is also suggested to prevent response error and unnecessary burden on patients when completing questionnaires (Mes et al., 2019). A four-phased practical framework has been developed by van der Wees et al. to support the selection and implementation of PROs in patient care (van der Wees et al., 2019). The phases include 1) determining the objective for using PROs, 2) selecting PROs, 3) developing a quality of healthcare indicator, and 4) using and continuously evaluating PROs. Moreover, Foster et al. illuminate the importance of tailoring PRO measures to the specific needs of patients and clinicians to ensure their successful implementation (Foster et al., 2018). To our knowledge, the patient perspective on the relevance, content, and use of PROs in MS treatment and care has yet to be investigated. Therefore, the present study helps fill this knowledge gap.

With the aim of contributing to the existing evidence, this qualitative study explores the perspectives of pwMS on the value of PROs in clinical encounters, on the most important aspects of living with MS that should be reflected in PROs, and on possible prospects and barriers for integrating PROs into clinical care.

2. Methods

2.1. Overview of study design

In this qualitative study, two focus groups interviews were conducted with five pwMS in one group and six in the other. Subsequently, nine individual interviews with pwMS were conducted to further investigate the identified domains of living with MS as well as explore possible potentials and barriers for integrating PROs in clinical care. An interview guide was developed for both interview types. The findings from the focus group interviews and the individual interviews were then combined to illuminate the perspectives of pwMS on PROs. Participation was voluntary, and participants were recruited through the Facebook site of the Danish MS Society. To be enrolled in the study, pwMS who signed up were asked to answer a few questions regarding demographic characteristics: age, sex, type of MS, and year of diagnosis. The inclusion criteria for participating in the study was defined as having a MS diagnosis based on self-reported answers to the questions. A total of 39 people volunteered to participate, and 20 were selected. Based on the reported demographic characteristics, the included participants were selected to reflect the general Danish MS population (Magyari et al., 2020). This purposive sampling method was used to ensure that the findings reflected perspectives from a broad range of pwMS in both focus group and individual interviews.

2.2. Patient interviews

Following written informed consent, the focus groups interviews and the individual interviews were conducted. An interview guide for both interview types was developed; covering themes such as identifying and elaborating on aspects of living with MS in relation to healthcare professionals, patient perspectives on how PROs may affect their treatment strategy, patient perspectives on motivation for and barriers to reporting PROs in clinical care, and, finally, patient perspectives on advantages and disadvantages of using PROs in clinical care.

The focus group interviews lasted about two hours, and the individual interviews ranged from 21 min to 73 min. A semi-structured interview guide was developed based on the findings from the group interviews. Due to the COVID-19 pandemic, the individual interviews were conducted online, and both group and individual interviews were audio-recorded and transcribed verbatim. A thematic analysis was then conducted by two of the authors based on quotes extracted from the transcription (Attride-Stirling, 2001).

3. Results

A total of 20 pwMS ranging in age from 40 to 69 years were interviewed, of whom 70% were female. All informants had a confirmed MS diagnosis, ranging from less than one year to 34 years. All three MS phenotypes were represented among the informants: 13 persons with relapsing-remitting MS, five persons with secondary progressive MS, and two persons with primary progressive MS (Table 1).

Table 1
Patient characteristics.

	Group interviews (n = 11)	Individual interviews (n = 9)	Overall (n = 20)
Gender			
Male, *n (%)*	4 (Mejdahl et al., 2018)	2 (Miller et al., 2020)	6 (Visser and van der Hiele, 2014)
Female, *n (%)*	7 (64)	7 (78)	14 (70)
Age (in years)			
Mean (SD)	52.7 (10.5)	51.8 (7.9)	52.3 (9.2)
Range	40–69	40–65	40–69
Years with confirmed MS diagnosis			
Mean (SD)	10.5 (8.5)	12.3 (11.6)	11.3 (9.8)
Range	1–24	0–34	0–34
MS type			
Relapsing-remitting MS, *n (%)*	7 (64)	6 (67)	13 (65)
Secondary progressive MS, *n (%)*	3 (Purks et al., 2017)	2 (Miller et al., 2020)	5 (Greenhalgh et al., 2005)
Primary progressive MS, *n (%)*	1 (Gunn et al., 2021)	1 (Hillert and Stawiarz, 2015)	2 (Zajicek et al., 2012)

Overall, the interview findings highlighted three main themes regarding patient perspectives on the value of PROs in clinical encounters: the most important aspects of living with MS and the perceived opportunities and barriers for integrating PROs into clinical care. Fig. 1 illustrates these main themes as well as subthemes described under each main theme. The following sections are a result of a condensed analysis.

3.1. Patient perspectives on the value of PROs in clinical encounters

3.1.1. Promoting patient involvement in clinical care

Overall, the informants were motivated to report PROs and believed them to be relevant in clinical encounters. Some informants believed that PROs may promote patient involvement in clinical care and strengthen patients' empowerment, while a few others expressed doubts about how PROs would change the quality of the treatment they received.

3.1.2. PROs leading to a more multifaceted agenda for clinical consultations

The majority of informants stated that reporting PROs in electronic surveys before clinical consultations can lead to a more multifaceted agenda for the clinical encounter. The informants viewed this positively, as they believed that PROs would not only help the neurologist understand the state of their health and life situation but would help them as well by inspiring reflection on their disease-related challenges. Moreover, some informants believed that PROs would make the consultation more efficient and provide them more time to ask questions about other relevant health-related subjects.

3.1.3. Different use of PROs among MS phenotypes

Differences among MS phenotypes were detected in the thematic analysis. Informants diagnosed with primary or secondary progressive MS found it difficult to comprehend how PROs would benefit them and their care compared to those with relapsing-remitting MS. This difference was seemingly attributed to the fact that no or few treatments are available for people with a progressive type of MS, which means limited contact with healthcare professionals and the healthcare system in general.

3.1.4. Different needs of PROs during MS care trajectory

The need for stating PROs was perceived differently among the informants, seemingly shaped by how lengthy their MS diagnosis was. Those with shorter disease trajectories said they were motivated to report PROs as their knowledge of how MS affects daily life was limited at this stage of their care trajectory. It emerged that these informants found it more difficult to distinguish between symptoms and challenges related to MS compared to informants with longer disease trajectories. Moreover, informants with shorter disease trajectories expressed concerns about reporting PROs correctly as well as becoming aware of MS-related symptoms they might experience in the future by learning about PROs.

3.2. Patient perspectives on the most important domains of living with MS

A total of 28 aspects of living with MS were identified, reflecting a broad range of concerns and symptoms among the informants. The described characteristics have been grouped into five main categories (Table 2). The informants were asked to prioritize which aspects were of most importance to them when seeing a neurologist, with the majority reporting that prioritizing a few aspects was difficult, because the challenges they faced often varied throughout their care. However, most informants highlighted quality of life, fatigue, cognitive impairments, family, and work life as important characteristics that were relevant to pwMS. Moreover, the informants argued that the highlighted domains could initiate conversations on other aspects of the disease as well. Additionally, many informants described how it could be beneficial to

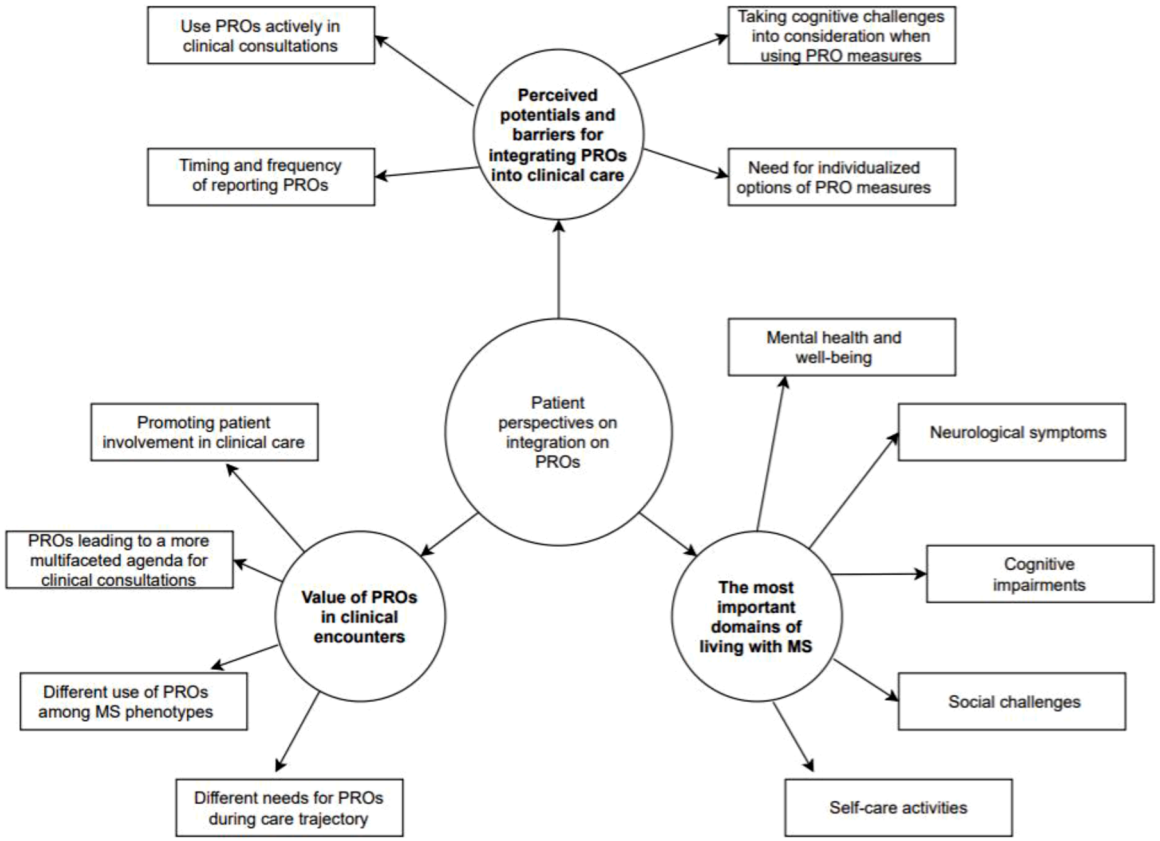


Fig. 1. Illustration of thematic network.

Table 2
Identified aspects of living with MS.

Neurological symptoms	Cognitive impairments	Mental health and well-being	Self-care activities	Social challenges
Gait disturbance	Memory challenges	Quality of life	Diet	Family life
Balance problems	Lack of energy	Mood	Physical training	Friends
Bladder problems	Concentration challenges	Fatigue		Work life
Bowel problems	Finding words	Worries about the future		Social support
Sexual problems		Depression		Participation in social activities
Visual impairment		Stress		
Sensory disturbance				
Emotional lability				
Pain				
Fine motor skills				
Spasticity				

include PROs regarding sexual, bladder, and bowel problems, because pwMS are often reluctant to talk about these topics. If these subjects were included in PROs, patients would be more likely to discuss them in clinical encounters according to the informants.

3.3. Patient perspectives on potentials and barriers for integrating PROs in clinical care

3.3.1. Timing and frequency of reporting PROs

The informants had varying opinions about the timing and frequency of sharing PROs. Only a few wanted to report PROs frequently to detect fluctuations of function and symptoms in more detail. However, a majority stated that reporting PROs without a subsequent clinical consultation was not meaningful and was a perceived waste of time. These informants explained that they could not see how they would benefit from reporting PROs without having a conversation with a healthcare professional, preferably a neurologist. However, reporting PROs immediately before a clinical consultation was received positively, as this was considered beneficial for discussions of treatment options during consultations.

3.3.2. Use PROs actively in clinical consultations

There was agreement among the informants that integration of PROs required that the clinicians be willing and able to use PROs actively in the clinical encounter, especially to respond to changes in health status or the lack thereof and to adjust the clinical care plan accordingly. Thus, clinicians' feedback on PROs was believed to be essential for the informants' motivation to complete the questionnaires when asked. Furthermore, several informants expressed concern about missing the complexity of living with MS when reporting PROs; however, if these outcomes were discussed in a subsequent clinical consultation, they would have an opportunity to elaborate on their answers, thereby managing the complexity of MS.

3.3.3. Taking cognitive challenges into considerations when using PRO measures

Several informants expressed the importance of considering the cognitive impairments that pwMS often experience when they are asked to report PROs electronically. One important feature was mentioned: allowing the possibility for patients to see their responses at any time, to guard against forgetfulness. Some informants said it is important to allow pwMS to begin stating PROs at one time and then finalize them later to accommodate issues with maintaining focus and concentration. Furthermore, many informants said such as cognitive impairments are often neglected in clinical consultations and that PROs may enhance their recognition.

3.3.4. Need for individualized options of PRO measures

Informants described how the burden of MS symptoms varies between individuals and over time, and how this issue may complicate the use of fixed PROs, as certain symptoms and functions could be relevant to some pwMS at one time and other symptoms and functions could be important later. Therefore, the informants argued that the individual PRO measures should be flexible and adapted to the individual patient's challenges. Moreover, most informants suggested that an open text option be available in a PRO system to provide information on additional functions and symptoms that neurologists may not relate to MS.

4. Discussion

This qualitative study aimed to examine MS patients' perspectives on the value of PROs as well as the opportunities for and problems with integrating these outcomes into MS clinical care. The findings indicate that pwMS were motivated to report PROs and believed them to be relevant in clinical encounters. Some pwMS even demonstrated that integrating PROs in clinical care could enhance patient involvement and lead to a more multifaceted agenda for clinical consultations. However, differences in the perceived need for stating PROs emerged relating to the stage in the patient's MS care trajectory and according to MS phenotypes. The study findings identified a broad range of aspects of living with MS, including neurological symptoms, cognitive impairments, mental health and well-being, self-care activities, and social challenges. These aspects were recognized as important for pwMS to state as part of PROs integrated into clinical encounters. Several opportunities and barriers for integrating PROs in clinical care emerged. These included the timing and frequency of reporting PROs, consideration of cognitive impairments, the need for individualized options for PRO measures, and the need to actively use PROs to adjust treatment approaches in clinical encounters.

A recent study by Miller et al. (Miller et al., 2020) found that pwMS stated preferences for completing multifaceted questionnaires prior to clinical encounters, which support our findings. Moreover, findings from Miller et al. as well as from the present study emphasize the difficulty of anticipating which concerns and aspects are important to the individual patient, therefore highlighting the importance of tailoring PROs to the individual patient's challenges and impairments. Consequently, tailoring questionnaires are necessary for pwMS to feel involved in their own treatment and care as well as to provide a multifaceted approach in the clinical encounter.

Furthermore, our findings demonstrate that pwMS express a preference for individualized options for PRO measures if they are to perceive them as meaningful for their health and life situations. Studies suggest that a patient response burden is often a challenge when integrating PROs into clinical practice, and that tailoring these outcomes to the individual patient may have the potential to reduce this burden (Gensheimer et al., 2018; Atkinson et al., 2019). Moreover, Atkinson et al., when examining predictive factors of patient response burden, found that oncology patients with cognitive impairments were more likely to report higher patient response burden compared to oncology patients with no cognitive impairments (Atkinson et al., 2019). This finding demonstrates the importance of being aware of the patient burden when integrating PROs in clinical care among patients with cognitive impairments such as pwMS.

To accommodate patients' cognitive impairments, short questionnaires have been suggested (Greenhalgh et al., 2005). However, a 2011 review involving pwMS, investigating the relationship between patient response burden and questionnaire length, found it preferable to select PRO measures based on the content of the outcomes rather than the length alone (Rolstad et al., 2011). The present study's findings also underline the value of adjusting PROs to the cognitive impairments of

pwMS. Moreover, concerns about whether pwMS with cognitive impairments can validly self-report PROs such as quality of life are broadly discussed in the literature (Purks et al., 2017; Goverover et al., 2005; Baumstarck et al., 2014; Visser and van der Hiele, 2014). Purks et al. reported concerns from healthcare professionals regarding how effectively PROs can be captured among patients with cognitive decline (Purks et al., 2017). Furthermore, Goverover et al. demonstrated that cognitive impairments among pwMS were negatively associated with self-awareness and the reliability of self-reported information (Goverover et al., 2005). However, other studies suggested that pwMS with cognitive impairments were reliable when stating PROs (Baumstarck et al., 2014; Visser and van der Hiele, 2014). In the present study, pwMS did not perceive self-reporting as an issue relating to their cognitive impairments; nevertheless, the informants said cognitive impairments is highly important to discuss with their neurologist, and that this impairment is often neglected in clinical consultations.

The current literature regarding opportunities and barriers to using and implementing PROs in clinical practice focus, in particular, on quality-of-life measures (Gutteling et al., 2008; Baumstarck et al., 2013; Greenhalgh, 2009). Even though quality-of-life was also highlighted as an important domain in the present findings, our study further indicates that the integration of PROs should include a wider range of characteristics that are considered relevant by the informants. However, our findings highlight that potentials and barriers related to the implementation of quality-of-life measures in clinical care should also apply to other PRO measures. Gutteling et al. (Gutteling et al., 2008) demonstrated that patients with chronic liver disease lacked basic computer skills, which challenged them in stating PROs. Even when acceding to these challenges by implementing a user-friendly eHealth system, patients still found it difficult to state PROs. Moreover, Gutteling et al. found that clinicians believed that health-related quality-of-life measures provide new and useful information on the patient and have the potential to save time in the clinical consultation. However, this potential was emphasized specifically among patients who were challenged in their well-being (Gutteling et al., 2008). Another study found that neurologists did not recognize quality-of-life measures in the same way as objective routine measures when managing the care of pwMS (Baumstarck et al., 2013). Moreover, a recent Danish qualitative study investigating neurologists' views on using PROs in clinical care suggested that even though neurologists saw the potential for application of PROs in MS care, skepticism regarding the data quality derived from PROs endured (SR Gunnersen, 2021). These findings indicate discrepancies in patient preferences found in the present study and preferences from clinicians relating to the use of PROs in clinical care. Therefore, these discrepancies should be addressed when aiming to integrate PROs into clinical care.

Additionally, our findings suggest that the motivation of pwMS to report PROs was conditioned by clinicians' active use of patients' PRO responses in clinical consultations. Girgis et al., who investigated the feasibility and acceptability of an eHealth system for collecting PROs among cancer patients in specialized care, found that only a limited number of patients experienced a discussion of their reported PROs during clinical consultations. Additionally, although patients wished to discuss their reported data, they were not given the opportunity. The authors also highlight that patients who discussed their PROs with a clinician found it beneficial in facilitating communication and increasing recognition and acknowledgement of their concerns (Girgis et al., 2019). From a patient perspective, the present study indicates that patients' motivation to report PROs is conditioned by neurologists' explicit use of these PROs in clinical encounters. As suggested by other studies, neurologists' acceptance and knowledge of the strengths and shortcomings of PROs is critical when integrating them in clinical care (Baumstarck et al., 2013; Greenhalgh, 2009; Mejdahl et al., 2018).

The present study used a purposive sampling method (Greenhalgh and Taylor, 1997), which secured a diverse group of patients with MS in relation to age, sex, and years lived with MS. Thus, this method ensured broad perspectives on integration of PROs in MS treatment and care. Data analyses were conducted throughout the data collection phase. Recruitment of participants ended when no new themes were generated during preliminary results, hence data saturation was considered achieved. However, this study includes only patient perspectives of stating and using PROs in clinical care; perspectives from clinicians and researchers are necessary to fully understand how to include PROs in MS clinical care and treatment. Therefore, the applicability of the study findings may be limited in real-world settings.

In conclusion, the use of PROs in care and management of MS bears important potential for enhanced patient involvement, allowing the possibility of a broader discussion to take place in clinical consultations. However, to adequately capture and support the needs of pwMS in clinical encounters, PROs should be comprehensive and encompass a broad range of MS aspects, such as neurological symptoms, cognitive impairments, mental health and well-being, self-care activities, and social challenges. Barriers for integration of PROs into clinical care are important to address with the aim of preventing their misuse of lack of use. Future studies should focus on the synergy between perspectives from both pwMS and clinicians to understand how integration of PROs in clinical care can succeed.

Role of funding source

The study is funded by grant A39648 from the Danish MS Society

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authorship statement

Katrine Westergaard: Formal analysis, Investigation, Writing – Original Draft, Visualization.

Lasse Skovgaard: Conceptualization, Methodology, Writing – Review & Editing, Supervision.

Melinda Magyari: Conceptualization, Methodology, Writing – Review & Editing, Supervision.

Maria Kristiansen: Conceptualization, Methodology, Investigation, Writing – Review & Editing, Supervision, Project administration.

References

Dobson, R., Giovannoni, G., 2019. Multiple sclerosis - a review. Eur. J. Neurol. 26 (1), 27–40. Jan.

Barin, L., Salmen, A., Disanto, G., Babačić, H., Calabrese, P., Chan, A., et al., 2018. The disease burden of Multiple Sclerosis from the individual and population perspective: which symptoms matter most? Mult. Scler. Relat. Disord. 25, 112–121. Oct.

Giovannoni, G., 2006. Multiple sclerosis related fatigue. J. Neurol. Neurosurg. Psychiatry 77 (1), 2–3. Jan.

Meyer-Moock, S., Feng, Y.-.S., Maeurer, M., Dippel, F.-.W., Kohlmann, T., 2014. Systematic literature review and validity evaluation of the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC) in patients with multiple sclerosis. BMC Neurol. 14 (58).

Cheschmavar, M., Mirmosayyeb, O., Badihian, N., Badihian, S., Shaygannejad, V., 2020. Rituximab and glatiramer acetate in secondary progressive multiple sclerosis: a randomized clinical trial. Acta Neurol. Scand.

Kapoor, R., Ho, P.-.R., Campbell, N., Chang, I., Deykin, A., Forrestal, F., et al., 2018. Effect of natalizumab on disease progression in secondary progressive multiple sclerosis (ASCEND): a phase 3, randomised, double-blind, placebo-controlled trial with an open-label extension. Lancet Neurol. 17 (5), 405–415.

Benito-León, J., Morales, J.M., Rivera-Navarro, J., Mitchell, A.J., 2003. A review about the impact of multiple sclerosis on health-related quality of life. Disabil. Rehabil. 25 (23), 1291–1303.

Nowinski, C.J., Miller, D.M., Cella, D., 2017. Evolution of patient-reported outcomes and their role in multiple sclerosis clinical trials. Neurotherapeutics 14 (4), 934–944. Oct.

Gunn, H., Stevens, K.N., Creanor, S., Andrade, J., Paul, L., Miller, L., et al., 2021. Balance right in multiple sclerosis (BRiMS): a feasibility randomised controlled trial of a falls prevention programme. Pilot Feasibility Stud. 7 (2).

Zajicek, J.P., Hobart, J.C., Slade, A., Barnes, D., Mattison, P.G., 2012. Multiple sclerosis and extract of cannabis: results of the MUSEC trial. J. Neurol. Neurosurg. Psychiatry 83 (11), 1125–1132.
Hillert, J., Stawiarz, L., 2015. The Swedish MS registry - clinical support tool and scientific resource. Acta Neurol. Scand. 132, 11–19.
Myhr, K.M., Grytten, N., Torkildsen, Ø., Wergeland, S., Bø, L., Aarseth, J.H., 2015. The Norwegian multiple sclerosis registry and biobank. Acta Neurol. Scand. 132, 24–28.
Black, N., 2013. Patient reported outcome measures could help transform healthcare. BMJ 346. Jan 28(jan28 1):f167–f167.
Snyder, C.F., Aaronson, N.K., Choucair, A.K., Elliott, T.E., Greenhalgh, J., Haylard, M.Y., et al., 2012. Implementing patient-reported outcomes assessment in clinical practice: a review of the options and considerations. Qual. Life Res. 21 (8), 1305–1314.
Gunnersen S.R., Magyari M., Skovgaard L., Kristiansen M. Patient reported outcome measures in multiple sclerosis: a systematic review [Unpublished results]. 2021.
Wiering, B., de Boer, D., Delnoij, D., 2017. Patient involvement in the development of patient-reported outcome measures: a scoping review. Health Expect. 20 (1), 11–23. Feb.
Mes, M.A., Chan, A.H.Y., Wileman, V., Katzer, C.B., Goodbourn, M., Towndrow, S., et al., 2019. Patient involvement in questionnaire design: tackling response errror and burden. J Pharm. Policy Pract. 12 (17).
van der Wees, P.J., Verkerk, E.W., Verbiest, M.E.A., Zuidgeest, M., Bakker, C., Braspenning, J., et al., 2019. Development of a framework with tools to support the selection and implementation of patient-reported outcome measures. J. Patient-Rep. Outcomes 3 (75).
Foster, A., Croot, L., Brazier, J., Harris, J., O'Cathain, A, 2018. The facilitators and barriers to implementing patient reported outcome measures in organisations delivering health related services: a systematic review of reviews. J. Patient-Rep. Outcomes [Internet] 2 (46). Available from: https://jpro.springeropen.com/articles/10.1186/s41687-018-0072-3#Sec26.
Magyari, M., Joensen, H., Laursen, B., Koch-Henriksen, N., 2020. The Danish multiple sclerosis registry. Brain Behav.
Attride-Stirling, J., 2001. Thematic networks: an analytic tool for qualitative research. Qual. Res. 1 (3), 385–405. Dec.
Miller, D.M., Moss, B., Rose, S., Li, H., Schindler, D., Weber, M., et al., 2020. Obtaining patient priorities in a multiple sclerosis comprehensive care center: beyond patient-reported outcomes. J. Patient Exp. 7 (4), 541–548.
Gensheimer, S.G., Wu, A.W., Snyder, C.F., 2018. Oh, the places we'll go: patient-reported outcomes and electronic health records. Patient - Patient-Centered Outcomes Res. 11, 591–598.
Atkinson, T.M., Schwartz, C.E., Goldstein, L., Garcia, I., Storfer, D.F., Li, Y., et al., 2019. Perceptions of response burden associated with completion of patient-reported outcome assessments in oncology. Value Health 22 (2), 225–230.
Greenhalgh, J., Long, A.F., Flynn, R., 2005. The use of patient reported outcome measures in routine clinical practice: lack of impact or lack of theory? Soc. Sci. Med. 60 (4), 833–843.
Rolstad, S., PhLic, J.A., Rydén, A., 2011. Response burden and questionnaire length: is shorter better? a review and meta-analysis. Value Health 14 (8), 1101–1108.
Purks, J.L., Wilhelm, E.E., Shoulson, I., Creveling, J., Dorsey, E.R., Irony, T., et al., 2017. Inaugural conference on incorporating patient-reported outcomes and patient preference information into clinical research, clinical care, and risk-benefit assessments for neurodegenerative diseases. Patient - Patient-Centered Outcomes Res. 10 (5), 541–544. Oct.
Goverover, Y., Chiaravalloti, N., DeLuca, J., 2005. The relationship between self-awareness of neurobehavioral symptoms, cognitive functioning, and emotional symptoms in multiple sclerosis. Mutiple Scler. 11, 203–212.
Baumstarck, K., Boucekine, M., Boyer, L., Aghababian, V., Parola, N., Reuter, F., et al., 2014. Quantification of relevance of quality of life assessment for patients with cognitive impairment: the suitability indices. BMC Neurol. 14 (78).
Visser, L.H., van der Hiele, K., 2014. Self-reports of executive functioning in multiple sclerosis: to trust or not to trust. Neurodegener. Dis. Manag. 4 (2).
Gutteling, J.J., Busschbach, J.J.V., A de Man, R., Darlington, A.-.S, 2008. Logistic feasibility of health related quality of life measurement in clinical practice: results of a prospective study in a large population of chronic liver patients. Health Qual. Life Outcomes 6 (97).
Baumstarck, K., Boyer, L., Boucekine, M., Michel, P., Pelletier, J., Auquier, P., 2013. Measuring the quality of life in patients with multiple sclerosis in clinical practice: a necessary challenge. Mult Scler Int 2013, 1–8.
Greenhalgh, J., 2009. The applications of PROs in clinical practice: what are they, do they work, and why? Qual. Life Res. 18 (1), 115–123. Feb.
Gunnersen S.R., Lynning M., Skovgaard L. Neurologists' views on patient reported outcomes in multiple sclerosis care [Unpublished results]. 2021.
Girgis, A., Durcinoska, I., Arnold, A., Delaney, G.P, 2019. Interpreting and acting on the pro scores from the patient-reported outcomes for personalized treatment and care (PROMPT-Care) eHealth system. Med. Care 57, S85–S91.
Mejdahl, C.T., Schougaard, L.M.V., Hjollund, N.H., Riiskjær, E., Lomborg, K., 2018. Exploring organisational mechanisms in PRO-based follow-up in routine outpatient care - an interpretive description of the clinician perspective. BMC Health Serv. Res. 18 (1), 546. Dec.
Greenhalgh, T., Taylor, R., 1997. How to read a paper: papers that go beyond numbers (qualitative research). BMJ 315 (7110), 740–743. Sep 20.