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ORIGINAL RESEARCH

Hopelessness in Patients with Early-Stage Relapsing-Remitting Multiple Sclerosis

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Background: Hopelessness is a risk factor for depression and suicide. There is little information on this phenomenon among patients with relapsing-remitting multiple sclerosis (RRMS), one of the most common causes of disability and loss of autonomy in young adults. The aim of this study was to assess state hopelessness and its associated factors in early-stage RRMS.

Methods: A multicenter, non-interventional study was conducted. Adult patients with a diagnosis of RRMS, a disease duration ≤ 3 years, and an Expanded Disability Status Scale (EDSS) score of 0–5.5 were included. The State-Trait Hopelessness Scale (STHS) was used to measure patients´ hopelessness. A battery of patient-reported and clinician-rated measurements was used to assess clinical status. A multivariate logistic regression analysis was conducted to determine the association between patients' characteristics and state hopelessness.

Results: A total of 189 patients were included. Mean age (standard deviation-SD) was 36.1 (9.4) years and 71.4% were female. Median disease duration (interquartile range-IQR) was 1.4 (0.7, 2.1) years. Symptom severity and disability were low with a median EDSS (IQR) score of 1.0 (0, 2.0). A proportion of 65.6% (n=124) of patients reported moderate-to-severe hopelessness. Hopelessness was associated with older age (p=0.035), depressive symptoms (p=<0.001), a threatening illness perception (p=0.001), and psychological and cognitive barriers to workplace performance (p=0.029) in the multivariate analysis after adjustment for confounders.

Conclusion: Hopelessness was a common phenomenon in early-stage RRMS, even in a population with low physical disability. Identifying factors associated with hopelessness may be critical for implementing preventive strategies helping patients to adapt to the new situation and cope with the disease in the long term.

Keywords: relapsing-remitting multiple sclerosis, hopelessness, depressive symptoms, workplace difficulties, suicide

Introduction

Hopelessness is a psychological construct defined as negative expectations characterized by the feeling that one lacks control over events in the future and is a known risk factor for depression and suicide behavior.[1,2] Hopelessness can either represent

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a personality trait or a state in response to negative events. It is a phenomenon associated with poor outcome that has been studied in the general population and in patients with several medical conditions, including cancer and ischemic heart disease.[3–5]

Multiple sclerosis (MS) is a chronic autoimmune neurological disease that causes disability and poor quality of life mainly in active people between 20 and 40 years of age.[6,7] Most patients have a relapsing-remitting form of the disease (RRMS), characterized by attacks or relapses of sensorial symptoms, weakness, vision and gait problems followed by periods of stability with recovery that may be complete or incomplete.[6,8] The uncertainty of the long-term trajectory of the disease, the frequency and severity of residual symptoms, and the lack of curative treatments provide a context for the development of hopelessness, anxiety and mood disorders among MS patients.[7,9–12] The risk of suicide is almost two times higher in patients with MS than in the general population, especially at the time of diagnosis.[10] However, there is limited information about the phenomenon of hopelessness in patients with a recent diagnosis of MS.[13,14] As a modifiable risk factor in suicidal behavior, the aim of this study was to assess the presence of state hopelessness and its associated factors in early-stage RRMS.

Methods

A non-interventional, cross-sectional study was conducted at 21 hospital-based MS Care Units in Spain. We recruited adult patients with a diagnosis of RRMS (2017 revised McDonald criteria), a disease duration no longer than 3 years, and an Expanded Disability Status Scale (EDSS) score from 0 to 5.5 in the context of their routine follow-up visits.[15,16] Patients were invited to participate in the study by their treating neurologists in the context of their regular follow-up visits.

This study was reviewed and approved by the ethical review board of the Hospital Universitari Arnau de Vilanova (Lleida, Spain) and performed in accordance with the 1964 Helsinki Declaration and its later amendments. All participants provided a written informed consent.

Measures

The State-Trait Hopelessness Scale (STHS) was used to measured patients´ hopelessness.[17] The STHS is a validated, self-rated instrument to differentiate trait (13 items) and state (10 items) hopelessness in research and clinical practice. Each subscale is measured on a 4-point Likert scale ranging from 1 (strongly disagree) to 4 (strongly agree). Higher scores indicate higher levels of hopelessness.[17] A cut-off score ≥1.8 was used to define the presence of moderate-to-severe trait and state hopelessness.[5] We focused on state rather than trait hopelessness, as this can be addressed by short-term interventions that could be implemented in the multidisciplinary setting of MS Care Units.

Table 1 shows details of patient-reported and clinician-rated outcome measures administered. The SymptoMScreen (SyMS), 5-item Modified Fatigue Impact Scale (MFIS-5), a pain visual analog scale, Hospital Anxiety and Depression Scale (HADS), Multiple Sclerosis Impact Scale (MSIS-29), Brief-Illness Perception Questionnaire (B-IPQ), Stigma Scale for Chronic Illness (SSCI-8), 5-item Perceived Deficit Questionnaire (PDQ-5) and Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ-23) were used to assess patients´ perception of symptom severity, fatigue, pain, mood and anxiety, health-related quality of life, illness representation, perception of stigma, cognition, and work-related problems, respectively.[18–25] The EDSS, Symbol Digit Modalities Test (SDMT), 9-Hole Peg Test (9-HPT), and Timed 25-Foot Walk (T25-FW) were administered by clinicians to assess disability, cognition, hand dexterity, and gait, respectively.[16,26–28] Questionnaires were administered through an electronic tablet and completed online at the hospital.

Statistical Analysis

Demographic and clinical characteristics were summarized using frequencies (percentages) and mean (standard deviation) or median (interquartile range) as appropriate. P-values <0.05 were considered statistically significant.

A multivariate logistic regression analysis was conducted to assess the association between state hopelessness (STHS state score) and demographic, clinical characteristics, and patients' perspectives. Bivariate analyses were performed using logistic regression, taking the STHS state score as the dependent variable and each study variable as the independent variable. The multivariate analysis included those variables that were significant (p-value <0.10) in the previous analysis as the independent variables. These variables were further selected through stepwise regression using the Akaike information criterion (AIC), which chooses the model with the best quality as the final model.

Table 1 Outcome Measures

Outcome	Measure	Scoring and Interpretation	Range
Symptom severity	SyMS (self-rated)	The SyMS assesses MS symptom severity across twelve neurologic domains. Each item is assessed on a 7-point Likert scale from 0 (not at all affected) to 6 (total limitation). Higher scores indicate more severe symptom endorsement.	0–72
Disability	EDSS	The EDSS is a measure to quantify disability in eight functional systems. It is an ordinal rating system ranging from 0 (normal) to 10 (death) in 0.5 increments interval.	0–10
Fatigue	MFIS-5 (self-rated)	The MFIS-5 assesses physical, cognitive, and psychosocial components of fatigue. Each item scores on a 5-point Likert scale from 0 (never) to 4 (almost always). Higher scores indicate more severe fatigue.	0–20
Pain	VAS (self-rated)	Visual analog scale with higher scores indicating a higher level of pain.	0–100
Mood and Anxiety	HADS (self-rated)	The HADS is a 14-item, self-assessment scale to measure symptoms of anxiety and depression. Each item is scored on a 4-point Likert scale from 0 to 3. A total subscale score >10 indicates a probable case of anxiety or depression, respectively.	0–21
Quality of life	MSIS-29 (self-rated)	The MSIS-29 measures the impact of MS on health-related quality of life. It consists of two composite domains including physical (20 items) and psychological impacts (9 items). Items are rated using a 4-point Likert scale from 1 (not at all) to 4 (extremely). Higher scores indicate greater impact.	20–80 (physical) 9–36 (psychological)
Illness representations	B-IPQ (self-rated)	The B-IPQ assesses cognitive and emotional illness representations. It consists of eight items rated on a scale from 0 (minimum) to 10 (maximum). Higher scores indicate a threatening illness perception.	0–80
Stigma	SSCI-8 (self-rated)	The SSCI-8 assesses internalized and experienced stigma across neurological conditions. Each item is rated on a 5-point Likert scale from 1 (never) to 5 (always). A cut-off score >8 indicates the presence of stigmatization.	8–40
Work-related problems	MSWDQ-23 (self-rated)	The MSWDQ-23 assesses the extent of physical, psychological/cognitive, and external difficulties experienced in the workplace. Each item is scored on a 5-point Likert scale from 0 (never) to 4 (almost always). All the subscales and the total scale are scored as a percentage by summing the observed item scores, divided by the total possible item scores in each subscale, then multiplying the value by 100. Higher scores indicate greater difficulties.	0–100
Hand dexterity	9-HPT	The 9-HPT assesses upper extremity function by measuring the time spent in placing and removing nine pegs.	Maximum of 300 seconds
Gait	T-25FW	The T25-FW evaluates patients' lower extremity function by walking 25 feet.	Maximum of 180 seconds
Cognition	SDMT	The SDMT measures patient attention and information processing speed. A cut-off of ≤49 correct substitutions is used to identify patients with cognitive problems.	0–110
	PDQ-5 (self-rated)	The PDQ-5 assesses cognitive complaints on four subscales. Each of the 5 items is scored from 0 (never) to 5 (very often). Higher scores indicate greater difficulties.	0–5

Abbreviations: 9-HPT, 9-Hole Peg Test; B-IPQ, Brief Illness Perception Questionnaire; EDSS, Expanded Disability Status Scale; HADS, Hospital Anxiety and Depression Scale; MFIS-5, 5-item Modified Fatigue Impact Scale; MSIS-29, Multiple Sclerosis Impact Scale; MSWDQ-23, 23-item Multiple Sclerosis Working Difficulties Questionnaire; PDQ-5, 5-item Perceived Deficit Questionnaire; SSCI-8, Stigma Scale for Chronic Illness; SDMT, Symbol Digit Modalities Test; SyMS, SymptoMScreen; T25-FW, Timed 25-Foot Walk; VAS, Visual Analogue Scale.

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Results

A total of 189 patients were included in the study. The mean age (SD) was 36.1 (9.4) years and 71.4% were female. The median disease duration (IQR) was 1.4 (0.7, 2.1) years and the median EDSS score was 1.0 (0, 2.0). Patients perceived low symptom severity, with fatigue, sensory symptoms and anxiety being the most affected dimensions. A proportion of 65.6% (n=124) of patients reported moderate-to-severe state hopelessness. Forty-seven (24.9%) and thirteen (6.9%) patients had anxiety and depressive symptoms, respectively. Sociodemographic and clinical characteristics of the sample are shown in Table 2.

Multivariate analysis showed that older age (OR=1.05, 95% CI 1.00–1.10; p=0.035), depressive symptoms (OR=1.80, 95% CI 1.40–2.40; p=<0.001), a threatening illness perception (OR=1.10, 95% CI 1.04–1.20; p=0.001), and the presence of psychological and cognitive barriers to workplace performance (OR=1.06, 95% CI 1.01–1.11; p=0.029) were predictors of moderate-to-severe state hopelessness. Bivariate and multivariate analysis are shown in Table 3.

Table 2 Sociodemographic and Clinical Characteristics

	N=189
Age, years, mean (SD)	36.1 (9.4)
Sex (female), n (%)	135 (71.4)
Education, n (%)	
University	151 (79.9)
Living status, n (%)	
With a partner/family members	164 (86.8)
Working status, n (%)	
Partial or full-time employed	130 (68.8)
Time since disease onset, years, median (IQR)	1.4 (0.7, 2.1)
Number of relapses since first attack, mean (SD)	1.8 (8.4)
Number of patients under DMT, n (%)	132 (69.8)
EDSS score, median (IQR)	1.0 (0, 2.0)
9-HPT (dominant hand) score, seconds, mean (SD)	20.2 (7.5)[a]
T25-FW score, seconds, mean (SD)	5.8 (3.6)[b]
SDMT score, mean (SD)	51.7 (14.7)[c]
≤49 correct answers, n (%)	81 (43.1)
SyMS score, mean (SD)	12.0 (10.8)
B-IPQ score, mean (SD)	38.0 (11.8)
MSIS-29	
Physical impact score, mean (SD)	29.2 (11.3)
Psychological impact score, mean (SD)	17.2 (6.6)
MFIS-5 score, mean (SD)	6.2 (5.1)
Pain VAS score, mean (SD)	14.1 (23.1)
STHS	
Trait score, mean (SD)	2.0 (0.5)
State score, mean (SD)	2.0 (0.5)
State score ≥1.8, n (%)	124 (65.6)
HADS	
Anxiety score, mean (SD)	7.8 (4.3)
Depression score, mean (SD)	4.1 (3.9)
Anxiety, probable cases, n (%)	47 (24.9)
Depression, probable cases, n (%)	13 (6.9)
SSCI-8 score, mean (SD)	10.4 (3.9)
>8, n (%)	107 (56.6)

(*Continued*)

Table 2 (Continued).

	N=189
PDQ-5 score, mean (SD)	4.9 (4.4)
MSWDQ-23 total score, median (IQR)	11.4 (4.6, 27.3)[b]
Physical barriers, median (IQR)	9.4 (3.1, 25.0)[b]
Psychological/cognitive barriers, median (IQR)	11.4 (4.5, 27.3)[b]
External barriers, median (IQR)	12.5 (0, 37.5)[b]

Notes: [a]N=187, [b]N=183, [c]N=188.

Abbreviations: 9-HPT, 9-Hole Peg Test; B-IPQ, Brief Illness Perception Questionnaire; DMT, Disease-modifying therapy; EDSS, Expanded Disability Status Scale; HADS, Hospital Anxiety and Depression Scale; IQR, Interquartile range; MFIS-5, 5-item Modified Fatigue Scale; MSIS-29, Multiple Sclerosis Impact Scale; MSWDQ-23, 23-item Multiple Sclerosis Work Difficulties Questionnaire; PDQ-5, Perceived Deficits Questionnaire; SD, Standard deviation; SDMT, Symbol Digit Modalities Scale; SSCI-8, Stigma Scale for Chronic Illness; STHS, State-Trait Hopelessness Scale; SyMS, SymptoMScreen; T25-FW, Timed 25-Foot Walk; VAS, Visual Analogue Scale.

Table 3 Bivariate and Multivariate Logistic Regression Analysis

Bivariate Analysis - Variables	**OR**	**95% CI**	**p-value**
Age	1.05	1.01–1.08	0.010
Sex	1.64	0.85–3.15	0.135
Education, university vs no university	2.07	0.10–53.5	0.612
Living status, alone vs with a partner/family	1.10	0.41–2.73	0.837
Time since diagnosis	0.76	0.51–1.13	0.175
EDSS score	1.20	0.90–1.62	0.248
9-HPT score	1.03	1.00–1.10	0.245
T25-FW score	0.71	0.33–1.50	0.369
SDMT, >49 vs ≤49 correct answers	1.21	0.66–2.25	0.535
SyMS score	1.11	1.04–1.13	<0.001
B-IPQ score	1.11	1.08–1.20	<0.001
MSIS-29 Physical impact score	1.04	1.02–1.10	0.001
MSIS-29 Psychological impact	1.05	1.03–1.10	<0.001
MFIS-5 score	1.20	1.11–1.30	<0.001
Pain VAS score	1.02	1.00–1.04	0.018
HADS Anxiety score	3.94	1.74–10.20	0.002
HADS Depression score	1.64	1.40–2.10	<0.001
SSCI-8 score	3.12	1.70–5.90	<0.001
PDQ-5 score	1.13	1.05–1.23	0.003
MSWDQ-23 total score	1.05	1.03–1.08	<0.001
MSWDQ-23 Physical barriers score	1.04	1.02–1.07	0.001
MSWDQ-23 Psychological/cognitive barriers score	1.05	1.03–1.10	<0.001
MSWDQ-23 External barriers score	1.04	1.02–1.06	<0.001
Under DMT	1.00	0.48–2.20	0.998
Multivariate analysis - Variables	**OR**	**95% CI**	**p-value**
Age	1.05	1.00–1.10	0.035
B-IPQ score	1.10	1.04–1.20	0.001
HADS Anxiety score	0.30	0.10–1.24	0.099
HADS Depression score	1.80	1.40–2.40	<0.001
MSWDQ-23 Physical barriers score	0.94	0.03–0.89	0.096
MSWDQ-23 Psychological/cognitive barriers score	1.06	1.01–1.11	0.029

Abbreviations: 9-HPT, 9-Hole Peg Test; B-IPQ, Brief Illness Perception Questionnaire; CI, Confidence interval; DMT, Disease-modifying therapy; EDSS, Expanded Disability Status Scale; HADS, Hospital Anxiety and Depression Scale; MFIS-5, 5-item Modified Fatigue Scale; MSIS-29, Multiple Sclerosis Impact Scale; MSWDQ-23, 23-item Multiple Sclerosis Work Difficulties Questionnaire; MSWS-12, Multiple Sclerosis Walking Scale; OR, Odds ratio; PDQ-5, Perceived Deficits Questionnaire; SDMT, Symbol Digit Modalities Scale; SSCI-8, Stigma Scale for Chronic Illness; SyMS, SymptoMScreen; T25-FW, Timed 25-Foot Walk; VAS, Visual Analogue Scale.

Discussion

The impact of being diagnosed early in life with a chronic disease without curative treatment and an uncertain prognosis has a negative impact on most MS patients.[9,29] Problems already common in the early phase of the disease such as fatigue, depressive symptoms, cognitive difficulties, and motor impairments together with the fear of disability progression affect patients' quality of life and decision-making ability.[9,29–31] Functional impairment and productivity loss already occur at a low level of physical disability.[7] The pooled suicide rate ratio at diagnosis was 2.12 (95% CI 1.84–2.46) in a meta-analysis of 16 studies focused on suicide and multiple sclerosis.[10]

Hopelessness has traditionally been considered one of the risk factors for suicide.[32] This type of negative perception was found in 23% of cancer patients and 27–52% of patients with ischemic heart disease during their hospitalization.[33,34] However, no previous studies analyzed hopelessness in MS patients at early stages of the disease. In our study, hopelessness was a common phenomenon in a sample of patients with early-stage RRMS with low physical disability. Hopelessness was significantly associated with older age, a threatening illness perception, depressive symptoms, and perceived psychological and cognitive problems affecting the ability to work.

Patients' beliefs and expectations about a disease influence their emotional reactions and coping resources, and have been associated with quality of life and treatment adherence.[35] MS patients' perspectives and preferences are dynamic and may change along the disease trajectory following clinical events and contextual factors.[36–38] In a recent systematic review, Luca et al found that MS patients´ illness perceptions predicted physical, psychological, functioning, and disease management outcomes.[39] High emotional impact, illness attribution to psychological causes, number of symptoms, and functional limitations due to MS were associated with worse outcomes. Poor self-perception of physical condition in MS patients was associated with negative beliefs about treatment efficacy and poor adherence.[31,40] In addition, the self-perception of cognitive difficulties predicted presenteeism and unemployment since diagnosis.[41]

Interestingly, all of the impacted symptom domains that were associated in our study with hopelessness were identified from patient-reported assessment instruments (PROs), including the B-IPQ, HADS, and MSWDQ-23. These findings may support the complementary usefulness of including PROs in addition to routine neurological examination.[42,43]

Our study has some limitations. First, a selection bias may have influenced the prevalence of hopelessness as more motivated or cooperative patients may have chosen to participate in the study. Second, the study population may not be representative of the full spectrum of patients with early-stage RRMS as we only included patients with mild-to-moderate disability (EDSS score $\leq$ 5.5). Third, the cross-sectional study design limits the ability to establish causal relationships between the factors assessed and hopelessness. Another limitation is the lack of information collected on different factors known to be related to hopelessness, such as the perception of social support or disease knowledge.[44,45]

Conclusion

Hopelessness was a common phenomenon in an early-stage RRMS population. Early identification of factors associated with hopelessness in patients with RRMS may enable multidisciplinary teams to conduct a comprehensive approach aimed at training patients to understand their disease, prevent and manage mood disorders, and undertake early cognitive rehabilitation. Further studies with a longitudinal design are needed to understand the whole spectrum of mechanisms involved in hopelessness and MS.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

1. Balsamo M, Carlucci L, Innamorati M, et al. Further insights into the beck hopelessness scale (BHS): unidimensionality among psychiatric inpatients. *Front Psychiatry*. 2020;11:727. doi:10.3389/fpsyt.2020.00727
2. McMillan D, Gilbody S, Beresford E, et al. Can we predict suicide and non-fatal self-harm with the Beck Hopelessness Scale? A meta-analysis. *Psychol Med*. 2007;37(6):769–778. doi:10.1017/S0033291706009664
3. Assari S, Lankarani MM. Depressive symptoms are associated with more hopelessness among white than black older adults. *Front Public Health*. 2016;4:82. doi:10.3389/fpubh.2016.00082
4. Luo J, Li L, Reangsing C, et al. Effects of psychotherapy on hope/hopelessness in adults with cancer: a systematic review and meta-analysis. *Int J Behav Med*. 2022;29(6):691–704. doi:10.1007/s12529-021-10051-9
5. Dunn SL, DeVon HA, Buursma MP, et al. Reliability and validity of the state-trait hopelessness scale in patients with heart disease and moderate to severe hopelessness. *J Cardiovasc Nurs*. 2020;35(2):126–130. doi:10.1097/JCN.0000000000000647
6. McGinley MP, Goldschmidt CH, Rae-Grant AD. Diagnosis and treatment of multiple sclerosis: a review. *JAMA*. 2021;325(8):765–779. doi:10.1001/jama.2020.26858

7. Maurino J, Martínez-Ginés ML, García-Domínguez JM, et al. Workplace difficulties, health-related quality of life, and perception of stigma from the perspective of patients with multiple sclerosis. *Mult Scler Relat Disord*. 2020;41:102046. doi:10.1016/j.msard.2020.102046
8. Pitt D, Lo CH, Gauthier SA, et al. Toward precision phenotyping of multiple sclerosis. *Neurol Neuroimm Neuroinfl*. 2022;9(6):e200025. doi:10.1212/NXI.0000000000200025
9. Nielsen J, Saliger J, Montag C, et al. Facing the unknown: fear of progression could be a relevant psychological risk factor for depressive mood states among patients with multiple sclerosis. *Psychother Psychosom*. 2018;87(3):190–192. doi:10.1159/000487329
10. Shen Q, Lu H, Xie D, Wang H, Zhao Q, Xu Y. Association between suicide and multiple sclerosis: an updated meta-analysis. *Mult Scler Relat Disord*. 2019;34:83–90. doi:10.1016/j.msard.2019.06.012
11. Alejos M, Vázquez-Bourgon J, Santurtún M, Riancho J, Santurtún A. Do patients diagnosed with a neurological disease present increased risk of suicide? *Neurologia*. 2023;38(1):41–46. doi:10.1016/j.nrleng.2020.03.005
12. Shin JS, Kwon YN, Choi Y, et al. Comparison of psychiatric disturbances in patients with multiple sclerosis and neuromyelitis optica. *Medicine*. 2019;98(38):e17184. doi:10.1097/MD.0000000000017184
13. Patten SB, Metz LM. Hopelessness ratings in relapsing-remitting and secondary progressive multiple sclerosis. *Int J Psychiatry Med*. 2002;32 (2):155–165. doi:10.2190/2G2N-WE19-NM47-JNY8
14. Luca M, Chisari MG, D'Amico E, et al. Hopelessness in multiple sclerosis: psychological and organic correlates. *J Psych Psych Dis*. 2019;3:241–244. doi:10.26502/jppd.2572-519X0078
15. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17 (2):162–173. doi:10.1016/S1474-4422(17)30470-2
16. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33(11):1444–1452. doi:10.1212/WNL.33.11.1444
17. Dunn SL, Olamijulo GB, Fuglseth HL, et al. The state-trait hopelessness scale: development and testing. *West J Nurs Res*. 2014;36(4):552–570. doi:10.1177/0193945913507634
18. Meca-Lallana J, Maurino J, Hernández-Pérez MÁ, et al. Psychometric properties of the symptom screen questionnaire in a mild disability population of patients with relapsing-remitting multiple sclerosis: quantifying the patient's perspective. *Neurol Ther*. 2020;9(1):173–179. doi:10.1007/s40120-020-00176-6
19. Meca-Lallana V, Brañas-Pampillón M, Higueras Y, et al. Assessing fatigue in multiple sclerosis: psychometric properties of the five-item Modified Fatigue Impact Scale (MFIS-5). *Mult Scler J Exp Transl Clin*. 2019;5(4):2055217319887987. doi:10.1177/2055217319887987
20. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*. 1983;67(6):361–370. doi:10.1111/j.1600-0447.1983.tb09716.x
21. Hobart J, Lamping D, Fitzpatrick R, et al. The multiple sclerosis impact scale (MSIS-29): a new patient-based outcome measure. *Brain*. 2001;124 (Pt 5):962–973. doi:10.1093/brain/124.5.962
22. Basu S, Poole J. The brief illness perception questionnaire. *Occup Med*. 2016;66(5):419–420. doi:10.1093/occmed/kqv203
23. Ballesteros J, Martínez-Ginés ML, García-Domínguez JM, et al. Assessing stigma in multiple sclerosis: psychometric properties of the eight-item stigma scale for chronic illness (SSCI-8). *Int J MS Care*. 2019;21(5):195–199. doi:10.7224/1537-2073.2018-053
24. Sullivan MJ, Edgley K, Dehoux E. A survey of multiple sclerosis: i. Perceived cognitive problems and compensatory strategy use. *Canadian. J Rehabil*. 1990;4(2):99–105.
25. Honan CA, Brown RF, Hine DW. The multiple sclerosis work difficulties questionnaire (MSWDQ): development of a shortened scale. *Disabil Rehabil*. 2014;36(8):635–641. doi:10.3109/09638288.2013.805258
26. López-Góngora M, Querol L, Escartín A. A one-year follow-up study of the symbol digit modalities test (SDMT) and the PACED AUDITORY SERIAL ADDITION TEst (PASAT) in relapsing-remitting multiple sclerosis: an appraisal of comparative longitudinal sensitivity. *BMC Neurol*. 2015;15:40. doi:10.1186/s12883-015-0296-2
27. Feys P, Lamers I, Francis G, et al. The Nine-Hole Peg Test as a manual dexterity performance measure for multiple sclerosis. *Mult Scler*. 2017;23 (5):711–720. doi:10.1177/1352458517690824
28. Goldman MD, Motl RW, Scagnelli J, Pula JH, Sosnoff JJ, Cadavid D. Clinically meaningful performance benchmarks in MS: timed 25-foot walk and the real world. *Neurology*. 2013;81(21):1856–1863. doi:10.1212/01.wnl.0000436065.97642.d2
29. Thrue C, Riemenschneider M, Hvid LG, et al. Time matters: early-phase multiple sclerosis is accompanied by considerable impairments across multiple domains. *Mult Scler*. 2021;27(10):1477–1485. doi:10.1177/1352458520936231
30. Cattaneo D, Gervasoni E, Anastasi D, et al. Prevalence and patterns of subclinical motor and cognitive impairments in non-disabled individuals with early multiple sclerosis: a multicenter cross-sectional study. *Ann Phys Rehabil Med*. 2022;65(1):101491. doi:10.1016/j.rehab.2021.101491
31. Saposnik G, Sotoca J, Sempere ÁP, et al. Therapeutic status quo in patients with relapsing-remitting multiple sclerosis: a sign of poor self-perception of their clinical status? *Mult Scler Relat Disord*. 2020;45:102354. doi:10.1016/j.msard.2020.102354
32. Klonsky ED, Saffer BY, Bryan CJ. Ideation-to-action theories of suicide: a conceptual and empirical update. *Curr Opin Psychol*. 2018;22:38–43. doi:10.1016/j.copsyc.2017.07.020
33. Meggiolaro E, Berardi MA, Andritsch E, et al. Cancer patients' emotional distress, coping styles and perception of doctor-patient interaction in European cancer settings. *Palliat Support Care*. 2016;14:204–211. doi:10.1017/S1478951515000760
34. Dunn SL, Corser W, Stommel M, et al. Hopelessness and depression in the early recovery period after hospitalization for acute coronary syndrome. *J Cardiopulm Rehabil*. 2006;26:152–159. doi:10.1097/00008483-200605000-00007
35. Hagger MS, Orbell S. The common sense model of illness self-regulation: a conceptual review and proposed extended model. *Health Psychol Rev*. 2022;16(3):347–377. doi:10.1080/17437199.2021.1878050
36. Eskyte I, Manzano A, Pepper G, et al. Understanding treatment decisions from the perspective of people with relapsing remitting multiple Sclerosis: a critical interpretive synthesis. *Mult Scler Relat Disord*. 2019;27:370–377. doi:10.1016/j.msard.2018.11.016
37. Różycka J. How I see is how I feel. Identification of illness perception schema and its association with adaptation outcomes in multiple sclerosis - a 5-year prospective study. *PLoS One*. 2021;16(10):e0258740. doi:10.1371/journal.pone.0258740
38. Sinnakaruppan I, Macdonald K, McCafferty A, et al. An exploration of the relationship between perception of control, physical disability, optimism, self-efficacy and hopelessness in multiple sclerosis. *Int J Rehabil Res*. 2010;33:26–33. doi:10.1097/MRR.0b013e32832e6b16

39. Luca M, Eccles F, Perez Algorta G, et al. Illness perceptions and outcome in multiple sclerosis: a systematic review of the literature. *Mult Scler Relat Disord*. 2022;67:104180. doi:10.1016/j.msard.2022.104180
40. Wilski M, Kocur P, Górny M, et al. Perception of multiple sclerosis impact and treatment efficacy beliefs: mediating effect of patient's illness and self-appraisals. *J Pain Symptom Manage*. 2019;58(3):437–444. doi:10.1016/j.jpainsymman.2019.06.013
41. Honan CA, Brown RF, Batchelor J. Perceived cognitive difficulties and cognitive test performance as predictors of employment outcomes in people with multiple sclerosis. *J Int Neuropsychol Soc*. 2015;21(2):156–168. doi:10.1017/S1355617715000053
42. McGinley MP, Lapin B. The value of patient-reported outcome measures for multiple sclerosis. *Mult Scler*. 2022;28(10):1489–1490. doi:10.1177/13524585221111675
43. Zaratin P, Vermersch P, Amato MP, et al. The agenda of the global patient reported outcomes for multiple sclerosis (PROMS) initiative: progresses and open questions. *Mult Scler Relat Disord*. 2022;61:103757. doi:10.1016/j.msard.2022.103757
44. Buursma MP, Tintle NL, Boven E, et al. Lack of perceived social support in patients with ischemic heart disease is associated with hopelessness. *Arch Psychiatr Nurs*. 2020;34(2):14–16. doi:10.1016/j.apnu.2019.12.001
45. Claflin SB, Bessing B, van der Mei I, et al. Gains in multiple sclerosis knowledge following completion of the understanding multiple sclerosis online course are maintained six months after course completion. *Mult Scler Relat Disord*. 2022;67:104085. doi:10.1016/j.msard.2022.104085