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Psychometric Properties of LUN-MS: A New Questionnaire to Identify the Unmet Needs of People With Multiple Sclerosis

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ABSTRACT

BACKGROUND: We developed a 29-item Questionnaire, Long-term Unmet Needs in MS (LUN-MS) to identify the unmet needs of people with multiple sclerosis (pwMS).

OBJECTIVE: To assess acceptability, test-retest reliability, internal consistency, and validity of the LUN-MS.

METHODS: Participants completed the LUN-MS and MSIS-29 twice, four weeks apart. Acceptability was assessed by looking at the response rate in each time point. Reliability was calculated by comparing the response during the two time points using Cohen's weighted kappa. Using principal component analysis, the dimensionality of the questionnaire's items was reduced, to five domains and the internal consistency of each domain was assessed using Cronbach's alpha. Concurrent validity was tested by comparing the total LUN-MS score against MSIS-29 and EQ-5D-3L using Pearson's product-moment correlation coefficient.

RESULTS: Among 88 participants, rate of completion at time points-1 and 2 was 96 and 80% respectively. Test-retest reliability for individual items was between fair to near-perfect (weighted Cohen's kappa 0.39-0.81). The unmet needs could be divided into five internally consistent domains (Cronbach's alpha 0.83-0.74): neuropsychological, ambulation, physical, interpersonal relationship and informational. Concurrent validity with MSIS-29 ($r=0.705$, $P<.001$) and EQ-5D-3L ($r=0.617$, $P<.001$) were good.

CONCLUSION: LUN-MS is a reliable, valid, and acceptable tool to identify the unmet needs of pwMS.

KEYWORDS: Multiple sclerosis, unmet needs, patient reported outcome measure, rehabilitation, neurological conditions

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Background

Health, defined as a state of complete physical, psychological and social wellbeing and not merely the absence of disease or infirmity, is the amalgamation of three core domains – biological, psychological and social needs.¹ *Need* denotes the capacity to benefit from a specific health intervention in pursuance of an acceptable quality of life² and unmet needs are health needs that remain unattainable within the current service provisions.³

Disease modifying drugs (DMDs) are effective in reducing the activity of Multiple Sclerosis (MS). The medical team's focus is currently on the modification of course of MS using DMDs and management of objective symptoms like spasticity and weakness. People with MS (pwMS) experience needs which are not associated with objective neurological signs or symptoms. Many of these biopsychosocial needs are

inadequately addressed by the services.⁴⁻⁶ These unmet needs, may perpetuate a steady decline of their overall quality of life (QoL). With the advent of expensive disease-modifying therapies for MS, the focus of many service providers has also shifted to pharmacological needs, at the expense of rehabilitation and psychosocial needs.⁷ A study from South of England on unmet needs of 93 people with disability (28 of participants had MS), showed that 83 had at least one unmet need. The unmet needs spanned a variety of domains like information, finance, care, social and intellectual fulfilment. These are not usually captured by the current assessments for MS.⁸ A study from five European countries, including UK showed that pwMS reported an average of 2.9 unmet needs.⁹ A study from Ireland reported at least one, non-pharmacological unmet need in 170 of 325 people with MS.⁷



The pwMS consistently reported that the ‘invisible symptoms’ of MS, such as fatigue, pain, sexual and psychological disorders have all been associated with health related distress.^{10,11} Current monitoring tools used in MS such as the Expanded Disability Status Scale (EDSS)¹² addresses mostly the physical aspects of MS and do not address these invisible symptoms. Patient Reported Outcome Measures (PROM) measure a patient’s health status or health related quality of life at a single point in time through self-completed questionnaires. Most of the PROMs in MS focus on specific domains such the 12-Item MS Walking Scale (MSWS-12).¹³ Multiple Sclerosis Impact Scale 29 (MSIS-29), a multi-domain PROM, measures the physical and psychological impact of pwMS.¹⁴ It is not designed to identify the unmet needs and does not cover issues like information about MS, psychological issues and relationships. In its consensus statement, the steering group of the MS in 21st century initiative recommended that, to deliver optimum disease management, it is essential to identify the unmet needs of PwMS.¹⁵ There is a need to develop a PROM to identify the unmet needs of pwMS.

Longer-term Unmet Needs after Stroke (LUNS) is a valid, reliable, and acceptable 22-item tool used for identifying the long-term unmet needs in post-stroke patients.¹⁶ We obtained permission from the authors of LUNS to modify it to suit the needs of pwMS. We developed a 29-item questionnaire called the Long-term Unmet Needs in MS (LUN-MS) through a process of review of relevant literature, consultations with health care professionals including neurologists, neurorehabilitation specialists and MS nurse specialists and group consultations with pwMS and their family members.⁴ The LUN-MS is a 29-item self-reported questionnaire with each item scoring in 3-point Likert scale ranging from (1) ‘No, I don’t have this problem’, (2) ‘Yes, I have this problem, but I don’t need any help with it’, and (3) ‘Yes, this is a problem, and I would like help’ (Appendix). The Flesch-Kincaid reading level is 5.5 and Flesch reading ease is 60.8%.

This article outlines the psychometric evaluation of LUN-MS in terms of its acceptability, test-retest reliability, component structure and validity in line with the COSMIN guidelines for PROMs.¹⁷ This study received ethical approval from the Health Research Authority (HRA), North of Scotland Research Ethics Service (IRAS Project ID: 241772) and the Research Ethics Committee of The University of Sheffield.

Methods

Participants

This study was conducted at a regional MS centre of a tertiary teaching hospital in United Kingdom. The participants were identified by MS nurses and doctors from outpatient clinics and day care services delivering DMDs. Those attending remote consultations (telephone or video) were also included in the study. The inclusion criteria were (a) patients diagnosed with MS (by a consultant neurologist) attending the hospital

MS clinic, or Neuro Day-Case Unit (NDCU) (b) ability to provide informed consent (c) ability to complete the questionnaires (d) sufficient communication skills in English. Consequently, participants who lacked sufficient knowledge of English to read and understand the questionnaires were excluded. Those associated with neurological, cardiac, musculoskeletal and pulmonary diseases which can affect their unmet needs were excluded.

Measures

Participant’s clinical information were collected from their hospital records. Participants were asked to complete a paper questionnaire pack at each of the two separate time points (Time point-1 and Time point-2), four weeks apart (Table 1). Content of the questionnaire packs specific to each time point is further detailed in Table 1. The participants were asked to complete the questionnaires by themselves, if possible. The participants who cannot complete the questionnaire due to their impairments, could seek the assistance of the family members and/or carers of the participants to transcribe the participant’s responses on to the paper questionnaire. The participants were given the options of either completing the questionnaire during the hospital visit or to take the questionnaire packs home and return the completed questionnaires by post.

Other PROM in the questionnaire packs include MSIS-29¹⁴ and EuroQoL EQ-5D-3L.¹⁸ The MSIS-29 is a 29-item self-rated outcome measure which identifies the impact of MS in the physical (20 items) and psychological (9 items) domains.¹³ The EQ-5D-3L consist of the EQ-5D descriptive system and the EQ visual analogue scale (VAS).¹⁹ The EQ-5D-3L descriptive system measures patients’ health state in five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each of which has three levels of response: no problems, some problems and extreme problems. The EQVAS is a vertical visual analogue scale measuring patient’s self-rated health state and ranges from 0 (*worst imaginable health state*) to 100 (*best imaginable health state*).¹⁸ The patient-reported Kurtzke Expanded Disability Status Scale (EDSS)¹² ambulation score was also administered during the study, which was a modification of the EDSS mobility component, allowing participants to self-rate their motor function through a 5-point ordinal response scale.

Data on participant’s demography (age, gender) and health condition information (duration since MS diagnosis, type of MS, use of DMDs, EDSS) were collected from their electronic patient records (EPR), clinical notes and DMD treatment/funding records.

Analysis

The data was analysed using SPSS version 28 and JASP version 0.16.3.^{20,21,22} Prior to analysis, the datasets were cross-examined by four different investigators for their face validity,

Table 1. Questionnaire pack content.

TIME POINT	QUESTIONNAIRE PACK CONTENT	PAGE
1	Instructions for completion	1
	Participant Consent Form	2
	Long-term Unmet Needs in Multiple Sclerosis (LUN-MSv2) questionnaire (Appendix)	3-5
	LUN-MS “top three needs” questions	6
	Participant satisfaction questionnaire	7
	Multiple Sclerosis Impact Scale (MSIS-29) ¹⁴	8-9
	EuroQoL EQ-5D-3L ¹⁸	10-11
	Patient-reported Kurtzke Expanded Disability Status Scale (EDSS) ¹² -Ambulation Score	12
	Study team contact information	13
2	Instructions for completion	1
	Clinical status monitoring questions	2
	Long-term Unmet Needs in Multiple Sclerosis (LUN-MSv2) questionnaire (Appendix)	3-5
	LUN-MS ‘top three needs’ questions	6
	Participant satisfaction questionnaire	7
	Multiple Sclerosis Impact Scale (MSIS-29) ¹⁴	8-9
	Study team contact information	10

Questionnaire pack content at Time point-1 and Time point-2.

presence of univariate outliers and any missing data. Descriptive statistics (measures of central tendency and dispersion) were used to summarise participants’ demographics and clinical information. Missing values were analysed using Little’s missing completely at random (MCAR) test to establish their likely missing mechanism.¹⁹ The degree of skewness and kurtosis of LUN-MS response was also measured at individual item level to determine if each item meet the normality assumption.²³

Acceptability. The acceptability of LUN-MS was determined by: (1) the percentage of participants completing the questionnaire and (2) the responses to the satisfaction questionnaire. The satisfaction questionnaire comprised of five close-ended questions and two open-ended questions (Table 2). This is a bespoke questionnaire developed by the study team. We assessed the 2 core components defining a tool’s acceptability: usability and accessibility.²³ The first question required the participants to comment on any needs not covered by the questionnaire. The second question allowed participants to comment any aspects of the questionnaire. Responses to the open-ended satisfaction indicators were examined qualitatively through thematic analysis. In this context, the usability of this questionnaire was effectively captured by the satisfaction questions whilst accessibility of the questionnaire was measured by both the overall participant’s response rate and the open-ended satisfaction questions.

Test-retest reliability. Participants responded to a second pack of questionnaires at Time point-2, four weeks after Time point-1, to assess the test-retest reliability of the LUN-MS and MSIS-29. The clinical status monitoring questions were used to identify patients experiencing any worsening of existing symptoms or new MS symptoms. Those that reported any such changes were excluded from the reliability analysis. The test-retest reliability was evaluated using item-level values instead of the total score values as this facilitates identification of problematic items that are prone to inconsistencies and allowed the authors to further investigate on them. Use of the total score values could potentially obscure any variabilities introduced at item-level and create a misleading impression of consistency, as it may overlook individual items that demonstrate inconsistent responses across multiple administrations of the test. The intra-rater reliability was initially assessed by *percent agreement*, measuring the proportion of participants who consistently gave the same response at both time points. Item-level responses from both time points were cross-tabulated and coded according to their level of need. As this method may disregard agreement due to chance, weighted Cohen’s Kappa (κ) statistic was selected as an auxiliary measure of intra-rater reliability between the two-time points.²⁴ Weighted κ considers the severity of misclassifications in an ordinal scale unlike unweighted kappa which treats all disagreements equally. Weighted κ values across all 29 items of both LUN-MS v2 and MSIS-29 were calculated.

Table 2. Satisfaction questionnaire close-ended questions.

SATISFACTION QUESTIONNAIRE	DESCRIPTION	RESPONSE SCALE
1	I'd be happy to use this questionnaire again as part of a research study	(1) Strongly disagree (2) Disagree
2	I'd be happy to use this questionnaire again as part of my routine MS clinic appointment	(3) Neither agree or disagree (4) Agree (5) Strongly agree
3	The questionnaire covers all of the problems I have that are caused by my MS	
4	The questionnaire is:	(1) Much too long (2) Too long (3) About right (4) Too short (5) Much too short

Satisfaction questionnaire for the Long-term Unmet Needs in multiple sclerosis (LUN-MS) questionnaire.

Weighted κ values were interpreted as follows: no agreement (≤ 0), slight agreement (0.01-0.20), fair agreement (0.21-0.40), moderate agreement (0.41-0.60), substantial agreement (0.61-0.80), near-perfect agreement (0.81-0.99) and perfect agreement (1.00).²⁵ κ values across all 29 items of both LUN-MS v2 and MSIS-29 were juxtaposed with their corresponding percent agreements to identify any significant numerical discordance. We also included the results for percent agreement as stipulated by the COSMIN framework.¹⁷

Component analysis. Principal component analysis (PCA) was integrated into the questionnaire's validation framework to identify different components within the questionnaire.²⁶ An oblique (oblimin) rotation method was adopted to allow a certain degree of laxity towards potential collinearity between the extracted components. Eigen decomposition was based on the variance-covariance matrix, justified by the lack of need for variable normalisation in this sample. The number of underlying components was tentatively inferred from the generated pattern matrix and component eigenvalues (λ). Kaiser criterion (λ greater than 1 rule) was applied to establish the absolute lower bound of eigen values tolerated for component retention.²⁷ Comparative dimensionality assessment by the more robust parallel analysis (Monte Carlo method) was deemed appropriate given the propensity of the former method to overinflate λ at the sample level.²⁸ Outcomes from both methods later formed the basis of the underpinning theoretical justification for the final number of principal components retained.

Internal consistency of the proposed unidimensional constructs was assessed using the intraclass correlation coefficients (ICC) function in SPSS. The data were analysed using a 'two-way mixed effects, consistency, multiple measurement' model, ICC (3, k) to generate the Cronbach's alpha, α , reliability coefficients for each component.^{29,30,31} The calculation of Cronbach's alpha was done for establishing component internal consistency and not as an assessment of component unidimensionality. Alpha value of 0.6 to 0.7 indicates acceptable internal consistency.^{32,33}

Validity. *Concurrent validity*³⁵ was assessed by measuring the correlation between LUN-MS v2 response with other validated concurrent measures (MSIS-29, EuroQoL EQ-5D-3L and the EQ VAS). The bivariate correlation was determined using the Pearson product-moment correlation coefficient.

Construct validity was assessed through *convergent* and *discriminant* validity. Convergent validity looked at how closely two measures of the same construct were related and conversely, discriminant validity was established if two measures, each measuring an entirely different construct, were in fact unrelated to each other.³⁴ To establish convergent validity, the correlation of specific component with their corresponding surrogate measures were analysed (monotrait-heteromethod correlation). The comparator instruments used include MSIS-29 Physical, MSIS-29 Psychological, EQ-5D-3L Mobility, EQ-5D-3L Self-Care, EQ-5D-3L Usual Activities, EQ-5D-3L Pain/Discomfort, EQ-5D-3L Anxiety/Depression, EQ vertical visual analogues scale (EQ VAS) and patient-reported EDSS ambulation score. Priori hypotheses were made for each latent constructs and their corresponding surrogate measures. As per the COSMIN, we proposed the following expected relationship between each latent construct and their respective comparator instruments:

- *Neuropsychological:* MSIS-29 Psychological and EQ-5D-3L Anxiety/Depression.
- *Ambulation:* MSIS-29 Physical, EQ-5D-3L Mobility and Patient-reported EDSS ambulation score.
- *Physical:* MSIS-29 Physical, EQ-5D-3L Mobility, EQ-5D-3L Usual Activities and EQ-5D-3L Pain/Discomfort.
- *Interpersonal relationship:* MSIS-29 Psychological and EQ-5D-3L Anxiety/Depression.
- *Informational:* MSIS-29 Physical, MSIS-29 Psychological, EQ-5D-3L Self-Care, EQ-5D-3L Usual Activities and EQ VAS.

A correlation value of 0.50 and above signified acceptable convergent validity.

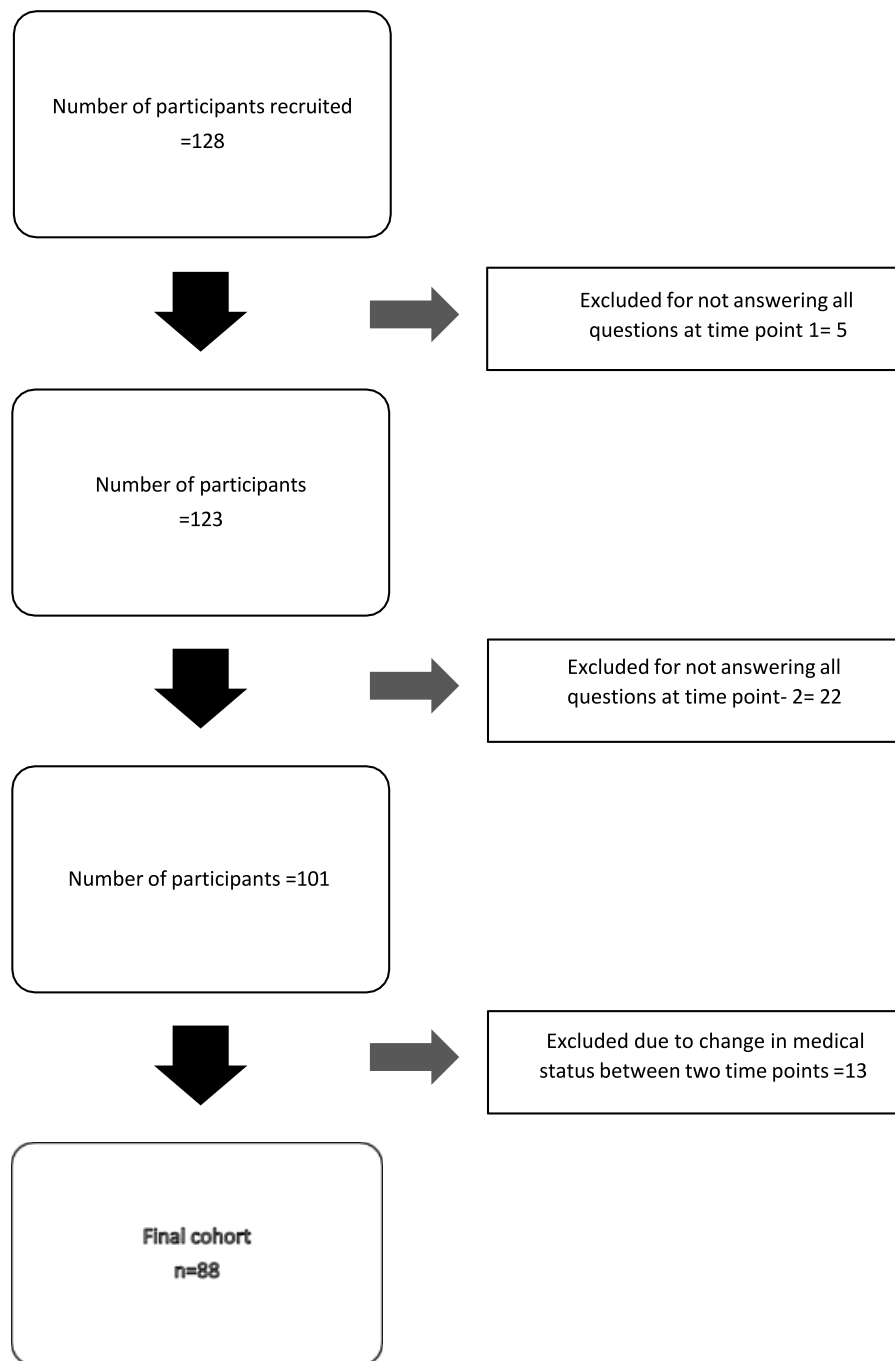


Figure 1. The flow of participants through the study with reasons for exclusion at each stage.

Discriminant validity was analysed by looking at the hetero-trait-heteromethod correlations and inter-component correlation coefficients. Sufficient distinction was achieved when the correlation coefficient does not exceed the upper limit of 0.80 to 0.85 when assessing the discriminant validity.³⁶

Results

Study population, missing data and normality testing

146 pwMS were invited to take part in the study (Figure 1), of which 128 (88%) gave consent. Among them, 101 participants completed the questionnaire at both time points. We

excluded 13 participants who experienced either relapse or disease progression between time points 1 and 2. Data from the 88 participants who completed the questionnaire packs at both time points were included in the analysis. The demographics and clinical information of the study cohort is shown in Table 3.

The number of missing item responses was 14 (0.4%) at Time point-1 and 27 (1.1%) at Time point-2. The maximum number of missing responses in any single questionnaire item was two. Little's MCAR test (Time point-1 $P=0.537$; Time point-2 $P=.400$) failed to reject the null hypothesis that the

Table 3. Descriptive statistics for LUN-MS patient cohorts.

PARTICIPANT COHORT	COMPLETED T1 QUESTIONNAIRE PACK (N=123) N (%)	COMPLETED BOTH T1 AND T2 QUESTIONNAIRE PACKS (N=101) N (%)	COMPLETED T1 AND T2 QUESTIONNAIRE PACKS, NO CHANGES IN CLINICAL STATUS (N=88) N (%)	EXCLUDED DUE TO REPORTED CHANGES IN CLINICAL STATUS AT T2 (N=13) N (%)
Median age/range	45/17-74	45/17-74	43.5/17-74	46/21-59
Gender: Male (%)	25 (20)	20 (20)	18 (20)	2 (15)
Gender: Female (%)	98 (80)	81 (80)	70 (80)	11 (85)
Median duration of MS (months)/range	93.5/2-610	88/2-610	81.5/2-610	167/41-345
Participants with RRMS	109 (89)	93 (92)	82 (93)	11 (85)
Participants with SPMS	10 (8)	7 (7)	5 (6)	2 (15)
Participants with PPMS	4 (3)	1 (1)	1 (1)	0 (0)
Median EDSS/range	5.5/0-7.5	5.5/0-7.5	5.5/0-7.5	6.5/3.5-6.5
Participants on DMTs	111 (90)	94 (93)	82 (93)	12 (92)
Face-to-face group	111 (90)	86 (85)	75 (85)	11 (85)
Postal group	12 (10)	15 (15)	13 (16)	2 (15)

Descriptive statistics comparing Long-term Unmet Needs in multiple sclerosis (LUN-MS) patient cohorts. T1-Time point-1, T2-Time point-2, MS-multiple sclerosis, RRMS-relapsing-remitting multiple sclerosis, SPMS-secondary progressive multiple sclerosis, PPMS-primary progressive multiple sclerosis, EDSS-Expanded Disability Status Scale, DMT-disease modifying therapy.

data was MCAR. Normality analysis of LUN-MS individual item responses revealed twelve items (4, 7-10, 17-20, 26-28) with right-skewness (skew level exceeding +1), indicating that participants were more likely to be unaffected by these health issues. No item had kurtosis value exceeding six, though two items (items 4 and 8) were relatively leptokurtic, suggesting moderate departure from normality.

Acceptability

Among the 128 participants, 123 (96%) responded to the questionnaire at Time point-1 and 101 (80%) at Time point-2 (Figure 1). Eleven participants (9%) required prompting to return the questionnaire. Among the 88 participants, 83% (n=73) were happy to use the LUN-MS questionnaire as part of a research study and 78% (n=69) of respondents were keen on using this questionnaire as part of their routine MS clinic appointment. While 72% (n=63) of respondents agreed that this questionnaire addressed all their MS-related concerns, 16% (n=14) neither agreed nor disagreed with this notion and 12% (n=11) expressed disagreement with it. 97% (n=85) of respondents agreed that the length of this questionnaire was about right.

The open-ended satisfaction questions received 68 responses, 30% (n=20) of which were on the general perception of the questionnaire including remarks on its comprehensiveness and user experience. Thirteen percent (n=9) of the responses focused on logistical issues with the study. Meanwhile,

57% (n=39) of the responses were specific suggestions and feedbacks on different items in the questionnaire. Table 4 summarises the results of thematic analysis conducted on the open-ended questions. The comments supported the need for the questionnaire and complemented the structure of the questionnaire. It also reflected some of the patient's experiences with unmet needs such as, 'I'm left in limbo and find it hard to contact services' and 'as a young female, it is the pregnancy and planning for children that I am most concerned about'.

Test-retest reliability

Eighty-seven percent (n=88) of respondents reported no fluctuations in their MS symptoms between the two time points. We assessed the reliability using responses from these 88 participants. The frequency of responses to each item for these 88 participants is shown in Table 5. Table 6 shows the frequency of responses for the 35 participants who were excluded from the analysis (excluded for not returning their questionnaire packs at Time point-2 (n=22), excluded due to a change in medical status between the two time points (n=13)). Item-specific percent agreement (%), weighted Cohen's Kappa (κ) and agreement level (based on weighted κ) for LUN-MS and MSIS-29 are shown in Tables 7 and 8, respectively. Percent agreement of LUN-MS ranged from 58-95%. Weighted κ ranged from 0.39 to 0.81; fair-2 items, moderate-15 items, substantial-10 items, and near-perfect-2 items. Percent agreement for MSIS-29 ranged from 39-65% and weighted κ

Table 4. Thematic analysis of the open-ended satisfaction questions.

THEME	ILLUSTRATIVE QUOTES
General perception, (n=20)	<p>'Very good questionnaire. You seemed to have covered most aspects'</p> <p>'The "I would like help" column is a little vague. Could maybe include something to say what kind of help might be on offer'</p> <p>'Regarding questions 1-5, I always appreciate further information but don't find that lack of information is a problem. I am aware of how to find out more as and when I need to'</p> <p>'It would be very useful to know what help is on offer. What will result from me ticking the box that says I need help with something?'</p>
Technicality and participant's intrinsic factor, (n=9)	<p>'I cannot see a list to find my 3 most important problems'</p> <p>'Some answers such as limitations in activities are due to COVID restrictions, not my MS'</p>
Item-related, (n=39)	<p>'I think it may be a part of mobility but balance is a big topic by itself'</p> <p>'Swallowing problems not related to food or drink – difficulty swallowing saliva'</p> <p>'As a young female, it is the pregnancy and planning for children that I am most concerned about. It feels as if many treatments do not work well for women wanting to plan a family.'</p> <p>'I would like help on how to deal with itching and help with heat and cold making symptoms worse.'</p> <p>'You have covered emotions, moods etc but there is nothing regarding acceptance or the impact this can have on you. Or even the "rollercoaster" this can take you on.'</p> <p>'I often feel like I'm left in limbo and find it hard to contact services because I feel I'm pestering them'.</p>

Thematic analysis of the open-ended satisfaction questions. Common themes extracted: General perception (n=20), Technicality & participant's intrinsic factor (n=9), Item-related (n=39).

ranged from 0.05 to 0.51. The test-retest reliability of LUN-MS questionnaire was better than that of MSIS-29. These questionnaires assessed a range of needs (LUNSMS) and impact of different impairments on patients physical and psychological well being (MSIS-29). Therefore the research team choose to analyse the reliability of individual questions rather than the total score.

Principal component analysis

Eigen value decomposition of the variance matrix resulted in eight principal components with λ over 1 (accounted for 71% of the cumulative multivariate variability) (Table 9). Results from the comparative parallel analysis suggested a two-component model but this only account for 37% of the overall variance, as opposed to 71% from the eight-component model derived by Kaiser criterion. For this reason, we have decided to opt for the eight-component solution as the initial baseline model.

Of the eight components extracted, seven components had a minimum of three variables each. The eighth component, Pregnancy and Emotional Support (PES) however, was only explained by two variables (items 4 and 29), both of which accounted for a cumulative 5% of the total variance. Despite satisfactory compliance to Kaiser criterion, retention of PES was poorly substantiated solely from its λ due to the tendency of such method to over-extract principal components. We decided to abandon the PES component as this was only explained by two of the measured variables instead of the recommended lower threshold of three, and the total common variance explained by this component was insignificant when compared to other components. We included item 4 in the

informational component and item 29 into the interpersonal relation component based on their next largest cross-loading values (Table 10).

We unified the domain 3 (Physical A) and domain 7 (Physical B), which were only marginally distinct under a single common domain 'Physical Needs'. Due to the homogeneous nature of the fifth (General Information) and the sixth (Health-related Information) domains, we merged them into a single domain labelled as 'Informational Needs'. The final five domains were neuropsychological needs, ambulation needs, physical needs, interpersonal relationship needs and informational needs.

Table 10 displayed the internal consistency (Cronbach's alpha reliability coefficient) for each LUN-MS domain used in validity analysis. α values were high, ranging from 0.736 to 0.834 across all five domains.

Validity

Bivariate correlation between the total LUN-MS v2 score and other validated concurrent measures were significant (MSIS-29: $r=0.705$, $P<.001$; EQ-5D-3L: $r=0.617$, $P<.001$) (Figure 2). Negative correlation was noted between the total LUN-MS v2 score and EQ VAS, $r=-0.429$, $P<.001$ (Figure 2). Convergent and discriminant validity for each hypothetical construct was described in Table 11. A heuristic approach was taken when determining the threshold value for each correlation coefficient, given the nature of each surrogate measure not exactly evaluating the targeted latent construct as intended. Table 12 outlined the inter-domain correlation matrix, used as part of the discriminant validity assessment. None of the correlation coefficients, r , exceeded the 0.80 to 0.85 upper threshold limit.

Table 5. Frequencies of individual item responses at Time point-1 and Time point-2.

ITEM	DESCRIPTION	TIME POINT-1 (N=88)				TIME POINT-2 (N=88)			
		(1)	(2)	(3)	MISSING	(1)	(2)	(3)	MISSING
1	Information on treatments/trials	40	19	27	2	44	15	28	1
2	Information on support services	37	21	29	1	41	17	28	2
3	Information on lifestyle, diet and exercise	42	15	31	0	41	23	23	1
4	Pregnancy/family planning	78	2	8	0	78	4	5	1
5	Information on new symptoms	42	18	28	0	45	19	23	1
6	Walking	30	38	20	0	34	33	20	1
7	Swollen feet, oedema, pressure sores	72	10	6	0	71	8	8	1
8	Eating and drinking	75	9	4	0	72	13	2	1
9	Vision	59	24	4	1	61	18	7	2
10	Speaking/making voice heard	70	14	4	0	73	7	6	2
11	Bowel/bladder dysfunction	44	25	19	0	45	24	18	1
12	Pain	35	29	23	1	34	34	19	1
13	Spasms/stiffness	36	23	29	0	33	29	24	2
14	Grip/difficulty using hands	52	18	18	0	45	36	6	1
15	Fatigue	18	33	37	0	17	40	30	1
16	Sleep disturbances	31	31	26	0	31	30	26	1
17	Financial organisation	69	8	11	0	70	9	8	1
18	Home adaptations	61	13	14	0	66	10	11	1
19	Travelling and transportation	59	19	10	0	60	17	10	1
20	Future planning and possible supports	63	11	14	0	65	14	8	1
21	Low mood	33	36	19	0	25	39	23	1
22	Emotional control (i.e., emotional lability)	38	34	16	0	42	30	15	1
23	Worry/anxiety	26	44	18	0	28	44	16	0
24	Memory problems	28	24	36	0	26	36	26	0
25	Advice on occupational/recreational adaptations	45	23	20	0	52	21	15	0
26	Physical/sexual relationship	62	18	8	0	62	17	9	0
27	Emotional relationship with partner	67	8	13	0	68	12	7	1
28	Impact on other family members	61	14	13	0	54	20	14	0
29	Lack of understanding from peers	50	22	16	0	48	23	17	0

Frequencies of individual item responses at Time point-1 and Time point-2 (n=88). Response: (1) 'No, I don't have this problem,' (2) 'Yes, I have this problem, but I don't need any help with it' and (3) 'Yes, this is a problem, and I would like help'. Columns 6 and 10 illustrated the number of missing responses at each Time point.

Discussion

The PROMs used in MS research, such as MSIS-29 and MSWS-12, identify limitations and functional impairments and do not directly assess the unmet needs of pwMS. The previous studies on unmet needs of pwMS did not use PROMS. They used

questionnaires and semi structured interviews administered by trained researchers. These questionnaires were neither designed as PROM nor for administration in a clinic setting.^{7,8} Our study showed that the LUN-MS is a valid and reliable tool to identify the unmet needs of pwMS. The tool has good concurrent and

Table 6. Frequencies of individual item responses at Time point-1 from 35 participants who completed their questionnaires at Time point-1 but were later excluded in analysis.

ITEM	DESCRIPTION	TIME POINT-1 (N=35)			
		(1)	(2)	(3)	MISSING
1	Information on treatments/trials	19	4	12	0
2	Information on support services	11	9	15	0
3	Information on lifestyle, diet and exercise	14	5	15	1
4	Pregnancy/family planning	30	1	3	1
5	Information on new symptoms	14	6	14	1
6	Walking	8	15	12	0
7	Swollen feet, oedema, pressure sores	16	12	7	0
8	Eating and drinking	17	11	7	0
9	Vision	21	8	6	0
10	Speaking/making voice heard	23	8	4	0
11	Bowel/bladder dysfunction	10	9	16	0
12	Pain	13	11	10	1
13	Spasms/stiffness	8	11	15	1
14	Grip/difficulty using hands	11	16	7	1
15	Fatigue	8	13	14	0
16	Sleep disturbances	13	13	8	1
17	Financial organisation	29	2	4	0
18	Home adaptations	20	9	6	0
19	Travelling and transportation	20	9	6	0
20	Future planning and possible supports	22	4	8	1
21	Low mood	16	11	8	0
22	Emotional control (i.e., emotional lability)	15	11	9	0
23	Worry/anxiety	10	19	6	0
24	Memory problems	9	13	13	0
25	Advice on occupational/recreational adaptations	13	11	10	1
26	Physical/sexual relationship	24	10	1	0
27	Emotional relationship with partner	25	9	1	0
28	Impact on other family members	22	8	5	0
29	Lack of understanding from peers	23	4	8	0

Frequencies of individual item responses at Time point-1 from 35 participants who completed their questionnaires at Time point-1 but were later excluded in analysis. Thirty-five respondents were excluded from the total of 123 responses received in Time point-1. Response: (1) 'No, I don't have this problem'; (2) 'Yes, I have this problem, but I don't need any help with it' and (3) 'Yes, this is a problem, and I would like help'. Column 6 illustrated the number of missing responses at Time point-1.

construct validity. The test-retest reliability was satisfactory for all 29 individual items, with most items having moderate to substantial level of agreement. The MSIS-29 is an established research tool in MS. We wanted to compare the reliability of our tool

against the reliability of an existing PROM in MS. The comparison of test-retest reliability between the LUN-MS and MSIS-29 showed that the reliability of individual items of LUN-MS is equivalent or better than that of the MSIS-29.

Table 7. Test-retest reliability of LUN-MS.

ITEM	DESCRIPTION	PERCENT AGREEMENT (%)	WEIGHTED COHEN'S KAPPA (κ)	AGREEMENT LEVEL
11	Bowel/bladder dysfunction	75.9	0.809	Near perfect
4	Pregnancy/family planning	95.4	0.808	Near perfect
10	Speaking/making voice heard	87.2	0.785	Substantial
25	Advice on occupational/recreational adaptations	67.1	0.712	Substantial
12	Pain	69.8	0.699	Substantial
6	Walking	71.3	0.688	Substantial
15	Fatigue	67.8	0.676	Substantial
23	Worry/anxiety	72.7	0.650	Substantial
17	Financial organisation	86.2	0.644	Substantial
24	Memory problems	59.1	0.638	Substantial
27	Emotional relationship with partner	79.3	0.610	Substantial
2	Information on support services available	68.2	0.608	Substantial
16	Sleep disturbances	58.6	0.600	Moderate
1	Information on treatments/trials available	65.9	0.580	Moderate
14	Grip/difficulty using hands	70.1	0.571	Moderate
9	Vision	71.8	0.562	Moderate
22	Emotional control (i.e., emotional lability)	59.8	0.546	Moderate
18	Home adaptations	77.0	0.546	Moderate
13	Spasms/stiffness	58.1	0.544	Moderate
21	Low mood	58.6	0.543	Moderate
8	Eating and drinking	82.8	0.543	Moderate
29	Lack of understanding from peers	64.8	0.542	Moderate
26	Physical/sexual relationship	77.2	0.539	Moderate
3	Information on lifestyle, diet and exercise	66.7	0.527	Moderate
20	Future planning and possible supports	67.8	0.501	Moderate
19	Travelling and transportation	69.0	0.493	Moderate
5	Information on future symptoms management	63.2	0.451	Moderate
28	Impact on other family members	65.9	0.390	Fair
7	Swollen feet, oedema, pressure sores	77.0	0.386	Fair

Test-retest reliability of the 29 items in the Long-term Unmet Needs in multiple sclerosis (LUN-MS) questionnaire. Individual item percent agreement (%), weighted Cohen's Kappa (κ) and agreement level (based on weighted Cohen's Kappa value) are shown in columns 3, 4 and 5 respectively.

Principal component analysis served as a guide to identify patterns and associations between the questionnaire items. We used clinical rationale to group the thematically linked items into five domains (neuropsychological, ambulation, physical, interpersonal relationship and informational). The domains demonstrated significant unidimensional reliability, indicating robust inter-correlations among the variables within each respective domain.

In line with the COSMIN, as there exists no 'gold standard' PROM, we decided to not assess the criterion validity of LUN-MS.¹⁷ The strong correlation between the total LUN-MS score with the total MSIS-29 and EQ-5D-3L scores signalled good concurrent validity. Significant monotrait-heteromethod correlations with chosen surrogate measures evaluating specific domain implied good convergent validity for all hypothetical constructs (Table 11). The results for the

Table 8. Test-retest reliability of MSIS-29.

ITEMS	DESCRIPTION	PERCENT AGREEMENT (%)	WEIGHTED COHEN'S KAPPA (κ)	AGREEMENT LEVEL
9	Tremor	64.7	0.512	Moderate
6	Clumsiness	49.4	0.433	Moderate
14	House-bound	55.4	0.394	Fair
2	Grip	59.5	0.377	Fair
4	Balance	55.3	0.371	Fair
23	Mental fatigue	45.2	0.354	Fair
20	Urgency (bowel/bladder)	56.0	0.348	Fair
3	Load lifting	54.8	0.332	Fair
26	Irritable/impatient/short tempered	51.8	0.332	Fair
1	Physically demanding task	51.8	0.308	Fair
28	Lack of confidence	58.8	0.299	Fair
27	Concentration problems	52.9	0.293	Fair
18	Time spent on completing tasks	49.4	0.290	Fair
24	Worries related to MS	45.2	0.285	Fair
7	Stiffness	48.8	0.280	Fair
15	Difficulties in using hands	53.6	0.228	Fair
17	Transportation issues	61.2	0.219	Fair
29	Depressed	52.9	0.216	Fair
5	Mobility	48.2	0.215	Fair
10	Spasms	48.2	0.197	Slight
12	Dependent on other people	52.4	0.194	Slight
13	Limitations in social/leisure activities	48.2	0.186	Slight
21	Feeling unwell	44.7	0.182	Slight
11	Impaired motor control	41.7	0.157	Slight
19	Difficulties in doing things spontaneously	45.9	0.133	Slight
8	Heavy arms/legs	47.6	0.123	Slight
22	Sleep difficulties	44.7	0.079	Slight
25	Anxious/tense	41.2	0.060	Slight
16	Intolerance to work/daily activities	38.8	0.046	Slight

Test-retest reliability of the 29 items in the Multiple Sclerosis Impact Scale (MSIS-29) questionnaire. Individual item percent agreement (%), weighted Cohen's Kappa (κ) and agreement level (based on weighted Cohen's Kappa value) are shown in columns 3, 4 and 5 respectively.

discriminant validity were mixed, with neuropsychological and ambulation domains showing good discriminant validity while physical and interpersonal relationship showed ambiguous discriminant validity. Discriminant validity was not done for informational needs due to lack of an established PROM to measure against it.

The physical needs domain of LUN-MS showed significant correlation with the psychological component of MSIS-29 ($r=0.58$), suggesting codependency between the three elements (Table 11). This was partly explained by the classification difference of certain symptoms, with the MSIS-29 labelling sleep disturbances and fatigue as psychological

Table 9. Component loadings of LUN-MS.

COMPONENT	ITEM	NP	AMB	PA	IR	GI	HRI	PB	PES
Neuropsychological (NP)	23	0.83	0.07	-0.06	0.17	-0.02	0.11	0.00	0.08
	21	0.79	0.01	0.14	0.01	0.16	-0.05	-0.04	0.09
	22	0.63	-0.04	0.22	0.19	-0.11	-0.03	0.09	0.20
	24	0.55	0.07	0.10	-0.05	0.15	0.16	0.30	-0.14
Ambulation (AMB)	19	0.10	0.79	0.11	0.01	0.09	-0.23	-0.13	0.05
	18	0.07	0.74	0.01	-0.19	0.14	0.11	0.08	-0.07
	7	-0.25	0.59	-0.09	0.14	0.08	0.15	0.32	0.22
	6	0.01	0.51	0.01	0.29	0.04	0.27	0.10	-0.18
Physical A (PA)	15	0.22	-0.12	0.65	-0.15	0.07	0.13	0.14	0.02
	16	0.29	-0.12	0.61	-0.07	0.33	-0.23	0.06	0.10
	13	-0.03	0.24	0.61	-0.02	-0.16	0.24	0.19	-0.25
	14	-0.03	0.31	0.58	0.21	0.08	-0.02	-0.21	-0.13
	11	0.05	0.38	0.52	0.07	-0.23	0.21	0.03	0.06
	12	0.18	-0.07	0.42	-0.01	0.32	0.23	0.07	-0.08
Interpersonal relationship (IR)	26	0.17	-0.09	-0.03	0.85	-0.11	0.13	-0.06	-0.11
	27	0.01	0.02	-0.06	0.80	0.19	0.01	0.09	0.06
	28	-0.02	0.25	0.18	0.42	0.06	-0.18	0.10	0.32
General information (GI)	17	0.02	0.24	0.02	-0.04	0.75	-0.03	-0.08	0.02
	20	0.03	0.06	-0.01	0.10	0.65	0.16	-0.11	-0.12
	2	0.05	-0.04	0.02	0.07	0.56	0.39	0.20	-0.06
	25	0.20	0.35	0.06	0.20	0.46	-0.13	0.10	-0.09
Health-related information (HRI)	5	0.36	0.01	0.05	0.07	0.06	0.73	-0.04	0.00
	1	-0.14	0.06	0.30	0.16	0.06	0.54	-0.06	0.32
	3	-0.27	-0.03	0.16	0.17	0.34	0.52	0.11	0.10
Physical B (PB)	9	-0.17	-0.12	0.20	0.14	-0.01	-0.16	0.82	0.03
	10	0.27	0.16	-0.16	-0.13	-0.03	0.15	0.77	-0.05
	8	0.09	0.10	0.09	0.40	-0.08	-0.29	0.41	-0.14
Pregnancy and emotional support (PES)	4	0.10	0.00	-0.07	-0.16	-0.16	0.13	-0.05	0.82
	29	0.25	0.03	-0.03	0.28	0.26	-0.12	0.09	0.55

Abbreviations: The eight components identified were: NP, Neuropsychological; AMB, Ambulation; PA, Physical A; IR, Interpersonal Relationship; GI, General Information; HRI, Health-related Information; PB, Physical B; PES, Pregnancy and Emotional Support. Component loadings for the Long-term Unmet Needs in multiple sclerosis (LUN-MS) questionnaire. A lower threshold of 0.4 was chosen for the loadings.

elements, whereas we have grouped them with the physical symptoms. The initial study on MSIS-29 also demonstrated a significant inter-construct correlation between its physical and psychological scales ($r=0.62$).¹⁴

The LUN-MS enabled the participants to identify whether the needs were met or unmet rather than simply acknowledging the presence or absence of needs. This allows

to distinguish between those whose needs were already met and those with unmet health needs. The strong correlation between the total LUN-MS score and MSIS-29 indicates that unmet needs correlate with the impact of MS in person's physical and psychological wellbeing. The items 4, 7, 8 and 10 showed floor effect on the normality testing due to the lack of dispersion between the responses.³⁵ This could either

Table 10. Cronbach's alpha (α) reliability coefficient for each LUN-MS domain.

COMPONENT	ITEM	DESCRIPTION	CRONBACH'S ALPHA (α)	95% CONFIDENCE INTERVAL
Neuro-psychological (NP)	21	Low mood	0.834	(0.770, 0.884)
	22	Emotional control (i.e., emotional lability)		
	23	Worry/anxiety		
	24	Memory problems		
Ambulation (AMB)	6	Walking	0.752	(0.656, 0.827)
	7	Swollen feet, oedema, pressure sores		
	18	Home adaptations		
	19	Travelling and transportation		
Physical (P)	8	Eating and drinking	0.789	(0.717, 0.846)
	9	Vision		
	10	Speaking/making voice heard		
	11	Bowel/bladder dysfunction		
	12	Pain		
	13	Spasms/stiffness		
	14	Grip/difficulty using hands		
	15	Fatigue		
Interpersonal relationship (IR)	26	Physical/ sexual relationship with partner	0.736	(0.631, 0.816)
	27	Emotional relationship with partner		
	28	Impact on other family members		
	29	Lack of understanding from others		
Informational (I)	1	Information on treatments/trials available	0.754	(0.671, 0.821)
	2	Information on support services available		
	3	Information on lifestyle, diet and exercise		
	4	Information on pregnancy-related concerns/family planning		
	5	Information on future symptoms management		
	17	Advice on financial organisation		
	20	Future planning and possible supports		
	25	Advice on occupational/recreational adaptations		

Abbreviations: The five domains used in validity analysis include: NP, Neuropsychological; AMB, Ambulation; P, Physical; IR, Interpersonal Relationship; I, Informational. Cronbach's alpha (α) reliability coefficient for each of the Long-term Unmet Needs in multiple sclerosis (LUN-MS) questionnaire's domain (native and joint component).

be due to these needs being infrequent or adequate service provisions were already in place to meet the specific needs. Nevertheless, this did not affect the core purpose of LUN-MS, which is to identify the unmet needs of pwMS.

The participants found the questionnaire to be acceptable and accessible. Minimal missing values were evident from the missing data analysis and were regarded as MCAR, eliminating potential intrinsic components to the missing

mechanism. This questionnaire has the potential to be used as a pre-clinic appointment checklist by patients, allowing them to prepare for their upcoming visits and prioritise what they need to ask their clinicians during the brief clinical encounter. A completed LUN-MS questionnaire could draw the attention of clinicians to the unmet needs of pwMS thus the limited appointment time could be used efficiently to focus on these needs.

Scatterplot Matrix of LUN-MS v2 with MSIS-29, EuroQoL EQ-5D-3L & EQ VAS

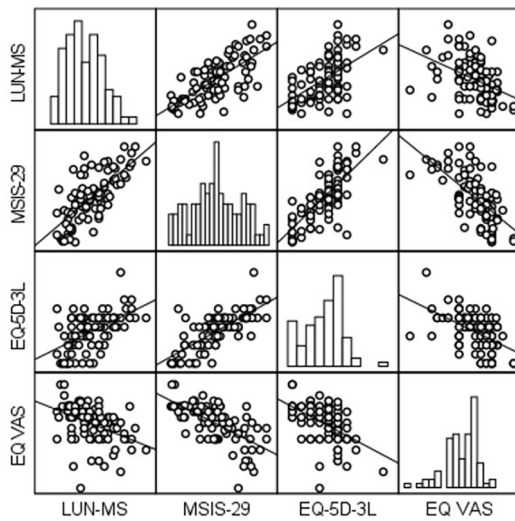


Figure 2. Scatterplot matrix of long-term Unmet Needs in multiple sclerosis (LUN-MS) with Multiple Sclerosis Impact Scale (MSIS-29), EuroQoL EQ-5D-3L and EQ vertical visual analogue scale (EQ VAS).

UK MS Register, a national digital platform for MS collects data from directly from the NHS clinical record and from pwMS via an online ‘portal’.¹⁰ Our next aim is to explore the option of integrating LUN-MS into UK MS Register. In our opinion, the data on unmet needs could identify gaps in service provisions for pwMS in different geographical areas. It also could help to identify the unmet needs of different social and ethnic groups. It could also be used as a powerful tool to monitor the effect of service or policy changes. LUN-MS could also provide valuable data for clinical audits which would ultimately facilitate service planning and delivery of care to pwMS.

Limitations

This is a single centre study done in a tertiary MS centre in NHS England with 93% (n=82) of participants on DMDs. The results were derived from pwMS that are mostly already on DMDs. The median EDSS for the study cohort was 5.5 (disability level that affects full daily activities but still able to

Table 11. Correlation coefficient between each LUN-MS domains and their concurrent measures.

DOMAIN	ITEM	CONCURRENT MEASURE	PEARSON'S R	P-VALUE
Neuropsychological	21-24	MSIS-29 physical*	0.368	<.001
		MSIS-29 psychological *	0.774	<.001
		EQ-5D-3L Mobility	0.186	.086
		EQ-5D-3L self-care	0.202	.063
		EQ-5D-3L usual activities	0.165	.128
		EQ-5D-3L pain/discomfort*	0.322	.002
		EQ-5D-3L anxiety/depression*	0.517	<.001
		EQ VAS*	-0.351	<.001
		Patient-reported EDSS ambulation	-0.066	.552
Ambulation	6-7, 18-19	MSIS-29 physical*	0.615	<.001
		MSIS-29 psychological*	0.344	<.001
		EQ-5D-3L mobility*	0.531	<.001
		EQ-5D-3L self-care*	0.414	<.001
		EQ-5D-3L usual activities*	0.431	<.001
		EQ-5D-3L pain/discomfort *	0.308	.004
		EQ-5D-3L Anxiety/depression*	0.229	.034
		EQ VAS*	-0.334	.002
		Patient-reported EDSS ambulation*	0.539	<.001

(Continued)

Table 11. (Continued)

DOMAIN	ITEM	CONCURRENT MEASURE	PEARSON'S <i>r</i>	P-VALUE
Physical	8-16	MSIS-29 physical*	0.570	<.001
		MSIS-29 psychological*	0.583	<.001
		EQ-5D-3L mobility*	0.444	<.001
		EQ-5D-3L self-care*	0.289	.008
		EQ-5D-3L usual activities*	0.351	.001
		EQ-5D-3L pain/discomfort*	0.465	<.001
		EQ-5D-3L anxiety/depression*	0.283	.009
		EQ VAS*	-0.299	.006
		Patient-reported EDSS ambulation	0.120	.286
Interpersonal relationship	26-29	MSIS-29 physical*	0.399	<.001
		MSIS-29 psychological*	0.472	<.001
		EQ-5D-3L mobility*	0.292	.006
		EQ-5D-3L self-care*	0.215	.046
		EQ-5D-3L usual activities	0.207	.056
		EQ-5D-3L pain/discomfort*	0.253	.019
		EQ-5D-3L anxiety/depression*	0.367	<.001
		EQ VAS	-0.196	.071
		Patient-reported EDSS ambulation	0.178	.107
Informational	1-3, 4, 5, 17, 20, 25	MSIS-29 physical*	0.463	<.001
		MSIS-29 psychological*	0.515	<.001
		EQ-5D-3L mobility*	0.352	.001
		EQ-5D-3L self-care*	0.226	.040
		EQ-5D-3L usual activities*	0.309	.004
		EQ-5D-3L pain/discomfort*	0.312	.004
		EQ-5D-3L anxiety/depression*	0.293	.007
		EQ VAS*	-0.429	<.001
		Patient-reported EDSS ambulation*	0.243	.030

The correlation coefficient between each domains of Long-term Unmet Needs in multiple sclerosis (LUN-MS) hypothetical construct (component) and their corresponding concurrent measures. The concurrent measures used include the Multiple Sclerosis Impact Scale (MSIS-29) Physical component, Multiple Sclerosis Impact Scale (MSIS-29) Psychological component, EQ-5D-3L 5 health dimensions (Mobility, Self-Care, Usual Activities, Pain/Discomfort, Anxiety/Depression), EQ vertical visual analogue scale (EQ VAS) and patient-reported Kurtzke Expanded Disability Status Scale (EDSS) Ambulation score. The Pearson product-moment correlation coefficient (Pearson's *r*) for each concurrent measure is listed in the fourth column, alongside its 2-tailed significance value (*P*-value) in the next column. Concurrent measures with statistically significant bivariate correlation were written in bold and labelled with "*".

ambulate for about 100m without walking aids¹²), with only 15% (n = 13) of the participants having an EDSS score of 6.0 or above (requiring assistance to walk), indicating a lack of representation for those on the higher burden of disability. In UK, recommended stopping criteria for DMD is EDSS of 7.0 (inability to walk). Even though 93% of our participants were

receiving DMD, the median EDSS was unexpectedly high (5.5), the reason behind this anomaly remains unexplained. We did not calculate the sample size based on number of questions before the study.

We used proxy tools (MSIS-29 and EQoL EQ-5D-3L) to validate LUN-MS. The LUN-MS questionnaire alone does

Table 12. LUN-MS inter-domain correlation matrix.

DOMAIN	NP	AMB	P	IR	I
Neuropsychological (NP)	1.000	–	–	–	–
Ambulation (AMB)	0.286	1.000	–	–	–
Physical (P)	0.565	0.522	1.000	–	–
Interpersonal Relationship (IR)	0.468	0.402	0.408	1.000	–
Informational (I)	0.525	0.571	0.574	0.530	1.000

Abbreviations: The hypothetical constructs measured were: NP, Neuropsychological; AMB, Ambulation; P, Physical; IR, Interpersonal Relationship; I, Informational. Inter-domain correlation matrix of Long-term Unmet Needs in multiple sclerosis (LUN-MS). Two-tailed significance value (P -value) were $P < .001$ across all correlation coefficients except for NP with AMB, which was at $P < .01$.

not provide insights into the underlying reasons behind the unmet needs. As we have eliminated individuals who experienced disease-related events during the study period, we were unable to comment whether the needs were dependent on activity of MS. The exclusion of individuals experiencing disease-related events during the study period was necessary as the evaluation of test-retest reliability required patients with stable MS between the administrations of the two questionnaire packs. However, we understand that including the patients experiencing a relapse to be important as unmet needs are likely to arise when patients experience such events during their disease. Further work is necessary to include pwMS who are currently experiencing disease-related events, as this can provide valuable insights into their specific unmet needs.

The COSMIN systematic review for PROMs stated that correlations with instruments measuring similar latent construct should be 0.50 or greater and correlations with instruments measuring related but dissimilar constructs should be 0.30 to 0.50.¹⁷ As the PROMs we used for comparisons were not measuring the same latent constructs, we evaluated the convergent validity for each construct on an individual basis in relation to their respective discriminant correlation values.

A major part of this study took place while the restrictions related to COVID-19 pandemic were in place. It is possible that some of the responses were influenced by the restrictions associated with the pandemic and.

Conclusion

This study showed that LUN-MS is a valid and reliable measure to assess the unmet needs of pwMS. The pwMS found LUN-MS questionnaire acceptable. A nationwide study using LUN-MS on platforms such as the UK MS register could facilitate identification of unmet needs in pwMS in the UK.

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REFERENCES

1. World Health Organization. *Constitution of the World Health Organization*. 45th ed. World Health Organization; 2005.
2. Wright J, Williams R, Wilkinson JR. Development and importance of health needs assessment. *BMJ*. 1998;316:1310-1313.
3. Aragon MJ, Chalkley M, Goddard MK. Defining and Measuring Unmet Need to Guide Healthcare Funding: Identifying and Filling the Gaps. *Centre for Health Economics, University of York*; 2017.
4. Kirkland C. *Identifying the Unmet Needs in patients with Multiple Sclerosis: Developing the LUN-MS Questionnaire*. Master thesis. Neurology Academy; 2018.
5. Senders A, Sando K, Wahbeh H, et al. Managing psychological stress in the multiple sclerosis medical visit: patient perspectives and unmet needs. *J Health Psychol*. 2016;21:1676-1687.
6. Lorefice L, Mura G, Coni G, et al. What do multiple sclerosis patients and their caregivers perceive as unmet needs? *BMC Neurol*. 2013;13:1-8.
7. Lonergan R, Kinsella K, Fitzpatrick P, et al. Unmet needs of multiple sclerosis patients in the community. *Mult Scler Relat Disord*. 2015;4:144-150.
8. Kerstan P, George S, McLellan L, Smith JAE, Mullee MA. Met and Unmet needs reported by severely disabled people in southern England. *Disabil Rehabil*. 2000;16: 737-744.
9. Kerstan P, McLellan DL, Gross-Pajou K, et al. A questionnaire assessment of unmet needs for rehabilitation services and resources for people with multiple sclerosis: results of a pilot survey in five European countries. *Clin Rehabil*. 2000;14:42-49.
10. Moore H, Nair KP, Baster K, et al. Fatigue in multiple sclerosis: a UK MS-register based study. *Mult Scler Relat Disord*. 2022;64:103954.
11. White CP, White MB, Russell CS. Invisible and visible symptoms of multiple sclerosis: which are more predictive of health distress? *J Neurosci Nurs*. 2008;40:85-95.
12. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33:1444.
13. Hobart JC, Riazi A, Lamping DL, et al. Measuring the impact of MS on walking ability: the 12-Item MS Walking Scale (MSWS-12). *Neurology*. 2003;60:31-36.
14. Hobart J, Lamping D, Fitzpatrick R, Riazi A, Thompson A. The multiple sclerosis impact scale (MSIS-29) a new patient-based outcome measure. *Brain*. 2001;124:962-973.
15. Members of the MS in 21st Century Steering Group. Unmet needs, burden of treatment and patient engagement in multiple sclerosis: A combined perspective from MS in the 21st century steering group. *Mult Scler Relat Disord*. 2018;19:153-160.
16. LoTS Care LUNS Study Team. Validation of the longer-term unmet needs after stroke (LUNS) monitoring tool: a multicentre study. *Clin Rehabil*. 2013;27:1020-1028.
17. Prinsen CA, Mokkink LB, Bouter LM, et al. COSMIN guideline for systematic reviews of patient-reported outcome measures. *Qual Life Res*. 2018; 27:1147-1157.
18. The EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16:199-208.

19. Little RJ. A test of missing completely at random for multivariate data with missing values. *J Am Stat Assoc.* 1988;83:1198-1202.

20. IBM Corp. IBM SPSS Statistics for Windows, Version 28.0. IBM Corp; 2021.

21. JASP Team. JASP (Version 0.16.3) [Computer software]; 2022.

22. Alexandre B, Reynaud E, Osiurak F, et al. Acceptance and acceptability criteria: a literature review. *Cogn Technol Work.* 2018;20:165-177.

23. Kline RB. *Principles and practice of structural equation modeling.* Vol., 3, 2nd ed. Guilford; 2005.

24. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas.* 1960;20:37-46.

25. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med.* 2012;22:276-282.

26. Shlens J. A tutorial on principal component analysis. Preprint. Posted online April 3, 2014. arXiv:1404.1100. doi:10.48550/arXiv.1404.1100

27. Kaiser HF. The application of electronic computers to factor analysis. *Educ Psychol Meas.* 1960;20:141-151.

28. Braeken J, Van Assen MA. An empirical Kaiser criterion. *Psychol Methods.* 2017;22:450.

29. McGraw KO and Wong SP. Forming inferences about some intraclass correlation coefficients. *Psychol Methods.* 1996;1:30.

30. Shrout PE, Fleiss JL. Intraclass correlations uses in assessing rater reliability. *Psychol Bull.* 1979;86:420.

31. Cronbach LJ. Coefficient alpha and the internal structure of tests. *Psychometrika.* 1951;16:297-334.

32. Ursachi G, Horodnic IA, Zait A. How reliable are measurement scales? External factors with indirect influence on reliability estimators. *Procedia Econ Finance.* 2015;20:679-686.

33. Nunnally JC. *Psychometric Theory 3E.* Tata McGraw-Hill Education; 1994.

34. Cronbach LJ, Meehl PE. Construct validity in psychological tests. *Psychol Bull.* 1955;52:281.

35. Koedel C, Betts J. Value added to what? How a ceiling in the testing instrument influences value-added estimation. *Educ Finance Policy.* 2010;5:54-81.

36. Brown TA. *Confirmatory factor analysis for applied research.* Guilford publications; 2015 Jan 7.

Appendix

Please read each statement and answer it as follows

Tick 'YES This is a problem and I would like help with it' if you currently have this problem and would like help.

Tick 'YES I have this problem but I don't need help with it' if you have had this problem but it currently isn't something you would like help with

Tick 'NO I don't currently have this problem' if this is something not bothering you at the moment

	YES THIS IS A PROBLEM AND I WOULD LIKE HELP	YES I HAVE THIS PROBLEM BUT I DON'T NEED HELP WITH IT	NO I DON'T CURRENTLY HAVE THIS PROBLEM
1.	I would like more information about the different treatment or trials available for MS		
2.	I would like more information about extra MS support services in my area		
3.	I would like more information about how to look after myself, such as exercise, diet and lifestyle		
4.	I would like more information about MS and pregnancy/family planning		
5.	I would like to know more about what to do if I have a new symptom or problem		
6.	I have difficulty walking and would like help with this		
7.	I have problems because I'm not very mobile (e.g. swollen feet, pressure sores) and would like help with this		
8.	I have problems eating and drinking and need some help with this		
9.	I have problems with my vision and need some help with this		
10.	I have problems speaking or making my voice heard and need some help with this		
11.	I would like help on bowel/bladder management and care		
12.	I would like help for managing pain		
13.	I would like help managing spasms or stiffness		
14.	I have problems with my grip or using my hands and would like help with this		
15.	I have fatigue and would like advice on how to manage this		
16.	I have sleep disturbances and would like advice on how to manage this		
17.	I need some help/advice on organising my finances (work/benefits)		
18.	I need help making adaptations to my home		
19.	I find it difficult to get around and would like some help with this (i.e., wheelchair, access to transport etc.)		

(Continued)

	YES THIS IS A PROBLEM AND I WOULD LIKE HELP	YES I HAVE THIS PROBLEM BUT I DON'T NEED HELP WITH IT	NO I DON'T CURRENTLY HAVE THIS PROBLEM
20	I would like advice on planning for the future to ensure my wishes are met		
21	I sometimes have low mood and would like help with this		
22	I sometimes feel my emotions are out of control and would like help with this		
23	I sometimes feel worried or anxious and would like help with this		
24	I find my memory has worsened since being diagnosed with MS and would like help with this		
25	I would like advice on how to adapt to be able to do the things I used to enjoy/ need to do but now find difficult (e.g., leisure or work activities)		
26	I am worried about my physical and/or sexual relationship with my partner and would like some advice on this		
27	I feel like MS has put a strain on my relationship with my partner and would like advice on how to cope with this		
28	I am worried about how other family members are affected by MS and would like some advice on this		
29	I feel other people like my boss or friends don't understand MS and I'd like advice on how to cope with this		