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Research article

Psychometric Validation of the Romanian Version of the Multiple Sclerosis Impact Scale (MSIS-29): Reliability and Validity Coefficients in a Cohort of Patients with Multiple Sclerosis

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Abstract: The Multiple Sclerosis Impact Scale (MSIS-29) is a widely used patient-reported outcome measure assessing the physical and psychological impact of multiple sclerosis (MS). A validated Romanian version is currently unavailable. To translate, cross-culturally adapt, and validate the Romanian version of the MSIS-29 in patients with multiple sclerosis. The study was conducted in two phases: translation and cross-cultural adaptation following international guidelines, followed by a psychometric validation in a cohort of 28 patients with MS. Acceptability, internal consistency (Cronbach's alpha), test-retest reliability (intraclass correlation coefficient), construct validity (exploratory factor analysis), convergent validity (correlation with EDSS), and known-groups validity were assessed. The Romanian MSIS-29 showed promising internal consistency (Cronbach's α = 0.96 for physical scale, 0.91 for psychological scale) and test-retest reliability (ICC = 0.94 and 0.91). Due to the small sample size (n=28), exploratory factor analysis was performed instead of exploratory factor analysis; exploratory factor analysis yielded a two-factor solution that may resemble the original structure; however, no confirmatory conclusions can be drawn, and these findings are hypothesis-generating only. Convergent validity was supported by correlations with EDSS (r = 0.72 for physical scale, r = 0.41 for psychological scale). Known-groups comparisons showed significantly higher scores in patients with progressive MS and higher disability, although subgroup sizes were very small. No floor or ceiling effects were observed, and missing data were 0%. The Romanian version of the MSIS-29 demonstrates acceptable preliminary reliability and validity. However, due to the small sample size, all results, particularly the factor structure and subgroup comparisons, must be interpreted as exploratory and hypothesis generating. Large scale confirmatory studies (N ≥ 200) are needed before the scale can be used definitively in clinical practice or research

Keywords: MSIS-29; validation; patient-reported outcome measure; quality of life; Romania; psychometric properties; reliability; validity.

1. Introduction

The validation of questionnaires and assessment scales in the language in which they are administered represents an essential step in medical research, ensuring that the instruments used measure the intended concepts in a valid and reliable manner, while preserving their psychometric properties regardless of linguistic or cultural context [1]. The use of translated but unvalidated instruments can lead to measurement errors and misinterpretation of data, affecting both clinical practice and the results of scientific studies [2].

Patient-reported outcome measures (PROMs) have gained increasing recognition in clinical research and routine practice as they provide valuable insights into

the patient's perspective on their health status, symptom burden, and quality of life [3]. These instruments complement objective clinical measures by capturing subjective experiences that may not be adequately reflected in traditional physician-assessed outcomes. In chronic neurological conditions such as multiple sclerosis, where the disease trajectory is unpredictable and the impact on daily functioning is profound, PROMs are particularly valuable for comprehensive patient assessment [4].

Multiple sclerosis (MS) is a chronic, inflammatory, and neurodegenerative disease of the central nervous system, characterized by demyelination and axonal loss, leading to progressive neurological disability [5]. It is one of the most common causes of neurological disability in young adults, with a worldwide prevalence of approximately 2.8 million people [6]. The disease typically manifests between the ages of 20 and 40 years, with a female-to-male ratio of approximately 3:1 [7]. The clinical course of MS is heterogeneous, ranging from relapsing-remitting forms (RRMS) to progressive phenotypes (primary progressive MS - PPMS, and secondary progressive MS - SPMS), each with different trajectories of disability accumulation [8].

The impact of MS on patients' lives extends far beyond the physical symptoms. Patients commonly experience a wide range of impairments, including motor deficits, sensory disturbances, visual problems, fatigue, cognitive dysfunction, bladder and bowel dysfunction, and emotional disturbances such as depression and anxiety [9]. These symptoms collectively contribute to limitations in activities of daily living, reduced social participation, unemployment, and diminished quality of life [10]. Therefore, comprehensive assessment of MS patients should encompass not only neurological impairment measured by scales such as the Expanded Disability Status Scale (EDSS) but also the patient's perception of how the disease affects their daily functioning and psychological well-being [11].

The Multiple Sclerosis Impact Scale (MSIS-29) is a disease-specific, patient-reported outcome measure developed by Hobart and colleagues at King's College Hospital and the National Hospital for Neurology and Neurosurgery in London [12]. It was designed to assess the physical and psychological impact of MS from the patient's perspective, addressing the need for a rigorously developed, psychometrically robust instrument that could be used in both clinical trials and routine practice. The development process involved extensive qualitative work with MS patients, item reduction techniques, and rigorous psychometric testing, resulting in a 29-item questionnaire with two distinct subscales: a 20-item physical impact scale and a 9-item psychological impact scale [12].

The MSIS-29 asks patients to rate the impact of MS on various aspects of their lives over the previous two weeks, using a Likert-type response scale ranging from 1 (not at all) to 5 (extremely). The physical scale includes items related to mobility, dexterity, physical fatigue, and activities of daily living, while the psychological scale encompasses items related to mood, anxiety, cognitive function, and social participation [12]. Scores for each subscale are calculated by summing the relevant items and transforming them to a 0-100 scale, with higher scores indicating greater impact of the disease.

Since its publication, the MSIS-29 has undergone extensive psychometric evaluation and has demonstrated excellent measurement properties. Studies have confirmed its high internal consistency, with Cronbach's alpha coefficients consistently exceeding 0.90 for both subscales [13,14]. Test-retest reliability has been shown to be excellent, with intraclass correlation coefficients above 0.80 [15]. The scale has also demonstrated good responsiveness to clinical change, making it suitable for longitudinal assessment and clinical trials [16]. Furthermore, the two-factor structure (physical and psychological) has been confirmed in multiple populations through exploratory factor analysis [17].

The MSIS-29 has been validated in numerous languages and cultural contexts, reflecting its widespread international acceptance as a gold-standard PROM in MS research. Validated versions currently exist in Danish [18], Dutch [19], German [20],

Spanish [21], Turkish [22], Italian [23], French [24], Portuguese [25], Chinese [26], and Persian [27], among others. These validation studies have consistently confirmed the robust psychometric properties of the scale across different populations, supporting its use as a reliable and valid measure of MS impact. The availability of multiple validated versions enables international multicenter studies and facilitates cross-cultural comparisons of MS impact [28].

In Romania, multiple sclerosis affects approximately 8,000-9,000 people, with an estimated prevalence of 40-50 per 100,000 inhabitants [29]. This gap is particularly problematic for Romanian patients because unvalidated instruments may introduce measurement errors that affect clinical decision-making, limit the comparability of Romanian research with international studies, and potentially lead to inappropriate interpretations of disease impact in a population with distinct cultural and healthcare system characteristics. Without a formally validated version, Romanian clinicians cannot reliably interpret MSIS-29 scores, and Romanian patients remain excluded from international multicenter trials requiring validated patient-reported outcome measures.

The use of unvalidated versions may compromise the accuracy and reliability of the data obtained, limiting the comparability of Romanian studies with international research and potentially affecting clinical decision-making [30].

The process of validating a questionnaire in a new language involves several methodological steps, including forward and backward translation, cross-cultural adaptation, and comprehensive psychometric testing [31-33].

Aim of the study

The study was to conduct a comprehensive psychometric validation of the Romanian version of the Multiple Sclerosis Impact Scale (MSIS-29) in a cohort of patients with multiple sclerosis, thereby providing Romanian clinicians and researchers with a standardized, reliable, and valid patient-reported outcome measure for assessing the physical and psychological impact of the disease.

At present, although the MSIS-29 has been informally used in some clinical settings and research studies in Romania, a formal validation process following international methodological standards has not been performed. Consequently, the psychometric properties of the Romanian version remain unknown, and the interpretability of scores obtained with the current unvalidated version is questionable.

2. Materials and Methods

2.1 Study design

This study was conducted in two distinct phases. The first phase involved the translation and cross-cultural adaptation of the original English version of the MSIS-29 into Romanian, following established international guidelines for the validation of patient-reported outcome measures [41,42]. The second phase was primarily cross-sectional in design for most psychometric analyses (internal consistency, construct validity, convergent validity, known-groups validity), but included a longitudinal component for test-retest reliability assessment, in which a subset of clinically stable patients completed the questionnaire on two occasions 14 days apart. As such, the overall design is best described as a prospective, observational study with both cross-sectional and longitudinal elements.

2.2 Translation and cross-cultural adaptation process

The translation and cross-cultural adaptation of the MSIS-29 into Romanian followed the standardized methodology proposed by Beaton et al. [42] and the ISPOR task force guidelines [43], comprising the following stages:

Stage 1: Forward translation

Two independent forward translations from English to Romanian were performed

by two bilingual translators whose native language was Romanian. The first translator was a neurologist with clinical expertise in multiple sclerosis, familiar with the medical concepts underlying the questionnaire. The second translator was a professional linguist with no medical background, providing a translation that reflected the language used by the general population. Both translators worked independently and produced two distinct Romanian versions (T1 and T2).

Stage 2: Synthesis of translations

The two translators, together with a recording observer (the principal investigator), met to synthesize the two forward translations into a single consensus version (T1-2).

Stage 3: Back translation

The synthesized Romanian version (T1-2) was then back-translated into English by two independent bilingual translators who were native English speakers, fluent in Romanian, and blinded to the original English version. Neither back-translator had medical training, ensuring that the back translation reflected the meaning of the Romanian version without medical interpretation. This process produced two back-translated English versions (BT1 and BT2).

Stage 4: Expert committee review

An expert committee was convened to review all translations (original, forward translations, synthesized version, and back translations) and develop the pre-final Romanian version. The committee consisted of:

- Two neurologists specializing in multiple sclerosis
- One rehabilitation physician
- One psychometrician with experience in questionnaire validation
- One professional linguist
- The four translators involved in the forward and back translation processes

Stage 5: Cognitive debriefing (pre-testing)

The pre-final Romanian version was administered to a pilot sample of 15 patients with multiple sclerosis (separate from the main validation cohort) to assess comprehensibility, clarity, and acceptability. Patients were asked to complete the questionnaire and then participated in a cognitive interview to identify any items that were difficult to understand, ambiguous, or culturally inappropriate.

Stage 6: Final version

The expert committee reviewed the cognitive debriefing results and finalized the Romanian version of the MSIS-29, which was used in the main validation study.

2.3 Study population and setting

This validation study was conducted at the Neurology Department of the Rehabilitation Hospital in Iasi, Romania, between January 2025 and December 2025.

Inclusion criteria:

- Confirmed diagnosis of multiple sclerosis according to the revised McDonald criteria 2017 [44]
- Age ≥ 18 years
- Ability to understand and complete the questionnaire independently or with minimal assistance
- Signed informed consent to participate in the study

Exclusion criteria:

- Age < 18 years

- Presence of a clinical relapse or corticosteroid treatment within the last 30 days (to avoid acute symptom fluctuations affecting responses)
- Severe cognitive impairment that prevented understanding of the questionnaire items (as judged by the attending neurologist). It should be noted that no standardized cognitive screening instrument (e.g., MMSE or MoCA) was used; the exclusion relied solely on clinical judgment.
- Presence of other significant neurological, psychiatric, or medical conditions that could substantially impact quality of life independently of MS (e.g., stroke, Parkinson's disease, major depression, active malignancy)

This sample size (n = 28) is acceptable for preliminary assessments of acceptability, internal consistency, and test-retest reliability. However, it is important to note that larger samples (typically N ≥ 200 or 5–10 cases per item) are required for exploratory factor analysis [45,46]. Therefore, the factor analytic results presented in this study should be considered exploratory and require confirmation in larger independent samples. This sample size is comparable to several preliminary validation studies of the MSIS-29 [47,48], although more recent validation studies have employed larger cohorts.

2.4 Data collection procedures

All eligible patients who agreed to participate provided written informed consent before enrollment. Data were collected through a combination of clinical interview, neurological examination, and self-administered questionnaires.

Clinical and demographic data:

The following variables were collected for each patient:

- Demographic characteristics: age, gender, educational level (years of education), occupational status
- Clinical characteristics: disease duration (years from diagnosis), clinical form of MS (relapsing-remitting, secondary progressive, primary progressive), number of relapses in the last two years, current disease-modifying treatment
- Disability assessment: Expanded Disability Status Scale (EDSS) score [49], assessed by a certified neurologist on the same day as questionnaire administration

Questionnaire administration:

Patients completed the Romanian version of the MSIS-29 during their routine clinical visit, in a quiet room without time pressure. The questionnaire was self-administered, but a trained researcher was available to provide assistance if needed, particularly for patients with visual or motor impairments affecting their ability to write.

2.5 Instruments

Multiple Sclerosis Impact Scale (MSIS-29):

The MSIS-29 is a 29-item, self-administered questionnaire that assesses the physical (20 items) and psychological (9 items) impact of multiple sclerosis over the previous two weeks [50]. Each item is rated on a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely). Subscale scores are calculated by summing the item responses and transforming them to a 0-100 scale using the formula:

Physical score = [(sum of 20 physical items - 20) / 80] × 100

Psychological score = [(sum of 9 psychological items - 9) / 36] × 100

Higher scores indicate greater impact of the disease on the patient's life. The original English version has demonstrated excellent psychometric properties, including high internal consistency (Cronbach's $\alpha > 0.90$ for both subscales), good test-retest reliability (ICC > 0.80), and strong construct validity [50,51].

Expanded Disability Status Scale (EDSS):
The EDSS is a physician-assessed scale that quantifies neurological impairment and disability in multiple sclerosis [49]. It consists of eight functional system scores (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral, and other) and an ambulation score, combined to generate a total score ranging from 0 (normal neurological examination) to 10 (death due to MS). The EDSS is the most widely used disability measure in MS clinical practice and research [52]. In this study, EDSS scores were categorized as mild (0-3.5), moderate (4.0-6.0), and severe (6.5-9.5) disability, based on established conventions [53].

2.6 Statistical analysis

Statistical analysis was performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA) and JASP version 0.18.3 (University of Amsterdam, Netherlands). The significance level was set at $\alpha = 0.05$ for all analyses. Normality of the continuous variables was assessed using the Shapiro-Wilk test and visual inspection of Q-Q plots. All MSIS-29 subscale scores and EDSS scores were found to be non-normally distributed ($p < 0.05$ for Shapiro-Wilk test), therefore non-parametric tests were used for all correlational and group comparison analyses.

Descriptive statistics: Continuous variables were expressed as mean, standard deviation (SD), median, minimum, and maximum. Categorical variables were expressed as frequencies and percentages.

Acceptability: Missing data were quantified. Floor and ceiling effects were defined as >15% of patients achieving the lowest (0) or highest (100) possible score.

Reliability:

- Internal consistency was assessed using Cronbach's alpha coefficient for each subscale, with values ≥0.90 considered excellent for individual patient assessment.
- Test-retest reliability was evaluated using the intraclass correlation coefficient (ICC), two-way random effects model, absolute agreement definition (ICC(2,1)), with values >0.90 indicating excellent reliability. The 95% confidence intervals were calculated using bootstrapping (1000 resamples).

Validity:

- **Construct validity:** Given the small sample size (n = 28), which is below the recommended minimum of 5–10 cases per item for exploratory factor analysis (CFA), an exploratory factor analysis (EFA) was conducted instead. EFA was performed using principal axis factoring with varimax rotation. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity were used to assess the suitability of the data for factor analysis. Factor extraction was based on eigenvalues > 1 and inspection of the scree plot. Factor loadings ≥ 0.40 were considered meaningful. Results from this EFA should be interpreted as hypothesis-generating and require confirmation in larger samples.
- **Convergent validity:** Spearman's rank correlation coefficient (rho) was used to examine the relationship between MSIS-29 subscale scores and EDSS scores due to non-normal distributions.
- **Known-groups validity:** Differences between clinical subgroups were compared using the Mann-Whitney U test (for two groups) or Kruskal-Wallis test (for three or more groups), as appropriate.

Additional analyses: Exploratory analyses examined correlations between MSIS-29 scores and demographic/clinical variables using Spearman's rho for continuous variables and Mann-Whitney U test for categorical variables.

3. Results

3.1 Demographic and clinical characteristics of the study population

A total of 28 patients with multiple sclerosis were included in the final analysis, after the exclusion of one patient from the initial database due to incomplete data. The demographic and clinical characteristics of the study population are presented in Table 1.

The study group comprised 21 women (75.0%) and 7 men (25.0%), with a female-to-male ratio of 3:1, consistent with the known epidemiology of multiple sclerosis. The mean age of the patients was 47.64 years (SD = 11.43), ranging from 23 to 70 years. The mean disease duration was 8.96 years (SD = 6.84), with a median of 7.00 years, reflecting a wide range from recently diagnosed patients to those with long-standing disease.

Regarding the clinical form of MS, the majority of patients (n = 24, 85.7%) had relapsing-remitting multiple sclerosis (RRMS), while 4 patients (14.3%) had progressive forms (3 with secondary progressive MS and 1 with primary progressive MS). This distribution is representative of the general MS population, where RRMS accounts for approximately 85% of cases at disease onset. The mean EDSS score was 3.14 (SD = 1.76), with a median of 2.75, indicating a predominantly mild to moderate level of disability in the study cohort. When categorized by disability severity, 18 patients (64.3%) had mild disability (EDSS < 4.0), 8 patients (28.6%) had moderate disability (EDSS 4.0-6.0), and 2 patients (7.1%) had severe disability (EDSS > 6.0).

The mean number of relapses in the previous two years was 2.64 (SD = 2.20), and the mean educational level was 13.93 years (SD = 3.91), indicating a relatively well-educated population.

Table 1. Demographic and clinical characteristics of the study population

Variable	Value
Gender, n (%)	
Female	21 (75.0)
Male	7 (25.0)
Age (years)	
Mean (SD)	47.64 (11.43)
Median (range)	48.50 (23-70)
Disease duration (years)	
Mean (SD)	8.96 (6.84)
Median (range)	7.00 (1-25)
Clinical form of MS, n (%)	
Relapsing-remitting (RRMS)	24 (85.7)
Secondary progressive (SPMS)	3 (10.7)
Primary progressive (PPMS)	1 (3.6)
EDSS score	
Mean (SD)	3.14 (1.76)
Median (range)	2.75 (1.0-6.5)
EDSS category, n (%)	
Mild disability (EDSS < 4.0)	18 (64.3)
Moderate disability (EDSS 4.0-6.0)	8 (28.6)
Severe disability (EDSS > 6.0)	2 (7.1)
Number of relapses (last 2 years)	
Mean (SD)	2.64 (2.20)
Median (range)	2.00 (1-12)
Educational level (years)	
Mean (SD)	13.93 (3.91)
Median (range)	14.00 (4-23)

3.2 MSIS-29 scores

The mean MSIS-29 physical scale score was 46.82 (SD = 24.31), with a median of 45.00 and a range from 5.00 to 91.25. The mean MSIS-29 psychological scale score was 42.86 (SD = 22.54), with a median of 38.89 and a range from 5.56 to 86.11. These scores indicate a moderate level of disease impact in the study population, with considerable variability reflecting the heterogeneity of disability levels (Table 2).

Table 2. MSIS-29 subscale scores in the study population

MSIS-29 subscale	Mean (SD)	Median	Minimum	Maximum
Physical scale (0-100)	46.82 (24.31)	45.00	5.00	91.25
Psychological scale (0-100)	42.86 (22.54)	38.89	5.56	86.11

3.3 Acceptability

Missing data: There were no missing responses for any of the 29 items of the MSIS-29 across the 28 patients, indicating excellent data completeness (0% missing data). All patients completed all items without omission.

Time to completion: The mean time required to complete the questionnaire was 8.4 minutes (SD = 2.3 minutes), ranging from 5 to 14 minutes. This demonstrates that the Romanian MSIS-29 is feasible for use in routine clinical practice without causing excessive burden to patients.

Floor and ceiling effects: No floor or ceiling effects were observed for either subscale. For the physical scale, no patient achieved the minimum possible score of 0, and only one patient (3.6%) achieved a score close to the maximum (91.25), below the 15% threshold considered indicative of a ceiling effect. For the psychological scale, no patient achieved the minimum score of 0, and no patient achieved the maximum score of 100. These findings indicate that the Romanian MSIS-29 has good discriminative ability across the full range of disease impact.

3.4 Reliability

Internal consistency: The Romanian MSIS-29 demonstrated excellent internal consistency for both subscales. Cronbach's alpha coefficient was 0.96 for the physical scale (20 items) and 0.91 for the psychological scale (9 items), both exceeding the recommended threshold of 0.90 for individual patient assessment. Corrected item-total correlations ranged from 0.58 to 0.89 for the physical scale and from 0.62 to 0.84 for the psychological scale, all exceeding the acceptable threshold of 0.30, indicating that each item contributes meaningfully to its respective subscale (Table 3).

Table 3. Internal consistency of the Romanian MSIS-29

Subscale	Number of items	Cronbach's α	Corrected item-total correlation (range)
Physical scale	20	0.96	0.58 - 0.89
Psychological scale	9	0.91	0.62 - 0.84

Test-retest reliability: In the stable subgroup of 15 patients who completed the MSIS-29 on two occasions 14 days apart, the intraclass correlation coefficients (ICC) demonstrated excellent stability. For the physical scale, the ICC was 0.94 (95% CI: 0.88-0.97), and for the psychological scale, the ICC was 0.91 (95% CI: 0.83-0.95). These

values indicate excellent test-retest reliability according to established criteria, confirming that the Romanian MSIS-29 produces stable scores over time in clinically stable patients.

3.5 Validity

3.5.1 Construct validity – exploratory factor analysis

Due to the limited sample size (n=28), which is far below the recommended minimum of 5–10 cases per item (i.e., 145–290 patients) for exploratory factor analysis (CFA), a confirmatory analysis was not possible. No exploratory factor analysis was performed, and no fit indices (CFI, TLI, RMSEA) were computed. The EFA results are strictly exploratory and hypothesis-generating. Instead, an exploratory factor analysis (EFA) was conducted to generate hypotheses about the factor structure of the Romanian MSIS-29 in this sample. The following results are strictly exploratory and hypothesis-generating; they do not confirm the factor structure.

The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.78, and Bartlett's test of sphericity was significant ($\chi^2 = 1243.56$, df = 406, $p < 0.001$), indicating that the correlation matrix was suitable for factor analysis. Principal axis factoring with varimax rotation extracted two factors with eigenvalues > 1, explaining 68.4% of the total variance. The first factor (eigenvalue = 14.2) explained 49.0% of the variance and corresponded to the physical items (loadings 0.58–0.91). The second factor (eigenvalue = 5.6) explained 19.4% of the variance and corresponded to the psychological items (loadings 0.54–0.88). Cross-loadings were minimal (< 0.30).

hese exploratory results suggest a two-factor structure that may be similar to the original MSIS-29, but no confirmatory claims can be made. Because the sample size (n=28) is very small, this finding is strictly hypothesis-generating. It does not confirm the two-factor structure; confirmation requires a exploratory factor analysis in a much larger sample (N ≥ 200). However, no confirmatory conclusions can be drawn from this EFA. The factor solution is likely unstable at n=28 and requires confirmation through CFA in a much larger, independent Romanian sample (N ≥ 200).

3.5.2 Convergent validity

Spearman's rank correlation coefficients between MSIS-29 subscale scores and EDSS scores are presented in Table 4. As hypothesized, there was a strong positive correlation between the MSIS-29 physical scale and EDSS ($r = 0.72$, $p < 0.001$), indicating that greater physical disability is associated with higher perceived physical impact of the disease. The correlation between the MSIS-29 psychological scale and EDSS was moderate ($r = 0.41$, $p = 0.03$), consistent with the expectation that psychological impact is less directly related to physical disability.

Table 4. Correlations between MSIS-29 subscales and EDSS

MSIS-29 subscale	Spearman's rho	p-value	Interpretation
Physical scale	0.72	< 0.001	Strong correlation
Psychological scale	0.41	0.03	Moderate correlation

3.5.3 Known-groups validity

The Romanian MSIS-29 demonstrated excellent ability to discriminate between groups of patients with different clinical characteristics, supporting its known-groups validity (Table 5).

Comparison by clinical form: Patients with progressive forms of MS (SPMS and PPMS, n = 4) had significantly higher scores on both MSIS-29 subscales compared to patients with RRMS (n = 24). The mean physical scale score was 78.75 (SD = 9.46) in progressive MS versus 41.50 (SD = 21.53) in RRMS ($p < 0.001$). Similarly, the mean psychological scale score was 65.28 (SD = 12.47) in progressive MS versus 39.15 (SD = 21.53) in RRMS ($p = 0.02$).

Comparison by disability level: Patients with moderate-to-severe disability (EDSS ≥ 4.0, n = 10) had significantly higher MSIS-29 scores compared to patients with mild disability (EDSS < 4.0, n = 18). The mean physical scale score was 67.50 (SD = 16.82) in the moderate-to-severe group versus 35.28 (SD = 19.46) in the mild group ($p < 0.001$). The mean psychological scale score was 55.56 (SD = 20.84) versus 35.80 (SD = 20.42), respectively ($p = 0.02$).

Comparison by disease duration: Patients with longer disease duration (≥ 10 years, n = 11) had significantly higher physical scale scores compared to those with shorter disease duration (< 10 years, n = 17): 59.55 (SD = 23.84) versus 38.97 (SD = 21.53) ($p = 0.02$). The difference in psychological scale scores (48.99 vs. 38.89) did not reach statistical significance ($p = 0.24$), although the trend was in the expected direction.

Table 5. Known-groups validity of the Romanian MSIS-29

Group comparison	N	Physical scale mean (SD)	p-value	Psychological scale mean (SD)	p-value
Clinical form					
RRMS	24	41.50 (21.53)	< 0.001	39.15 (21.53)	0.02
Progressive MS	4	78.75 (9.46)		65.28 (12.47)	
Disability level					
Mild (EDSS < 4.0)	18	35.28 (19.46)	< 0.001	35.80 (20.42)	0.02
Moderate-severe (EDSS ≥ 4.0)	10	67.50 (16.82)		55.56 (20.84)	
Disease duration					
< 10 years	17	38.97 (21.53)	0.02	38.89 (22.24)	0.24
≥ 10 years	11	59.55 (23.84)		48.99 (22.98)	

3.6 Exploratory analyses

3.6.1 Correlations with demographic variables

Correlations between MSIS-29 scores and demographic variables are presented in Table 6. Age showed a moderate positive correlation with the physical scale ($r = 0.43$, $p = 0.02$) but not with the psychological scale ($r = 0.18$, $p = 0.36$), indicating that older patients report greater physical impact of MS. Educational level showed a weak negative correlation with both subscales, suggesting that higher education may be associated with slightly lower perceived disease impact, although these correlations did not reach statistical significance. There was no significant difference in MSIS-29 scores between male and female patients ($p > 0.05$ for both subscales).

Table 6. Correlations between MSIS-29 scores and demographic variables

Variable	Physical scale	Psychological scale
Age (years)	r = 0.43, p = 0.02	r = 0.18, p = 0.36
Educational level (years)	r = -0.21, p = 0.28	r = -0.19, p = 0.32
Gender (male vs. female)	p = 0.42	p = 0.38

4. Discussion

Authors This study evaluated the psychometric properties of the Romanian version of the Multiple Sclerosis Impact Scale (MSIS-29) in a cohort of 28 patients with multiple sclerosis. The preliminary results suggest that the Romanian MSIS-29 may be a valid, reliable, and acceptable instrument for assessing the physical and psychological impact of MS in Romanian patients, although these findings require confirmation in larger samples.

Summary of main findings

The Romanian MSIS-29 showed excellent internal consistency, with Cronbach's alpha coefficients of 0.96 for the physical scale (20 items) and 0.91 for the psychological scale (9 items). These values exceed the recommended threshold of 0.90 for individual patient assessment [54] and are comparable to those reported in other international validation studies [55-57].

Test-retest reliability was excellent, with intraclass correlation coefficients of 0.94 for the physical scale and 0.95% CI: 0.88-0.97) and 0.91 (95% CI: 0.83-0.95) for the psychological scale, indicating stable scores over time in clinically stable patients. These values exceed the recommended standard of 0.90 for excellent reliability [58].

Regarding validity, due to the limited sample size, exploratory factor analysis (EFA) was conducted instead of exploratory factor analysis. The EFA suggested a two-factor structure consistent with the original scale, but this finding is hypothesis-generating only and requires confirmation in larger samples. No confirmatory fit indices (e.g., CFI, TLI, RMSEA) were computed.

Convergent validity was demonstrated by strong correlation between the physical scale and EDSS ($r = 0.72$, $p < 0.001$) and moderate correlation between the psychological scale and EDSS ($r = 0.41$, $p = 0.03$). Known-groups validity was confirmed by significantly higher scores in patients with progressive MS ($p < 0.001$), higher disability levels ($p < 0.001$), and longer disease duration ($p = 0.02$).

Acceptability was excellent, with no missing data, a mean completion time of 8.4 minutes, and no floor or ceiling effects observed for either subscale.

Comparison with other validation studies

While the preliminary results suggest that the Romanian MSIS-29 may have psychometric properties broadly comparable to those reported in larger validation studies, this must not be interpreted as evidence of equivalence. The small sample size (n=28) renders all such comparisons unstable and potentially misleading. Definitive comparisons require a larger confirmatory study.The preliminary results obtained with the Romanian version are directionally consistent with those reported in larger validation studies from other countries. However, due to the small sample size, these similarities must be interpreted with caution and do not constitute confirmatory evidence.

In the Danish validation study, Broch et al. reported Cronbach's alpha values of 0.95 for the physical scale and 0.92 for the psychological scale, with ICC values of 0.92 and 0.89, respectively [59].

The Dutch validation study by van der Linden et al. demonstrated Cronbach's alpha values of 0.94 for the physical scale and 0.91 for the psychological scale, with a correlation between the physical scale and EDSS of $r = 0.68$ [60], slightly lower than our observed correlation of 0.72 but still within the strong correlation range.

Similarly, the Spanish validation study by Vázquez Navarrete et al. reported Cronbach's alpha values of 0.95 for the physical scale and 0.93 for the psychological scale, with a correlation between the physical scale and EDSS of r = 0.71 [61], virtually identical to our findings.

The Turkish validation study by Bingöl et al. found Cronbach's alpha values of 0.94 for the physical scale and 0.90 for the psychological scale, with ICC values of 0.93 and 0.90, respectively [62], again confirming the robust psychometric properties of the scale across different populations.

The German validation study by Schäffler et al. confirmed the two-factor structure of the MSIS-29 using exploratory factor analysis (CFA) in a large sample. We did not perform CFA because our sample size (n=28) was far below the required minimum. Consequently, no fit indices (CFI, TLI, RMSEA) could be calculated, and no comparison between our exploratory results and the German CFA results is possible. Our exploratory factor analysis (EFA) is hypothesis-generating only and should not be misinterpreted as providing confirmatory evidence. The Norwegian validation study by Broch et al. also demonstrated excellent psychometric properties, with Cronbach's alpha values of 0.96 for the physical scale and 0.93 for the psychological scale, and confirmed the two-factor structure through factor analysis [64].

A systematic review by Hobart et al. examined the psychometric properties of the MSIS-29 across multiple validation studies and concluded that it is one of the most robust patient-reported outcome measures available in MS research, with consistently high reliability and validity across different language versions [65].

Clinical implications

If confirmed in larger studies, the availability of a validated Romanian version of the MSIS-29 could have several important clinical implications.

First, it provides Romanian neurologists and rehabilitation physicians with a standardized, psychometrically robust instrument for quantifying the impact of MS from the patient's perspective. This complements objective clinical measures such as the EDSS and enhances comprehensive patient assessment [66].

Second, the MSIS-29 can be used to monitor disease progression and treatment response over time. The absence of floor and ceiling effects and the excellent test-retest reliability make it suitable for longitudinal assessment in both clinical practice and research settings [67].

Third, the validated Romanian version enables the inclusion of Romanian patients in international multicenter studies that require the use of validated patient-reported outcome measures. This facilitates cross-cultural comparisons and contributes to the global MS research effort [68].

Fourth, the MSIS-29 can improve patient-physician communication by providing a structured framework for discussing disease impact. Patients often underreport symptoms during routine clinical consultations, and the use of a standardized questionnaire can help identify areas of concern that might otherwise be overlooked [69].

Comparison with other MS-specific instruments

Several other patient-reported outcome measures are available for MS, including the Functional Assessment of Multiple Sclerosis (FAMS) [70], the Multiple Sclerosis Quality of Life-54 (MSQOL-54) [71], and the Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL) [72]. However, the MSIS-29 offers several advantages: it is shorter than the MSQOL-54, has been more extensively validated than the FAMS, and has demonstrated superior psychometric properties in head-to-head comparisons [73].

MSIS-29 with the FAMS and the SF-36 in a large sample of MS patients and found that the MSIS-29 had better discriminative ability and responsiveness than the other instruments [74]. Similarly, Hoogervorst et al. compared the MSIS-29 with the EDSS and the MS Functional Composite and found that the MSIS-29 provided unique information not captured by these clinician-administered scales [60].

Several subgroup and psychometric analyses were performed despite the limited sample size, including comparisons involving very small subgroups (e.g., progressive MS, n = 4). These findings should therefore be interpreted cautiously and considered preliminary rather than definitive.

Strengths and limitations

Strengths of this study include the rigorous translation and cross-cultural adaptation process following international guidelines, the comprehensive psychometric evaluation including exploratory factor analysis, and the use of a well-characterized clinical sample with diverse disease characteristics.

Several limitations of this study must be acknowledged. First, the sample size (n = 28) is the most important limitation. While this sample size may be acceptable for preliminary assessment of internal consistency and test-retest reliability, it is substantially below the recommended minimum for exploratory factor analysis (which requires 5–10 cases per item, i.e., 145–290 patients for the 29-item MSIS-29). Consequently, we were unable to perform a exploratory factor analysis and instead conducted an exploratory factor analysis, which should be interpreted as hypothesis-generating rather than confirmatory. The results of the EFA require replication in a much larger Romanian cohort. Second, the sample was predominantly composed of patients with relapsing-remitting MS (85.7%) and mild to moderate disability, limiting generalizability to progressive forms and severe disability. Third, the cross-sectional design precluded assessment of responsiveness to clinical change. Fourth, the study was conducted at a single center in one geographic region of Romania. Multicenter studies including patients from different regions of Romania and a larger sample size (ideally N ≥ 200) are needed to confirm the psychometric properties of the Romanian MSIS-29, particularly its factor structure.

5. Conclusions

In this study, the Romanian version of the MSIS-29 showed preliminary, hypothesis-generating results: internal consistency estimates were high (though imprecise), test-retest reliability was good (in a very small stable subsample), and an exploratory factor analysis suggested a two-factor structure resembling the original. However, all these findings are provisional and require confirmation in a large, adequately powered study.The scale was well-accepted by patients, with no missing data and no floor or ceiling effects.

However, these findings must be interpreted with extreme caution due to the small sample size (N = 28). The small sample precluded exploratory factor analysis, made the factor structure unstable, reduced the precision of reliability estimates, and rendered subgroup comparisons underpowered. Therefore, all results presented here are exploratory and hypothesis-generating, not confirmatory.

The Romanian MSIS-29 cannot yet be recommended for definitive clinical or research use.Instead, it should be considered a promising instrument that requires further validation in a large, multicenter Romanian cohort (N ≥ 200) with exploratory factor analysis, more precise reliability estimates, and adequately powered subgroup analyses. Only after such confirmatory studies can the scale be confidently adopted in routine practice.

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