ORIGINAL ARTICLE

Two Multiple Sclerosis Quality-of-Life Measures: Comparison in a National Sample

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ABSTRACT: ***Background:*** Multiple sclerosis (MS) has a profound impact on patients' health-related quality of life (HRQoL). It is unclear how HRQoL can be best assessed for different purposes. This study aimed to compare two HRQoL questionnaires of differing lengths for feasibility of administration, patient perceptions and psychometric properties. ***Methods:*** This was an open-label, 24-month study in 334 patients with relapsing MS treated with subcutaneous interferon β-1a. At baseline and months 6, 12, 18 and 24, patients completed the Multiple Sclerosis International Quality of Life (MusiQoL) and Multiple Sclerosis Quality of Life-54 (MSQOL-54) questionnaires and compared them using an evaluation questionnaire. HRQoL scores over time and psychometric properties (correlations with clinical disease measures, relative validity and responsiveness to change) of the questionnaires were assessed. ***Results:*** A minority of patients had missing items on either HRQoL measure. Completion time was significantly shorter for MusiQoL versus MSQOL-54 ($p < 0.0001$). Patients felt that MusiQoL was easier to use than MSQOL-54 but preferred MSQOL-54 in terms of thoroughness. Mean HRQoL scores increased significantly from baseline to 24 months; correlations of both measures were stronger with an anxiety and depression measure than with disability or recent relapse occurrence. Relative validity and responsiveness to change were similar for both instruments. ***Conclusion:*** The shorter MusiQoL is suitable for evaluating HRQoL in patients with MS and may be more practical to administer than the more thorough MSQOL-54.

RÉSUMÉ: Comparaison, dans un échantillon national, de deux mesures de la qualité de vie dans la sclérose en plaques : ***Contexte:*** La sclérose en plaques (SP) a un impact important sur la qualité de vie reliée à la santé (QVS) chez les patients qui en sont atteints. La meilleure façon d'évaluer la QVS à différentes fins demeure à préciser. Le but de l'étude était de comparer deux questionnaires de QVS de différente longueur pour évaluer la faisabilité d'administration, les perceptions des patients et les propriétés psychométriques. ***Méthode:*** Il s'agit d'une étude ouverte de 24 mois portant sur 334 patients atteints de SP cyclique traités par l'interféron ß-1a sous-cutané. Les patients ont complété les questionnaires *Multiple Sclerosis International Quality of Life* (MusiQoL) et *Multiple Sclerosis Quality of Life-54* (MSQOL-54) au début de l'étude, à 6, 12, 18 et 24 mois du début et ils les ont comparés au moyen d'un questionnaire d'évaluation. Les scores au QVS et les propriétés psychométriques (corrélations avec les mesures de la maladie clinique, la validité relative et la capacité d'adaptation au changement) des questionnaires ont été évalués. ***Résultats:*** L'une ou l'autre des mesures de la QVS comportait des items manquants pour une minorité de patients. Le temps requis pour compléter les questionnaires était significativement plus court pour le MusiQoL que pour le MSQOL-54 ($p<0,0001$). Les patients estimaient que le MusiQoL était plus facile à utiliser que le MSQOL-54, mais préféraient le MSQOL-54 qui est plus approfondi. Les scores moyens aux QVS avaient augmenté significativement à 24 mois par rapport aux scores initiaux. Les corrélations entre les deux mesures étaient plus fortes pour la mesure de l'anxiété et de la dépression que pour l'invalidité ou une récurrence récente de la maladie. La validité relative et l'adaptation au changement étaient semblables pour les deux instruments. ***Conclusion:*** Le Questionnaire MusiQoL, qui est plus court, est approprié pour évaluer la QVS chez les patients atteints de SP et peut être plus pratique à administrer que le MSQOL-54 qui est plus approfondi.

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Although clinical assessment of patients with multiple sclerosis (MS) tends to focus on physical disability, the importance of monitoring health-related quality of life (HRQoL) is increasingly recognized.[1-4] HRQoL instruments can provide additional information on disease impact by assessing mental and social health dimensions of QoL, such as psychological state and social interaction, which would not be evaluated using observer-based measures focusing on physical disability.[5]

Some HRQoL instruments are available for use in patients with MS, including generic and MS-specific measures.[2,4,6] Instruments specific to MS may offer a more comprehensive assessment of the disease's impact on health compared with generic instruments, but they do not enable cross-disease comparisons.[7-9] One of the most widely used MS-specific questionnaires is the Multiple Sclerosis Quality of Life-54 (MSQOL-54) instrument.[9,10] This questionnaire includes the generic Short-Form 36-item QoL instrument, supplemented with 18 MS-specific items that were based on

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expert opinion and literature review. Reliability and validity in MS patient samples in several countries have been reported.[11,12]

The MS International QoL (MusiQoL) questionnaire is a self-administered, multi-dimensional, MS-specific questionnaire that is available in 14 languages.[13] This questionnaire was developed from patient interviews and designed specifically to reflect patients' perspectives of how MS affects their daily lives. The MusiQoL questionnaire has been validated internationally across 15 countries in approximately 2000 patients with different types and severities of MS[13] and has also been validated locally in several countries.[14-20]

This study aimed to assess and compare the feasibility of administration, patient-perceived acceptability, content relevance and psychometric properties of the MusiQoL and MSQOL-54 questionnaires in patients with relapsing MS treated with subcutaneous (sc) interferon (IFN) β-1a.

Methods

Study design and treatment

This was a Phase IV, observational, open-label, single-arm, 24-month study conducted between July 2005 and June 2011 across 34 MS clinics in Canada (ClinicalTrials.gov identifier: NCT01141751). Patients received treatment with sc IFN β-1a, 44 or 22 μg three times weekly (tiw). The study was conducted in accordance with the International Conference on Harmonisation/ Good Clinical Practice Guidelines and local regulations. An institutional review board or independent ethics committee approved the protocol at each centre before study initiation. All patients gave written informed consent.

Patients

For inclusion in the study, patients were required to have a confirmed diagnosis of relapsing MS according to the McDonald (2001) diagnostic criteria[21] and to be eligible for, and willing to start, treatment with sc IFN β-1a tiw as prescribed by their treating physician. Patients were excluded if they were unable to complete the HRQoL questionnaires without assistance at baseline (Day 1) or if they had taken disease-modifying drugs within the last month (or 30 days) prior to study entry.

Study procedures and assessments

Clinic visits were scheduled at baseline and months 6, 12, 18 and 24. Patients who withdrew from the study were invited to return for an early termination (ET) visit. At baseline, patients underwent a physical examination, and their demographic data and medical history were collected. Patients completed the MusiQoL and MSQOL-54 questionnaires at baseline and each subsequent visit. The content of these questionnaires is detailed in Supplemental files 1 and 2. For both questionnaires, dimension (scale) and global (summary) scores are expressed on a scale of 0 (poorest QoL) to 100 (best possible QoL). The MusiQoL questionnaire yields one global index score and nine dimension scores, while MSQOL-54 produces two global scores (physical and mental health composite scores) and 14 dimension scores. At baseline, MusiQoL was usually completed first, followed by MSQOL-54, and the sequence was reversed at each subsequent visit. Time to completion was recorded for the administration of each measure; calculated durations of >60 minutes were recorded as 60 minutes. At each visit, patients compared the two HRQoL instruments for perceived acceptability and content relevance using a seven-item, self-administered evaluation questionnaire (Supplemental file 3).

Other assessments at each visit included: number of relapses over the previous six months; Expanded Disability Status Scale (EDSS) score; clinical global impression (CGI) rating (mild, moderate or severe disease); and rating of change in health status ("*Since the last completion of the questionnaire, the health status of the subject: has deteriorated; has remained stable; has improved; or is unknown*") over the previous six months or since the last study visit, as assessed by the examiner. A relapse was defined as a new or worsening neurological symptom, in the absence of fever, lasting for ≥24 hours, accompanied by an objective change (i.e. symptomatic) in the relevant Kurtzke Functional Systems examination[22] and preceded by ≥30 days of clinical stability or improvement. Additional self-administered measures were the Hospital Anxiety and Depression Scales (HADS).

Study endpoints

The primary endpoints were the number of missing items on the MusiQoL and MSQOL-54 questionnaires, the time taken to complete each questionnaire and responses to the seven-item evaluation questionnaire comparing the two HRQoL instruments at each visit. Secondary endpoints included HRQoL scores over time and the relationship between HRQoL scores and number of relapses, EDSS scores and HADS subscores at baseline, 24 months and ET visit.

Analyses comparing the associations and construct validity of the two HRQoL questionnaires at baseline were scale–scale correlations and relative validity, which examined the extent to which the global scores were associated with CGI rating (mild or moderate/severe), HADS subscores (normal 0–7; possible 8–10; case >10) and employment status (employed or unemployed).[23]

Responsiveness to change in HRQoL was assessed using effect size relative to the following external criteria for HRQoL change: change in categorization of HADS subscores (normal 0–7; possible 8–10; case >10) between baseline and six months; examiner's global rating of change in health status at six months (improved, same or worsened); and change in CGI rating between baseline and six months (improved, same or worsened).[24] (We used baseline and six months for this analysis because the 'changed' groups were very small at the later follow-ups due in part to attrition over time.)

Statistical analyses

Data were analysed using SAS version 9.2 software (SAS Institute, Cary, NC, USA) and p-values were not adjusted for multiple comparisons.

To detect a difference of 2.882 in the mean MusiQoL global index scores at baseline and 24 months, assuming a standard deviation (SD) of 14.480 and using a paired *t*-test with a two-sided significance level of 0.05, 200 patients were required. With 68–73% of patients expected to experience clinical activity over 24 months (based on historical data[25]) and 20% expected to discontinue the study, the planned sample size was 360 patients. This sample size was considered sufficient to estimate the null hypothesis that 50% of patients who responded preferred MusiQoL, with a precision of 23% and a two-sided risk of 5%.

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Two-sided p-values for the primary endpoints were calculated assuming the null hypothesis that 50% of patients who responded preferred one measure or the other, using the binary proportion for one-way tables. Paired differences were estimated using the two-sided Wilcoxon matched pairs signed-rank test.

A Generalized Estimating Equation approach was used to analyse the effects of the order in which the two questionnaires were administered on the results for Questions 1–5 of the evaluation questionnaire. The analysis was performed using the GENMOD procedure with a binomial distribution, logit link and an unstructured correlation modelling the probability that MSQOL-54 was preferred. An intercept-only model using all available data (the ET data were allocated to month 6, 12, 18 or 24) provided a probability estimate, 95% confidence interval and p-value based on a robust standard error accommodating the correlation between time points. A second model, using the time point variable only, tested whether patient preferences varied at study visits.

Spearman correlation coefficients were calculated to estimate the relationships between HRQoL global scores and number of relapses, EDSS scores and HADS subscores and between global scores on the two questionnaires, with −1, 0 and +1 corresponding to perfect negative correlation, no correlation and perfect positive correlation, respectively.

For the relative validity analyses, F-ratios were computed for the global and dimension scores of each HRQoL measure across CGI rating, HADS and employment status categories using one-way analysis of variance. The global or dimension score with the highest F-ratio for a given criterion variable was judged to be the most sensitive to differences across categories of that criterion variable. Relative validity was calculated by dividing the F-ratio of each HRQoL global or dimension score with a reference scale, corresponding to the smallest F-ratio obtained for a global or dimension score on either of the two HRQoL measures.[26]

In the responsiveness-to-change analyses, the changed group for each of the external criteria included patients with improved or worsened status at six months, with the sign reversed for patients with worsening status over this time. To estimate responsiveness, effect sizes were calculated as the raw score change in the changed group divided by the baseline SD and classified as small (0.20–0.49), medium (0.50–0.79) or large (≥0.80).[27]

Results

Patients

A total of 334 patients were enrolled into the study. Patient disposition is shown in Figure 1. Baseline sociodemographic and disease characteristics are presented in Table 1. At enrollment, the median time since diagnosis of MS was four months. The mean (SD) time on study was 19.5 (7.2) months, and median (range) time on study was 23.5 (0.0–30.8) months. The percentages of patients completing MusiQoL first (before MSQOL-54) at baseline and months 12 and 24 were 96%, 94% and 97%, respectively; the percentages of patients completing MSQOL-54 first (before MusiQoL) at months 6 and 18 were 93% and 92%, respectively. Fifty-nine percent (81 of 138) study participants who withdrew from the study before 24 months attended an early termination (ET) visit, at which study data were collected; only 57 (17%) of all study enrollees had no ET or 24-month follow-up data. At the ET visit, MusiQoL was completed first by 70% of patients.

Ease of administration of MusiQoL vs MSQOL-54

Few patients had missing items on either questionnaire but, at each visit, the proportion of missing items was numerically lower for MusiQoL (7.2–12.8%) compared with MSQOL-54 (11.1–16.4%), although the differences were not statistically significant. The impact of missing questionnaire items on global and dimension score calculations is shown in Supplemental files 4 and 5.

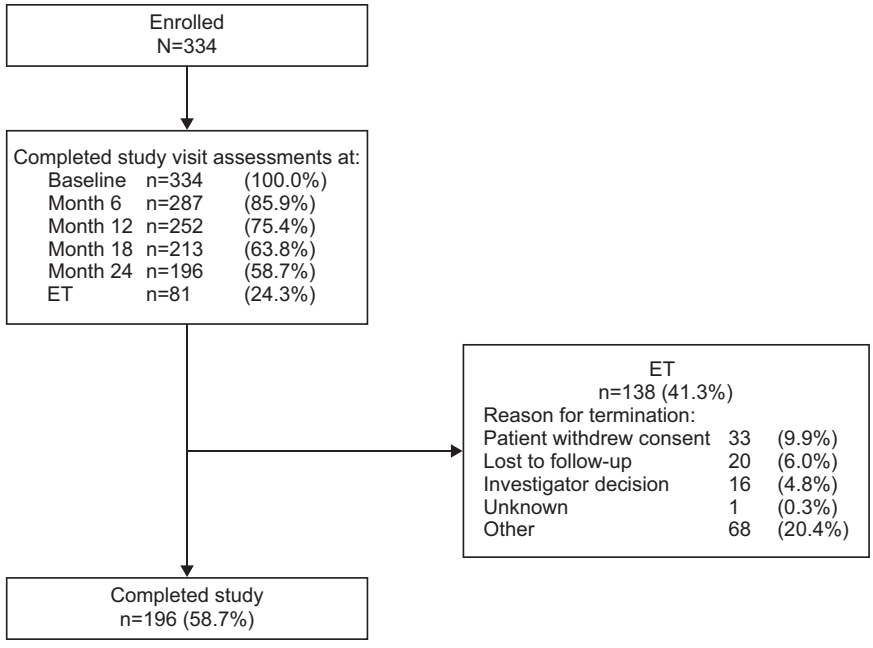

Figure 1: *Patient disposition. ET = early termination.*

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Table 1: Sociodemographics and disease characteristics at baseline and over time

Characteristic	(N = 334)
Baseline sociodemographic and disease characteristics	
Age, years, mean (SD)	38.7 (9.3)
Female, n (%)	254 (76.0)
Caucasian, n (%)	309 (92.5)
Employment status, n (%)	
Student	20 (6.0)
Full-time, part-time or retired workers	227 (68.0)
Unemployed	86 (25.7)
Never employed outside the home	1 (0.3)
MS classification, n (%)	
Relapsing–remitting	319 (95.5)
Secondary-progressive	6 (1.8)
Clinically isolated syndrome	9 (2.7)
Time since MS symptoms onset, months, median (range)	26.0 (0–422)
Time since MS diagnosis, months, median (range)[a]	4.0 (0–386)
Previously received disease-modifying drugs, n (%)	68 (20.4)
HRQoL scores, mean (SD)	
MusiQoL global index[a]	71.9 (14.8)
MSQOL-54 physical health[b]	60.9 (19.7)
MSQOL-54 mental health[c]	65.6 (20.5)
EDSS score, n (%)	
0	39 (11.7)
1.0–1.5	116 (34.7)
2.0–2.5	97 (29.0)
3.0–3.5	46 (13.8)
4.0–4.5	17 (5.1)
5.0–5.5	9 (2.7)
6.0–6.5	10 (3.0)
≥ 7.0	0
Mean (SD)	2.0 (1.4)
HADS subscore, mean (SD)	
Anxiety[d]	7.1 (4.1)
Depression[e]	4.4 (3.5)
Clinical global impression, n (%)	
Mild	264 (79.0)
Moderate	63 (18.9)
Severe	4 (1.2)
Unknown	3 (0.9)
Changes from baseline in HRQoL scores and clinical disease characteristics over time	
Paired change from baseline in HRQoL score, mean (SD) points	
MusiQoL global index	
At 24 months[f]	2.5 (12.0); p = 0.002
At ET[g]	0.3 (13.3); NS
MSQOL-54 physical health composite	
At 24 months[f]	2.2 (15.3); p < 0.05
At ET[g]	0.3 (14.4); NS
MSQOL-54 mental health composite	
At 24 months[f]	4.3 (19.1); p < 0.001
At ET[g]	1.3 (19.2); NS
Number of relapses experienced during the previous 6 months, mean (SD)	
At 24 months[f]	0.13 (0.39)
At ET[g]	0.22 (0.50)
Paired change from baseline in EDSS score, mean (SD) points	
At 24 months[f]	0.1 (1.0); NS
At ET[g]	0.1 (1.0); NS
Paired change from baseline in HADS anxiety subscore, mean (SD) points	
At 24 months[f]	− 1.0 (3.6); p < 0.0001
At ET[g]	− 0.5 (3.5); NS
Paired change from baseline in HADS depression subscore, mean (SD) points	
At 24 months[f]	− 0.2 (3.0); NS
At ET[g]	0.0 (2.5); NS

[a]n = 333; [b]n = 313; [c]n = 331; [d]n = 328; [e]n = 329; [f]n = 196; [g]n = 81.
EDSS = Expanded Disability Status Scale; ET = early termination; HADS = Hospital Anxiety and Depression Scale; HRQoL = health-related quality of life; MSQOL-54 = MS Quality of Life-54; MusiQoL = MS International Quality of Life; n = number; NS = not significant (p ≥ 0.05); SD = standard deviation.

Across visits, the proportion of patients for whom a particular global or dimension score could not be calculated ranged from 0% to 18.5% for MusiQoL (Supplemental file 4) and 0% to 16.0% for MSQOL-54 (Supplemental file 5). The mean time spent to complete the questionnaire at each visit was significantly shorter for MusiQoL compared with MSQOL-54 (4.5–5.9 min vs 10.1–12.5 min, respectively; p < 0.0001 for paired difference at all time points).

Patient preferences for MusiQoL vs MSQOL-54

At each visit, a numerically higher proportion of patients indicated that MusiQoL was more user-friendly than MSQOL-54 (50.2–61.7% vs 38.3–49.8%), with the difference reaching significance (p = 0.001) at months 6 and 18. A numerically higher proportion of patients reported that MusiQoL was easier to read, understand and answer compared with MSQOL-54 at baseline, months 6 and 18 and ET (54.5–61.4% vs 38.6–45.5%; the difference was significant [p < 0.01] at months 6 and 18). At months 12 and 24, patients reported that that MusiQoL and MSQOL-54 were similarly easy to read, understand and answer (51.0 vs 49.0% and 49.2 vs 50.8%, respectively).

At all time points, a higher proportion of patients felt that MSQOL-54, compared with MusiQoL, contained questions that were more closely related to their daily QoL (54.4–79.5% vs 20.5–45.6%; p < 0.0001 at baseline, months 12 and 24 and ET; p < 0.05 at month 18) and more specific to MS (54.7–65.6% vs 34.4–45.3%; p < 0.0001 at baseline and month 12; p < 0.05 at months 18 and 24 and ET). Significantly more patients indicated

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Table 2: Analyses of the effects of the order of questionnaire administration on responses to Questions 1–5 of the evaluation questionnaire using all available data at each study visit

Questions 1–5 of evaluation questionnaire	GEE estimate (SE)	p-value	Probability MSQOL-54 preferred* (95% CI)	Questionnaire preferred	Variation of preference at each time point
1. Which questionnaire is more user-friendly?	–0.24 (0.07)	0.0006	0.44 (0.41, 0.47)	MusiQoL	Yes
2. Identify which questionnaire you felt is easier to read, understand and answer	–0.25 (0.07)	0.0002	0.44 (0.41, 0.47)	MusiQoL	No
3. Which questionnaire covers questions that are more closely related to your daily quality of life?	0.81 (0.07)	<0.0001	0.69 (0.66, 0.72)	MSQOL-54	Yes
4. Which questionnaire has questions that are more specific to MS?	0.41 (0.07)	<0.0001	0.60 (0.57, 0.63)	MSQOL-54	No
5. Which quality of life questionnaire would you recommend to others?	0.56 (0.07)	<0.0001	0.64 (0.60, 0.67)	MSQOL-54	Yes

*$e^{Estimate} / (1 + e^{Estimate})$.

CI = confidence interval; GEE = Generalized Estimating Equation; MSQOL-54 = Multiple Sclerosis Quality of Life-54; MusiQoL = MS International Quality of Life; SE = standard error.

that they would recommend MSQOL-54 over MusiQoL to others at baseline, months 12 and 24 and ET (63.9–72.9% vs 27.1–36.1%; $p < 0.0001$ at baseline and months 12 and 24; $p < 0.05$ at ET). There was no significant difference between MSQOL-54 and MusiQoL at month 6 (49.8% vs 50.2%) and month 18 (54.4% vs 45.6%) in response to this question.

Detailed data for evaluation questions 1–5 are provided in Supplemental file 6. Generalized Estimating Equation analyses of these data across study visits showed that across all study follow-up time points (thus regardless of order of administration overall), patients significantly preferred MusiQoL for user-friendliness and ease-of-use, but significantly preferred MSQOL-54 for closest relevance to daily QoL, being more specific to MS and for recommendation to others (Table 2). The extent or magnitude of patient preferences for user-friendliness of the MusiQoL, closest relevance to daily QoL for the MSQOL-54, and recommendation to others for the MSQOL-54 were influenced by the order of questionnaire administration; however, the particular measure that was preferred for each question (analysed across the entire set of time points) was no different due to order of administration.

On a five-point scale of ease-of-use ranging from 'very difficult' to 'very easy', patients rated both the MusiQoL and MSQOL-54 instruments toward the easy end of the scale (mean scores 4.3–4.4 vs 4.2–4.3; $p < 0.05$ for paired difference in favour of MusiQoL at baseline, months 6 and 18 and ET). Overall impressions of MusiQoL and MSQOL-54 on an 11-point visual analogue scale (0 = poor, 10 = excellent) were high, with mean scores of 7.9–8.1 and 7.9–8.3, respectively, across all time points ($p < 0.05$ for paired difference in favour of MusiQoL at Month 6 and MSQOL-54 at baseline and Months 12 and 24).

HRQoL scores over time and correlations with clinical disease measures

Changes from baseline in HRQoL scores and clinical disease characteristics over time are presented in Table 1. From baseline to 24 months, significant mean paired improvements were observed in MusiQoL global index and MSQOL-54 physical and mental health composite scores. Numerical improvements were also observed in HRQoL global scores from baseline to ET, but these were not statistically significant. The mean number of relapses experienced during the previous 6 months was slightly higher at ET compared with month 24. Mean EDSS scores remained stable from baseline to month 24 and ET. A significant mean paired decrease from baseline to month 24 was observed for HADS anxiety subscores; however, the mean paired decrease from baseline in HADS anxiety subscores at ET and HADS depression subscores at 24 months and ET did not reach statistical significance.

At baseline, month 24 and ET, the MusiQoL global index and MSQOL-54 physical and mental health composite scores showed similar weak to moderate negative correlations with EDSS scores and moderate to strong negative correlations with HADS subscores (Table 3). All three global HRQoL scores showed similar very weak to weak negative correlations with relapses in the last 6 months at month 24 and ET.

Scale–scale correlations

Spearman correlation coefficients between the MusiQoL global index score and MSQOL-54 physical and mental health composite scores at baseline were 0.74 and 0.74, respectively ($p < 0.0001$ for both associations).

Relative validity

The MusiQoL global index score and MSQOL-54 physical health composite scores had similar high relative validity for discriminating between different categories of CGI rating (Table 4). With respect to HAD anxiety subscores, the relative validity of the MusiQoL global score was similar to the MSQOL-54 physical health composite score but lower than the mental health composite score. Relative validities of the MusiQoL and MSQOL-54 global scores were similar and low in magnitude with respect to HAD depression subscores. Global scores for both instruments had high relative validity with respect to employment status, although the MSQOL-54 physical health composite score had the highest value.

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Table 3: Correlation coefficients for HRQoL scores and clinical disease measures at baseline, 24 months and ET

	MusiQoL global index score	MSQOL-54 physical health composite score	MSQOL-54 mental health composite score
Number of relapses in last 6 months			
Baseline	–	–	–
Month 24	−0.08	−0.20*	−0.15*
ET	−0.19	−0.23	−0.18
EDSS score			
Baseline	−0.34***	−0.44***	−0.23***
Month 24	−0.29***	−0.41***	−0.24**
ET	−0.45***	−0.56***	−0.35*
HADS anxiety subscore			
Baseline	−0.57***	−0.49***	−0.67***
Month 24	−0.59***	−0.45***	−0.64***
ET	−0.61***	−0.61***	−0.74***
HADS depression subscore			
Baseline	−0.76***	−0.77***	−0.78***
Month 24	−0.78***	−0.74***	−0.79***
ET	−0.82***	−0.83***	−0.81***

*$p < 0.05$; **$p < 0.001$; ***$p < 0.0001$.
EDSS = Expanded Disability Status Scale; ET = early termination; HADS = Hospital Anxiety and Depression Scale; HRQoL = health-related quality of life; MSQOL-54 = MS Quality of Life-54; MusiQoL = MS International Quality of Life.

Responsiveness to change

The MusiQoL and MSQOL-54 summary scores had similar small or medium effect sizes relative to change in HAD anxiety and depression subscore classifications from baseline to six months, and examiner's global rating of health status at six months (Table 5). Neither MusiQoL nor MSQOL-54 was responsive to change in CGI rating.

Discussion

To our knowledge, this is the first comparison between MusiQoL and MSQOL-54, although MusiQoL has previously been compared with the Short-Form 36-item QoL instrument for the purpose of validation in different languages.[14-20] Our findings show that the MusiQoL and MSQOL-54 instruments were both well received by patients, consistent with previous observations that HRQoL measures are associated with high patient acceptability,[3] and had similar psychometric properties.

For each instrument, few patients missed any items and most indicated that the questionnaire was easy to use and rated the questionnaire favourably on a visual analogue scale. Patients preferred MSQOL-54 over MusiQoL in terms of thoroughness; however, a greater proportion of patients perceived that MusiQoL was more user-friendly and easier to read, understand and answer, compared with MSQOL-54. The rating of MSQOL-54 as more relevant to MS, and as the measure patients would recommend to others, was unexpected given that MusiQoL was developed from patient interviews. This finding warrants further investigation. The MusiQoL questionnaire is shorter than other MS-specific instruments and, accordingly, patients spent significantly less time completing MusiQoL than MSQOL-54. A previous study has indicated that questionnaire length does not seem to be a drawback for patients with MS,[28] and the results from the present study suggest that patients do not appear to mind completing a longer questionnaire. Nevertheless, the shorter completion time could be advantageous for patients and clinicians if time is limited, and MusiQoL is likely to be more convenient to administer than MSQOL-54.

The two questionnaires had similar and good evidence for construct validity, with the MusiQoL performing as well as the longer MSQOL-54. Higher scores on both questionnaires were moderately to strongly correlated with lower HADS subscores, and moderately to weakly correlated with EDSS scores. We note that there was relatively little variation in EDSS in this study's sample, which was in the direction of milder MS. Without variation, it is difficult to demonstrate associations between constructs but certainly HRQoL has been shown to be associated with ambulation status in prior studies in which a broader range of mobility status was represented.[10] Only weak correlations were observed between MusiQoL and MSQOL-54 global scores and relapses in the last six months at month 24; however, this may be explained by the low number of patients (n = 21) who had experienced a relapse in the last six months at this time point. Strong correlations were found between MusiQoL and MSQOL-54 scores at baseline.

Regarding potential limitations, our sample did not include more severely disabled patients and half were diagnosed within the prior four months, as eligibility criteria included that patients *not* be on treatment and that patients *would* be willing to start medication. Thus, it is possible that these comparative findings about HRQoL measures may not be generalizable to MS patients at later stages or who have more disability. For 17% of study participants we had neither 24-month nor ET data; it is possible that those for whom we had no data might have been either

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Table 4: Relative validity analyses for MusiQoL and MSQOL-54 at baseline

	MusiQoL global index score	MSQOL-54 physical health composite score	MSQOL-54 mental health composite score
CGI rating			
Mild: mean QoL score (n)	74.2 (263)	63.9 (249)	67.1 (261)
Moderate/severe: mean QoL score (n)	63.3 (67)	48.5 (63)	59.7 (67)
F-ratio	31.4	34.0	7.1
Relative validity	51.9	56.3	11.7
HADS anxiety subscore			
Normal (0–7): mean QoL score (n)	78.1 (179)	68.8 (167)	76.2 (178)
Possible (8–10): mean QoL score (n)	67.7 (85)	54.6 (81)	59.0 (85)
Case (>10): mean QoL score (n)	60.6 (64)	47.2 (61)	44.5 (64)
F-ratio	49.2	41.2	99.6
Relative validity	15.6	13.1	31.6
HADS depression subscore			
Normal (0–7): mean QoL score (n)	75.7 (261)	65.7 (246)	71.4 (260)
Possible (8–10): mean QoL score (n)	60.0 (53)	43.3 (49)	47.4 (53)
Case (>10): mean QoL score (n)	46.3 (15)	35.6 (14)	32.7 (15)
F-ratio	68.3	50.9	72.3
Relative validity	6.8	5.1	7.2
Employment status			
Employed: mean QoL score (n)	73.9 (220)	64.9 (208)	68.6 (219)
Unemployed: mean QoL score (n)	65.4 (86)	49.5 (79)	57.0 (86)
F-ratio	20.9	39.0	20.7
Relative validity	99.7	185.7	98.6

CGI = clinical global impression; HADS = Hospital Anxiety and Depression Scale; MSQOL-54 = MS Quality of Life-54; MusiQoL = MS International Quality of Life; n = number; QoL = quality of life.
For CGI rating and HADS subscores, relative validity was calculated with reference to the lowest F-ratio obtained on any health-related QoL global or dimension score (CGI: lowest F-ratio = 0.6 for MSQOL-54 – Emotional well-being; HADS anxiety: lowest F-ratio = 3.2 for MSQOL-54 – Change in health; HADS depression: lowest F-ratio = 10.0 for MusiQoL – Relation with family). For employment status, the lowest F-ratio obtained was 0.0768 for MusiQoL – Sentimental and Sexual Life, but this value was considered too low to be used as a reference scale; therefore, the second lowest F-ratio (0.2 for MusiQoL – Relation with family) was used instead. Data for dimension scores are not shown in the table.

'sicker', and unable to make it to study visits, or healthier, perhaps feeling no need to complete the study.

Relative validities of the MusiQoL and MSQOL-54 summary scores were generally similar across the external criteria tested. Responsiveness to change for MusiQoL and MSQOL-54, according to the external criteria examined, was comparable in effect size and interpretation, although the responsiveness was typically small (or at most medium) in magnitude. However, it should be noted that the subgroups of patients with improved or worsened status were relatively small. Furthermore, external change criteria were selected after the initial data collection had commenced and were consequently limited to variables already included in the data set; these criteria, particularly the examiner ratings, may not have been ideal for assessing HRQoL change. More definitive assessment of comparative responsiveness to change and relative validity would need larger patient populations with a broader range of stages of disease, as well as external criteria determined *a priori* so that the most appropriate measures of those criteria could be incorporated.

In this patient population receiving treatment with sc IFN β-1a, 44 or 22 μg tiw, improvements were observed in MusiQoL and MSQOL-54 summary scores from baseline to month 24. However, as this study did not include a comparison group and it was not possible to collect follow-up data on all patients who withdrew before study completion, any potential treatment effect on HRQoL would need to be investigated further in controlled studies.

In summary, these findings demonstrate that both the MusiQoL and MSQOL-54 questionnaires are suitable instruments for the evaluation of HRQoL in patients with MS. Although some patients preferred MSQOL-54 for some endpoints, the correlations of the HRQoL measurements were similar with both instruments. When the ease and efficiency of administration is considered, the MusiQoL questionnaire is likely to be a more practical tool to use in clinical practice.

Disclosures

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Table 5: Responsiveness of MusiQoL and MSQOL-54 summary scores to change relative to external criteria for health-related quality of life change

External criterion for change	MusiQoL global index score	MSQOL-54 physical health composite score	MSQOL-54 mental health composite score
HADS anxiety subscore			
n changed/n	99/281	90/260	98/279
Effect size	0.346	0.330	0.453
Interpretation	Small	Small	Small
HADS depression subscore			
n changed/n	54/282	47/260	54/280
Effect size	0.596	0.572	0.709
Interpretation	Medium	Medium	Medium
Examiner's global rating of health status			
n changed/n	79/284	73/263	78/283
Effect size	0.343	0.342	0.359
Interpretation	Small	Small	Small
CGI			
n changed/n	41/282	37/263	41/281
Effect size	0.043	0.075	0.133
Interpretation	No effect	No effect	No effect

CGI = clinical global impression; HADS = Hospital Anxiety and Depression Scale; MSQOL-54 = MS Quality of Life-54; MusiQoL = MS International Quality of Life; n = number.
n (changed) is the number of patients with improved or worsened external criterion status from baseline to six months; n is all patients with a quality of life and external criterion measurement at baseline and six months (at six months only for examiner's global rating of health status).
Effect size is the raw score change in the changed group divided by the baseline standard deviation, classified as small (0.20–0.49), medium (0.50–0.79) or large (≥0.80).

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KF was an employee of EMD Serono, a division of EMD Inc., Canada, at the time the study was conducted. EMD Inc., Canada is a subsidiary of Merck KGaA, Darmstadt, Germany. LL has served on advisory boards, received honoraria and conducted clinical trials with Biogen Canada, Novartis Canada, EMD Serono Canada, Teva Neurosciences and Sanofi-Aventis.

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Supplementary material

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