Mood Associated With Health- and Social Care–Related Quality of Life in Patients With Advanced Multiple Sclerosis

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ABSTRACT

BACKGROUND: Individuals with advanced multiple sclerosis (MS) have complex care requirements and are more likely to use long-term facilities. This study determined the associations between mood and social care–related quality of life (SCRQOL), and health-related quality of life (HRQOL) and examined the association between HRQOL and SCRQOL.

METHODS: Baseline data from a cohort study were used. Patients completed questionnaires, including the Hospital Anxiety and Depression Scale (HADS), Adult Social Care Outcomes Toolkit (ASCOT), and EuroQOL 5D-5L (EQ-5D-5L) and EQ-Visual Analogue Scale (EQ-VAS). Linear regression analyses were employed to assess the relationships between mood and both outcomes of QOL while controlling for relevant confounding factors (βs; 95% CI). The cross-sectional association between SCRQOL and HRQOL was examined using Pearson correlation coefficients (*r*).

RESULTS: A total of 75 patients, with a mean age of 56.1 years and a disease duration of 17.3 years, were enrolled from a long-term care facility in the Netherlands. Results showed that after controlling for confounders, HADS is an independent determinant of ASCOT (βs = −.368; 95% CI, −.581 to −.154) and EQ-5D-5L (βs = −.297; 95% CI, −.507 to −.087). Also, there are significant but weak correlations between ASCOT and EQ-5D-5L ($r = 0.242$; 95% CI, .015-.468), between ASCOT and EQ-VAS ($r = 0.230$; 95% CI, .003-.457) and between EQ-5D-5L and EQ-VAS ($r = 0.227$; 95% CI, .000-.454).

CONCLUSIONS: Mood, especially the depression component, is an important determinant of both HRQOL and SCRQOL in advanced MS. Focusing on mood in health care and social care may contribute to the improvement of QOL in a broader sense.

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Multidisciplinary rehabilitation and symptom management is critical for people with more advanced multiple sclerosis (MS)[1,2] because progression of the disease is associated with complex physical and psychosocial needs and decreased health-related quality of life (HRQOL).[3,4]

Individuals in the advanced phases of MS have complex care requirements and more extensive use of long-term care facilities, including both health care and social care services.[4] Although no uniform definition of advanced MS exists,[5-7] it is characterized by physical impairments, multiple MS symptoms at the same time, and dependence on others for many care and support needs. Because HRQOL does not measure the impact of these complex care and support needs, it has been argued that a wider concept of QOL should be used. Objectives of many social care services should include aspects of QOL beyond HRQOL, such as control over daily life, supporting physical functioning, cleanliness and comfort, personal safety, and social participation and involvement. These aspects are primarily concerned with reducing the effects of impairments on daily life[8,9] and are collectively called social-care–related quality of life (SCRQOL). SCRQOL is defined as "the aspects of an individual's quality of life that can be affected by social care." Earlier studies in frail, older adults (ie, age 64 or older) have shown the value of taking both HRQOL and SCRQOL into account when considering QOL.[10-12] Similar to frail, older adults, advanced MS threatens aspects of SCRQOL, like control over daily life, occupation, and social participation and involvement.[13] It is therefore important to consider the wider concept of health and take into account both HRQOL and SCRQOL when MS progresses.

Mood disturbances, ie, the presence of anxiety and depression symptoms, are among the most common psychological symptoms in MS, with reported prevalence rates of 22.1% for anxiety and 30.5% for depression.[14,15] It is well known that both MS and mood have a major impact on HRQOL. Reduced HRQOL among people with MS is significantly associated

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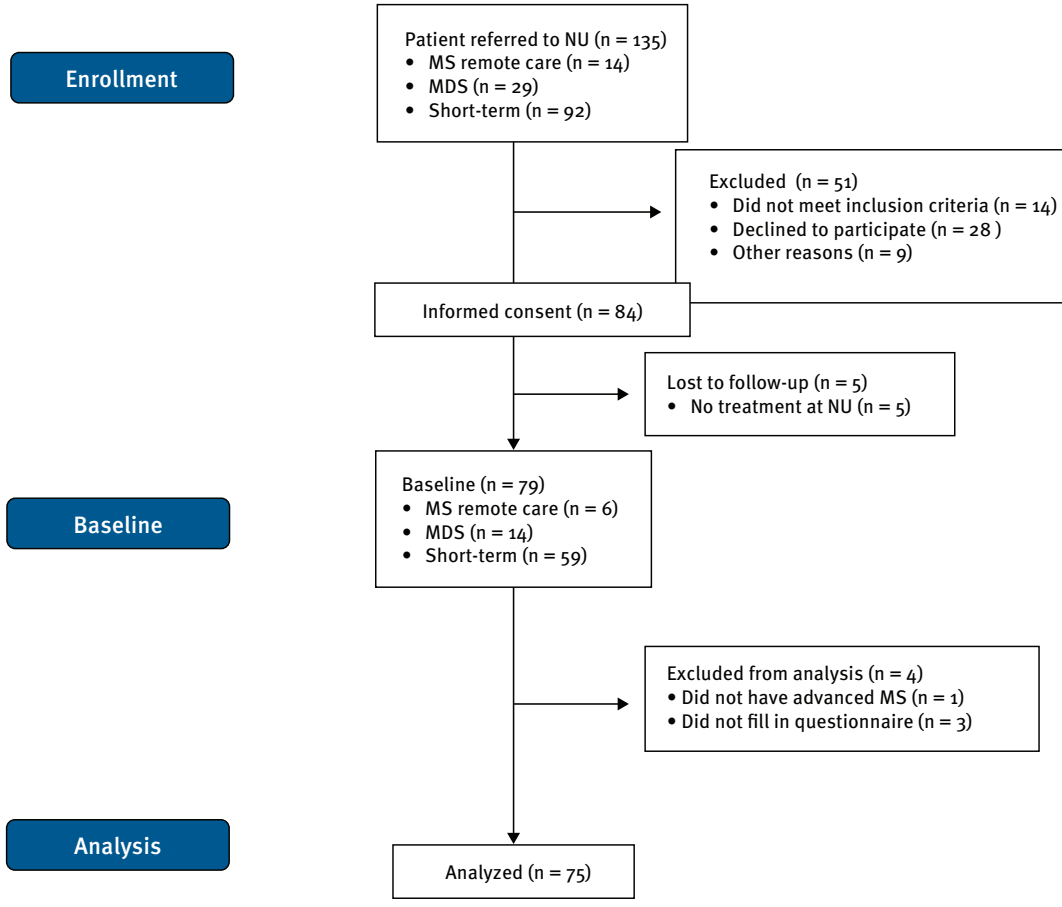
FIGURE 1. Flow Diagram



MDS, multidisciplinary screening group; MS remote care, multiple sclerosis remote care group; NU, Nieuw Unicum; Short-stay, short-stay residential group.

with mood disturbances.[16] To our knowledge, no studies have investigated the association between mood and SCRQOL in MS and the association between mood and HRQOL in a population with advanced MS.

Other factors have been found to be related to both mood and HRQOL in MS, including gender,[17,18] fatigue,[19] pain,[20,21] spasticity,[22] disease duration,[23,24] severity of MS,[17,23] and motor[25] and cognitive function.[26] These factors may confound the association between mood and HRQOL and SCRQOL.

Understanding the impact of mood on the wider concept of QOL may contribute to developing, improving, and evaluating interventions to enhance QOL in advanced MS[27] and can inform professionals providing social care services. Therefore, the aim of this study is to determine the relationship between mood and HRQOL and SCRQOL among patients with advanced MS. First, we examine the association between HRQOL and SCRQOL. Second, we assess whether mood is associated with HRQOL and SCRQOL.

METHODS

Study Design and Participants

Baseline data were from a previous 1.5-year-long longitudinal cohort study. The study cohort was adults diagnosed with MS and in the later stages of the disease who visited the long-term care facility Nieuw Unicum (NU) in the Netherlands for first-time treatment consultation between January 2018 and January 2020. There were no restrictions for referral to the center based on the Dutch health care system. The participants came from 1 of 3 groups of center-offered care: (1) remote care (ie, an online coaching program including advice and support provided by an MS nursing consultant), (2) multidisciplinary screening (ie, an individually tailored 1- or 2-day assessment by a multidisciplinary team of different medical and allied health care professionals with treatment advice as an outcome), and (3) short-stay care for 1 to 6 weeks to optimize health and functioning and/or to offer relief to caregivers at home. Written informed consent was obtained from all patients.

All individuals with MS who were referred to NU from December 2017 until December 2019 were asked to participate (**FIGURE 1**). After assessing outliers and after consideration within the research team, 1 participant was excluded because they did not meet the criteria for an advanced MS diagnosis.

Study size estimation was based on the previous longitudinal cohort study. The study was approved by the Medical Research Ethics Committee (METc Amsterdam UMC, VUmc; registration number 2017.519).

Demographic information (ie, age, gender, education) and disease characteristics (ie, type of MS, disease duration, MS severity, motor and cognitive functioning) were collected by telephone or in individual meetings at the center. Education levels were defined using the International Standard Classification of Education 2011.[28]

TABLE 1 contains the sociodemographic and clinical characteristics. Seventy-five participants with a mean age of 56.1 years (SD 9.2) were included. Slightly more women (53%) than men participated. The mean disease duration was 17.3 years (SD 9.6), and the median EDSS score was 7.0 (range 3.5-9.0).

TABLE 1. Sociodemographic and Clinical Characteristics (N = 75)

	Total population n (%)	Male n = 35 (47%)	Female n = 40 (53%)
Type of MS			
RR	8 (12%)	3 (8.6%)	5 (12.5%)
SP	26 (34%)	15 (42.9%)	18 (45.0%)
PP	33 (43%)	15 (42.9%)	11 (27.5%)
Unknown	8 (11%)	2 (5.6%)	6 (15.0%)
Treatment group at NU			
MS remote care	5 (8%)	3 (8.6%)	2 (5.0%)
MDS	13 (17%)	6 (17.1%)	7 (17.5%)
Short-stay	57 (75%)	26 (74.3%)	31 (77.5%)
Education*			
Low	22 (29%)	7 (20.0%)	15 (37.5%)
Medium	28 (37%)	12 (34.3%)	16 (40.0%)
High	24 (33%)	15 (42.9%)	9 (22.5%)
Unknown	1 (1.3%)	1 (2.8%)	–
Mean (SD; range)			
Age, y	56.1 (9.2; 25.0-71.0)	57.2 (8.9; 40.0-71.0)	55.2 (9.4; 25.0-68.0)
MS duration, y	17.3 (9.6; 1.0-39.0)	17.7 (10.0; 2.0-39.0)	16.9 (9.3; 1.0-37.0)
ASCOT index	0.62 (0.21; 0.10-1.00)	0.67 (0.18; 0.19-1.00)	0.57 (0.22; 0.10-0.92)
EQ-5D-5L index Dutch Tariff	0.31 (0.29; −0.33 to 0.92)	0.34 (0.29; −0.18 to 0.92)	0.27 (0.28; −0.33 to 0.83)
EQ-5D-5L index UK Tariff	0.37 (0.26; −0.20 to 0.95)	0.40 (0.26; −0.04 to 0.95)	0.34 (0.26; −.20 to 0.86)
EQ-VAS	50.1 (19.4; 0.0-90.0)	50.2 (18.8; 10.0-0.0)	50.1 (20.2; 0.0-90.0)
HADS total	12.8 (7.8; 0.0-31.0)	9.6 (6.3; 0.0-24.0)	15.7 (7.9; 1.0-31.0)
HADS-A	6.1 (4.6; 0.0-17.0)	4.3 (3.7; 0.0-13.0)	7.6 (4.7; 0.0-17.0)
HADS-D	6.7 (4.2; 0.0-18.0)	5.3 (3.4; 0.0-13.0)	8.3 (4.4; 1.0-18.0)
Median (IQR; 25%-75%)			
EDSS	7.0 (1.0; 6.5-7.5)	7.0 (1.0; 6.5-7.5)	7.0 (1.0; 6.5-7.5)
FIM	99.0 (34.0; 75.0-109.0)	101.0 (23.3; 84.0-107.3)	97.0 (35.8; 73.0-108.8)
FIM motor	68.0 (34.0; 43.0-77.0)	68.5 (22.0; 52.0-74.0)	66.5 (39.3; 38.5-77.8)
FIM cognitive	33.0 (3.0; 31.0-34.0)	33.0 (4.5; 30.5-34.0)	33.0 (5.0; 30.0-35.0)
Pain NRS	5.0 (6.0; 1.0-7.0)	3.0 (6.0; 1.0-7.0)	5.5 (5.7; 1.3-7.0)
Spasticity NRS	4.0 (6.0; 0.0-6.0)	4.0 (6.0; 1.0-7.0)	3.0 (5.0; 0.0-5.0)
CIS20R-f	44.0 (13.5; 37.5-51.0) (n = 73)	43.5 (15.8; 34.5-50.3) (n = 34)	45.0 (12.0; 40.0-52.0) (n = 39)

ASCOT, Adult Social Care Outcome Toolkit; CIS20R-f, Checklist Individual Strength-Fatigue; EDSS, Expanded Disability Status Scale; EQ-5D-5L, EuroQOL 5-dimensional 5-level; EQ-VAS, EuroQOL Visual Analogue Scale; FIM, Functional Independence Measure; HADS, Hospital Anxiety and Depression Scale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; ISCED, International Standard Classification of Education 2011; MDS, multidisciplinary screening; MS, multiple sclerosis; NRS, Numerical Rating Scale; PP, primary progressive; RR, relapsing-remitting; SP, secondary progressive; Short-stay, short-stay residential.

*Low, ISCED 0-2 ‹ upper secondary; Medium, ISCED 3-4; High, ISCED 5-8 › postsecondary nontertiary

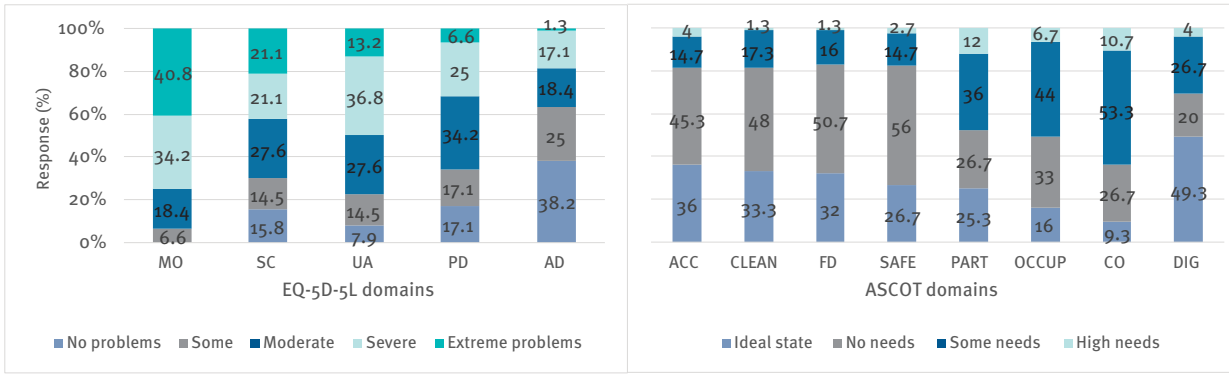
Measurements

Participants completed questionnaires at study onset and at 3, 6, 12, and 18 months. Questionnaires could be filled in on paper or digitally, and researcher assistance was available.

The Hospital Anxiety and Depression Scale (HADS) was used to measure mood state.[29] This self-reported scale consists of 14 items rated on a 4-point Likert scale ranging from 0 to 3 with an anxiety (HADS-A) and depression (HADS-D) subscale (7 items each). This results in a total score between 0 and 42, and a subscale score between 0 and 21, with higher scores indicating higher levels of distress. The HADS has a high sensitivity and specificity in relation to clinical interviews in MS patients.[30]

HRQOL was measured using the EuroQOL 5D questionnaire (EQ-5D) which has 2 parts, the EQ-5D 5-level (EQ-5D-5L) descriptive system and the EuroQOL Visual Analogue Scale (EQ-VAS).[31] The EQ-5D-5L measures health in 5 dimensions—mobility, self-care, usual activities, pain/discomfort, and anxiety/depression—and, by applying the Dutch Tariff valuation set, can be converted into an overall utility index score ranging from −.446 for the worst state to 1 for the mildest state.[32] The UK Tariff valuation set was used to compare index scores with other populations.[33] The EQ-VAS is a vertical visual analog scale to indicate current overall health. The participant rates their health on a scale ranging from 0, "the worst health you can imagine," to 100, "the best health you can imagine." The EQ-5D is found

FIGURE 2. Proportion of Participants Responding to Each Domain of the EQ-5D-5L and ASCOT



ACC, accommodation; AD, anxiety/depression; ASCOT, Adult Social Care Outcome Toolkit; CLEAN, cleanliness; CO, control; DIG, dignity; EQ-5D-5L, EuroQol-5 dimensional; FD, food and drink; MO, mobility; OCCUP, occupation; PART, social participation; PD, pain/discomfort; SAFE, safety; SC, self-care; UA, usual activities.

to be valid and reliable in disabled populations, such as individuals with acute stroke and Parkinson disease.[34]

The Dutch version of the Adult Social Care Outcomes Toolkit (ASCOT) was used to measure SCRQOL.[35] The preference-based ASCOT was developed to help users broadly evaluate social care services. It quantifies the impact of services in domains of quality of life most affected by social care with 9 items and 8 domains: control over daily life, personal cleanliness and comfort, meals and nutrition, personal safety, social participation and involvement, occupation, accommodation cleanliness and comfort, and dignity. Each domain is scored on a 4-point Likert scale, ranging from ideal to worst imaginable state with high needs.[8,9,35] Overall utility index scores can be calculated and range from –0.171, "high needs on all domains," to 1, "the ideal state of SCRQOL." The Dutch translation of the ASCOT is valid, reliable, and comparable to the original English version.[36]

Severity of MS was measured using a telephone version of the Expanded Disability Status Scale (EDSS).[37] EDSS scores range from 0, "no disability," to 10, "death due to MS."[38]

Motor and cognitive functioning were assessed using the Functional Independence Measure (FIM).[39] The FIM consists of a 13-category motor subscale and 5-category cognitive subscale that assess the level of functional independence. Each item is scored ranging from 1, "total assistance," to 7, "complete independence." Motor subscores can range from 13 to 91 and cognitive subscores can range from 5 to 35. The FIM is a responsive, reliable, and valid measure of disability.[39]

Pain and spasticity were assessed using a numerical rating scale (NRS).[40] Patients rated average pain intensity during the last 24 hours from 0, "no pain," to 10, "pain as bad as could be." Patients rated their spasticity over the last 24 hours from 0, "no spasticity," to 10, "worst possible spasticity." High test-retest reliability and good validity for pain were observed in patients with rheumatoid arthritis[41] and the scale was found to be valid and reliable for spasticity in MS research.[42]

Fatigue was rated using the subjective fatigue subscale of the Checklist Individual Strength (CIS20R-f).[43] The subscale consists of 8 items on a 7-point Likert scale. A summary score is the sum of points scored on the 8 items, which results in a score ranging between 8 and 56. Higher scores reflect higher levels of perceived fatigue. Test-retest reliability of the fatigue subscale of the CIS20R-f is good.[44]

Statistical Analysis

Descriptive statistics were calculated for demographic and disease characteristics.

The association between HRQOL and SCRQOL concepts was examined using Pearson correlation coefficients (*r*) with 95% CI. Correlations were interpreted as weak (< 0.3), moderate (≥ 0.3, < 0.5), or strong (≥ 0.5).[45]

Linear regression analyses were used to investigate whether mood is a determinant of both QOL outcomes. To determine differences in strength of association between mood and QOL constructs, standardized regression coefficients (βs) and 95% CIs were compared. No difference in strength was presumed when the standardized regression coefficient was included in the association 95% CI of the other QOL construct.

In step 1, univariable linear regression analyses were performed to assess the associations between mood and QOL. In step 2, these univariable models were subsequently adjusted for sex, disease duration, MS severity, motor function, cognitive function, pain, spasticity, and fatigue. When the unstandardized regression coefficient of mood changed by more than 15% after adjustment, this variable was considered a confounder.[46] In step 3, all relevant confounders from step 2 were added to a final model to determine the unconfounded association of mood with QOL. In step 4, the standardized regression coefficients of anxiety and mood were compared to study their relative contribution to QOL.

RESULTS

Association Between QOL Concepts

The mutual relationship between the QOL measures appeared to be weak with significant Pearson correlation coefficients between ASCOT and EQ-5D-5L ($r = 0.242$; 0.015-0.468), between ASCOT and EQ-VAS ($r = 0.230$; 0.003-0.457), and between EQ-5D-5L and EQ-VAS ($r = 0.227$; 0.000-0.454). **FIGURE 2** shows

the proportion of participants responding to each domain of the ASCOT and EQ-5D-5L.

Relationship of Mood to QOL Concepts

TABLE S1 shows the results of the regression analyses between mood and SCRQOL and HRQOL. In step 1, significant inverse associations were found between mood, SCRQOL, and HRQOL, but not between mood and personal overall health status. Fatigue was an important confounder in the relationships between mood and SCRQOL and HRQOL, and pain was an important confounder only in the relationship between mood and HRQOL. After correcting for confounding (step 3), mood was still a significant determinant of SCRQOL (βs = −0.368; −0.581 to −0.154) and HRQOL (βs = -0.297; −0.507 to −.087). In step 4, the relative effect of HADS-D was found to be considerably stronger than HADS-A for both SCRQOL and HRQOL.

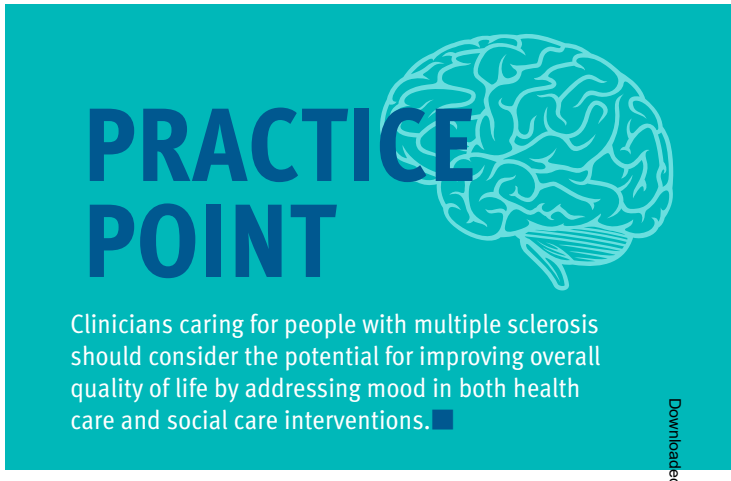
DISCUSSION

Our study shows that mood, especially as measured by HADS-D, is inversely and equally associated with both HRQOL and SCRQOL among patients with advanced MS. HRQOL and SCRQOL were only weakly correlated, indicating that these concepts measure different aspects of QOL.

Our results in an advanced MS population are in line with findings in other populations; our data show the mean utility index score of the HRQOL measure EQ-5D-5L is lower than the utility index score of the SCRQOL measure ASCOT. This emphasizes that these QOL measures have different underlying constructs. Comprehensive QOL assessments should therefore include measurement of these different concepts of QOL, especially in people requiring complex social care services.

Although HRQOL and SCRQOL are likely measuring different aspects of QOL, both are strongly associated with mood, with a stronger relative effect for depression. An increase of 1 standard deviation in mood leads to a 0.474 standard deviation decrease in SCRQOL index score and a 0.428 standard deviation decrease in HRQOL index score. These results are in line with a recent systematic review that shows mood is a strong risk factor for a lower HRQOL in MS,[16] although none of the studies consisted only of people with advanced MS.

A relationship was found between SCRQOL, as measured with ASCOT, and mood, measured by different instruments, in frail, older adults in 3 studies.[11,12,47] One study showed that the ASCOT was correlated with the 12-Item Short Form Health Survey mental health component ($r = 0.50$) in frail adults aged 65 years or older in the Netherlands.[12] Other studies conducted in England found a correlation with the Geriatric Depression Scale ($r = -0.69$) in social care users 70 years of age and older,[47] and with the General Health Questionnaire ($r = -0.58$) in people 65 years or older who are using social care services.[11] Next to HRQOL, generating more knowledge about SCRQOL in advanced MS and its related factors (eg, mood) may contribute insight into the broader picture of QOL for this population.



No significant relationship was found between mood and HRQOL via EQ-VAS assessment. Since the relationship with the other QOL instruments was so robust, we argue that this may be because overall health status is a more encompassing construct than general QOL, which is not fully captured by the EQ-5D-5L and ASCOT separately.

According to the World Health Organization, QOL is a broad concept affected in a complex way by a person's physical health, psychological state, level of independence, social relationships, personal beliefs, and their relationship to salient features of their environment.[48] As such, not all aspects of this definition can be captured in the QOL instruments (eg, personal beliefs, relationship to salient environmental features). In addition, in an online survey, 97% of individuals with MS (n = 237) felt that the EQ-5D-5L did not capture all important aspects of well-being that added significant burden to their HRQOL.[49] They cited fatigue, balance, and dizziness, which are not included in the ASCOT. Therefore, other factors might play a more prominent role in judgment of personal overall health status.

In our study, fatigue confounded the association of mood with HRQOL as well as the association of mood with SCRQOL. Pain had only a confounding effect in the association of mood with HRQOL. Although it is known that fatigue and pain are associated with HRQOL and mood in individuals with MS,[20] the role of these factors in SCRQOL has not been investigated. A possible reason that pain was not a confounder in the association of mood with SCRQOL is that the EQ-5D-5L specifically assesses the level of pain/discomfort, while the ASCOT does not. Pain and fatigue are important factors in QOL, but their influence depends on the QOL construct used. These factors, next to mobility and upper-extremity function, are highlighted as the key symptoms in MS symptom management and rehabilitation.[50]

No confounding effects of sex, disease duration, severity of MS, cognitive functioning, or spasticity were found in the association between QOL and mood. In the literature, findings about their role in mood and QOL are inconsistent; some studies[17,18,22,23,26,51] found an association between the variables and mood or QOL, while other studies did not.[52-56]

Limitations

Patients in our cohort have varying levels of physical impairment (EDSS ≥ 3.5). However, most have several complex needs and utilize both health and social care services to maintain their QOL, which likely indicates an advanced stage of MS. Considering the characteristics of advanced MS in the literature, it can be argued whether advanced MS should be defined only when physical impairment is present or whether the definition of advanced MS should also include more intangible characteristics like psychosocial needs.[7]

Another limitation is the collection of data from 1 center; the study population may not be representative of the larger population of individuals with advanced MS.

The present study is cross-sectional and did not have this capability, but future research should use longitudinal assessments to study time-dependent cause-and-effect relationships, as it is likely that QOL and mood are not stable but vary over time.

In addition, future research could consider other instruments that focus on aspects of QOL beyond health (eg, the ICEpop CAPability measure for Adults[57]) and on HRQOL other than the EQ-5D, such as disease-specific instruments, especially since reviewers of the EQ-5D have reported the low coverage of QOL domains relevant to MS.[58] However, disease-specific instruments typically do not incorporate utility scores, which are important when conducting economic evaluations of future interventions in health care.

CONCLUSIONS

In summary, mood was inversely and equally strongly associated with both HRQOL and SCRQOL, which were found to be distinct but complementary concepts of QOL. Depression was considerably more strongly associated with both HRQOL and SCRQOL than anxiety. Fatigue was a confounder in both models, whereas pain only distorted the association between mood and HRQOL. Focusing on mood in both health care and social care for individuals with advanced MS may contribute to improved QOL in a broader sense. ■

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TABLE S1. Regression Model Between Mood (HADS) and Social Care–Related Quality of Life (ASCOT) and Health-Related Quality of Life (EQ-5D) (N = 75)

	ASCOT				EQ-5D-5L				EQ-VAS		
Independent variable	βu (95% CI)	Δ(%)	Bs (95% CI)	R^2	βu (95% CI)	Δ(%)	Bs (95% CI)	R^2	βu (95% CI)	Bs (95% CI)	R^2
Step 1											
Mood	−.013 (−.018 to −.007)		−.474 (−.679 to −.269)	22.5	−.016 (−.025 to −.008)		−.428 (−.639 to −.217)	18.3	−.468 (−1.042 to .106)	−.187 (−.416 to .042)	3.5
Step 2											
Sex	−.012 (−.018 to −.006)	−7.7			−.017 (−.025 to −.008)	6.3					
MS duration	−.013 (−.018 to −.007)	0.0			−.016 (−.023 to −.008)	0.0					
EDSS	−.013 (−.018 to −.007)	0.0			−.016 (−.022 to −.010)	0.0					
FIM motor	−.013 (−.018 to −.007)	0.0			−.018 (−.024 to −.011)	12.5					
FIM cognitive	−.012 (−.017 to −.007)	−7.7			−.016 (−.024 to −.008)	0.0					
Pain	−.012 (−.018 to −.007)	−7.7			−.012 (−.019 to −.005)	−25.0					
Spasticity	−.013 (−.018 to −.007)	0.0			−.015 (−.023 to −.007)	−6.3					
CIS20R-f	−.010 (−.015 to −.004)	−23.1			−.012 (−.021 to −.003)	−25.0					
Step 3											
Mood	−.010 (−.015 to −.004)	−23.1	−.368 (−.58 to- −.154)	29.2	−.011 (−.019 to −.003)	−31.3	−.297 (−.507 to −.087)	36.4	-	-	-
Step 4											
Anxiety	−.007 (−.019 to.004)		−.165 (−.418 to −.087)		−.006 (−.022 to .010)		−.092 (−.350 to −.165)		-	-	-
Depression	−.018 (−.031 to −.006)		−.371 (−.623 to −.118)		−.027 (−.045 to −.009)		−.393 (−.650 to −.135)		-	-	-

Δ(%), proportional change in βu; Bs, standardized β coefficient; βu, unstandardized β coefficient; ASCOT, Adult Social Care Outcome Toolkit; CIS20R-f, Checklist Impact Scale Revised-Fatigue; EDSS, Expanded Disability Status Scale; EQ-5D-5L, EuroQol 5-dimensional 5-level; EQ-VAS, EuroQol Visual Analogue Scale; FIM, Functional Independence Measure; HADS, Hospital Anxiety and Depression Scale; R^2, proportion of variance.
Step 1: effect of mood unadjusted for confounding
Step 2: effect of individual confounders
Step 3: effect of mood adjusted for relevant (Δ›15%) confounding
Step 4: relative effect of the 2 components, anxiety (HADS-A) and depression (HADS-D) of mood adjusted for relevant confounding