



## Original article

## Unmet needs influence health-related quality of life in people with multiple sclerosis



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## ABSTRACT

**Background:** People with MS are a heterogeneous population with varying difficulties and needs that are influenced by the individual experience of the disease, symptoms and disease course. The aim of the present study was to identify factors that influence health-related quality of life in a sample of subjects with MS, specifically health and social care-related needs and demographic and disease characteristics.

**Methods:** Individuals with a definite diagnosis of MS were identified through MS out-patient clinics and local branches of the Italian MS Society. The EQ-5D-3L utility index was used to describe health profiles and as an overall measure of perceived HRQoL. The number of unmet health and social care-related needs was used to describe the impact of unmet needs on HRQoL. Multiple regression analyses were performed using a hierarchical approach.

**Results:** Data was analyzed from 1013 subjects. Overall, 83% of subjects reported at least one health or social care-related need as being unmet and subjects with a higher number of unmet needs had lower HRQoL ( $p < 0.001$ ). The number of unmet needs was entered at the first step with a statistically significant effect (Cox-Snell  $R^2$  0.15, BIC 870.9, AIC 851.2). Clinical variables, included in the second step, contributed significantly to explaining the variability between models (Cox-Snell  $R^2$  0.43, BIC 481.0, AIC 446.6), and the addition of socio-demographic factors further accounted for variability (Cox-Snell  $R^2$ , 0.46, BIC 461.0, AIC 402.0).

**Conclusions:** The study demonstrated that a higher number of both health and social care-related unmet needs predicted lower HRQoL. The health profile of the sample identified all domains of the EQ-5D-3L as being important in determining HRQoL. Data confirms that unmet needs alone are significantly related to reduced HRQoL, although the multifactorial and complex nature of MS makes it a challenge to identify the combination of aspects that fully predict variability in quality of life.

## 1. Introduction

Multiple sclerosis (MS) is a disabling disease of the central nervous system with an unpredictable course that affects around 2.3 million people in the world, with as many as 600,000 in Europe and more than 109,000 in Italy (Compston et al., 2003; Browne et al., 2014; Battaglia et al., 2017). The effects of MS are wide-ranging, having an impact on physical, psychological, social and economic well-being (Kobelt et al., 2017). Furthermore, it is known that psychological, psychiatric and social issues related to MS play a major role in health-related quality of life (HRQoL) (Prisnie et al., 2018; Hayarat et al.,

2019). Consequently, people with MS are a heterogeneous population with varying difficulties and needs that are influenced by the individual experience of the disease, symptoms and disease course. The clinical care of patients with MS is focused on disease management, alleviating symptoms and maintaining functional ability and HRQoL (Giovannoni et al., 2016). In recent years, there has been an increased focus on the association between health and social care-related needs and HRQoL in health services research (Calvert et al., 2013; van Walsem et al., 2017). Despite general awareness of the need for comprehensive healthcare for patients with MS, there is a lack of research investigating the state of health and social care service delivery

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and its impact on HRQoL. An earlier study assessed HRQoL and healthcare services in patients with long-term neurological conditions (MS, Huntington's disease, amyotrophic lateral sclerosis and Parkinson's disease), and reported that often individuals did not receive the services that could have positively influence their HRQoL (Calvert et al., 2013). An Italian study in MS demonstrated that subjects had a considerable number of unmet needs regarding healthcare and social support, indicating that many individuals were not receiving the comprehensive care they needed (Ponzio et al., 2015). Studies specifically investigating the potential association between the status of health and social care-related needs and its influence on HRQoL in MS have not been identified in the literature.

## 2. Aim

The aim of the present study was to identify factors that influence HRQoL in a sample of subjects with MS, specifically health and social care-related needs, and demographic and disease characteristics.

## 3. Methods

### 3.1. Sample

Potential subjects were invited to participate in the study through a contact e-mail on the MS Society website, randomly invited to participate from local branch contact lists and consecutively recruited at MS clinics. At MS clinics, an MS Society volunteer informed individuals of the study and acquired consent to be contacted later for a telephone interview by a member of the research team.

Data were collected using a questionnaire completed directly by the subject or through a telephone interview. The study was conducted according to the Declaration of Helsinki guidelines for human subject research.

### 3.2. Instruments

The EQ-5D-3L questionnaire measures HRQoL (EuroQol Group, 1990). The first of this two-part instrument includes five single-item dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension is measured on a 3-point scale (1 = no problem, 2 = some problems, 3 = extreme problems). The combination of problems on the five dimensions related to each individual are converted into a utility index score (ranging from -0.380 to 1.000) based on the population preference-based value sets derived from the Time-Trade-Off (TTO) technique (Scalone et al., 2013). The second part of the EQ-5D-3L consists of a visual analogue scale (EQ-VAS) ranging from 0 (poorest condition) to 100 (best possible health condition).

The level of disability was determined using the self-Expanded Disability Status Scale (EDSS) (Tacchino et al., 2019). The EDSS score was dichotomized using a cut-off score of 6 (EDSS < 6, "low" disability; EDSS ≥ 6, "high" disability) since it represents an important functional milestone of clinical disability (Kurtzke et al., 1983).

Health and social care-related needs were assessed with a questionnaire specifically developed for a recent study on the needs of people with MS (Ponzio et al., 2019). Participants were asked to identify their needs during the previous year from a list of 12 items and to report whether they perceived that the need was satisfied or not. The answers were coded as *not perceived as a need* (0), *need satisfied* (1) and *need unmet* (2). Health care-related needs investigated were rehabilitation, psychological support, technical aids, medications and residential care. Social care-related needs included financial support, personal assistance, transportation, eliminating architectural barriers, managing bureaucracy, workplace adaptation and career guidance. Socio-demographic information (age, gender, education, marital and occupational status) and clinical characteristics (disease duration,

relapses in the last three months, disability level and use of DMT) were also recorded.

For the purpose of this study, the EQ-5D-3L utility index was used to describe both health profiles and as an overall measure of perceived HRQoL (EuroQol Research Foundation, 2018). The number of unmet health and social care-related needs was used to describe the impact of unmet needs on HRQoL.

### 3.3. Statistical analyses

Descriptive statistics of mean values and standard deviations (SD) were calculated for sociodemographic and clinical characteristics. Frequencies and proportions (%) were computed for nominal variables. A health status profile for the general sample was based on the calculation of the number and percent of each level of EQ-5D-3L scores (1 = no problem, 2 = some problems and 3 = extreme problems) for the five dimensions. The mean value and SD of the HRQoL VAS-score were calculated. The mean number of total unmet needs was calculated. Test for trend was used to verify the presence of a trend across categorical variables.

The relationship between each of the independent variables (number of unmet needs, clinical and socio-demographic variables) and the dependent variable (utility index) was analyzed using simple linear regression (data not reported). Tobit regression models with upper censoring at 1.0 were used to assess the influence of the variables on HRQoL (Austin et al., 2000). Variables that correlated with an utility index with  $p < 0.05$  were retained. Multiple regression analyses were performed using a hierarchical approach (a block-wise analysis). Independent variables were entered into the models in three steps: Step 1. HRQoL, number of health-related needs and number of social care-related needs; Step 2. clinical variables (disability level, disease duration); Step 3. socio-demographic variables (gender, age, years of education, employment status). Results are presented as coefficients and standard errors. Specification errors and the goodness of fit of the models were examined using Cox-Snell  $R^2$ , Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC). A higher  $R^2$  score, lower AIC and lower BIC indicate a better fit with the models. The analyses were performed using Stata Statistical Software, release 15 (StataCorp, 2017).

## 4. Results

A total of 1,351 eligible subjects were recruited and 1,014 provided signed informed consent to participate. One subject did not complete the EQ-5D-3L questionnaire and was therefore not included in the analysis. Data was analyzed from 1,013 subjects. Table 1 provides demographic and disease information.

**Table 1**  
Demographic and clinical characteristics (N = 1,013).

Age in years, mean (SD)		49.8 (12.8)
Female, %		69.4%
Education, %	Primary school	31.0%
	High school	48.6%
	University degree	20.4%
Marital status, %	Married	55.1%
	Other	44.9%
Occupational status, n (%)	Currently employed	37.4%
	Unemployed	62.6%
Duration of MS disease in years, mean (SD)		15.3 (10.2)
Relapses in the last 3 months, %		15.6%
DMT user, %		63.3%
Disability level, %	Low (EDSS < 6)	54.0%
	High (EDSS ≥ 6)	46.0%
EQ-5D index utility scores, mean (SD)	Italian value set	0.648 (0.340)

DMT = disease modifying treatment; EDSS = Expanded Disability Status Scale; SD = standard deviation

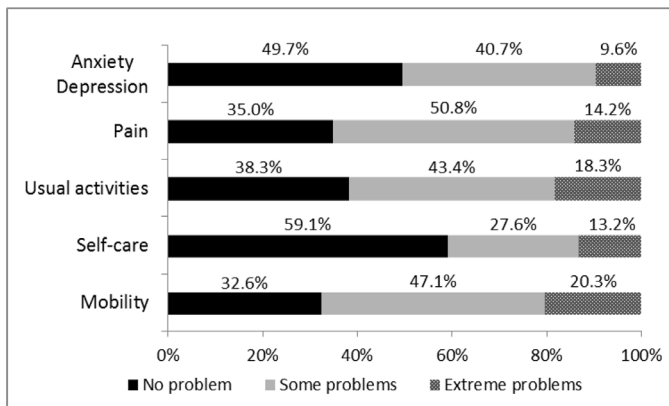


Fig. 1. Health profile of subjects based on EQ-5D-3L dimensions.

The health profile resulted in all five domains of HRQoL representing problems (some or extreme) for a large proportion of subjects: 67.4% mobility, 65% pain/discomfort, 61.7% usual activities, 50.3% anxiety/depression and 40.8% self-care (Fig. 1). The EQ-5D-3L utility index had a mean score of 0.648 ( ± 0.340). HRQoL measured by the EQ-5D VAS resulted in a mean score of 63.0 ( ± 20.3).

Subjects reported a mean of 1.37 ( ± 1.11) health-related needs and 2.26 ( ± 1.70) social care-related needs. A mean of 0.86 ( ± 0.92) health care needs and a mean of 0.85 ( ± 1.09) social care-related needs were reported to have been met. Overall, 83% of subjects reported at least one health care or social care-related need as being unmet, specifically, 62.5% reported at least one unmet health care need and 68.2% at least one unmet social care-related need.

4.1. Relationship between number of unmet needs and HRQoL

Fig. 2 shows the mean EQ-5D-3L utility index for the number of needs, stratified into three categories: no unmet needs, one unmet need and two or more unmet needs. Results of the hierarchical regression analysis of the association between the number of unmet needs and HRQoL are presented in Table 2. Overall, subjects with a higher number of unmet needs had lower HRQoL, demonstrated by a statistically significant trend for both health care and social care-related needs (p < 0.001). Table 2 how the step-wise inclusion of additional covariates improved the fit of the models to the HRQoL data. The number of unmet needs was entered at the first step with a statistically significant effect (Cox-Snell R<sup>2</sup> 0.15, BIC 870.9, AIC 851.2). Clinical variables, included in the second step, contributed significantly to explaining the variability between models (Cox-Snell R<sup>2</sup> 0.43, BIC 481.0, AIC 446.6), and the addition of socio-demographic factors further accounted for

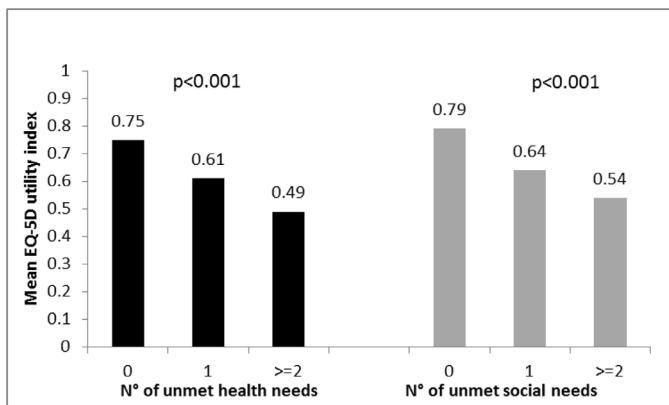


Fig. 2. Mean index for number of health and social care-related needs P value is test for trend.

variability (Cox-Snell R<sup>2</sup>, 0.46, BIC 461.0, AIC 402.0).

The strongest model for predicting HRQoL (step 3) demonstrated that for each unit increase in the number of unmet needs, there was an associated decrease of 0.05 (unmet health needs) and 0.03 (unmet social-related needs) points in utilities. Similarly, higher disability (>6 EDSS) was associated with a decrease of 0.31 points in utilities compared to lower disability. Disease duration of one year was associated with a decrease of 0.01 points in utilities. Each one-year increase in age was associated with a decrease of 0.01 points in utilities. A higher level of education was associated with a significant increase in HRQoL measured in utilities (0.06 points for a university-level education), while employment was associated with an increase in utilities by 0.08 points.

5. Discussion

While resources to meet the needs of Italians with MS are available in theory, research has clearly pointed to an inequitable distribution of health and care-related services in different geographic areas of the country (Tacchino 2017; Ponzio 2019). This in part is due to the complexities of the National Health Service, in which 19 regions and two autonomous provinces each have significant autonomy in determining the macro structure of their health systems and relevant differences exist between regions in terms of wealth, and thus, health and social care service availability (For more details refer to international.commonwealthfund.org/countries/italy/). Given the Italian healthcare landscape, it is apparent that a high proportion of people living with MS experience unmet needs related to their disease (Ponzio 2019). The current study confirmed this with 83% of subjects reporting at least one need being unmet. This is the first report of the impact of unmet needs on HRQoL in the context of MS. Subjects in the present study had lower quality of life than the general population, compared on the EQ-5D-3L, demonstrated by both the mean utility index (0.648 vs. 0.915 general population) and the EQ-VAS score (63.0vs. 78.2 general population) (Scalone et al., 2015). The study demonstrated that a higher number of both health and social care-related unmet needs predicted lower HRQoL.

The health profile of the sample identified all domains of the EQ-5D-3L as being important in determining HRQoL. This is consistent with several reports that have linked mobility impairment, pain and mood disorders to reduced quality of life (Zwibel et al., 2009; Barin et al., 2018; Prisnie et al., 2018; Yalachkov et al., 2019). The domain of pain and discomfort is an important issue in MS, and is correlated with depression (Zwibel et al., 2009). In the current study 57% of subjects who reported pain as a problem also reported depression and anxiety. Untreated depression has been shown to increase the burden of MS in different ways, and is considered a primary determinant of quality of life (Ziemssen et al., 2009; Prisnie et al., 2018; Yalachkov et al. 2019). Further, the EQ domain of “usual activities”, which includes work, study, maintaining the home, family and leisure activities, problematic for two-thirds of the current sample, have also been reported as factors that influence quality of life, as well as being impacted by symptoms like mood and mobility problems (Zwibel et al., 2009; Longeran et al., 2015). Taken in sum, the results confirm that the health profile of MS is a multidimensional phenomenon influenced by the different symptoms of the disease and by the complex interconnection between symptoms.

The three-step regression analysis demonstrated that unmet health and social care-related needs alone were significantly related to reduced HRQoL. The addition of disease-related variables, including disability level, disease duration and disease modifying therapy, accounted for the most relevant variability between models. A higher level of disability and longer disease duration negatively correlated with HRQoL, while the use of a disease modifying treatment appears to have a role in predicting better quality of life. A higher level of disability being predictive of having unmet needs has been reported in the literature (Zheng et al., 2014; Göksel et al., 2011; Baumstarck et al.,

**Table 2**  
Hierarchical regression analysis predicting HRQoL.

	Step 1 $\beta$ (SE), p value	Step 2	Step 3
N° unmet health needs	-0.11 (0.02), <0.001	-0.06 (0.01), <0.001	-0.05 (0.01), <0.001
N° unmet social needs	-0.07 (0.01), <0.001	-0.03 (0.01), <0.001	-0.03 (0.01), <0.001
Disability levels (low EDSS <6)		-0.36 (0.02), <0.001	-0.31 (0.02), <0.001
Duration of MS disease		-0.01 (0.01), <0.001	-0.01 (0.01), 0.017
DMT use (no DMT use)		0.06 (0.02), 0.005	0.04 (0.02), 0.065
Gender (male)			0.01 (0.02), 0.314
Age			-0.01 (0.01), 0.002
Educational (primary school)			
High school			0.01 (0.02), 0.955
University degree			0.06 (0.03), 0.016
Occupational (unemployed)			0.08 (0.02), <0.001
Cox-Snell R <sup>2</sup>	0.15	0.43	0.46
BIC	870.9	481.0	461.0
AIC	851.2	446.6	402.0

$\beta$  = regression coefficient; SE=standard error; DMT=disease modifying treatment; AIC=Akaike information criteria; BIC=Bayes information criteria. Text in parentheses provides the reference category.

2015). One study found that unmet social needs significantly related to progressive MS and more disease years (Longeran et al., 2015). While our study did not differentiate between disease courses, progressive forms of MS are typically associated with higher disability. In a study reported by Prisnie et al. disease severity was predictive of lower quality of life on the mental composite score on the SF-12, a commonly used quality of life measure, but was not predictive of the physical component (Prisnie et al., 2018). One study reported discordant results, finding that problems were common in even mildly disabled subjects (Eriksson et al., 2019). Finally, the use of a disease modifying treatment is associated with prevention of worsening and with improvement of HRQoL (Jongen et al., 2017), supporting the current results. Adding demographic variables to the regression analysis further explained HRQoL. While an older age negatively correlated with HRQoL, female gender, a higher level of education and being employed predicted better quality of life. These results confirm other reports in the literature (Prisnie et al., 2018; Yalachkov et al., 2019; Eriksson et al., 2019), with the exception of age not being particularly relevant in one study (Eriksson et al., 2019).

While the combination of unmet needs, disease-related and demographic factors together were strongly predictive, these combined variables did not fully account for HRQoL and thus, other aspects clearly have a role. While the analysis allows for a finite number of covariates to be assessed, other factors such as coping skills, personality traits, social support, financial status and non-MS comorbidities, have a role in accounting for variability in HRQoL in part, and there are likely others (Longergan et al., 2015; Zarbo et al., 2016; Mikula et al., 2015; Costa et al., 2017; Conway et al., 2017).

### 5.1. Limitations

Caution should be used in interpreting the present findings as indicative of a causal relationship between HRQoL and independent variables due to the cross-sectional study design. Further, although the EQ-5D-3L has been widely used in assessing HRQoL, it is a generic questionnaire and not specific for MS, and thus does not specifically address some aspects of MS that are relevant.

## 6. Conclusions

The current study confirms that unmet health and social care-related needs alone are significantly related to reduced HRQoL, although the multifactorial and complex nature of MS makes it a challenge to identify the combination of aspects that fully predict variability in quality of life. Currently there is no definitive cure for MS and while disease modifying therapies may have a modest effect on HRQoL, there

are other pharmacological and non-drug interventions, including rehabilitation, that can address factors that put individuals at risk for reduced quality of life, such as symptom management that addresses mood disorders, pain and impaired mobility.

Importantly, addressing HRQoL in MS is inevitably related to the equitable availability and allocation of services and support that address health and social care-related needs. This requires evidence-based policy-making on the social determinants of health (WHO 2008). The scope of future research in this area should include linking the individual perception of unmet needs to evidence of a lack of appropriate and accessible services and focus on identifying the source or sources of the problem be it resource limitations, skewed priorities, culture, history, political environment or other factors.

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## CRediT authorship contribution statement

**Michela Ponzio:** Visualization, Writing - original draft, Project administration, Formal analysis. **Andrea Tacchino:** Writing - original draft. **Concetta Vaccaro:** Visualization, Writing - original draft. **Silvia Traversa:** . **Giampaolo Brichetto:** . **Mario Alberto Battaglia:** . **Michele Messmer Uccelli:** Visualization, Writing - original draft, Project administration.

## Declaration of Competing Interest

The authors declare that they have no conflicts of interest affecting this article.

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