Multiple sclerosis patients valuing their own health status: valuation and psychometric properties of the 15D

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Abstract

An ongoing debate on decision and cost-utility analyses is whether to use preferences of general public or patients. The aim of this study was to replicate the valuation procedure of the multi-attribute utility generic measure, 15D, using a sample of multiple sclerosis (MS) patients and to assess its psychometric properties. Consecutive outpatient MS patients were recruited from two MS centers in Greece. The three-stage valuation procedure was applied and, with the use of elicited preference weights, an MS patients' algorithm was developed. The original Finnish value set derived from healthy individuals was also used to calculate scores and a comparison between the two algorithms was made. A total of 64 MS patients were evaluated. The 15D scores obtained with the MS patients' valuation algorithm were higher than the original one. The derived utilities differed significantly with respect to age, depressive symptoms, Expanded Disability Status Scale score and clinical form. MS patients indicated as most important domains mobility, mental functioning and vitality. Cronbach's alpha was estimated 0.876 and correlations between relevant dimensions of the instruments were moderate to high. The 15D was generally feasible and reliable in patients with MS and the valuation system yielded acceptable psychometric properties.

Introduction

Multiple sclerosis (MS) is a chronic and potentially highly disabling disease of the central nervous system.[1] It is an unpredictable disease with a wide spectrum of consequences in physical and mental health which undoubtedly impacts significantly upon quality of life.[2]

Health-related quality of life (HRQoL) is a multidimensional concept that includes physical, mental, and social health and represents a subjective perception reported by the patient.[3] Generic tools of HRQoL can be classified as health profiles and utility measures, which are called multi-attribute utility instruments (MAUIs) and are based on the decision theory.

The interest for HRQoL in MS is relatively new. For many years the MS research was focused on estimation of impairment and disability,[2] as measured by the Expanded Disability Status Scale (EDSS). The two last decades HRQoL in MS has been studied with increasing intensity and it is being utilized more often as an endpoint.[4] HRQoL assessment in MS has essentially restricted on the use of health profiles and the SF-36 is routinely used.[2,4] Criticisms of the appropriateness of the SF-36 and other generic HRQoL instruments have focused on the fact that item content of these scales does not reflect all aspects of HRQoL considered important for MS patients.[5] As a result, MS specific HRQoL instruments have proliferated the last few years in order to tackle this problem. The combination of a generic profile and a disease specific instrument is generally recommended increasing their ability to capture subject's real health status, however none of them could be used in cost-utility analyses because they lack the necessary properties.[6] Until recently, assessment of utilities in studies of MS was not frequent. No gold standard instrument has been established yet, although the most commonly used is the EQ-5D, and comparisons of available measures are rather rare.[5]

The 15D is a MAUI and it could be a useful utility measure for MS patients in many aspects. Nowadays, several new therapies are becoming available in the field of MS (*e.g.* monoclonic antibodies), which may have a positive benefit for disease course, but are also related to potentially severe adverse events. Thus, they may have significant impact on all aspects of life and if there is more than one treatment among which health care providers and patients must choose, the use of utility assessment becomes more relevant in a decision-making context.[7] This notion is enhanced by the fact that MS mainly affects young people in fully productive age, with direct and indirect costs being relatively high, which underlines the necessity to perform economic evaluation studies. The patient's perspective in evaluating health system and management of disease is increasingly recognized.[8] Patient-derived data are progressively more accepted as an important assessment domain in clinical research for most chronic conditions, including MS.[9] In particular, concerning MAUIs, involvement of patients is recommended mainly in the development of descriptive systems and in some cases in creating condition specific instruments, in order to enhance the content validity of these measures.[10] In the health states assessment literature there is an ongoing debate whether to use utilities of healthy people or patients.[11,12] In general, patient's participation in valuation of MAUIs has been investigated adequately for some instruments such as EQ-5D and Health Utilities Index (HUI) but not enough for 15D. Specifically for the 15D, values for different health states are derived from healthy people and it is doubtful whether these are valid reflections of patients' true perceptions of the disutility of disease.[13] Hence, it is worth mentioning that for decisions concerning benefits of medical interventions or for highlighting patients' willingness to accept potentially life-saving treatments with possible negative effects it is important to assess if patients' values are actually represented by these measurements. From this perspective, the valuation procedure of the 15D seems to be meaningful and requisite. To our knowledge, utility values of MS patients with the 15D have not been extensively investigated worldwide and no such studies have ever been conducted in Greece.

The primary goal of this study was to replicate, using the Greek version of the 15D instrument, the three-stage valuation proce-

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dure, in a sample of MS patients; moreover, a main objective of the study was to assess its psychometric properties.

Materials and Methods

Sample and data

This study adopted a cross-sectional design. Sixty-four consecutive patients were recruited from the outpatient assessment clinics of AHEPA University Hospital and Greek MS Society Center in Thessaloniki. The patients comprised a wide spectrum from recently diagnosed to more severe cases referred for consultation on disease management.

The following inclusion criteria were used: diagnosis of MS according to McDonald criteria, any type of the disease, age over 18 years, EDSS score ≤6.5, having Greek as native language; and having given written informed consent. The main exclusion criteria were: illiteracy, patients with a main diagnosis other than MS, acute major comorbidities present, suffering from dementia (Mini Mental State Examination score, MMSE <24), having experienced a relapse during the last month and having experienced a severe traumatic event in the last two months. The study was approved by the Greek MS Society and AHEPA hospital ethics committees.

The questionnaires were administered by face-to-face interviews from an experienced interviewer. Socio-demographic data were also obtained. The EDSS was assessed by a neurologist experienced in MS. Severity of depressive symptoms was evaluated with the Greek version of the Center for Epidemiologic Studies Depression Scale (CES-D Scale) and cognitive function with the MMSE.

Instruments

Three HRQoL questionnaires were administered. The Greek versions of the 15D and the SF-36 were used as generic tools and MusiQoL as disease-specific.

Description and valuation of the 15D

The 15D is a relatively brief, 15-dimensional, MAUI that can be used both as a profile and health utility measure.[14] It depicts health status, assessing 15 attributes, namely: breathing, mental function, speech (communication), vision, mobility, usual activities, vitality, hearing, eating, elimination, sleeping, distress, discomfort and symptoms, sexual activity and depression. Each dimension has five levels of severity: level 1 is the best (no health problems at that moment) and level 5 is the worst (severe health problems). Subsequently, the classification comprises many billions of distinct health states. A single index score is obtained by incorporating population based value sets to the dimensions.

The valuation system of the 15D comprised a three-stage procedure through which a set of preference or utility weights was elicited from the sample of MS patients. These weights were used to compute a single-index score over all the dimensions from the health state descriptive system. The maximum score is 1 (no problems on any dimension) and the minimum score is 0 (being dead). The formula employed to generate the summary 15D score is the following:[14]

$$V_H = I_j(x_j)[w_j(x_j)] \quad (1)$$

where $I_j(x_j)$ is the average relative importance people attach to various levels of dimension $j(j=1,2,...,15)$, and $wj(xj)$ is the average value that the respondents place on various levels of dimension j.

According to this formula, a value is assigned to each dimension level, and these are multiplied by a weight representing the relative importance of that dimension and summed to derive a single index.

Importance weights were obtained by asking MS patients to indicate the relative importance of each dimension from the viewpoint of HRQoL on an adjacent importance scale (0-100 ratio scale). The most important dimension was placed at the top (at 100). Individual values given to a dimension by patients were averaged and transformed in order the sum of weights to equal unity. Importance weights were elicited with reference to both the top and bottom level of each dimension and means (standard deviations, SDs) and 95% confidence intervals (CIs) were computed. Importance weights for the intermediate levels were extrapolated linearly from the weights of the extreme ends in relation to the distance between level values.[14]

The level values were elicited similarly by using a 0 to 100 ratio scale where the patients placed the most desirable level at 100. In addition to the five levels, the states of being unconscious and dead were also valued for each dimension. The individual values given to a level were averaged and divided by 100 to obtain the desirability value of that level. Therefore, the within-dimension values reflect the distance between the levels on a 0 to 1 scale and subsequently the goodness of the levels relative to the absence of problems on the dimension and to being dead. The preference weight for a level of a dimension was then obtained by multiplying the level value by the importance weight of that dimension. A simple computer algorithm was used to associate the preference weights to the responses on the 15D questionnaire.[14]

SF-36

The SF-36 is the most widely used generic instrument of HRQoL. It includes 36 self-administered items distributed over eight domains: PF, Physical Function; RP, Role Physical; BP, Bodily Pain; GH, General Health; VT, Vitality; SF, Social Functioning; RE, Role Emotional and MH, Mental Health. The first four scales measure physical health (physical component-PCS) while the last four mental health (mental component-MCS). Scores are valued between 0 (worst health) and 100 (best health).[15]

MusiQoL

The MusiQoL is a well-validated, self-administered, disease-specific questionnaire that comprises 31 items describing nine dimensions and yielding a global index score. Each dimension is named according to its constitutive items, as follows: Activity of Daily Living – ADL, Psychological Well-Being – PWB, Symptoms – SPT, Relationships with Friends – RFr, Relationships with Family – Rfa, Relationships with Health Care System – RHCS, Sentimental and Sexual Life – SSL, Coping – COP, and Rejection – REJ.[16] Each item is scored on a six-point Likert scale and for negatively worded items, scores are reversed; thus, higher scores indicate a higher level of HRQoL, on a 0 – 100 scale.[16]

The MusiQoL is a patient focused questionnaire developed by an independent scientific steering committee in conjunction with MS patients, neurologists and health economists. The MusiQoL is the only disease specific MS HRQoL questionnaire not adapted from a generic instrument and the only one directly based on MS patients' perspective.

Statistical analysis

Statistical analysis was performed using SPSS v17.0 (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Normally distributed continuous data were reported by mean and SD otherwise by median and range. Categorical variables were described by counts and percentages. For continuous variables, the significance of the differences between groups was analyzed using *t*-test or the Mann–Whitney test. $P<0.05$ signified statistical significance.

The 15D utilities were examined with *t*-tests and analysis of variance (ANOVA) and utilities from the MS patients and original scoring algorithms were compared using the paired samples *t*-test.

The following psychometric properties were examined: feasibility and data quality, logical consistency, sensitivity, reliability, convergent and discriminant construct validity. Feasibility and data quality were determined to be high if the percentages of missing data for the various items were low. Logical consistency was exam-

ined by the percentage of respondents who attributed a lower value to a logical better level of health. Discriminatory power was assessed through floor and ceiling effects. Reliability was tested using Cronbach's coefficient alpha, both overall and with an item deleted from the scale. Values exceeding 0.70 were considered satisfactory.[17] Additionally, the acceptance cut-off for item-total correlations was 0.30.[18] Convergent and discriminant construct validity were investigated with the multitrait-multimethod analysis.[19] Intercorrelations of corresponding items or scales of the different questionnaires were assessed. A finding of higher correlations between items measuring related phenomena, than between non-corresponding items, would support construct validity. Spearman correlations of less than 0.30 were considered weak evidence of validity, 0.30 to 0.59 moderate, and greater than 0.59 strong.[18] Moreover, construct validity was also examined by comparing the ability of the HRQoL measures to distinguish groups of subjects known to differ in specific socio-demographic or clinical variables (*known-groups* validity), using criteria from the literature.[20] In this study, the variables assessed were the following: gender, age, depressive symptoms, EDSS score and clinical form of MS. Confirmation of the assumptions that women, older patients, patients with depressive symptoms, higher EDSS scores and progressive clinical forms of MS report lower HRQoL, would provide evidence of discriminant construct validity.

Results

Detailed demographic and clinical information is shown in Table 1. The average importance weights were computed for the top and bottom of each of the 15 dimensions and were expressed as means (SD) and 95% CIs. In pairwise comparisons, most of the average importance weights from the top differed significantly from those from the bottom (Table 2). The subjects, at the top of the dimensions, designated mobility, mental function and vitality as the most important health attributes, whereas hearing and speech as the least important ones. Respectively, at the bottom of the dimensions, the lack of mobility was indicated as the least desirable health state (lowest importance weight) and the inability to perform usual activities as the most desirable (highest importance weight) in relation to other ominous health states.

The average value for each level and the importance weights for intermediate levels for each of the 15 dimensions are presented in Table 3. The calculation of these levels was based on the previously described methodology and the MS patients scoring algorithm for the 15D derived from these values.

Concerning the feasibility and data quality, no missing data were observed and scores were computable for all patients. Logical consistency was evaluated for the five levels of each dimension with no *non-logical* answers. Sensitivity was acceptable; minimal floor effects were recorded while ceiling effects were in general moderate to high. The most considerable ceiling effects were recorded on the dimensions of eating, hearing and speech, 93.8, 87.5 and 82.5%, respectively, implying reduced discriminatory power for these particular dimensions, at least in this specific sample. Internal consistency was satisfactory for most dimensions (Table 3). Overall Cronbach's alpha for all dimensions included was 0.876, thus fulfilling the 0.70 criterion. Alpha coefficient was reduced or remained unchanged when one dimension (item) was deleted from the scale in most cases (14 of 15), suggesting that their presence contributes to the overall reliability. Only the exclusion of the hearing resulted in a (slightly) improved Cronbach's alpha, a finding in line with the item-total correlation that was lower than 0.30.

Construct validity was estimated by comparing the 15D scores with those from the MusiQoL and SF-36 as well as with CES-D and EDSS scores. The direction, magnitude, statistical significance and pattern of correlations were consistent with predictions. In particular, for the hypothesized associations high correlations were shown between related items while associations between non-corresponding items were lower (Table 4). Concerning total scores, Spearman correlation coefficients provided strong evidence of construct validity between the instruments. The correlation of the 15D and the MusiQoL was 0.765 for the MS patients' valuation and 0.712 for the original value set.

Moreover, the ability of the two valuation systems to discriminate groups of patients was another evidence strengthening construct validity (Table 5). The MS patients' algorithm steadily generated higher 15D utilities than the original one and both showed satisfactory discriminant ability. The results confirmed the assumptions that women, older patients, patients with depressive symptoms, higher EDSS scores and progressive clinical forms of MS would report lower HRQoL. All the above-mentioned differences, with the exception of gender, were found to be statistically significant ($P<0.05$).

Discussion

To the best of our knowledge, this is the first attempt to create a scoring algorithm of the 15D based on valuations for the different health states by a sample of MS patients rather than by healthy individuals. Furthermore, this is the first study in which the 15D is administered to a sample of Greek MS patients and the results reported here point out that the Greek version demonstrates in general satisfactory reliability and construct validity.

A considerable debate of the research community is whose preferences should be used to value health states. To date, there is the dilemma mainly between the patient or general population perspective. Several arguments exist for and against of either approach. Patients are familiar with particular health states and have the knowledge and experience of impaired health as well as the ability to judge better their own good. On the other hand, they

Table 1. Demographic and disease characteristics of the study sample.

	Value
Total sample, n	64
Gender, n (%)	
Male	24 (37.5)
Female	40 (62.5)
Age, years (mean±SD)	39.3±8.94
20-29	9 (14.1%)
30-39	23 (35.9%)
40-49	22 (34.4%)
50-59	10 (15.6%)
Education level, n (%)	
≤ 6 years of education	4 (6.3)
7-9	6 (9.4)
10-12	29 (45.3)
>12	25 (39)
Marital status, n (%)	
Single (never married)	17 (26.6)
Married/engaged	41 (64)
Widowed - divorced	6 (9.4)
Residence, n (%)	
Urban	44 (68.8)
Rural	20 (31.2)
Current employment status, n (%)	
Employed full time	22 (34)
Employed part time	4 (6.2)
Unemployed	16 (25)
Retired	17 (26.6)
Student	5 (7.8)
Disease duration, years (median range)	6 (0-31)
EDSS score (%)	
≤2.5	24 (37.5)
3.0-4.5	30 (46.9)
5.0-6.5	10 (15.6)
MMSE score, median (range)	28 (24-30)
CES-D score, mean ± SD	14.55±11.49
Current disease course, n (%)	
Relapsing-remitting	44 (68.8)
Secondary progressive	5 (7.8)
Primary progressive	7 (10.9)
Relapsing progressive	4 (6.3)
Clinically isolated syndrome	4 (6.3)

EDSS, expanded disability status scale; MMSE, mini-mental status scale examination.

may provide biased values because of their personal interest and in a degree they may compromise their own benefits by giving higher values.[11,21] However, none of these perspectives could be considered ideal and the choice depends on the specific decision making framework.

In general, the patients tend to assign higher health state utilities than the general public, a finding consistent in the literature, which was also observed in our study.[11,12] Our valuation was performed by patients suffering from MS whereas the original one by healthy population and this could possibly explain the discrepancy in the obtained utilities. Healthy respondents is more possible to focus on the negative aspects of the disease without recognizing any adaptation to an unfavorable health state while chronic patients seem to overvalue health states. Interestingly, someone could investigate the change of these health states valuations over the course of time where coping mechanisms may be developed by patients.[22] Moreover, a recent meta-analysis has shown that according the elicitation methods patients gave higher valuations than non-patients using a visual analog scale and such ratio scales were used in our valuation procedure.[12] Finally, another probable explanation for this finding could be ethnic differences as Greek people may valued higher specific dimensions than Finish. However, a previous study demonstrated that cross-country differences of utility scores, at least in patients with MS at similar disease severity levels, were in general minimal, fact that enhances the notion that this valued version could be used worldwide.[23]

Both valuation systems were compared and showed that the obtained scores were valid reflections of the different demographic and disease factors. Thus, the 15D health state utilities derived with the original Finnish value set differed significantly with respect to age, depressive symptoms, EDSS score and clinical form, just as they did using the MS patients' valuation. Moreover, another important observation was that the scores with the MS patients' algorithm demonstrated higher correlation with MusiQoL. Taking into account that the later is a disease specific question-

Table 2. Average importance weights for the bottom and top of the 15D dimensions (n=59).

Dimension	Top of dimension		Bottom of dimension		P*
	Mean (±SD)	95% CI	Mean (±SD)	95% CI	
Mobility	0.073 (±0.013)	0.069-0.076	0.013 (±0.020)	0.007-0.019	<0.001
Vision	0.066 (±0.014)	0.062-0.070	0.038 (±0.051)	0.024-0.052	<0.001
Hearing	0.062 (±0.013)	0.059-0.066	0.104 (±0.168)	0.580-0.150	NS
Breathing	0.067 (±0.014)	0.063-0.070	0.053 (±0.045)	0.040-0.065	<0.05
Sleeping	0.064 (±0.018)	0.059-0.069	0.073 (±0.066)	0.055-0.091	NS
Eating	0.064 (±0.013)	0.061-0.068	0.037 (±0.050)	0.023-0.050	<0.001
Speech	0.062 (±0.015)	0.058-0.066	0.071 (±0.083)	0.048-0.094	NS
Elimination	0.067 (±0.010)	0.065-0.070	0.060 (±0.073)	0.040-0.080	<0.05
Usual activities	0.068 (±0.010)	0.065-0.071	0.123 (±0.139)	0.086-0.162	<0.001
Mental function	0.073 (±0.013)	0.070-0.077	0.034 (±0.037)	0.024-0.044	<0.001
Discomfort/symptoms	0.064 (±0.012)	0.061-0.067	0.054 (±0.053)	0.039-0.068	<0.05
Depression	0.069 (±0.013)	0.065-0.072	0.063 (±0.055)	0.048-0.078	NS
Distress	0.067 (±0.010)	0.064-0.070	0.086 (±0.066)	0.068-0.104	NS
Vitality	0.072 (±0.010)	0.069-0.074	0.100 (±0.135)	0.063-0.137	NS
Sexual activity	0.063 (±0.018)	0.057-0.067	0.091 (±0.152)	0.049-0.132	NS

*Mean weights compared with paired-samples t-test. SD, standard deviation; CI, confidence interval; NS, non-significant.

Table 3. Average values and level importance weights for each 15D dimension and internal consistency (n=63).

Dimension	Average value for each level [Wj(Xj)]							Level importance weight (Ij)					Item-total correlation	Alpha (item deleted)
	1	2	3	4	5	Uncon	Dead	1	2	3	4	5		
Mobility	1	0.754	0.495	0.233	0.067	0.013	0	0.073	0.057	0.040	0.024	0.013	0.614	0.866
Vision	1	0.826	0.609	0.403	0.141	0.013	0	0.066	0.060	0.053	0.047	0.038	0.526	0.874
Hearing	1	0.844	0.590	0.321	0.123	0.013	0	0.062	0.070	0.082	0.095	0.104	0.237	0.877
Breathing	1	0.809	0.609	0.378	0.140	0.012	0	0.067	0.064	0.061	0.057	0.053	0.348	0.876
Sleeping	1	0.835	0.658	0.399	0.189	0.011	0	0.064	0.066	0.068	0.071	0.073	0.709	0.853
Eating	1	0.752	0.519	0.267	0.077	0.012	0	0.064	0.057	0.050	0.042	0.037	0.384	0.876
Speech	1	0.792	0.585	0.370	0.194	0.014	0	0.062	0.064	0.067	0.069	0.071	0.478	0.873
Elimination	1	0.752	0.523	0.301	0.121	0.013	0	0.067	0.065	0.063	0.061	0.060	0.647	0.874
Usual activities	1	0.800	0.571	0.403	0.189	0.015	0	0.068	0.082	0.098	0.110	0.124	0.644	0.862
Mental function	1	0.760	0.515	0.315	0.116	0.014	0	0.073	0.062	0.052	0.043	0.034	0.621	0.869
Discomfort/symptoms	1	0.822	0.535	0.353	0.137	0.012	0	0.064	0.062	0.058	0.056	0.054	0.453	0.864
Depression	1	0.798	0.574	0.359	0.190	0.013	0	0.069	0.067	0.066	0.064	0.063	0.540	0.864
Distress	1	0.811	0.608	0.410	0.225	0.012	0	0.067	0.072	0.077	0.082	0.087	0.430	0.873
Vitality	1	0.834	0.605	0.398	0.221	0.013	0	0.072	0.078	0.086	0.094	0.100	0.765	0.855
Sexual activity	1	0.801	0.532	0.267	0.125	0.012	0	0.062	0.069	0.077	0.086	0.091	0.626	0.862

naire, this finding could also support the expedience of the valuation procedure in an MS sample.

In previous studies, the 15D has shown good psychometric properties in terms of feasibility, reliability, validity and responsiveness[14,24] and it has been also used in MS patients.[25] The 15D scores were valid for deriving QALYs gained for resource allocation decisions.[14] Validations of the questionnaire have been performed in Greece not only in the general population[26,27] but also in coronary artery disease patients.[28] The present study examined the psychometric properties of the Greek MS patients valuation algorithm and the overall results of the instrument were in general satisfactory. Floor effects were not identified while ceiling effects were moderate for dimensions expected to be affected by MS, a phenomenon that could affect the sensitivity of the instrument. All dimensions, except hearing, showed acceptable internal consistency. Correlations between corresponding items of the measures were high and significant, whilst low correlations were evidenced between items examining different constructs. In addition, 15D scores differentiated between known

Table 4. Spearman's correlation coefficients between 15D with CES-D, EDSS and MusiQoL.

	CES-D	EDSS	ADL	PWB	SPT	RFR	RFA	SSL	COP	REJ	RHCS	MusiQoL Total score
Mobility	0.312**	0.759	−0.694	NS	−0.296**	NS	NS	−0.342*	NS	−0.365*	−0.258*	−0.522
Vision	NS	0.532	−0.513	NS	−0.544	NS	NS	NS	NS	NS	−0.382*	−0.406*
Hearing	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Breathing	NS	NS	NS	NS	NS	0.266**	NS	NS	NS	NS	NS	NS
Sleeping	0.488	0.535	−0.572	−0.430	−0.403*	NS	NS	−0.404*	NS	NS	−0.268*	−0.488
Eating	0.399*	0.318*	−0.358*	NS	NS	NS	NS	−0.367*	NS	NS	NS	−0.367*
Speech	0.362**	0.270*	−0.336*	−0.248**	−0.322**	NS	NS	−0.303**	NS	NS	NS	−0.354
Elimination	0.286**	0.740	−0.622	NS	−0.421*	NS	NS	−0.290*	NS	−0.299*	NS	−0.429
Usual activities	0.440	0.753	−0.812	NS	−0.350*	NS	NS	−0.362*	NS	−0.421*	−0.263**	−0.450
Mental function	0.402*	0.275*	-0.332*	-0.352*	-0.599	NS	-0.270**	-0.281**	NS	NS	NS	-0.441
Discomfort/symptoms	0.270**	0.271**	−0.294**	−0.295**	NS	NS	−0.335*	NS	NS	NS	−0.373*	NS
Depression	0.721	0.255**	−0.302**	−0.726	−0.336*	NS	−0.276*	−0.455	NS	NS	−0.295**	−0.523
Distress	0.429	NS	NS	−0.519	NS	NS	−0.387*	−0.339	NS	NS	NS	−0.311
Vitality	0.711	0.485	−0.694	−0.473	−0.363*	NS	−0.327*	−0.595	NS	NS	−0.360*	−0.649
Sexual activity	0.449	0.484	−0.559	NS	−0.332*	NS	NS	−0.745	−0.267**	NS	−0.375*	0.661
Total score 15D MS patients	−0.717	−0.727*	0.797	0.513	0.607	NS	0.273**	0.607	NS	0.327*	0.435	0.765

P<0.001, *P<0.01, **P<0.05, NS, non-significant.

Table 5. Mean 15D scores from multiple sclerosis patients and original valuations by demographic and clinical variables.

Variable	N (%)	15D score		P-value#
		MS patients valuation	Original valuation	
Gender				
Male	24 (37.5)	0.875	0.827	<0.001
Female	40 (62.5)	0.862	0.816	<0.001
P-value*		0.656	0.739	
Age				
20-29	9 (14.1)	0.940	0.907	<0.05
30-39	23 (35.9)	0.919	0.868	<0.001
40-49	22 (34.4)	0.841	0.790	<0.001
50-59	10 (15.6)	0.756	0.693	<0.001
P-value°		<0.001	<0.001	
CES-D				
Depressive	11 (17)	0.724	0.659	<0.001
Non depressive	53 (83)	0.897	0.853	<0.001
P-value*		<0.05	<0.05	
EDSS				
0-2.5	24 (37.5)	0.935	0.901	<0.001
3-4.5	30 (46.9)	0.866	0.814	<0.001
5-6.5	10 (15.6)	0.705	0.639	<0.001
P-value°		<0.001	<0.001	
Clinical form				
CIs	4 (6.3)	0.916	0.876	<0.05
RR	44 (68.7)	0.897	0.855	<0.001
PR	4 (6.3)	0.771	0.700	<0.001
SP	7 (10.9)	0.722	0.652	<0.001
PP	5 (7.8)	0.844	0.795	0.056
P-value°		<0.001	<0.001	

*Mean 15D scores by sex, CES-D compared with t-tests. °Mean 15D scores by age, EDSS and clinical form compared with ANOVA. #Mean 15D scores from MS patients and original valuation compared with paired samples t-tests. MS, Multiple Sclerosis; EDSS, expanded disability status scale; CIs, confidence intervals.

groups of patients, supporting *known-groups* construct validity. Finally, previous studies showed that depressive mood and physical impairment in MS patients are independent predictors affecting QoL, finding that was confirmed as depression and EDSS scores were highly correlated with 15D and MusiQoL scores.[29,30] Interestingly, this is an important characteristic for ascertaining the relative clinical usefulness of a MAUI as outcome measure since it supports the relation between health utilities and neurological impairment.[31]

In this study the 15D was preferred because, compared with more frequently used utility instruments (SF-6D, EQ-5D), it includes additional questions about vision, elimination and sexual activity. MS unambiguously encompasses most of the 15 attributes addressed in the 15D and in combination with measures of social life and relationships, which are clearly included in MusiQoL, a thorough assessment into the patient's needs, disabilities and concerns is feasible. A recent study by Kuspinar and colleagues has shown that from the top 10 most important domains for MS patients, SF-6D included six of them followed by EQ-5D and HUI 2 with four.[32] These data suggest the need of a more appropriate instrument. The 15D contains six of them and appears to constitute an interesting alternative option. A relative disadvantage of the 15D is that it has not been validated yet to the same extent with the previous scales. Of note, our study through the valuation procedure demonstrated MS patients' values about specific dimensions and highlighted that mobility, mental function and vitality were the most important domains for them, an outcome being in agreement, at least for the first two, with the study mentioned above.

Limitations of the study

The patients of this study were sampled from two MS centers so they may not be fully representative of the overall MS population in Greece. Another limitation was that patients with high EDSS score (>6.5) were not included, a fact that could influence the valuation of some dimensions. Finally, this study only assessed some psychometric properties of the 15D, yet not its factor analytic aspects. Anagnostopoulos and colleagues concluded that there might be issues related to the item/dimension orthogonality or even the limited aspects of quality of life captured by the instrument at least in the general population.[27] This implies that further research is needed to fully clarify 15D's role in measuring the quality of life of MS patients.

Conclusions

In conclusion, the valuation system generated results demonstrating in general satisfactory psychometric properties of 15D in MS patients as well as comparability to the original Finnish value set. In any case, some ceiling effects and lower than required reliabilities have been evidenced for certain items, yet not the most important ones for MS patients. The 15D patients' valuated form could have several implications in the research of HRQOL in MS considering patients' real perceptions and judgments about their own disease as medical decisions, health care evaluation and planning may be influenced by these valuations. Further cross-sectional studies could provide supplementary evidence on the psychometric and factor analytic soundness of the 15D in MS patients and longitudinal studies on its ability to detect changes in HRQoL over time, taking into account the impact of this value set.

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