

VALIDATION OF THE SLOVENIAN VERSION OF MULTIPLE SCLEROSIS QUALITY OF LIFE (MSQOL-54) INSTRUMENT

POTRDITEV SLOVENSKE VERZIJE VPRAŠALNIKA O KAKOVOSTI ŽIVLJENJA PRI MULTIPLI SKLEROZI (MSQOL-54)

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ABSTRACT

Purpose. To cross-culturally adapt and validate Multiple Sclerosis Quality of Life-54 (MSQOL-54) instrument.

Keywords:

multiple sclerosis, MSQOL-54 instrument, reliability, validity, Slovenia

Methods. The study which enrolled 134 Slovenian multiple sclerosis (MS) patients was conducted from March to December 2013. The internal consistency of the MSQOL-54 instrument was evaluated by Cronbach's alpha coefficient (α), and its dimensionality assessed by the principal component analysis (PCA).

Results. The whole instrument had high internal consistency ($\alpha=0.88$), as well as the majority of its twelve subscales ($\alpha=0.83-0.94$). The results of the PCA showed two components with eigenvalue greater than 1, explaining 59.4% of the cumulative variance. Further results indicated good construct validity of the instrument with the physical health-related-quality-of-life subscales loading highly on the physical component, and mental health-related-quality-of-life subscales loading highly on the mental component.

Conclusion. The Slovenian version of the MSQOL-54 instrument proved to be an internally consistent and accurate tool, well accepted by the Slovenian MS patients. The adequate psychometric properties warrant the scientifically sound version of the MSQOL-54 instrument, which is from now on at disposal to all health professionals dealing with MS patients in Slovenia.

IZVLEČEK

Namen. Medkulturno prilagoditi in potrditi Vprašalnik o kakovosti življenja pri multipli sklerozi (MSQOL-54).

Ključne besede:

multipla skleroza, vprašalnik MSQOL-54, zanesljivost, veljavnost, Slovenija

Metode. Študija, ki je vključevala 134 slovenskih bolnikov z multiplo sklerozo (MS), je potekala od marca do decembra 2013. Notranja skladnost prevedenega vprašalnika je bila ocenjena s Cronbachovim koeficientom alfa (α), njegova dimenzionalnost pa z analizo glavnih komponent (AGK).

Rezultati. Prevedeni vprašalnik kot celota je imel visoko notranjo skladnost ($\alpha=0,88$), prav tako tudi večina njegovih dvanajstih podlestvic ($\alpha=0,83-0,94$). Rezultati AGK so pokazali na dve pomembni komponenti, s katerima je moč pojasniti 59,4% skupne variance. Rezultati so pokazali tudi dobro konstruktivno veljavnost instrumenta, saj so se podlestvice, ki merijo telesno komponento z zdravjem povezane kvalitete življenja dobro skladale s telesno komponento, ugotovljeno v analizi, podlestvice, ki merijo duševno komponento z zdravjem povezane kvalitete življenja, pa dobro z duševno komponento, ugotovljeno v analizi.

Zaključek. Slovenska različica MSQOL-54 se je izkazala za notranje skladno in natančno orodje, ki so ga slovenski bolniki z MS dobro sprejeli. Ustrezne psihometrične lastnosti kažejo na znanstveno zanesljivo različico instrumenta MSQOL-54, ki je zdaj na razpolago vsem zdravstvenim delavcem, ki se v Sloveniji ukvarjajo z bolniki z MS.

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1 INTRODUCTION

Multiple sclerosis (MS) is a chronic neurological disease complexly deteriorating the health of the patients (1). According to the World Health Organisation MS is classified among major public health problems (2) and in Europe, it is considered the leading cause of non-traumatic disability in young adults (3). The effect of disability in daily living is reported to be greater in comparison to other chronic diseases (4-6).

The impact of MS on health has been determined mainly through the physical disability measures over the past years. The gold standard for assessing physical disability in clinical settings has been the Kurtzke's Expanded Disability Status Scale (EDSS) (7). However, health has not only the physical component, but is rather a state of complete physical, mental, and social well-being (8). Conventional physical disability scales omit mental and social health dimensions that substantially contribute to the patient's overall quality of life. Moreover, the difficulties which are perceived important by patients substantially differ from those ones which doctors assess based on physical disability measures (9). Health-related-quality-of-life (HRQoL) instruments are increasingly recognized as indispensable tools for clinicians, not only to systematically assess patients' self-perceived HRQoL, but also to tailor care and therapy programmes according to the patient's individual needs (10), which is a novel treatment approach in the increasingly important new field of medicine, i.e. a personalised medicine. Patient-reported outcomes are also known to improve a patient-doctor communication, because the patients receive a positive signal that the physicians are interested in an array of issues concerning their illness, which, in turn, makes them feel understood. In addition, the patients are empowered being able to participate in the decision-making process related to the personalized treatment approach (5).

There exist a wide range of instruments for measuring the HRQoL concept. The generic ones are applicable to different populations and allow comparisons among them, but they do not address specific areas of concern to specific population groups, e.g. MS patients. The instrument Multiple Sclerosis Quality of Life-54 (MSQOL-54) was the first disease-specific HRQoL instrument which included items covering specific MS symptoms and signs (11). This instrument captures the whole burden experienced by MS patients and provides a more complete picture of their health and well-being (1). The instrument was initially developed in the US in the English language, and ever since it has been adapted to, and validated in numerous other languages (12-20).

Information about the burden of MS in Slovenia is sparse. The existing data showed the prevalence of 83/100,000 in early 1990s (3), while the newest available data showed even higher prevalence (>100/100,000) (21), classifying Slovenia among countries with the highest prevalence worldwide. In addition, due to a long life-span, the disability burden of the Slovenian MS patients is even higher nowadays (22).

To our knowledge, the HRQoL construct was not assessed among Slovenian MS patients yet, and no translated, adapted, and psychometrically sound Slovenian version of MSQOL-54 exists. So far, only two generic instruments measuring HRQoL were translated into Slovenian language and psychometrically tested, i.e. the generic SF-36 instrument (23) and the EQ-5D instrument (24).

It is very important for clinical as well as for research purposes to know whether the psychometric instrument reliably and validly measures what it intends to measure in each specific population within a specific culture.

Therefore, the aim of the present study was to prepare a valid Slovenian translation of the MSQOL-54 instrument for measurement of HRQoL of Slovenian MS patients in a context of a salutogenic approach to this vulnerable population group. In this frame, the objectives of the study were a forward-backward translation and linguistic validation of MS-18 module as well as psychometric testing of the complete MSQOL-54 instrument.

2 METHODS

The present cross-sectional study, in which the methodological approach similar to other comparable studies was used (12,14-19,25,26), was a part of a larger research project on the impact of the sense of coherence on quality of life and self-rated health in MS patients in Slovenia. In this project, it was planned to measure the quality of life with the MSQOL-54 instrument. Before using it for this purpose, the instrument was required to be validated in the observed population.

2.1 Observed Population

Out of all consecutive 207 patients, scheduled for a regular follow-up at the Department of Neurology of the University Clinical Centre Maribor between March and December 2013, all those who met the inclusion criteria, being the diagnosis of MS according to McDonald's criteria (27) and age 18+ years, were invited to participate in the study. Exacerbation of MS in the period of 30 days prior the scheduled neurological examination (a current, ongoing active phase of the disease) and co-existing other chronic diseases were considered as exclusion criteria (12, 16-19).

2.2 Translation and Linguistic Validation

2.2.1 Description of MSQOL-54 Instrument

The MSQOL-54 is an instrument, developed by the UCLA Department of Neurology (28), created by adding 18 items relevant to MS patients, i.e. MS-18 module, to the generic HRQoL instrument, i.e. the Short-Form-36 Health Survey (SF-36) (11, 29). The instrument has two main dimensions and several sub-dimensions (28); consequently, it is comprised of 12 subscales (physical health, role limitations due to physical problems, role limitations due to emotional problems, pain, emotional well-being, energy, health perceptions, social function, cognitive function, health distress, sexual function, the overall quality of life) and two single-item measures (change in health, satisfaction with sexual function) (28). These subscales are summarized into the two summary composite scores: the physical health composite score (PHC) (comprised of physical health, role limitations due to physical problems, pain, energy, health perceptions, social function, health distress and sexual function subscales) and the mental health composite score (MHC) (comprised of role limitations due to emotional problems, emotional well-being, cognitive function, health distress and the overall quality of life subscales) (28).

2.1.2 The Translation into the Slovenian Language

After obtaining the written permission of the author of the original MS-18 module, two well-qualified translators performed the translation of this module into Slovenian. The translators were certified, bilingual, bicultural, with distinct professional backgrounds, the first being a professional literary translator and the second one a professional medical translator. A single preliminary draft was synthesized from the two forward translations by a group consisting of the members of the narrower research team (all of them being physicians), nurses, specialized in care for MS patients, MS patients, and translators. Afterwards, a certified translator, native in English, who had never seen the original English instrument, translated the preliminary version back into English.

Finally, the aforementioned group compared the original and the back-translated version to identify semantic and conceptual discrepancies. Subsequently, the differences between the original and the translated versions were addressed in a group discussion by using the method of voting and ranking. The solutions with the highest total ranking were accepted in the final version. This stage led to the Slovenian version of MS-18 module which was linguistically most equivalent to the original. The Slovenian version of MSQOL-54 was created by adding the Slovenian SF-36 questionnaire (23) to the linguistically adapted Slovenian MS-18 module.

2.3 Administration of the Instrument and Other Data Acquisition

In the presence of the neurology resident and two MS nurses, each participant completed the Slovenian version of MSQOL-54 instrument. Assistance in reading, writing, and explanation was provided, if required.

Along with the MSQOL-54 instrument the socio-demographic data (gender: male, female; age; education: primary, secondary, college or higher; employment status: employed, unemployed, retired; marital status: single, married/cohabiting; area of living: rural, urban) were also collected. The clinical data, i.e. the MS duration in years, the disease course (primary progressive, secondary progressive, relapsing-remitting), clinical worsening of MS in the past year prior the neurological examination, excluding the period of 30 days prior the examination (a relapse of relapsing-remitting type of MS or an increase of the EDSS score by 1 point in progressive type of MS; yes, no), the immunomodulatory therapy (yes, no), and the EDSS score were extracted from the patients' medical records.

2.4 Acceptability of the Instrument

Acceptability was assessed by estimating the mean time-to-complete the questionnaire (recommended administration time 11-18 min (30)), the percentage of missing data, and the assistance required by the patients in terms of reading, writing, or explanation of the questionnaire's items.

2.5 Psychometric Validation

The Expectation-Maximization technique was used to replace the missing values, and the descriptive statistics to describe the study participants' characteristics.

In order to assess the instrument's reliability, the internal consistency was assessed by calculating the Cronbach's alpha coefficient (α), ranging from 0-1, the latter meaning perfect internal consistency. The instrument was considered as internally consistent, if $\alpha \geq 0.70$ (31).

In order to assess the construct validity, the dimensionality of the instrument was assessed by conducting the principal component analysis (PCA) on 12 instrument subscales with varimax orthogonal rotation (32). A preliminary analysis concerning the data screening, assumption testing and sampling adequacy was performed using the Kaiser-Meyer-Olkin (KMO) statistic with appropriate values >0.5 and the Bartlett's sphericity test with $p \leq 0.05$. The components with associated eigenvalues >1 were retained in the analysis. Component loadings were used to indicate the inclusion of variables into the separate components. SPSS statistical software version 19.0 was used as statistical tool (SPSS Inc., Chicago, IL, USA).

3 RESULTS

3.1 Study Group Characteristics

Out of 207 MS patients initially considered for inclusion, 134 were finally enrolled in the study, while 73 did not meet inclusion criteria: 55 (75.3%) had comorbidity, 2 (2.7%) had a recent exacerbation of MS, and 16 (21.9%) refused to participate in the study.

Among participants, there were 42 males (31.3%) and 92 (68.7%) females. The mean age was 43.2 ± 11.1 years (age range: 21-72 years). All other participants' characteristics are presented in the Table 1.

Table 1. Characteristics of the multiple sclerosis (MS) patients for validation of the Slovenian version of Multiple Sclerosis Quality of Life-54 questionnaire (n=134).

Characteristic	Category	No. (%)/ Median; Min-Max; Q1-Q3
Education	Primary	16 (11.9)
	Secondary	94 (70.1)
	College or higher	24 (17.9)
Employment status	Employed	63 (47.0)
	Unemployed	18 (13.4)
	Retired	53 (39.6)
Marital status	Single	44 (32.8)
	Married/ cohabiting	90 (67.2)
Area of living	Rural	80 (59.7)
	Urban	54 (40.3)
Disease duration (years)		8; 0-33; 4-12.25
Disease course	Primary progressive	6 (4.5)
	Secondary progressive	23 (17.2)
	Relapsing- remitting	105 (78.4)
Clinical worsening of the disease*	Yes	51 (38.1)
	No	83 (61.9)
Immunomodulatory therapy	Yes	92 (68.7)
	No	42 (31.3)
EDSS		3.0; 0.0-8.0; 1.625-4.5

LEGEND: Q1 - the first quartile; Q3 - the third quartile; *- clinical worsening of the disease in the past year prior the neurological examination, excluding the period of 30 days prior the examination (a relapse of relapsing-remitting type of MS or an increase of the EDSS score by 1 point in progressive type of MS; EDSS - Expanded Disability Status Scale score

3.2 Acceptability Analysis Results

The average time to complete the questionnaire was 15.9 ± 8.9 minutes. Most of the participating patients (94.8%) did not require additional explanation of the translated items. Thirty-two patients (23.9%) needed assistance in reading and writing due to the visual or upper extremity impairments. The percentage of missing data was generally low, ranging from 0.8% to 3.7% (Table 2).

Table 2. The total number and percentage of missing answers within a subscale/single item measure in the Slovenian version of Multiple Sclerosis Quality of Life-54 questionnaire validation study.

Subscale/Item	N of items	Total N of answers	N of missing answers	% of missing answers
Subscales				
Physical health	10	1323	17	1.3
Role limitations due to physical problems	4	525	11	2.1
Role limitations due to emotional problems	3	396	6	1.5
Pain	3	397	5	1.2
Emotional well-being	5	655	15	2.2
Energy	5	660	10	1.5
Health perceptions	5	664	6	0.9
Social function	3	395	7	1.7
Cognitive function	4	531	5	0.9
Health distress	4	532	4	0.8
Sexual function	4	520	16	3.0
Overall quality of life	2	264	4	1.5
Single-item measures				
Change in health	1	133	1	0.8
Satisfaction with sexual function	1	129	5	3.7

3.3 Psychometric Validation Results

3.3.1 Reliability

The whole instrument had a high internal consistency ($\alpha=0.88$), as well as the majority of the separate subscales. Exceptions were the health perception, and the social function subscales (Table 3).

3.3.2 Validity

The KMO statistic verified a sampling adequacy for the analysis (KMO=0.88), and the Bartlett's test indicated sufficiently large correlations between the subscales for the PCA ($p<0.001$). The results of the PCA showed that only the first two components had the eigenvalues exceeding 1, accounting for 59.4% of the total variance (Table 4). Consequently, only these two components were retained in the analysis. In Table 5, the component loadings after rotation are shown. The emotional well-being, the cognitive function, the health distress, and the overall quality of life subscales all related to the mental dimension of MSQOL-54 and loaded highly on component 1, suggesting this component is, in fact, the mental component. The physical health, the role limitations due to physical problems, the pain, the health perceptions, the social, and the sexual function subscales all related to the physical dimension of MSQOL-54 and loaded highly on component 2, suggesting this component as the physical component. The energy subscale, originally the subcomponent in the physical health component, also showed a high loading on mental health. The role limitations due to emotional problems subscale was the only subscale loading about equally on both components.

Table 3. Statistical description and the Cronbach's Alpha (α) for the Slovenian version of Multiple Sclerosis Quality of Life-54 questionnaire subscales/single item measures (n=134).

Subscale/Item	N of items	Mean	SD	α
Subscales				
Physical health	10	55.7	29.6	0.94
Role limitations due to physical problems	4	33.1	41.0	0.90
Role limitations due to emotional problems	3	62.7	41.3	0.83
Pain	3	65.9	24.0	0.89
Emotional well-being	5	74.4	15.9	0.84
Energy	5	55.2	19.2	0.84
Health perceptions	5	44.6	14.8	0.58
Social function	3	72.8	19.3	0.68
Cognitive function	4	71.4	23.2	0.91
Health distress	4	72.0	19.9	0.85
Sexual function	4	71.4	28.2	0.90
Overall quality of life	2	67.8	15.9	0.86
Single-item measures				
Change in health*	1	45.3	22.6	
Satisfaction with sexual function*	1	61.4	25.7	

LEGEND: SD - standard deviation; * - α was not computed because the scale is based on a single item.

Table 4. Component loadings after rotation in the Slovenian version of Multiple Sclerosis Quality of Life-54 questionnaire validation study (n=134).

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of variance	Cum. %	Total	% of variance	Cum. %	Total	% of variance	Cum. %
1	5.906	49.2	49.2	5.906	49.2	49.2	3.659	30.5	30.5
2	1.219	10.2	59.4	1.219	10.2	59.4	3.466	28.9	59.4
3	0.938	7.8	67.2						
4	0.765	6.4	73.6						
5	0.625	5.2	78.8						
6	0.564	4.7	83.5						
7	0.479	4.0	87.5						
8	0.423	3.5	91.0						
9	0.349	2.9	93.9						
10	0.277	2.3	96.2						
11	0.257	2.1	98.4						
12	0.198	1.6	100.0						

Table 5. Component loadings after rotation in the Slovenian version of Multiple Sclerosis Quality of Life-54 questionnaire validation study (n=134).

Subscale	Rotated factor loadings	
	Component 1 Mental component	Component 2 Physical component
Physical health	0.129	0.854
Role limitations due to physical problems	0.184	0.792
Role limitations due to emotional problems	0.472	0.475
Pain	0.275	0.570
Emotional well-being	0.874	0.104
Energy	0.750	0.407
Health perceptions	0.415	0.536
Social function	0.474	0.654
Cognitive function	0.754	0.174
Health distress	0.698	0.320
Sexual function	0.202	0.590
Overall quality of life	0.701	0.432

4 DISCUSSION

The results of this study showed that the Slovenian version of the MSQOL-54 instrument successfully passed the evaluation for cultural equivalence as well as fulfilled the required psychometric criteria. The instrument was well accepted by the Slovenian MS patients, with the majority of them stating there were no items difficult to interpret. Almost all the patients completed the questionnaire within the recommended period, indicating that it was easy to understand and manageable to accomplish. The greater portion of participants could fill in the questionnaire without any intervention by the research team, which is in line with the preferred self-administered mode. Nevertheless, in one sixth of the patients, the MSQOL-54 instrument was administered as an interview due to the visual or upper extremity impairments. Therefore, the acceptability is likely to improve if the questionnaire is administered in settings where help is accessible. The percentage of the missing answers was low, except for the items referring to the sexual function and satisfaction with the sexual function. A pattern of a higher percentage of the missing answers in the sexual function subscale was detected in the original US study as well as in other similar studies dealing with MSQOL-54 validation (11, 12, 15, 18, 19). This could be explained by a traditional perception of sexuality as a taboo in many cultures.

The individual subscales and the complete instrument had a high internal consistency, indicating an internally consistent instrument. However, in the health perception and the social function subscales, it was below the recommended cut-off point. The aforementioned subscales also had the lowest coefficients in the original US study and in several other published MSQOL-54 validation studies (11, 14, 17-19). The health perception subscale contains items that cover quite broad aspects of health self-evaluation, and this might explain the relative lack of consistency. Furthermore, the social function subscale contains only three items, therefore its reduced reliability could be attributed to the low number of items. In this study, two underlying dimensions of the instrument's construct have been confirmed. The two extracted components by the PCA represented the physical and the mental HRQoL dimensions. The analysis also revealed that subscales, which in the original US study (11) are related to the physical HRQoL dimension and unrelated to mental HRQoL dimension, loaded highly on the physical component. Likewise, the subscales originally intended to pertain in the mental dimension, made up the mental component in our study, too. Therefore, the Slovenian MSQOL-54 instrument has good discriminant validity. An exception from the aforementioned was the energy subscale, which was originally stapled as the physical dimension subscale, while in our study, it appeared to fit more into the mental component. Similarly, to our finding, two other studies evidenced that the energy subscale measured by MSQOL-54 was primarily an emotional component (14, 17). Moreover, in our study, the role limitations due to emotional problems subscale had equal loadings on both components. Likewise, in the Israeli validation study (14), this subscale emerged together with the role limitations due to physical problems subscale as a separate dimension, suggesting that patients view role limitations as unitary, tending to overlook the source of the limitations.

There are some limitations of this study. Firstly, a relatively small number of participants were included in the study; however, the number was still sufficient to permit fair conclusions. Moreover, one could argue that item response theory statistics has not been used in the present study since this methodology is increasingly used for the purpose of psychometric validation of instruments. However, most of the studies reporting the validation of the translated versions of the MSQOL-54 instrument in the past used the classical methodology. In order to make our results comparable to the results of other similar studies, a classic methodology was used in our study as well. Furthermore, one could argue that no method of measurement of the stability of the instrument over time, e.g. the test-retest method, was used in the present study. However, the reliability of

the measurement can be evaluated using measurement stability methods and/or measurement equivalence methods. The later were developed in the social science research for the situations in which it is not possible to perform repeated measurements, because the measured phenomenon changes or could change over time (33). As we assumed that the phenomenon measured in our study could change over time, the measurement at the same time was used and the internal consistency method was used as an appropriate method (33). Finally, only the exploratory factor analysis was performed; however, the intention of the study was to explore if data collected by the translated version of the instrument fit the expected pattern.

Nonetheless, the study has also some important strengths. Firstly, the rigorously performed forward-backward translation process provided a good quality translation of the MSQOL-54 instrument to the Slovenian language, making it available to all Slovenian experts dealing with MS patients in clinical settings as well as for the research purposes. Secondly, this study provided the information on the psychometric properties when used in Slovenian MS patients. According to the results of this study, the Slovenian MSQOL-54 instrument is valid and reliable, and the users can trust it, and use it as a valid and reliable measurement tool. These benefits give the opportunity for treating MS patients in Slovenia in accordance to personalised medicine approach. Finally, the study could be another step in the implementation of a comprehensive approach to managing major public health problems in Slovenia.

There are still many challenges left in researching both the properties of the MSQOL-54 instrument and the content of the instrument itself. With a focus on studying the properties of the Slovenian version of the instrument, further evaluation is needed. Our work can be continued by assessing the instrument's responsiveness, exploring the relations between the MSQOL-54 dimensions and another HRQoL instrument, as well as by performing the confirmatory factor analysis, while working on larger clinical data sets. With a wider focus, at the content level of the instrument, another challenge for researchers could be to combine the MS-18 module with another HRQoL instrument than SF-36, e.g. the EQ-5D (34).

5 CONCLUSION

The Slovenian version of the MSQOL-54 proved to be internally consistent and accurate tool, well accepted by the Slovenian MS patients. The adequate psychometric properties warrant the scientifically sound Slovenian version of the MSQOL-54 instrument, which is from now on at disposal to all health professionals dealing with MS patients in Slovenia.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING

The study received no funding.

ETHICAL CONSIDERATIONS AND PERMISSIONS

The study was launched after receiving permissions to use MSQOL-54 and SF-36 instruments from their developers. It was approved by the Medical Ethics Committee of the Republic of Slovenia on 17 July 2012 (approval No. 24k/07/12).

REFERENCES

- Benito-Leon J, Manuel Morales J, Rivera-Navarro J, Mitchell A. A review about the impact of multiple sclerosis on health-related quality of life. *Disabil Rehabil* 2003; 25: 1291-1303.
- WHO. Neurological disorders: public health challenges. Geneva: WHO, 2006.
- Pugliatti M, Rosati G, Carton H, Riise T, Drulovic J, Vecsei L, Milanov I. The epidemiology of multiple sclerosis in Europe. *Eur J Neurol* 2006; 13: 700-22.
- Hermann BP, Vickrey B, Hays RD, Cramer J, Devinsky O, Meador K et al. A comparison of health-related quality of life in patients with epilepsy, diabetes and multiple sclerosis. *Epilepsy Res* 1996; 25: 113-8.
- Rudick R. Multiple sclerosis therapeutics. Boca Raton, FL: CRC Press, 1999.
- Murphy N, Confavreux C, Haas J, Konig N, Roullet E, Sailer M et al. Quality of life in multiple sclerosis in France, Germany, and the United Kingdom: cost of multiple sclerosis study group. *J Neurol Neurosurg Psychiatry* 1998; 65: 460-6.
- Kurtzke J. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983; 33: 1444-52.
- Nutbeam D. Health promotion glossary. Geneva: WHO Collaborating Centre for Health Promotion, 1998.
- Rothwell PM, McDowell Z, Wong CK, Dorman PJ. Doctors and patients don't agree: cross sectional study of patients' and doctors' perceptions and assessments of disability in multiple sclerosis. *BMJ* 1997; 314: 1580-3.
- Provinciali L, Ceravolo MG, Bartolini M, Logullo F, Danni M. A multidimensional assessment of multiple sclerosis: relationships between disability domains. *Acta Neurol Scand* 1999; 100: 156-62.
- Vickrey BG, Hays RD, Harooni R, Myers LW, Ellison GW. A health-related quality of life measure for multiple sclerosis. *Qual Life Res* 1995; 4: 187-206.
- Solari A, Filippini G, Mendozzi L, Ghezzi A, Cifani S, Barbieri E et al. Validation of Italian multiple sclerosis quality of life 54 questionnaire. *J Neurol Neurosurg Psychiatry* 1999; 67: 158-62.
- Acquadro C, Lafortune L, Mear I. Quality of life in multiple sclerosis: translation in French Canadian of the MSQoL-54. *Health Qual Life Outcomes* 2003; 1: 70.
- Miller A, Dishon S. Health-related quality of life in multiple sclerosis: psychometric analysis of inventories *Mult Scler* 2005; 11: 450-8.

15. Idiman E, Uzunel F, Ozakbas S, Yozbatiran N, Oguz M, Callioglu B et al. Cross-cultural adaptation and validation of multiple sclerosis quality of life questionnaire (MSQOL-54) in a Turkish multiple sclerosis sample. *J Neurol Sci* 2006; 240: 77-80.
16. Heiskanen S, Merilainen P, Pietila AM. Health-related quality of life-testing the reliability of the MSQOL-54 instrument among MS patients. *Scand J Caring Sci* 2007; 21: 199-206.
17. Ghaem H, Borhani Haghighi A, Jafari P, Nikseresht AR. Validity and reliability of the Persian version of the multiple sclerosis quality of life questionnaire. *Neurol India* 2007; 55: 369-75.
18. Pekmezovic T, Kistic Tepavcevic D, Kostic J, Drulovic J. Validation and cross-cultural adaptation of the disease-specific questionnaire MSQOL-54 in Serbian multiple sclerosis patients sample. *Qual Life Res* 2007; 16: 1383-7.
19. Fuvesi J, Bencsik K, Benedek K, Matyas K, Meszaros E, Rajda C et al. Cross-cultural adaptation and validation of the "Multiple sclerosis quality of life instrument" in Hungarian. *Mult Scler* 2008; 14: 391-8.
20. Tadic D, Dajic V. Quality of life in patients with multiple sclerosis in Republic of Srpska. *Med Glas (Zenica)* 2013; 10: 113-9.
21. Multiple Sclerosis International Federation. Atlas of MS 2013: mapping multiple sclerosis around the world. London: Multiple Sclerosis International Federation, 2013.
22. Vidmar G, Burger H, Marincek C. Time trends in ability level and functional outcome of stroke and multiple sclerosis patients undergoing comprehensive rehabilitation in Slovenia. *Zdr Varst* 2011; 50: 24-33.
23. Marn-Vukadinovic D, Jamnik H. Validation of the short form-36 health survey supported with isokinetic strength testing after sport knee injury. *J Sport Rehabil* 2011; 20: 261-76.
24. Prevolnik Rupel V, Ogorevc M. The EQ-5D health states value set for Slovenia. *Zdr Varst* 2012; 51: 128-40.
25. Rosato R, Testa S, Bertolotto A, Confalonieri P, Patti F, Lugaresi A et al. Development of a short version of MSQOL-54 using factor analysis and item response theory. *PLoS One* 2016; 11: e0153466.
26. Vucic L, Glisic B, Kistic-Tepavcevic D, Vucic U, Drulovic J, Pekmezovic T. Cross-cultural adaptation and validation of the disease specific questionnaire OQLQ in Serbian patients with malocclusions. *Zdr Varst* 2016; 55: 166-73.
27. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011; 69: 292-302.
28. UCLA. Multiple sclerosis quality of life (MSQOL)-54 instrument. Los Angeles, CA: UCLA, 1995. Available Feb 1, 2017 from: https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/MSQOL54_995.pdf.
29. Ware J, Snow K, Kosinski M, Grandek B. SF-36 health survey: manual and interpretation guide. Boston, MA: The Health Institute, New England Medical Center, 1993.
30. National Multiple Sclerosis Society. Multiple Sclerosis Quality of Life-54 (MSQOL-54). Available Feb 1, 2017 from: [http://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-Researchers/Clinical-Study-Measures/Multiple-Sclerosis-Quality-of-Life-54-\(MSQOL-54\)](http://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-Researchers/Clinical-Study-Measures/Multiple-Sclerosis-Quality-of-Life-54-(MSQOL-54)).
31. Kline P. Handbook of psychological testing. 2nd ed. London: Routledge, 1999.
32. Schmitt TA. Current methodological considerations in exploratory and confirmatory factor analysis. *J Psychoeduc Assess* 2011; 29: 304-21.
33. Ferligoj A, Leskošek K, Kogovšek T. Zanesljivost in veljavnost merjenja. Metodološki zvezki 10. Ljubljana: Univerza v Ljubljani, FDV, 1995.
34. AAOS. EQ-5D. Available Jul 22, 2017 from: <https://www.aaos.org/uploadedFiles/EQ5D3L.pdf>.