QUALITY OF LIFE AND HEALTH OF PATIENTS IN EARLY STAGES OF MULTIPLE SCLEROSIS

Klaudija Duka Glavor[1], Marina Titlić[2] & Gorka Vuletic[3]

[1]*Department of Neurology, General Hospital Zadar, Zadar, Croatia*
[2]*Department of Neurology, University Hospital Centre Split, Split, Croatia*
[3]*Department of Psychology, Faculty of Humanities and Social Science in Osijek, Osijek, Croatia*

SUMMARY

Background: *Multiple sclerosis is a chronic neurologic condition with a variety of symptoms which have a great impact on quality of life even in the early stages. The aim of this study was to investigate, and to compare overall subjective quality of life with self-perceived health in patients with early stages of MS.*

Subjects and methods: *Thirty patients with MS (22 women, 8 men; mean age 37.3±9.7years; relapsing-remitting MS; EDSS<2.5; all on immunomodulatory therapy: IFN, GA) were enrolled in the study. The QOL was assessed using the Personal well-being index (PWI) and health was measured by the Short Form 36-Item Health Survey (SF-36) questionnaire.*

Results: *Results indicate that MS patients in early stage experience similar health and quality of life, comparing to the general adult population. Analysis of self-reported change in health by categories showed that 50% patients access their health about the same as a year before, 9 rate their health as worse as one year before and 5 rate their health even better. Correlation analysis revealed that SF-36 domain Mental health correlates with most PWI domains.*

Conclusion: *This study demonstrates that MS patients in early stage experience similar quality of life as general adult population. Also, it was revealed that health domain Mental health is correlated with various quality of life domains, suggesting that mental health is of great significance for subjective quality of life perception. However, it is important to emphasize the distinction between the health and quality of life, due to the fact that one can perceive his/hers own health as impaired, but at the same time can have satisfactory quality of life.*

Key words: *multiple sclerosis - quality of life - SF-36 - personal wellbeing index*

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INTRODUCTION

Multiple sclerosis (MS) is a chronic neurologic condition with a variety of symptoms which have a great impact on quality of life even in the early stages (Nourbakhsh et al. 2016). Next to the individual's motor, visual, brainstem or sphincter symptoms (Benito-Leon et al. 2002), which are expressed through the most widely used Kurtzke Expanded Disability Status Scale (EDSS score), there are other manifestations of MS that have a detrimental influence on overall functioning and quality of life, such as cognitive impairment, depression, anxiety (Marrie et al. 2018), fatigue and pain (Fischer et al. 1999).

The objective picture of MS given by the symptoms, clinical picture, MR specific patterns of the central nervous system, neurophysiological tests and the previously mentioned EDSS score are completed by the subjective state of individual comments of each MS patient, which are usually expressed throughout generic and disease specific quality of life questionnaires. Studies have shown that QOL is an important measure of future morbidity, mortality, and the measure of the impact of disease as an outcome measure in clinical trials (Pittock et al. 2004). Moreover, the level of impact of the wide range of health problems associated with MS

needs to be understood in terms of patients' own perceptions of those impacts and the degree to which they affect their lives (Hemmet et al. 2004).

Traditional endeavour in the treatment of chronic disorders was focused to the relief of symptoms and to prognosis improvement. However, contemporary approach of healthcare tends to achieve and maintain the highest possible level of quality of life within the specific limits inflicted by the disorder and to maximise daily life functioning, since the full recovery has been very unlikely (Opara et al. 2010).

Quality of life

Quality of life refers to an individual's perception of standing in a specific cultural, social and environmental context (World Health Organization 1999, Vuletić & Misajon 2011). Although quality of life has been traditionally linked to economic variables and therefore treated as a possession of wealthy societies, it is clear nowadays that wealth represents an inadequate indicator of quality of life. For that reason the distinction between the concepts of objective and subjective quality of life has been suggested.

While objective quality of life encompasses previously mentioned economic aspects, such as GDP,

subjective quality of life includes life satisfaction and happiness. Life satisfaction is defined as cognitive evaluation of one's entire life or different life domains (Andrews & Withey 1976, Campbell et al. 1976, Vuletić 2004). Furthermore, life satisfaction represents cognitive, long-term aspect of quality of life, whereas happiness refers to emotional, short-term aspect of quality of life (Yang & Srinivasan 2016). However, life satisfaction is mostly used as a measure of quality of life.

Prior research suggest that self-report measures represent more useful and precise quality of life indicator, when compared to objective indicators, such as income. For that reason, different self-report measures have been developed and frequently used in order to obtain the highly useful information regarding one's subjective quality of life (Williams & Wood-Dauphinee 1989).

There are two types of subjective quality of life measures: generic and disease specific measures. While generic measures can be applied to a wide variety of patients, specific instruments are focused on issues related to the individual disease states or patient groups. Since the applicability of generic measures has originated from their coverage of the broad range that includes functioning, disability and distress, which are all necessary in order to understand one's status, generic measures are used more often in scientific and clinical research (Guyatt 1997).

Health

In 1948 the World Health Organisation formulated a definition of health, which defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (1948; Ware et al. 1981). Although many challenges were confronted to this definition due to the absoluteness of the word "complete" in relation to the concept of wellbeing, this definition emphasized multidimensional nature of health.

In order to fully understand one's health perception, self-perceived measures of health have been applied. Such measures capture individuals' subjective assessment of their health through examining various health domains, such as physical, psychological and role function. In both clinical and public health settings, subjective perceptions of health often have greater saliency for functioning and survival, comparing to physiological and clinical assessments (Vuletić et al. 2006). Subjective measures of health status have been advocated as a useful proxy for objective measures. In some studies the question about the global self-rated health has been found to be a powerful predictor of the mortality within a targeted population group (Idler & Benyamini 1997). A self-administered health status questionnaire provides with the subjective assessments

of both individual and collective health status (Vuletić et al. 2006).

Health is one of the most important determinants of quality of life, especially among the population of chronic patients. However, it is not correct to equalize the health with the quality of life, considering that health is not the only quality of life determinant. Quality of life refers to the multidimensional construct that encompasses multiple domains besides the health. In order to fully understand one's quality of life and health it is needed to apply both quality of life and health measures.

Furthermore, it is highly important to emphasize that the presence of chronic condition, therefore impaired health, does not automatically imply low quality of life. For that reason it is recommended to investigate both health and quality of life in order to identify relationships among various health and quality of life domains, which contributes to the better understanding of their mutual relation.

Since self-perceived health has been representing an important indicator of health status as well as the disease course and the outcome, this research focused on multidimensional measurement of health, subjective quality of life and relationship between the two of them. Generic measures of subjective quality of life have been applied in order to both explore the subjective quality of life among MS patients and compare the results with the normative data for the general population.

SUBJECTS AND METHODS

This single-center, cross-sectional study was carried out at Neurology Department, General Hospital Zadar, Croatia between 2010 and 2012. The study protocol was approved by General Hospital Zadar Ethics Committee. All participants signed the written informed consent for their participation. The study was designed and executed in accordance with World Medical Association Declaration of Helsinki 2013 (Lily et al. 2004).

MS patients in our study were enrolled consecutively during their routine outpatient visits at the GH Zadar. Inclusion criteria were 18-55 years old Croatian patients of both sexes with early stage of relapsing remitting MS diagnosed according to Dublin Panel on Diagnosis of MS revision of Mc Donald criteria 2010 (Jongen et al. 2010), the diagnostic criteria used at that time. All patients were on immunomodulatory therapy (ING, GA), available at that time in Croatia, Kurtzke Expanded Disability Status Scale (EDSS)≤2.5 (mild disability in one or minimal disability in two functional systems). Inclusion criteria for all participants were the ability to understand and write the questionnaires by their own. Exclusion criteria for MS patients were: active disease (relaps).

Health status questionnaire SF-36

Health and health related quality of life were measured multidimensionally by *Health status questionnaire SF-36*, Croatian version (Maslić Seršić & Vuletić 2006). SF-36 is a multidimensional health questionnaire comprising 36 questions (Ware et al. 1993). It represents a theoretically based and empirically authenticated operationalization of two general health concepts – physical and psychological health – and their two general manifestations, functioning and wellbeing. Hence the four types of scales or conceptually diverse health measurements relative to the following health assessments or indicators: a) functioning on the level of behaviour, b) estimated wellbeing, c) limitations of the social life and realization of central life roles, and d) personal self-assessment of the overall health. At the manifestation level, each questionnaire item relates to one of the following eight health indicators: physical functioning (PF) (10 items); role limitation due to physical problems (RP) (4 items); bodily pain (BP) (2 items); perception of general health (GH) (5 items); vitality and energy (VE) (4 items); social functioning (SF) (2 items); role limitation due to emotional problems (RE) (3 items); mental health (MH) (5 items); changes in health (CH) as one item referring to changes in health relative to one year ago (five levels from 'how much the condition is better than a year ago' to 'how much the condition is worse than a year ago'), not expressed as a scale, but still useful for the evaluation of average change in the health status over a period of one year prior to monitoring, and was presented separately from results on 8 dimensions.

Personal Wellbeing Index - Adult Questionnaire (PWI-A)

PWI-A (International Wellbeing Group 2013) was used as multidimensional measure of subjective quality of life. It comprises seven scales assessing satisfaction on seven life domains: standard of living, health, achievements in life, close relationships, safety, community connectedness and future security. Answers are given on an 11-point Likert scale where 0 denotes "not satisfied at all" and 10 means complete satisfaction. Overall index (PWI) is expressed as an arithmetic mean of the results across the seven domains. Results were transformed and presented in the form of percentage of scale maximum (%SM), range 0-100 %SM.

The data was statistically analysed by SPSS software for Windows, version 20.0, SPSS inc., Chicago. Il, SAD. In order to describe the results methods of descriptive statistics was used.

The results from quality of life and health questionnaires are conventionally reported as a mean score for each dimension. Spearman's correlation coefficient (rho) was used to test the correlation between variables. The level of significance was set at p<0.05.

RESULTS

Study included 30 patients with early stage of relapsing remitting MS (8 M; 22 F), age 37.39 years (SD=9.497) (Table 1). Female MS patients were somewhat older than male ones, while age of male and female participants was equal. MS patients were less educated. Effects of these possible confounders were controlled by multivariate analysis. All participants answered all of the questions of both questionnaires and were used in the analysis.

Table 1. Descriptive statistics for health status dimensions

SF-36 dimensions	M	SD
Physical Functioning	69.33	30.505
Role limitation due to Physical problems	62.50	40.869
Role limitation due to Emotional problems	68.89	36.022
Social Functioning	77.92	18.477
Mental Health	68.27	14.362
Energy Vitality	57.50	18.135
Pain	66.33	22.664
General Health Perception	53.80	20.865

Patients reported quite good health. Somewhat lower on Energy and General health perception, but Croatian open adult population show similar scores on those dimensions (7). Comparing MS patients' results to Croatian general adult population, it can be seen that MS patient group report even higher average scores on Social functioning, Mental health and Energy/Vitality dimension (Table 2, Figure 1).

Table 2. Change in health in relation to one year ago

Change in health	N	%
Much better	1	3.3
Somewhat better	4	13.3
About the same	16	53.3
Somewhat worse	2	6.7
Much worse	7	23.3

Distribution of answers by categories shows that over 50% patients access their health about the same as a year before. 9 patients rate their health as worse as one year before and 5 rate their health even better (Table 3).

Results show that the subjective QOL is within the normative range expected for the global population, which is between 60 and 80 %SM although there are patients in the group who have low QOL. Average domain scores were relatively high and indicate satisfaction with life on different life domains. However, there are patients with low scores on specific domains and additional attention should be focus on them individually in further clinical work during regular check-ups.

In order to examine the relationship between health status and subjective quality of life dimensions Spearman's rho correlation coefficient was used due to small sample size. Results are shown in table 4.
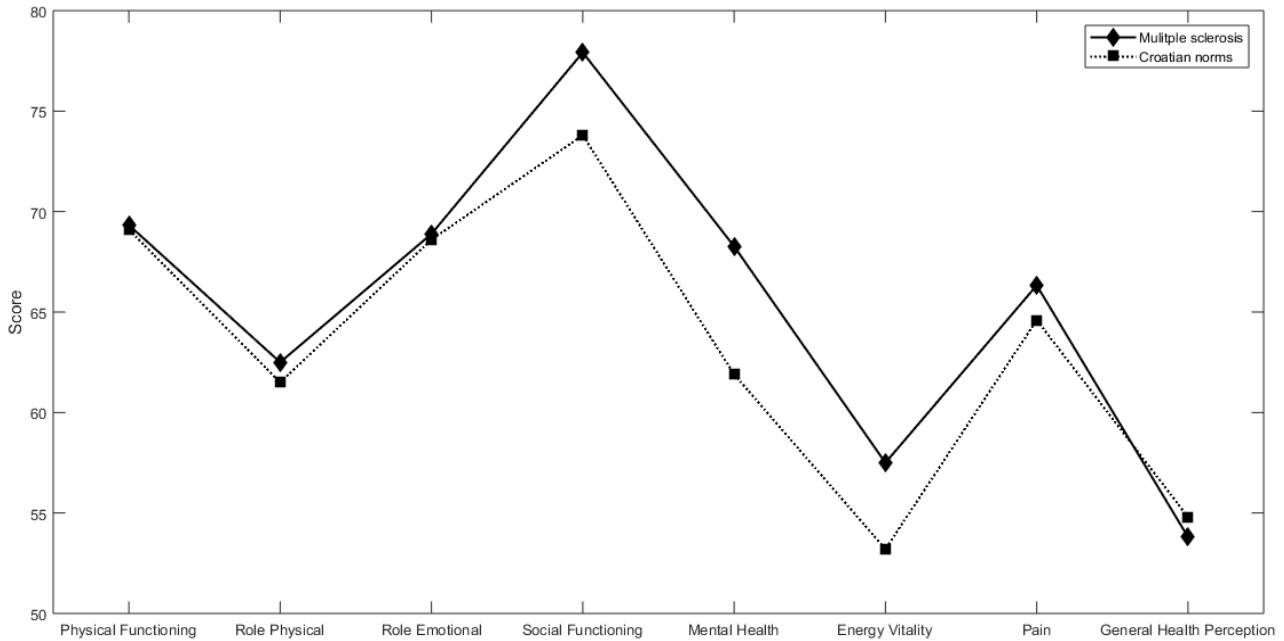
Figure 1. Health status profiles for MS patients and general Croatian adult population

Table 3. Descriptive statistics for quality of life dimensions and overall Index (PWI)

QOL DOMAINS	M	SD	Observed min.	Observed max.
Standard of living	58.33	20.69	10	90
Health	61.33	20.30	20	100
Achievements in life	67.00	23.07	20	100
Close Relationships	77.67	20.63	40	100
Safety	72.33	23.29	20	100
Community connectedness	70.67	22.43	30	100
Future security	60.33	22.36	20	100
PWI	66.81	17.19	32.86	91.43

Table 4. Coefficients of correlation among subjective quality of life and health status variables

SF36 dimension		PWI	Standard	Health	Achievements in life	Close Relationships	Safety	Community connectedness	Future security
Physical	r	0.068	0.049	0.200	0.013	0.129	-0.013	0.065	0.067
Functioning	p	0.722	0.797	0.290	0.944	0.497	0.947	0.735	0.723
Role limitation	r	0.044	0.060	0.171	0.021	-0.061	0.046	0.147	0.013
due to Physical problems	p	0.816	0.754	0.366	0.914	0.749	0.810	0.437	0.947
Pain	r	0.153	0.233	0.336	-0.002	0.067	-0.004	0.171	0.172
	p	0.421	0.216	0.070	0.990	0.726	0.985	0.365	0.364
Energy Vitality	r	0.292	0.272	0.381*	0.222	0.278	0.202	0.224	0.209
	p	0.117	0.146	0.038	0.238	0.136	0.284	0.234	0.267
General Health	r	0.259	0.245	0.506**	0.111	0.270	0.118	0.315	0.237
Perception	p	0.167	0.192	0.004	0.558	0.150	0.536	0.090	0.208
Mental Health	r	0.450*	0.409*	0.255	0.347	0.495**	0.505**	0.375*	0.271
	p	0.013	0.025	0.173	0.061	0.005	0.004	0.041	0.147
Role limitation	r	0.299	0.404*	0.253	0.321	0.317	0.245	0.158	0.170
due to Emotional problems	p	0.108	0.027	0.177	0.084	0.088	0.192	0.405	0.370
Social Functioning	r	0.222	0.172	0.198	0.183	0.273	0.304	0.215	0.053
	p	0.237	0.363	0.295	0.334	0.144	0.102	0.254	0.782

* p<0.05;   ** p<0.01

In table 4 the relationship between overall QOL and health status dimensions was presented. Results have shown that several dimensions of the overall QOL (standard of living, close relationships, safety, and community connectedness) were significantly correlated to health status dimension of mental health, as the QOL domain of health was significantly related only to general health and vitality dimension.

DISCUSSION

The aim of this study was to compare the impact of various symptoms of MS patients with an early stage (EDSS <2.5) of disease to health population based normative samples by using the Croatian version of SF-36 and Croatian version of the PWI. In general, patients with MS in our study reported quite good health, compared with the normative scores of the Croatian adult population. Interestingly, MS patients reported on much higher average results on Social functioning, Mental health and Energy/Vitality dimensions, comparing to the adult population. Even though MS patients scored somewhat lower results on Energy/ Vitality and General health perception, Croatian open adult population demonstrated similar scores on those dimensions. Next to the eight health domains, an item on retrospective review of change in general health to the period of one year was applied. According to the results, over 50% of patients reported no change in general health in the past year. This finding is in line with the results of the study that included Croatian open adult population (Jureša et al. 2000, Maslić Sersić & Vuletić 2006).

A population-based cohort study by Pittock et al. (2004) revealed that patients with MS in Olmsted County performed worse than the general US population on the SF-36 dimensions Physical functioning, Vitality and General health. However, they scored similarly to the general US population on dimensions Mental health, Pain, Role emotional and Social functioning, suggesting that these findings may not be clinically meaningful. These results are partially in accordance with the present study, showing that people with MS report quite a good QOL, despite their reported disability.

Another study was conducted in order to compare the impact of multiple sclerosis and Parkinson's disease on health perception with general adult population in United Kingdom (Riazi et al. 2003). Both neurologic conditions had significantly worse health comparing to the general population in all eight SF-36 domains. Patients with MS obtained poorer results on Physical functioning and Role physical. Nevertheless, they reported better scores on Mental health. People with low EDSS score who are able to walk without the usage of any aid also had scored significantly worse on all dimensions, comparing to the general adult UK population. Similar pattern can be noticed in the present study and the study of Riazi et al. (2003), whereby in both studies MS patients reported lower scores on Role limitation due to Physical problems and higher scores in Mental health. Furthermore, similar findings were also found in Norwegian and Canadian study population (Riazi et al. 2003).

Based on the previous research, it has been observed that MS patients are more likely to experience worse health across the eight SF-36 domains, comparing to the general adult population (Nortvedt et al. 1999), which is assumed on the basis of the comorbidity analysis (Marrie & Hanwell 2013) and in comparison with epilepsy and diabetes patients (Hermann et al. 1996). Nevertheless, present study revealed that patients in early stage of MS expressed similar or even better health than the general adult population across the eight health domains. This finding could be partially explained by the impossibility of direct comparison among participants from different studies due to the sample characteristics: it is possible that participants from the present study might slightly differ from the other MS patients in severity of symptoms or level of functionality, in a way that the participants from the present study experience significantly less disability and distress in relation to the participants from the other studies. Effectiveness of the EDSS score as an outcome measure in patients with MS has been investigated, suggesting that the EDSS score is only moderately useful as an outcome measure in the early stages of MS, which might lead to the greater heterogeneity of MS patients (de Groot et al. 2006).

The Croatian version of the Personal Wellbeing Index was been validated and published in 2011 by Kaliterna-Lipovčan and colleagues. According to the results, Croatian citizens are most satisfied with the domains of family and friends, acceptance by the community and feelings of physical safety, followed by the domain they were least satisfied with, which is the standard of living. Similar results were found in the Third European Quality of life Survey in 2011, counting 27 EU countries. The follow up study that focused on gender and age differences in wellbeing of Croatian's citizen in 2013 revealed there are more changes in age than in gender, suggesting that wellbeing declines with age, without any systematic gender differences in the overall score and different life domains. The highest decline throughout the age was found in satisfaction with health.

When results from the present study were compared to general Croatian population scores (Kaliterna-Lipovčan et al. 2011), it was discovered that the PWI index, as well as the PWI dimension scores were in accordance with both average scores obtained from the general Croatian population (Kaliterna-Lipovčan et al. 2011) and with the average scores found in Western countries (Cummins 1995).

As it can be seen from the Table 3, MS patients rated their satisfaction with standard of living, future security and health lower, in contrast to the satisfaction with safety and close relationships. Similar findings were found in the Croatian study (Kaliterna-Lipovčan et al. 2011). Even though patients with MS evaluated their satisfaction in different life domains to be lower than the average result obtained from the general population, they expressed higher satisfaction in the domain of safety, comparing to the general population. These findings may be explained with the fact that personal wellbeing is the mirror of social and economic situation in a country. As young patients with MS, they might feel "safer" in the current healthcare and social system. Both groups were almost equally satisfied with their life achievements and close relationships. Considering these facts, it cannot be concluded that overall subjective QOL in patients with early phase of MS is significantly damaged. Also, in a recently published research, differences between subgroups of MS patients were found regarding QOL. The longer the disorder duration and the more severe and progressive the MS, the lower the patient's experienced QOL was. Considering that, it was expected that the results on PWI are going to be similar to the general adult population, since participants included in the present study have been in early stage of MS (EDSS<2.5).

To the author's knowledge there weren't any studies with early stages of MS patients (EDSS<2.5) comparatively exploring using health and subjective QOL while both constructs were measured multidimensionally. There were only few studies using the PWI questionnaire to assess subjective quality of life in patients with different neurological conditions (Geyh et al. 2010, Morgan et al. 2014). For example, Morgan et al. (2014) assessed wellbeing and health status aspects of health-related quality of life (HRQOL) in adult patients with cerebral palsy (CP). Furthermore, they explored the relationship of mobility decline and falls with HRQOL. In comparison to the mean value of PWI from the present study (M=66.81, SD=17.19), CP patients scored 65.2%SM in PWI. The difference can be attributed to the absence of physical handicap in MS patients from the present study, but also to the fact that patients with developmental impairments are often considered "healthier", comparing to the patients with physical impairments (Pender 1987). This is also supported by even lower value of the overall PWI index in patients with traumatic spinal cord injury (Geyh 2010). It is possible that patients who lived with disabilities throughout their whole life have a slightly different understanding of "health" and life expectancy than those who have recently acquired certain disability, such as spinal cord injury (Morgan 2014).

The second aim of the present study was to explore correlations between the measures of health and quality of life. Results indicate that SF-36 domain Mental health significantly correlates with the following PWI domains: standard of living, close relationships, safety and community connectedness. In addition, SF-36 domains Physical Functioning, Role Limitation due to Physical and Emotional Problems, Pain, and Social Functioning have not been significantly associated with the overall QOL, measured by the PWI, as with the QOL domains. The QOL domain of health significantly correlates with SF-36 domains General health and Vitality. Hence, it is obvious that health, especially physical health, does not have to necessarily reduce the subjective QOL. Mental health or psychological state of the patient seem to be of higher importance for the subjective perception of QOL. Furthermore, it is believed that MS patients are more focused on their mental health, emotional problems and vitality in relation to their physical disability (Rothwell et al. 1997, Benito-Leon et al. 2002).

Studies have demonstrated that, next to psychiatric comorbidities (Marrie et al. 2018), personality (Benedict et al. 2001, Zarbo et al. 2016) and temperament (Salhofer-Polanyi et al. 2018) also have a great influence on quality of life of MS patients. The recent case-control study of neurological diseases and risk of suicide attempt by Eliasen et al. (2018) revealed that newly diagnosed (within 3 months) patient with a neurological disease had an even higher risk of attempting suicide with no sign of gender difference, and that patients with MS have a 1.5 times increased risk of attempting suicide, compared to the general population. This guides us to the importance of detecting and medicating these psychological changes early in the course of MS, thereby improving their QOL.

Few limitations of the research have been recognized. First of all, the sample of MS patients is relatively small (N=30). Moreover, there is unequal number of male (N=8) and female participants. Secondly, only MS patients in early stages (EDSS<2.5) were included in research. However, if the other subgroups of MS patients were included, they could have been compared according to the severity of symptoms and distress.

CONCLUSION

Present study examined health and quality of life of MS patients in early stage in relation to the general Croatian population. Furthermore, correlation between health and quality of life has been explored. Results indicate that MS patients in early stage experience similar health and quality of life, comparing to the general adult population. When it comes to the health domains, greatest differences between MS patients and general adult population have been noticed regarding Mental health, Social Functioning and Energy/vitality. As far as the QOL domains, MS patients reported on similar or slightly lower QOL, expect for the domain safety, which was evaluated more positively by the MS

patients. In addition, results demonstrated the conceptual difference between the health and QOL. According to the correlation analysis, only a few health domains correlate significantly with QOL domains, meaning that health and QOL measures encompass different constructs, and therefore, leading to conclusion that impaired health does not necessarily imply lower quality of life. These findings contribute to the better comprehension of the complex relationship between the health and subjective perception of quality of life of MS patients who are currently in early stage of the disease, suggesting that in early stage of MS quality of life is still maintained at the average level.

Contribution of individual authors:

Klaudia Duka Glavor: study design of the article; data collection, literature searches; writing the manuscript; approval of the final version.

Marina Titlić: study design, revisioning the manuscript; approval of the final version.

Gorka Vuletić: study design, statistical analysis and interpretation of results, approval of the final version.

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Correspondence:

Klaudia Duka Glavor, MD
Department of Neurology, General Hospital Zadar
Boze Pericica 5, 23000 Zadar, Croatia
E-mail: klaudia.duka@du.t-com.hr