The effects of fatigue, depression and the level of disability on the health-related quality of life of glatiramer acetate-treated relapsing-remitting patients with multiple sclerosis in Hungary

Zsanett Fricska-Nagy[a], Judit Füvesi[a], Csilla Rózsa[b], Sámuel Komoly[c], Gábor Jakab[d], Tünde Csépány[e], Zita Jobbágy[f], Gyula Lencsés[g], László Vécsei[a,h], Krisztina Bencsik[a]

Hungarian Multiple Sclerosis Study Group

[a]Department of Neurology, Faculty of Medicine, Albert Szent-Györgyi Clinical Centre, University of Szeged, 6 Semmelweis Str., 6725, Szeged, Hungary

[b]Department of Neurology, Ferenc Jahn Hospital of South-Pest, 1 Köves Road, 1204, Budapest, Hungary

[c]Department of Neurology, Faculty of Medicine, University of Pécs, 2 Rét Str., 7623, Pécs, Hungary

[d]Department of Neurology, Uzsoki Street Hospital, 29-41 Uzsoki Str., 1145, Budapest, Hungary

[e]Department of Neurology, Faculty of Medicine, University of Debrecen, 98 Nagyerdei Str., 4012, Debrecen, Hungary

[f]Department of Neurology, Bács-Kiskun County Hospital, 38 Nyíri Road, 6000, Kecskemét, Hungary

[g]Department of Sociology, University of Szeged, 30-34 Petőfi S. Str., 6722, Szeged, Hungary

2
[h]MTA-SZTE Neuroscience Research Group, Szeged, Hungary

Email addresses:

fricskanagy@gmail.com

judit.fuvesi@gmail.com

rozsa.csilla@jahndelpest.hu

komoly.samuel@pte.hu

jakabgbp@yahoo.com

csepany@edu.med.unideb.hu

zitajobbagy@freemail.hu

lencses@socio.u-szeged.hu

vecsei.laszlo@med.u-szeged.hu

bencsik.krisztina@med.u-szeged.hu

Corresponding author:

Krisztina Bencsik MD, PhD

Department of Neurology

Albert Szent-Györgyi Clinical Centre

University of Szeged

Semmelweis u. 6

H-6725, Szeged

3
HUNGARY

e-mail.: bencsik.krisztina@med.u-szeged.hu

fax: +36 62/545-597

Abstract

Background: The common symptoms of multiple sclerosis are fatigue, depression, cognitive dysfunction, pain and sexual dysfunction, which influence the health-related quality of life of the patients.

Objective: We aimed to determine the correlations between the health-related quality of life, the level of disability, fatigue and depression in glatiramer acetate-treated patients with multiple sclerosis in Hungary.

Methods: The Hungarian versions of the Multiple Sclerosis Quality of Life-54, Fatigue Impact Scale and Beck Depression Inventory questionnaires were completed by 428 relapsing-remitting multiple sclerosis patients treated with glatiramer acetate from 19 Hungarian centers.

Results: The prevalence of fatigue was found to be 62.4%. The prevalence of depression was lower (13.4%) than that described in previous studies (36-54%) among patients with multiple sclerosis. Significant differences in the health-related quality of life were found between fatigued and non-fatigued patients. The level of disability, fatigue, depression and the duration of the disease correlated significantly with the quality of life. However, linear regression analysis indicated that the quality of life was predicted by the level of disability, depression, social and cognitive fatigue, but not by physical fatigue.

Conclusions: Decreasing the disease activity in multiple sclerosis with immunomodulatory therapy, together with improvements of the diagnostics and treatment of the accompanying depression and fatigue are of high priority to improve the health-related quality of life of patients with multiple sclerosis.

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Keywords: Multiple sclerosis; Fatigue; Depression; Health-related quality of life; Immunomodulatory therapy.

Highlights:

- The prevalence of fatigue and depression was found to be 62.4% and 13.4%, respectively.
- Significant differences in the quality of life were found between fatigued and non-fatigued patients.
- The quality of life was predicted by EDSS, depression, social and cognitive fatigue.

1. Introduction

Multiple sclerosis (MS) is a chronic disease, which, via its various symptoms, impairs the patients' ability to move and work, as well as their level of well-being. Although the Expanded Disability Status Scale (EDSS) is generally used to determine the level of disability of patients with multiple sclerosis, several aspects of multiple sclerosis are not measurable with this scale (Kurtzke, 1983). In recent years, measurement of the health-related quality of life (HRQoL) became a useful tool to assess the burden of MS. HRQoL is a multidimensional parameter which relates to physical, mental and social health, and which is estimated by using general, combined and specific questionnaires (Hadgkiss et al., 2013). The common symptoms of multiple sclerosis are fatigue, depression, cognitive dysfunction, pain and sexual dysfunction, which synergistically influence the health-related quality of life (Crayton et al., 2004).

Fatigue is found in 40-90% of patients with multiple sclerosis (Lerdal et al., 2003), and fundamentally influences their daily routine. The patients' capability of moving is better during the morning hours, but they need resting periods during longer activities. Fatigue also limits the patients' personal interactions; moreover, it can even lead to losing their jobs. A patient with multiple sclerosis was reported, who presented fatigue as the only manifestation of an acute MS relapse (Flachenecker & Meissner, 2008). Futhermore, in another study, the correlation of fatigue and a cognitive sign of MS, alertness, was confirmed (Weinges-Evers et al., 2010). Three forms of fatigue have been described: physical, cognitive and social fatigue (Bakshi,

2003; Vucic et al., 2010).

The diagnosis and treatment of depression are essential in multiple sclerosis cases. Patten et al. concluded that major depression occurs in 15.7% of individuals with multiple sclerosis, which means a 2.3 times higher risk than in the normal population (Patten et al., 2003). A survey by Ziemssen et al. suggested that major depression may occur in approximately 50% of patients with multiple sclerosis (Ziemssen, 2009). Only a small proportion of patients with multiple sclerosis receive effective treatment for their depression, and this situation, besides putting their uninterrupted

immunomodulatory therapy at risk, can lead to more severe fatigue, with a resulting negative influence on their health-related quality of life (Sadovnick et al., 1996).

Among the various modes of immunomodulatory therapy, the interferons can cause flu-like symptoms and fever, which can lead to secondary fatigue (Plosker, 2011). Sleep disorders can also cause secondary fatigue. Studies showed that sleep medical therapy may improve MS related fatigue (Veauthier et al., 2013; Veauthier & Paul, 2014). Furthermore, one of the adverse events of interferon beta treatment is depression. It was suggested that interferon beta induces secondary depression due to inhibition of serotonin production, however, long-term studies did not prove this hypothesis (Loftis & Hauser, 2004; Reder et al., 2014). For our study, we selected a group of glatiramer acetate-treated patients with multiple sclerosis, since the adverse events of glatiramer acetate (depression, flu-like symptoms, fever) are less common than those of interferon beta.

The aim of our study was to determine the prevalence of fatigue and

depression in glatiramer acetate-treated patients with multiple sclerosis. Since we expected that fatigue negatively influences the health-related quality of life, we compared this parameter in fatigued and non-fatigued patients. We analyzed the correlation of fatigue, depression, clinical disability and the disease duration with the health-related quality of life.

2. Methods

2.1. Participants

Data on 428 relapsing-remitting patients with multiple sclerosis treated with glatiramer acetate were collected from 19 Hungarian multiple sclerosis centers. The relevant socio-demographic and disease-related data were obtained from the multiple sclerosis registers at the centers. The diagnosis was confirmed according to the 2005 modification of the McDonald criteria for relapsing-remitting multiple sclerosis (McDonald et al., 2001; Polman et al., 2005). Patients were included in the study according to the following inclusion criteria: the patients had a relapsing-remitting form of multiple sclerosis, glatiramer acetate treatment period was longer than one year, the patients were in remission for at least 30 days, the patients were off steroid therapy for more than 30 days, the patients had an EDSS score between zero and 5.5, and the patients were more than 18 years old.

2.2. Ethics

The personal data on the patients were subject to strict confidentiality. All participants received appropriate information about the study both in

written form and orally. They gave their written consent to statistical evaluation of their answers. The study was approved by the Science and Research-ethics Committee of the Medical Science Council in Hungary (3462-0/2010-1018EKU (197/PI/10)) and was in full accord with the Declaration of Helsinki. The same, ethically approved information sheet and consent form were given to the participating patients at each center.

2.3 Measures

The most frequently utilized questionnaire in multiple sclerosis to measure quality of life is the Multiple Sclerosis Quality of Life Questionnaire (MSQoL-54), which is a combined questionnaire, developed for English-speaking patients. It contains general questions regarding the quality of life (Short Form-36) and 18 specific questions for patients with multiple sclerosis (Vickrey et al., 1995). The MSQoL-54 enables the comparison of the quality of life of patients with multiple sclerosis with that of the general population and with that of patients with other diseases. The total of 54 questions can be divided into 14 groups: 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, Overall quality of life, Sexual function, Satisfaction with sexual function and Change in health. The MSQoL-54 was validated for the Hungarian language (Füvesi et al., 2008), and the first survey with this questionnaire was performed in Hungary in 2010 (Füvesi et al., 2010). Apart from determining the health-related quality of life of multiple sclerosis patients, the survey demonstrated that 62% of the patients had at least one

concomitant disease. Depression was found in 20.3% of the patients with multiple sclerosis.

The pathophysiology of fatigue is not well understood, and the objective characterization of fatigue is difficult. Recently, it was shown that fatigue is associated with the alterations of basal ganglia functional connectivity and with altered parameters of saccade like ocular motor movements, therefore testing these may lead to a better quantification of fatigue (Finke et al., 2012; Finke et al., 2015). However, questionnaires are widely used for this purpose. Although they are somewhat subjective, they yield useful information about the patients' everyday life. The most frequently used questionnaires are the Fatigue Severity Scale (FSS) (Krupp et al., 1989), the Fatigue Impact Scale (FIS) (Fisk et al., 1994), and the Modified Fatigue Impact Scale (MFIS) (Achiron et al., 2015). While the FSS is one-dimensional, measuring only physical fatigue, the FIS and MFIS assess all three aspects of fatigue. The completed FIS questionnaire contains 40 statements, the MFIS is a 21-item scale, each with a score ranging from 0 to 4 points, giving information on the last 4 weeks. The Hungarian version of the FIS was validated in 2011 (Losonczi et al., 2011).

The Beck Depression Inventory - First Edition (BDI-I.) provides 21 grouped assertions on how the patient has been feeling in the last week. Each question has a set of at least four possible answers. With a total score above 21 points, the patient is regarded to have depression (Beck et al., 1961).

2.4. Statistical analysis

Statistical analysis was carried out with the Statistical Package for Social Sciences (SPSS 19.0, SPSS Inc., http://www.spss.com); the level of significance was predefined at $p < 0.05$. For determination of the prevalence of fatigue and depression, we used frequency analysis. Correlation coefficients and partial correlation coefficients were applied to assess the influence of the EDSS score, depression, fatigue and the disease duration on the quality of life. The predictors of the quality of life were determined by linear regression. The data on the fatigued and the non-fatigued patients were compared with the independent samples t-test. Our study is an exploratory pilot study, so no correction for multiple comparisons was made.

3. Results

3.1. Demographic and clinical measures

The average age of the patients was 43.6 years (95% confidence interval [CI] 42.6–44.6), the male to female ratio was 1:2.8, the mean disease duration of multiple sclerosis from date of diagnosis was 11.2 years (95% CI 10.6–11.9), the mean duration of glatiramer acetate treatment was 6.6 years (95% CI 6.2–6.9) and the median EDSS score was 2.0 (95% CI 2.2–2.5). The percentage of the married respondents was 60.7%, and 83.8% had one or two children. Around 66% had participated successfully in secondary education, and about 33% had done so in higher-level education. The distribution of patients among the multiple sclerosis centers is shown in Table I.

3.2. Main outcome measures

As concerns the responses to the MSQoL-54, FIS and BDI questionnaires by the 428 glatiramer acetate-treated relapsing-remitting patients with multiple sclerosis in this multicentre study, 402 and 381 patients answered all questions in the FIS and BDI questionnaires, respectively. In each question group of the MSQoL-54, an average of 60 of the questionnaires could not be evaluated because of missing data. An exception was the question group relating to the sexual function and the satisfaction with the sexual function, which were incomplete in more than 80 cases.

The FIS scores indicated that the prevalence of fatigue was 62.4% (251 of 402 patients). The prevalence of depression was 13.4% (51 of 381 patients). Among the 278 patients who filled in both questionnaires completely, no one had depression without fatigue. However, 35 of the 168 fatigued patients also had depression (20.8%). Non-fatigued patients assessed their health-related quality of life significantly higher than patients with fatigue in all question groups of the MSQoL-54 questionnaire (Table II).

By means of correlation analysis, we examined the correlation of the EDSS score, depression, the three dimensions of fatigue and the disease duration with the health-related quality of life, as examined with the MSQoL-54. Depression and the three dimensions of fatigue influenced all the subscales of the MSQoL-54 questions significantly negatively. The EDSS score correlated significantly negatively with all aspects of the MSQoL-54, except for the cognitive function scale. The disease duration had a significant negative correlation with the quality of life, with the exception of the mental health, the cognitive function and the satisfaction with the sexual function

(Table III).

Regression analysis revealed that the overall quality of life was significantly predicted by the EDSS score, depression and social fatigue (Table IV). When the patients were grouped on the basis of the presence of depression, it emerged that in patients with depression, social fatigue was the only factor that predicted the quality of life (Table V). At question 54 of the MSQoL-54, the patients verbally evaluate their quality of life (terrible (1) - unhappy (2) - mostly grumbler (3) -mixed (4) - mostly satisfied (5) - satisfied (6) - happy (7)). Regression analysis showed that the verbal characterization of the quality of life was predicted by the EDSS score, depression, social and cognitive fatigue ($R^2=0.389$, $p<0.05$). As concerns the cognitive and the sexual quality of life, we found significant effects of depression and cognitive fatigue (Tables VI, VII).

4. Discussion

The standardized prevalence of multiple sclerosis in Csongrád County, Hungary is 83.7/100,000, 69% of the patients show the relapsing-remitting clinical form (Zsíros et al., 2014), and 78% of the relapsing-remitting patients is treated with immunomodulatory therapy. The 428 patients examined in our study represent almost 10% of the Hungarian MS patients treated with immunomodulatory therapy, and more than 50% of the Hungarian MS patients treated with glatiramer acetate.

In this multicentre, cross-sectional study of Hungarian, relapsing-remitting multiple sclerosis patients treated with glatiramer acetate, we found a considerable prevalence of fatigue and depression. We also showed that

these factors significantly contribute to the health-related quality of life of our patients. The 62.4% prevalence of fatigue after a mean disease duration of 11.23 years is in line with the literature data (Lerdal et al., 2003). Many international studies found that glatiramer acetate therapy may improve fatigue (Jongen et al., 2010; Jongen et al., 2014; Metz et al., 2004; Ziemssen et al., 2008).

In previous studies, the prevalence of depression among patients with multiple sclerosis was found to be 36-54% (Ziemssen, 2009). Surprisingly, in our study, the prevalence was significantly lower (13.4%). The risk factors for depression in multiple sclerosis include the female gender, an age under 35 years, a family history of major depression and stress (Patten et al., 2000). Chwastiak et al. reported that depression correlated with a lower level of education, a younger age and the absence of social support, while a survey in Sarajevo, Bosnia and Herzegovina indicated that depression is more frequent among younger and middle-aged patients with a higher educational level and an unmarried status (Chwastiak et al., 2002; Alajbegovic et al., 2011). In the general population, depression is 1.7 to 2 times more frequent in females than in males (Kessler et al., 1993), however, the above-mentioned studies did not detect this ratio in patients with MS.

The low prevalence of depression in our study may result from the interaction of a number of factors. The majority of the respondent patients were married with one or two children. However, most of the patients (about 70%) declined to answer questions about their family status. The freely available phone service of multiple sclerosis nurses may also significantly influence the occurrence of depression among patients. This ensures stable

and well-functioning medical support for patients with multiple sclerosis. The participants in this study had a relatively low median EDSS score, indicating a low level of physical disability. If introduced within a few years after the onset of multiple sclerosis, glatiramer acetate not only reduces the activity of the disease, but may also have an antidepressant effect (Tsai, 2007; Johnson, 2012).

Our correlation analysis also demonstrated that depression significantly influences the health-related quality of life. Depression has a strong influence on all aspects of the quality of life, and it can also mask the effects of fatigue, the EDSS score or the duration of the disease on quality of life.

Our results suggest that it is important to diagnose depression among multiple sclerosis patients, since depression can worsen their health-related quality of life, and its presence can influence the choice of immunomodulatory therapy. For patients with multiple sclerosis, who are susceptible to depression, glatiramer acetate is to be recommended since depression may occur as an adverse event of interferon beta therapy.

Depression in multiple sclerosis is often not well-diagnosed, and is not effectively treated (Marrie et al., 2009). The diagnosis is missed in around 23-30% of the cases, and around 20-36% of the patients are claimed to receive inadequate treatment of depression (McGuigan, & Hutchinson, 2006). The effective treatment of depression is essential since, if left untreated, it may decrease the level of patient compliance, which may result in the cessation of immunomodulatory therapy.

According to several previous studies, fatigue can decrease the health-related quality of life significantly (Benedict et al., 2005; Janardhan & Bakshi,

2002; Lobentanz et al., 2004; Mitchell et al., 2005). In these studies, fatigue was examined as a one-dimensional factor. Our results are partly contradictory to these findings, which may be explained by our different approach. We examined the three dimensions of fatigue separately, and found that physical fatigue does not predict the quality of life of multiple sclerosis patients. Social and cognitive fatigue, however, exerts significantly negative effects on the health-related quality of life. We cannot measure these with the EDSS, and it is not sure that the patients are willing to talk about their social difficulties or about their inability to lead a social life due to multiple sclerosis. We have to consider and strive to decrease the level of social fatigue, and thereby raise the patients' quality of life perceptibly.

In the past decade, various surveys have emphasized the importance of depression and fatigue in multiple sclerosis, showing that these parameters, together with the EDSS score and the disease duration, significantly influence the health-related quality of life of patients with multiple sclerosis (Miller et al., 2003; Pittion-Vouyovitch et al., 2006). Recent studies in Iran and Poland on the influence of fatigue and depression on the health-related quality of life in multiple sclerosis yielded data that are in line with our results (Kargarfard et al., 2012; Papuc, & Stelmasiak, 2012).

5. Conclusions

Our study draws attention to the importance of estimation and follow-up of both social and cognitive fatigue and depression in multiple sclerosis. Besides the determination of the EDSS score, it is necessary to consider these symptoms as parameters, which influence the health-related quality of life.

Their treatment adds further values to immunomodulatory therapy, and hence provides a better life for patients with multiple sclerosis.

Competing interests

The authors declare that there is no competing of interest.

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Hungarian Multiple Sclerosis Study Group: Éva Langane, Margit Török (Dept. of Neurology, A. Szent-Györgyi Clinical Centre, University of Szeged, Szeged, Hungary); Judit Matolcsi, Gedeonné Jakab, Tünde Závodni, (Dept. of Neurology, F. Jahn Hospital of South-Pest, Budapest, Hungary); László Bors, Zsolt Illés, Anita Trauninger, Mária Deák (Dept. of Neurology, University of Pécs Medical School, Pécs, Hungary); Gabriella Katona, Ilona Mayer, Zsuzsanna Győri, Zoltánné Szépvölgyi (Dept. of Neurology, Uzsoki St. Hospital, Budapest, Hungary); Zsolt Mezei, Jánosné Virág (Dept. of Neurology, University of Debrecen, Debrecen, Hungary); Gézáné Szőke (Dept. of Neurology, Bács-Kiskun County Hopital, Kecskemét, Hungary); István Deme, Zsolt Győrbíró, Majorné Márta Novák (Dept. of Neurology, M. Kaposi Hospital, Kaposvár, Hungary); Zsuzsanna Nagy, Rózsa Báger, Péterné Barti (Dept. of

Neurology, L. Markusovszky Hospital, Szombathely, Hungary); Botond Cseh, Tibor Kollár, Istvánné Tószegi, Éva Kubiczi (Dept. of Neurology, BAZ County Hospital, Miskolc, Hungary); Péter Diószeghy, Zsuzsa Magyar, Károlyné Hengsperger (Dept. of Neurology, A. Jósa Hospital, Nyíregyháza, Hungary); Erzsébet Bense, Judit Kánya, Ivánné Ildikó Simon (Dept. of Neurology, Gy. Kenézy Hospital, Debrecen, Hungary); András Guseo, Jánosné Boda, Sárosdiné Márta Horváth (Dept. of Neurology, St. György Hospital, Székesfehérvár, Hungary); Attila Csányi, Gábor Rum, Lugosiné Erika Huszár (Dept. of Neurology, A. Petz County Hospital, Győr, Hungary); Gabriella Molnár, Gizella Szabóné Dudás (Dept. of Neurology, Tolna County Hospital, Szekszárd, Hungary); Ágnes Köves, Gyöngyi Györök, Kissné Gizella Bartos (Dept. of Neurology, Zs. Bajcsy Hospital, Budapest, Hungary); Mária Sátori, Miklós Hernádi, Mária Budavári (Dept. of Neurology, K. Vaszary Hospital, Esztergom, Hungary); Adrien Jóri (Dept. of Neurology, St. István Hospital, Budapest, Hungary); Zsuzsanna Lohner, Éva Juhász, Józsefné Henger (Dept. of Neurology, Hungarian Military Health Centre, Budapest, Hungary).

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	Centers	No. of patients
1.	Dept. of Neurol., F. Jahn Hosp. of South-Pest, Budapest, Hungary	48
2.	Dept. of Neurol., Hungarian Military Hosp., Budapest, Hungary	3
3.	Dept. of Neurol., St. István Hosp., Budapest, Hungary	4
4.	Dept. of Neurol., Univ. of Debrecen, Debrecen, Hungary	25
5.	Dept. of Neurol., Gy. Kenézy Hosp., Debrecen, Hungary	18
6.	Dept. of Neurol., A. Petz County Hosp., Győr, Hungary	11
7.	Dept. of Neurol., M. Kaposi Hosp., Kaposvár, Hungary	24
8.	Dept. of Neurol., Bács-Kiskun County Hosp., Kecskemét, Hungary	25
9.	Dept. of Neurol., BAZ County Hosp., Miskolc, Hungary	21
10.	Dept. of Neurol., A. Jósa Hosp., Nyíregyháza, Hungary	19
11.	Dept. of Neurol., Univ. of Pécs Med. School, Pécs, Hungary	40
12.	Dept. of Neurol., Univ. of Szeged, Szeged, Hungary	74
13.	Dept. of Neurol., Tolna County Hosp., Szekszárd, Hungary	9
14.	Dept. of Neurol., St. György Hosp., Székesfehérvár, Hungary	16
15.	Dept. of Neurol., G. Hetényi County Hosp., Szolnok, Hungary	18
16.	Dept. of Neurol., L. Markusovszky Hosp., Szombathely, Hungary	22
17.	Dept. of Neurol., K. Vaszary Hosp., Esztergom, Hungary	6
18.	Dept. of Neurol., Uzsoki St. Hosp., Budapest, Hungary	38
19.	Dept. of Neurol., Zs. Bajcsy Hosp., Budapest, Hungary	7

Table I. Hungarian multiple sclerosis centers participating in the study

		N	Mean	Std. deviation	Std. error mean	*t*-test for equality of means*t*-test for equality of means						
						t	df	Sig. (2-tailed)	Mean difference	Std. error difference	95% CI of the diff.	
											Lower	Upper
"Overall, how would you rate your own quality of life?"	no fatigue	131	7.69	1.608	0.14	12.386	323	0.001	2.326	0.188	1.957	2.696
	fatigue	194	5.36	1.695	0.122	12.514	288.797	0.001	2.326	0.186	1.96	2.692
"Which best describes how you feel about your life as a whole?"	no fatigue	131	5.39	1.113	0.097	10.513	325	0.001	1.379	0.131	1.121	1.637
	fatigue	196	4.01	1.194	0.085	10.661	291.742	0.001	1.379	0.129	1.124	1.634
Overall quality of life scale %	no fatigue	131	75.013	14.852	1.298	13.144	325	0.001	23.014	1.751	19.57	26.459
	fatigue	196	51.998	15.943	1.139	13.331	291.92	0.001	23.014	1.727	19.617	26.412
General health scale %	no fatigue	131	65.473	20.318	1.775	15.132	325	0.001	31.441	2.078	27.353	35.528
	fatigue	196	34.032	17.021	1.216	14.613	244.674	0.001	31.441	2.152	27.203	35.679
Cognitive function scale %	no fatigue	130	85.692	17.239	1.512	11.423	323	0.001	26.923	2.357	22.286	31.56
	fatigue	195	58.769	22.888	1.639	12.074	318.167	0.001	26.923	23.02	22.536	31.31
Sexual function scale %	no fatigue	128	88.997	16.367	1.447	8.192	311	0.001	24.973	3.049	18.975	30.972
	fatigue	185	64.024	31.68	2.329	9.108	290.671	0.001	24.973	2.742	19.577	30.37
Bodily pain scale %	no fatigue	131	82.924	21.171	1.85	12.938	323	0.001	32.913	2.544	27.908	37.918
	fatigue	194	50.01	23.347	1.676	13.185	296.503	0.001	32.913	2.496	28.001	37.826

Table II. Health-related quality of life of patients with or without fatigue

		EDSS	Cognitive fatigue	Physical fatigue	Social fatigue	BDI	Duration of disease
Physical Functioning Scale	r	-0.541	-0.455	-0.707	-0.651	-0.423	-0.201
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Role-Physical Scale	r	-0.422	-0.516	-0.655	-0.66	-0.452	-0.209
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Role-Emotional Scale	r	-0.241	-0.581	-0.578	-0.643	-0.523	-0.153
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.003
Bodily Pain Scale	r	-0.315	-0.567	-0.66	-0.655	-0.478	-0.138
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.008
Pain Scale (Vickrey)	r	-0.304	-0.581	-0.666	-0.674	-0.526	-0.145
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.005
Mental Health Scale	r	-0.181	-0.556	-0.569	-0.649	-0.716	-0.047
	p	0.0001	0,0001	0.0001	0.0001	0.0001	0.367
Vitality Scale	r	-0.328	-0.578	-0.723	-0.721	-0.591	-0.125*
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.016
Energy Scale (Vickrey)	r	-0.294	-0.577	-0.695	-0.705	-0.591	-0.134
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.01
General Health Scale	r	-0.358	-0.59	-0.698	-0.712	-0.563	-0.135
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.009
Social Functioning Scale	r	-0.272	-0.57	-0.643	-0.705	-0.58	-0.11*
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.033
Social Function Scale (Vickrey)	r	-0.352	-0.605	-0.685	-0.739	-0.588	-0.151
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.003
Cognitive Function Scale	r	-0.084	-0.764	-0.528	-0.648	-0.603	-0.057*
	p	0.106	0.0001	0.0001	0.0001	0.0001	0.276
Health Distress Scale	r	-0.292	-0.56	-0.649	-0.701	-0.617	-0.1*
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.053
Overall Quality of Life Scale	r	-0.369	-0.545	-0.617	-0.675	-0.674	-0.133
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.01
Sexual Function Scale	r	-0.224	-0.442	-0.517	-0.549	-0.486	-0.122*
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.022
Reported Health Transition Scale	r	-0.262	-0.273	-0.412	-0.387	-0.317	-0.143
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.006
Satisfaction with Sexual Function Scale	r	-0.211	-0.406	-0.426	-0.471	-0.525	-0.097*
	p	0.0001	0.0001	0.0001	0.0001	0.0001	0.071

Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Table III. Correlation of the level of disability, fatigue, depression and the duration of MS with the HRQoL

Coefficients[a]

	Unstandardized coefficients		Standardized coefficients		
	B	Std. error	Beta	*t*	Sig.
(Constant)	18.184	0.306		59.46	0.0001
EDSS	-0.394	0.108	-0.155	-3.654	**0.0001**
Cognitive fatigue	0.057	0.029	0.152	1.947	0.052
Physical fatigue	0.032	0.033	0.094	0.996	0.320
Social fatigue	-0.148	0.023	-0.785	-6.329	**0.0001**
Depression	-1.742	0.478	-0.152	-3.643	**0.0001**

[a] Dependent variable: overall quality of life scale (N=349, R^2=0.519)

Table IV. Predictors of the overall quality of life scale by linear regression

		Coefficients[a]				
		Unstandardized coefficients		Standardized coefficients		
		B	Std. error	Beta	*t*	Sig.
No depression	(Constant)	18.287	0.312		58.698	0.0001
	EDSS	-0.436	0.114	-0.186	-3.843	**0.0001**
	Cognitive fatigue	0.058	0.031	0.157	1.875	0.062
	Physical fatigue	0.023	0.034	0.069	0.661	0.509
	Social fatigue	-0.143	0.025	-0.768	-5.780	**0.0001**
Depression	(Constant)	14.996	2.238		6.702	0.0001
	EDSS	-0.102	0.384	-0.046	-0.264	0.793
	Cognitive fatigue	0.05	0.094	0.133	0.529	0.600
	Physical fatigue	0.115	0.116	0.275	0.998	0.325
	Social fatigue	-0.177	0.081	-0.707	-2.200	**0.034**

[a] Dependent variable: overall quality of life scale (N=305 and 44, R^2=0.448 and 0.170, respectively)

Table V. Predictors of the overall quality of life scale among patients without or with depression by linear regression

Coefficients[a]					
	Unstandardized coefficients		Standardized coefficients		
	B	Std. error	Beta	*t*	Sig.
(Constant)	85.468	2.060		41.499	0.0001
Depression	-10.716	3.389	-0.142	-3.162	**0.002**
EDSS	1.344	0.744	0.082	1.806	0.072
Cognitive fatigue	-27.332	2.988	-0.55	-9.147	**0.0001**
Physical fatigue	-2.642	3.693	-0.051	-0.715	0.475
Social fatigue	-6.473	3.891	-0.13	-1.663	0.097

[a] Dependent variable: cognitive function scale % (N=276, R^2=0.527)

Table VI. Predictors of the cognitive quality of life by linear regression

Coefficients[a]					
	Unstandardized coefficients		Standardized coefficients		
	B	Std. error	Beta	*t*	Sig.
(Constant)	91.62	3.077		29.774	0.0001
Depression	-16.605	5.130	-0.182	-3.237	**0.001**
EDSS	-1.705	1.121	-0.086	-1.521	0.129
Cognitive fatigue	-14.892	4.468	-0.249	-3.333	**0.001**
Physical fatigue	0.511	5.503	0.008	0.093	0.926
Social fatigue	-11.049	5.799	-0.185	-1.905	0.058

[a] Dependent variable: sexual function scale % (N=271, R^2=0.273)

Table VII. Predictors of the sexual quality of life by linear regression