

# Maintaining quality of life in multiple sclerosis

## Fact, fiction, or limited reality?

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### ABSTRACT

Health-related quality of life (HRQOL) is an important marker for health-related impacts on individuals with chronic diseases. This HRQOL study compares multiple sclerosis (MS) patients to a socio-demographically-matched healthy control group. HRQOL was assessed by means of a modular instrument (DEFU/DEFIS), which allows comparisons between diseased and healthy individuals. Main goal of the study was to obtain pertinent data to build a more reliable theoretical framework concerning HRQOL in MS. Another aim was to test the hypothesis of the so-called happiness paradox, according to which disabled individuals could maintain reasonable levels of HRQOL. Results show that MS individuals present lower levels of HRQOL in comparison to healthy controls, arguing against the happiness paradox hypothesis. Preservation of HRQOL levels against certain levels of disability may be restricted to a group of patients.

**Key words:** multiple sclerosis, health related quality of life, DEFU/DEFIS, happiness paradox.

### Mantendo a qualidade de vida na esclerose múltipla: fato, ficção ou realidade circunscrita?

### RESUMO

A qualidade de vida relacionada à saúde (QVRS) é um indicador importante do impacto das doenças crônicas sobre a vida dos indivíduos. Esse estudo propõe uma comparação da qualidade de vida de uma amostra de portadores de esclerose múltipla (EM) e uma amostra pareada de indivíduos saudáveis, avaliada pelos questionários DEFU / DEFIS. O objetivo é contribuir para a construção de um referencial teórico a respeito do impacto das doenças crônicas e de seus tratamentos no bem-estar dos pacientes, assim como de investigar a hipótese do paradoxo da felicidade, segundo a qual os pacientes manteriam um bom nível de sensação de bem-estar apesar de suas incapacidades causadas pela doença. Os resultados mostraram que pacientes com EM apresentam graus mais baixos de QVRS do que indivíduos sadios, o que não corrobora a existência do paradoxo da felicidade. No entanto, é possível que a preservação da QVRS apesar das vicissitudes associadas à doença possa ser restrita a um grupo de pacientes.

**Palavras-chave:** esclerose múltipla, qualidade de vida relacionada à saúde, DEFU/DEFIS, paradoxo da felicidade.

Multiple sclerosis (MS) is the most common acquired neurological disease in young adults<sup>1</sup>. Patients with MS have worse physical functioning and report higher incidence and prevalence of depres-

sion than patients with different neurological illness and the general population<sup>2,3</sup>. Many studies have found physical impairments related to the disease and functions related to arms, legs and vision count

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among the most frequent impaired domains<sup>4</sup>. Fatigue is another common symptom, occurring in almost 75% of MS patients and may be sometimes most disabling as it interferes with daily activities<sup>5</sup>. The presence of depressive symptoms could be associated with the experienced of chronic conditions and unpredictable course or/and with lesions in specific regions of central nervous system<sup>3</sup>. These elements including impaired cognition, pain, visual disturbances and degrading social function contribute to the global understanding of the impact of MS on patient's life<sup>5,6</sup>. Studies comparing Health-related quality of life (HRQOL) in patients with chronic diseases to that of normal individuals are essential to build an objective benchmark of their impact on the functionality and well-being perceptions of affected individuals. Few studies have compared MS patients to the healthy population regarding the impact of disease on different areas of functionality in everyday life<sup>2,5</sup>.

Some researchers have pointed to the fact that many individuals with chronic health conditions apparently recovered their levels of welfare, configuring what has been called happiness, well-being or quality of life paradox<sup>7</sup>. Moderately preserved HRQOL, eventually observed in at least some patients with chronic diseases, led to the hypothesis that quality of life may depend more on the individual's subjective conditions (and thus on constitutional factors) than on objective measures, as factually determined by third parties<sup>8</sup>.

In this study we compare MS patients to a socio-demographically-matched healthy control group regarding their HRQOL and assess the value of psychosocial functioning and HRQOL measures as discrimination markers between MS patients and healthy individuals. Additionally we investigated the existence of the happiness paradox hypothesis. The main goal of the present study was to compare HRQOL in MS patients with normal controls in order to obtain a quantitative estimate of eventual impairments or preservation of this construct.

## METHOD

### Subjects

Study participants comprised 20 MS patients and 20 healthy individuals, comparable on socio-demographic variables such as gender, age and years of formal education. The Clinical Research Ethics Board of the Federal University of Minas Gerais approved the study. The diagnosis was established by experienced neurologists according to the McDonald criteria<sup>9</sup> and the disease course was classified according to the international consensus<sup>10</sup>. Control participants were selected from a larger sample of 131 individuals among university students, middle-level nurse technicians and middle-level fundamental level teachers considering comparable socio-demographic

variable such as sex, age, and formal schooling. A tolerance of 4 years was accepted for selection according to age and formal schooling. No significant statistical differences were observed between the two groups regarding age ( $t = -0.03$ ;  $df = 48$ ;  $p > 0.05$ ) and formal schooling ( $t = -0.04$ ;  $df = 48$ ;  $p > 0.05$ ).

### Instruments

In this study we used the Ambulatory Index (AI)<sup>11</sup> and the Expanded Disability Status Scale (EDSS)<sup>12</sup> to assess neurological disability, whereas fatigue was evaluated by the Fatigue Severity Scale (FSS)<sup>13</sup> which has been employed in some studies in Brazilian population<sup>14,15</sup>. The Beck Depression Inventory (BDI)<sup>16</sup> was used to assess depression in all participants. It was validated for the Brazilian population<sup>17</sup> and has been used in Brazilian MS patients<sup>15,18</sup>.

The Brazilian Version of the Functional Assessment of Multiple Sclerosis (DEFU Scale) - The DEFU scale is the validated version to the Portuguese language in Brazil<sup>16</sup> of the Functional Assessment of Multiple Sclerosis (FAMS) developed by Cella and coworkers in 1996<sup>19</sup>. It consists of general questions, which allow comparisons between different diseases or health conditions, and a specific part, which deals with perceptions of patients about symptoms or aspects of the functionality in a given condition, including, cancer, multiple sclerosis and HIV<sup>20</sup>. The FAMS/DEFU scale covers five areas related to HRQOL: [1] satisfaction with life (e.g., "I am content with the quality of my life right now", "I am frustrated by my condition"), [2] affect (e.g., "I am able to enjoy the life", "I am depressed about my condition"); [3] motivation (e.g., "I feel motivated to do things"), [4] functionality (e.g., "I have to limit my social activity because of my condition", "I have trouble walking"), and [5] disease symptoms (e.g., "I feel weak all over", "I have pain").

The Functional Assessment of Healthy Individuals (DEFIS) is a self-report scale for assessing HRQOL of healthy individuals<sup>21</sup>, adapted from the DEFU<sup>18</sup>. Its content is equivalent to that of DEFU, and has adequate internal consistency (alpha coefficients higher than 0.85) and high accuracy for discrimination between MS individuals and normal controls. It aims to compare patients with chronic conditions such as MS to healthy individuals as HRQOL is concerned, providing a ground to the understanding of the impact of various chronic diseases and their treatments on patients. The DEFIS scale consists of 44 statements, grouped in the six following areas which correspond to the DEFU questionnaire: [1] mobility, [2] symptoms, [3] emotional state, [4] personal satisfaction, [5] thinking and fatigue and [6] social and family situation. The response alternatives are formatted in a Likert scale varying from 0 (Never) to 4 (Always). The total score is calculated from the sum of the scores of all

**Table 1.** Descriptive statistics for questionnaires' performance.

Questionnaires	MS				Healthy controls			
	Mean	sd	Kolmogorov-Smirnov	Sig	Mean	sd	Kolmogorov-Smirnov	Sig
DEFU / DEFIS	94.00	20.96	0.44	0.99	124.80	6.60	0.98	0.29
BDI	18.20	9.11	0.49	0.97	6.00	3.39	0.57	0.90
FSS	47.70	12.83	0.80	0.549	21.00	12.35	0.74	0.64

MS: multiple sclerosis; SD: standard deviation; SIG: significance degree; DEFU: Brazilian version of the functional assessment of multiple sclerosis; DEFIS: the functional assessment of healthy individuals; BDI: Beck depression inventory; FSS: fatigue severity scale.

**Table 2.** Effect sizes for group comparisons.

Questionnaires	Cohen's d coefficient	Degree of overlap (%)	Interpretation
DEFU/DEFIS	-1.98	<29%	Large
BDI	1.78	<29%	Large
FSS	2.12	<29%	Large

DEFU: Brazilian version of the functional assessment of multiple sclerosis; DEFIS: the functional assessment of healthy individuals; BDI: Beck depression inventory; FSS: fatigue severity scale.

alternatives endorsed, using the arithmetic inverse score for the statements made in a negative way. Responses are coded such that the higher the total score found, the better the subjective evaluation of HRQOL.

### Statistical analyses

For statistical analysis we used the t test for independent samples, Cohen's d coefficient to examine effect sizes for the found differences, nonparametric ROC analyses<sup>22</sup> to test the discriminating power of employed instruments, and Wilcoxon tests to compare individual item scores between the groups of MS patients and healthy individuals regarding performance on different domains. Initially, univariate descriptive statistical analyses were conducted to verify the distribution characteristics of the scores in the instruments. To check if data were normally distributed we used analysis of Kolmogorov-Smirnov's Zs, which indicated the adequacy of data to perform parametric analysis (all total scores at  $p > 0.05$ ). Statistical analysis was performed with SPSS version 15.0, and statistical significance level at  $p < 0.05$ . The parametric nature of scores distribution was ascertained by means of visual inspection of histograms, box-plots, and Kolmogorov-Smirnov analyses.

### RESULTS

Participants comprised 75% women and 25% men with age ranging from 24 to 55 years (mean 39.88,  $sd = 10.28$ ) in the MS group whereas corresponding distribution in the control group were 80% women and 20% men, 24 to 55 years old (mean 37.68,  $sd = 10.44$ ). The mean formal schooling was 10.64 ( $sd = 3.57$ ) years in the MS group and

9.32 ( $sd = 4.20$ ) years in the control group. Mean duration of disease after diagnosis was 11.00 ( $sd = 8.97$ ) years. Sixty percent of patients ( $n = 12$ ) had relapsing-remitting disease. Mean AI was 2.65 ( $sd = 2.67$ ), mean EDSS was 3.9 ( $sd = 2.48$ ). Ninety percent of patients ( $n = 18$ ) were being treated with disease - modifying drugs and 65% ( $n = 13$ ) received antidepressant medication. In comparison, only 5% ( $n = 1$ ) individuals in the control group were in use of antidepressant medications. Analyses of the performance on the employed instruments showed that MS patients got a higher score, indicating higher prevalence of fatigue and depression symptoms in MS patients than in the control group (Table 1).

The mean scores at DEFU/DEFIS were also worse in the MS group than in the healthy individuals group. On the other hand no significant correlations were found between neurological disability measures (AI, EDSS) and psychosocial self-report instruments (FSS, BDI, DEFU) in the MS group (Spearman's  $\rho$  between  $-0.40$  and  $0.29$ ). The groups of MS patients and healthy individuals were different regarding their performance on the employed instruments at  $p < 0.001$ : DEFU/DEFIS ( $t = 6.14$ ;  $df = 19$ ;  $IC_{95}$ : 20.30 to 41.30), BDI ( $t = -5.56$ ;  $df = 19$ ;  $IC_{95}$ :  $-16.79$  to  $-7.61$ ) and FSS ( $t = -7.05$ ;  $df = 19$ ;  $IC_{95}$ :  $-34.63$  to  $-18.77$ ). Cohen's d coefficients showed effect sizes in the large range meaning that overlapping for the scores in the groups was small (Table 2).

The largest between-groups difference was found for the HRQOL measures. Individual between-groups item comparisons were then conducted with the Wilcoxon test. Significant differences emerged for the total scores in all six assessed domains. Comparisons for all individual items in the Cognition/Fatigue domain reached significance. Statistically significant differences were found for 29/44 items, most notably for Item 25 ("I am content with the quality of my life right now"), which assesses life satisfaction or subjective well-being.

ROC analysis showed that the areas under the curves were 0.929 ( $se = 0.041$ ,  $p < 0.001$ ,  $IC_{95}$ : 0.829 to 1.00) for DEFU/DEFIS, 0.891 ( $se = 0.057$ ,  $p < 0.05$ ,  $IC_{95}$ : 0.776 to 1.00) for BDI, and 0.929 ( $se = 0.040$ ,  $p < 0.05$ ,  $IC_{95}$ : 0.840 to 1.00) for FSS. It suggested that DEFU/DEFIS is a valid tool to discriminate MS patients from healthy controls.

## DISCUSSION

HRQOL measures pursue the important goal of assessing the disease impact in patients' terms. In HRQOL questionnaires the patient is invited to self-assess his/her life satisfaction (general or overall well-being), emotional or psychiatric symptoms such as anxiety or depression (cognitive component, evaluation of emotional feelings), symptoms of the disease (such as pain, fatigue etc.), and the functional impact disease (such as ability to ambulate, self-care, occupational performance, social and family participation, etc.)<sup>23</sup>. HRQOL measures allow a more comprehensive understanding of the impact of disease on the patient's life, providing additional information to those obtained by the traditional objective clinical instruments as, for example, the EDSS<sup>11</sup>. Although it represents an important advance in health care, HRQOL assessment is characterized by many problems awaiting solution. One problem concerns the multidimensionality of the construct, making it difficult to define what exactly is being evaluated, and possibly thus withdrawing meaning of an overall score for quality of life<sup>24</sup>.

One of the most important challenges is the comparison of HRQOL levels among individuals with various chronic health conditions and with the normal population<sup>6</sup>. Concerning MS results from the scanty studies comparing MS patients to healthy individuals are conflicting. In an analysis of 60 MS patients and matched healthy controls it was demonstrated that MS patients got lower scores on all functional attributes of the Health Utilities Index Mark (HUIM3), a self-report measure of HRQOL: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain and discomfort<sup>5</sup>. Opposite results were obtained by other authors<sup>2</sup>, who found that MS patients had significant lower scores than the general population regarding physical functioning, vitality, and general health dimensions, but not in other HRQOL domains such as pain, emotions, mental health, and social functioning.

Our results clearly show that perceived HRQOL levels of MS patients in the first half of the disease course and with relatively mild levels of impairment are consistently and significantly lower when compared to socio-demographically matched controls. Moreover, effect sizes were large and accuracy of the instruments high in discriminating MS from healthy individuals. Analysis by domain scores also showed consistent significant effects favoring the healthy sampling. Statistically significant differences were found for 29/44 items. However, as the sample size is small, this is not a definitive study and further investigations with larger samples should be conducted.

An important objective of the present study was to investigate the happiness paradox hypothesis. According to the disability paradox or happiness paradox hypothesis, a

proportion of disabled individuals would maintain or regain HRQOL against the odds of chronic and/or progressively disabling diseases. Each individual's self and psychosocial functioning would be characterized by a range of optimal values or attractors towards which she would tend to return, even after major life events affecting health and well-being<sup>25</sup>. An opposite view holds that satisfaction with life depends substantially on objective factors such as youth, health, education, marriage, among others<sup>26</sup>.

A study of 153 moderately to severely disabled patients with different conditions including MS found that 54.3% had good or excellent HRQOL rates. In spite of some methodological weakness of the study it suggested the existence of the happiness paradox<sup>6</sup>. On the other hand results from two longitudinal prospective series from Britain and Germany<sup>27</sup> show that individuals' well-being perceptions changed in relation to the occurrence of disability. Lower levels of subjective well-being started for some time before individuals were officially declared physically disabled, and this declining course of well-being perceptions persisted afterwards. This suggests that if existent, adaptation mechanisms may be limited.

In this paper we are drawing attention to the necessity of comparing HRQOL perceptions of individuals with diseases such as MS with those of the healthy population. As intraindividual comparisons before disease inception are virtually impossible to obtain, between-group comparisons with the normal population are essential to assess degree of HRQOL impact. Paradoxically, this has not been adequately considered in the literature<sup>6</sup>.

The lack of appropriate comparisons has led to formulations such as the happiness paradox hypothesis<sup>8</sup> which could be the result of methodological shortcomings in previous studies<sup>26</sup>, inappropriate effect size<sup>8,9</sup> and the use of qualitative methods<sup>7</sup>.

Finding that a major, or at least expressive group of MS patients could maintain their HRQOL perceptions would be good news, and it could also encourage patients and professionals to pursue improvements in HRQOL perceptions. If HRQOL perceptions depend on individual or subjective factors, such as a "set point", then it should always be possible to adopt proper psychotherapeutic measures to improve them. On the reverse side, awareness that subjective factors play a major role in HRQOL perceptions would be detrimental to those patients unable to cope adequately with the disease consequences.

Theoretically, our results clearly profile against the disability paradox hypothesis. And this is most remarkable as the sample is small. This result should be expanded in further studies focusing specifically on comparisons by domains. It could be that differences were observed relating to symptoms, impairment or disability, and even so more general life satisfaction or well-being could be pre-

served in the patients. Content analysis of the DEFUS indicates that only Item 25 is explicitly pertinent to life satisfaction or subjective well-being. A more suitable instrument such as the Satisfaction with Life Scale (SWLS)<sup>28</sup> may yield more focus on the issue.

Clinical implications are also clear cut. It makes little to assess HRQOL perceptions without a healthy comparative benchmark. HRQOL perceptions should also be cross-sectionally compared across patients with different individual or disease profiles, as well as longitudinally, as the disease progresses and impairment and disability accumulate. Comparisons of HRQOL perceptions from different patients with the disability level, patients with different levels of disability, disease courses, or under different therapeutic regimens, as well between patients and healthy individuals are essential to gauge clinicians' expectations of patients' responses and when/which intervention is necessary.

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