

4

IMPACT OF RECENTLY DIAGNOSED MULTIPLE SCLEROSIS ON QUALITY OF LIFE, ANXIETY, DEPRESSION AND DISTRESS OF PATIENTS AND PARTNERS

Abstract

Objectives: Studies demonstrating reduced quality of life and psychological well-being in MS have typically investigated patients within more advanced stages of disease. The aim of the present paper was to evaluate the emotional burden and quality of life of recently diagnosed MS patients and their partners. **Methods:** Data on health-related quality of life (SF-36), anxiety and depression (HADS) and disease-related distress (IES) were obtained in 101 patients and their partners (n=78). **Results:** On average eight months after diagnosis (range 0 – 24 months), 34% of the patients and 40% of the partners had clinically high levels of anxiety, and 36% of the patients and 24% of the partners had levels of severe distress. Scores of anxiety, depression and distress were higher in patients with more functional limitations (EDSS \geq 3.0). Quality of life was significantly poorer in patients compared to controls, particularly among those with higher disability. **Conclusions:** Both patients and their partners demonstrated high levels of anxiety and distress in the early period after the diagnosis. These findings indicate careful attention by health care professionals to identify those who may benefit from further psychological support.

CHAPTER 4

Introduction

Multiple sclerosis (MS) has a major impact on the lives of patients and their partners. In patients, the disease substantially interferes with daily activities and family, social and working life, disturbs emotional well-being, and reduces quality of life.^[1-8] Similar negative consequences on well-being, quality of life and employment have also been found in partners of MS patients.^[9-11] This psychosocial impact of the disease in patients and partners was found to be significantly associated with the patients' severity of disability.^[2-6,8,9,11]

Studies on quality of life and psychological well-being in MS have mainly been conducted among patients who were at more advanced stages of disease. In the above-mentioned studies, the average illness duration varied between 8 and 16 years and median scores on the Expanded Disability Status Scale (EDSS) varied between 3.5 and 5.0.^[1-11] The impact of the disease on quality of life and psychological outcomes of patients and their partners in earlier phases of disease has not been examined. In the early period after diagnosis, patients and their partners may still have to cope with the uncertainty and the prospect of potential serious disability. Also, the uncertainty about unexplained symptoms that had evoked anxiety and distress before the diagnosis may prolong in the period thereafter. On the other hand, at an early stage most patients may still face relatively good health with limited need for care and assistance in daily activities. This would predict that quality of life of patients and their partners may not be reduced in an early phase of disease.

The aim of the present study was to investigate the emotional burden of MS in patients and partners in order to determine the need for psychological support in the early period of disease. For this purpose, we assessed health-related quality of life, anxiety, depression and distress (i.e. the intrusion and avoidance of thoughts and feelings that relate to MS) in recently diagnosed patients and their partners. Psychological outcomes were related to disability status (EDSS) and compared with scores from a general population sample. Finally, we examined differences in psychological well-being between patients and their partners within couples.

Methods

Participants and procedures

In the period of March 1999 – December 2000, consecutive patients were recruited through the Departments of Neurology of the Erasmus MC (Rotterdam), three hospitals within the region of this academic hospital, and the VU Medical Center (Amsterdam). Patients were eligible if they were diagnosed as having definite or probable MS^[12] no longer than two years before study entry, were

IMPACT OF RECENTLY DIAGNOSED MULTIPLE SCLEROSIS

between 18 and 55 years old and had given informed consent. Patients with serious comorbidity of other neurological or systemic diseases or with insufficient understanding of the Dutch language were excluded. Of the 120 patients who met the inclusion criteria, 101 agreed to participate in the study. Patients who declined participation mentioned the emotional burden (n=3) or a lack of interest (n=3). Nine others declined without additional comments and four never responded to our reminders. Ninety of them (89%) had a partner, of whom 78 (87%) did participate. Two partners were excluded due to insufficient understanding of the Dutch language, six were not living with the patient and for that reason not invited by the patient, and four refused for unknown reasons.

Patients underwent a neurological examination, participated in an interview and filled out questionnaires. The questionnaires were sent one week before the neurological examination and had to be given back one week later, before the at-home interview. At that time, partners were given their questionnaires, and requested to complete these in another room during the interview with the patient. Functional limitations were assessed by a physician and rated on the EDSS.^[13] As the present population of recently diagnosed patients is relatively homogeneous with regard to time since first symptoms, EDSS can be regarded as an indicator of disease progression.^[13] The study protocol was approved by the medical ethical committees of the participating hospitals.

Instruments

Patients and partners were asked to evaluate their health-related quality of life during the week prior to the examinations using the SF-36.^[14] The SF-36 is a validated and commonly used instrument for the self-evaluation of physical and mental health. The questionnaire comprises four physical health scales (physical functioning, role-physical functioning, bodily pain and general health) and four mental health scales (vitality, social functioning, role-emotional functioning and mental health). A shortcoming of the SF-36 is its insensitivity to change and the significant floor and ceiling effects in several dimensions.^[15] For this study, both the insensitivity to change and the ceiling effects imply that minor differences in QoL between patients, partners and general population controls may not be detected. Items are summed per scale and transformed into scores between 0 (poor health) and 100 (optimal health).^[14] In our study, Coefficient α ranged from 0.74 to 0.94, indicating good reliability of the scales. Quality of life scores of healthy controls were obtained from a nationwide, population-based study that was conducted to provide Dutch normative data for the SF-36.^[16] Original data on quality of life, age and sex were available for analysis (n = 1742).

CHAPTER 4

The intensity of feelings of anxiety and depression during the past seven days was measured by the Hospital Anxiety and Depression Scale (HADS).^[17] Both scales include seven items that are summed into a total score with a possible range of 0-21. High scores indicate higher levels of anxiety and depression. Scores between 8 and 10 are considered clinically borderline and 11 or higher are considered clinically definite levels of anxiety and depression.^[17] Internal consistency reliability in this study was good: Coefficient α was 0.83 for the anxiety and 0.81 for the depression scale. Data on anxiety and depression of a general population sample were derived from published results of a Dutch validation study of the HADS.^[18] Mean age of this population sample ($n = 199$) was 39.9 years and 54% were women.

Disease-related psychological distress was measured using the Impact of Event Scale (IES).^[19] This questionnaire addresses the psychological distress of having MS by focusing on the intensity of thoughts and feelings that relate to the disease within the past seven days. The questionnaire includes two scales: a 7-item intrusion scale (range 0 – 35) and an 8-item avoidance scale (0 – 40). Intrusion refers to the degree of being overwhelmed by thoughts and feelings about MS. Items include e.g. 'Any reminder brought back feelings about it' and 'I had dreams about it'. Avoidance refers to the tendency to keep off these thoughts and feelings, and is measured by items such as 'I tried not to think about it' and 'I stayed away from any reminders of it'. Answers were given on a 4-point scale with 0 = not at all, 1 = rarely, 3 = sometimes and 5 = often. In this study, Coefficient α was 0.82 for the intrusion scale and 0.75 for the avoidance scale. Intrusion and avoidance are positively correlated.^[20] Although this seems paradoxical, avoidance can be thought of as a way of coping with high levels of intrusive thoughts: if thoughts and feelings are too disturbing, patients may restore emotional equilibrium by avoidance. This co-occurrence of intrusion and avoidance is expressed in a total distress score obtained by summation of the intrusion and avoidance scores.^[19] Total scores of 26 and higher indicate a high risk of developing a stress disorder.^[21] Since intrusion and avoidance are relevant only in subjects who are confronted with the disease, no comparisons were made to general population controls.

Statistical analysis

To test overall differences in quality of life (SF-36) between patients, partners and controls, we performed univariate analysis of variance with age and sex as covariates. Similar analyses were performed to compare quality of life in two groups of disability status (EDSS) for patients and partners separately. EDSS 3.0 was taken as a cut-off score to distinguish between no to minimal disability (0 - 2.5)

IMPACT OF RECENTLY DIAGNOSED MULTIPLE SCLEROSIS

and moderate to severe disability (3.0 - 10.0).^[13] Student's t-tests were performed to compare psychological well-being between high and low EDSS groups for patients and partners separately. Differences in psychological well-being between patients and partners were compared using paired t-tests. A p-value lower than 0.05 was considered statistically significant.

Results

Characteristics of patients and partners

General and clinical characteristics of patients and partners are presented in Table 1. Fifty-nine patients were recruited through the Erasmus MC, 32 through the VU medical center and 10 through local hospitals within the region of the academic centers. Thirty-seven percent of the patients had EDSS scores ≥ 3.0 . Higher EDSS scores were found among male patients (median EDSS 3.0 versus 2.0 in females; $p = 0.05$), in older patients (correlation coefficient $\rho = 0.22$; $p = 0.03$) and in those with definite MS (2.5 versus 2.0 in probable MS; $p = 0.02$). EDSS tended to be higher in patients with a longer time since first symptoms ($\rho = 0.19$; $p = 0.06$). Time since diagnosis ranged from 0 to 24 months (mean 7.8 months), and was not significantly related to EDSS ($\rho = -0.06$; $p = 0.58$).

Quality of life

Overall, recently diagnosed MS patients reported significantly poorer quality of life on all SF-36 scales compared to controls from the general population ($p < 0.05$),

Table 1 General characteristics of MS patients and their partners

	Patients (n = 101)	Partners (n = 78)
Age (years; mean \pm SD)	37.5 \pm 9.5	39.3 \pm 8.7
Sex (women)	70%	36%
Diagnosis		
Definite MS	90%	
Probable MS	10%	
EDSS (median; range)	2.5 [0.0 – 7.0]	
EDSS < 3.0	63%	58%*
EDSS ≥ 3.0	37%	42%*
Time since first symptoms (years; mean \pm SD)	3.7 \pm 4.6 (median 2.1)	
Time since diagnosis (months; mean \pm SD)	7.8 \pm 6.5 (median 5.1)	

* Categorization based on EDSS score of patient.

CHAPTER 4

except for the SF-36 bodily pain scale ($p = 0.67$). SF-36 scores of patients were significantly correlated to their level of disability as measured by the EDSS ($p < 0.001$).

Figure 1 shows mean SF-36 scores of MS patients and controls from the general population. The center of the graph indicates poorest possible health status, representing lowest scores (0) on all scales. Differences between the three groups were significant at all scales ($p < 0.001$). Post-hoc analyses of between-group differences demonstrated that patients with high EDSS scores (≥ 3.0) evaluated their mental and physical health significantly poorer on all SF-36 scales compared with controls. Yet, also patients with low disability (EDSS < 3.0) had significantly poorer SF-36 general health ($p < 0.001$), role-physical functioning ($p < 0.001$), vitality ($p < 0.001$) and physical functioning ($p = 0.01$) than controls. Disease duration from first symptoms was related to two out of eight SF-36 scales: patients with a longer time since their first symptoms reported significantly more

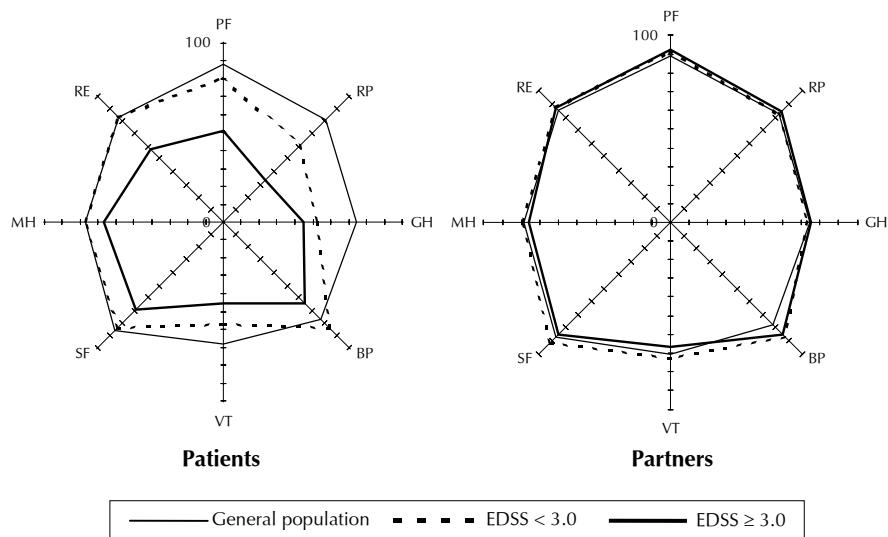


Figure 1 Quality of life of MS patients and partners related to severity of disability (EDSS)

Values are mean scores of SF-36 scales. PF = physical functioning, RP = role-physical functioning, GH = general health, BP = bodily pain, VT = vitality, SF = social functioning, MH = mental health, RE = role-emotional functioning. The center of the graph represents the lowest possible score on each scale. Grouping of partners was based on the patient's EDSS score. Differences between the three groups were tested by univariate ANOVA. In patients, the differences were significant at all scales ($p < 0.001$). In partners, none of the differences were significant, except bodily pain ($p = 0.003$).

IMPACT OF RECENTLY DIAGNOSED MULTIPLE SCLEROSIS

pain ($\rho = -0.32$, $p = 0.002$) and tended to report poorer physical functioning ($\rho = -0.19$, $p = 0.06$). SF-36 quality of life was not significantly related to time since diagnosis. Partners did not differ significantly in mean SF-36 scores from general population controls, except that they reported less pain ($p = 0.001$). Their SF-36 scores were not related to patients' status of functional disability as measured by the EDSS (Figure 1).

Anxiety, depression and psychological distress.

Both patients and partners had significantly higher levels of anxiety than controls from a Dutch population sample (mean score of anxiety in patients 6.6 versus 5.1 in controls; $p = 0.003$; mean score of partners 6.4 versus 5.1, $p = 0.012$).^[18] Thirty-four percent of the patients and 40% of the partners had clinically relevant levels of anxiety (score ≥ 8). Patients and partners did not differ from controls in their mean scores of depression (mean score in patients 3.8 versus 3.4 in controls; $p = 0.41$; mean score of partners 3.7 versus 3.4; $p = 0.56$). Figure 2 shows mean scores of anxiety and depression of patients and partners in two groups divided by the patients' EDSS scores. The figure shows that patients with more functional limitations (EDSS ≥ 3.0) had significantly higher levels of anxiety ($p = 0.05$) and depression ($p < 0.001$) compared to patients with fewer limitations. In a stratified analysis, patients with a high EDSS score were found more anxious ($p = 0.001$) and depressed ($p < 0.001$) than controls. Yet, patients with fewer functional limitations (EDSS < 3.0) did not significantly differ from controls in their levels of anxiety ($p = 0.20$) and depression ($p = 0.14$). In partners, anxiety and depression were not significantly related to the patient's severity of disability (Figure 2).

Figure 2 also demonstrates mean scores of intrusion and avoidance of thoughts and negative feelings about MS. Again, intrusion ($p = 0.01$) as well as avoidance ($p = 0.02$) were significantly related to disability status in patients, but not in partners. Severe distress (defined as the sum of intrusion and avoidance scores > 25) was found in 36% of patients and 24% of the partners. In total, 48% of the patients and 46% of the partners had clinically relevant levels either of anxiety, depression or distress. Neither in patients nor in partners were anxiety, depression and distress associated with time since first symptoms or time since diagnosis.

Comparison between patients and partners

Overall, patients demonstrated a greater tendency to avoid MS-related feelings and thoughts than partners (mean score of avoidance 11.1 versus 7.1; $p < 0.001$), but they did not differ significantly in their levels of anxiety (means 6.6 versus 6.4; $p = 0.76$), depression (3.8 versus 3.7; $p = 0.76$) and intrusion (10.3 versus 9.9;

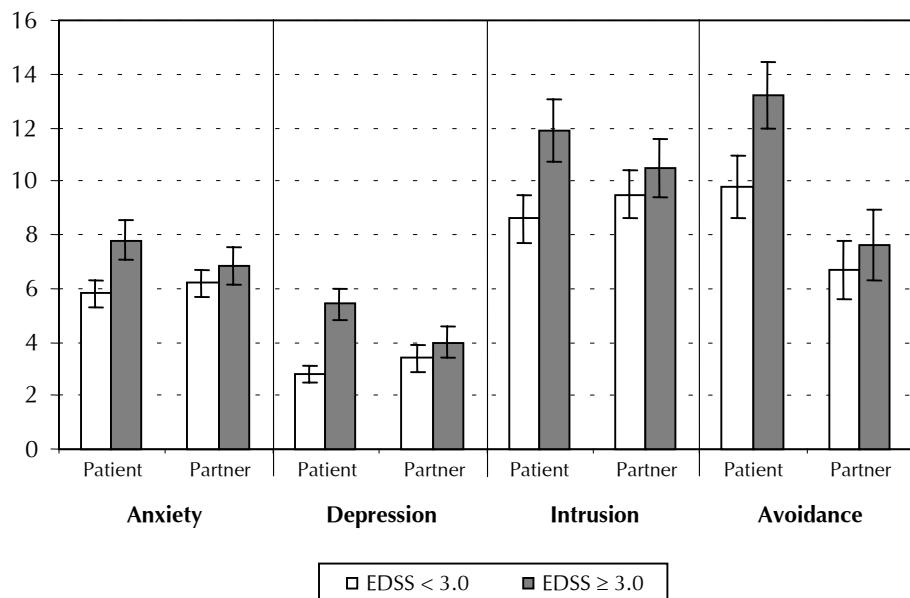


Figure 2 Anxiety, depression, intrusion and avoidance of patients and partners

Bars represent mean values (\pm standard errors) of the Hospital Anxiety and Depression scale and the Impact of Event scale (intrusion and avoidance).

$p = 0.67$). Given these similarities in overall mean scores of psychological well-being, correlations between scores of patients and partners were moderate (anxiety $r = 0.31$, $p = 0.006$; depression $r = 0.36$, $p = 0.001$; intrusion $r = 0.10$, $p = 0.37$ and avoidance $r = 0.27$, $p = 0.02$). This suggests that there were substantial differences within couples, with patients having poorer psychological well-being than partners in some couples, and better in others.

Discussion

In the early phase after diagnosis of MS, patients and their partners experienced a substantial emotional burden of the disease: approximately 50% of the patients and partners had clinically relevant levels of either anxiety or distress. Compared to general population controls, SF-36 scores were significantly lower in patients, also in those with no to minimal disability (EDSS < 3.0). Disturbances in psychological well-being and quality of life were more prevalent among patients with more disability (EDSS ≥ 3.0). In partners, psychological well-being and SF-36 quality of life were not related to the patients' EDSS scores.

IMPACT OF RECENTLY DIAGNOSED MULTIPLE SCLEROSIS

Previous studies demonstrating that psychological well-being and quality of life are reduced in MS patients and inversely related to disability status, have typically investigated MS patients within the more advanced stages of disease.^[2-8] Our data show that a major impact of the disease on the quality of both physical and mental health was also found in recently diagnosed patients. Compared to SF-36 scores of patients with an average disease duration of 10-15 years,^[2,4] our patients generally reported equal or better quality of life, except that our patients had substantially *lower* scores on the general health scale. Various reasons may explain the poorer quality of life and high emotional burden in this early phase of disease. First, quality of life may be reduced because patients already experienced practical consequences of their disability, as indicated by the lower SF-36 scores of patients with higher disability. Second, in judging the quality of their current physical health condition, patients may still compare their health status with their condition before they became ill.^[22] That is, in the evaluation of their health status, patients with a recent diagnosis may focus more on the *loss* in functional ability, rather than on the functional ability itself. This may explain the poorer quality of life of patients with relatively mild limitations (EDSS < 3.0) as well as the poorer evaluations of general health. Finally, patients may feel more uncertain and bothered about the implications of these early limitations for their future disability. The latter may be most prominent for those with more functional limitations and particularly contribute to their high emotional burden. In partners, psychological well-being and quality of life were not related to the level of functional limitations of the patient. This suggests that emotional problems in partners, at least in early phases of the disease, were not due to the burden of care. Instead, the high levels of anxiety and intrusion of partners may reflect their worry about the patient's future disability and the possible impact of the disease for *their* lives.

The origin of anxiety and depression in MS patients is still unclear, but psychosocial, i.e. a response to the burden of having an invalidating disease, and pathogenic, i.e. related to the cerebral pathology, causes are considered.^[23,24] Compared to general population controls, we found significantly increased levels of anxiety but not of depression. Patients did not differ from partners in their levels of anxiety, suggesting that anxiety is a reactive response on the disclosure of diagnosis.^[24,25] In line with previous studies in later phases of disease,^[6,24,26] we also found more symptoms of depression among patients with higher disability in our population of recently diagnosed patients. Yet, the fact that both levels of anxiety and depression were similar in patients and partners argues in favor of the view that, at least in an early phase of disease, depression is a result of the accumulated burden of adverse stressful experiences.^[27]

CHAPTER 4

Quality of life scales are widely considered as broader measurements of the impact of disease as compared to the EDSS.^[2,28,29] The widely-used SF-36 may not be sufficient in studies that also aim to address the emotional burden of disease.^[15] In this study, scores on the SF-36 mental health scale were not substantially reduced compared to controls, whereas patients and partners did report significantly more symptoms of anxiety than controls, and had high levels of intrusion and avoidance. Although the mental health scale of the SF-36 was related to anxiety ($r = -.57$, $p < 0.001$), depression ($r = -.60$, $p < 0.001$), intrusion ($r=-.43$, $p < 0.001$) and avoidance ($r=-.47$, $p < 0.001$), the SF-36 failed to indicate the considerable disturbances in emotional well-being that we found in our population. Therefore, we advocate the use of specific screening scales for the assessment of symptoms of anxiety, depression or distress as they prove to have additive value over generic quality of life instruments.

Further follow-up studies are needed to elucidate the course of anxiety and distress in patients and partners in the early period after diagnosis. This will be necessary to identify those who will remain anxious and distressed for a longer period and who may need further psychological support. Another issue that deserves further investigation is the finding of considerable differences in psychological well-being within couples. Although it may be advantageous for a couple when at least one of the spouses is not profoundly distressed, these discrepancies may also hamper mutual support in the adaptation to the disease and potentially threaten the relationship between spouses.

In conclusion, this study demonstrates that MS patients as well as their partners experience a substantial emotional burden in the early phase after diagnosis. About half of the patients and partners had clinically high levels of anxiety and distress. These clinically high levels of anxiety and distress of patients and partners ask for attention of health care professionals, to observe those who may need further psychological support.

References

- [1] **Solari A, Radice D.** Health status of people with multiple sclerosis: a community mail survey. *Neurol Sci* 2001; 22:307-15.
- [2] **Nortvedt MW, Riise T, Myhr KM, Nyland HI.** Quality of life in multiple sclerosis: measuring the disease effects more broadly. *Neurology* 1999; 53:1098-103.
- [3] **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.
- [4] **The Canadian Burden of Illness Study Group.** Burden of illness of multiple sclerosis: Part II: Quality of life. *Can J Neurol Sci* 1998; 25:31-8.
- [5] **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.

IMPACT OF RECENTLY DIAGNOSED MULTIPLE SCLEROSIS

- [6] **Fruewald S, Loeffler-Stastka H, Eher R, Saletu B, Baumhacki U.** Depression and quality of life in multiple sclerosis. *Acta Neurol Scand* 2001; 104:257-61.
- [7] **Brumet DG, Hopman WM, Singer MA, Edgar CM, MacKenzie TA.** Measurement of health-related quality of life in multiple sclerosis patients. *Can J Neurol Sci* 1996; 23:99-103.
- [8] **Kroencke DC, Denney DR, Lynch SG.** Depression during exacerbations in multiple sclerosis: the importance of uncertainty. *Mult Scler* 2001; 7:237-42.
- [9] **Hakim EA, Bakheit AM, Bryant TN, Roberts MW, McIntosh-Michaelis SA, Spackman AJ et al.** The social impact of multiple sclerosis--a study of 305 patients and their relatives. *Disabil Rehabil* 2000; 22:288-93.
- [10] **Knight RG, Devereux RC, Godfrey HP.** Psychosocial consequences of caring for a spouse with multiple sclerosis. *J Clin Exp Neuropsychol* 1997; 19:7-19.
- [11] **Aronson KJ.** Quality of life among persons with multiple sclerosis and their caregivers. *Neurology* 1997; 48:74-80.
- [12] **Poser CM, Paty DW, Scheinberg L, McDonald WI, Davis FA, Ebers GC et al.** New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol* 1983; 13:227-31.
- [13] **Kurtzke JF.** Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983; 33:1444-52.
- [14] **Ware JE, Sherbourne CD.** The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30:473-83.
- [15] **Freeman JA, Hobart JC, Langdon DW, Thompson AJ.** Clinical appropriateness: a key factor in outcome measure selection: the 36 item short form health survey in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2000; 68:150-6.
- [16] **Aaronson NK, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R et al.** Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998; 51:1055-68.
- [17] **Zigmond AS, Snaith RP.** The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67:361-70.
- [18] **Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM.** A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med* 1997; 27:363-70.
- [19] **Horowitz M, Wilner N, Alvarez W.** Impact of Event Scale: a measure of subjective stress. *Psychosom Med* 1979; 41:209-18.
- [20] **Sundin EC, Horowitz MJ.** Impact of event scale: psychometric properties. *Br J Psychiat* 2002; 180:205-9.
- [21] **Chemtob CM, Tomas S, Law W, Cremniter D.** Postdisaster psychosocial intervention: a field study of the impact of debriefing on psychological distress. *Am J Psychiatry* 1997; 154:415-7.
- [22] **Carver CS, Scheier MF.** Scaling back goals and recalibration of the affect system are processes in normal adaptive self-regulation: understanding 'response shift' phenomena. *Soc Sci Med* 2000; 50:1715-22.
- [23] **Feinstein A.** Depression associated with multiple sclerosis: an etiological conundrum. *Can J Psychiatry* 1995; 40:573-6.
- [24] **Zorzon M, de Masi R, Nasuelli D, Ukmar M, Mucelli RP, Cazzato G et al.** Depression and anxiety in multiple sclerosis. A clinical and MRI study in 95 subjects. *J Neurol* 2001; 248:416-21.
- [25] **Joffe RT, Lippert GP, Gray TA, Sawa G, Horvath Z.** Mood disorder and multiple sclerosis. *Arch Neurol* 1987; 44:376-8.
- [26] **Lynch SG, Kroencke DC, Denney DR.** The relationship between disability and depression in multiple sclerosis: the role of uncertainty, coping, and hope. *Mult Scler* 2001; 7:411-6.
- [27] **Alonso AA.** The experience of chronic illness and post-traumatic stress disorder: the consequences of cumulative adversity. *Soc Sci Med* 2000; 50:1475-84.
- [28] **Amato MP, Ponziani G, Rossi F, Liedl CL, Stefanile C, Rossi L.** Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. *Mult Scler* 2001; 7:340-4.
- [29] **Thompson AJ, Hobart JC.** Multiple sclerosis: assessment of disability and disability scales. *J Neurol* 1998; 245:189-96.

