What drives quality of life in multiple sclerosis?

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Summary

**Background:** Extensive use of the EDSS measure of disease severity by clinicians, and the EQ-5D measure of quality of life by healthcare decision-makers, may not adequately reflect patient perceptions of the range and impact of their symptoms.

**Aim:** To investigate the perceptions of MS patients in relation to specific symptoms and their general health-related quality of life.

**Design:** Questionnaire-based surveys.

**Methods:** Two consecutive postal surveys were sent to people whose contact details were on the database of the MS Trust. The first was sent to all 8614. Of 3403 respondents, 1992 agreed to participate in a second survey.

**Results:** In the first survey (response rate 40%), 1993 respondents (88%) reported moderate or severe fatigue; of 266 receiving disease-modifying therapy, 109 (41%) felt it improved their fatigue. In the second (response rate 78%), mean EQ-5D Index and z scores on the related quality of life deficit were significantly lower for respondents with relapsing or progressive disease than for those with benign disease. In the former groups (total n = 1178), over 90% reported problems with mobility and usual activities, and over 80% reported problems with pain. The lowest mean SF-36 scores were for role-physical, physical functioning and vitality, vitality being higher in respondents receiving beta interferon vs. those who were not (p<0.0001). Vitality was highly correlated with social functioning (0.58), general health (0.51) and mental health (0.50).

**Discussion:** Fatigue can profoundly disrupt the occupational and social functioning of MS patients, but is not directly captured in either the EDSS or the EQ-5D. Further investigation of the patient-perceived benefits of disease-modifying therapy, particularly in relation to symptoms of fatigue, may be valuable.

Introduction

There is already a considerable literature on the impact of multiple sclerosis (MS) on quality of life (QoL), including some recent postal surveys using the EQ-5D and SF-36 questionnaires.¹⁻³ However, assessment of quality of life presents difficulties in a long-term chronic condition that is susceptible to considerable variations in the incidence and severity of symptoms, both between patients and for the same patients over time.

The extensive use of the EDSS scale⁴ by health professionals as a measure of disease severity may not adequately reflect patients' own perceptions of the impact of symptoms on their overall health status and their quality of life. For example, the EDSS is heavily weighted towards mobility and does not fully reflect patients' problems in other areas of health such as pain and levels of vitality.⁵ MS patients' perceptions of the overall benefits of neurorehabilitation have also been found to correlate poorly with physician outcome measures related to functional improvement only.⁶
Most importantly, 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. The aim of the present study was therefore to generate observational data on the perceptions of people with MS, in relation both to the impact of specific symptoms and to their general health-related quality of life.

Methods

Data were collected via two consecutive postal surveys of people whose contact details were on the database of the MS Trust. The first survey was sent to all 8614 contacts on this database: 2265 responses were received from people with MS, plus 1138 responses from informal (i.e. unpaid) carers of people with MS, giving an overall response rate of 40%. The number of people with MS in the original contact population is not known, so an accurate response rate for this subgroup cannot be calculated, but it represents one of the largest surveys of its kind in an MS population. This survey concentrated on generating descriptive data on symptomatology; no demographic or clinical data were collected.

Following responses to the first survey, a subset of 1992 respondents who agreed to participate in a second survey were sent a further questionnaire. In this second survey, 1554 responses were received from people with MS, giving a response rate of 78%. The findings of this survey therefore reflect the perceptions of a large but self-selected group, such selection being based on consent to participate (although respondents did not know what the subject area of the second survey would be).

The second survey included the EQ-5D and SF-36 quality of life questionnaires. These are well-validated generic questionnaires designed to measure health-related quality of life, but are not specific to MS. A key reason for inclusion of the EQ-5D was its increasing use by healthcare decision-makers such as the UK’s National Institute for Clinical Excellence (NICE) in evaluating the effectiveness and cost-effectiveness of different treatments. The SF-36 is also widely used. It has more domains than the EQ-5D, and has been shown to provide appropriate measures of quality of life for people with MS.

The second survey also generated data on respondents’ perceptions of their disease state and whether they were receiving disease-modifying therapy.

The first part of the EQ-5D defines health in terms of five dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Within each dimension there are three levels of response, indicating no problems, some problems or extreme problems on that dimension. Taken together, this descriptive system defines a total of 243 unique health states. Responses can be converted into a single weighted index score (the EQ-5D Index) using population preference scores. This was the focus of the present analysis.

EQ-5D Index scores can range from 1 (full health) to –0.594. These Index scores can also be transformed into a z score to represent the difference between the reported score and the mean of the general population in a given 10-year age group and gender, based on UK population norms for the EQ-5D.

The SF-36 defines health in terms of eight dimensions: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Scores for each dimension can range from 100 (full health) to zero. The focus of the present analysis was on each dimension separately, since one overall composite score cannot be calculated (although separate composite scores can be calculated for the physical and mental components).

In the second survey, respondents were grouped according to their own reporting of the frequency of relapses and whether they perceived relapses to be followed by complete recovery. Group 1 comprised patients with benign disease (defined in the questionnaire as ‘infrequent relapses with long intervals between relapses’). Group 2 comprised patients with relapsing disease, with or without disease progression. Within this group, a distinction was made between (Group 2a) respondents currently in remission (when they completed the questionnaire) and (Group 2b) respondents currently in relapse. Group 3 comprised patients with progressive disease without relapses.

In the second survey, there were 131 respondents (8.4%) who reported that they were receiving disease-modifying therapy with a beta interferon drug. Additional analysis was undertaken on this subgroup. Nineteen (1.2%) were receiving treatment with glatiramer acetate, but these data were excluded, on the basis that this subgroup was too small for analysis.

Bivariate analysis included correlation coefficients being calculated between the SF-36 dimensions scores. In addition, one-sided t-tests were used to compare the mean EQ-5D Index scores and mean EQ-5D z scores between disease groups.
Mean EQ-5D z scores and mean SF-36 dimension scores were also compared between those patients receiving disease-modifying therapy and those who were not.

Multiple regression analysis was carried out to identify variables that could predict EQ-5D Index scores and scores for each of the SF-36 dimensions.

**Results**

Among the respondents to the first survey who provided data on the length of time since their diagnosis of MS \( (n = 2230) \) the mean period since diagnosis was 12 years (SD 9.3 years).

The findings from this phase of the research indicated that a wide range of different symptoms are experienced, with all respondents reporting more than one symptomatic problem. Fatigue is particularly pronounced, with 96% of respondents reporting this as a problem, and 88% of all respondents saying the level of this problem was ‘moderate’ or ‘severe’. Table 1 shows the relative prevalence and severity of each pre-coded symptom.

In addition, Table 1 shows the proportion of respondents in the first survey who were receiving disease-modifying therapy and felt that their symptoms improved with such therapy. Over half these respondents felt their pain and loss of mobility improved, and over 40% felt their problems with speech and swallowing and problems with fatigue improved. Clearly, these data cannot be regarded in the same way as data from a controlled trial, but they are helpful indicators of patients’ own perceptions of the impact of medication on their symptoms.

This first survey found that the mean number of relapses in the last 12 months was 1.7 (SD 2.5). However, amongst those respondents experiencing relapses \( (n = 1080) \), the mean number of relapses in the last 12 months was 3.2 (SD 2.7). To investigate the influence of relapses further, data from the second survey distinguished between patients in different relapse states.

Respondents to the second survey \( (n = 1554) \) had a mean period since diagnosis of 13 years (SD 10.1) and a mean age of 51.9 years (SD 11.9).

The second survey allowed calculation of mean EQ-5D Index scores by disease group (Figure 1). Respondents with relapsing or progressive disease (Groups 2a, 2b and 3) experienced significantly poorer quality of life than respondents with benign disease (Group 1) \( (p < 0.001 \) for all three comparisons). In the former groups, the proportion reporting some or extreme problems on Mobility and Usual Activities was >90% and that reporting some or extreme problems on Pain was >80% (Table 2).

The SF-36 data show the greatest impact (lowest mean scores) on Role-Physical (21.2), Physical Functioning (27.9) and Vitality (30.9) (Figure 2). This reinforces the importance of the physical symptoms reported in the first survey, such as balance and dizziness and loss of mobility. It also confirms the importance of fatigue (or lack of vitality), and is consistent with the high proportion of respondents reporting problems with mobility and usual activities on the EQ-5D.

<table>
<thead>
<tr>
<th>Symptomatic problem</th>
<th>Respondents experiencing the problem ( (n = 2265) )</th>
<th>Respondents classifying impact of the problem as ‘moderate’ or ‘high’ ( (n = 2265) )</th>
<th>Respondents reporting symptom improvement on disease-modifying therapy ( (n = 266) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>96%</td>
<td>88%</td>
<td>41%</td>
</tr>
<tr>
<td>Balance and dizziness problems</td>
<td>92%</td>
<td>74%</td>
<td>27%</td>
</tr>
<tr>
<td>Loss of mobility</td>
<td>91%</td>
<td>79%</td>
<td>52%</td>
</tr>
<tr>
<td>Sensory problems</td>
<td>88%</td>
<td>54%</td>
<td>28%</td>
</tr>
<tr>
<td>Bladder problems</td>
<td>87%</td>
<td>70%</td>
<td>39%</td>
</tr>
<tr>
<td>Loss of memory and concentration</td>
<td>87%</td>
<td>52%</td>
<td>17%</td>
</tr>
<tr>
<td>Spasticity</td>
<td>82%</td>
<td>54%</td>
<td>34%</td>
</tr>
<tr>
<td>Vision problems</td>
<td>82%</td>
<td>41%</td>
<td>21%</td>
</tr>
<tr>
<td>Pain</td>
<td>81%</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Bowel problems</td>
<td>74%</td>
<td>45%</td>
<td>36%</td>
</tr>
<tr>
<td>Sexual problems</td>
<td>70%</td>
<td>42%</td>
<td>33%</td>
</tr>
<tr>
<td>Tremor</td>
<td>68%</td>
<td>30%</td>
<td>35%</td>
</tr>
<tr>
<td>Speech and swallowing problems</td>
<td>68%</td>
<td>26%</td>
<td>42%</td>
</tr>
</tbody>
</table>
Bivariate analysis of the eight dimensions of the SF-36 indicated that Role-Emotional was highly correlated with Mental Health (correlation coefficient 0.61). Vitality, Role-Physical and Physical Functioning were highly correlated with Social Functioning (correlation coefficients of 0.58, 0.57 and 0.51 respectively). Vitality was also strongly correlated with both General Health (0.51) and Mental Health (0.50).

In the analysis of these data, potential confounding factors are age and gender. In order to normalize for these factors, quality of life ‘deficits’ based on EQ-5D z scores were calculated using normative data from large population studies. The results of this analysis indicate that, as with the Index scores by disease group shown in Figure 3, respondents with relapsing or progressive disease (Groups 2a, 2b and 3) have significantly greater deficits compared to respondents with benign disease ($p < 0.001$ for all three comparisons). It is also apparent that respondents with relapsing disease but currently in relapse have a significantly greater deficit than those currently in remission ($p = 0.0009$) (Figure 3).

Analysis was also undertaken in relation to current disease-modifying therapy, expanding on the
preliminary findings of the first survey. Of the 131
respondents receiving therapy with a beta interferon
drug, 105 (80.2%) were in the relapsing disease
groups (2a and 2b).

The mean EQ-5D deficit for the beta interferon
group overall was 0.571 (SD 0.268), compared to
a mean for the non-beta interferon group of 0.427
(SD 0.34). Although the respondent numbers are
much smaller in the beta interferon group, there
is a significant overall difference between these
mean scores ($p<0.0001$). There was also a
significantly higher mean score for the beta inter-
feron group on the SF-36 Vitality dimension
($p<0.0001$).

In the relapsing respondent groups (Groups 2a
and 2b), multiple regression analysis was under-
taken to determine the drivers of EQ-5D Index
scores and individual scores on each of the
SF-36 dimensions. Age and gender were included
as explanatory variables in all cases. Whether a
respondent was in relapse or remission was signifi-
cant in explaining the EQ-5D Index and seven of the
eight SF-36 dimensions ($p<0.05$). In the Physical
Functioning dimension, whether the respondent
was in relapse or remission was of borderline
significance ($p=0.061$).

Whether a respondent was receiving beta inter-
feron was significant ($p<0.05$) in relation to seven
of the SF-36 dimensions (Physical Functioning
was of borderline significance) but not in relation
to the EQ-5D Index.

In Group 2 overall, receiving beta interferon
was a significant explanatory variable in relation
to Role-Physical ($p<0.001$), Bodily Pain ($p<0.021$),
General Health ($p<0.001$), Vitality ($p<0.001$),
Social Functioning ($p<0.001$), Role-Emotional
($p<0.001$) and Mental Health ($p=0.003$). Years
since diagnosis was not significant in any regres-
sions for this group of respondents.

Discussion

It is clear from these two surveys that people
with MS experience a wide range of symptoms
that affect their quality of life. The first survey
indicated that most patients experience multiple
symptoms; while the precise combination of symp-
toms may be different for different people, there
is no evidence of discrete groups reporting indi-
vidual symptoms.

In particular, the overwhelming prevalence of
fatigue is important. In the present study it was
found that lack of ‘vitality’ was highly correlated
with Social Functioning, General Health and
Mental Health. The impact of fatigue/lack of vitality
may not have received sufficient recognition in
the implementation of care for people with MS,
partly because it is not directly captured in the
EDSS measure of disease severity. Neither is it
captured in the EQ-5D, the measure of quality of
life which is increasingly being used by health
policy decision-makers.

Nevertheless, other studies have shown that
MS-related fatigue can profoundly disrupt the
occupational and social functioning of patients.11–15
Previous research has also shown that fatigue has
a significant impact on both mental and physical
health-related quality of life, and its influence on
the latter is independent of the EDSS.16

The present study has shown that the most
pronounced quality of life deficits in comparison
with age and gender-specific norms are apparent
amongst patients with relapsing and progressive
disease. The deficit is also significantly worse for
patients actually experiencing a relapse, as com-
pared to those in remission.

One limitation of this study is the fact that, despite
the large numbers of survey respondents, the true
response rate for people with MS and the extent
of any response bias are unknown. The analysis of
reported quality of life for patients receiving treatment with beta interferon versus those not receiving beta interferon is not based on randomized, controlled trial data. Other papers have reported such data based on studies using both the SF-36 \cite{17,18} and the EQ-5D.\cite{19}

Nevertheless, these observational findings do indicate superior quality of life for those receiving treatment in the progressive disease group as reported on the EQ-5D, and superior vitality across the overall respondent base as reported on the SF-36. In multiple regression analysis, whether a patient was receiving beta interferon was a significant explanatory variable in relation to seven of the eight dimensions of the SF-36. Further investigation of the patient-perceived benefits of disease-modifying treatment, particularly in relation to symptoms of fatigue, may consequently be valuable.

**Acknowledgements**

The authors would like to express their gratitude to all the people with MS and their carers who responded to the surveys reported in this paper.

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**References**