Quality of Life Is Favorable for Most Patients With Multiple Sclerosis

A Population-based Cohort Study

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Background: Quality of life (QOL) is becoming an increasingly important factor in measurement of disease impact as well as an outcome measure in clinical trials.

Objectives: To study the QOL of patients with multiple sclerosis (MS) in a population-based prevalence cohort and compare it with the general US population.

Design: Population-based prevalence cohort.

Setting: Olmsted County, Minn, population.

Participants: All patients with definite MS (N = 201) alive and residing in Olmsted County on December 1, 2000.

Intervention: None.

Main Outcome Measures: The expanded disability status scale (EDSS) and the Multiple Sclerosis Quality of Life Health Survey (MSQOL-54), which consisted of Short Form 36 (SF-36) with an additional 18 items pertinent to MS.

Results: The MSQOL-54 form was completed by 185 patients. Patients with MS had worse scores than the general US population with respect to physical functioning, vitality, and general health dimensions of the SF-36 QOL measure. Many QOL domains (pain, role emotional, mental health, and social functioning) were, however, similar for the 2000 MS cohort compared with the general US population. Duration of MS and EDSS score correlated significantly with physical functioning (P < .001). The QOL correlation with EDSS score was less than expected. No significant difference in the scores for the 8 QOL dimensions were found for patients with quick vs slow progression (quick progression defined as < 5 years from onset to EDSS score of 3). The majority of patients with MS (77%) were mostly satisfied or delighted with their QOL.

Conclusion: Though MS can cause significant disability, most patients with MS in the Olmsted County prevalence cohort continue to report a good QOL.

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THERE HAS BEEN A GROWING interest in quality of life (QOL) in multiple sclerosis (MS), though few have studied QOL in a population-based prevalence cohort. Immunomodulatory therapies have a beneficial effect on relapse rate, disease activity measurements using neuroimaging, and short-term disability. Contemporary studies are beginning to assess the effects of these treatments on QOL, which may be more important to patients than disability.

The natural history of MS with regard to disability and QOL, based on community-based cohort studies, is a benchmark against which both treatment and placebo outcome groups can be compared.

In this study, we measured the QOL of the Olmsted County, Minn, 2000 prevalence cohort and compared it with the general population.

METHODS

THE STUDY COMMUNITY AND STUDY DESIGN

We identified all known cases of MS in Olmsted County using the Mayo Clinic’s (Rochester, Minn) computerized centralized diagnostic index. Definite (clinical and laboratory supported) MS cases were identified using the Poser criteria. The majority of patients in Olmsted County received their care at the Mayo Clinic, with the remainder receiving care at either the Olmsted Medical Group, Rochester, or the Olmsted Community Hospital, Rochester. The indices of the Rochester Epidemiology Project allowed retrieval of all diagnoses regardless of health care provider. All records were reviewed by a neurologist (S.J.P., W.T.M., J.H.N., or M.R.) to confirm the diagnosis and extract medical information. Definite MS cases who were residents of Olmsted County on December 1, 2000, and had an established residence in Olmsted County for at least 1 year prior to this formed the prevalence cohort.
CLINICAL EVALUATION AND PATIENT INTERVIEW

Patients were interviewed and examined in a clinic setting. Home and nursing home evaluations were performed when patients were unable to attend the clinic. Telephone interviews were performed for patients unwilling to be seen. We recorded demographic data, date of MS onset, and use of immunomodulatory treatment by review of medical records supplemented by patient reporting. A full neurologic examination was performed and neurologic disability assessed with the use of the expanded disability status scale (EDSS), or if the patient was not examined, then the EDSS score was estimated from interview or review of case records. Patients were required to be at these specific EDSS scores for at least 6 months. Course of MS was categorized as relapsing remitting, secondary progressive, or primary progressive. At the end of the face-to-face or telephone interview, the patients completed the Multiple Sclerosis Quality of Life Health Survey (MSQOL-54) consisting of the Short Form 36 (SF-36) along with 18 additional items pertinent to patients with MS.

The SF-36 part of the MSQOL-54 consists of 36 questions, 35 of which are compressed into 8 multi-item scales: (1) physical functioning is a 10-question scale that captures abilities to deal with the physical requirement of life, such as carrying groceries, walking, climbing stairs, and dressing; (2) role physical is a 4-item scale that measures the extent to which physical capabilities limit activity; (3) bodily pain is a 2-item scale that evaluates the perceived amount of pain experienced during the previous 4 weeks and the extent to which that pain interfered with normal work activities; (4) general health is a 5-item scale that evaluates general health in terms of personal perception; (5) vitality is a 4-item scale that assesses feelings of pep, energy, and tiredness; (6) social functioning is a 2-item scale that assesses the extent and amount of time, if any, that physical health or emotional problems interfered with family, friends, and other social interactions during the previous 4 weeks; (7) role emotional is a 3-item scale that evaluates the extent, if any, to which emotional factors interfere with work or other activities; and (8) mental health is a 5-item scale that evaluates feelings principally of anxiety and depression. The scales are assessed quantitatively, each on the basis of answers to 2 to 10 multiple-choice questions, and a score between 0 and 100 is calculated with a higher score indicating a better state of health. The additional 18 QOL items pertinent to patients with MS are described in the “Results” section and pertain to bowel and bladder dysfunction and sexual, other health, and cognitive problems.

RESULTS

We identified 201 patients with clinically or laboratory-supported definite MS. One hundred forty (70%) were women. The median age of onset of disease was 31 years, and the median duration of follow-up for the entire cohort was 19.3 years (range, 0.9-70.7). One hundred thirty patients were in the relapsing-remitting category; 60 were in the secondary progressive category. Only 11 were classified as having primary progressive MS. The median EDSS score was 3.0 (range, 0-9.5) for the prevalence cohort. The distribution for the EDSS score for the entire cohort is shown in Figure 1.

Fifty patients (25%) had been on at least 1 of the immunomodulatory drugs (interferon β-1a, interferon β-1b, glatiramer acetate). Thirty-four of these had relapsing-remitting MS and 16 had secondary progressive MS at the time of the study. The median duration of treatment was 13.4 months (interquartile range, 8.7-24.2) for interferon β-1a, 15.6 months (interquartile range, 10.5-37.3) for interferon β-1b, and 14.8 months (interquartile range, 5.0-28.9) for glatiramer acetate. Twenty-two patients (44%) stopped their initial drug and half of these patients did not restart another.

Of the 2000 prevalence cohort, 178 (89%) of the patients underwent a face-to-face interview and repeated neurologic examination within 14 months of the prevalence date and 14 patients underwent a telephone interview. While 9 patients refused to participate actively in the study, recent medical records (with neurologic evaluations in all) made it possible for them to be included in most of the assessments. One hundred eighty-five patients (92%) completed the MSQOL-54; 6 patients were unable because of severe dementia, and 10 refused.

The unadjusted raw scores for the total MS cohort and the MS subtypes (relapsing remitting, secondary progres-
Table 1. Unadjusted Short Form 36 (SF-36) Data*

<table>
<thead>
<tr>
<th>SF-36 Dimensions†</th>
<th>All Patients</th>
<th>Patients With RRMS (n = 120)</th>
<th>Patients With SPMS (n = 55)</th>
<th>Patients With PPMS (n = 10)</th>
<th>P Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>50.6 (38.2)</td>
<td>71.7 (28.9)</td>
<td>12.7 (16.8)</td>
<td>7.0 (14.0)</td>
<td>.001</td>
</tr>
<tr>
<td>Role physical</td>
<td>60.1 (39.5)</td>
<td>71.3 (37.2)</td>
<td>40.9 (37.1)</td>
<td>32.5 (23.7)</td>
<td>.001</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>77.1 (24.4)</td>
<td>77.7 (24.4)</td>
<td>75.8 (24.7)</td>
<td>77.9 (25.2)</td>
<td>.46</td>
</tr>
<tr>
<td>General health</td>
<td>59.9 (22.6)</td>
<td>63.5 (21.1)</td>
<td>55.0 (24.2)</td>
<td>44.7 (21.0)</td>
<td>.36</td>
</tr>
<tr>
<td>Vitality</td>
<td>48.4 (22.8)</td>
<td>51.5 (22.8)</td>
<td>40.1 (21.7)</td>
<td>55.5 (18.5)</td>
<td>.001</td>
</tr>
<tr>
<td>Social functioning</td>
<td>78.5 (24.2)</td>
<td>83.3 (20.3)</td>
<td>68.4 (28.6)</td>
<td>76.3 (26.0)</td>
<td>.001</td>
</tr>
<tr>
<td>Role emotional</td>
<td>89.7 (25.2)</td>
<td>90.0 (24.3)</td>
<td>87.3 (29.0)</td>
<td>100 (0.0)</td>
<td>.001</td>
</tr>
<tr>
<td>Mental health</td>
<td>78.6 (15.5)</td>
<td>78.5 (15.2)</td>
<td>78.3 (16.6)</td>
<td>81.6 (14.6)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis. *Values are expressed as mean (SD). †Physical functioning refers to limitations in physical activities because of health problems; role physical, limitations in usual role activities because of physical health problems; bodily pain, the perceived amount of pain and the extent to which it interfered with normal activities; general health, general health in terms of personal perception; vitality, feelings of pep, energy, and tiredness; social functioning, limitations in social activities because of physical or emotional problems; role emotional, limitations in usual role activities because of emotional problems; mental health, feelings principally of anxiety and depression.

Table 2. Standardized Age- and Sex-Adjusted Short Form 36 (SF-36) Data by Multiple Sclerosis Type*

<table>
<thead>
<tr>
<th>SF-36 Dimensions†</th>
<th>All Patients</th>
<th>Patients With RRMS (n = 120)</th>
<th>Patients With SPMS (n = 55)</th>
<th>Patients With PPMS (n = 10)</th>
<th>P Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>36.8 (17.4)</td>
<td>44.5 (14.5)</td>
<td>22.7 (12.8)</td>
<td>22.1 (12.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Role physical</td>
<td>45.1 (11.6)</td>
<td>47.3 (11.6)</td>
<td>41.2 (10.7)</td>
<td>39.7 (10.7)</td>
<td>.002</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>52.3 (10.2)</td>
<td>52.1 (10.3)</td>
<td>52.6 (9.9)</td>
<td>53.4 (9.9)</td>
<td>.92</td>
</tr>
<tr>
<td>General health</td>
<td>45.4 (11.3)</td>
<td>46.3 (11.0)</td>
<td>44.5 (11.7)</td>
<td>40.7 (11.7)</td>
<td>.25</td>
</tr>
<tr>
<td>Vitality</td>
<td>44.5 (10.9)</td>
<td>45.8 (11.0)</td>
<td>41.0 (10.2)</td>
<td>48.2 (10.2)</td>
<td>.01</td>
</tr>
<tr>
<td>Social functioning</td>
<td>48.3 (10.7)</td>
<td>50.0 (9.4)</td>
<td>44.5 (12.5)</td>
<td>48.4 (12.5)</td>
<td>.006</td>
</tr>
<tr>
<td>Role emotional</td>
<td>52.6 (7.6)</td>
<td>52.5 (7.5)</td>
<td>52.2 (8.3)</td>
<td>55.9 (8.3)</td>
<td>.36</td>
</tr>
<tr>
<td>Mental health</td>
<td>52.1 (8.5)</td>
<td>52.2 (8.5)</td>
<td>51.8 (6.7)</td>
<td>53.4 (6.7)</td>
<td>.85</td>
</tr>
<tr>
<td>Physical component score</td>
<td>39.2 (12.7)</td>
<td>44.8 (11.4)</td>
<td>29.4 (7.7)</td>
<td>25.5 (7.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mental component score</td>
<td>54.2 (8.6)</td>
<td>52.6 (8.2)</td>
<td>56.3 (8.3)</td>
<td>62.5 (8.3)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis. *Values are expressed as mean (SD). †Physical functioning refers to limitations in physical activities because of health problems; role physical, limitations in usual role activities because of physical health problems; bodily pain, the perceived amount of pain and the extent to which it interfered with normal activities; general health, general health in terms of personal perception; vitality, feelings of pep, energy, and tiredness; social functioning, limitations in social activities because of physical or emotional problems; role emotional, limitations in usual role activities because of emotional problems; mental health, feelings principally of anxiety and depression. ‡P values are based on an analysis of variance model comparing the 3 types of multiple sclerosis. Scores are standardized so that the general US population is represented by a mean (SD) of 50 (10). Standardized means lower than 50 for the multiple sclerosis population indicate a worse score (ie, a worse state of health) than the general US population; means higher than 50 indicate a better score (ie, a better state of health).
significant as well as clinically meaningful (Table 2) (Figure 3). The secondary progressive group perceived their social functioning and vitality as worse than the relapsing-remitting and primary progressive groups.

Figure 2. Comparison of quality of life scores for the multiple sclerosis (MS) prevalence cohort (n=185) and the general US population. A, Physical function scores. Refers to limitations in physical activities because of health problems. B, Role physical scores. Refers to limitations in usual activities because of physical health problems. C, Bodily pain scores. Refers to the perceived amount of pain and the extent to which it interferes with normal activities. D, General health perception scores. E, Vitality scores. Refers to feelings of pep, energy, and tiredness. F, Social function scores. Refers to limitations in social activities because of physical or emotional problems. G, Role emotional scores. Refers to limitations in usual activities because of emotional problems. H, Mental health scores. Refers to feelings principally of anxiety and depression.
Physical functioning, role physical, general health, social functioning, and vitality dimensions were significantly correlated with the EDSS score (Table 3). There was a very weak correlation between bodily pain, role emotional, or mental health dimensions and EDSS score. The correlation between EDSS score and self-rated QOL scale score (0 [worst] to 10 [best]) was significant but weaker than expected ($r = -0.37$; $P < .001$) (Figure 4).

Duration of MS from onset only correlated significantly with physical functioning ($r = -0.37$; $P < .001$) but none of the other QOL dimensions (Table 3).

Rate of progression was analyzed with respect to QOL. No significant differences in the scores for the 8 QOL dimensions were found between patients with quick vs slow progression (quick progression defined as <5 years from onset to EDSS score of 3).

Results of the additional QOL questions as part of the MSQOL-54 are presented in Table 4. Questions relating to overall satisfaction with sexual function revealed that 98 patients (53%) were very or somewhat satisfied, 26 (14%) were somewhat or very dissatisfied, and 61 (33%) were neither satisfied nor dissatisfied. When patients were asked to describe how they felt about their life as a whole, 142 (77%) were mostly satisfied or delighted whereas only 7 (4%) were mostly dissatisfied or described their lives as terrible at the time of interview.
Determining clinically important differences in health status measures is of paramount importance because what may be statistically significant may have no clinical importance. For this study, we used a cutoff of 3 based on similar methods of analyses published by others.25,26 Differences greater than 3 more or less than the mean 50 for the age- and sex-matched US population were considered clinically meaningful.

In our study, the application of the SF-36 in a cross-sectional fashion provided an overview of QOL for a community-based population at a single point in time. Only 25% of our prevalence cohort received immunomodulatory treatment, and those who did were on therapy for a mean duration of less than 2 years. It is unlikely that this duration of treatment in such a small proportion of patients affected either the level of disability or QOL.

The physical functioning, physical role dimensions, and the physical-component scores were worse for the MS cohort compared with the general US population. In contrast, however, bodily pain, role emotional, and social functioning were generally not clinically different from the general US population, possibly reflecting the coping skills of patients with long-term progressive illnesses to adjust and compensate socially and emotionally. These findings differed somewhat from a previous population-based study in Norway, which found lower mean scores for all SF-36 health dimensions compared with sex- and age-matched scores in a general population.3 The Norwegian community-based cohort was, however, similar to our cohort. They had a similar mean EDSS score (4.1 vs 3.8), age at disease onset (33 vs 31 years), age at examination (47 vs 52 years), duration of disease (14 vs 19 years), and proportion of women (61% vs 70%), though there was a higher percentage of patients with primary progressive MS in the Norway cohort compared with ours (20% vs 5%).

A study of 136 patients with MS by Wang et al32 found that patients with lifetime depression had significantly lower MSQOL-54 scores for domains of energy, mental health, cognitive function, general health, and role emotional than those without depression.

The relatively good performance of our patient cohort in the mental health dimension is notable. Patients with severe dementia (n = 6) were not asked to complete the QOL assessments, and these patients, if included would obviously have lowered the scores in those dimensions of QOL. The 2000 Olmsted County MS population had a median EDSS score of 3.0 (range, 0-9.5) and a higher proportion of patients with relapsing-remitting MS (65%) than many other population-based MS studies.33 In addition, previous studies based on this population have shown a more favorable functional status than previously recognized.34 This will likely have a similar beneficial effect on overall QOL.

The EDSS is the most commonly used measure of impairment/disability in MS studies, though it is heavily influenced by limb and gait dysfunction. Previous studies have shown a correlation between EDSS score and most dimensions of the SF-36, though correlation was highest for physical functioning. This reflects the heavy weighting of the EDSS for mobility.3 In this study, we found that QOL is impaired, though not as much as might be ex-

### Table 3. Correlation of Short Form 36 (SF-36) Scales With Expanded Disability Status Scale (EDSS) Score and Duration of Multiple Sclerosis From Onset (N = 185)

<table>
<thead>
<tr>
<th>SF-36 Dimension*</th>
<th>EDSS Score Correlation (P Value)</th>
<th>Duration From Onset Correlation (P Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>-0.47 (&lt;.001)</td>
<td>-0.37 (&lt;.001)</td>
</tr>
<tr>
<td>Role physical</td>
<td>-0.45 (&lt;.001)</td>
<td>-0.09 (.20)</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>-0.15 (.04)</td>
<td>-0.07 (.36)</td>
</tr>
<tr>
<td>General health</td>
<td>-0.31 (&lt;.001)</td>
<td>-0.03 (.68)</td>
</tr>
<tr>
<td>Vitality</td>
<td>-0.26 (.003)</td>
<td>-0.02 (.78)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>-0.37 (&lt;.001)</td>
<td>-0.09 (.22)</td>
</tr>
<tr>
<td>Role emotional</td>
<td>-0.05 (.46)</td>
<td>-0.01 (.89)</td>
</tr>
<tr>
<td>Mental health</td>
<td>-0.05 (.50)</td>
<td>0.07 (.36)</td>
</tr>
</tbody>
</table>

*Physical functioning refers to limitations in physical activities because of health problems; role physical, limitations in usual role activities because of physical health problems; bodily pain, the perceived amount of pain and the extent to which it interfered with normal activities; general health, general health in terms of personal perception; vitality, feelings of pep, energy, and tiredness; social functioning, limitations in social activities because of physical or emotional problems; role emotional, limitations in usual role activities because of emotional problems; mental health, feelings principally of anxiety and depression.

**Figure 4.** Self-rated quality of life score (0=worst, 10=best) vs expanded disability status scale (EDSS) score. To avoid overlap, points have been shifted slightly along both axes.

It is generally believed among health care professionals that illness and injury profoundly affect patients’ QOL. In addition to mortality and morbidity, QOL is becoming an increasingly important measure of the impact of disease and as an outcome measure in clinical trials.

The most widely used measure of health-related QOL in the United States is the SF-36.27-30 The SF-36 has been widely applied to the general population as well as people with cancer and other highly prevalent diseases.27-30 Recent studies in MS have investigated QOL in MS clinics, cross-sectional population-based cohorts, in association with magnetic resonance imaging, and as an outcome measure in MS clinical trials.27,20,21 The QOL data on prevalence cohorts have been lacking despite promising to contribute important information about the impact of disease on a community as well as allowing for comparisons with the general population and patients with other diseases.
pected from EDSS measurements, and there was no correlation between EDSS score and pain, role emotional, or mental health.

In a random sample of 203 patients with MS from a population register, Ford et al found no significant difference in QOL across disease course groups (early relapsing-remitting, secondary progressive relapsing, and primary progressive and benign) in sharp contrast to differences in disability. In their analyses, there was a trend of QOL measures consistent with the hypothesis that adjustment to disability occurs with age and increasing duration of disease. In contrast, we found that duration of disease was only significantly positively associated with 1 (physical functioning) of 8 QOL dimensions.

Although many patients with MS have significant disability, most patients with MS in the Olmsted County community continue to report a good QOL. Though they are worse with respect to the physical and social functioning domains of QOL, they did not have clinically meaningful differences in their perception of pain, cognitive problems, or emotional problems affecting their QOL when compared with the general US population. Future studies will need to address the role of psychiatric morbidity, religious belief, financial status, and home and social environment as well as support networks on QOL, which may have an important role in different communities but were not addressed in our study.

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Author Contributions: Study concept and design (Drs Pittock, Mayr, McClelland, and Rodriguez); acquisition of data (Drs Pittock and Mayr); analysis and interpretation of data (Drs Pittock, McClelland, Jorgensen, Weigand, Noseworthy, and Rodriguez); drafting of the manuscript (Drs Pittock, McClelland, Jorgenson, Noseworthy, and Rodriguez); critical revision of the manuscript for important intellectual content (Drs Pittock, Mayr, McClelland, Jorgensen, Weigand, Noseworthy, and Rodriguez); statistical expertise (Drs Pittock, McClelland, Jorgensen, Weigand, and Rodriguez); obtained funding (Dr Mayr); administrative, technical, or material support (Dr Pittock); study supervision (Drs Noseworthy and Rodriguez).

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